of membranes with HPLC will be limited to problems where due consideration is given their current limitations in terms of the molecular weight and polarity of analyte.

The results obtained in this paper depend on the operation of the hollow fiber membranes in the mode (*18*) in which the fluid sample stream flows *through* the capillary tube. This approach can be contrasted with that in which the permselected analyte itself moves through the capillary which is surrounded by fluid analyte (Figure 8). The permeation step is identical, but the method used herein has substantial analytical advantages. These include the efficiency of analyte transport by the fluid into the heart of the analyzer, applicability of flow injection analysis as a means of introducing standard samples and of controlling contact times, and the fact that the molecules emerge from the membrane directly into a low-pressure environment where they are effectively transported through the ionization region.

ACKNOWLEDGMENT

We express our appreciation to Weldon Vaughn for his precision machining and George Tsao and Norm Jensen for the fermentation samples.

LITERATURE CITED

(1) Westover, L. B.; Tou, J. C.; Mark, J. H. *Anal. Chem.* **1974**, *46*, 568.
(2) Weaver, J. C.; Abrams, J. H. *Rev. Sci. Instrum.* **1979**, *50*, 478.
(3) Jones, P. R.; Yang, S. K. *Anal. Chem.* **1975**, *47*, 1000.
(4) Kallos, G. J.; Mahle, N. H. *Anal. Chem.* **1983**, *55*, 813.
(5) Calvo, K. C.; Weisenberger, C. R.; Anderson, L. B.; Klapper, M. H. *Anal. Chem.* **1981**, *53*, 981.
(6) Eustache, H.; Histi, G. *J. Membr. Sci.* **1981**, *8*, 105.
(7) Tou, J. C.; Kallos, G. T. *Anal. Chem.* **1974**, *46*, 1866.
(8) Evans, J. E.; Arnold, J. T. *Environ. Sci. Technol.* **1975**, *9*, 1134.
(9) Woldring, S.; Owens, G.; Woolford, D. C. *Science (Washington, D.C.)* **1966**, *153*, 885.
(10) Roberts, M.; Cotton, E. T.; Owens, G.; Watkins, G. M. *Med. Biol. Eng.* **1975**, *13*, 535.
(11) Weaver, J. C.; Mason, M. K.; Jarrell, J. A.; Peterson, J. W. *Biochim. Biophys. Acta* **1976**, *438*, 296.
(12) Calvo, K. C.; Weisenberger, C. R.; Anderson, L. B.; Klapper, M. H. *J. Am. Chem. Soc.* **1983**, *105*, 6935.
(13) Pungor, E.; Pecs, M.; Szigeti, L.; Nyeste, L. *Anal. Chim. Acta* **1984**, *163*, 185.
(14) Llewellyn, P. M.; Littlejohn, D. P. U.S. Patent 3 429 105, Feb 1969.
(15) Schmidt, W. J.; Meyer, H. D.; Schugerl, K. *Anal. Chim. Acta* **1984**, *163*, 101.
(16) Heinzle, E.; Moes, J.; Griot, M.; Kramer, H.; Dunn, I. J.; Bourne, J. R. *Anal. Chim. Acta* **1984**, *163*, 219.
(17) Reuss, M.; Piehl, H.; Wagner, F. *Eur. J. Appl. Microbiol.* **1975**, *1*, 323.
(18) Brodbelt, J. S.; Cooks, R. G. *Anal. Chem.* **1985**, *57*, 153.
(19) Bier, M. E.; Cooks, R. G.; Brodbelt, J. S.; Tou, J. C.; Westover, L. G. U.S. Patent pending.
(20) Yost, R. A.; Fetterolf, D. D. *Mass Spectrom. Rev.* **1983** *2*, 1.
(21) Cooks, R. G.; Busch, K. L. *J. Chem. Educ.* **1982**, *13*, 535.

RECEIVED for review July 29, 1986. Accepted November 3, 1986. This work was funded by the National Science Foundation (CHE 84-08258).

Electron Capture Negative Ion Chemical Ionization Mass Spectrometry of Derivatized Chlorophenols and Chloroanilines

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The electron capture negative ion chemical ionization mass spectra of electrophoric derivatives (perfluoroacyl, pentafluorobenzyl, pentafluorobenzoyl, 3,5-bis(trifluoromethyl)-benzoyl, and (pentafluorophenyl)methanimine) of chloro-substituted phenols and anilines have been investigated. The formation of analyte-specific anions in the spectra of the derivatives is strongly influenced by the nature of the electrophoric group and the summed electron-donating or -withdrawing properties of the aromatic ring substituents. Hammett linear free energy relationships can be used to predict the stability of molecular anions, the direction of fragmentation pathways, and the usefulness of a given derivative for analytical purposes by using selective-ion monitoring. The influence of ion source temperature on the ionically induced dissociation of the derivatives was examined. The relative molar responses of different derivatives under conditions of GC–negative ion chemical ionization mass spectrometry and GC–electron capture detection were comparable.

At least three of the most sensitive techniques for the detection of organic compounds at the trace level are based on the process of gas-phase electron capture. These are the electron capture detector utilized in gas chromatography (GC–ECD), the conventional mass spectrometer operated in the electron capture negative ion chemical ionization mode (EC-NCIMS), and the atmospheric pressure ionization mass spectrometer (API-MS). In each case, extremely low detection limits, approaching the low femtogram (10^{-15} g) range, have been demonstrated for compounds amenable to electron capture (*1–3*). In general, this ionization process is based on the production of near thermal energy electrons (ca. 0 eV) followed by electron–molecule reactions creating organic anions in the gas phase. The ionization efficiency of molecules by this process is highly structure dependent. This feature allows for selective techniques, with high sensitivity for favorable cases. The presence of structural elements possessing low level unoccupied molecular orbitals is found to facilitate this ionization. This translates to compounds containing halogens, nitro groups, and highly conjugated systems.

Unfortunately, many compounds of interest are not inherently electrophoric and must be converted to a suitable volatile derivative for analysis by any of the aforementioned EC techniques. A vast literature base has developed over the last 20 years concerning the synthesis of EC derivatives for the GC–ECD (*4–6*). Hunt (*2*, *7*) has pioneered the use of popular GC–ECD derivative methodology for the analysis of nonelectrophoric compounds by negative ion mass spectrometric techniques. To be of use in EC-NCIMS, the derivatized molecule must not only favor the capture of electrons but, just as important, stabilize the negative charge in a manner in which anions characteristic of the derivative or original analyte

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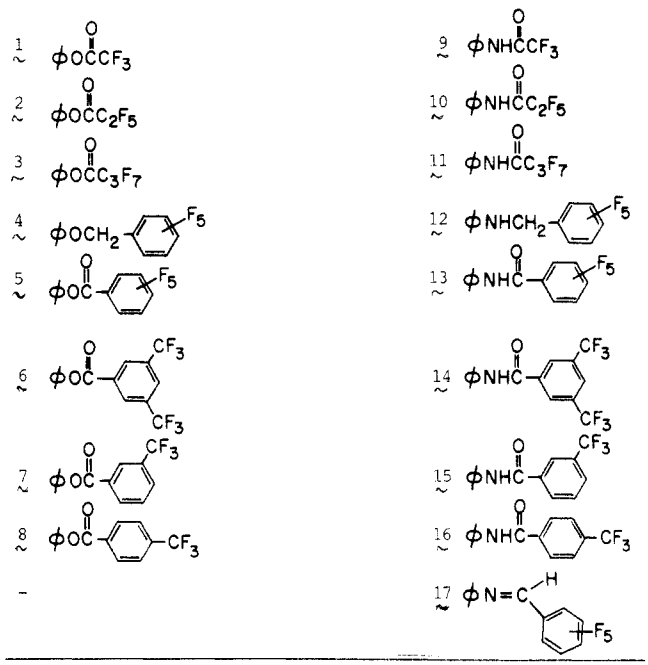
Table I. Structures of Phenol and Aniline Derivatives ($\phi = C_6H_5$)



predominate in the mass spectrum. In many instances, the observed fragmentation of derivatives contains a preponderance of ions stemming from the introduced electrophore. For instance, acidic and alcoholic catecholamine metabolites converted to the corresponding pentafluoropropionyl derivatives have been shown to fragment under EC-NCIMS conditions to primarily a series of ions at m/z 128, 147, and 163 corresponding to the fragments $C_2F_4CO^-$, $C_2F_5CO^-$, and $C_2F_5CO_2^-$, respectively (*8*). This presents a limitation to the application of selected ion monitoring techniques, GC–SIM–MS, since the presence of ions specific to the original analyte is necessary for unequivocal characterization. Therefore, when a derivative is selected for the quantitative analysis of a compound by EC-NCIMS, major considerations in terms of derivative selection include (1) good chromatographic performance, (2) high synthetic yields, (3) high ionization efficiency, and (4) high relative abundance of analyte-specific ions.

