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Analysis of semivolatile organic compounds by headspace gas chromatography

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ABSTRACT

Through an unconventional application of static headspace gas chromatography (GC), organic solutes of low volatility were determined at sub mg/l or lower levels in organic matrices of higher volatility as well as in aqueous matrices. Organic compounds such as phenol, biphenyl, diphenyl ether, 1,3,5-triethylbenzene, diphenylethanes, and monochlorobiphenyl with boiling points as high as 291°C were determined in complex matrices by headspace GC without preconcentration or other sample handling.

INTRODUCTION

Static and dynamic headspace analysis have been widely used with gas chromatography (GC) for analysis of trace amounts of volatile organic components. Dynamic headspace analysis is used for concentration of volatiles in matrices such as biological fluids and environmental samples. The main reasons for using headspace analysis are to avoid injecting compounds with high boiling points that may not elute from the column and to increase the amount of solutes of interest reaching the detector. Dirty or complex samples drastically affect quantitative results, shorten the lifetime of capillary columns, and increase the down time of the instrument. Headspace analysis, when applicable, alleviates the problems associated with dirty and complex samples. Headspace analysis of volatile components in a wide range of matrices is covered in the literature [1–8].

Determination of residual solvents in high-boiling pharmaceutical formulations is an excellent example of using static headspace analysis. Due to the difference in volatility between residual solvents and drugs, the solvents can be selectively injected into the GC system without injecting the drug. Residual monomers in the associated polymers are often analyzed by headspace GC.

Determinations of semivolatile and non-volatile components are usually made by direct injection of the sample into the gas or liquid chromatograph or by selective extraction into another solvent followed by gas or liquid chromatographic analysis. Adsorption onto solid adsorbents followed by solvent extraction is another popular approach for analysis of non-volatile components. Non-volatile compounds such as lactic acid and succinic acid [9] have been methylated in a headspace vial, and then the volatile methyl esters were determined by headspace analysis.

The sensitivity of static headspace analysis depends on several factors such as the volume ratio of the gas and liquid phases and the partition coefficient of the analyte between the liquid and gas phases at the equilibrium temperature used [10]. The sensitivity of the headspace technique can be improved by increasing the concentration of the analyte in the headspace in equilibrium with the liquid phase. Depending on the matrix, this can be done by adjusting the pH, adding a solvent, adding salt, or increasing the equilibration temperature. For example, the sensitivity of the headspace analysis of residual monomers in polymers has been increased by spiking the polymer solution with water [11]. This sensitivity enhancement has been attributed to decreased solubility of the monomers in the solution

which increases the equilibrium concentration of the monomers in the headspace. For a detailed discussion of the methods for increasing sensitivity of static headspace analysis and applications of these techniques, see refs. 10 and 12.

Many improvements have been made in headspace technology. The most important is automation, which reduces deviations in the sample size injected. Another improvement is the ability to work at higher temperatures. Some headspace analyzers allow the sample to be heated to 200°C and the valve, sample loop, and transfer line to 250°C. The higher temperature of the sample increases the sensitivity of the analysis, while the higher temperature of the transfer line reduces carry-over effect. Thus, the higher temperature capabilities extend the range of compounds that can be determined by the headspace technique. However, the risk of degrading the sample or bursting the container or losing the analyte due to chemical interaction with the vial septum must be considered when using the high temperatures.

In this work, headspace analysis with matrix modifiers and/or high equilibrium temperatures was used to determine semivolatile components such as phenol, biphenyl, diphenyl ether, 1,3,5-triethylbenzene, 1,1-diphenylethane, and 1,2-diphenylethane in an aqueous matrix and monochlorobiphenyls in an organic matrix of moderate volatility.

EXPERIMENTAL

Chemicals

n-Propylbenzene, 1,3,5-triethylbenzene, 1,2-diphenylethane, and biphenyl were obtained from Aldrich (Milwaukee, WI, USA). Dimethyl sulfoxide and phenol were obtained from Fisher Scientific (Pittsburgh, PA, USA). 2-Phenylphenol was obtained from Mobay Chemical (now known as Miles). 1,1-Diphenylethane was synthesized in the laboratory, and diphenyl ether was obtained from the Dow Chemical (Midland, MI, USA).

