THIOPHANATE-METHYL in air 5606

$C_{12}H_{14}N_4O_4S_2$ MW: 342.40 CAS: 23564-05-8 RTECS: BA3675000

METHOD: 5606, Issue 1 **EVALUATION: PARTIAL** **Issue 1: 15 March 2003**

OSHA: N/A
NIOSH: N/A
ACGIH: N/A

PROPERTIES: colorless prisms; MP 181.5–182.5 °C; soluble in acetone, methanol, chloroform, acetonitrile, slightly soluble in other organics, insoluble in water

SYNONYMS: Topsin-M; [1,2-phenylenebis(iminocarbonothioyl)]bisdimethyl ester carbamic acid

SAMPLING

SAMPLER: FILTER/SOLID SORBENT TUBE (OVS-2 tube: 11 mm quartz fiber filter; XAD-2, 270 mg/140 mg)

FLOW RATE: 0.1 L/min to 1 L/min

VOL-MIN: 20 L @ 0.1 L/min [see Evaluation of Method, Note 1.]
-MAX: 480 L

SHIPMENT: 4 °C

SAMPLE STABILITY: at least 28 days at 4 °C

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: not determined

BIAS: not determined

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

ACCURACY: not determined

MEASUREMENT

TECHNIQUE: HPLC, UV detector

ANALYTE: thiophanate-methyl

EXTRACTION: 2 mL 40% isopropanol:60% acetonitrile

INJECTION VOLUME: 5 µL

MOBILE PHASE: A = 2% *n*-propanol in water, 0.02 *M* TEA-PO_4, pH adjusted to 7.0 ± 0.1 using phosphoric acid; B = 2% *n*-propanol in acetonitrile; gradient from 20% B to 70% B (20 min), decreasing to 20% B (2 min), hold at 20% B (5 min)

COLUMN: reversed phase C-18, 4 µm, 250 × 2.00 mm (or equivalent)

DETECTOR: UV @ 200 nm [see Evaluation of Method, Note 2.]

CALIBRATION: solutions prepared in extraction solvent

RANGE: 5 to 650 µg/sample

ESTIMATED LOD: 0.76 µg/sample

PRECISION ($\bar{S}_r$): 0.0318

APPLICABILITY: This method was developed for the determination of thiophanate-methyl in air samples for a fungicide field study of orchard workers, and was meant to be used in conjunction with NMAM 5601 for the determination of carbendazim and captan as well. Recoveries of thiophanate-methyl may be lower when carbendazim, thiophanate-methyl, and captan are present in the same sample due to chemical interactions. The working range for this method is 0.025–5.67 mg/m^3 based on a 100-L sample.

INTERFERENCES: Potential interferences to the analysis of thiophanate-methyl include other organic compounds, in particular other pesticides or fungicides that have the same retention time on a C-18 column. Positive identification may be confirmed by dual column chromatography using an appropriate alternative LC column. **NOTE:** It is possible to see a peak at the retention time for carbendazim, 9.8 minutes, since carbendazim is a decomposition product of thiophanate-methyl.

OTHER METHODS: This method is based in part on NMAM 5601 [1] for the development work. As such, several of the compounds listed in NMAM 5601can also be analyzed in conjunction with thiophanate-methyl using this method.

REAGENTS:

1. Isopropanol*, HPLC grade.
2. Acetonitrile*, HPLC grade.
3. Triethylamine (TEA)*, HPLC grade.
4. Water, deionized.
5. Ortho-phosphoric acid*, >85% by weight, ACS grade or better grade.
6. Extraction solvent: 40% isopropanol/60% acetonitrile (v/v).
7. Thiophanate-methyl stock solution, 10 mg/mL. Prepare in acetonitrile and store in refrigerator.
8. TEA-PO_4 preservative. Dissolve 1.4 mL of TEA in 90 mL of deionized water in a 100-mL volumetric flask. Add phosphoric acid to lower pH to 7.0 ± 0.1 as indicated by a calibrated pH meter. Bring volume to 100 mL with water. Keep tightly capped and refrigerated. Solution stable for 12 months.
9. Mobile phase A. Combine 20 mL of *n*-propanol and 2.8 mL TEA in a 1-L volumetric flask and bring to volume using deionized water. Adjust pH to 7.0 ± 0.1 with phosphoric acid using a pH meter. Final concentrations: 2% *n*-propanol, 0.02 M TEA-PO_4. Degas prior to use.
10. Mobile phase B. Add 20 mL of *n*-propanol to acetonitrile in a 1-L volumetric flask and bring to volume with acetonitrile. Degas prior to use.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: OSHA Versatile Sampler (OVS-2 tube), 13-mm OD inlet, 6-mm OD outlet. Front section contains 270 mg 20/60 mesh XAD-2 sorbent held in place by an 11-mm diameter quartz fiber filter and Teflon® ring, separated from the back section of 140 mg XAD-2 sorbent by a short plug of polyurethane foam. The tube is available commercially.
2. Personal sampling pump: 1 L/min with flexible and inert connection tubing.
3. High performance liquid chromatograph (HPLC) with UV detector.
4. Autosampler capable of 5-µL injections.
5. Analytical column: Phenomenex® Synergi™ 4 µm Hydro-RP 80A (250 × 2.00 mm) or equivalent [see Note 3].
6. Vials, 4-mL and 2-mL, glass with PTFE-lined caps.
7. Syringes, 50-µL ,1-mL, and 5-mL.
8. Volumetric flasks, 5-mL, 100-mL, and 1-L.
9. Syringe filter, PTFE, 4-mm, 0.45-µm pore.
10. Forceps.
11. Small vial/tube rotator.
12. pH meter.
13. Graduated cylinder, 50-mL.
14. Pipettes, glass, disposable, 2-mL.
15. Funnel, plastic.
16. Bagged refrigerant.

SPECIAL PRECAUTIONS: Thiophanate-methyl: Avoid inhaling vapors or dust; avoid skin contact. Wear gloves and suitable clothing when handling pure material. Solvents: Avoid skin contact and open flame. Use in a hood. Phosphoric acid: Avoid skin contact. See Note 1.

SAMPLING:

1. Calibrate each personal sampling pump with representative sampler in line.
2. Connect the sampler to the personal sampling pump with flexible tubing. Place sampler vertically, with the large end down, in the breathing zone.
3. Sample at an accurately known flow rate between 0.1 and 1 L/min for a total sampling volume of up to 480 L. Record volume, and document presence of any known or potential interferences.
4. Cap both ends of the sampler with plastic caps and pack securely with bagged refrigerant for shipment.

SAMPLE PREPARATION:

5. Remove cap from large end. Transfer PTFE retainer ring, filter, and front XAD-2 resin section to a 4-mL vial. Transfer the polyurethane foam divider plug along with the back-up XAD-2 resin bed to a second 4-mL vial.
6. Add 2 mL of extraction solvent to each vial and cap each vial using a PTFE-lined cap.
7. Mix by rotating the vials end-over-end for approximately one hour.

NOTE: If this method is being combined with NMAM Method 5601 for benomyl, then at the end of the mixing period allow the samples to sit at room temperature overnight. This will allow any possible residual benomyl to convert to carbendazim.

8. Filter an aliquot into a 2-mL autosampler vial through a 4-mm, 0.45-µm PTFE filter.

CALIBRATION AND QUALITY CONTROL:

9. Determine retention times for thiophanate-methyl using the column and chromatographic conditions as shown on page 5606-1. The approximate retention time of thiophanate-methyl using the current chromatographic conditions is 14.1 minutes. (See Figures 1–3.)
10. Calibrate daily with at least six working standards covering the working range for thiophanate-methyl.
11. Determine desorption efficiency (DE) for each lot of OVS-2 tubes used for sampling in the calibration range. Prepare three tubes at each of five levels plus three media blanks.
    a. Remove cap and PTFE retainer ring from large end of sampler tube (to prevent wicking behind the ring). Apply known volume of calibration solution to face of quartz filter.
       NOTE: Spike no more than 30 µL at a time. If more must be applied, connect the sampler to a vacuum pump with a flow ≤1 L/min, then apply spiking solution in aliquots of 15–30 µL. Allow 15 minutes for the solvent to evaporate between each aliquot, to prevent wicking along the sides of the tube in the back-up section (5% or more may deposit on the walls of the tube).
    b. Cap and allow to stand a minimum of one hour.
    c. Include an unspiked sampler as a media blank.
    d. Desorb (steps 5 through 8) and analyze together with working standards (steps 11 and 12).
    e. Prepare a graph of DE vs. µg thiophanate-methyl recovered.
12. Prepare analyst spike samples when field samples are received and store them together. Analyze with the field samples, blanks, and the liquid standards.

