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Polymerization Inhibitors and Promoters for Unsaturated Polyester Resins; Use of Solid Phase MicroExtraction and Gas Chromatography Coupled to Mass Spectrometry for the Determination of 4-tert-Butyl Catechol and Acetylacetone

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ABSTRACT
This paper reports a contribution of three on-sample derivatization sampling techniques for acetylacetone, 4-*tert*-butyl catechol and its oxidated derivatives 4-*tert*-butyl-1,2-benzoquinone determination in unsaturated polyester resins. The use of *O*-(2,3,4,5,6, pentafluorobenzyl)-hydroxylamine, trimethyloxonium tetrafluoroborate and *O*-methyl-hydroxylamine is combined with automated head space/solid phase microextraction and gas chromatography/mass spectrometry analysis. For an innovative powerful meaning in high-throughput routine, the generality of the structurally informative mass spectrometry fragmentation patterns together with the chromatographic separation are also investigated. The detection limits for these polymerization inhibitors and promoters are less than 27 pg for one mg of unsaturated polyester resin. In this study a new autosampler platform is proposed by using the Multi Fiber Exchange device in a *xyz* robotic system. We promote these methods as the analytical reference in the polyester resin field. The introduction of dedicated, automated, and robotic systems allowed a friendly use of MS apparatus for high-throughput screening and it reduces the costs of monitoring campaigns.
Keywords: unsaturated polyester resins, 4-*tert*-butyl catechol, acetylacetone, solid phase microextraction, gas chromatography

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INTRODUCTION

Global unsaturated polyester resins (UPR) market is expected to witness growth owing to commercial use in fiberglass reinforced plastics which have extensive applications in the construction industry. Therefore, worldwide production is expected to increase by more than 30% by 2020 (7,000 kilo tonnes) [1]. The invention of UPR is ascribed to Carleton Ellis. The first patents with regard to polyester resins emerged in the 1930s. Commercial production started in 1941 already reinforced with glass fibers for radar domes, also referred to as radomes [2, 3]. High ambient storage temperatures or long storage times, result in preliminary self-polymerization of these resins. A monetary loss due to the deterioration of the work ability of the resins occurs. So, inhibitors are used to increase the lifetime.

The existing methods for UPR characterization are nuclear magnetic resonance spectroscopy, size exclusion chromatography, and gas chromatography (GC) [4-6]. The main drawbacks in these analytical procedures are the use of solvents and/or cleanup steps, which have been reported to extract and eliminate most of the interfering compounds from the UPR, thus impeding their identification and quantification. Moreover, these procedures result in a large number of manual operations, uncertainty of the determination, higher overall cost and possible analyte loss.

In the last 10 years, miniaturization has attracted much attention in analytical chemistry and has driven solvent and sample savings, sample enrichment, rapid sample preparation, and easier automation. Sample preparation remains one of the more time-consuming and error-prone aspects of analytical chemistry. To overcome drawbacks of conventional extraction techniques, alternative miniaturized methods have been proposed both as solid phase microextraction, as Solid Phase MicroExtraction (SPME) [7-9], MicroExctraction by Packed Sorbent (MEPS) [10], Stir Bar Sorptive Extraction (Twister, SBSE) [11], Solid Phase Dynamic Extraction (Magic Needle, SPDE) [12], In-Tube Extraction (ITEX) [13] and liquid phase microextraction like Single-Drop MicroExtraction (SDME) [14], Hollow Fiber Liquid-Phase Microextraction (HF-LPME) [15,16], Dispersive Liquid–Liquid Microextraction (DLLME) [17], Solvent Bar MicroExtraction (SBME) [18]. On-sample derivatizations applied in miniaturized extraction systems and their simultaneous GC and liquid chromatography analysis has been described for the determination of analytes in aqueous matrices [19, 20]. These methods employ a sample derivatization technique to convert such polar substances into hydrophobic compounds whose volatility is sufficiently high for a GC determination. Within analytical chemistry, the SPME analysis is considered one of major breakthroughs that shaped 20th-century analytical chemistry [21]. SPME integrates sampling, extraction, concentration and sample introduction into a single step and the extraction requires no polluting organic solvent.

