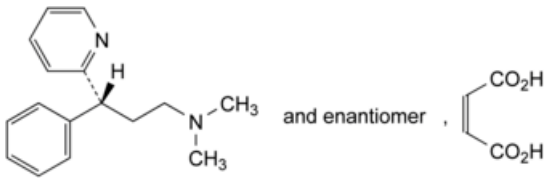
Edition: BP 2025 (Ph. Eur. 11.6 update)

Pheniramine Maleate

General Notices

(Ph. Eur. monograph 1357)



$C_{20}H_{24}N_2O_4$ 356.4 *132-20-7*

Action and use

Histamine H_1 receptor antagonist; antihistamine.

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DEFINITION

(3*RS*)-*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.

Reference solution (b) Dissolve 0.10 g of *pheniramine maleate CRS* in *methanol R* and dilute to 5.0 mL with the same solvent.

Plate *TLC silica gel F_{254} plate R*.

Mobile phase *water R*, *anhydrous formic acid R*, *methanol R*, *di-isopropyl ether R* (3:7:20:70 *V/V/V/V*).

Application 5 µL.

Development Over 2/3 of the plate.

Detection Examine in ultraviolet light at 254 nm.

Results The chromatogram obtained with the test solution shows 2 clearly separated spots; the upper spot is similar in position and size to the spot in the chromatogram obtained with reference solution (a); the lower spot is similar in position and size to the lower spot in the chromatogram obtained with reference solution (b).

TESTS

Solution S

Dissolve 2.0 g in *water R* and dilute to 20.0 mL with the same solvent.

Appearance of solution

Solution S is clear (2.2.1) and not more intensely coloured than reference solution BY_6 (*2.2.2, Method II*).

pH (2.2.3)

4.5 to 5.5.

Dissolve 0.20 g in 20 mL of *carbon dioxide-free water R*.

Related substances

Liquid chromatography (2.2.29).

Solvent mixture *acetonitrile R*, mobile phase A (10:90 *V/V*).

Test solution Dissolve 20.0 mg of the substance to be examined in the solvent mixture and dilute to 20.0 mL with the solvent mixture.

Reference solution (a) Dissolve 10.0 mg of *pheniramine impurity A CRS* and 10 mg of *4-benzylpyridine R* (impurity B) in 10.0 mL of the solvent mixture and dilute to 100.0 mL with the solvent mixture.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Reference solution (c) Dilute 1.0 mL of reference solution (a) to 50.0 mL with the solvent mixture.

Reference solution (d) Dilute 1.0 mL of the test solution to 10.0 mL with reference solution (a). Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Column:

— *size*: *l* = 0.30 m, *Ø* = 3.9 mm;

— *stationary phase*: *octadecylsilyl silica gel for chromatography R* (10 µm).

Mobile phase:

— *mobile phase A*: dissolve 5.056 g of *sodium heptanesulfonate R* in 900 mL of *water R*, adjust to pH 2.5 with *dilute phosphoric acid R* and dilute to 1000 mL with *water R*;

— *mobile phase B*: *acetonitrile R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 2	90	10
2 - 37	90 → 62	10 → 38

Flow rate 1 mL/min.

Detection Spectrophotometer at 264 nm.

Injection 20 µL.

Identification of impurities Use the chromatogram obtained with reference solution (a) to identify the peaks due to impurities A and B.

Relative retention With reference to pheniramine (retention time = about 31 min): maleic acid = about 0.1; impurity A = about 0.9; impurity B = about 0.97.

System suitability Reference solution (d):

— *resolution*: minimum 1.5 between the peaks due to impurity B and pheniramine.

Limits:

— *impurity A*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (c) (0.2 per cent);

— *impurity B*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);

— *total*: maximum 1.0 per cent;

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent); disregard the peak due to maleic acid.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo* at 60 °C for 3 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.130 g in 50 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

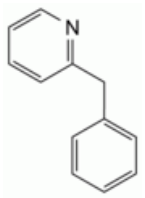
1 mL of *0.1 M perchloric acid* is equivalent to 17.82 mg of $C_{20}H_{24}N_2O_4$.

STORAGE

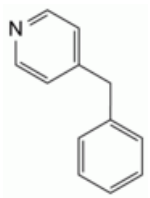
Protected from light.

IMPURITIES

Specified impurities *A, B.*



A. 2-benzylpyridine,



B. 4-benzylpyridine.

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