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ATMOSPHERIC PRESSURE IONIZATION MASS SPECTROMETRY

STUDIES OF NEGATIVE ION FORMATION FOR DETECTION AND QUANTIFICATION PURPOSES

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SUMMARY

The analytical system described here consists of a gas chromatograph, an atmospheric pressure ionization mass spectrometer designed for operation in the negative ion mode, and a computer. The gas stream from the gas chromatograph is split in order to obtain concurrent but separate detection with a standard electron capture detector and with the mass spectrometer. The ion source of the mass spectrometer is also a duplicate of the standard electron capture detector, so that simultaneous monitoring of the ions and monitoring of the electron capture detection response can also be carried out for the reaction chamber.

Negative ions observed under atmospheric pressure ionization conditions are almost always anions of strong gas phase acids. These may be formed by reaction with a gas phase basic ion, or by electron capture reactions. A few organic compounds form stable radical M^- ions. Most pesticides, herbicides and fungicides, as well as numerous toxic compounds that are now environmental hazards, form stable anions and show an electron capture response. Most ordinary organic compounds do not form stable negative ions at atmospheric pressure and do not show an electron capture response. The results suggest that an analytical system of this kind will be useful for the detection and quantification of many environmentally hazardous compounds.

INTRODUCTION

The most powerful methods of organic chemical analysis now available for the study of complex mixtures are based upon the use of analytical systems with mass spectrometric (MS) detection. In their present form, these systems employ a combination of gas or liquid chromatography and positive ion MS with computer-based data analysis.

Several years ago we initiated a study of negative ion MS, using atmospheric pressure ionization (API) conditions, with the aim of developing analytical systems comparable to those now in use but based upon negative ion rather than positive ion MS. This work had two objectives. One was to determine if analytical systems of this

kind would be useful in toxicological and environmental studies. Many compounds that are cytotoxic show a response with electron capture (EC) detectors; these include many pesticides, herbicides, fungicides and such diverse halogen-containing compounds as polychlorobiphenyls, polybromobiphenyls, chlorinated dibenzodioxins and bromine-substituted flame retardants. Analytical procedures employed in the past for the detection and quantification of these compounds were almost always based upon gas chromatography with EC detection, and the results were not always reliable because the detection process provided essentially no structural information or structural specificity. It was our view that analytical systems based upon a combination of a gas or liquid chromatograph and a negative ion mass spectrometer would prove to be more effective in these applications than the present systems, since interference would not be expected from most of the ordinary compounds present in samples of biological tissues, soils or water. It was also believed that direct knowledge of the chemical events occurring under EC detector conditions would be helpful from both theoretical and practical points of view, since the detector is widely used.

The analogy between an analytical system which includes a gas or liquid chromatograph, a positive ion mass spectrometer and a computer, and a similar system with a negative ion mass spectrometer, is easily realized. In fact, if the mass spectrometer is of the electrical field type, it is possible to design a mass spectrometer[1,2] which can be used in either mode without the delay required for magnetic field changes, or with a capability for detecting both positive and negative ions during the same analysis through rapid switching of circuits with two multipliers[3]. The analogy, however, virtually ends at this point. There is a large corpus of knowledge relating to positive ion MS for organic compounds, and considerable experience has been gained in many laboratories in the design and use of analytical systems based on both magnetic and electrical field mass spectrometers. There is very little background information about negative ion MS and, until recently, the prevailing view of this field was that significant new knowledge was not likely to result from further studies. This view was due in part to the absence of commercially available instruments, and in part to the fact that negative ion mass spectra of organic compounds are usually relatively simple and easily interpreted. In addition, ordinary electron impact conditions are unsatisfactory for negative ion formation. The fact that the amount of structural information contained in a negative ion mass spectrum is far less than that contained in a positive ion mass spectrum is not necessarily a great disadvantage in analytical work. In quantitative procedures, for example, it is advantageous to employ conditions which result in relatively simple mass spectra made up of stable ions. Stable negative ions are formed by a great variety of compounds that are cytotoxic, and that have been released into the environment purposely or by accident. Some of these compounds are mutagenic. It is important to have analytical capabilities to detect these substances in biological tissues and in soils, foods, air and water. Since the concentration of compounds of interest is usually low, and since most samples are initially of great complexity in composition, a means of selective detection is advantageous. The wide use of gas chromatography (GC) with EC detection for analyses of this kind is due to the selective behavior of EC detectors. The disadvantage of EC detection is that virtually no specific structural information is associated with a response, and slight differences in conditions may affect the response. These disadvantages have led in the past to mistakes both in identity and in quantification.

Some of the difficulties inherent in air analyses with EC detection have been described recently[4].

The initial problem was to define or classify reactions leading to negative ions which occur at atmospheric pressure and which can be effected by thermal electrons or by ion molecule reactions. Earlier observations[5,6] of negative ion mass spectra at low pressure are of considerable interest, but are not directly comparable to our results. Our conditions involve ionization at atmospheric pressure in several different ways. The conditions employed have been (a) ionization by thermal electrons, in nitrogen with as little interference as possible from traces of oxygen and water, (b) ionization by ion molecule reactions with the gaseous superoxide ion (O_2^-) as the reagent, and (c) ionization by thermal electrons in argon–methane carrier gas. Ionization by adduct formation was not studied.

