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NEGATIVE ION CHEMICAL IONIZATION GAS CHROMATOGRAPHY-MASS SPECTROMETRY OF SOME DERIVATIVES OF TRI-, TETRA- AND PENTACHLOROPHENOLS

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SUMMARY

The methane negative ion gas chromatographic (GC)–mass spectrometric and electron capture GC behaviour of tri-, tetra- and pentachlorophenols have been investigated as their pentafluorobenzyl ethers, pentafluorobenzoate esters, heptafluorobutyrate esters, trifluoroacetate, acetate and 2,4-dinitrophenyl ether derivatives. The derivatives of choice for optimum detection of chlorophenols are the pentafluorobenzyl ether and pentafluorobenzoate ester because of the strong negative ion signal which is derived from the chlorinated phenol, rather than reagent moieties, in each instance. Using this procedure the chlorophenols present in an industrial starch adhesive and in water collected near an industrial dumping site were determined.

INTRODUCTION

Intensive use of 2,4,6-trichlorophenol (2,4,6-TCP), 2,3,4,6-tetrachlorophenol (2,3,4,6-TeCP) and pentachlorophenol (PCP) and their salts as preservatives and biocides has resulted in this group of compounds becoming one of the most ubiquitous of the environmental pollutants[1]. Many chlorophenols are highly toxic[2,3] while they, and their microbiologically methylated products (polychloroanisoles), possess odour and taste spoiling properties to which humans have very low thresholds of detection[4,5]. It is therefore of considerable importance to develop sensitive and specific analytical techniques for the trace detection of these compounds in such complex matrices as environmental and biological extracts as well as food samples and food packaging materials.

Diverse chromatographic techniques have been used in this regard. By gas chromatography (GC) or high-performance liquid chromatography (HPLC), many chlorophenol isomers, or their derivatives, have been totally or partially separated[6–11]. To improve GC properties, and to maximize the response available with electron capture detectors, chlorophenols have been derivatized as their alkyl ethers[12,13],

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acetyl esters[14,15], heptafluorobutyrate (HFB) esters[16] and nitroaromatic ethers[17]. In addition, attempts have been made to analyse chlorophenols directly on specially treated GC columns[18,19] and by HPLC[9-11,20,21].

However, in spite of the prodigious advances in resolution and sensitivity, both GC and HPLC techniques suffer from being non-specific methods of detection. A confirmatory technique based on mass spectrometry (MS) and involving either GC–MS or LC–MS is required for the specific identification of these pollutants[7,8,12,18,22]. The sensitivity of detection of polychlorinated aromatic systems by GC–electron-capture detection (ECD) may be 2–3 orders of magnitude greater than conventional electron or chemical ionization (EI or CI) mass spectrometry. These latter methods lack the sensitivity for practical support of GC–ECD analysis of traces of chlorophenols present in complex matrices.

Electron capture negative ion chemical ionization mass spectrometry (NICI-MS)[23-25] provides a sensitivity of detection comparable to GC–ECD with the important advantage that it furnishes evidence of molecular structure and can be used for compound identification. As with GC–ECD, only those molecules possessing a positive electron affinity will be ionized under EC–NICI conditions. Dissociative or non-dissociative processes, or ejection of the captured electron, are all possible repercussions of the ionization process. The neutral chemical ionization gas in this instance serves as a moderator gas to stabilize anions through collisional deactivation. In recent years both this mode of NICI-MS, and that using negative anions to promote ionization of sample molecules, have been extensively applied in environmental analyses to exploit the superior sensitivity and selectivity of detection available with many toxic pollutants[26-30]. Dougherty and co-workers[31-33] have developed a multi-residue screening procedure utilizing dichloromethane–methanol–isobutane, and solid probe sample introduction for the NICI-MS analysis of polychlorinated aromatics in environmental samples, food, human tissue and body fluids, and PCP and 2,3,4,6-TeCP were detected in nearly all cases. Bayer and Lowe[22] briefly reported a NICI-GC–MS qualitative and quantitative analysis of phenolic priority pollutants which had been derivatized as their pentafluorobenzyl ether derivatives.

