2,4- AND 2,6-TOLUENEDIAMINE (in the presence of isocyanates) 5516

$CH_3C_6H_3(NH_2)_2$ MW: 122.17 CAS: 2,4-: 95-80-7 2,6-: 823-40-5 RTECS: 2,4-: XS9625000 2,6-: XS9750000

METHOD: 5516, Issue 2 **EVALUATION: PARTIAL** **Issue 1: 15 May 1989** **Issue 2: 15 August 1994**

OSHA : no PEL
NIOSH: 2,4-: lowest feasible; carcinogen
ACGIH: no TLV

PROPERTIES: 2,4-: solid; MP 99 °C
2,6-: solid; MP 106 °C

SYNONYMS: 2,4-: 4-methyl-1,3-benzenediamine; 2,4-diaminotoluene
2,6-: 2-methyl-1,3-benzenediamine; 2,6-diaminotoluene

SAMPLING

SAMPLER: IMPINGER (solution of 1-(2-methoxyphenyl)-piperazine in toluene, 15 mL)

FLOW RATE: 1 L/min

VOL-MIN: 30 L @ 10 µg/m^3
-MAX: 500 L

SHIPMENT: routine

SAMPLE STABILITY: at least 2 weeks @ 25 °C in the dark [1]

FIELD BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: not studied

BIAS: not determined

OVERALL PRECISION ($\hat{S}_{rT}$): not determined

ACCURACY: not determined

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTES: 2,4- and 2,6-bisacetamidotoluene

PREPARATION: acetylate 4 hour, evaporate, redissolve in 1.5 mL methanol

INJECTION VOLUME: 10 µL

MOBILE PHASE: programmed; sodium acetate in acetonitrile/water at pH 6.0; 1.0 mL/min; ca. 20 °C

COLUMN: 10 cm x 8-mm octadecylsilylated silica (C_{18}), 5-µm particle size, in Waters RCM-100 radial compression module

CALIBRATION: standard solution of analytes in methanol

RANGE: 0.3 to 3 µg per sample [1]

ESTIMATED LOD: 0.1 µg per sample [1]

PRECISION ($\hat{S}_r$): 0.06 @ 0.74 to 0.89 µg per sample [1]

APPLICABILITY: The working range is 3 to 30 µg/m^3 for a 100-L air sample. This method, based on that of Warwick et al. for isocyanates [2], determines 2,4- and 2,6-toluenediamine in air in the presence of isocyanates. Samples from polyurethane foam plants were analyzed simultaneously for 2,4- and 2,6-toluenediamine and 2,4- and 2,6-toluene diisocyanate [1].

INTERFERENCES: m-Phenylenediamine interferes in the determination of 2,4-toluenediamine.

OTHER METHODS: Holdren et al. [3] reported a similar method using N-(4-nitrobenzyl)propylamine in toluene for sampling and HPLC with electrochemical detection. Other methods are: (a) absorb on Tenax GC, desorb in toluene, GC [4]; (b) absorb on silica gel, desorb in 2-butanone, GC [5]; (c) sample in aqueous acid, work up, GC of free amines [6] or bis(hepta-fluorobutyryl)amides [7,8]; (d) sample in ethanolic KOH, workup, LC of free amine [9,10] or GC of bis(pentafluoropropionyl) amides [11]; (e) sample with sulfuric acid-coated filter, work up, GC of bis(heptafluorobutyrl)amides [12]. Some of these methods [3,9-11] can b e used for the simultaneous determination of toluenediamines and toluene diisocyanates.

REAGENTS:

1. Toluene, reagent grade.
2. 1-(2-Methoxyphenyl)piperazine, purified (see APPENDIX A).
3. Sampling medium: 43 µg/mL 1-(2-methoxyphenyl)piperazine in toluene.
4. 2,4-Toluenediamine*, reagent grade.
5. 2,6-Toluenediamine*, reagent grade.
6. Acetic anhydride, reagent grade.
7. Methanol, reagent grade.
8. Mobile phase A: Dissolve 60 mg anhydrous sodium acetate in 1 L of 12% acetonitrile in distilled water. Add 17% (V/V) aqueous acetic acid. Bring pH to 6.0.
9. Mobile phase B: Acetonitrile, chromatographic quality.
10. Water, distilled deionized.
11. Sodium acetate, anhydrous.
12. 2,4-Bisacetamidotoluene, See APPENDIX B).
13. 2,6-Bisacetamidotoluene, (See APPENDIX B).
14. Calibration stock solution, 0.5 µg/µL. Dissolve 5 mg each of 2,4- and 2,6-bisacetamidotoluene in methanol. Dilute to 10 mL.
15. Nitrogen, prepurified.
16. Pentane*, purified.