The prototype analytical system used in this work included a packed column gas chromatograph, an API mass spectrometer operated in negative ion mode (with positive ion mode available for obtaining additional information) and a small computer. The effluent stream from the gas chromatograph was split, so that direct comparisons could be made for EC responses and for stable negative ion MS data.

EXPERIMENTAL

Analytical system

A schematic diagram of the mass spectrometer with a reaction chamber treated as an EC detector is shown in Fig. 1. The system includes a Hewlett-Packard Model 5710A gas chromatograph. A 6 ft. × 2 mm I.D. column, with Applied Science Labs. 3% Poly-S 179 on 100–120 mesh Gas-Chrom Q packing, was used for this

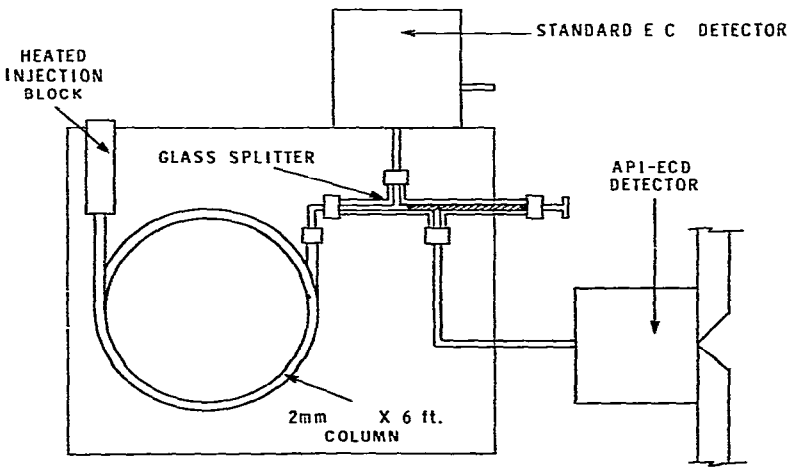


Fig. 1. Schematic diagram of assembly for an analytical system including a gas chromatograph and an API negative ion mass spectrometer. The effluent stream from the gas chromatograph is split to provide detection both with a standard EC detector and the API mass spectrometer. The source of the API instrument was constructed to the same dimensions as the EC detector, so that EC responses could be measured both in the usual way and in the source chamber which provides the ions for mass analysis. The API mass spectrometer and computer elements have been described previously[1]. Both positive and negative ion mass spectra were obtained for all compounds.

work. The carrier gas was Linde Specialty Gases argon–methane (95:5), which was passed through an Alltech Assoc. OXY-TRAP prior to use. Other gases were nitrogen and nitrogen–oxygen for ionization observations. The effluent from the gas chromatographic column was passed through an all-glass splitter (Scientific Glass Engineering) to both a standard Hewlett-Packard Model 18713A EC detector, and a special API source designed and built to be physically and electrically identical to the standard EC detector. Matheson Model LF-100 mass flow meters were used to monitor the inlet carrier gas flow and the exit flow from the EC detector. The splitter was adjusted for unity ratio based upon these measured flows. The connecting line to the API–EC source was 1/16 in. glass-lined stainless-steel tubing, separately heated using the auxiliary temperature controller available on the chromatograph. All connecting tubing, fittings and the splitter were silanized prior to assembly. The inlet block and the API connecting lines were maintained at 250°.

A schematic diagram of the API–EC source is shown in Fig. 2. The gas inlet and exit lines were positioned, as nearly as possible, to be the same as in the standard EC detector. The ionization chamber dimensions, center electrode and nickel-63 foil were identical to the standard EC detector. The ions formed in this detector were sampled through a 20 μm aperture into the mass spectrometer section where they were mass analyzed and detected. The center electrodes of both the standard EC detector and the API–EC detector were connected to separate Hewlett-Packard Model 2709A linear EC control units. Both detectors were operated in a constant current, variable frequency pulsed mode.

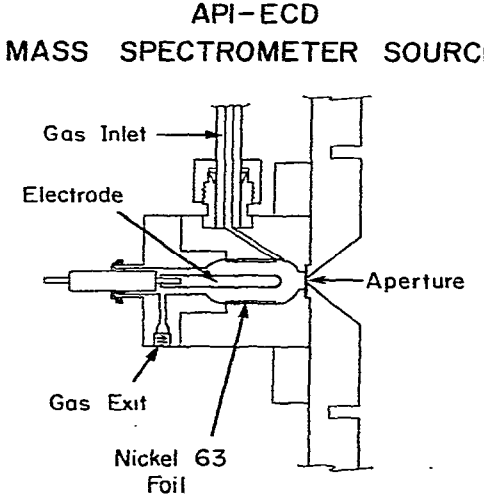


Fig. 2. Schematic diagram showing construction of the API source. The reaction chamber duplicates the standard EC detector which is in the usual position. Measurements of EC detector response can be made with this source at the same time that sample ions are undergoing mass analysis.

