

acidify with 12 mL of dilute nitric acid, and filter the solution into a Nessler tube. Wash the test tube and the filter with three 5-mL portions of hot water, adding the washings to the filtrate. After cooling, add water to make 50 mL, then add 1 mL of silver nitrate TS, mix well, and allow to stand for 5 minutes: the turbidity of the solution does not exceed that of the following control solution.

Control solution: Prepare in the same manner as described above, using 0.20 mL of 0.01 mol/L hydrochloric acid VS.

(3) Non-volatile residue—Heat 2.0 g of *d*-Camphor on a water bath until sublimation is complete, then dry the residue at 105°C for 3 hours: the mass of the residue does not exceed 1.0 mg.

**Assay** Weigh accurately about 0.1 g each of *d*-Camphor and *d*-Camphor Reference Standard, add exactly 5 mL each of the internal standard solution, dissolve in dehydrated methanol to make 100 mL, and use these solutions as the sample solution and the standard solution. Perform the test with 2  $\mu$ L each of these solutions as directed under the Gas Chromatography according to the following conditions, and calculate the ratios,  $Q_T$  and  $Q_S$ , of the peak area of *d*-camphor to that of the internal standard.

$$\begin{aligned} \text{Amount (mg) of } C_{10}H_{16}O \\ = \text{amount (mg) of } d\text{-Camphor Reference Standard} \\ \times \frac{Q_T}{Q_S} \end{aligned}$$

**Internal standard solution**—A solution of methyl salicylate in ethanol (99.5) (1 in 25).

**Operating conditions**—

Detector: A hydrogen flame-ionization detector.

Column: A glass column 3 mm in inside diameter and 3 m in length, which is packed with 10% of polyethylene glycol 20 M for gas chromatography supported on 180- to 250- $\mu$ m mesh silanized siliceous earth for gas chromatography.

Column temperature: A constant temperature of about 160°C

Carrier gas: Nitrogen

Flow rate: Adjust the flow rate so that the retention time of *d*-camphor is about 6 minutes.

**System suitability**—

System performance: When the procedure is run with 2  $\mu$ L of the standard solution under the above operating conditions, *d*-camphor and the internal standard are eluted in this order with the resolution between these peaks being not less than 7.

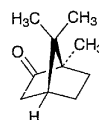
System repeatability: When the test is repeated 6 times with 2  $\mu$ L of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of *d*-camphor to that of the internal standard is not more than 1.0%.

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

## *dl*-Camphor

### Synthetic Camphor

*dl*-カンフル



and enantiomer

$C_{10}H_{16}O$ : 152.23

(1*RS*,4*RS*)-Bornan-2-one [21368-68-3]

*dl*-Camphor contains not less than 96.0% of  $C_{10}H_{16}O$ .

**Description** *dl*-Camphor occurs as colorless or white, translucent crystals, crystalline powder or masses. It has a characteristic, agreeable odor, and has a slightly bitter taste followed by a pleasant, cooling sensation.

It is freely soluble in ethanol (95), in diethyl ether and in carbon disulfide, and slightly soluble in water.

It slowly volatilizes at room temperature.

**Identification** Dissolve 0.1 g of *dl*-Camphor in 2 mL of methanol, add 1 mL of 2,4-dinitrophenylhydrazine TS, and heat for 5 minutes on a water bath: an orange-red precipitate is formed.

**Optical rotation**  $[\alpha]_D^{20}$ :  $-1.5 - +1.5^\circ$  (5 g, ethanol (95), 50 mL, 100 mm).

**Melting point** 175 – 180°C

**Purity** (1) Water—Shake 1.0 g of *dl*-Camphor with 10 mL of carbon disulfide: the solution is clear.

(2) Chlorinated compounds—Mix 0.20 g of finely powdered *dl*-Camphor with 0.4 g of sodium peroxide in a dry, hard glass test tube. Suspend the tube at an angle of 45° by means of a clamp placed at the upper end, and heat the tube gently, starting near the upper end, and gradually bringing the heat toward the lower part of the tube until incineration is complete. Dissolve the residue in 20 mL of warm water, acidify with 12 mL of dilute nitric acid, and filter the solution into a Nessler tube. Wash the test tube and the filter with three 5-mL portions of hot water, adding the washings to the filtrate. After cooling, add water to make 50 mL, then add 1 mL of silver nitrate TS, mix well, and allow to stand for 5 minutes: the turbidity of the solution does not exceed that of the following control solution.

