01/2008:1196
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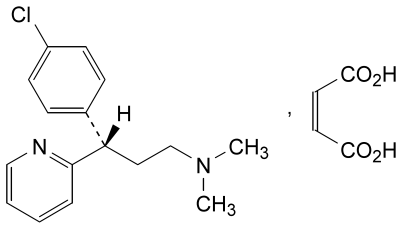
DEXCHLORPHENIRAMINE MALEATE

Dexchlorpheniramini maleas



$C_{20}H_{23}ClN_2O_4$ M_r 390.9
[2438-32-6]

DEFINITION

(3*S*)-3-(4-Chlorophenyl)-*N*,*N*-dimethyl-3-(pyridin-2-yl)propan-1-amine (*Z*)-butenedioate.

Content: 98.0 per cent to 100.5 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: very soluble in water, freely soluble in ethanol (96 per cent), in methanol and in methylene chloride.

IDENTIFICATION

First identification: A, C, E.

Second identification: A, B, D, E.

A. Specific optical rotation (see Tests).

B. Melting point (*2.2.14*): 110 °C to 115 °C.

C. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs of *potassium bromide R*.

Comparison: *dexchlorpheniramine maleate CRS*.

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

Test solution. Dissolve 0.10 g of the substance to be examined in *methanol R* and dilute to 5.0 ml with the same solvent.

Reference solution. Dissolve 56 mg of *maleic acid R* in *methanol R* and dilute to 10 ml with the same solvent.

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

Mobile phase: *water R, anhydrous formic acid R, methanol R, di-isopropyl ether R* (3:7:20:70 *V/V/V/V*).

Application: 5 µl.

Development: over a path of 12 cm.

Drying: in a current of air for a few minutes.

Detection: examine in ultraviolet light at 254 nm.

Results: the chromatogram obtained with the test solution shows 2 clearly separated spots. The upper spot is similar in position and size to the spot in the chromatogram obtained with the reference solution.

E. To 0.15 g in a porcelain crucible add 0.5 g of *anhydrous sodium carbonate R*. Heat over an open flame for 10 min. Allow to cool. Take up the residue with 10 ml of *dilute nitric acid R* and filter. To 1 ml of the filtrate add 1 ml of *water R*. The solution gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 2.0 g in *water R* and dilute to 20.0 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*).

pH (*2.2.3*): 4.5 to 5.5.

Dissolve 0.20 g in 20 ml of *water R*.

Specific optical rotation (*2.2.7*): + 22 to + 23 (dried substance), determined on solution S.

Related substances. Gas chromatography (*2.2.28*).

Test solution. Dissolve 10.0 mg of the substance to be examined in 1.0 ml of *methylene chloride R*.

Reference solution. Dissolve 5.0 mg of *brompheniramine maleate CRS* in 0.5 ml of *methylene chloride R* and add 0.5 ml of the test solution. Dilute 0.5 ml of this solution to 50.0 ml with *methylene chloride R*.

Column:

– *material*: glass;
– *size*: *l* = 2.3 m, Ø = 2 mm;
– *stationary phase*: acid- and base- washed *silanised diatomaceous earth for gas chromatography R* (135-175 µm) impregnated with 3 per cent *m/m* of a mixture of 50 per cent of poly(dimethyl)siloxane and 50 per cent of poly(diphenyl)siloxane.

Carrier gas: *nitrogen for chromatography R*.

Flow rate: 20 ml/min.

Temperature:

– *column*: 205 °C;
– *injection port and detector*: 250 °C.

Detection: flame ionisation.

Injection: 1 µl.

Run time: 2.5 times the retention time of dexchlorpheniramine.

System suitability: reference solution:

– *resolution*: minimum 1.5 between the peaks due to dexchlorpheniramine and brompheniramine.

Limits:

– *impurities A, B*: for each impurity, not more than 0.8 times the area of the peak due to dexchlorpheniramine in the chromatogram obtained with the reference solution (0.4 per cent);
– *total*: not more than twice the area of the peak due to dexchlorpheniramine in the chromatogram obtained with the reference solution (1 per cent).

Enantiomeric purity. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 10.0 mg of the substance to be examined in 3 ml of *water R*. Add a few drops of *concentrated ammonia R* until an alkaline reaction is produced. Shake with 5 ml of *methylene chloride R*. Separate the layers. Evaporate the lower, methylene chloride layer to an oily residue on a water-bath. Dissolve the oily residue in *2-propanol R* and dilute to 10.0 ml with the same solvent.