There are two separate analog EC detector signals; one from the standard EC detector and one from the API–EC detector. In principle, the API–EC source alone would be sufficient. The standard EC source was retained to demonstrate that the outputs from both the EC and API–EC sources were identical.

The computer program[1,2] was modified to permit the sampling of both analog EC signals and up to two channels of selected ion monitoring data as a function of time. The accumulated data for a GC run were plotted on a standard X–Y recorder in correct time relationships.

The usual mode of GC operation was isothermal.

Compounds and samples

All compounds were used as received; purification was achieved through GC separation when the analytical system was used. Some observations were made by probe introduction of samples with an earlier design of the source[1]. Descriptions of procedures for plasma samples will be published separately.

RESULTS AND DISCUSSION

Negative ion formation with thermal electrons and without added reagents

When pure nitrogen is used as a carrier gas in the instrument shown in Figs. 1 and 2, an organic compound introduced into the reaction chamber in the gas stream is subjected to both positive and negative ionizing conditions. Negative ions are formed by reaction with thermal electrons, and positive ions are formed by charge transfer reactions with N_4^+ and N_3^+ ions[7]. For most organic compounds, the observed ions are likely to be positive ions resulting from protonation reactions due to $(H_2O)H^+$ from water which is always present in trace concentration. In early experiments with an API mass spectrometer[1], and with a "Plasma Chromatograph"[8,9], the observed positive ions were formed in this way. If it is desired to produce stable positive ions, however, it is more appropriate to use the $C_4H_9^+$ ion as a reagent[7]. The positive ions are the same as those which are obtained in isobutane chemical ionization MS at 0.5–1 Torr. While the use of nitrogen (or helium or argon) alone for API positive ion MS is not recommended for this reason, it is an effective and useful method for negative ion mass MS when stable negative ions are formed by direct

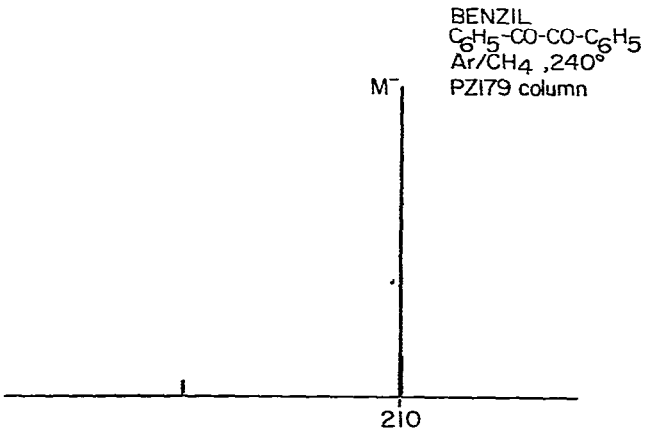


Fig. 3. Negative ion mass spectrum of benzil taken in argon–methane carrier gas. The source temperature was 240°. The ion corresponds to M^-. The same result was obtained with nitrogen as the carrier gas, and with a nitrogen–oxygen gas stream with probe introduction of the sample.

electron attachment ("electron capture"). For example, *o*- and *p*-quinones, and *α,β*-diketones such as benzil, have relatively high electron affinities and will form M^- ions through reaction with thermal electrons. This is illustrated in Fig. 3 for benzil in argon–methane, but the results are the same in nitrogen. Water and oxygen do not interfere with the reaction; O_2^- formed from traces of oxygen present in the carrier gas will also react by charge transfer to form M^-, and the effect of traces of water is to form MH^+ ions which can be observed in the positive ion mode.

This ionization condition resembles that used at the time of the original observations of Lovelock and Lipsky[10] which later led to the development of the EC detector. The use of argon–methane as a carrier gas with pulsed detection is now the preferred mode of operation for EC detectors. Our results suggest that the use of nitrogen as a carrier gas is desirable for qualitative and mechanistic studies of electron attachment reactions, and that this condition is useful when it is desired to demonstrate the formation of M^- ions or to define reaction sequences which are initiated by M^- formation. This is particularly important when chlorine-containing substances are under study. In many instances M^- ions of chlorine-substituted compounds are not highly stable and are likely to undergo transformations which result in chlorine elimination. An interesting example of this effect is found in the contrasting ionization reactions of flunitrazepam and N-methylclonazepam in nitrogen, and in nitrogen containing oxygen as a reagent. Flunitrazepam forms a stable $(M - 58)^-$ ion which is apparently derived from $(M - H)^-$ by loss of the neutral molecule methyl isocyanate (CH_3NCO). This reaction occurs in an environment containing oxygen as a reagent. In pure nitrogen, the expected product would be M^-, and this ion was observed. Under API conditions with nitrogen containing a trace of oxygen, the only ion observed is the stable $(M - 58)^-$ ion; this is shown in Fig. 4. This figure also shows that the chloro analog forms $(M - 37)^-$ in addition to $(M - 58)^-$ ions [or $(M - 61)^-$ for the deuterated analog], and that this reaction

