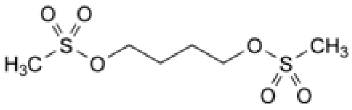
Edition: BP 2025 (Ph. Eur. 11.6 update)

Busulfan

General Notices

(Ph. Eur. monograph 0542)



$C_6H_{14}O_6S_2$ 246.3 *55-98-1*

Action and use

Cytotoxic alkylating agent.

Preparation

Busulfan Tablets

Ph Eur

DEFINITION

Butane-1,4-diyl di(methanesulfonate).

Content

99.0 per cent to 100.5 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Very slightly soluble in water, freely soluble in acetone and in acetonitrile, very slightly soluble in ethanol (96 per cent).

mp

About 116 °C.

IDENTIFICATION

First identification: A.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (*2.2.24*).

Comparison *busulfan CRS*.

B. Thin-layer chromatography (*2.2.27*).

Test solution Dissolve 20 mg of the substance to be examined in 2 mL of *acetone R*.

Reference solution Dissolve 20 mg of *busulfan CRS* in 2 mL of *acetone R*.

Plate *TLC silica gel G plate R*.

Mobile phase *acetone R*, *toluene R* (50:50 *V/V*).

Application 5 µL.

Development Over a path of 15 cm.

Drying In a current of warm air.

Detection Spray with *anisaldehyde solution R* and heat at 120 °C.

Results The principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

C. To 0.1 g add 5 mL of *1 M sodium hydroxide*. Heat until a clear solution is obtained. Allow to cool. To 2 mL of the solution add 0.1 mL of *potassium permanganate solution R*. The colour changes from purple through violet to blue and finally to green. Filter and add 1 mL of *ammoniacal silver nitrate solution R*. A precipitate is formed.

D. To 0.1 g add 0.1 g of *potassium nitrate R* and 0.25 g of *sodium hydroxide R*, mix and heat to fusion. Allow to cool and dissolve the residue in 5 mL of *water R*. Adjust to pH 1-2 using *dilute hydrochloric acid R*. The solution gives reaction (a) of sulfates (*2.3.1*).

TESTS

Appearance of solution

The solution is clear (*2.2.1*) and not more intensely coloured than reference solution B_7 (*2.2.2, Method II*).

Dissolve 0.25 g in 20 mL of *acetonitrile R*, dilute to 25 mL with *water R* and examine immediately.

Acidity

Dissolve 0.20 g with heating in 50 mL of *anhydrous ethanol R*. Add 0.1 mL of *methyl red solution R*. Not more than 0.05 mL of *0.1 M sodium hydroxide* is required to change the colour of the indicator.

Loss on drying (*2.2.32*)

Maximum 2.0 per cent, determined on 1.000 g by drying *in vacuo* at 60 °C.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

To 0.250 g add 50 mL of *water R*. Shake. Boil under a reflux condenser for 30 min and, if necessary, make up to the initial volume with *water R*. Allow to cool. Using 0.3 mL of *phenolphthalein solution R* as indicator, titrate with *0.1 M sodium hydroxide* until a pink colour is obtained.

1 mL of *0.1 M sodium hydroxide* is equivalent to 12.32 mg of $C_6H_{14}O_6S_2$.

STORAGE

In an airtight container, protected from light.

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