Chromatographic system

Chromatographic studies were carried out with a Varian 3400 gas chromatograph equipped with both flame ionization and electron-capture detectors and a Varian Genesis headspace analyzer. The headspace analyzer was connected to the gas chromatograph via a transfer line through the split injector. A 30 m × 0.25 mm I.D. column with 0.25 μm DB-FFAP was obtained from J & W Scientific (Folsom, CA, USA) and a 60 m × 0.32 mm I.D. column with 1.0 μm Rt_x-20 was obtained from Restek (Bellefonte, PA, USA). Other GC conditions are described in the figure captions.

Non-aqueous samples

Several solutions of *o*-, *m*- and *p*-chlorobiphenyls were prepared in the range from 2 mg/l to 47 mg/l in *n*-propylbenzene. The solvent, *n*-propylbenzene, was chosen as representative of organic matrices with moderate volatility. Aliquots (5 ml) were transferred to 20-ml headspace vials.

The vials were equilibrated at 150°C for 15 min. A 1-ml aliquot of the headspace above the solution was injected into the gas chromatograph via a transfer line that was held at 190–230°C. Electron-capture detection (ECD) was used with these analyses.

Aqueous samples

A stock solution of *n*-propylbenzene, 1,3,5-triethylbenzene, biphenyl, diphenyl ether 1,1-diphenylethane, 1,2-diphenylethane, and 2-phenylphenol was prepared in dimethyl sulfoxide. Dilute solutions were prepared by successive dilutions of the stock solution in water. The vials were equilibrated at 95°C for 20 min. For comparison, dilute solutions were also prepared in *n*-propylbenzene. These were equilibrated at two temperatures, 95°C and 135°C, for 20 min. The transfer line was held at 230°C. Flame ionization detection (FID) was used with these analyses. Other conditions are the same as for non-aqueous analysis. Higher equilibration temperatures of aqueous samples was not attempted because of the associated complexity of the analysis at those conditions.

A water solution containing 5 μg/l phenol was prepared. Analysis of a 5-ml aliquot of the phenol solution was performed. Analysis of phenol solutions that were spiked with either 1-ml or 2-ml aliquots of *n*-propylbenzene to make a total sample volume of 5 ml was performed and compared to the unspiked sample analysis.

RESULTS AND DISCUSSION

Non-aqueous samples

Determination of monochlorobiphenyls in complex matrices has been routinely done by GC, however, the procedure is tedious. A typical sample preparation consists of concentrating the analytes on a solid adsorbent and then washing them off with a solvent. The resulting solution is analyzed by GC. Headspace analysis is an appealing alternative to the adsorption and concentration of the monochlorobiphenyl analytes. However, due to their low volatility this would be an unconventional application of the headspace technique. Nonetheless, headspace GC analysis with high equilibration and vapor transfer temperatures was investigated for the determination of low levels of monochlorobiphenyls. The boiling points and vapor pressures of the compounds of interest at various temperatures are listed in Table I. The data in Table I are only indicative of what happens in the vials during equilibration. The partitioning in the phases is a very important factor and affects the sensitivity of the analysis. A 15-min equilibration at 150°C produced adequate analyte concentrations in the vapor phase for the purpose of this study. No optimization of the equilibration time was done. Steady-state conditions might not have been achieved for all solutes in a 15-min period. Manual injection of the headspace sample via a syringe is problematical because vapors can condense in the syringe. Instead, a valve injector was used. By maintaining the valve and transfer line at 190–230°C vapor condensation was avoided.

TABLE I

PHYSICAL PROPERTY DATA

Data obtained from the Dow physical property data bank.

