GLUTARALDEHYDE 2531

$O=CH(CH_2)_3CH=O$ MW: 100.12 CAS: 111-30-8 RTECS: MA2450000

METHOD: 2531, Issue 3 **EVALUATION: FULL** **Issue 1: 15 May 1989**
Issue 3: 20 January 2016

OSHA: No PEL
NIOSH: C 0.2 ppm
(1 ppm = 4.09 mg/m³ @ NTP)

PROPERTIES: Oil; d 0.72 g/mL @ 20 °C; BP 188 °C; MP −14 °C; VP 2.2 kPa (17 mmHg) @ 20 °C

SYNONYMS: Glutaric dialdehyde; 1,5-pentanedial

SAMPLING

SAMPLER: SOLID SORBENT TUBE (10% 2-(hydroxymethyl)piperidine on XAD-2, 120 mg/60 mg)

FLOW RATE: 0.01 L/min to 0.08 L/min, or 0.2 L/min for 20 min

VOL-MIN: 4 L @ 0.2 ppm
-MAX: 39 L

SHIPMENT: Routine

SAMPLE STABILITY: At least 5 weeks @ 25 °C [1]

FIELD BLANKS: 2 to 10 field blanks per set

MEDIA BLANKS: 10 per set

ACCURACY

RANGE STUDIED: 0.8 mg/m³ to 9 mg/m³ [1] (22 L samples)

BIAS: 0.3%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.087 [1]

ACCURACY: ±17.4%

MEASUREMENT

TECHNIQUE: GAS CHROMATOGRAPHY, FID

ANALYTE: Oxazolidine derivative of glutaraldehyde

DESORPTION: 2 mL toluene; 60 min ultrasonic

INJECTION: 1 µL splitless; split vent time 30 s

TEMPERATURE-INJECTOR: 250 °C
-DETECTOR: 280 °C
-COLUMN: 1 min @ 70 °C; 20 °C/min; hold 2 min @ 290 °C

CARRIER GAS: Helium, 0.5 mL/min; makeup 2.9 mL/min

COLUMN: Capillary, 10 m × 0.25 mm, 5% phenyl, 95% methyl polysiloxane (US Pharmacopeia (USP) phase G27)

CALIBRATION: Standard glutaraldehyde solutions spiked on sorbent

RANGE: 3 µg to 180 µg per sample [1]

ESTIMATED LOD: 1 µg per sample [2]

PRECISION ($\bar{S}_r$): 0.093 [2] @ 5 µg to 50 µg per sample [1]

APPLICABILITY: The working range is 0.03 ppm to 2 ppm (0.14 mg/m³ to 8 mg/m³) for a 22 L air sample; the method is sensitive enough for ceiling determinations. The method is suitable for the simultaneous determination of furfural and glutaraldehyde.

INTERFERENCES: None have been observed.

OTHER METHODS: This is a new method. A wide-bore 10 m capillary column is an alternate chromatographic column.

REAGENTS:

1. Toluene,* chromatographic quality.
2. 2-(Hydroxymethyl)piperidine. Recrystallize several times from isooctane until there is one major peak (>95% of area) by GC analysis. Store in desiccator.
3. XAD-2 resin.
4. Glutaraldehyde,* 250 g/L solution in water.
5. Glutaraldehyde stock solution, 10 µg/µL (see Appendix A).
6. Glutaraldehyde oxazolidine (see Appendix B) stock solution, 2 mg/mL. Add 20 mg to toluene and dilute to 10 mL.
7. Sulfuric acid,* 0.01 mol/L.
8. Sodium hydroxide,* 0.01 mol/L.
9. Sodium sulfite, 1.13 mol/L. Dissolve 14.2 g reagent grade sodium sulfite in deionized, distilled water and dilute to 100 mL. Prepare fresh immediately before use.
10. Water, deionized, then distilled.
11. Hydrogen,* prepurified.
12. Air, filtered.
13. Helium,* prepurified.
14. Magnesium sulfate.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

