Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Chromatography A, 1058 (2004) 107–112
JOURNAL OF CHROMATOGRAPHY A
www.elsevier.com/locate/chroma

Determination of aldehydes and ketones using derivatization with 2,4-dinitrophenylhydrazine and liquid chromatography–atmospheric pressure photoionization-mass spectrometry

Suze M. van Leeuwen, Laurens Hendriksen, Uwe Karst*

Department of Chemical Analysis and MESA+ Institute for Nanotechnology, University of Twente, P.O. Box 217, 7500 AE Enschede, The Netherlands

Abstract

Atmospheric pressure photoionization-mass spectrometry (APPI-MS) is used for the analysis of aldehydes and ketones after derivatization with 2,4-dinitrophenylhydrazine (DNPH) and liquid chromatographic separation. In the negative ion mode, the $[M - H]^-$ pseudomolecular ions are most abundant for the carbonyls. Compared with the established atmospheric pressure chemical ionization (APCI)-MS, limits of detection are typically lower using similar conditions. Automobile exhaust and cigarette exhaust samples were analyzed with APPI-MS and APCI-MS in combination with an ion trap mass analyzer. Due to improved limits of detection, more of the less abundant long-chain carbonyls are detected with APPI-MS in real samples. While 2,4-dinitrophenylazide, a known reaction product of DNPH with nitrogen dioxide, is detected in APCI-MS due to dissociative electron capture, it is not observed at all in APPI-MS.

Keywords: Atmospheric pressure photoionization; Carbonyls; 2,4-Dinitrophenylhydrazine

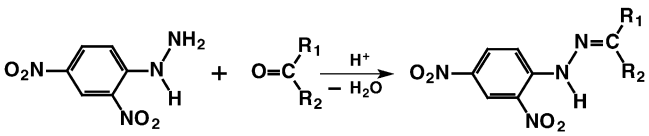
1. Introduction

The analysis of aldehydes and ketones in air samples is an important task in the fields of occupational medicine and atmospheric chemistry. Due to their reactivity, a stabilization of the carbonyls prior to analysis is advantageous. Therefore, a large number of derivatization reagents for aldehydes has been introduced in the last decades. Many of these use an aromatic hydrazine group, which reacts with aldehydes and ketones in acidic media under formation of the respective hydrazones [1]. 2,4-Dinitrophenylhydrazine (DNPH) is known for this purpose since more than 20 years [2–4] and has become the most popular reagent for the analysis of aldehydes. After derivatization (see Scheme 1), the hydrazones are separated by reversed-phase liquid chromatography and detection is performed by UV–vis absorption spectroscopy. Due to its good performance for the analysis of liquid and gas phase samples, the DNPH method has been introduced as national and international standard method by several standardization bodies [5–7]. As the resolving power of liquid chromatography is limited for the DNPH derivatives and as the number of carbonyl compounds is strongly increasing with increasing alkyl chainlength, UV–vis detection is not sufficient for the analysis of DNPH derivatives of higher aldehydes and ketones with four or more carbon atoms [8]. Furthermore, problems are described for the analysis of formaldehyde in the presence of ozone [9,10] or nitrogen dioxide [11], as potentially coeluting compounds are formed. Recently, it was found out that the analysis of unsaturated aldehydes in the gas phase may be accompanied by interferences, when a large excess of reagent is still present after sampling and when strongly acidic pH is used [12].

Mass spectrometric detection of the hydrazones by using atmospheric pressure chemical ionization (APCI) in the negative ion mode was introduced in 1998 by Oehme and coworkers [13]. They used an ion trap mass spectrometer and investigated the fragmentation pathways of reference compounds. Soon thereafter, other groups adapted this method to investigate various types of air samples [14–16]. Oehme

* Corresponding author. Tel.: +31 53 489 2983; fax: +31 53 489 4645.
E-mail address: u.karst@utwente.nl (U. Karst).

0021-9673/$ – see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.chroma.2004.08.149



Scheme 1. Derivatization of carbonyls with 2,4-dinitrophenylhydrazine.

and coworkers later refined their method with respect to fragmentation pathways [17] and quantitative aspects [18]. Van den Bergh et al. [19,20] applied the method to study oxidation products formed in the reaction between alpha- and beta-pinene and OH radicals. Manini and coworkers [21] determined patterns of biologically relevant aldehydes, e.g., acrolein or 4-hydroxynonenal, in exhaled breath using DNPH derivatization and LC with tandem mass spectrometric detection. Richardson et al. [22] and Zwiener et al. [23] determined aldehydes by LC–MS in ozonated drinking waters and outdoor swimming pools after chlorination, respectively.

