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Electron impact induced multiple rearrangements of aralkyl nitro and nitroso compounds and multiple hydrogen rearrangements in cumyl and related cations

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Electron impact induced multiple rearrangements of aralkyl nitro and nitroso compounds and multiple hydrogen rearrangements in cumyl and related cations

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HISTORICAL

The widespread usage of mass spectrometry as a research tool for the solution of structural problems has been one of the most significant developments in organic chemistry in the past few years (1, 2). The usefulness of the mass spectrum in the structural elucidation of a compound can be seriously limited, however, by molecular rearrangement prior to or during the fragmentation of either the molecular ion or daughter ions. Early approaches to structural problems using mass spectrometry adopted the view that the fragment lost and ion produced represented a structural unit of the original molecule. These early workers found, however, that many of the ions formed, especially in the mass spectra of hydrocarbons, could not be correlated with the known structure and thus mass spectrometry was all but abandoned for a period of time as a tool for structure determination. Considerable work has accumulated in the past decade, however, which illustrates that the correct explanation of molecular rearrangement phenomena can make valuable contributions to the solution of structural problems by mass spectrometry.

Detection of Electron Inpact Rearrangement Reactions

The products of a thermal, photochemical or solution reaction may be collected and examined to determine whether or not molecular rearrangement occurred. Because the products of a

mass spectral reaction cannot be collected, other methods must be employed to determine whether the products result from simple bond cleavage or molecular rearrangement processes.

The various product ions produced upon electron impact may be viewed as formed through a series of competitive and consecutive unimolecular reactions (3). The rate at which these decompositions occur determines whether or not product ions will be observed in the mass spectrum and how intense these ions will be if they are observed. Consequently a knowledge of the rate constant for simple bond cleavage reactions and rearrangement reactions becomes important for determining which ions in the mass spectrum are associated with which type of process.

In simplest form, the quasi-equilibrium theory of mass spectrometry relates the unimolecular ion reaction rate constant k to internal energy E, activation energy E°, frequency factor v and effective number of harmonic oscillators s, by Equation 1 (4, p. 16). Such an expression will lead to a

$$k = v\left(\frac{E-E^\circ}{E}\right)^{s-1} \qquad \text{Equation 1}$$

variety of k vs E curves of which the extremes are represented by the curve for a rearrangement reaction as opposed to the curve for a simple bond cleavage reaction. Simple bond cleavage reactions are generally processes of high frequency factors and high activation energies while rearrangement reactions are characterized by low frequency factors and low

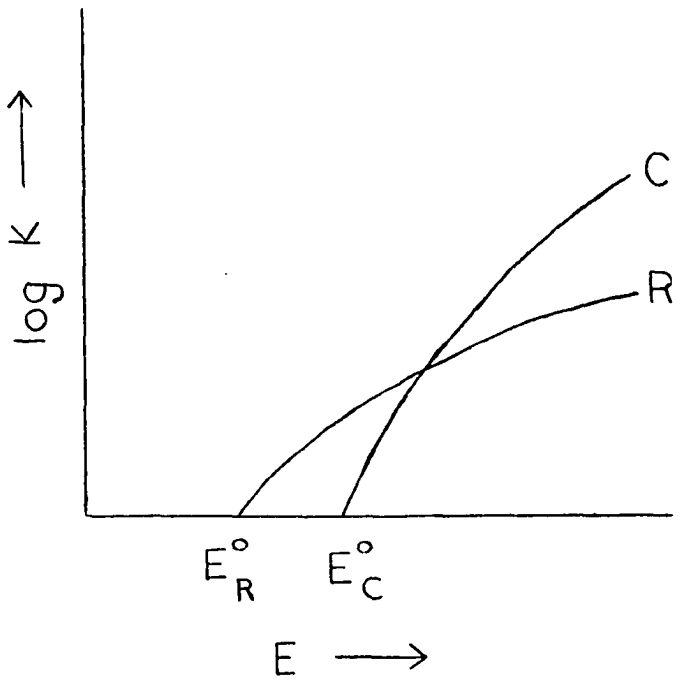


Figure 1. Idealized k vs E curves for hypothetical competing rearrangement (R) and simple cleavage (C) reactions (5)

activation energies (6). Low frequency factors would be anticipated for reactions with rigid steric requirements such as those necessary for many rearrangement reactions. Because rearrangement reactions necessarily involve bond formation as well as bond breakage, these reactions generally have lower activation energies (7).

If the energy imparted to the molecule upon electron impact is smaller than the activation energy for a particular reaction, then the molecule obviously will not fragment by that pathway . Therefore, one can discriminate against the higher activation energy processes by simply imparting a smaller amount of energy to the molecule. This is accomplished

by lowering the energy of the bombarding electrons. At electron energies of 10-20eV (typical low-voltage spectra) it will frequently be the case that the average energy of the molecules will be slightly in excess of the activation energy for simple cleavage reactions. This will make the contribution of the $\frac{E-E^\circ}{E}$ term to the rate constant small even though the power to which it is raised is a large number for organic molecules. The larger value of the term $\frac{E-E^\circ}{E}$ for a competing rearrangement reaction will be magnified greatly because of the large power to which it is raised. The power, s, is a large number because the typical organic molecule has a large number of effective harmonic oscillators. The overall effect may give the competing rearrangement reaction a larger rate constant despite the fact that the frequency factor is lower.

At 70eV the energy is much greater than the activation energy for both simple cleavage and rearrangement reactions and the frequency factor becomes more important in determining the rate constant. In practice, one measures the spectrum at 70eV and then observes which fragment ions become more important as the electron energy is lowered. These fragment ions are more likely to have resulted from rearrangement reactions.

Chupka has suggested that mass spectral fragmentations which have low frequency factors should show abundant

metastable ions (8). Ions which fragment after leaving the source are accelerated at the mass of the ion prior to fragmentation (called the parent mass or m_1) but are dispersed by the magnetic field as the mass of the fragment ion (called the daughter ion or m_2). This results in the appearance of a diffuse peak (called a metastable peak) at a mass m* which is approximated by Equation 2. Ions decomposing with a rate constant of approximately 10^5 $sec.^{-1}$

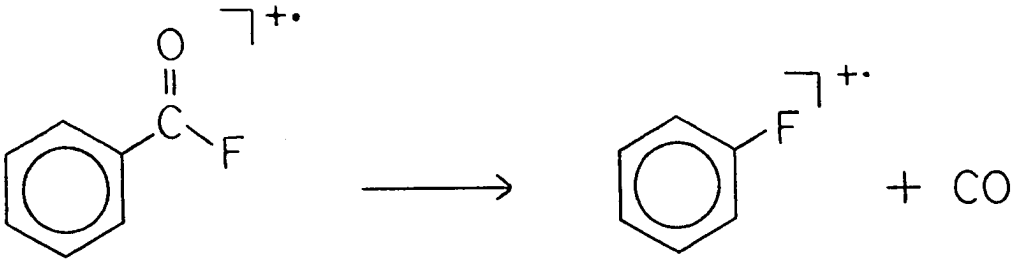
$$m^* = \frac{m_2^2}{m_1} \qquad \text{Equation 2}$$

have lifetimes which result in decomposition in the field-free region thereby producing metastable ions while those ions whose rate constant for fragmentation is greater than 10^6 sec^{-1} decompose in the source. Surprisingly, no attempt to utilize Chupka's suggestion as an aid for the detection of rearrangements appeared in the literature for nine years. McLafferty and Fairweather studied several well known simple cleavage and rearrangement reactions and postulated that a process producing an abundant ion does not involve a rearrangement if the corresponding metastable ion is not abundant (9). Brown has recently presented convincing experimental evidence that the metastable ion for a fragmentation involving a rearrangement reaction is more intense than the metastable ion for a competing cleavage reaction when both metastable ions are present (5). It appears that the careful

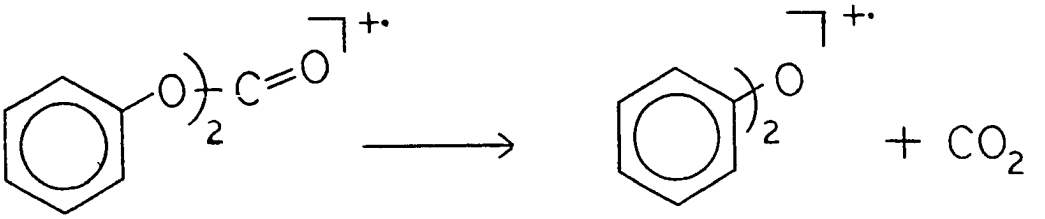
study of metastable ions and their intensities at varying electron energies may be a useful method to aid in the detection of mass spectral rearrangements.

The measurement of the appearance potential of an ion (defined as the minimum energy of the ionizing electrons that can produce a large enough quantity of the ion to be detected) is another technique which has been employed in detecting rearrangements. The measured appearance potential of an ion should agree with an appearance potential calculated from other data such as ionization potential, heat of formation and bond dissociation data if the structure assumed for the ion is correct. Perhaps the most famous usage of this type of data was the suggestion that the $C_7H_7^+$ ion in the mass spectrum of toluene could not be the benzyl cation (10). A difference of 16 kcal/mole was noted in the measured ionization potential of the benzyl free radical and the ionization potential of C_7H_7 which was calculated by using the appearance potential for the m/e 91 ion in the spectra of toluene and bibenzyl (11, 12). Subsequent data has indicated that the $C_7H_7^+$ ion in these compounds is better represented by the tropylium ion structure.

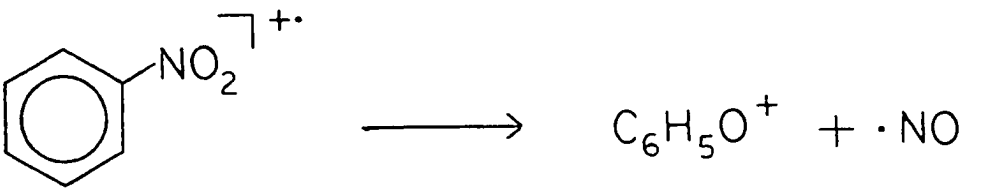
One of the simplest methods for the detection of mass spectral rearrangements is an arithmetic approach in which one looks for ions in the spectrum whose mass suggests that they contain bonded atoms which were not bonded together in the



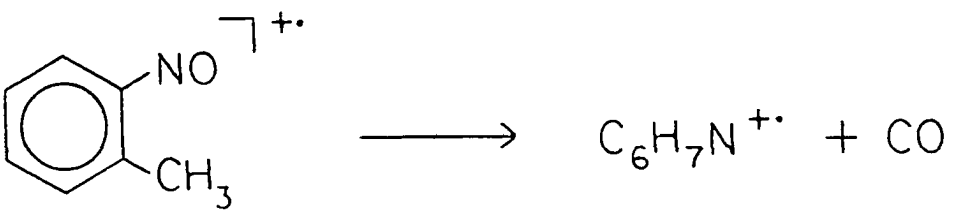
Equation 3



Equation 4



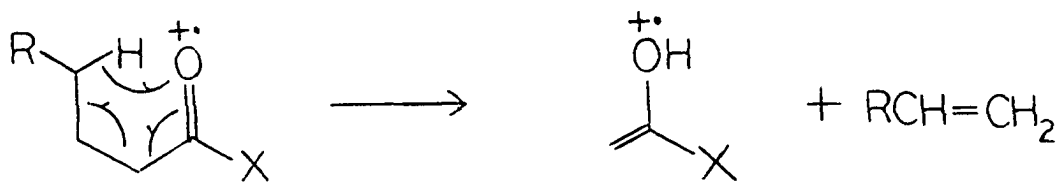
Equation 5



Equation 6

original molecule. Alternatively, a knowledge of the neutral species ejected can also suggest a rearrangement process. Equations 3-6 represent only a few of the numerous ways in which these approaches may be applied in detecting rearrangement reactions (13).

Perhaps the most commonly employed method of studying mass spectral rearrangements is the use of isotopically labelled compounds. In these cases the mass spectra of unlabelled and isotopically labelled compounds are compared in order to determine mechanistic features of a reaction which is known or suspected to involve rearrangement. Frequently additional unknown rearrangement reactions will be uncovered. An example of how this technique aids in determining the features of a rearrangement was the establishment by deuterium labelling that the well known McLafferty rearrangement involves a gamma hydrogen transfer as illustrated in Equation 7 (14, p. 155).



Equation 7

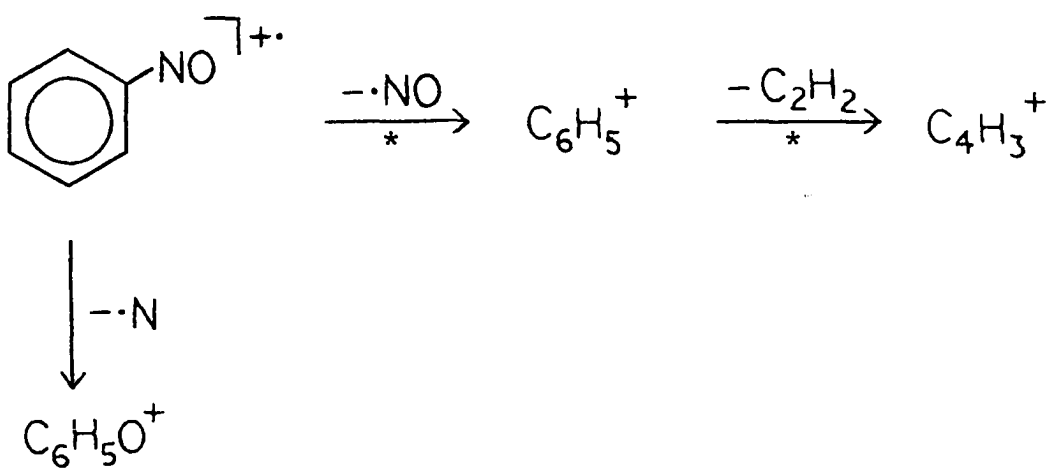
A very recent technique for detecting rearrangements involves the comparison of the field ionization spectrum with the mass spectrum (15, 16). Because of the extremely short

period of time for normal fragmentation following field ionization, the intensity of the rearrangement ions are very small in the field ionization spectrum compared to ions formed by a single step direct bond cleavage.

Mass Spectral Rearrangements of Aralkyl Nitroso and Nitro Compounds

The possible mass spectral interrelationship of C-nitroso compounds with related nitrogenous compounds such as aryl and olefinic nitro compounds (14, p. 518, 17) hydroxylamines (18) nitrones (19) and azoxy compounds (20) is of interest due to the large number of interesting rearrangement reactions these compounds undergo upon electron impact. Many of the rearrangements which the related nitrogenous compounds undergo are multiple rearrangements and the possibility exists for similar multiple rearrangements in the spectra of C-nitroso compounds. For the purposes of these studies, both rearrangements involving several migrations prior to fragmentation and a rearrangement and fragmentation followed by another rearrangement and fragmentation will be considered as multiple rearrangements. The following discussion will center on previous work which has been directed toward the elucidation of the mass spectral behavior of aromatic nitro and nitroso compounds. These studies are most important because the work described in this dissertation deals with aralkyl nitro and nitroso compounds.

In spite of widespread research activities with C-nitroso compounds, the powerful technique of mass spectrometry has been sparingly applied to these compounds and little is known of their gas phase cation chemistry (14, p. 523, 21, 22, 23). Nitrosobenzene is known to form an intense molecular ion (65% relative intensity) which fragments by loss of the functional group to give the base peak at m/e 77 (14, p. 523). The $C_6H_5^+$ ion subsequently expels a molecule of acetylene and a more recent study utilizing the labelled

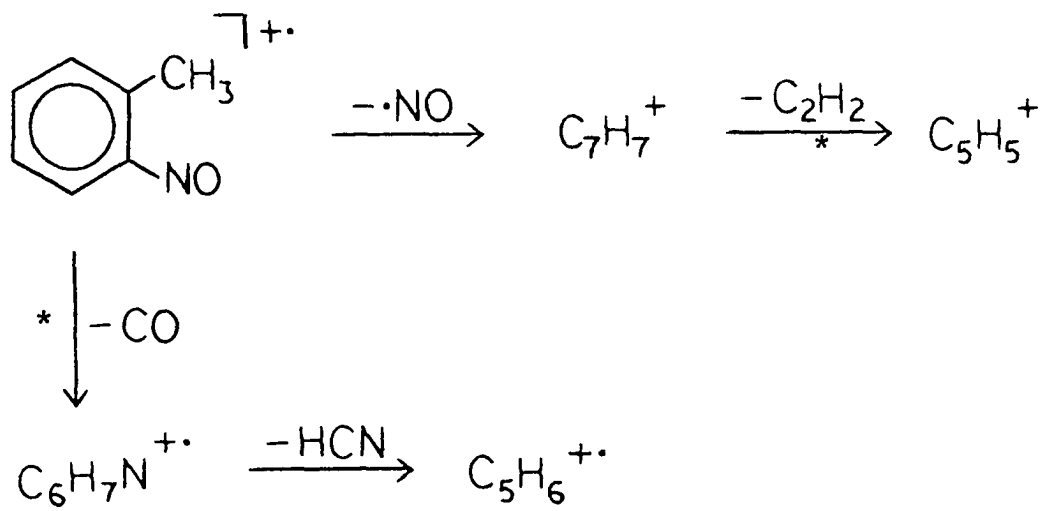


Scheme 1. Fragmentation of nitrosobenzene

compound, 2,4,6-d_3-nitrosobenzene, provided convincing evidence that the hydrogen atoms in the M-·NO ion underwent rearrangement to the extent that they were randomized prior to the expulsion of acetylene (23). A minor loss of a nitrogen atom from the molecular ion was also noted. This reaction is of considerable interest due to the possible relationship with

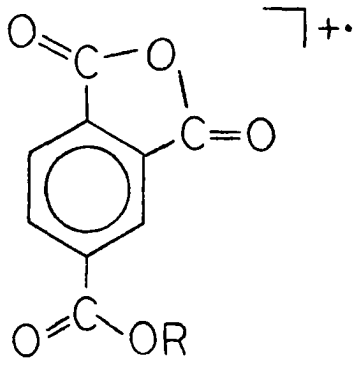
the well known nitro-nitrite rearrangement observed in aromatic nitro compounds.

The base peak in the 70eV spectrum of the nitrosotoluenes is also formed by the loss of the functional group (21). The M-·NO ion of these compounds expels a molecule of acetylene producing the $C_5H_5^+$ ion. In addition, the mass spectrum of the ortho isomer displays a prominent M-CO ion which is formed in a metastable process. As the bombarding electron energy is lowered, the M-CO ion increases in importance while the M-·NO ion decreases. If the carbon atom that is lost in this process is the methyl carbon atom, as has been suggested, then this rearrangement would require a triple hydrogen migration prior to or during fragmentation. This would be a rearrangement of considerable interest because only two other

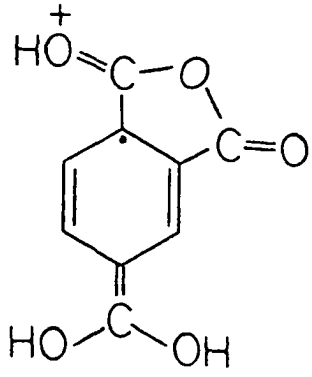


Scheme 2. Fragmentation of ortho-nitrosotoluene

multiple rearrangements involving a triple hydrogen migration prior to fragmentation have been documented as such in the literature although others may exist. Katoh and Djerassi were able to determine by deuterium labelling that the neutral ethanol molecule ejected from the molecular ion of n-heptyl vinyl ether contained the three vinyl hydrogen atoms and one hydrogen from C_3, C_4 and C_5 of the heptyl group (24). Meyerson noted that long chain esters of compound (1) underwent decomposition by a triple hydrogen migration from the alkyl chain and he suggested that resonance stabilized structures such as (2) may represent the product ion (25). The



(1)

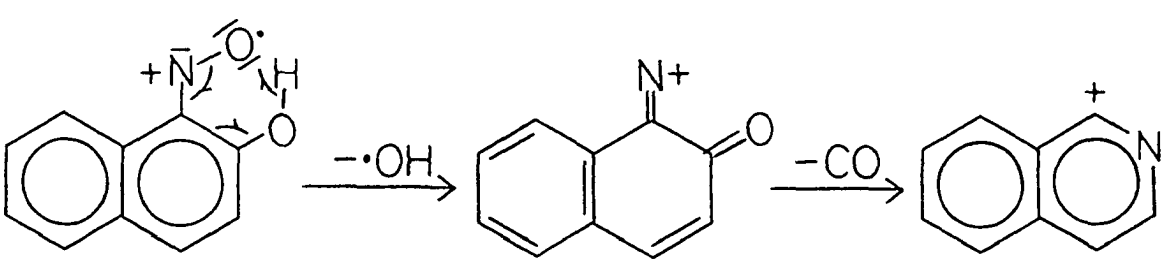


(2)

triple hydrogen migration involved in the formation of the M-CO ion of ortho-nitrosotoluene probably involves migration to both the ring and the nitrogen atom and an anilinium radial cation structure has been suggested for the m/e 93 ion.

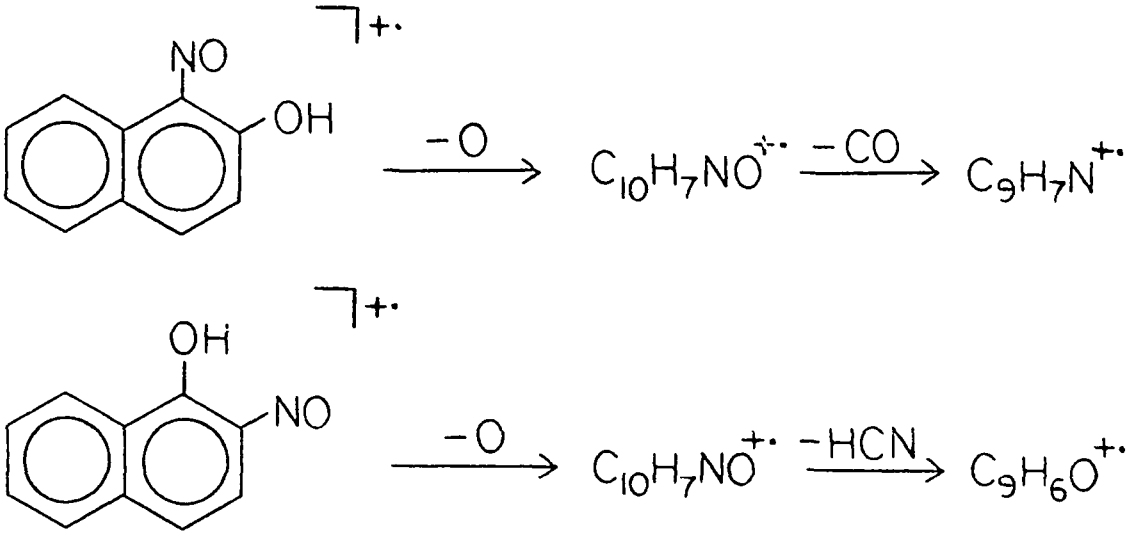
The mass spectra of a few para-nitrosoaniline derivatives, para-nitrosophenol, 1-nitroso-2-naphthol and 2-nitroso-1-

naphthol have been examined (21). The mass spectra of the para-nitrosoaniline derivatives show that these compounds behave unexceptionally upon electron impact. The mass spectrum of para-nitrosophenol shows fragmentation occurs through both the nitroso and phenol substituents giving M-·NO and M-CO ions of comparable abundance. In addition, an ion at m/e 109 of 10% intensity relative to the molecular ion (m/e 123, 100% relative intensity) appears in the spectrum. The composition of this M-14 ion was reported to be C_6H_7NO, but this clearly cannot be correct because only five hydrogen atoms are present in the original molecule. This M-14 ion is most likely formed by loss of a nitrogen atom from the molecular ion, a process which is considerably more important in the spectrum of this compound than in the spectra of nitrosobenzene and the nitrosotoluenes. If the nitroso and hydroxy groups are ortho to each other as in the nitrosonaphthols which were studied, the expulsion of a hydroxyl radical becomes quite favorable presumably due to an ortho-effect as shown in Scheme 3. The M-·OH ion of both



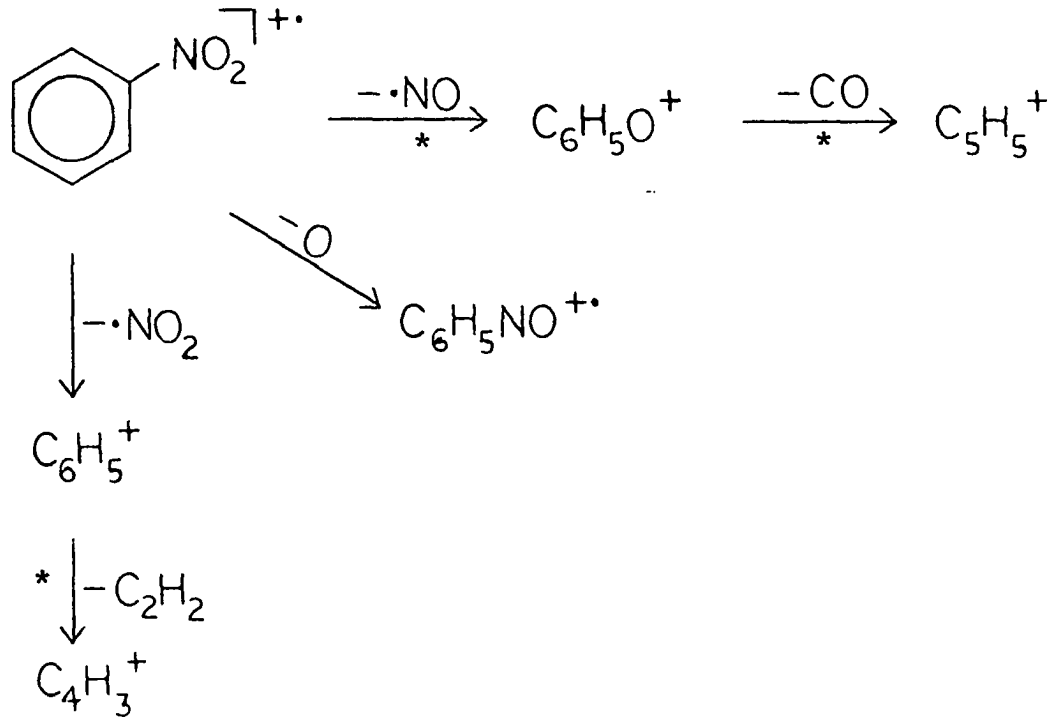
Scheme 3. Mechanism for loss of ·OH from 1-nitroso-2-naphthol

nitrosonaphthols studied fragments further by loss of carbon monoxide providing the intense ions observed at m/e 128. These nitrosonaphthols can be distinguished from each other by mass spectrometry because the base peak in the spectrum of 1-nitroso-2-naphthol is due to the loss of CO from the M-O ion while the base peak in the spectrum of 2-nitroso-1-naphthol is the M-·OH ion. An interesting difference is noted in the behavior of the M-O ions as that ion formed from 2-nitroso-1-naphthol expels a molecule of hydrogen cyanide while the M-O ion of 1-nitroso-2-naphthol loses carbon monoxide as shown in Scheme 4. No explanation for this phenomenon has been proposed (21).



Scheme 4. Different mass spectral behavior of iosmeric nitrosonaphthols

Considerably more is known of the gas phase cation chemistry of aralkyl nitro compounds containing the nitro group substituted on the aromatic ring. The mass spectrum of nitrobenzene reveals a one step loss of nitric oxide to form both

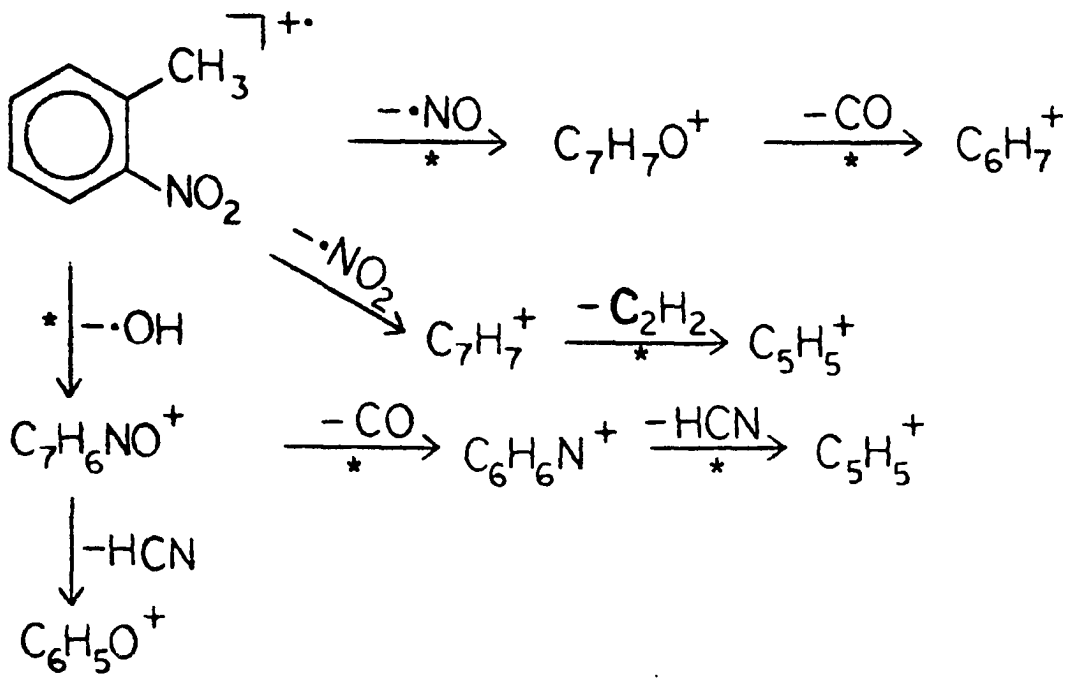


Scheme 5. Fragmentation of nitrobenzene

the M-·NO ion and the NO^+ ion (26). The M-·NO ion fragments further by loss of carbon monoxide producing the $C_5H_5^+$ ion. Beynon proposed that the loss of nitric oxide occurred by an initial rearrangement of the nitro group to a nitrite group (27). Considerable other work which will not be discussed here has supported this proposal. The base peak in the 70eV

spectrum of nitrobenzene corresponds to the simple cleavage of the nitro group producing the $C_6H_5^+$ ion which then expels a molecule of acetylene in a metastable process. Only a minor loss (1%) of an oxygen atom is observed.

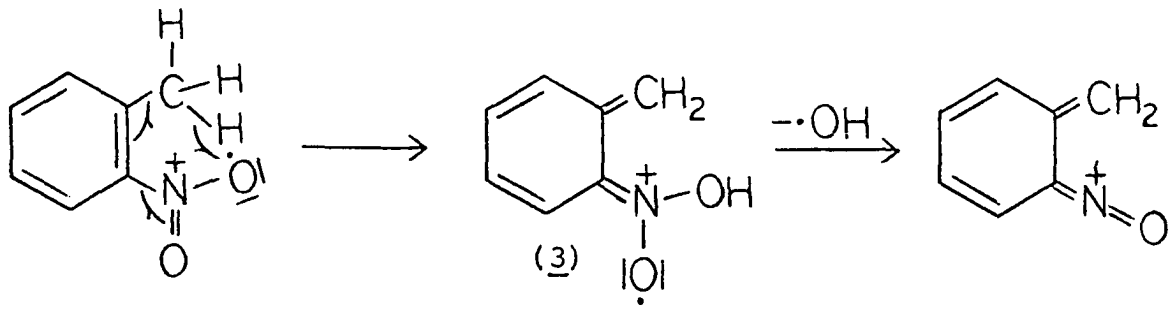
The mass spectra of the nitrotoluenes show M-O, M-·NO and M-·NO_2 ions, but the ortho isomer undergoes additional fragmentation due to interaction of the methyl and nitro groups (27, 28). The base peak in the spectrum of ortho-nitrotoluene arises by loss of a hydroxyl radical from the



Scheme 6. Fragmentation of ortho-nitrotoluene

molecular ion, a process which is followed by loss of either hydrogen cyanide or carbon monoxide producing the ions at m/e 92 and 93. The m/e 92 ion subsequently expels a molecule

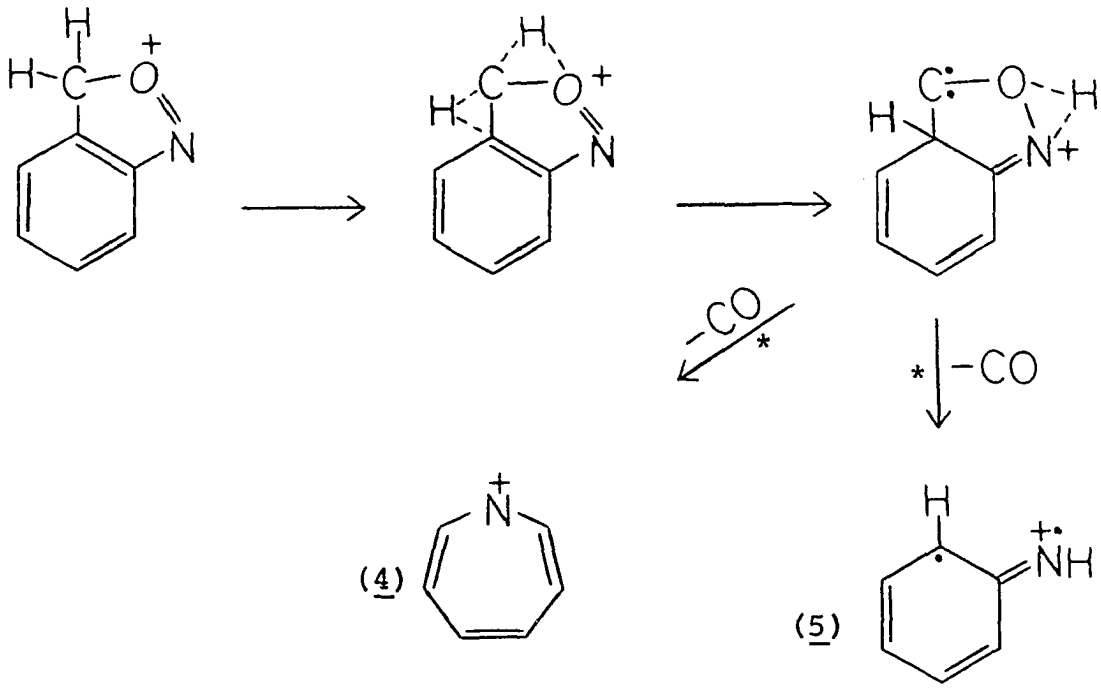
of HCN in a metastable process. Competition from this group of reactions evidently reduces the importance of the M-O, M-·NO and M-·NO_2 ions relative to those observed in the spectra of the meta and para isomers. Because the meta and para compounds do not show the primary loss of a hydroxyl radical and the associated reactions, the hydrogen atoms of the methyl group are implicated in the hydroxyl loss and this inference is confirmed by deuterium labelling. The occurrence of a large isotope effect indicates that the reaction may occur through the rearranged intermediate (3) shown in Scheme 7. This implies that the M-·OH ion arises from the nitro rather than



Scheme 7. Possible mechanism for ·OH loss from ortho-nitrotoluene

the nitrite form of the molecular ion and this is further supported by the fact that the M-·OH ion expels $C^{13}O$ if the ortho methyl group is labelled with a carbon-thirteen atom (29). A possible mechanism is shown in Scheme 8, but the authors were unable to distinguish whether the structure of the product ion was better represented as (4) or (5). Deuterium labelling has established that the loss of HCN

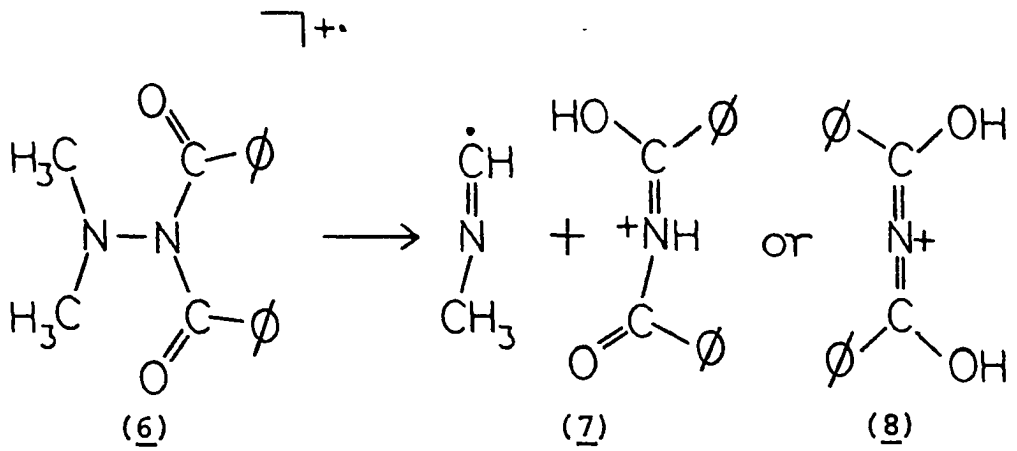
from the m/e 92 ion (M-·OH-CO) involves primarily a hydrogen from the original methyl group. This series of rearrangements



Scheme 8. Possible mechanism for CO loss from the M-·OH ion of ortho-nitrotoluene

represents three consecutive rearrangements, the second of which requires a double hydrogen migration prior to or during the loss of carbon monoxide.

Double hydrogen transfers prior to or during fragmentation are more common than the triple hydrogen transfers previously discussed, but are still relatively unusual mass spectral rearrangements. A recent study established by deuterium labelling that two hydrogen atoms from the same methyl group of 1,1-dimethyl-2,2-dibenzoyl hydrazine (6)



(6) (7) (8)

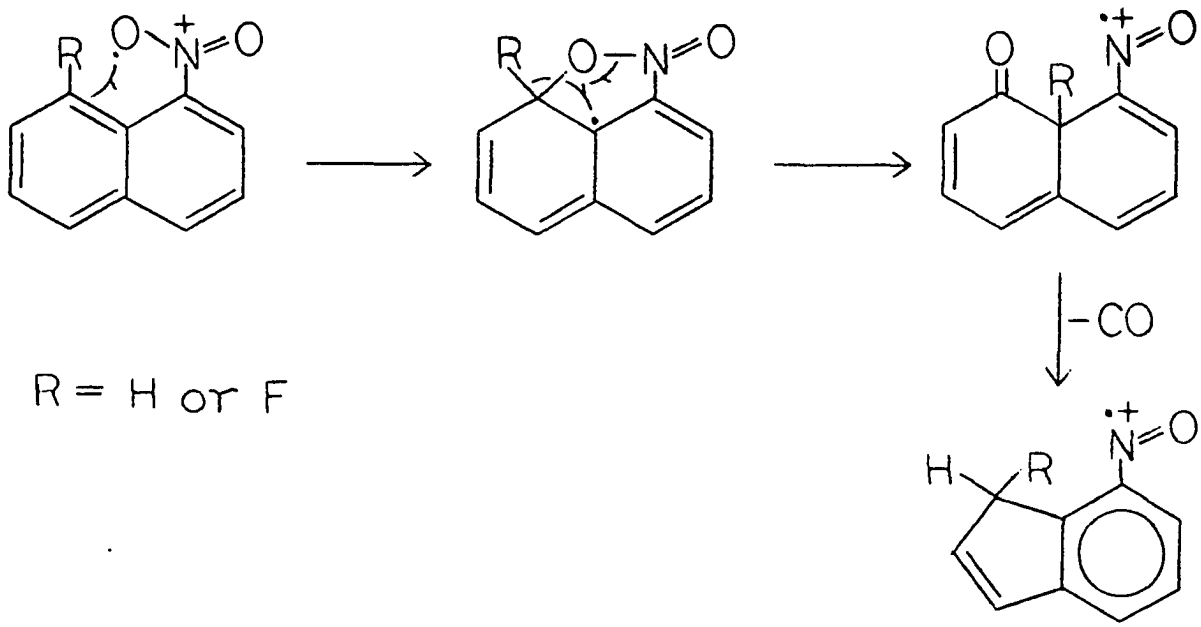
Scheme 9. Loss of $C_2H_4N\cdot$ from (6)

migrated prior to or during N-N bond fission to give either (7) or (8) as the product ion as shown in Scheme 9 (30). Other well studied examples of double hydrogen migrations include the transfer of two hydrogen atoms prior to or during the loss of the alkyl fragment from the alcohol portion of aliphatic esters producing a product ion which may be represented by a protonated carboxylic acid ion as shown in Equation 8 (31, 32, 33, 34, 35).

$$RCOOR'^{+\cdot} \rightarrow RCO_2H_2^{+} + R'\text{-}2H^{\cdot} \qquad \text{Equation 8}$$

The mass spectra of the nitronaphthalenes are similar to the nitrobenzenes in that they show intense molecular ions which fragment to give M-O, M-·NO and M-·NO_2 ions (36, 37). The base peak in the spectra of the two isomeric nitronaphthalenes is formed by the simple bond cleavage of the nitro group.

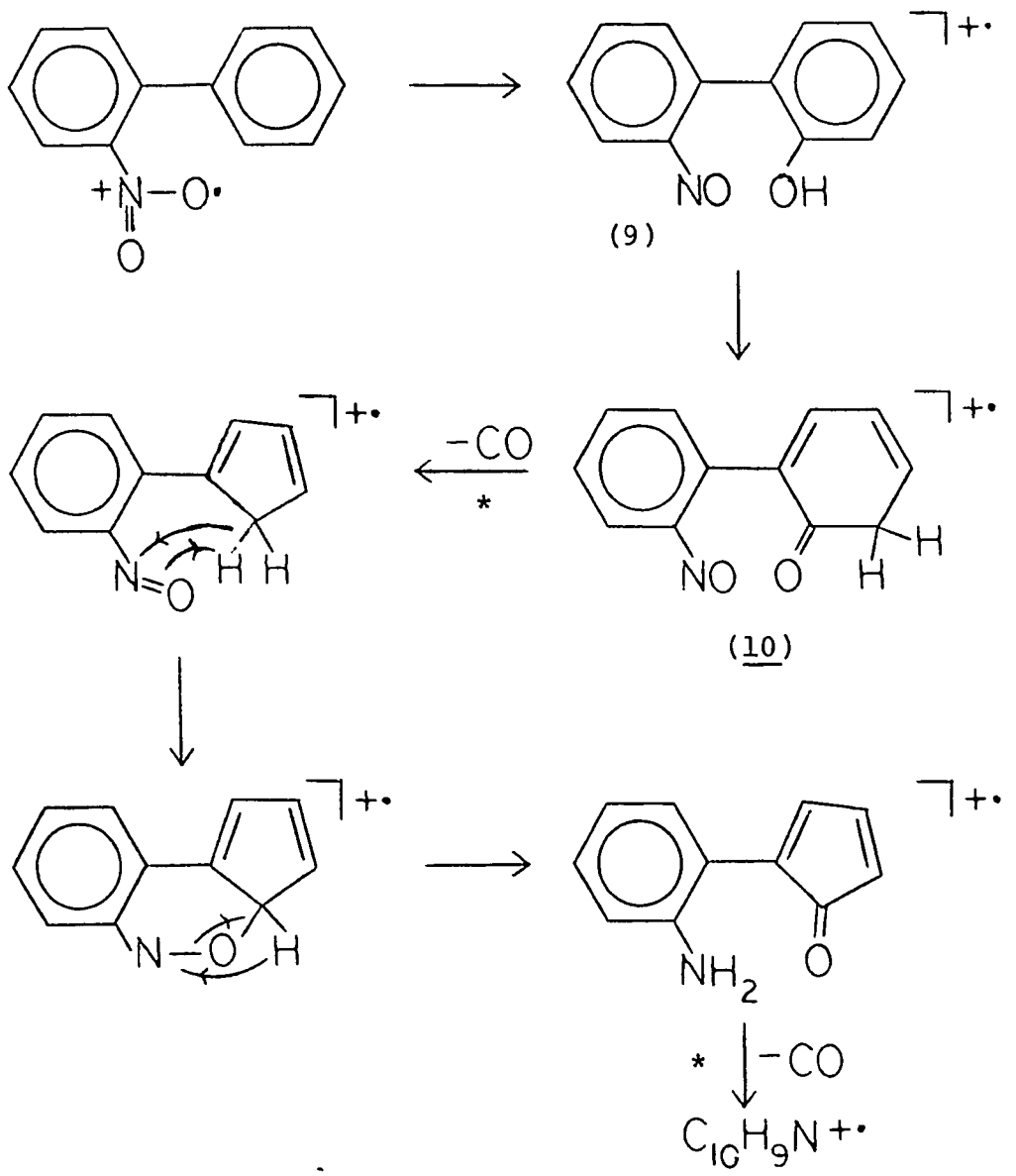
The mass spectrum of 1-nitronaphthalene is unusual because carbon monoxide is lost from the molecular ion (36, 37). The absence of this fragmentation in the mass spectrum of nitrobenzene and 2-nitronaphthalene led to the suggestion that the carbon atom involved in this fragmentation is the 8-carbon atom and this was confirmed by carbon-thirteen labelling. This loss of carbon monoxide from 1-nitronaphthalenes is not general and is known to occur only when the 8 position contains a hydrogen or flourine atom. This suggests that the initial step does not involve abstraction of the peri-atom by oxygen as flourine abstraction by oxygen seems unlikely. The mechanism shown in Scheme 10 has been suggested.



Scheme 10. Mechanism for loss of CO from 1-nitronaphthalene and 8-flouro-1-nitronaphthalene

The mass spectra of the isomeric nitrobiphenyls have been recorded and that of 2-nitrobiphenyl shows several rearrangement processes involving interaction between the nitro group and the ortho-phenyl ring (28). The mass spectrum of the 2-isomer shows the metastable loss of a hydroxyl radical but this M-·OH ion is considerably less important than the M-·OH ion in the spectrum of ortho-nitrotoluene. This is not surprising as the abstraction of an aromatic hydrogen by an oxygen atom of the nitro group would be expected to be more difficult than abstraction of a benzylic hydrogen atom. Other reaction pathways are also available to the molecular ion and these processes act to further diminish the importance of the M-.OH ion.

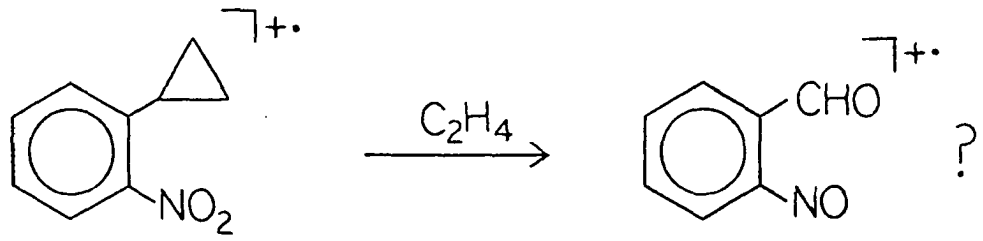
The most interesting fragmentation of 2-nitrobiphenyl is the sequential loss of two molecules of carbon monoxide. A metastable ion was observed for both of the CO losses. It has been suggested that the initial rearrangement involves an isomerization to a nitrosophenyl phenol structure such as the intermediate (9) in Scheme 11. This intermediate would be expected to lose carbon monoxide by undergoing further rearrangement to a cyclohexadienone intermediate like (10). This is, of course, the same type of an intermediate which has been suggested for the loss



Scheme 11. Mechanism for two successive losses of CO from 2-nitrobiphenyl

of carbon monoxide in phenol itself (38). A double hydrogen migration is suggested to precede the loss of the second molecule of carbon monoxide (see Scheme 11).

