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Determination of Hydroxyaromatic Compounds in Complex Mixtures by Tandem Mass Spectrometry

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Derivatization of alkylated hydroxyaromatics with *N*-methyl-bis(trifluoracetamide) is used for a rapid screening for alkylated hydroxyaromatic compounds in complex mixtures by tandem mass spectrometry. Applications are based on a detailed investigation of the fragmentation reactions of derivatized alkylated phenols, 2,3-dihydroindenols, indenols, 1,2,3,4-tetrahydronaphthols and naphthols. As shown by daughter-ion mass spectra obtained in different field-free regions of a BEQQ-instrument, the loss of CF_3COOH, CF_3CO^+ or CF_3COO^+, respectively, is common for the compounds studied and can be used for their detection by means of neutral mass loss scans.

INTRODUCTION

Alkylated phenols (more generally alkylated hydroxyaromatic compounds) can be found in many crude industrial products, waste water, etc. The determination of hydroxyaromatics or even a rapid screening for these compounds in complex matrices is difficult and time consuming if gas chromatographic or gas chromatographic/mass spectrometric methods are applied.

Tandem mass spectrometry (MS/MS) techniques have been extensively used for the investigation of ion structures as well as the mechanism and energetics of ion fragmentation. However, the number of reports dealing with analytical applications of MS/MS methods is comparably small although these methods allow the determination of single compounds in complex matrices using daughter-ion scans or the detection of classes of compounds fragmenting via one common daughter ion by means of parent-ion scans. Neutral mass loss scans can be taken into account if the compounds of interest lose the same neutral. The above-mentioned techniques were used by Cooks and co-workers[1–3] and other workers,[4,5] for the detection of alkylated phenols or other hydroxy substituted aromatic compounds in coal-derived liquids. However, the parent scans applied by Cooks and co-workers are limited to homologous series of alkylated phenols, thiophenols, 2,3-dihydroindenols etc.[2,3]

The loss of H_2O which can be observed by neutral mass loss scans is not relevant or intensive enough for several types of hydroxyaromatics to ensure a reliable detection under electron-impact conditions. An improvement of the MS/MS methods discussed above can be achieved by derivatization of the hydroxy group. Among the possible derivatization reagents, e.g. *N,O*-bis(trimethylsilyl)acetamide[6] or acetic anhydride,[7] *N*-methyl-bis(trifluoracetamide) (MBTFA)[8] yields the best results.

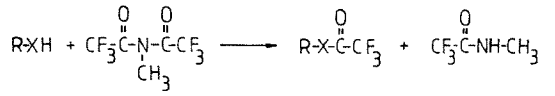
The reaction (Scheme 1) is simple to perform and results in a quantitative formation of trifluoracetylated compounds. The mass spectra of the TFA derivatives display an intensive molecular ion and a typical mass spectrometric fragmentation pattern permitting a reliable identification from complex mixtures. In this paper we report fragmentation pathways of trifluoracetylated alkylated phenols, naphthols, 2,3-dihydroindenols, indenols and 1,2,3,4-tetrahydronaphthols. Neutral mass loss scans were used for the detection of these compounds in industrial products.

EXPERIMENTAL

Mass spectra were recorded on a VG ZAB-HSQ mass spectrometer with BEQQ configuration equipped with a combined EI/CI source. The source temperature was held at 200 °C. The source accelerating potential was 8 kV.

Daughter-ion, parent-ion or neutral mass loss spectra were obtained in each of the three field-free regions (1st–3rd FFR) of the instrument. Collision-induced dissociation spectra were recorded by introducing argon collision gas in the appropriate collision cell at an estimated pressure of 10^{-6} mbar.

Most of the chemicals were obtained commercially or prepared by standard literature methods.[9–12] The purity of all compounds was checked by mass spectrometric analysis. According to the literature[8] pyridine was used as a solvent for the derivatization with MBTFA (Merck). The derivatization reaction was complete after 2 h. Other derivatives were prepared by the methods described in Refs 6 and 7.



