$CH_3OC_6H_4NH_2$ MW: 123.16 CAS: (o-) 90-04-0 (p-) 104-94-9 RTECS: (o-) BZ5410000 (p-) BZ5450000

METHOD: 2514, Issue 2 **EVALUATION: FULL** **Issue 1: 15 May 1985** **Issue 2: 15 August 1994**

OSHA : 0.5 mg/m^3 (skin)
NIOSH: 0.5 mg/m^3 (skin); o-isomer suspect carcinogen
ACGIH: 0.1 ppm (skin) (0.5 mg/m^3)
(1 ppm = 5.03 mg/m^3 @ NTP)

PROPERTIES: o-isomer: liquid; d 1.092 g/mL @ 15 °C; BP 225 °C; MP 5 °C; VP 0.1 mm Hg @ 27 °C
p-isomer: solid; MP 57 °C; BP 246 °C

SYNONYMS: o-isomer: 2-aminoanisole; 2-methoxybenzenamine; o-methoxyaniline
p-isomer: 4-aminoanisole; 4-methoxybenzenamine; p-methoxyaniline

SAMPLING

SAMPLER: SOLID SORBENT TUBE (XAD-2, 150 mg/75 mg)

FLOW RATE: 0.5 to 1.0 L/min

VOL-MIN: 24 L
-MAX: 320 L

SHIPMENT: routine

SAMPLE STABILITY: at least 1 week @ 25 °C

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.13 to 0.58 mg/m^3 [1] (225-L samples)

BIAS: 0.12%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.068 [1]

ACCURACY: ± 13.3%

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTE: o-anisidine and p-anisidine

DESORPTION: 5 mL methanol; stand 15 min

INJECTION VOLUME: 10 µL

MOBILE PHASE: 35% acetonitrile/65% water @ 1.2 mL/min; ambient temperature

COLUMN: 50 cm x 2-mm ID stainless steel packed with µ-Bondapak C_{18} or equivalent

DETECTOR: UV absorption @ 254 nm

CALIBRATION: analytes dissolved in methanol

RANGE: 12 to 360 µg per sample (each isomer) [2]

ESTIMATED LOD: 0.35 µg per sample [2]

PRECISION ($\hat{S}_r$): 0.029 @ 30 to 240 µg per sample [1]

APPLICABILITY: The working range is 0.06 to 0.8 mg/m^3 (0.012 to 0.16 ppm) for a 200-L air sample.

INTERFERENCES: None identified.

OTHER METHODS: This revises Method S163 [2]. This method replaces P&CAM 168 [3] because XAD-2 has a much greater capacity than silica gel for o-anisidine at high humidity [1].

REAGENTS:

1. p-Anisidine, reagent grade.*
2. o-Anisidine, reagent grade.*
3. Methanol, HPLC grade.*
4. Acetonitrile, HPLC grade.*
5. Water, distilled, deionized.
6. Methylene chloride.
7. Calibration stock solution, 15.0 mg/mL p-anisidine and 15.3 mg/mL o-anisidine. Dissolve 750 mg p-anisidine and 700 µL o-anisidine in methanol to make 50 mL solution.
8. HPLC mobile phase: 35% acetonitrile/65% water. Filter (5-µm PTFE) and degas prior to use.

* See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: glass tube, 7 cm long, 8-mm OD, 6-mm ID, with plastic caps, containing two sections of 20/50 mesh XAD-2 (front = 150 mg; back = 75 mg) separated and held in place by plugs of silylated glass wool. Pressure drop across the tube must be <3.4 kPa (2.5 cm Hg) at 1 L/min airflow. Tubes are commercially available, (SKC Cat. No. 226-30-05, or equivalent).
2. Personal sampling pump, 0.5 to 1 L/min, with flexible connecting tubing.
3. HPLC with UV absorption detector at 254 nm, integrator and column (page 2514-1).
4. Vials, 20-mL, scintillation.
5. Pipet, 5-mL.
6. Syringes, 10-µL, readable to 0.1 µL.
7. Volumetric flasks, 5- and 50-mL.

SPECIAL PRECAUTIONS: Anisidine can irritate the skin. Methanol and anisidine can be absorbed through the skin. Avoid inhalation of vapors of these compounds and of acetonitrile [4].

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Uncap the sampler immediately before sampling. Attach sampler to personal sampling pump with flexible tubing.
3. Sample at an accurately known flow rate between 0.5 and 1.0 L/min for a total sample size of 24 to 320 L. Do not sample at less than 0.5 L/min.
4. Cap the samplers. Pack securely for shipment.