Accordingly, we developed three innovative methods for the determination of acetylacetone, 4-tert-butyl catechol (TBC) and its oxidated derivatives 4-tert-butyl-1,2-benzoquinone (TBBC) in UPR, in which automated head space (HS)/SPME technique after

on-sample derivatization is coupled to GC/mass spectrometry (MS). The aim of this work is a high-throughput assay with a molecular discrimination perfomed by structurally informative MS fragmentation patterns. Finally, we proposed a new off-line platform, called SPME Multi Off-Line Sampler, coupled to MultiFiber Exchange (MFX) installed on a *xyz* autosampler.

EXPERIMENTAL

On-sample derivatization

Dilution of UPR

As indicated in a previous paper [22], 100 mg of UPR were dissolved in 10 mL of chloroform (CAS n. 67-66-3). The resulting solution was diluted 1/10 in dimethylsulfoxide (CAS n. 67-68-5). The third solution was made by 1/100 to 1/10 000 water dilutions.

TBC by trimethyloxonium tetrafluoroborate

2 mL of water diluted UPR were transferred into a 10 mL autosampler vial with a magnetic stirring bar and mixed with 40 µL of the internal standard (IS) TBC methyl-D6 methanol solution (50 µg/mL). To convert the TBC (CAS n. 98-29-3, Cat. n. 19670, Aldrich) into its methylether, derivatization with trimethyloxonium tetrafluoroborate (TMO, CAS n. 420-37-1, Cat. n. 281077, Aldrich) was performed at room temperature in two steps. While stirring, about 20 mg of Na_2CO_3 (CAS n. 497-19-8) were added and within 4 minutes approximately 30 mg of solid TMO were added in two aliquots. After 1 minute the solution was neutralized with about 15 mg of $NaHCO_3$ (CAS n. 144-55-8). This procedure was repeated again. Finally, for HS by polyacrylate 85 µm Fast Fit Assemblies (FFA) SPME fiber (Cat. n. FFA 57294-U, Supelco), NaCl (0.5 g) (CAS n. 7647-14-5) was added and the vials were processed by extraction. For TBC-dimethylether, the mass number of the target ion was m/z=179 and the confirming ion was m/z=194.

Acetylacetone by O-(2,3,4,5,6, pentafluorobenzyl)-hydroxylamine

2 mL of water diluted UPR were transferred into a 10 mL autosampler vial and mixed with 10 µL cyclohexanone (CAS n. 108-94-1, Cat. n. 398241 Sigma-Aldrich) IS solution (240 µg/mL) plus 100 µL of 40 mg/mL *O*-(2,3,4,5,6, pentafluorobenzyl)-hydroxylamine hydrochloride (PFBHA, CAS n. 57981-02-9, Cat. n. 76735, Sigma-Aldrich) aqueous solution. The condition used for full reaction to convert the acetylacetone (CAS n. 123-54-6, Cat. n. 005581, Sigma-Aldrich) into its PFB-*bis*-oximes was 20 hours at room temperature. The SPME-HS sampling was performed by 30 µm polydimethylsiloxane (PDMS) FFA SPME fiber (Cat. n. FFA 57289-U, Supelco). The target and the confirming ions were m/z=181 and m/z=236, 293, respectively.

TBBC by methoxylamine

2 mL of water diluted UPR were transferred into a 10 mL autosampler vial and mixed with 10 µL TBBC methyl-D9 IS solution 240 µg/mL plus 300 µL of 80 mg/mL *O*-

methylhydroxylamine hydrochloride (MHA, CAS n. 593-56-6, Alfa Aesar Cat. n. A19188) aqueous solution. The condition used for full reaction to convert the TBBC (CAS n. 1129-21-1) into its methyl-*bis*-oxime was 20 hours at room temperature. The SPME-HS sampling was performed by 30 µm PDMS FFA SPME fiber. The confirming ion was m/z=222.