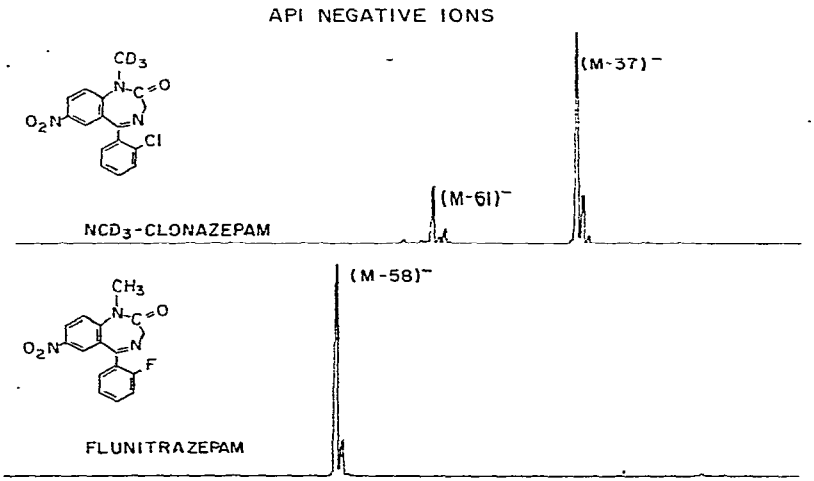


Fig. 4. Negative ion mass spectra observed for flunitrazepam and for NCD_3-clonazepam. The samples were introduced by probe with a nitrogen gas stream which contained traces of oxygen. The temperature was 250°.

sequence involves loss of chlorine. Fig. 5 shows that the reaction is temperature dependent, and that at a lower temperature M^- ions are formed. The loss of hydrogen chloride involves a cyclization reaction which requires activation anergy. The alternate pathway of ionization $(M - H)^- \rightarrow (M - 58)^-$ also occurs due to oxygen. When sufficient oxygen is present as a reagent, the formation of M^- by electron attachment is suppressed (because of the absence of thermal electrons which are replaced by O_2^- ions), but $(M - H)^-$ is formed and is immediately converted to $(M - 58)^-$. $(M - 37)^-$ ions are found for N-methylclonazepam only under conditions of M^- formation. For quantitative analytical purposes, the ionization condition of choice is that leading to $(M - 58)^-$ ions through initial formation of $(M - H)^-$ by reaction with a basic reagent ion.

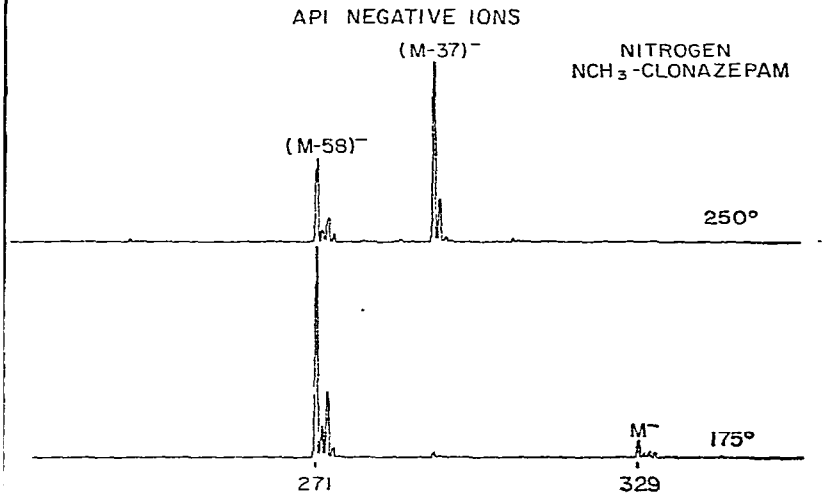


Fig. 5. Negative ion mass spectra for N-methylclonazepam observed at 175° and 250° with probe injection and a nitrogen gas stream which contained traces of oxygen.

Negative ion formation by reaction with the superoxide ion O_2^-

Oxygen has a relatively high electron affinity (0.48 eV), and with thermal electrons the ion which is formed is O_2^-. The extent to which additional ions are formed depends upon the concentration of oxygen, the temperature and the water concentration; these ions are usually O_4^- and the hydrates $(H_2O)_nO_2^-$ and $(H_2O)_nO_4^-$. Fig. 6 shows the ion products formed under API conditions at 100° for an oxygen concentration in nitrogen corresponding to 1.5 Torr pressure. Although only traces of water are present in the carrier gas, this is sufficient to be detected as $(H_2O)O_2^-$.

Several types of reactions with organic compounds are known to occur for O_2^- ions. The O_2^- ion is a relatively strong base in the gas phase, and many organic compounds can be ionized to $(M - H)^-$ ions by proton transfer to O_2^-. This was an early finding in negative ion studies under API conditions[11]. Ionization to $(M - H)^-$ has been observed for a variety of substituted phenols and for compounds such as barbiturates and diphenylhydantoin. This is illustrated in Fig. 7. Nitrosubstituted

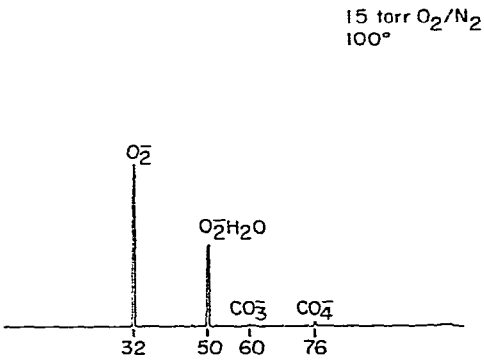


Fig. 6. Negative ions present in the source at 100° for a nitrogen–oxygen gas mixture with the concentration of oxygen corresponding to 1.5 Torr pressure. Traces of water are detected as $(H_2O)O_2^-$ ions. The ions CO_3^- and CO_4^- are due to the addition of O_2^- to CO and CO_2 present as trace impurities. The dimer ion O_4^- is present at higher concentrations of oxygen.

aromatic compounds often show strongly acidic properties; 2,4,6-trinitrotoluene, for example, is a strong gas phase acid.

