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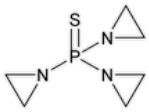
# Thiotepa



$C_6H_{12}N_3PS$ 189.22

Aziridine, 1,1',1"-phosphinothioylidynetris-;

Tris(aziridin-1-yl)phosphine sulfide CAS RN®: 52-24-4; UNII: 905Z5W3GKH.

## DEFINITION

Thiotepa contains NLT 97.0% and NMT 102.0% of thiotepa ($C_6H_{12}N_3PS$), calculated on the anhydrous basis.

[**Caution—**Great care should be taken to prevent inhaling particles of Thiotepa or exposing the skin to it.]

## IDENTIFICATION

***Change to read:***

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

## ASSAY

• **Procedure**

**Buffer:** 13.6 g/L of monobasic potassium phosphate in water. Adjust with 35 g/L of dibasic sodium phosphate to a pH of 7.0.

**Mobile phase:** Acetonitrile and *Buffer* (13:87)

**System suitability solution:** Transfer 10 mg of USP Thiotepa RS to a 4-mL vial, add 2 mL of methanol, and mix. Add 50 µL of 0.1% phosphoric acid solution. Place a cap on the vial, and heat at 65° for 50 s. Cool the solution, add 1 mL of methanol, and mix. [Note—The preparation generates methoxythiotepa.]

**Standard solution:** 1.5 mg/mL of USP Thiotepa RS in water

**Sample solution:** 1.5 mg/mL of Thiotepa in water

**Chromatographic system**

(See *Chromatography* ⟨621⟩, *System Suitability*.)

**Mode:** LC

**Detector:** 215 nm

**Column:** 4.6-mm × 15-cm; 5-µm packing L1

**Flow rate:** 1 mL/min

**Injection volume:** 20 µL

**System suitability**

**Samples:** *System suitability solution* and *Standard solution*

[Note—The relative retention times for thiotepa and methoxythiotepa are about 1.0 and 1.3, respectively.]

**Suitability requirements**

**Resolution:** NLT 3 between methoxythiotepa and thiotepa, *System suitability solution*

**Relative standard deviation:** NMT 0.73%, *Standard solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of thiotepa ($C_6H_{12}N_3PS$) in the portion of Thiotepa taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

$r_U$ = peak response of thiotepa from the *Sample solution*

$r_S$ = peak response of thiotepa from the *Standard solution*

$C_S$ = concentration of USP Thiotepa RS in the *Standard solution* (mg/mL)

$C_U$ = concentration of Thiotepa in the *Sample solution* (mg/mL)

**Acceptance criteria:** 97.0%–102.0% on the anhydrous basis

## IMPURITIES

• **Organic Impurities**

**Buffer, Mobile phase,** and **System suitability solution:** Proceed as directed in the *Assay*.

**Peak identification solution:** Dissolve 15 mg of USP Thiotepa RS in 10 mL of water, add 1 g of sodium chloride, boil in a water bath for 10 min, and cool. [Note—The preparation generates thiotepa chloroethyl analog.]

**Standard solution:** 3.5 µg/mL of USP Thiotepa RS in water

**Sample solution:** 3.5 mg/mL of Thiotepa in water

**Chromatographic system:** Proceed as directed in the *Assay*, with a run time NLT 4 times the retention time of the thiotepa peak.

**System suitability**

**Sample:** *System suitability solution*

[Note—The relative retention times for thiotepa and methoxythiotepa are about 1.0 and 1.3, respectively.]

**Suitability requirements**

**Resolution:** NLT 3 between methoxythiotepa and thiotepa, *System suitability solution*

**Analysis**

**Samples:** *Peak identification solution*, *Standard solution*, and *Sample solution*

Calculate the percentage of each impurity in the portion of Thiotepa taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

$r_U$ = peak response of each impurity from the *Sample solution*

$r_S$ = peak response of thiotepa from the *Standard solution*

$C_S$ = concentration of USP Thiotepa RS in the *Standard solution* (mg/mL)

$C_U$ = concentration of Thiotepa in the *Sample solution* (mg/mL)

**Acceptance criteria:** See *Table 1*. Disregard any impurity peaks less than 0.05%.

**Table 1**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Thiotepa | 1.0 | — |
| Thiotepa chloroethyl analog[a] | 3.75 | 0.15 |
| Any individual unspecified impurity | — | 0.1 |
| Total unspecified impurities | — | 0.2 |

[a] *P,P*-Bis(aziridin-1-yl)-*N*-(2-chloroethyl)phosphinothioic amide.

## SPECIFIC TESTS

• **Water Determination,** *Method I* ⟨921⟩**:** NMT 2.0%

## ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, and store in a refrigerator.

- **USP Reference Standards ⟨11⟩**

  USP Thiotepa RS

**Auxiliary Information** - Please check for your question in the FAQs before contacting USP.

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| THIOTEPA | Documentary Standards Support | SM32020 Small Molecules 3 |
| REFERENCE STANDARD SUPPORT | RS Technical Services<br>RSTECH@usp.org | SM32020 Small Molecules 3 |

**Chromatographic Database Information:** Chromatographic Database

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