Many of the perfluorinated acylation and alkylation reagents that have been described in the GC–ECD literature (*4*) will produce stable derivatives of a variety of functionalities that satisfy criteria 1 and 2. However, as noted in a review of the EC-NCIMS technique (*8*), systematic studies on the suitability of different electrophoric derivatives for the analysis of specific compounds by EC-NCIMS have not yet appeared. We report here on an examination by EC-NCIMS of five of the most popular EC derivatives (trifluoroacetyl, pentafluoropropionyl, heptafluorobutyryl, pentafluorobenzoyl, and pentafluorobenzyl), as well as several novel EC derivatives, of a series of test analytes. These derivatives were compared in terms of their fulfillment of criteria 3 and 4 above. Selected as test analytes were a number of chlorinated phenols and anilines. This selection was based, in part, on the substantial environmental concerns surrounding these compounds. Moreover, the aromatic hydroxy and amino functionalities are pervasive in the realm of industrially and biologically important chemicals, and their associated intermediates, degradation products, and metabolites.

The structures of the derivatives studied are presented in Table I. Hunt has previously reported the EC-NCIMS spectra of 5, 13, and 17 (*2, 7*). Shang-Zhi and Duffield reported the spectra of a number of derivatives of pentachlorophenol, 2,3,4,6-tetrachlorophenol, and 2,4,6-trichlorophenol (*9*). Unfortunately, these studies obtained spectra in a range above m/z 60, thus failing to observe the ion Cl^- (m/z 35 and 37), a prominent signal in the EC-NCIMS of many chlorinated species (*10–12*). In this work, we focused on the influence of both the analyte and final derivative structure on the resulting fragmentation pattern under methane EC-NCIMS conditions. A useful parameter to evaluate changes in the observed spectra was found to be the Hammett free energy relationship (*13*). Indeed, for several of the series of chlorinated derivatives, a correlation exists between the log ratio of analytically important ions and the Hammett σ substituent constants.

EXPERIMENTAL SECTION

Reagents. Solvents used included methanol, cyclohexane, methylene chloride, and ethyl acetate and were residue grade (J. T. Baker). All derivatization reagents, phenols, and anilines were purchased from Aldrich and used as received. Stock solutions of the individual phenols and anilines were prepared by diluting each compound to a concentration of approximately 1 $\mu g/\mu L$ in methanol. All glassware and syringes were treated with hexamethyldisilazane (*14*) to minimize losses due to surface adsorption.

Instrumentation. All GC–MS analyses were carried out on a Finnigan 4021 GC–MS equipped with a 15-m DB-5 capillary column (J&W, 0.25-μm film) directly inserted into the ion source. Helium (Matheson, UHP) was used as carrier gas, while methane (Matheson, UHP) served as the CI reagent gas. The ion source tuning was carried out in the negative ion mode by using perfluorotributylamine. Typical MS operating parameters included: 70-eV ionizing potential, 0.40-mA filament current, 0.30-torr source pressure, and 1000-V electron multiplier setting. The Finnigan-Incos data system was programmed to scan the range from m/z 18 to 500 in 0.50 s for the full scan runs. In the case of the SIM experiments, the mass spectrometer was scanned over one amu in 0.25 s. The GC oven was initially set at 110 °C and ramped linearly at 15 °C/min to 300 °C. Injections were made by using the on-column technique (*15*) utilizing an injector and fused silica needle syringe supplied by J&W. For the chlorinated compounds, only the most intense peak in each isotope cluster is reported here. The expected isotope pattern was observed in all instances. In the instances where no molecular anion $M^{\bullet-}$ could be observed, derivative structures were confirmed by using both methane positive chemical ionization and electron-impact MS.

For the GC–ECD study, a Varian Model 3700 gas chromatograph equipped with a Varian constant-current variable-frequency ^{63}Ni electron-capture detector and a Varian Model 11095 temperature programmable on-column injector was used. The GC–ECD chromatograms were recorded with a Spectra-Physics Model 4270 digital integrator. The identical 15-m DB-5 column utilized in the GC–MS experiments was installed in the GC–ECD. The carrier and ECD makeup gases were helium (UHP, Matheson) and nitrogen (UHP, Matheson), respectively. Flow rates, measured at 20 °C, were 5 cm^3/min for helium and 25 cm^3/min for nitrogen. Injections were made by using a 5-μL syringe equipped with a stainless-steel needle (Varian). The on-column injector was initially set at 100 °C and heated to a temperature of 290 °C at a rate of 180 °C/minute upon sample injection. The GC oven was kept at 120 °C for 1.0 min after injection and ramped linearly at 20 °C/min to 220 °C. The detector temperature was maintained at 300 °C.

Preparation of Derivatives. A. Phenols. Appropriate volumes of the methanol solutions containing the five chlorophenols (3-Cl, 4-Cl, 3,4-Cl_2, 3,5-Cl_2, and 3,4,5-Cl_3) and phenol itself were transferred to a 1-mL reacti-vial (Pierce) to give 10 μg of each compound. The methanol was removed under a gentle nitrogen stream, and the appropriate solvent and reagents were added immediately.

1. Trifluoroacetates (1) and Pentafluoropropionates (2). Ethyl acetate (200 μL), triethylamine (1 μL), and the perfluoroanhydride (10 μL) were added to the analyte, and the solution was allowed to react for 30 min at 75 °C. The mixture was then cooled, brought to dryness via nitrogen, and transferred to another vessel by using 0.5-mL aliquots of cyclohexane. The solution was further diluted to give a concentration of 1.0 ng/μL for each derivative.

2. Heptafluorobutyrates (3), Pentafluorobenzoates (5), 3,5-Bis(trifluoromethyl)benzoates (6), 3-(Trifluoro-

Table II. EC-NCI Mass Spectra of Phenol Derivatives

derivative	rel abundance $M^{\bullet-}$	rel abundance ArO^-	other
1	0	0.2	$CF_3CO_2^-$ (100)
2	0	0	$C_2F_5CO^-$ (100), $C_2F_4CO^-$ (23)
3	0	0	$C_3F_7CO^-$ (100), $C_3F_6CO^-$ (6)
4	0	100	
5	100	5	$C_6F_5^-$ (8)
6	100	2	
7	100	1	$CF_3C_6H_4CO_2^-$ (80)
8	100	1	$CF_3C_6H_4CO_2^-$ (19)

Table III. EC-NCI Mass Spectra of Aniline Derivatives

derivative	rel abundance $M^{\bullet-}$	rel abundance $(M - HF)^-$	other
9	0	0	$(M - H)^-$ (100)
10	0	100	$(M - H_2F)^-$ (2)
11	0	100	
12	0	100	$(M - H_2F)^-$ (30)
13	0	35	$(M - H_2F)^-$ (100)
14	100		$(M - H)^-$ (57)
15	80		$(M - H)^-$ (100)
16	100		$(M - H)^-$ (30)
17	100	1	

methyl)benzoates (7), and 4-(Trifluoromethyl)benzoates (8). The above procedure (A.1) was followed with two exceptions. The quantity of derivatization reagent (heptafluorobutyric anhydride or the appropriate benzoyl chloride) was decreased to 5 μL, and the cyclohexane solution was subjected to a wash with distilled water (3 × 0.5 mL). These changes facilitated the removal of these less volatile derivatization reagents prior to the nitrogen drying step.

3. Pentafluorobenzyl Ethers (4). The extractive alkylation procedure of Ehrsson (*16*) was adapted. To the reacti-vial containing 10 μg of each phenol was added methylene chloride (0.5 mL), an aqueous solution of 0.2 M tetrabutylammonium sulfate in 0.1 M NaOH (0.5 mL), and pentafluorobenzyl bromide (1 μL). After the reaction was allowed to proceed for 15 min with constant shaking at room temperature, the aqueous layer was discarded and the organic layer washed with distilled water (2 × 0.5 mL). Next, the methylene chloride was removed via a nitrogen stream, and the contents were transferred to a clean vessel with cyclohexane and diluted to a concentration of 1 ng/μL.

