

Trimethyltin chloride determination by hydride generation — gas phase molecular absorption spectrometry

A sequential application of experimental designs

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Abstract

In this paper, a sequential experimental design is applied to optimize the determination of trimethyltin chloride (TMT) by hydride generation-gas phase molecular absorption spectrometry. The TMT is converted into gaseous trimethyltin hydride by adding a sodium tetrahydroborate (III) solution. The hydride generated is collected in a liquid nitrogen cryogenic trap. This is revolatilized, driven to the quartz flow cell and measured with gas phase molecular absorption spectrometry with diode array detection. A Plackett-Burman design is used to study the parameters affecting the production, collection and measurement of the hydrides. The optimization of these parameters is achieved using a central composite design. PLS, MLR and univariate calibration are applied to the spectra obtained. The detection and quantification limits are 1.5 and 4.6 ng ml⁻¹, respectively, and the relative standard deviation ($n = 10$) at 15 ng ml⁻¹ was 5.5%. An interference study is presented. ©2000 Elsevier Science B.V. All rights reserved.

Keywords: Hydride generation; Gas phase molecular absorption spectrometry; Trimethyltin chloride; Experimental design

1. Introduction

Organotin compounds are mainly used in agriculture, as biocides, antifouling paints, catalysts and PVC stabilizers [1]. Organometallic species are more toxic than their inorganic salts; the toxic potential of organotin compounds increases with the degree of alkylation and decreases with the increasing chain length of the substituents [2]. The lipidic and hydrophobic properties of these compounds facilitate their accumulation in marine organisms. The environmental methylation

of tin by the action of microorganisms contributes to the presence of methyltins in the environment [3].

Several techniques have been developed for the determination of organotin compounds. The current methods usually involve a separation technique such as high performance liquid chromatography (HPLC) [4,5] or gas chromatography (GC) [6,7] coupled to a tin detection method such as atomic absorption spectrometry (AAS) [8,9], atomic emission spectrometry (AES) [10], mass spectrometry (MS) [4,11], flame photometric detection (FPD) [6] or microwave-induced plasma atomic emission spectrometry (MIP-AES) [7]. Hydride generation with sodium tetrahydroborate (III) [12] or sodium tetraethyl borate [13] and alkylation by Grignard reagents [14]

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are used to turn the ionic organotin compounds into stable and volatile species.

Gas phase molecular absorption spectrometry (GP-MAS), introduced by Syty in 1973 [15], is based on the measurement of the absorption of molecular species in the gas phase, generated at room temperature. The introduction of diode-array systems as the detector allows the investigator to obtain the volatile spectrum generated over a wide wavelength range. This allows the application of multivariate calibration methods or the study of the changes produced in the structure of the molecule generated [16]. Several applications of GPMAS have been developed for the determination of sulphur compounds [17], nitrogenated compounds [18], halides [19], covalent hydride volatiles [20] and more recently, arsenic and tin organo-metals [21].

In this paper, the optimization of the trimethyltin chloride determination by HG-GPMAS is presented, achieved by the sequential application of the experimental design. In this strategy each group of experiments is based on the previous group. The experimental design allows a large number of factors to be screened simultaneously to determine which of them has a significant effect on the analytical signal, and the factors can be optimized to give the best possible results with a relatively low number of experiments.

The optimization study was performed using a statistical model of the Plackett-Burmann design [22] to evaluate the significance of each factor. A statistical model of central composite design [23] was used to study the influence of the interaction between variables and the optimum conditions. Multivariate calibration [24] was studied in artificial aqueous samples. A study of interferences was performed for the determination of TMT by this technique.

