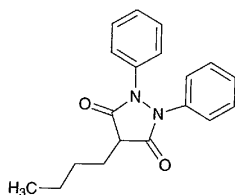


## Phenylbutazone

フェニルブタゾン

C<sub>19</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>: 308.37

4-Butyl-1,2-diphenylpyrazolidine-3,5-dione [50-33-9]

Phenylbutazone, when dried, contains not less than 99.0% of C<sub>19</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>.

**Description** Phenylbutazone occurs as a white to slightly yellowish white, crystalline powder. It is odorless, and is at first tasteless but leaves a slightly bitter aftertaste.

It is freely soluble in acetone, soluble in ethanol (95) and in diethyl ether, and practically insoluble in water.

It dissolves in sodium hydroxide TS.

**Identification (1)** To 0.1 g of Phenylbutazone add 1 mL of acetic acid (100) and 1 mL of hydrochloric acid, and heat on a water bath under a reflux condenser for 30 minutes. Add 10 mL of water, and cool with ice water. Filter, and to the filtrate add 3 to 4 drops of sodium nitrite TS. To 1 mL of this solution add 1 mL of 2-naphthol TS and 3 mL of chloroform, and shake: a deep red color develops in the chloroform layer.

(2) Dissolve 1 mg of Phenylbutazone in 10 mL of dilute sodium hydroxide TS, and dilute with water to make 100 mL. Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

**Melting point** 104 – 107°C

**Purity (1)** Clarity of solution—Dissolve 1.0 g of Phenylbutazone in 20 mL of sodium hydroxide solution (2 in 25), and allow to stand at 25 ± 1°C for 3 hours: the solution is clear. Determine the absorbance of this solution at 420 nm as directed under the Ultraviolet-visible Spectrophotometry: it is not more than 0.05.

(2) Heavy metals—Proceed with 20 g of Phenylbutazone according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(3) Arsenic—Prepare the test solution with 1.0 g of phenylbutazone, according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(4) Readily carbonizable substances—Dissolve 1.0 g of Phenylbutazone in 20 mL of sulfuric acid, and allow to stand at 25 ± 1°C for exactly 30 minutes: the solution is clear. Determine the absorbance of this solution at 420 nm: it is not more than 0.10.

**Loss on drying** Not more than 0.5% (1 g, in vacuum, silica gel, 4 hours).

**Residue on ignition** Not more than 0.10% (1 g).

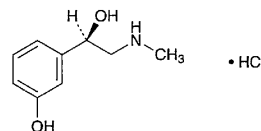
**Assay** Weigh accurately about 0.5 g of Phenylbutazone, previously dried, dissolve in 25 mL of acetone, and titrate with 0.1 mol/L sodium hydroxide VS until the solution shows a blue color which persists for 15 seconds (indicator: 5 drops of bromothymol blue TS). Perform a blank determination with a mixture of 25 mL of acetone and 16 mL of water, and make any necessary correction.

Each mL of 0.1 mol/L sodium hydroxide VS  
= 30.838 mg of C<sub>19</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>

**Containers and storage** Containers—Tight containers.

## Phenylephrine Hydrochloride

塩酸フェニレフリン

C<sub>9</sub>H<sub>13</sub>NO<sub>2</sub>·HCl: 203.67

(1R)-1-(3-Hydroxyphenyl)-2-methylaminoethanol monohydrochloride [61-76-7]

Phenylephrine Hydrochloride, when dried, contains not less than 98.0% and not more than 102.0% of C<sub>9</sub>H<sub>13</sub>NO<sub>2</sub>·HCl.

**Description** Phenylephrine Hydrochloride occurs as white crystals or crystalline powder. It is odorless, and has a bitter taste.

It is very soluble in water, freely soluble in ethanol (95), and practically insoluble in diethyl ether.

The pH of a solution of Phenylephrine Hydrochloride (1 in 100) is between 4.5 and 5.5.

**Identification (1)** To 1 mL of a solution of Phenylephrine Hydrochloride (1 in 100) add 1 drop of copper (II) sulfate TS and 1 mL of a solution of sodium hydroxide (1 in 5): a blue color is produced. To the solution so obtained add 1 mL of diethyl ether, and shake vigorously: no blue color develops in the diethyl ether layer.

(2) To 1 mL of a solution of Phenylephrine Hydrochloride (1 in 100) add 1 drop of iron (III) chloride TS: a persistent purple color is produced.

(3) Dissolve 0.3 g of Phenylephrine Hydrochloride in 3 mL of water, add 1 mL of ammonia TS, and rub the inner side of the test tube with a glass rod: a precipitate is produced. Collect the precipitate, wash with a few drops of ice-cold water, and dry at 105°C for 2 hours: it melts between 170°C and 177°C.

(4) A solution of Phenylephrine Hydrochloride (1 in 100) responds to the Qualitative Tests (2) for chloride.

**Optical rotation** [α]<sub>D</sub><sup>20</sup>: –42.0 – –47.5° (after drying, 0.5 g, water, 10 mL, 100 mm).

**Melting point** 140 – 145°C

**Purity (1)** Clarity and color of solution—Dissolve 1.0 g

of Phenylephrine Hydrochloride in 10 mL of water: the solution is clear and colorless.

(2) Sulfate—Take 0.5 g of Phenylephrine Hydrochloride, and perform the test. Prepare the control solution with 0.50 mL of 0.005 mol/L sulfuric acid VS (not more than 0.048%).