The mass spectra of the three isomeric cyclopropyl nitrobenzenes have been reported (39). The meta and para isomers showed similar spectra including an unusual M-17 ion of low intensity. The spectrum of ortho isomer is distinctive from the spectra of the meta and para isomers because of the presence of a large M-28 ion. The composition of this ion was established by high resolution mass spectrometry as $C_7H_5NO_2^{+\cdot}$ thus indicating the loss of ethylene from the molecular ion. Interaction of the ortho nitro group with the cyclopropane ring evidently promotes the loss of ethylene and the structure of the M-28 ion was suggested to be a rearranged ion, possibly an ortho-nitrosobenzaldehyde ion (39).

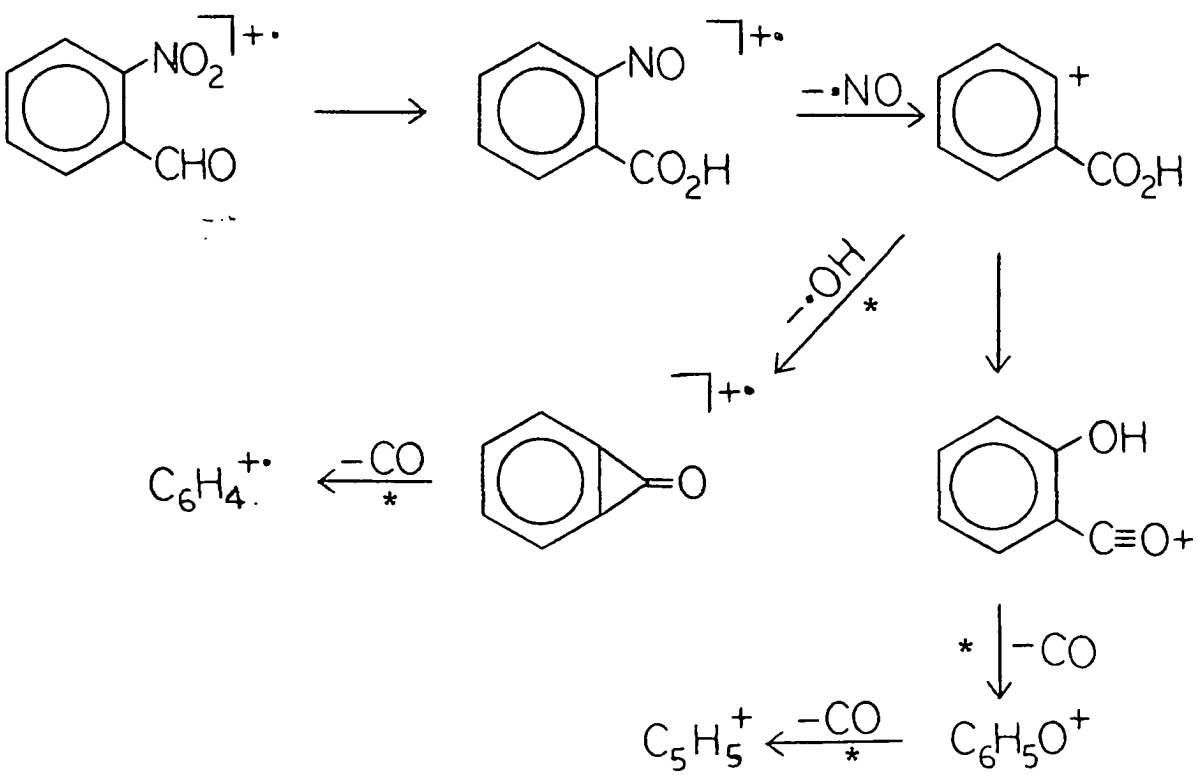


Scheme 12. Loss of ethylene from 2-nitro-cyclopropylbenzene

There are other examples in the literature where nitro and nitroso compounds have been proposed to form common product ions upon electron impact. These studies are relevant

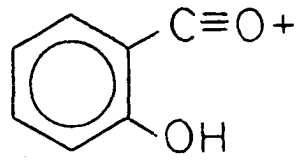
to the present study because several comparisons of the behavior of product ions of nitro and nitroso compounds will be made.

The first proposal of the intervention of common ions in the spectra of nitro and nitroso compounds was based on analogy to the known photochemical transformation of ortho-nitrobenzaldehyde to ortho-nitrosobenzoic acid (40). The original fragmentation sequence of ortho-nitrobenzaldehyde proposed the possible conversion to ortho-nitrosobenzoic acid upon electron impact as shown in Scheme 13. This was later

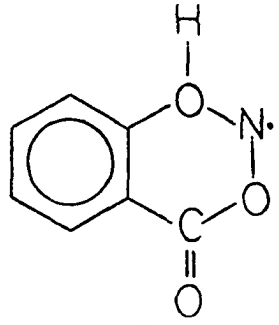


Scheme 13. Proposed fragmentation of ortho-nitrobenzaldehyde

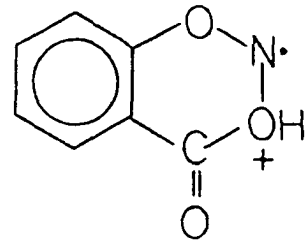
deemed unlikely because the m/e 104 ion (originally explained as the loss of a hydroxyl radical from the M-·NO ion) was considerably less intense in the spectrum of ortho-nitrosobenzoic acid than in the spectrum of ortho-nitrobenzaldehyde. Furthermore, the molecular ion of ortho-nitrosobenzoic acid is the base peak in its spectrum while the molecular ion of ortho-nitrobenzaldehyde is very small (1%) (41). It has been proposed that the intense m/e 104 ion of ortho-nitrobenzaldehyde arises by the one step loss of NO_2H from the molecular ion. The m/e 121 ion present in the spectra of ortho-nitrobenzoic acid (M-·NO_2), ortho-nitrosobenzoic acid (M-·NO) and ortho-nitrobenzaldehyde (M-·NO) fragments by two successive loses of carbon monoxide. The proposed structure for this common ion is (11) and may be formed in the aldehyde via expulsion of ·NO from intermediates of nitrite form such as (12) and (13) (41).



(11)

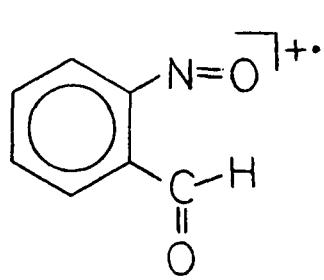


(12)

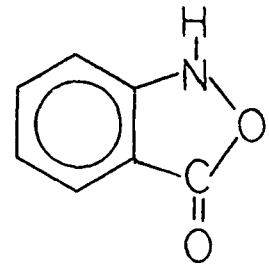


(13)

The mass spectrum of ortho-nitrobenzyl alcohol shows a weak molecular ion which loses water to form the m/e 135 ion. This ion fragments by loss of C_2O_2 (probably as two successive CO losses) and by loss of CO_2 which is followed by loss of HCN. The spectrum of ortho-nitrosobenzaldehyde is remarkably similar and thus the two compounds were proposed to fragment through the common intermediate (14) or (15) (41). The mass spectrum of (15) has been studied and the same fragmentations were observed (42).



(14)



(15)

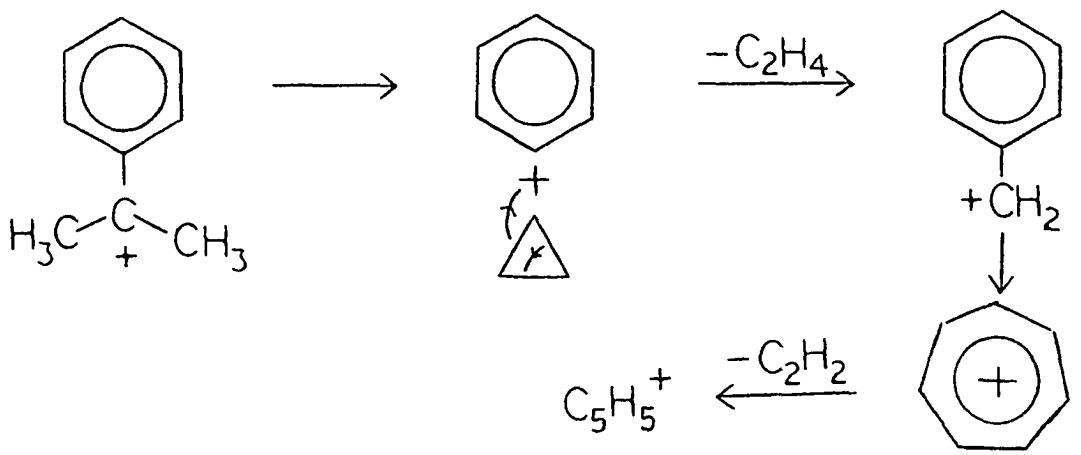
Mass Spectral Rearrangements of Cumyl and Related Cations

Several of the aralkyl nitro and nitroso compounds which were investigated in the studies to be presented contained iso-propyl and tert-butyl groups substituted on the aromatic ring. The rearrangements and fragmentations that these structural units undergo, become important for interpreting some of the rearrangements and fragmentations of the aralkyl nitro and nitroso compounds containing iso-propyl and tert-butyl groups.

Upon electron impact the moderately intense molecular ion of cumene (25% relative intensity) undergoes beta cleavage of a methyl group to produce the base peak at m/e 105. This $C_8H_9^+$ ion then loses a molecule of acetylene producing the m/e 79 ion which subsequently loses a molecule of hydrogen to give the m/e 77 ion (4, p. 458). Although the structures of the $C_8H_9^+$ and $C_6H_5^+$ ions formed from this compound and others has attracted considerable interest (4, pp. 475-487), these ions do not play a prominent role in the spectra of the aralkyl nitro and nitroso compounds. Cumene shows a very small (1%) M-1 peak and thus the cumyl cation does not play an important role in the fragmentation of cumene.

The molecular ion of tert-butylbenzene also undergoes beta cleavage of a methyl group to form the base peak at m/e 119 and this ion subsequently expels a molecule of ethylene to produce the m/e 91 ion. The mass spectrum of alpha-^{13}C-tert-butylbenzene has been examined, and the data from this compound forms the basis for the proposal of one of the most intriguing of all mass spectral rearrangements. Upon electron impact, the labelled compound forms the cumyl cation with complete retention of the label. This M-15 ion then expels ethylene, but only 37% of the original label is retained in the product ion (43). Rylander and Meyerson proposed that the initial cumyl cation rearranged to an intermediate ion in

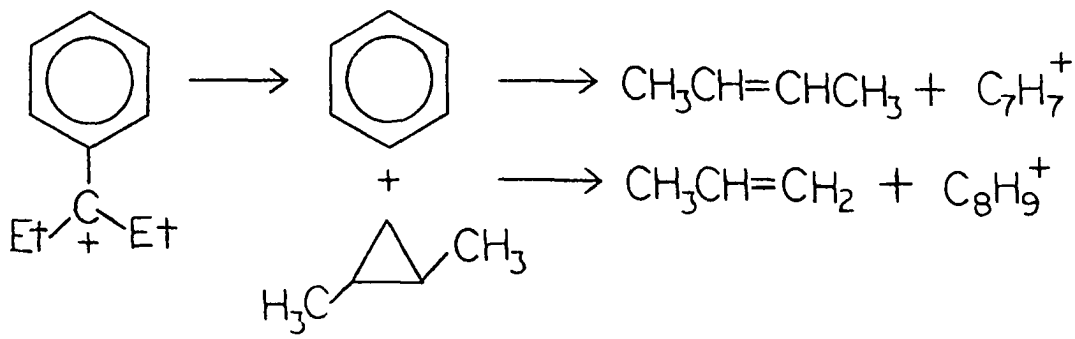
which the three side chain carbon atoms became symmetrical with respect to the phenyl group. The simplest formulation of such an ion is a cyclopropane molecule with a symmetrically located phenyl ion. This phenylated cyclopropane could be envisioned as losing the ethylene molecule in three equivalent ways thereby accounting for the retention of about one-third of the label in the product ion. By the migration of only two bonds, as shown in Scheme 14, the phenylated cyclopropane intermediate would form a benzyl cation which could



Scheme 14. Mechanism for loss of ethylene from cumyl cations

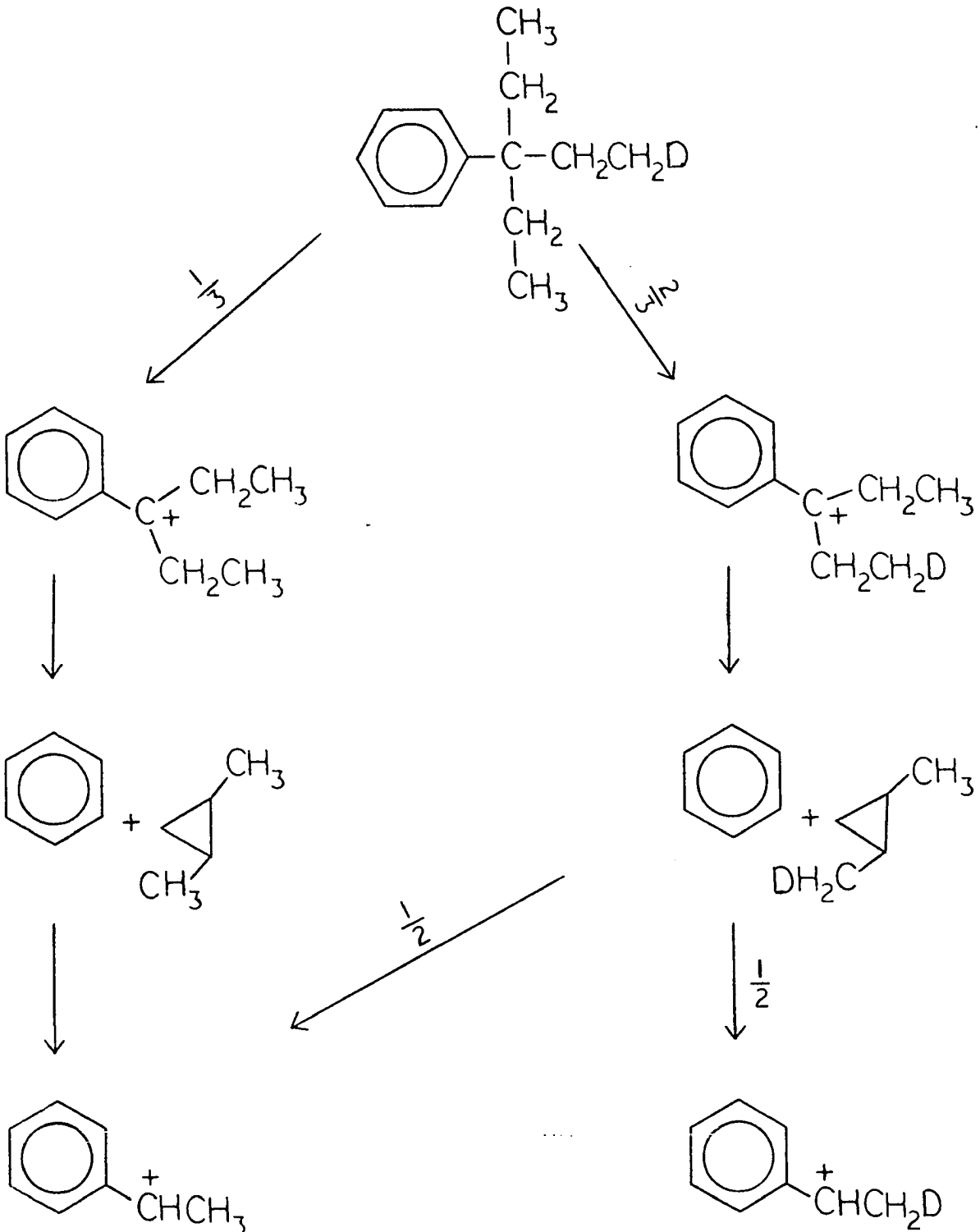
then rearrange to the tropylium ion and fragment as such. There is still some question as to whether all benzyl cations rearrange to tropylium ions or whether only those which undergo further fragmentation rearrange (44). The exact mechanism by which benzyl cations rearrange to tropylium ions is also an area of current interest (45, 46).

The concept of an intermediate phenylated cyclopropane species has proven useful for the explanation of the behavior of other alkylbenzenes upon electron impact. The loss of propylene and butylene from the $C_{11}H_{15}^+$ ion formed by the initial beta cleavage of an ethyl group in the molecular ion of 3-ethyl-3-phenylpentane is postulated as occurring through a phenylated dimethylcyclopropane cation as shown in Scheme 15 (4, p. 514).



Scheme 15. Fragmentation of the m/e 147 ion of 3-ethyl-3-phenylpentane

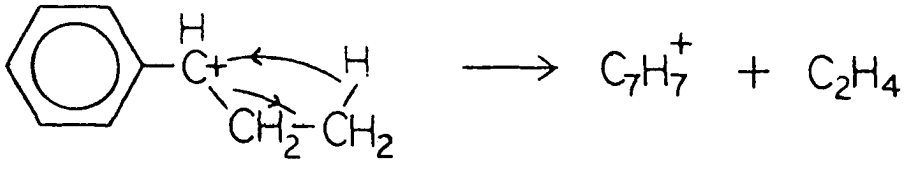
The observed label retentions of 65% in the $C_{11}H_{15}^+$ ion and 33% in the $C_8H_9^+$ ion in the spectrum of 3-ethyl-3-phenylpentane-1-d agree well with the retentions of 67% and 33% which would be predicted by Scheme 16. Schemes 15 and 16 predict a 0% label retention in the $C_7H_7^+$ ion of 3-ethyl-3-phenylpentane-1-d and the 6% observed retention was rationalized as arising by the fragmentation of $C_9H_{10}D^+$ ions to $C_7H_6D^+$ ions.



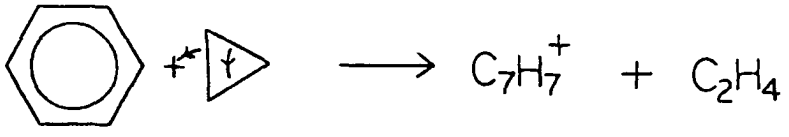
Scheme 16. Fragmentation of 3-ethyl-3-phenylpentane-1-d

The mass spectrum of 3-phenylpentane also showed initial <u>beta</u> cleavage of an ethyl group to form $\phi\overset{+}{C}HCH_2CH_3$ ions which subsequently lose ethylene to form $C_7H_7^+$ ions. Meyerson and Hart studied the labelled compounds, 3-phenylpentane-1-d and 3-phenylpentane-3-d, and suggested that the $\phi\overset{+}{C}HCH_2CH_3$ ion from 3-phenylpentane lost ethylene by a combination of Mechanisms I and II in a 10:90 ratio as shown in Scheme 17 (47). The operation of two mechanisms was involved because 3-phenylpentane-3-d showed an energy dependent retention of more deuterium than one would predict from a process like Mechanism II which randomizes all side chain hydrogen atoms.

Nibbering and DeBoer, upon examining the mass spectra



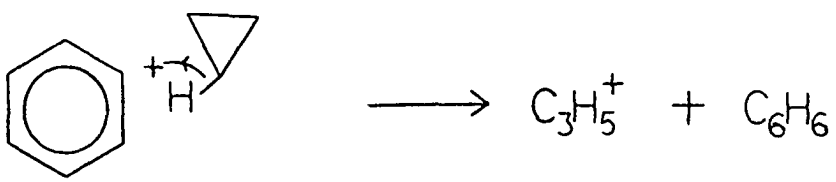
Mechanism I



Mechanism II

Scheme 17. Fragmentation of the m/e 147 ion of 3-phenylpentane

of 1-phenyl-1-nitropropane, 1-phenyl-2-nitropropane and some deuterated analogs, proposed that the M-·NO_2 ion lost ethylene through an intermediate phenylated cyclopropane cation in which the cyclopropane hydrogen atoms were scrambled prior to fragmentation (48, 49). In addition, a new reaction of the phenylated cyclopropane was proposed in which the phenyl ring abstracts a hydride ion from the cyclopropane ring thereby forming a $C_3H_5^+$ ion. A metastable ion for the reaction m/e 119 → m/e 41 was observed (48).



Scheme 18. Formation of $C_3H_5^+$ from a phenylated cyclopropane

The concept of a phenylated cyclopropane intermediate has been further strengthened by the observation of the analogous methylated cyclopropane and protonated cyclopropane ions in the mass spectra of some aliphatic hydrocarbons (50, 51, 52, 53).

RESULTS AND DISCUSSION

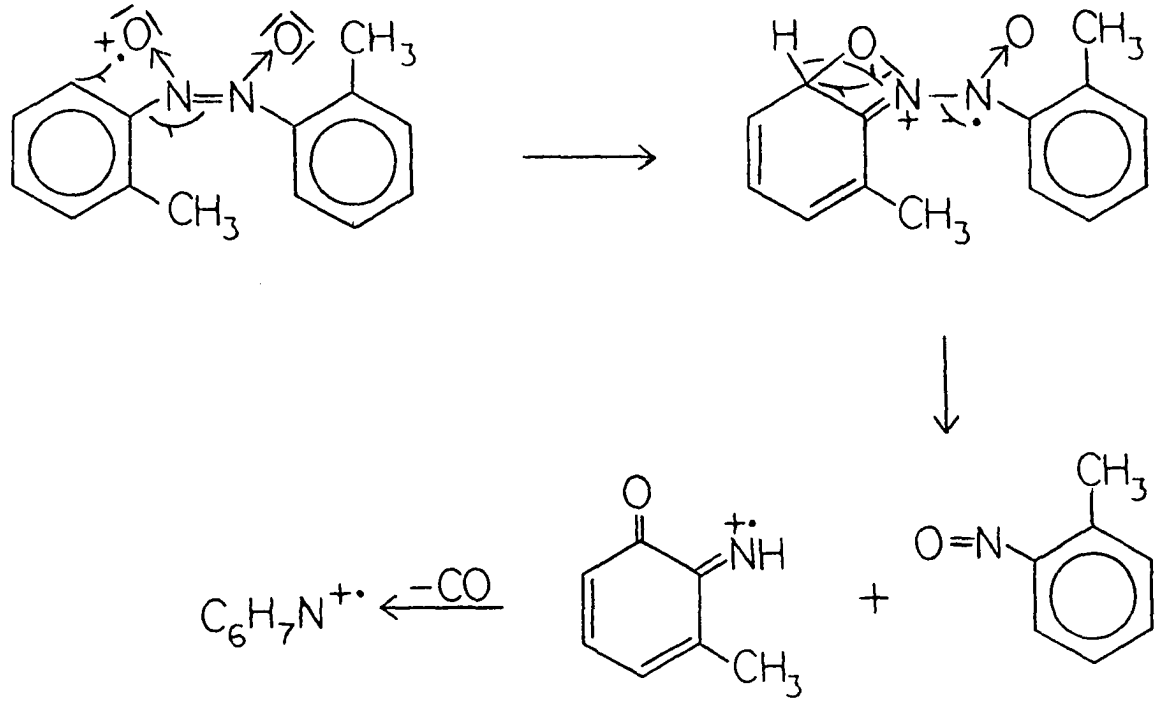
The widespread research activities with C-nitroso compounds have shown that these compounds have some very interesting and unusual properties. One of the most interesting characteristics of these compounds is their ability to exist as either monomers or dimers depending upon the conditions to which they are subjected (54, 55). In the study of the fragmentation and rearrangement reactions of aralkyl nitroso compounds upon electron impact it is important to establish whether the molecular species undergoing electron bombardment is monomeric or dimeric. Different conclusions about the mechanisms of some of the rearrangement reactions might be reached depending on whether the parent ion was that of the monomer or dimer.

The existence of a dimeric molecular ion of a nitroso compound in the mass spectrometer would certainly be established if either the dimeric molecular ion or daughter ions whose mass is greater than the mass of the monomer could be measured. None of the compounds investigated in these studies have ever shown peaks in the mass spectrum at a higher mass than those expected for a monomeric species under our conditions. Unfortunately, this does not prove the non-existence of nitroso dimers in the mass spectrometer because of the possibility that the dimer might undergo very rapid cleavage to the monomer or to other daughter ions of lower mass than

the monomer. If the dimer fragmented only to the monomer, difficulty in determining the mechanism for further fragmentation would result because this monomer could either be a radical cation or a cation depending upon the neutral species eliminated. A situation which would cause even more serious mechanistic difficulties would be if the initial interaction leading to a fragmentation that produces a species of smaller mass than the monomer actually occurs in the dimer and this interaction causes the dimer to fragment to the monomer.

A different mechanistic interpretation for the formation of the M-CO ion of ortho-nitrosotoluene than that previously discussed could be proposed in the absence of other conclusive data if the initial interaction occurred in the dimer. Dimers of aryl nitroso compounds are known to be less stable than those of alkyl nitroso compounds (54). However, dimers of aryl nitroso compounds containing ortho substituents are more stable than those without ortho substituents. Two reports in the literature document the presence of dimeric nitroso alkanes in the mass spectrometer. Collin noted a peak of 11% intensity at m/e 90 in the mass spectrum of nitrosomethane (22) and Tou and Chang have recently found that 1-chloro-2-nitrosocycloalkanes exist as dimers under their mass spectral conditions (56). It is also interesting to note that the base peak in the field ionization spectrum of 1-chloro-2-nitrosocycloalkanes is the molecular ion of the dimer. These

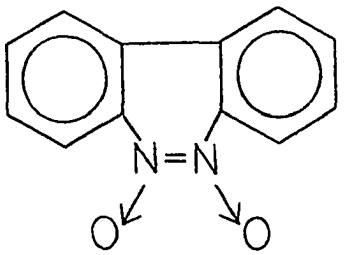
facts indicate that there is a possibility that the dimer of ortho-nitrosotoluene may form a molecular ion which could influence fragmentation but not be detected. The mechanism shown in Scheme 19 is highly improbable, but nevertheless indicates that it is possible to envision the dimer of ortho-nitrosotoluene as the precursor to the m/e 93 ion in the absence of other conclusive data.



Scheme 19. Possible mechanism for loss of carbon monoxide from the dimer of ortho-nitrosotoluene

Several pieces of evidence other than the fact that ions of a mass greater than the monomer have never been measured in these studies indicate that the initially formed molecular ions of all the compounds studied are monomeric. Nitroso

compounds are known to exist as colorless or light yellow dimers in the solid phase, but usually are converted to the blue or green colored monomer when liquified, vaporized or dissolved (54). Several of the compounds investigated, including some with ortho substituents, sublimed onto a cold finger as a light green fog which gradually changed to light yellow or colorless crystals. The pressure employed in these sublimations was considerably higher than the pressure in the mass spectrometer and a lower dimer concentration would be anticipated at lower pressure. In an effort to determine what fragmentation might be expected from a dimeric aryl nitroso compound, the mass spectrum of compound (16), an internal cis-nitroso dimer, was measured. If an important electron impact process in dimeric nitroso compounds was the initial formation of the monomer, then the fragmentations of compound (16) might be expected to be similar to that of 2-nitrosobiphenyl (compound (17)). However, compound (16) does not lose carbon monoxide from its molecular ion while 2-nitrosobiphenyl shows a peak which is appropriate for the loss of carbon monoxide from the monomer (see Figure 11). A prominent fragmentation of compound (16) is the loss of ·NO. This fragmentation was also observed in the mass spectra of dimeric nitrosomethane (22) and the dimeric 1-chloro-2-nitrosocycloalkanes (56) and may represent the primary fragmentation mode of the molecular ion of dimeric nitroso



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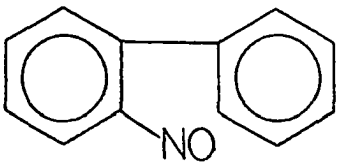


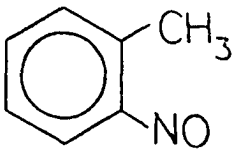
(17)

compounds. All of the available evidence strongly indicates that the initially formed molecular ion is that of the monomer and the following discussion will be based upon that assumption.

Carbon Monoxide Loss from Nitroso and Nitro Compounds

One of the goals at the outset of these studies was to determine the mechanistic features of the reaction leading to the formation of the M-CO ion in the mass spectrum of ortho-nitrosotoluene. During the course of these studies Schroll and co-workers published a paper in which they proposed that the reaction involved a triple hydrogen migration and loss of the methyl carbon atom. However, they presented little substantiating evidence for this mechanism (see page 11) (21).

Compounds (18)-(24) were investigated in the present study and the data obtained provides convincing evidence in favor of a triple hydrogen migration and the loss of the



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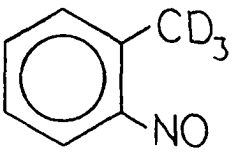

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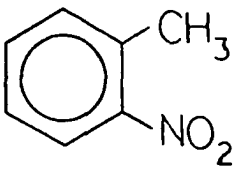
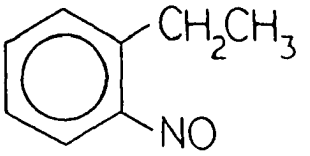
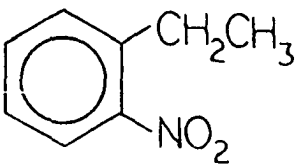


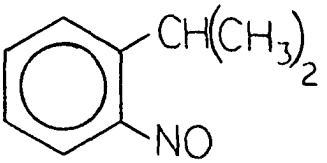
(20)



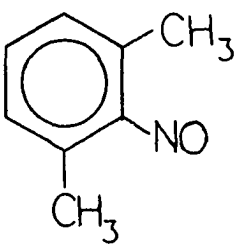
(21)



(22)



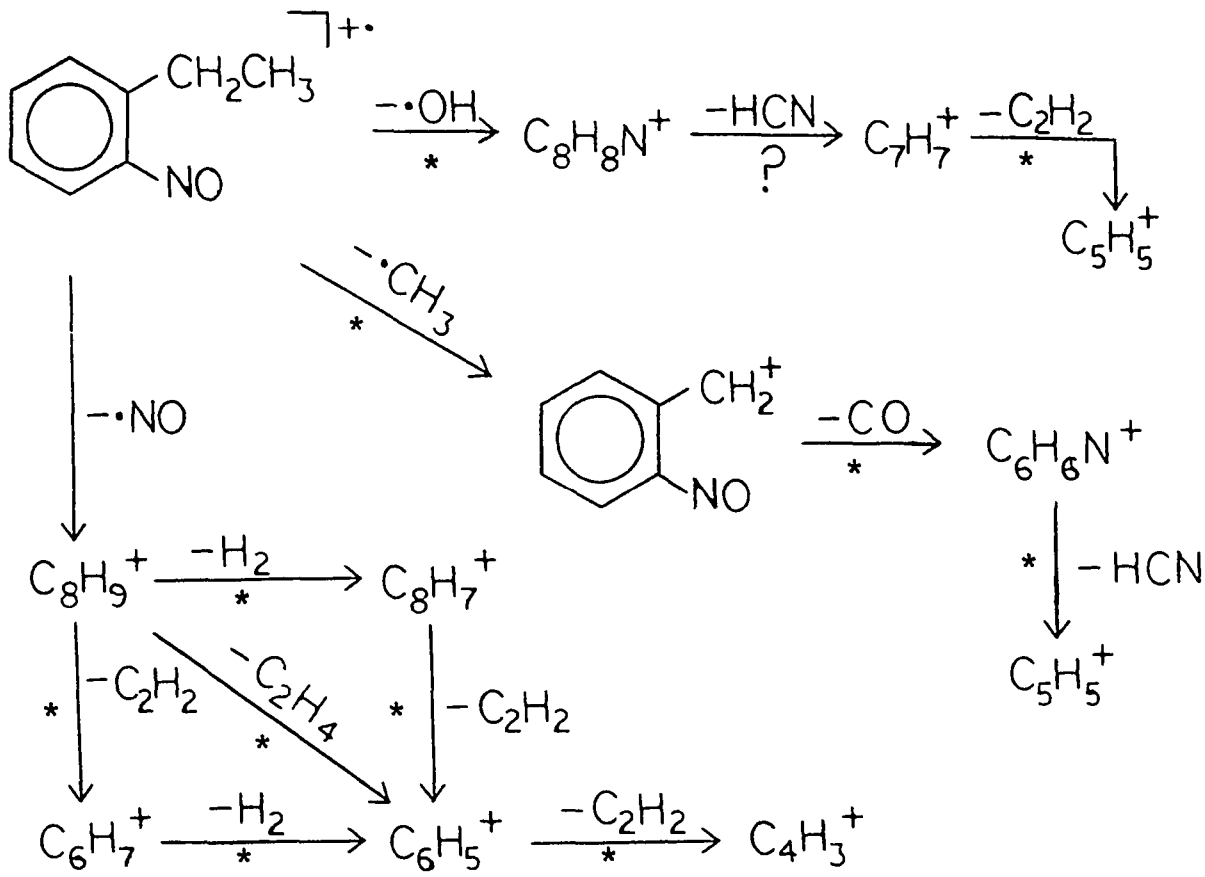
(23)



(24)

methyl carbon atom.

The molecular ion of ortho-nitroso-ethylbenzene (21) loses a methyl group, an ethyl group, the nitroso group and a hydroxyl radical. The other main fragmentations are illustrated in Scheme 20 (also see Figure 2), but the pathway of interest in relation to the present discussion is the fate of the M-·CH_3 (m/e 120) ion. This ion initially contains the same arrangement of atoms expected for the M-·OH ion of ortho-nitrotoluene and undergoes the same mode of fragmentation (27, 28); that is, loss of carbon monoxide and hydrogen cyanide in successive steps. The intensity ratio of m/e 120:m/e 92 (M-·CH_3:M-·CH_3-CO) as well as the shape and



Scheme 20. Fragmentation of ortho-nitroso-ethylbenzene

intensity of the metastable ions are approximately the same when the spectra of compounds (20) and (21) are recorded using similar conditions.

One of the difficulties encountered in these types of comparisons is the necessity of forming the ions under as nearly similar experimental conditions as possible in order to make meaningful qualitative and quantitative comparisons. The quantitative nature of the spectra of the nitro and nitroso compounds utilized in these studies was found to depend on the mode of sample introduction into the ion source. A

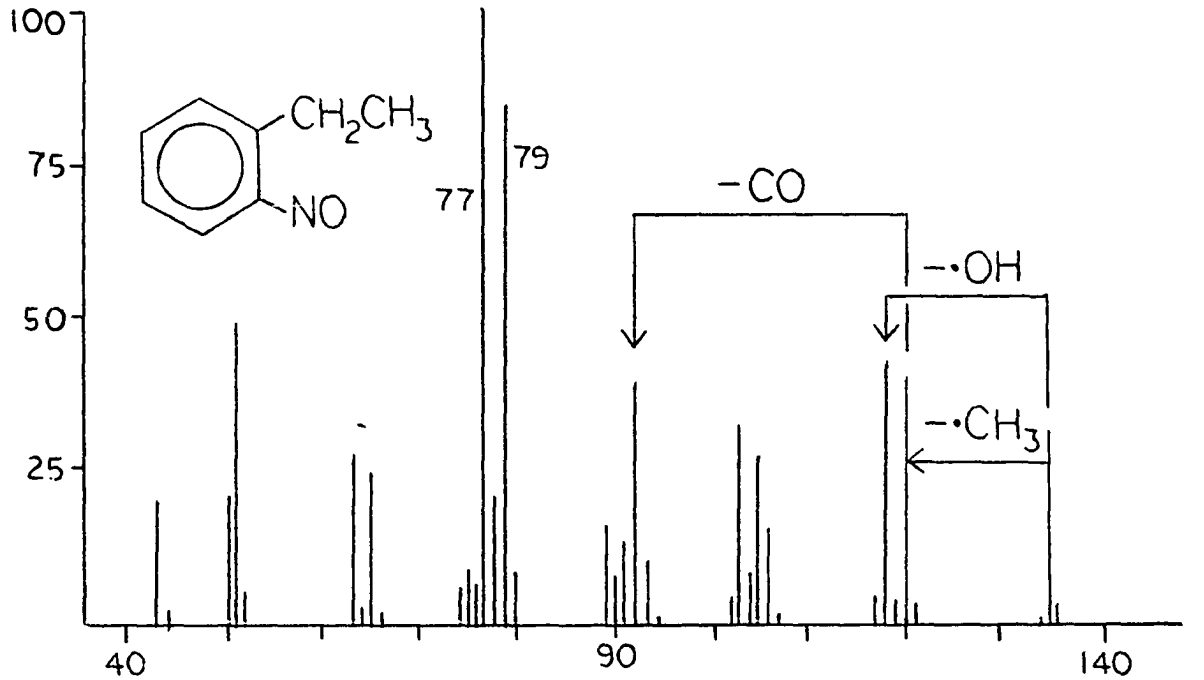


Figure 2. Mass spectrum of ortho-nitroso-ethylbenzene

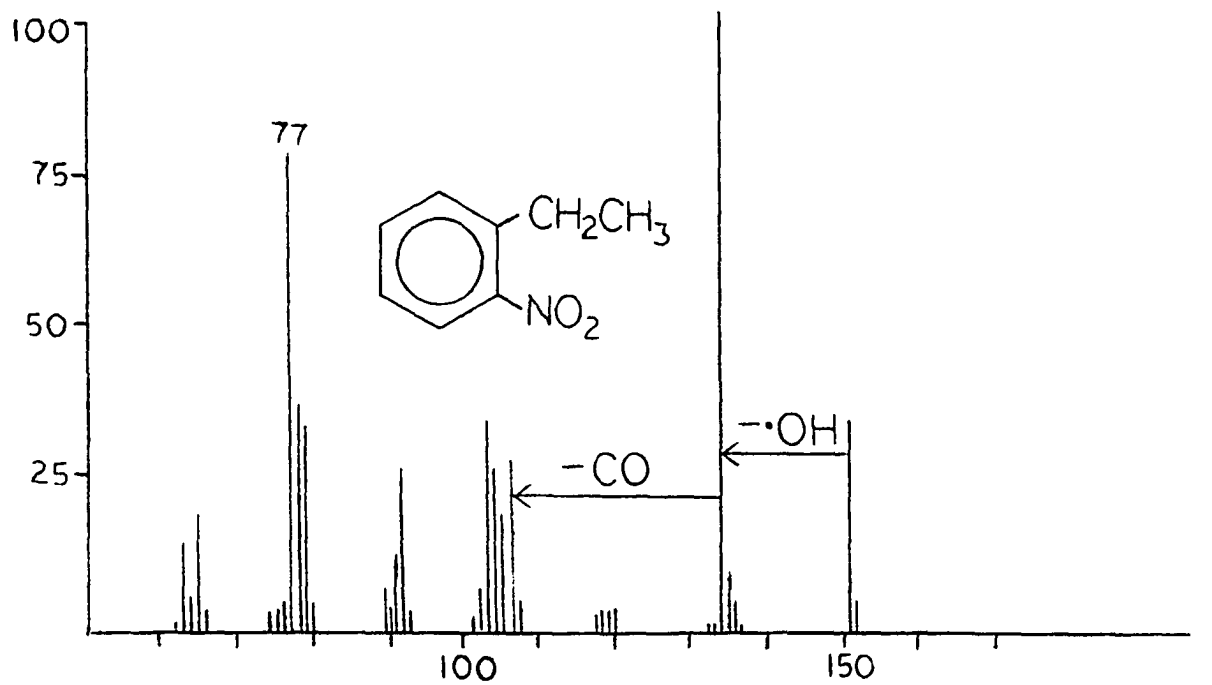
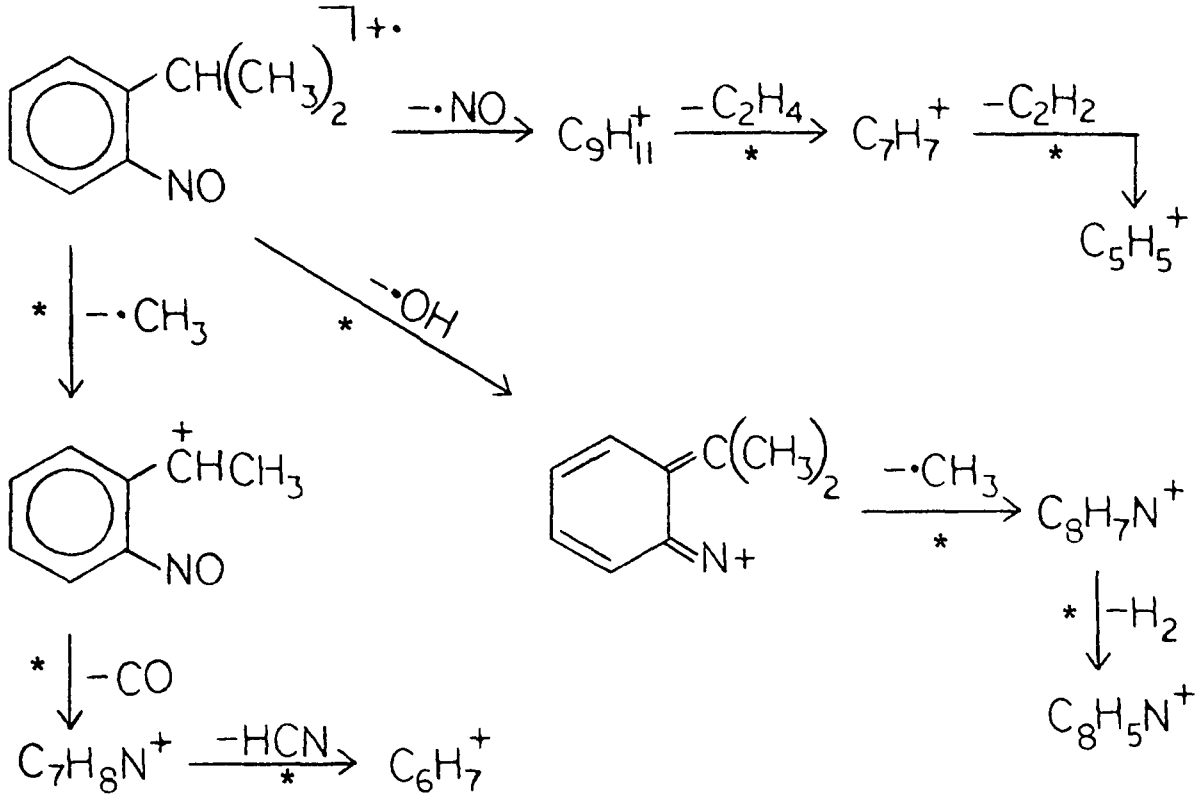


Figure 3. Mass spectrum of ortho-nitro-ethylbenzene

maximum correlation of data was found when the liquid compounds were absorbed on molecular seives and inserted directly into the ionization chamber. The nitro compounds produced more intense fragment ions when inserted into the ionization chamber via a heated inlet system thus making the spectra appear quantitatively different.

The intensity ratio of m/e 92:m/e 65 ($M-\cdot CH_3-CO$:$M-\cdot CH_3-CO-HCN$) in the mass spectra of ortho-nitrotoluene and ortho-nitroso-ethylbenzene could not be compared meaningfully even when the method of sample introduction is the same because of the unequal contribution of the fragmentation of the m/e 91 ion to the m/e 65 ion in the two compounds. However, the comparison of the m/e 120 ion to the m/e 92 ion suggests the same mechanism and intermediate is involved in the loss of carbon monoxide from the m/e 120 ion. Carbon-thirteen labelling in ortho-nitrotoluene established that the carbon atom lost was from the methyl group (see page 17), and thus it is suggested here that the carbon atom lost from the m/e 120 ion of ortho-nitroso-ethylbenzene is the original alpha carbon atom and the process involves a double hydrogen migration prior to expulsion of carbon monoxide.