Compound	Boiling point (°C)	Vapor pressure data	
		Temperature (°C)	Pressure (Pa)
o-Chlorobiphenyl	275.7	95	198
		135	1418
		150	2640
m-Chlorobiphenyl	291.5	95	109
		135	867
		150	1661
p-Chlorobiphenyl	291.5	95	116
		135	863
		150	1636
n-Propylbenzene	159.2	95	13 823
		135	52 191
		150	79 549
1,3,5-Triethylbenzene	218.7	95	1675
Biphenyl	253.1	95	570
Diphenyl ether	258.1	95	359
1,1-Diphenylethane	272.6	95	214
1,2-Diphenylethane	280.8	95	161
o-Phenylphenol	286.2	95	116
Phenol	181.9	95	4343

The partitioning of the analytes between the liquid phase and the vapor phase is an important factor in determining the sensitivity of the analysis. Several factors contribute to the low concentration of such high boiling compounds in the vapor phase: the high boiling point, the low vapor pressure and favorable partitioning in the liquid phase. However, the use of sensitive, selective detection, such as ECD, can overcome the low concentrations of those semivolatiles in the vapor phase. This is especially useful in complex samples where many compounds may be present and may complicate the analysis if a universal detection system, such as FID, were used.

Fig. 1 shows a chromatogram for *o*-, *m*- and *p*-chlorobiphenyls in *n*-propylbenzene. The combination of high equilibration temperature and a selective detector allows the analysis of such semivolatiles by the static headspace technique.

Linearity plots for concentrations that range from 2 to 47 mg/l gave a correlation coefficient, r, of 0.99 for each isomer. The relative precision ranged between 24 and 27% at the 95% confidence level for 6, 2, and 6 mg/l concentration level of *o*-, *m*- and *p*-chlorobiphenyls, respectively.

Aqueous samples

Semivolatile solutes in an aqueous matrix represent a difficult challenge for headspace GC because the sample equilibration temperature must be below the boiling point of the matrix. In order to avoid the hazards associated with high pressure in the headspace vial, the equilibration temperature of aqueous samples should be limited to a maximum of 100°C.

To demonstrate the analysis of semivolatile compounds in an aqueous matrix, a standard solution that contained *n*-propylbenzene, 1,3,5-triethylben-

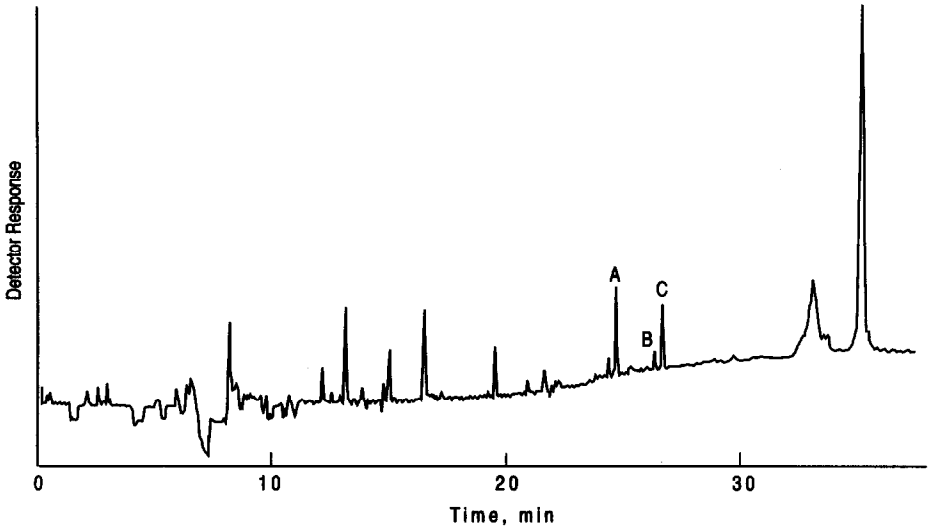

Fig. 1. Gas chromatogram of a headspace sample of a solution that contained monochlorobiphenyls. Oven temperature: 80°C for 1 min then to 280°C at 8°C/min with a 10-min final hold; column: 60 m × 0.32 mm I.D. coated with 1.0-μm Rt_x-20; detector: electron capture at 350°C; injector: split (68 ml/min), 300°C. Peak identification: A = *o*-chlorobiphenyl (6.4 mg/l), B = *m*-chlorobiphenyl (2.2 mg/l), C = *p*-chlorobiphenyl (6.6 mg/l).

