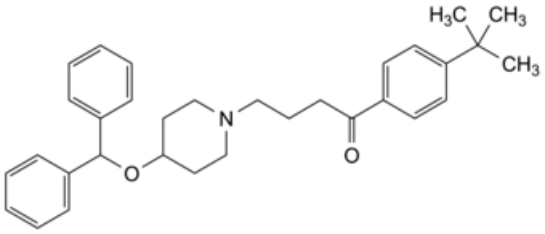
Edition: BP 2025 (Ph. Eur. 11.6 update)

Ebastine

General Notices

(Ph. Eur. monograph 2015)



$C_{32}H_{39}NO_2$ 469.7 *90729-43-4*

Action and use

Histamine H_1 receptor antagonist; antihistamine.

Ph Eur

DEFINITION

1-(4-*tert*-Butylphenyl)-4-[4-(diphenylmethoxy)piperidin-1-yl]butan-1-one.

Content

99.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water, very soluble in methylene chloride, sparingly soluble in methanol.

mp

About 86 °C.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison ebastine CRS.

TESTS

Related substances

Liquid chromatography (2.2.29).

Solution A Dilute 12 mL of phosphoric acid R and 12 mL of diethylamine R in 800 mL of water for chromatography R, adjust to pH 6.0 with diethylamine R and dilute to 1000 mL with water for chromatography R.

Test solution Dissolve 25 mg of the substance to be examined in the mobile phase and dilute to 10.0 mL with the mobile phase.

Reference solution (a) Dissolve 5 mg of bis(diphenylmethyl) ether R (impurity H) in the mobile phase and dilute to 50.0 mL with the mobile phase. Dilute 0.5 mL of the solution to 5.0 mL with the test solution. Dilute 3.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (b) 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.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: base-deactivated end-capped octadecylsilyl silica gel for chromatography R (5 µm);

— *temperature*: 40 °C.

Mobile phase Solution A, methanol R2, acetonitrile R1 (20:38:42 *V/V/V*).

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 210 nm.

Autosampler Set at 15 °C.

Injection 10 µL.

Run time 1.5 times the retention time of ebastine.

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

Relative retention With reference to ebastine (retention time = about 27 min): impurity H = about 0.9.

System suitability Reference solution (a):

— resolution: minimum 2 between the peaks due to impurity H and ebastine.

Calculation of percentage contents:

— for each impurity, use the concentration of ebastine in reference solution (b).

Limits:

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

— *total*: maximum 0.2 per cent;

— *reporting threshold*: 0.05 per cent.

Sulfates (*2.4.13*)

Maximum 100 ppm.

Suspend 2.5 g in 25 mL of *dilute nitric acid R*. Boil under a reflux condenser for 10 min. Cool and filter.

Water (*2.5.12*)

Maximum 0.5 per cent, determined on 0.500 g.

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*).

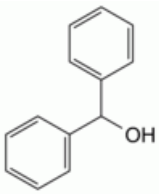
1 mL of *0.1 M perchloric acid* is equivalent to 46.97 mg of $C_{32}H_{39}NO_2$.

STORAGE

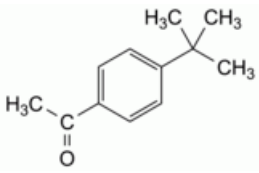
Protected from light.

IMPURITIES

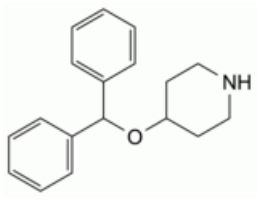
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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, F, G, H.



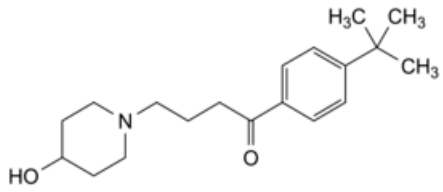
A. diphenylmethanol (benzhydrol),



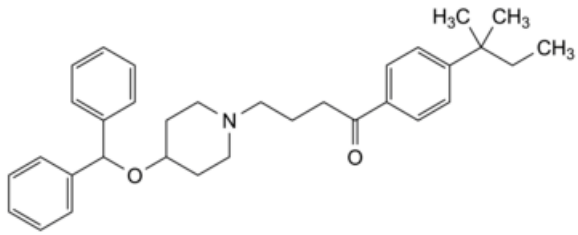
B. 1-(4-*tert*-butylphenyl)ethan-1-one,



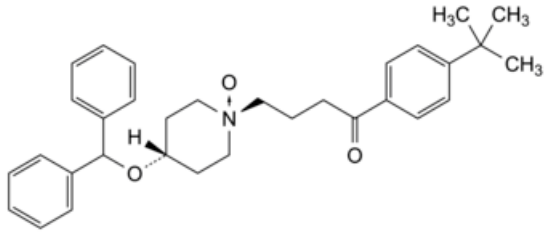
C. 4-(diphenylmethoxy)piperidine,



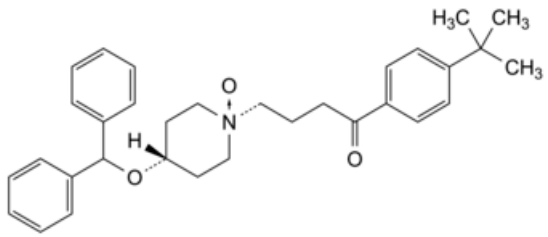
D. 1-(4-*tert*-butylphenyl)-4-(4-hydroxypiperidin-1-yl)butan-1-one,



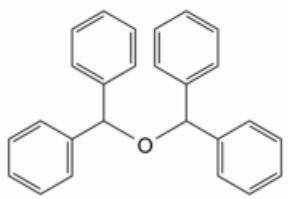
E. 4-[4-(diphenylmethoxy)piperidin-1-yl]-1-[4-(2-methylbutan-2-yl)phenyl]butan-1-one,



F. (1*s*,4*s*)-1-[4-(4-*tert*-butylphenyl)-4-oxobutyl]-4-(diphenylmethoxy)piperidine *N*-oxide,



G. (1*r*,4*r*)-1-[4-(4-*tert*-butylphenyl)-4-oxobutyl]-4-(diphenylmethoxy)piperidine *N*-oxide,



H. [oxybis(methanetriyl)]tetrakisbenzene (bis(diphenylmethyl) ether).