Scheme 1

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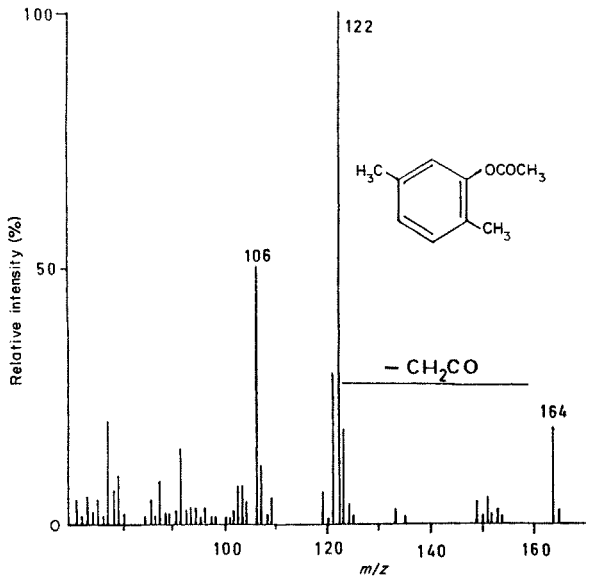


Figure 1. EI mass spectrum of acetylated 2,5-dimethylphenol.

RESULTS AND DISCUSSION

With respect to the analytical determination of hydroxyaromatic compounds in complex matrices, several derivatizing reagents have been tested. The derivatization using *N,O*-bis(trimethylsilyl)acetamide[6] does not result in a facile mass spectrometric identification.

A characteristic fragmentation of the acetylated phenols, recently reported for chlorophenols,[7] is given by the elimination of ketene producing in the following compounds a spectrum similar to the original phenol spectrum (Fig. 1). In addition, the molecular ions of other derivatives tested have a low abundance. Both facts prevent a sensitive detection of hydroxyaromatics in complex mixtures.

Suitable results could be obtained using MBTFA for the derivatization (Scheme 1). As shown in Fig. 2(a), the trifluoracetylated compounds exhibit characteristic mass spectra. The most important fragmentation pathways of these derivatives are discussed below in more detail.

Alkylated phenols

If trifluoracetyl derivatives of phenols contain at least one hydrogen atom in an *ortho*-position to the trifluoracetyl group, a McLafferty-rearrangement occurs in the ion source and in the 1st–3rd FFR of the instrument. In this case the most abundant daughter ion, both unimolecularly and induced by collisions (CID), is caused by the neutral mass loss of trifluoracetic acid. Beside this the molecular ion loses CF_3CO and CF_3 radicals. The abundance of the corresponding product ions can be increased by collisional activation. The mass spectrum and the collision-induced dissociation/mass-analysed ion kinetic energy (CID/MIKE) spectrum of trifluoracetylated 2,5-dimethylphenol are shown in Figs 2(a) and (b).

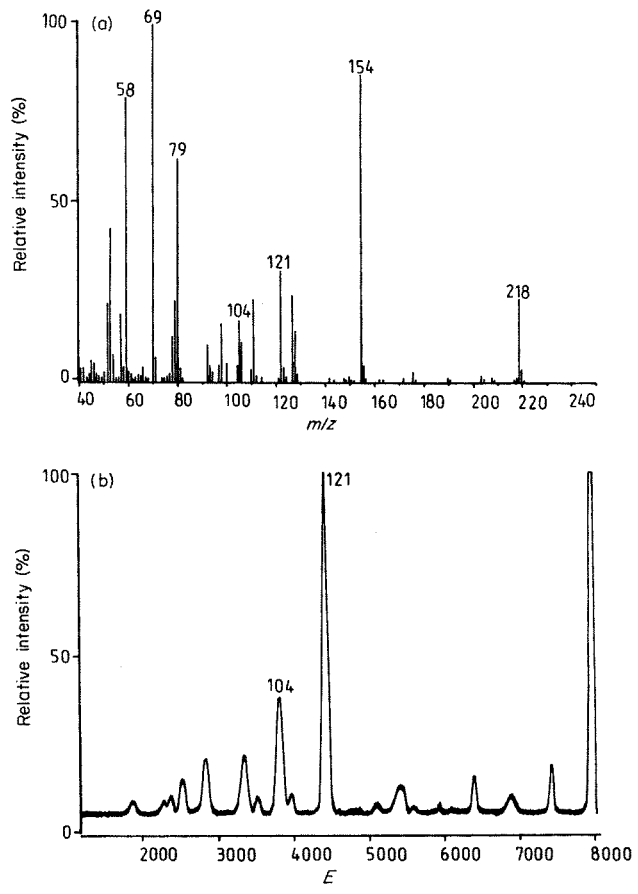


Figure 2. (a) EI mass spectrum and (b) CID/MIKE spectrum of trifluoracetylated 2,5-dimethylphenol.