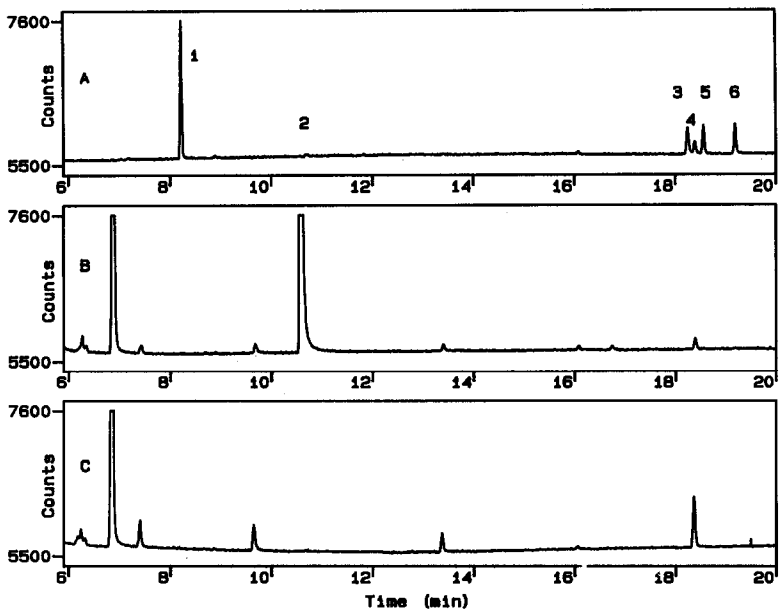

Fig. 2. (A) Gas chromatogram for semivolatiles in water. Oven temperature: 80°C for 1 min then to 230°C at 6°C/min; column: 30 m × 0.25 mm I.D. coated with 0.25-μm BD-FFAP; detector: flame ionization at 300°C; injector: split (68 ml/min), 250°C. Peak identification: 1 = 1,3,5-triethylbenzene (0.40 mg/l), 2 = dimethyl sulfoxide, 3 = biphenyl (0.23 mg/l), 4 = diphenyl ether (0.28 mg/l), 5 = 1,1-diphenylethane (0.19 mg/l), 6 = 1,2-diphenylethane (0.50 mg/l). Sample size: 5 ml. (B) Same as in (A) except solution was prepared in *n*-propylbenzene. (C) Same as (B) except that 2 ml *n*-propylbenzene was replaced with 2 ml water.

zene, biphenyl, diphenyl ether, 1,1-diphenylethane, 1,2-diphenylethane, and 2-phenylphenol was prepared in dimethyl sulfoxide and diluted with water to concentrations ranging from 13 to 693 μg/l. To contrast the behavior of these analytes in water to their behavior in an organic matrix, a solution that contained all the solutes except for *n*-propylbenzene was prepared in *n*-propylbenzene. Solute concentrations in this solution ranged from 170 to 500 μg/l. The sample prepared in *n*-propylbenzene was equilibrated at two different temperatures, 95°C and 135°C, before analysis by headspace.

Only diphenyl ether and dimethyl sulfoxide were detected at both equilibration temperatures. However, analysis of the water solution showed very good response for all the components except dimethyl sulfoxide and 2-phenylphenol. The relative precision for the determination of each of these components (*i.e.*, all except dimethyl sulfoxide and 2-phenylphenol) at a concentration of 200 μg/l ranged from 8.6 to 12.9% at the 95% confidence level. In a separate experiment the detection limit for 2-phenylphenol was found to be 3.4 mg/l with a signal-to-noise ratio (*S/N*) of 3. Thus, the conditions reported here were not suitable for the determination of sub mg/l concentrations of 2-phenylphenol.

