**DOXYLAMINE HYDROGEN SUCCINATE**

Doxylamine hydrogensuccinate

\[ C_{22}H_{24}N_2O_8 \]

\[ M, 388.5 \]

**DEFINITION**

\[ N,N\text{-dimethyl-2-[(1RS)-1-phenyl-1-(pyridin-2-yl)ethoxy]ethanamine hydrogen butanedioate} \]

**Content:** 99.0 per cent to 101.0 per cent (anhydrous substance).

**CHARACTERS**

**Appearance:** a white or almost white powder.

**Solubility:** very soluble in water, freely soluble in alcohol.
IDENTIFICATION

First identification: C.
Second identification: A, B.

A. Melting point (2.2.14): 103 °C to 108 °C.
B. Dissolve 0.200 g in 0.1 M hydrochloric acid and dilute to 100.0 ml with the same solvent. Dilute 1.0 ml of the solution to 100.0 ml with 0.1 M hydrochloric acid. Examined between 230 nm and 350 nm (2.2.25), the solution shows an absorption maximum at 262 nm. The specific absorbance at the maximum is 229 to 243 (anhydrous substance).
C. Infrared absorption spectrophotometry (2.2.24).

Comparison: Ph. Eur. reference spectrum of doxylamine hydrogen succinate.

TESTS

Appearance of solution. The solution is clear (2.2.1) and colourless (2.2.2, Method II).

Dissolve 0.4 g of the substance to be examined in water R and dilute to 20 ml with the same solvent.

Optical rotation (2.2.7): -0.10° to +0.10°.

Dissolve 2.50 g of the substance to be examined in water R and dilute to 25.0 ml with the same solvent.

Related substances. Gas chromatography (2.2.28).

Test solution. Dissolve 0.650 g of the substance to be examined in 20 ml of 0.1 M hydrochloric acid. Add 3 ml of a 100 g/l solution of sodium hydroxide R and extract 3 times with 25 ml of methylene chloride R. Combine the methylene chloride extracts and filter using hydrophobic phase-separation filter paper. Rinse the filter with 10 ml of methylene chloride R and combine the rinsings with the methylene chloride extracts. Evaporate the solvent under reduced pressure at a temperature not exceeding 40 °C. Dissolve the residue in 20.0 ml of ethanol R.

Reference solution (a). Dilute 1.0 ml of the test solution to 200.0 ml with ethanol R.

Reference solution (b). Dissolve 40 mg of doxylamine impurity A CRS and 40 mg of 2-benzoylpyridine R in ethanol R and dilute to 20 ml with the same solvent. Dilute 1 ml of this solution to 20 ml with ethanol R.

Column:
- material: fused silica,
- size: l = 30 m, Ø = 0.53 mm,
- stationary phase: poly(dimethyl)(diphenyl)siloxane R (film thickness 1.5 µm).

Carrier gas: helium for chromatography R.
Flow rate: 7 ml/min.

Temperature:

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Temperature (°C)</th>
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</thead>
<tbody>
<tr>
<td>Column</td>
<td>0 - 12 160 → 220</td>
</tr>
<tr>
<td></td>
<td>12 - 27 220</td>
</tr>
<tr>
<td>Injection port</td>
<td>250</td>
</tr>
<tr>
<td>Detector</td>
<td>250</td>
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</tbody>
</table>

Detection: flame ionisation.
Injection: 1 µl.

System suitability: reference solution (b):
- resolution: minimum 1.5 between the peaks due to impurity A and impurity D.

Limits:
- any impurity: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent).
- total: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (1 per cent).
- disregard limit: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Water (2.5.12): maximum 0.5 per cent, determined on 2.00 g.

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

ASSAY

Dissolve 0.150 g in 50 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 19.43 mg of C21H28N2O5.

IMPURITIES

A. N,N-dimethyl-2-[1(RS)-1-phenyl-1-(pyridin-4-yl)ethoxy]ethanamine,

B. R1 = CH3, R2 = H: (1RS)-1-phenyl-1-(pyridin-2-yl)ethanol,

C. R1 = H, R2 = CH2-CH2-N(CH3)2: N,N-dimethyl-2-[1(RS)-1-phenyl(pyridin-2-yl)methoxy]ethanamine,

D. phenyl(pyridin-2-yl)methanone (2-benzoylpyridine).