The most favoured loss from 2,6-alkylated trifluoracetylated phenol ions is that of CF_3CO and CF_3COO radicals, suggesting that the aromatic hydrogen atom in the *o*-position is involved in the elimination of CF_3COOH in the corresponding derivatives. However, in the molecular ions of unsubstituted trifluoracetoxybenzene the loss of CO becomes predominant. The MIKE spectrum is given in Fig. 3(a). The structure of the corresponding daughter ion (*m/z* 162) is most probably that of ionized trifluoromethyl phenyl ether which is supported by the appropriate MIKE spectrum. The CID/MIKE spectrum and the 3rd FFR daughter-ion spectrum show fragment ions due to the loss of CO (*m/z* 134), OCF_2 (*m/z* 96), $^{\cdot}CF_3$ (*m/z* 93) and $C_6H_5O^{\cdot}$ (*m/z* 69). However, some less abundant fragmentations, e.g. C_5H_5, could be observed only in the MIKE spectrum. The 3rd FFR daughter-ion spectrum of *m/z* 162 ions is identical to that of *m/z* 162 ions formed by a consecutive reaction starting from the molecular ion of trifluoracetylated phenol. Both spectra are shown in Figs 3(a) and (c). The small differences concerning the abundances of the daughter ions should be caused by a slightly different collison gas pressure used in the experiments. The reactions *m/z* 190 → *m/z* 162 → *m/z* 96, and *m/z* 190 → *m/z* 162 → *m/z* 93 are observed without collision gas (indicated pressure in the analyser region was 2×10^{-8} mbar) and therefore should be unimolecular.[13]

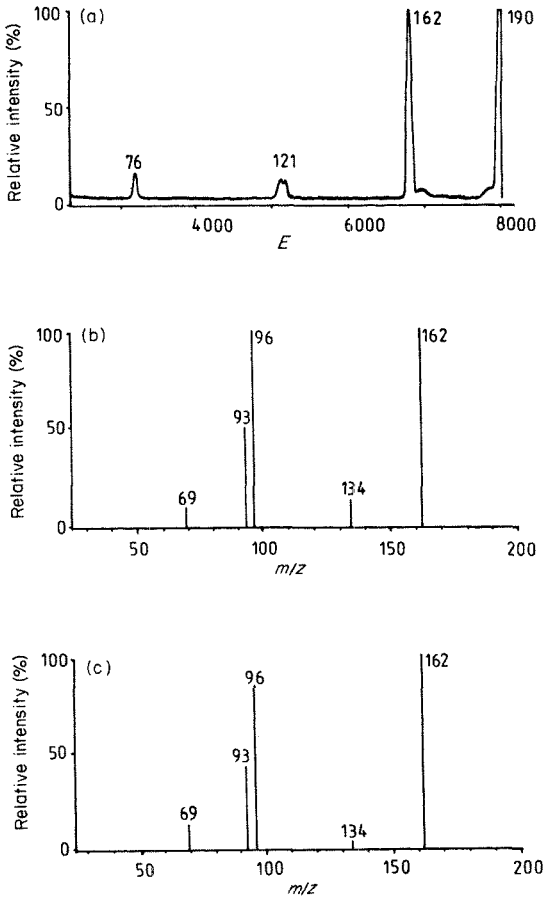


Figure 3. (a) MIKE spectrum of selected molecular ions of trifluoracetylated phenol (*m/z* 190). (b) 3rd FFR CID daughter-ion spectrum of selected *m/z* 162 ions. (c) Consecutive 3rd FFR daughter ion scan (*m/z* 190 (B) → *m/z* 162 (E) → daughters (Q)).