Four years ago, Bruins and coworkers introduced atmospheric pressure photoionization (APPI), a new method for the analysis of non-polar analytes by LC–MS [24]. A vacuum ultraviolet (VUV) lamp is used as source of photons with an energy of approximately 10 eV. A dopant is added to obtain a great abundance of dopant photoions, which then react with the analytes. The ion source is similar to an APCI source, with the major difference that the corona discharge needle is replaced by a VUV lamp. The method has rapidly become commercially available for the state-of-the-art instruments of most major LC–MS manufacturers, and has already been covered in recent reviews [25,26]. The number of publications in this field is therefore increasing rapidly, with some papers being devoted to fundamental investigations, e.g., about negative ion-APPI-MS [27], solvent [28] or dopant [29,30] effects. Most papers in this field, however, focus on novel applications for the analysis of analytes with low polarity, e.g., flavonoids [31], anabolic steroids [32], idoxifene and its metabolites [33], hydrophobic peptides [34] and even polycyclic aromatic hydrocarbons [35]. However, nitroaromatics have not been studied by APPI-MS yet, and the DNPH derivatives are particularly interesting because of their broad application and the established use of APCI-MS for their analysis. For this reason, a method for the determination of aldehydes based on DNPH derivatization, LC separation and APPI-MS detection has been developed. The results are compared with those obtained with APCI-MS detection.

2. Experimental section

2.1. Chemicals

DNP hydrazone standards (DNPH derivatives of formaldehde, acetaldehyde, acrolein, 2-butanone, *p*-tolualdehyde and 1-hexanal) were synthesized according to [8]. Solvents for LC were acetonitrile and water, both LC–MS grade, purchased from Biosolve Ltd. (Valkenswaard, The Netherlands). DNPH coated sampling cartridges were purchased from Supelco (Bellefonte, PA, USA).

2.2. Instrumentation

For the LC–MS setup, an Agilent Technologies (Waldbronn, Germany) HP1100 liquid chromatograph consisting of binary gradient pump model G1312A, autosampler model G1313A and diode array detector model G1315B was coupled to an Esquire 3000*plus* ion trap mass spectrometer from Bruker Daltonics (Bremen, Germany), equipped with Agilent/Syagen Photomate® atmospheric pressure photoionization source and atmospheric pressure chemical ionization source. Equipment for active air sampling was a Buck I.H. Pump (Supelco), connected to a DC-Lite DryCal® flow calibrator (Supelco).

2.3. Air sampling

Car exhaust samples were obtained by active sampling over a DNPH coated silica gel cartridge. Sampling was performed in a distance of 5 cm behind the exhaust pipes of the car. Sample volumes were approximately 3 L for car 1 (diesel fuelled) and car 2 (regular fuelled). For car 3 (regular fuelled) it was about 4 L. A flow rate of 1 L/min was applied for all sampling experiments. Cigarette smoke samples were obtained by water jet pump-assisted smoking of filter cigarettes over two cartridges, one for sampling and one as backup to control possible breakthroughs of the analytes. Due to this methodology, the exact sample volume could not be determined. The cigarettes were burnt down completely until the filter.

The sample loaded cartridges were eluted with 10 mL of acetonitrile. This solution was directly injected into the HPLC system.

2.4. Analysis

Separations of the standard compounds were performed on column I, a Discovery® C_{18} column of 150 mm × 3 mm and 5 μm particle size with a 2 cm × 3 mm precolumn of the same packing material (Supelco). The samples from automobile exhaust and cigarette smoke were separated on column II, which is based on LiChrospher RP-18 ec material (Merck, Darmstadt, Germany) in ChromCart cartridges (Macherey-Nagel, Düren, Germany) with dimensions of 200 mm × 3 mm and 5 μm particle size. The respective gradients for columns I and II are shown in Table 1, where solvent A is water and solvent B is acetonitrile. Flow rates for both columns were 0.5 mL/min and injection volumes were 10 μL in all cases. For all measurements, both for the standards as well as for the samples, triple injections were made. Limits of detection and quantification are based on an estimation of S/N = 3 and 10, respectively, calculated from the chromatogram traces in the respective concentration range.

