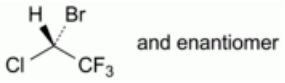
Edition: BP 2025 (Ph. Eur. 11.6 update)

Halothane

General Notices

(Ph. Eur. monograph 0393)



$C_2HBrClF_3$ 197.4 *151-67-7*

Action and use

General anaesthetic.

Ph Eur

DEFINITION

(*RS*)-2-Bromo-2-chloro-1,1,1-trifluoroethane to which 0.01 per cent *m/m* of thymol has been added.

CHARACTERS

Appearance

Clear, colourless, mobile, heavy, non-flammable liquid.

Solubility

Slightly soluble in water, miscible with anhydrous ethanol.

IDENTIFICATION

First identification: B.

Second identification: A, C.

A. Distillation range (see Tests).
B. Infrared absorption spectrophotometry (2.2.24).

Preparation Examine the substance in a 0.1 mm cell.

Comparison *Ph. Eur. reference spectrum of halothane*.

C. Add 0.1 mL to 2 mL of *2-methyl-2-propanol R* in a test-tube. Add 1 mL of *copper edetate solution R*, 0.5 mL of *concentrated ammonia R* and a mixture of 0.4 mL of *strong hydrogen peroxide solution R* and 1.6 mL of *water R*

(solution A). Prepare a blank at the same time (solution B). Place both tubes in a water-bath at 50 °C for 15 min, cool and add 0.3 mL of *glacial acetic acid R*. To 1 mL of each of solutions A and B add 0.5 mL of a mixture of equal volumes of freshly prepared *alizarin S solution R* and *zirconyl nitrate solution R*. Solution A is yellow and solution B is red.

To 1 mL of each of solutions A and B add 1 mL of *buffer solution pH 5.2 R*, 1 mL of *phenol red solution R* diluted 1 to 10 with *water R* and 0.1 mL of *chloramine solution R*. Solution A is bluish-violet and solution B is yellow.

To 2 mL of each of solutions A and B add 0.5 mL of a mixture of 25 volumes of *sulfuric acid R* and 75 volumes of *water R*, 0.5 mL of *acetone R* and 0.2 mL of a 50 g/L solution of *potassium bromate R* and shake. Warm the tubes in a water-bath at 50 °C for 2 min, cool and add 0.5 mL of a mixture of equal volumes of *nitric acid R* and *water R* and 0.5 mL of *silver nitrate solution R2*. Solution A is opalescent and a white precipitate is formed after a few minutes; solution B remains clear.

TESTS

Acidity or alkalinity

To 20 mL add 20 mL of *carbon dioxide-free water R*, shake for 3 min and allow to stand. Separate the aqueous 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.

Relative density (*2.2.5*)

1.872 to 1.877.

Distillation range (*2.2.11*)

It distils completely between 49.0 °C and 51.0 °C and 95 per cent distills within a range of 1.0 °C.

Volatile related substances

Gas chromatography (*2.2.28*).

Internal standard *trichlorotrifluoroethane CRS*.

Test solution (a) The substance to be examined.

Test solution (b) Dilute 1.0 mL of *trichlorotrifluoroethane CRS* to 20.0 mL with the substance to be examined. Dilute 1.0 mL of the solution to 100.0 mL with the substance to be examined. Dilute 1.0 mL of this solution to 10.0 mL with the substance to be examined.

Column:

— *size*: *l* = 2.75 m, Ø = 5 mm;

— *stationary phase*: *silanised diatomaceous earth for gas chromatography R* (180-250 µm), the first 1.8 m being impregnated with 30 per cent *m/m* of *macrogol 400 R* and the remainder with 30 per cent *m/m* of *dinonyl phthalate R*;

— *temperature*: 50 °C.

Carrier gas *nitrogen for chromatography R*.

Flow rate 30 mL/min.

Detection Flame ionisation.

Injection 5 µL.

Limit Test solution (b):

— *total*: not more than the area of the peak due to the internal standard, corrected if necessary for any impurity with the same retention time as the internal standard (0.005 per cent).

Thymol

Gas chromatography (2.2.28).

Internal standard solution Dissolve 0.10 g of menthol R in methylene chloride R and dilute to 100.0 mL with the same solvent.

Test solution To 20.0 mL of the substance to be examined add 5.0 mL of the internal standard solution.

Reference solution Dissolve 20.0 mg of thymol R in methylene chloride R and dilute to 100.0 mL with the same solvent. To 20.0 mL of this solution, add 5.0 mL of the internal standard solution.

Column:

— *material*: fused silica;

— *size*: *l* = 15 m, Ø = 0.53 mm;

— *stationary phase*: methylpolysiloxane R (film thickness 1.5 µm).

Carrier gas nitrogen for chromatography R.

Flow rate 15 mL/min.

Temperature:

— *column*: 150 °C;

— *injection port*: 170 °C;

— *detector*: 200 °C.

Detection Flame ionisation.

Injection 1.0 µL.

Limit:

— *thymol*: 0.75 times to 1.15 times the area of the corresponding peak in the chromatogram obtained with the reference solution (0.008 per cent *m/m* to 0.012 per cent *m/m*).

Bromides and chlorides

To 10 mL add 20 mL of water R and shake for 3 min. To 5 mL of the aqueous layer add 5 mL of water R, 0.05 mL of nitric acid R and 0.2 mL of silver nitrate solution R1. The solution is not more opalescent than a mixture of 5 mL of the aqueous layer and 5 mL of water R.

Bromine and chlorine

To 10 mL of the aqueous layer obtained in the test for bromides and chlorides add 1 mL of potassium iodide and starch solution R. No blue colour is produced.

Non-volatile matter

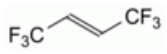
Maximum 20 mg/L.

Evaporate 50 mL to dryness on a water-bath and dry the residue in an oven at 100-105 °C for 2 h. The residue weighs a maximum of 1 mg.

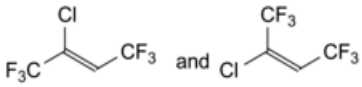
STORAGE

In an airtight container, protected from light, at a temperature not exceeding 25 °C. The choice of material for the container is made taking into account the particular reactivity of halothane with certain metals.

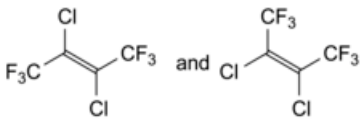
IMPURITIES



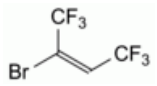
A. (*E*)-1,1,1,4,4,4-hexafluorobut-2-ene,



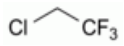
B. (*EZ*)-2-chloro-1,1,1,4,4,4-hexafluorobut-2-ene (*cis* and *trans*),



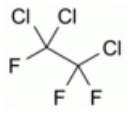
C. (*EZ*)-2,3-dichloro-1,1,1,4,4,4-hexafluorobut-2-ene (*cis* and *trans*),



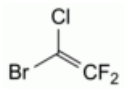
D. (*E*)-2-bromo-1,1,1,4,4,4-hexafluorobut-2-ene,



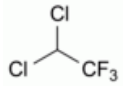
E. 2-chloro-1,1,1-trifluoroethane,



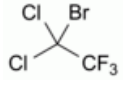
F. 1,1,2-trichloro-1,2,2-trifluoroethane,



G. 1-bromo-1-chloro-2,2-difluoroethene,



H. 2,2-dichloro-1,1,1-trifluoroethane,



I. 1-bromo-1,1-dichloro-2,2,2-trifluoroethane,

J. 1,2-dichloro-1,1-difluoroethane.

Ph Eur