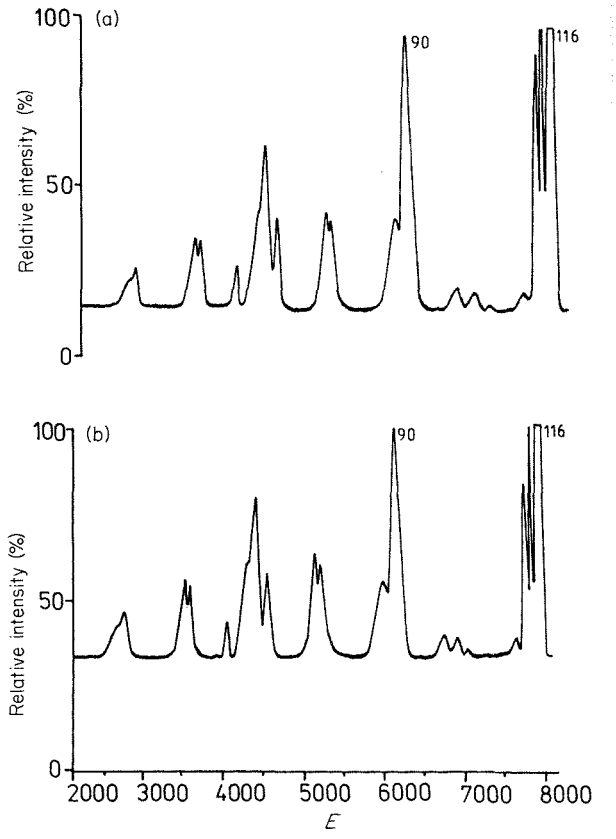


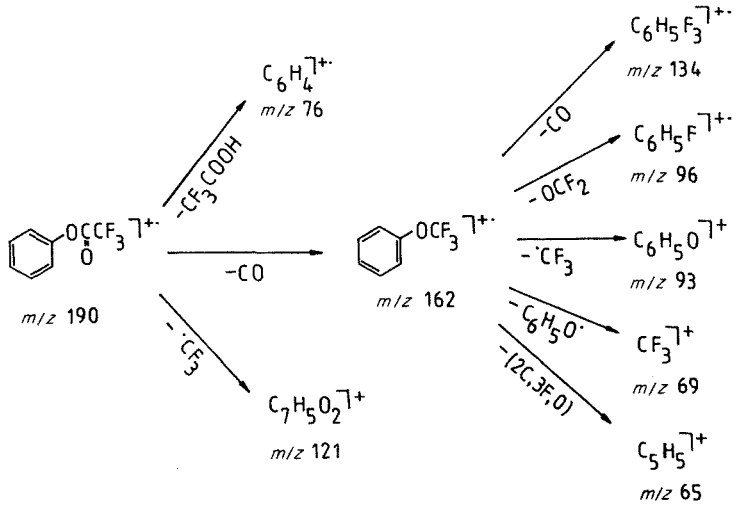
Figure 4. (a) CID/MIKE spectrum of the molecular ion of indene and (b) of *m/z* 116 ions produced by a McLafferty rearrangement from 3-trifluoracetoxy-2,3-dihydroindene.

The fragmentation reactions for trifluoracetylated phenol and alkylated phenols are summarized in Scheme 2.

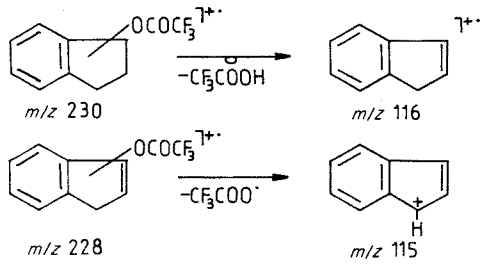
Alkylated 2,3-dihydroindenols and indenols

Derivatized 2,3-dihydroindenols fragment exclusively by a McLafferty rearrangement as discussed above (Scheme 3, upper part). The ions formed have the same structure as the corresponding indene molecular ions. The CID/MIKE spectra of the unsubstituted indene molecular ion (*m/z* 116) and the same ion obtained from 3-trifluoracetoxy-2,3-dihydroindene are shown in Fig. 4. Both spectra are quite similar and confirm the fragmentation reaction given in the upper part of Scheme 3. In some of the alkylated compounds the loss of CF_3COOH occurs from the $[M - alkyl]^+$ ions.

The CID/MIKE spectra of indenols show predominant peaks due to the loss of CF_3COO radicals



Scheme 2



Scheme 3

(Scheme 3, lower part). This simple bond cleavage yields in the case of trifluoracetoxyindene ions with a mass-to-charge ratio of 115. The CID/MIKE spectrum of the m/z 115 ions is the same as that for the $[M - 1]^+$ ion of indene which is shown in Fig. 6(a).

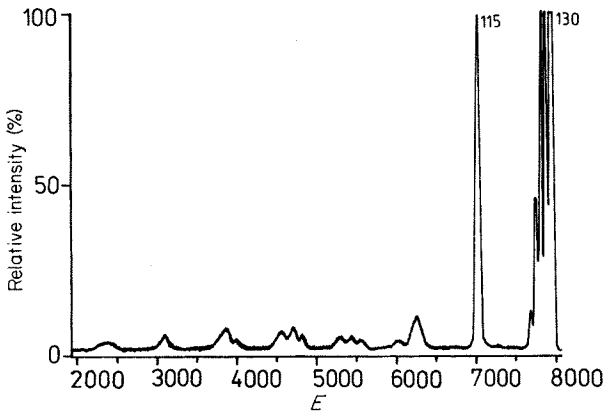


Figure 5. CID/MIKE spectrum of m/z 130 ions from 1-acetoxy-1,2,3,4-tetrahydronaphthalene.

