Determination of low concentrations of trimellitic anhydride in air

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Abstract

Trimellitic anhydride is used in the polymer industry as a hardener in epoxy formulations and as a component in paint resins and surface coatings. It has been reported to be a severe respiratory irritant and to cause pulmonary oedema, immunological sensitisation and asthma-like symptoms. It has been previously analysed as the corresponding acid by high-performance liquid chromatography with ultraviolet detection, and with flame ionisation detection after esterification to trimethyl trimellitate. In this study, the trimellitate ester was assayed by gas chromatography using electron-capture detection. The detection limit, $0.6 \mu g/m^3$ (12 l of air sample; sampling rate 0.2 l/min), was superior compared with methods using flame ionisation or ultraviolet detection and also in view of the occupational reference value, $0.04 mg/m^3$. The method will also be suitable for short-term sampling of the anhydride.

1. Introduction

Trimellitic anhydride (TMA; CAS No. 552-30-7; M_r 192.13; vapour pressure at 25°C $1.6 \cdot 10^{-5}$ Pa) [1] is a common industrial chemical used in the production of coatings, enamels and plasticisers for plastics. It is used also at elevated temperatures (ca. 200°C) as a multifunctional hardener for epoxy resins [2].

TMA is considered to be an extremely toxic substance [3–5]. In exposed humans, it can cause non-cardiac pulmonary oedema, immunological sensitisation and severe respiratory irritation. In many countries, the occupational reference value for this compound has been set as low as 0.04 mg/m^3, this being in most cases the ceiling value [6,7].

Sampling of airborne TMA has been carried out with poly(vinyl chloride) (PVC) copolymer membrane filters [8] or glass fibre filters [9–11]. PVC filter cassettes mounted on 10-mm cyclonic separators [12] have been used for collecting respirable particles while vapours have been sampled with Tenax tubes [9]. Apart from Tenax tubes, even charcoal tubes, two types of silica gel tubes, octadecyl silica gel, XAD-2 resin and Chromosorb 104 adsorption tubes have been tested for sampling TMA [1]. Tenax and Chromosorb 104 were the most promising sampling media for TMA vapours.

After sampling, the sampling medium is eluted with a mixture acidic acetonitrile and water [9] or with a dilute sodium hydroxide solution [10,11]. TMA in the eluate is then determined as its corresponding acid using high-performance liquid chromatography (HPLC) with ultraviolet (UV) detection. Alternatively, the filters are extracted with methanol, the extract derivatised

with boron trifluoride–methanol, and TMA assayed as its trimethyl ester by gas chromatography (GC) with flame ionisation detection (FID) [8,12,13]. Solutions consisting of diazomethane in diethyl ether have also been used for derivatisation of the anhydride and the corresponding acid, followed by GC–FID [14].

The detection limits of the above methods are roughly on the same level as the current occupational reference value. However, large sample volumes are required for determination of concentrations close to the reference value. On the other hand, nothing is known about the lowest concentrations causing sensitisation. Therefore, it would also be important to be able to measure TMA at any concentration suspected of causing allergy.

We modified the NIOSH method [8] where TMA is determined as the corresponding methyl ester, i.e. trimethyl trimellitate (TME), by GC–FID. It has been found that phthalate esters with a conjugated structure resembling that of trimellitic esters, sometimes cause considerable contamination in the electron-capture detection (ECD) in environmental analyses [15]. TME could thus be assumed to yield a good response by ECD. Using ECD, one could easily reach a detection limit corresponding to 0.6 μg TMA/m^3 air with samples of 12 l.

2. Experimental

2.1. Chemicals

The chemicals used were boron trifluoride–methanol (BF$_3$ 14%; E. Merck, Darmstadt, Germany), methanol and acetonitrile (Lab-Scan, Dublin, Ireland), methyl tert.-butyl ether (MTBE; Rathburn Chemicals, Walkerburn, UK), pyridine (Pierce, Rockford, IL, USA), dimethyl phthalate (DMP) and phthalic anhydride (PA) (E. Merck). The solvents were of HPLC grade (dried with anhydrous sodium sulphate), and the other chemicals of analytical grade.

