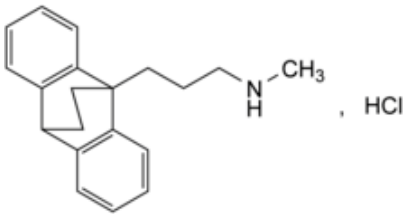
Edition: BP 2025 (Ph. Eur. 11.6 update)

Maprotiline Hydrochloride

General Notices

(Ph. Eur. monograph 1237)



$C_{20}H_{24}ClN$ 313.9 *10347-81-6*

Action and use

Antidepressant.

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DEFINITION

3-(9,10-Ethanoanthracen-9(10*H*)-yl)-*N*-methylpropan-1-amine hydrochloride.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Slightly soluble in water, freely soluble in methanol, soluble in ethanol (96 per cent), sparingly soluble in methylene chloride, very slightly soluble in acetone.

It shows polymorphism (5.9).

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D.

A. Ultraviolet and visible absorption spectrophotometry (2.2.25).

Test solution Dissolve 10 mg in *1 M hydrochloric acid* and dilute to 100 mL with the same acid.

Spectral range 250-300 nm.

Absorption maxima At 265 nm and 272 nm.

Absorption minimum At 268 nm.

Absorbance ratio A_{272}/A_{265} = 1.1 to 1.3.

B. Infrared absorption spectrophotometry (2.2.24).

Comparison *maprotiline hydrochloride CRS*.

If the spectra obtained show differences, dissolve the substance to be examined and the reference substance separately in *methanol R*, evaporate to dryness and record new spectra using the residues.

C. Thin-layer chromatography (2.2.27).

Test solution Dissolve 25 mg of the substance to be examined in *methanol R* and dilute to 5 mL with the same solvent.

Reference solution (a) Dissolve 25 mg of *maprotiline hydrochloride CRS* in *methanol R* and dilute to 5 mL with the same solvent.

Reference solution (b) Dissolve 10 mg of *maprotiline impurity D CRS* in reference solution (a) and dilute to 2 mL with reference solution (a).

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

Mobile phase *ethyl acetate R*, *dilute ammonia R1*, *2-butanol R1* (4:5:14 *V/V/V*).

Application 5 µL.

Development Over half of the plate.

Drying In a current of warm air.

Detection Examine in ultraviolet light at 254 nm.

System suitability Reference solution (b):

— the chromatogram shows 2 clearly separated principal spots.

Results The principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a).

D. Dilute 0.5 mL of solution S (see Tests) to 2 mL with *methanol R*. The solution gives reaction (a) of chlorides (2.3.1).

TESTS

Solution S

Dissolve 1.0 g in *methanol R* and dilute to 20 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*).

Related substances

Liquid chromatography (*2.2.29*).

Test solution Dissolve 0.10 g of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (a) Dilute 1.0 mL of the test solution to 10.0 mL with the mobile phase. Dilute 2.0 mL of this solution to 100.0 mL with the mobile phase.

Reference solution (b) Dissolve 1.0 mg of *maprotiline impurity D CRS* in the test solution and dilute to 10.0 mL with the test solution.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: *silica gel for chromatography R* (5 µm).

Mobile phase Dissolve about 0.580 g of *ammonium acetate R* in 200 mL of *water R* and add 2 mL of a 70 g/L solution of *concentrated ammonia R*; add 150 mL of *2-propanol R* and 650 mL of *methanol R*; the resulting apparent pH value is between 8.2 and 8.4.

Flow rate 1 mL/min.

Detection Spectrophotometer at 272 nm.

Injection 20 µL.

Run time 1.5 times the retention time of maprotiline.

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

Relative retention With reference to maprotiline (retention time = about 10 min): impurity A = about 0.3; impurity B = about 0.5; impurity C = about 0.7; impurity D = about 0.8; impurity E = about 1.3.

System suitability Reference solution (b):

— *resolution*: 1.8 to 3.2 between the peaks due to impurity D and maprotiline; if necessary, adjust the pH of the mobile phase, in steps of 0.1 pH unit, by adding a 50 per cent *V/V* solution of *acetic acid R* if the resolution is less than 1.8, or by adding a 70 g/L solution of *concentrated ammonia R* if the resolution is greater than 3.2.

Limits:

— *impurities A, B, C, D, E*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

— *unspecified impurities*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

— *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent);

— *disregard limit*: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Loss on drying (*2.2.32*)

Maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 80 °C at a pressure not exceeding 2.5 kPa for 6 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

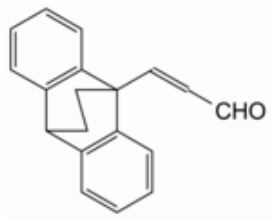
ASSAY

Dissolve 0.250 g in a mixture of 5 mL of *0.1 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.

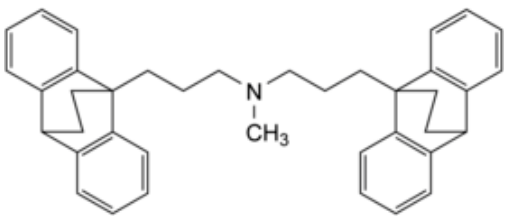
1 mL of *0.1 M sodium hydroxide* is equivalent to 31.39 mg of $C_{20}H_{24}ClN$.

IMPURITIES

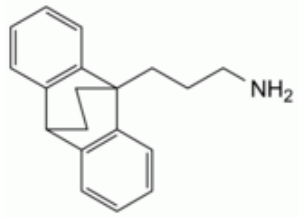
Specified impurities *A, B, C, D, E.*



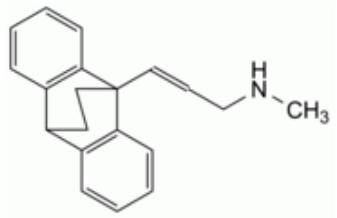
A. 3-(9,10-ethanoanthracen-9(10*H*)-yl)prop-2-enal,



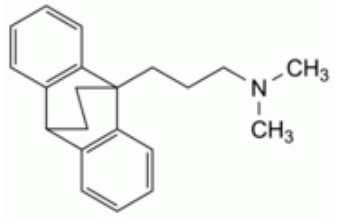
B. 3-(9,10-ethanoanthracen-9(10*H*)-yl)-*N*-[3-(9,10-ethanoanthracen-9(10*H*)-yl)propyl]-*N*-methylpropan-1-amine,



C. 3-(9,10-ethanoanthracen-9(10*H*)-yl)propan-1-amine,



D. 3-(9,10-ethanoanthracen-9(10*H*)-yl)-*N*-methylprop-2-en-1-amine (dehydromaprotiline),



E. 3-(9,10-ethanoanthracen-9(10*H*)-yl)-*N,N*-dimethylpropan-1-amine.

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