Suitable derivatization is crucial for both GC–ECD and NICI-MS analyses and we now report an investigation of various derivatizing agents for chlorophenol detection by both techniques. Three chlorophenols (2,4,6-tri-, 2,3,4,6-tetra- and penta-) were investigated as their respective acetates (Ac), pentafluorobenzyl (PFBz) ethers, pentafluorobenzoate (PFB) esters, heptafluorobutyrate (HFB) esters, trifluoroacetates (TFA) and 2,4-dinitrophenyl (2,4-DNP) derivatives. The NICI fragmentation of these compounds is presented together with their GC behaviour on different columns. The PFBz ether and PFB ester are the derivatives of choice for the trace analysis of these chlorophenols and high femtogram (fg) levels of detection are routinely accessible by both GC–ECD and NICI-MS using these derivatives.

EXPERIMENTAL

Chemicals

Chlorophenols and pentafluorobenzoyl chloride were obtained from Fluka (Buchs, Switzerland). These compounds were recrystallized, dried and standard solutions prepared in acetone (0.5 μg/μl). Pentafluorobenzyl bromide, trifluoroacetic

anhydride and heptafluorobutyric anhydride were purchased from Pierce (Rockford, IL, U.S.A.). 2,4-Dinitrofluorobenzene and [$^2H_6$]acetic anhydride were supplied by Sigma (St. Louis, MO, U.S.A.). Acetic anhydride was purchased from May and Baker (Sydney, Australia). All solvents were redistilled prior to use and procedural blanks were analysed by GC–ECD or HPLC before sample analyses.

Instrumentation

A Packard 427 gas chromatograph equipped with a ^{63}Ni source and Model 902 electron capture detector was used. Separations were carried out on all-glass columns (1.8 m × 3 mm) packed with 3% OV-17 on Gas-Chrom Q (100–120 mesh) (Applied Science, State College, PA, U.S.A.). The carrier gas was nitrogen (flow-rate 20 ml/min) and the electron capture detector scavenger flow-rate was 20 ml/min.

A Waters Assoc. HPLC system equipped with a Model 440 UV detector (wavelength 254 nm) and a C_{18} µBondapak column (10 µm, 30 cm × 3.9 mm) was used with a mobile phase consisting of methanol (58%), water (containing 0.5% acetic acid) (35%) and acetonitrile (7%) at a flow-rate of 1.1 ml/min.

GC–MS data were recorded on a Finnigan quadrupole 3200 chemical ionization system interfaced to a Finnigan Incos Model 2300 data system. The mass spectrometer was scanned from m/z 60 to 660 in 2 sec. GC separations were conducted on glass U-shaped columns (1.8 m × 2 mm I.D.) packed with 3% OV-17 or 3% OV-101 (see above). The GC–MS interface oven and transfer line were maintained at 260–280°C. Negative ion mass spectra were recorded with a Finnigan PPINICI module. The electron multiplier voltage was 1.1 kV, the filament emission 1.0 mA and the ionizing energy 100–110 eV. Chemically pure methane or nitrogen (Matheson, Coleman & Bell, East Rutherford, NJ, U.S.A.) served as the GC carrier gas with a flow-rate of 20 ml/min and also as the CI moderator gas (ion source pressure 0.8–0.9 Torr). The diverter valve was opened for 45 sec following sample injection; 15 sec later the GC oven was temperature programmed and the data system activated and the MS scan commenced.

Chemical derivatization[34]

To the chlorophenol (1–5 µg) in a 2-ml Reacti-Vial were added pyridine (1 µl) and acetone (400 µl). For PFBz ether formation, potassium carbonate (0.1 mg) replaced pyridine and for 2,4-DNP ether formation xylene was used instead of acetone. The appropriate derivatizing agent (10–15 µl) was added and the reaction mixture heated at 60°C for 30 min (2,4-DNP ether at 100°C for 1 h). After cooling, the solvent was removed (nitrogen), hexane (0.5 ml) added and the organic phase washed briefly with water (0.5 ml). The TFA derivatives are easily hydrolyzed by water and these derivatives were not subjected to the final water wash, while for the 2,4-DNP ethers 0.1 *M* sodium hydroxide replaced water for this step. The organic phase was dried (sodium sulphate) and diluted to the desired concentration for instrumental analysis. Methane PICI-GC–MS was used to confirm the authenticity of the products from the expected [MH]$^+$ and fragmentation pattern.