MEASUREMENT:

13. Set the liquid chromatograph according to manufacturer's recommendations. Set the wavelength for detection at 200 nm and flow rate at 0.200 mL/min.
14. Inject a 5-µL sample aliquot with autosampler or sample injection valve.
    NOTE: If peak area of a sample is greater than the area of the highest standard, dilute with extraction solvent and reanalyze. Apply the appropriate dilution factor in the calculations.
15. Measure peak area of the analyte.

CALCULATIONS:

16. Determine the mass, µg, of thiophanate-methyl found in the sampler filter and front sorbent section (W_f), back-up sorbent section (W_b), and the media blank front (B_f) and back-up (B_b) sorbent sections from a standard curve.
17. Calculate concentration, C, of thiophanate-methyl 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:

This method was evaluated with a recovery study over the range of 79.5–567 µg/sample, using spiked laboratory samples, with average recoveries in the range of 89.9–100%. The storage study was completed at 159 µg/sample with recovery averages of 91.6% to 99.8% over the 28 days of the study

when the samples were stored at refrigerator temperatures. Calibration standards have been prepared and evaluated up to a level of 324 µg/ml. This amount equates to 648 µg/sample for field samples.

This method was developed to be used in conjunction with NMAM 5601 for the analysis of thiophanate-methyl, carbendazim, and captan. In laboratory prepared samples, it was found that the recoveries of thiophanate-methyl may decrease and those of carbendazim may increase due to chemical interactions and the decomposition of thiophanate-methyl to carbendazim [2].

NOTES:

1. There are no established RELs or PELs for thiophanate-methyl. A REL of 5 mg/m^3 was assumed for the sampling requirements of this analyte. This method can comfortably measure thiophanate-methyl in solution at 5 µg/mL.

2. Thiophanate-methyl has an ultraviolet absorption maximum at 266 nm that may be a more appropriate wavelength for analysis. However, this method was developed to analyze several other fungicides concurrently with the thiophanate-methyl. One of these analytes has an absorption maximum at 195–200 nm, and 200 nanometers was selected as the wavelength of choice for this analysis. If it is known that the only analyte present in the sample is thiophanate-methyl, then it would be more advantageous to use a detector wavelength of 266 nm.

3. The major part of this work was performed on a Phenomenex® KingSorb™ C-18, 5 µm, 250 × 2 mm column. However, a direct replacement column, the Phenomenex® Synergi™, 4 µm, Hydro-RP, 250 × 2 mm column, was suggested by the manufacturer, which would provide better separation and resolution. Retention times on the Synergi™ column are similar to those on the KingSorb™ column. (See Figures 1 & 2.) A small adjustment to the mobile phase gradient was all that was required to achieve the same separation and retention time. The Synergi™, Hydro-RP column was also able to resolve carbendazim (another fungicide included in the same overall project) from imidaclorpid, a potential interference in the field samples. The KingSorb™ column was not able to separate these two materials under any conditions that would not severely impact any of the other analytes.

REFERENCES:

[1] NIOSH [1998]. Method 5601: Organonitrogen Pesticides. In: Cassinelli ME, O'Connor PF, eds. NIOSH Manual of Analytical Methods (NMAM), 4th ed, 2nd supplement. Cincinnati, OH: National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 98-119.
[2] Jaycox, LB, Andrews RN [2003]. Thiophanate-methyl in Air Backup Data Report. Cincinnati, OH: National Institute for Occupational Safety and Health,Division of Applied Research and Technology (unpublished, May).
[3] Lin J, Reynolds JM, Perkins JB [1996]. Backup Data Report Carbamate, Urea, and Sulfenimide Pesticides, unpublished.