Table 1
Gradient profiles used for the separation of the DNPH derivatives

	Column I								Column II							
Time (min)	0	0.5	11.0	12.0	12.5	16.0	16.5	21.0	0	1.5	7.5	10	13.5	14.5	20.0	
Concentration B (%)	60	60	75	75	100	100	60	Stop	49	49	65	80	80	49	Stop	

Mass spectra were recorded in the full scan mode, scanning from m/z = 50 to 350. The detector was employed in the negative ion mode, and the ion count cumulative target for the ion trap mass analyzer was 5000, with a maximum accumulation time of 200 ms. Ion source parameters were 0 V on the transfer capillary, 65 psi nebulizer gas of 250 °C and 3.0 L/min of drying gas with a temperature of 225 °C. In case where the APCI source was employed, a current of 2000 nA was applied to the corona. All other parameters were the same for APPI and APCI.

3. Results and discussion

First investigations showed already that the DNPH derivatives can be detected well using LC–APPI-MS without dopant. As in case of APCI-MS, the most abundant ion for the derivatives is the $[M - H]^-$ pseudomolecular ion in the negative ion mode. An APPI(−) mass spectrum of the acetaldehyde DNPH derivative is presented in Fig. 1. The $[M - H]^-$ peak with an m/z = 223 is observed with highest intensity, and without consideration of quantitative aspects, the mass spectrum is identical to that obtained with APCI-MS. Kostiainen and coworkers [27] reported deprotonation as well as electron capture as typical ionization mechanisms for negative ion APPI, using toluene as dopant. They analyzed several model compounds, including *p*-dinitrobenzene, which is similar to the analytes used in our study. The data obtained in that study support the assumption that the ionization process is initiated by thermal electrons formed in the photoionization of toluene. A series of further reactions is then observed depending on the individual analytes. For *p*-dinitrobenzene,

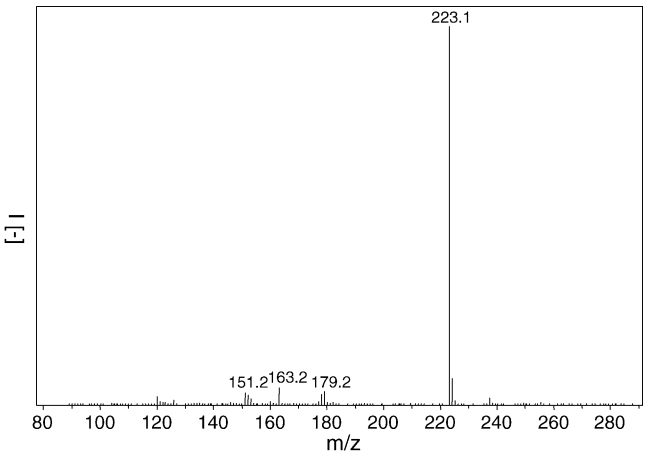


Fig. 1. APPI(−) mass spectrum of the DNPH derivative of acetaldehyde.

non-dissociative electron capture was observed, and deprotonation occured frequently for analytes with lower electron affinity [27]. The findings observed in this study cannot be explained with these data, as the absence of dopant should not lead to ionization of the analytes. For the case of acetonitrile in positive ion photoionization, the group of Traldi [28] describes possible acetonitrile rearrangements after photoexcitation. For the species they assumed to be the most reasonable photoionization product of acetonitrile, no protonating action can be invoked, since it is an odd-electron molecular ion. Owing to this fact, they argue, this ion has a considerable proton affinity and could therefore, in the positive ion mode, react with neutral acetonitrile to produce protonated species. In the negative ion mode, as exploited in the present study, this photoexcitated acetonitrile species could possibly act as deprotonating agent for the DNP hydrazones. However, additional work is required to investigate the exact mechanism(s) of APPI with and without dopant.

The instrumental parameters were optimized in the following for both APPI-MS and APCI-MS to allow a fair comparison between the two techniques. It turned out that most instrumental parameters have identical optimum values for both ion sources. This is not surprising, because the setups of the ion sources are identical, with the only exception that the VUV lamp replaces the corona discharge needle. Preliminary results on other groups of compounds indicate, in comparison to available literature data that the need for a dopant may be strongly dependent on the model of the APPI source.

