MDHS

Methods for the Determination of Hazardous Substances
Health and Safety Laboratory

HSE
Health & Safety Executive

89

Dimethyl sulphate and diethyl sulphate in air

Laboratory method using thermal desorption, gas chromatography-mass spectrometry

March 1998

INTRODUCTION

Requirements of the COSHH Regulations

1 The Control of Substances Hazardous to Health (COSHH) Regulations 1994[1] are designed to ensure that the exposure of people at work to substances which could cause health damage is either prevented, or where that is not reasonably practicable, adequately controlled. Employers are required to make an assessment of the health risk created by such work, and to prevent or control exposure to the substances involved. The COSHH regulations also require that persons who may be exposed to substances hazardous to health receive suitable and sufficient information, instruction and training. Employers must ensure that their responsibilities under the COSHH Regulations are fulfilled before allowing employees to undertake any procedure described in this MDHS.[1]

Properties and uses

2 Dimethyl sulphate, DMS, is a clear, colourless oily liquid with a very slight odour. It is soluble in water and most organic solvents. Dimethyl sulphate is used as a methylating agent in organic syntheses and the production of pharmaceuticals, and as a quaternising agent in dyestuffs manufacture.

3 Diethyl sulphate, DES, is a clear, colourless oily liquid with a slight ‘peppermint’ odour. It is sparingly soluble in water and miscible with many polar organic solvents. Diethyl sulphate is used as an ethylating agent in the dyestuffs and pharmaceuticals industries.

Health effects

4 Both the liquid and vapour forms of these dialkyl sulphates are harmful to the skin, eyes and mucous membranes. There are no warning properties (no smell or initial irritation) and the symptoms are delayed by a few hours. Under the EU Dangerous Substances Directive 67/548/EEC as amended and adapted to technical progress (as implemented in Great Britain by the Chemicals (Hazard Information and Packaging for Supply) Regulations (CHIP)[5]), they are classified as category 2 carcinogens (may cause cancer). DES is also classified as a category 2 mutagen (may cause heritable genetic damage).

Exposure

5 Both DMS and DES are used within enclosed plant and the potential for airborne exposure is thought to be minimal and limited to short periods of time. During normal operations the potential for exposure may exist during the coupling/uncoupling of road tankers, maintenance, the removal of test samples, venting and drum discharge.

Exposure limits

6 The maximum exposure limit (MEL) is at present 0.05 ppm (0.26 mg/m^3 for DMS and 0.32 mg/m^3 for DES) related to an 8 hour time weighted average (TWA) reference period.[6]

Analytical methods

7 This is not a ‘reference’ method in the strict analytical sense of the word. There are frequently several alternative methods available for the determination of a particular analyte. With the exception of a few cases, where an exposure is linked to a specific method (eg rubber fume or asbestos), the use of methods not included in the MDHS series is acceptable provided that they have been shown to have the accuracy and reliability appropriate to the application.

8 This method has been validated to demonstrate that it complies with BS EN 482 *Workplace atmospheres - General requirements for the performance of procedures for the measurement of chemical agents*.[3] If an alternative method is used it is necessary to demonstrate that it also meets these performance requirements.

SCOPE

9 This MDHS describes a method for determination of the concentration of DMS and DES in air using thermal

desorption gas chromatography-mass spectrometry. The method is suitable for sampling over the range 15 minutes to 8 hours.

10 The method covers the concentration range 0.01 ppm (0.05 mg/m^3) to 0.2 ppm (1.0 mg/m^3) for 15 minute or 8 hour sampling.

11 HSG173[2] advises employers about how they should conduct investigations into the nature, extent and control of exposure to substances hazardous to health which are present in workplace air. The objective of air monitoring is usually to determine worker exposure, and therefore the procedures described in this method are for personal sampling in the breathing zone. The method may also however be used for background or fixed location sampling.

PRINCIPLE

12 A measured volume of air is drawn through a sorbent tube containing Tenax TA. After sampling, the tube is thermally desorbed and analysed by gas chromatography. Separation is achieved using a BP-1 (or equivalent) capillary column and separated species are detected using a mass selective detector.

SAMPLING EQUIPMENT

Samplers

13 Samples should be collected onto sorbent tubes containing 200 mg Tenax TA (particle size 0.18-0.25 mm, 60-80 mesh). (Tenax is a registered trademark of the Akzo Research Co.) The sorbent tubes should be compatible with the thermal desorption apparatus to be used. The sorbent should be preconditioned by heating in an inert atmosphere at 250°C for 16 hours before packing the tubes.