2. Experimental

2.1. Apparatus

All measurements were made with a Hewlett-Packard (HP) model 8451 diode-array Spectrophotometer equipped with an HP 98155A keyboard, an HP 9121 disk drive for bulk data storage, an HP Thinkjet printer and HP 7475A graphics plotter. A Hellma 174QS 1 cm quartz flow cell was used, together with a peristaltic pump (Cole Parmer Instrument 7554-20),

an Agitamic Heidolph MR 3003 with temperature control via a platinum probe, a Mettler PJ 3600 Delta Range, a Dewar (21) Dilvac and a Schott ISO 250/1000 ml generator flask. The generation scheme and procedure system are already described in previous papers [21]. The statistical designs were created and analyzed with the Statistica 5.0 software package [25]. Parvus 3.0 [26] was used for multicomponent analysis.

2.2. Reagents

Stock solutions of $1000 \mu\text{g ml}^{-1}$ TMT (as Sn) were made by dissolving the corresponding chloride, $\text{C}_3\text{H}_9\text{SnCl}$ from Aldrich (Sigma-Aldrich, USA), in water. Working standards were prepared by serial dilution of the stock solutions with water, immediately before use. Aqueous solutions of sodium tetrahydroborate (III), NaBH_4 from Carlo Erba (Milan, Italy) were prepared immediately prior to use. The hydrochloric acid (37%, 1.186 g ml^{-1}) and acetic acid (80% m/m, 1.070 g ml^{-1}) were RPE grade from Carlo Erba. Working solutions were prepared daily by diluting the concentrated solutions with water. All water used was doubled-distilled. The calcium chloride was dried granular RE grade from Carlo-Erba. The carrier gases were nitrogen and hydrogen (C-50 Carbueros Metalicos).

2.3. Experimental design

The absorbance response of trimethyltin hydride by HG-GPMAS, whose absorbance spectrum is shown in Fig. 1, is considered as a function of the several factors selected on the basis of previous results [20] and in function of the bibliography found [12,27]: reductor flow, reductor concentration, acid type, gas flow rate during hydride generation, revolatilizing temperature, carried time, carrier gas type, time at room temperature, revolatilizing time, sample volume and pH. In order to obtain the best conditions for the TMT determination, an optimization based on the experimental design was used.

The first stage of the optimization consisted in a study of the variables which affect the system. In order to identify the significant factors, a Plackett-Burman design involving 12 runs was used. This experimental

