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AN ALTERNATIVE METHOD FOR THE ANALYSIS OF PHENOL AND O-, M-, AND P-CRESOL BY CAPILLARY GC/FID

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An alternative method for the sampling and simultaneous analysis of phenol, o-, m-, and p-cresol, employing XAD-7 as a sorbent for the collection of each analyte, is described. Desorption was achieved with methanol followed by analysis of all samples using gas chromatography with flame ionization detection. The separation of all analytes was achieved on a Stabilwax-DA capillary column. Sample collection and preparation was improved over current methods used at the National Institute for Occupational Safety and Health. The results obtained when a Stabilwax-DA capillary column was used in the analysis, as compared to those obtained using a Stabilwax capillary column, indicated achievement of baseline separation of the analytes. Peak resolution and overall peak shape were enhanced by the use of the Stabilwax-DA column. Lower limits of detection were achieved for each analyte. Desorption efficiency and storage stability results (30 days) were acceptable. Sample stability in solution and on solid sorbent tubes was examined. The relative standard deviation of the analytical portion of the method was found to be 0.045. This method provides a simplified, concise, simultaneous analysis of phenol, o-, m-, and p-cresol.

Phenol, and the related o-, m-, and p-cresol isomers, members of the class of aromatic organic compounds collectively referred to as phenols, are used throughout industry on an ever-expanding scale. According to the most recent National Occupational Exposure Survey (NOES) data, over 600,000 workers are potentially exposed to phenol and another 40,000 to o-, m-, and p-cresol in the preparation of various phenolic resins, pharmaceuticals, disinfectants, and plastics.[1] The National Institute for Occupational Safety and Health (NIOSH) has established a recommended exposure limit (REL) of 5 ppm for phenol and 2.3 ppm for the cresol isomers.[2–4] In addition, the American Conference of Government Industrial Hygienists (ACGIH) has established a threshold limit value (TLV®) of 5 ppm, and the Occupational Safety and Health Administration (OSHA) has established a permissible exposure limit (PEL) of 5 ppm exposure for phenol and the cresol isomers.[5–6]

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Recently, in addition to concerns about workplace exposure to phenol and the cresol isomers, attention has been directed toward the detection of these compounds in the exhalant air of patients afflicted with lung carcinomas, highlighting new concerns about phenol exposure in cigarette smoke.[7] A number of methods currently exist for the sampling and analysis of both phenol and the cresol isomers.[8–13] Various sampling techniques were employed in these methods. Phenol previously has been sampled by the use of silica gel solid sorbent tubes[11–12], bubblers containing 0.1 N NaOH[9], bubblers containing 0.1 N NaOH followed by derivatization with p-nitrobenzene diazonium tetrafluoroborate[13], and collection on XAD-7 high surface area acrylate-ester polymeric solid sorbent sampling tubes.[8] Sampling techniques employed for the cresol isomers have been limited to collection on solid sorbent tubes such as silica gel [10,12] and XAD-7.[8] Subsequent analysis of each analyte routinely has been performed either by gas chromatography with flame ionization detection (GC/FID) or by high performance liquid chromatography with ultraviolet detection (HPLC/UV).[8–13]

Although these methods generally have achieved satisfactory sampling and analytical results, each has associated with it certain disadvantages either in the sampling procedure or the analytical procedure. The use of bubblers for the air sampling of phenol and the cresol isomers was bulky, time consuming, and resulted in reduced worker acceptance.[9] Certain disadvantages associated with the analysis of these analytes included multiple solvent preparations for use in gradient elutions, collection of the analytes on varying sampling media, and the successful derivatization of the analytes.[8,13]

Phenol and the related cresol isomers, when collected on silica gel solid sorbent tubes, exhibited unacceptable results because the accuracy of the procedure was affected by poor sample collection efficiency.[10,11] Sample collection efficiency was affected by external factors such as conditions of high relative humidity, duration of sampling time, and the amount of solid sorbent present in the silica gel tubes.[12] While the use of high performance liquid chromatography (HPLC) provided excellent sensitivity (ng levels), it required longer and more detailed sample preparation, and could not achieve the total resolution of the cresol isomers.[8] Earlier gas chromatographic analyses lacked the overall sensitivity achieved by the