Ionization to $(M - H)^-$ ions which undergo cyclization is a relatively rare occurrence, but this is believed to be the ionization route followed by flunitrazepam, as indicated in the previous section.

Substitution may occur with O_2^- as the reagent, and this is important for some

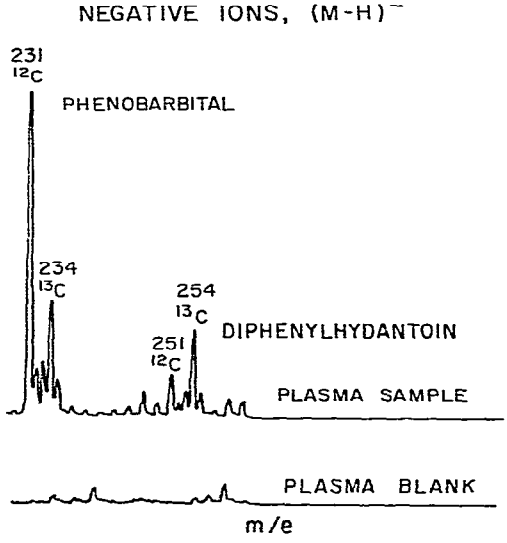
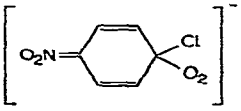


Fig. 7. Analysis of a plasma extract containing phenobarbital and diphenylhydantoin with an API negative ion analytical system. The sample was injected in solvent form (chloroform) and without a GC separation. The internal reference compounds were the same drugs containing three ^{13}C atoms; these were added to the plasma at the time of extraction. These drugs are strong gas phase acids, and the ions correspond to the anions $(M-H)^-$.

chlorine-containing compounds. The nature of the reaction under API conditions was studied in detail for *p*-nitrochlorobenzene[2]. The ion molecule reactions are:

$$\begin{array}{llllll} & O_2 & & & & M \\ (1) & \downarrow e & (3) & (4) & & e\downarrow \quad (2) \\ & O_2^- + M \longrightarrow & [MO_2]^- & \rightleftharpoons & O_2 + & M^- \\ & & \downarrow (6) & (5) & & \\ & & [M - Cl + O]^- + & ClO\cdot & & \end{array}$$

When oxygen is present as a reagent in high concentration, reaction 2 is suppressed, and the reaction of O_2^- with *p*-chloronitrobenzene leads to the formation of the *p*-nitrophenoxide ion and the ClO· neutral radical which is not detected. When the concentration of oxygen is very low, reactions 2, 4 and 6 become the chief route of phenoxide formation. The presence of M^- can be demonstrated, and as the oxygen concentration nears zero, reaction 4 is suppressed and the ratio of M^-/phenoxide$^-$ increases. Appropriate experiments with $^{18}O_2$ were carried out to determine that hydrolysis of the parent halide with water did not contribute to the ion product. The nature of the intermediate state $[MO_2]^-$ is unknown, but since the reaction does not occur for *m*-chloronitrobenzene, it is likely that the structure



is a requirement; the reaction of *o*-chloronitrobenzene could proceed by an analogous structure.

Another example of this circumstance is shown in Figs. 8 and 9. The chlorosulfonate ester Tetradifon, when ionized in nitrogen containing as little oxygen as possible, forms $(M - HCl)^-$ ions by a reaction that involves a cyclization (Fig. 8). The sequence is probably:

$$\begin{aligned} M &\rightarrow M^- \\ M^- &\rightarrow Cl^- + (M - Cl)\cdot \\ (M - Cl)\cdot &\rightarrow (M - HCl) + H\cdot \\ (M - HCl) &\rightarrow (M - HCl)^- \end{aligned}$$

The ions that are observed in low yield are Cl^- and $(M - HCl)^-$. When sufficient oxygen is present, the product is $(M - Cl + O)^-$ as shown in Fig. 9. The ion yield of $(M - Cl + O)^-$ is much greater than that of $(M - HCl)^-$, and $(M - Cl + O)^-$ is a phenoxide ion corresponding to a relatively strong acid. The existence of two competing pathways of ionization, one of which involves oxygen as a reagent, suggests that EC detector responses observed for compounds that react with oxygen under ionizing conditions are likely to be variable and to be dependent upon the trace oxygen concentration in the carrier gas. It is not desirable to introduce traces of oxygen into an EC detector, but this can be done under API conditions. The usual recommendation for EC detectors is to remove oxygen from the carrier gas.

