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Journal of Chromatography A, 863 (1999) 147–155

JOURNAL OF CHROMATOGRAPHY A

www.elsevier.com/locate/chroma

Determination of polar pesticides with atmospheric pressure chemical ionisation mass spectrometry–mass spectrometry using methanol and/or acetonitrile for solid-phase desorption and gradient liquid chromatography

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Received 20 May 1999; received in revised form 6 August 1999; accepted 19 August 1999

Abstract

Thirty-seven polar pesticides, mainly triazines, phenylurea herbicides and phenoxy acids, were determined by LC–atmospheric pressure chemical ionisation MS–MS with methanol and acetonitrile as the organic modifiers. For most pesticides, detection limits were the same irrespective of the modifier. However, for the phenylurea herbicides, propachlor, carbetamide, triadimefon, triadimenol, triethylcitrate, benzothiazole and metazachlor, the results were much poorer in the presence of acetonitrile; in several cases, no meaningful results were obtained at all. When carrying out trace enrichment of 100 ml water samples on a 10×2 mm I.D. solid-phase extraction precolumn containing a polymeric sorbent, rapid desorption with a small volume of pure organic solvent and the introduction of a T-piece in between the solid-phase extraction precolumn and the analytical column was necessary. Aliquots of 300 μl of acetonitrile were optimal for the complete desorption of all analytes from the sorbent. With methanol as the modifier and when using an identification criterion of three ions, the detection limits for most analytes, in the full-scan mode, were 10–100 ng/l. The linearity of the procedure, which was tested at the 0.1 and 1 μg/l levels, was satisfactory in the positive, but not in the negative ionisation mode. The procedures were used to analyse surface water samples.

Keywords: Pesticides; Triazines; Phenylurea herbicides; Phenoxy acids

1. Introduction

The liquid chromatographic (LC) analysis of pesticides in environmental matrices is often performed with acetonitrile instead of methanol as the organic modifier, mainly because of its higher elution strength for late-eluting analytes and hydrophobic interferences. In addition, acetonitrile is favoured over methanol when diode array UV detection is used, as for example in the SAMOS (system for automated monitoring of organic micropollutants in surfacewater) approach [1,2] because of its lower UV cut-off.

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0021-9673/99/$ – see front matter
PII: S0021-9673(99)00898-5

In our laboratory most LC–UV, and also LC–MS, analyses are performed with acetonitrile as the modifier. However, when methanol is used instead of acetonitrile, the detectability of many analytes in LC–atmospheric pressure chemical ionisation (APCI)–MS is much better [3]. However, in on-line solid-phase extraction (SPE)–LC procedures it is not easy to maintain the system performance when acetonitrile is replaced by methanol. Especially with a polymeric sorbent in the precolumn and a C_{18}-bonded silica in the analytical column, which is an often used combination for the analysis of pesticides, the use of methanol can cause problems because, contrary to acetonitrile, it cannot elute the microcontaminants efficiently from the highly retaining polymeric phase without creating substantial extra peak broadening on the analytical column.

In this paper the detectability of 37 pesticides (see Table 1) in LC–APCI–MS–MS (positive, and negative ionisation modes) was studied with acetonitrile and methanol as the modifiers. The efficient desorption of the pesticides from the polymeric precolumn to the alkyl-bonded analytical column was found to require the use of a small volume of pure organic solvent. The optimised procedure was used to analyse several real-life samples.

2. Experimental

2.1. Apparatus

The liquid chromatograph was connected in series with a UV detector and a mass spectrometer. A PROSPEKT (Spark Holland, Emmen, The Netherlands) sample handling module was used to concentrate the analytes from the water samples and a CM4000 gradient pump (Milton Roy, Riviera Beach, FL, USA) to deliver the eluents. Separation was performed on a 250×4.6 mm I.D. 5 μm Supelcosil LC-18-DB column (Supelco, Bellefonte, PA, USA). It was protected by a guard column (Supelguard LC-18-DB, Supelco, USA). An LKB (Bromma, Sweden) Model 2150 pump was used to deliver the acetonitile desorption solvent at a flow-rate of 0.1 ml/min.