The mass spectrum of ortho-nitrosocumene (23) shows the same type of initial fragmentation as ortho-nitroso-ethylbenzene. The molecular ion loses a methyl group, a hydroxyl radical and the nitroso group (also see Figures 4 and 5). The



Scheme 21. Fragmentation of ortho-nitrosocumene

M-·CH_3 (m/e 134) ion subsequently expels carbon monoxide and hydrogen cyanide in successive steps, a sequence which is also similar to that observed for ortho-nitroso-ethylbenzene. The initial loss of a hydroxyl radical from the molecular ion of ortho-nitro-ethylbenzene (see Figure 3) produces an m/e 134 ion which contains the same arrangement of atoms expected for the m/e 134 ion of ortho-nitrosocumene and this m/e 134 ion also shows the successive loss of carbon monoxide and hydrogen cyanide. The intensity ratio, m/e 134:m/e 106, is approximately the same in both compounds as is the shape and intensity of the corresponding metastable ions. A

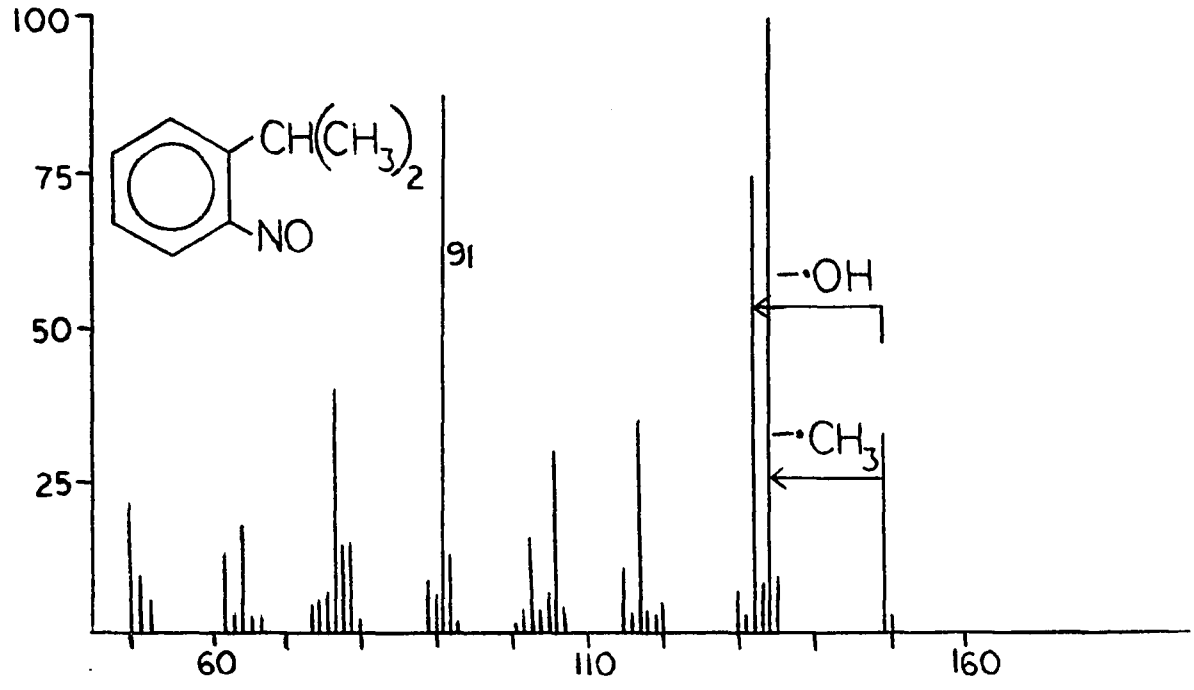


Figure 4. Mass spectrum of ortho-nitrosocumene

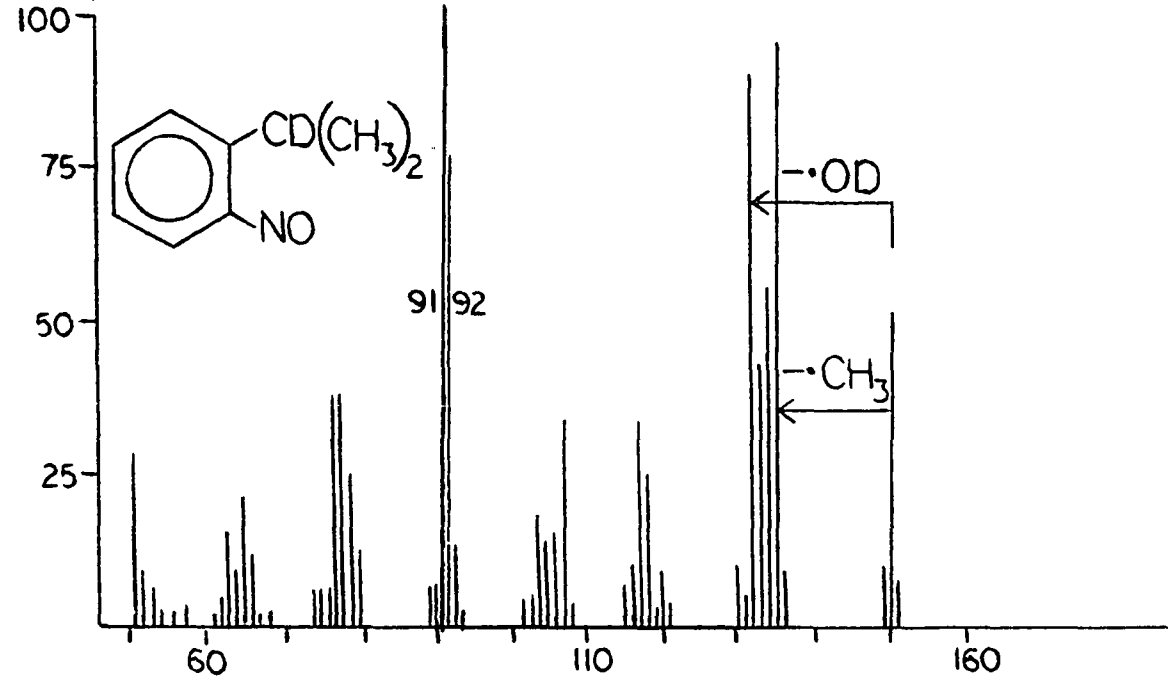
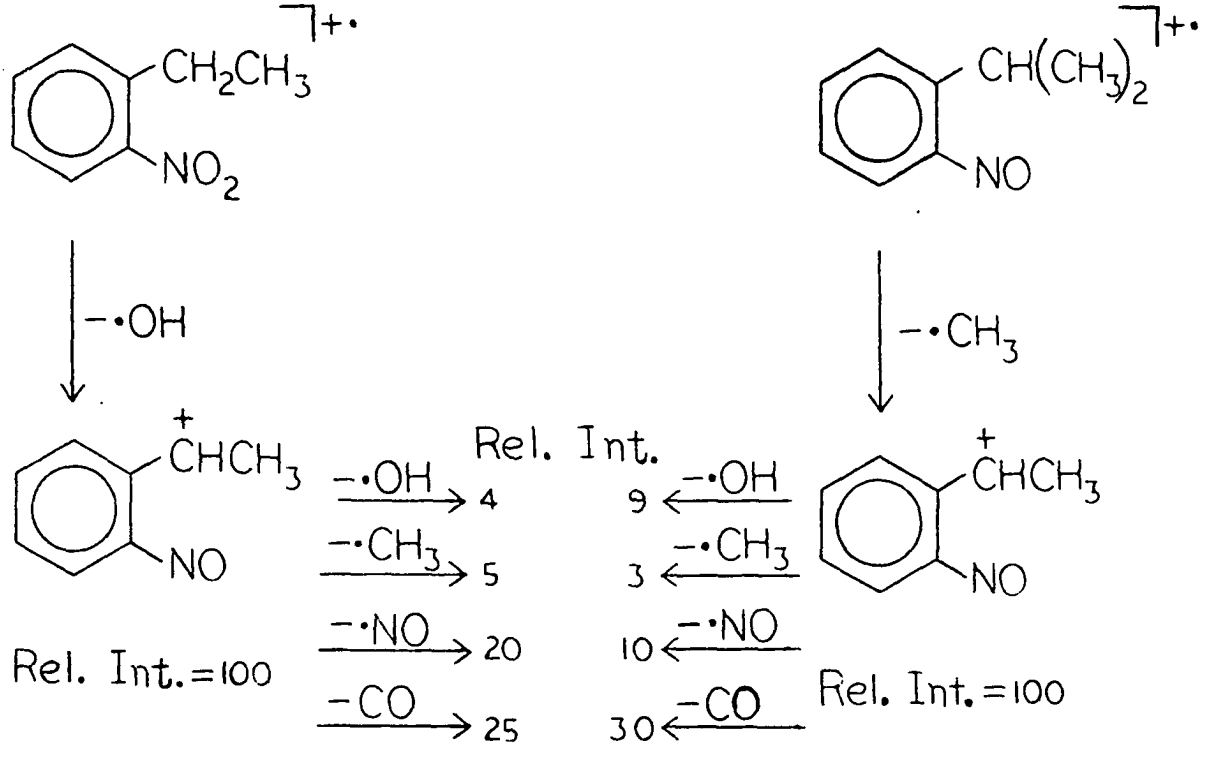


Figure 5. Mass spectrum of ortho-nitrosocumene-α-d

mechanism similar to the proposed mechanism for the loss of carbon monoxide from the m/e 120 ion of ortho-nitrotoluene and ortho-nitroso-ethylbenzene can be envisioned by invoking a double transfer prior to fragmentation. In this case, a methyl group and a hydrogen atom would be transferred back to the ring and nitrogen atom. The product ion produced following fragmentation could have a methyl-azatopylium cation structure or a methyl-aniline cation structure but no proof for either structural formulation of m/e 106 was obtained.

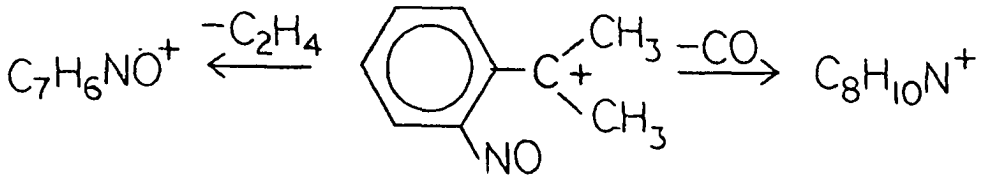
Additional proof for the proposal that the m/e 134 ions in the spectra of ortho-nitroethylbenzene and ortho-



Scheme 22. Common ions in the spectra of ortho-nitroethylbenzene and ortho-nitrosocumene

nitrosocumene are identical was obtained by comparing the relative intensities of all the fragment ions formed from the m/e 134 ions as shown in Scheme 22. The small differences observed in the intensities of the fragment ions could be attributed to the energy difference that would exist in the m/e 134 ions due to the fact that one is formed by a rearrangement reaction while the other is formed by a simple cleavage reaction.

A logical extension to test the generality of the proposed double rearrangement would be to determine if the M-·CH_3 ion of ortho-nitroso-tert-butylbenzene and/or the M-·OH ion of ortho-nitrocumene would expel carbon monoxide. This process could be viewed as a unique double methyl migration. Unfortunately, the m/e 148 ion of ortho-nitroso-tert-butylbenzene does not show a metastable ion for the reaction m/e 148 → m/e 120. High resolution mass spectrometry establishes that the m/e 120 ion present in the spectrum is a mixture of $C_7H_6NO^+$ and $C_8H_{10}N^+$ ions. The origin of these isobaric ions could be interpreted as arising from the M-·CH_3 ion by loss of ethylene and carbon monoxide (see page 46). The loss of ethylene could be rationalized as occurring through a phenylated cyclopropane intermediate (see page 28) while the loss of carbon monoxide might involve a double methyl migration.



The intensity ratio m/e 148:m/e 120 differs significantly in ortho-nitrocumene and ortho-nitroso-tert-butylbenzene, and while this fact alone does not eliminate the possibility of a common intermediate for the m/e 148 ion, it also does not lend support to one. Due to a very large number of competing fragmentations the intensities of the m/e 148 and m/e 120 ions of ortho-nitroso-tert-butylbenzene are small (<10%) and thus may not be reliable for comparison purposes. These intensities were fairly reproducible on two trials, but because of the difficulties involved in preparing, purifying and storing ortho-nitroso-tert-butylbenzene no more spectra of this compound were recorded. A metastable ion for the reaction m/e 148 → m/e 120 might not be expected for ions of such small intensity.

The m/e 148 (M-·OH) ion in the spectrum of ortho-nitrocumeme (see Figures 6 and 7) is the base peak and the m/e 120 ions (shown to be a mixture of $C_7H_6NO^+$ and $C_8H_{10}N^+$ by high resolution mass spectrometry) have a total intensity of 27%. An intense metastable ion corresponding to the reaction m/e 148 → m/e 120 is also present and its shape is similar to

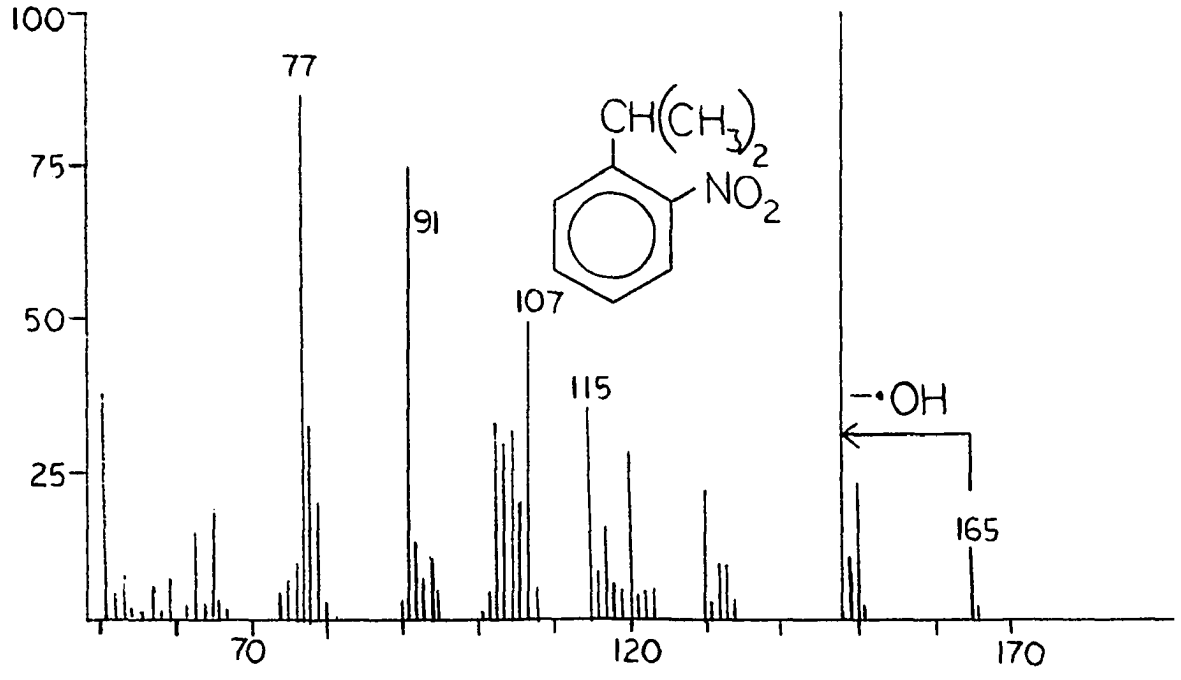


Figure 6. Mass spectrum of ortho-nitrocumene

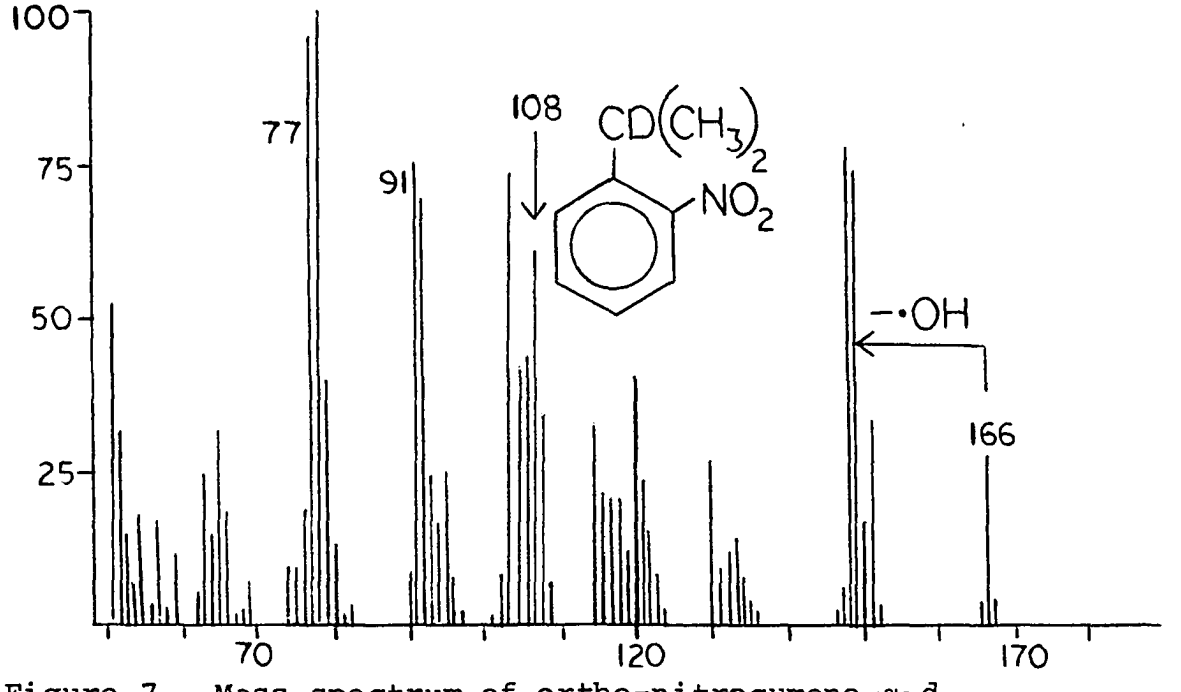
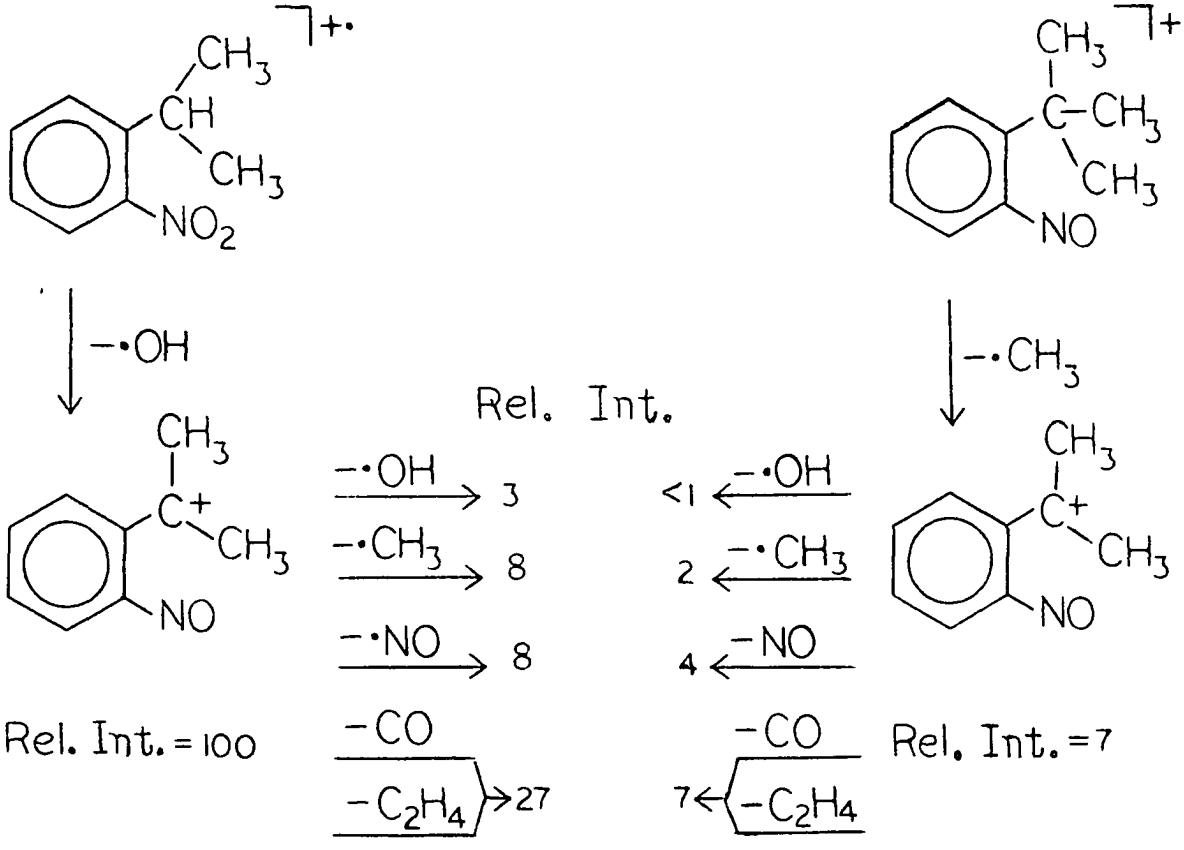


Figure 7. Mass spectrum of ortho-nitrocumene-α-d

the shape of the metastables observed for the other double migrations that were previously proposed. While this does not prove that a double methyl migration occurs prior to loss of carbon monoxide from the M-·OH ion of ortho-nitrocumene, it does indicate the feasibility of this mechanistic interpretation.

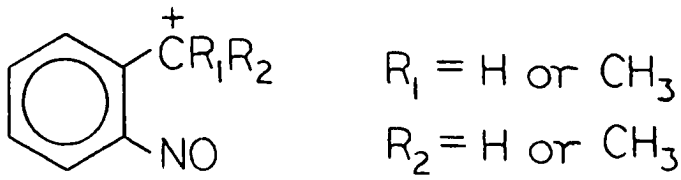
The possibility that the m/e 148 ions of ortho-nitrocumeme and ortho-nitroso-tert-butylbenzene might be identical was further explored by comparing the relative intensities of all the fragment ions produced from the m/e 148 ions (see Scheme 23). Although the ratios of the parent m/e 134 ions to



Scheme 23. Common ions in the spectra of ortho-nitrosocumene and ortho-nitroso-tert-butylbenzene

daughter ions are considerably different, it is interesting to note that the intensity of the daughter ions produced in the spectrum of the nitro compound are about four times those of the nitroso compound except for the loss of ·NO which is only twice as large. If the m/e 148 ions are identical, the differences in the ratios of the m/e 148 ions to their daughter ions could be rationalized because different energies might be expected for the m/e 148 ions.

All of these reactions establish that ions with structure (25) probably fragment by loss of carbon monoxide following a double transfer of R groups to the ring and nitrogen atom. This supports but does not prove that a triple hydrogen



(25)

migration occurs prior to the loss of carbon monoxide from the molecular ion of ortho-nitrosotoluene. Further evidence supporting this mechanism was obtained by studying the mass spectrum of 2,6-dimethyl-nitrosobenzene (24) (see Figure 8). The intensity of the M-CO ion of compound (24) was 25-30% greater than the M-CO ion of ortho-nitrosotoluene. A larger M-CO ion might have been anticipated if the ortho methyl carbon atom is the carbon atom which is lost.

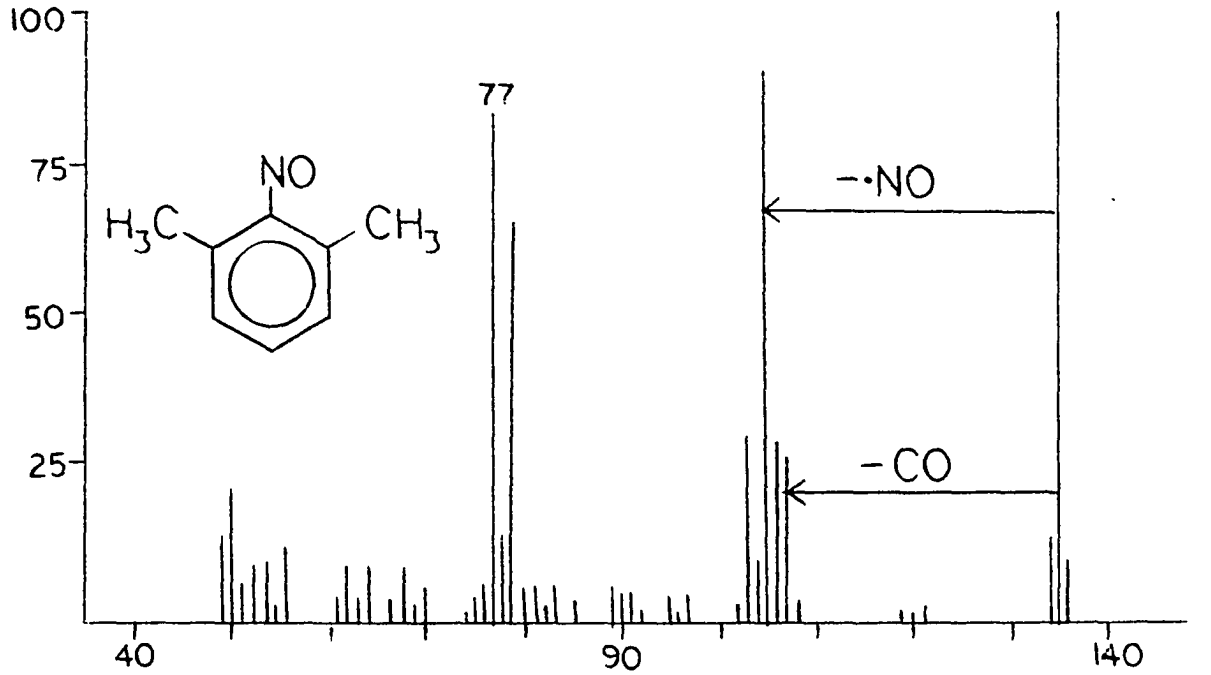


Figure 8. Mass spectrum of 2,6-dimethyl-nitrosobenzene

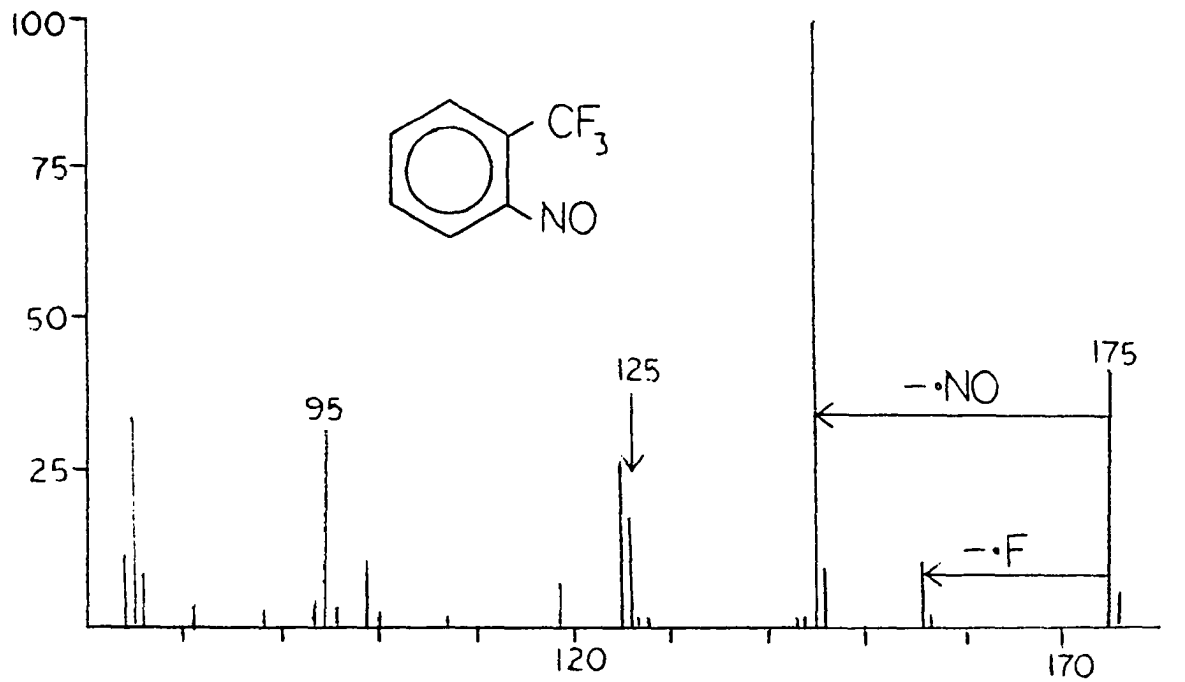


Figure 9. Mass spectrum of ortho-triflouromethyl-nitroso-benzene

The most conclusive evidence supporting the proposed triple hydrogen transfer was obtained by studying the spectrum of the labelled compound (19). The spectrum of (19) should exhibit an isotope effect manifested as a retardation of carbon monoxide loss if the carbon-hydrogen bonds are broken with subsequent rebonding prior to carbon monoxide loss. The method utilized for the preparation of the labelled compound produced material which was 81%-d_3 and 19%-d_2 and the spectra reported in Table 1 are uncorrected for both incomplete labelling and naturally occurring isotopes. The fact that the

Table 1. Mass spectra of ortho-nitrosotoluene (18) and ortho-nitrosotoluene-α,α,α-d_3 (19) at 70eV and 20eV

m/e	70eV (20eV) (18)	70eV (20eV) (19)
124		51 (100)
123		13 (23)
122	7 (9)	4 (8)
121	51 (100)	(1)
120	6 (10)	
96		9 (20)
95		11 (14)
94	2	100 (86)
93	14 (46)	26 (20)
92	12 (7)	6 (3)
91	100 (40)	5
90	4	2
69		Trace (1)
68		2 (8)
67	1.5	22 (9)
66	9 (2)	40 (4)
65	62 (7)	21
64	4	8

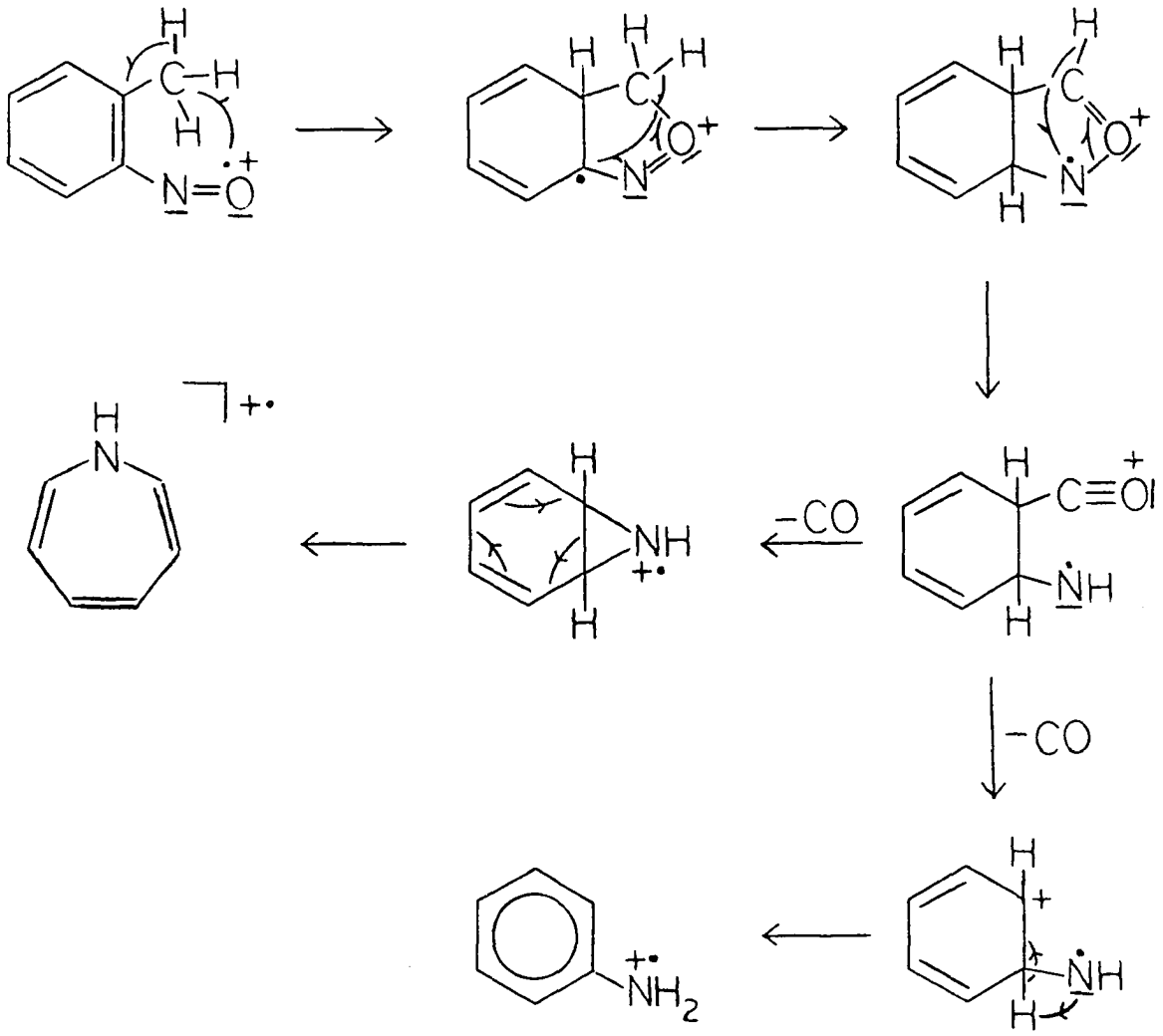
molecular ions of ortho-nitrosotoluene and the labelled compound containing three deuterium atoms both have a relative intensity of 51% allows the isotope effect to be calculated by a direct comparison of the M-CO ions. The intensity of the M-CO ion in the labelled compound is 5/14 (uncorrected) smaller than in the nonlabelled compound. Correction for the natural abundance of carbon-thirteen and division by three for the number of carbon-deuterium bonds which must be broken gives a value of 12.7% at 70eV for the retardation of the M-CO reaction per carbon-deuterium bond. As the electron energy is lowered the M-CO ion becomes more important relative to the M-·NO ion but the rate at which it increases in importance is less in the labelled compound compared to the nonlabelled compound. This is evidenced by an increase in the isotope effect to 20% per carbon-deuterium bond at 20eV. The only rationale for this puzzling observation is that the slightly higher energy process of breaking three carbon-deuterium bonds is discriminated against compared to breaking three carbon-hydrogen bonds by imparting a smaller initial energy to the molecules.

The spectrum of the labelled compound was studied in detail in an attempt to elucidate the structure of the m/e 93 (M-CO) ion of ortho-nitrosotoluene. A very interesting possibility is that the m/e 93 ion is a ring expanded azepine radical cation. Azepine, which is still an unknown substance,

is an 8π electron system and would not be expected to be stabilized (57). However, the azepine radical cation may represent a 7π electron substance and this should have different stability than the neutral molecule. Another possible structure for the M-CO ion of ortho-nitrosotoluene is the aniline radical cation structure proposed by Schroll and coworkers (21).

The labelled compound shows the expected 3 a.m.u. mass shift in the molecular ion, the m/e 91 (tropylium ion) and the m/e 93 ion. The ion at m/e 66 in the spectrum of the unlabelled compound is formed by loss of HCN from the m/e 93 ion. This ion is mass shifted to m/e 68 and m/e 69 by loss of DCN and HCN from the m/e 96 ion of the labelled compound. At 70eV, the m/e 68 ion is in part formed by loss of C_2H_2 from the deuterated tropylium ion at m/e 94. By reducing the electron energy, the elimination of acetylene from the tropylium ion is reduced to essentially zero but both the m/e 68 and m/e 69 ions remain. At 16eV metastable ions are present for both the loss of HCN and DCN from the m/e 96 ion with the latter process being favored. This is in agreement with the fact that the hydrogens originally bonded to the methyl carbon atom are primarily lost in the expulsion of HCN from the M-·OH-CO ion of ortho-nitrotoluene (see page 18). These observations probably do not eliminate either the azepine or aniline radical cation structures for the m/e 93

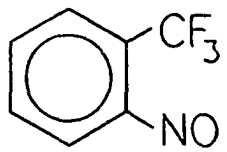
ion because deuterium labelling experiments of Meyerson demonstrate that both N-H and C-H hydrogen atoms are lost as HCN from the aniline radical cation using 70eV electrons (58). One can only speculate on the behavior of azepine upon electron impact but it would not be surprising if azepine lost HCN from the molecular ion with the source of hydrogen



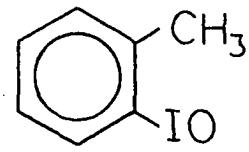
Scheme 24. Possible mechanism for CO loss in ortho-nitrosotoluene

being both the original N-H and C-H hydrogen atoms (58). A plausible mechanism for the loss of carbon monoxide from the molecular ion of ortho-nitrosotoluene is suggested in Scheme 24.

The mass spectra of compounds (26) and (27) were



(26)



(27)

recorded to see if either of the interacting groups could be changed and still show the ortho effect loss of carbon monoxide and the triple migration. The triflouromethyl compound (26) (see Figure 9) might have been expected to show loss of carbon monoxide on the basis that 1-nitronaphthalene and 8-flouro-1-nitronaphthalene both lose carbon monoxide by a process which expels the eight-carbon atom (see page 20). However, other studies have indicated that the triflouromethyl group does not enter into ortho effect reactions (59). The fragmentations of ortho-triflouromethyl-nitrosobenzene are characteristic of an aromatic triflouromethyl group and an aromatic nitroso group and no loss of carbon monoxide was observed. This observation adds further strength to the proposed mechanism for CO loss from the molecular ion of ortho-nitroso-toluene as flourine migration to nitrogen would not be antici-

pated. The valence electron structure of the iodoso compound (27) differs from ortho-nitrosotoluene by only two electrons. The iodoso group is the only group other than a nitroso group that can form a double bond to oxygen and a single bond to only one other group and is thus also structurally similar to the nitroso compound. Ortho-iodosotoluene lost an oxygen atom to give the base peak and also the iodoso group to give the $C_7H_7^+$ cation, but did not lose carbon monoxide.

Two other nitroso compounds which expel a molecule of carbon monoxide from the molecular ion are 1-nitrosonaphthalene (see Figure 10) and 2-nitrosobiphenyl (see Figure 11). The moderately intense (43%) molecular ion of 1-nitrosonaphthalene forms the base peak by the direct cleavage of the nitroso group and this M-·NO ion expels a molecule of acetylene in a metastable process. This series of reactions corresponds to the fragmentation of nitrosobenzene (see page 10). The mass spectrum of 2-nitrosonaphthalene is similar to the 1-isomer but lacks the 10% peak due to loss of carbon monoxide from the molecular ion. By analogy with the nitronaphthalenes (see page 20), the carbon atom lost is probably the 8-carbon atom and a mechanism similar to that of Scheme 10 is suggested in Scheme 25.

This may indicate that the M-O ion of 1-nitroso-2-naphthol (see page 13) actually has a structure corresponding

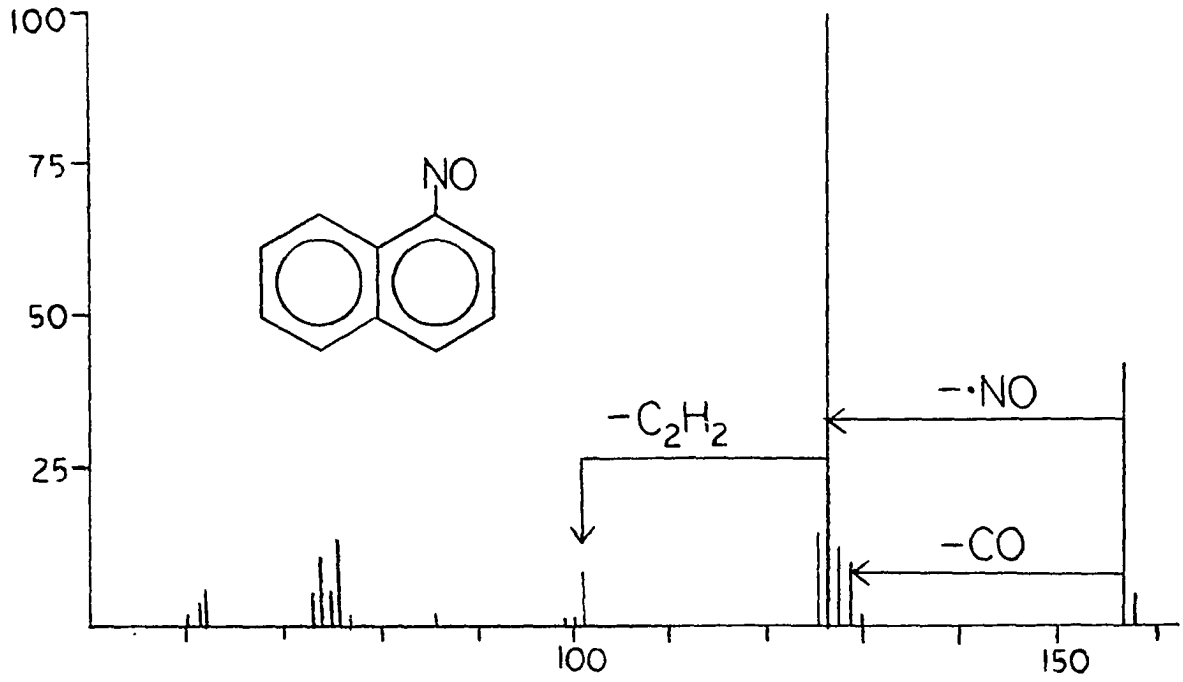


Figure 10. Mass spectrum of 1-nitrosonaphthalene

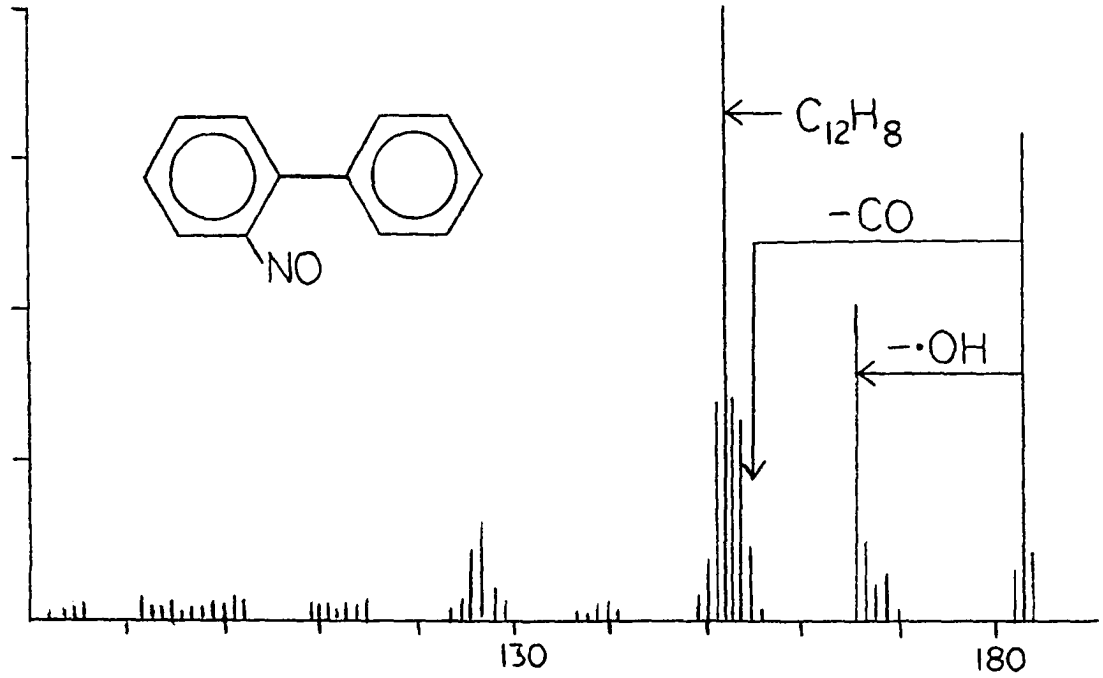
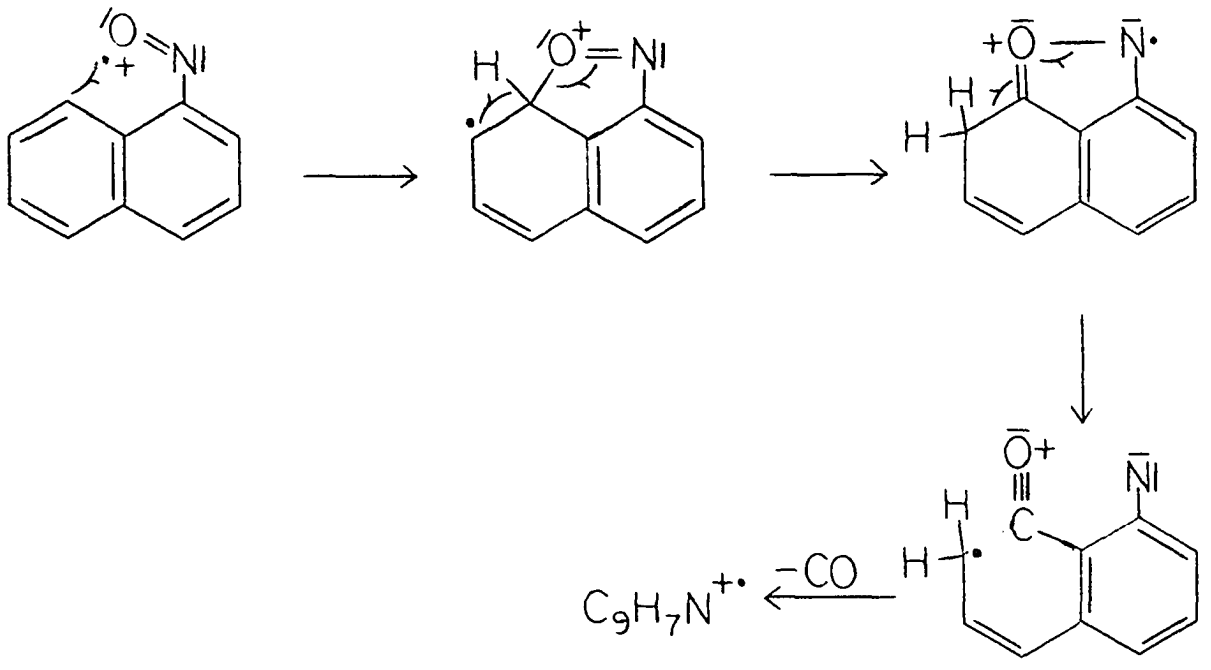
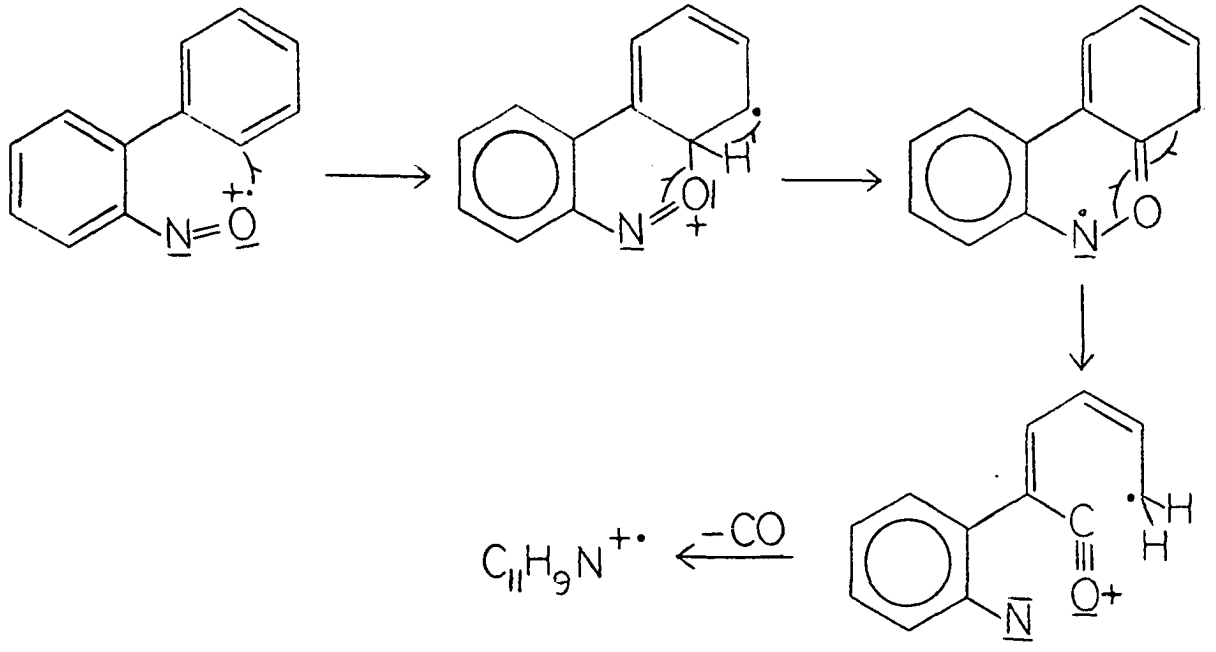


Figure 11. Mass spectrum of 2-nitrosobiphenyl



Scheme 25. Possible mechanism for CO loss in 1-nitroso-naphthalene



Scheme 26. Possible mechanism for CO loss in 2-nitroso-biphenyl

to the molecular ion of 1-nitrosonaphthalene because the M-O ion subsequently lost carbon monoxide (22). However, if this is true, the M-O ion of 2-nitroso-1-naphthol might be expected to have a structure corresponding to the molecular ion of 2-nitrosonaphthalene. The mass spectrum of 2-nitrosonaphthalene does not show loss of HCN, a process which is shown by the M-O ion of 2-nitroso-1-naphthol. Thus the behavior of the nitrosonaphthols upon electron impact remain unsolved unless different mechanisms are involved in the loss of an oxygen atom from the molecular ions.

Based upon analogy with the nitro-biphenyls (see page 21), a mechanism similar to that of Scheme 25 is suggested in Scheme 26 for the loss of carbon monoxide from the molecular ion of 2-nitrosobiphenyl. The base peak in the spectrum corresponds to loss of NOH and the resulting $C_{12}H_8^+$ ion probably has the biphenylene structure.