On-line SPME conditions and xyz robotic apparatus

Automation of the GC procedure was achieved using a new Flex autosampler (EST Analytical, Fairfield, USA). For HS-SPME absorption, a pulsed agitation (on for 2 s at 500 rpm and off for 4 s, 50 °C) was carried out for incubation, before automatically introducing the fiber into the vial in the same conditions. After the absorption, the SPME fiber was introduced into the GC injector port by *xyz* autosampler.

Off-line SPME sampling and *xyz* robotic apparatus

The SPME Multi Off-Line Sampler (Chromline, Prato, Italy) is designed to be used with FFA SPME fibers. The holder works as a support to expose the SPME fiber into the vial, placed on plate of the 32-position magnetic stirrer (Chromline). After the exposure FFA SPME fibers are automatically removed by the Multi Off-Line Sampler and placed into a 45-position tray, allowing the exchange of SPME fibers on the Flex autosampler. Desorption of sampled fibers was perfomed into the GC instrument equipped with Merlin Microseal System (Cat. n. 24817-U, Sigma-Aldrich). A connection with the Laboratory Information Management System (Bika Lab System) allowed a user-programmable suite.

GC/MS

Analysis were performed with a Varian 3900 GC equipped with electronic flow control and a 320-MS (Varian Inc.) detector. A MEGA-5-MS fused silica capillary column (internal diameter 0.25 mm, length 30 m and film thickness 0.25 µm, Cat. No. MS-5-025-025-30, MEGA, Legnano, Italy) was used. TBC and TBBC analysis were performed with column temperature set to 50 °C for 1 min and then increased at 10 °C/min to 240 °C (total run time 20.00 min). In acetylacetone (CAS n. 123-54-6) determination, column oven was set to 40 °C for 2 min and then increased at 25 °C/min to 210 °C, 3 °C/min to 230 °C and finally 30 °C/min to 300 °C for 2.2 min (total run time 20.00 min). Desorption of the analytes was performed introducing the SPME fiber into the 1079 Varian GC injector port (10:1 split mode) for 4 min. The MS was operated in single quadrupole and electron ionization (EI) source with electron energy of 70 eV. Helium (99.999%) at a flow rate of 1.2 mL/min was used as carrier gas.

SYNTHESIS

TBC-D6

Methylation of the catecholic hydroxyls with methyl iodide-D3 (CAS n. 865-50-9) afforded TBC-D6 in good yield (**Figure 1**). Methyl iodide-D3 (5.00 g, 34.5 mmol) was added to a suspension of 4-tert-butyl catechol (2.39 g, 14.4 mmol) and K_2CO_3 (5.97 g, 43.2 mmol) (CAS

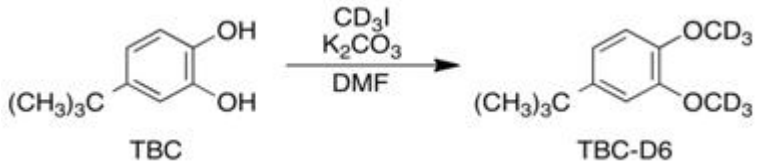

Figure 1. Methylation of TBC with methyl iodide-D3

n. 584-08-7). The mixture was heated at 60 °C for 16 hours, then poured on 200 mL of water, extracted three times with Et_2O (CAS n. 60-29-7), the combined organic layers were dried over anhydrous Na_2SO_4 (CAS n. 7757-82-6), filtered and evaporated. The resulting residue was purified by flash column chromatography on silica gel [25% CH_2Cl_2 (CAS n. 75-09-2) in petroleum ether (CAS n. 8032-32-4)] to give pure TBC-D6 (2.44 g, 85% yield). 1H-NMR (400 MHz, CDCl3) δ 6.92-6.88 (m, 2H), 6.77 (d, 1H), 1.30 (s, 9H); 13C-NMR (100 MHz, CDCl3) δ 148.2, 146.6, 143.7, 116.9, 110.6, 109.0, 55.61, 55.60, 34.2, 31.3; ESI-MS: m/z 201.31 [M+H]+.