(3) Ketone—Dissolve 0.20 g of Phenylephrine Hydrochloride in 1 mL of water, and add 2 drops of sodium pentacyanonitrosylferrate (III) TS, 1 mL of sodium hydroxide TS and then 0.6 mL of acetic acid (100): the solution has no more color than the following control solution.

Control solution: Prepare as directed above without Phenylephrine Hydrochloride.

**Loss on drying** Not more than 0.5% (1 g, 105°C, 2 hours).

**Residue on ignition** Not more than 0.20% (1 g).

**Assay** Weigh accurately about 0.1 g of Phenylephrine Hydrochloride, previously dried, dissolve in 40 mL of water contained in an iodine flask, add exactly measured 50 mL of 0.05 mol/L bromine VS, then add 5 mL of hydrochloric acid, and immediately stopper tightly. Shake the mixture, and allow to stand for 15 minutes. To this solution add 10 mL of potassium iodide TS carefully, stopper tightly immediately, shake thoroughly, allow to stand for 5 minutes, and titrate with 0.1 mol/L sodium thiosulfate VS (indicator: 1 mL of starch TS). Perform a blank determination.

$$\begin{aligned} \text{Each mL of 0.05 mol/L bromine VS} \\ = 3.3945 \text{ mg of } C_9H_{13}NO_2 \cdot HCl \end{aligned}$$

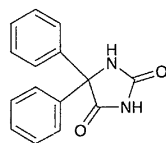
**Containers and storage** Containers—Tight containers.

Storage—Light-resistant.

## Phenytoin

### Diphenylhydantoin

フェニトイン



$C_{15}H_{12}N_2O_2$ : 252.27

5,5-Diphenylimidazolidine-2,4-dione [57-41-0]

Phenytoin, when dried, contains not less than 99.0% of  $C_{15}H_{12}N_2O_2$ .

**Description** Phenytoin occurs as a white, crystalline powder or granules. It is odorless and tasteless.

It is sparingly soluble in ethanol (95) and in acetone, slightly soluble in diethyl ether, and practically insoluble in water.

It dissolves in sodium hydroxide TS.

Melting point: about 296°C (with decomposition).

**Identification** (1) Dissolve 0.02 g of Phenytoin in 2 mL of ammonia TS, and add 5 mL of silver nitrate TS: a white precipitate is produced.

(2) Boil a mixture of 0.01 g of Phenytoin, 1 mL of ammonia TS and 1 mL of water, and add dropwise 2 mL of a mixture prepared from 50 mL of a solution of copper (II) sulfate pentahydrate (1 in 20) and 10 mL of ammonia TS: a red, crystalline precipitate is produced.

(3) Heat 0.1 g of Phenytoin with 0.2 g of sodium hydroxide, and fuse: the gas evolved turns moistened red litmus paper blue.

(4) Add 3 mL of chlorinated lime TS to 0.1 g of phenytoin, shake for 5 minutes, and dissolve the oily precipitate in 15 mL of hot water. After cooling, add 1 mL of dilute hydrochloric acid dropwise, then add 4 mL of water. Filter the white precipitate thus obtained, wash with water, and press it with dry filter paper to remove the accompanying water. Dissolve the precipitate with 1 mL of chloroform, add 5 mL of diluted ethanol (99.5) (9 in 10), and rub the inner surface of the flask to produce a white, crystalline precipitate. Collect the precipitate, wash with ethanol (95), and dry: the melting point is between 165°C and 169°C.

**Purity** (1) Clarity and color of solution—Dissolve 0.20 g of Phenytoin in 10 mL of 0.2 mol/L sodium hydroxide VS: the solution is clear and colorless. Then heat the solution: no turbidity is produced. Cool, and mix the solution with 5 mL of acetone: the solution is clear and colorless.

(2) Acid or alkali—Shake 2.0 g of phenytoin with 40 mL of water for 1 minute, filter, and perform the following tests using this filtrate as the sample solution.

(i) To 10 mL of the sample solution add 2 drops of phenolphthalein TS: no color develops. Then add 0.15 mL of 0.01 mol/L sodium hydroxide VS: a red color develops.

(ii) To 10 mL of the sample solution add 0.30 mL of 0.01 mol/L hydrochloric acid VS and 5 drops of methyl red TS: a red to orange color develops.

(3) Chloride—Dissolve 0.30 g of Phenytoin in 30 mL of acetone, and add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution from 30 mL of acetone, 0.60 mL of 0.01 mol/L hydrochloric acid VS and 6 mL of dilute nitric acid, and add water to 50 mL (not more than 0.071%).

(4) Heavy metals—Proceed with 1.0 g of Phenytoin according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

**Loss on drying** Not more than 0.5% (2 g, 105°C, 2 hours).

**Residue on ignition** Not more than 0.10% (1 g).

**Assay** Weigh accurately about 0.5 g of Phenytoin, previously dried, dissolve in 40 mL of ethanol (95) with the aid of gentle heating, add 0.5 mL of thymolphthalein TS immediately, and titrate with 0.1 mol/L sodium hydroxide VS until a light blue color develops. Then add 1 mL of pyridine, 5 drops of phenolphthalein TS and 25 mL of silver nitrate TS, and titrate with 0.1 mol/L sodium hydroxide VS until a light red color, which persists for 1 minute, develops.

$$\begin{aligned} \text{Each mL of 0.1 mol/L sodium hydroxide VS} \\ = 25.227 \text{ mg of } C_{15}H_{12}N_2O_2 \end{aligned}$$

**Containers and storage** Containers—Well-closed containers.