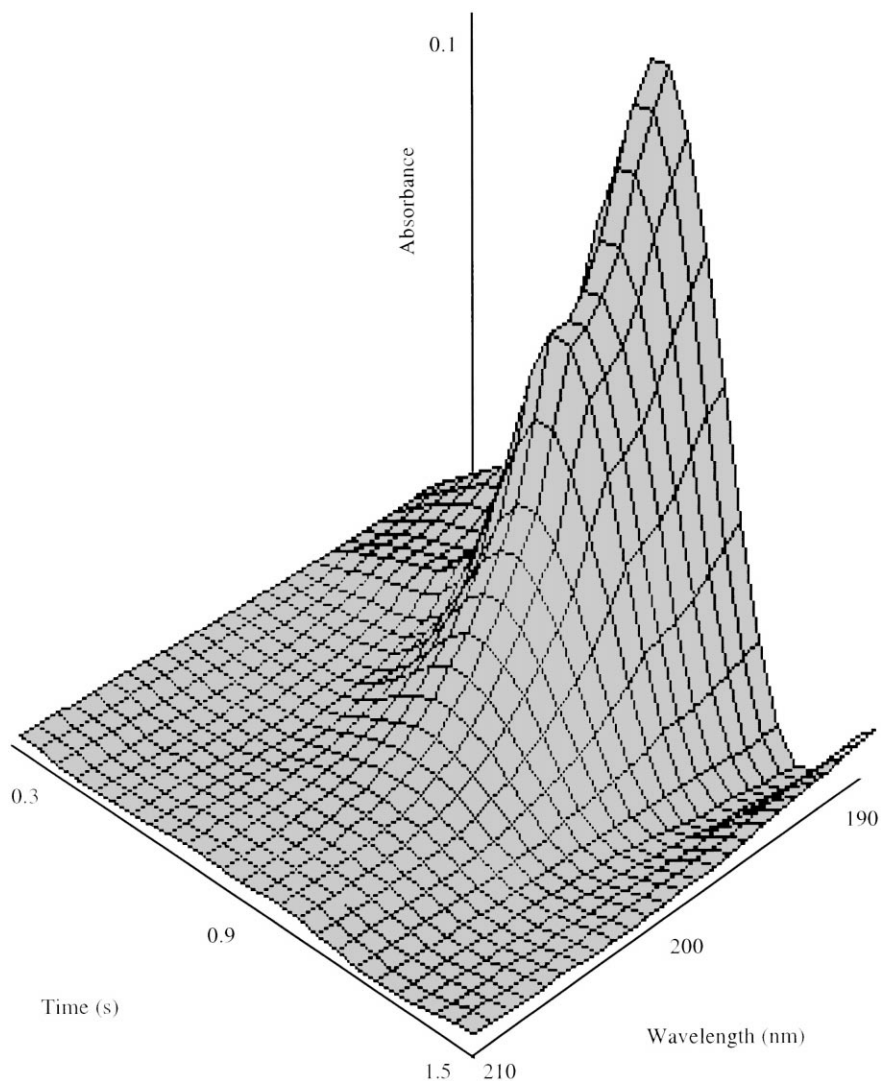


Fig. 1. Three-dimensional absorption molecular spectrum of trimethyltin hydride.

design allows a large number of factors to be screened simultaneously to determine which of them has a significant effect on the response and to fix the values of the non-continuous variables (sample volume, acid type and carrier gas type). This design supposes that only the principal effects influence the absorbance signal; the interactions among the variables are not considered. The levels of control are listed in Table 1.

The second step of the optimization was the study of the influence of the interaction between variables

and the obtaining of the optimum conditions. To do this, a five level central composite rotatable design ($\alpha = 1.6861$) was performed. In this design, each of the variables had five coded levels $-\alpha$, -1 , 0 , $+1$ and $+\alpha$ and required a total of 14 experimental runs and three central points; these were carried out with three replicates per run. This model allows the direct evaluation of the variables considered, and also the first-order interactions and quadratic terms. Table 3 shows the design matrix for the experimental design.

Table 1
Factors and levels used in the Plackett-Burman design

Factors	Levels	
	Low (-)	High (+)
A: Reductor flow (ml min ⁻¹)	2	10
B: Reductor concentration (%)	0.5	4.0
C: Sample volume (ml)	150	750
D: Acid type	Acetic acid	Hydrochloric acid
E: pH	1	4
F: Gas flow rate (ml min ⁻¹)	200	500
G: Carried time (min)	2.0	5.0
H: Carrier gas type	H ₂	N ₂
I: Time at room temperature (min)	1.5	3.0
J: Revolatilizing temperature (°C)	60	90
K: Revolatilizing time (min)	0.5	1.5

By using this design, it is possible to fit the experimental data into a polynomial mathematical model, an equation that relates the absorbance of the trimethyltin hydride measured at 192 nm to the significant factors obtained in the previous step. The equation on which this model is based is:

$$y = \beta_0 + \sum \beta_i x_i + \sum \beta_{ij} x_i x_j + \sum \beta_{ii} x_i^2 + \varepsilon \quad (1)$$

where y is the predicted response, β_{ii} is the adjusting coefficient and x_i, x_j are the factors studied.

The experiments were carried out with three replicates per run, to obtain a value for the experimental

error. Randomization was used in order to obtain a random distribution of unknown systematic errors.

3. Optimization of experimental parameters

Table 2 shows the Plackett-Burman design, the mean response obtained (absorbance of the trimethyltin hydride measured at 192 nm) and the main effects of the factors. The sample amount was 123 μ g trimethyltin chloride (as Sn).