Hydroxyl Radical Loss

The loss of a hydroxyl radical from the molecular ion of ortho-nitrotoluenes and other aromatic nitro compounds to form an even electron daughter ion is a well known example of an "ortho effect" reaction (29). The ortho substituted aralkyl nitro and nitroso compounds which have been investigated in this study also undergo this reaction. A priori, it might have been expected that ortho-nitrosotoluene would

show a large M-·OH ion, but this process is unimportant. However, an intense M-·OH ion appears in the spectra of ortho-nitroso-ethylbenzene (43%) and ortho-nitrosocumene (75%).

The intensity of the M-·OH ion was found to depend on both the particular functional group (·NO_2 vs ·NO) and the alkyl group in the ortho compounds studied. Table 2 shows the percent of the total ion current carried by the M-·OH ion and the percent of the total ion current carried by the sum of the M-·OH ion and all ions which are derived from the M-·OH ion. The only ions utilized in the summation were those which are proven to be daughter ions of the M-·OH ion by the presence of the appropriate metastable ion or those which could not have arisen from any other reasonable precursor ion except by fragmentation of the M-·OH ion and its daughter ions.

Table 2. Percent of the total ion current of the M-·OH ion and the (summation of the M-·OH ion and derived ions)[a] of ortho alkyl nitro and nitroso benzenes

ortho alkyl group	Nitro	Nitroso
Methyl	22.8% (75%)	.43% (.43%)
Ethyl	18.6% (29.6%)	6.8% (10%)
iso-Propyl	10.4% (16.6%)	11.2% (22.8%)
tert-Butyl	.78% (.85%)	3.9% (8.6%)

[a]Only ions of greater than m/e 50 which at least 1% of the base peak were used in the summation.

The successive substitution of methyl groups for the methyl hydrogen atoms of ortho-nitrotoluene produces a steady decrease in the importance of the M-·OH process; a process which, as seen from Table 2, accounts for three-fourths of the total ion current in the spectrum of ortho-nitrotoluene, but less than 1% of the total ion current in the spectrum of ortho-nitro-tert-butylbenzene. These facts indicate that the loss of a hydroxyl radical occurs through a six-membered transition state since a decrease in the number of alpha hydrogen atoms from three to zero produces a corresponding decrease in the importance of the M-·OH process. The magnitude of this decrease is also affected by the additional fragmentations which iso-propyl and tert-butyl groups can undergo that a methyl group cannot. One of these is the very favorable beta cleavage of a methyl group from iso-propyl and tert-butyl groups.

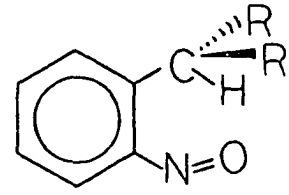
The data obtained for ortho-nitrosotoluene, ortho-nitroso-ethylbenzene and ortho-nitrosocumene suggest that the loss of a hydroxyl radical may occur through a seven-membered transition state. However, if this is true, ortho-nitroso-tert-butylbenzene might have been expected to show a considerably more important M-·OH process than that observed.

In order to clarify whether a 6 or 7 membered transition state is involved in the loss of a hydroxyl radical from the molecular ion of the ortho nitroso compounds, ortho-

nitrosocumene-α-d was prepared and the mass spectrum of this compound is shown in Figure 5. The spectrum of ortho-nitroso-cumene-α-d showed that at least 3/4 of the time the alpha hydrogen (deuterium) atom was involved in the loss of the hydroxyl radical. Since there are six beta hydrogen atoms and only one alpha hydrogen (deuterium) atom, the loss of a hydroxyl radical involving an alpha hydrogen (deuterium) atom is favored by a statistically corrected factor of greater than 95:5 for ortho-nitrosocumene-α-d. This fact would seem to indicate that the loss of a hydroxyl radical should be more important than it is in ortho-nitroso-ethylbenzene and considerably more important than it is in ortho-nitrosotoluene. These molecules contain two and three alpha hydrogen atoms respectively, as compared to only one in ortho-nitrosocumene.

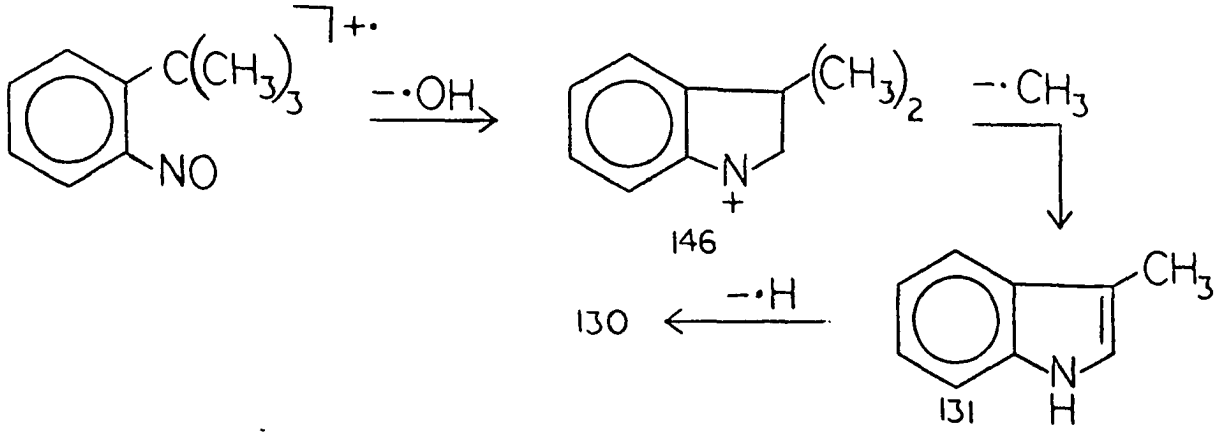
A reasonable interpretation of all the data suggests that the reaction occurs from the preferred conformation (28).

(28)



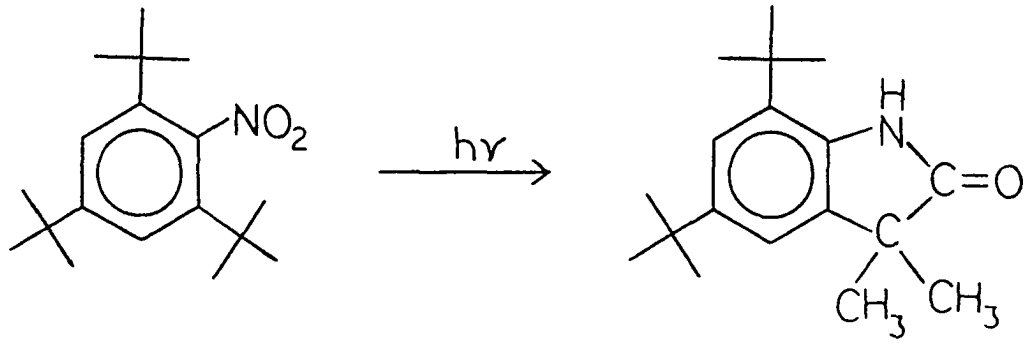
The additional methyl groups of ortho-nitroso-ethylbenzene and ortho-nitrosocumene increase the equilibrium concentration of the reactive conformation (28) as a result of decreasing the steric interaction of the bulky methyl groups with the nitroso functionality. The fact that ortho-

nitroso-tert-butylbenzene shows as important an M-·OH process as it does may be related to product ion stability. Although no proof for the following structures was obtained, it is a plausible assumption that the m/e 146 ion (M-·OH) and some of its daughter ions may have ring closed systems as shown in Scheme 27. Something of a precedent for the possible



Scheme 27. Possible structures of the M-·OH ion and its daughter ions in ortho-nitroso-tert-butylbenzene

formation of ring closed systems is the photochemical dehydration of 2,4,6-tri-tert-butyl-nitrobenzene as shown in Equation 9 (60).



Equation 9

Interestingly, ortho-nitrocumene shows a slightly smaller preference for alpha hydrogen abstraction. Ortho-nitrocumene-α-d_1 abstracts the alpha hydrogen (deuterium) atom only half the time, a statistically corrected 86% preference. This smaller preference when compared to the corresponding nitroso compound may be rationalized on the basis of the greater steric requirement for a nitro group compared to a nitroso group. It is possible for the nitroso and iso-propyl groups to become oriented in such a manner that little steric repulsion, if any, occurs. However, it is impossible to eliminate all steric interaction between ortho nitro and iso-propyl groups. This forces one of the oxygen atoms of the nitro group to be located in a position where it is more capable of abstracting a hydrogen atom from the methyl group. The fact that ortho-nitro-tert-butylbenzene does not undergo as much ·OH loss as the corresponding nitroso compound may be rationalized by either the greater steric hindrance of the nitro group in obtaining a seven-membered transition state as opposed to the nitroso group or the ring-closed product ions one might envision are less stable.

Appreciable loss of a hydroxyl radical is observed only in the spectrum of one other nitroso compound investigated, namely 2-nitrosobiphenyl. This reaction would presumably involve the 2' hydrogen atom, i.e., from the unsubstituted ring, although no investigation of this possibility was carried out.

A similar fragmentation from the molecular ion of beta-nitrostyrenes is site specific (17).

Methyl Group Loss

The direct cleavage of a methyl group from the molecular ion in the nitro and nitroso compounds studied was found to depend on both the functional group ($\cdot NO$ vs $\cdot NO_2$) and whether it was ortho or para to the alkyl group as shown in Table 3.

The base peak in the spectra of the isomeric nitro-tert-butylbenzenes is the $M-\cdot CH_3$ ion (see Figures 12 and 13), but the existence of various ortho-effect reactions decreases the amount of the total ion current carried by the $M-\cdot CH_3$ ion

Table 3. Percent of the total ion current carried by the $M-\cdot CH_3$ ion

Alkyl Group	Nitro	Nitroso
ortho-Methyl	0%	.5%
ortho-Ethyl	.85%	6.3%
ortho-iso-Propyl	2.2%	15.1%
ortho-tert-Butyl	10.5%	1.5%
para-Methyl	0%	0%
para-iso-Propyl	20.2%	.75%
para-tert-Butyl	42.5%	8.9%

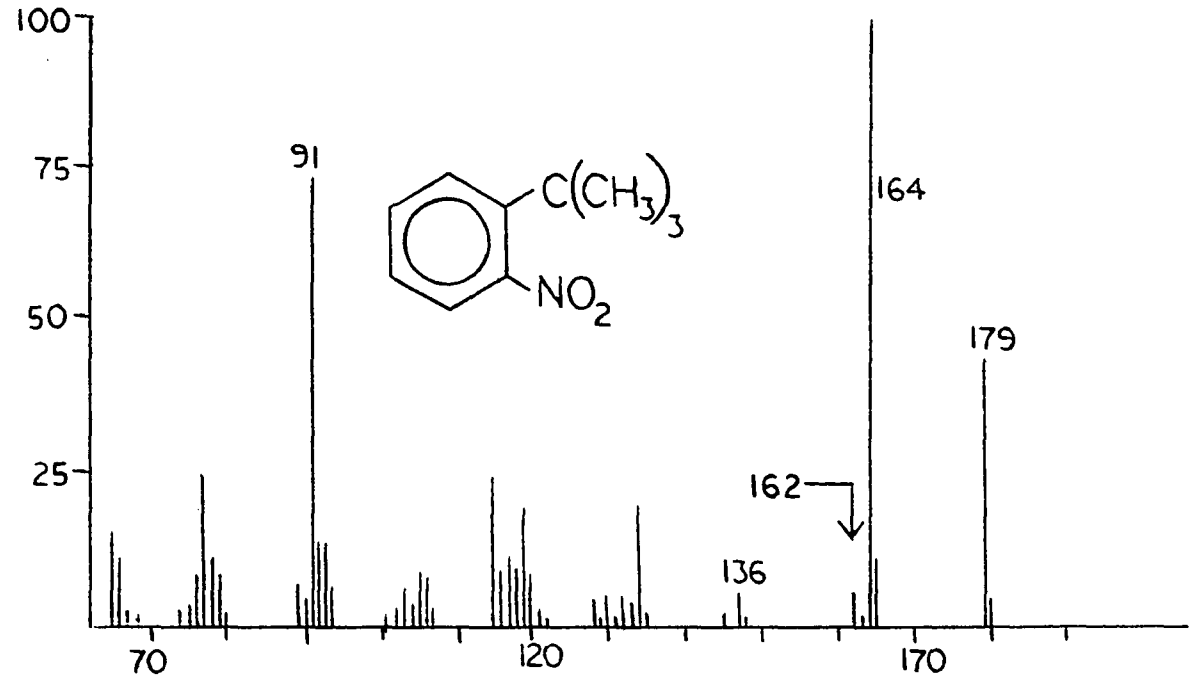


Figure 12. Mass spectrum of ortho-nitro-tert-butylbenzene

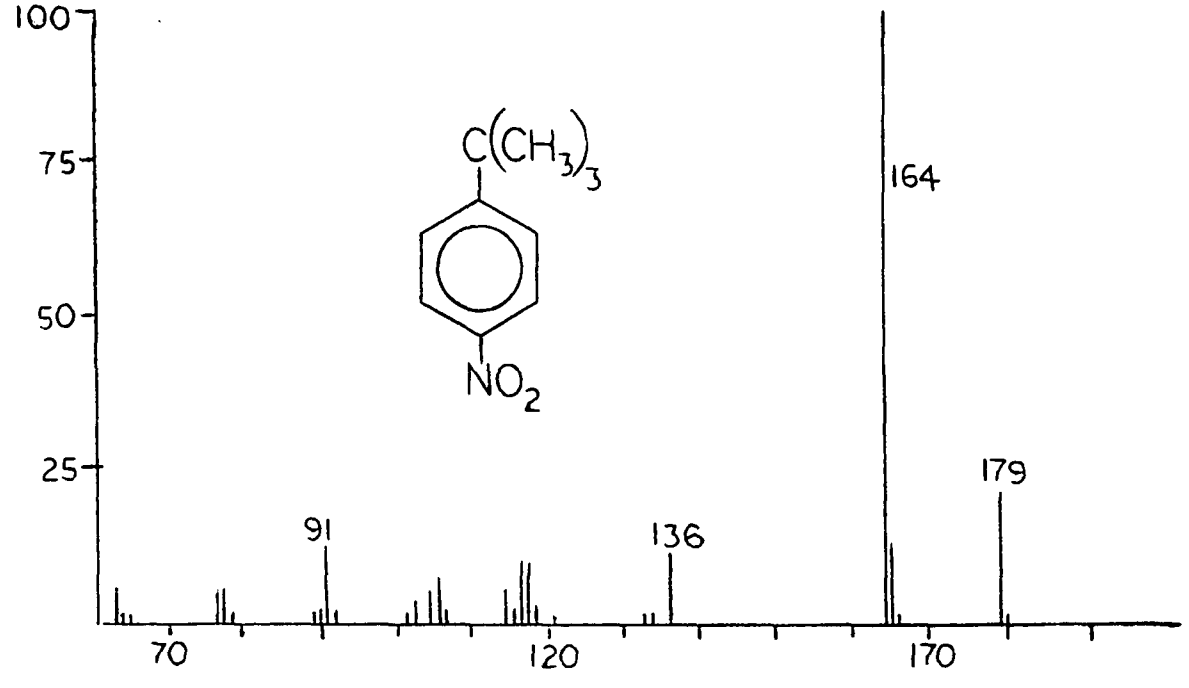


Figure 13. Mass spectrum of para-nitro-tert-butylbenzene

of the ortho compound relative to the para compound by a factor of four. This effect is also observed in the spectra of the nitrocumenes and nitroso-tert-butylbenzenes, (see Figures 14 and 15), but not the nitrosocumenes.

The relatively large M-·CH_3 ions in the spectra of ortho-nitroso-ethylbenzene and ortho-nitrosocumene subsequently undergo the successive losses of carbon monoxide and hydrogen cyanide in important ortho effect metastable reactions which were previously discussed. The ion current carried by the M-·CH_3, M-·CH_3-CO and M-·CH_3-CO-HCN ions of ortho-nitroso-ethylbenzene accounts for 17.7% of the total while the ion current carried by the M-·CH_3, M-·CH_3-CO and M-·CH_3-CO-HCN ions of ortho-nitrosocumene accounts for 24.8% of the total ion current. Thus less than 40% of the M-·CH_3 ions of ortho-nitrosocumene undergo the ortho effect reactions while 65% of the M-·CH_3 ions of ortho-nitroso-ethylbenzene undergo the same set of reactions. This is in agreement with the proposed mechanism because the transfer of a methyl group and a hydrogen atom would seemingly be more difficult than the transfer of two hydrogen atoms.

The M-·CH_3 ion of ortho-nitroso-tert-butylbenzene also shows the successive loss of carbon monoxide and hydrogen cyanide but to a much smaller extent. This could be related to the unfavorable process of transferring two methyl groups as opposed to two hydrogen atoms. However, two new unique

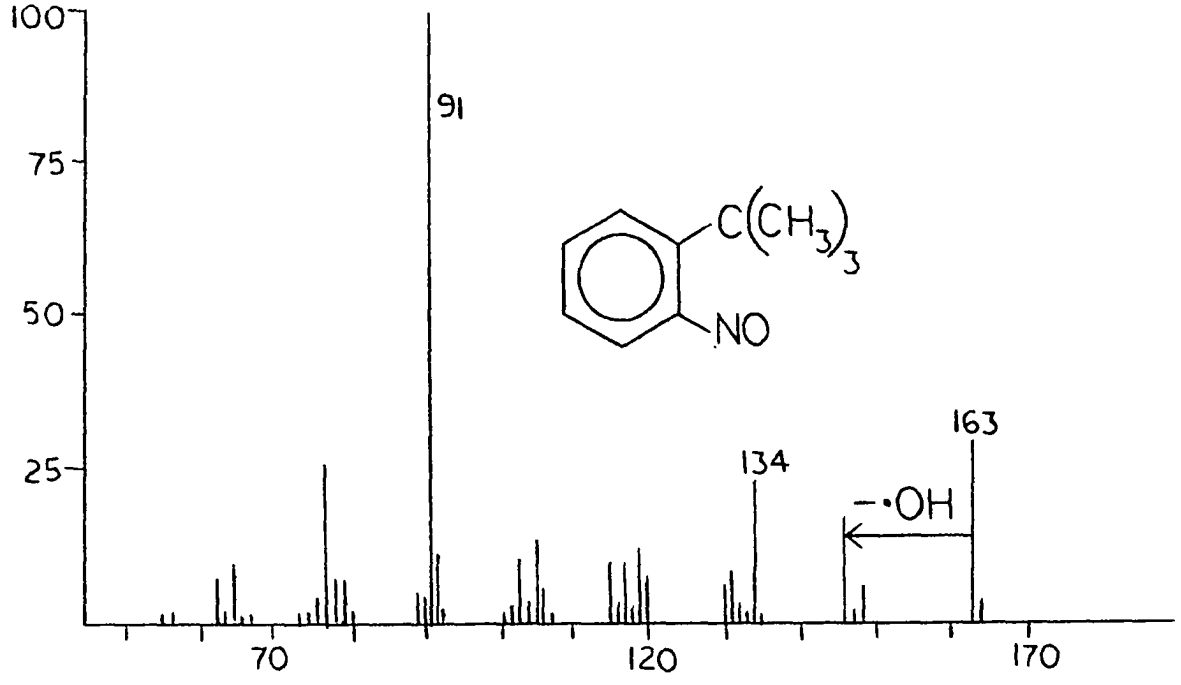


Figure 14. Mass spectrum of ortho-nitroso-tert-butylbenzene

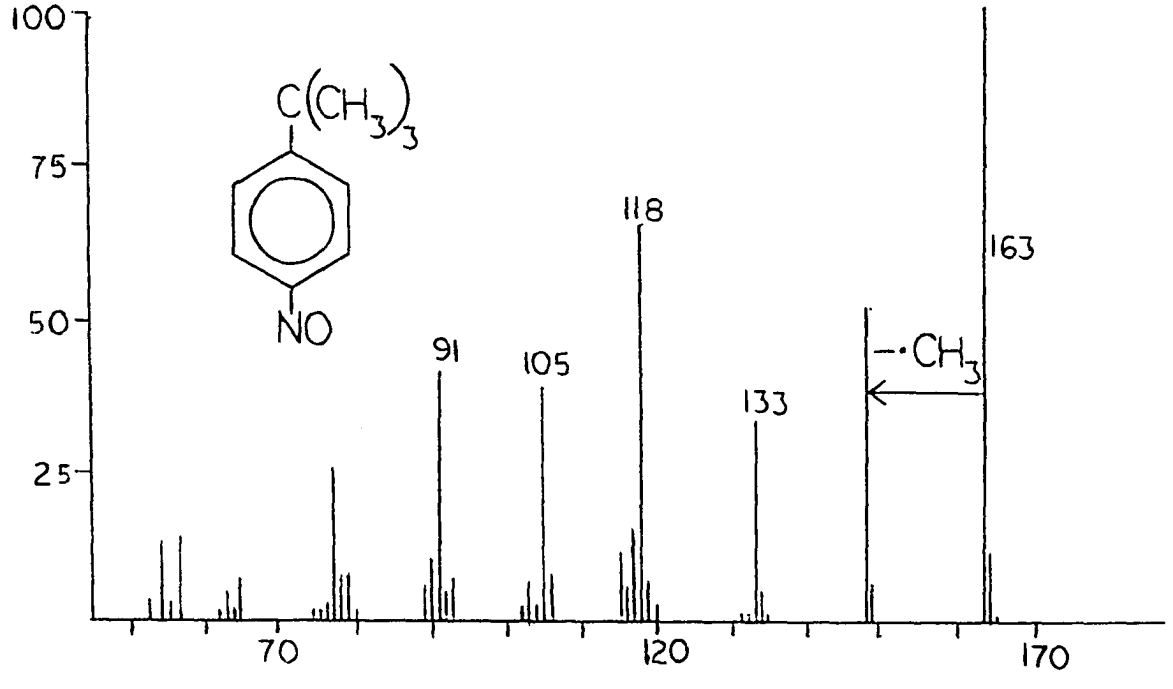
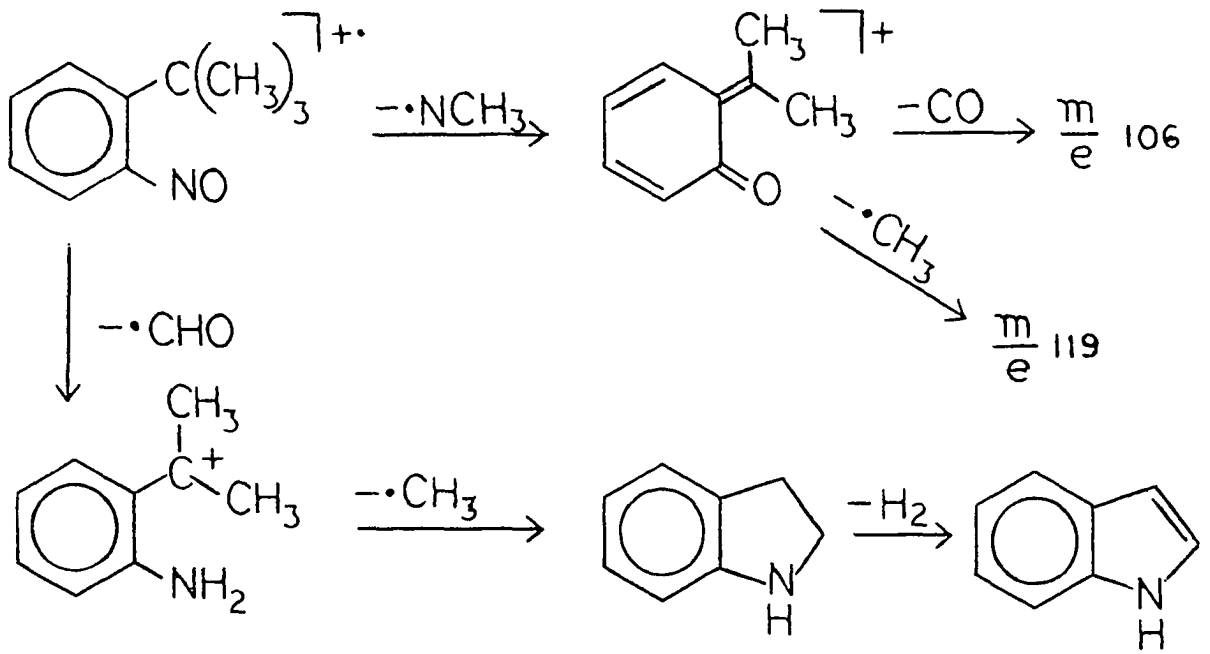


Figure 15. Mass spectrum of para-nitroso-tert-butylbenzene

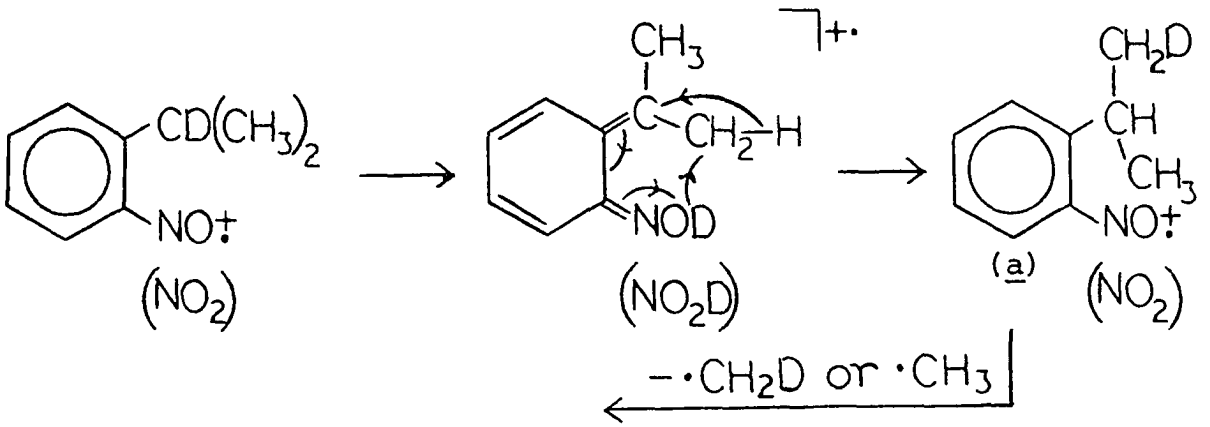
ortho effect reactions of moderate intensity (5.6% of the total ion current) also act to further decrease the importance of other processes. These ortho effect reactions both form m/e 134 ions whose composition are $C_9H_{10}O$ and $C_9H_{12}N$ as established by high resolution mass spectrometry. Some possible ion structures and their subsequent fragmentations are suggested in Scheme 28.



Scheme 28. Partial fragmentation of ortho-nitroso-tert-butylbenzene

A very interesting rearrangement was discovered by studying the label retention in the M-·CH_3 ion of alpha deuterio labelled nitro and nitrosocumenes. Ortho-nitrocumene-α-d showed 90-94% loss of ·CH_3 methyl groups and 6-10% loss of

$\cdot CH_2D$ methyl groups while ortho-nitrosocumene-α-d showed a less specific 78-83% loss of $\cdot CH_3$ methyl groups and 17-22% loss of $\cdot CH_2D$ methyl groups. The correspondingly labelled para compounds lost only $\cdot CH_3$ methyl groups. A plausible mechanism for this unusual rearrangement is suggested in Scheme 29. This mechanism is in agreement with the fact that



Scheme 29. Proposed mechanism for $\cdot CH_3$ and $\cdot CH_2D$ loss in ortho-nitro and nitrosocumenes

the loss of a hydroxyl radical in the nitro compound is less specific than in the nitroso compound because the less specific hydrogen abstraction by a nitro group would result in a smaller amount of ion (a) and thus a more specific loss of a $\cdot CH_3$ methyl group. This type of scrambling was not detected in the tert-butyl compounds studied which were labelled with two $\cdot CD_3$ methyl groups because of the unimportance of the M-·OH process in these compounds.

Loss of the Functional Group and Tropylium Ion Formation

The direct cleavage of the nitro or nitroso group from the molecular ion of similarly substituted aralkyl nitro and nitroso compounds produces daughter ions which have the same initial structure when the charge is retained by the aralkyl group. These daughter ions should also be energetically similar because the formation of M-·X (X = NO or NO_2) ions involves cleavage of a carbon-nitrogen bond and the fragment lost (a nitro or nitroso group) is small. Small energy differences can be rationalized on the basis that the nitro group might carry more excess vibrational energy away from the aralkyl ion than the nitroso group due to dissipation into the extra nitrogen-oxygen bond. These factors taken alone would indicate that the intensity of the M-·X (X = NO or NO_2) ions should be quite similar. However, competing fragmentations also affect the intensity of the fragment ions and some of these competing fragmentation involve different types of reactions in the nitro and nitroso compounds and thus have different effects on the intensity of the M-·X ions.

Table 4 shows the percent of total ion current carried by the M-·X (X = NO_2 or NO) ions in some of the aralkyl nitro and nitroso compounds studied. The nitro and nitrosotoluenes provide an excellent example of how competing fragmentations

Table 4. Percent of total ion current of M-·X (X = NO_2 or NO) ion

Substituent	Nitro	Nitroso
ortho-Methyl	14.9%	29.8%
ortho-Ethyl	2.4%	4.3%
ortho-iso-Propyl	.8%	.7%
ortho-tert-Butyl	.6%	.4%
para-Methyl	31.8%	34%
para-iso-Propyl	3.2%	14.6%
para-tert-Butyl	.4%	5.9%

may alter the intensity of a product ion. The intensity of the M-·NO_2 ion in the mass spectrum of ortho-nitrotoluene is considerably less than in all the other nitro and nitroso-toluenes studied even though the M-·X (X = NO or NO_2) ion is probably the tropylium ion in all of these compounds. The reduced importance of this fragmentation is due to the extremely important ortho effect loss of a hydroxyl radical from the molecular ion.

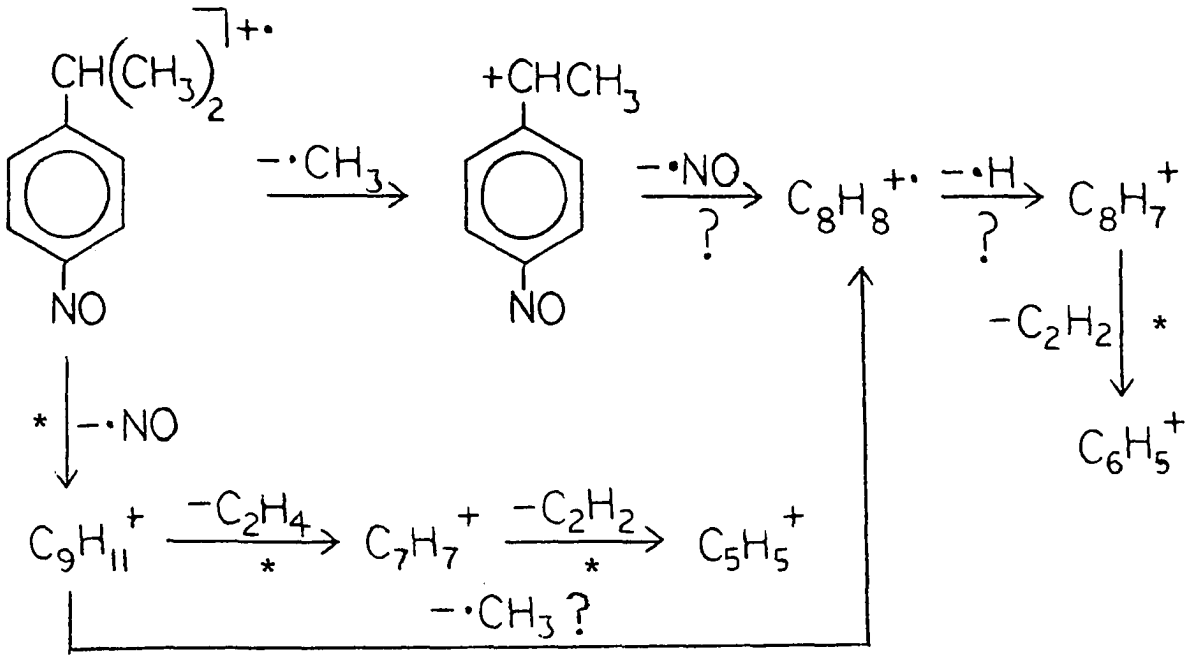
The M-·NO_2 ion in the mass spectrum of para-nitrotoluene carries slightly less of the total ion current (31.8%) than the M-·NO ion in para-nitrosotoluene (34%) because 2.3% of the total ion current in the spectrum of para-nitrotoluene is accounted for by the pathway involving the nitro-nitrite rearrangement. The ortho effect loss of carbon monoxide from the molecular ion of ortho-nitrosotoluene accounts for the

smaller amount of the total ion current carried by the M-·NO ion in the ortho compound (29.8%) as compared to the M-·NO ion (34%) of para-nitrosotoluene.

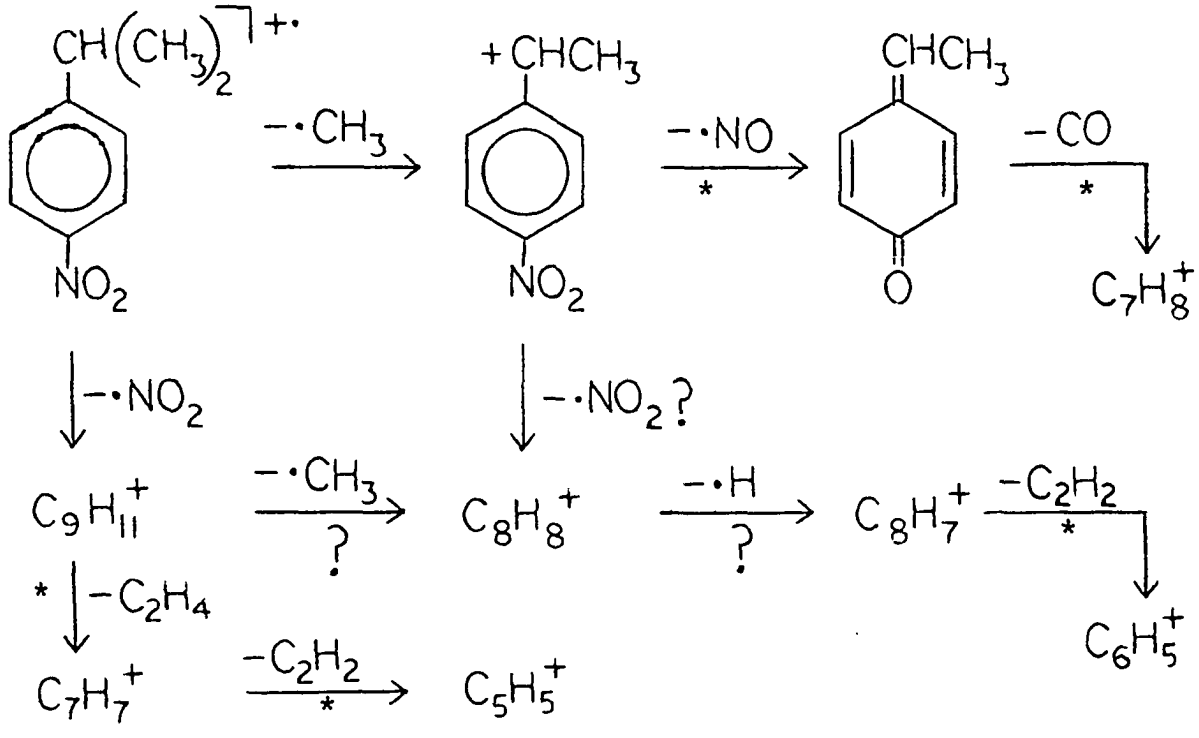
The loss of the nitro or nitroso group from the molecular ions of ortho-nitro and nitrosocumene is unimportant because of the dominance of the ortho effect loss of a hydroxyl radical. Another important ortho effect reaction in the mass-spectrum of ortho-nitrosocumene is the initial cleavage of a methyl group followed by successive losses of carbon monoxide and hydrogen cyanide (see page 42) and this pathway further diminishes the importance of the M-·NO ion.

The M-·NO ion of para-nitrosocumene (see Figures 16 and 17 and Scheme 30) carries a much larger share of the total ion current (14.6%) than the M-·NO_2 ion of para-nitrocumene (3.2%) (see Figures 18 and 19). However, para-nitrocumene apparently has a greater tendency to fragment through the iso-propyl group than para-nitrosocumene as evidenced by the percent of the total ion current carried by the M-·CH_3 ions in the nitro (20.2%) (also see Scheme 31) and nitroso (.8%) compounds.

The tert-butyl substituted compounds, like the iso-propyl compounds, have unimportant M-·X (X = NO or NO_2) ions in both ortho compounds and the para nitro compound and a relatively important M-·NO ion in the para nitroso compound (see Scheme 32). It is interesting to recall that the base



Scheme 30. Fragmentation of <u>para</u>-nitrosocumene



Scheme 31. Fragmentation of <u>para</u>-nitrocumene

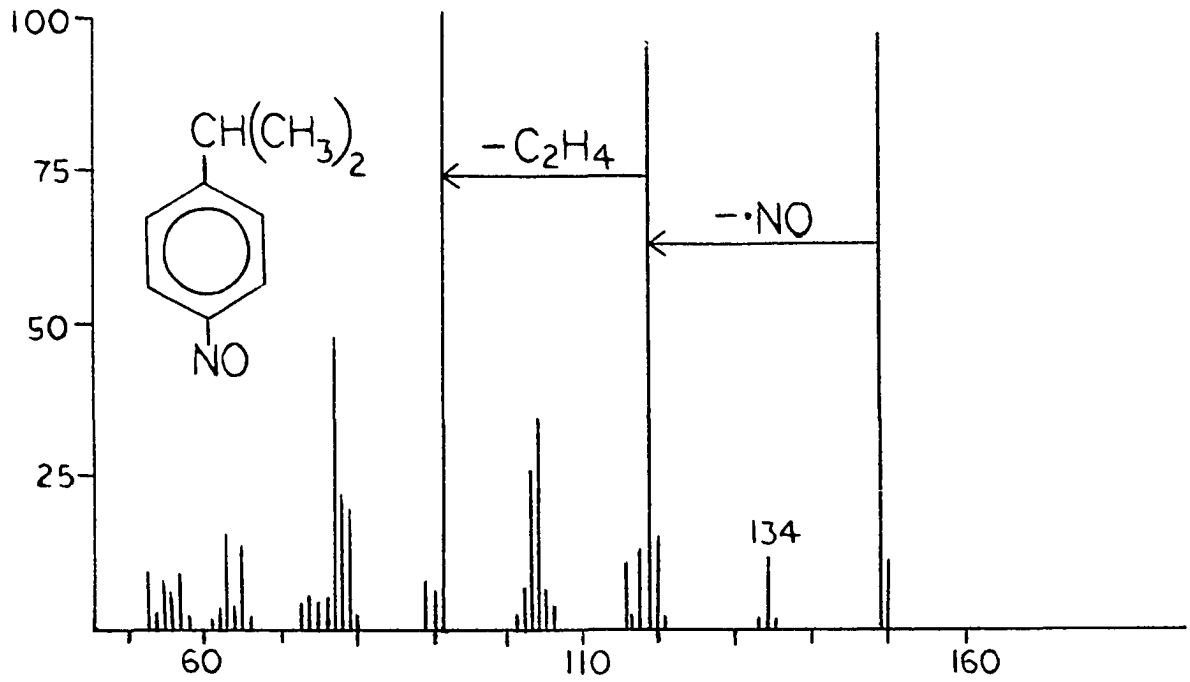


Figure 16. Mass spectrum of para-nitrosocumene

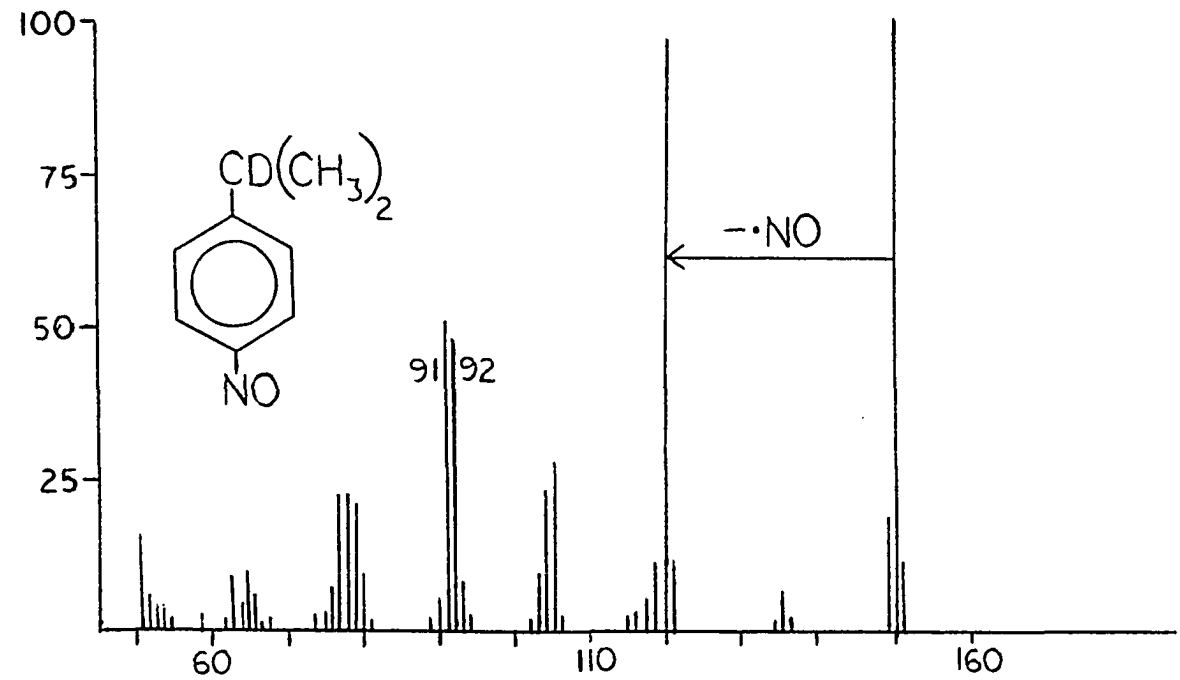


Figure 17. Mass spectrum of para-nitrosocumene-α-d

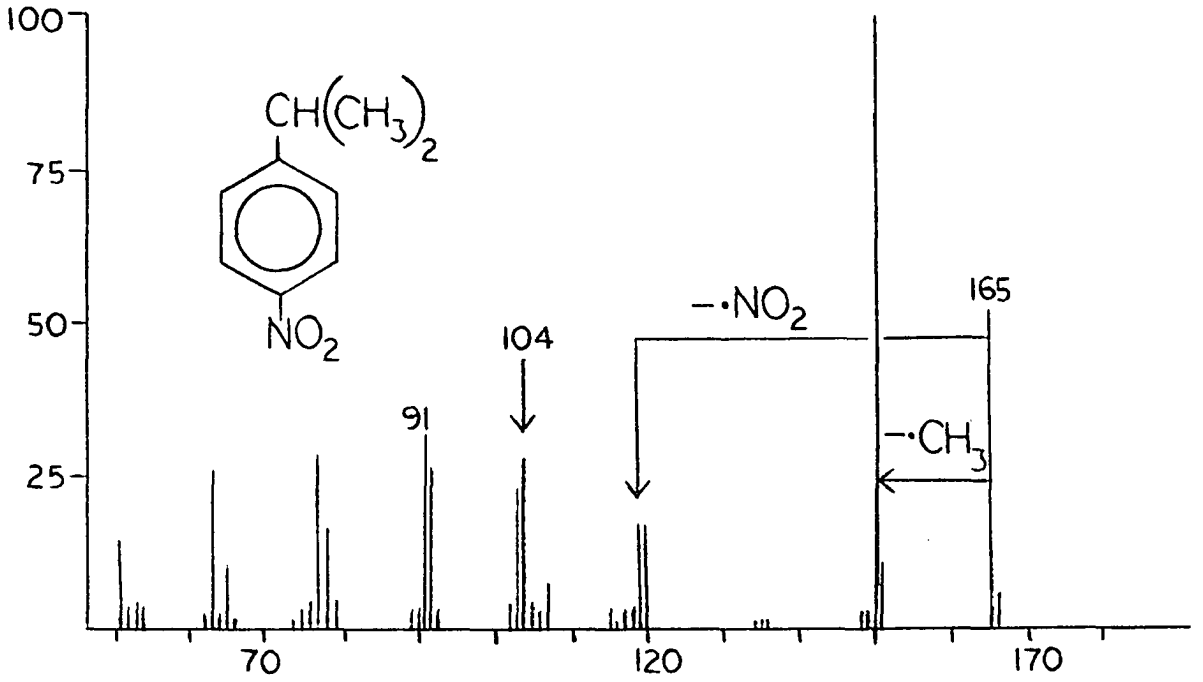


Figure 18. Mass spectrum of para-nitrocumene

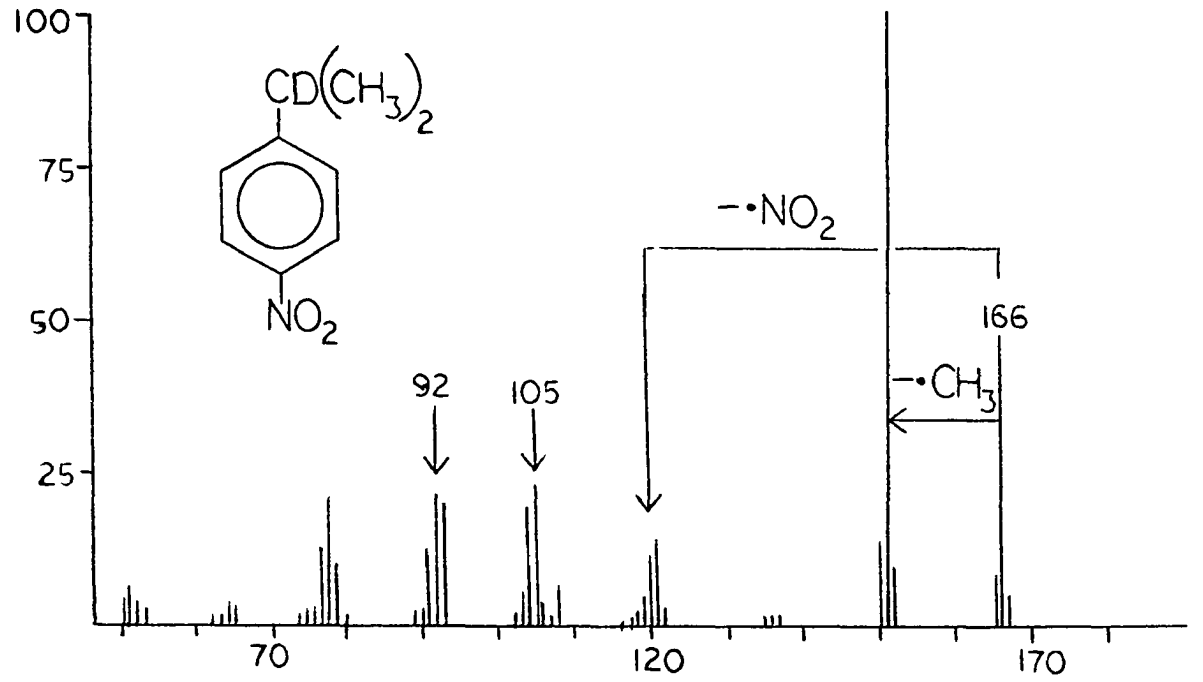
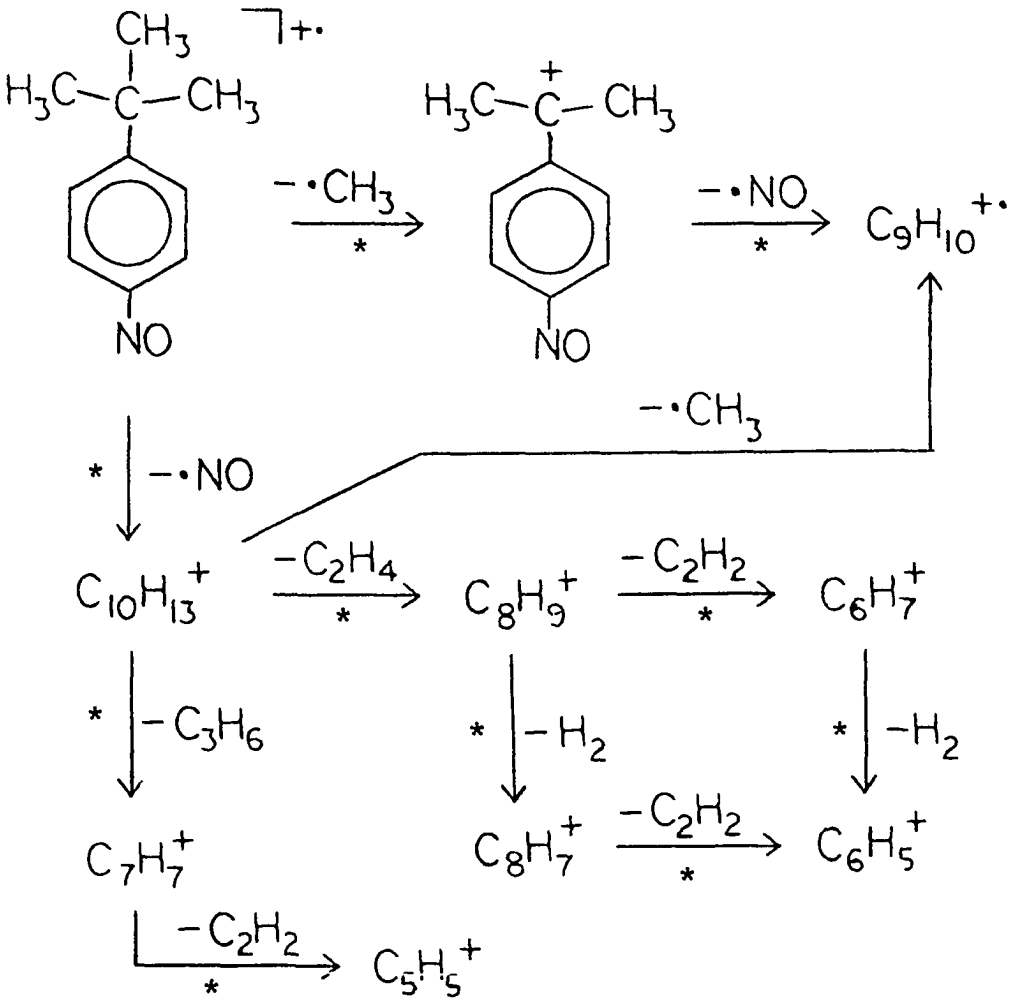


Figure 19. Mass spectrum of para-nitrocumene-α-d

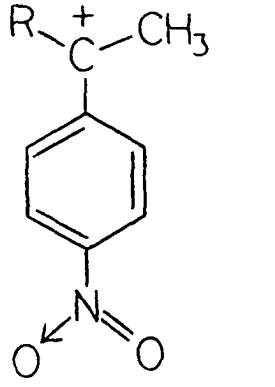


Scheme 32. Fragmentation of para-nitroso-tert-butylbenzene

peak in the spectra of both ortho and para-nitro-tert-butylbenzene is the M-·CH_3 ion. However, ortho effect reactions reduce the importance of the M-·CH_3 ion of the ortho compound relative to the para compound (10.5% of the total ion current compared to 42.5% of the total ion current). It can be concluded that, in the absence of ortho effects, the cleavage of a nitro group is unfavorable relative to the competitive beta cleavage of an iso-propyl or tert-butyl group

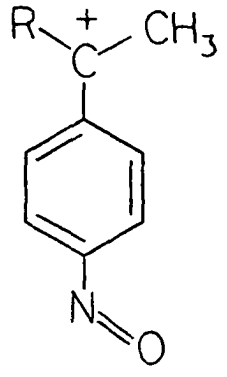
in a given molecule. Cleavage of a nitroso group is favored over competitive beta cleavage of an iso-propyl or tert-butyl group.

