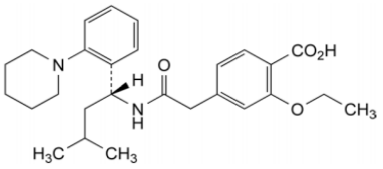
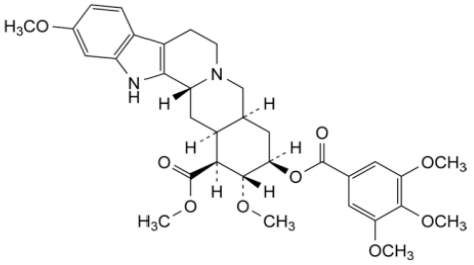


E. 2-ethoxy-4-[2-[[(1*R*)-3-methyl-1-[2-(piperidin-1-yl)phenyl]butyl]amino]-2-oxoethyl]benzoic acid.

01/2008:0528

RESERPINE

Reserpinum



$C_{33}H_{40}N_2O_9$ M_r 609
[50-55-5]

DEFINITION

Methyl 11,17α-dimethoxy-18β-[(3,4,5-trimethoxybenzoyl)oxy]-3β,20α-yohimban-16β-carboxylate.

Content:

– *reserpine*: 98.0 per cent to 102.0 per cent (dried substance),
– *total alkaloids*: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or slightly yellow, small crystals or crystalline powder, darkening slowly on exposure to light.

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

IDENTIFICATION

First identification: B.

Second identification: A, C, D, E.

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

Test solution. Dissolve 20.0 mg in *chloroform R* and dilute to 10.0 mL with the same solvent. Dilute 1.0 mL of this solution to 100.0 mL with *ethanol (96 per cent) R*. Examine immediately.

Spectral range: 230-350 nm.

Absorption maximum: at 268 nm.

Specific absorbance at the absorption maximum: 265 to 285.

Over the range 288-295 nm, the curve shows a slight absorption minimum followed by a shoulder or a slight absorption maximum; over this range, the specific absorbance is about 170.

B. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *reserpine CRS*.

C. To about 1 mg add 0.1 mL of a 1 g/L solution of *sodium molybdate R* in *sulfuric acid R*. A yellow colour is produced which becomes blue within 2 min.

D. To about 1 mg add 0.2 mL of a freshly prepared 10 g/L solution of *vanillin R* in *hydrochloric acid R*. A pink colour develops within 2 min.

E. Mix about 0.5 mg with 5 mg of *dimethylaminobenzaldehyde R* and 0.2 mL of *glacial acetic acid R* and add 0.2 mL of *sulfuric acid R*. A green colour is produced. Add 1 mL of *glacial acetic acid R*. The colour becomes red.

TESTS

Specific optical rotation (*2.2.7*): – 116 to – 128 (dried substance).

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

Oxidation products. Dissolve 20 mg in *glacial acetic acid R* and dilute to 100.0 mL with the same acid. The absorbance (*2.2.25*) measured immediately at the absorption maximum at 388 nm is not greater than 0.10.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 0.500 g by drying at 60 °C over *diphosphorus pentoxide R* at a pressure not exceeding 667 Pa for 3 h.

Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 0.5 g.

ASSAY

Total alkaloids. Dissolve 0.500 g in a mixture of 6 mL of *acetic anhydride R* and 40 mL of *anhydrous 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 60.9 mg of total alkaloids.

Reserpine. *Protect the solutions from light.* Moisten 25.0 mg with 2 mL of *ethanol (96 per cent) R*, add 2 mL of *0.25 M sulfuric acid* and 10 mL of *ethanol (96 per cent) R*, and warm gently to dissolve. Cool and dilute to 100.0 mL with *ethanol (96 per cent) R*. Dilute 5.0 mL of this solution to 50.0 mL with *ethanol (96 per cent) R*. Prepare a reference solution in the same manner using 25.0 mg of *reserpine CRS*. Place 10.0 mL of each solution separately in 2 boiling-tubes, add 2.0 mL of *0.25 M sulfuric acid* and 2.0 mL of a freshly prepared 3 g/L solution of *sodium nitrite R*. Mix and heat in a water-bath at 55 °C for 35 min. Cool, add 1.0 mL of a freshly prepared 50 g/L solution of *sulfamic acid R* and dilute to 25.0 mL with *ethanol (96 per cent) R*. Measure the absorbance (*2.2.25*) of each solution at the absorption maximum at 388 nm, using as the compensation liquid 10.0 mL of the same solution prepared at the same time in the same manner, but omitting the sodium nitrite.

Calculate the content of $C_{33}H_{40}N_2O_9$ from the absorbances measured and the concentrations of the solutions.

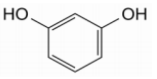
STORAGE

Protected from light.

01/2008:0290

RESORCINOL

Resorcinolum



$C_6H_6O_2$ M_r 110.1
[108-46-3]

DEFINITION

Resorcinol contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of benzene-1,3-diol, calculated with reference to the dried substance.