* See SPECIAL PRECAUTIONS

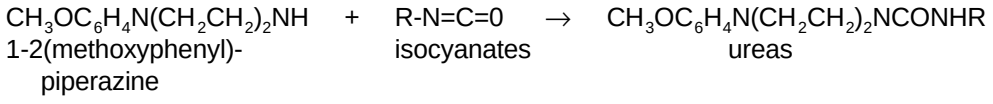
EQUIPMENT:

1. Sampler: midget impinger, 25-mL.
2. Personal sampling pump, 1 L/min, with flexible connecting tubing.
3. Liquid chromatograph (HPLC) with 229-nm UV detector, recorder, integrator, and column (page 5516-1).
4. Vials, 4-mL and 20-mL, glass, with PTFE-lined caps.
5. Pipets, pasteur, 14.6-cm, glass disposable.
6. Volumetric flasks, 10-mL.
7. Syringes, 10- and 100-µL.
8. Pipets, 2-mL (graduated) and 15-mL, glass, with pipet bulb.
9. Water bath.
10. Hotplate, spark-free, 35 to 50 °C.
11. Evaporator, Mini-Vap, six-port, or equivalent.
12. pH meter.
13. Beakers, 250-mL.
14. Flask, filtration, 500-mL.
15. Funnel, Buchner, fritted glass, 100-mL.
16. Vacuum pump.
17. Vacuum desiccator.
18. Watchglass.

SPECIAL PRECAUTIONS: 2,4-Toluenediamine is a cancer suspect agent [13]; 2,6-Toluenediamine may be mutagenic [14]. Handle these chemicals carefully in a hood or glove box, and avoid working-surface contamination which

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Transfer 15.0 mL sampling medium to an impinger.
3. Connect the assembled impinger to a sampling pump.
4. Sample 30 to 500 L of air at an accurately measured sampling rate of 1 L/min. When it is necessary to add solvent for proper impinger operation during sampling, add only toluene.
   NOTE: The reagent in the sampling medium reacts with isocyanates present to form ureas, thus preventing reaction of the isocyanate with the toluenediamines.



5. Transfer sample solution, including condensed water, to a 20-mL vial for shipment. Rinse impinger with 1 to 2 mL toluene. Add rinsings to sample solution.

SAMPLE PREPARATION:

6. Add 25 µL acetic anhydride to acetylate the 2,4- and 2,6-toluenediamine and excess 1-(2-methoxyphenyl)piperazine. Allow 4 hours for completion of reactions. Evaporate sample to dryness under a gentle stream of nitrogen while warming to 40 to 50 °C on a hotplate. Redissolve residue in 1.5 mL methanol.
   NOTE: The acetylation reaction for 2,4-toluenediamine to produce 2,4-bisacetamidotoluene is:

$$\underset{\text{2,4-toluenediamine}}{CH_3C_6H_3(NH_2)_2} + \underset{\text{acetic anhydride}}{2CH_3COOCOCH_3} \rightarrow \underset{\text{2,4-bisacetamidotoluene}}{CH_3C_6H_3(NHCOCH_3)_2} + \underset{\text{acetic acid}}{2\ CH_3COOH}.$$

CALIBRATION AND QUALITY CONTROL:

7. Calibrate daily with at least six working standards.
   a. Using aliquots of calibration stock solution, prepare working standards of 2,4- and 2,6-bisacetamidotoluene in methanol covering the range 0.1 to 3 µg/mL each.
   b. Analyze these with the unknown and blank samples (steps 9 through 11).
   c. Prepare calibration graphs (peak height vs. µg 2,4- and 2,6-toluenediamine per sample). Multiply the concentration (µg/mL) of bisacetamidotoluene by 0.889 mL to obtain the quantity (µg) of toluenediamine per sample.
      NOTE: The factor 0.889 includes the MW of toluenediamine (122.17), the MW of bisacetamidotoluene (206.24), and the 1.5-mL solution volume from step 6.
8. Prepare three quality control samples by adding known quantities of 2,4- and 2,6-toluenediamine to 15 mL of sampling medium and analyze (steps 9 through 11).

