Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 2	100	0
2 - 15	100 → 38.5	0 → 61.5

Flow rate: 1.5 mL/min.

Detection: spectrophotometer at 215 nm.

Injection: 10 µL.

Identification of impurities: use the chromatogram obtained with reference solution (b) to identify the peak due to impurity E.

Relative retention with reference to benzocaine (retention time = about 10 min): impurity E = about 0.9.

System suitability: reference solution (b):

– *resolution*: minimum 5.0 between the peaks due to impurity E and benzocaine.

Calculation of percentage contents:

– for each impurity, use the concentration of benzocaine in reference solution (a).

Limits:

– *unspecified impurities*: for each impurity, maximum 0.10 per cent;

– *total*: maximum 0.2 per cent;

– *reporting threshold*: 0.05 per cent.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo*.

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

ASSAY

Carry out the determination of primary aromatic amino-nitrogen (*2.5.8*), using 0.400 g dissolved in a mixture of 25 mL of *hydrochloric acid R* and 50 mL of *water R*.

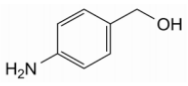
1 mL of *0.1 M sodium nitrite* is equivalent to 16.52 mg of $C_9H_{11}NO_2$.

STORAGE

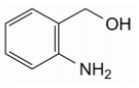
Protected from light.

IMPURITIES

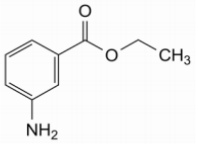
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical use (2034)*. It is therefore not necessary to identify these impurities for demonstration of compliance. See also *5.10. Control of impurities in substances for pharmaceutical use*): *A, B, C, D, E, F, G, H.*



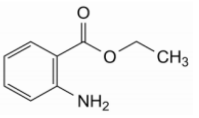
A. (4-aminophenyl)methanol,



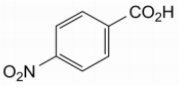
B. (2-aminophenyl)methanol,



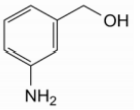
C. ethyl 3-aminobenzoate,



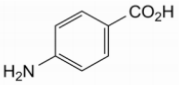
D. ethyl 2-aminobenzoate,



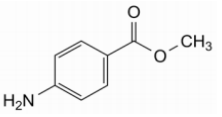
E. 4-nitrobenzoic acid,



F. (3-aminophenyl)methanol,



G. 4-aminobenzoic acid,



H. methyl 4-aminobenzoate.

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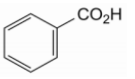
BENZOIC ACID

Acidum benzoicum



$C_7H_6O_2$ M_r 122.1

[65-85-0]

DEFINITION

Benzenecarboxylic acid.

Content: 99.0 per cent to 100.5 per cent.

CHARACTERS

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

Solubility: slightly soluble in water, soluble in boiling water, freely soluble in ethanol (96 per cent) and in fatty oils.

IDENTIFICATION

A. Melting point (*2.2.14*): 121 °C to 124 °C.

B. Solution S (see Tests) gives reaction (a) of benzoates (*2.3.1*).

TESTS

Solution S. Dissolve 5.0 g in *ethanol (96 per cent) R* and dilute to 100 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Carbonisable substances. Dissolve 0.5 g with shaking in 5 mL of *sulfuric acid R*. After 5 min, the solution is not more intensely coloured than reference solution Y_5 (*2.2.2, Method I*).

Oxidisable substances. Dissolve 0.2 g in 10 mL of boiling *water R*. Cool, shake and filter. To the filtrate add 1 mL of *dilute sulfuric acid R* and 0.2 mL of *0.02 M potassium permanganate*. After 5 min, the solution is still coloured pink.

Halogenated compounds and halides: maximum 300 ppm.

All glassware used must be chloride-free and may be prepared by soaking overnight in a 500 g/L solution of nitric acid R, rinsed with water R and stored full of water R. It is recommended that glassware be reserved for this test.

Solution (a). Dissolve 6.7 g in a mixture of 40 mL of *1 M sodium hydroxide* and 50 mL of *ethanol (96 per cent) R* and dilute to 100.0 mL with *water R*. To 10.0 mL of this solution add 7.5 mL of *dilute sodium hydroxide solution R* and 0.125 g of *nickel-aluminium alloy R* and heat on a water-bath for 10 min. Allow to cool to room temperature, filter into a 25 mL volumetric flask and wash with 3 quantities, each of 2 mL, of *ethanol (96 per cent) R*. Dilute the filtrate and washings to 25.0 mL with *water R*. This solution is used to prepare solution A.

Solution (b). In the same manner, prepare a similar solution without the substance to be examined. This solution is used to prepare solution B.