HPLC method and failed to achieve the complete separation of the cresol isomers.[9–12]

Therefore, considering the limitations presented in the current methods for the sampling and analysis of phenol and the cresol isomers, this article describes a procedure designed for the low microgram level detection of both phenol and the cresol isomers simultaneously; complete baseline separation of phenol and the o-, m-, and p-cresol isomers; minimal sample preparation; and improved sample recovery over current NIOSH methods. Prior use of XAD-7 solid sorbent collection tubes has been shown to provide the best combination of desorption efficiency (DE) results, increased sampling capacity under conditions of high relative humidity, and minimal breakthrough of analytes.[8] Thus, analyte collection on XAD-7 sorbent tubes combined with recent advances in capillary gas chromatography (CGC), as described in this article, results in an improved method for the collection and analysis of phenol and the cresol isomers.

EXPERIMENTAL

The reagents used were methanol (99.9+%, Baxter Scientific, Obetz, Ohio); phenol (99+%, Aldrich Chemical Co., Milwaukee, Wis.); o-cresol (99%, Aldrich Chemical Co.); m-cresol (97%, Aldrich Chemical Co.); and p-cresol (99%, Aldrich Chemical Co.). The solid sorbent used was Amberlite XAD-7 (glass tubes containing two separate sections of 100 mg and 50 mg; SKC, Inc, Eighty Four, Pa.).

In this study, XAD-7 polymer solid sorbent tubes were syringe spiked with a solution containing a mixture of phenol and each individual cresol isomer at approximately 10 μg (3× the limit of detection, LOD); 30 μg (10× LOD); and 120 μg (30× LOD) level, where LOD is defined as the mass of analyte that gives a signal 3σ above the mean blank signal (δ = standard deviation of the blank signal). The limit of quantitation (LOQ) is defined as the mass of analyte 3.3 times the LOD having a recovery of greater than 75%.[14] To confirm the desorption efficiency (DE) results reported in OSHA Method 32 and to determine long-term storage stability, six tubes at each level were analyzed at 1, 15, and 30 days after storage in the dark at 5°C. Previous data indicated that each analyte was stable when stored at ambient temperature for 14 days.[8] Freshly prepared calibration standards in methanol solvent were used for each analysis, ranging from 1 to 518 μg/sample. The front and back sections of each XAD-7 solid sorbent tube were placed into 4 mL glass vials and desorbed in 2 mL of methanol ultrasonically for one hour. One milliliter aliquots were then transferred from the 4 mL glass vials to autosampler vials for analysis by GC/FID.

An experiment was designed to determine the effect that high humidity would have on the collection and recovery of phenol and the cresol isomers from both XAD-7 tubes and silica gel tubes. It has been previously reported that the collection of various analytes on silica gel is reduced under conditions of high relative humidity, while XAD-7 remains unaffected by high humidity.[12–15] To six silica gel tubes and six XAD-7 tubes a mixture of the analytes was applied to the inner glass wall with a syringe and warm humid air was pulled through the system for two hours to give a total volume of 24 L. The relative humidity of the system was measured to be 80%.

TABLE I. Comparison of Results from Phenol and Cresol Isomers Analysis on Both Stabilwax and Stabilwax-DA Fused Silica Capillary Columns

Characteristic	*Stabilwax*	*Stabilwax-DA*
Peak Resolution (splitless injection)	partial b	baseline
Peak Shape	broadened	sharp
Initial Temperature	170°C (isothermal)	160°C (programmed)
Precision (RSD)	0.206	0.045
Column Stability (analyte interactions)	moderate	very good
LOD	6 μg	< 1 μg

Analysis of each analyte was performed on an HP5890 (Hewlett Packard Corp, Avondale, Pa.) gas chromatograph using flame ionization detection. Partial separation of the analytes was achieved on a Stabilwax fused silica capillary column (30-m, 0.32 mm ID, 0.25 μm film thickness, Restek Corp., Bellefonte, Pa.) at 170°C isothermally while complete separation of the analytes was achieved using a Stabilwax-DA fused silica capillary column (30-m, 0.32 mm ID, 1.0 μm film thickness, Restek Corp.) programmed from 160°C to 225°C at 3°C/min. The composition of the column coating was 100%

