CHARACTERS

A bright-red to dark-red, crystalline powder, very slightly soluble in water, slightly soluble in alcohol.

IDENTIFICATION

A. Dissolve 10 mg in a 10 g/L solution of *sodium carbonate R* and dilute to 200.0 mL with the sodium carbonate solution. Dilute 5.0 mL of the solution to 100.0 mL with a 10 g/L solution of *sodium carbonate R*. Examined between 400 nm and 630 nm (*2.2.25*), the solution shows an absorption maximum at 558 nm. The specific absorbance at the maximum is 1900 to 2100.

B. Dissolve about 10 mg in 1 mL of *dilute sodium hydroxide solution R* and add 9 mL of *water R*. The solution is deep red. To 5 mL of the solution add a slight excess of *dilute sulfuric acid R*. The colour becomes orange.

C. To 5 mL of the solution prepared for identification test B add 1 mL of *0.0167 M bromide-bromate* and 1 mL of *dilute hydrochloric acid R*, shake and allow to stand for 15 min. Make alkaline with *dilute sodium hydroxide solution R*. An intense violet-blue colour is produced.

TESTS

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

*Test solution*. Dissolve 0.1 g of the substance to be examined in *0.1 M sodium hydroxide* and dilute to 5 mL with the same solvent.

*Reference solution*. Dilute 0.5 mL of the test solution to 100 mL with *0.1 M sodium hydroxide*.

Apply separately to the plate 10 µL of each solution. Develop over a path of 15 cm using a mixture of 25 volumes of *glacial acetic acid R*, 25 volumes of *water R* and 100 volumes of *tert-pentyl alcohol R*. Allow the plate to dry in air until the solvent has evaporated and expose the plate to the vapour from *concentrated ammonia R*. Examine in ultraviolet light at 254 nm. Not more than one spot, apart from the principal spot, appears in the chromatogram obtained with the test solution and this spot is not more intense than the spot in the chromatogram obtained with the reference solution (0.5 per cent).

**Insoluble matter**. To 1.0 g of the finely powdered substance to be examined add 12 mL of *sodium hydrogen carbonate solution R*. Allow to stand for 1 h, shaking frequently. Dilute to 100 mL with *water R* and allow to stand for 15 h. Centrifuge at 2000 *g* to 3000 *g*, for 30 min, decant the supernatant liquid and wash the residue with 25 mL of a 10 g/L solution of *sodium hydrogen carbonate R* and then 25 mL of *water R*. Dry at 100 °C to 105 °C. The residue weighs not more than 5 mg (0.5 per cent).

**Loss on drying** (*2.2.32*). Not more than 1.0 per cent, determined on 1.00 g of the powdered substance to be examined by drying in an oven at 105 °C.

**Sulfated ash** (*2.4.14*). Not more than 0.2 per cent, determined on 0.5 g.

ASSAY

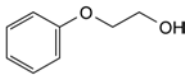
Dissolve 0.900 g in 15 mL of *1 M sodium hydroxide* and dilute to 250.0 mL with *water R*. To 10.0 mL of the solution in a glass-stoppered flask add 25 mL of *glacial acetic acid R*, 20.0 mL of *0.0167 M potassium bromate*, 5 mL of a 100 g/L solution of *potassium bromide R* and 5 mL of *hydrochloric acid R*. Allow to stand protected from light for 15 min, add 10 mL of a 100 g/L solution of *potassium iodide R* and titrate immediately with *0.1 M sodium thiosulfate*, using 0.1 mL of *starch solution R* as indicator.

1 mL of *0.0167 M potassium bromate* is equivalent to 4.43 mg of $C_{19}H_{14}O_5S$.

**01/2008:0781**

# PHENOXYETHANOL

## Phenoxyethanolum



$C_8H_{10}O_2$ $M_r$ 138.2
[122-99-6]

DEFINITION

2-Phenoxyethanol.

*Content*: 99.0 per cent *m/m* to 100.5 per cent *m/m*.

CHARACTERS

*Appearance*: colourless, slightly viscous liquid.

