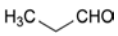
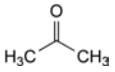
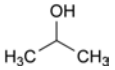


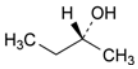
C. propanal,



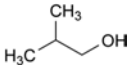
D. propanone (acetone),



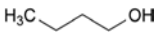
E. isopropyl alcohol (2-propanol),



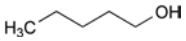
F. butan-2-ol (*sec*-butanol),



G. 2-methylpropan-1-ol (isobutanol),



H. butan-1-ol (*n*-butanol),



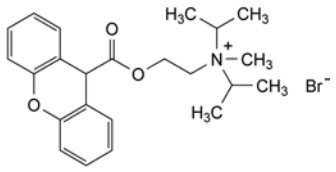
I. pentan-1-ol (*n*-pentanol),

J. hexan-1-ol (*n*-hexanol).

01/2008:0857
corrected 6.0

PROPANTHELINE BROMIDE

Propanthelini bromidum



$C_{23}H_{30}BrNO_3$ M_r 448.4
[50-34-0]

DEFINITION

N-Methyl-*N*,*N*-bis(1-methylethyl)-2-[(9*H*-xanthen-9-ylcarbonyl)oxy]ethanaminium bromide.

Content: 98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or yellowish-white, slightly hygroscopic powder.

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

IDENTIFICATION

A. Ultraviolet and visible absorption spectrophotometry (*2.2.25*).

Test solution. Dissolve 60 mg in *methanol R* and dilute to 100.0 mL with the same solvent. Dilute 10.0 mL of this solution to 100.0 mL with *methanol R*.

Spectral range: 230-350 nm.

Absorption maxima: at 246 nm and 282 nm.

Specific absorbance at the absorption maxima:

– at 246 nm: 115 to 125;
– at 282 nm: 57 to 63.

B. Dissolve 0.2 g in 15 mL of *water R* and add 1 mL of *strong sodium hydroxide solution R*. Boil for 2 min and cool slightly. Add 7.5 mL of *dilute hydrochloric acid R* and filter. Wash the residue with *water R* and recrystallise from *ethanol (50 per cent V/V) R*. Dry at 100-105 °C for 1 h. Dissolve about 10 mg of the residue in 5 mL of *sulfuric acid R*. The solution has an intense yellow colour and shows an intense yellowish-green fluorescence when examined in ultraviolet light at 365 nm.

C. Dissolve 50 mg in 0.1 mL of *water R* in a 25 mL flask and add 1 mL of a saturated solution of *potassium permanganate R*. Attach a fractionating column and a condenser, with the end of the delivery tube immersed in 1 mL of *water R* in a test-tube placed in a bath of iced water. Distil fairly vigorously and continue heating for 1 min after a dry residue has been obtained in the flask. Prepare a blank by introducing into an identical test-tube a volume of *water R* equal to that of the distillate. Place the tubes in a bath of iced water. To each tube, add 0.5 mL of a 20 per cent *V/V* solution of *morpholine R* and 0.5 mL of a freshly prepared 50 g/L solution of *sodium nitroprusside R*. Mix and allow to stand at 0 °C for 5 min, and then at room temperature for 3 min. No blue colour develops in either tube. Add 1 g of *ammonium sulfate R*, mix and allow to stand for 15 min. A stable, intense pink colour develops in the test solution. A brownish-yellow colour develops in the blank.

D. It gives reaction (a) of bromides (*2.3.1*).

TESTS

Appearance of solution. The solution is clear (*2.2.1*).

Dissolve 0.6 g in *water R* and dilute to 20 mL with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).

Solvent mixture: *acetonitrile R*, *water R* (40:60 *V/V*).

Test solution (a). Dissolve 6 mg of the substance to be examined in the solvent mixture and dilute to 50 mL with the solvent mixture.

Test solution (b). Dissolve 6 mg of the substance to be examined in 30 mL of the solvent mixture. Add 5 mL of reference solution (b) and dilute to 50 mL with the solvent mixture.

Test solution (c). Dissolve 6 mg of *xanthydrol R1* and 6 mg of the substance to be examined in the solvent mixture, then dilute to 50 mL with the solvent mixture.

Reference solution (a). Dissolve 6 mg of *xanthydrol R1* in the solvent mixture and dilute to 50 mL with the solvent mixture.

Reference solution (b). Dilute 5 mL of reference solution (a) to 50 mL with the solvent mixture.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;
– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: mixture of equal volumes of *acetonitrile R* and of a solution containing 28 g/L of *sodium perchlorate R* and 11 g/L of *phosphoric acid R*, adjusted to pH 3.8 with *strong sodium hydroxide solution R* and then with *0.1 M sodium hydroxide*.

Flow rate: 1 mL/min.

Detection: spectrophotometer at 206 nm.

Injection: 20 µL of test solutions (a), (b), (c) and reference solution (a).

Run time: twice the retention time of propantheline.

System suitability: test solution (c):

– in the chromatogram obtained with test solution (a), there is no peak corresponding to the principal peak in the chromatogram obtained with reference solution (a);
– *resolution*: minimum 8.0 between the peaks due to propantheline and xanthydrol.

