– *total*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);

– *disregard limit*: the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent); disregard the peaks due to the blank and maleic acid.

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 105 °C for 4 h.

Sulfated 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*).

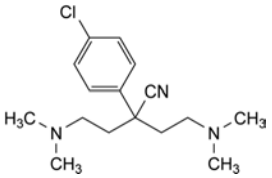
1 mL of *0.1 M perchloric acid* is equivalent to 19.54 mg of $C_{20}H_{23}ClN_2O_4$.

STORAGE

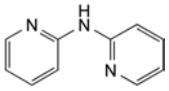
Protected from light.

IMPURITIES

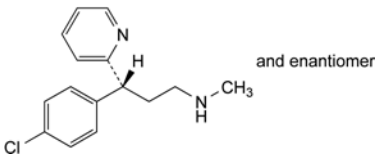
Specified impurities: A, B, C, D.



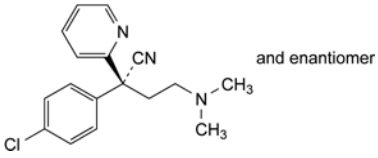
A. 2-(4-chlorophenyl)-4-(dimethylamino)-2-[2-(dimethylamino)ethyl]butanenitrile,



B. *N*-(pyridin-2-yl)pyridin-2-amine (2,2′-dipyridylamine),



C. (3*RS*)-3-(4-chlorophenyl)-*N*-methyl-3-(pyridin-2-yl)propan-1-amine,

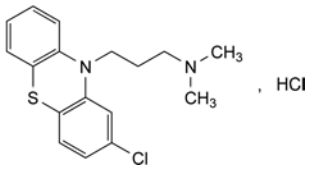


D. (2*RS*)-2-(4-chlorophenyl)-4-(dimethylamino)-2-(pyridin-2-yl)butanenitrile.

01/2008:0475
corrected 7.0

CHLORPROMAZINE HYDROCHLORIDE

Chlorpromazini hydrochloridum



$C_{17}H_{20}Cl_2N_2S$ M_r 355.3
[69-09-0]

DEFINITION

3-(2-Chloro-10*H*-phenothiazin-10-yl)-*N*,*N*-dimethylpropan-1-amine hydrochloride.

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

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: very soluble in water, freely soluble in ethanol (96 per cent).

It decomposes on exposure to air and light.

mp: about 196 °C.

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D.

A. Ultraviolet and visible absorption spectrophotometry (*2.2.25*). *Prepare the solutions protected from bright light and measure the absorbances immediately.*

Test solution. Dissolve 50.0 mg in a 10.3 g/L solution of *hydrochloric acid R* and dilute to 500.0 mL with the same solution. Dilute 5.0 mL of the solution to 100.0 mL with a 10.3 g/L solution of *hydrochloric acid R*.

Spectral range: 230-340 nm.

Absorption maximum: at 254 nm and 306 nm.

Specific absorbance at the absorption maximum:

– *at 254 nm*: 890 to 960.

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *chlorpromazine hydrochloride CRS*.

C. Identification test for phenothiazines by thin-layer chromatography (*2.3.3*): use *chlorpromazine hydrochloride CRS* to prepare the reference solution.

D. It gives reaction (b) of chlorides (*2.3.1*).

TESTS

pH (*2.2.3*): 3.5 to 4.5. *Carry out the test protected from light and use freshly prepared solutions.*

Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 10 mL with the same solvent.

Related substances. Liquid chromatography (*2.2.29*). *Carry out the test protected from light and use freshly prepared solutions.*

Test solution. Dissolve 40 mg of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (a). Dissolve 4 mg of *chlorpromazine impurity D CRS* in the mobile phase and dilute to 10.0 mL with the mobile phase. To 1 mL of this solution add 1 mL of the test solution and dilute to 100.0 mL with the mobile phase.

Reference solution (b). Dilute 1.0 mL of the test solution to 20.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (c). Dissolve 4.0 mg of *chlorpromazine impurity A CRS* in the mobile phase and dilute to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 100.0 mL with the mobile phase.