Reactions of this kind occur for hexachlorobenzene and for the polychloro-

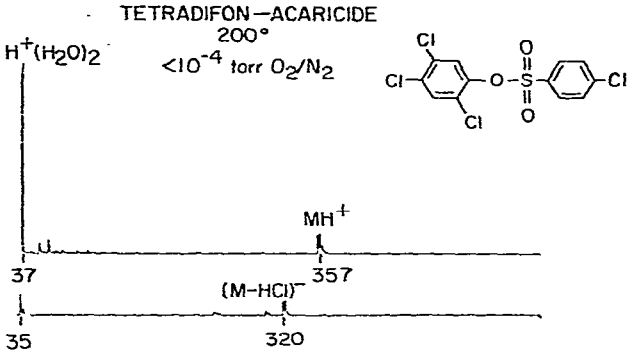


Fig. 8. Negative ion mass spectra observed for Tetradifon with an API negative ion analytical system. The carrier gas was nitrogen. An oxygen scrubber was used, and the oxygen concentration was below 10^{-4} Torr. The major negative ions correspond to Cl^- and $(M-HCl)^-$. The source temperature was 200°. The positive ion mass spectrum shows that the compound was present in the source and was protonated through reactions arising from traces of water in the carrier gas.

biphenyls. They have also been observed under negative ion chemical ionization conditions. For example, Dougherty *et al.*[12] and Hunt *et al.*[13] found phenoxide ions as products from chloronitrobenzenes and polychlorobiphenyls; under these conditions with trace concentrations of oxygen the products included M^- ions, and the reaction probably proceeded primarily through the sequence 2,4,6 rather than 1,3,6. It is assumed that reaction 3 is not reversible, and that the charge transfer sequence 3,4 does not occur because the rate of reaction 6 is faster than that of reaction 4. A somewhat similar reaction has been reported to occur under other conditions for aromatic hydrocarbons, but the mechanism has not been defined. The negative ion mass spectra of benzene[6] and of polycyclic aromatic hydrocarbons[14] have been reported to contain phenoxide ions. This is apparently a general reaction occurring for aromatic

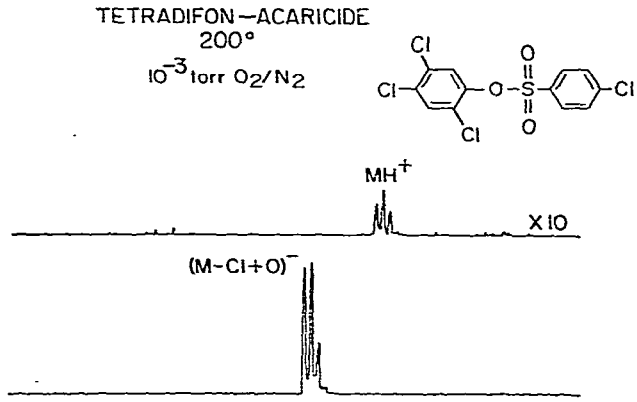


Fig. 9. Negative ion mass spectrum observed for Tetradifon with an API negative ion analytical system. The carrier gas was nitrogen containing oxygen at a concentration of 10^{-3} Torr. The negative ions correspond to $(M-Cl+O)^-$. The reaction leading to $(M-HCl)^-$ was suppressed. The ion yield was greatly improved over that shown in Fig. 8. The sample size and conditions of operation were the same for both Figs., with the exception that nitrogen–oxygen was used as the carrier gas for this Fig., and nitrogen alone was used for Fig. 8.

compounds under ionizing conditions with oxygen present in trace concentration. It is not known if the reacting ionic species is M^-, $(M - H)^-$, O_2^- or O^-, but it is unlikely that water is involved, as suggested earlier[6].

Negative ion formation in argon–methane

Argon containing 5% methane is frequently used as a carrier gas when analyses are carried out with EC detection. Both positive and negative ionizing conditions are present. Stable negative ions which are observed under API conditions should correspond to M^- or to transformation products derived from M^- but not from $(M - H)^-$. Figs. 3 and 10 show the result found for benzil. A stable M^- ion is formed. Although many positive ions are also present in the reaction chamber, the rate of formation of M^- ions exceeds the rate of loss of M^- by reaction with positive ions or by conversion to other ions. It is not possible by direct MS observations to determine if the neutral radical $MH^\cdot$ is present, although this would result from protonation of M^- and might be expected as a reaction product. Fig. 10 shows the responses observed simultaneously for the standard EC detector, for the reaction chamber of the mass spectrometer when treated as an EC detector, and for API MS detection of M^-. These results suggest that the observed EC response is due to the formation of stable M^- ions, as postulated in early studies of EC detection.