The PFBz ether derivative of PCP was prepared in mg amounts and recrystallized from acetone–water. A stock solution was made up in toluene at a concentration of 1 ppm. This solution was sequentially diluted for the estimation of this compound's detection limit by NICI-MS and GC–ECD detection.

Analysis of chlorophenols present in industrial starch adhesive

Starch adhesive (5 g) was processed by the method previously developed[35] for the HPLC analysis of chlorophenols to yield a methanolic solution (1 ml), and aliquots (20 μl each) were injected three times into the HPLC apparatus. The peaks corresponding to 2,3,4,6-TeCP and PCP were each collected separately, adjusted to pH 9 with 1 M sodium hydroxide and the organic solvent removed *in vacuo*. The residue was acidified (2 M sulphuric acid) to pH 3 extracted with hexane (2 × 1 ml) and derivatized as the PFBz ether as described above. The resulting solution was diluted (1:100) and 1 μl injected for both GC–ECD and NICI-GC–MS analyses.

For an independent analysis of the same sample, without HPLC separation adhesive (0.5 g) in water (100 ml) was acidified to pH 2 with 2 M sulphuric acid and steam distilled to yield 40 ml of distillate. A portion (10 ml) was acidified (2 M sulphuric acid) to pH 3, extracted with hexane and the residue, after removal of the organic solvent, derivatized with PFBz-Br. The derivatized sample in hexane (1 ml) was diluted 1:10^4 when injection (1 μl) intersected the 0.1–1 pg response of the electron-capture detector for these derivatives.

Identification of chlorophenols in a water sample collected adjacent to an industrial dump

Surface water (2 l) was collected from an industrial dump site near Shanghai and extracted with hexane (3 × 50 ml). The organic phase was concentrated to 3–5 ml (Büchi Rotavapor) and then to 0.3 ml with nitrogen gas. This concentrate was reacted with PFBz-Br to yield a final volume of 0.2 ml. Aliquots (2 μl) were then injected for methane NICI-GC–MS analysis. One minute after sample injection the GC column (3% OV-101) was temperature programmed from 80°C to 300°C at 8°C/min.

RESULTS AND DISCUSSION

Three chlorophenols, 2,4,6-TCP, 2,3,4,6-TeCP and PCP, were initially investigated as they represent the most common environmental pollutants within this

TABLE I

RETENTION TIMES OF SIX DERIVATIVES OF THREE CHLOROPHENOLS USING NICI-GC-MS

The GC oven temperature was programmed at 10°C/min. Separations were completed using 3% OV-17 on Gas-Chrom Q.

Derivative	Retention time (min)			Initial temp. (°C)
	2,4,6-TCP	2,3,4,6-TeCP	PCP	
PFBz	6.3	8.3	10.2	130
PFB	6.0	8.0	9.7	150
HFB	3.5	6.0	7.7	90
TFA	3.3	5.5	7.2	90
2,4-DNP ether	5.2	6.3	8.0	220
Acetate	2.5	6.2	8.7	120

group of compounds. Six derivatives were prepared of each of these compounds and their GC retention times are recorded in Table I. All the derivatives showed symmetrical peak shapes by GC–ECD analyses.

These same compounds were then subjected to an EC-NICI-GC–MS investigation. Prior to this their PICI mass spectra were recorded to verify from the $[MH]^+$ and fragmentation patterns the correct identity of each derivative. Both the PICI- and NICI-MS of the derivatives of these three chlorophenols are summarized in Table II. The PI spectra all showed easily recognizable $[MH]^+$ (base peak for the 2,4-DNP, HFB, TFA and Ac derivatives). The PFBz and PFB analogues had ions of masses 181 $[C_6F_5CH_2]^+$ and 195 $[C_6F_5CO]^+$ as their respective base peaks for all three chlorophenols.