An analysis of the results gave the Pareto chart shown in Fig. 2. The Pareto chart shows the ANOVA effect estimates and their significance (an effect that exceeds the critical t -value for $\alpha = 0.05$ may be considered significant). As can be seen, the significant effects were reductor concentration, sample volume, acid type, gas flow rate, carried time and carrier gas type. The sign of the main effects showed whether the response would be improved or decreased when a given factor went from the lower level to the higher level, and determined the new experimental domain to be explored to obtain response optimization.

The sample volume, acid type and carrier gas type were non-continuous variables. Sample volume and the carrier gas type showed negative signs and these were fixed as 150 ml, and hydrogen gas. However, the acid type showed a positive sign and was fixed as HCl. The reductor concentration, flow generation

Table 2
Experimental matrix and results for the Plackett-Burman design

Runs	Factors											Response (192 nm)
	A	B	C	D	E	F	G	H	I	J	K	
8	+	-	+	-	-	-	+	+	+	-	+	0.0619
12	+	+	-	+	-	-	-	+	+	+	-	0.1253
9	-	+	+	-	+	-	-	-	+	+	+	0.0637
6	+	-	+	+	-	+	-	-	-	+	+	0.4774
3	+	+	-	+	+	-	+	-	-	-	+	0.2557
11	+	+	+	-	+	+	-	+	-	-	-	0.6329
7	-	+	+	+	-	+	+	-	+	-	-	0.6268
4	-	-	+	+	+	-	+	+	-	+	-	0.0432
2	-	-	-	+	+	+	-	+	+	-	+	0.5217
5	+	-	-	-	+	+	+	-	+	+	-	0.0012
10	-	+	-	-	-	+	+	+	-	+	+	0.1272
1	-	-	-	-	-	-	-	-	-	-	-	0.1204
Effect	0.008	0.101	-0.231	0.126	-0.006	0.174	0.286	-0.138	-0.005	-0.004	-0.003	

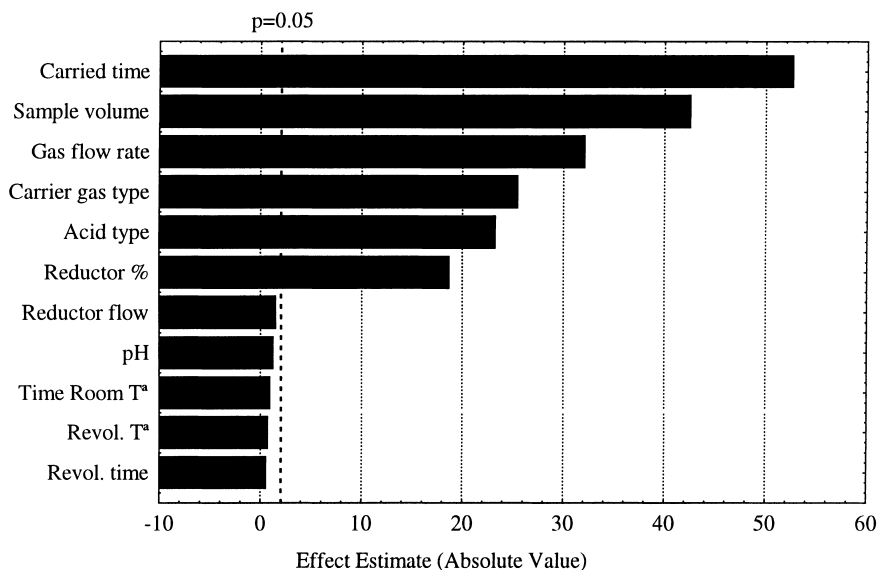


Fig. 2. Pareto chart for the standardized effects in the Plackett-Burman design. The dotted vertical line indicates the statistical significance bounds for the effects.

and carried time were significant and positive effects, so that the region of their higher level was studied further. The reductor flow, pH, time at room temperature, revolatilizing temperature and revolatilizing time were not significant effects and these were fixed at the values of 5 ml min^{-1} , 1, 1.5 min, 90°C and 30 s, respectively. The variables related to the revolatilization phase of the volatile species (time at room temperature, revolatilizing temperature and revolatilizing time) did not show significant effects on the absorbance signal. This reflects the high stability of the compound generated, trimethyltin hydride, in the gas phase.