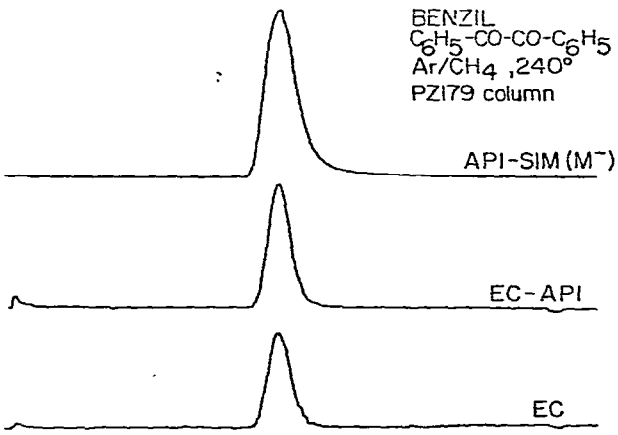


Fig. 10. Responses observed for benzil with an API negative ion analytical system. The EC response is for the standard EC detector; the EC–API response is for the API source treated as an EC detector: and the API–SIM(M^-) response is for the M^- ion of benzil using the technique of selected ion detection. In another run (not shown) a similar experiment with the API system in positive ion mode showed that benzil was present in the source during the EC–API response. The carrier gas was argon–methane and the source temperature was 240°.

Many analyses for pesticides, herbicides and fungicides are carried out by gas chromatography with EC detection, and it is usually assumed that the response is due to the formation of M^- ions or to ions formed by dissociative EC. Fig. 11 shows the responses observed for methyl parathion for the EC detector, for the API reaction chamber treated as an EC detector, and for API MS detection of $(M - 15)^-$. The negative ion mass spectrum of methyl parathion under API conditions is shown in

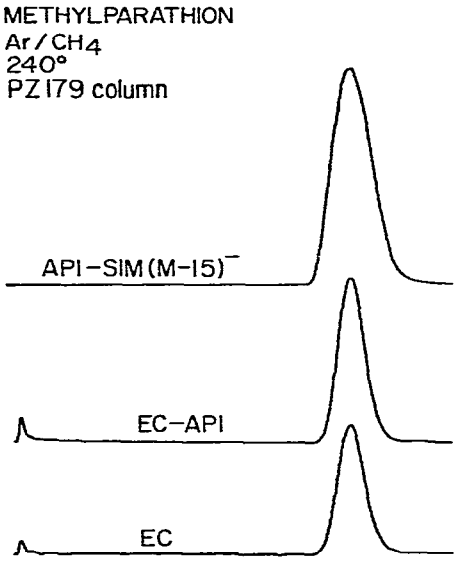


Fig. 11. Responses observed for methyl parathion with an API negative ion analytical system. The EC response is for the standard EC detector; the EC–API response is for the API source treated as an EC detector; and the API–SIM$(M-15)^-$ response is for the $(M-CH_3)^-$ ion of methyl parathion using the technique of selected ion detection. The carrier gas was argon–methane and the source temperature was 240°.

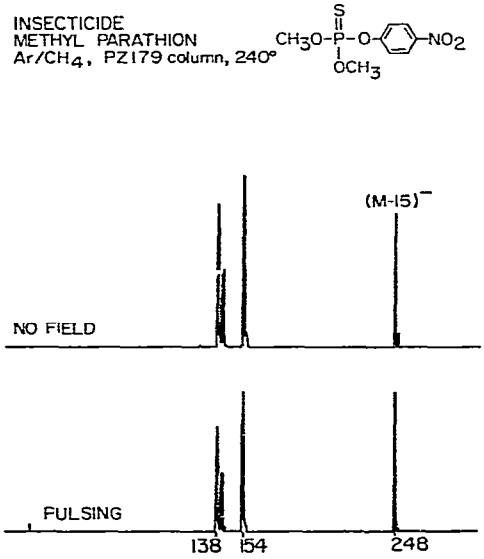


Fig. 12. Negative ion mass spectra observed for methyl parathion with an API negative ion analytical system. The spectra were taken while the sample was in the source as a peak as indicated in Fig. 11. The spectrum observed with the API–EC source in operation is shown as the "pulsing" record. The "no field" mass spectrum was taken without operation of the API–EC detector. The spectra are identical. Simultaneous operation of the API–EC detector and the API mass spectrometer does not affect the mass spectrum. The conditions of operation were the same as for Fig. 11.

Fig. 12. The major ionic products are ions of 138, 154 and 248 a.m.u. An ion corresponding to M^- was not observed, but the loss of a methyl group leading to $(M - 15)^-$ corresponds to the ion at *m/e* 248. The 154-a.m.u. ion is the thionitrophenoxide ion resulting from rearrangement and cleavage, while the 138-a.m.u. ion is the nitrophenoxide ion. The ion at 141 a.m.u. is probably the phosphate anion resulting from loss of a nitrophenyl radical. These are the ions that would be expected for this thiophosphate ester. All correspond to anions of strong gas phase acids. Thus, while the radical ion M^- is very likely the ion which is formed initially, the product ions are anions of acids and not radical ions. This is related to observations made earlier for oxygen substitution reactions; the reason for phenoxide formation from *p*-chloronitrobenzene is the gas phase acidity of *p*-nitrophenol. It would appear that negative radical ions will rearrange or cleave whenever highly stable anions are possible reaction products.