B. Anilines. 1. Trifluoroacetamides (9), Pentafluoropropionamides (10), Heptafluorobutyramides (11), (Pentafluorobenzyl)amines (12), Pentafluorobenzamides (13), 3,5-Bis(trifluoromethyl)benzamides (14), 3-(Trifluoromethyl)benzamides (15), and 4-(Trifluoromethyl)benzamides (16). The reactions were conducted as described in procedure A.2, above, by using 10 μg each of aniline and the five chloroanilines (3-Cl, 4-Cl, 3,4-Cl_2, 3,5-Cl_2, and 3,4,5-Cl_3).

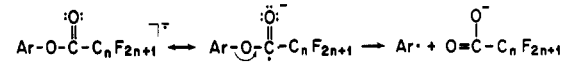
2. (Pentafluorophenyl)methanimines (17). To the reacti-vial containing the anilines was added ethyl acetate (200 μL) and pentafluorobenzaldehyde (1.0 mg). The mixture was heated at 75 °C for 1 h, cooled, and isolated as in A.2, above.

In addition to the microgram scale derivatizations, three derivatives of phenol (4–6) were prepared on a 0.5-g scale by using similar conditions and adding the derivatization reagents in a 1:1 molar ratio with phenol. The products were recrystallized from 95% ethanol to give white needles with sharp melting points (4, mp 74 °C; 5, mp 68 °C; 6, mp 34 °C). Silica gel TLC revealed in each case only one UV absorbing spot (ethyl acetate/hexane, 1:9).

RESULTS AND DISCUSSION

Initially, eight derivatives of phenol and nine derivatives of aniline were prepared and EC-NCIMS spectra recorded by using methane as a moderator gas and an ion source temperature of 200 °C. The spectra are summarized in Tables II (phenols) and III (anilines). In general, all of the aniline derivatives 9–17 exhibit ions suitable for GC–SIM–MS analysis; either the molecular anion $M^{\bullet-}$ or fragment ions characteristic of aniline are produced in high abundance. However, for phenol only the aryl derivatives 4–8 provide analyte specific ions. The nature of the spectra of the derivatives 4–17 was found to change with chlorine substitution on the phenol or aniline ring, and, furthermore the spectral patterns also exhibited a strong dependence on ion source temperature. The following discussion covers these results in more detail.

Scheme I



Scheme II

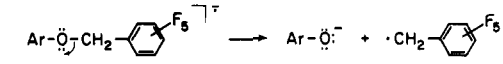


Table IV. EC-NCI Mass Spectra of Pentafluorobenzyl Ethers

$Cl_xPhOCH_2C_6F_5$	rel abundance Cl_xPhO^-	rel abundance Cl^-
H	100	
4-Cl	100	0.9
3-Cl	100	1.9
3,4-Cl_2	100	4.8
3,5-Cl_2	100	7.5
3,4,5-Cl_3	100	20

A. Phenol Derivatives. I. Alkyl Perfluoroacyl Derivatives. The alkyl perfluoroacyl derivatives 1–3, popular in the GC–ECD determination of phenols (*17*, *18*), are not suitable for GC–SIM–MS analysis under EC-NCIMS conditions. For these compounds, retention of the negative charge with the fluoroacyl moiety leads to formation of anions derived from the derivatization reagent and not the original phenol analyte (Scheme I). Since these derivatives were found to be of little potential use in the case of phenols, additional substituted phenols were not examined.

II. Pentafluorobenzyl Ether Derivatives. The alkylation of phenols with pentafluorobenzyl bromide and subsequent analysis by GC–ECD is a well-known analytical approach (*16*, *19–21*). Under EC-NCIMS conditions, 4 undergoes a dissociative electron capture process to produce the phenoxide anion (ArO^-) as the sole peak in the mass spectrum (Scheme II). The ion ArO^- is of course characteristic of the original phenol and should be useful for quantitation by GC–SIM–MS. The absence of an ion at m/z 181, corresponding to the pentafluorobenzyl anion, is noteworthy since none of the ion current is carried by nonspecific ions. Murphy (*22*) has previously reported the absence of the m/z 181 ion in the EC-NCIMS spectra of pentafluorobenzyl esters of prostaglandins and has attributed this to the lower relative stability of the pentafluorobenzyl anion vs. the corresponding radical species. Hence, in contrast to the alkyl perfluoroacyl derivatives, negative charge is preferrentially retained by the phenoxide moiety.

Table IV contains the EC-NCIMS spectra of the five chlorinated phenols studied. Other than the substituted phenoxide species, the only additional ion noted in the spectra of these compounds is the chloride anion, Cl^-, which is found to increase in relative abundance with the extent of chlorination.

III. Pentafluorobenzoate Esters. Lester has detected chlorinated phenols at the ppb level by GC–ECD of derivative 5 formed by treatment with pentafluorobenzoyl chloride (*23*). Under EC-NCIMS conditions, the molecular anion $M^{\bullet-}$ is

Table V. EC-NCI Mass Spectra of Pentafluorobenzoate Esters

	rel abundance							
$Cl_xPhOC(O)C_6F_5$	$M^{\bullet-}$	$(M-20)^-$	$(M-64)^-$	Cl_xPhO^-	m/z 196^{-a}	m/z 167^{-b}	m/z 148^{-c}	Cl^-
H	100	2.5	1.2	5	3.2	6	3.7	
4-Cl	100	14	8	6.3	6	21	1.4	16
3-Cl	100	8	8	25	5.5	38	3.5	22
3,4-Cl_2	78	19	16	44	14	58	3	100
3,5-Cl_2	53	10	13	90	20	100	8	72
3,4,5-Cl_3	8.5	4.5	4	73	31	100	6	89

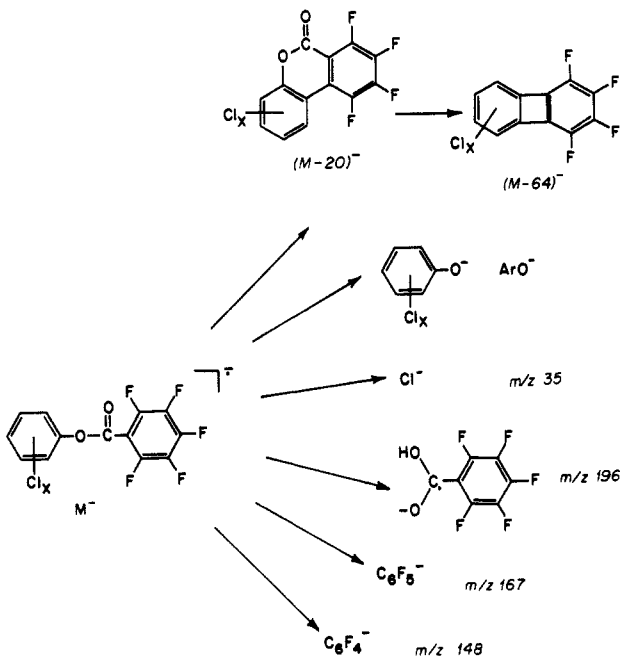
$^a C_6F_5COH^-$. $^b C_6F_5^-$. $^c C_6F_4^-$.

Table VI. EC-NCI Mass Spectra of 3,5-Bis(trifluoromethyl)benzoate Esters

	rel abundance				
$Cl_xPhOC(O)Ph(CF_3)_2$	$M^{\bullet-}$	Cl_xPhO^-	m/z 257^{-a}	m/z 213^{-b}	Cl^-
H	100	2	0	1	
4-Cl	100	4.9	33	2	1
3-Cl	100	6.7	46	2	5
3,4-Cl_2	78	11	100	3	11
3,5-Cl_2	85	17	100	3	12
3,4,5-Cl_3	41	21	100	4	47

$^a (CF_3)_2C_6H_3CO_2^-$. $^b C_6H_3(CF_3)_2^-$.