Limits: test solution (b):

– *any impurity*: for each impurity, not more than the area of the peak due to xanthydrol (1.0 per cent), and not more than one such peak has an area greater than or equal to 0.5 times the area of the peak due to xanthydrol (0.5 per cent);
– *disregard limit*: disregard any peak with a retention time relative to propantheline of less than 0.2 (bromide); disregard the peak due to xanthydrol.

Loss on drying (*2.2.32*): maximum 1.0 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 0.400 g in 50 mL of *acetic anhydride R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* corresponds to 44.84 mg of $C_{23}H_{30}BrNO_3$.

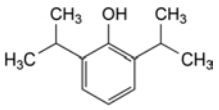
STORAGE

In an airtight container.

01/2008:1558

PROPOFOL

Propofolum



$C_{12}H_{18}O$ M_r 178.3
[2078-54-8]

DEFINITION

2,6-Bis(1-methylethyl)phenol.

Content: 98.0 per cent to 102.0 per cent.

This monograph applies to propofol prepared using distillation for purification.

CHARACTERS

Appearance: colourless or very light yellow, clear liquid.

Solubility: very slightly soluble in water, miscible with hexane and with methanol.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *propofol CRS*.

TESTS

Refractive index (*2.2.6*): 1.5125 to 1.5145.

Related substances. Liquid chromatography (*2.2.29*).

Test solution (a). Dissolve 1.00 g of the substance to be examined in *hexane R* and dilute to 10.0 mL with the same solvent.

Test solution (b). Dissolve 0.240 g of the substance to be examined in *hexane R* and dilute to 100.0 mL with the same solvent.

Reference solution (a). Dissolve 5 µL of the substance to be examined and 15 µL of *propofol impurity J CRS* in *hexane R* and dilute to 50.0 mL with the same solvent.

Reference solution (b). Dilute 0.1 mL of *propofol for peak identification CRS* (containing impurities E and G) to 1.0 mL with *hexane R*.

Reference solution (c). Dilute 1.0 mL of test solution (a) to 100.0 mL with *hexane R*. Dilute 1.0 mL of this solution to 10.0 mL with *hexane R*.

Reference solution (d). Dissolve 0.240 g of *propofol CRS* in *hexane R* and dilute to 100.0 mL with the same solvent.

Column:

– *size*: *l* = 0.20 m, Ø = 4.6 mm;
– *stationary phase*: *silica gel for chromatography R* (5 µm).

Mobile phase: *anhydrous ethanol R, acetonitrile R, hexane R* (1.0:7.5:990 *V/V/V*).

Flow rate: 2.0 mL/min.

Detection: spectrophotometer at 275 nm.

Injection: 10 µL of test solution (a) and reference solutions (a), (b) and (c).

Run time: 7 times the retention time of propofol.

Identification of impurities: use the chromatogram obtained with reference solution (b) to identify the peaks due to impurities G and E.

Relative retention with reference to propofol (retention time = about 3 min): impurity G = about 0.5; impurity I = about 0.6; impurity B = about 0.7; impurity N = about 2.3; impurity D = about 2.5; impurity P = about 2.9; impurity A = about 3.0; impurity C = about 3.4; impurity E = about 4.0; impurity F = about 5.8; impurity H = about 6.4.

System suitability: reference solution (a):

– *resolution*: minimum 4.0 between the peaks due to impurity J and propofol.

Limits:

– *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity E = 0.25; impurity G = 5.0;
– *impurity G*: not more than twice the area of the peak due to propofol in the chromatogram obtained with reference solution (c) (0.2 per cent);
– *impurity E*: not more than 0.1 times the area of the peak due to propofol in the chromatogram obtained with reference solution (c) (0.01 per cent);
– *unspecified impurities*: for each impurity, not more than 0.5 times the area of the peak due to propofol in the chromatogram obtained with reference solution (c) (0.05 per cent);
– *total*: not more than 3 times the area of the peak due to propofol in the chromatogram obtained with reference solution (c) (0.3 per cent);
– *disregard limit*: 0.3 times the area of the peak due to propofol in the chromatogram obtained with reference solution (c) (0.03 per cent), except for impurity E.

Impurities J, K, L and O. Gas chromatography (*2.2.28*).

Test solution. Dissolve 40.0 mg of the substance to be examined in *methylene chloride R* and dilute to 10.0 mL with the same solvent.

Reference solution (a). Dilute 1.0 mL of the test solution to 100.0 mL with *methylene chloride R*. Dilute 1.0 mL of this solution to 10.0 mL with *methylene chloride R*.

Reference solution (b). Dissolve 5 µL of *propofol impurity J CRS* (corresponding to 5 mg) in *methylene chloride R* and dilute to 100 mL with the same solvent. Dilute 1.0 mL of this solution to 25 mL with *methylene chloride R*.

Reference solution (c). Dissolve 4 mg of *propofol CRS* in reference solution (b) and dilute to 1 mL with the same solution.

Column:

– *material*: fused silica;
– *size*: *l* = 30 m, Ø = 0.32 mm;
– *stationary phase*: *polymethylphenylsiloxane R* (film thickness 0.5 µm).

Carrier gas: *helium for chromatography R*.

Flow rate: 1.7 mL/min.

Split ratio: 1:5.