A triple stage quadrupole mass spectrometer (TSQ-700, Finnigan MAT, San José, CA, USA) equipped with an APCI interface and a DEC 5000 data system computer was used. Typical instrument parameters used as default were: sheath gas 420 kPa (positive mode) or 260 kPa (negative mode); auxilliary gas, off; vaporizer temperature, 375°C; capillary temperature, 180°C; scan time, 0.5–1 s. The conversion dynode was set at −20 kV (positive mode) or +20 kV (negative mode), the electron multiplier at 1.9 kV and the electrometer amplifier gain at 10^{-7} A/V. Argon (quality 5.0, Hoekloos, Schiedam, The Netherlands) was used as the collision gas at 0.3–0.4 Pa. The RF-only (radio frequency) daughter scan mode was used at two cut-off masses: m/z 70 at a collision offset (COFF) of −23 V (positive mode) or 23 V (negative mode), and m/z 71 at a COFF of −7 V (positive mode) or 8 V (negative mode). Scans at high and low COFF (−23 V, 23 V or −7 V or 8 V, respectively) were alternated, and each scan was followed by a scan over the ranges of m/z 45–320 (positive mode) and m/z 30–400 (negative mode), with a scan time of 1 s. The two cut-off masses m/z 70 and m/z 71 are used to filter the high and low COFF signals. The MS–MS correction factor (MSMSC) was set to zero. Details of this procedure are reported in Refs. [4,5].

2.2. Reagents

Acetonitrile, methanol, water, glacial acetic acid were of analytically or HPLC-grade quality and were obtained from J.T. Baker (Deventer, The Netherlands). All analytes were from Riedel-de Haën (Hannover, Germany) or Promochem (Wesel, Germany).

Stock solutions of [$^2H_5$]ethylamineatrazine (atrazine-d_5) and 2,4-dichlorophenoxy acetic acid (2,4-D ring d_3, 2,4-D-d_3) (Cambridge Isotope Laboratories, Andover, MA, USA) were prepared by dissolving 5 mg in 100 ml (atrazine-d_5) or 50 ml (2,4-D-d_3) of methanol. These solutions were diluted to 0.5 mg/l (atrazine-d_5) or 1 mg/l (2,4-D-d_3) in methanol.

Stock solutions of the analytes were prepared by dissolving 25 mg of each analyte in 50 ml methanol

Table 1
Repeatability of quantitation ions (1 μg/l, $N=7$) at low and high COFF (first/second result, respectively)

Positive mode			Negative mode		
Analyte	Quantitation		Analyte	Quantitation	
	Ion	RSD (%)		Ion	RSD (%)
Desethylatrazine	188	5	Chloridazon	220	8
	146	2		220	5
Benzothiazole	136	3	Bromacil	259	6
	136	6		259	6
Metribuzin	215	2	Fluroxypyr	253	7
	187	6		253	8
Lenacil	235	3	Bentazon	239	4
	153	5		197	3
Metabenzthiazuron	222	3	2,4-D-d_3	222	0
	165	4		164	0
Chlortoluron	213	1	2,4-D	219	5
	72	5		161	4
Atrazine-d_5	221	0	MCPA[a]	199	7
	179	0		141	4
DEET	192	4	DNOC	197	7
	119	2		180	5
Diuron	233	3	2,4-DP[a]	233	3
	72	5		161	4
Triadimenol	296	3	MCPP[a]	213	8
	70	3		141	5
Triadimefon	294	4	2,4,5-T[a]	253	5
	197	3		195	3
Desisopropylatrazine	174	5	Warfarin	307	5
	96	14		250	7
Carbetamide	237	5	2,4-DB	247	7
	120	6		161	4
Simazine	202	3	MCPB	227	6
	124	6		141	7
Triethylcitrate	277	4	2,4,5-TP	267	5
	157	5		195	6
Propazine	230	2	Dinoseb	239	8
	146	5		194	6
Atrazine	216	2	Dinoterb	239	10
	174	4		239	8
Isoproturon	207	3	Pentachlorophenol	265	8
	72	6		265	5
Monolinuron	215	5			
	126	8			
Propachlor	212	2			
	170	6			
Metazachlor	278	2			
	134	6			