Sampling pumps

14 Sampling pumps, complying with the provisions of BS EN1232,[8] with an adjustable flow rate, incorporating a flowmeter or a flow fault indicator, capable of maintaining the selected flow rate to within ±5% of the nominal value throughout the sampling period, and capable of being worn by persons without impeding normal work activity.

Flowmeter

15 Flowmeter, portable, capable of measuring the appropriate flow rate to within ±5%, and calibrated against a primary standard.[8] Flowmeters incorporated in sampling pumps are not suitable for accurate measurement of the flow rate. However, they can be useful for monitoring the performance of samplers, provided they have adequate sensitivity.

Ancillary equipment

16 Flexible plastic tubing, of a diameter suitable for making a leakproof connection from the sample to the sampling pump; belts or harnesses to which the sampling pump can be conveniently fixed, unless the pump is sufficiently small to fit into the worker’s pocket.

LABORATORY APPARATUS

Glassware

17 A selection of laboratory glassware: including beakers and volumetric flasks.

Disposable gloves

18 Disposable gloves, impermeable, to avoid the possibility of contamination from the hands and to protect them from contact with harmful substances. Nitrile rubber gloves are suitable.

Micropipettes

19 A set of adjustable positive displacement micropipettes, calibrated against a primary standard, for the preparation of calibration and sample solutions.[4]

Syringes

20 A microsyringe capable of dispensing volumes of 5 µl and 10 µl.

REAGENTS

21 During the analysis, use only reagents of a recognised analytical grade. Suitable personal protection (eg gloves and safety spectacles) should be used when handling the reagents listed below. Diethyl ether is highly flammable. Exposure by contact with skin or eyes, or by inhalation of the vapour, should be avoided, and all operations involving solvents should be carried out in the fume cupboard. Do not pipette by mouth.

Diethyl ether

22 Inhibitor-free HPLC or spectrophotometric grade diethyl ether.

Dimethyl sulphate

23 Pure (99%+) dimethyl sulphate.

Diethyl sulphate

24 Pure (99%+) diethyl sulphate.

Dimethyl/diethyl sulphate stock solution

25 Pipette 750 µl dimethyl and/or diethyl sulphate into a 100 ml volumetric flask containing diethyl ether and make up to volume with diethyl ether. The resulting stock solution is 10 µg/µl DMS or 8.8 µg/µl DES.

Laboratory detergent solution

26 A laboratory grade detergent suitable for cleaning of labware, diluted with water according to the manufacturer’s instructions.

Gases

27 Air, clean, dry, compressed and regulated for supply to the automated thermal desorption apparatus.

28 Helium, clean, compressed and regulated for supply to the gas chromatograph as the carrier gas.

SAMPLING

Preparation of sampling equipment

29 Recondition the Tenax tubes before use by heating slowly under inert carrier gas to 250°C and maintaining that temperature for 10 minutes. Cap the clean tubes.

30 Connect each Tenax tube to a sampling pump using plastic tubing ensuring that no leaks can occur. Switch on the pump, attach the calibrated flowmeter to the sampling head so that it measures the flow through the tube, and set the appropriate flow rate with an accuracy of ±5%. The flow rate through the Tenax tubes should be 200 ml/min. Switch off the pump and cap the tube to prevent contamination during transport to the sampling position.

Collection of samples

31 Fix the Tenax tube to the worker, on the lapel and as close to the mouth and nose as possible.[3] Then place the sampling pump in a convenient pocket or attach it to the worker in a manner that causes the minimum inconvenience, eg to a belt around the waist. When ready to begin sampling, remove the protective cap from the sampling tube and switch on the pump. Record the time at the start of the sampling period, and if the pump is equipped with an elapsed time indicator, ensure that this is set to zero.

32 Monitor the performance of the sample periodically, at least every two hours. Measure the flow rate with the calibrated flowmeter and record the measured value. Terminate sampling and consider the sample to be invalid if the flow rate is not maintained to within ±5% of the nominal value throughout the sampling period.

33 Regular observation of the flow fault indicator is an acceptable means of ensuring that the flow rate of flow-stabilised pumps is maintained satisfactorily, provided that the flow fault indicator indicates malfunction when the flow rate is outside ±5% of the nominal value.

34 At the end of the sampling period, measure the flow rate with an accuracy of ±5% using the calibrated flow-meter, switch off the sampling pump, and record the flow rate and the time. Also observe the reading on the elapsed time indicator, where fitted, and consider the sample to be invalid if the reading on the elapsed time indicator and the timed interval between switching on and switching off the sampling pump do not agree to within ±5%, since this may suggest that the sampling pump has not been operating throughout the sampling period. Disconnect the tube from the sampling pump and cap the ends of the tube.