Table 1. $T_{0.5}$ values for H and C_2H_2 loss from m/z 115 ions (precursor ions: indene, 1- and 2-trifluoracetoxynaphthalene); values are given in meV

Precursor (m/z)	Indene	1-Trifluoracetoxy-naphthalene	2-Trifluoracetoxy-naphthalene
114	13.5	24.7	91.0
89	91.1	146.0	117.0
65	41.2	70.6	83.0

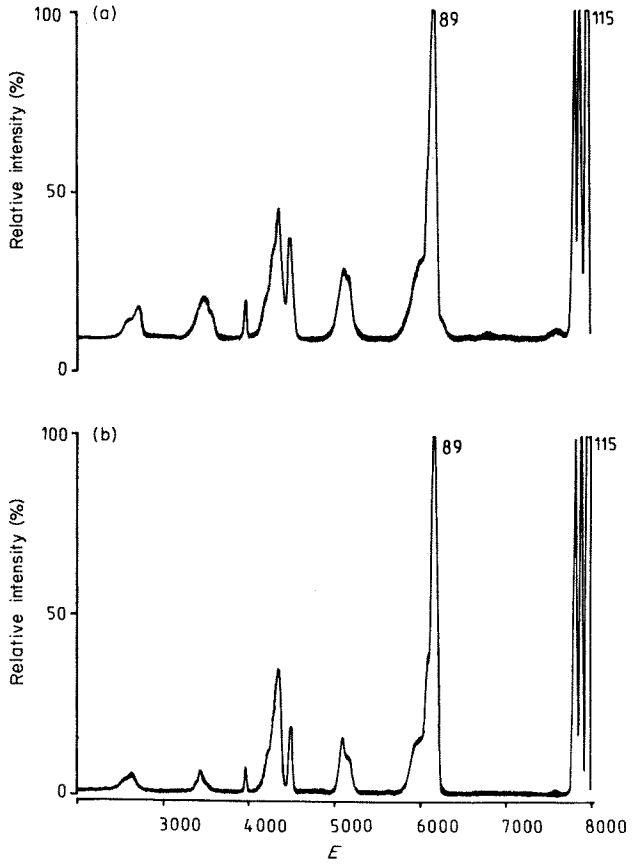
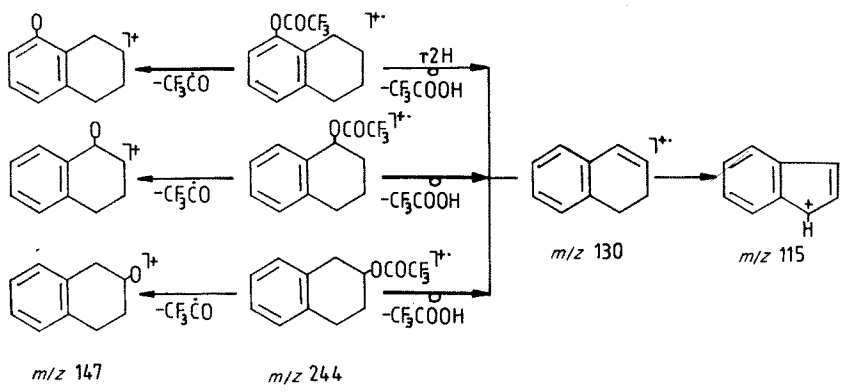


Figure 6. CID/MIKE spectra of mass-selected m/z 115 ions. Precursor ions: (a) indene, and (b) 1-trifluoracetoxynaphthalene.

Alkylated 1,2,3,4-tetrahydronaphthols

Three different 1,2,3,4-tetrahydronaphthols were chosen to study the fragmentation reactions of these compounds having the trifluoracetoxy group in the 1-, 2-, or 8-position of the molecule (see Scheme 4). If the aromatic ring contains the CF_3COO substituent, then α-cleavage is preferred instead of the McLafferty rearrangement. This rearrangement dominates in compounds in which the saturated ring is substituted by the trifluoracetoxy group provided that there is at least one hydrogen atom in the α-position. Considering the compounds shown in Scheme 4, the product of the



