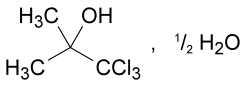
01/2008:0383
corrected 6.0

CHLOROBUTANOL HEMIHYDRATE

Chlorobutanolum hemihydricum



$C_4H_7Cl_3O,{}^1/_2H_2O$ M_r 186.5
[6001-64-5]

DEFINITION

1,1,1-Trichloro-2-methylpropan-2-ol hemihydrate.

Content: 98.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or almost white, crystalline powder or colourless crystals, sublimes readily.

Solubility: slightly soluble in water, very soluble in ethanol (96 per cent), soluble in glycerol (85 per cent).

mp: about 78 °C (without previous drying).

IDENTIFICATION

A. Add about 20 mg to a mixture of 1 ml of *pyridine R* and 2 ml of *strong sodium hydroxide solution R*. Heat in a water-bath and shake. Allow to stand. The pyridine layer becomes red.

B. Add about 20 mg to 5 ml of *ammoniacal silver nitrate solution R* and warm slightly. A black precipitate is formed.

C. To about 20 mg add 3 ml of *1 M sodium hydroxide* and shake to dissolve. Add 5 ml of *water R* and then, slowly, 2 ml of *iodinated potassium iodide solution R*. A yellowish precipitate is formed.

D. Water (see Tests).

TESTS

Solution S. Dissolve 5 g in *ethanol (96 per cent) R* and dilute to 10 ml with the same solvent.

Appearance of solution. Solution S is not more opalescent than reference suspension II (*2.2.1*) and not more intensely coloured than reference solution BY_5 (*2.2.2, Method II*).

Acidity. To 4 ml of solution S add 15 ml of *ethanol (96 per cent) R* and 0.1 ml of *bromothymol blue solution R1*. Not more than 1.0 ml of *0.01 M sodium hydroxide* is required to change the colour of the indicator to blue.

Chlorides (*2.4.4*): maximum 100 ppm.

To 1 ml of solution S add 4 ml of *ethanol (96 per cent) R* and dilute to 15 ml with *water R*. When preparing the standard, replace the 5 ml of *water R* by 5 ml of *ethanol (96 per cent) R*.

Water (*2.5.12*): 4.5 per cent to 5.5 per cent, determined on 0.300 g.

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

ASSAY

Dissolve 0.100 g in 20 ml of *ethanol (96 per cent) R*. Add 10 ml of *dilute sodium hydroxide solution R*, heat in a water-bath for 5 min and cool. Add 20 ml of *dilute nitric acid R*, 25.0 ml of *0.1 M silver nitrate* and 2 ml of *dibutyl phthalate R* and shake vigorously. Add 2 ml of *ferric ammonium sulphate solution R2* and titrate with *0.1 M ammonium thiocyanate* until an orange colour is obtained.

1 ml of *0.1 M silver nitrate* is equivalent to 5.92 mg of $C_4H_7Cl_3O$.

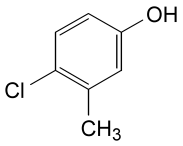
STORAGE

In an airtight container.

01/2008:0384

CHLOROCRESOL

Chlorocresolum



C_7H_7ClO M_r 142.6
[59-50-7]

DEFINITION

4-Chloro-3-methylphenol.

Content: 98.0 per cent to 101.0 per cent.

CHARACTERS

Appearance: white or almost white, crystalline powder or compacted crystalline masses supplied as pellets or colourless or white crystals.

Solubility: slightly soluble in water, very soluble in ethanol (96 per cent), freely soluble in fatty oils. It dissolves in solutions of alkali hydroxides.

IDENTIFICATION

A. Melting point (*2.2.14*): 64 °C to 67 °C.

B. To 0.1 g add 0.2 ml of *benzoyl chloride R* and 0.5 ml of *dilute sodium hydroxide solution R*. Shake vigorously until a white, crystalline precipitate is formed. Add 5 ml of *water R* and filter. The precipitate, recrystallised from 5 ml of *methanol R* and dried at 70 °C, melts (*2.2.14*) at 85 °C to 88 °C.

C. To 5 ml of solution S (see Tests) add 0.1 ml of *ferric chloride solution R1*. A bluish colour is produced.

TESTS

Solution S. To 3.0 g, finely powdered, add 60 ml of *carbon dioxide-free water R*, shake for 2 min and filter.

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution BY_6 (*2.2.2, Method II*).

Dissolve 1.25 g in *ethanol (96 per cent) R* and dilute to 25 ml with the same solvent.

Acidity. To 10 ml of solution S add 0.1 ml of *methyl red solution R*. The solution is orange or red. Not more than 0.2 ml of *0.01 M sodium hydroxide* is required to produce a pure yellow colour.

Related substances. Gas chromatography (*2.2.28*): use the normalisation procedure.

Test solution. Dissolve 1.0 g of the substance to be examined in *acetone R* and dilute to 100 ml with the same solvent.

Column:

– *material*: glass;

– *size*: *l* = 1.80 m, Ø = 3-4 mm;

– *stationary phase*: *silanised diatomaceous earth for gas chromatography R* impregnated with 3-5 per cent *m/m* of *polymethylphenylsiloxane R*.

