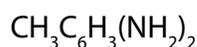


2,4- and 2,6-TOLUENEDIAMINE (in the presence of isocyanates)

5516



MW: 122.17

CAS: 2,4-: 95-80-7

RTECS: 2,4-: XS9625000

CAS: 2,6-: 823-40-5

RTECS: 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

APPLICABILITY: The working range is 3 to 30 µg/m³ 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(heptafluorobutryl)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(heptafluorobutryl)amides [12]. Some of these methods [3,9–11] can be 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:

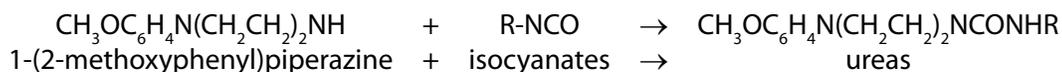
1. Sampler: midget impinger, 25-mL.
2. Personal sampling pump, 1 L/min, with flexible connecting tubing.
3. Liquid chromatograph (HPLC) with 229-nm UV detector, recorder, integrator, and column (page 5516-1).
4. Vials, 4-mL and 20-mL, glass, with PTFE-lined caps.
5. Pipets, pasteur, 14.6-cm, glass disposable.
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 might occur by spillage or by dissipation of fine powder from opening of containers or making transfers. Pentane is highly volatile and flammable. Take adequate precautions while handling pentane.

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.

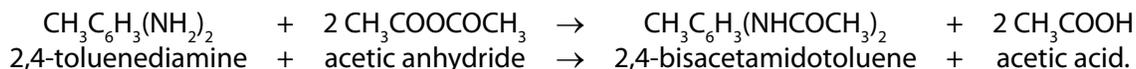


5. Transfer sample solution, including condensed water, to a 20-mL vial for shipment. Rinse impinger with 1 to 2 mL toluene. Add rinsings to sample solution.

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 $^{\circ}\text{C}$ on a hotplate. Redissolve residue in 1.5 mL methanol.

NOTE: The acetylation reaction for 2,4-toluenediamine to produce 2,4-bisacetamidotoluene is:

**CALIBRATION AND QUALITY CONTROL:**

7. Calibrate daily with at least six working standards.
- 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 $\mu\text{g}/\text{mL}$ each.
 - Analyze these with the unknown and blank samples (steps 9 through 11).
 - Prepare calibration graphs (peak height vs. μg 2,4- and 2,6-toluenediamine per sample). Multiply the concentration ($\mu\text{g}/\text{mL}$) 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:
- Linear gradient 100% A to 90% A over $t = 0$ to 8 min.
 - 90% A to 40% A over $t = 8$ to 19 min following the convex gradient $\%A = 90 - 31(t - 8)^{1/5}$.
 - Hold at 40% A for 1 min, or as long as necessary to clear the column.
 - 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 h 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.

REFERENCES:

- [1] Arnold, J. E. and A. W. Teass. Unpublished research, NIOSH (1985).
- [2] Warwick, C. J., D. A. Bagon, and C. J. Purnell. "Application of Electrochemical Detection to the measurement of Free Monomeric Aromatic and Aliphatic isocyanates in Air by High-performance Liquid Chromatography," *Analyst*, 106, 676–685 (1981).
- [3] Holdren, M. W., C. W. Spicer, and R. M., Riggin. "Gas Phase Reaction of Toluene Diisocyanate with Water Vapor," *Am. Ind. Hyg. Assoc. J.*, 45, 626–633 (1984).
- [4] Menzies, K. T., J. Worthington and B. Belinky. "2,4-Dinitrotoluene, 2,4-Diaminotoluene," in "Short-Term Method Development and Chemical Analysis: Final Report," Contract No. 210-89-0099, National Institute for Occupational Safety and Health, Cincinnati, OH, 213–222 (June, 1982), available as Stock No. PB-84-181-817 from NTIS, Springfield, VA 22161.
- [5] Becher, G. "Glass Capillary Columns in the Gas Chromatographic Separation of Aromatic Amines. II. Application to Samples from Workplace Atmospheres using Nitrogen-Selective Detection," *J. Chromatogr.*, 211, 103–110 (1981).
- [6] Audunsson, G. and L. Mathiasson. "Simultaneous Determination of Amines and Isocyanates in Working Atmospheres by Gas-Liquid Chromatography," *J. Chromatogr.*, 261, 253–264 (1983).
- [7] Skarping, G., C. Sango, and B. E. F. Smith. "Trace Analysis of Isocyanates in Industrial Atmospheres Using Gas Chromatography and Electron-Capture Detection," *J. Chromatogr.*, 208, 313–321 (1981).
- [8] Bishop, R. W., T. A. Ayers, and G. G. Esposito. "A Gas Chromatographic Procedure for the Determination of Airborne MDI and TDI," *Am. Ind. Hyg. Assoc. J.*, 44, 151–155 (1983).
- [9] Nieminen, E. H., L. H. Saarinen, and J. T. Laakso, "Simultaneous Determination of Aromatic Isocyanates and Some Carcinogenic Amines in the Work Atmosphere by Reversed-phase High-performance Liquid Chromatography," *Journal of Liquid Chromatography*, 6, 453–469 (1983).
- [10] Darlene, M., L. Mathiasson, G. Skarping, C. Sango, and J. F. Sandstrom, "Trace Analysis of Airborne Aromatic Isocyanates and Related Aminoisocyanates and Diamines Using High-Performance Liquid Chromatography with Ultraviolet and Electrochemical Detection," *J. Chromatogr.*, 435, 469–481 (1988).
- [11] Skarping, G., L. Renman, G. Sango, L. Mathiasson, and M. Darlene, "Capillary Gas Chromatographic Method for the Determination of Complex Mixture of Isocyanates and Amines," *J. Chromatogr.*, 346, 191–204 (1985).

- [12] Elskamp, C. J., "Benzidine; 3,3'-Dichlorobenzidine; 2,4-Toluenediamine; 2,6-Toluenediamine. Method 65," OSHA Analytical Laboratory, Salt lake City, Utah (1987).
- [13] NIOSH [1988], Registry of Toxic Effects of Chemical Substances, data base: 2,4-Toluenediamine. D.V. Sweet, Ed., U. S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Division of Standards Development and Technology Transfer.
- [14] *Ibid.*, 2,6-Toluenediamine.

METHOD WRITTEN BY:

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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.