Scheme 4

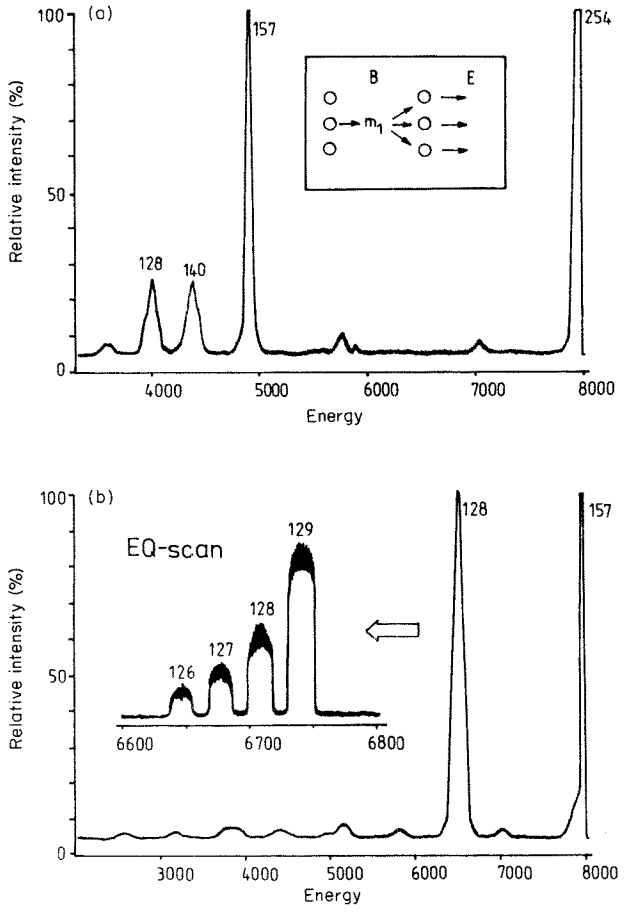


Figure 7. CID/MIKE spectrum of (a) 1-methyl-2-acetoxynaphthalene molecular ions and (b) *m/z* 157 ions obtained by loss of CF_3COO radicals. The EQ-scan for *m/z* 128 is given in the insert.

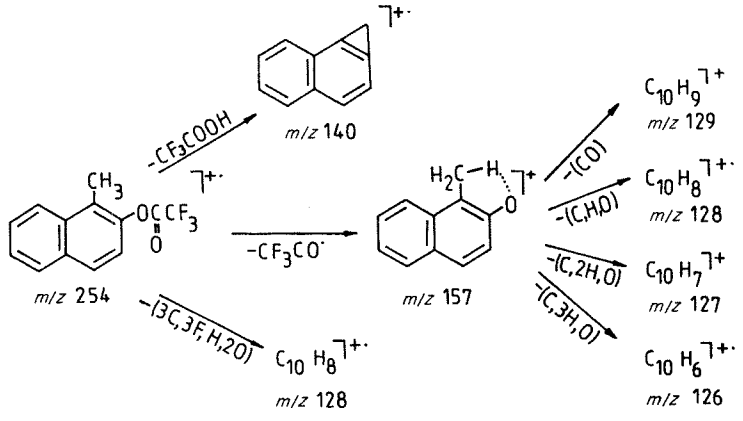
McLafferty rearrangement is a 1,2-dihydronaphthalene radical cation (*m/z* 130). However, in any case the ion *m/z* 130 rearranges to the same structure. This can be deduced from the CID/MIKE spectra which are identical for all *m/z* 130 ions. One of the resulting spectra is shown in Fig. 5. The elimination of CF_3COOH from 8-trifluoracetoxy-1,2,3,4-tetrahydronaphthalene must be accompanied by a hydrogen rearrangement to yield the 1,2-dihydronaphthalene ion. The extension of the π-electron system should be a plausible reason for this reaction. As can be seen from Fig. 5, the most abundant fragmentation of the 1,2-dihydronaphthalene cations is a ring contraction (loss of CH_3). The resulting ion with *m/z* 115 has a similar CID/MIKE spectrum as observed for the indenyl cation (Fig. 6(a)).

Alkylated naphthols

There was no evidence for a McLafferty rearrangement in the ion source, or in any of the field-free regions, for these compounds. Instead of this the spectra show peaks due to the elimination of $CF_3CO^{\cdot}$, and with lower probability, $CF_3COO^{\cdot}$ radicals. The stabilized $[C_{10}H_7O]^+$ ions undergo further fragmentation. The most-favoured loss, observed both unimolecularly and induced by collisions in the field-free regions, is that of carbon monoxide. Therefore, the question arises if both $[C_{10}H_7O]^+$ ions react to the same product by loss of CO and ring contraction. The CID/MIKE spectra recorded for the resulting $[C_9H_7]^+$ ions show very small differences in comparison with the spectrum observed for the $[M-1]^+$ ion of indene. The spectra of $[C_9H_7]^+$ ions obtained by using 1-trifluoracetoxynaphthalene and indene as precursor ions are shown in Fig. 6. Both ions produce a prominent peak at *m/z* 89 and are distinguished only by differences in the intensities of the peaks at *m/z* 114, 113, 57.5 (M^{2+}) and 51. To facilitate the structural assignment the kinetic energy release for the following metastable decompositions of each $[C_9H_7]^+$ ion has been considered:

$$m/z\ 115 \begin{cases} \rightarrow m/z\ 114 \\ \rightarrow m/z\ 89 \\ \rightarrow m/z\ 65 \end{cases}$$

