IDENTIFICATION

A. Dilute 1 mL to 100 mL with *water R*. The solution is strongly acid (*2.2.4*).

B. 0.2 mL of the solution obtained in identification test A gives the reaction of nitrates (*2.3.1*).

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution Y_6 (*2.2.2, Method II*).

Dilute 2 mL to 10 mL with *water R*.

Chlorides (*2.4.4*): maximum 0.5 ppm.

To 5 g add 10 mL of *water R* and 0.3 mL of *silver nitrate solution R2* and allow to stand for 2 min protected from light. Any opalescence is not more intense than that of a standard prepared at the same time in the same manner using 13 mL of *water R*, 0.5 mL of *nitric acid R*, 0.5 mL of *chloride standard solution (5 ppm Cl) R* and 0.3 mL of *silver nitrate solution R2*.

Sulfates (*2.4.13*): maximum 10 ppm.

To 15 g add 0.2 g of *sodium carbonate R*. After carbon dioxide has evolved, evaporate to dryness. Dissolve the residue in 15 mL of *distilled water R*.

Iron (*2.4.9*): maximum 10 ppm.

Dissolve the residue obtained in the test for sulfated ash in 1 mL of *dilute hydrochloric acid R* and dilute to 20 mL with *water R*. Dilute 1 mL of this solution to 10 mL with *water R*.

Sulfated ash: maximum 0.01 per cent.

Carefully evaporate 20.00 g to dryness. Moisten the residue with a few drops of *sulfuric acid R* and ignite to dull red.

ASSAY

To 0.750 g add 50 mL of *water R* and titrate with *1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *1 M sodium hydroxide* is equivalent to 63.0 mg of HNO_3.

STORAGE

Protected from light.

01/2008:1550

NITRIC OXIDE

Nitrogenii oxidum

NO M_r 30.01
[10102-43-9]

DEFINITION

Content: minimum 99.0 per cent *V/V* of NO.

This monograph applies to nitric oxide for medicinal use.

CHARACTERS

Appearance: colourless gas which turns brown when exposed to air.

Solubility: at 20 °C and at a pressure of 101 kPa, 1 volume dissolves in about 21 volumes of water.

PRODUCTION

Carbon dioxide. Gas chromatography (*2.2.28*).

Gas to be examined. The substance to be examined.

Reference gas: mixture containing 3000 ppm *V/V* of *carbon dioxide R1* in *nitrogen R*.

Column:

- *material*: stainless steel;
- *size*: *l* = 3.5 m, Ø = 2 mm;
- *stationary phase*: *ethylvinylbenzene-divinylbenzene copolymer R*;
- *temperature*: 50 °C.

Carrier gas: *helium for chromatography R*.

Flow rate: 15 mL/min.

Detection: thermal conductivity.

Injection: loop injector.

System suitability:

- the chromatograms obtained show a clear separation of carbon dioxide from nitric oxide.

Limit:

- *carbon dioxide*: not more than the area of the corresponding peak in the chromatogram obtained with the reference gas (3000 ppm *V/V*).

Nitrogen. Gas chromatography (*2.2.28*).

Gas to be examined. The substance to be examined.

Reference gas: mixture containing 3000 ppm *V/V* of *nitrogen R* in *helium for chromatography R*.

Column:

- *material*: stainless steel;
- *size*: *l* = 3.5 m, Ø = 2 mm;
- *stationary phase*: *molecular sieve for chromatography R* (0.5 nm);
- *temperature*: 50 °C.

Carrier gas: *helium for chromatography R*.

Flow rate: 15 mL/min.

Detection: thermal conductivity.

Injection: loop injector.

System suitability:

- the chromatograms obtained show a clear separation of nitrogen from nitric oxide.

Limit:

- *nitrogen*: not more than the area of the corresponding peak in the chromatogram obtained with the reference gas (3000 ppm *V/V*).

Nitrogen dioxide: maximum 400 ppm *V/V*.

Ultraviolet absorption spectrophotometry analyser.

Gas to be examined. The substance to be examined.

Reference gas (a): *nitrogen R1*.

Reference gas (b): mixture containing 400 ppm *V/V* of *nitrogen dioxide R* in *nitrogen R*.

Apparatus:

- an ultraviolet-visible light source (analytical wavelength about 400 nm);
- a sample gas cell through which the feed gas flows;
- a closed reference gas cell containing *nitrogen R1* in parallel with the sample gas cell;
- a rotating chopper which feeds light alternately through the reference gas cell and the sample gas cell;
- a semiconductor detector which generates a frequency modulated output whose amplitude is a measure of the difference of absorption of the sample gas and the reference gas.

