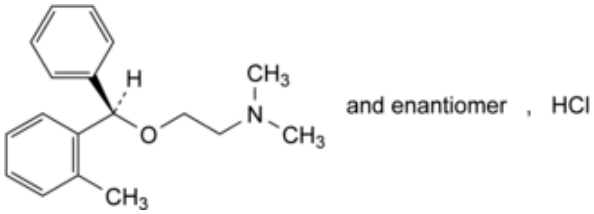
Edition: BP 2025 (Ph. Eur. 11.6 update)

Orphenadrine Hydrochloride

General Notices

(Ph. Eur. monograph 1760)



$C_{18}H_{24}ClNO$ 305.9 *341-69-5*

Action and use

Anticholinergic.

Preparation

Orphenadrine Hydrochloride Tablets

Ph Eur

DEFINITION

(*RS*)-*N,N*-Dimethyl-2-[(2-methylphenyl)phenylmethoxy]ethanamine hydrochloride.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Freely soluble in water and in ethanol (96 per cent).

mp

About 160 °C.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison orphenadrine hydrochloride CRS.

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

TESTS

Appearance of solution

The solution is clear (2.2.1) and its absorbance (2.2.25) at 436 nm has a maximum of 0.050.

Dissolve 0.70 g in ethanol (96 per cent) R and dilute to 10.0 mL with the same solvent.

Related substances

Gas chromatography (2.2.28): use the normalisation procedure.

Test solution Dissolve 0.300 g of the substance to be examined in water R and dilute to 50 mL with the same solvent. Add 2 mL of concentrated ammonia R and shake with 3 quantities, each of 10 mL, of toluene R. To the combined upper layers add anhydrous sodium sulfate R, shake, filter and evaporate the filtrate by suitable means, at a temperature not exceeding 50 °C. Take up the residue with toluene R and dilute to 20.0 mL with the same solvent.

Reference solution (a) Dissolve 20 mg of orphenadrine hydrochloride CRS and 20 mg of orphenadrine impurity E CRS in 20 mL of water R. Add 1 mL of concentrated ammonia R and shake with 3 quantities, each of 5 mL, of toluene R. To the combined upper layers add anhydrous sodium sulfate R, shake, filter and evaporate the filtrate by suitable means, at a temperature not exceeding 50 °C. Take up the residue with toluene R and dilute to 20.0 mL with the same solvent.

Reference solution (b) Dissolve the contents of a vial of orphenadrine for peak identification CRS (containing impurities A, B, C, D and F) in 1.0 mL of toluene R.

Column:

— *size*: *l* = 60 m, Ø = 0.32 mm;

— *stationary phase*: phenyl(5)methyl(95)polysiloxane R (film thickness 1.0 µm).

Carrier gas helium for chromatography R.

Flow rate 1 mL/min.

Split ratio 1:25.

Temperature:

— *column*: 240 °C;

— *injection port and detector*: 290 °C.

Detection Flame ionisation.

Injection 2 µL.

Run time 1.3 times the retention time of orphenadrine.

Identification of impurities Use the chromatogram supplied with *orphenadrine for peak identification CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A, B, C, D and F. Use the chromatogram obtained with reference solution (a) to identify the peak due to impurity E.

Relative retention With reference to orphenadrine (retention time = about 13 min): impurity B = about 0.5; impurity A = about 0.6; impurity D = about 0.8; impurity C = about 0.9; impurity E = about 0.98; impurity F = about 1.1.

System suitability Reference solution (a):

— *resolution*: minimum 1.5 between the peaks due to impurity E and orphenadrine.

Limits:

— *impurities A, B, C, D, E, F*: for each impurity, not more than 0.3 per cent;

— *unspecified impurities*: for each impurity, not more than 0.10 per cent;

— *total*: not more than 1.0 per cent;

— *disregard limit*: 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 for 3 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.250 g in 50 mL of *acetic anhydride R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

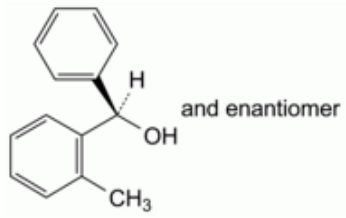
1 mL of *0.1 M perchloric acid* is equivalent to 30.59 mg of $C_{18}H_{24}ClNO$.

STORAGE

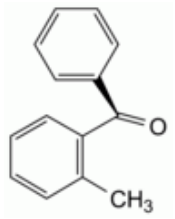
Protected from light. If the substance is sterile, store in a sterile, airtight, tamper-evident container, protected from light.

IMPURITIES

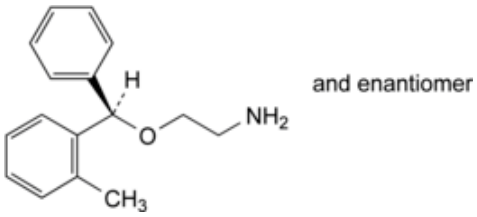
Specified impurities *A, B, C, D, E, F.*



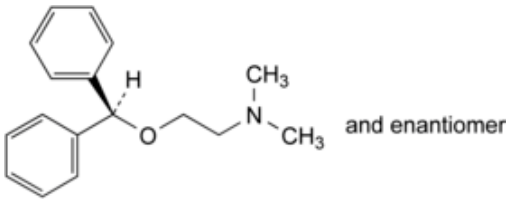
A. (*RS*)-(2-methylphenyl)phenylmethanol (2-methylbenzhydrol),



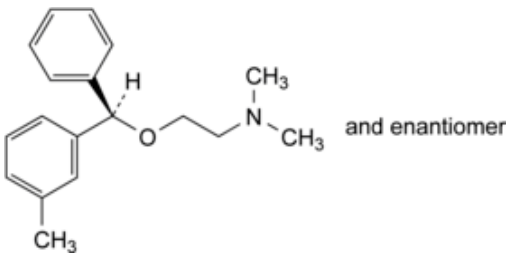
B. (2-methylphenyl)phenylmethanone (2-methylbenzophenone),



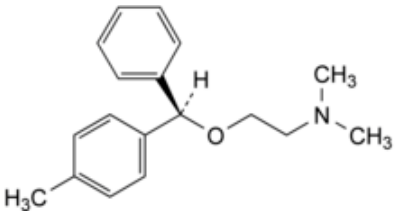
C. (*RS*)-2-[(2-methylphenyl)phenylmethoxy]ethanamine,



D. 2-(diphenylmethoxy)-*N*,*N*-dimethylethanamine (diphenhydramine),



E. (*RS*)-*N,N*-dimethyl-2-[(3-methylphenyl)phenylmethoxy]ethanamine (*meta*-methylbenzyl isomer),



and enantiomer

F. (*RS*)-*N,N*-dimethyl-2-[(4-methylphenyl)phenylmethoxy]ethanamine (*para*-methylbenzyl isomer).

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