The difference in responses of dimethyl sulfoxide and diphenyl ether is related to the difference in partition coefficients of those solutes between *n*-propylbenzene and water. Due to the different interaction and partition of the solutes in the different solvents, the response of certain compounds will be more favorable in one solvent *versus* another. Addition of water to the *n*-propylbenzene solution enhanced the response of diphenyl ether but decreased the response of dimethyl sulfoxide which is more soluble in water than is diphenyl ether. Representative chromatograms that demonstrate the difference in responses are shown in Fig. 2.

The importance of the matrix effect described above is clearly illustrated in the determination of phenol. Determination of μg/l levels of phenol by headspace analysis under the conditions described above cannot be achieved in an aqueous matrix because of the favorable partitioning into the water phase. However, addition of an immiscible solvent, such as *n*-propylbenzene, in which phenol has considerable partitioning, enhances the sensitivity tremendously. Fig. 3 shows a comparison of chromatograms obtained for 5 μg/l phenol in water. Fig. 3A is for a water blank. Fig. 3B, C, and D show the enhancement of the response of phenol due to the addition of 0-, 1- and 2-ml aliquots of *n*-propylbenzene. Several experiments were performed to determine how changes in the relative volumes of water, *n*-propylbenzene, and gas phase would affect the analysis. In all cases, the addition of *n*-propylbenzene improved the sensitivity of the analysis. This sensitivity enhancement cannot be explained by favorable partitioning of the solute since phenol was found to partition almost equally between the two solvents. The addition of a non-electrolyte, *n*-propylbenzene, increases the activity coefficient of phenol. This increases the vapor pressure of phenol which enhances the sensitivity of the analysis.

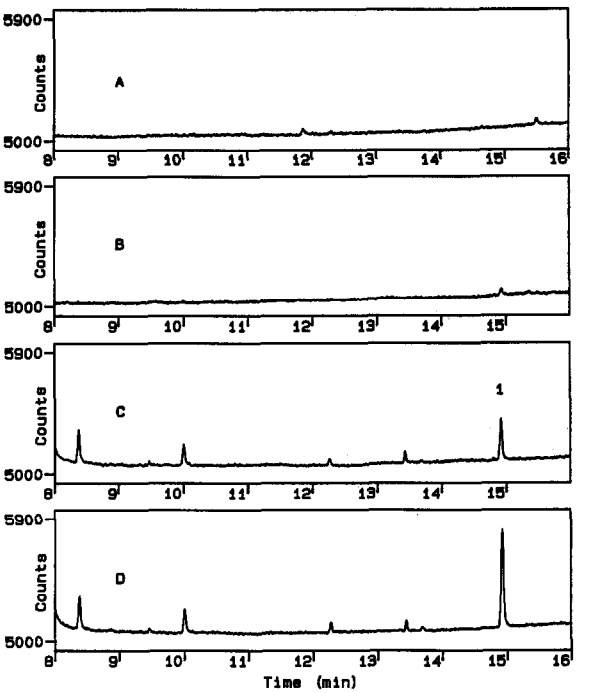

Fig. 3. Gas chromatograms of phenol in water. (A) Water blank; (B) sample size: 5 ml water solution containing 5 μg/l phenol; (C) sample size: 4 ml water solution + 1 ml *n*-propylbenzene; (D) same as (C) but sample size 3 ml water + 2 ml *n*-propylbenzene. Peak identification: 1 = phenol. Oven temperature: 70°C for 3 min then to 210°C at 12°C/min. Other conditions are same as in Fig. 3.

Carry-over effects were studied for non-aqueous and aqueous analysis. A solvent blank run was

analyzed after each sample. No interference or carry-over was noticed when this procedure was practiced.

CONCLUSIONS

The range of compounds that can be determined by static headspace GC has been extended to include semivolatile materials with boiling points as high as 291°C. High equilibration temperatures and matrix modifiers were used to increase the vapor concentration of semivolatile solutes in aqueous and organic matrices of moderate volatility. A selective detector can be used to enhance the response of the analytes relative to other matrix components. Sub mg/l detection levels were demonstrated for some of the semivolatile solutes.

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