Analysis:

- set the zero of the instrument using reference gas (a) through the sample gas cell at a flow rate of 1 L/min;
- adjust the span while feeding reference gas (b) through the sample gas cell at a flow rate of 1 L/min;

– feed the gas to be examined through the sample gas cell at a flow rate of 1 L/min, read the value from the instrument output and calculate, if necessary, the concentration of nitrogen dioxide.

Nitrous oxide. Gas chromatography (*2.2.28*).

Gas to be examined. The substance to be examined.

Reference gas: mixture containing 3000 ppm *V/V* of *nitrous oxide R* in *nitrogen R*.

Column:

– *material*: stainless steel;
– *size*: *l* = 3.5 m, Ø = 2 mm;
– *stationary phase*: *ethylvinylbenzene-divinylbenzene copolymer R*;
– *temperature*: 50 °C.

Carrier gas: *helium for chromatography R*.

Flow rate: 15 mL/min.

Detection: thermal conductivity.

Injection: loop injector.

System suitability:

– the chromatograms obtained show a clear separation of nitrous oxide from nitric oxide.

Limit:

– *nitrous oxide*: not more than the area of the corresponding peak in the chromatogram obtained with the reference gas (3000 ppm *V/V*).

Water (*2.5.28*): maximum 100 ppm *V/V*.

Assay. Determine the content of nitric oxide by difference using the mass balance equation after determining the sum of the impurities described under Production.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *Ph. Eur. reference spectrum of nitric oxide*.

STORAGE

Compressed at a pressure not exceeding 2.5 MPa (25 bar) measured at 15 °C, in suitable containers complying with the legal regulations.

IMPURITIES

Specified impurities: A, B, C, D, E.

A. CO_2: carbon dioxide,

B. N_2: nitrogen,

C. NO_2: nitrogen dioxide,

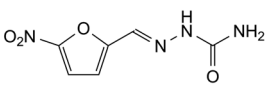
D. N_2O: nitrous oxide,

E. H_2O: water.

04/2013:1135

NITROFURAL

Nitrofuralum



$C_6H_6N_4O_4$ M_r 198.1
[59-87-0]

DEFINITION

2-[(5-Nitrofuran-2-yl)methylene]diazanecarboxamide.

Content: 97.0 per cent to 103.0 per cent (dried substance).

CHARACTERS

Appearance: yellow or brownish-yellow, crystalline powder.

Solubility: very slightly soluble in water, slightly soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: B.

Second identification: A, C, D.

A. Ultraviolet and visible absorption spectrophotometry (*2.2.25*). *Carry out the test protected from bright light.*

Test solution. Use the solution prepared for the assay.

Spectral range: 220-400 nm.

Absorption maxima: at 260 nm and 375 nm.

Absorbance ratio: A_{375}/A_{260} = 1.15 to 1.30.

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *nitrofural CRS*.

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

Test solution. Dissolve 10 mg of the substance to be examined in *methanol R* and dilute to 10 mL with the same solvent.

Reference solution. Dissolve 10 mg of *nitrofural CRS* in *methanol R* and dilute to 10 mL with the same solvent.

Plate: *TLC silica gel G plate R*.

Mobile phase: *methanol R*, *nitromethane R* (10:90 *V/V*).

Application: 5 µL.

Development: over a path of 15 cm.

Drying: in air.

Detection: spray with *phenylhydrazine hydrochloride solution R*.

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.

D. Dissolve about 1 mg in 1 mL of *dimethylformamide R* and add 0.1 mL of *alcoholic potassium hydroxide solution R*. A violet-red colour is produced.

TESTS

pH (*2.2.3*): 5.0 to 7.0.

To 1.0 g add 100 mL of *carbon dioxide-free water R*. Shake and filter.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 0.100 g of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (a). Dissolve 10.0 mg of *nitrofural impurity B CRS* in the mobile phase and dilute to 20.0 mL with the mobile phase. Dilute 1.0 mL of the solution to 100.0 mL with the mobile phase.

Reference solution (b). Dissolve 10 mg of the substance to be examined and 10 mg of *nitrofurantoin R* in the mobile phase and dilute to 100.0 mL with the mobile phase. Dilute 5.0 mL of the solution to 100.0 mL with the mobile phase.

Reference solution (c). Dissolve with the aid of ultrasound the contents of a vial of *nitrofural for peak identification CRS* (containing impurities A and B) in 1.0 mL of the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;
– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: *acetonitrile R*, *water R* (40:60 *V/V*).

Flow rate: 1 mL/min.

Detection: spectrophotometer at 310 nm.

Injection: 20 µL.

Run time: 10 times the retention time of nitrofural.