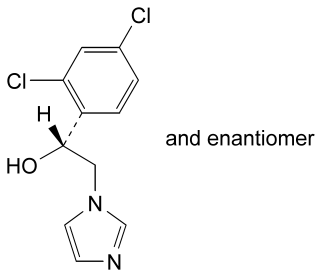
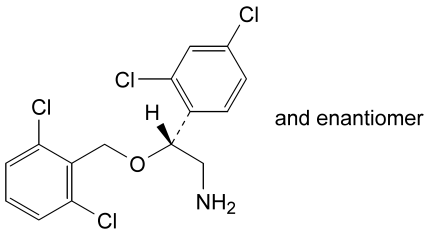


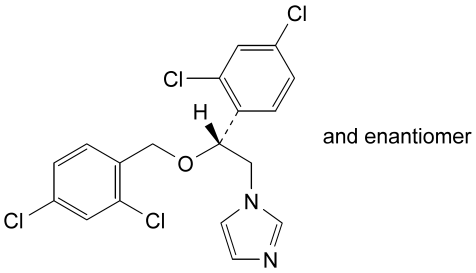
and enantiomer

B. (1*RS*)-1-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-yl)ethanol,



and enantiomer

C. (2*RS*)-2-[(2,6-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)-ethanamine,



and enantiomer

D. 1-[(2*RS*)-2-[(2,4-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole.

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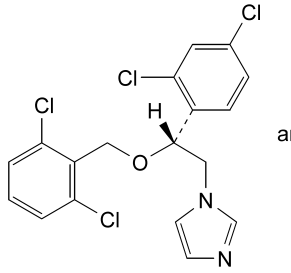
corrected 6.0

ISOCONAZOLE NITRATE

Isoconazoli nitras



and enantiomer , HNO_3

$C_{18}H_{15}Cl_4N_3O_4$ M_r 479.1
[40036-10-0]

DEFINITION

1-[(2*RS*)-2-[(2,6-Dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)-ethyl]-1*H*-imidazole nitrate.

Content: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white powder.

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

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D.

A. Melting point (*2.2.14*): 178 °C to 182 °C.

B. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *isoconazole nitrate CRS.*

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

Test solution. Dissolve 30 mg of the substance to be examined in *methanol R* and dilute to 5 ml with the same solvent.

Reference solution (a). Dissolve 30 mg of *isoconazole nitrate CRS* in *methanol R* and dilute to 5 ml with the same solvent.

Reference solution (b). Dissolve 30 mg of *isoconazole nitrate CRS* and 30 mg of *econazole nitrate CRS* in *methanol R*, then dilute to 5 ml with the same solvent.

Plate: *TLC octadecylsilyl silica gel plate R.*

Mobile phase: *ammonium acetate solution R, dioxan R, methanol R* (20:40:40 *V/V/V*).

Application: 5 µl.

Development: over a path of 15 cm.

Drying: in a current of warm air for 15 min.

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. It gives the reaction of nitrates (*2.3.1*).

TESTS

Solution S. Dissolve 0.20 g in *methanol R* and dilute to 20.0 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution Y_7 (*2.2.2, Method II*).

Optical rotation (*2.2.7*): – 0.10° to + 0.10°, determined on solution S.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 0.100 g of the substance to be examined in the mobile phase and dilute to 10.0 ml with the mobile phase.

Reference solution (a). Dissolve 2.5 mg of *isoconazole nitrate CRS* and 2.5 mg of *econazole nitrate CRS* in the mobile phase, then dilute to 100.0 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 5.0 ml of this solution to 20.0 ml with the mobile phase.

Column:

– *size*: *l* = 0.1 m, Ø = 4.6 mm;

– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (3 µm).

Mobile phase: dissolve 6.0 g of *ammonium acetate R* in a mixture of 300 ml of *acetonitrile R*, 320 ml of *methanol R* and 380 ml of *water R*.

Flow rate: 2 ml/min.

Detection: spectrophotometer at 235 nm.

Equilibration: with the mobile phase for about 30 min.

Injection: 10 µl.