2.2. Sampling

For sampling of airborne TMA, glass fibre filters (binder-free, Type AE, diameter 1 cm, pore size 0.3 μm; SKC, Eighty Four, PA, USA) and Tenax tubes (No. 226-35, SKC) mounted in series and a flow-rate of 0.2 l/min produced by SKC Aircheck Samplers, Model 224-43 XR, were used.

2.3. Derivatisation

For the analysis, the filters and the Tenax polymer were separately desorbed overnight with 2 ml methanol, with 0.2 pmol phthalic anhydride as an internal standard. Filter fibres and Tenax corns were removed from the solution by centrifugation (2000 g) and then washed with an additional 1 ml methanol which was thereafter combined with the desorption solution. After addition of 5 mg fine sodium chloride (for drying purposes), the solution was evaporated to near dryness and esterified with 150 μl boron trifluoride–methanol solution at 100°C for 1 h. After cooling, the solution was again carefully evaporated to near dryness under a nitrogen stream and the residue dissolved in 1 ml of MTBE. A 40-μl volume of pyridine was added to the MTBE solution, and the precipitate formed was removed by centrifugation (2000 g). Acetonitrile (0.5 ml) was added to 0.5 ml of the clear supernatant, and the mixture was used for GC analysis. As TME is a polar compound, the addition of the more polar acetonitrile to the solvent avoided the memory effect which otherwise might occur in chromatography.

2.4. Gas chromatography

The apparatus consisted of a Hewlett-Packard series 5790A gas chromatograph (Palo Alto, PA, USA) with a Ni^{63} electron-capture detector and a HP 5 column (5% phenylmethyl silicone; 25 m × 0.32 mm I.D., 0.17 μm). The temperature program for the column oven was 60°C for 0.5 min, 15°C/min, and 250°C for 3 min. The injector temperature was 230°C and that of the

detector 250°C. Helium was used as the carrier gas at a flow-rate of 1 ml/min, and argon with 5% of methane as an additional detector gas at 56 ml/min. These conditions gave a retention time of 15.04 min for TME.

2.5. Identity confirmation

The identity of the ester was confirmed by mass spectrometry (Hewlett-Packard, HP-5989A MS Engine) using electron impact ionisation at 70 eV. The optimal esterification period was determined by infrared (IR) spectrometry (20 SXC Fourier transform IR spectrometer; Nicolet, Madison, WI, USA). The anhydride was esterified as described above, but the heating was stopped alternatively after 15, 30, 45 or 60 min. After solvent evaporation, the ester was mixed with dried potassium bromide powder, and the mixture was pressed onto disks for IR spectroscopy.

2.6. Calibration

Calibration was performed with external standards by the phase (solid–liquid) balance method, i.e. a glass fibre filter or the contents of a Tenax tube of the same batch and in the same amount as for the samples were added to 2 ml of a standard solution of TMA in methanol. The standard solutions were allowed to stabilise overnight before derivatisation of TMA in the same way as with the samples. PA was used as an internal standard.

3. Results and discussion

A plot of $\ln KT^{3/2}$ versus T^{-1} [15] has been used to provide insight into the detection mechanism of a compound and to indicate its optimum temperature (T) for ECD. Since K, electron-capture affinity, is proportional to the peak area, A, recorded on the chromatogram, K can be replaced by A in the plot. The graph for TME (Fig. 1) with its positive slope, indicates that TME is detected non-dissociatively and that the
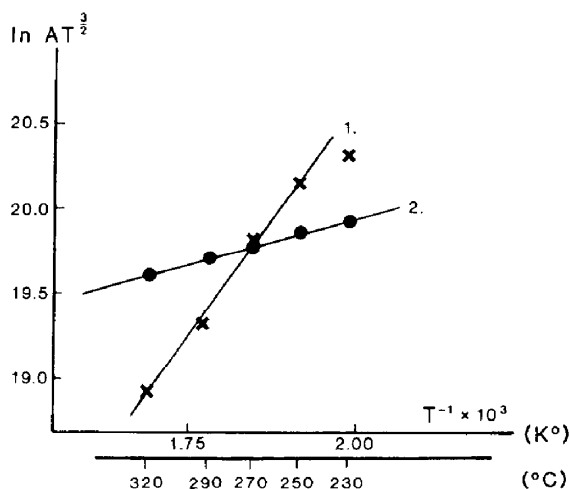