In four 25 mL volumetric flasks, place separately 10 mL of solution (a), 10 mL of solution (b), 10 mL of *chloride standard solution (8 ppm Cl) R* (used to prepare solution C) and 10 mL of *water R*. To each flask add 5 mL of *ferric ammonium sulfate solution R5*, mix and add dropwise and with swirling 2 mL of *nitric acid R* and 5 mL of *mercuric thiocyanate solution R*. Shake. Dilute the contents of each flask to 25.0 mL with *water R* and allow the solutions to stand in a water-bath at 20 °C for 15 min. Measure at 460 nm the absorbance (*2.2.25*) of solution A using solution B as the compensation liquid, and the absorbance of solution C using the solution obtained with 10 mL of *water R* as the compensation liquid. The absorbance of solution A is not greater than that of solution C.

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

ASSAY

Dissolve 0.200 g in 20 mL of *ethanol (96 per cent) R* and titrate with *0.1 M sodium hydroxide*, using 0.1 mL of *phenol red solution R* as indicator, until the colour changes from yellow to violet-red.

1 mL of *0.1 M sodium hydroxide* is equivalent to 12.21 mg of $C_7H_6O_2$.

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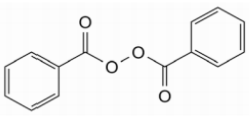
corrected 7.0

BENZOYL PEROXIDE, HYDROUS

Benzoylis peroxidum cum aqua



$C_{14}H_{10}O_4$ M_r 242.2 (anhydrous substance)
Anhydrous benzoyl peroxide: [94-36-0]

DEFINITION

Content:

– *dibenzoyl peroxide*: 70.0 per cent to 77.0 per cent;
– *water*: minimum 20.0 per cent.

CHARACTERS

Appearance: white or almost white, amorphous or granular powder.

Solubility: practically insoluble in water, soluble in acetone, soluble in methylene chloride with the separation of water, slightly soluble in ethanol (96 per cent).

It loses water rapidly on exposure to air with a risk of explosion.

Mix the entire sample thoroughly before carrying out the following tests.

IDENTIFICATION

First identification: B

Second identification: A, C, D.

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

Solution A. Dissolve 80.0 mg in *ethanol (96 per cent) R* and dilute to 100.0 mL with the same solvent. Dilute 10.0 mL of the solution to 100.0 mL with *ethanol (96 per cent) R*.

Solution B. Dilute 10.0 mL of solution A to 100.0 mL with *ethanol (96 per cent) R*.

Spectral ranges: 250-300 nm for solution A; 220-250 nm for solution B.

Absorption maxima: at 274 nm for solution A; at 235 nm for solution B.

Shoulder: at about 282 nm for solution A.

Absorbance ratio: A_{235}/A_{274} = 1.17 to 1.21.

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *Ph. Eur. reference spectrum of hydrous benzoyl peroxide.*

C. Dissolve about 25 mg in 2 mL of *acetone R*. Add 1 mL of a 10 g/L solution of *diethylphenylenediamine sulfate R* and mix. A red colour develops which quickly darkens and becomes dark violet within 5 min.

D. To 1 g add 5 mL of *ethanol (96 per cent) R*, 5 mL of *dilute sodium hydroxide solution R* and 10 mL of *water R*. Boil the mixture under reflux for 20 min. Cool. The solution gives reaction (c) of benzoates (*2.3.1*).

TESTS

Acidity. Dissolve a quantity of the substance to be examined containing the equivalent of 1.0 g of dibenzoyl peroxide in 25 mL of *acetone R*, add 75 mL of *water R* and filter. Wash the residue with two quantities, each of 10 mL, of *water R*. Combine the filtrate and the washings and add 0.25 mL of *phenolphthalein solution R1*. Not more than 1.25 mL of *0.1 M sodium hydroxide* is required to change the colour of the indicator. Carry out a blank test.

Related substances. Liquid chromatography (*2.2.29*). *Prepare the solutions immediately before use.*

Test solution. Dissolve a quantity of the substance to be examined containing the equivalent of 0.10 g of dibenzoyl peroxide in *acetonitrile R* and dilute to 50 mL with the same solvent.

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

Reference solution (b). Dissolve 30.0 mg of *benzoic acid R* in the mobile phase and dilute to 100.0 mL with the mobile phase. Dilute 1.0 mL of the solution to 10.0 mL with the mobile phase.

Reference solution (c). Dissolve 50.0 mg of *ethyl benzoate R* in the mobile phase and dilute to 100.0 mL with the mobile phase. Dilute 1.0 mL of the solution to 100.0 mL with the mobile phase.

Reference solution (d). Dissolve 50.0 mg of *benzaldehyde R* in the mobile phase and dilute to 100.0 mL with the mobile phase. Dilute 1.0 mL of the solution to 100.0 mL with the mobile phase.