TBC-D9

In a flame dried Schlenk flask under N_2 atmosphere, *tert*-butanol-D10 (CAS n. 53001-22-2) (300 mg, 3.56 mmol) was added to a solution of catechol (CAS n. 120-80-9) (392 mg, 3.56 mmol) in trifluoroacetic acid-D (CAS n. 599-00-8) (4.5 mL) and D_2SO_4 (CAS n. 13813-19-9) (200 uL). The obtained yellow solution was stirred at 40 °C overnight. The reaction was diluted with CH_2Cl_2, washed twice with water and then twice with a saturated solution of $NaHCO_3$ and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by flash column chromatography on silica gel [20% ethyl acetate (CAS n. 141-78-6) in petroleum ether] obtaining pure TBC-D9 (90 mg, 15% yield) as an oil. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 6.77-6.83 (m, 2H), 6.58 (s, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 144.9, 142.7, 140.6, 118.0, 115.9, 113.4, 34.0; ESI-MS: *m/z* 198.16 $[M+Na]^+$.

TBBC-D9

To obtain TBBC-D9, TBC-D9 was first synthesized following the procedure reported for the preparation of the protonated analogue [23]. Briefly, catechol was alkylated at position 4 with *tert*-butanol-D10 under acidic conditions of trifluoroacetic acid-D and D_2SO_4. The deuterated environment proved to be essential for the obtainment of the fully deuterated compound, as otherwise the *tert*-butyl cation D9 can exchange with the protic medium leading to the formation of partially deuterated derivatives. Oxidation of the catechol by $NaIO_4$ (CAS n. 7790-28-5) under phase transfer conditions provided the correspondent ortho-quinone TBBC-D9. In detail, to a solution of TBC-D9 (80 mg, 0.46 mmol) in CH_2Cl_2 (45 mL) shielded from light, a solution of $NaIO_4$ (103 mg, 0.48 mmol) in H_2O (5 mL) was added. To this mixture tetrabutylammonium bromide (CAS n. 64-20-0) (148 mg, 0.46 mmol) was added. The reaction was vigorously stirred in the dark for 1 hour. After diluting the reaction with CH_2Cl_2, the organic phase was collected and washed twice with H_2O, then dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by flash column chromatography

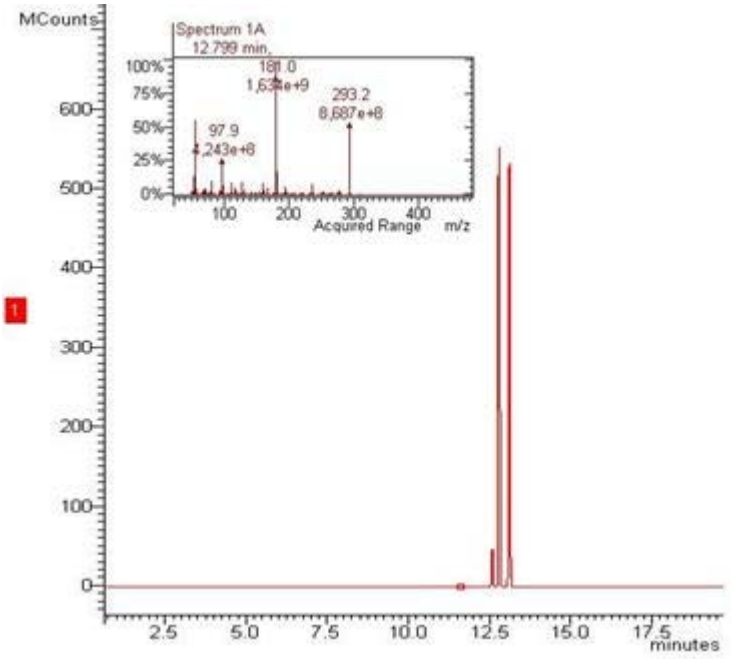

Figure 2. GC chromatogram and EI-MS spectrum of the three stereoisomers of acetylacetone-bis-PFB-oxime

on silica gel (25% ethyl acetate in petroleum ether) obtaining pure TBBC-D9 (16 mg, 20% yield) as a green solid. M.p. = 61-62 °C; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.19 (dd, 1H), 6.38 (d, 1H), 6.27 (d, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 190.44, 162.25, 140.20, 129.53, 123.94, 35.77; ESI-MS: *m/z* 196.14 $[M+Na]^+$.