The methane EC-NICI mass spectra of 2,4,6-TPC, 2,3,4,6-TeCP and PCP, as their respective 2,4-DNP, HFB, TFA and Ac derivatives, were dominated by the product anions of resonance dissociation, $[OR]^-$, corresponding to the derivatizing agent plus the phenolic oxygen atom, except for the 2,4-DNP analogue which produced R^-. In addition the sensitivity of detection of the acetoxy and 2,4-DNP ether derivatives was found to be significantly lower than of the other compounds investigated. The PFBz ether and PFB ester derivatives of selected chlorophenols (Table II) had their base peak anions (90% relative abundance for the PCP-PFB) corresponding to the chlorophenol anion (expulsion in each instance of perfluorobenzyl and perfluorobenzoyl radicals respectively) and no other peak exceeded 10% relative abundance. Thus, for the identification of trace quantities of chlorophenols with EC-NICI-GC–MS, the PFBz or PFB ester derivatives are preferred because of the retention of the chlorophenol entity with its characteristic chlorine isotope patterns in the most abundant anionic species. For chlorophenol detection in complex mixtures (as discussed below) we elected to use the PFBz ether derivative because of the increased per cent total ionization of its base peak anions relative to the PFB ester analogues.

The acetoxy derivatives of the chlorophenols were examined under methane NICI conditions to gauge the effect of tri-, tetra- and pentachlorophenyl substitution on the detection response and fragmentation behaviour of these compounds. As expected the acetoxy derivatives, especially the TCP acetates, gave far weaker negative ion detection responses than did their PFBz analogues. Within the acetoxy compounds the following order of detection was observed: PCP > 2,3,4,6-TeCp > 2,4,6-TCP in the ratio of 70:25:1. The NICI mass spectra of the acetoxy chlorophenols showed molecular anions for PCP and 2,3,4,6-TeCP compounds, while the TCP isomers had weak $[M - H]^-$ and others (2,4,5- and 2,3,5-TCP respectively) lacked $[M]^-$ and $[M - H]^-$.

Fragmentation of the $[M]^-$ of PCP and 2,3,4,6-TeCP acetates occurred by the elimination of CH_2CO and $Cl^{\cdot}$ radicals. A species equivalent to $[M - 19]^-$ resulted from the elimination of $Cl^{\cdot}$ with concomitant oxygen abstraction (from traces of oxygen present in the ion source), and the product ion had a chlorine isotope pattern consistent with this chain of events. In the case of PCP a further loss of $Cl^{\cdot}$ plus CH_2CO with oxygen capture from the ion source produced the anion of mass 225 (6% relative abundance) which remained at this mass in the spectrum of the $^2H_3$-labelled acetate.

Loss of ketene (CH_2CO) from the $[M - Cl]^-$ species accounts for a prominent

TABLE II

PRINCIPAL IONS OBSERVED IN THE METHANE PI AND NI CHEMICAL IONIZATION MASS SPECTRA OF SOME DERIVATIZED CHLOROPHENOLS

Correct isotope ratio intensities were observed for all chlorinated ions. For ions containing multiple chlorine atoms the lowest mass ion within the cluster is recorded. m/z (relative abundance); fragments less than 10% relative abundance are not listed.