Fig. 1. Temperature dependence of the ECD response towards a fixed mass of trimethyl trimellitate (1; 0.71 pmol) and of dimethyl phthalate (2; 3.7 pmol). A = Area counts of the peaks; T = temperature (K).

detector response is stronger at lower temperatures. For a fixed amount of TME, the detector response was about six times stronger at 225°C than at 350°C (Fig. 2). Injection temperatures higher than 230°C caused the ester to decompose back to the anhydride [16], which was also
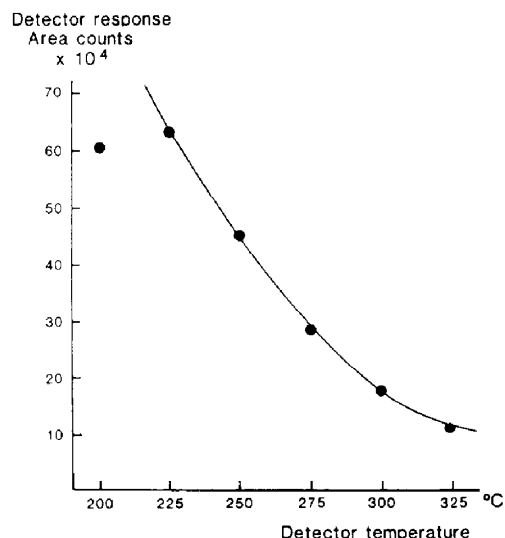

Fig. 2. Effect of the detector temperature on the detector response of a fixed mass (0.47 pmol) of trimethyl trimellitate.

evident in the chromatogram as a broad anhydride peak.

The identity of TME was confirmed by mass spectrometry. Fig. 3 shows a molecular ion at m/z 252 and a confirmatory ion at m/z 221 corresponding to the loss of an OCH_3 group [14]. The identity of the ester was also confirmed by IR spectrometry (Fig. 4). After a 30-min esterification period at 100°C, no sign of the anhydride was apparent in the wavenumber range 1860–1780 cm^{-1}, which is specific for anhydrides [17]. It was therefore also concluded that the esterification had been adequate.

A chromatogram of an external standard and of a sample collected on a glass fibre filter from the factory air are presented in Fig. 5. The chromatograms also show an internal standard (DMP) at 10.34 min. The ratio between the

responses of the same molar amounts of TME and DMP at the detection temperature used (250°C) was 4 (response factor).

A calibration graph prepared with external standards is presented in Fig. 6. The regression is linear ($y = 35.96x + 0.065$; $r = 0.999$) up to a concentration of 0.5 μg/ml. The relative standard deviation of the method (including sampling and analysis) was 6.3% when measuring a concentration of 0.04 mg/m^3 ($n = 6$) of TMA in the air of an exposure chamber (6 m^3). The concentration in the chamber was developed by heating an epoxy hardener (4% TMA) in an open Petri dish (165 cm^2) at 185°C and using a fan to mix the emitted vapour with the chamber air.