The cause of this phenomenon brings up the question of product ion stability. Loss of a methyl group from the molecular ion of the para-nitro and para-nitroso iso-propyl and tert-butyl substituted benzenes would produce products ions which could be represented by structures (29) and (30).



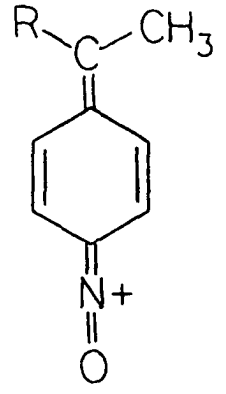
R= H or CH_3

(29)



R= H or CH_3

(30)



(30')

The lone pair of electrons available in the nitroso group would seem to favor resonance stabilization of the cation by a structure such as (30'), a situation which is not possible in the nitro compound. However, structure (30') would not have a completely overlapping set of p orbitals because the nitrogen-oxygen pi bond would be orthogonal to the rest of the p orbitals. It is possible, however, for the nitro

compound to have a completely overlapping set of p orbitals thus allowing delocalization of electrons throughout the system. However, this resonance structure would place the positive charge on oxygen and would not be expected to make an important contribution to the overall picture. A nitro group is usually thought of as a group which tends to destabilize positive charge both inductively and by resonance and thus product ion structure does not seem to be the answer. Other explanations which would invoke charge localization effects or comparisons of ionization potentials are not reasonable because of the specificity of this behavior in the iso-propyl and tert-butyl compounds.

A further important item to consider when comparing intensities of ions in the mass spectrometer is that the intensity is not only determined by how much of the ion is formed but also reflects the amount of the further fragmentation of the ion. Thus, a low intensity ion may be formed in large quantities but further rapid fragmentation lowers the intensity observed. One ion which seemingly must arise, at least in part if not totally, from the further decomposition of the M-·X (X = NO or NO_2) ions of the iso-propyl and tert-butyl nitro and nitrosobenzenes is the $C_7H_7^+$, m/e 91 ion, which most likely is the tropylium ion. Formally, the formation of the tropylium ion would seem to involve loss of the functional group and incorporation of one side chain

carbon atom and three side chain hydrogen atoms with the six ring carbon atoms and four ring hydrogen atoms. The percent of the total ion current carried by the tropylium ion is shown in Table 5.

Table 5. Percent of the total ion current carried by the tropylium

Substituent	Nitro	Nitroso
ortho-Methyl	14.9%	29.8%
ortho-Ethyl	2.4%	2.2%
ortho-iso-Propyl	7.4%	14.0%
ortho-tert-Butyl	15.5%	21.5%
para-Methyl	31.8%	34.0%
para-iso-Propyl	7.1%	15.4%
para-tert-Butyl	4.7%	7.1%

The fact that the M-·X ion (X = NO or NO_2) of all the nitro and nitrosocumenes studied is a precursor to the $C_7H_7^+$ ion is established by a similarly shaped metastable which is appropriate for the fragmentation m/e 119 → m/e 91. The ratio of the intensity of the m/e 119 ion to the m/e 91 ion is larger in the para compounds than in the ortho compounds (para-nitrocumene .45, ortho-nitrocumene .10, para-nitrosocumene .95, ortho-nitrosocumene .05). This may indicate that the m/e 119 ions formed from the ortho compounds fragment more readily to tropylium ions than the m/e 119 ions in the

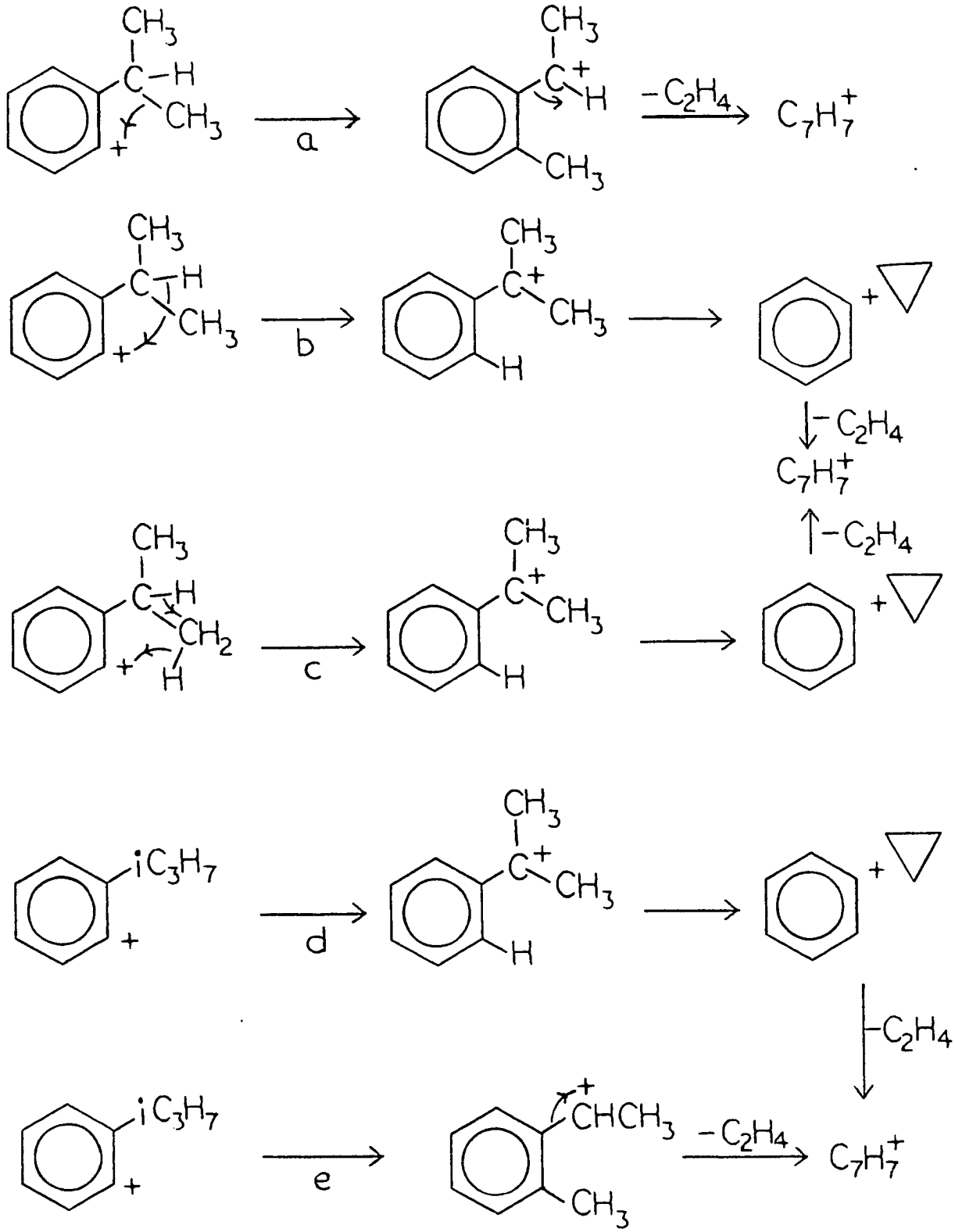
para compounds. It should be noted that other pathways may contribute to tropylium ion formation in the ortho compounds but these are not believed to be major sources of the tropylium ion. Thus the ratio of m/e 119:m/e 91 would be larger in the ortho compounds if only the tropylium ions formed from m/e 119 were considered but still would not approach the value observed in the para compounds.

Another feature of these spectra which appears to give an anomalous result is the wide difference in the ratio of the m/e 119:m/e 91 ions in the two para compounds (para-nitrocumene .45, para-nitrosocumene .95). It is true that the nitro compound undergoes the nitro-nitrite rearrangement in two different fragmentation pathways, namely loss of ·NO from both the molecular and the M-·CH_3 ions, in each case followed by CO loss. This should act to decrease the M-·NO_2 ion, but one would also expect a corresponding decrease in the tropylium ion. Comparison of the ratios of the M-·X (X = NO_2 or NO) ion to the tropylium ion in the spectra of para-nitro-tert-butylbenzene (.1) and para-nitroso-tert-butylbenzene (.8) leads to the same result. While no explanation can be offered for these observations, it is interesting to note that the results are qualitatively similar.

Several mechanisms by which the m/e 119 ions of the nitro and nitrosocumenes form tropylium ions can be envisioned, all of which involve multiple rearrangements. Mechanism a of

Scheme 33 involves an initial intact methyl group transfer followed by loss of the elements of ethylene. Mechanism b would involve transfer of an alpha hydrogen atom to the ring to form the cumyl cation which could subsequently rearrange to a phenylated cyclopropane cation and fragment as such while mechanism c involves initial beta hydrogen transfer followed by rearrangement to the cumyl cation and subsequent fragmentation. Mechanism d involves an initial random hydrogen transfer followed by rearrangement to the cumyl cation and fragmentation as such while mechanism e involves initial transfer of a random methyl group. Of course, any combination of any of these mechanisms or other less likely mechanisms might also be operating. The initial transfer to the aromatic ring of a methyl group or a hydrogen atom does not have to be to the ortho position. It is, however, a reasonable assumption that an initial cleavage in the para position could produce rearrangement to give a vacant ortho position.

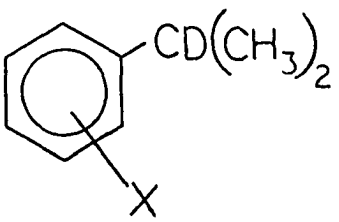
Assuming the cumyl cation to phenylated cyclopropane cation rearrangement leads to the tropylium ion one would expect that cleavage of a para functional group and subsequent hydrogen migration from the side chain to the ring would involve more molecular reorganization than cleavage of an ortho functional group followed by hydrogen migration from the side chain to the ring. This molecular reorganization of



Scheme 33. Some possible mechanisms for ethylene loss from $\overset{+}{C}_6H_4$iPr ions

the para compounds would require more energy and thus a smaller fraction of the cumyl cations formed would have enough energy to further rearrange to phenylated cyclopropane cations. Alternatively, a larger fraction of the m/e 119 ions generated by cleavage of the para group might not have enough energy to rearrange to cumyl cations and thus a smaller fraction of the m/e 119 ions would fragment to tropylium ions.

The labelled compounds (31)-(34) can be used to distinguish between some of the mechanistic possibilities. The tropylium



(31) X = o-NO

(32) X = p-NO

(33) X = o-NO_2

(34) X = p-NO_2

ions formed from compounds (31)-(34) would all be $C_7H_7^+$ ions if mechanism a were the only mechanism operating while they would all be $C_7H_6D^+$ ions if mechanism b were the only mechanism operating. Mechanism c would give a mixture of m/e 91 and m/e 92 tropylium ions in a ratio of 2:1 assuming that the hydrogen atoms of the cyclopropane ring are randomized prior to ethylene loss. Mechanisms d and e would both

form m/e 91 and m/e 92 tropylium ions in a ratio of 4:3.

The spectrum of para-nitrocumene has a very large m/e 92 ion (M-·CH_3-·NO-CO) and thus is useless for quantitative studies on the m/e 119 → m/e 91 fragmentation. Fortunately, both ortho and para-nitrosocumene have m/e 92 ions which are formed almost entirely from the carbon-thirteen isotope peak of the m/e 91 ion. The m/e 92 ion of ortho-nitrocumene has a relative intensity of 16%, half of which is due to the carbon-thirteen isotope peak and the other half to the M-·CH_3-·NO-CO ion. Therefore it was decided that the two nitroso compounds (31) and (32) would be the best ones to study the fragmentation m/e 119 → m/e 91.

The method of synthesis produced labelled material which was shown by low voltage mass spectrometry to be 83% alpha-d_1 and 17% d_0. Mechanism a would still produce only m/e 91 tropylium ions while mechanism b would form m/e 91 and m/e 92 tropylium ions in a ratio of 17:83. Mechanism c would produce $\frac{5.17}{6} \times \frac{4.17}{5} \times \frac{3.17}{4} \times 100\% = 57\%$ m/e 91 tropylium ions and 43% m/e 92 tropylium ions while mechanisms d and e would both produce $\frac{6.17}{7} \times \frac{5.17}{6} \times \frac{4.17}{5} \times 100\% = 63.5\%$ m/e 91 tropylium ions and 36.5% m/e 92 tropylium ions. The spectrum of ortho-nitrosocumene-α-d showed 59.8% of the tropylium ions at m/e 91 and 40.2% at m/e 92 while 58.4% of the tropylium ions were at m/e 91 and 41.6% at m/e 92 in the para isomer. The best estimate from the spectrum of ortho-

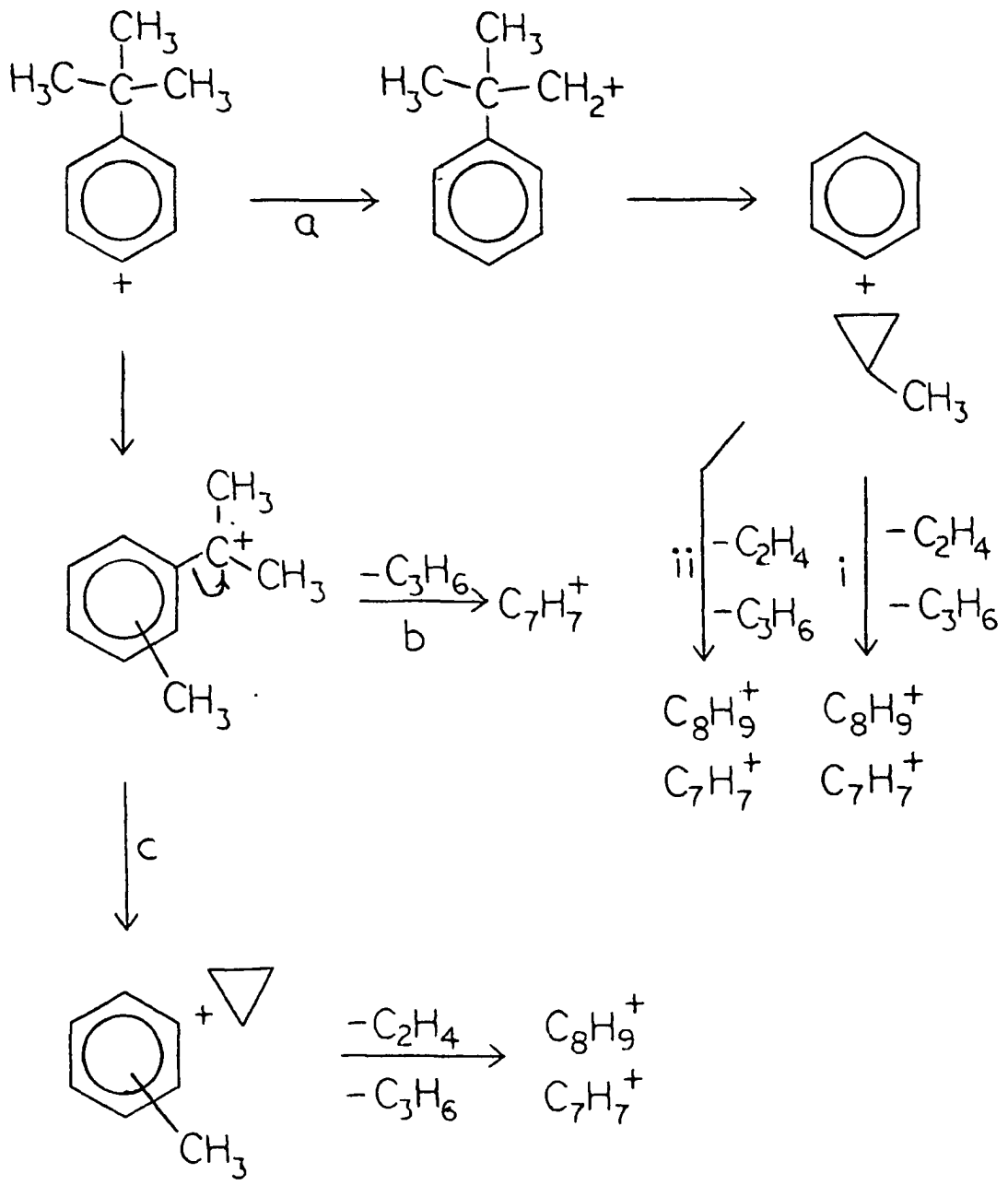
nitrocumene-α-d was 58.5% d_0 and 41.5% d_1 tropylium ions. The retention of the label in the tropylium ion indicates that the more attractive mechanistic possibilities of those proposed are either c, d or e. On the basis of other mass spectral data mechanisms c and d would seem to be more firmly established than e and thus it was decided to investigate the phenylated cyclopropane intermediate in greater depth than previous investigations. The results of these investigations uncovered additional rearrangements and are discussed beginning on page 98.

The m/e 133 ions (M-·X, X = NO_2 or NO) in the spectra of para-nitro and nitroso-tert-butylbenzene are established as the precursors to the tropylium ions by the presence of a metastable ion for the reaction m/e 133 → m/e 91 + C_3H_6. The spectrum of the nitroso compound also has a metastable ion for the loss of C_2H_4 from the m/e 133 ion. It is impossible to tell (without utilizing metastable defocusing techniques) if the corresponding metastable is present in the spectrum of the nitro compound because of the presence of large metastable ion for the loss of ·NO by the nitro-nitrite rearrangement from the M-·CH_3-C_2H_4 ion. It also is not clear whether the corresponding ortho compounds show these metastable ions because of the presence of other metastable ions produced from various ortho effect reactions.

Some of the several possible mechanisms which will be

considered in the present discussion for the fragmentation of the m/e 133 ion of para-nitroso-tert-butylbenzene are shown in Scheme 34. The M-·NO ion could undergo an initial hydrogen transfer from the side chain to the aromatic ring (path a) and the remaining C_4H_8 side chain could then rearrange to form a phenylated methylcyclopropane cation. This ion, once formed, could fragment by loss of ethylene or propylene to form the m/e 91 and m/e 105 ions. The initial process might be viewed as involving the transfer of a methyl group to the aromatic ring followed by loss of C_3H_6 through an unrearranged ion to give the m/e 91 ion (path b). Ethylene loss through a cationated cyclopropane type of intermediate would give the m/e 105 ion (path c). The initial methyl group transfer could have also been followed by immediate further rearrangement to the cationated cyclopropane which then undergoes loss of either cyclopropane or ethylene to form the m/e 91 and m/e 105 ions respectively.

The labelled compounds (35), (36) and (37) were prepared in an attempt to elucidate the mechanistic details of the fragmentation of the m/e 133 ion. The azoxy compounds were prepared instead of the nitroso compounds because of the experimental case in preparing and purifying the labelled materials on a small scale as opposed to the difficulties involved in the small scale preparation of the corresponding labelled nitroso compounds. As can be seen from Figure 20,



i all eight side chain H's randomized prior to loss of C_2H_4 and C_3H_6

ii only the five cyclopropyl side chain H's randomized prior to loss of C_2H_4 and C_3H_6

Scheme 34. Some possible mechanisms for ethylene and propylene loss from $\overset{+}{C}_6H_4$tBu ions

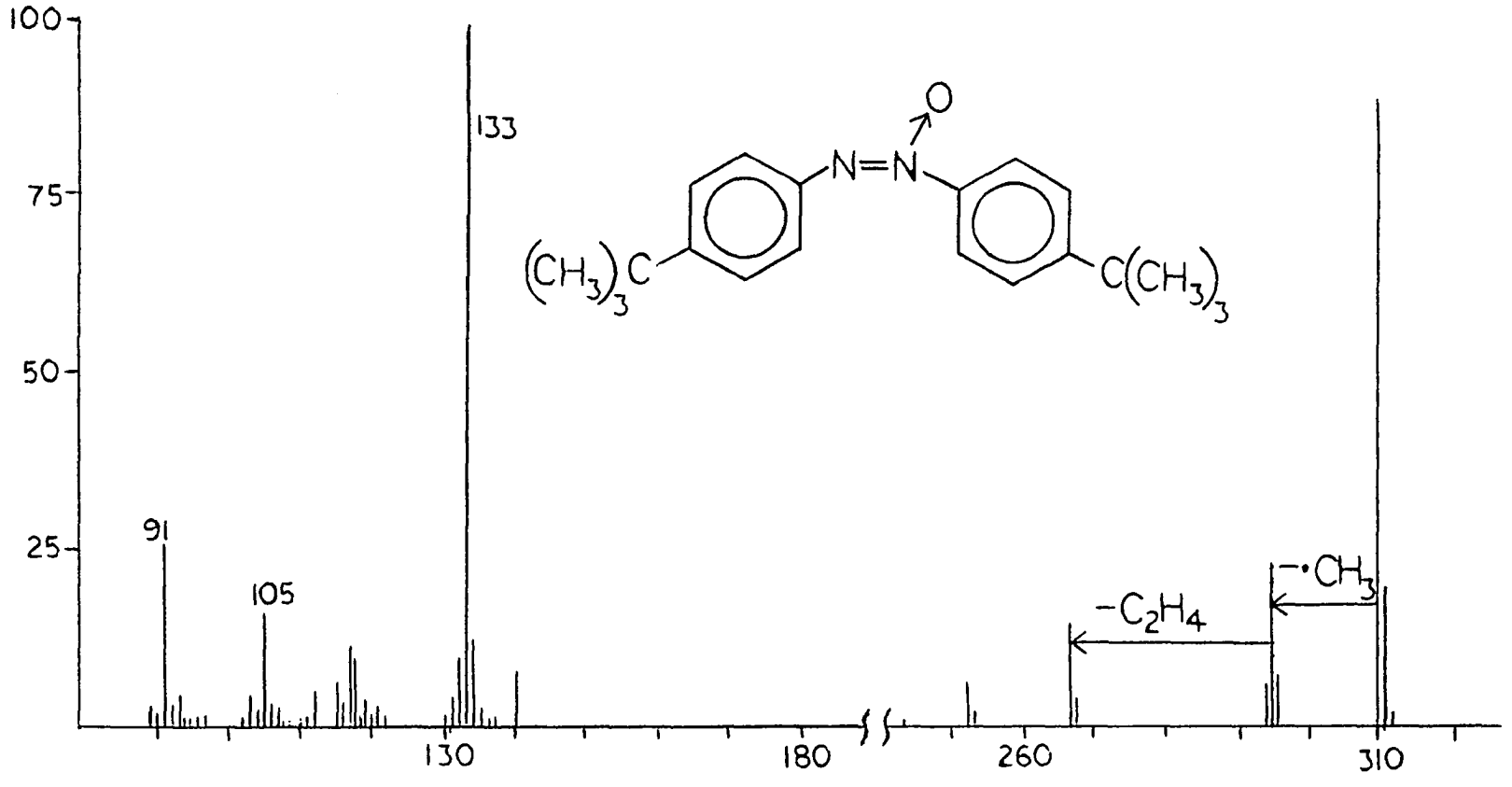
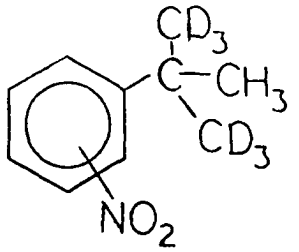
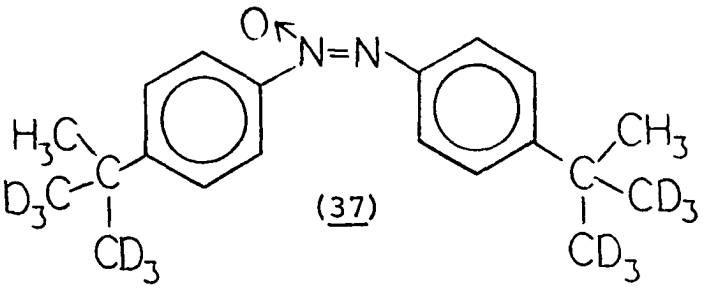


Figure 20. Mass spectrum of 4,4'-di-tert-butylazoxybenzene

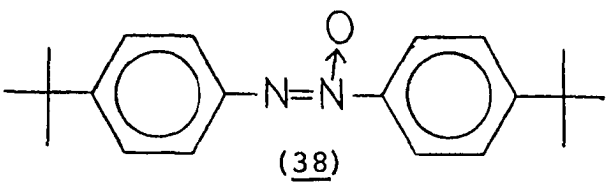


(35) ortho

(36) para



(37)

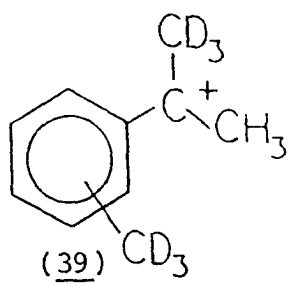


(38)

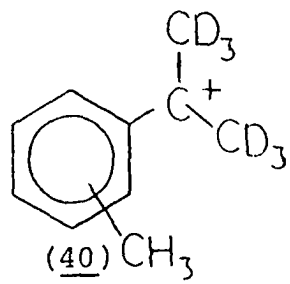
the base peak in the spectrum of the unlabelled azoxy compound is the m/e 133 ion. There is a considerable difference in the ratios of the m/e 133:m/e 91 ions and the m/e 133:m/e 105 ions in the azoxy compound as compared to those ratios in para-nitroso-tert-butylbenzene. This might have been anticipated because the large fragment lost in forming the m/e 133 ion in the azoxy compound could carry away a large amount of the excess vibrational energy and thus give m/e 133 ions of lower average energy. Fewer of these ions would have enough energy to fragment further and thus a smaller amount of the m/e 91 and m/e 105 ions would be observed. The spectra of unlabelled ortho and para-nitro-tert-butylbenzene (see Figures 12 and 13) show that deuterium analogs would not be useful for the determination of label retention in the m/e 105 region but would be useful for determining label retention in the m/e 91 region. The azoxy compound is most useful for determining

label retentions in the m/e 105 region, but can also be used as an aid in determining label retentions in the m/e 91 region.

An intact methyl group transfer to the aromatic ring in the $C_6H_4C(CH_3)(CD_3)_2^+$ ions produced from compounds (35), (36) and (37) would produce ions (39) and (40) in a ratio of 2:1. The loss of $C_3H_3D_3$ from the side chain of (39) would

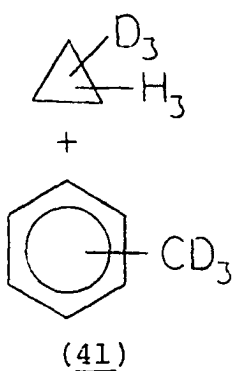


(39)

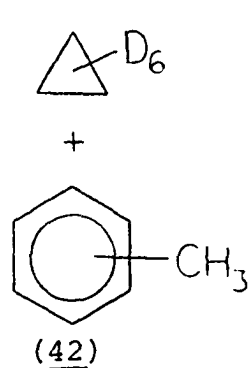


(40)

lead only to m/e 94 and loss of C_3D_6 from (40) would lead only to m/e 91, thereby producing a 2:1 ratio of m/e 94 to m/e 91 if paths b or c of Scheme 34 are the only source of tropylium ions. The loss of ethylene from the side chain of (39) to give $C_8H_xD_y^+$ (x+y=9) (probably methyl tropylium ions) through the cationated cyclopropane (41) (path c) in which the cyclopropane hydrogen atoms are randomized would give



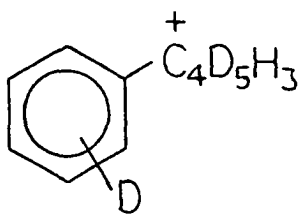
(41)



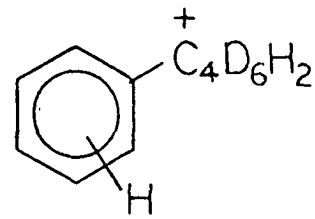
(42)

methyltropylium ions at m/e 108, 109 and 110 in a ratio of 1:3:1. The loss of ethylene through the corresponding cationated cyclopropane intermediate (42) would form methyltropylium ions of only m/e 107. Assuming a 2:1 ratio of (39) to (40) produces a 2:1 ratio of (41) to (42), the overall ratio of m/e 107:m/e 108:m/e 109:m/e 110 becomes 5:2:6:2.

An initial random hydrogen atom transfer from the side chain to the aromatic ring in the $\overset{+}{C}_6H_4C(CH_3)(CD_3)_2$ ion (path a of Scheme 34) would produce a 2:1 ratio of (43) to (44). If



(43)

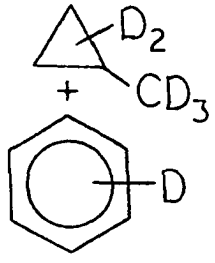


(44)

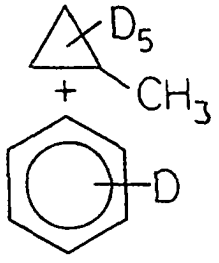
the remainder of the side chain hydrogen (deuterium) atoms are randomized prior to propylene loss, the tropylium ion formed from (43) would be 5/8 x 4/7 = 10/28 $C_7H_4D_3^+$, 2(5/8 x 3/7) = 15/28 $C_7H_5D_2^+$ and 3/8 x 2/7 = 3/28 $C_7H_6D^+$. The tropylium ion formed from (44) by the same mechanism would be 6/8 x 5/7 = 15/28 $C_7H_5D_2^+$, 2(6/8 x 2/7) = 12/28 $C_7H_6D^+$ and 2/8 x 1/7 = 1/28 $C_7H_7^+$. The combination of these values in a 2:1 ratio gives an overall ratio for m/e 91:m/e 92:m/e 93:m/e 94 of 1:18:45:20.

The random loss of ethylene from the side chain of (43) would form methyltropylium ions which would be 4(3/8 x 2/7 x 1/6) = 1/14 $C_8H_7D_2^+$, 6(3/8 x 2/7 x 5/6 x 4/5) = 6/14 $C_8H_6D_3^+$, 4(3/8 x 5/7 x 4/6 x 2/5) = 6/14 $C_8H_5D_4^+$ and 5/8 x 4/7 x 3/6 x 2/5 = 1/14 $C_8H_4D_5^+$. The random loss of ethylene from the side chain of (44) would form 6(2/8 x 1/7) = 3/14 $C_8H_7D_2^+$, 4(2/8 x 6/7 x 5/4 x 4/5) = 8/14 $C_8H_6D_3^+$ and 6/8 x 5/7 x 4/6 x 3/5 = 3/14 $C_8H_5D_4^+$ ions. The statistical combination in a 2:1 ratio gives a ratio of 5:20:15:2 for m/e 107:m/e 108:m/e 109:m/e 110.

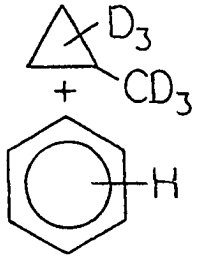
Another mechanism which can be envisioned for path a of Scheme 34 would involve rearrangement to a phenylated methylcyclopropane cation in which the methyl group was one of the initial intact methyl groups and only the other five cyclopropyl hydrogen atoms were randomized prior to loss of propylene. The ion formed by initial deuterium atom transfer



(45)



(46)



(47)

from the side chain to the ring would form two phenylated methylcyclopropanes (45) and (46), of equal intensity by this pathway while the ion formed by initial hydrogen atom transfer

would only form (47). The overall ratio of (45):(46):(47) would be 1:1:1 because of the 2:1 ratio of (43) to (44). Propylene loss from (45) would form 2/5 x 1/4 = 1/10 $C_7H_4D_3^+$, 2(2/5 x 3/4) = 6/10 $C_7H_5D_2^+$ and 3/5 x 2/4 = 3/10 $C_7H_6D^+$ ions while propylene loss from (47) would form 3/5 x 2/4 = 3/10 $C_7H_5D_2^+$, 2(3/5 x 2/4) = 6/10 $C_7H_6D^+$ and 2/5 x 1/4 = 1/10 $C_7H_7^+$ ions. By this mechanism (46) would only produce $C_7H_4D_3^+$ ions. The overall ratio m/e 91:m/e 92:m/e 93:m/e 94 would thus be 1:9:9:11. Ethylene loss from (45) would form 2/5 $C_8H_4D_5^+$ and 3/5 $C_8H_5D_4^+$ ions while ethylene loss from (47) would form 3/5 $C_8H_5D_4^+$ and 2/5 $C_8H_6D_3^+$ ions. The only ion formed from (46) by ethylene loss would be $C_8H_7D_2^+$ and thus the ratio m/e107:m/e 108:m/e 109:m/e 110 would be 5:2:6:2 Table 6 summarizes the calculations for the label retentions expected for various proposed mechanisms of Scheme 34.

As can be seen by looking at the spectra in Figures 21, 22 and 23, the label retention in the tropylium ion region is approximately the same for m/e 91-96. The best average of the intensity of these ions after subtracting out contributions for incomplete labelling and natural abundance carbon-thirteen gives a ratio of 1.64:1.70:2.62:3.64:1.17:1.0 for m/e 91:m/e 92:m/e 93:m/e 94:m/e 95:m/e 96. The value for label retention in the methyltropylium ion is most reliably obtained from the labelled azoxy compound (37) and gives a ratio of 1.67:2.25:2.95:1.8:1.0 for m/e 107:m/e 108:

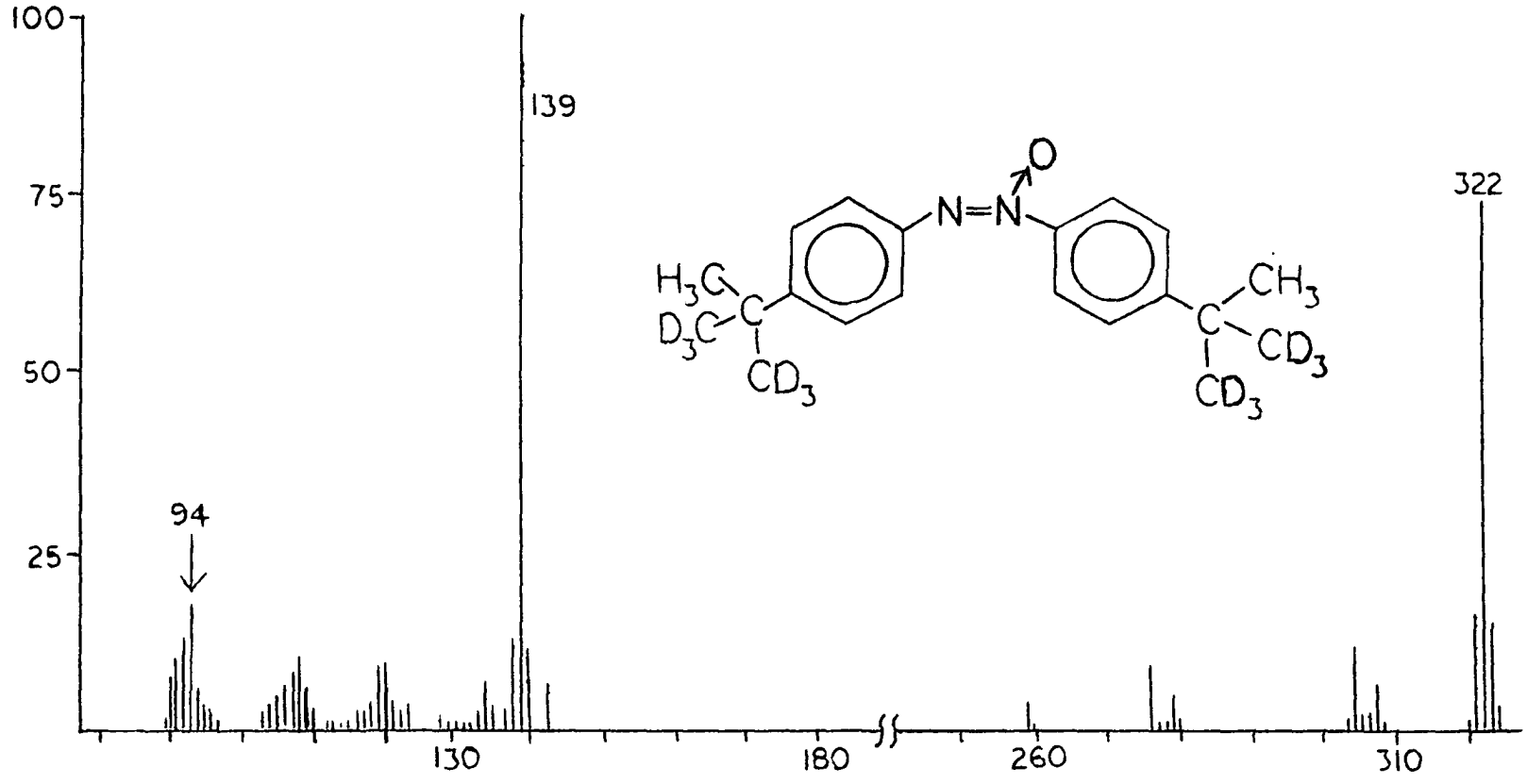


Figure 21. Mass spectrum of 4,4'-bis-(2-methyl-1,1,1,3,3,3-d_6-iso-propyl)-azoxybenzene

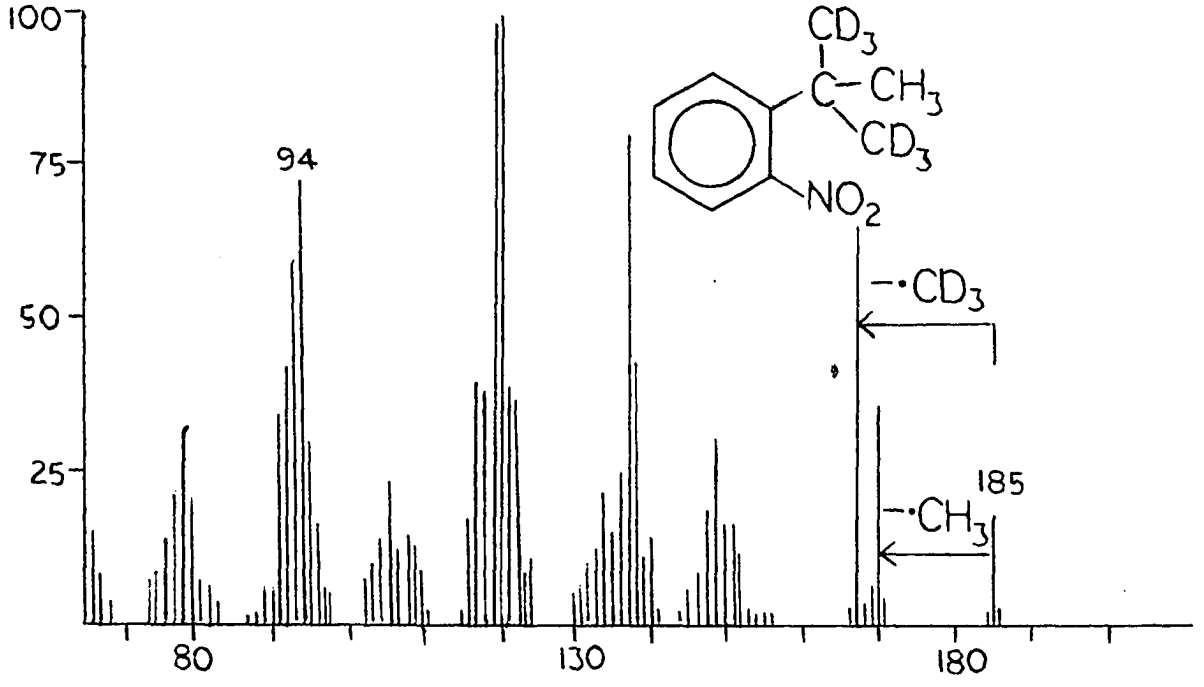


Figure 22. Mass spectrum of 2-methyl-2-(o-nitrophenyl)-1,1,1,3,3,3-d_6-propane (source temp. +200°)

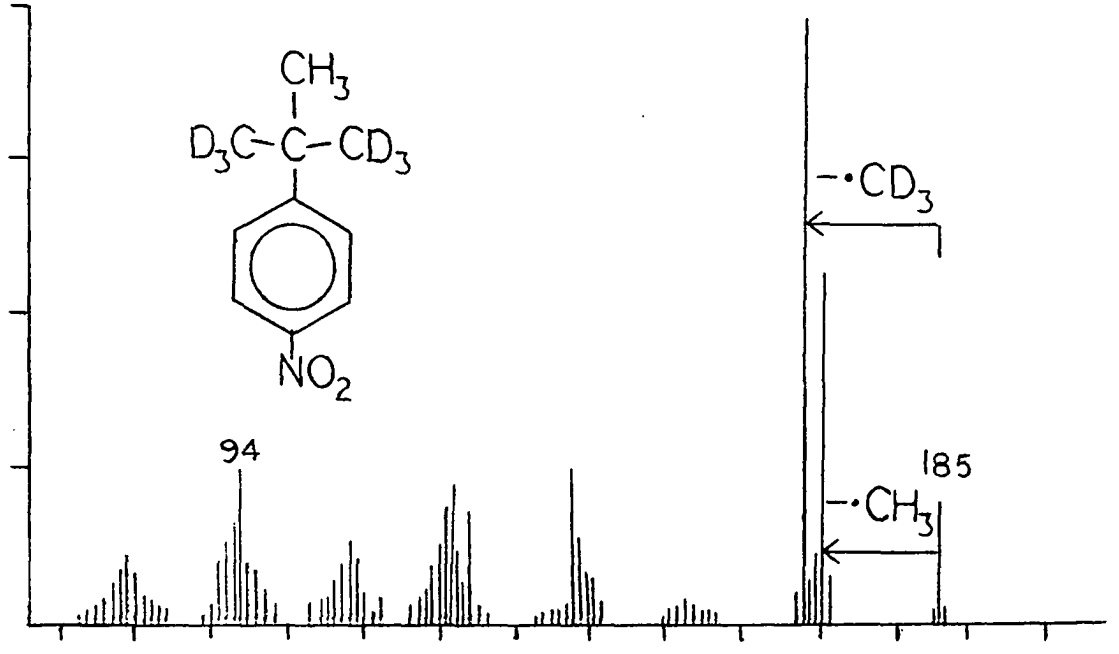


Figure 23. Mass spectrum of 2-methyl-2-(p-nitrophenyl)-1,1,1,3,3,3-d_6-propane (source temp. +200°)

Table 6. Ratios of labelled tropylium and methyl tropylium ions formed from $\overset{+}{C}_6H_4C(CH_3)(CD_3)_2$ ions by the various mechanisms of Scheme 34

m/e	Mech. a, pathi Rel. Int.	Mech. a, pathii Rel. Int.	Mech.b or c Rel. Int.
91	1	1	1
92	18	9	0
93	45	9	0
94	20	11	2
107	5	5	5
108	20	2	2
109	15	6	6
110	2	2	2

m/e 109:m/e 110:m/e 111. The experimental ratios are considerably different than the theoretical ratios predicted by any of the proposed mechanisms. Furthermore, the label retention observed in the tropylium ions at m/e 95 and m/e 96 and in the methyltropylium ion at m/e 111 are not predicted by any of the mechanisms. A mechanism involving the total scrambling of all hydrogen atoms prior to loss of C_2H_4 or C_3H_6 from the m/e 133 ion would predict the existence of tropylium ions at m/e 91-m/e 97 and methyltropylium ions at m/e 107-m/e 111. However, the calculated ratio of m/e 91:m/e 92:m/e 93:m/e 94:m/e 95:m/e 96:m/e 97 for this mechanism is 1:42:315:700:525:126:7 and that of m/e 107:

m/e 108:m/e 109:m/e 110:m/e 111 is 3:28:63:42:7. This is clearly in much poorer agreement than any of the other proposed mechanisms with the experimental result.