Table 3 gives the design matrix for the five level central composite rotatable design and the mean response obtained. The sample amount was $59 \mu\text{g}$ trimethyltin chloride (as Sn).

After the estimation of the factor's main effects, their significance was computed by means of an ANOVA test. As the factors have a significant effect, the variance of the data set was larger than the variance of the residuals. This was confirmed by the Fischer variance ratio (F), the ratios of the respective mean square effect and the mean square error; the p values indicate when the main effect of each factor

is statistically significant ($p < 0.05$). The results from the ANOVA study are shown in Table 4. As can be seen, reductor concentration and carried time were significant effects. Also, the quadratic terms were significant. The lineal term of the gas flow rate was not significant in the interval studied, whereas the interaction between the gas flow rate and the carried time did have a significant effect. This fact would not have been observed if the optimization had been done variable by variable.

The coefficient of multiple determination (r^2) was 0.9505, indicating that the variables explained the data fairly well. The resulting equation of the mathematical model postulated, which was obtained by processing the design responses, is:

$$y = 1.25E - 02 + 1.50E - 02x_A - 7.61E - 03x_C - 1.35E - 03x_A^2 - 1.32E - 07x_B^2 - 2.17E - 03x_C^2 + 1.94E - 03x_Ax_C + 2.79E - 05x_Bx_C$$

If a mathematical relationship between the variables is known, response surface mapping is an effective method for locating the optimum and for the interpretation of the most influential interactions. Fig. 3 shows the response surfaces for the significant interactions.

Table 3
Mean response values obtained for TMT from a two-level central 2^3 + star rotatable composite experimental design

Runs	Normalized points			Variables			Response (192 nm)
	x	y	z	Reductor (% w/v)	Gas flow rate (ml min ⁻¹)	Carried time (min)	
4	-1	-1	-1	2.0	375	3.0	0.0708
8	-1	-1	+1	2.0	375	5.0	0.0526
12	-1	+1	-1	2.0	625	3.0	0.0569
13	-1	+1	+1	2.0	625	5.0	0.0670
2	+1	-1	-1	6.0	375	3.0	0.0229
15	+1	-1	+1	6.0	375	5.0	0.0346
14	+1	+1	-1	6.0	625	3.0	0.0166
11	+1	+1	+1	6.0	625	5.0	0.0278
9	-∞	0	0	0.6	500	4.0	0.0098
17	+∞	0	0	7.4	500	4.0	0.0624
10	0	-∞	0	4.0	290	4.0	0.0466
5	0	+∞	0	4.0	710	4.0	0.0445
16	0	0	-∞	4.0	500	2.3	0.0540
6	0	0	+∞	4.0	500	5.7	0.0365
1	0	0	0	4.0	500	4.0	0.0516
7	0	0	0	4.0	500	4.0	0.0526
3	0	0	0	4.0	500	4.0	0.0537

Fig. 3(a) shows the response surface function developed by the model for reductor concentration and carried time; it was observed that the maximum response was obtained for reductor concentrations between 5% and 7%, and carried times between 2 and 4 min, with maxima at 6% and 3 min, respectively. Fig. 3(b) shows the response surface function developed by the model for gas flow rate and carried time. The function showed an extensive maximum zone which covered

practically all the interval studied; this zone is situated above the line which joins the points at which both variables were at the high level with the points for which both were at the low level. Interpolating the results obtained for the previous interaction (carried time = 3 min) on this response surface, a value of 300 ml min⁻¹ was obtained for the gas flow rate.