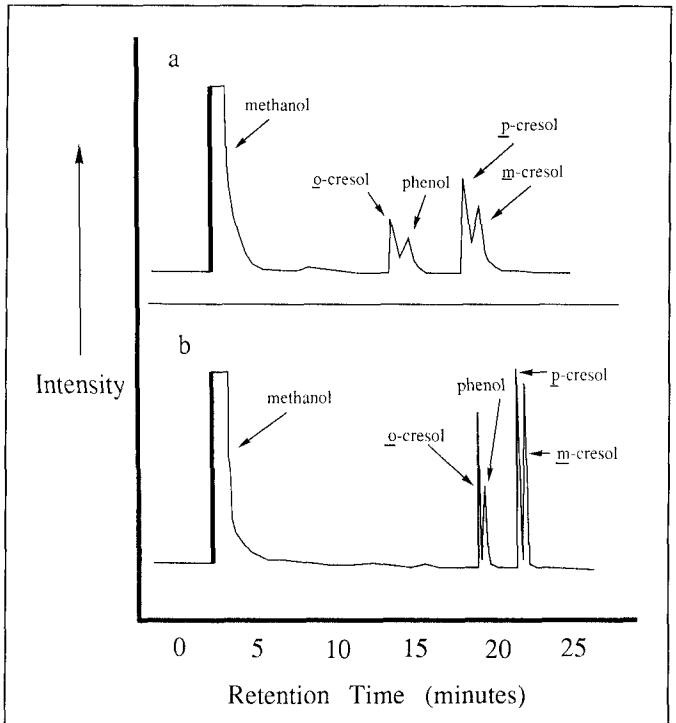

FIGURE 1. Comparison of phenol (~50 μg) and individual cresol isomers (~50 μg) when injected splitless onto Stabilwax (a) and Stabilwax-DA (b) fused capillary columns.

TABLE II. Results of the Combined Desorption Efficiency Storage Stability Study

Storage Period (d)	Initial Loading	Avg. Recovery (%)[A] Phenol	o-Cresol	m-Cresol	p-Cresol
1	30 × LOD	97.2	90.3	91.2	99.7
15	30 × LOD	92.2	84.7	89.7	94.8
30	30 × LOD	88.3	81.9	83.5	85.2
1	10 × LOD	97.2	101.6	88.3	78.4
15	10 × LOD	87.6	100.2	85.0	76.0
30	10 × LOD	82.6	91.2	79.8	69.8
1	3.3 × LOD	94.0	96.8	94.4	85.7
15	3.3 × LOD	86.3	94.8	93.0	85.2
30	3.3 × LOD	80.7	86.2	85.2	75.1
LOD (μg/sample)		3	3	3	3
LOQ (μg/sample)		10	10	11	11

[A] Average recovery is compiled from six samples

Carbowax PEG. Sample volume was 1 μL injected at a split ratio of 10:1 and splitless as specified. Helium was used as the carrier gas. The column flow was set at 1—2 cc/min. The injector port temperature was 250°C, and the detector temperature was 300°C. Quantitation of the integration results obtained from an HP 3392A ALS was based on a least-squares analysis of a standard calibration curve. The identities and retention times of each analyte were confirmed by performing the analysis on both the Stabilwax and the Stabilwax-DA fused silica capillary columns and by use of peak spiking techniques.

RESULTS AND DISCUSSION

This research initially was aimed at identifying a fused silica capillary column that would allow for the baseline separation of phenol and the individual cresol isomers (o-, m-, and p-). A Stabilwax fused silica capillary column allowed for the baseline separation of these analytes when a split injection mode (approximately 40:1) was employed. However, on further investigation using a Stabilwax-DA fused silica capillary column, it was determined that the separation of phenol and the cresol isomers could be achieved up to levels of 50—60 μg/sample when using splitless injections. In addition, when compared to the results obtained using the Stabilwax column, better peak shape and resolution, precision of the results, and lower LODs for each analyte were obtained when the analysis was performed on the Stabilwax-DA fused silica capillary column (see Table I). A comparison of the chromatograms is depicted in Figure 1.

