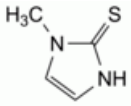
Edition: BP 2025 (Ph. Eur. 11.6 update)

Thiamazole

General Notices

(Ph. Eur. monograph 1706)



$C_4H_6N_2S$ 114.2 *60-56-0*

Action and use

Thionamide antithyroid.

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DEFINITION

1-Methyl-1,3-dihydro-2*H*-imidazole-2-thione.

Content

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

CHARACTERS

Appearance

White or pale brown, crystalline powder.

Solubility

Freely soluble in water, freely soluble in methylene chloride, freely soluble or soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: A, C.

Second identification: A, B, D.

A. Melting point (2.2.14): 143 °C to 146 °C.
B. Dissolve 25 mg in 10 mL of a 0.28 per cent *V/V* solution of *sulfuric acid R* and dilute to 50.0 mL with the same solution. Dilute 1.0 mL of this solution to 100.0 mL with a 0.28 per cent *V/V* solution of *sulfuric acid R*. Examined between 200 nm

and 300 nm (2.2.25), the solution shows 2 absorption maxima, at 211 nm and 251 nm. The ratio of the absorbance measured at the absorption maximum at 251 nm to that measured at the absorption maximum at 211 nm is 2.5 to 2.7.

C. Infrared absorption spectrophotometry (2.2.24).

Preparation Discs.

Comparison *thiamazole CRS*.

D. Thin-layer chromatography (2.2.27).

Test solution Dissolve 5.0 mg of the substance to be examined in *methanol R* and dilute to 5.0 mL with the same solvent.

Reference solution (a) Dissolve 5.0 mg of *thiamazole CRS* in *methanol R* and dilute to 5.0 mL with the same solvent.

Reference solution (b) Dissolve 5.0 mg of *2-methylimidazole R* in *methanol R* and dilute to 5.0 mL with the same solvent. Dilute 1.0 mL of this solution to 2.0 mL with the test solution.

Plate *TLC silica gel F_{254} plate R*.

Mobile phase *concentrated ammonia R1*, *2-propanol R*, *toluene R* (1:24:75 *V/V/V*).

Application 10 µL.

Development Over 2/3 of the plate.

Drying In air.

Detection Examine in ultraviolet light at 254 nm.

System suitability Reference solution (b):

— expose the plate to iodine vapour for 30 min; the chromatogram shows 2 clearly separated spots.

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 reference solution (a).

TESTS

Solution S

Dissolve 2.0 g in *water 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 B_6 (2.2.2, *Method II*).

Related substances

Gas chromatography (2.2.28).

Test solution Dissolve 0.100 g of the substance to be examined in *chloroform R* and dilute to 10.0 mL with the same solvent.

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

Reference solution (b) Dissolve 5.0 mg of *thiamazole impurity A CRS*, 5.0 mg of *1-methylimidazole R1* and 5.0 mg of *thiamazole impurity C CRS* in *chloroform R* and dilute to 50.0 mL with the same solvent. Dilute 1.0 mL of this solution to 10.0 mL with *chloroform R*.

Column:

— *material*: fused silica,

— *size*: *l* = 30.0 m, Ø = 0.25 mm,

— *stationary phase*: *base-deactivated phenyl(5)methyl(95)polysiloxane R* (film thickness 0.5 µm).

Carrier gas *helium for chromatography R*.

Flow rate 1.5 mL/min.

Split ratio 3:20.

Temperature:

	Time (min)	Temperature (°C)
Column	0 - 2	100
	2 - 7	100 → 250
	7 - 22	250
Injection port		150
Detector		250

Detection Flame ionisation.

Injection 1 µL.

Relative retention With reference to thiamazole (retention time = about 6.5 min): impurity A = about 0.3; impurity B = about 0.4; impurity C = about 0.7.

System suitability Reference solution (b):

— *resolution*: minimum 1.5 between the peaks due to impurity A and impurity B.

Limits:

— *impurities A, B, C*: for each impurity, not more than the area of the corresponding 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 (a) (0.1 per cent),

— *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 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).

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.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

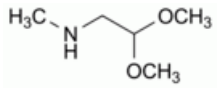
ASSAY

Dissolve 0.250 g in 75 mL of *water R*. Add 15.0 mL of *0.1 M sodium hydroxide*, mix and add with stirring, about 30 mL of *0.1 M silver nitrate*. Continue the titration with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*).

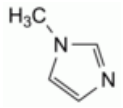
1 mL of *0.1 M sodium hydroxide* is equivalent to 11.42 mg of $C_4H_6N_2S$.

IMPURITIES

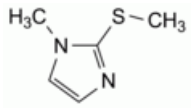
Specified impurities *A, B, C.*



A. 2,2-dimethoxy-*N*-methylethanamine,



B. 1-methyl-1*H*-imidazole,



C. 1-methyl-2-(methylsulfanyl)-1*H*-imidazole.

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