It can be seen that the factors which significantly affect the determination of TMT by HG-GPMAS are

Table 4
ANOVA for the two-level central 2^3 + star rotatable composite design

Source of variation	Sum of squares	Degrees of freedom	Mean square	F-ratio	p-value
A: Reductor %	0.01201	1	0.01201	626.29	0.0000
(Reductor %) ²	0.00081	1	0.00081	42.22	0.0000
B: Gas flow rate	0.00002	1	0.00002	0.96	0.3332
(Gas flow rate) ²	0.00012	1	0.00012	6.13	0.0179
C: Carried time	0.00043	1	0.00043	22.31	0.0001
(Carried time) ²	0.00013	1	0.00013	6.82	0.0129
AB	0.00007	1	0.00007	3.67	0.0629
AC	0.00036	1	0.00036	18.91	0.0001
BC	0.00029	1	0.00029	15.22	0.0004
Error	0.00073	38	0.00002		
Total SS ^a	0.01472	47			

^aSum of squares.

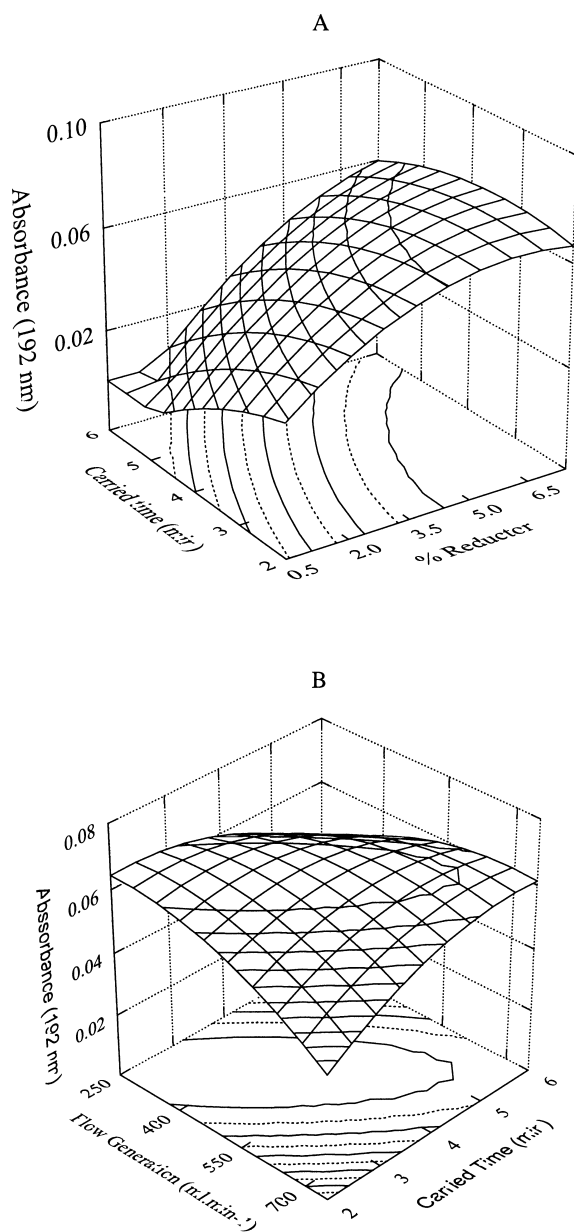


Fig. 3. Response surface and level curves obtained from the central composite design.

those which are related to the generation stage: reductor concentration, gas flow rate and carried time. The optimum generation of the hydride requires an energetic reduction (high reductor concentration) and medium values for gas flow rate and carried

time. These observations confirm the stability of trimethyltin hydride in the gas phase, as noted above.

Resulting from this study, the optimum working conditions to obtain the highest absorbance responses were selected. These are: reductor concentration 6%; carried time 3 min and flow generation 300 ml min⁻¹.

