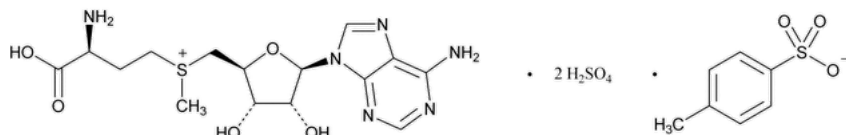


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S-Adenosyl-L-methionine Disulfate Tosylate

Former Title: Ademetionine Disulfate Tosylate



$C_{22}H_{34}N_6O_{16}S_4$ 766.80

S-(Adenosyl)-L-methionine disulfate tosylate;

(3S)-5'-[(3-Amino-3-carboxypropyl)methylsulfonio]-5'-deoxy adenosine, disulfate-methylbenzenesulfonate CAS RN®: 97540-22-2.

DEFINITION

S-Adenosyl-L-methionine Disulfate Tosylate is the disulfate–tosylate mixed salt of a mixture of diastereoisomers of the S-adenosyl-L-methionine ion. It contains NLT 95.0% and NMT 105.0% of S-adenosyl-L-methionine disulfate tosylate ($C_{22}H_{34}N_6O_{16}S_4$) calculated through the content of S-adenosyl-L-methionine ($C_{15}H_{23}N_6O_5S^+$), calculated on the anhydrous basis.

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 S-adenosyl-L-methionine in the *System suitability solution*, as obtained in the *CONTENT OF S-ADENOSYL-L-METHIONINE*.

COMPOSITION

• CONTENT OF S-ADENOSYL-L-METHIONINE

Solution A: 10 mL of glacial acetic acid in 500 mL of water. Add 2.06 g of sodium 1-hexanesulfonate, and dilute with water to 1000 mL.

Mobile phase: Acetonitrile and *Solution A* (15:85)

System suitability solution: 400 µg/mL each of [USP S-Adenosyl-L-methionine Disulfate Tosylate RS](#) and [USP S-Adenosyl-L-homocysteine RS](#)

Standard solution A: 400 µg/mL of [USP S-Adenosyl-L-homocysteine RS](#)

Standard solution B: 200 µg/mL from *Standard solution A*

Standard solution C: 80 µg/mL from *Standard solution A*

Sample solution: 20 mg of S-Adenosyl-L-methionine Disulfate Tosylate in 40 mL of water. Stir for 30 min, then dilute with water to 50.0 mL.

Transfer 1.0 mL of the solution to a 1.5-mL microcentrifuge tube, and centrifuge for 1 min. Use a portion of the supernatant.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 260 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

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

[NOTE—The relative retention times for S-adenosyl-L-homocysteine and S-adenosyl-L-methionine disulfate tosylate are about 0.68 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between S-adenosyl-L-homocysteine and S-adenosyl-L-methionine

Tailing factor: NMT 1.5, *Standard solution B*

Relative standard deviation: NMT 2.0% for S-adenosyl-L-homocysteine, *Standard solution B*

Analysis

Samples: *Standard solution A*, *Standard solution B*, *Standard solution C*, and *Sample solution*

[NOTE—Record the chromatograms, and measure the area of the S-adenosyl-L-homocysteine peak in all three *Standard solutions* and the S-adenosyl-L-methionine disulfate tosylate peak in the *Sample solution*.]

Plot a calibration curve of the peak area of the *Standard solutions* versus the corresponding S-adenosyl-L-homocysteine concentration, in mg/mL, and draw the straight line best fitting the three points. From the calibration curve, and using the peak area of S-adenosyl-L-methionine from the chromatogram from the *Sample solution*, determine the concentration, C, in mg/mL, of S-adenosyl-L-methionine as S-adenosyl-L-homocysteine in the *Sample solution*.

Calculate the percentage of $C_{15}H_{23}N_6O_5S^+$ in the portion of S-Adenosyl-L-methionine Disulfate Tosylate taken:

$$\text{Result} = (C/C_U) \times (M_{r1}/M_{r2}) \times 100$$

C = concentration of S-adenosyl-L-methionine as S-adenosyl-L-homocysteine obtained from the linear regression line (mg/mL)

C_U = concentration of S-Adenosyl-L-Methionine Disulfate Tosylate in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of S-adenosyl-L-methionine, 399.44

M_{r2} = molecular weight of S-adenosyl-L-homocysteine, 384.41

Acceptance criteria: 49.5%–54.7% on the anhydrous basis, equivalent to 95.0%–105% of S-adenosyl-L-methionine disulfate tosylate on the anhydrous basis

• **CONTENT OF SULFATE**

Mobile phase: 8.0 mM sodium carbonate and 1.0 mM sodium bicarbonate in water

Standard solution: 0.18 mg/mL of potassium sulfate

Sample solution: 0.5 mg/mL of S-Adenosyl-L-methionine Disulfate Tosylate

Chromatographic system

(See [Chromatography \(621\), System Suitability.](#))

Mode: LC

Detector: Ion detector with suppressed conductivity

Column: 4.0-mm × 25-cm; 7-μm packing L74

Column temperature: 30°

Flow rate: 1 mL/min

Injection size: 25 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 8200 theoretical plates

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

[NOTE—Measure the area of the sulfate peak.]

Calculate the percentage of sulfate (SO_4) in the portion of S-Adenosyl-L-methionine Disulfate Tosylate taken:

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

r_U = peak response of sulfate from the *Sample solution*

r_S = peak response of sulfate from the *Standard solution*

C_S = concentration of sulfate (SO_4) in the *Standard solution* (mg/mL)

C_U = concentration of S-Adenosyl-L-methionine Disulfate Tosylate in the *Sample solution* (mg/mL)

Acceptance criteria: 23.5%–26.5%

SPECIFIC TESTS

• **pH (791):** 1.0–2.0, in an aqueous solution (1 in 20)

• **WATER DETERMINATION, Method Ia (921):** NMT 3.0%

• **ISOMERIC RATIO**

Buffer: Transfer 4.2 g of citric acid monohydrate and 2.03 g of sodium dihydrogen phosphate dihydrate to a 1-L volumetric flask, and dissolve in and dilute with water to volume.

Mobile phase: 4.0 g of sodium dodecyl sulfate and 440 mL of acetonitrile. Dilute with *Buffer* to 1 L.

Standard solution: 1.0 mg/mL of [USP S-Adenosyl-L-methionine Disulfate Tosylate RS](#)

Sample solution: 1.0 mg/mL of S-Adenosyl-L-methionine Disulfate Tosylate

Chromatographic system

(See [Chromatography \(621\), System Suitability.](#))

Mode: LC