[a] See Table 2.

or methanol–water (50:50, v/v). Stock solutions were kept at −20°C. From the stock solutions, mixtures of 5 mg/l (analytes and 2,4-D-d_3) and 2.5 mg/l atrazine-d_5 were prepared and diluted with methanol. These solutions were kept at +4°C and used to prepare standard solutions.

2.3. Samples

The samples in this study were blanks (tapwater), mixed standards (1 μg analyte/l) in tapwater, control samples (tapwater spiked with a mixture of analytes at 0.16 μg analyte/l and spiked surface water (Rhine and Meuse riverwater spiked with a mixture at 1 μg analyte/l).

To every 150 ml (surface) water sample were added 150 μl of atrazine-d_5 (0.5 mg/l) in the positive mode and 150 μl 2,4-D-d_3 (1 mg/l) and 0.5 ml glacial acetic acid for analyses in the negative mode as the internal standard. 100 ml of the sample were concentrated by the PROSPEKT system at a flow-rate of 4 ml/min.

Precolumns (10×2 mm I.D.) packed with polymer PLRP-S (Polymer Laboratories, Church Stretton, UK) were conditioned with 2 ml of methanol followed by 2 ml of water. After pre-concentration, the analytes were on-line desorbed to the analytical column. With the acetonitrile gradient, the LC eluent was directed via the precolumn to desorb the analytes. With the methanol gradient, the LC eluent was on-line mixed with the acetonitrile desorption flow in the T-piece. The flow-rate of the gradient was 0.9 ml/min and for the desorption solvent it was 0.1 ml/min.

The LC eluent consisted of (A) methanol (or acetonitrile)–water (5:95) containing 3 ml glacial acetic acid/l; and (B) methanol (or acetonitrile) containing 3 ml glacial acetic acid/l. The gradient run was 5 min isocratic at 100% A, and then linearly to 100% B in 50 min. During the first 3 min of the gradient run, the desorption pump was connected on-line to the T-piece (as shown in Fig. 1).

3. Results and discussion

In a previous paper [4] the development of an on-line SPE–LC–MS–MS method was reported using the Rf-only daughter scan mode with positive ionisation and a thermospray interface. The method was validated for 40 analytes, using acetonitrile as the organic modifier. In the full-scan mode the detection limits ranged from 0.03 to 1 μg/l. Somewhat surprisingly the triazines had detection limits of 0.03–0.08 μg/l, while the phenylurea herbicides had detection limits of 0.2–1 μg/l. With an APCI interface, and using the same system, the results