The only mechanism of those proposed which gives an m/e 91:m/e 94 ratio close to the observed ratio of 1.64:3.64 is the mechanism involving an initial intact methyl group transfer. However, this mechanism does not predict the existence of ions at m/e 92, 93, 95 and 96. If this is the mechanism which is operating, the existence of tropylium ions at m/e 92, 93, 95 and 96 might be explained by the operation of another mechanism or a deuterium isotope effect. The additional rearrangements of cationated cyclopropanes, which were referred to earlier, also contribute to the label retention observed in this system and these rearrangements are discussed in the next section of this thesis prior to making final conclusions on the mechanism for m/e 133 → m/e 91 in these systems.

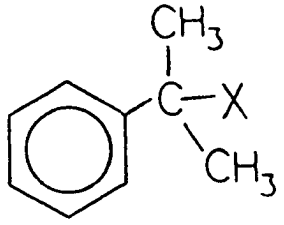
Hydrogen Rearrangements in the Phenylated Cyclopropane Cation

It has previously been noted that many iso-propyl and tert-butyl substituted compounds, such as aralkyl nitro, nitroso, azo and azoxy compounds, expel a molecule of ethylene from the $C_9H_{11}^+$, m/e 119, and the $C_{10}H_{13}^+$, m/e 133 ions, respectively. Neither cumene nor tert-butylbenzene undergo

loss of ethylene from the molecular ion, but the M-·CH_3 ion of tert-butylbenzene does undergo ethylene loss though a proposed phenylated cyclopropane cation (see page 28). An analogous mechanism for ethylene loss from the m/e 119 (M-substituent) and m/e 133 (M-substituent) ions of the substituted iso-propyl and tert-butyl compounds can be envisioned if the m/e 119 ion undergoes an initial hydrogen migration to the ring from the side chain and the m/e 133 ion undergoes an initial methyl migration from the ring to the side chain. These rearranged ions could further rearrange to cationated cyclopropanes and react as such. Because of the difficulty of interpreting the deuterium labelling experiments in light of the existing sparse deuterium labelling which has been performed on possible precursors to phenylated cyclopropane cations (4, Chapter 10, 47, 48), more extensive deuterium labelling was performed and this led to the discovery of new hydrogen rearrangements involving the phenylated cyclopropane cation.

The Dimethyl-Phenyl-Carbonium Ion

Loss of ·X from the molecular ion of a variety of compounds such as (48)-(53) produces dimethyl-phenyl-carbonium ions (cumyl cations) which subsequently undergo a metastable loss of ethylene to form m/e 91 ions. The m/e 91 ion is

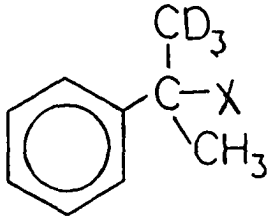


(48) X=CO_2H (51) X=CH_2OMes

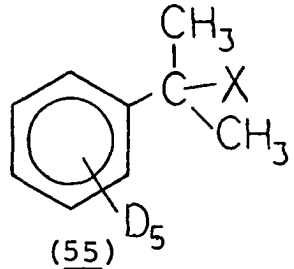
(49) X=CO_2CH_3 (52) X=OCH_3

(50) X=$CO_2CH_2CH_3$ (53) X=CH_3

assumed to have a tropylium structure. If the cumyl cation is generated by loss of ·X from a compound labelled such as (54), and this cumyl cation (m/e 122) expels ethylene by a



(54)



(55)

process involving a phenylated cyclopropane intermediate in which all side chain carbon and hydrogen atoms are randomized prior to ethylene loss, then the tropylium ion would be a 1:3:1 ratio of m/e 91:m/e 92:m/e 93. This type of a mechanism would produce cumyl cations at m/e 124 by loss of ·X from the molecular ion of (55) and tropylium ions at m/e 96 by ethylene loss utilizing the side chain carbon and hydrogen atoms of the m/e 124 ion.

The mass spectrum of compound (49) has very few ions other than the molecular ion, the M-·CO_2CH_3 ion, the tropylium ion and the hydrocarbon ions at m/e 77, 78 and 79 (see Figure 24). Compound (54) (X=CO_2CH_3) was prepared and its mass spectrum showed the expected 3 a.m.u. shift in the

molecular ion and the M-·CO_2CH_3 ion as compared to compound (49) (see Figure 25). Table 7 shows the ratios of the m/e 91-m/e 94 tropylium ions (corrected for natural abundance carbon-thirteen and a 2.7% d_2 impurity) formed at various electron energies. The m/e 91 ion is assigned an arbitrary value of 1.00. Only the 12.5 and 13eV spectra approximate a

Table 7. Ratio of m/e 91-m/e 94 in compound (54)

m/e	70eV	25eV	20eV	18eV	16eV
94	.24	.20	.17	.19	.22
93	1.96	2.01	2.10	2.00	2.12
92	5.38	6.06	6.62	6.73	7.13
91	1.00	1.00	1.00	1.00	1.00
m/e	15eV	14eV	13.5eV	13eV	12.5eV
94	-[a]				
93	1.77	1.29	.98	.83	.87
92	6.85	5.41	4.04	2.83	3.14
91	1.00	1.00	1.00	1.00	1.00

[a]m/e 94 could not be measured accurately below 13eV.

1:3:1 ratio for m/e 91:m/e 92:m/e 93. As can be seen from Table 7 an increase in electron energy causes an increase in the m/e 92 and m/e 93 ions relative to the m/e 91 ion. The maximum ratios of m/e 92 and m/e 93 to m/e 91 are reached at 16eV and then the ratios show a slight decrease. The label retention in the tropylium ion is too large for a process which

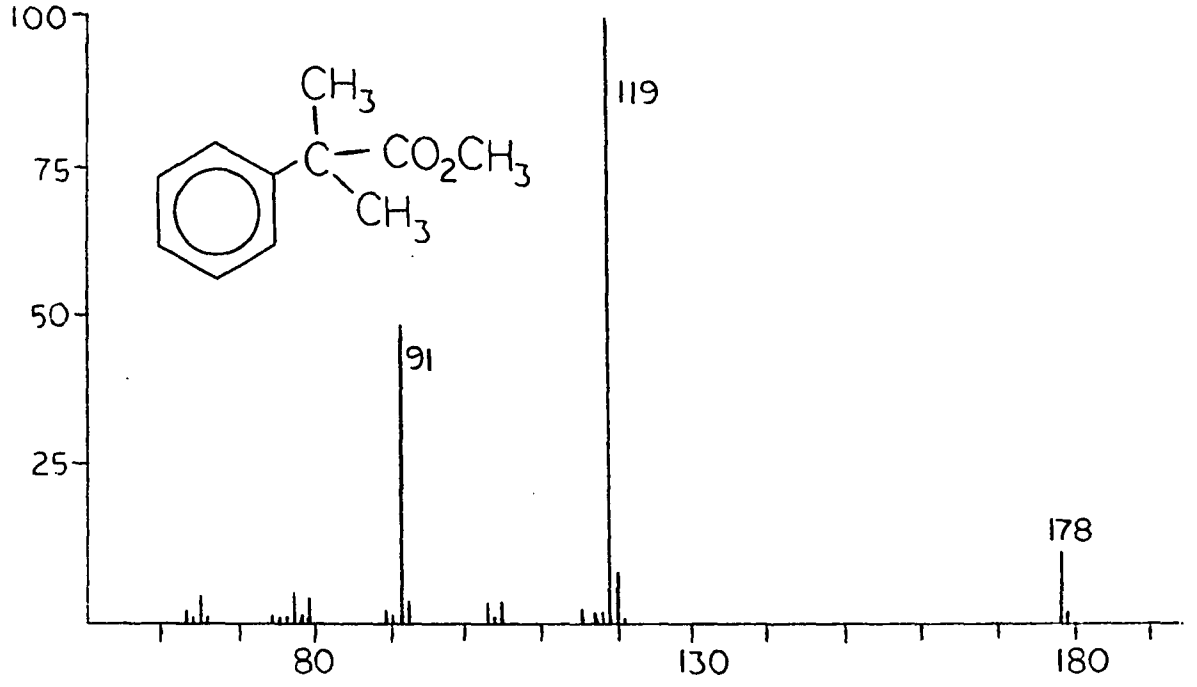


Figure 24. Mass spectrum of methyl-2-methyl-2-phenyl-propionate

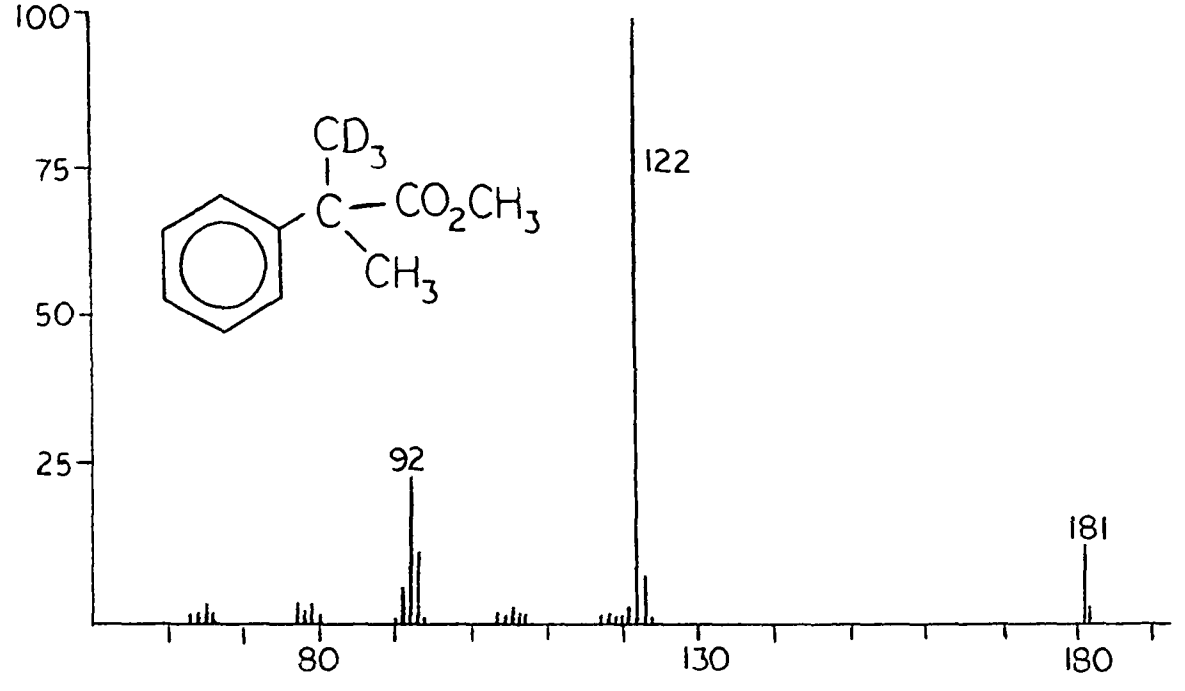


Figure 25. Mass spectrum of methyl-1,1,1-d_3-2-methyl-2-phenyl-propionate

simply randomizes side chain hydrogen atoms prior to ethylene loss and this is further evidenced by the formation of a small amount of tropylium ions containing all three deuterium atoms.

The fact that label retention varies with electron energy may indicate that more than one mechanism is operating above 13eV. A deuterium isotope effect, possibly energy dependent, of the correct magnitude may also be operating and this could cause the ethylene molecule which is formed to contain more hydrogen atoms than would be predicted by the phenylated cyclopropane mechanism. However, compound (55) was prepared and its mass spectrum (see Figure 26) revealed that the mechanism for ethylene loss involved hydrogen rearrangements other than those involved in randomizing only side chain hydrogen atoms.

Table 8 shows the ratio of the m/e 94:m/e 95:m/e 96 ions (corrected for natural abundance carbon-thirteen, a 7.2%

Table 8. Ratios of m/e 94-96 in compound (55)

m/e	70eV	18eV	16eV	15eV	14eV	13eV
96	1.00	1.00	1.00	1.00	1.00	1.00
95	.45	.44	.42	.39	.31	.25
94	.10	.10	.09	.09	.08	-[a]

[a] m/e 94 could not be measured accurately below 14eV.

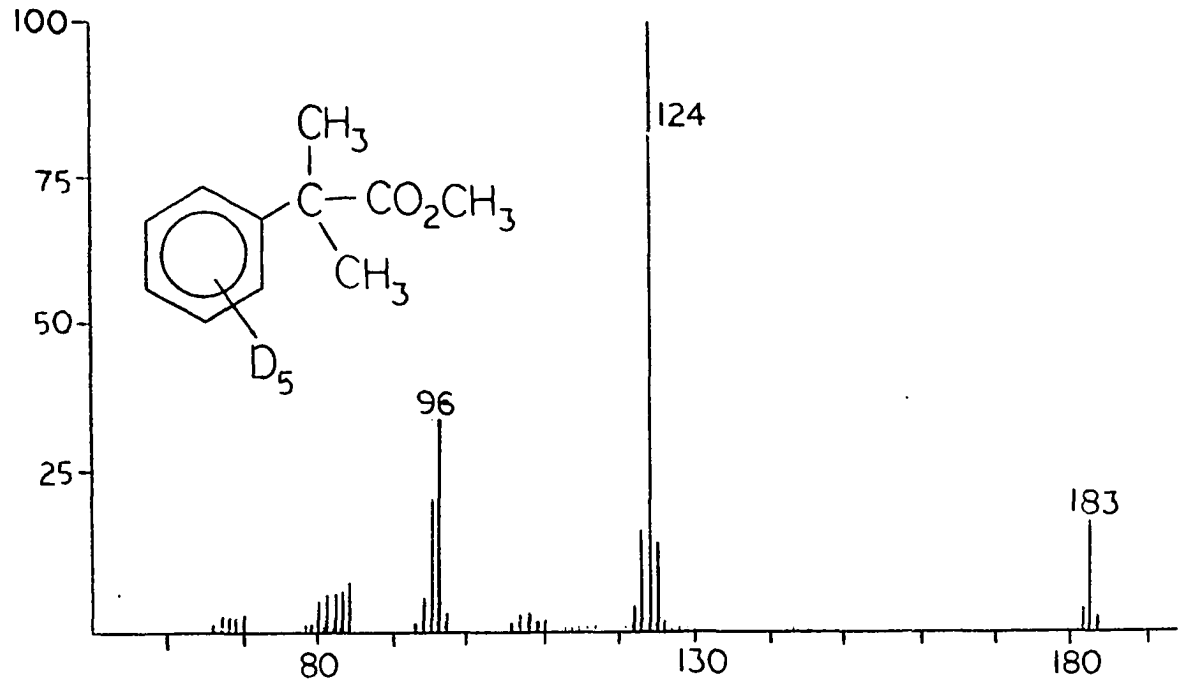


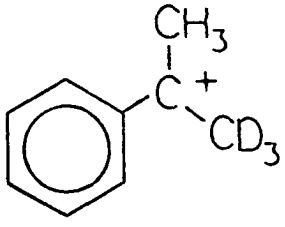
Figure 26. Mass spectrum of methyl-2-methyl-2-phenyl-d_5-propionate

d_4 impurity and a .6% d_6 impurity) at various electron energies taking the value of m/e 96 as 1.00. The d_6 impurity is discussed briefly on page 126 of this thesis.

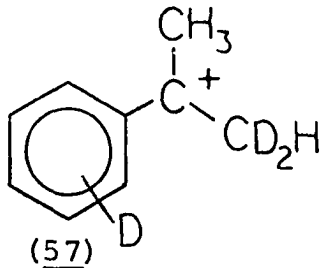
The expected 5 a.m.u. shift occurs in the molecular ion and the M-.CO_2CH_3 ion, but not in the tropylium ion (see Figure 26). The data in Table 8 clearly indicates an energy dependent loss of C_2H_4, C_2H_3D and $C_2H_2D_2$ from the m/e 124 ion of (55). Any plausible mechanism for ethylene loss from the cumyl cation in light of the deuterium labelling experiments on compounds (54) and (55) and the carbon-thirteen labelling experiment of Meyerson (43) would involve an energy dependent process or processes which partially scrambles ring

and side chain hydrogen atoms, but not carbon atoms. If the cumyl cation really does rearrange to a phenylated cyclopropane intermediate prior to ethylene loss, the partial scrambling of ring and side chain hydrogen atoms could occur either in the cumyl cation or the rearranged intermediate. Empirical calculations were carried out to determine the extent of ring and side chain hydrogen scrambling at 70eV. These calculations indicated that a possible mechanism could involve 35-45% of the cumyl cations undergoing exchange of one ring hydrogen atom for one side chain deuterium atom and then 20-30% of the cations undergoing a second exchange.

A sample calculation shows that if a 45:30 mixture of ions (56) and (57) undergo ethylene loss by randomizing the



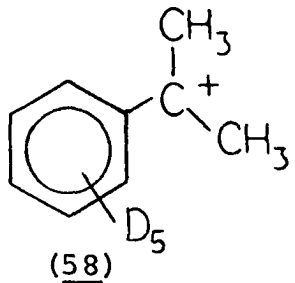
(56)



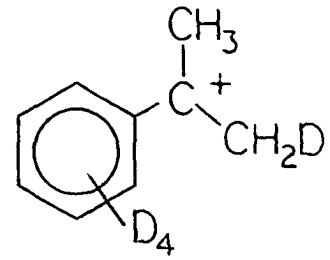
(57)

side chain hydrogen and deuterium atoms that (56) would produce a 9:27:9 ratio of m/e 93:m/e 92:m/e 91 and (57) would produce a 2:16:12 ratio of m/e 94:m/e 93:m/e 92. Adding these together gives a 2:25:39:9 ratio of m/e 94:m/e 93:m/e 92:m/e 91. This roughly approximates the data at higher eV in Table 7. A 45:60 ratio of (58) and (59) would produce a

ratio of 20:85 for m/e 95:m/e 96 by randomizing side chain hydrogen and deuterium atoms prior to ethylene loss. It should



(58)



(59)

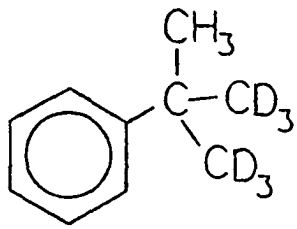
be noted that a 45:60 ratio of (58):(59) is produced by the same amount of ring and side chain scrambling which produces a 45:30 ratio of (56):(57) because half of the exchange in (57) results in no net change in the ion structure. The 85:20 ratio of m/e 96:m/e 95 does not agree as well with Table 8 as the ratio of m/e 91:m/e 92:m/e 93:m/e 94 did with Table 7.

The reason for the small discrepancy is not clear but it is possible that a deuterium isotope effect is acting on the rate determining step of the mechanism. Although it will not be shown here, the calculated ratios better approximate the observed ratios when the second exchange is also considered. The ratios were also somewhat dependent on the method of sample insertion and all the values given are for insertion via the high temperature inlet.

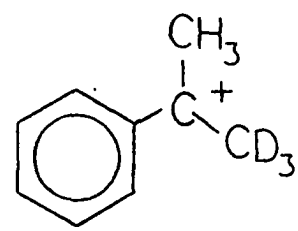
Scrambling between ring and side chain hydrogen atoms which is far short of that required to effect complete loss of position identity has been observed in the loss of a methyl

radical in para-xylene (4, Chapter 10, 61) and in the loss of a methyl radical from polymethylbenzenes (62). The label retention in the M-·CH_3 ion of various labelled xylenes suggested a 50:50 chance for exchanging one ring and side chain hydrogen atom. The data for the polymethylbenzenes was in agreement with the proposed mechanism for para-xylene with the additional possibility of the operation of a second exchange. No consistent mechanism has been proposed for this data which would also explain the results of carbon-thirteen labelling in these systems. The effect observed in compounds (54) and (55) is similar to these results of Meyerson (61, 62).

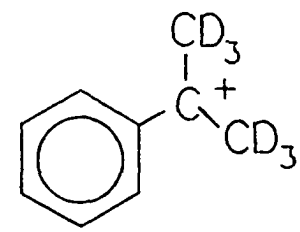
To further document the generality of this type of rearrangement, compound (60) was prepared and subjected to mass spectral analysis (see Figure 27). The initial beta



(60)



(61)



(62)

cleavage of a methyl radical gave a 1:.55 ratio of m/e 122:m/e 125. One would have anticipated a 2:1 ratio for m/e 122:m/e 125 but apparently an isotope effect either slightly favors the loss of ·CH_3 over ·CD_3 from the molecular ion or slightly favors the fragmentation of the m/e 122 ions

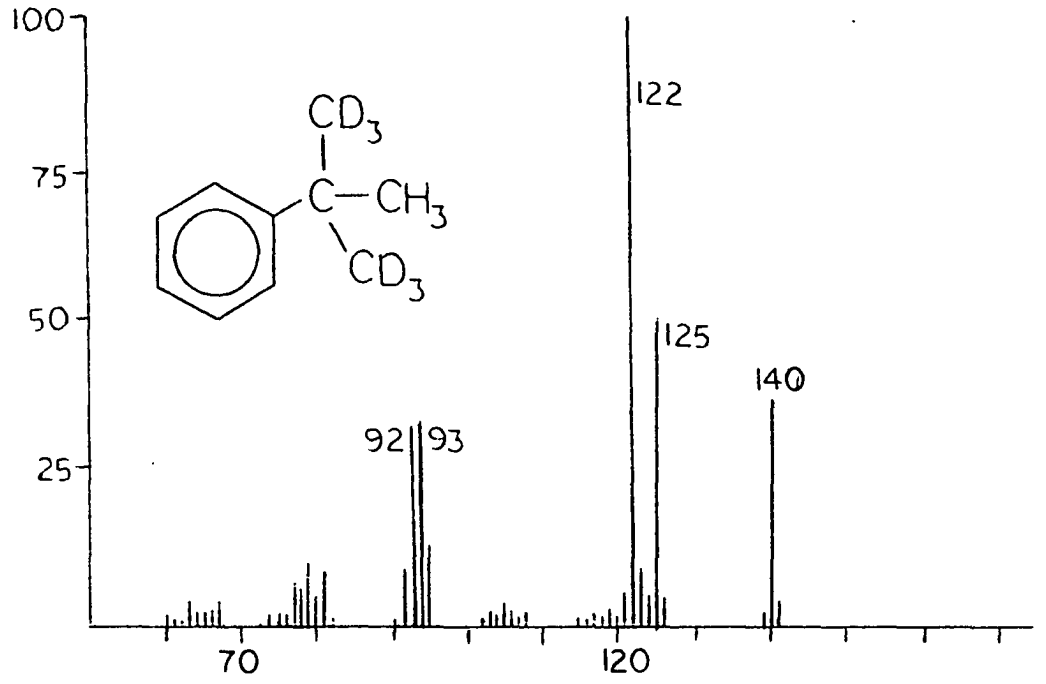


Figure 27. Mass spectrum of 2-methyl-2-phenylpropane-1,1,1, 3,3,3-d_6

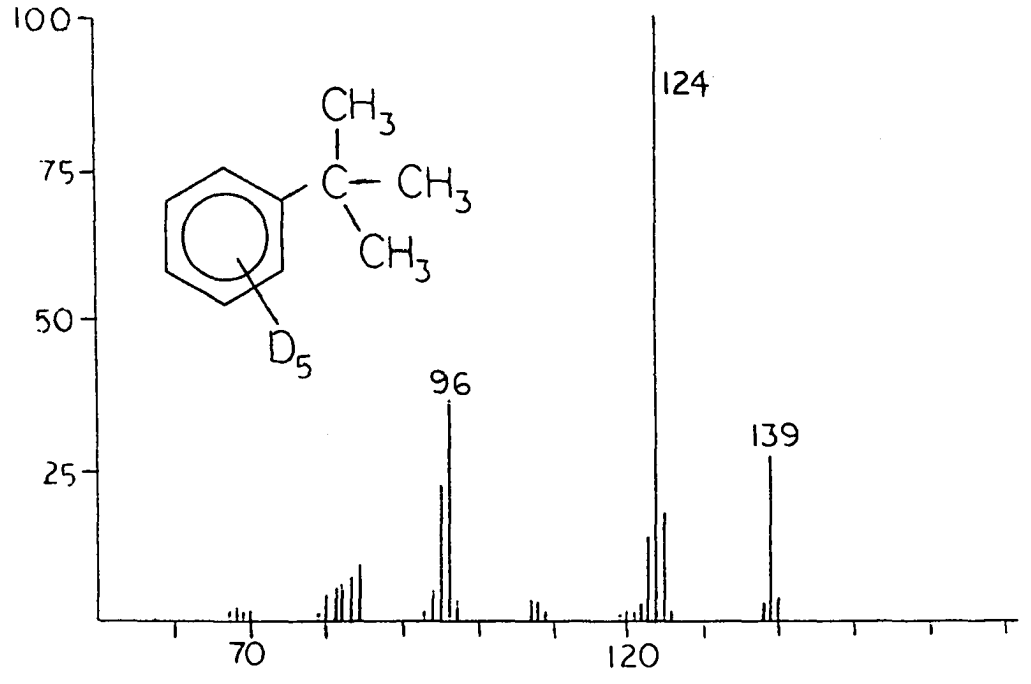
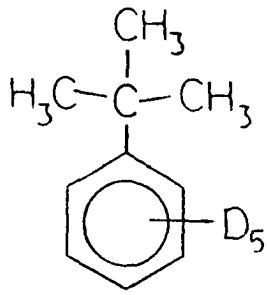
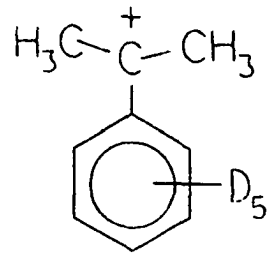


Figure 28. Mass spectrum of 2-methyl-2-phenyl-d_5-propane

(61) relative to the m/e 125 ions (62). If only side chain hydrogen and deuterium atoms were involved in ethylene loss from (61) a 1:3:1 ratio of m/e 91:m/e 92:m/e 93 would be produced while ion (62) would give only m/e 93 if only side chain deuterium atoms were involved in ethylene loss. Combining these in a ratio of 1:.55 gives a ratio of 20:60:75 for m/e 91:m/e 92:m/e 93. The ring labelled compound (63) should produce only m/e 96 tropylium ions if only side chain hydrogen atoms are involved in ethylene loss from ion (64).



(63)



(64)

Table 9 shows the ratio of the m/e 91:m/e 92:m/e 93:m/e 94 ions (corrected for natural abundance carbon-thirteen and an 8% d_5 impurity) in the spectrum of compound (60) (see Figure 27) taking the m/e 91 ion as 1.00. Table 10 shows the ratio of the m/e 94:m/e 95:m/e 96 ions (corrected for natural abundance carbon-thirteen, a 10.3% d_6 impurity and an 11.8% d_4 impurity) in compound (63) taking the m/e 96 ion as 1.00. The data from Tables 9 and 10 are in excellent

Table 9. Ratio of m/e 91-94 in compound (60)

m/e	70eV	20eV	16eV	12eV
94	1.42	1.46	1.18	
93	4.24	5.27	4.11	2.66
92	4.27	5.55	4.85	2.56
91	1.00	1.00	1.00	1.00

Table 10. Ratio of m/e 94-96 in compound (63)

m/e	70eV	16eV	15eV	13eV
96	1.00	1.00	1.00	1.00
95	.44	.35	.31	.26
94	.14	.10	.07	

agreement with that in Tables 7 and 8 thus indicating that the nature of the ·X group lost from the molecular ion does not affect the subsequent rearrangements of the cumyl cation.

The Ethyl-Phenyl-Carbonium Ion

The mass spectrum of 3-phenylpentane (see Figure 29) shows an initial beta cleavage of an ethyl group to form a $\phi\overset{+}{C}HCH_2CH_3$ ion (m/e 119) which subsequently expels a molecule of ethylene to form $C_7H_7^+$ ions which probably have the tropylium structure. Deuterium labelling experiments (47) led to the suggestion that the $\phi\overset{+}{C}HCH_2CH_3$ ions lost ethylene by the combination of mechanisms shown in Scheme 17. However,

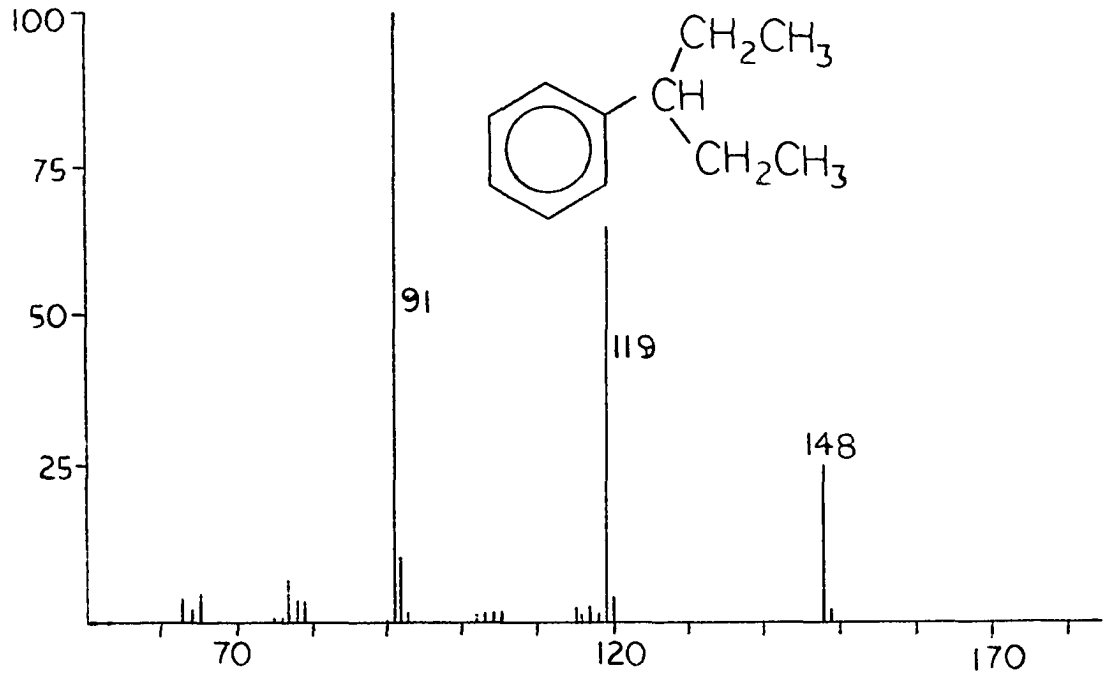


Figure 29. Mass spectrum of 3-phenylpentane

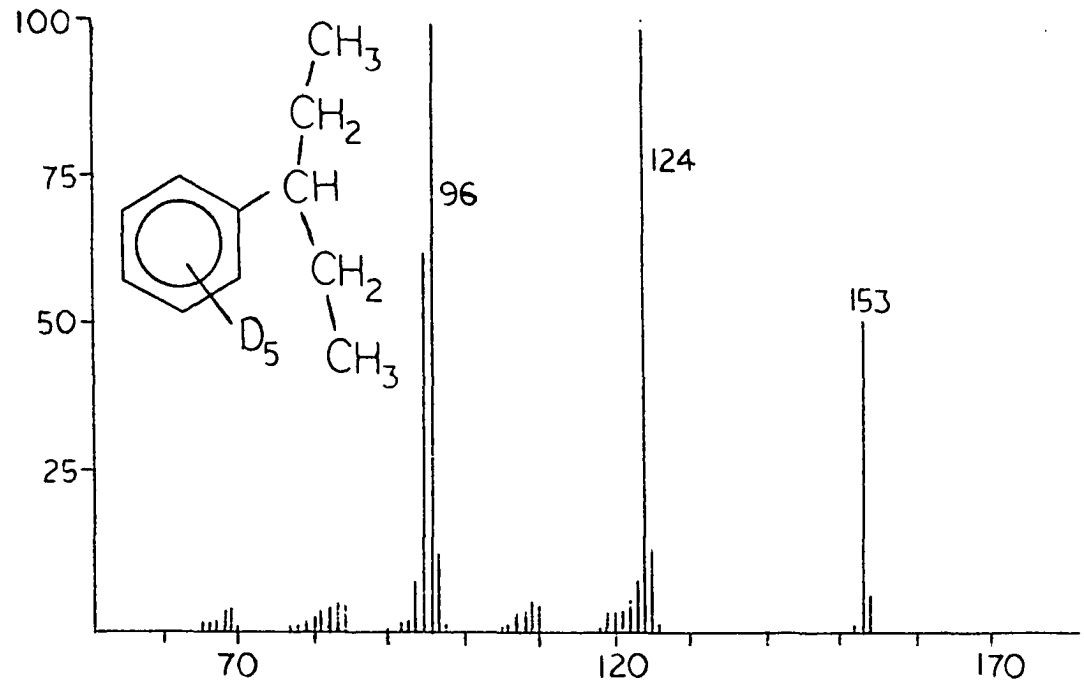


Figure 30. Mass spectrum of 3-phenylpentane-d_5

the deuterium labelling data obtained for 3-phenylpentane-3-d could be interpreted differently if a partial scrambling occurs between the ring and side chain hydrogen atoms. In order to investigate this possibility, 3-phenyl-d_5-pentane was prepared and subjected to mass spectral analysis.

A 5 a.m.u. shift is observed for the molecular ion and the M-·CH_2CH_3 ion (see Figure 30), thereby further substantiating the observation that the loss of an ethyl radical occurs through an unrearranged ion (47). However, as can be clearly seen from both Figure 30 and Table 11, the loss of ethylene from the m/e 119 ions is an energy dependent process in which part of the ethylene lost contains some of the initial ring deuterium atoms. The data presented in Table 11 has been corrected for natural abundance carbon-thirteen and a 2.9% d_4 impurity and the m/e 96 ion is assigned a value of 1.00. The partial scrambling of ring and side chain hydrogen atoms accounts for the increase in the retention

Table 11. Ratio of m/e 94-96 in 3-phenyl-d_5-pentane

m/e	70eV	30eV	25eV	20eV	16eV
96	1.00	1.00	1.00	1.00	1.00
95	.50	.40	.26	.15	.08
94	.10	.07	.05	.01	-

of the deuterium label in the tropylium ion at increasing ionizing voltages which was observed by Meyerson and Hart (47).

The data obtained from 3-phenyl-d_5-pentane suggested that Meyerson and Hart's data on 3-phenylpentane-1-d should be reinvestigated (47). The compound, 3-phenylpentane-1,1,1,5,5,5-d_6, was chosen for the study for several reasons: (a) initial beta cleavage of an ethyl group would produce only m/e 122 ions as opposed to the mixture of m/e 119 and m/e 120 ions formed in the spectrum of 3-phenylpentane-1-d, (b) utilizing three gamma deuterium atoms in the $\phi\overset{+}{C}HCH_2CH_3$ ions instead of only one would produce tropylium ions in which the label retention could be measured more accurately, (c) the method of synthesis produced 96.3% d_6 and 3.7% d_5 products as opposed to the 12% d_0, 84% d_1 and 4% d_2 3-phenylpentane-1-d used previously thereby making the corrections for incomplete labelling easier. The mass spectrum of 3-phenylpentane-1,1,1,5,5,5-d_6 is shown in Figure 31.

Table 12 shows the ratio of label retention observed in the tropylium ion (corrected for natural abundance carbon-thirteen and a 1.85% d_2 impurity in the m/e 122 ion) with the m/e 91 ion assigned a value of 1.00. As can be seen from Table 12, the m/e 91 and m/e 93 ions are approximately equal in intensity at all energies while the m/e 92 ion decreases at energies above 20eV. If only mechanism II of

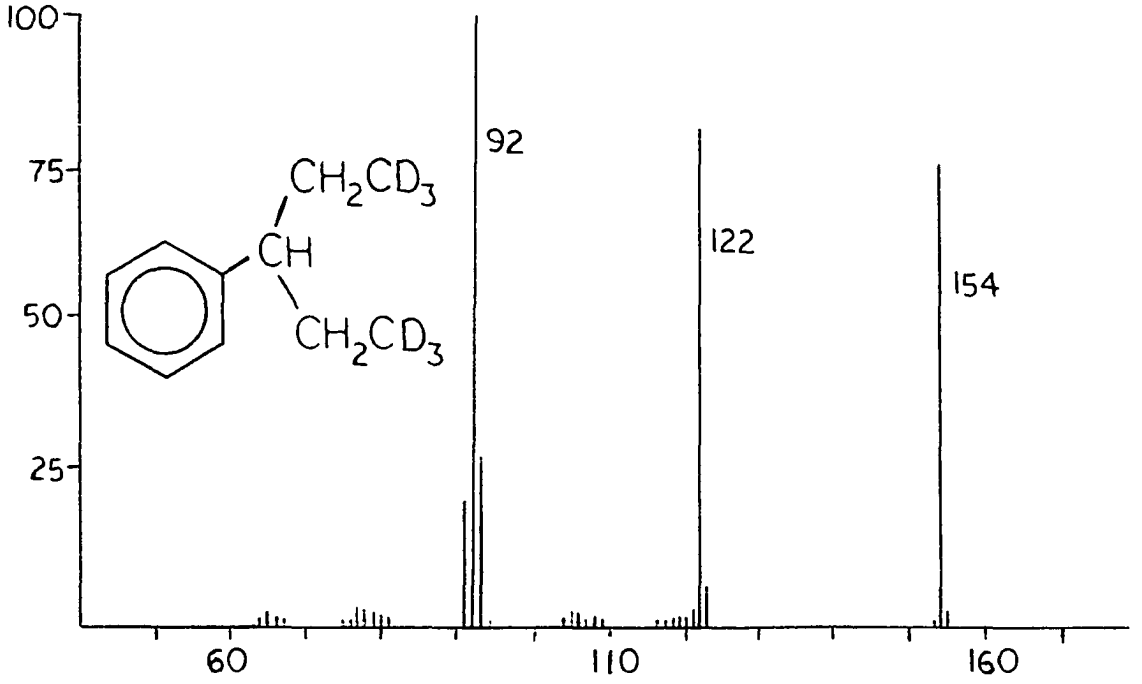


Figure 31. Mass spectrum of 3-phenylpentane-1,1,1,5,5,5-d_6

Table 12. Ratio of m/e 91-93 in 3-phenylpentane-1,1,1,5,5,5-d_6

m/e	70eV	25eV	20eV	18eV	16eV
93	.95	.92	1.00	1.00	.96
92	5.63	5.92	7.50	7.50	7.50
91	1.00	1.00	1.00	1.00	1.00

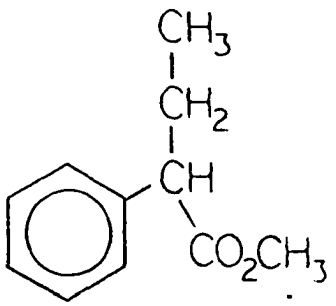
Scheme 17 were operating, that is, an intermediate such as a phenylated cyclopropane which randomizes only side chain hydrogen atoms prior to ethylene loss, then a 1:3:1 ratio for m/e 91:m/e 92:m/e 93 would be observed. If only mechanism I of Scheme 17 were operating, $\phi\overset{+}{C}HCH_2CD_3$ ions would form only

m/e 92 tropylium ions. The data is in agreement with the proposal of Meyerson and Hart that ethylene is lost by a combination of these two mechanisms but suggests a ratio of 47:53 for mechanism II:mechanism I at low eV. This changes to 34:46 at higher eV indicating that mechanism I plays a less important role relative to mechanism II at increasing ionizing energy. The fact that the m/e 91 and m/e 93 ions are nearly equal at all ionizing energies indicates that no exchange occurs between the ring and gamma hydrogen atoms in this system. This further implies that the exchange observed between the aromatic ring hydrogen atoms and the alpha hydrogen atoms (and probably also the beta hydrogens although this possibility in this system has not been investigated) occurs before rearrangement to the phenylated cyclopropane intermediate. Exchange of a ring deuterium atom for a beta hydrogen atom in 3-phenyl-d_5-pentane would result in loss of label by either mechanism.

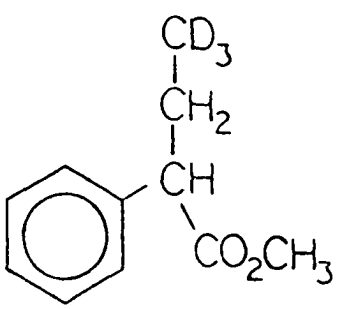
Another interesting point about the partial scrambling is the amount that occurs in the ethyl-phenyl-carbonium ion as compared to the amount that occurs in the dimethyl-phenyl-carbonium ion. Comparison of Table 11 with Tables 8 and 10 indicate more scrambling in the ethyl-phenyl-carbonium ion than in the dimethyl-phenyl-carbonium ion at 70eV, but less at 16eV. This may indicate that the scrambling between alpha and ring hydrogen atoms is favored over scrambling between

beta and ring hydrogen atoms at higher eV, but the reverse is true at lower eV. Another plausible explanation would involve different mechanisms for scrambling in dimethyl-phenyl-carbonium ions and ethyl-phenyl-carbonium ions.

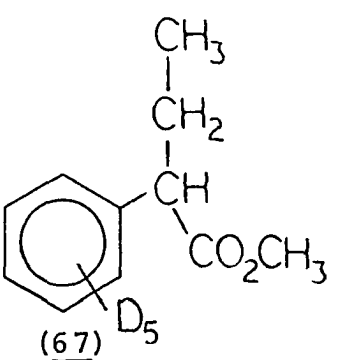
Compounds (65), (66) and (67) were prepared and their mass spectra (see Figures 32-34) were investigated to see if, as observed for the dimethyl-phenyl-carbonium ion, the scrambling was independent of the group lost. However, these



(65)



(66)



(67)

compounds lose both $\cdot CO_2CH_3$ and HCO_2CH_3. The loss of methyl formate in similar systems has recently been observed (63). At 70eV, the M-$\cdot CO_2CH_3$ ion is four times as intense as the M-HCO_2CH_3 ion in compounds (65), (66) and (67) but at 12eV the ratio of the M-$\cdot CO_2CH_3$ ion to the M-HCO_2CH_3 ion is 6:5. The M-HCO_2CH_3 is undoubtedly a precursor to part of the tropylium ions and thus the ratios observed for the m/e 91-93 ions of (66) and the m/e 94-96 ions of (67) represent a combination of mechanisms I and II of Scheme 17 and the tropylium ion formed from the M-HCO_2CH_3 ion. These observations may

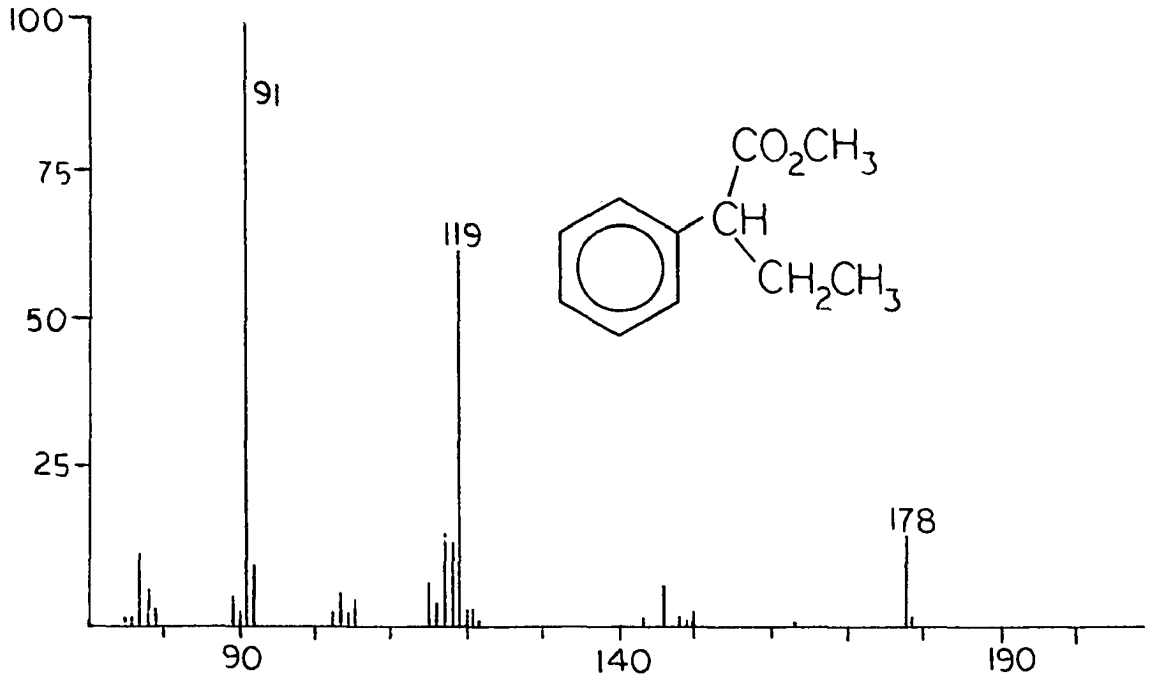


Figure 32. Mass spectrum of methyl-2-phenyl-butyrate

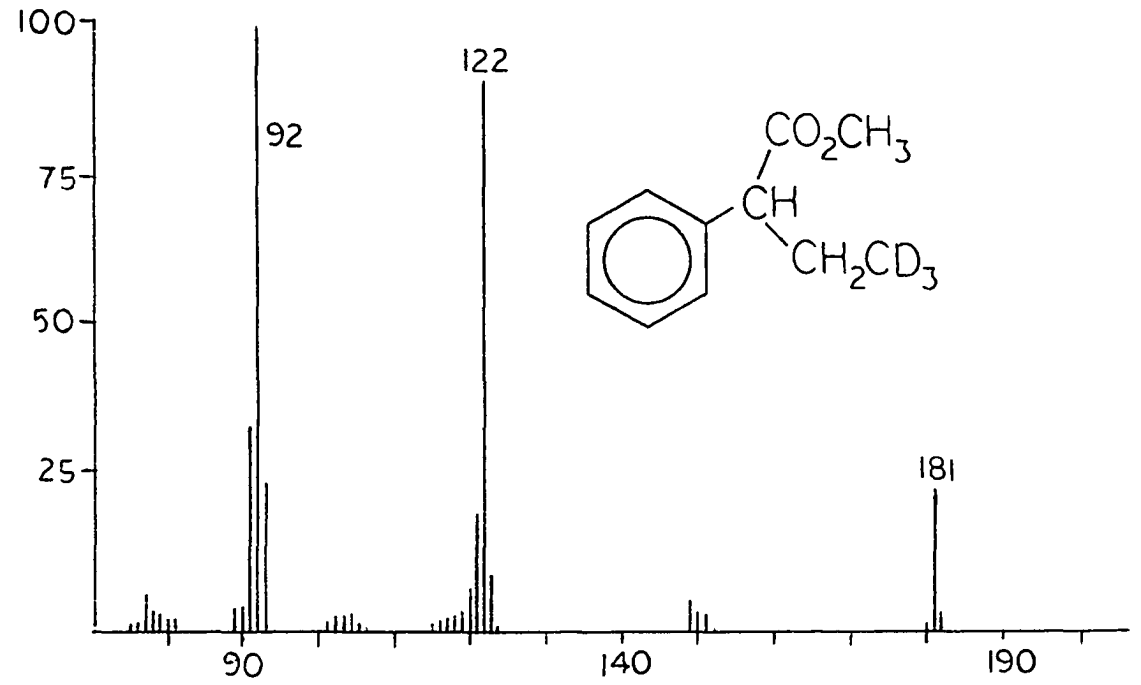


Figure 33. Mass spectrum of methyl-4,4,4-d_3-2-phenyl-butyrate

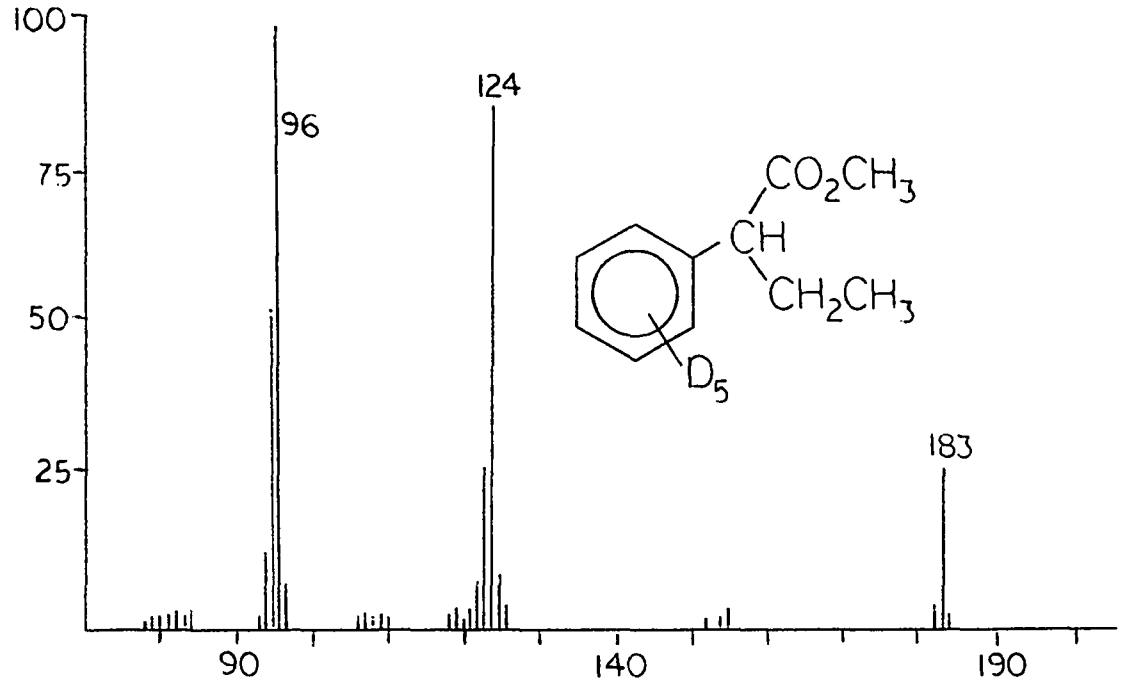


Figure 34. Mass spectrum of methyl-2-phenyl-d_5-butyrate

also be pertinent to the recent studies of Nibbering and DeBoer who have generated $\phi\overset{+}{C}HCH_2CH_3$ cations by the loss of a functional group (48, 49).

