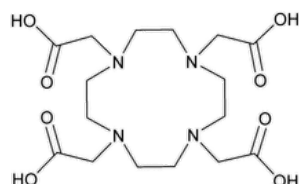


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Add the following:

^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-tetrayl)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	



Documents

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