Reference solution (a). Dissolve 10.0 mg of *dexchlorpheniramine maleate CRS* in 3 ml of *water R*. Add a few drops of *concentrated ammonia R* until an alkaline reaction is produced. Shake with 5 ml of *methylene chloride R*. Separate the layers. Evaporate the lower, methylene chloride layer to an oily residue on a water-bath. Dissolve the oily residue in *2-propanol R* and dilute to 10.0 ml with the same solvent.

Reference solution (b). Dissolve 10.0 mg of *chlorphenamine maleate CRS* in 3 ml of *water R*. Add a few drops of *concentrated ammonia R* until an alkaline reaction is produced. Shake with 5 ml of *methylene chloride R*. Separate the layers. Evaporate the lower, methylene chloride

layer to an oily residue on a water-bath. Dissolve the oily residue in *2-propanol R* and dilute to 10.0 ml with the same solvent.

Reference solution (c). Dilute 1.0 ml of the test solution to 50 ml with *2-propanol R*.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;

– *stationary phase*: *amylose derivative of silica gel for chromatography R*.

Mobile phase: *diethylamine R, 2-propanol R, hexane R* (3:20:980 *V/V/V*).

Flow rate: 1 ml/min.

Detection: spectrophotometer at 254 nm.

Injection: 10 µl.

Under these conditions the peak of the (*S*)-isomer appears first.

System suitability:

– *resolution*: minimum 1.5 between the peaks due to the (*R*)-enantiomer and to the (*S*)-enantiomer in the chromatogram obtained with reference solution (b);

– the retention times of the principal peaks in the chromatograms obtained with the test solution and reference solution (a) are identical ((*S*)-enantiomer).

Limits:

– *(R)-enantiomer*: not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (2 per cent);

– *any other impurity*: for each impurity, not more than 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.5 per cent).

Heavy metals (*2.4.8*): maximum 20 ppm.

1.0 g complies with test C. Prepare the reference solution using 2 ml of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 65 °C for 4 h.

Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.150 g in 25 ml of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

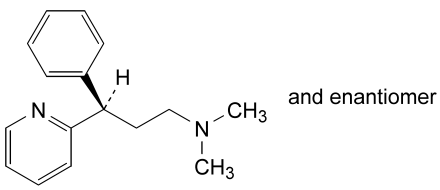
1 ml of *0.1 M perchloric acid* is equivalent to 19.54 mg of $C_{20}H_{23}ClN_2O_4$.

STORAGE

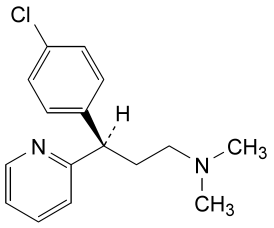
Protected from light.

IMPURITIES

Specified impurities: A, B.



A. (3*RS*)-*N,N*-dimethyl-3-phenyl-3-(pyridin-2-yl)propan-1-amine,

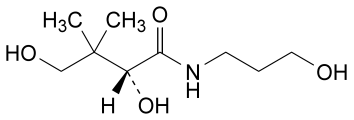


B. (3*R*)-3-(4-chlorophenyl)-*N,N*-dimethyl-3-(pyridin-2-yl)propan-1-amine.

01/2008:0761

DEXPANTHENOL

Dexpanthenolum



$C_9H_{19}NO_4$ M_r 205.3

[81-13-0]

DEFINITION

Dexpanthenol contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of (2*R*)-2,4-dihydroxy-*N*-(3-hydroxypropyl)-3,3-dimethylbutanamide, calculated with reference to the anhydrous substance.

CHARACTERS

A colourless or slightly yellowish, viscous hygroscopic liquid, or a white or almost white, crystalline powder, very soluble in water, freely soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D.

A. It complies with the test for specific optical rotation (see Tests).

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *dexpanthenol CRS*. Examine the substances using discs prepared as follows: dissolve the substance to be examined and the reference substance separately in 1.0 ml of *anhydrous ethanol R* to obtain a concentration of 5 mg/ml. Place dropwise 0.5 ml of this solution on a disc of *potassium bromide R*. Dry the disc at 100-105 °C for 15 min.

C. Examine the chromatograms obtained in the test for 3-aminopropanol. The principal spot in the chromatogram obtained with test solution (b) is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (a).

D. To 1 ml of solution S (see Tests) add 1 ml of *dilute sodium hydroxide solution R* and 0.1 ml of *copper sulphate solution R*. A blue colour develops.

TESTS

Solution S. Dissolve 2.500 g in *carbon dioxide-free water R* and dilute to 50.0 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution B_6 (*2.2.2, Method II*).