CHARACTERS

A colourless or slightly pinkish-grey, crystalline powder or crystals, turning red on exposure to light and air, very soluble in water and in alcohol.

IDENTIFICATION

A. Melting point (*2.2.14*): 109 °C to 112 °C.

B. Dissolve 0.1 g in 1 mL of *water R*, add 1 mL of *strong sodium hydroxide solution R* and 0.1 mL of *chloroform R*, heat and allow to cool. An intense, deep-red colour develops which becomes pale yellow on the addition of a slight excess of *hydrochloric acid R*.

C. Thoroughly mix about 10 mg with about 10 mg of *potassium hydrogen phthalate R*, both finely powdered. Heat over a naked flame until an orange-yellow colour is obtained. Cool and add 1 mL of *dilute sodium hydroxide solution R* and 10 mL of *water R* and shake to dissolve. The solution shows an intense green fluorescence.

TESTS

Solution S. Dissolve 2.5 g in *carbon dioxide-free water R* and dilute to 25 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution B_5 or R_5 (*2.2.2, Method II*) and remains so when heated in a water-bath for 5 min.

Acidity or alkalinity. To 10 mL of solution S add 0.05 mL of *bromophenol blue solution R2*. Not more than 0.05 mL of *0.1 M hydrochloric acid* or *0.1 M sodium hydroxide* is required to change the colour of the indicator.

Related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel G R* as the coating substance.

Test solution. Dissolve 0.5 g of the substance to be examined in *methanol R* and dilute to 10 mL with the same solvent.

Reference solution. Dilute 0.1 mL of the test solution to 20 mL with *methanol R*.

Apply separately to the plate 2 µL of each solution. Develop over a path of 15 cm using a mixture of 40 volumes of *ethyl acetate R* and 60 volumes of *hexane R*. Allow the plate to dry in air for 15 min and expose it to iodine vapour. Any spot in the chromatogram obtained with the test solution, apart from the principal spot, is not more intense than the spot in the chromatogram obtained with the reference solution (0.5 per cent).

Pyrocatechol. To 2 mL of solution S add 1 mL of *ammonium molybdate solution R2* and mix. Any yellow colour in the solution is not more intense than that in a standard prepared at the same time in the same manner using 2 mL of a 0.1 g/L solution of *pyrocatechol R*.

Loss on drying (*2.2.32*). Not more than 1.0 per cent, determined on 1.00 g of powdered substance by drying in a desiccator for 4 h.

Sulfated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.500 g in *water R* and dilute to 250.0 mL with the same solvent. To 25.0 mL of the solution in a ground-glass-stoppered flask add 1.0 g of *potassium bromide R*, 50.0 mL of *0.0167 M potassium bromate*, 15 mL of *chloroform R* and 15.0 mL of *hydrochloric acid R1*. Stopper the flask, shake and allow to stand in the dark for 15 min, shaking occasionally. Add 10 mL of a 100 g/L solution of *potassium iodide R*, shake thoroughly, allow to stand for 5 min and titrate with *0.1 M sodium thiosulfate*, using 1 mL of *starch solution R* as indicator.

1 mL of *0.0167 M potassium bromate* is equivalent to 1.835 mg of $C_6H_6O_2$.

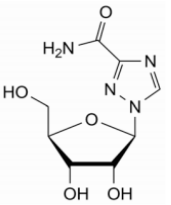
STORAGE

Store protected from light.

01/2017:2109

RIBAVIRIN

Ribavirinum



$C_8H_{12}N_4O_5$ M_r 244.2

[36791-04-5]

DEFINITION

1-β-D-Ribofuranosyl-1*H*-1,2,4-triazole-3-carboxamide.

Content: 98.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

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

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *ribavirin CRS*.

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in *methylene chloride R*, evaporate to dryness and record new spectra using the residues.

TESTS

pH (*2.2.3*): 4.0 to 6.5.

Dissolve 0.200 g in *carbon dioxide-free water R* and dilute to 10.0 mL with the same solvent.

Specific optical rotation (*2.2.7*): − 33 to − 37 (dried substance).

Dissolve 0.250 g in *water R* and dilute to 25.0 mL with the same solvent. Determine the specific optical rotation within 10 min of preparing the solution.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 50.0 mg of the substance to be examined in *water for chromatography R* and dilute to 100.0 mL with the same solvent.

Reference solution (a). In order to produce impurity A *in situ*, mix 5.0 mL of the test solution and 5.0 mL of a 42 g/L solution of *sodium hydroxide R* and allow to stand for 90 min. Neutralise with 5.0 mL of a 103 g/L solution of *hydrochloric acid R* and mix well.

Reference solution (b). Dilute 1.0 mL of the test solution to 100.0 mL with *water for chromatography R*. Dilute 1.0 mL of this solution to 10.0 mL with *water for chromatography R*.