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Note

Determination of dimethyl sulfate in air by reversed-phase liquid chromatography

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The toxicity of dimethyl sulfate has been recognized for years, and prior to 1973, a threshold limit value (TLV) of 1 ppm was assigned by the American Conference of Government Industrial Hygienists (ACGIH). Evidence obtained in 1966 and subsequent years regarding the carcinogenic action of dimethyl sulfate in animals led to the recommendation in 1973 of a tentative change in the TLV to 0.01 ppm. This value was not accepted after the two-year trial period ended, but instead the current ceiling limit of 0.1 ppm was adopted[1]. In the G.F.R., still a limit of 0.01 ppm is used.

The determination of dimethyl sulfate in air at the required level obviously requires a very sensitive method of analysis. A spectrophotometric method sensitive to approximately 40 ppb* has been reported[2], but it requires sampling with an impinger containing pyridine, making it inconvenient for personal monitoring. A procedure involving preconcentration of the sample on an organic adsorber followed by analysis on a gas chromatograph–mass spectrometer system has reached a detection limit of 1 ppb with a sample size of only 1 l[3,4]. While this represents the limit of detectability reported to date, it requires the use of elaborate and expensive apparatus. At the lower levels, the procedure also requires strict attention to such details as precleaning of the adsorption tubes and deactivation of glass surfaces. The method of analysis recommended by a supplier of dimethyl sulfate involves sampling with a silica gel adsorption tube, reaction of the trapped dimethyl sulfate with sodium *p*-nitrophenoxide in acetone solution, and determination of the resulting *p*-nitroanisole by gas chromatography with electron-capture detection[5]. This method also gives ppb sensitivity, but it suffers from several disadvantages. A long period of heating at the end of each chromatographic run is necessary to clear the interference from the excess derivatizing agent. In addition, the sensitivity is limited by the presence of several interfering peaks. A variation on this procedure has also been reported[6], using thin-layer chromatography for estimation of the *p*-nitroanisole. The present work was carried out with the aim of improving the utility of this approach for routine use in monitoring of the workplace air.

* In this article, the American billion (10^9) is meant.

EXPERIMENTAL

Materials

Dimethyl sulfate was purchased from Eastman Kodak. Sodium *p*-nitrophenoxide was purchased from Eastman and was dried in a vacuum oven overnight at 100°C before use. Diethyl ether, methanol, and acetone were analytical grade.

Derivatization solution

Approximately 2 g of dried sodium *p*-nitrophenoxide was stirred with 50 ml acetone until the solution was saturated. The solids were allowed to settle, and the supernatant liquid was decanted for use.

Instrumentation

Liquid chromatography was carried out with a Spectra-Physics 8000B liquid chromatograph. Quantitation was done by peak area integration with the SP-4000 data system. A Valco injection valve with a 10-μl loop was used for injection, and a Spectra-Physics 8400 variable-wavelength detector was set at 305 nm. The separations were carried out on a 10-μm Alltech C_8 column, 25 cm length. The analytical conditions were: solvent, methanol–water (55:45); flow-rate, 1 ml/min; detector sensitivity, 0.02 a.u.f.s.; analysis time, 20 min.

Preparation and analysis of samples

A metered sample of air was drawn over a NIOSH-type small silica gel sampling tube, with two separated sections containing 150 and 75 mg of silica gel, respectively. The front and back sections were added to separate 10-ml volumetric flasks. To each flask was added 2 ml derivatization solution and approximately 100 mg dried sodium *p*-nitrophenoxide. The flasks were allowed to stand at room temperature for 2 h with occasional shaking. To each flask was added 7.5 ml 1 *N* sodium hydroxide and 1 ml of the internal standard (*p*-nitrophenetole) solution in diethyl ether (9 mg/l). The flasks were stoppered and shaken, and the layers were allowed to separate. A portion of the ether layer was removed for liquid chromatographic analysis. The solution was found to be stable indefinitely following the phase separation, provided that it was protected from evaporation. However, extended standing in contact with the aqueous phase prior to phase separation generated interfering impurities by oxidation of the derivatization solution.