4. Analytical characteristics

Under the experimental conditions obtained in Section 2, calibration studies were made for the trimethyltin chloride. The regression equation was obtained by simple linear regression, multiple linear regression (MLR) and partial least square regression (PLSR). The absorbance was obtained on a wavelength interval from 190 to 210 nm. For the univariate regression, the wavelength selected was 192 nm; the MLR results were obtained after reducing by stepwise selection the total set of 20 predictors to an optimum subset (190 and 196 nm). For PLS, in order to select the number of factors, a cross-validation method, leaving out one sample at a time, was used.

Based on the IUPAC, the detection and quantification limits of the technique are 1.5 and 4.6 ng ml⁻¹; the values reported are the mean of five replicates. The linear response range above 500 ng ml⁻¹ was obtained. The values for precision (expressed as relative standard deviation) and accuracy were 5.5 and 98%, respectively. These were obtained by the replicate analysis of 20 standard solutions containing 10 times the corresponding detection limit and taken on different days.

To compare the different calibration models, the prediction error (PE) in the calibration was calculated. This is an indication of the error in the analysis

$$\text{PE (\%)} = \frac{\sqrt{\sum [y_i - \hat{y}_i]^2}}{\sum [\hat{y}_i]} \times 100$$

Table 5
Statistical parameters of the calibration

	Univariate	MLR	PLS
R ²	0.9990	0.9992	0.9988
PE (%)	3.32	2.55	2.70

Table 6
Results obtained in the resolution of the artificial samples of TMT

Added (ng ml ⁻¹)	Univariate		MLR		PLSR	
	Found ^a (ng ml ⁻¹)	Relative error ^b (%)	Found ^a (ng ml ⁻¹)	Relative error ^b (%)	Found ^a (ng ml ⁻¹)	Relative error ^b (%)
23.5	21.7	7.8	22.9	4.2	22.9	4.5
29	26.1	16.3	31.9	10.0	29.3	2.9
73.2	74.2	2.6	72.4	1.2	73.3	0.3
117	128.6	9.9	117.6	4.0	118.7	1.6
PE (%)	9.0		4.3		2.6	

^aMean of three independent determinations.

^bRelative error (%) = $(\sum |y_i - \hat{y}_i| / N) / (y_i) \times 100$.

and the square of the correlation coefficient (R^2), which is an indication of the quality of fit of all the data to a model:

$$R^2 = 1 - \frac{\sum_{i=1}^N (y_i - \hat{y}_i)^2}{\sum_{i=1}^N (y_i - \bar{y})^2}$$

where y_i is the standard concentration of analyte in sample i , \hat{y}_i is the estimated concentration of the analyte in sample i , \bar{y} represents the mean of standard concentrations and N is the total number of samples. In Table 5, the values obtained for the two statistical parameters are summarized. It can be seen that the best results were obtained using MLR, which gave the best correlation coefficient and the lowest prediction error.

The proposed calibration methods applied to the absorption spectra allowed the resolution of drinking water fortified with trimethyltin compound. In Table 6, the results obtained in the resolution of the synthetic samples of trimethyltin chloride are shown. The PE was calculated to compare the results obtained. It can be seen that the prediction error values were significantly lower when multivariate methods were used; within this group, the best results were obtained using PLS.

5. Interference study

Studies on the effect of different ions on the absorbance signal were carried out. Solutions containing trimethyltin chloride (TMT) and various concentrations of the potential interferents, one at a time, were subjected to the optimal HG-GPMAS conditions and the signals obtained by this method were compared

with the signals obtained without the interference. All experiments were performed in triplicate.

