– *sum of contents of palmitic acid and stearic acid*: minimum 90.0 per cent.

Free propylene glycol: maximum 5.0 per cent, determined as prescribed under Assay.

Total ash (*2.4.16*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Size-exclusion chromatography (*2.2.30*).

Test solution. In a 15 mL flask, weigh about 0.2 g (*m*), to the nearest 0.1 mg. Add 5.0 mL of *tetrahydrofuran R* and shake to dissolve. Heat gently, if necessary. Reweigh the flask and calculate the total mass of solvent and substance (*M*).

Reference solutions. In four 15 mL flasks, weigh, to the nearest 0.1 mg, about 2.5 mg, 5.0 mg, 10.0 mg and 20.0 mg of *propylene glycol R*. Add 5.0 mL of *tetrahydrofuran R* and shake to dissolve. Weigh the flasks again and calculate the concentration of propylene glycol in milligrams per gram for each reference solution.

Column:

– *size*: *l* = 0.6 m, Ø = 7 mm,

– *stationary phase*: *styrene-divinylbenzene copolymer R* (particle diameter 5 µm, pore size 10 nm).

Mobile phase: *tetrahydrofuran R*.

Flow rate: 1 mL/min.

Detection: differential refractometer.

Injection: 40 µL.

Relative retention with reference to propylene glycol: diesters = about 0.78, monoesters = about 0.84.

Limits:

– *free propylene glycol*: from the calibration curve obtained with the reference solutions, determine the concentration (*C*) in milligrams per gram in the test solution and calculate the percentage content in the substance to be examined using the following expression:

$$\frac{C \times M}{m \times 10}$$

– *monoesters*: calculate the percentage content of monoesters using the following expression:

$$\frac{A}{A + B} \times (100 - D)$$

A = area of the peak due to the monoesters,

B = area of the peak due to the diesters,

D = percentage content of free propylene glycol + percentage content of free fatty acids which is determined using the following expression:

$$\frac{I_A \times 270}{561.1}$$

I_A = acid value.

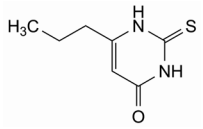
STORAGE

Protected from light.

01/2017:0525

PROPYLTHIOURACIL

Propylthiouracilum



$C_7H_{10}N_2OS$ M_r 170.2
[51-52-5]

DEFINITION

Propylthiouracil contains not less than 98.0 per cent and not more than the equivalent of 100.5 per cent of 2,3-dihydro-6-propyl-2-thioxopyrimidin-4(1*H*)-one, calculated with reference to the dried substance.

CHARACTERS

White or almost white, crystalline powder or crystals, very slightly soluble in water, sparingly soluble in alcohol. It dissolves in solutions of alkali hydroxides.

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D.

A. Melting point (*2.2.14*): 217 °C to 221 °C.

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *propylthiouracil CRS*. Examine as discs prepared using 1 mg of substance and 0.3 g of *potassium bromide R*.

C. Examine the chromatograms obtained in the test for impurity A and related substances in ultraviolet light at 254 nm before exposure of the plate to iodine vapour. The principal spot in the chromatogram obtained with test solution (b) is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a).

D. To about 20 mg add 8 mL of *bromine water R* and shake for a few minutes. Boil until the mixture is decolourised, allow to cool and filter. To the filtrate add 2 mL of *barium chloride solution R1*. A white precipitate is formed whose colour does not become violet on the addition of 5 mL of *dilute sodium hydroxide solution R*.

TESTS

Impurity A and related substances. Examine by thin-layer chromatography (*2.2.27*), using a *TLC silica gel GF_{254} plate R*.

Test solution (a). Dissolve 0.1 g of the substance to be examined in *methanol R* and dilute to 10 mL with the same solvent.

Test solution (b). Dilute 1 mL of test solution (a) to 10 mL with *methanol R*.

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

Reference solution (b). Dissolve 50 mg of *thiourea R* in *methanol R* and dilute to 100 mL with the same solvent. Dilute 1 mL of this solution to 100 mL with *methanol R*.

Reference solution (c). Dilute 1 mL of test solution (a) to 100 mL with *methanol R*.