Determination of recovery efficiency

A solution of dimethyl sulfate in dry hexane (0.5 mg/ml) was injected onto the front portion of silica gel on each of three tubes for each level tested. The tubes were allowed to equilibrate for 1 h, and desorption and analysis were carried out in the usual manner.

RESULTS AND DISCUSSION

Since the problems encountered with the electron-capture gas chromatographic method of analysis were due primarily to the presence of excess derivatizing reagent, attempts were made initially to remove this excess. Washing of an organic

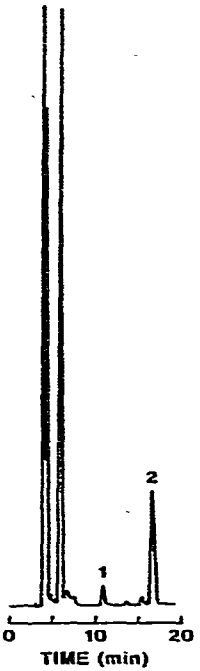

Fig. 1. Chromatogram of *p*-nitroanisole from derivatization of 1 μg dimethyl sulfate adsorbed on silica gel. Alltech C_8 column (5 μm, 25 cm). Mobile phase: methanol–water (55:45), flow-rate 1 ml/min. Peaks: 1 = *p*-nitroanisole; 2 = *p*-nitrophenetole (internal standard).

solution of the product with aqueous sodium hydroxide was effective in removing the sodium *p*-nitrophenoxide and thus eliminating the long period of heating required at the end of each run. However, small interfering peaks remained, one near the retention time of *p*-nitroanisole. Aside from the interference problem, the sensitivity and collection efficiency of the method were quite satisfactory. A possible solution to the problem would be to change the method for separation and detection of the *p*-nitroanisole. The extremely high UV absorbance of this derivative suggested the possibility of using liquid chromatography with a UV detector for the measurement. We were encouraged in this approach by the high sensitivity reported for use of this derivative with thin-layer chromatography for analysis of dimethyl sulfate in air down to 0.01 ppm (ref. 6).

Only minor modifications in the derivatization method were required to adapt the analysis to liquid chromatography. The volume of derivatizing reagent was reduced from 5 to 2 ml, and at the end of the reaction, the solution was diluted with 1 *N* sodium hydroxide and extracted with diethyl ether containing *p*-nitrophenetole as an internal standard. The separation could be carried out conveniently by reversed-phase chromatography on a C_8 column eluted with either 55% methanol or 40% acetonitrile in water. The UV detector was set at 305 nm, the absorbance maximum for *p*-nitroanisole. As seen by the chromatogram in Fig. 1, the detection limit of the method is below 1 μg of dimethyl sulfate per sample. The procedure gave a linear

TABLE I

RECOVERY OF DIMETHYL SULFATE INJECTED ON SILICA GEL TUBES

Amount injected (μg)	*Recovery (%)*
1	103
2.5	97
5	97

standard curve in the concentration range corresponding to 1–25 μg dimethyl sulfate per tube.

The sample capacity for an adsorption tube was found to be at least 10 l of air. With this volume, the detection limit of approximately 0.5 μg corresponds to 0.01 ppm. If necessary, the limit could be pushed lower by concentration of the solution before injection or by use of a larger injector loop. The recovery of dimethyl sulfate from the tubes was studied by direct injection of aliquots of a hexane solution and analysis in the usual way after 1 h of equilibration. As seen in Table I, the recovery was not significantly different from 100% at any level.

The procedure as modified offers a relatively simple way to analyze dimethyl sulfate in air at levels well below the current TLV. The relative standard deviation of the method for six determinations at the 2 μg/tube level was 2%.

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