

**Loss on drying** (2.2.32): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

**Sulfated ash** (2.4.14): maximum 0.1 per cent, determined on 1.0 g.

#### ASSAY

Dissolve 0.220 g in 50 mL of *alcohol R*. Add 5.0 mL of 0.01 M *hydrochloric acid*. Titrate with 0.1 M *sodium hydroxide* determining the end-point potentiometrically (2.2.20). Read the volume added between the 2 points of inflexion.

1 mL of 0.1 M *sodium hydroxide* is equivalent to 28.38 mg of  $C_{15}H_{22}ClNO_2$ .

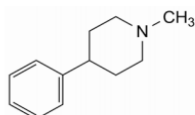
#### STORAGE

In an airtight container, protected from light.

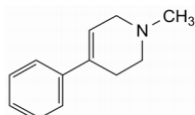
#### LABELLING

The label states, where applicable, that the substance is suitable for use in the manufacture of parenteral preparations.

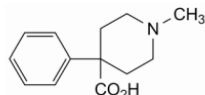
#### IMPURITIES



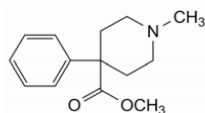
A. 1-methyl-4-phenylpiperidine (MPP),



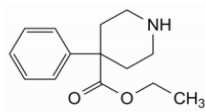
B. 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP),



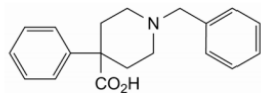
C. 1-methyl-4-phenylpiperidine-4-carboxylic acid,



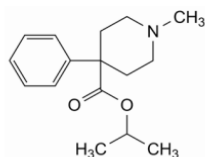
D. methyl 1-methyl-4-phenylpiperidine-4-carboxylate,



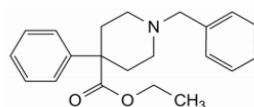
E. ethyl 4-phenylpiperidine-4-carboxylate,



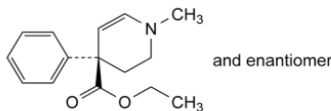
F. 1-benzyl-4-phenylpiperidine-4-carboxylic acid,



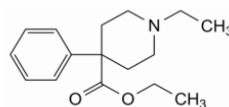
G. 1-methylethyl 1-methyl-4-phenylpiperidine-4-carboxylate,



H. ethyl 1-benzyl-4-phenylpiperidine-4-carboxylate,



I. ethyl (4RS)-1-methyl-4-phenyl-1,2,3,4-tetrahydropyridine-4-carboxylate,



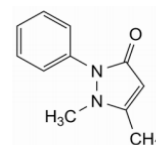
J. ethyl 1-ethyl-4-phenylpiperidine-4-carboxylate.



01/2017:0421

## PHENAZONE

### Phenazonum



$C_{11}H_{12}N_2O$   
[60-80-0]

$M_r$  188.2

#### DEFINITION

1,5-Dimethyl-2-phenyl-1,2-dihydro-3H-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,  $\varnothing = 6.0$  mm;
- stationary phase: spherical octadecylsilyl silica gel for chromatography R (5  $\mu$ m).

**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  $\mu$ L.

**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.

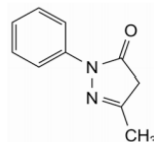
1 mL of 0.05 M iodine is equivalent to 9.41 mg of  $C_{11}H_{12}N_2O$ .

**STORAGE**

Protected from light.

**IMPURITIES**

Specified impurities: A.



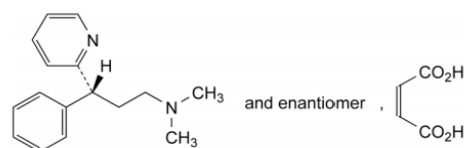
A. 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one.



01/2017:1357

## PHENIRAMINE MALEATE

### Pheniramini maleas



$C_{20}H_{24}N_2O_4$   
[132-20-7]

$M_r$  356.4

**DEFINITION**

(3RS)-N,N-Dimethyl-3-phenyl-3-(pyridin-2-yl)propan-1-amine (Z)-butenedioate.

**Content:** 99.0 per cent to 101.0 per cent (dried substance).

**CHARACTERS**

**Appearance:** white or almost white, crystalline powder.

**Solubility:** very soluble in water, freely soluble in ethanol (96 per cent), in methanol and in methylene chloride.

**IDENTIFICATION**

**First identification:** C.

**Second identification:** A, B, D.

A. Melting point (2.2.14): 106 °C to 109 °C.

B. Ultraviolet and visible absorption spectrophotometry (2.2.25).

**Test solution.** Dissolve 40.0 mg in 0.1 M hydrochloric acid and dilute to 100.0 mL with the same acid. Dilute 5.0 mL of the solution to 50.0 mL with 0.1 M hydrochloric acid.

**Spectral range:** 220-320 nm.

**Absorption maximum:** at 265 nm.

**Shoulder:** at 261 nm.

**Specific absorbance at the absorption maximum:** 200 to 220.

C. Infrared absorption spectrophotometry (2.2.24).

**Comparison:** pheniramine maleate CRS.

D. Thin-layer chromatography (2.2.27).

**Test solution.** Dissolve 0.10 g of the substance to be examined in methanol R and dilute to 5.0 mL with the same solvent.

**Reference solution (a).** Dissolve 65 mg of maleic acid R in methanol R and dilute to 10 mL with the same solvent.