MEASUREMENT:

9. Set up the HPLC system according to the manufacturer's recommendations and to the conditions given on page 5516-1. The mobile phase program is:
   a. Linear gradient 100% A to 90% A over t = 0 to 8 min.
   b. 90% A to 40% A over t = 8 to 19 min following the convex gradient % A = 90 - 31 (t - 8) $^{1/5}$.
   c. Hold at 40% A for 1 min, or as long as necessary to clear the column.
   d. Return to 100% A and hold for 7 min before the next run.
   NOTE: If only 2,4- and 2,6-toluenediamine are to be quantified, the mobile phase program may be modified to hasten elution of the ureas derived from the isocyanates.
10. Inject a 10-µL aliquot of solution from step 6 or step 7b.
11. Measure the peak heights. Adjusted retention times for some compounds of interest are:

2,6-bisacetamidotoluene	5.2 min
1,4-bisacetamidobenzene	7.8 min
1,3-bisacetamidobenzene	9.4 min
2,4-bisacetamidotoluene	9.7 min
1-acetyl-4-(2-methoxyphenyl)piperazine	14.3 min
urea derivative of 2,6-toluene diisocyanate	17.0 min
urea derivative of 2,4-toluene diisocyanate	18.3 min

CALCULATIONS:

12. Using the calibration graphs, determine the mass, µg, of 2,4- and of 2,6-toluenediamine in each sample (W) and in the average media blank (B).
13. Calculate the concentration, C, of 2,4- and of 2,6-toluenediamine in the air volume sample, V (L):

$$C = \frac{(W - B)}{V}, \text{ mg/m}^3.$$

EVALUATION OF METHOD: [1]

The relationship of peak height and concentration of 2,4- and 2,6-bisacetamidotoluene in methanol was found to be essentially linear over the ranges 0.05 to 141 µg/mL and 0.14 to 84 µg/mL, respectively. The time required for completion of the acetylation reaction was determined using samples equivalent to 0.7 µg of 2,4-toluenediamine and 0.9 µg of 2,6-toluenediamine in 15 mL of sampling medium. Aliquots (2 mL) were treated with 10 µL of acetic anhydride and allowed to stand 0.25 to 6 hrs before further workup and analysis. The acetylation of 2,6-toluenediamine was the slower reaction, but it appeared complete after 4 h. Sample stability was studied using solutions of 2,4- and 2,6-toluenediamine in sampling medium at levels corresponding to 0.89 and 0.74 µg per sample, respectively. The recoveries, ranging from 97% to 106%, suggested the samples were stable under the conditions of storage -- 1, 7, and 14 days at room temperature in the dark. The potential for interference from isocyanates was investigated by drawing air containing 7.3 µg each of 2,4- and 2,6-toluene diisocyanate through samples of 0.9 µg each of 2,4- and 2,6-toluenediamine in 15 mL of sampling medium. The recoveries from these samples, averaging 95%, suggested that, when compared to identical samples not treated with toluene diisocyanate, a small but statistically significant negative bias was caused by the isocyanate. Using the data from all of the recovery experiments, the relative standard deviation (S_r) for 2,4-toluenediamine (0.74 and 0.83 µg per sample) ranged from 0.01 to 0.08 with a pooled average ($\bar{S}_r$) of 0.05 and for 2,6-toluenediamine (0.89 µg per sample) ranged from 0.02 to 0.14 with a pooled average ($\bar{S}_r$) of 0.06.

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APPENDIX A:

PURIFICATION OF 1-(2-METHOXYPHENYL)PIPERAZINE:

Place 25 g 1-(2-methoxyphenyl)piperazine (yellowish white solid) in a 250-mL beaker. Add ca. 125 mL pentane. Bring to a boil (CAUTION: Pentane is FLAMMABLE) on a water bath and allow to boil until all but a small amount of yellow oil is in solution. The 1-(2-methoxyphenyl)piperazine will melt as it is warmed in the pentane. Decant the solution into a clean beaker, cover with a watchglass, and cool in the freezer for 2 to 3 h. Collect the resulting white needles in a Buchner funnel using suction filtration and dry them in a vacuum desiccator. The crystals are hygroscopic and melt at 26 to 29 °C. Store them in an airtight container in a refrigerator.

APPENDIX B:

SYNTHESIS OF 2,4- AND 2,6-BISACETAMIDOTOLUENE:

Place 0.5 g of 2,4- or 2,6-toluenediamine in a 250-mL beaker. Add ca. 100 mL of distilled water and warm to dissolve the compound. Filter the solution, if necessary. Chill the solution in an ice bath, then slowly add 5 mL acetic anhydride and stir. After keeping the mixture at least 1 h in the ice bath, collect the solid product by suction filtration. Recrystallize the product from water by dissolving it in boiling water, filtering the hot solution, chilling the filtrate in a refrigerator, and collecting the precipitate by suction filtration. Dry the precipitate in a vacuum desiccator.

2,4-Bisacetamidotoluene recrystallizes as white needles and melts at 230 °C.

2,6-Bisacetamidotoluene recrystallizes as brownish needles and melts at ca. 318 °C.