Apply separately to the plate 10 µL of each solution. Develop over a path of 15 cm using a mixture of 0.1 volumes of *glacial acetic acid R*, 6 volumes of *2-propanol R* and 50 volumes of *chloroform R*. Allow the plate to dry in air. Examine in ultraviolet light at 254 nm. Expose the plate to iodine

vapour for 10 min. In the chromatogram obtained with test solution (a), any spot corresponding to impurity A is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.05 per cent) and any spot apart from the principal spot and any spot corresponding to impurity A is not more intense than the spot in the chromatogram obtained with reference solution (c) (1.0 per cent).

Loss on drying (*2.2.32*). Not more than 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

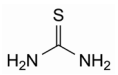
To 0.300 g add 30 mL of *water R* and 30.0 mL of *0.1 M sodium hydroxide*. Boil and shake until dissolution is complete. Add 50 mL of *0.1 M silver nitrate* while stirring, boil gently for 5 min and cool. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*). The volume of *0.1 M sodium hydroxide* used is equal to the sum of the volume added initially and the volume used in the final titration.

1 mL of *0.1 M sodium hydroxide* is equivalent to 8.511 mg of $C_7H_{10}N_2OS$.

STORAGE

Store protected from light.

IMPURITIES

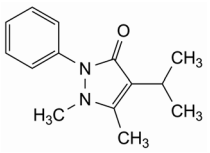


A. thiourea.

01/2017:0636

PROPYPHENAZONE

Propyphenazonum



$C_{14}H_{18}N_2O$ M_r 230.3
[479-92-5]

DEFINITION

1,5-Dimethyl-4-(1-methylethyl)-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 slightly yellowish, crystalline powder.

Solubility: slightly soluble in water, freely soluble 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*): 102 °C to 106 °C.

B. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *propyphenazone CRS.*

C. Thin-layer chromatography (*2.2.27*).
Test solution. Dissolve 80 mg of the substance to be examined in *methanol R* and dilute to 5 mL with the same solvent.
Reference solution. Dissolve 80 mg of *propyphenazone CRS* in *methanol R* and dilute to 5 mL with the same solvent.
Plate: *TLC silica gel F_{254} plate R.*
Mobile phase: *butanol R, cyclohexane R, ethyl acetate R* (10:45:45 *V/V/V*).
Application: 5 µL.
Development: over 2/3 of the plate.
Drying: in a current of hot air for 15 min.
Detection: examine in ultraviolet light at 254 nm.
Results: the principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with the reference solution.

D. To 1 mL of solution S (see Tests) add 0.1 mL of *ferric chloride solution R1*. A brownish-red colour appears which becomes yellow on addition of 1 mL of *dilute hydrochloric acid R*.

TESTS

Solution S. Dissolve 2 g in a mixture of equal volumes of *carbon dioxide-free water R* and *ethanol (96 per cent) R* and dilute to 50 mL with the same mixture of solvents.

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 becomes pink. Add 0.4 mL of *0.01 M hydrochloric acid*; the solution becomes colourless. Add 0.2 mL of *methyl red solution R*. The solution becomes orange or red.

Related substances. Liquid chromatography (*2.2.29*).
Test solution. Dissolve 20.0 mg of the substance to be examined in the mobile phase and dilute to 20.0 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 1 mg of the substance to be examined and 1 mg of *phenazone R* (impurity A) in the mobile phase and dilute to 10.0 mL with the mobile phase.
Column:
– *size*: *l* = 0.25 m, Ø = 4.0 mm;
– *stationary phase*: *end-capped octylsilyl silica gel for chromatography R* (5 µm).
Mobile phase. Dissolve 13.7 g of *potassium dihydrogen phosphate R* in 900 mL of *water R*, adjust to pH 5.2 with *dilute sodium hydroxide solution R* and dilute to 1000 mL with *water R*. Mix 60 volumes of the solution and 40 volumes of *acetonitrile R1*.
Flow rate: 1.2 mL/min.
Detection: spectrophotometer at 210 nm.
Injection: 20 µL.
Run time: 4 times the retention time of propyphenazone.
Relative retention with reference to propyphenazone (retention time = about 7 min): impurity A = about 0.4.
System suitability: reference solution (b):
– *resolution*: minimum 4.0 between the peaks due to impurity A and propyphenazone.
Limits:
– *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);