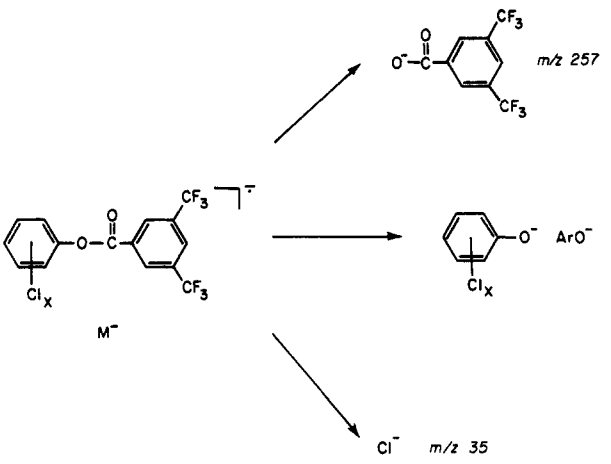
Scheme III



quite stable and represents the base peak in the spectrum. Apparently the conjugated carbonyl–aromatic system is capable of stabilizing the additional electron, and fragmentation is minimal. Upon chlorination, however, an increase in intensity of many of the fragment ions is observed as indicated in the spectra summarized in Table V. The fragmentation pathways of the pentafluorobenzoate esters of the chlorinated phenols are outlined in Scheme III.

IV. 3,5-Bis(trifluoromethyl)benzoate Esters. The use of the reagent 3,5-bis(trifluoromethyl)benzoyl chloride for the synthesis of electrophoric derivatives for EC-NCIMS has been reported by Murray (*24*) for the analysis of the drug clonidine, a secondary amine. The ester prepared from treatment of phenol with this reagent produces a derivative that exhibits a base peak corresponding to the molecular ion $M^{\bullet-}$. Table VI summarizes the EC-NCIMS spectra for the chlorinated phenol derivatives, and Scheme IV outlines their fragmentation. Even though derivatives of type **5** and **6** share the benzoate functionality, the different substitution on the

Scheme IV



aromatic ring of the electrophore, pentafluoro vs. 3,5-bis(trifluoromethyl), changes dramatically the fragmentation pattern. When the two sets of derivatives (Tables V and VI) are compared, two features can be noted. First, the number and intensity of nonspecific fragment ions is greater in the case of the pentafluorobenzoate esters. Second, the relative intensity of the molecular ion, $M^{\bullet-}$, is always enhanced in the 3,5-bis(trifluoromethyl)benzoate ester. Thus the stabilization of negative charge is highly dependent on the structure of the benzoyl ester.

V. Substituent Effects. A common feature of the three sets of chlorophenol derivatives discussed above is the increased fragmentation noted as the number of chlorines on the phenol ring is increased. Significantly, the application of the Hammett linear energy relationships can be shown to provide an insight into these observations. The correlation of ion abundances in the mass spectra of substituted aromatic compounds with the substituent Hammett σ values has found use in mass spectrometry (*25–27*). Typically, the log ratios of molecular ion intensities to selected fragment ions or ratios (R) of two fragment ions are calculated and plotted vs. the appropriate σ value. A plot fit to the equation $\log R = \rho\sigma + b$ with a reasonable correlation coefficient (r^2) is significant, as the change in ion abundances in a mass spectrum can then be predicted for further substituent changes. For multiply substituted aromatics, the sum of the individual σ values, $\sum\sigma$,

Table VII. Values of $\sum\sigma$ for Chlorinated Derivatives[a]

Cl_xPh^-	$\sum\sigma$	Cl_xPh^-	$\sum\sigma$
H	0.00	3,4-Cl_2	0.60
4-Cl	0.23	3,5-Cl_2	0.74
3-Cl	0.37	3,4,5-Cl_3	0.97

[a] Reference 28.

is calculated (*27*). Table VII lists the $\sum\sigma$ values calculated for the chlorinated compounds in this report (*28*).

For the purposes of this study, we have been interested in isolating the factors responsible for the production of ions characteristic of the phenol and aniline derivatives so as to permit the selection of electrophoric derivatives on a predictive basis and thus facilitate the development of selective quantitative methods. Plotting the log ratios of the intensities of analytically important ions for the three sets of phenol derivatives has resulted in linear Hammett plots with excellent correlation coefficients. Presented in Table VIII are the values of ρ, b, and r^2 obtained from linear regression analysis of the plots log I_{Cl^-}/I_{Aro^-} vs. $\sum\sigma$ for the pentafluorobenzyl ethers and log $I_{Aro^-}/I_{M\cdot^-}$ vs. $\sum\sigma$ for the two sets of benzoate esters. The results from experiments conducted at five different ion source temperatures are included.

The absolute value of ρ, the slope of the Hammett plot, is a measure of the degree of influence the substituents exert in directing the fragmentation. Chlorine is assigned positive σ values, reflecting electron-withdrawing properties at both the meta (σ = 0.37) and para (σ = 0.23) positions. There is a wide range in the absolute magnitude in ρ values for these derivatives, demonstrating the degree to which each type of derivative is affected by substitution. For the benzoate esters, as the value $\sum\sigma$ becomes more positive, the abundance of the molecular ion $M^{\cdot-}$ diminishes, while the abundances of the fragment ions increases. The ratio of the two ions potentially useful for quantitation, $I_{Aro^-}/I_{M\cdot^-}$, increases sharply as the value of $\sum\sigma$ increases ($\rho > 0$). This may be attributed in part to the increasing ability of the phenoxide anion to stabilize the resulting charge as chlorine substitution increases. In the case of the benzyl ethers, only two ions, both fragments, are observed in the mass spectra. The increase in the abundance of Cl^- with the increase in chlorine substitution in the molecule is not surprising. However, the linear Hammett plots indicate that the actual site of substitution is a major factor in the observed ratio I_{Aro^-}/I_{Cl^-}.

Since the changes in substitution on the phenol portion of the derivatives were found to lead to significant mass spectral changes, we next considered the effect of changes in fragmentation brought about by changing the substituent $\sum\sigma$ value for the benzoate ring. A convenient set of derivatives for this purpose is those bearing the electrophores shown in compounds **6**, **7**, and **8**. In these examples, the number and position of electrophoric trifluoromethyl groups are varied. A series of chlorophenols was derivatized with the appropriate substituted benzoyl chloride reagents, and the EC-NCIMS

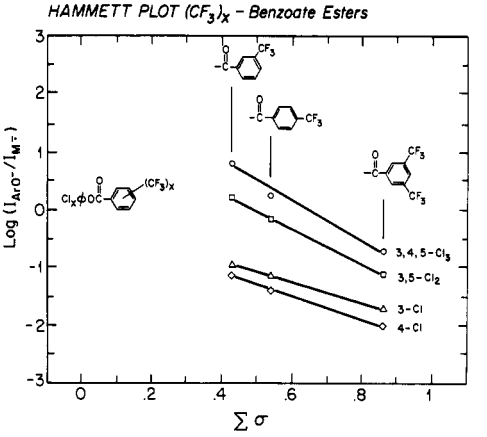


Figure 1. Hammett plot for 3,5-bis(trifluoromethyl)benzoate esters.

spectra were recorded at an ion source temperature of 200 °C. Figure 1 shows the Hammett plots observed for these derivatives. In this instance, the log ratio $I_{Aro^-}/I_{M\cdot^-}$ is plotted vs. the $\sum\sigma$ value for the benzoate ring (σ_m = 0.43 and σ_p = 0.54 for CF_3). In contrast to the change in the ratio $I_{Aro^-}/I_{M\cdot^-}$ observed by varying $\sum\sigma$ on the phenol ring ($\rho > 0$), the increase in $\sum\sigma$ on the benzoate ring leads to a decrease in $I_{Aro^-}/I_{M\cdot^-}$ ($\rho < 0$). Presumably, a higher value of $\sum\sigma$ on the benzoate ring leads to stabilization of the molecular anion $M^{\cdot-}$ formed by initial electron capture, suggesting that the site of electron capture is most likely the carbonyl group of the benzoate ring.

As noted earlier, an EC-NCIMS study conducted on derivatives of the chlorophenols 2,4,6-trichlorophenol, 2,3,4,6-tetrachlorophenol, and pentachlorophenol has been published (*9*). The authors reported that the spectra were dominated by the phenoxide anions. It is important to note, however, that all their spectra were not scanned below m/z 60. Our results illustrate that for valid linear free energy relationship calculations inclusion of the chloride anion abundances is necessary, at least for the simple pentafluorobenzyl derivatives of chlorophenols.