The Diethyl-Phenyl-Carbonium Ion

It was next decided to investigate the proposed phenylated dimethyl cyclopropane intermediate (4, Chapter 10) to see if ring and side chain hydrogen atoms were scrambled prior to propylene and butylene loss. Compounds (68), (69) and (70) were chosen as precursors to the diethyl-phenyl-carbonium ion because of the experimental ease in obtaining the labelled compounds and the spectra (see Figures 35-37)

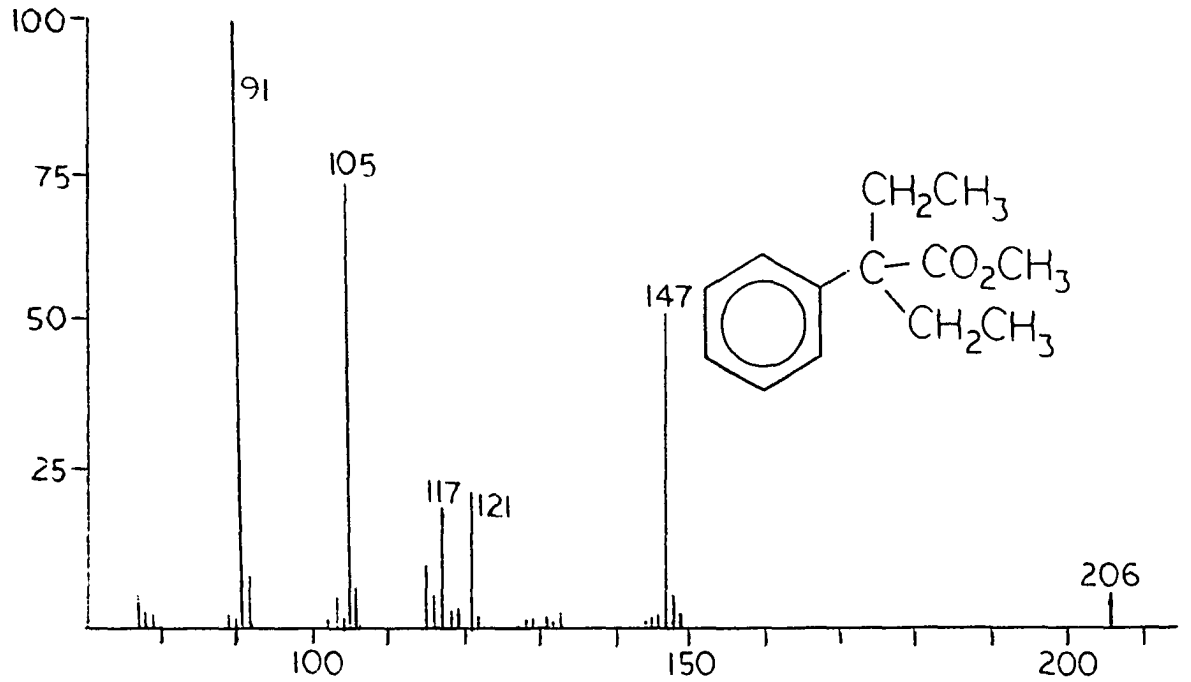


Figure 35. Mass spectrum of 3-carbomethoxy-3-phenylpentane

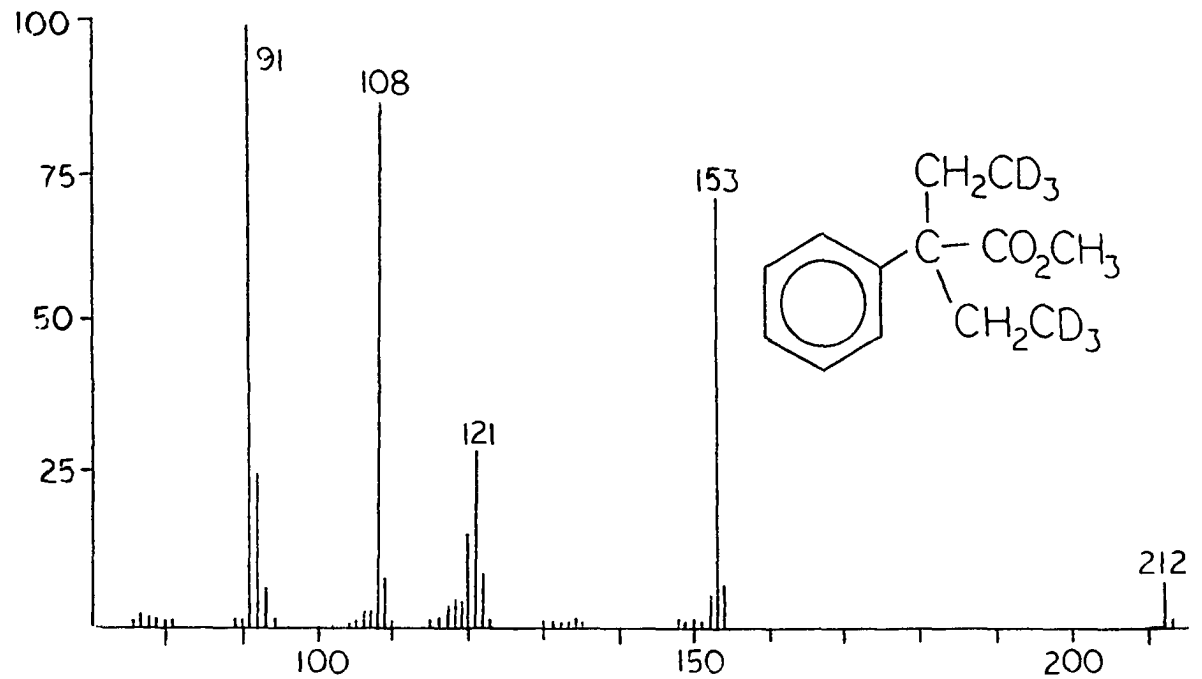


Figure 36. Mass spectrum of 3-carbomethoxy-3-phenylpentane-1,1,1,5,5,5-d_6

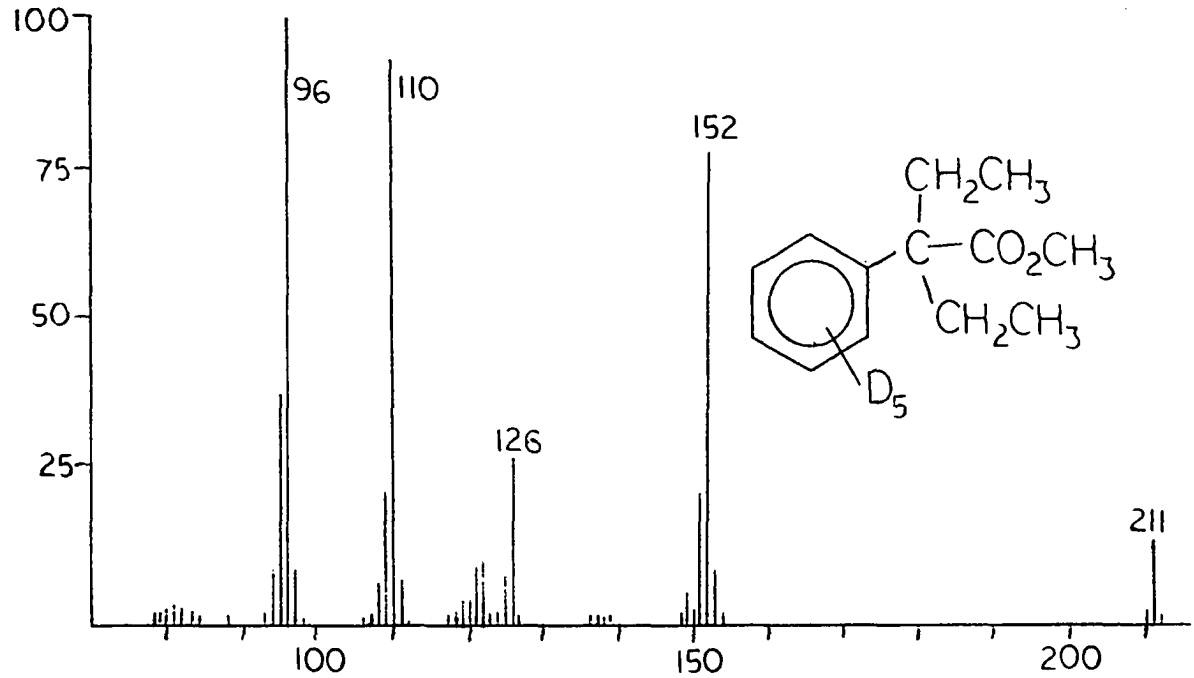
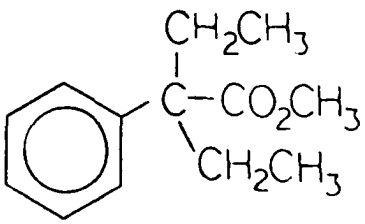


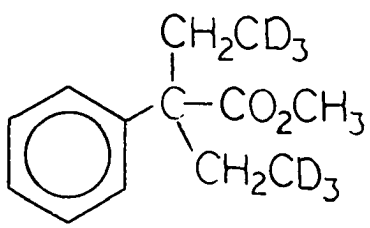
Figure 37. Mass spectrum of 3-carbomethoxy-3-phenyl-d_5-pentane

indicated only a small M-HCO_2CH_3 ion compared to that observed in the spectra of (65), (66) and (67).

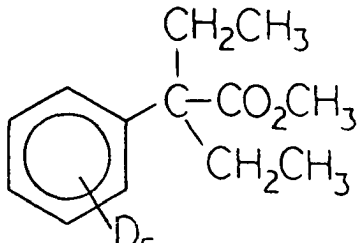
Compound (69) showed the expected 6 a.m.u. shift in the molecular ion and the M-·CO_2CH_3 ion as compared to compound (68). The m/e 105 ion of (68) was shifted cleanly to m/e 108 in (69), but the tropylium ion was 81% m/e 91, 14% m/e 92 and 5% m/e 93. A path such as that shown in Scheme 35



(68)



(69)

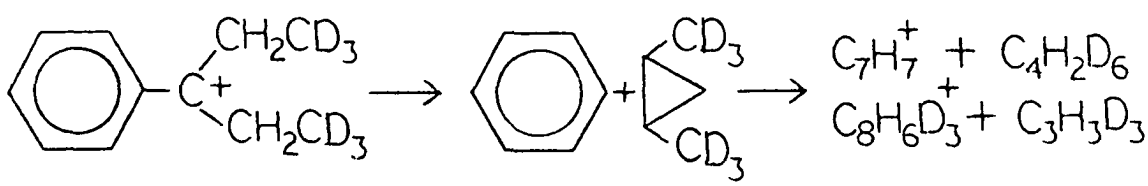


(70)

would produce only m/e 91 tropylium ions. Results obtained

with 3-phenylpentane-1,1,1,5,5,5-d_6 indicated that ring and gamma hydrogen atoms did not scramble and this is further substantiated by the formation of only m/e 108 ions in the spectrum of (69). This implies that the m/e 92 and m/e 93 tropylium ions arise from another source. It was previously observed that the mass spectrum of 3-ethyl-3-phenylpentane-1-d showed a 6% m/e 92 tropylium ion and the source was rationalized as the metastable loss of C_2H_4 from $C_9H_{10}D^+$ ions. This process was also observed in the spectrum of (68) and thus the $C_9H_{11}^+$ ion, the M-·CO_2CH_3 ion and the hydrocarbon ions of m/e 121, 117 and 115 of (68) are all possible precursors to the m/e 92 and 93 tropylium ions in (69). Not unexpectedly, the m/e 92 and 93 ions decrease at lower electron energies.

Table 13 shows the ratios observed for the m/e 108, 109 and 110 ions and the m/e 94, 95 and 96 ions (corrected for natural abundance carbon-thirteen, a 17.1% d_4 impurity and a 1.6% d_3 impurity) in the mass spectrum of (70). The scrambling observed in this system appears to be less than in the other systems studied. This may be due to the steric interference of the bulky methyl groups which could act to hinder the scrambling of the ring and beta hydrogen atoms.



Scheme 35. Formation of m/e 91 and m/e 108 in (69)

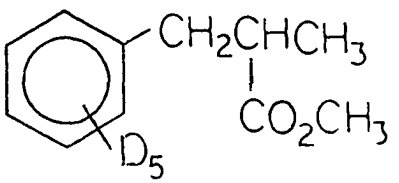
Table 13. Ratio of m/e 108-110 and m/e 94-96 in (70)[a]

m/e	70eV	20eV	18eV	16eV
110	1.00	1.00	1.00	1.00
109	.06	.03	.02	.02
108	.01	-	-	-
96	1.00	1.00	1.00	1.00
95	.12	.09	.07	.02
94	.02	.01	.01	-

[a]The ratio of m/e 110 to 96 is not 1.00 at any eV.

The Benzyl-Methyl-Carbonium Ion

The mass spectrum of compound (71) (see Figure 38) was examined and the main fragmentation was found to be loss



(71)

of HCO_2CH_3 rather than $\cdot CO_2CH_3$. Part of the tropylium ion formed is generated by the fragmentation of the M-HCO_2CH_3 ion and part is formed by simple beta cleavage which initially gives benzyl cations and these may rearrange to tropylium ions. The M-$\cdot CO_2CH_3$ has a relative intensity of 13% in (71) and apparently undergoes scrambling and rearrangement to a

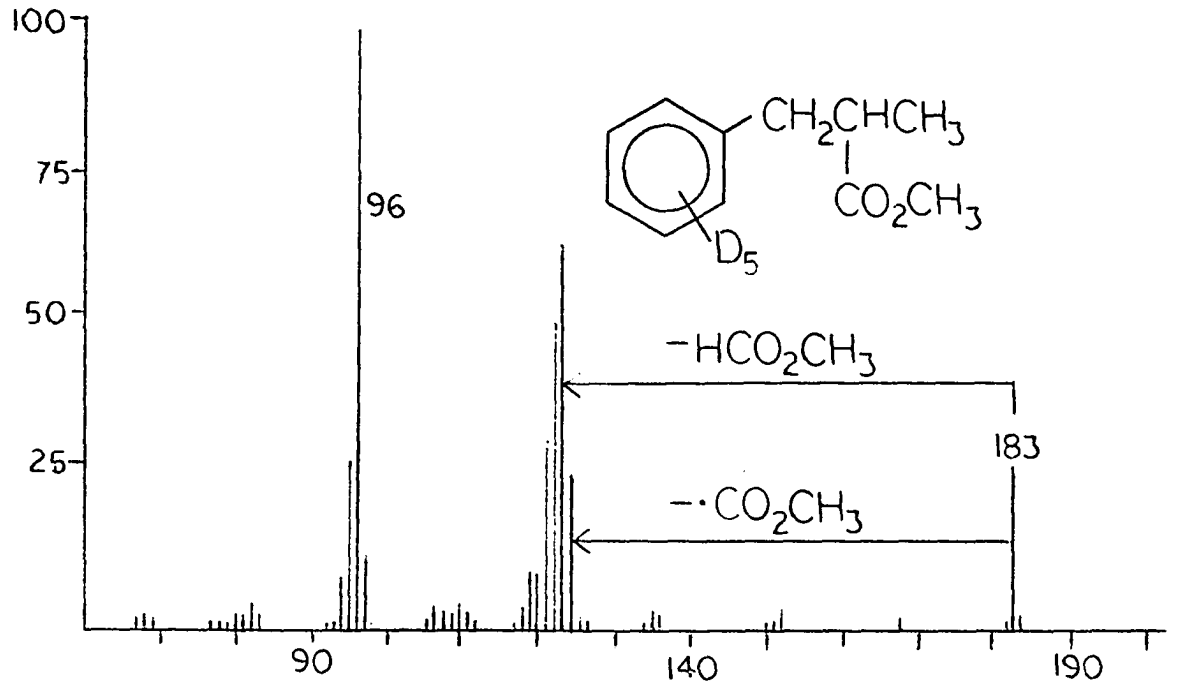
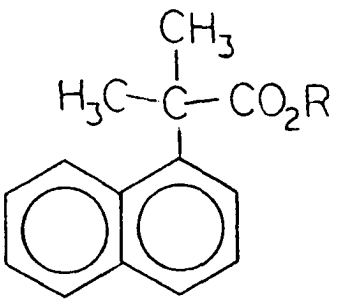


Figure 38. Mass spectrum of methyl-2-methyl-3-phenyl-d_5-propionate

phenylated cyclopropane prior to ethylene loss. The tropylium ion at 70eV was found to be 85% d_5, 11% d_4 and 4% d_3. This changed to 98% d_5 and 2% d_4 at 20eV and finally to 100% d_5 and 0% d_4 at 14eV. This decrease of scrambled tropylium ion parallels the decrease in importance of the M-$\cdot CO_2CH_3$ ion relative to the M-HCO_2CH_3. The amount of scrambling observed is again different and apparently is determined by the initial system. This system is the only one studied in which the group which is cleaved is not a benzylic group. This implies that many systems might undergo similar rearrangements but the detection will be difficult because of more favorable competing fragmentations.

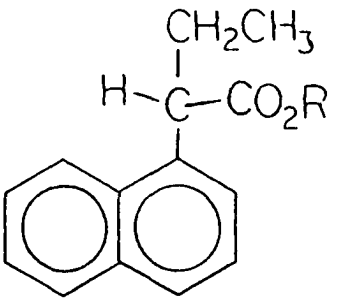
A Few Other Possible Arylated Cyclopropanes

The naphthalene compounds (72)-(77) were prepared and the mass spectra were recorded to determine if other arylated



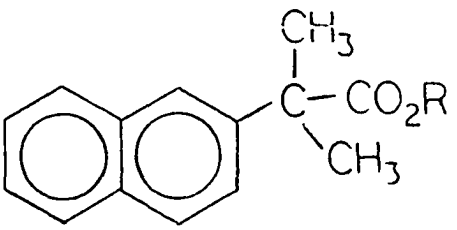
(72) R=H

(73) R=CH_3



(74) R=H

(75) R=CH_3



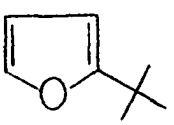
(76) R=H

(77) R=CH_3

cyclopropanes might exist in the mass spectrometer other than phenylated cyclopropanes. These compounds all showed loss of the $\cdot CO_2R$ group followed by ethylene loss. The ratio of the M-$\cdot CO_2R$ ion to the M-$\cdot CO_2R$-C_2H_4 ion in (72) and (73) was essentially the same as in (76) and (77) and thus the reaction was not affected greatly by position of the fragmenting group on the naphthalene ring. The ratio of the M-$\cdot CO_2CH_3$ ion to the M-$\cdot CO_2CH_3$-C_2H_4 ion in (72) and (73) did differ from the ratio observed in (74) and (75). This was also observed in the phenyl case. Although no labelling experiments were

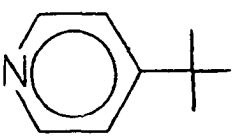
performed,a mechanism involving a naphthylated cyclopropane might be envisioned for ethylene loss from the M-·CO_2R ion. Presumably the same type of scrambling of ring and side chain hydrogen atoms previously observed could occur but probably to a different extent than that observed in the phenyl compounds.

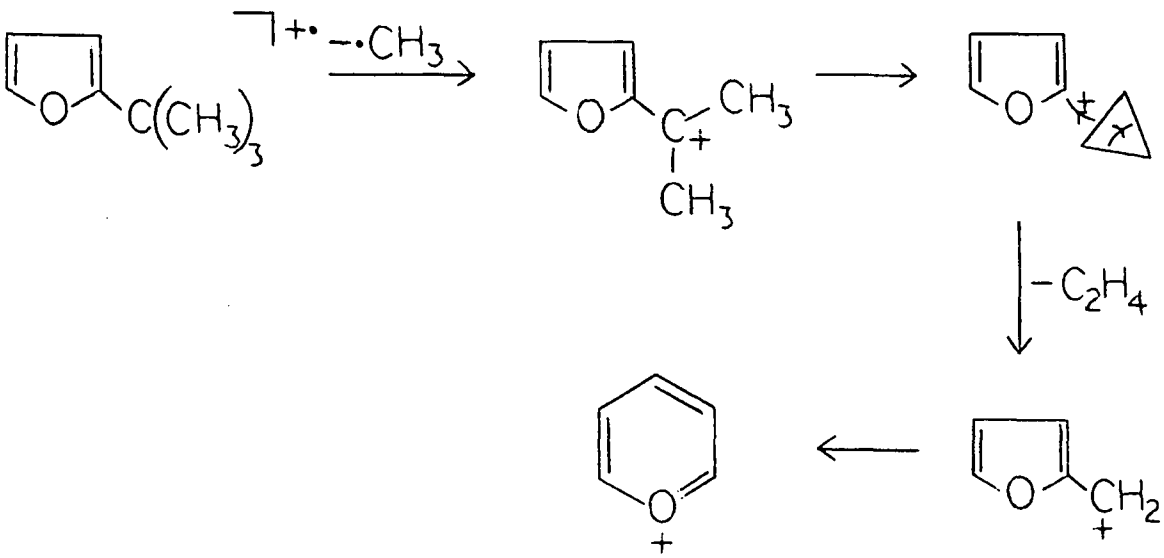
Commercial samples of 2-tert-butylfuran (78) and 4-tert-butylpyridine (79) were also subjected to mass spectral analysis to determine if heteroaromatic rings could also form arylated cyclopropanes in the mass spectrometer. The molecular ions of both compounds lost a methyl group and the M-·CH_3 ion then lost ethylene in a metastable process. Although no labelling experiments have been performed, a mechanism involving an arylated cyclopropane intermediate such as that shown in Scheme 36 could be envisioned. This mechanism could be coupled with a process that partially scrambles ring and side chain hydrogen atoms prior to ethylene loss. A ring expansion similar to that proposed in the last step of the mechanism in the furan case has previously been proposed (64). It has been pointed out that the M-·H ion of gamma-picoline may not undergo ring expansion such as that observed for the M-·H ion of toluene (65).



(78)

(79)





Scheme 36. Possible fragmentation mechanism in (78)

Formation of d_6 Products in Friedel-Crafts Alkylation of Benzene-d_6

The first attempt to prepare 2-methyl-2-phenyl-d_5-propionic acid by the alkylation of d_6-benzene with alpha-bromo-iso-butyric acid in the presence of anhydrous aluminum chloride resulted in the isolation of the desired product which was shown by mass spectrometry to contain a 15% d_6 impurity. The mass spectral fragmentation pattern further established that the impurity contained five ring deuterium atoms while the sixth deuterium atom was incorporated in the methyl group. A 20% d_6 impurity was obtained in the first attempt to prepare 2-methyl-2-phenyl-d_5-propane by the alkylation of d_6-benzene with tert-butylchloride in the presence of anhydrous aluminum chloride. The mass spectral fragmentation pattern established that there were five ring deuterium atoms and one methyl

deuterium atom. A similar difficulty had not been encountered in preparing the corresponding side chain labelled compounds.

The method of preparation had involved one major difference in that benzene was used in a very large excess compared to the labelled halides while only minimal amounts of d_6-benzene had been used for the preparation of the ring labelled compounds. It was decided to rerun the alkylation of d_6-benzene using about a ten molar excess of d_6-benzene as compared to the 2 or 3 molar excess used previously. Trial experiments with unlabelled benzene were performed to find the minimal reaction times and temperatures which would produce a reasonable yield of product. Using increased amounts of d_6-benzene and minimal reaction times and temperatures, the amount of d_6 product was reduced to .6% in the alkylation with alpha-bromo-iso-butyric acid and 10.3% with tert-butylchloride.

The exact conditions employed are reported in the experimental section. The mechanism for the formation of this unusual product is unknown. There does not appear to be any good precedent for this process in the literature.

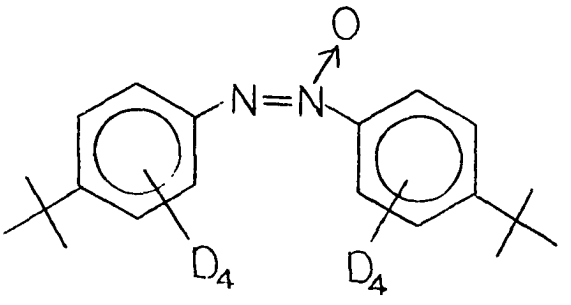
Loss of Ethylene from the M-·X Ion of iso-Propyl and tert-Butyl Substituted Compounds

Several possible mechanisms were previously proposed which might account for the way in which ethylene is lost from the m/e 119 ion of nitro and nitrosocumenes. Deuterium labelling

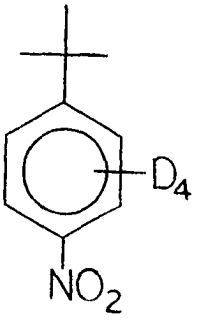
experiments established that a possible mechanism might involve a random hydrogen transfer from the side chain to the aromatic ring followed by rearrangement to a phenylated cyclopropane and fragmentation as such. Another possible mechanism involved an initial beta hydrogen transfer. The fact that precursors to phenylated cyclopropanes have been shown to undergo a partial scrambling of ring and side chain hydrogen atoms prior to rearrangement to the cyclopropane intermediate must be considered as part of either mechanism. This partial scrambling always results in the retention of more label in the tropylium ion when the label is initially in the side chain. On this basis an initial beta hydrogen transfer (mechanism d of Scheme 33) would be favored if the subsequent process following the hydrogen transfer to the ring is the partial scrambling of ring and side chain hydrogen atoms and finally rearrangement to the phenylated cyclopropane and fragmentation as such.

Several mechanisms were previously proposed for the loss of propylene and ethylene from the m/e 133 ion (M-•X) of substituted $XC_6H_4C(CH_3)_3$ compounds. The only mechanims which approached the observed ratio for the m/e 91:m/e 94 ions in compounds (35), (36) and (37) involved an initial intact methyl group transfer prior to loss of C_3H_6. The loss of C_2H_4 from the m/e 133 ion was also observed. However, the formation of ions at m/e 92, 93, 95, 96 and 111 in the

spectra of (35), (36) and (37) left all of the proposed mechanisms very much in doubt. Compounds (80) and (81) were prepared and as can be seen from Figures 39 and 40 a partial scrambling of ring and side chain hydrogen atoms is involved



(80)



(81)

in the loss of ethylene and propylene from the M-·X ion. There is considerable, but far less than complete, scrambling of ring and side chain hydrogen atoms and it is conceivable that this might account for the ratios observed for the m/e 91-97 and m/e 107-111 regions in compounds (35), (36) and (37). Deuterium labelling data establishes that the actual mechanism for these fragmentations is very complicated.

Nitrogen Atom Loss in Nitrosoanisoles

Probably the most unique fragmentation of the nitroso compounds studied is the direct expulsion of a nitrogen atom from the molecular ion. The aralkyl nitroso compounds were found to give only very small M-·N ions which were all less than five percent relative intensity. However, this

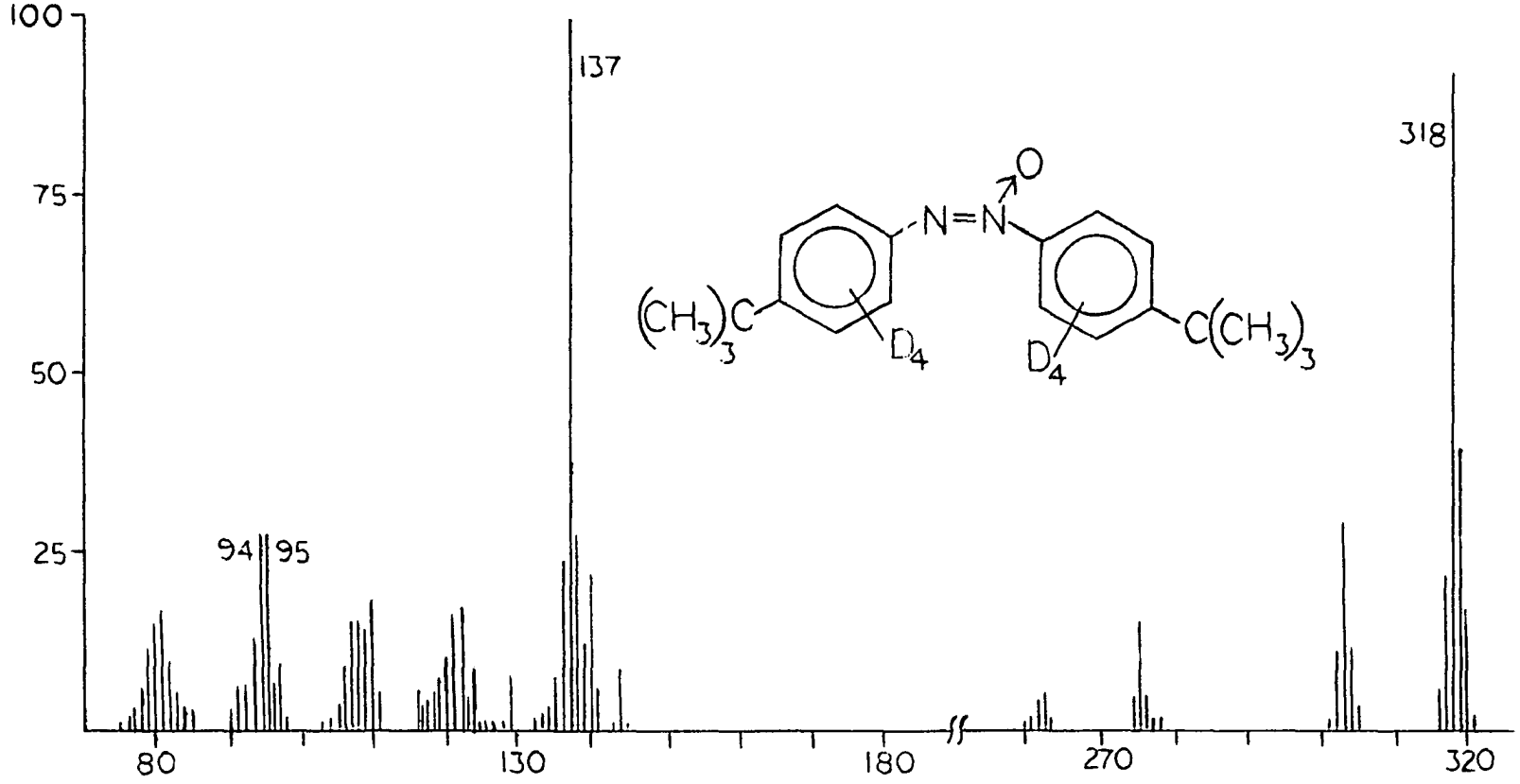


Figure 39. Mass spectrum of 4,4'-di-tert-butyl-2,3,5,6,2',3',5',6'-d_8-azoxybenzene

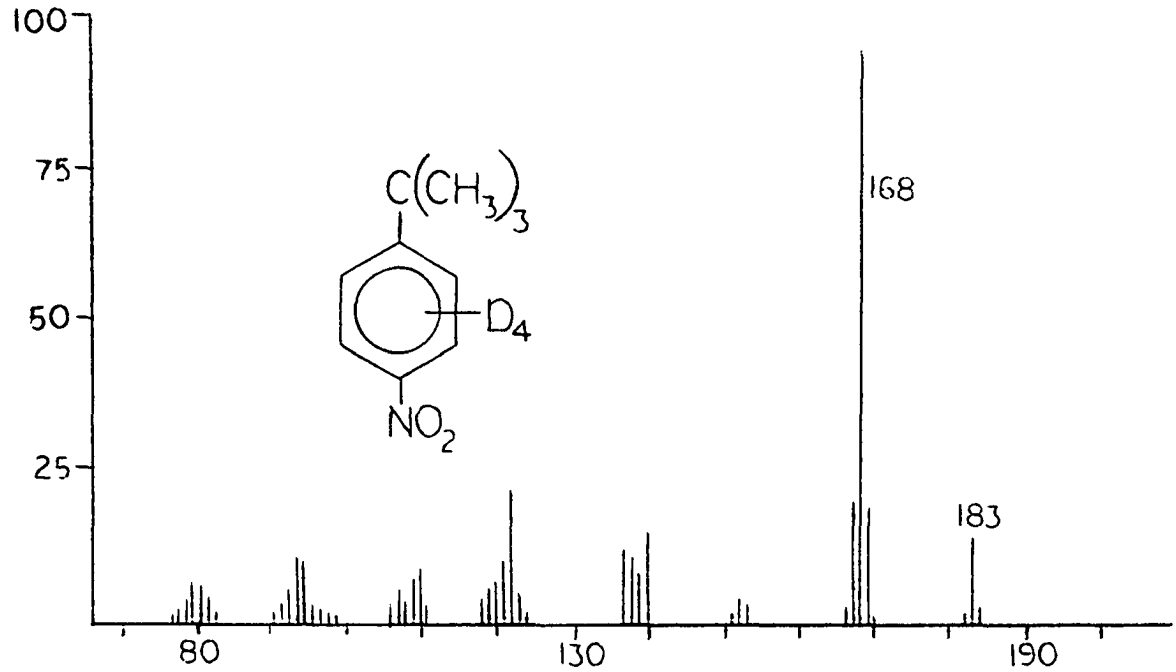


Figure 40. Mass spectrum of 4-nitro-2,3,5,6-d_4-tert-butylbenzene (source temp. +150°)

fragmentation was found to be very important in the mass spectra of nitrosoanisoles. The interest in these compounds originated when pronounced differences in the spectra were noted which were dependent on the method of sample insertion into the source of the mass spectrometer. The initial studies indicated that the loss of a nitrogen atom from the molecular ion of nitrosoanisoles could be thermally enhanced in the mass spectrometer. The loss of a nitrogen atom from the molecular ion of aralkyl nitroso compounds could not be thermally enhanced. This unusual process may be related mechanisticly to the well known nitro-nitrite rearrangement observed in aryl nitro compounds (26).

In Table 14 the intensities of the abundant ions of ortho, meta and para-nitrosoanisole obtained under direct insertion (no heat) and heated (200°C) inlet conditions are compared.

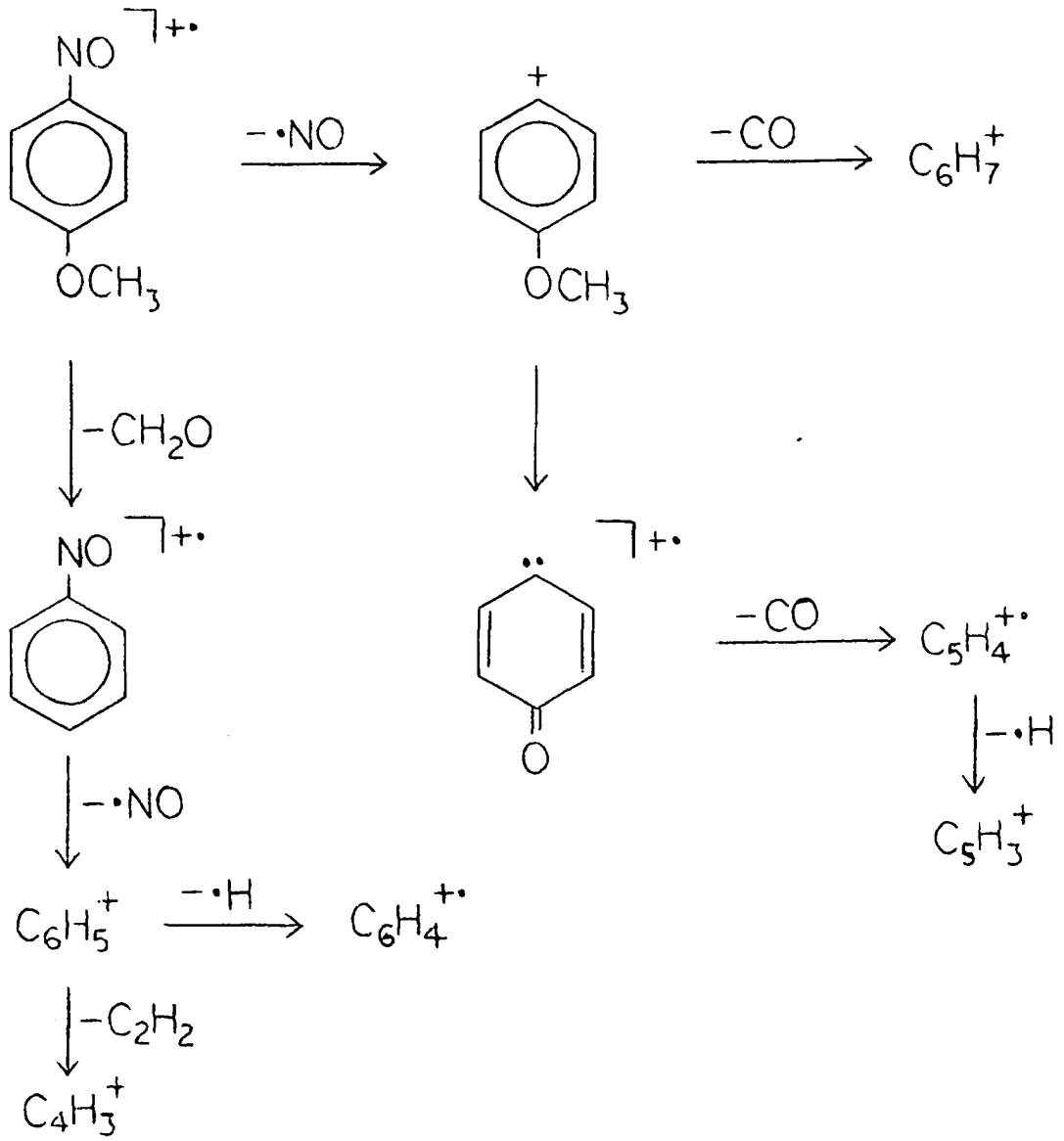
Table 14. 70eV mass spectra of ortho, meta and para-nitrosoanisole using direct insertion inlet and heated (200°C) inlet systems

m/e	ortho direct (heated)	meta direct (heated)	para direct (heated)
137	94 (31)	85 (89)	97 (27)
135	- (5)	- Trace	- (7)
123	2 (49)	Trace (8)	<1 (73)
122	Trace (2)	Trace (1)	<1 (3)
121	1 (5)	Trace (Trace)	<1 (2)
120	3 (6)	Trace -	Trace (1)
119	- (16)	- -	- -
109	6 (6)	- -	- (9)
108	27 (69)	5 (6)	5 (100)
107	1 (1)	62 (55)	63 (31)
106	2 (5)	2 (2)	2 (2)
105	1 (-)	- (-)	- (-)
93	12 (15)	6 (10)	6 (3)
92	100 (66)	74 (85)	79 (31)
91	2 (10)	1 (1)	- (13)
80	41 (74)	Trace (3)	3 (30)
79	99 (46)	6 (5)	5 (4)
78	24 (17)	11 (11)	10 (5)
77	100 (100)	100 (100)	100 (29)
76	20 (9)	11 (10)	11 (4)
75	12 (-)	6 (-)	6 (-)
65	11 (20)	4 (6)	4 (10)
64	90 (44)	50 (57)	47 (15)
63	80 (43)	31 (34)	30 (12)
62	21 (15)	10 (8)	8 (5)
53	19 (27)	7 (7)	8 (17)
52	42 (34)	5 (5)	13 (14)
51	84 (50)	18 (16)	21 (8)

The fragmentations using the direct inlet system are characteristic of aryl nitroso and aryl methoxyl groups and Scheme 37 shows the fragmentations observed for the meta and para isomers. The only unusual reaction is loss of carbon monoxide from m/e 107, an ion which high resolution mass spectrometry defines as a mixture of isobaric ions with compositions C_6H_5NO and C_7H_7O. The $C_7H_7O^+$ ion is the source of the m/e 79 ion and the process involves a methyl group migration to the electron deficient aromatic ring followed by carbon monoxide expulsion. Some precedent for this rearrangement was found by examining the mass spectra of the isomeric nitroanisoles and para-bromoanisole. The M-·NO_2 ion of the nitroanisoles and the M-·Br ion of para-bromoanisole show metastable losses of carbon monoxide.

An alternate major fragmentation of m/e 107 (C_7H_7O) is the loss of a methyl group to form m/e 92 (no m* observed), a relatively rare Even Electron ion → Odd Electron ion fragmentation process. The structure of the m/e 92 ion is well accommodated by the quinone-methide formulation (66) depicted in Scheme 37 since the observed subsequent loss of carbon monoxide (m* at m/e 44.6) could form an m/e 64 ion with the cyclopentadienylidene structure.

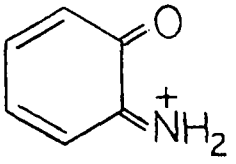
Ortho-nitrosoanisole exhibits distinct differences in its mass spectral chemistry as a result of ortho effects: (1) the m/e 107 ion is much less intense, possibly as a result



Scheme 37. Fragmentation of para-nitroanisole

of a more rapid loss of $\cdot CH_3$ to produce a more stable α-keto-carbene, (2) a new intense ion at m/e 108 (C_6H_6NO by HRMS) is present. This m/e 108 ion subsequently expels a molecule of carbon monoxide in a metastable process. The structure of this ion could reasonably be formulated as (82) although other

possibilities such as ring expansion certainly exist. The m/e 108 ion is not present in either the meta or para isomers when the direct insertion system is used.



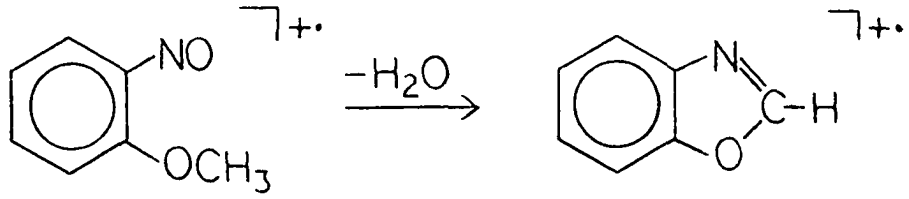
(82)

Pronounced thermal effects on the mass spectra of nitrosoanisoles are apparent from the data listed in Table 14. The loss of a nitrogen atom from the molecular ion becomes very important in the spectra of ortho and para-nitrosoanisole, but not the meta isomer. The m/e 123 ion in both the ortho and para compounds undergoes the loss of a methyl group to form the m/e 108 ion (m* observed). Therefore, when the compounds are inserted via a heated inlet system the m/e 108 ion in the ortho and para compounds must be at least in part an ion of composition $C_6H_4O_2$. This m/e 108 ion subseqeuntly expels a molecule of carbon monoxide in a metastable process to give the m/e 80 ion which further loses another molecule of carbon monoxide in a metastable process to give the m/e 52 ion. It can be noted from Table 14 that the ortho and para compounds both show more intense m/e 80 ions on the heated inlet system. The most plausible structure for this m/e 108 ion would be a quinone structure. No meta-quinone isomer is possible, of course, and probably this explains the near

absence of thermal effects on the mass spectrum of meta-nitrosoanisole. Our efforts to measure the m/e 108 ion by high resolution mass spectrometry using a glass heated inlet system fails to give an m/e 108 ion in the para compound and gives only a C_6H_6NO ion in the ortho compound. In fact, the spectra recorded on the high resolution mass spectrometer using the glass heated inlet system were identical to those obtained using the direct insertion system of the CH4 spectrometer. Therefore, it is concluded that the pronounced effects were caused by metal catalysis in the heated inlet system. Metal catalyzed eliminations are not uncommon processes (14, p. 7). The absence of these effects in the direct inlet system and the heated glass inlet system further indicated that the expulsion of a nitrogen atom could be a thermally aided but not thermally initiated process. The mechanism of this observed nitrogen expulsion is not known but it can be noted that para-nitrosophenol, para-bromo-nitrosobenzene and para-nitroso-N, N-dimethylaniline all showed an increased loss of a nitrogen atom when inserted via a heated metal inlet system as opposed to direct insertion. None of these M-·N ions approached the magnitude of that observed in para-nitroso-anisole but it is significant that the common feature of all the groups studied is their ability to stabilize a quinone type structure by resonance. The driving force for this unusual elimination of nitrogen in ortho and para-nitroso-anisole is probably related to the stability of the product

ion formed.