RESULTS AND DISCUSSION

Sampling of UPR by HS/SPME sampling and following GC/MS analysis has aroused interest in the authors of this work and has been investigated as a possible alternative to conventional methods. The aim of this paper is to provide a simple, fast, sensitive, and organic-solvent free innovative procedure for analysis of polymerization inhibitors and promoter in UPR. So, to achieve successful method, two fundamental requisites were satisfied by the Authors.

Carbonyl and hydroxyl functional groups on-sample derivatizations

On-sample derivatization of carbonyl group to hydrazones and oximes is frequently used. The procedure involves derivatization of the analyte with 2,4-dinitrophenylhydrazine (CAS n. 119-26-6) [24], 2,4,6-trichlorophenylhydrazine [25], pentafluorophenylhydrazine (CAS n. 828-73-9) [26], PFBHA and MHA. These last two reacts in weakly acidic media (pH 4–6) with CO- groups to produce the corresponding oximes.

The GC/EI positive ion MS base peak for all PFB-derivatives is *m/z* 181, the pentafluorotropylium cation [27] (**Figure 2**).

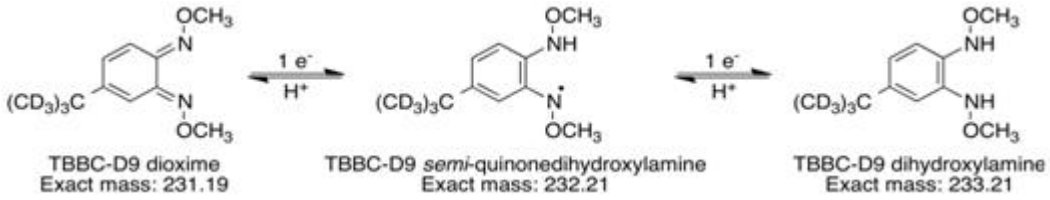

Figure 3. Redox equilibria in TBBC-D9 dioxime

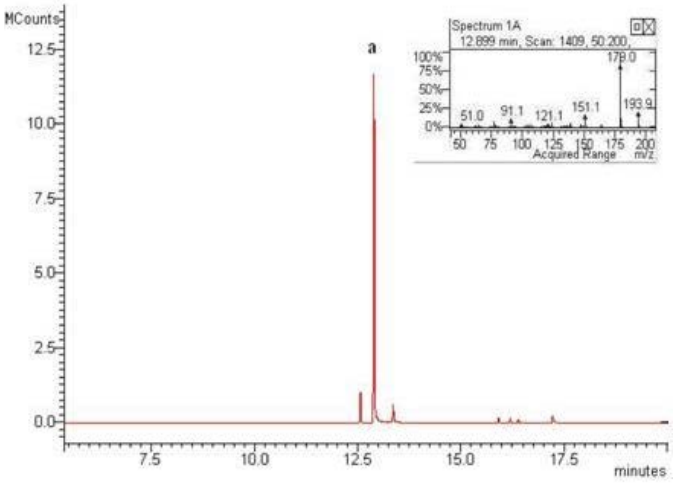

Figure 4. GC chromatogram and EI-MS spectrum of the TBC-bis-methylether

Differently, a characteristic base peak was not observed for methyloxime derivatives of model carbonyl compounds [28]. Methyloxime derivatives produce several abundant fragment ions with low molecular weight that result from simple cleavage or rearrangement followed by fragmentation [29]. We releaved that the o-quinones readily react with MHA to give the corresponding bis-oximes, and the reaction can be pushed to completion if an excess of hydroxylamine is used [30]. The presence of different peaks in the mass spectrum of TBBC-D9 after the derivatization with MHA can be explained taking into account the redox equilibria which quinones and related molecules undergo by simple monoelectronic transfer [31]; indeed the mass peaks that were observed correspond to the TBBC-D9 dioxime, TBBC-D9 *semi*-quinonedihydroxylamine and TBBC-D9 quinonedihydroxylamine which coexist in equilibrium (**Figure 3**).