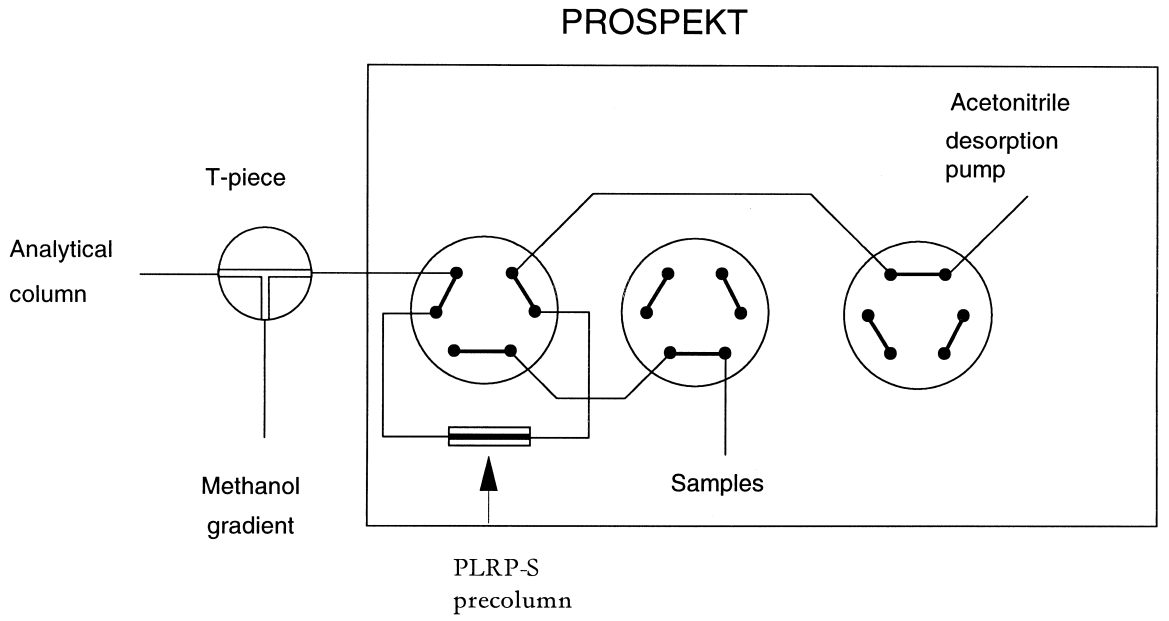

Fig. 1. Set-up for the procedure using acetonitrile desorption and a methanol–water gradient.

were identical. Therefore, confirmation of phenylurea herbicides at the target level of 0.1 μg/l was not possible. However, a preliminary study [3] showed much better detectability of the phenylureas in the positive mode with methanol instead of acetonitrile as the organic modifier. Even the use of a relatively small percentage of acetonitrile in the methanol solvent significantly reduced the analyte detectability compared with pure methanol. In the negative mode the test analytes showed a comparable detectability with both modifiers. This phenomenon also has been recently reported by Temesi and Law [7] and may be due to the lower proton affinity of methanol (PA= 761 kJ/mol) compared with acetonitrile (PA=787 kJ/mol) and the ion formation within the LC–MS interface, i.e., the liquid-to-gas phase transition process, which for phenylurea herbicides is probably better with methanol than with acetonitrile [6].

To determine the influence of both modifiers on detection limits in LC–MS, 37 analytes, mainly the same as used in one of our earlier studies [4], were studied in the positive and negative modes.

3.1. Precolumn desorption

A methanol gradient does not effectively desorb analytes from a polymeric precolumn onto an alkyl-bonded silica analytical column. Therefore, rapid desorption of the analytes from the polymeric precolumn with a small volume of pure methanol, i.e., the same solvent as the modifier used for gradient elution, was studied. In this set-up, a T-piece has to be installed after the precolumn (see Fig. 1), and the LC eluent is not used to desorb the precolumn but is mixed with the pure methanol in the T-piece. The flow-rate of the desorption solvent was set at 0.1 ml/min and the gradient flow at 0.9 ml/min. In order to obtain efficient mixing at the prevalent high flow-rate differences, co-axial mixing, as shown in Fig. 1, was found to be required. Desorption with 200–500 μl, i.e., during 2–5 min, did not affect re-concentration on the top of the analytical column or separation of the first eluting peaks, although the starting concentration of methanol increased from 5 to 14.5% methanol, due to the methanol desorption contribution. One should note that the first 5 min of the gradient were isocratic.

The repeatability of the methanol desorption showed excellent relative standard deviations (RSDs) for the two base peaks of most analytes recorded at both low and high COFF. Typical values were 1–6% RSD ($N=7$) for data recorded in the positive and 5–10% for data recorded in the negative mode. However, very poor repeatability, with RSDs of 25–40%, was found for the phenolic analytes dinitro ortho cresol (DNOC), dinoseb, dinoterb and pentachlorophenol. Probably, the binding energy of the charge-transfer complexation of the polymeric sorbent and the phenolic analytes is rather strong, and adversely affects their rapid and reproducible release. Desorption with 300 μl of a methanol–acetonitrile (50:50, v/v) mixture did not improve the results, but desorption with 300 μl pure acetonitrile gave satisfactory results for all analytes, i.e., all analytes were effectively reconcentrated on the top of the analytical column, and the first eluting peaks were well separated and RSDs <10%. Desorption with 300 μl of acetonitrile was, therefore, used in all further experiments.