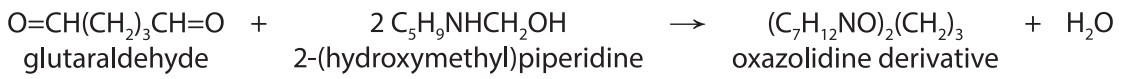
1. Sampler: resin-filled sampling tube; glass tube, 10 cm long, 6-mm OD, 4-mm ID, flame-sealed ends and plastic caps, containing two sections of 40/60 mesh 2-(hydroxymethyl)piperidine-coated XAD-2 (see Appendix C). Sorbent sections are retained and separated by small plugs of silanized glass wool. Pressure drop across the tube at 0.10 L/min airflow must be less than 0.76 kPa (5.7 mmHg). Tubes are commercially available.
2. Personal sampling pump, 0.01 L/min to 0.08 L/min, with flexible connecting tubing.
3. Gas chromatograph, flame ionization detector, integrator, and column (page 2531-1).
4. Ultrasonic bath.
5. Vials, glass, 4 mL, with septum and plastic screw caps.
6. Flasks, volumetric, 10 mL, 25 mL, and 50 mL.
7. Pipets, TD, 1 mL, 2 mL, and 10 mL with pipet bulb.
8. Pipets, disposable, 2 mL.
9. Syringes, 10 µL (readable to 0.1 µL), 25 µL, and 50 µL.
10. File.
11. Beakers, 50 mL.
12. pH meter.
13. Magnetic stirrer.
14. Burets, 50 mL.
15. Flasks, round-bottomed, 100 mL.
16. Soxhlet extraction apparatus.
17. Vacuum oven.
18. Distillation apparatus.

SPECIAL PRECAUTIONS: Glutaraldehyde can irritate the mucous membranes and act on the central nervous system [3]. Toluene is flammable. Sulfuric acid is highly corrosive and sodium hydroxide is caustic. All work with these compounds should be performed in a well-ventilated hood. Use proper protective clothing including gloves, safety glasses, and laboratory coat. Users must be familiar with the proper use of flammable and nonflammable gases, cylinders, and regulators.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Break ends of the sampler immediately before sampling. Attach sampler to personal sampling pump with flexible tubing.
3. Sample at an accurately know flow rate between 0.01 and 0.08 L/min for a total sample size of 4 L to 39 L. For ceiling determination, sample at 0.2 L/min for 20 min.

   NOTE: The aldehyde reacts with the 2-(hydroxymethyl)piperidine to form an oxazolidine derivative in the sorbent bed during sampling (see equation below). Sampling rate is limited by the speed of this reaction. Sampling rates above 0.1 L/min for extended periods may cause breakthrough owing to incomplete reaction, possibly invalidating the sample.



SAMPLE PREPARATION:

4. Score each sampler with a file in back of the back sorbent section.
5. Break sampler at score line. Remove and place back glass wool plug and back sorbent section in a vial.
6. Transfer front section with remaining glass wool plugs to a second vial.
7. Add 2.0 mL toluene to each vial. Screw cap tightly onto each vial.
8. Agitate vials in an ultrasonic bath for 60 min.
   NOTE: Desorption efficiency is affected by the amount of time that the vials are allowed to spend in the ultrasonic bath. A minimum of 60 min residence time in the ultrasonic bath is required to ensure adequate desorption.

CALIBRATION AND QUALITY CONTROL:

9. Prepare glutaraldehyde oxazolidine standard solutions.
   a. Add known amounts of glutaraldehyde oxazolidine stock solution (equivalent to the range of the samples) to toluene in 10 mL volumetric flasks and dilute to the mark.
   b. Analyze (steps 12 and 13) with samples and blanks for qualitative identification of derivative peaks.
10. Calibrate daily with at least five working standards covering the range of the samples.
    a. Weigh 120 mg portions of unused sorbent from media blanks into vials.
    b. Add aliquiots of glutaraldehyde stock solution or dilutions thereof. Cap vials and allow them to stand overnight at room temperature.
    c. Desorb (steps 7 and 8) and analyze (steps 12 and 13) with samples and blanks.
    d. Prepare calibration graph (combined peak area vs. µg glutaraldehyde).
       NOTE: Because the working standards are prepared on media blanks, no additional blank correction or desorption efficiency correction is necessary. Check desorption efficiency occasionally in the range of interest (see Appendix D).
11. Analyze three quality control blind spikes to ensure that the calibration graph is in control.

MEASUREMENT:

12. Set gas chromatograph to manufacturer's recommendations and to conditions given on page 2531-1. Inject 1 µL sample aliquot.
    NOTE: If the amount of oxazolidine in the aliquot exceeds the capacity of the column, dilute the sample with toluene and apply the appropriate dilution factor in calculations.
13. Measure total peak area of the two analyte peaks.
    NOTE: On the recommended column, the oxazolidine derivative gives two peaks, since the diastereoisomers are resolved; t_r for the glutaraldehyde derivative = 9.4 min and 9.7 min; t_r for 2-(hydroxymethyl)piperidine = 2.6 min for these conditions.