35 Carefully record the sample identity and all relevant sampling data. Calculate the mean flow rate by averaging the flow rate measurements throughout the sampling period and calculate the volume of air sampled, in litres, by multiplying the flow rate in litres per minute by the sampling time in minutes.

36 With each batch of ten samples, submit for analysis at least two unused Tenax tubes from the same lot of tubes used for sample collection. Subject these blank tubes to the same handling procedure as the samples, but draw no air through them.

Transportation

37 Ensure that the Tenax tubes are securely capped for transportation.

ANALYSIS

38 Wear disposable gloves during analysis to reduce the possibility of contamination and to protect the hands from harmful solvents/reagents.

Cleaning of glassware

39 Before use, clean all glassware to remove any residual grease or chemicals. Firstly soak overnight in laboratory detergent solution and then rinse thoroughly with water.

Preparation of calibration standards

40 Prepare at least six calibration standard solutions to cover the range 30 to 10 000 ng/µl by adding by pipette the appropriate volume of stock solution (paragraph 25) to separate, labelled volumetric flasks. Dilute to the mark with diethyl ether, stopper and mix thoroughly.

41 Tenax tubes are spiked with 5 or 10 µl of the calibration solution of the appropriate dialkyl sulphate to obtain tubes in the range 2.4 µg to 48 µg to cover 0.1 to 2 times the exposure limit (0.05 ppm) for 8 hour samples. Prepare a fresh set of calibration standards with each batch of samples.

Thermal desorption

42 Apparatus for the two-stage thermal desorption of the sorbent tubes and transfer of the desorbed vapours via an inert gas flow into a gas chromatograph will be required.

43 Desorption conditions should be chosen such that desorption from the sample tube is complete, and no sample loss occurs. Typical parameters are:

Desorb temp	250°C
Desorb time	5 min
Transfer line	200°C
Cold trap low	-30°C
Cold trap high	250°C
Trap hold time	10 min

44 The split valve is placed at the chromatograph end of the transfer line. A typical split ratio is 100:1.

Chromatography

45 The gas chromatograph conditions are shown in Table 1. Gas flow valves should be capable of delivering the helium to the capillary column at the required flow rate/column pressure (±5%). Other GC columns may be suitable but have not been laboratory tested. An electronic/computer-controlled data collection system is recommended.

Table 1 Chromatographic conditions

Column dimensions	60 m x 0.25 mm
Oven temperature 2 (T_2)	120°C
Phase/thickness	BP-1; 0.25 µm
Time at T_2	0 min
Carrier gas/pressure	Helium; 20 psi
Oven ramp 2	20°C min^{-1}
Initial oven temperature (T_1)	35°C
Oven temperature 3 (T_3)	200°C
Time at T_1	0 min
Time at T_3	0 min
Oven ramp 1	5°C min^{-1}
Total run time	21 min

Mass spectrometry

46 A mass selective detector is used in selective ion monitoring mode.

47 For analysis of DMS the following ions are measured: 66, 95, 96, 125 (0-14 min).

48 For analysis of DES the following ions are measured: 59, 99, 111, 125, 139 (14-21 min).

System calibration

49 Run the calibration standards in order of increasing concentration. Determine the chromatographic peak areas for the required alkyl sulphate peak(s). Under the conditions described, the retention times are as follows:

DMS	9.7 min
DES	14.6 min

50 Check the calibration graph by analysing a Tenax tube spiked with an independently prepared control solution. If the result does not agree with the previous calibration line within 10%, prepare fresh standards and carry out a new calibration.

51 From the pipetted volumes and volumes spiked onto each Tenax tube, calculate the dimethyl and/or diethyl sulphate content of each standard. Plot the concentration against the peak area values, and determine the best-fit line.

Samples

52 Run the sample and blank Tenax tubes. For each sample determine the chromatographic peak areas for the dimethyl and/or diethyl sulphate and use the calibration graph to relate this to the concentration on the sample tube, C_s, in µg.

CALCULATION OF RESULTS

Volume of air sample

53 Calculate the volume, V_s, in litres, of each air sample.

Concentration of dialkyl sulphate in air

54 Calculate the dimethyl/diethyl sulphate concentration in each air sample, ρ, in micrograms per cubic metre (µg m^{-3}), using the equation:

$$\rho = C_s / V_s \times 100$$

METHOD PERFORMANCE

Detection limits

55 The qualitative and quantitative detection limits for DMS and DES, defined as the concentration which gives a signal to noise ratio of 3:1 and 10:1 respectively, are typically around 4 ng and 13 ng per sample respectively. For a 15 minute sample taken at a flow rate of 200 ml/minute, these figures correspond to qualitative and quantitative detection limits of 1.5 µg m^{-3} (0.3 ppb) and 4.3 µg m^{-3} (0.9 ppb) respectively.