VI. Temperature Effects. An increase in fragment ion abundances with increasing source temperature has been a general behavior reported for EC-NCIMS (*29*). We have obtained EC-NCIMS spectra of the phenol derivatives **4**, **5**, and **6** over the range of ion source temperatures between 100 and 300 °C and have noted some significant trends. In reviewing the change in relative ion abundances for the chlorinated series of derivatives **4** (Figure 2), **5** (Figure 3), and **6** (Figure 4) two points can be made. First, the changes in ion abundances are most pronounced for the higher chlorinated compounds, with the derivatives of phenol itself showing little change. Second, the temperature effects are minimal for compounds undergoing dissociative electron capture (i.e., **6**) and most significant for compounds capable of nondissociative ionization.

B. Aniline Derivatives. I. Alkyl Perfluoroacyl Derivatives. Three alkyl perfluoroacyl derivatives have been

Table VIII. Hammett ρ Constants for Phenol Derivatives[a]

	derivative (ion ratio, R)								
	$ROCH_2C_6F_5$ (Aro^-/Cl)			$ROC(O)C_6F_5$ ($Aro^-/M^{\cdot-}$)			$ROC(O)C_6H_3(CF_5)_2$ ($Aro^-/M^{\cdot-}$)		
source temp, °C	ρ	r^2	b	ρ	r^2	b	ρ	r^2	b
100	−1.49	0.991	2.16	1.49	0.978	−1.45	0.847	0.889	−1.56
150	−1.59	0.993	2.15	1.80	0.978	−1.44	1.18	0.985	−1.52
200	−1.77	0.996	2.41	2.37	0.960	−1.52	1.42	0.990	−1.71
250	−1.80	0.995	2.36	3.05	0.968	−1.63	1.95	0.990	−1.91
300	−1.83	0.995	2.31	4.24	0.976	−1.61	2.26	0.975	−1.96

[a] $\log R = \rho\sum\sigma + b$; r^2 = correlation coefficient.

Table IX. EC-NCI Mass Spectra of Trifluoroacetamides

	rel abundance						
$Cl_xPhNHC(O)CF_3$	$M^{\bullet-}$	$(M - H)^-$	$(M - HF)^-$	$(M - HCl)^-$	$(M - H_2Cl_2)^-$	CF_3^-	Cl^-
H	0	100	0			0	
4-Cl	100	1	3	75	0	5	63
3-Cl	34	1	4	100	0	4	51
3,4-Cl_2	8	0	0	100	2	9	27
3,5-Cl_2	4	0	0	100	5	8	26
3,4,5-Cl_3	0	0	0	100	11	3	11

Table X. EC-NCI Mass Spectra of Pentafluoropropionamides

	rel abundance					
$Cl_xPhNHC(O)CF_2CF_3$	$M^{\bullet-}$	$(M - HF)^-$	$(M - H_2F)^-$	$(M - HCl)^-$	$(M - H_2F_2)^-$	Cl^-
H	0	100	2		3	
4-Cl	0	100	2	1	1	1
3-Cl	0	100	2	2	2	1
3,4-Cl_2	0	100	1	5	3	4
3,5-Cl_2	0	100	2	4	6	4
3,4,5-Cl_3	0	100	1	12	4	9

Table XI. EC-NCI Mass Spectra of Heptafluorobutyramides

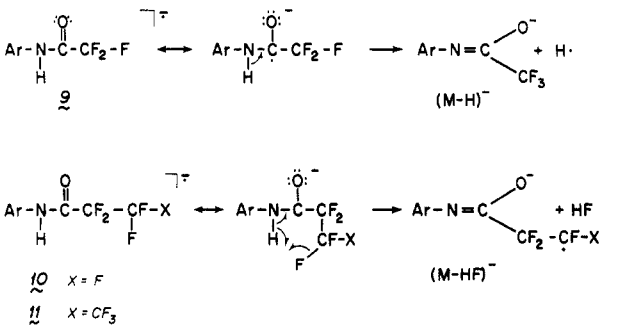
	rel abundance					
$Cl_xPhNHC(O)CF_2CF_2CF_3$	$M^{\bullet-}$	$(M - HF)^-$	$(M - H_2F)^-$	$(M - HCl)^-$	$(M - H_2F_2)^-$	Cl^-
H	0	100	0		2	
4-Cl	0	100	0	0	2	1
3-Cl	0	100	0	1	3	1
3,4-Cl_2	0	100	0	3	4	1
3,5-Cl_2	0	100	0	3	2	4
3,4,5-Cl_3	0	100	1	4	2	9

Table XII. EC-NCI Mass Spectra of (Pentafluorobenzyl)amines

	rel abundance					
$Cl_xPhNHCH_2C_6F_5$	$M^{\bullet-}$	$(M - HF)^-$	$(M - H_2F)^-$	$(M - H_3F)^-$	$(M - HF - HCl)^-$	Cl^-
H	0	100	30	15		
4-Cl	0	100	46	15	11	7
3-Cl	0	100	37	11	77	53
3,4-Cl_2	0	100	23	7	73	56
3,5-Cl^2	0	24	0	0	100	66
3,4,5-Cl_3	0	2	0	0	100	29

examined for the determination of anilines by EC-NCIMS: trifluoroacetamides (**9**), pentafluoropropionamides (**10**), and heptafluorobutyramides (**11**). Under methane EC-NCIMS conditions, these derivatives were observed to produce characteristic fragment ions unlike the situation noted earlier for phenols in Table II. The spectra for the series of the chlorinated aniline derivatives **9**–**11** are summarized in Tables IX–XI. The spectra of both the pentafluoropropionamides (**10**) and the heptafluorobutyramides (**11**) are dominated by the $(M - HF)^{\bullet-}$ ion, with no molecular anion $M^{\bullet-}$ and few additional fragment ions. Similar trends were also observed with the derivatized chloroanilines. In contrast, the EC-NCIMS spectra of the trifluoroacetamides (**9**) exhibited more dramatic changes as a function of chlorine substitution. Derivative **9** produced essentially the $(M - H)^-$ ion. However, with the addition of chlorine atoms to the aniline ring, significant abundances of molecular anion $M^{\bullet-}$ and fragments $(M - HCl)^{\bullet-}$ and Cl^- were observed. Experiments carried out by using ring labeled [$^2H_5$]aniline confirm that the hydrogen bonded to the nitrogen atom is eliminated to form both the $(M - H)^-$ ion in **9** and the $(M - HF)^{\bullet-}$ ion in **10** and **11**. The differences in fragmentation between the trifluoroacetyl derivatives **9** and those of the larger fluoroacyl homologues (**10** and **11**) may be the result of the steric demands of the elimination process that involves a six-member ring intermediate leading to the formation of the $(M - HF)^{\bullet-}$ ion. Conceivably a minimum length of the perfluorocarbon chain is critical to sustain the fragmentation process (*30*) (Scheme V).

Scheme V



9

10 X = F

11 X = CF_3

II. (Pentafluorobenzyl)amines. Under EC-NCIMS conditions, the pentafluorobenzyl derivatives of anilines, **12**, were found to undergo considerable fragmentation (Table XII). Major ions include $(M - HF)^{\bullet-}$, $(M - H_2F)^-$, $(M - HF - HCl)^{\bullet-}$, and Cl^-, whose relative abundances were strongly affected by the chlorine ring substitution. Unlike the corre-

Table XIII. EC-NCI Mass Spectra of Pentafluorobenzanilides

	rel abundance					
$Cl_xPhNHC(O)C_6F_5$	$M^{\bullet-}$	$(M - HF)^-$	$(M - H_2F)^-$	$(M - H_2F_2)^-$	$(M - HF - HCl)^-$	Cl^-
H	1	35	100	6		
4-Cl	0	52	100	3	2	4
3-Cl	0	81	100	3	7	4
3,4-Cl_2	0	100	80	2	9	14
3,5-Cl_2	0	100	17	0	11	12
3,4,5-Cl_3	0	100	10	0	9	33

Table XIV. EC-NCI Mass Spectra of 3,5-Bis(trifluoromethyl)benzanilides

	rel abundance				
$Cl_xPhNHC(O)C_6H_3(CF_3)_2$	$M^{\bullet-}$	$(M - H)^-$	$(M - HCl)^-$	m/z 242$^-$[a]	Cl^-
H	100	57		2	
4-Cl	100	50	1	9	0.1
3-Cl	100	51	2	4	0.5
3,4-Cl_2	100	48	17	10	7
3,5-Cl_2	100	46	19	7	7
3,4,5-Cl_3	100	47	99	16	31

[a] $HCOC_6H_3(CF_3)_2^-$.

