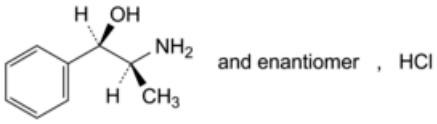
Edition: BP 2025 (Ph. Eur. 11.6 update)

Phenylpropanolamine Hydrochloride

General Notices

(Ph. Eur. monograph 0683)



$C_9H_{14}ClNO$ 187.7 *154-41-6*

Action and use

Adrenoceptor agonist.

Ph Eur

DEFINITION

(1*RS*,2*SR*)-2-Amino-1-phenylpropan-1-ol hydrochloride.

Content

99.0 per cent to 101.5 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Freely soluble in water and in ethanol (96 per cent), practically insoluble in methylene chloride.

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D.

A. Melting point (*2.2.14*): 194 °C to 197 °C.
B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison *phenylpropanolamine hydrochloride CRS*.

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

Test solution Dissolve 20 mg of the substance to be examined in *ethanol (96 per cent) R* and dilute to 10 mL with the same solvent.

Reference solution Dissolve 10 mg of *phenylpropanolamine hydrochloride CRS* in *ethanol (96 per cent) R* and dilute to 5 mL with the same solvent.

Plate *TLC silica gel G plate R*.

Pretreatment Spray with a 20 g/L solution of *disodium tetraborate R*, using 8 mL for a plate 100 mm x 200 mm and dry in a stream of cold air for 30 min.

Mobile phase *concentrated ammonia R*, *ethanol (96 per cent) R*, *butanol R* (6:24:70 *V/V/V*).

Application 10 µL as bands of 10 mm by 3 mm.

Development Over 1/2 of the plate.

Drying In a current of warm air.

Detection Allow to cool, then spray with a 2 g/L solution of *ninhydrin R* in *ethanol (96 per cent) R* and heat at 110 °C for 15 min.

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. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S

Dissolve 1.25 g in *water R* and dilute to 25 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 *methyl red solution R* and 0.2 mL of *0.01 M sodium hydroxide*. The solution is yellow. Add 0.4 mL of *0.01 M hydrochloric acid*. The solution is red.

Related substances

Liquid chromatography (*2.2.29*).

Buffer solution Dissolve 3.4 g of *potassium dihydrogen phosphate R* in 500 mL of *water for chromatography R* and adjust to pH 2.5 with *phosphoric acid R*.

Test solution Dissolve 25.0 mg of the substance to be examined in *methanol R* and dilute to 25.0 mL with the same solvent.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with *methanol R*. Dilute 1.0 mL of this solution to 10.0 mL with *methanol R*.

Reference solution (b) Dissolve 5 mg of *cathine hydrochloride R* (1*S*,2*S*-enantiomer of impurity A) in *methanol R* and dilute to 50 mL with the same solvent. Dilute 1 mL of the solution to 10 mL with *methanol R*. Dilute 1 mL of this solution to 10 mL with the test solution.

Column:

— *size*: *l* = 0.075 m, Ø = 3.0 mm;

— *stationary phase*: *octadecylsilyl silica gel for chromatography R* (1.8 µm);

— *temperature*: 40 °C.

Mobile phase:

— *mobile phase A*: *acetonitrile R1*, buffer solution (2:98 *V/V*);

— *mobile phase B*: *water for chromatography R*, *acetonitrile R1* (30:70 *V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 6	100	0
6 - 14	100 → 48	0 → 52
14 - 18	48	52

Flow rate 0.56 mL/min.

Detection Spectrophotometer at 206 nm.

Injection 1 µL.

Identification of impurities Use the chromatogram obtained with reference solution (b) to identify the peak due to impurity A.

Relative retention With reference to phenylpropanolamine (retention time = about 3 min): impurity A = about 1.2.

System suitability Reference solution (b):

— *peak-to-valley ratio*: minimum 2.0, where H_p = height above the baseline of the peak due to impurity A and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to phenylpropanolamine.

Calculation of percentage contents:

— for each impurity, use the concentration of phenylpropanolamine hydrochloride in reference solution (a).

Limits:

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.2 per cent;

— *reporting threshold*: 0.05 per cent.

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.

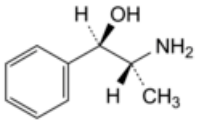
ASSAY

Dissolve 0.150 g in a mixture of 5.0 mL of *0.01 M hydrochloric acid* and 50 mL of *ethanol (96 per cent) R*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

1 mL of *0.1 M sodium hydroxide* is equivalent to 18.77 mg of $C_9H_{14}ClNO$.

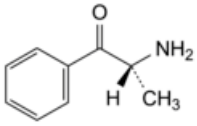
IMPURITIES

Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) A, B, C, D, E.



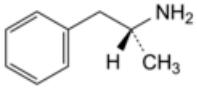
and enantiomer

A. (1*RS*,2*RS*)-2-amino-1-phenylpropan-1-ol (racemic cathine, racemic norpseudoephedrine),



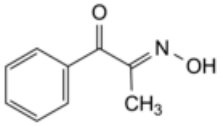
and enantiomer

B. (2*RS*)-2-amino-1-phenylpropan-1-one (racemic cathinone),



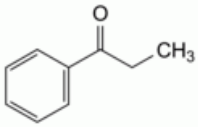
and enantiomer

C. (2*RS*)-1-phenylpropan-2-amine (amfetamine),



and (*Z*)-isomer

D. (2*EZ*)-2-(hydroxyimino)-1-phenylpropan-1-one (α-isonitrosopropiophenone),



E. 1-phenylpropan-1-one (propiophenone).

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