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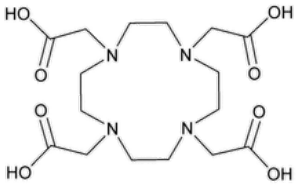
Add the following:

▲Tetraxetan



$C_{16}H_{28}N_4O_8$ 404.42

1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid;

2,2',2",2"'-(1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetryl)tetraacetic acid. CAS RN®: 60239-18-1.

DEFINITION

Tetraxetan contains NLT 98.5% and NMT 101.5% of tetraxetan ($C_{16}H_{28}N_4O_8$), calculated on the anhydrous basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K

• **B.** The retention time of the tetraxetan peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the test for *Organic Impurities*.

ASSAY

• **Procedure**

Sample solution: Dissolve 150 mg of Tetraxetan in 15 mL of water and add 30 mL of methanol.

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Direct titration

Titrant: 0.1 N sodium hydroxide VS

Endpoint detection: Potentiometric

Analysis

Sample: *Sample solution*

Titrate with *Titrant* using a glass electrode and a silver–silver chloride electrode system. Perform a blank determination and make any necessary correction.

Calculate the percentage of tetraxetan ($C_{16}H_{28}N_4O_8$) in the portion of Tetraxetan taken:

$$\text{Result} = [(V - B) \times N \times F/W] \times 100$$

V = volume of *Titrant* consumed by the *Sample solution* to reach the first endpoint (mL)

B = blank *Titrant* volume (mL)

N = normality of the *Titrant* (mEq/mL)

F = equivalency factor for tetraxetan, 202.2 mg/mEq

W = weight of the sample taken (mg)

Acceptance criteria: 98.5%–101.5% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

- **Organic Impurities**

Buffer: 0.6 g/L of monobasic sodium phosphate in water. Adjust with phosphoric acid to a pH of 2.1.

Solution A: Acetonitrile and water (50:50)

Solution B: *Buffer*

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	1	99
30	40	60
40	90	10
41	1	99
60	1	99

System suitability solution: 10 mg/mL of USP Tetraxetan RS and 30 µg/mL of USP Tetraxetan Related Compound A RS in water

Sensitivity solution: 5 µg/mL of USP Tetraxetan RS in water

Sample solution: 10 mg/mL of Tetraxetan in water

Chromatographic system

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

Mode: LC

Detector: UV 200 nm

Column: 4.6-mm × 15-cm; 3-µm packing L109

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Sensitivity solution*

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between tetraxetan and tetraxetan related compound A, *System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of each individual impurity in the portion of Tetraxetan taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of each impurity

r_T = sum of all the peak responses

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Tetraxetan	1.0	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Tetraxetan related compound A	1.4	0.20
Any individual unspecified impurity	—	0.10
Total impurities	—	0.50

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I*: NMT 15.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Tetraxetan RS

USP Tetraxetan Related Compound A RS

2,2',2''-[10-(2-Ethoxy-2-oxoethyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triyl]triacetic acid.

$C_{18}H_{32}N_4O_8$ 432.47▲ (USP 1-May-2021)

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

Topic/Question	Contact	Expert Committee
TETRAXETAN	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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