The separation of the DNP hydrazones was carried out according to literature descriptions [8] using reversed phase C_{18} column and a binary gradient of acetonitrile and water. The instrumental limits of detection were determined for a series of derivatives of compounds, which are either of special relevance or represent interesting groups of carbonyls as aliphatics, unsaturated compounds or aromatics. It is obvious from Table 2 that the limits of detection and the limits of quantification are in all cases better for APPI-MS when compared with APCI-MS. The differences vary with the individual compounds and range from a factor of 1.2–8. For most compounds, the limits of detection are between 2.9 and 8.8 nmol/L, with formaldehyde reaching only 24 nmol/L. The linear ranges of the substances on the used ion trap instrument cover two decades of concentration when using APPI-MS and at least three decades for APCI-MS. The correlation coefficient for the calibration function is good in both cases, with slight advantages for APCI-MS.

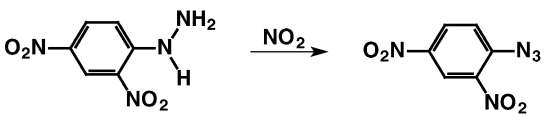
Oehme et al. have discussed the fragmentation schemes of the DNPH derivatives using APCI(−) in detail [13,17,18]. For the substances investigated with APPI-MS in this work,

Table 2
Analytical figures of merit for selected standard compounds obtained with APPI-MS and APCI-MS

	APPI			APCI		
	LOD ($\times 10^{-9}$ M)	LOQ ($\times 10^{-9}$ M)	R	LOD ($\times 10^{-9}$ M)	LOQ ($\times 10^{-9}$ M)	R
Formaldehyde	24	80	0.986	70	234	0.998
Acetaldehyde	8.8	29	0.993	73	244	0.996
Acrolein	3.9	13	0.991	12	41	0.998
2-Butanone	4.3	14	0.989	5.3	18	0.995
p-Tolualdehyde	2.9	9.7	0.995	8.7	29	>0.999
1-Hexanal	3.7	12	0.993	5.8	19	>0.999

the fragmentation pathways were identical. In principle, the compounds, which were observed in APCI-MS could also be detected in APPI-MS. As major exception, 2,4-dinitrophenylazide (DNPA), the reaction product of DNPH with nitrogen dioxide (see Scheme 2) is not observed at all in APPI-MS. This compound has recently been investigated by APCI-MS, and it was detected after dissociative electron capture as $[M - N_2]^-$ at an m/z = 181 [36]. The $[M]^-$ or $[M - H]^-$ peaks are not observed at all. As explained before, no thermal electrons should be produced without the use of a dopant. Therefore, this ionization mechanism of electron capture should not occur in the APPI-MS interface. Ionization via deprotonation as described for the DNP hydrazones can be excluded for the DNPA, due to the fact that DNPA is likely to have a higher proton affinity than the deprotonating solvent species, because only protons at an aromatic ring could possibly be abstracted. This may explain why no ionization is obtained at all for this analyte. The lack of ionization can be considered as an advantage, as interferences by this compound in mass spectrometric analysis are therefore not possible. On the other hand, the degree of information, which can be obtained, is reduced, and the possibility to determine nitrogen dioxide besides the hydrazones is excluded as well.

After characterization of the system, real samples from different sources were analyzed with the goal to compare the suitability of APPI-MS with APCI-MS concerning the detection of trace compounds in highly contaminated samples. For this purpose, automobile exhaust and cigarette smoke were selected. Sampling was carried out using commercial cartridges, which contain DNPH-coated silica gel with low background of the aldehydes. Two cartidges were used for each sample, one for quantification and one to control possible breakthroughs of the analytes, which are most likely to occur in case of high analyte concentrations and high flow rates during sampling. It should also be considered that sterically hindered ketones often react slower with DNPH than aldehydes, thus increasing the likelihood of a breakthrough.



Scheme 2. Derivatization of NO_2 with 2,4-dinitrophenylhydrazine.