Carrier gas: *nitrogen for chromatography R*.

Flow rate: 30 ml/min.

Temperature:

– *column*: 125 °C;

– *injection port*: 210 °C;

– *detector*: 230 °C.

Detection: flame ionisation.

Run time: 3 times the retention time of chlorocresol.

Retention time: chlorocresol = about 8 min.

Limits:

– *total*: maximum 1 per cent;

– *disregard limit*: disregard the peak due to the solvent.

Non-volatile matter: maximum 0.1 per cent.

Evaporate 2.0 g to dryness on a water-bath and dry the residue at 100-105 °C. The residue weighs not more than 2 mg.

ASSAY

In a ground-glass-stoppered flask, dissolve 70.0 mg in 30 ml of *glacial acetic acid R*. Add 25.0 ml of *0.0167 M potassium bromate*, 20 ml of a 150 g/l solution of *potassium bromide R* and 10 ml of *hydrochloric acid R*. Allow to stand protected from light for 15 min. Add 1 g of *potassium iodide R* and 100 ml of *water R*. Titrate with *0.1 M sodium thiosulphate*, shaking vigorously and using 1 ml of *starch solution R*, added towards the end of the titration, as indicator. Carry out a blank titration.

1 ml of *0.0167 M potassium bromate* is equivalent to 3.565 mg of C_7H_7ClO.

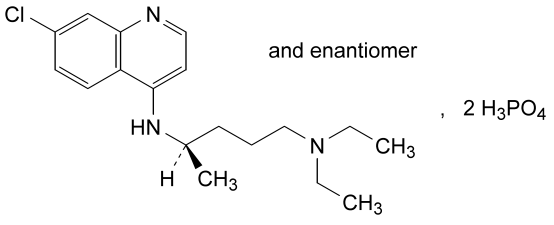
STORAGE

Protected from light.

01/2008:0544
corrected 6.0

CHLOROQUINE PHOSPHATE

Chloroquini phosphas



$C_{18}H_{32}ClN_3O_8P_2$ M_r 515.9
[50-63-5]

DEFINITION

Chloroquine phosphate contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of N^4-(7-chloroquinolin-4-yl)-N^1,N^1-diethylpentane-1,4-diamine bis(dihydrogen phosphate), calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder, hygroscopic, freely soluble in water, very slightly soluble in alcohol and in methanol.

It exists in 2 forms, one of which melts at about 195 °C and the other at about 218 °C.

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D.

A. Dissolve 0.100 g in *water R* and dilute to 100.0 ml with the same solvent. Dilute 1.0 ml of this solution to 100.0 ml with *water R*. Examined between 210 nm and 370 nm (*2.2.25*), the solution shows absorption maxima at 220 nm, 235 nm, 256 nm, 329 nm and 342 nm. The specific absorbances at the maxima are respectively 600 to 660, 350 to 390, 300 to 330, 325 to 355 and 360 to 390.

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with the base isolated from *chloroquine sulphate CRS*. Record the spectra using solutions prepared as follows: dissolve separately 0.1 g of the substance to be examined and 80 mg of the reference substance in 10 ml of *water R*, add 2 ml of *dilute sodium hydroxide solution R* and shake with 2 quantities, each of 20 ml, of *methylene chloride R*; combine the organic layers, wash with *water R*, dry over *anhydrous sodium sulphate R*, evaporate to dryness and dissolve the residues separately, each in 2 ml of *methylene chloride R*.

C. Dissolve 25 mg in 20 ml of *water R* and add 8 ml of *picric acid solution R1*. The precipitate, washed with *water R*, with *alcohol R* and finally with *methylene chloride R*, melts (*2.2.14*) at 206-209 °C.

D. Dissolve 0.1 g in 10 ml of *water R*, add 2 ml of *dilute sodium hydroxide solution R* and shake with 2 quantities, each of 20 ml, of *methylene chloride R*. The aqueous layer, acidified by the addition of *nitric acid R*, gives reaction (b) of phosphates (*2.3.1*).

TESTS

Solution S. Dissolve 2.5 g in *carbon dioxide-free water R* and dilute to 25 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution BY_5 or GY_5 (*2.2.2, Method II*).

pH (*2.2.3*). The pH of solution S is 3.8 to 4.3.

Related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel* GF_{254} *R* as the coating substance.

Test solution. Dissolve 0.50 g of the substance to be examined in *water R* and dilute to 10 ml with the same solvent.

Reference solution (a). Dilute 1 ml of the test solution to 100 ml with *water R*.

Reference solution (b). Dilute 5 ml of reference solution (a) to 10 ml with *water R*.

Apply to the plate 2 µl of each solution. Develop over a path of 12 cm using a mixture of 10 volumes of *diethylamine R*, 40 volumes of *cyclohexane R* and 50 volumes of *chloroform R*. Allow the plate to dry in air. Examine in ultraviolet light at 254 nm. Any spot in the chromatogram obtained with the test solution, apart from the principal spot, is not more intense than the spot in the chromatogram obtained with reference solution (a) (1.0 per cent) and not