Table 7 presents the results from the studies of interferents for the species that produce variation in the absorbance signal (192 nm). This effect was studied for several [Int.] / [TMT] concentration ratios, both in ($\mu\text{g ml}^{-1}$) as values of % error, defined by the equation:

$$\% \text{ error} = \frac{\text{Abs}_{(\text{TMT} + \text{Interferent})} - \text{Abs}_{(\text{TMT})}}{\text{Abs}_{(\text{TMT})}} \times 100$$

Those elements which gave rise to a signal depression of less than one standard deviation of the expected response were deemed not to interfere.

We observed no interferences from up to 200 $\mu\text{g ml}^{-1}$ concentrations of the following elements: Na(I), K(I), Ca(II), Ba(II), Sr(II), Mg(II), Mn(II), Hg(II), Cd(II), Zn(II), V(V), Mo(VI), Al(III), Cr(III), NH_4^+ , Te(VI), Sn(IV), Bi(III), Pb(II), Ge(IV), MnO_4^- , Br^- , F^- and I^- . The normal amounts of reagents commonly used for digestion and acidification (chloride, sulphate and nitrate) did not show any effect either.

Depression of the signal was observed in the presence of Co(II), Ni(II), Cu(II), Ag(I), Fe(II), Fe(III) and Cr(VI).

Significant interference effects were seen from the sulphide ion and the elements which form volatile hydrides under the generation conditions. Sb(III), Sb(V), Sn(II), As(III), As(V), Se(IV) and the $\text{S}^{=}$ anion caused a quantitative increase in the absorbance signal which can be used for the simultaneous determination of mixtures of several elements by the obtaining of this completed spectrum and the application of multivariate calibration methods.

Table 7
Results from the interference study

Interferent	[Int.]/[TMT] ratio	Error (%)	Interferent	[Int.]/[TMT] ratio	Error (%)
Sb(III)	0.5	19	Co(II)	10	–
	1	54		50	–27
	1.5	94		100	–57
	2	116		200	–60
	2.5	162		400	–65
Sb(V)	1	18	Ni(II)	10	–48
	2	39		50	–61
	4	100		100	–71
	8	167		200	–76
As(III)	0.5	31	Cu(II)	10	–
	0.75	48		50	–16
	1.5	72		100	–45
	2	97		200	–48
	3	145		400	–49
As(V)	0.5	39	Ag(I)	5	–
	1	96		25	–6
	2.5	128		100	–19
	3.5	189		200	–45
Se(IV)	1	54	Fe(II)	300	–
	2	51		500	–9
	6.5	49		750	–32
	20	63		1000	–54
	50	96		2000	–93
Sn(II)	25	21	Fe(III)	100	–
	50	71		250	–9
	100	143		500	–12
	200	202		1000	–14
NO ₂	75	–	Cr(VI)	100	–
	200	–16		150	–15
	500	–47		200	–26
	1000	–90		500	–54
				1000	–82
S ⁼	1	72			
	2	91			
	4	119			
	6	181			

6. Conclusions

The optimization method, based on experimental design techniques, allows us to improve a determination of trimethyltin chloride by HG-GPMAS. With the Plackett-Burman design used in this work, the variables which affect the determination were identified: reductor concentration, carried time, flow generation,

volume sample, carrier gas and acid media. This design allows a reduction in the number of factors to be studied, from 11 to 3, and establishes a new region to study.

The proposed experimental design methodology allows the finding of the optimal conditions for the determination of trimethyltin chloride by HG-GPMAS, together with an identification of the interactions

between the factors studied, parameters which cannot be obtained when optimization of one factor at a time is used. It can be concluded that the factor which most influences the response is the reducing agent concentration.

The application of multivariate methods improves the results obtained when the classical univariate calibration is used. With the use of a diode-array molecular absorption spectrometer as the detector, the spectra of the generated volatiles can be obtained over a wide wavelength range; this use allows the application of a multivariate calibration system. Furthermore, the different effects that the various interferences present on the analytical signal can be observed. The completed spectra obtained for the interfering compounds allows, in some cases, the simultaneous determination of several compounds.

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