CALCULATIONS:

14. Determine the mass, µg, of glutaraldehyde found in the sample front (W_f) and back (W_b) sorbent sections.
    NOTE: If $W_f > W_b / 10$, report breakthrough and possible sample loss.
15. Calculate concentration, C, of glutaraldehyde in the air volume sampled, V (L):

$$C = \frac{W_f + W_b}{V}, \text{ µg/L or mg/m}^3.$$

EVALUATION OF METHOD:

Atmospheres were generated by injection of an aqueous solution of glutaraldehyde by syringe pump into a heated block injector and flash vaporization into a stream of air flowing at a fixed rate [1]. Relative humidity during generation was controlled at 80% ±5%. The generator and sampling manifold systems have been described previously [4]. Concentration of glutaraldehyde vapor was independently verified by the 2,4-dinitrophenylhydrazine procedure of Lipari and Swarin [5]. No bias with dynamically-generated atmospheres was observed with the method over the range 0.8 mg/m^3 to 8 mg/m^3 using 22 L air samples. Desorption efficiencies on statically-spiked samples averaged 87% in the ranges 5 µg to 50 µg per sample. Recovery averaged 1.10 with S_r = 0.043 for twelve tubes spiked with 67 µg glutaraldehyde [6].

REFERENCES:

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APPENDIX

A. Preparation and Standardization of Glutaraldehyde Stock Solution (about 10 µg/µL)

Dilute 1 mL of 250 g/L aqueous glutaraldehyde to 25 mL with distilled, deionized water to make the glutaraldehyde stock solution. Put 10.0 mL of 1.13 mol/L sodium sulfite solution in a beaker and stir magnetically. Adjust pH to between 8.5 and 10 with base or acid. Record the pH. Add 1.0 mL glutaraldehyde stock solution. The pH should be about 12. Titrate the solution back to its original pH with 0.01 mol/L sulfuric acid. If the endpoint pH is overrun, back-titrate to the endpoint with 0.01 mol/L sodium hydroxide. Calculate the concentration, C_s, of the glutaraldehyde stock solution:

$$C_s = \frac{(C_a V_a - C_b V_b) \times 50.06}{V_s}, \text{ µg/µL},$$

where: 50.06 = MW of glutaraldehyde divided by 2,
C_a = concentration (mol/L) of sulfuric acid,
V_a = volume of sulfuric acid (mL) used for titration,
C_b = concentration (mol/L) of sodium hydroxide,
V_b = volume of sulfuric acid (mL) used for titration, and
V_s = volume of glutaraldehyde stock solution (1.0 mL).

B. Synthesis of Glutaraldehyde Oxazolidine

Place a solution of purified 2-(hydroxymethyl)piperidine (0.57 g, 5 mmol) in 10 mL of toluene in a 50 mL round-bottomed flask. Several 2 mL portions of toluene can be used to rinse residual 2-(hydroxymethyl) piperidine from the container used for weighing. Add magnesium sulfate (2.5 g) to the round-bottomed flask to dry the glutaraldehyde solution as it is added and to remove the water which forms during the reaction. Add a solution of 1 mL of 250 g/L aqueous glutaraldehyde (0.25 g, 2.5 mmol) in 10 mL of toluene to the 2-(hydroxymethyl)piperidine solution dropwise with stirring over 1 h. Stir the solution overnight, then filter to remove the magnesium sulfate. Remove the toluene from the solution at reduced pressure by rotary evaporation. The product is a yellow viscous oil, about 90% to 95% pure.
NOTE: Exact amounts of reagent are required for this synthesis since excess glutaraldehyde can cause appreciable formation of the mono-oxazolidine derivative of glutaraldehyde.

C. Sorbent Preparation (optional if commercially prepared tubes are used)

Extract XAD-2 sorbent 4 h in a Soxhlet extractor with a mixture of equal volumes of acetone and methylene chloride. Replace with fresh solvent and repeat. Vacuum dry overnight. Add 1 g purified 2-(hydroxymethyl)piperidine in 50 mL toluene for each 9 g extracted XAD-2 sorbent. Allow this mixture to stand 1 h with occasional swirling. Remove the solvent by rotary evaporation at 37 °C and dry at 0.13 kPa (1 mmHg) at ambient temperature for approximately 1 h. To determine the amount of background for each batch, extract several 120 mg portions of the coated sorbent with toluene and analyze (steps 7, 8, 9, 10, 11, 12, and 13). No blank peak is expected for glutaraldehyde.

D. Desorption Efficiency

The determination of desorption efficiency (DE) is not necessary when using the calibration procedure in step 10. If desired, the following procedure can be used to determine DE:

1. Prepare and analyze a set of glutaraldehyde oxazolidine standard solutions (step 9.a) and a set of working standards (step 10), including media blanks.
2. Treating the working standards as unknowns, read the mass (µg) of oxazolidine found in each working standard (W), and in the average media blank (B).
3. Using the mass of glutaraldehyde, µg, spiked onto the working standard (W_o) and the stoichiometric conversion factor between glutaraldehyde and glutaraldehyde oxazolidine (2.94), calculate the desorption efficiency $(W - B) / (W_o \times 2.94)$.
4. Prepare a graph of DE vs. µg glutaraldehyde recovered per sample $(W - B) / 2.94$.