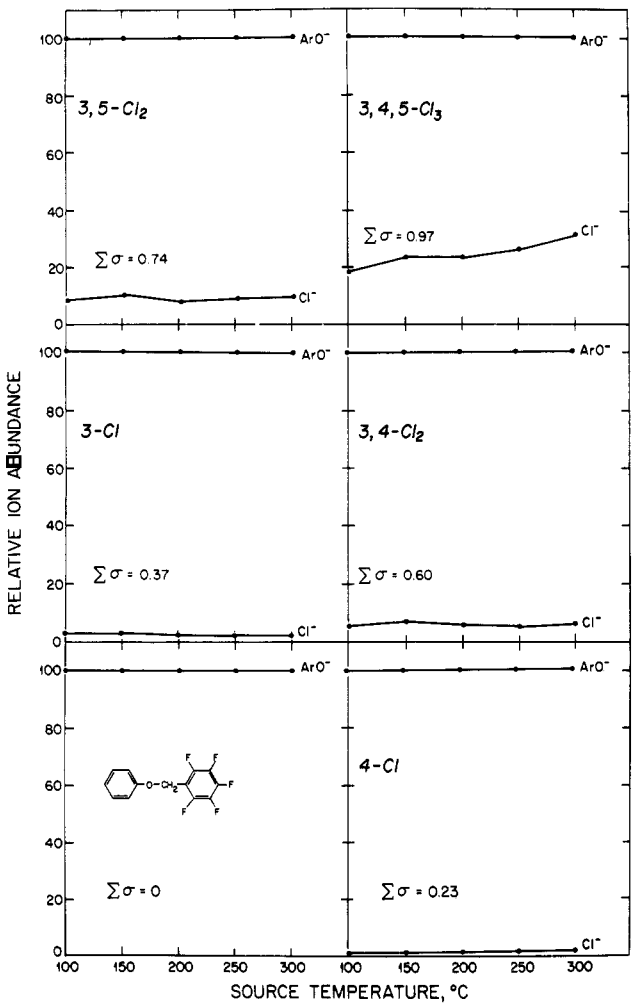


Figure 2. Relative ion abundances vs. ion source temperature for pentafluorobenzyl ethers.

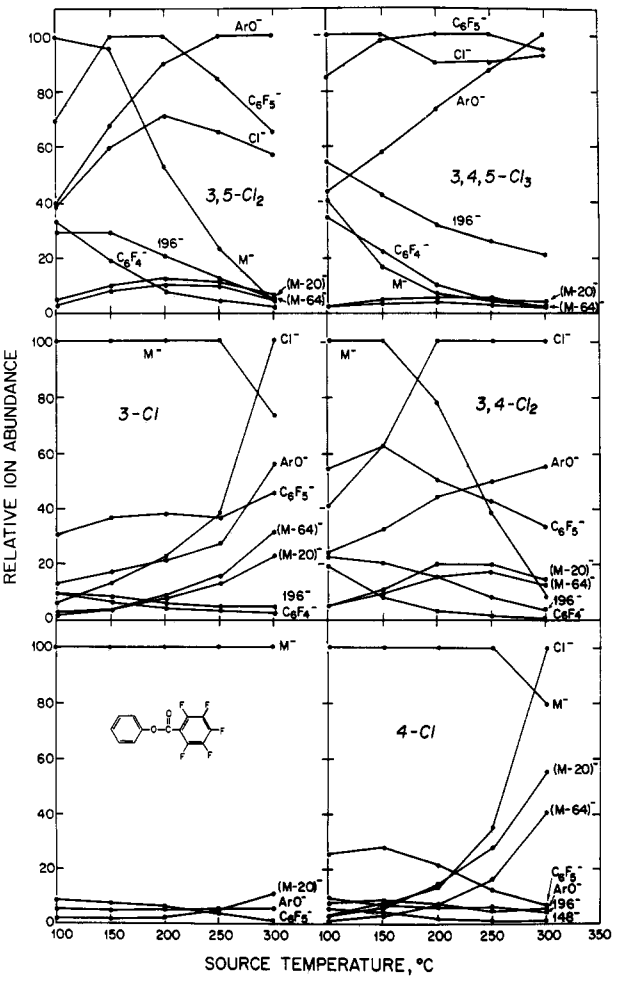


Figure 3. Relative ion abundances vs. ion source temperature for pentafluorobenzoate esters.

sponding phenol derivatives (4), no $(M - 181)^-$ ion corresponding to the fragment $ArNH^-$ was observed.

III. Pentafluorobenzanilides. In contrast to the case of phenol, the spectra of the derivatives obtained from treatment of the chlorinated anilines with pentafluorobenzoyl chloride did not exhibit a molecular anion, $M^{\bullet-}$, under EC-NCIMS conditions. For these derivatives, the spectra were dominated by the fragments $(M - HF)^{\bullet-}$ and $(M - H_2F)^-$ (Table XIII and Scheme VI). For the case of aniline itself, the ion $(M - H_2F)^-$ was the base peak. With chlorine substitution on the ring the relative abundances of the $(M - HF)^{\bullet-}$ ion and chloride ion Cl^- increased, while that of the $(M - H_2F)^-$ ion decreased.

IV. 3,5-Bis(trifluoromethyl)benzanilides. The molecular anion $M^{\bullet-}$ was the base peak in the EC-NCIMS spectra

Table XV. EC-NCI Mass Spectra of (Pentafluorophenyl)methanimines

$Cl_xPhN{=}CHC_6F_5$	rel abundance					
	$M^{\bullet-}$	$(M - HF)^-$	$(M - HCl)^-$	$(M - F - Cl)^-$	$C_6F_5^-$	Cl^-
H	100	1			2	
4-Cl	100	1	0	1	3	1
3-Cl	100	2	0	0.5	3	0.5
3,4-Cl_2	100	0.3	1	2	3	2
3,5-Cl_2	100	2	0.3	1	3	2
3,4,5-Cl_3	100	0.1	2	3	3	4

Table XVI. Hammett ρ Constants for Aniline Derivatives[a,b]

	derivative			
	$RNHC(O)CF_3$ (9) $(M - HCl)^-/M^{\bullet-}$	$RNHCH_2C_6F_5$ (12) $(M - HF - HCl)^-/(M - HF)$	$RNH(O)CC_6F_5$ (13) $(M - H_2F)^-/(M - HF)^-$	$RNHC(O)C_6H_3(CF_3)_2$ (14) $(M - HCl)^-/M^{\bullet-}$
ρ	3.05	3.24	−1.64	2.71
r^2	0.987	0.909	0.925	0.974
b	−0.75	−1.66	0.61	−2.62

[a] $\log R = \rho\sum\sigma + b$; r^2 = correlation coefficient. [b] Ion source temperature, 200 °C.

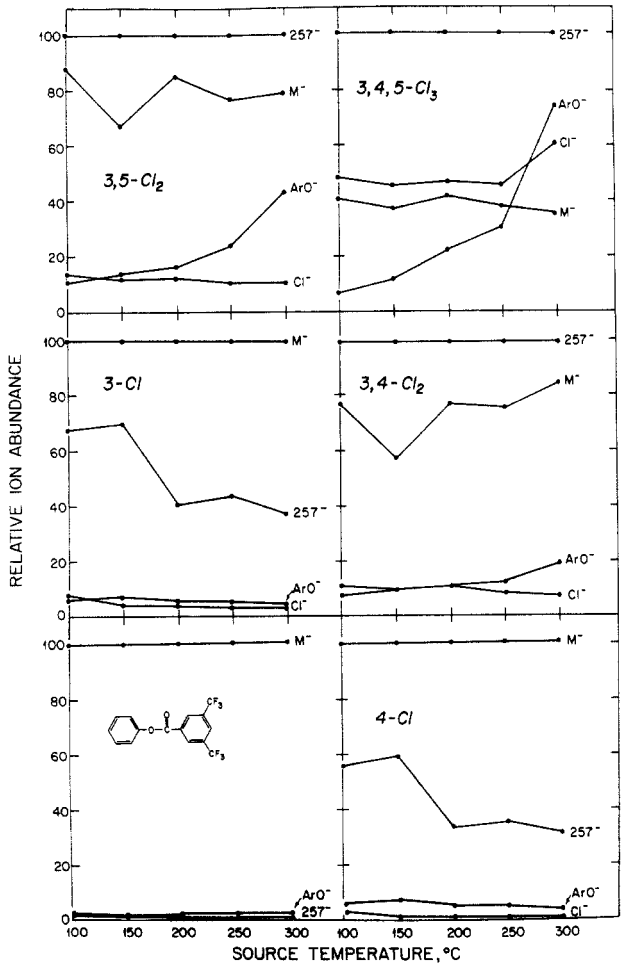
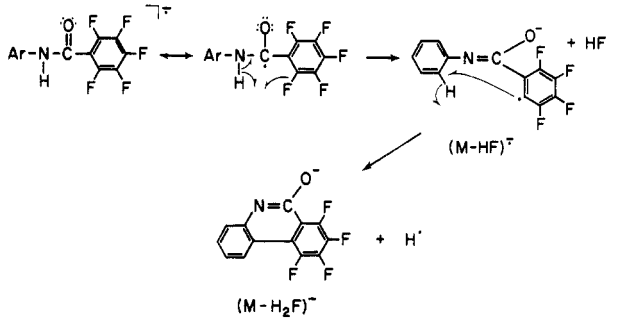