As was mentioned previously in the experimental section, a combined desorption efficiency/storage stability study was conducted for each analyte at 3.3× LOD, 10× LOD, and 30× LOD. The relationship between these analyte spiking levels and their REL/PEL values is as follows: the 3.3× LOD level is approximately 0.02× the REL/PEL, while the 30× LOD is approximately 0.2× the REL/PEL. Normally, desorption efficiencies/storage stability studies are preformed at analyte concentrations 0.1×, 0.5×, and 1.0× the REL/PEL, but to more accurately represent the analyte concentrations found on field samples lower microgram level analyte spikes were used in this research. The results of the combined desorption efficiency/storage stability study (Table II) indicated that the desorption efficiencies determined for each analyte after one day were quite acceptable, well above the 75% recovery required at the LOQ level as stipulated by this laboratory's currently accepted quality control protocol.[14]

TABLE III. Comparison of Collection and Recovery Results of Phenol and Cresol Isomers on XAD-7 and Silica Gel at 80% Relative Humidity

Sorbent	N	Phenol	o-Cresol	m-Cresol	p-Cresol
XAD-7	6	95.3	93.1	97.2	95.6
Silica Gel	6	41.7	26.9	76.3	77.1

Samples analyzed after 15 days, when compared to samples analyzed after 1 day, exhibited recovery differences of less than 10%. This complies with the criteria established in the NIOSH validation protocol.[16] In addition, the storage stability for each analyte was found to be acceptable for 30 days, with the only exception being p-cresol falling under the 75% recovery level after 30 days at the 10× LOD level. When necessary, appropriate desorption efficiency corrections would have to be applied to field sample results.

When phenol and the cresol isomers were collected under conditions of high relative humidity (80%) on XAD-7 sorbent media, the recovery of all analytes was greater than 93%. Analyte recovery from silica gel was significantly reduced, especially for phenol (41.7%) and o-cresol (26.9%). These results confirm previous reports that when sampling under conditions of high humidity, the ability of silica gel to quantitatively collect the analytes of interest is greatly reduced. The results are reported in Table III.

Further investigations of the analytical aspects of the method determined that the results were consistently reproducible. Retention time (Rt) variations were consistently less than ± 0.1 min for each analyte when the analyses were performed on the Stabilwax-DA fused silica capillary column. The precision of results was determined from duplicate injections of eight standard calibration solutions ranging from 0.5 to 319 μg per sample. The overall precision of the method was 0.045 when the analyses were performed on the Stabilwax-DA fused silica capillary column, compared to 0.206 when the analyses were performed on the Stabilwax fused silica capillary column. Overall analytical precision was derived from data pooled from an average of the standard deviations of all sample analyses obtained from peak area values. It should be noted that these analytes were found to exhibit a time-dependent rate of decomposition in solution over a period of several days when stored at 5°C. The level of decomposition was estimated to be ~50%. Therefore, it is recommended that fresh calibration standards be prepared daily to prevent any possible analyte loss due to sample decomposition in solution.

CONCLUSION

The method described in this report provides a number of improvements over currently available methods. It allows for the

complete baseline separation of phenol and all cresol isomers while at the same time providing a reproducible low limit of detection (LOD). The use of XAD-7 solid sorbent tubes as the sampling media essentially eliminates the effects of humidity (a common problem associated with the previously used silica gel sorbent tubes) and improves sample recovery. Sample collection and preparation for analysis is easier and simpler with better analyte recoveries than in existing NIOSH chromatographic methods. The use of a Stabilwax-DA fused silica capillary column improves peak resolution and analyte peak separations and prevents column degradation by acidic compounds such as phenol and the cresol isomers.

A precise, simultaneous, high-quality method for the quantitative analysis of phenol and the cresol isomers has been described and may be used to improve the measurement of occupational exposures to phenol, o-, m-, and p-cresol.

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