3.2. Mass selection and validation

Generally, confirmation of the presence of an analyte in a sample is performed by comparing the mass spectrum of the sample and a standard acquired in the same series. If this procedure has to be automated, one should consider that the (varying) percentages of acetonitrile and/or methanol may well have an effect on the ionisation and fragmentation of the analyte in LC–APCI–MS(–MS).

As a first step, we determined the repeatability of the acquisition of mass spectral data for the acetonitrile-as-modifier situation, using data files recorded over a three-month period ($N=7–10$). To this end, ions with a relative abundance >5% compared to the base peak (ion abundance ratio) were selected. With all but four analytes, metabenzthiazuron, 4-(2,4-dichlorophenoxy)butyric acid (2,4-DB), 4-chloro-2-methyl-phenoxybutyric acid (MCPB) and 2-(2,4,5-trichlorophenoxy)propionic acid (2,4,5-TP), the protonated or deprotonated molecular ion was the base peak. For most test analytes, the repeatabilities of the ion abundance ratios were good (RSDs=2–15%). However, ten analytes could not be detected at the 1 μg/l spiking level used or showed poor RSDs (30–100%). These were diuron, isoproturon, mono-

linuron, benzothiazole, propachlor, metazachlor, carbetamide, triadimefon, triadimenol and triethylcitrate.

Next, the repeatability of the selected ion abundance ratios was determined with methanol as the modifier and acetonitrile as the desorption solvent. The repeatability was excellent for almost all ion abundance ratios (RSDs<10%), and for most analytes more than five ions could be selected with RSD<20%, except for benzothiazole (four ions), chlortoluron (four ions), chloridazon (four ions) and lenacil (two ions). It should be emphasized that good results were also obtained for the ten test compounds that could not be detected at the 1 μg/l level with acetonitrile as the modifier (cf. before) and for the ion abundance ratios that gave high RSDs with that solvent.

The ion abundance ratios observed for the analytes in spiked surface water were essentially the same as those recorded for the standard solutions, in both the positive and negative modes. This illustrates the high selectivity of the whole procedure.

Because the procedure will be used for semi-quantitative purposes, a limited validation study was performed. First, the repeatability was tested using the quantitation data of the base peaks observed at both the low and high COFF voltages. The data of Table 1 show that the RSDs are 2–10% ($N=7$), except for desisopropylatrazine. The results for positive and negative modes were adjusted for the internal standards, atrazine-d_5 and 2,4-D-d_3, respectively. The RSDs of the high COFF values for most analytes in the positive mode were slightly higher than those of the low COFF values, whereas the opposite was true for the RSDs in the negative mode. We have no explanation for this phenomenon.

Next, detection limits were calculated for all the ions present in the mass spectra that were used in the above procedure. For this purpose the signal intensities of 1 μg/l solutions of all analytes were

Table 2
Detection limits (LOD) for the analyte ions that produce the third best result using methanol (MeOH) or acetonitrile (ACN) as the modifier[a]

Positive mode			Negative mode		
Analyte	LOD (ng/l)		Analyte	LOD (ng/l)	
	MeOH	ACN		MeOH	ACN
Atrazine	10	10	MCPA[b]	20	10
Atrazine-d_5	10	10	MCPP[b]	20	10
Desethylatrazine	20	10	MCPB	80	70
Desisopropylatrazine	200	100	2,4-D	30	20
Propazine	20	10	2,4-D-d_3	20	10
Simazine	20	10	2,4-DP[b]	20	10
Metribuzin	30	30	2,4-DB	70	50
Diuron	10	—	2,4,5-T[b]	30	20
Chlortoluron	20	90	2,4,5-TP	20	10
Isoproturon	30	—	Chloridazon	150	250
Monolinuron	30	—	Bromacil	10	10
DEET	20	20	Fluroxypyr	60	20
Benzothiazole	80	1500	Bentazon	30	20
Propachlor	10	—	DNOC	40	30
Metazachlor	10	—	Warfarin	20	10
Carbetamide	10	700	Dinoseb	20	10
Triadimefon	20	130	Dinoterb	20	20
Triadimenol	10	340	Pentachlorophenol	20	20
Triethylcitrate	50	1000			
Metabenzthiazuron	10	10			