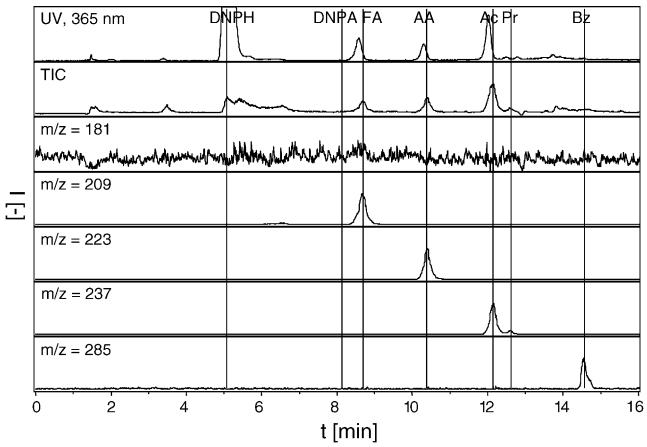


Fig. 2. LC–APPI(−)-MS chromatograms and UV trace of the analysis of a car exhaust sample, including the mass traces of DNPH, DNPA and the 2,4-dinitrophenylhydrazones of formaldehyde (FA), acetaldehyde (AA), acetone (Ac), propanol (Pr) and benzaldehyde (Bz).

In Figs. 2 and 3, the chromatogram of an automobile exhaust sample of a car applying regular fuel is presented using APPI-MS (Fig. 2) and APCI-MS (Fig. 3). In the total ion current as well as in the UV–vis detector trace at 365 nm, only few peaks are observed in Fig. 2. It should be noted that the time delay between the UV trace and the MS traces of Fig. 2 is due to using the detectors in sequence with a transfer line, which provides a delay of a few seconds. The concentration of formaldehyde, acetaldehyde and the saturated C_3 carbonyls (acetone, propanal) in the exhaust sample is very high, but

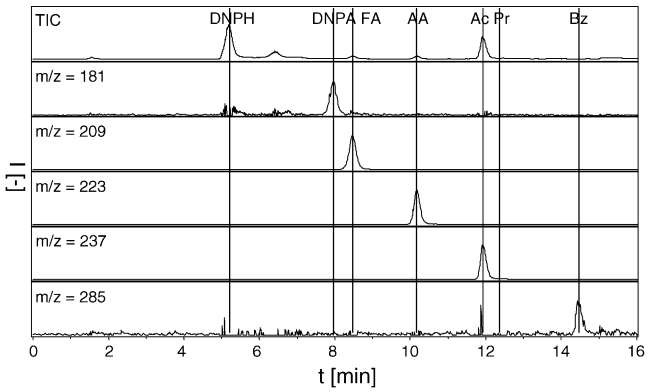


Fig. 3. LC–APCI(−)-MS chromatograms of the analysis of a car exhaust sample. For abbreviations, see Fig. 2.

Table 3
List of carbonyls detected with S/N ≥ 3 in the automobile exhaust and cigarette smoke samples

		DNPA	A	B	C	D	E
Diesel	APPI	–	C_1–C_6	C_1–C_2	C_3–C_6	C_7–C_8	C_8
	APCI	×	C_1–C_3	C_1	C_3	–	–
Regular fuel 1	APPI	–	C_1–C_6	C_1–C_2	C_3–C_7	C_7–C_8	C_8
	APCI	×	C_1–C_6	C_1	C_3–C_7	C_7–C_8	C_8
Regular fuel 2	APPI	–	C_1–C_6	C_1–C_3	C_3–C_7	C_7–C_8	C_8
	APCI	×	C_1–C_6	C_1–C_2	C_3–C_7	C_7–C_8	C_8
Cigarette	APPI	–	C_1–C_7	C_1–C_5	C_3, C_5	–	–
	APCI	×	C_2–C_5	C_1, C_3–C_4	C_3, C_5	–	–

A: saturated, not alicyclic; B: saturated hydroxycarbonyls or carboxylic acids; C: one double bond or saturated ring; D: aromatic; E: phenolic.