Trialkyloxonium ions (Meerwein salts), R3O+, with various counterions such as SbF6−, BF4−, SbCl6−, and PF6−are excellent alkylating agents for nucleophiles containing heteroatoms such as N, O, or S [32]. With TMO a methyl group of the oxonium ion reacts with the anion of the a –OH functional group to form the methyl ether. The MS spectrum of TBC-*bis*-methylether is indicated in **Figure 4**.

Table 1. Physical properties and partition coefficients of the TBBC-methyl-*bis*-oxime [a], acetylacetone-PFB-*bis*-oximes[b] and TBC-dimethylether[c] using SPARC software (http://www.archemcalc.com/index.html).

SMILES strings	CAS n.	T_{eb} °C	D_{water} cm^2/s	D_{air} cm^2/s	K_H atm/(mol/m^3)	P_{vap} Pa
CO\N=C1/C=C(C=C/C1=N\OC)C(C)(C)C [a]	unknown	373	$5*10^{-6}$	$4*10^{-2}$	$5.21*10^{-5}$	$1*10^{-2}$
Fc2c(CO\N=C(\C)CC(/C)=N\OCc1c(F)c(F)c(F)c(F)c1F)c(F)c(F)c(F)c2F [b]	unknown	348	$4*10^{-6}$	$3*10^{-2}$	$7.1*10^{-5}$	$2*10^{-5}$
COc1cc(ccc1OC)C(C)(C)C [c]	41280-64-2	269	$6*10^{-6}$	$5*10^{-2}$	$1.3*10^{-6}$	1.9

Verify the suitability to HS-SPME technique

The first objective was to develop the derivatization conditions onto HS-SPME technologies to obtain compounds which are stable under a variety of conditions and easily amenable of sampling and analysis. The PA and PDMS absorptive liquid coatings were chosen for the SPME sampling of a very complex matrix such as UPR because of the lack of competition between the analytes. The HS-SPME techniques were described in a previous work by examining a three-phase system in which a liquid polymeric coating, a HS and an aqueous solution were involved [33]. The mass (n) of analytes absorbed by a coating after the equilibrium has been reached is related to the overall equilibrium of analytes in a three-phase system

$$n = (C_0V_1V_2K_1K_2)/(K_1K_2V_1 + K_2V_3 + V_2)$$

where K_1 is the SPME coating/HS partition coefficient, K_2 is the HS/aqueous matrix partition coefficient, C_0 is the initial concentration of the analyte in the aqueous solution, and V_1, V_2 and V_3 are the volumes of the coating, the aqueous solution, and the HS, respectively. Since K values of the analytes (where $K = K_1 \times K_2$) are often very close to the octanol–water partition coefficient (K_{ow}), and $K_2 = K_H/RT$, where K_H is Henry's constant (C_0, concentration gas phase/C_0, concentration liquid phase). It derives that the equilibrium is controlled by K_{ow} and K_H values. Therefore, the constant of distribution estimated from physicochemical tables or by using the structural unit contribution method can anticipate trends in SPME analysis. The K_H of the TBC-dimethylether, acetylacetone-PFB-oximes and TBBC-methyl-bis-oxime derivatives were 1.3, 71 52 and atm cm^3/mol, which were in agreement with that reported by Pacenti et al [34], and indicated that HS-SPME is efficient for compounds with the K_H higher than 0.17 atm cm^3/mol (**Table 1**).

Furthermore, we found better sensitivity using HS-SPME by an increase in the ion strength by adding bivalent salts instead monovalent salts. The solubility decrease of the methyloxime in the presence of inorganic salts is quantified by the Setschenow equation [35]

$$\log S_0/S = \log \gamma = K_{s\,(salt,solute)}\, C$$

Table 2. Calibration curve. Accuracy and precision of acetylacetone-PFB-*bis*-oximes and TBC-dimethylether analytical methods.

