ACETAZOLAMIDUM

Acetazolamide

Molecular formula. C₄H₆N₄O₃S₂

Relative molecular mass. 222.2

Graphic formula.



Chemical name. *N*-(5-Sulfamoyl-1,3,4-thiadiazol-2-yl)acetamide; *N*-[5-(amino-sulfonyl)-1,3,4-thiadiazol-2-yl]acetamide; 5-acetamido-1,3,4-thiadiazole-2-sulfonamide: CAS Reg. No. 59-66-5.

Description. A white, or almost white, crystalline powder; occurless.

Solubility. Very slightly soluble in water; slightly soluble in ethanol (~ 750 g/l) TS; practically insoluble in ether R and chloroform R.

Category. Carbonic anhydrase inhibitor.

Storage. Acetazolamide should be kept in a well-closed container.

REQUIREMENTS

General requirement. Acetazolamide contains not less than 99.0% and not more than 101.0% of C₄H₆N₄O₃S₂, calculated with reference to the dried substance.

Identity tests

A. Carry out the examination as described under "Spectrophotometry in the infrared region" (vol. 1, p. 40). The infrared absorption spectrum is concordant with the spectrum obtained from acetazolamide RS or with the *reference spectrum* of acetazolamide.

B. Dissolve 25 mg in 5 ml of water, add 0.15 ml of sodium hydroxide (1 mol/l) VS and 0.1 ml of copper(II) sulfate (80 g/l) TS; a bluish green colour or precipitate is formed.

formed. Filter (keep the filtrate for test C), wash the precipitate with water and dry at 105 °C. Melting temperature, about 159 °C (salicylic acid).

C. Heat the filtrate from test B with 2 ml of ethanol ($\sim 750 \text{ g/l}$) TS and 2 ml of sulfuric acid ($\sim 1760 \text{ g/l}$) TS; ethyl acetate, perceptible by its odour (proceed with caution), is produced.

Heavy metals. Use 1.0 g and 25 ml of acetone R for the preparation of the test solution as described under "Limit test for heavy metals", procedure 2 (vol. 1, p. 118); determine the heavy metal content according to Method A (vol. 1, p. 119); not more than 20 μ g/g.

Solution in ethanol. A solution of 1.0 g in 10 ml of ethanol (\sim 750 g/l) TS is clear and colourless.

Solution in alkali. A solution of 0.5 g in 10 ml of warm sodium carbonate (50 g/l) TS is clear.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry to constant weight at ambient temperature under reduced pressure (not exceeding 0.6 kPa or about 5 mm of mercury) over silica gel. desiccant, R; it loses not more than 5.0 mg/g.

Salicylic acid. Dissolve 0.50 g in sufficient ethanol (~750 g/l) TS to produce 25 ml and transfer 10 ml to a comparison tube. Dissolve separately 0.040 g of salicylic acid R in sufficient water to produce 100 ml. Transfer 1 ml of this solution to a second comparison tube and add to it 10 ml of ethanol (~750 g/l) TS. Add water to both tubes to make 50 ml, followed by 1 ml of ferric ammonium sulfate TS1, mix and allow to stand for 1 minute. The violet colour of the test solution is not more intense than that of the reference solution when compared as described under "Colour of liquids" (vol. 1, p. 50); the salicylic acid content is not more than 2.0 mg/g.

Assay. To about 0.20 g, accurately weighed, add 50 ml of carbonate-free sodium hydroxide (0.1 mol/l) VS, and boil under reflux for 10 minutes. Titrate the excess of alkali with sulfuric acid (0.05 mol/l) TS, using phenolphthalein/ethanol TS as indicator. Repeat the operation without the substance being examined and make any necessary corrections. Each ml of carbonate-free sodium hydroxide (0.1 mol/l) VS is equivalent to 9.008 mg of $C_9H_8O_4$.

Identity test

Dissolve 0.14 g in 1 ml of sodium hydroxide (1 mol/l) VS and add 5 ml of water; this solution yields the reaction described under "General identification tests" as characteristic of salicylates (vol. 1, p. 114).