Figure 4. Relative ion abundances vs. ion source temperature for 3,5-bis(trifluoromethyl)benzoate esters.

of the anilines derivatized with 3,5-bis(trifluoromethyl)benzoyl chloride (Table XIV). Similar to the situation noted with the phenols, the change from a pentafluoro to a 3,5-bis(trifluoromethyl) electrophore had a major effect on the fragmentation pattern. No $(M - HF)^{\bullet-}$ ion was produced, and the major fragments include $(M - H)^-$, $(M - HCl)^{\bullet-}$, and Cl^-. An ion derived from the derivative moiety, at m/z 242, was also present.

V. (Pentafluorophenyl)methanimines. The formation of a Schiff's base derivative by treatment of primary amines

Scheme VI



with pentafluorobenzaldehyde has been utilized in both GC–ECD (*31*) and EC-NCIMS (*7*). Among the aniline derivatives studied here, the (pentafluorophenyl)methanimines of type **17** produced EC-NCIMS spectra with the least fragmentation (Table XV). Indeed, even for the chlorinated compounds, the molecular anion remained the base peak, accounting for over 80% of the total ion current. This reflects the stability of the highly conjugated anion formed upon initial electron capture.

VI. Substituent Effects. In a manner analogous to the phenols discussed above, the aniline derivatives examined in this study also exhibited fragmentation patterns under EC-NCIMS conditions that were consistent with the Hammett linear free energy relationships. Three types of derivatives (**10**, **11**, and **17**) showed very little variation in their mass spectral patterns as the number and position of chlorine substituents on the ring were varied. For the case of the Schiff's base, series **17**, this is not surprising given the inherent high stability of the molecular anion. The derivatives in the series **10** and **11** exhibited only minor changes in ion abundances with increased chlorination, probably due to the very facile loss of HF (Scheme VI). However, derivatives of the type **9**, **12**, **13**, and **14** produced EC-NCIMS spectra that showed considerable ion abundance variation with changes in chlorine substitution in agreement with the Hammett equation. This is illustrated in Table XVI that shows the Hammett equation constants obtained from linear regression analysis of the analytically most important ion abundance ratios.

When the conformity of the aniline and the phenol derivatives with the Hammett equation is compared, generally higher correlation coefficients may be noted for the phenols. For the anilines, the worst cases are for derivatives of type **12** and **13** where the ion ratios compared are formed via

Table XVII. GC-SIM-MS Relative Molar Response

compd	ion monitored	rel molar response (RMR)[a] 150 °C[b]	200 °C[b]	250 °C[b]
$PhOCH_2C_6F_5$, 4	m/z 93 ($C_6H_5O^-$)	1.8	2.1	2.5
$PhOC(O)C_6F_5$, 5	m/z 288 ($M^{\bullet-}$)	0.73	1.1	1.0
$PhOC(O)C_6H_3(CF_3)_2$, 6	m/z 234 ($M^{\bullet-}$)	0.15	0.18	0.15

[a] RMR expressed in terms of area counts per picomole × 10^6. [b] Source temperature.

Table XVIII. GC-ECD Relative Molar Response

compd	rel molar response, RMR[a]	RMR referenced to compd 5[b]
$PhOCH_2C_6F_5$, 4	3.9	1.3
$PhOC(O)C_6F_5$, 5	3.0	1.0
$PhOC(O)C_6H_3(CF_3)_2$, 6	0.59	0.20

[a] RMR expressed in terms of area counts per picomole × 10^6. [b] Calculated by dividing the RMR values for each compound by the RMR value of compound 5.

multistep processes. Thus it would appear that other factors, in addition to the simplified Hammett treatment, influence the mode of fragmentation of the molecular anion and other secondary fragments. Nevertheless, the selection of a derivative that yields abundant analyte-related ions for SIM can still be aided by applying the Hammett principles.

C. Relative Sensitivity. Any one type of the derivatives that produce abundant analyte-specific ions are, in principle, good candidates for trace level analysis by GC–SIM–MS using EC-NCIMS. For the examples considered in this study this criterion is met by most of the substituted anilines as long as the facile elimination of HF, HCl, or other related processes that yield analyted-related ions is a priori known. In the case of the phenols, derivatives of the type **4**, **5**, or **6** appear best suited for analytical purposes by GC–SIM–MS in the EC-NCI mode.

In previous work utilizing GC–ECD (*4–6*), it has been reported that significant differences in sensitivity exist among electrophoric derivatives of a specific analyte. The phenolic derivatives **4**, **5**, and **6** were used as models to assess the extent to which such differences in sensitivity may also exist under EC-NCIMS conditions. The experiment was carried out under selected ion monitoring conditions (500 pg injected) over a range of source temperatures. As shown in Table XVII, at all ion source temperatures studied, the relative molar responses remained in the order **4** > **5** > **6**. It was further reasoned that, since all three of these compounds produce spectra composed of essentially a single ion, the differences in the MS response may also reflect the electron capturing ability of the compounds under methane EC-NCIMS conditions. Accordingly, we compared these molar response ratios to those exhibited for the same derivatives by the similar technique of GC–ECD. The data obtained, Table XVIII, indicate that the derivatives produce signals in the identical order as for the EC-NCIMS experiments, with some change in the ratio of responses between the three derivatives. This correlation does not imply that identical processes are taking place in the two detectors. However, unlike the information obtained with the mass spectrometer, the data from the ECD detector reveal little about the actual electron capture mechanism (i.e., dissociative vs. nondissociative) taking place in the ECD. A number of studies have been conducted on ECD detectors in combination with atmospheric ionization mass spectrometers (*32–34*) in order to study the actual ECD ionization products. None of these studies utilized any of the common electrophoric derivatives of the type discussed here. Consequently the identity of the anionic products formed in the ECD remains unknown.

In conclusion, the data presented here show that selection of the appropriate electrophoric derivative is an important consideration in order to carry out trace level analysis by GC–EC-NCIMS. It is also shown that linear free energy relationships can be employed to predict stability of molecular anions, the direction of fragmentation pathways, and thus the extent to which a derivative will be useful under selective ion monitoring conditions. To that effect, the ion source temperature is an additional parameter that may play an important role in the efficient use of the EC-NCIMS selective ion detection process. Finally, the comparison of the molar responses of derivatives of the type **4**, **5**, and **6** when used in the GC–ECD vs. the GC–EC-NCIMS mode provides some interesting new insights regarding the operation of the two detectors. It appears, from the present data, that the EC-NCIMS and ECD are very similar in their mode of operation although, clearly, more information will be necessary before any definitive conclusions can be made. Work along these lines is currently in progress.