Calibration curve point	acetylacetone-PFB-bis-oximes		TBC-dimethylether	
	Concentration (pg/mg)			
	Nominal	Measured (mean, n=5)	Nominal	Measured (mean, n=5)
1	80	78	100	75
2	160	159	200	202
3	320	321	400	407
4	640	640	800	817
5	1280	1280	1600	1604
6	2560	2559	3200	3193
Response factor plot				
Least-squares linear regression plot parameters (m=slope b=intercept)	m = 0.5361 b = 0.6457		m = 0.5868 b = 8.621	
Coefficient of correlation	0.99		0.99	
Standard Error	0.556		8.199	
Method Detection Limits				
LOD (pg/mg)	1.9		27	
LOQ (pg/mg)	9.2		125	
Accuracy and Precision				
Within session accuracy (%)	6.7		7.0	
Within session repeatability (%)	0.9		3.7	
Inter session repeatability (%)	3.1		3.8	

where S_0 is the solubility of the solute in water, S is the solubility in the presence of salt, γ is the activity coefficient of the solute, K_s is the Setschenow constant and C is the salt concentration. As some Authors showed [36, 37, 38], we noticed that the salt mixture ammonium sulfate (CAS n. 7783-20-2) and sodium dihydrogen phosphate (CAS n. 10049-21-5) (ratio 4/1, 0.7 g) increase the salting out factor of 1.6 rather than the more commonly salt sodium chloride.

In light of what indicated above the authors present the final results. As indicated in **Table 2** the resulting calibration curves for TBC-dimethylether and acetylacetone-PFB-bis-oximes were linear in the investigated range, showing a correlation coefficients >0.99. Accuracy was within 15% of the theoretical concentration, in line with the requirement of US Food and Drug Administration.

The new autosampler platform proposed in this study integrate the MFX device. Several sample preparation steps immediately before sample injection have been automated, allowing just-in-time sample preparation. Following an example to show the advantages of the use of SPME FFA Multi Off-Line Sampler (**Figure 5**), we assume an extraction time of 40 minutes for TBC-*bis*-methylether and acetylacetone-PFB-*bis*-oximes equilibrium in a SPME three phase

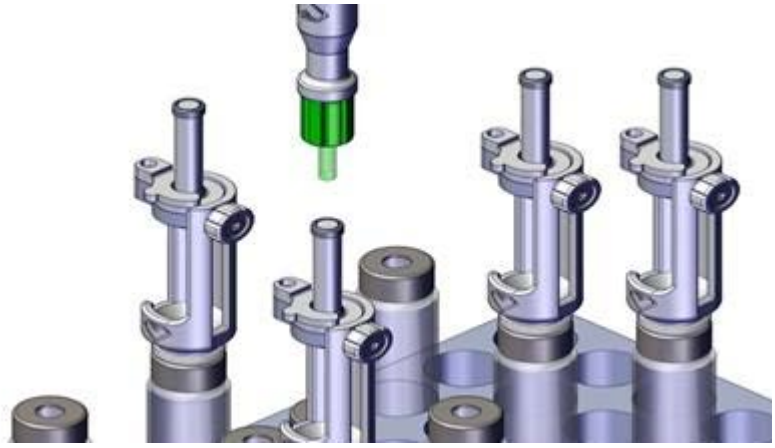

Figure 5. SPME 32-position Multi Off-Line Sampler

system and analysis time of 20 minutes. The results are excellent, with reduction of the total analysis time of 725 minutes (30 samples processed) respect to conventional SPME on-line analysis.

CONCLUSIONS

Our data suggest that automated SPME extraction coupled with GC/MS may be a viable alternative for quantitative TBC and acetylacetone analyses. New sample preparation techniques are being increasingly introduced because of the considerable need for information management, the automation of sample preparation, and the integration of data management into the analytical process. As a future perspective, we wish to expand the application of this methodology by carrying out the quantitative TBBC determination.

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