Melting range. 158-161 °C.

Heavy metals. Use 2.0 g and 15 ml of ethanol (~750 g/l) TS for the preparation of the test solution as described under "Limit test for heavy metals", Procedure 2 (vol. 1, p. 118); determine the heavy metals content according to Method A (vol. 1, p. 119); not more than $20 \ \mu g/g$.

Chlorides. Dissolve 1.7 g in 40 ml of boiling water, cool and filter. Add 2 ml of nitric acid (\sim 130 g/l) TS to the filtrate and proceed as described under "Limit test for chlorides" (vol. 1, p. 112); the chloride content is not more than 0.15 mg/g.

Sulfates. Dissolve 2.5 g in 40 ml of boiling water, cool, filter, and proceed with the filtrate as described under "Limit test for sulfates" (vol. 1, p. 116); the sulfate content is not more than 0.2 mg/g.

Solution in ethanol. A solution of 1.0 g in 10 ml of ethanol (\sim 750 g/l) TS is clear and colourless.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry to constant weight over silica gel, desiccant, R at ambient temperature; it loses not more than 5.0 mg/g.

Assay. Dissolve about 0.3 g, accurately weighed, in 15 ml of neutralized ethanol TS and add 20 ml of water. Titrate with carbonate-free sodium hydroxide (0.1 mol/l) VS, using phenolphthalein/ethanol TS as indicator. Repeat the operation without the substance being examined and make any necessary corrections. Each ml of carbonate-free sodium hydroxide (0.1 mol/l) VS is equivalent to 13.81 mg of $C_3H_6O_3$.

Chemical name. (2S,5R,6R)-6-[(R)-2-Amino-2-phenylacetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicy:lo[3.2.0]heptane-2-carboxylic acid; $[2S-[2\alpha,5\alpha,6\beta(S^*)]]$ -6-[(aminophenylacetyl)amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0]heptane-2-carboxylic acid; CAS Reg. No. 69-53-4 (anhydrous). (2S,5R,6R)-6-[(R)-2-Amino-2-phenylacetamido]-3,3-dimethyl-7-oxo-4-thia-1carbinyle[2.2.0]heptane. 2 acid and a set of the set

azabicyclo[3.2.0]heptane-2-carboxylic acid trihydrate; $[2S-[2\alpha, 5\alpha, 6\beta(S^*)]]$ -6-[(aminophenylacetyl)amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid trihydrate; CAS Reg. No. 7177-48-2 (trihydrate).

Description. A white or almost white, crystalline powder; odourless or almost odourless.

Solubility. Slightly soluble in water; practically insoluble in ethanol (\sim 750 g/l) TS, chloroform R, and ether R.

Category. Antibiotic.

Storage. Ampicillin should be kept in a tightly closed container, protected from light and stored at a temperature not exceeding 25 °C.

Labelling. The designation on the container of Ampicillin should state whether the substance is in the anhydrous form or is the trihydrate.

Additional information. Even in the absence of light, Ampicillin is gradually degraded on exposure to a humid atmosphere, the decomposition being faster at higher temperatures.

REQUIREMENTS

General requirement. Ampicillin contains not less than 95.0% and not more than 102.0% of $C_{16}H_{19}N_3O_4S$, calculated with reference to the anhydrous substance.

Identity tests

• Either test A or test B may be applied.

A. Carry out the examination as described under "Spectrophotometry in the infrared region" (vol. 1, p. 40). For the anhydrous form the infrared absorption spectrum is concordant with the spectrum obtained from ampicillin RS or with the *reference spectrum* of ampicillin.

For the trihydrate the infrared absorption spectrum is concordant with the spectrum obtained from ampicillin trihydrate RS or with the *reference spectrum* of ampicillin trihydrate.

B. To 2 mg in a test-tube add 1 drop of water followed by 2 ml of sulfuric acid $(\sim 1760 \text{ g/l})$ TS and mix; the solution is colourless. Immerse the test-tube for