LITERATURE CITED

(1) Corkill, A.; Joppich, M.; Kuttab, H.; Giese, R. W. *Anal Chem.* **1982**, *54*, 481–485.
(2) Hunt, D. F.; Stafford, G. C., Jr.; Crow, F. W.; Russell, J. W. *Anal. Chem.* **1976**, *48*, 2098–2105.
(3) Siegel, M. W.; McKeown, M. C. *J. Chromatogr.* **1976**, *122*, 397–413.
(4) Zlatkis, A.; Poole, C. F. *Electron Capture. Theory and Practice in Chromatography*; Elsevier: New York, 1981; Chapter 8.
(5) Poole, C. F.; Zlatkis, A. *Anal. Chem.* **1980**, *52*, 1002A–1016A.
(6) Knapp, D. R. *Handbook of Analytical Derivatization Reactions*; Wiley: New York, 1979.
(7) Hunt, D. F.; Crow, F. W. *Anal. Chem.* **1978**, *50*, 1781–1784.
(8) Faull, K. F.; Barchas, J. D. In *Methods of Biochemical Analysis*; Glick, D., Ed.; Wiley: New York, 1983; Vol. 29, pp 325–383.
(9) Shang-Zhi, S.; Duffield, A. M. *J. Chromatogr.* **1984**, *284*, 157–165.
(10) Dougherty, R. C. *Biomed. Mass Spectrom.* **1981**, *8*, 283–292.
(11) Crow, F. W.; Bjorseth, A. F.; Knapp, K. T.; Bennett, R. *Anal. Chem.* **1981**, *53*, 619–625.
(12) Betowski, L. D.; Webb, H. M.; Sauter, A. D. *Biomed. Mass. Spectrom.* **1983**, *10*, 369–376.
(13) Grunwald, E. *CHEMTECH* **1984**, *14*, 698–705.
(14) Fenimore, D. C.; Davis, M.; Whitford, J. H.; Harrington, C. A. *Anal. Chem.* **1976**, *48*, 2289–2290.
(15) Grob, K.; Grob, K., Jr. *J. Chromatogr.* **1978**, *151*, 311–320.
(16) Ehrrson, H.; Brotell, H.; Glyllenhaal, O. *J. Chromatogr.* **1973**, *78*, 293–301.
(17) Ehrsson, H.; Walle, T.; Brotell, H. *Acta Pharm. Suec.* **1971**, *8*, 319–328.
(18) Lamparski, L. L.; Nestrick, T. J. *J. Chromatogr.* **1978**, *156*, 143–150.
(19) Lee, H.-B.; Weng, L.-D.; Chau, A. S. Y. *J. Assoc. Off. Anal. Chem.* **1984**, *67*, 1086–1091.
(20) Davis, B. *Anal. Chem.* **1977**, *49*, 832–834.
(21) Kawahara, F. H. *Anal. Chem.* **1968**, *40*, 1009–1010.
(22) Strife, R. J.; Murphy, R. C. *J. Chromatogr.* **1984**, *305*, 3–12.
(23) Bulsson, R. S. K.; Kirk, P. W. W.; Lester, J. N. *J. Chromatogr. Sci.* **1984**, *22*, 339–342.
(24) Murray, S.; Davies, D. S. *Biomed. Mass Spectrom.* **1984**, *11*, 435–440.
(25) Bursey, M. M. In *Advances in Linear Free Energy Relationships*; Chapman, N. B., Shorter, J., Eds.; Plenum: New York, 1972; pp 445–461.
(26) Bentley, T. W.; Johnstone, R. A. W. In *Advances in Physical Organic Chemistry*; Gold, V., Ed.; Academic: New York, 1970; Vol. 8, pp 151–269.
(27) Exner, O. In *Advances in Linear Free Energy Relationships*; Chapman, N. B., Shorter, J. Eds.; Plenum: New York, **1972**; pp 2–69.
(28) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*; Harper and Row: New York, 1976; p 62.
(29) Miwa, B. J.; Garland, W. A.; Blumenthal, P. *Anal. Chem.* **1981**, *53*, 793–797.
(30) Low, G. K. C.; Duffield, A. M. *Biomed. Mass Spectrom* **1984**, *11*, 177–181.

(31) Moffat, A. C.; Horning, E. C.; Matin, S. B.; Rowland, M. J. Chromatogr. 1971, 66, 255-260.
(32) Grimsrud, E. P.; Kim, S. H., Gobby, P. L. Anal. Chem. 1979, 51, 223-229.
(33) Horning, E. C.; Carroll, D. I.; Dzidic, I.; Lin, S. N.; Stilwell, R. N., Thenot, J. P. J. Chromatogr. 1977, 142, 481-495.
(34) Siegel, M. W.; McKeown, M. C. J. Chromatogr. 1976, 122, 397-413.

RECEIVED for review May 5, 1986. Accepted October 10, 1986.

This work was supported by funds provided from the National Institutes of Health (Grants RR07143, NS 15439, NCICA35843), Grant CR 812740 from the Reproductive Effects Assessment Group of the U.S. Environmental Protection Agency, and an ACS Analytical Division Graduate Fellowship sponsored by the Analytical Chemists of Pittsburgh (T.M.T.). Contribution no. 294 from the Barnett Institute of Chemical Analysis.

Application of Isotope Dilution Inductively Coupled Plasma Mass Spectrometry to the Analysis of Marine Sediments

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Isotope dilution inductively coupled plasma mass spectrometry (ICP-MS) has been applied to the determination of 11 trace elements (Cr, Ni, Zn, Sr, Mo, Cd, Sn, Sb, Tl, Pb, and U) in the marine sediment reference materials MESS-1 and BCSS-1. Accuracy and, especially, precision are better than those that can be easily achieved by other ICP-MS calibration strategies, as long as isotopic equilibration is achieved and the isotopes used for the ratio measurement are free of isobaric interferences by molecular species. The measurement of the isotope ratios on unspiked samples provides a sensitive diagnostic of such interferences.

The detection power of inductively coupled plasma mass spectrometry (ICP-MS) makes possible the determination in geological reference materials of many trace elements for which relatively few reliable values have been previously established (*1-4*). This lack of data in many cases prevents a full assessment of the accuracy of ICP-MS results. A partial solution to this problem is the use of stable isotope dilution techniques (*5*) which are immune to many of the sources of error which can adversely affect ICP-MS results obtained by other calibration strategies. This approach would, for example, be an effective means to compensate for the suppression of ion sensitivities by concomitant elements (*6*) observed in many of the early applications of ICP-MS (*4*, *7-9*). Also, more calibration drift can be tolerated in an isotope dilution analysis because an isotope ratio, rather than an absolute intensity measurement, is used in the calculation of the analyte concentration. This suggests that it may be easier to obtain accurate and precise ICP-MS results for solutions with appreciable dissolved solids concentrations if isotope dilution techniques are used.

Relatively little use has been made of isotope dilution techniques in ICP-MS. Its application to the determination of six trace metals in a coastal seawater sample after a separation by adsorption on silica-immobilized 8-hydroxyquinoline was recently reported (*10*). Ting and Janghorbani used a ^{57}Fe spike for the accurate determination of ^{54}Fe and ^{58}Fe in human fecal matter after a chemical separation (*11*). Taylor and Garbarino (*12*) have applied isotope dilution ICP-MS to the determination of trace elements in natural waters. Longerich et al. (*4*) briefly described the determination of samarium using a ^{147}Sm isotopic spike in three geological reference materials.

Table I. Operating Conditions for Isotopic Analysis by ICP-MS

ICP	
plasma Ar	14 L min^{-1}
auxiliary Ar	2.0 L min^{-1}
nebulizer Ar	0.9 L min^{-1}
rf power	1.2 kW
Mass Spectrometer	
sampler	nickel, 1.2-mm orifice
skimmer	nickel, 0.9-mm orifice
Operating Pressures	
interface region	~1 torr
mass spectrometer chamber	~4 × 10^{-5} torr
Lens Voltages	
photon stop (S2)	-7.0 V
Bessel box barrel (B)	+2.95 V
einzel lenses 1 and 3 (E1)	-12.0 V
Bessel box end lenses (P)	-11.3 V
einzel lens 2	-130 V
entrance a.c. rods	0 V
exit a.c. rods	-5 V

The purpose of the present work was to examine in detail the application of isotope dilution ICP-MS to the determination of trace elements in solutions of the marine sediment reference materials MESS-1 and BCSS-1. These materials were chosen with two objectives in mind: verification of the methodology by comparison of the results with published reliable values, and assessment of the potential of isotope dilution ICP-MS to contribute accurate data toward establishment of reliable values for additional elements.

EXPERIMENTAL SECTION

Instrumentation. The inductively coupled plasma mass spectrometer used for this work was an ELAN 250 from SCIEX Division of MDS Health Group Ltd. (Thornhill, Ontario, Canada) that had recently undergone a modification of the original ion optics by the manufacturer to improve stability and reduce suppression of analyte ion sensitivity by concomitant elements. This involved replacement of a set of ac rods between the skimmer and Bessel box lenses with a three-cylinder einzel lens and re-

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