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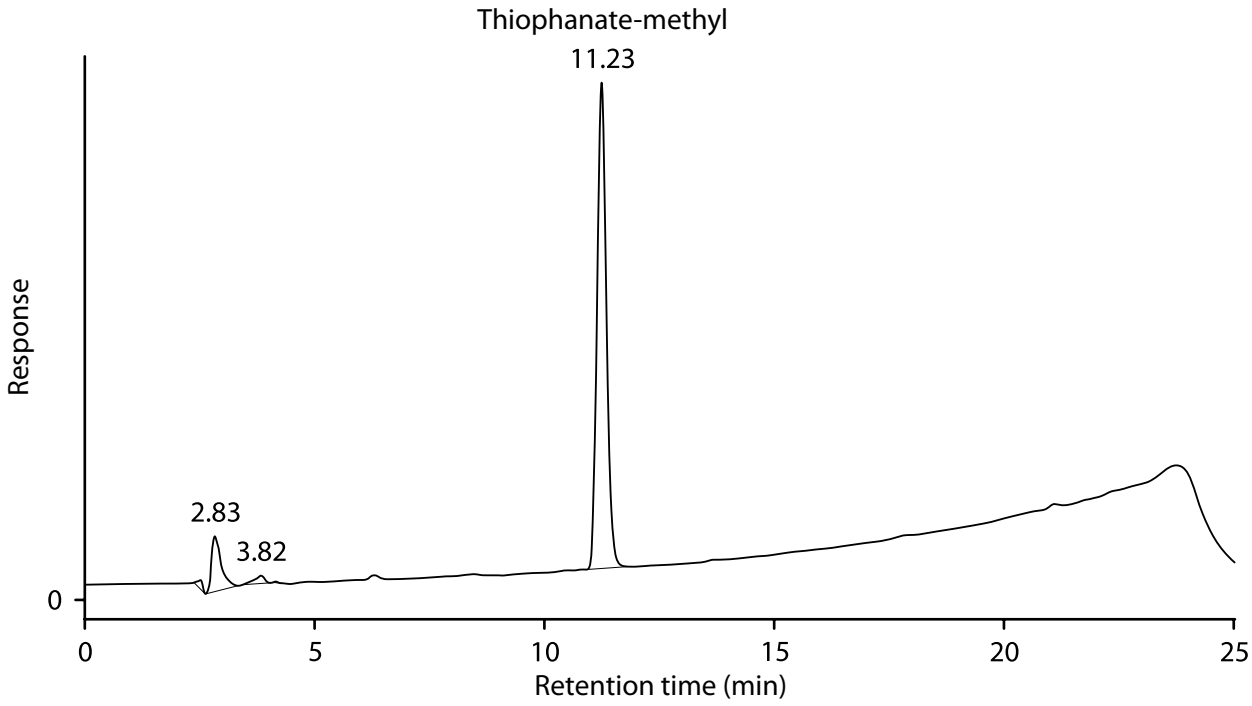

Figure 1. This is a typical chromatogram for a sample of thiophanate-methyl. This shows the response for a spike of 348 µg/sample of thiophanate-methyl on an OVS-2 tube, extracted and analyzed by this LC method using the Kingsorb™ column. On the Synergi™ column, the retention time for thiophanatemethyl is 14.1 minutes.