the later part of the chromatogram with many smaller peaks clearly confirms that only MS detection will provide useful information on the concentration of the higher aldehydes. The most obvious difference between the two figures is the mass trace of m/z = 181 for DNPA, which shows, due to the different ionization mechanism as explained above, a peak for APCI-MS, but not for APPI-MS. For the derivatives of the saturated carbonyls with a C_3 alkyl chain, the S/N for the first peak (acetone) is similar in both figures, while the second peak (propanal) can hardly be detected with APCI-MS, but is clearly observed in APPI-MS. This finding is in analogy to the fact that the difference between the limits of detection for APPI and APCI is quite small for ketones (compare with butanone, Table 2), while it is much larger for the lower aliphatic aldehydes (acetaldehyde). The effect of APPI-MS on higher aliphatic aldehydes like 1-hexanal (Table 2) is quite low. As an example for a less abundant compound, which is known to occur in exhaust samples, benzaldehyde with m/z = 285 was selected. The comparison between the two respective mass traces in Figs. 2 and 3 also confirms the findings stated in Table 2 for aromatics (*p*-tolualdehyde) that the limits of detection are lower for APPI-MS.

As different groups of carbonyls were studied by APCI-MS in earlier work of Oehme and coworkers [13], this investigation was extended to find out, which members of which of these groups can be detected in the real samples with a S/N ≥ 3. While DNPA is detected in all samples using APCI-MS, it is not detected at all in APPI-MS as explained above. For the other groups of carbonyls, APPI-MS allows to detect at least the same number of species in all cases. Often, significantly more carbonyl compounds are detected when using APPI-MS.

One unusual group of carbonyls mentioned in Table 3 is the group of carboxylic acids, which is not routinely determined using the DNPH method. Recent LC–MS investigations by Oehme and coworkers [13] had already indicated that hydroxylated carbonyls and/or carboxylic acids are derivatized. Although no dedicated reports on the determination of carboxylic acids via derivatization with 2,4-dinitrophenylhydrazine have been published, studies on their analysis after derivatization with the strongly related 2-nitrophenylhydrazine prior to UV–vis and/or MS analysis were carried out [37–39]. It was shown in these publications that the derivatization takes place slowly, indicating that under the typical conditions for air sampling of aldehydes, only an extremely low derivatization yield can be expected. This might, in combination with the short retention times of these highly polar compounds, be the reason why no attention was paid yet to possible interferences of the derivatives of the carboxylic acids on the determination of the aldehydes and ketones. However, for the actual air sampling conditions, it is not likely to have a high derivatization yield of carboxylic acids. Therefore, it is most likely that the observed peaks in the sample chromatograms, belonging to group B (Table 3), are the respective hydroxycarbonyls and not the carboxylic acids.

4. Conclusions

Dopant-free APPI-MS has shown to be an attractive alternative to APCI-MS, as the limits of detection typically are slightly lower and more different carbonyls can be detected at low levels in real samples from automobile exhaust and cigarette smoke. As no dopant is required, the technical effort for both methods is identical and routine analysis with APPI-MS in well possible. As could be expected, DNPA, which is ionized by dissociative electron capture in APCI-MS, is not detected at all in APPI-MS. At this stage, the only slight drawbacks of APPI-MS are a reduced linear range (of still two decades of concentration) and a slightly higher correlation coefficient of the calibration.

Acknowledgement

Financial support by the Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO, Den Haag, The Netherlands) is gratefully acknowledged.

References

[1] M. Vogel, A. Büldt, U. Karst, Fresenius J. Anal. Chem. 366 (2000) 781.