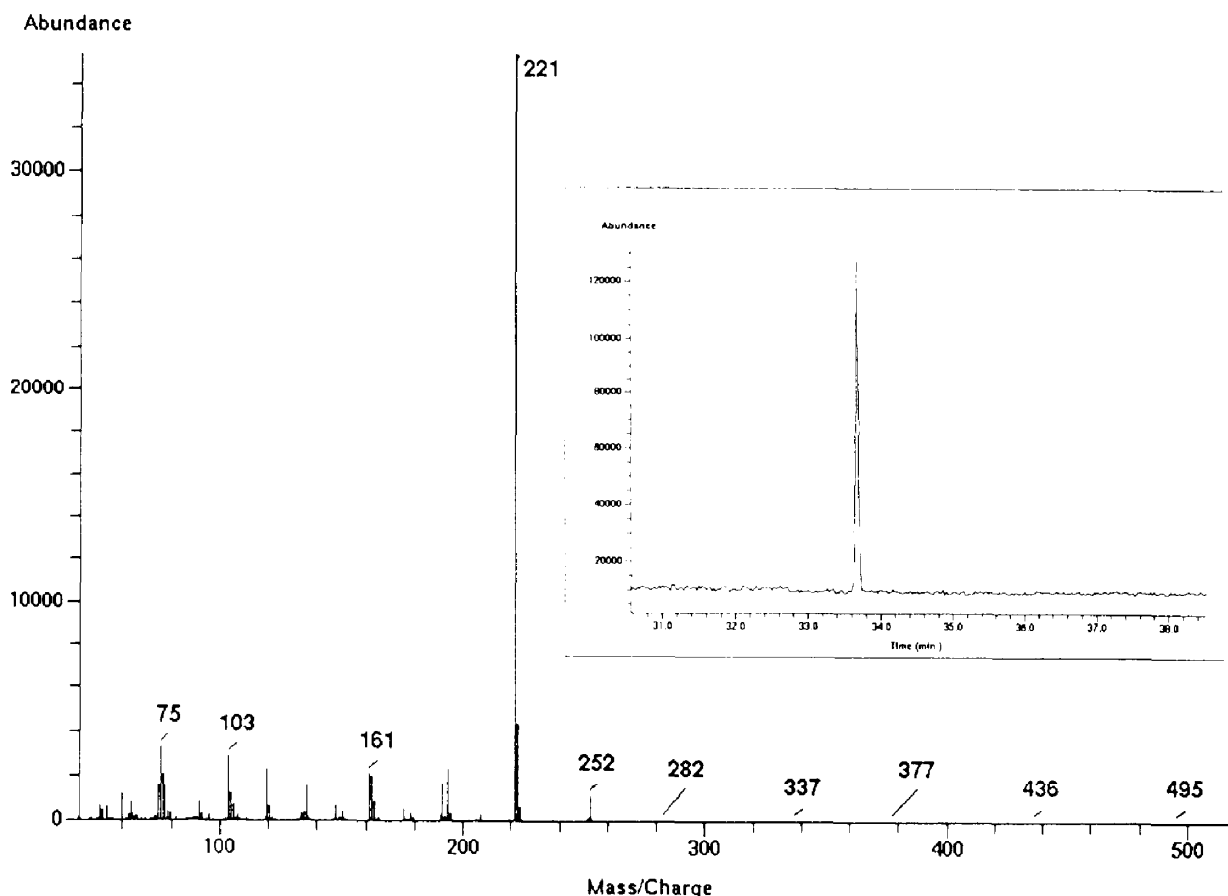TMA has a low vapour pressure, and, therefore, it can be expected to appear in the air as a