Chlorophenol	Derivative	Pentafluorobenzyl	Pentafluorobenzoate	2,4-Dinitrophenyl	Heptafluorobutyryl	Trifluoroacetyl	Acetyl
2,4,6-TCP	NI	195 (Cl_3) 100% $(M - 181)^-$	195 (Cl_3) 100% $(M - 195)^-$ 167 (Cl_0) 73% $(C_6F_5)^-$	167 (Cl_0) 100% 183 (Cl_0) 22% 195 (Cl_3) 10% $(M - 167)^-$	213 (Cl_0) 100% 195 (Cl_3) 20%	113 (Cl_0) 100%	195 (Cl_3) 100% 160 (Cl_2) 22%
	PI	181 (Cl_0) 100% 377 (Cl_3) 2% $(MH)^+$	195 (Cl_0) 100% 391 (Cl_3) 23% $(MH)^+$	363 (Cl_3) 100% $(MH)^+$	393 (Cl_3) 100% $(MH)^+$	293 (Cl_3) 100% $(MH)^+$	239 (Cl_3) 100% $(MH)^+$
2,3,4,6-TeCP	NI	229 (Cl_4) 100%	229 (Cl_4) 100% 167 (Cl_0) 73%	167 (Cl_0) 100% 183 (Cl_0) 30% 229 (Cl_4) 20%	213 (Cl_0) 100% 229 (Cl_4) 20%	113 (Cl_0) 100%	195 (Cl_3) 100% 229 (Cl_4) 50% 272 (Cl_4) 25%
	PI	181 (Cl_0) 100% 411 (Cl_4) 0.1% $(MH)^+$	195 (Cl_0) 100% 425 (Cl_4) 30% $(MH)^+$	397 (Cl_4) 100% $(MH)^+$	427 (Cl_4) 100% $(MH)^+$	327 (Cl_4) 100% $(MH)^+$	273 (Cl_4) 100% $(MH)^+$
PCP	NI	263 (Cl_5) 100%	167 (Cl_0) 100% 263 (Cl_5) 90%	167 (Cl_0) 100% 183 (Cl_0) 50% 263 (Cl_5) 15%	213 (Cl_0) 100% 263 (Cl_5) 30%	113 (Cl_0) 100%	306 (Cl_5) 100% 263 (Cl_5) 50% 229 (Cl_4) 60%
	PI	181 (Cl_0) 100% 445 (Cl_5) 0.1% $(MH)^+$	195 (Cl_0) 100% 459 (Cl_5) 22% $(MH)^+$	431 (Cl_5) 100% $(MH)^+$	461 (Cl_5) 100% $(MH)^+$	361 (Cl_5) 100% $(MH)^+$	307 (Cl_5) 100% $(MH)^+$

TABLE III

DETECTION LIMITS FOR PCP-PFBz ETHER BY NICI- AND PICI-GC–MS AND GC–ECD

	NICI	PICI	GC–ECD
Ion current monitored (m/z)	263	181	—
Signal:noise	5:1	2:1	10:1
Amount injected	0.1 pg	0.1 ng	0.1 pg

anion of mass 229, 195 and 161 in the NICI-MS of PCP, 2,3,4,6-TeCP and 2,4,6-TCP respectively. All these anions retained one deuterium atom when their $^2H_3$-labelled acetates were investigated.

The ion source temperature is known to effect NICI mass spectra. Hass et al.[36] reported that a change of 25°C in ion source temperature was sufficient to reduce the base peak of a polychlorodiphenyl ether to very low relative intensity. We have noted a similar effect with the molecular anion of PCP-Ac where this species was reduced from 100% to 0.4% relative abundance by increasing the ion source temperature
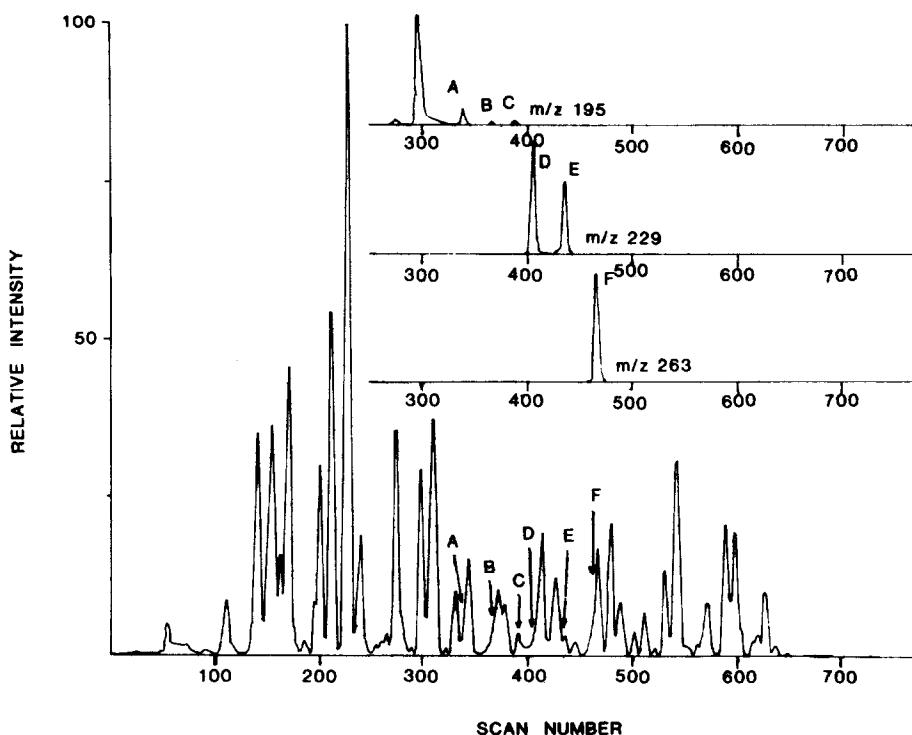