*Solubility*: slightly soluble in water, miscible with acetone, with ethanol (96 per cent) and with glycerol, slightly soluble in arachis oil and in olive oil.

IDENTIFICATION

*First identification: C.*

*Second identification: A, B, D.*

A. Refractive index (*2.2.6*): 1.537 to 1.539.

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

*Test solution*. Dissolve 80.0 mg in *water R* and dilute to 100.0 mL with the same solvent. Dilute 10.0 mL of this solution to 100.0 mL with *water R*.

*Spectral range*: 240-350 nm.

*Absorption maxima*: at 269 nm and 275 nm.

*Specific absorbances at the absorption maxima*:

– at 269 nm: 95 to 105;
– at 275 nm: 75 to 85.

C. Infrared absorption spectrophotometry (*2.2.24*).

*Comparison*: *phenoxyethanol CRS*.

D. Shake 2 mL with a mixture of 4 g of *potassium permanganate R*, 5.4 g of *sodium carbonate R* and 75 mL of *water R* for 30 min. Add 25 g of *sodium chloride R* and stir continuously for 60 min, filter and acidify with *hydrochloric acid R* to about pH 1.7. The melting point of the precipitate, after recrystallisation from *water R*, is 96 °C to 99 °C (*2.2.14*).

TESTS

**Relative density** (*2.2.5*): 1.105 to 1.110.

**Related substances**. Gas chromatography (*2.2.28*).

*Internal standard solution*. Dissolve 1.25 g of *methyl laurate R* in *methylene chloride R* and dilute to 25 mL with the same solvent.

*Test solution (a)*. Dissolve 5.0 g of the substance to be examined in *methylene chloride R* and dilute to 10.0 mL with the same solvent.

*Test solution (b)*. Dissolve 5.0 g of the substance to be examined in *methylene chloride R*, add 1.0 mL of the internal standard solution and dilute to 10.0 mL with *methylene chloride R*.

*Reference solution*. To 1.0 mL of test solution (a) add 10.0 mL of the internal standard solution and dilute to 100.0 mL with *methylene chloride R*.

*Column*:

– *material*: glass;
– *size*: *l* = 1.5 m, Ø = 4 mm,
– *stationary phase*: *silanised diatomaceous earth for gas chromatography R* (150-180 µm) impregnated with 3 per cent *m/m* of *polymethylphenylsiloxane R*.

*Carrier gas*: *nitrogen for chromatography R*.

*Flow rate*: 30 mL/min.

*Temperature*:

– *column*: 130 °C;

– *injection port and detector*: 200 °C.

*Detection*: flame ionisation.

*Injection*: 1 µL.

*Run time*: 5 times the retention time of phenoxyethanol.

*Elution order*: phenoxyethanol, methyl laurate.

*Retention time*: phenoxyethanol = about 5 min.

*System suitability*:

– *resolution*: minimum 12 between the peaks due to phenoxyethanol and methyl laurate in the chromatogram obtained with the reference solution;

– in the chromatogram obtained with test solution (a) there is no peak with the same retention time as the internal standard.

*Limit*:

– *total*: calculate the ratio (*R*) of the area of the peak due to phenoxyethanol to the area of the peak due to the internal standard from the chromatogram obtained with the reference solution; from the chromatogram obtained with test solution (b), calculate the ratio of the sum of the areas of any peaks, apart from the principal peak and the peak due to the internal standard, to the area of the peak due to the internal standard: this ratio is not greater than *R* (1.0 per cent).

**Phenol**: maximum 0.1 per cent.

Dissolve 1.00 g in 50 mL of *methylene chloride R*, add 1 mL of *dilute sodium hydroxide solution R* and 10 mL of *water R*. Shake. Wash the upper layer with 2 quantities, each of 20 mL, of *methylene chloride R* and dilute to 100.0 mL with *water R*. The absorbance (*2.2.25*) of the solution measured at the absorption maximum at 287 nm is not greater than 0.27.