Fig. 3. Mass spectrum of trimethyl trimellitate (M⁺ 252; M − OCH_3 221).
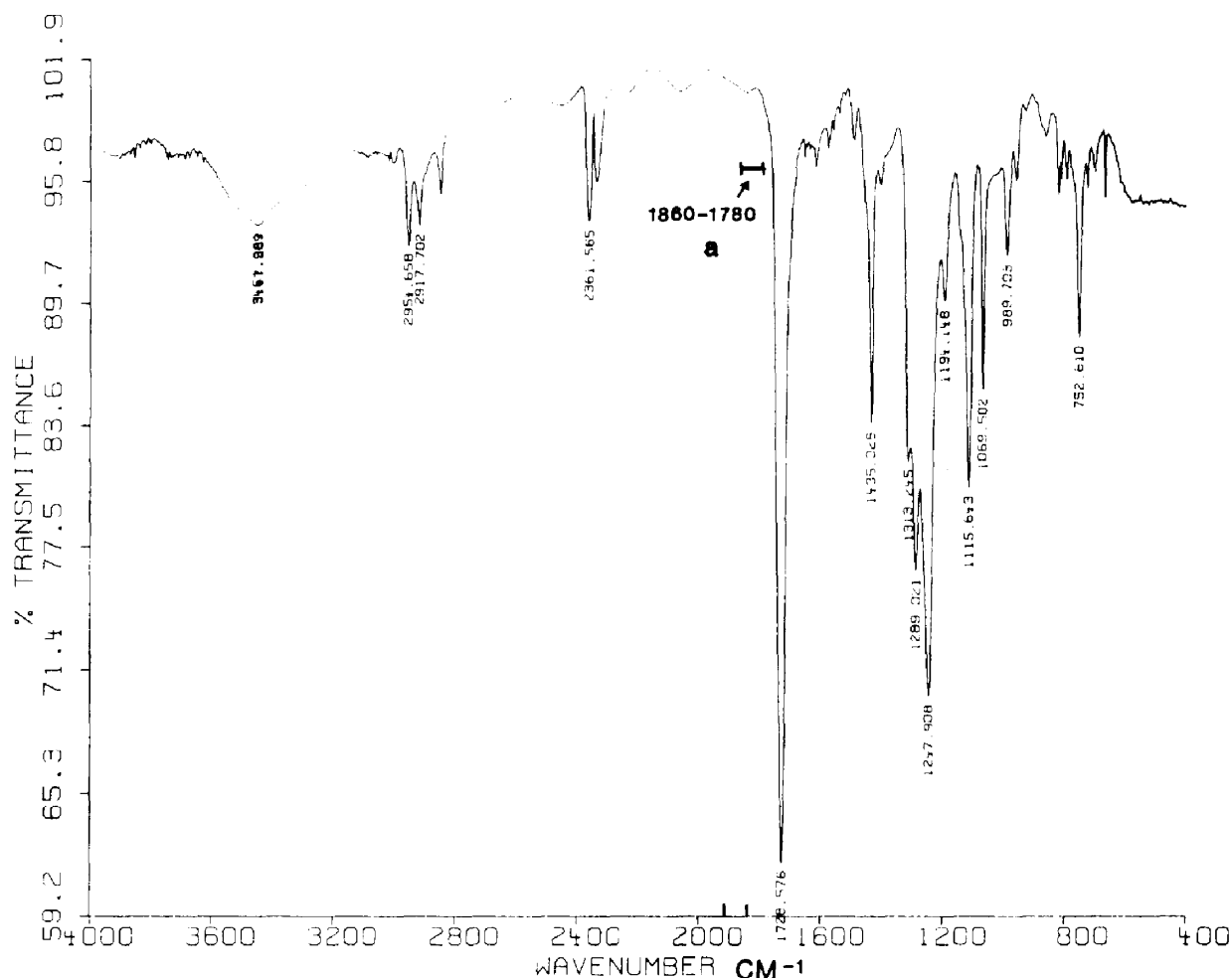
Fig. 4. Infrared spectrum of trimethyl trimellitate (a = wavenumber range for anhydrides).

mixture of gas and very fine particles [18]. Depending on TMA concentration in the air, 65 to 11% of the total amount of TMA retained was found on the filters and 35 to 89% in the Tenax tubes (Table 1). The anhydride was undetectable in the back-up sections of the tubes, indicating that no breakthrough had occurred in the tubes. The distribution of TMA between the filter and the Tenax tube did not seem to be significantly dependent on the sampling rate in the range of 0.2 to 0.5 l min^{-1}.

The anhydride, which reacts readily with water, may partly be converted to the corresponding acid in the moist ambient air. The same can happen on glass fibre filters, which are, unlike Tenax [19], polar material and may thus collect some water from the air. The esterification methods do not distinguish between the anhydride and the acid if present in the sample at the same time.