Fig. 1. Methane NICI–GC–MS total ion current trace recorded from an analysis of surface water collected near an industrial dump site. The mass chromatograms for m/z 195, m/z 229 and m/z 263 locate the GC retention time and peak profile of the individual chlorophenol-PFBz ether derivatives which were identified as follows: A = 2,4,6-TCP; B = 2,4,5- or 2,3,4-TCP; C = 3,4,5-TCP; D = 2,3,4,6-TeCP; E = 2,3,4,5-TeCP; F = PCP. The retention times were identical to those recorded with authentic standards under similar chromatographic conditions.

from 160°C to 200°C. When the PFBz ether derivative of the same phenol was subjected to a similar increase in ion source temperature the base peak remained at m/z 263.

A comparison of the detection levels of PCP-PFBz using methane NICI-MS, EC-GC and methane PICI-MS is shown in Table III. Selected ion monitoring using the ion of mass 263 (NI) and 181 (PI) was used to record the respective MS responses. The results indicate that NICI and GC–ECD yield similar detection responses which were 10^3 times that available with methane PICI mass spectrometry.

Two applications of the use of PFBz derivatization for chlorophenol determination were the confirmation of 2,3,4,6-TeCP and PCP in an industrial starch adhesive with, and without, prior HPLC fractionation. These compounds were present in the adhesive sample at concentrations of 50–80 ppm and are easily detectable using the NICI-GC–MS technique provided appropriate sample dilutions are made.

The analysis of the chlorophenol content of surface water collected at an industrial dump site was achieved using the technique of derivatizing the target compounds as their PFBz ethers following solvent extraction of the water sample. Fig. 1 demonstrates the complex total ion chromatogram (TIC) obtained by methane NICI-GC–MS analysis of the water sample. The chlorophenol ether derivatives are hidden within the complex peak profiles of other more concentrated constituents. However, using the mass chromatograms for anions characteristic of TCP, TeCP and PCP PFBz ether (m/z 195, 229 and 263 respectively), the target compounds can be localized (Fig. 1) and their mass spectra determined after subtraction of neighbouring background contributions. The mass spectra recorded over these mass chromatogram peak profiles displayed the required chlorine isotope patterns consistent with their identifications (Fig. 1). This and the GC retention times were sufficient to identify the chlorophenols bearing in mind that their methane NICI mass spectra (Table II) are essentially the same within the derivatized tri- and tetrachlorophenol isomers respectively.

CONCLUSIONS

We have developed a sensitive and specific method for the negative ion GC–MS analysis of chlorophenols. The technique utilizes pentafluorobenzyl ether derivatization, which because of the intense negative ion signal incorporating the chlorophenoxy portion of the derivatized molecule, is suitable for trace sample identification. The technique has been used for the detection of chlorophenols (easily recognized) from their characteristic multiple chlorine isotope patterns) in complex matrices such as starch adhesives and surface water.

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