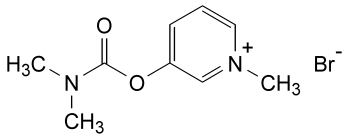
01/2008:1255
corrected 6.0

PYRIDOSTIGMINE BROMIDE

Pyridostigmini bromidum



$C_9H_{13}BrN_2O_2$ M_r 261.1
[101-26-8]

DEFINITION

3-(Dimethylcarbamoyloxy)-1-methylpyridinium bromide.

Content: 98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline, deliquescent powder.

Solubility: very soluble in water and in ethanol (96 per cent).

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *pyridostigmine bromide CRS*.

B. It gives reaction (a) of bromides (*2.3.1*).

TESTS

Solution S. Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 100 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Acidity or alkalinity. To 40 ml of solution S add a few drops of *methyl red solution R*. To 20 ml of this solution add 0.2 ml of *0.02 M sodium hydroxide*. The solution is yellow. To the other 20 ml add 0.2 ml of *0.02 M hydrochloric acid*. The solution is red.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 50 mg of the substance to be examined in the mobile phase at about 40 °C. Allow to cool and dilute to 50.0 ml with the mobile phase.

Reference solution (a). Dissolve 4 mg of *pyridostigmine impurity A CRS* and 4 mg of *pyridostigmine bromide CRS* in the mobile phase and dilute to 100.0 ml with the mobile phase. Dilute 5.0 ml of this solution 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 10.0 ml of this solution to 50.0 ml with the mobile phase.

Reference solution (c). Dilute 5.0 ml of reference solution (b) to 20.0 ml with the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4.0 mm;

– *stationary phase*: *base-deactivated octadecylsilyl silica gel for chromatography R* (5-10 µm).

Mobile phase: mix 30 volumes of *acetonitrile R* and 70 volumes of a 4.33 g/l solution of *sodium dodecyl sulphate R* previously adjusted to pH 2.0 with *phosphoric acid R*.

Flow rate: 1.1 ml/min.

Detection: spectrophotometer at 220 nm.

Injection: 20 µl.

Run time: twice the retention time of pyridostigmine.

System suitability: reference solution (a):

– *resolution*: minimum 1.5 between the peaks due to pyridostigmine and impurity A.

Limits:

– *impurities A, B*: for each impurity, not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.4 per cent), at most one such peak has an area greater than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent) and at most one further peak has an area greater than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent);

– *total*: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

– *disregard limit*: the area of the principal peak in the chromatogram obtained with reference solution (c) (0.05 per cent).

Heavy metals (*2.4.8*): maximum 20 ppm.

1.0 g complies with test C. Prepare the reference solution using 2 ml of *lead standard solution (10 ppm Pb) R*.

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

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

ASSAY

Dissolve 0.230 g in 10 ml of *anhydrous acetic acid R*. Add 40 ml of *acetic anhydride R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

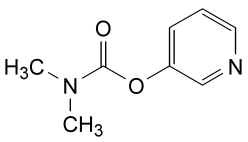
1 ml of *0.1 M perchloric acid* is equivalent to 26.11 mg of $C_9H_{13}BrN_2O_2$.

STORAGE

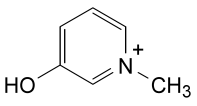
In an airtight container, protected from light. If the substance is sterile, store in a sterile, airtight, tamper-proof container, protected from light.

IMPURITIES

Specified impurities: *A, B.*



A. pyridin-3-yl dimethylcarbamate,



B. 3-hydroxy-1-methylpyridinium.

Monographs P