The analytical recovery of the anhydride (and the acid) from the spiked glass fibre filters was 100%, thus corroborating the previous results [9–11]. The recovery from Tenax polymer was 74.8 to 96.8% depending on the concentration (Table 2).

The collected samples can be stored at least four weeks at 6°C. Likewise, the esterified samples can be stored in dry solvent at 6°C for at least four weeks.
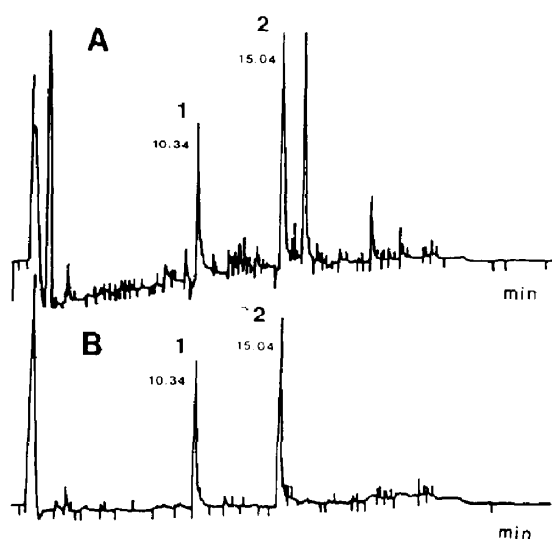
Fig. 5. Chromatograms of a sample (A) collected on a glass fibre filter and of a calibration standard (B) (0.22 μg/ml) of trimethyl trimellitate. TME (2) has a retention time of 15.04 min. Peak 1 is the internal standard, DMP (10.34 min; 0.72 μg/ml).

The detection limit of the ester in solution was 10 pg/μl (0.01 μg/ml), corresponding to 7.6 pg of the anhydride in each μl injected and 0.6 μg of the anhydride in each m^3 of air (12 l, sampling time 60 min). This detection limit is superior to methods using UV detection and FID, and good compared with the current occupational refer-
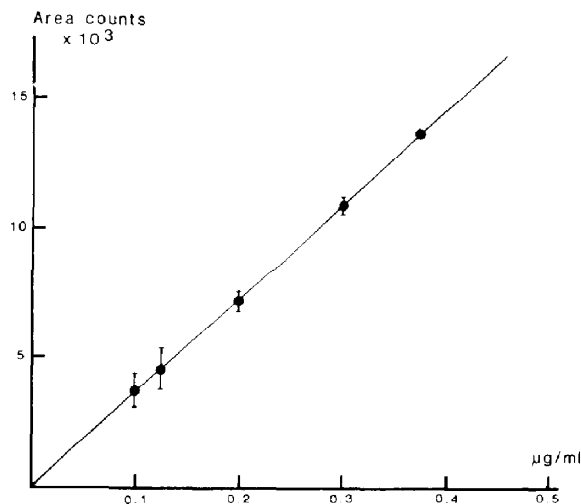

Fig. 6. Calibration graph for trimethyl trimellitate.

Table 1
Distribution of TMA fume between glass fibre filter and Tenax tube in the sampling apparatus (mean proportion, %, retained in each medium)

Concentration of TMA in air (mg/m^3) (± R.S.D., %)	Retained on filter (%)	Retained in Tenax tube (%)
0.042 (± 6.3)	65.2	34.8
0.026 (± 2.9)	11.3	88.7

R.S.D. = Relative standard deviation. Six samples were analysed at each of the two concentration levels. Of the six samples, two were collected at 0.2 l/min, two at 0.35 l/min and two at 0.5 l/min.

ence values (40 μg/m^3). The low detection limit also allows the use of short sampling periods, which might be valuable, e.g. when analysing profiles of fluctuating atmospheric concentrations. Such analyses are important when evaluating the role of peak concentrations in the development of allergy in workers [4].

Personal samples collected from the workplace of a patient with suspected work-derived asthma showed TMA concentrations ranging from 2 to 24 μg/m^3 of TMA in the air. The factory in question used epoxy resin which was hardened with TMA to produce components for the electronics industry.

