Drying: in air.

Detection: examine in ultraviolet light at 254 nm.

Results: the principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with the reference solution.

D. To 0.5 g add 0.1 g of *citric acid R* and 0.2 ml of *acetic anhydride R*. Heat cautiously for 1 min. A yellow colour is produced which turns first to orange, then to red and then to violet.

TESTS

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 25 mg of the substance to be examined in the mobile phase and dilute to 25.0 ml with the mobile phase.

Reference solution (a). Dissolve 25 mg of *nicotinic acid R* in the mobile phase and dilute to 25.0 ml with the mobile phase. To 0.5 ml of this solution add 0.5 ml of the test solution and dilute to 100 ml with the mobile phase.

Reference solution (b). Dilute 1.0 ml of the test solution to 100.0 ml with the mobile phase. Dilute 1.0 ml of this solution to 10.0 ml with the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4 mm,
– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: *acetic acid R, water R, acetonitrile R* (1:29:70 *V/V/V*).

Flow rate: 1 ml/min.

Detection: spectrophotometer at 261 nm.

Injection: 20 µl.

Run time: 3 times the retention time of methyl nicotinate.

Retention time: methyl nicotinate = about 3.3 min.

System suitability: reference solution (a):

– *resolution*: minimum 2 between the peaks due to impurity A and methyl nicotinate.

Limits:

– *impurity A*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent),
– *any other impurity*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent),
– *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent),
– *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Chlorides (*2.4.4*): maximum 200 ppm.

Dissolve 0.25 g in *water R* and dilute to 15 ml with the same solvent.

Water (*2.5.12*): maximum 0.5 per cent, determined on 2.000 g.

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

ASSAY

Dissolve 0.120 g in 50 ml of *glacial 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 13.71 mg of $C_7H_7NO_2$.

STORAGE

Protected from light.

IMPURITIES

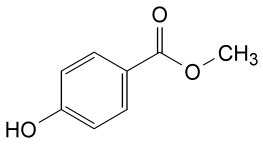
Specified impurities: A.

A. nicotinic acid.

01/2008:0409
corrected 6.0

METHYL PARAHYDROXYBENZOATE

Methylis parahydroxybenzoas



$C_8H_8O_3$ M_r 152.1
[99-76-3]

DEFINITION

Methyl 4-hydroxybenzoate.

Content: 98.0 per cent to 102.0 per cent.

CHARACTERS

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

Solubility: very slightly soluble in water, freely soluble in alcohol and in methanol.

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D.

A. Melting point (*2.2.14*): 125 °C to 128 °C.

B. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *methyl parahydroxybenzoate CRS*.

C. Examine the chromatograms obtained in the test for related substances.
Results: the principal spot in the chromatogram obtained with test solution (b) is similar in position and size to the principal spot in the chromatogram obtained with reference solution (b).

D. To about 10 mg in a test-tube add 1 ml of *sodium carbonate solution R*, boil for 30 s and cool (solution A). To a further 10 mg in a similar test-tube add 1 ml of *sodium carbonate solution R*; the substance partly dissolves (solution B). Add at the same time to solution A and solution B 5 ml of *aminopyrazolone solution R* and 1 ml of *potassium ferricyanide solution R* and mix. Solution B is yellow to orange-brown. Solution A is orange to red, the colour being clearly more intense than any similar colour which may be obtained with solution B.

TESTS

Solution S. Dissolve 1.0 g in *alcohol R* and dilute to 10 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*).

Acidity. To 2 ml of solution S add 3 ml of *alcohol R*, 5 ml of *carbon dioxide-free water R* and 0.1 ml of *bromocresol green solution R*. Not more than 0.1 ml of *0.1 M sodium hydroxide* is required to change the colour of the indicator to blue.

Monographs M

Related substances. Thin-layer chromatography (*2.2.27*).

Test solution (a). Dissolve 0.10 g of the substance to be examined in *acetone R* and dilute to 10 ml with the same solvent.

Test solution (b). Dilute 1 ml of test solution (a) to 10 ml with *acetone R*.

Reference solution (a). Dilute 0.5 ml of test solution (a) to 100 ml with *acetone R*.