Electron affinity studies carried out with EC detection response as the experimental basis for electron affinity ranking indicate that some polycyclic aromatic hydrocarbons have electron affinities similar to or higher than oxygen[15]. When these compounds were studied under API and EC argon–methane, a response was observed for both the EC detector and the API reaction chamber treated as an EC detector. This result is shown for benzanthracene in Fig. 13. Selected ion detection for MH^+ in the API mass spectrometer showed that benzanthracene was present in in the reaction chamber, but no negative ions were observed. The reasons for this

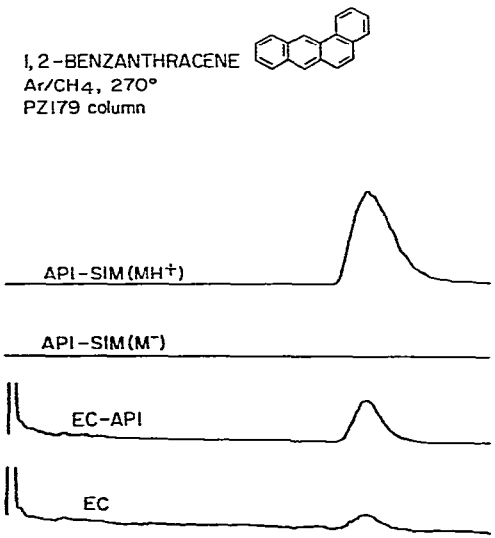


Fig. 13. Responses observed for 1,2-benzanthracene with an API negative ion analytical system. The carrier gas was argon–methane, and the source temperature was 270°. The EC response is for the standard EC detector; the EC–API response is for the API source treated as an EC detector; the API–SIM (M^-) response is for the M^- ion of 1,2-benzanthracene using the technique of selected ion detection; and the API–SIM (MH^+) response is for the MH^+ ion of benzanthracene using the technique of selected ion detection. The results indicate that 1,2-benzanthracene was in the API source and was detected in the same way by the EC and API–EC detectors, but that M^- ions were not present. Mass spectral scans showed no negative ion products corresponding to M^-, $(M-H)^-$ or $(M-H+O)^-$ derived from the hydrocarbon.

effect are not known. Ions corresponding to $(M - H + O)^-$, which are phenoxide ions resulting from reaction with oxygen, have been reported as ionic products under other ionizing conditions[14]. These ions were not observed. The conventional interpretation of a response observed under EC detector conditions is that stable negative ion formation is responsible for the effect. This interpretation is supported by all observations made in the course of this work, except for those relating to polycyclic aromatic hydrocarbons. Further studies are in progress to determine the origin of the EC detector response for these compounds.

Negative ion mass spectrometers

Three types of conditions and instruments have been used for the generation of negative ions in mass spectrometers. The API conditions used in this work involve the generation of thermal electrons in a carrier gas (argon–methane or nitrogen) at atmospheric pressure. The primary source of electrons is a ^{63}Ni foil; a corona discharge has been used in other applications[16–18]. A quadrupole mass analyzer is employed. The analytical instrument described by Siegel and McKeown[19] is similar in design to that used in our initial studies[1]. For the reasons discussed by Siegel and McKeown[19], the ultimate sensitivity of detection reached by API detection of negative ions should exceed that of EC detection. Subpicogram sensitivity of detection has been observed for both positive and negative ions with API systems.

Hunt and his colleagues modified a Finnigan chemical ionization (CI) quadrupole mass spectrometer to provide for the detection of negative ions, and to use a Townsend discharge as a primary source of electrons[14]. Recent reports and presentations[3,14,20] indicate that most negative ions observed under these conditions are the same as those observed under API conditions, with a few exceptions. The formation of M^-, $(M - H)^-$ and $(M - H + O)^-$ ions from polycyclic aromatic hydrocarbons in a CI source is in accord with earlier work under low pressure conditions, but these ions have not been observed under API conditions. Dougherty and his colleagues have also used a negative ion chemical ionization mass spectrometer to study ion molecule reactions involving the formation of adduct ions, as well as the direct formation of negative ions[12,21–23]. It is likely that in most instances negative ions observed under CI and API conditions will be the same; this will certainly be true for stable negative ions. CI negative ion mass spectrometers are now commercially available.

The formation of negative ions under low pressure conditions[5,6] is not directly comparable to negative ion formation under CI or API conditions. While the initial reaction under all conditions is probably M^- formation, followed most often by immediate conversion to $(M - H)^-$ ions, the relatively unstable negative ions observed under low pressure conditions are not seen under API or CI conditions.

CONCLUSION

Most pesticides, herbicides and fungicides, as well as many other types of compounds that are environmental hazards and are cytotoxic or mutagenic, form stable negative ions under API conditions. Many of these substances can be ionized directly in carrier gases such as argon–methane or nitrogen, while others are best ionized by reaction in nitrogen–oxygen. These environmentally hazardous materials are usually

present in biological tissues, foods, soils and water in low concentration, and the chief problem in detection and in quantitative analysis is interference from other sample components. Since some of these compounds (for example, polychlorobiphenyls) are now widely distributed, almost every analysis carried out for hazardous substances will require some evidence of identity for the compounds under analysis. Retention behavior does not provide adequate evidence of identity, and an EC detector response is observed for many toxic compounds. The most effective method of analysis is likely to be the use of analytical systems based upon API negative ion MS.

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