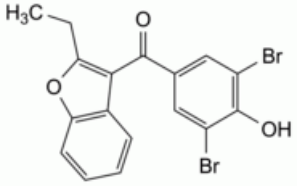
Edition: BP 2025 (Ph. Eur. 11.6 update)

Benzbromarone

General Notices

(Ph. Eur. monograph 1393)



$C_{17}H_{12}Br_2O_3$ 424.1 *3562-84-3*

Action and use

Uricosuric; treatment of hyperuricaemia.

Ph Eur

DEFINITION

(3,5-Dibromo-4-hydroxyphenyl)(2-ethylbenzofuran-3-yl)methanone.

Content

98.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water, freely soluble in acetone and in methylene chloride, sparingly soluble in ethanol (96 per cent).

mp

About 152 °C.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison benzbromarone CRS.

B. By means of a copper wire, previously ignited, introduce a small amount of the substance to be examined into the non-luminous part of a flame. The colour of the flame becomes green.

TESTS

Appearance of solution

The solution is clear (2.2.1) and not more intensely coloured than reference solution Y_5 (2.2.2, Method II).

Dissolve 1.25 g in dimethylformamide R and dilute to 25 mL with the same solvent.

Acidity or alkalinity

Shake 0.5 g with 10 mL of carbon dioxide-free water R for 1 min and filter. To 2.0 mL of the filtrate add 0.1 mL of methyl red solution R and 0.1 mL of 0.01 M hydrochloric acid. The solution is red. Add 0.3 mL of 0.01 M sodium hydroxide. The solution is yellow.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 0.125 g of the substance to be examined in 30 mL of methanol R and dilute to 50.0 mL with the mobile phase.

Reference solution (a) 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.

Reference solution (b) Dissolve 10 mg of benzarone CRS (impurity C) in the mobile phase and dilute to 20 mL with the mobile phase. To 5 mL of this solution add 1 mL of the test solution and dilute to 100 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: octadecylsilyl silica gel for chromatography R (5 µm).

Mobile phase glacial acetic acid R, acetonitrile R, water R, methanol R (5:25:300:990 *V/V/V/V*).

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 231 nm.

Injection 20 µL.

Run time 2.5 times the retention time of benzbromarone.

Relative retention With reference to benzbromarone: impurity A = about 0.6; impurity B = about 2.

System suitability Reference solution (b):

— resolution: minimum 10.0 between the peaks due to impurity C (1st peak) and benzbromarone (2nd peak).

Limits:

— *impurity A*: not more than 4 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.4 per cent);

— *impurity B*: not more than 10 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

— *sum of impurities other than A and B*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

— *disregard limit*: 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.02 per cent).

Halides expressed as chlorides (*2.4.4*)

Maximum 400 ppm.

Shake 1.25 g with a mixture of 5 mL of *dilute nitric acid R* and 15 mL of *water R*. Filter. Rinse the filter with *water R* and dilute the filtrate to 25 mL with the same solvent. Dilute 2.5 mL of this solution to 15 mL with *water R*.

Iron (*2.4.9*)

Maximum 125 ppm.

Moisten the residue obtained in the test for sulfated ash with 2 mL of *hydrochloric acid R* and evaporate to dryness on a water-bath. Add 0.05 mL of *hydrochloric acid R* and 10 mL of *water R*, heat to boiling and maintain boiling for 1 min. Allow to cool. Rinse the crucible with *water R*, collect the rinsings and dilute to 25 mL with *water R*. Dilute 2 mL of this solution to 10 mL with *water R*.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo* at 50 °C for 4 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.300 g in 60 mL of *methanol R*. Stir until completely dissolved and add 10 mL of *water R*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M sodium hydroxide* is equivalent to 42.41 mg of $C_{17}H_{12}Br_2O_3$.

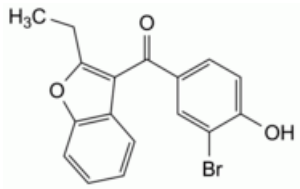
STORAGE

Protected from light.

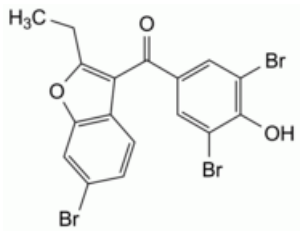
IMPURITIES

Specified impurities *A, B.*

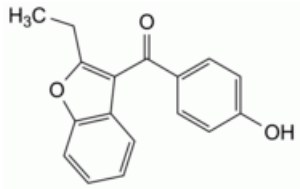
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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) *C.*



A. (3-bromo-4-hydroxyphenyl)(2-ethylbenzofuran-3-yl)methanone,



B. (6-bromo-2-ethylbenzofuran-3-yl)(3,5-dibromo-4-hydroxyphenyl)methanone,



C. (2-ethylbenzofuran-3-yl)(4-hydroxyphenyl)methanone (benzarone).

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