Reference solution (b). Dissolve 10 mg of *methyl parahydroxybenzoate CRS* in *acetone R* and dilute to 10 ml with the same solvent.

Reference solution (c). Dissolve 10 mg of *ethyl parahydroxybenzoate CRS* in 1 ml of test solution (a) and dilute to 10 ml with *acetone R*.

Plate: suitable octadecylsilyl silica gel with a fluorescent indicator having an optimal intensity at 254 nm as the coating substance.

Mobile phase: *glacial acetic acid R, water R, methanol R* (1:30:70 *V/V/V*).

Application: 2 µl.

Development: over a path of 15 cm.

Drying: in air.

Detection: examine in ultraviolet light at 254 nm.

System suitability: the chromatogram obtained with reference solution (c) shows 2 clearly separated principal spots.

Limits:

– *any impurity*: any spot in the chromatogram obtained with test solution (a), apart from the principal spot, is not more intense than the spot in the chromatogram obtained with reference solution (a) (0.5 per cent).

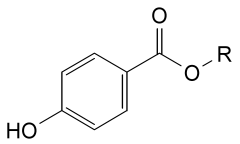
Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

To 1.000 g add 20.0 ml of *1 M sodium hydroxide*. Heat at about 70 °C for 1 h. Cool rapidly in an ice bath. Prepare a blank in the same manner. Carry out the titration on the solutions at room temperature. Titrate the excess sodium hydroxide with *0.5 M sulphuric acid*, continuing the titration until the second point of inflexion and determining the end-point potentiometrically (*2.2.20*).

1 ml of *1 M sodium hydroxide* is equivalent to 152.1 mg of $C_8H_8O_3$.

IMPURITIES



A. R = H: 4-hydroxybenzoic acid,

B. R = CH_2-CH_3: ethyl 4-hydroxybenzoate,

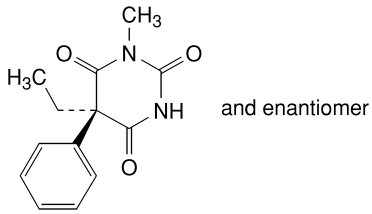
C. R = CH_2-CH_2-CH_3: propyl 4-hydroxybenzoate,

D. R = CH_2-CH_2-CH_2-CH_3: butyl 4-hydroxybenzoate.

01/2008:0189
corrected 6.0

METHYLPHENOBARBITAL

Methylphenobarbitalum



$C_{13}H_{14}N_2O_3$ M_r 246.3
[115-38-8]

DEFINITION

Methylphenobarbital contains not less than 99.0 per cent and not more than the equivalent of 102.0 per cent of (5*RS*)-5-ethyl-1-methyl-5-phenylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder or colourless crystals, practically insoluble in water, very slightly soluble in ethanol. It forms water-soluble compounds with alkali hydroxides and carbonates and with ammonia.

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D.

A. Determine the melting point (*2.2.14*) of the substance to be examined. Mix equal parts of the substance to be examined and *methylphenobarbital CRS* and determine the melting point of the mixture. The difference between the two melting points (which are about 178 °C) is not greater than 2 °C.

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *methylphenobarbital CRS*.

C. 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 *chloroform R* and dilute to 100 ml with the same solvent.

Reference solution. Dissolve 0.1 g of *methylphenobarbital CRS* in *chloroform R* and dilute to 100 ml with the same solvent.

Apply separately to the plate 10 µl of each solution. Develop over a path of 18 cm using the lower layer of a mixture of 5 volumes of *concentrated ammonia R*, 15 volumes of *alcohol R* and 80 volumes of *chloroform R*. Examine immediately in ultraviolet light at 254 nm. The principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with the reference solution.

D. To about 10 mg add 0.2 ml of *sulphuric acid R* and 0.1 ml of *nitric acid R*. Heat on a water-bath for 10 min. Cool in iced water and add 5 ml of *water R* and 5 ml of *strong sodium hydroxide solution R*. Add 5 ml of *acetone R*, shake and allow to stand. A dark-red colour develops in the upper layer.