[a] MeOH=Methanol as modifier, acetonitrile as desorption solvent; ACN=acetonitrile used in on-line gradient desorption mode.
[b] MCPA=4-Chloro-2-methyl-phenoxyacetic acid; MCPP=4-chloro-2-methyl-phenoxypropionic acid; 2,4-DP=4-(2,4-dichlorophenoxy)propionic acid; 2,4,5-T=2-(2,4,5-trichlorophenoxy)acetic acid.

Table 3
Comparison of SPE–LC–DAD and SPE–LC–MS–MS data for surface water samples suspected to contain diuron, atrazine and simazine

Sample	Concentration (μg/l)								
	Diuron			Atrazine			Simazine		
	DAD	MS (A)[a]	MS (M)[b]	DAD	MS (A)	MS (M)	DAD	MS (A)	MS (M)
013368	0.32	–[c]	0.30	0.24	0.26	0.23	0.04	0.04	0.04
014517	0.56	–	0.60	0.21	0.22	0.18	0.07	0.09	0.08
013384	0.29	–	0.35	0.05	0.05	0.05	0.16[e]	0.03	0.04
013915	0.94	–	0.14	0.39[d]	0.10	0.07	0.16[d]	0.04	0.03
014177	1.16	0.72	1.20	0.45	0.46	0.38	0.18	0.19	0.14

[a] MS (A)=On-line acetonitrile desorption and acetonitrile modifier.
[b] MS (M)=Acetonitrile (300 μl) desorption and methanol modifier.
[c] Below detection limit.
[d] Spectrum not correct.
[e] Spectrum correct.

determined, while the background noise in the positive mode was determined for some 20 ions and in the the negative mode for some ten ions. The mean background noise in the positive mode was found to be twice as high as the mean background noise in the negative mode. Three times the background noise was used as a criterion to calculate the detection limits of the test analytes. One criterion that is used rather widely in the Netherlands for LC–MS, if used for confirmation purposes, is that while the retention time of the analyte of interest must be equal to that of the analyte in the external standard solution to within 0.2%, at least three diagnostic ions must be determined while all ion abundance ratios should agree to within 50% of the established value.

Table 2 summarizes the results observed with both methanol and acetonitrile as the modifier. For obvious reasons, the data that are presented are those found for the third most abundant ion. Not surprisingly when discussing the mass selection, with acetonitrile as the modifier, the ten ions cited previously and chloridazon had detection limits of over 100 ng/l. The results obtained with methanol are more promising: all but two analytes (desisopropylatrazine and chloridazon) have detection limits of 10–80 ng/l. In other words, for quite a number of test compounds, the analyte detectability improved 5–50-fold compared with the 'acetonitrile-only' situation. Moreover, all test analytes (excepting lenacil: two ions only) can be determined.

As a final test, standard solutions containing 100 ng/l of all compounds, except desisopropylatrazine and chloridazon (cf. detection limits in Table 2), were analysed using a one-point calibration at 1 μg/l (through the origin) and two quantitation ions were studied for each compound. In the positive mode and with methanol as modifier, identification was of course no problem, but linearity was also rather satisfactory with 20% or less ($N=3$) deviation from the true value, i.e., the spiked 0.1 μg/l level, in all but three cases (triadimefon and triethylcitrate, both quantitation ions; benzothiazole, one quantitation ion). Compared with this promising result, the nega-

Table 4
Additional analytes found by SPE–LC–MS–MS in surface water samples of Table 3