Another thermally aided reaction is operating in ortho-nitrosoanisole to produce an m/e 119 ion by loss of the elements of water from the molecular ion. This reaction is an ortho effect elimination and the structure of the m/e 119 may be the well known benzoxazole structure. The m/e 119 ion loses CO to give m/e 91, a reaction which is characteristic of benzoxazole.



The mass spectra of 2-methyl-4-nitrosoanisole and 3-methyl-4-nitrosoanisole have also been examined. When the methyl group is ortho to the nitroso group one observes fragmentation characteristic of both ortho substituted aralkyl nitroso compounds and para-nitrosoanisole. When the methyl group is ortho to the methoxyl group the fragmentation is characteristic of only para-nitrosoanisoles. These compounds also undergo the thermally aided nitrogen elimination similar to a para-nitrosoanisole.

EXPERIMENTAL

Instruments and Methods

All medium resolution mass spectra were obtained on an Atlas MAT model CH4 single focusing mass spectrometer operated at 70 electron volts, 3000 volts accelerating potential and a total ionizing current in the range of 1-10 A. High resolution mass spectra were obtained using either an Atlas SMI-A or an AEI MS-902 spectrometer. Unless otherwise noted, medium resolution spectra were obtained by absorbing the liquid nitro and nitroso compounds on neutral alumina or crushed molecular seives and inserting into the ion source via the vacuum lock while the solid nitro and nitroso compounds were inserted directly into the ionization chamber. The remainder of the liquid samples investigated were run by vaporization into the stainless steel inlet system maintained at 120-140° and a source temperature of 180-220°.

Infrared spectra were obtained using either a Perkin-Elmer Model 21 spectrometer or a Beckman IR-12 spectrometer.

Nuclear magnetic resonance (nmr) spectra were obtained using a Varian Associates A-60 spectrometer or a Hitachi Perkin-Elmer R20B spectrometer. The solvent used to obtain the solution spectra is noted. The chemical shift values are reported in parts per million using delta values relative to the internal standard, tetramethysilane. The type of signal observed is reported as singlet (s), doublet (d), triplet (t),

quartet (q) or multiplet (m) and the number of hydrogen atoms represented by this signal is also given.

All gas liquid partition chromatography (glpc) was carried out on an F and M Model 500 gas chromatograph. Column material and operating conditions are reported for the individual compounds. Melting points were determined with a Kofler Hot Stage melting point apparatus and are uncorrected. Analyses were performed by Chemalytics Inc., Tempe, Arizona.

Source of Compounds

The necessary quantities of ortho-nitrotoluene, meta-nitrotoluene, para-nitrotoluene, ortho-nitro-ethylbenzene, 2-nitrobiphenyl, 2,6-dimethyl-nitrobenzene, 1-nitroso-2-naphthol, 2-nitroso-1-naphthol, ortho-nitroanisole, meta-nitroanisole, para-nitroanisole, tert-butylbenzene, 4-tert-butylpyridine, para-nitroso-N,N,-dimethylaniline, 2,2'-dinitro-biphenyl, 2-triflouromethyl-aniline, ortho-iodotoluene, 3-methyl-4-nitrosophenol and 2-methyl-4-nitrosophenol were obtained from Aldrich. Samples of para-nitrosophenol, ortho-nitrocumene, benzoxazole and 2-methyl-naphthalene were donated by Professor Glen Russell. Samples of para-nitro-nitroso-benzene and para-bromo-nitrosobenzene were donated by Dr. Phil Carpenter, a sample of 2-nitro-naphthalene was donated by Dr. Jeff Bechner and a sample of 1-nitroso-naphthalene was donated by Dr. John Stam. Consistent spectral properties were observed

for all of these compounds. The solid compounds were recrystallized prior to mass spectral analysis until the melting points were in agreement with literature values. The liquids were purified by glpc prior to mass spectral analysis.

Preparation of Compounds

General preparation of nitroso compounds

Many of the reported methods for the preparation of aromatic nitroso compounds give poor yields and unreproducible results. The desire to prepare aryl nitroso compounds with alkyl groups and deuterium labels led to an improved synthesis for many of the aralkyl compounds used in this study.

Various methods for the preparation of aromatic nitroso compounds have been reported. Amines may be oxidized directly to nitroso compounds by Caro's acid (67, 68) or peracetic acid (69). Nitro compounds may be reduced to hydroxyl amines (70) and the crude hydroxyl amine can then be oxidized without isolation to the nitroso compound by potassium dichromate (70), silver oxide (71) or ferric chloride (72). Procedures involving Caro's acid are sometimes difficult to reproduce and the yields are generally poor. If alkyl side chains larger than methyl are present in the molecule, procedures involving Caro's acid, peracetic acid and potassium dichromate appear to be useless.

The best yields of aryl nitroso compounds of reasonable

initial purity were obtained by the following modification of the ferric chloride method (72). In a typical preparation, 35 to 40 mmoles of the corresponding nitro compound are dissolved in 20 to 25 ml of ethanol and a solution of 20 mmoles of NH_4Cl dissolved in 5 to 10 ml of distilled water is added. The temperature is raised to 65° by an oil bath and 160 mmoles of zinc dust is added to the vigorously stirred solution. The heat of reaction raises the temperature of the solution to reflux, where it is maintained for 8 to 10 minutes. The solution, which has changed from yellow to colorless during this time, is filtered to remove unreacted zinc and zinc salts. The residue is washed at once with approximately 20 ml of a 50/50 mixture of hot water and ethanol, and the filtrate and washings are allowed to cool before being rapidly poured into 300 ml of an ice cold 5% solution of ferric chloride. Small pieces of ice are added, as necessary, to maintain a temperature between 5 and 10°C. The nitroso compound usually separates within one to two minutes but the solution is kept cold until it appears that product formation is complete. The solution is filtered and the product is purified by steam distillation, recrystallization (usually from ethanol), sublimation or a combination of these. Sublimation appears to be an excellent final purification method for preparing small quantities of material for spectral analysis (73). Some nitro compounds, such as 2-nitrobiphenyl, are

rather insoluble in ethanol, and cellosolve may be employed as a solvent medium. These quantities of materials appear to be ideal for control of the zinc reduction.

The following compounds were prepared by the above procedure:

ortho-nitrosotoluene: mp 72-73° (lit. (74) mp 72.5°)

meta-nitrosotoluene: mp 52-53° (lit. (75) mp 53-53.5°)

meta-nitrosotoluene: mp 47-48° (lit. (76) mp 48.5°)

ortho-nitroso-ethylbenzene: mp 59-60° (lit. (77) mp 61°)

ortho-nitrosocumene: mp 44-45° Anal. Calcd. for $C_{18}H_{22}N_2O_2$: C, 72.45; H, 7.44. Found: C, 72.31; H, 7.51.

2,6-dimethyl-nitrosobenzene: mp 141-42° (lit. (78) mp 141.5°)

meta-nitrosoanisole: mp 78-80° (lit. (79) mp 80°)

2-nitrosobiphenyl: mp 100-01° (lit. (80) mp 101°)

para-Nitrosocumene

The isolation and purification steps of the general procedure were modified because the product is a liquid. Only small amounts of a solid which rapidly decomposed was formed in the ferric chloride oxidation. However, the reaction mixture appeared to be dark green and upon extracting with two 100 ml portions of ether and removal of the ether by evaporation under reduced pressure a green oil was isolated. This was chromatographed on silica gel using Skelly B as an eluent. Two fractions were collected, the first of which proved to be a mixture of the starting nitro compound and the

desired product while the second fraction gave a 30% yield of the crude nitroso compound. This was purified for mass spectral and carbon hydrogen analysis by glpc using an LAC 446 column operated at 120°.

Anal. Calcd. for $C_9H_{11}NO$: C, 72.45; H, 7.44, Found: C, 72.51; H, 7.20.

2,4-Dinitro-tert-butylbenzene

Tert-butylbenzene was nitrated by the method of Biekart (81) and following workup an nmr spectrum of the product indicated a mixture of 4-nitro-tert-butylbenzene and 2,4-dinitro-tert-butylbenzene. The nitrated product was then subjected to the same nitrating conditions two more times and 2,4-dinitro-tert-butylbenzene was obtained in 53% yield following recrystallization from ethanol. The nmr spectrum (CCl_4) showed the following resonances: 1.43 (s, 9H); 7.68-8.5 (m, 3H), mp 60-61° (lit. (81) mp 60-61°).

4-Amino-2-nitro-tert-butylbenzene (81)

A solution of 55 g of $Na_2S \cdot 9H_2O$ and 7 g of sulphur in 85 ml of water was added dropwise over 1 1/2 hours to a vigorously stirred suspension of 25 g of 2,4-dinitro-tert-butylbenzene (.11 mmole) and 100 ml of water at 80°. The reaction mixture was stirred for two more hours at reflux and then cooled and extracted with ether. The etheral extract

was washed with three 300 ml portions of 3N hydrochloric acid. The acid solution was cooled and the amine hydrochloride salt precipitated and was collected by filtration. The amine hydrochloride salt was added to a mixture of concentrated ammonium hydroxide and ether. Evaporation of the ether under reduced pressure yielded 12.3 g (.064 mmole) of the free amine (57%). The nmr spectrum (CCl_4) showed the following resonances: 1.35 (s, 9H); 6.38-7.27 (m, 3H); 4.0 (broad s, 2H).

ortho-Nitro-tert-butylbenzene (81)

To a solution of 12 g of 4-amino-2-nitro-tert-butylbenzene (.062 mmole) in 36 ml of absolute ethanol was added 9.3 ml of concentrated sulfuric acid and the resulting mixture was cooled to near 0°C. The reaction mixture was allowed to warm to room temperature very slowly and finally was heated on the steam bath for 15 minutes. Then the reaction mixture was cooled to room temperature and extracted with 250 ml of ether. The etheral solution was washed with 200 ml of 10% sodium hydroxide and 200 ml of water, dried ($MgSO_4$) and the ether evaporated under reduced pressure yielding 5.54 g (.031 mole) of crude o-nitro-tert-butylbenzene (50%). The product was purified for mass spectral analysis by glpc using an LAC 446 column operated at 165°C. The nmr spectrum showed the following resonances: 1.40 (s, 9H); 7.1-7.7 (m, 4H).

ortho-Nitroso-tert-butylbenzene

The usual method of preparation was employed with the exception of the purification procedure. The mixture formed by adding the filtrate from the zinc reduction to the ice-cold ferric chloride solution was extracted with three 100 ml portions of ether. The ether was evaporated under reduced pressure and the crude product was chromatographed on silica gel using Skelly B as an eleunt. The desired product separated nicely from the crude mixture but an attempt to purify the product by glpc resulted in decomposition of the product. The product, which was a green oil, was purified for mass spectral and carbon-hydrogen analysis by rechromatographing on silica gel and drying under vacuum.

Anal. Calcd. for $C_{10}H_{13}NO$: C, 73.58; H, 8.03.
Found: C, 73.67; H, 7.63.

para-Nitroso-tert-butylbenzene

The usual method of preparation was employed with the exception of the isolation and purification procedure. The solid product obtained from the ferric chloride oxidation was collected and recrystallized from absolute ethanol but proved (mass spectrometry) to be 4,4-'-di-tert-butylazobenzene (m.p. 176-77°). Extraction of the filtrate from the ferric chloride reaction mixture with two 200 ml portions of ether yielded a green oil following evaporation of the

ether under reduced pressure. This oil was stored at 0° for two days during which time more of the azo compound solidified. This was filtered off and the remaining product was chromatographed on silica gel using Skelly B as an eleunt. Two fractions were collected, the first of which proved to be a mixture of the starting nitro compound and the desired nitroso compound. The second fraction produced a 16% yield of the light green liquid nitroso compound. The product was purified for mass spectral and carbon-hydrogen analysis using an LAC 446 column operated at 165°. The nmr spectrum of the crude product (CCl_4) showed the following resonances: 1.35 (s, 9H); 7.45-7.89 (AB m, 4H).

Anal. Calcd. for $C_{10}H_{13}HO$: C, 73.58; H, 8.03.
Found: C, 73.43; H, 7.78.

Toluene-α,α,α-d_3

Using the method of Renard and Leitch (82), 400 ml of anhydrous ether, 65 g of CH_3CO_2D (prepared by refluxing a mixture of deuterium oxide and freshly distilled acetic anhydride for 4 hours followed by fractionation (83)) and 60 g of zinc dust were placed in a three-necked flask equipped with a reflux condensor, addition funnel and mechanical stirrer and cooled by an external ice bath. A solution of 39.2 g of benzotrichloride (.2 mmole) dissolved in 200 ml of anhydrous ether was added over a four hour period. The addition funnel

was replaced with a reflux condensor and the reaction mixture was allowed to reflux for four more hours, cooled to room temperature and 400 ml of water was slowly added. The etheral solution was then extracted with three 200 ml portions of water, dried ($CaCl_2$) and the ether was removed by evaporation under reduced pressure. The product was then fractionated to give 11.3 g of pure product (65%).

ortho-Nitrotoluene-α,α,α-d_3

Using the method of Knowles and Norman (84), 10 g of toluene-α,α,α-d_3 (.106 mole) was slowly added to a vigorously stirred mixture of 5.5 g of conc. sulfuric acid and 2.5 g of water. The temperature was maintained below 10° for 10 minutes and then a mixture of 12.6 g of conc. sulfuric acid, 7.7 g of conc. nitric acid and 3 g of water was added dropwise at a rate which kept the temperature at 10°. The reaction mixture was kept at 10° for 15 more minutes, then allowed to warm to room temperature and 200 ml of water was added. The reaction mixture was then extracted with two 200 ml portions of ether and the combined etheral extracts were washed with 100 ml portions of water, sodium carbonate and water. Glpc analysis on an LAC 446 column operated at 165° showed 60% ortho, 3% meta and 37% para-nitrotoluene-α,α,α-d_3 present in 86% overall yield. Following preliminary partial vacuum distillation, this mixture was separated into the pure ortho

and para compounds by glpc. Low voltage mass spectrometry established the following label incorporation in the product: 81% d_3, 19% d_2.

ortho-Nitrosotoluene-α,α,α-d_3

This compound was prepared from the corresponding labelled nitro compound in 83% yield by the procedure previously described. The mp of the product after recrystallization from ethanol and sublimation was 72-72.5° and the mixed melting point with the non-deuterated compound was not depressed. Low voltage mass spectrometry established the following label incorporation in the product: 81% d_3, 19% d_2.

Cumene-α-d

Treatment of alpha-methyl-styrene with methanol and a few drops of 70% perchloric acid according to the method of Ziegler (85) gave, following workup and distillation, a 68% yield of 2-methoxy-2-phenylpropane. This compound was then used to prepare cumene-α-d by the following modification of Ziegler's procedure. A three-neck flask equipped with reflux condenser, dropping funnel, magnetic stirring bar and thermometer was evacuated and purged with dry nitrogen. Dry heptane (250 ml, freshly distilled from sodium hydride) was placed in the flask, 15.6 g of potassium (.4 mole) was added, and the flask and contents were heated to 70° using an oil bath. Then 33 g of 2-methoxy-2-phenylpropane (.22

mole) was added during one hour such that a temperature between 65 and 72° was maintained. After 1 1/2 hours at this temperature, a thick bright purple suspension had formed and no further reaction was visible during the next three hours. A solution of 10 g of deuterium oxide (.5 mole) in 50 ml of dry THF was added during 1 hour and the mixture gradually turned colorless as stirring was continued for a total of three hours. Water was added and the organic layer was separated and dried over magnesium sulfate. Cumene-α-d_1 was recovered by fractional distillation in 64.7% yield. Low voltage mass spectrometry established the following label incorporation in the product: 84% d_1; 16% d_0.

ortho and para-Nitrocumene-α-d

Cumene-α-d (11.36 g, .094 mole) was placed in a three-necked flask equipped with a power stirrer, dropping funnel and thermometer. A mixture of 8.6 g of 68% HNO_3 (.094 mole) and 14.7 g of 98% H_2SO_4 (.147 mole) was added dropwise during 1 1/2 hours with vigorous stirring. The temperature was maintained at 15-25°C during the addition. The reaction mix--ure was poured onto 200 g of cracked ice and extracted with 200 ml of ether. The ethereal extract was washed with two 50 ml portions of saturated $NaHCO_3$ and two 50 ml portions of water, dried over magnesium sulfate and concentrated. Glpc analysis using a LAC 446 column operated at 180° showed

cumene-α-d (4%) ortho-nitrocumene-α-d (25%) meta-nitrocumene-α-d (1%) and para-nitrocumene-α-d (70%). The ortho and para isomers were collected by glpc. Low voltage mass spectrometry established the following label incorporation in both compounds: 83% d_1; 17% d_0.

ortho-Nitrosocumeme-α-d

A mixture of 150 mg of ortho-nitrocumene-α-d, .03 g of ammonium chloride, 3 ml of ethanol and 1 ml of water was warmed by a steam bath to near reflux. Then .25 g of zinc dust was added and the mixture was vigorously stirred at or near reflux for 15 minutes. During this time, a solution of 2 ml of ethanol and 1 ml of water was added four times in order to replenish the solvents which were lost to evaporation. The unreacted zinc and zinc salts were filtered off and the residue was washed with 3 ml of warm ethanol. The washings and filtrate were then poured into 15 ml of an ice cold 5% ferric chloride solution. A 51% yield of the crude nitroso compound, which separated very slowly, was collected by filtration and had a melting point of 40-44°C. Washing this product with three 10 ml portions of hexane gave a colorless product melting from 43-44°. The mixed melting point with the unlabelled compound was not depressed. Low voltage mass spectrometry established the following label incorporation in the product: 83% d_1; 17% d_0.

para-Nitrosocumene-α-d

This compound was prepared by the same procedure as that used for the preparation of ortho-nitrosocumene-α-d. The crude product was purified by the method used for purification of para-nitrosocumene. Low voltage mass spectrometry established the following label incorporation in the product: 83% d_1; 17% d_0.

para-Nitrocumene

Cumene was nitrated and the para isomer was separated and purified as described on page 150.

para-Nitro-tert-butylbenzene

Tert-butyl benzene was nitrated and the para isomer was separated and purified as described on page 150.

ortho-Nitroanisole

Using a modification of the method of Lutz and Lytton (77), a flask containing 15 g of conc. sulfuric acid was cooled to 5° by an external ice bath and 10 g of potassium persulfate was added and stirred for 1 hour. The mixture was then added slowly to 300 ml of water containing enough ice to maintain a temperature of 0-5°C. This solution was neutralized with solid sodium carbonate, then made slightly acid (pH 6.4-6.6) with glacial acetic acid. Then 5 g of ortho-

anisidine was added and the reaction mixture was vigorously stirred for 20 minutes at 0-5°. The solid product was filtered (1.2 g, 21%) and recrystallized twice from ethanol. mp 101-02° (lit. (77) mp 101.5°).

ortho-Trifluoromethyl-nitrosobenzene

Caro's acid was prepared by the same method used in the preparation of ortho-nitrosoanisole and ortho-trifluoromethylaniline was added and the reaction mixture was stirred for 4 hours at 0-15°. The product, which was collected by filtration and recrystallized from ethanol, was obtained in a 63% yield. The nmr spectrum ($CDCl_3$) showed the following resonances: 6.28 (m, 1H); 7.44-8.14 (m, 3H), mp 61.5-62.5°.

Anal.: Calcd. for $C_{14}H_8F_6N_2O_2$: C, 48.01; H, 2.30.
Found: C, 47.80; H, 2.30.

para-Nitroanisole

Following the method of Hays, DeButts and Young (86), 10 g of para-nitrosophenol, 10 ml of methanol and 41 ml of toluene were placed in a 500 ml two-necked flask equipped with thermometer, magnetic stirring bar and vacuum distillation take off. The system was purged with nitrogen, brought to 45° and then .2 ml of conc. sulfuric acid added. After one hour the reaction mixture was neutralized with 1.3 ml of 1.5 N sodium hydroxide and diluted with 125 ml of toluene. Methanol and water

were removed by vacuum distillation of the toluene azeotropes. The reaction mixture was filtered, the phenol filtercake was washed three times with 50 ml portions of toluene, and the toluene was removed by vacuum distillation. The residue was dissolved in pentane, cooled to 0° and the product separated as beautiful blue-green crystals. The crystals were filtered rapidly and by keeping the product cold, it was possible to measure the melting point as 24-25° (lit. (86) 25°). The nmr spectrum (CCl_4) showed the following resonances: 3.9 (s, 3H); 6.81 (m, 2H); 7.8 (m, 2H).

3-Methyl-4-nitroanisole

This compound was prepared by the same method used for the preparation of para-nitrosoanisole. The nmr spectrum (CCl_4) showed the following resonances: 3.26 (s, 3H); 3.89 (s, 3H); 6.21-6.92 (m, 3H), mp 22-23° (lit. (87) 22°).

2-Methyl-4-nitrosoanisole

This compound was prepared by the same method used for the preparation of para-nitrosoanisole. The nmr spectrum (CCl_4) showed the following resonances: 2.27 (s, 3H); 3.94 (s, 3H); 6.83-8.15 (m, 3H), mp 52.5-54° (lit. (87) 53.5°).

2-Nitrosonaphthalene

A mixture of 15 ml of ethanol, 10 ml of 2-ethoxyethanol (cellosolve), 10 ml of water, .16 g of ammonium chloride and 1.2 g of 2-nitronaphthalene was heated to 70° and then 2 g of

zinc dust was added in small portions to the vigorously stirred solution over a five minute period. The temperature of the reaction mixture was then raised to 80° at which time the reduction appeared to start. After ten more minutes, the zinc salts and unreacted zinc were filtered from the then clear solution and washed with a small amount of hot water. Some solid began to precipitate out of the filtrate and thus 100 ml of ethanol was added to the filtrate to dissolve the precipitate. The filtrate was cooled and then poured into 150 ml of an ice-cold 5% ferric chloride solution. A solid product formed immediately and this was collected by filtration. This crude product was dissolved in a hot mixture of 50 ml of ethanol and 25 ml of acetone. Some material didn't dissolve and this was collected by filtration and tentatively identified (mass spectrum) as the azoxy compound. From the mother liquor .21 g of crude product was obtained by evaporation of the solvent.

This material was chromatographed on a silica-gel column using ether as an eleunt. Evaporation of the ether under reduced pressure yielded 90 mg of product which was recrystallized to give 2-nitrosonaphthalene. mp 60-63° (lit. (88) 62-64°).

ortho-Iodosotoluene

Following the procedure of Saltzman (89), ortho-iodotoluene was converted to ortho-iodosotoluene-diacetate by

stirring with 40% peracetic acid at 30° for two hours. The reaction mixture was then stored at 0° for one hour and the product was collected by filtration, washed with water and dried overnight in a vacuum desiccator.

Ortho-iodosotoluene-diacetate was converted to the desired product by stirring vigorously with 3N sodium hydroxide, After standing for two hours, water was added and the product is collected by filtration and vacuum dried.

1,1,1,3,3,3-d_6-2-Methyl-2-phenylpropane

Into a flame dried 250 ml three-necked flask equipped with a magnetic stirrer, reflux condensor and addition funnel was placed 1.44 g of magnesium turnings (.055 mole) and 75 ml of anhydrous ether (freshly distilled from CaH_2). A solution of 7.1 g of methyl iodide (.05 mole) in 25 ml of anhydrous ether was added dropwise over a ten minute period. After formation of the Grignard reagent was complete a solution of 3.2 g of d_6-acetone (.05 mole) in 30 ml of anhydrous ether was added dropwise over a ten minute period. This reaction mixture was then stirred at reflux for two hours, cooled to room temperature, treated with 200 ml of a saturated ammonium chloride solution and extracted with five 200 ml portions of ether. The etheral solution was dried ($MgSO_4$) and the product, 1,1,1,3,3,3-d_6-2-methyl-2-propanol, was collected by fractional distillation. Hydrogen chloride gas

was bubbled through the product for 1 hour at 15-20°C after which time 30 ml of water was added. The resulting mixture was extracted with 15 ml of benzene, the benzene solution was washed with 20 ml of saturated sodium bicarbonate, then with 20 ml of water and finally dried over $MgSO_4$. Anhydrous aluminum chloride (1 g) was then added to the benzene solution. This reaction mixture was stirred at room temperature for 2 hours and then poured onto 15 g of cracked ice. After the addition of 10 ml of dilute hydrochloric acid, the mixture was extracted with 50 ml of ether. The etheral solution was washed first with 30 ml of saturated sodium bicarbonate, then with 30 ml of water, dried ($MgSO_4$) and the solvents were evaporated under reduced pressure yielding 1.86 g of product (28%). The product, 1,1,1,3,3,3-d_6-2-methyl-2-phenylpropane was purified for mass spectral analysis by glpc using an LAC 446 column operated at 90°C. Low voltage mass spectrometry showed the following label incorporation in the product: 92% d_6; 8% d_5.

2-Methyl-2-(ortho-nitrophenyl)-1,1,1,3,3,3-d_6-propane and 2-Methyl-2-(para-nitrophenyl)-1,1,1,3,3,3-d_6-propane

The appropriately labelled tert-butylbenzene was nitrated by the method of Knowles and Norman (84) and the ortho and para products were separated by glpc using an LAC 446 column operated at 165°C. Low voltage mass spectral analysis showed the following label incorporation in the products:

ortho-isomer 92.2% d_6; 7.6% d_5; .2% d_4 .

para-isomer 91.6% d_6; 8.1% d_5; .2% d_4.

2,3,4,5,6-d_5-tert-Butylbenzene

A mixture of 5 ml of d_6-benzene and .65 g of anhydrous aluminum chloride was cooled to 5° and .46 g of tert-butylchloride (5 mmole) was added dropwise over a 5 minute period. The reaction mixture was stirred for 30 more minutes, then 10 ml of water was added slowly and the resulting mixture was extracted with 50 ml of ether. The etheral solution was dried ($MgSO_4$) and the solvents evaporated under reduced pressure yielding .62 g of product (92%). The product was purified for mass spectral analysis by glpc using an LAC 446 column operated at 95°C. Low voltage mass spectrometry showed the following label incorporation in the product: 10.3% d_6; 77.9% d_5; 11.8% d_4. The nmr spectrum and the mass spectral fragmentation pattern established that the d_6 product contained five ring deuterium atoms and one side chain deuterium atom.

4-Nitro-2,3,5,6-d_4-tert-butylbenzene and 2-Nitro-3,4,5,6-d_4-tert-butylbenzene

The appropriately labelled tert-butylbenzene was nitrated by the method of Knowles and Norman (84) and the ortho and para products were separated by glpc using an LAC 446 column operated at 170°. Low voltage mass spectral analysis showed the following label incorporation in the products:

ortho-isomer 10.3% d_5; 79.2% d_4; 10.5% d_3

para-isomer 10.2% d_5; 79.4% d_4; 10.3% d_3

The mass spectral fragmentation pattern established that the d_5 product contained four ring deuterium atoms and one side chain deuterium atom.

4,4'-di-tert-Butyl-azoxybenzene

Following the method of Lachman (90) for the preparation of azoxy compounds, a mixture of 8 g of 4-nitro-tert-butylbenzene, 8 g of sodium hydroxide and 40 ml of absolute methanol was stirred under reflux for three hours and the solid product which formed was collected by filtration. The product was recrystallized twice from a 50-50 chloroform-ether mixture giving 2.05 g of the light yellow azoxy compound (17%). No effort was made to recover more of the product. mp 143-44°.

Anal: Calcd. for $C_{20}H_{26}N_2O$: C, 77.34; H, 8.44.
Found: C, 77.54; H, 8.52.

2,3,5,6,2',3',5',6'-d_8-4,4'-di-tert-Butyl-azoxybenzene

A mixture of 80 mg of 2,3,5,6-d_4-nitro-tert-butylbenzene, 2 ml of absolute methanol and four pellets of solid sodium hydroxide was stirred at 60° for eight hours, then cooled to room temperature and diluted with 25 ml of water. The resulting mixture was extracted with 50 ml of ether, the

etheral solution was dried ($MgSO_4$) and the ether evaporated under reduced pressure to give 43 mg of the crude azoxy compound (60%). The product was recrystallized three times from ethanol to give the pure azoxy compound melting at 145-6°. The mixed melting point with the unlabelled material was not depressed. Low voltage mass spectrometry established the following label incorporation in the product: 1.9% d_{10}; 15.1% d_9; 67.4% d_8; 15.0% d_7; 4% d_6. The mass spectral fragmentation pattern established that the d_{10} and d_9 products contained 8 ring deuterium atoms.

Bis-4,4'-(2-methyl-1,1,1,3,3,3-d_6-iso-propyl)-azoxybenzene

The appropriately labelled nitro compound was converted to the azoxy compound by the procedure used to prepare the preceding compound. Low voltage mass spectrometry established the following label incorporation in the product: 82.1% d_{12}; 16.2% d_{11}; 1.6% d_{10}.

Methyl-2-methyl-2-phenyl-propionate

Thionyl chloride was added to iso-butyric acid and the product was brominated and converted to the alpha-bromo ester by treatment with methanol (91, p. 431). Treatment of benzene with the alpha-bromo ester and anhydrous aluminum chloride by the method of Schultz and Mickey (92) resulted in formation of the desired product in 40% yield. The product was purified for mass spectral analysis by glpc using an

LAC 446 column operated at 135°. The nmr spectrum (CCl_4) showed the following resonances: 1.51 (s, 6H); 3.58 (s, 3H); 7.1-7.3 (m, 5H).

Ethyl-2-methyl-2-phenyl-propionate (91,92)

This compound was prepared and purified by the same method used for the previous compound. The nmr spectrum (CCl_4) showed the following resonances: 1.10 (t, 3H); 1.51 (s, 6H); 4.03 (q, 2H); 7.05-7.33 (m, 5H).

Methyl-2-methyl-d_3-2-phenyl-propionate

A mixture of .36 g of sodium (16.5 mmole) and 25 ml of absolute ethanol was stirred until all of the metal had reacted, then cooled to room temperature and treated over a five minute period with the dropwise addition of 2.78 g of diethyl-methyl-malonate (16 mmole). This mixture was stirred near reflux for twenty minutes, cooled to room temperature and 2.32 g of methyliodide-d_3 (16 mmole) was added. After stirring at reflux for 2 hours, the reaction mixture was neutralized with 3 drops of glacial acetic acid and the alcohol was removed by distillation. Then 50 ml of water was added and the mixture was extracted with three 150 ml portions of chloroform. The chloroform was evaporated under reduced pressure and the residue was poured into 60 ml of 50% aqueous ethanol containing 6 g of KOH. This was stirred under reflux for 3 hours, cooled to room temperature

and about half of solvent was removed by evaporation under reduced pressure. Enough 6N H_2SO_4 was added to make the pH 1-2 and the resulting acidic solution was extracted with three 150 ml portions of ether. The etheral solution was dried ($MgSO_4$) and the ether evaporated under reduced pressure giving 1.7 g of product (80%). The resulting labelled dimethyl-malonic acid was placed in a 5 ml pear-shaped flask connected to a short path distillation apparatus and heated by an external oil bath at a temperature of 210° for 30 minutes and .91 g of product (82%) was collected in the receiving flask. The product acid, 2-methyl-3,3,3-d_3-propionic acid, was then brominated and benzene was alkylated with the resulting α-bromo acid and anhydrous $AlCl_3$ yielding .45 g (30%) of 2-methyl-d_3-2-phenyl-propionic acid (91,92). Treatment of the above acid with excess diazomethane in the usual manner gave the desired ester in 95% yield. The product was purified by glpc using an LAC 446 column operated at 135°C. Low voltage mass spectrometry established the following label incorporation in the product: 97.3% d_3; 2.7% d_2. The nmr spectrum (CCl_4) showed the following resonances: 1.51 (s, 3H); 3.58 (s, 3H); 7.1-7.3 (m, 5H).

Methyl-2-methyl-2-phenyl-d_5-propionate

A solution of .4 g of α-bromo-iso-butyric acid in 1 ml of d_6-benzene was added dropwise to a mixture of .5 g of anhydrous $AlCl_3$ and 5 ml of d_6-benzene. The reaction mixture was stirred

at 75° for 5 hours, then cooled to room temperature and treated with the dropwise addition of 10 ml of water followed by 3 ml of conc. HCl. The resulting mixture was extracted with 50 ml of ether and the etheral extract was washed once with 50 ml of water. The etheral solution was then extracted with 70 ml of 10% NaOH and the basic extracts acidified with 6N HCl. This acidic solution was then extracted with 75 ml of ether. The etheral solution was washed with two 50 ml portions of water, dried ($MgSO_4$) and the ether was evaporated under reduced pressure. An nmr spectrum showed approximately a 50-50 mixture of α-bromo-iso-butyric acid and 2-methyl-2-phenyl-d_5 propionic acid. This mixture was treated with excess diazomethane and the desired product was collected by glpc using an LAC 446 column operated at 135°C. Low voltage mass spectrometry established the following label incorporation in the product: .6% d_6; 92.2% d_5; 7.4% d_4. The nmr spectrum (CCl_4) showed the following resonances: 1.51 (s, 6H); 3.58 (s, 3H); 7.2 (trace).

3-Phenyl-d_5-pentane

Benzene-d_6 was brominated according to the procedure described in Vogel (91, p. 535) and following distillation of the product a solution of 2.43 g of bromobenzene-d_5 (.015 mole) in 5 ml of anhydrous ether was added to a mixture of .48 g of magnesium turnings (.02 mole) and 15 ml of anhydrous ether. The reaction mixture was kept at reflux for 45 minutes, then cooled to

room temperature and a solution of 1.52 g of 3-pentanone (.02 mole) in 10 ml of anhydrous ether was added over a 15 minute period and then sitrred at reflux for an additional 15 minutes. This reaction mixture was then cooled to room temperature and 50 ml of 5% HCl was added over a 30 minute period. The resulting mixture was poured into a separatory funnel containing 100 ml of ether. The organic layer was separated, washed with two 100 ml portions of water, dried ($MgSO_4$) and the ether was evaporated under reduced pressure yielding 2.10 g of 3-phenyl-d_5-3-pentanol (85%). A mixture of 15 drops of 85% phosphoric acid and 2.1 g of 3-phenyl-d_5-3-pentanol (.012 mole) was then stirred at 100° for 90 minutes, cooled to room temperature and poured into 50 ml of water. The resulting mixture was extracted with 50 ml of ether, the etheral solution was washed with two 50 ml portions of water, dried ($MgSO_4$) and the ether was evaporated under reduced pressure yielding 1.58 g of 3-phenyl-d_5-2-pentene (84%).

Using a typical hydrogenation apparatus, 1.51 g of 3-phenyl-d_5-2-pentene (.01 mole) was hydrogenated at room temperature and pressure in 50 ml of ethanol using 100 mg of Pd/C catalyst. Following workup in the usual manner, 1.44 g of 3-phenyl-d_5-pentane (94%) was isolated and purified for mass spectral analysis by glpc using an LAC 446 column operated at 105°C. Low voltage mass spectrometry established the following label incorporation in the product: 97.1% d_5;

2.9% d_4. The nmr spectrum (CCl_4) showed the following resonances: .78 (t, 6H); 1.33-1.91 (m, 4H); 2.05-2.45 (m, 1H).

Bromoethane-2,2,2-d_3

A solution of 6.4 g of acetic acid-d_4 (.10 mole) in 50 ml of anhydrous ether was added dropwise to a suspension of 5.7 g of lithium aluminum hydride (.15 mole) and then the mixture was stirred under reflux for 18 hours and worked up in the usual manner. Then 50 ml of water was added to the etheral solution and the resulting mixture was fractionated and the azetrope of ethanol-2,2,2-d_3 was collected. The product was brominated by treatment with a mixture of 50 ml of conc. HBr and 10 ml of conc. H_2SO_4 at 50°. The product was collected in a Dean-Stark trap and redistilled giving 9.62 g of bromoethane-2,2,2-d_3 (86%). The nmr spectrum (CCl_4) showed the following resonances: 3.37 (multiplet appropriate for hydrogen-deuterium coupling).

3-Phenylpentane-1,1,1,5,5,5-d_6

A solution of 1.78 g of bromoethane-2,2,2-d_3 (.015 mole) in 10 ml of anhydrous ether was added dropwise to .48 g of magnesium turnings and 10 ml of anhydrous ether. Upon completion of formation of the Grignard reagent a solution of .95 g of methyl benzoate (.007 mole) in 25 ml of anhydrous ether was added and the mixture was stirred overnight and worked up

in the usual manner giving 1.27 g of product which was found to be 70% 3-phenyl-3-pentanol-1,1,1,5,5,5-d_6 and 30% methyl benzoate. This mixture was dehydrated and hydrogenated by the same method as described for preparing 3-phenyl-d_5-pentane. The desired product was purified for mass spectral analysis by glpc using an LAC 446 column operated at 105°C. Low voltage mass spectrometry established the following label incorporation in the product: 96.3% d_6; 3.7% d_5. The nmr spectrum (CCl_4) showed only the following resonances: 1.37-1.90 (distorted broad d, 4H); 2.01-2.47 (m, 1H); 6.83-7.37 (m, 5H).

Methyl-2-phenyl-butyrate (93)

A mixture of 5.85 g of phenylacetonitrile (.05 mole), 5.45 g of ethyl bromide (.05 mole) and .1 g of benzyltriethylammonium chloride was added to 30 ml of 50% sodium hydroxide and stirred at 75° for 4 hours (93). The reaction mixture was cooled,diluted with 30 ml of water and extracted with 100 ml of ether. The etheral solution was washed with two 50 ml portions of water, dried ($MgSO_4$) and the ether evaporated under reduced pressure yielding 6.60 g of 2-phenylbutyronitrile (91%). A mixture of 2 g of 2-phenylbutyronitrile (.014 mole), 4 g of potassium hydroxide and 15 ml of ethylene glycol was stirred under reflux for 24 hours, then cooled to room temperature and diluted with 80 ml of water. The basic solution was extracted with one 80 ml

portion of ether and then acidified with 6N HCl. The acidic solution was then extracted with 80 ml of ether and the etheral extract was washed once with 80 ml of water, dried ($MgSO_4$) and the ether evaporated under reduced pressure yielding 1.6 g of 2-phenyl-butyric acid (76%). Treatment with diazomethane in the usual manner gave the ester which was purified for mass spectral analysis by glpc using an LAC 446 column operated at 135°C. The nmr spectrum (CCl_4) showed the following resonances: .87 (distorted t, 3H); 1.42-2.26 (m, 2H); 3.17-3.45 (m, 1H); 3.58 (s, 3H); 6.93-7.35 (m, 5H).

Methyl-2-phenyl-4,4,4-d_3-butyrate

This compound was prepared and purified by the same method as that described for the preparation of the unlabelled compound using bromoethane-2,2,2-d_3. Low voltage mass spectrometry established the following label incorporation in the product: 97.3% d_3; 2.7% d_2. The nmr spectrum (CCl_4) showed the following resonances: 1.40-2.27 (m, 2H); 3.31 (distorted t, 1H); 3.58 (s, 3H); 6.93-7.37 (m, 5H).

Phenyl-d_5-acetonitrile

Benzene-d_6 was acylated by treatment with anhydrous $AlCl_3$ and propionyl chloride (91, p. 535) and the product was converted to benzoic acid-d_5 in 68% overall yield by oxidation with 20% nitric acid (94). The product was reduced

to phenyl-d_5-methanol using lithium aluminum hydride and a mixture of 4.1 g of the alcohol and 15 ml of conc. HBr was stirred at reflux for 1 hour, then cooled to room temperature, diluted with 100 ml of water and extracted with 150 ml of ether. The etheral solution was washed with two 100 ml portions of water, dried ($MgSO_4$) and the ether evaporated under reduced pressure. The product was dissolved in 10 ml of 95% ethanol and this solution was added to a solution of 1.5 g of sodium cyanide in 5 ml of water. The reaction mixture was stirred at reflux for 2 hours, cooled to room temperature and diluted with 150 ml of water. This mixture was extracted with 150 ml of ether, washed once with 100 ml of water, dried ($MgSO_4$) and the solvents were evaporated under reduced pressure giving 3.15 g of phenyl-d_5-acetonitrile (81%). The nmr spectrum (CCl_4) showed the following resonances: 3.55 (s); 7.2 (trace).

3-Carbomethoxy-3-phenyl-pentane (93)

Phenylacetonitrile was dialkylated by the same method used to prepare the mono-alkylated material by using a 2:1 ratio of ethylbromide to phenylacetonitrile. The product was converted to the desired ester by the same method used to prepare methyl-2-phenyl-butyrate. Purification of the final product for mass spectral analysis was accomplished by glpc using an LAC 446 column operated at 150°. The nmr

spectrum (CCl_4) showed the following resonances: .7 (t, 6H); 1.98 (q, 4H); 3.58 (s, 3H); 7.17 (s, 5H).

3-Carbomethoxy-3-phenyl-1,1,1,5,5,5-d_6-pentane

This compound was prepared and purified by the same method used for the corresponding unlabelled compound with the exception of using bromoethane-2,2,2-d_3. Low voltage mass spectrometry established the following label incorporation in the product: 96.4% d_6; 3.6% d_5. The nmr spectrum (CCl_4) showed the following resonances: 1.98 (broad s, 4H); 3.58 (s, 3H); 7.17 (s, 5H).

3-Carbomethoxy-3-phenyl-d_5-pentane

This compound was prepared and purified by the same method used for the corresponding unlabelled compound with the exception of using phenyl-d_5-acetonitrile. Low voltage mass spectrometry established the following label incorporation in the product: 81.3% d_5; 17.1% d_4; 1.6% d_3. The nmr spectrum (CCl_4) showed the following resonances: .7 (t, 6H); 1.98 (q, 4H); 3.58 (s, 3H); 7.2 (trace).

Methyl-2-methyl-3-phenyl-d_5-propionate

Using the method of Nibbering (48), diethyl-methyl-malonate was alkylated with phenyl-d_5-methylbromide. The resulting malonic ester was hydrolyzed, decarboxylated and converted to the product ester by treatment with diazomethane.

The product was purified for mass spectral analysis by glpc using an LAC 446 column operated at 140°. Low voltage mass spectrometry established the following label incorporation in the product: 89.2% d_5; 10.8% d_4. The nmr spectrum (CCl_4) showed the following resonances: 1.1 (distorted d, 3H); 2.29-3.11 (complex m, 3H); 3.58 (s, 3H).

2-Methoxy-2-phenylpropane

This compound was prepared by the method of Ziegler (85). The nmr spectrum (CCl_4) showed the following resonances: 1.43 (s, 6H); 2.95 (s, 3H); 7.05-7.42 (m, 5H).

]-Methyl-1-mesyl-2-phenylpropane

The reduction of ethyl-2-methyl-2-phenyl-propionate with lithium aluminum hydride in the usual manner gave an 81% yield of 2-methyl-2-phenyl-1-propanol. Following the procedure of Tipson (95), treatment of 2-methyl-2-phenyl-1-propanol with mesyl chloride gave a 76% yield of the desired product. The nmr spectrum (CCl_4) showed the following resonances: 1.37 (s, 6H); 2.64 (s, 3H); 4.12 (s, 2H); 7.15-7.4 (m, 5H).

Methyl-2-(alpha-naphthyl)-butyrate

A mixture of 8.36 g of alpha-naphthyl-acetonitrile (.05 mole), 5.85 g of ethyl bromide (.05 mole) and .1 g of benzyl-triethylammonium chloride was added to 30 ml of 50% sodium hydroxide and stirred at 75° for eight hours. A 73% yield of crude 2-(alpha-naphthyl)-butyronitrile was isolated as previous-

ly described on page 165. The crude nitrile was then hydrolyzed as described on page 165 to give a 76% yield or crude 2-(alpha-naphthyl)-butyric acid. Treatment of the crude acid (mp 84-86° (lit. (96) 86-87°) with diazomethane gave the methyl ester in 95% yield. Final purification of the ester for mass spectral analysis was accomplished by glpc using an LAC 446 column operated at 175°. The nmr spectrum (CCl_4) showed the following resonances: .92 (t, 3H); 1.58-2.52 (m, 2H); 4.18 (distorted t, 1H); 3.55 (s, 3H); 7.15-8.16 (m, 7H).

Methyl-2-methyl-2-(alpha-naphthyl)-propionate (96)

A mixture of 8.36 g of alpha-naphthyl-acetonitrile (.05 mole), 15.6 g of methyl iodide (.11 mole) and .1 g of benzyl of triethyl ammonium chloride was added to 30 ml of 50% sodium hydroxide and stirred at 75° for 10 hours. The product was worked up in the usual manner and an nmr spectrum showed that only monoalkylation had occurred. The mono-alkylated product was subjected to the same alkylating conditions two more times before complete dialkylation occurred. The product was then hydrolyzed to 2-methyl-2-(alpha-naphthyl)-propionic acid in the manner described on page 165. Treatment of the crude acid with diazomethane gave the corresponding ester which was purified for mass spectral analysis by glpc using an LAC 446 column operated at 175°. The nmr spectrum (CCl_4) showed the following resonances: 1.61 (s, 6H); 3.58

(s, 3H); 7.2-7.85 (m, 7H).

2-Methyl-2-(beta-naphthyl)-propionic acid

A mixture of 14.2 g of 2-methyl-naphthalene (.1 mole), 17.8 g of N-bromosuccinimide (.1 mole) and 200 mg of benzoyl peroxide was dissolved in 200 ml of CCl_4 and stirred at reflux for 18 hours. The succinimide was filtered off, washed with CCl_4 and the filtrate and washings were combined. The solvent was removed under reduced pressure and the nmr spectrum showed the product to be mostly bromo-(beta-naphthyl)-methane. Treatment of this product with NaCN by the method of Adams and Thal (97) gave 10.2 g of crude beta-naphthyl-acetonitrile (62%). A mixture of 1 g of beta-naphthyl-acetonitrile (6 mmole), 28.4 g of methyl iodide (.2 mole), .1 g of benzyl triethyl ammonium chloride and 40 ml of 50% sodium hydroxide was stirred at reflux for 48 hours, cooled to room temperature and an 87% yield of the product was isolated as described on page 172. This was hydrolyzed to the product acid in 88% yield by the method described on page 165. The product was purified by recrystallization from absolute ethanol. mp 150-151° (lit. (96) mp 152-3°).

Methyl-2-methyl-2-(beta-naphthyl)-propionate

Treatment of 2-methyl-2-(beta-naphthyl)-propionic acid with diazomethane in the usual manner gave a 96% yield of the product. The product was purified for mass spectral analysis

by glpc using an LAC 446 column operated at 170°. The nmr spectrum (CCl_4) showed the following resonances: 1.64 (s, 6H); 3.59 (s, 3H); 7.17-7.81 (m, 7H).

Methyl-2-phenyl-d_5-butyrate

Phenyl-d_5-acetonitrile was converted to methyl-2-phenyl-d_5-butyrate using the same method that was used to prepare and purify the corresponding unlabelled compound. Low voltage mass spectrometry established the following label incorporation in the product: 82.7% d_5; 17.3% d_4. The nmr spectrum (CCl_4) showed the following resonances: .87 (distorted t, 3H); 1.42-2.27 (m, 2H); 3.17-3.45 (m, 1H); 3.58 (s, 3H); 7.2 (trace).

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