Run time: 1.5 times the retention time of isoconazole.

Retention time: econazole = about 10 min; isoconazole = about 14 min.

System suitability: reference solution (a):

– *resolution*: minimum 5.0 between the peaks due to econazole and isoconazole; if necessary, adjust the composition of the mobile phase.

Limits:

– *impurities A, B, C*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.25 per cent);

– *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

– *disregard limit*: 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent); disregard the peak due to the nitrate ion.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 2 h.

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

ASSAY

Dissolve 0.350 g in 75 ml of a mixture of 1 volume of *anhydrous acetic acid R* and 7 volumes of *methyl ethyl ketone R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

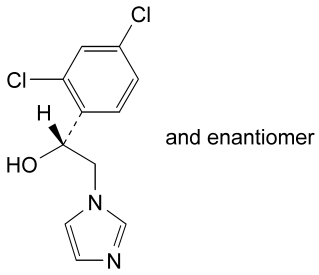
1 ml of *0.1 M perchloric acid* is equivalent to 47.91 mg of $C_{18}H_{15}Cl_4N_3O_4$.

STORAGE

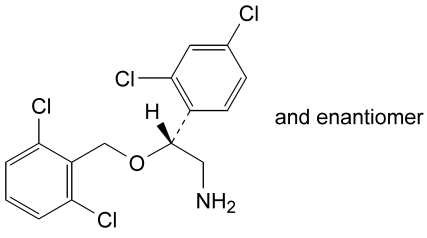
Protected from light.

IMPURITIES

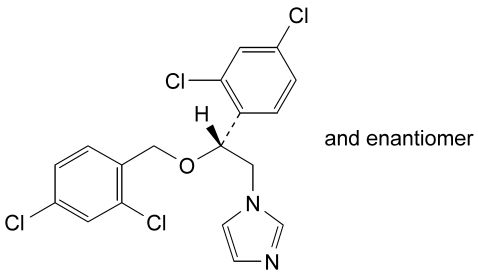
Specified impurities: *A, B, C.*



A. (1*RS*)-1-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-yl)ethanol,



B. (2*RS*)-2-[(2,6-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethanamine,



C. 1-[(2*RS*)-2-[(2,4-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole.

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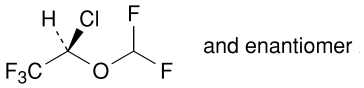
ISOFLURANE

Isofluranum



$C_3H_2ClF_5O$ M_r 184.5
[26675-46-7]

DEFINITION

(2*RS*)-2-Chloro-2-(difluoromethoxy)-1,1,1-trifluoroethane.

CHARACTERS

Appearance: clear, colourless, mobile, heavy liquid.

Solubility: practically insoluble in water, miscible with ethanol and trichloroethylene.

bp: about 48 °C.

It is non-flammable.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Preparation: examine the substance in the gaseous state.

Comparison: *Ph. Eur. reference spectrum of isoflurane.*

TESTS

Acidity or alkalinity. To 20 ml add 20 ml of *carbon dioxide-free water R*, shake for 3 min and allow to stand. Collect the upper layer and add 0.2 ml of *bromocresol purple solution R*. Not more than 0.1 ml of *0.01 M sodium hydroxide* or 0.6 ml of *0.01 M hydrochloric acid* is required to change the colour of the indicator.

Related substances. Gas chromatography (*2.2.28*).

Test solution. The substance to be examined.

Reference solution. To 80 ml of *ethanol R*, add 1.0 ml of the substance to be examined and 1.0 ml of *acetone R*, avoiding loss by evaporation. Dilute to 100.0 ml with *ethanol R*. Dilute 1.0 ml of the solution to 100.0 ml with *ethanol R*.

Column:

– *material*: fused silica,

– *size*: *l* = 30 m, Ø = 0.32 mm,

– *stationary phase*: *macrogol 20 000 R* (film thickness 0.25 µm).

Carrier gas: *helium for chromatography R.*

Flow rate: 1.0 ml/min.

Split ratio: 1:25.

Temperature:

– *column*: 35 °C,