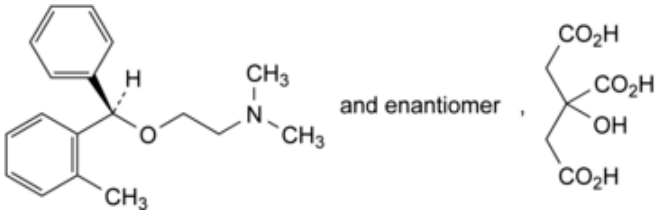
Edition: BP 2025 (Ph. Eur. 11.6 update)

# Orphenadrine Citrate

General Notices

*(Ph. Eur. monograph 1759)*




$C_{24}H_{31}NO_8$ 461.5 *4682-36-4*

**Action and use**

Anticholinergic.

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## DEFINITION

(*RS*)-*N,N*-Dimethyl-2-[(2-methylphenyl)phenylmethoxy]ethanamine dihydrogen 2-hydroxypropane-1,2,3-tricarboxylate.

**Content**

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

## CHARACTERS

**Appearance**

White or almost white, crystalline powder.

**Solubility**

Sparingly soluble in water, slightly soluble in ethanol (96 per cent).

**mp**

About 137 °C.

## IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

*Comparison* orphenadrine citrate CRS.

## 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 1.0 g in a 3.6 per cent *V/V* solution of hydrochloric acid R in ethanol (96 per cent) R and dilute to 10.0 mL with the same acid solution.

**Related substances**

Gas chromatography (2.2.28): use the normalisation procedure.

*Test solution* Dissolve 0.500 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 30 mg of orphenadrine citrate CRS and 30 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 of 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*: maximum 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 0.350 g in 50 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

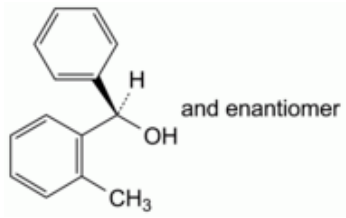
1 mL of *0.1 M perchloric acid* is equivalent to 46.15 mg of $C_{24}H_{31}NO_8$.

## STORAGE

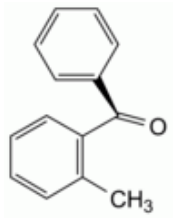
Protected from light. If the substance is sterile, store in a sterile, airtight, tamper-evident container, protected from light.

## IMPURITIES

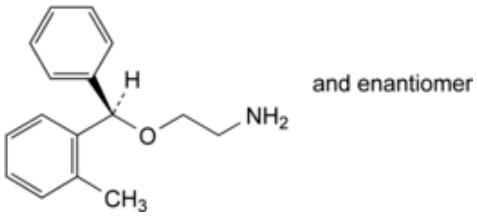
*Specified impurities* *A, B, C, D, E, F.*



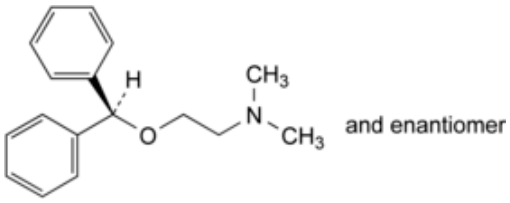

A. (*RS*)-(2-methylphenyl)phenylmethanol (2-methylbenzhydrol),



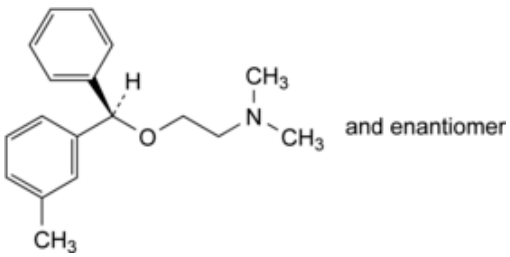

B. (2-methylphenyl)phenylmethanone (2-methylbenzophenone),



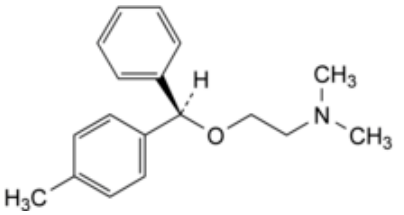

C. (*RS*)-2-[(2-methylphenyl)phenylmethoxy]ethanamine,




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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