Sample	Analyte	Concentration (μg/l)	
		Acetonitrile	Methanol
013368	Benzothiazole	–	0.08
	DEET	0.03	0.04
014177	Desethylatrazine	0.07	0.08
	Lenacil	–	0.14
	DEET	0.05	0.05
013915	Desethylatrazine	0.03	0.03
	DEET	0.05	0.05
014517	Desethylatrazine	0.06	0.06
	DEET	0.04	0.04
013384	Desethylatrazine	0.08	0.08
	Lenacil	–	0.06
	DEET	0.03	0.04

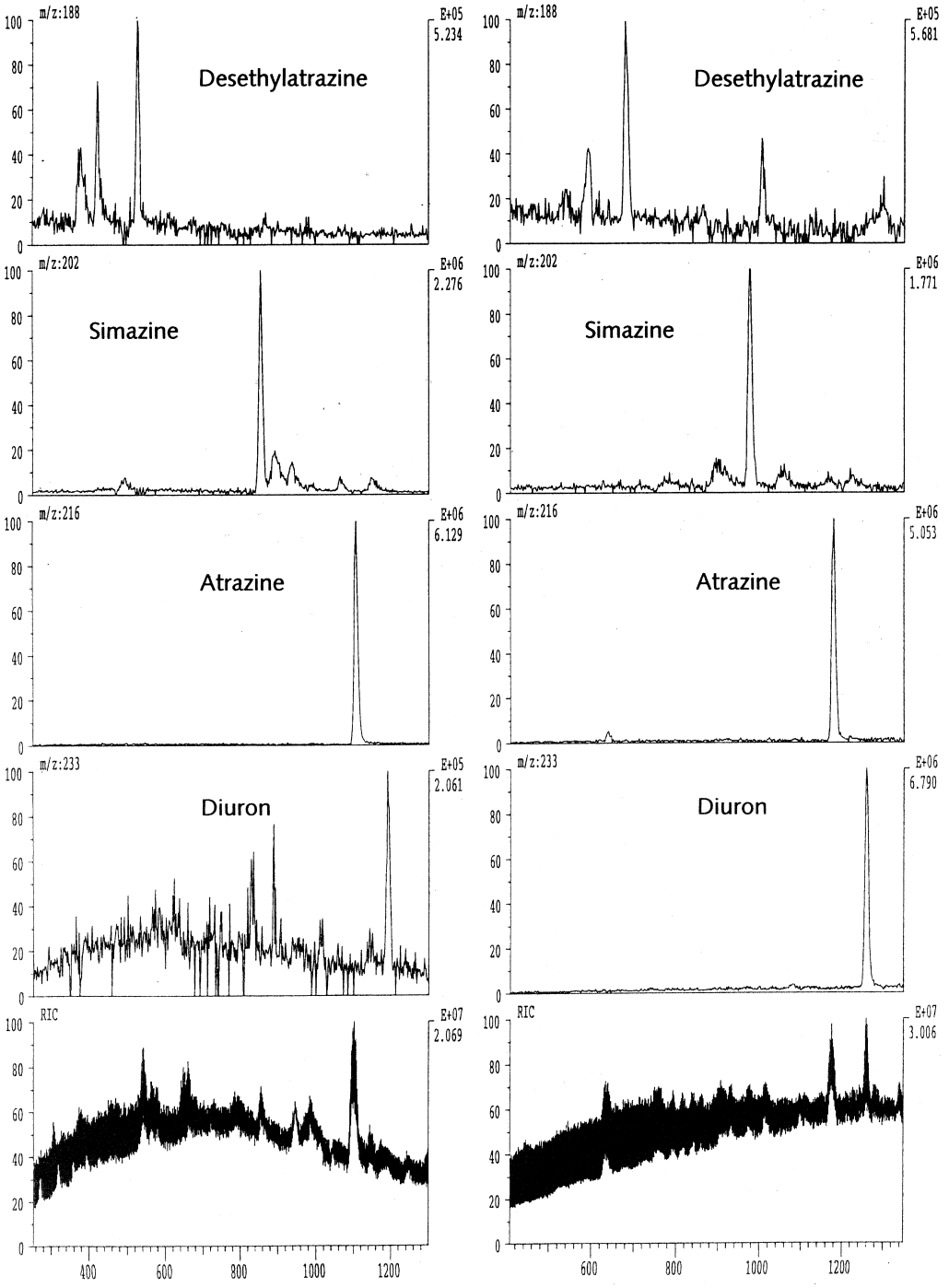

Fig. 2. Comparison of mass chromatograms of analytes found by SPE–LC–MS–MS in sample 014177 (see Tables 3 and 4) with acetonitrile (left) or methanol (right) as the modifier.

tive mode data were somewhat disappointing because all analytes showed deviations over 20%, which indicates distinct non-linearity at the lower concentration levels.

3.3. Application

Five surface water samples were analysed using both the acetonitrile-as-modifier and the methanol-as-modifier approaches. The samples were selected because over 0.1 μg/l of diuron had been found in all of them by means of SPE–LC–diode array detection (DAD). In addition, traces of atrazine and simazine had been detected.

Table 3 clearly shows that the LC–MS–MS results for diuron, with methanol-as-modifier, are in good agreement with the LC–DAD data except for sample 013915 (which presumably reflects the higher selectivity of MS detection). Note that the results are the mean value of the low and high COFF result of the quantitation ions (see Table 1 and Section 2). However, as was to be expected, the data obtained with acetonitrile-as-modifier are extremely poor. The results for atrazine and simazine were essentially the same irrespective of the modifier, also according to our expectations. The higher results occasionally found with DAD detection can again be attributed to the lower selectivity of that technique.