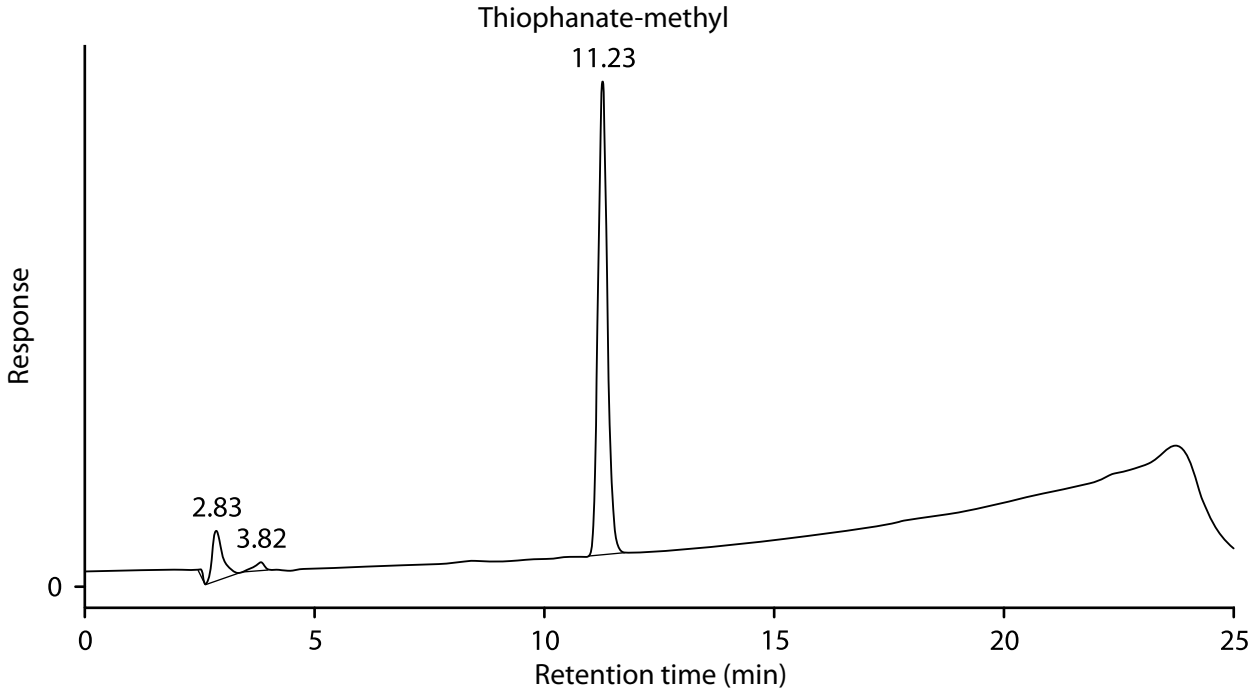

Figure 2. This is a typical chromatogram of a liquid calibration standard. This sample was analyzed with the Kingsorb™ column. The retention time on the Synergi™ column is 14.1 minutes.

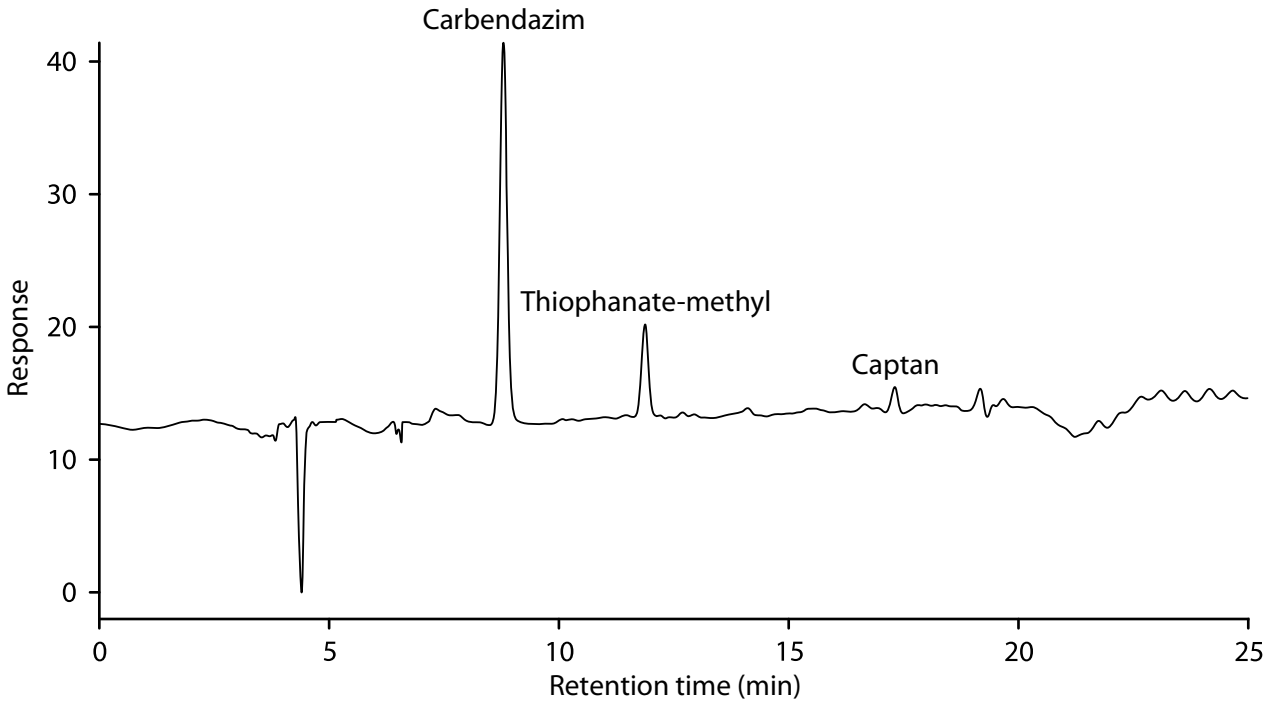

Figure 3. This chromatogram shows the three analytes of interest, carbendazim, thiophanate-methyl, and captan, which were extracted from a spiked OVS-2 sampling tube. This chromatogram has been background corrected by subtracting an OVS-2 blank analysis.