[2] K. Kuwata, M. Uebori, Y. Yamasaki, J. Chromatogr. Sci. 17 (1979) 264.
[3] R.K. Beasley, C.E. Hoffmann, M.L. Rueppel, J.W. Worley, Anal. Chem. 52 (1980) 1110.
[4] G. Andersson, K. Andersson, C.A. Nilsson, J.-O. Levin, Chemosphere 10 (1979) 823.
[5] American Society for Testing and Materials, Standard test method for the determination of formaldehyde and other carbonyl compounds in air (active sample methodology), designation D 5197–92, 1992.
[6] Environmental Protection Agency, Method for the determination of formaldehyde in ambient air using adsorbent cartridge followed by high performance liquid chromatography (HPLC), method TO-11, 1987.
[7] Deutsche Forschungsgemeinschaft, Analytische Methoden zur Bestimmung gesundheitsschädlicher Arbeitsstoffe-Luftanalysen, Bd. 1, Methoden-Nr. 1 Aldehyde, Methoden-Nr. 2 Aldehyde, VCH Verlagsgesellschaft Weinheim, 1996.
[8] W. Pötter, U. Karst, Anal. Chem. 68 (1996) 3354.
[9] D.F. Smith, T.E. Kleindienst, E.E. Hudgens, J. Chromatogr. 483 (1989) 431.
[10] R.R. Arnts, S.B. Tejada, Environ. Sci. Technol. 23 (1989) 1428.
[11] U. Karst, N. Binding, K. Cammann, U. Witting, Fresenius J. Anal. Chem. 345 (1993) 48.
[12] R. Schulte-Ladbeck, R. Lindahl, J.-O. Levin, U. Karst, J. Environ. Monit. 3 (2001) 306.
[13] S. Kölliker, M. Oehme, C. Dye, Anal. Chem. 70 (1998) 1979.
[14] E. Grosjean, P. Green, D. Grosjean, Anal. Chem. 71 (1999) 1851.
[15] A. Sakuragawa, T. Yoneno, K. Inoue, T. Okutani, J. Chromatogr. A 844 (1999) 403.
[16] G. Zurek, H. Luftmann, U. Karst, Analyst 124 (1999) 1291.
[17] S. Kölliker, M. Oehme, L. Merz, Rapid Commun. Mass Spectrom. 15 (2001) 2117.
[18] S. Brombacher, M. Oehme, C. Dye, Anal. Bioanal. Chem. 372 (2002) 622.
[19] V. Van den Bergh, I. Vanhees, R. de Boer, F. Compernolle, C. Vinckier, J. Chromatogr. A 896 (2000) 135.
[20] V. Van den Bergh, H. Coeckelberghs, I. Vanhees, R. de Boer, F. Compernolle, C. Vinckier, Anal. Bioanal. Chem. 372 (2002) 630.
[21] R. Andreoli, P. Manini, M. Corradi, A. Mutti, W.M.A. Niessen, Rapid Commun. Mass Spectrom. 17 (2003) 637.
[22] S.D. Richardson, T.V. Caughran, T. Poiger, Y.B. Guo, F.G. Crumley, Ozone Sci. Eng. 22 (2000) 653.
[23] C. Zwiener, T. Glauner, F.H. Frimmel, Anal. Bioanal. Chem. 372 (2002) 615.
[24] D.B. Robb, T.R. Covey, A.P. Bruins, Anal. Chem. 72 (2000) 3653.
[25] A. Raffaelli, A. Saba, Mass Spectrom. Rev. 22 (2003) 318.
[26] H. Hayen, U. Karst, J. Chromatogr. A 1000 (2003) 549.
[27] T.J. Kauppila, T. Kotiaho, R. Kostiainen, A.P. Bruins, J. Am. Soc. Mass Spectrom. 15 (2004) 203.
[28] E. Marotta, R. Seraglia, F. Fabris, P. Traldi, Int. J. Mass Spectrom. 228 (2003) 841.
[29] T.J. Kauppila, T. Kuuranne, E.C. Meurer, M.N. Eberlin, T. Kotiaho, R. Kostiainen, Anal. Chem. 74 (2002) 5470.
[30] M. Tubaro, E. Marotta, R. Seraglia, P. Traldi, Rapid Commun. Mass Spectrom. 17 (2003) 2423.
[31] J.P. Rauha, H. Vuorela, R. Kostiainen, J. Mass Spectrom. 36 (2001) 1269.
[32] A. Leinonen, T. Kuuranne, R. Kostiainen, J. Mass Spectrom. 37 (2002) 693.
[33] C.M. Yang, J. Henion, J. Chromatogr. A 970 (2002) 155.
[34] A. Delobel, F. Halgand, B. Laffranchise-Gosse, H. Snijders, O. Laprevote, Anal. Chem. 75 (2003) 5961.
[35] H. Moriwaki, M. Ishitaki, S. Yoshikawa, H. Miyakoda, J.F. Alary, Anal. Sci. 20 (2004) 375.
[36] H. Hayen, N. Jachmann, M. Vogel, U. Karst, Analyst 127 (2002) 1027.
[37] R. Peters, J. Hellenbrand, Y. Mengerink, Sj. Van der Wal, J. Chromatogr. A 1031 (2004) 35.
[38] H. Miwa, J. Chromatogr. A 881 (2000) 365.
[39] H. Miwa, Anal. Chim. Acta 465 (2002) 237.