4. Conclusions

Determination of trimellitic anhydride by GC–ECD is superior in sensitivity to other detection

Table 2
Recovery of spiked trimellitic anhydride amounts from sampling media

Amount of TMA (μg)	Recovery (%)	
	Glass fibre filter	Tenax polymer (± R.S.D., %)
1.127	100	96.8 ± 2.2
0.375	100	78.5 ± 5.1
0.209	100	77.8 ± 6.3
0.125	100	74.8 ± 8.0

Number of samples was 6 in each concentration.

methods used for determining this toxic compound. The good sensitivity permits also short-term sampling.

Acknowledgements

References

[1] R.E. McCoy, J.A. Pauls and R.L. Stoffer, *Am. Ind. Hyg. Assoc. J.*, 46 (1985) 704.

[2] C.E. Freitag, in H. Buchholz-Meisenheimer, J. Frenzel and R. Pfefferkorn (Editors), *Ullmanns Ensyklopädie der technischen Chemie.* Vol. 9, Verlag Chemie, Weinheim, 4th ed., 1975, p. 150.

[3] National Institute of Occupational Safety and Health (NIOSH), *Current Intelligence Bulletin 21: Trimellitic anhydride; Publication No. 78-121,* Department of Health, Education and Welfare, Cincinnati, OH, 1978.

[4] K.M. Venables, *Br. J. Ind. Med.,* 46 (1989) 222.

[5] *Toxicity Review 8,* Health and Safety Executive, London, 1983.

[6] *Threshold Limit Values and Biological Exposure Indices. 1993–1994,* American Conference of Governmental Industrial Hygienists, Cincinnati, OH, 1993.

[7] Anon., *Appl. Occup. Environ. Hyg.,* 6 (1991) 625.

[8] National Institute of Occupational Safety and Health (NIOSH), *Manual of Analytical Methods, Vol. 6, Method No. P and CAM 322; Trimellitic Anhydride,* US Department of Health, Education and Welfare, Washington, DC, 2nd ed., 1985.

[9] *Aromatic Carboxylic Acid Anhydrides in Air —Laboratory Method using Glass Fibre Filter/Tenax Tube Sampling and High Performance Liquid Chromatography (MDHS Series* No. 62), Health and Safety Executive, London, 1988.

[10] J. Purnell and C.J. Warwick, *J. High Resolut. Chromatogr. Chromatogr. Commun.,* 3 (1980) 482.

[11] R. Geyer, R.C. Jones and N. Mezin, *J. High Resolut. Chromatogr. Chromatogr. Commun.,* 9 (1986) 308.

[12] J. Palassis, J.C. Posner, E. Slick and K. Schulte, *Am. Ind. Hyg. Assoc. J.,* 42 (1981) 785.

[13] P.A. Biondi and M. Gagnasso, *J. Chromatogr.,* 109 (1975) 389.

[14] L.G. Rushing, J.R. Althaus and H.C. Thompson, *J. Anal. Toxicol.,* 6 (1982) 290.

[15] C.F. Poole and A. Zlatkis, in A. Zlatkis and C.F. Poole (Editors), *Electron Capture —Theory and Practice in Chromatography,* Elsevier, Amsterdam, 1982, pp. 151–190.

[16] M. Windholz, S. Budavari, L.Y. Stroumtsos and M. Noether Fertig (Editors), *The Merck Index, An Encyclopedia of Chemicals and Drugs,* Merck & Co., Rahway, NJ, 1976, p. 1244.

[17] C.J. Pouchert, *The Aldrich Library of FT-IR Spectra,* Edition I, Vol. 2, Aldrich, Milwaukee, WI, 1985, pp. 308, 334.

[18] C. Perez and S.C. Soderholm, *Appl. Occup. Environ. Hyg.,* 6 (1991) 859.

[19] U. Giese, in A. Kettrup (Editor), *Analyses of Hazardous Substances in Air,* Working Group Analytical Chemistry, Deutsche Forschungsgemeinschaft, VCH, Weinheim, Vol. 2, 1993, pp. 7–8.