SAMPLE PREPARATION:

5. Place the front and back sections of the sampler in separate vials. Discard the glass wool plugs.
6. Add 5.0 mL methanol to each vial. Cap each vial and swirl vigorously.
7. Allow to stand for 15 min. Analyze within one day.

CALIBRATION AND QUALITY CONTROL:

8. Calibrate daily with at least six working standards over the range 0.4 to 360 µg anisidine per sample for each isomer.
   a. Add a known volume of calibration stock solution, or a dilution thereof in methanol, to a 5-mL volumetric flask and dilute to the mark with methanol.
   b. Analyze together with samples and blanks (steps 11 and 12).
   c. Prepare calibration graph (peak area vs. µg analyte) for each isomer.
9. Determine desorption efficiency (DE) at least once for each lot of XAD-2 used for sampling in the concentration range of interest. Prepare four tubes at each of five levels.

a. Remove and discard the back sorbent section of a media blank sampler.
b. Inject a known amount (e.g., 1 to 20 µL) of calibration stock solution, or a dilution thereof in methanol, directly onto the front section with a microliter syringe.
c. Cap the tube. Allow to stand overnight.
d. Desorb (steps 5 through 7) and analyze with working standards (steps 11 and 12).
e. Prepare graphs of DE vs. µg isomer recovered.

10. Analyze three quality control blind spikes and three analyst spikes with each subsequent set from the same lot to ensure that the calibration graph and DE graph are in control.

MEASUREMENT:

11. Set HPLC to conditions given on page 2514-1. Inject sample aliquot.
NOTE: Sensitivity is ca. 0.083 absorbance unit/mg of either isomer in a 10-mL injection volume with a 1-cm flow cell. Approximate retention times are 7.5 min for p-anisidine and 12 min for o-anisidine.
12. Measure peak area.

CALCULATIONS:

13. Determine the quantities (sum of quantities of the o- and the p-isomers corrected for DE), mg of analytes found in the sample front (W_f) and back (W_b) sorbent sections, and in the average media blank front (B_f) and back (B_b) sorbent sections.
NOTE: If $W_b > W_f/10$, report breakthrough and possible sample loss.
14. Calculate the sum of the concentrations, C, of the isomers in the air volume sampled, V (L):

$$C = \frac{(W_f + W_b - B_f - B_b)}{V}, \text{ mg/m}^3.$$

EVALUATION OF METHOD:

Method S163 was issued on February 16, 1979 [2], and was validated over the range 0.13 to 0.58 mg/m^3 for the o-isomer and 0.12 to 0.58 mg/m^3 for the p-isomer using 225-L air samples [1,5]. The generation system was constructed so that samples were generated for both isomers at the same time. Concentrations were verified by an independent method using bubblers containing methanol and HPLC analysis [1]. The overall precision, $\hat{S}_{rT}$, for the combined sampling and measurement of both isomers was 0.068 with an average recovery of 100.7% for the o-isomer and 99.7% for the p-isomer [1], which represent non-significant biases for the isomers. A separate breakthrough test was conducted for each isomer with XAD-2. Samples were taken at ca. 1.0 L/min. o-Anisidine was generated at 1.03 mg/m^3 with a relative humidity of 81% at 21 °C. Breakthrough (3%) from 150 mg XAD-2 occurred after 236 min, but did not increase above this amount up to 479 min. p-Anisidine was generated at 1.04 mg/m^3 with a relative humidity of 82% at 20 °C. Breakthrough did not occur during the 361-min test. Samples containing both isomers were stored for one week at room temperature and found to be stable. Desorption efficiencies averaged 0.95 and 0.91 for o- and p-anisidine, respectively, in the range 30 to 240 µg per sample.

REFERENCES:

[1] NIOSH Backup Data Report S163 (unpublished, February, 1979).
[2] NIOSH Manual of Analytical Methods, 2nd ed., Vol. 5, S163, U.S. Department of Health, Education, and Welfare, Publ. (NIOSH) 79-141 (1979).
[3] Ibid., Vol. 1, P&CAM 168, U.S. Department of Health, Education, and Welfare, Publ. (NIOSH) 77-157-A (1977).

[4] NIOSH/OSHA Occupational Health Guidelines for Occupational Hazards, U.S. Department of Health and Human Services, Publ. (NIOSH) 81-123 (1981), available as GPO Stock #017-033-00337-8 from Superintendent of Documents, Washington, DC 20402.
[5] NIOSH Research Report - Development and Validation of Methods for Sampling and Analysis of Workplace Toxic Substances, U.S. Department of Health and Human Services, Publ. (NIOSH) 80-133 (1980).

METHOD REVISED BY:

Edward Slick, NIOSH/DPSE; S163 originally validated under NIOSH Contract 210-76-0123.