The $T_{0.5}$ values, calculated by means of the usual equation,[14] show remarkable differences (Table 1) suggesting the existence of isomeric ions formed simultaneously.



Scheme 5

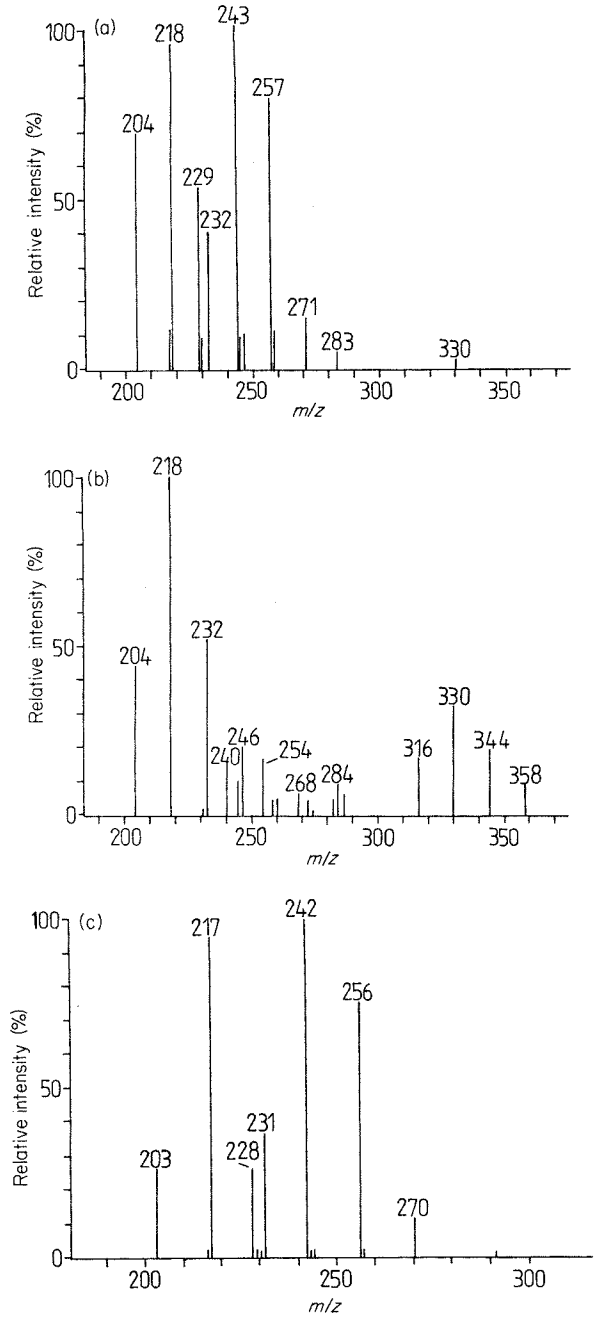


Figure 8. Constant neutral loss of (a) CF_3COOH (114 u), (b) $CF_3CO^{\cdot}$ (97 u) and (c) $CF_3COO^{\cdot}$ (113 u) obtained for a derivatized coal-derived liquid.

This is supported by the shape of the metastable peaks which is of a complex Gaussian type.[15] Hence, the assumption is justified that the $[C_{10}H_7O]^+$ ions isomerize to a certain extent prior to further fragmentation.