Interestingly, with both types of SPE–LC–MS–MS procedures, desethylatrazine, benzothiazole, lenacil (two ions) and DEET (*N*,*N*-diethyl-3-methylbenzamide) were found in all of the samples (Table 4), at very low levels which certainly would escape detection in SPE–LC–DAD. Thus, generally speaking, excellent agreement of the two sets of MS data is gratifying. Some analytes of one of the samples in Tables 3 and 4 detected with the acetonitrile-as-modifier and the methanol-as-modifier approaches are shown in Fig. 2

4. Conclusions

The efficient trace-level determination of polar analytes requires the use of polymer sorbents during SPE and their subsequent desorption with acetonitrile. However, for quite a number of analytes, MS detection is much better if a methanol–water rather than an acetonitrile–water gradient is used. In the present SPE–LC–APCI–MS–MS study of 37 polar pesticides, a 5–50-fold improved detectability was observed for the combined acetonitrile desorption–methanol gradient procedure compared with an 'acetonitrile-only' approach.

With 100 ml samples, detection limits (when using three diagnostic ions as a criterion), were below 100 ng/l in all but two instances. In addition, the repeatability of the ion abundance ratios in the full scan-mode was rather good (RSDs$<$10%, $N=7$). Quantitation was fully satisfactory in the positive mode, but less so in the negative mode, which indicates non-linearity at low analyte concentrations, i.e., 0.1 μg/l, in the latter case. The practicality of the procedure was demonstrated by analysing a series of surface water samples.

References

[1] U.A.Th. Brinkman, J. Slobodnik, J.J. Vreuls, Trends Anal. Chem. 13 (1994) 373–381.
[2] E. Papadopoulou, J. Patsias, J. Chromatogr. A 726 (1996) 99–113.
[3] J. Tiesnitsch, Technical Report, No. 98.081X, RIZA, Lelystad, The Netherlands, 1998.
[4] P.G.M. Kienhuis, R.B. Geerdink, A. Sijpersma, Anal. Meth. Instrum. 2 (1995) 236–246.
[5] P.G.M. Kienhuis, R.B. Geerdink, Trends Anal. Chem., in press.
[6] B.L.M. van Baar, in: D. Barcelo (Ed.), Applications of LC–MS in Environmental Chemistry, Elsevier, Amsterdam, 1996.
[7] D. Temesi, B. Law, LC·GC Int. March 1999, p. 175, 176, 179, 180.