ASSAY

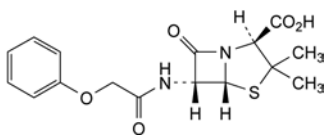
To 2.000 g in an acetylation flask fitted with an air condenser, add 10.0 mL of freshly prepared *acetic anhydride solution R1* and heat with frequent shaking in a water-bath for 45 min. Cool and carefully add 10 mL of *water R*. Heat for a further 2 min. Cool, add 10 mL of *butanol R*, shake vigorously and titrate the excess of acetic acid with *1 M sodium hydroxide* using 0.2 mL of *phenolphthalein solution R* as indicator. Repeat the procedure without the substance to be examined. The difference between the volumes used in the titrations represents the amount of acetic anhydride required for the acetylation of the substance to be examined.

1 mL of *1 M sodium hydroxide* is equivalent to 0.1382 g of $C_8H_{10}O_2$.

**01/2008:0148**
**corrected 6.1**

# PHENOXYMETHYLPENICILLIN

## Phenoxymethylpenicillinum



$C_{16}H_{18}N_2O_5S$ $M_r$ 350.4
[87-08-1]

DEFINITION

(2*S*,5*R*,6*R*)-3,3-Dimethyl-7-oxo-6-[(phenoxyacetyl)amino]-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

Substance produced by the growth of certain strains of *Penicillium notatum* or related organisms on a culture medium containing an appropriate precursor, or obtained by any other means.

*Content*: 95.0 per cent to 102.0 per cent for the sum of the percentage contents of phenoxymethylpenicillin and 4-hydroxyphenoxymethylpenicillin (anhydrous substance).

CHARACTERS

*Appearance*: white or almost white, slightly hygroscopic, crystalline powder.

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

IDENTIFICATION

*First identification: B.*

*Second identification: A, C, D.*

A. pH (see Tests).

B. Infrared absorption spectrophotometry (*2.2.24*).

*Comparison*: *phenoxymethylpenicillin CRS*.

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

*Test solution.* Dissolve 25 mg of the substance to be examined in 5 mL of *acetone R*.

*Reference solution (a).* Dissolve 25 mg of *phenoxymethylpenicillin CRS* in 5 mL of *acetone R*.

*Reference solution (b).* Dissolve 25 mg of *benzylpenicillin potassium CRS* and 25 mg of *phenoxymethylpenicillin potassium CRS* in 5 mL of *water R*.

*Plate*: *TLC silanised silica gel plate R*.

*Mobile phase*: mix 30 volumes of *acetone R* and 70 volumes of a 154 g/L solution of *ammonium acetate R* adjusted to pH 5.0 with *glacial acetic acid R*.

*Application*: 1 µL.

*Development*: over a path of 15 cm.

*Drying*: in air.

*Detection*: expose to iodine vapour until the spots appear and examine in daylight.

*System suitability*: reference solution (b):

– the chromatogram shows 2 clearly separated spots.

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

D. Place about 2 mg in a test-tube about 150 mm long and 15 mm in diameter. Moisten with 0.05 mL of *water R* and add 2 mL of *sulfuric acid-formaldehyde reagent R*. Mix the contents of the tube by swirling; the solution is reddish-brown. Place the test-tube on a water-bath for 1 min; a dark reddish-brown colour develops.

TESTS

**pH** (*2.2.3*): 2.4 to 4.0.

Suspend 50 mg in 10 mL of *carbon dioxide-free water R*.

**Specific optical rotation** (*2.2.7*): + 186 to + 200 (anhydrous substance).

Dissolve 0.250 g in *butanol R* and dilute to 25.0 mL with the same solvent.

**Related substances**. Liquid chromatography (*2.2.29*).

*Dissolution mixture.* To 250 mL of *0.2 M potassium dihydrogen phosphate R* add 500 mL of *water R*, adjust to pH 6.5 with an 8.4 g/L solution of *sodium hydroxide R* and dilute to 1000 mL with *water R*.

*Test solution (a).* Dissolve 50.0 mg of the substance to be examined in the dissolution mixture and dilute to 50.0 mL with the dissolution mixture.