A slightly different fragmentation pathway can be observed for alkylated and derivatized naphthols having the substituent in the *ortho* position. In the CID/MIKE spectrum of 1-methyl-2-trifluoracetoxynaphthalene, the most abundant fragmentation is the loss of the trifluoracetyl group. The CID/MIKE spectrum of the ion formed (*m/z* 157) shows a broad, unresolved signal around *m/z* 128. This signal can be resolved in its components by a simultaneous scan of the electrostatic and the quadrupole analyser. The spectra are shown in Fig. 7. It can be seen that the methyl group is also involved in the fragmentation which is indicated by the loss of CH_nO (n = 1–3). It is interesting to note that the fragmentation due to the loss of CH_nO (n = 1–3) is obviously caused by high-energy collisions only in the 2nd FFR. This conclusion can be drawn from the 3rd FFR daughter-ion spectra obtained with the quadrupole analyser. The spectra of mass-selected *m/z* 157 ions recorded with collision energies of ~10 eV show only one signal caused by the loss of CO (*m/z* 129). Applying higher collision energies (>100 eV) as well as a higher collision gas pressure, additional signals at *m/z* 128 and 127 are observed. Furthermore, consecutive daughter-ion spectra including the 2nd FFR and 3rd FFR reactions show that the loss of the trifluoracetyl radical and the loss of CO is a unimolecular reaction (sequence: *m/z* 254 → *m/z* 157 → *m/z* 129). The observed fragmentations are summarized in Scheme 5.

Applications

The fragmentation reactions described above of several types of derivatized alkylated hydroxyaromatic compounds indicate that the neutral mass loss caused by the trifluoracetyl group can be used for their determination. The neutral mass loss of 114 u (CF_3COOH) is suitable for the identification of alkylated phenols, 2,3-dihydroindenols and 1,2,3,4-tetrahydronaphthols, whereas the mass loss of 97 u ($CF_3CO^{\cdot}$) is characteristic for all classes of compounds studied, with the exception of indenols and 2,3-dihydroindenols.

The derivatization of simple phenols using MBTFA can be applied also to other hydroxyaromatics. However, the fragmentation of dihydroxybenzenes, hydroxybiphenyls and others shall not be discussed here in detail. Figure 8 shows an application of the neutral mass loss scans on a coal-derived liquid (80–360 °C fraction). With the help of Table 2 C_1–C_7 phenols, 2,3-dihydroindenols, up to C_4 naphthols and 1,2,3,4-tetrahydronaphthols, as well as C_1–C_4 dihydroxybenzenes, were identified (Fig. 8(a) and (b)). Figure 8(c) shows that also C_1–C_4 indenols are present in this complex mixture. Note that in the case of alkylated 2,3-dihydroindenols the loss of CF_3COOH occurs from the $[M - alkyl]^+$ ions (Fig. 8(a), odd *m/z* ratios). The same fragmentation is observed for some of the phenols (Fig. 8(c)).

The neutral mass loss scan described above indicates the advantage of a derivatization for a rapid screening of mixtures by the MS/MS methods. The detection limits for individual compounds reach 10–100 ppm (ng/µl inj.) if $(B/E)(1 - E)^{1/2}$ scans are applied, and are slightly better if the 3rd FFR reactions are monitored. An optimization of the collision gas pressure ($\sim 10^{-6}$ mbar in the appropriate FFR) and of the collision energies (30–40 eV) is important for maximum intensity.

In comparison with parent scans which can be applied only to those compounds having a common fragment ion the neutral mass loss spectra detect many

Table 2. Mass table of selected derivatized hydroxyaromatic compounds

Compound class	Expected mass-to-charge ratios			
	Unalkylated	C_1	C_2	C_3
Phenols	190	204	218	232
Indenols	228	242	256	270
2,3-Dihydroindenols	230	244	258	272
Naphthalenols	240	254	268	282
1,2,3,4-Tetrahydronaphthalenols	244	258	272	286
Decahydronaphthalenols	250	264	278	292
Biphenylenols and acenaphthalenols	266	280	294	308
Fluorenols	278	292	306	320
Phenanthrenols and anthracenols	290	304	318	332
Dihydroxybenzenes[a]	302	316	330	344
[b]	206	220	234	248
Dihydroxybiphenylenols and dihydroxyacenaphthalenols	378	392	406	420

[a] Both hydroxy groups derivatized.
[b] One hydroxy group derivatized.

more classes of hydroxy compounds. The parent scans are limited to the screening for alkylated phenols, 2,3-dihydroindenols and 1,2,3,4-tetrahydronaphthols, producing the hydroxytropylium ion.[3] Besides this, the parent spectra often show peaks which are caused by fragment ions leading also to the hydroxytropylium ion (m/z 107) ($[M-1]^+$, $[M-\text{alkyl}]^+$). Therefore the identification of the molecular ions which is the aim of the analysis is especially difficult if the molecule contains long alkyl side chains. However, the advantages of the methods presented in this paper are diminished partly by the inability to differentiate between isomeric compounds and by a difficult quantitative determination. To answer these questions a more time-consuming GC/MS analysis has to be accomplished.

Acknowledgements

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