Reference solution (d). Dissolve 4 mg of *promazine hydrochloride CRS* (impurity C) and 4.0 mg of *chlorpromazine impurity E CRS* in the mobile phase and dilute to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 100.0 mL with the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4.0 mm,
– *stationary phase*: *base-deactivated octylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: mix 0.2 volumes of *thiodiethylene glycol R* with 50 volumes of *acetonitrile R* and 50 volumes of a 0.5 per cent *V/V* solution of *trifluoroacetic acid R* previously adjusted to pH 5.3 with *tetramethylethylenediamine R*.

Flow rate: 1.0 mL/min.

Detection: spectrophotometer at 254 nm.

Injection: 10 µL.

Run time: 4 times the retention time of chlorpromazine.

Relative retention with reference to chlorpromazine (retention time = about 8 min): impurity A = about 0.4; impurity B = about 0.5; impurity C = about 0.7; impurity D = about 0.9; impurity E = about 3.4.

System suitability: reference solution (a):

– *resolution*: minimum 2.0 between the peaks due to impurity D and chlorpromazine.

Limits:

– *impurity A*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (c) (0.1 per cent);
– *impurities B, C, D*: for each impurity, not more than 0.6 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent);
– *impurity E*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (d) (0.1 per cent);
– *any other impurity*: for each impurity, not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent);
– *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent);
– *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Heavy metals (*2.4.8*): maximum 10 ppm.

1.0 g complies with test C. Prepare the reference solution using 1 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 105 °C.

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

ASSAY

Dissolve 0.250 g in a mixture of 5.0 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.

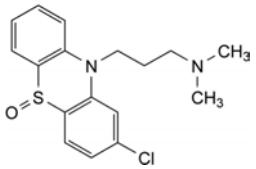
1 mL of *0.1 M sodium hydroxide* is equivalent to 35.53 mg of $C_{17}H_{20}Cl_2N_2S$.

STORAGE

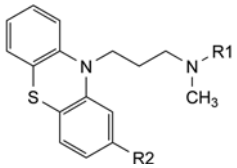
In an airtight container, protected from light.

IMPURITIES

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



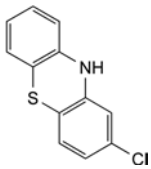
A. 3-(2-chloro-10*H*-phenothiazin-10-yl)-*N*,*N*-dimethylpropan-1-amine *S*-oxide (chlorpromazine sulfoxide),



B. R1 = $[CH_2]_3$-$N(CH_3)_2$, R2 = Cl: *N*-[3-(2-chloro-10*H*-phenothiazin-10-yl)propyl]-*N*,*N*′,*N*′-trimethylpropane-1,3-diamine,

C. R1 = CH_3, R2 = H: 3-(10*H*-phenothiazin-10-yl)-*N*,*N*-dimethylpropan-1-amine (promazine),

D. R1 = H, R2 = Cl: 3-(2-chloro-10*H*-phenothiazin-10-yl)-*N*-methylpropan-1-amine (desmethylchlorpromazine),

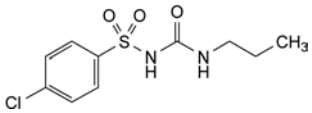


E. 2-chloro-10*H*-phenothiazine.

01/2008:1087
corrected 6.0

CHLORPROPAMIDE

Chlorpropamidum



$C_{10}H_{13}ClN_2O_3S$ M_r 276.7
[94-20-2]

DEFINITION

Chlorpropamide contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of 1-[(4-chlorophenyl)sulfonyl]-3-propylurea, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder, practically insoluble in water, freely soluble in acetone and in methylene chloride, soluble in alcohol. It dissolves in dilute solutions of alkali hydroxides.

It shows polymorphism (*5.9*).

IDENTIFICATION

First identification: C, D.

Second identification: A, B, D.

A. Melting point (*2.2.14*): 126 °C to 130 °C.

B. Dissolve 0.10 g in *methanol R* and dilute to 50.0 mL with the same solvent. Dilute 5.0 mL of the solution to 100.0 mL with *0.01 M hydrochloric acid*. Dilute 10.0 mL of the solution to 100.0 mL with *0.01 M hydrochloric acid*. Examined between 220 nm and 350 nm (*2.2.25*), the solution shows an absorption maximum at 232 nm. The specific absorption at the maximum is 570 to 630.