Overall uncertainty

56 The overall uncertainty for a measuring procedure is defined in BS EN 482 as 'the quantity used to characterise as a whole the uncertainty of the result given by a measuring procedure', and is quoted as a percentage combining bias and precision using the following equation:[3]

$$\text{Overall uncertainty} = \frac{\left| \bar{x} - x_{ref} \right| + 2s}{x_{ref}} \times 100$$

where :

$\bar{x}$	is the mean value of results of a number *n* of repeated measurements;
x_{ref}	is the true or accepted reference value of concentration;
s	is the standard deviation of measurements.

57 An additional 5% is usually added to the overall uncertainty percentage calculated using the equation in paragraph 12, to allow for the variability of the pump flow rate. The performance requirements quoted in BS EN 482 for overall uncertainty are ≤50% for samples in the range 0.1 to 0.5 LV and ≤30% for samples in the range 0.5 to 2.0 LV (LV = Limit Value).[3]

58 The overall uncertainty of the method was determined to be less than ±20% for samples in the range 0.1 to 0.5 LV and less than ±14% for samples in the range 0.5 to 2.0 LV.

Interferences

59 No interferences were identified.

Stability

60 Sample stability was investigated by spiking tubes with a solution of dialkyl sulphate and determining the analytical recovery after 14 days. The results indicated that samples are stable on Tenax tubes.

QUALITY CONTROL MEASURES

61 An appropriate level of quality control should be employed when using this method. Analytical quality requirements, guidance on the establishment of a quality assurance programme and details of internal quality control and external quality assessment schemes are fully described in MDHS 71.[7]

ADVICE

Advice on this method and the equipment used can be obtained from the Health and Safety Executive, Health and Safety Laboratory, Broad Lane, Sheffield S3 7HQ (telephone 0114 2892000, fax 0114 2892500, email info@hsl.gov.uk).

The Health and Safety Executive wishes, wherever possible, to improve the methods described in this series. Any comments that might lead to improvements would therefore be welcome and should be sent to the above address.

REFERENCES

1 Health and safety Executive *General COSHH ACOP (Control of Substances Hazardous to Health) and Carcinogens ACOP (Control of Carcinogenic Substances) and Biological Agents ACOP (Control of Biological Agents): Control of Substances Hazardous to Health Regulations 1994: Approved Codes of Practice* (6th edition) HSE Books 1997 ISBN 0 7176 1308 9[*]

2 Health and Safety Executive *Monitoring strategies for toxic substances* HSG173 HSE Books 1997 ISBN 0 7176 1411 5[*]

3 British Standards Institution *Workplace atmospheres - General requirements for the performance of procedures for the measurement of chemical agents* European Standard BS EN 482 BSI 1994 ISBN 0 580 236447*

4 British Standards Institution *Piston and/or plunger operated volumetric apparatus (POVA) Part 3: Methods of test* BS 7653-3 BSI 1993 ISBN 0 580 0221253[*]

5 *Chemicals (Hazard Information and Packaging for Supply) Regulations 1994* (SI 1994/3247)[*] HMSO ISBN 0 11 043877 9 as amended by the *Chemicals (Hazard Information and Packaging for Supply) (Amendment) Regulations 1996* (CHIP 96) SI 1996/1092 HMSO ISBN 0 11 054570 2 and *(Amendment) Regulations* 1997 (CHIP 97) SI 1997/1460 ISBN 0 11 063750 X

6 Health and Safety Executive *Occupational Exposure Limits* EH40/98 TSO 1998 ISBN 0 7176 1473 3[*]

7 Health and Safety Executive *Analytical quality in workplace air monitoring* MDHS 71 HSE Books 1991 ISBN 0 11 885976 5

8 Health and Safety Executive *General methods for the gravimetric determination of respirable and total inhalable dust* MDHS 14/2 HSE Books 1997 ISBN 0 7176 1295 3[*]

[*] Amendments may be made occasionally and readers should ensure that they are using the current edition.

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59 Manmade mineral fibres
60 Mixed hydrocarbons
61 Total hexavalent chromium compounds in air *colorimetric*
62 Aromatic carboxylic acid anhydrides
63 Butadiene *diffusive/thermal desorption/GC*
64 Toluene *charcoal diffusive/solvent desorption/GC*
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