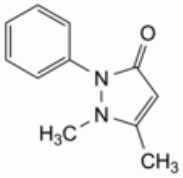
Edition: BP 2025 (Ph. Eur. 11.6 update)

Phenazone

General Notices

(Ph. Eur. monograph 0421)



$C_{11}H_{12}N_2O$ 188.2 *60-80-0*

Action and use

Analgesic; used to test hepatic drug-metabolizing activity.

Ph Eur

DEFINITION

1,5-Dimethyl-2-phenyl-1,2-dihydro-3*H*-pyrazol-3-one.

Content

99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder or colourless crystals.

Solubility

Very soluble in water, in ethanol (96 per cent) and in methylene chloride.

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D.

A. Melting point (2.2.14): 109 °C to 113 °C.
B. Infrared absorption spectrophotometry (2.2.24).

Comparison *phenazone CRS*.

C. To 1 mL of solution S (see Tests) add 4 mL of *water R* and 0.25 mL of *dilute sulfuric acid R*. Add 1 mL of *sodium nitrite solution R*; a green colour develops.
D. To 1 mL of solution S add 4 mL of *water R* and 0.5 mL of *ferric chloride solution R2*. A red colour develops which is discharged on the addition of *dilute sulfuric acid R*.

TESTS

Solution S

Dissolve 2.5 g in *carbon dioxide-free water R* and dilute to 50 mL with the same solvent.

Appearance of solution

Solution S is clear (2.2.1) and colourless (2.2.2, Method II).

Acidity or alkalinity

To 10 mL of solution S add 0.1 mL of *phenolphthalein solution R*; the solution is colourless. Add 0.2 mL of *0.01 M sodium hydroxide*; the solution is red. Add 0.25 mL of *methyl red solution R* and 0.4 mL of *0.01 M hydrochloric acid*; the solution is red or yellowish-red.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 50.0 mg of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (b) Dissolve 5 mg of *phenazone impurity A CRS* in the mobile phase, add 10 mL of the test solution and dilute to 20.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 50.0 mL with the mobile phase.

Reference solution (c) Dissolve 5.0 mg of *phenazone impurity A CRS* in the mobile phase and dilute to 20.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.15 m, Ø = 6.0 mm;

— *stationary phase*: spherical *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase Dissolve 6.8 g of *potassium dihydrogen phosphate R* in *water R* and dilute to 1000 mL with the same solvent. Add 2 mL of *triethylamine R* and adjust to pH 7.0 with *sodium hydroxide solution R*. Add 430 mL of *methanol R*.

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 254 nm.

Injection 10 µL.

Run time 3 times the retention time of phenazone.

Relative retention With reference to phenazone (retention time = about 13 min): impurity A = about 0.8.

System suitability Reference solution (b):

— *resolution*: minimum 3.0 between the peaks due to impurity A and phenazone.

Limits:

— *impurity A*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (c) (0.05 per cent);

— *unspecified impurities*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent);

— *total*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent);

— *disregard limit*: 0.3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.03 per cent).

Chlorides (*2.4.4*)

Maximum 100 ppm.

Dilute 10 mL of solution S to 15 mL with *water R*.

Sulfates (*2.4.13*)

Maximum 100 ppm.

Dissolve 1.5 g in *distilled water R* and dilute to 15 mL with the same solvent.

Loss on drying (*2.2.32*)

Maximum 1.0 per cent, determined on 1.000 g by drying *in vacuo* at 60 °C for 6 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.150 g in 20 mL of *water R*. Add 2 g of *sodium acetate R*, 1 mL of *dilute acetic acid R* and 25.0 mL of *0.05 M iodine*. Allow to stand protected from light for 30 min. Add 25 mL of *methylene chloride R* and shake until the precipitate dissolves. Titrate with *0.1 M sodium thiosulfate*, using 1 mL of *starch solution R*, added towards the end of the titration, as indicator. Carry out a blank titration.

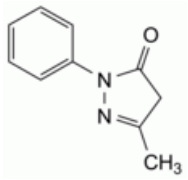
1 mL of *0.05 M iodine* is equivalent to 9.41 mg of $C_{11}H_{12}N_2O$.

STORAGE

Protected from light.

IMPURITIES

Specified impurities *A.*



A. 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one.

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