Control solution: Prepare in the same manner as described above, using 0.20 mL of 0.01 mol/L hydrochloric acid VS.

(3) Non-volatile residue—Heat 2.0 g of *dl*-Camphor on a water bath until sublimation is complete, then dry the residue at 105°C for 3 hours: the mass of the residue does not exceed 1.0 mg.

**Assay** Weigh accurately about 0.1 g each of *dl*-Camphor and *dl*-Camphor Reference Standard, add exactly 5 mL each of the internal standard solution, dissolve in dehydrated methanol to make 100 mL, and use these solutions as the sample solution and the standard solution, respectively. Per-

form the test with 2  $\mu\text{L}$  each of these solutions as directed under the Gas Chromatography according to the following conditions, and calculate the ratios,  $Q_T$  and  $Q_S$ , of the peak area of *dl*-camphor to that of the internal standard.

$$\begin{aligned} & \text{Amount (mg) of } \text{C}_{10}\text{H}_{16}\text{O} \\ &= \text{amount (mg) of } \textit{dl}\text{-Camphor Reference Standard} \\ & \quad \times \frac{Q_T}{Q_S} \end{aligned}$$

**Internal standard solution**—A solution of methyl salicylate in ethanol (99.5) (1 in 25).

**Operating conditions**—

Detector: A hydrogen flame-ionization detector.

Column: A glass column 3 mm in inside diameter and 3 m in length, which is packed with 10% of polyethylene glycol 20 M for gas chromatography supported on 180- to 250- $\mu\text{m}$  mesh silanized siliceous earth for gas chromatography.

Column temperature: A constant temperature of about 160°C.

Carrier gas: Nitrogen

Flow rate: Adjust the flow rate so that the retention time of *dl*-camphor is about 6 minutes.

**System suitability**—

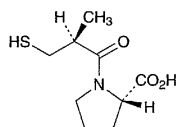
**System performance:** When the procedure is run with 2  $\mu\text{L}$  of the standard solution under the above operating conditions, *dl*-camphor and the internal standard are eluted in this order with the resolution between these peaks being not less than 7.

**System repeatability:** When the test is repeated 6 times with 2  $\mu\text{L}$  of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of *dl*-camphor to that of the internal standard is not more than 1.0%.

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

## Captopril

カプトプリル



$\text{C}_9\text{H}_{15}\text{NO}_3\text{S}$ : 217.29

(2*S*)-1-[(2*S*)-2-Methyl-3-sulfanylpropanoyl]pyrrolidine-2-carboxylic acid [62571-86-2]

Captopril contains not less than 98.0% of  $\text{C}_9\text{H}_{15}\text{NO}_3\text{S}$ , calculated on the dried basis.

**Description** Captopril occurs as white crystals or crystalline powder.

It is very soluble in methanol, freely soluble in ethanol (99.5), and soluble in water.

**Identification** Determine the infrared absorption spectrum of Captopril as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spec-

tra exhibit similar intensities of absorption at the same wave numbers.

**Optical rotation**  $[\alpha]_D^{25}$ :  $-125$  –  $-134^\circ$  (after drying, 0.1 g, ethanol (99.5), 10 mL, 100 mm).

**Melting point** 105 – 110°C

**Purity (1)** Heavy metals—Proceed with 1.0 g of Captopril 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).

(2) Arsenic—Prepare the test solution with 1.0 g of Captopril according to Method 1, and perform the test using Apparatus B (not more than 2 ppm).

(3) Related substances—Dissolve 0.20 g of Captopril in methanol to make exactly 10 mL, and use this solution as the sample solution. Separately, dissolve 0.015 g of 1,1'-[3,3'-dithiobis(2-methyl-1-oxopropyl)]-L-dipropine in methanol to make exactly 250 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10  $\mu\text{L}$  each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop with a mixture of toluene and acetic acid (100) (13:7) to a distance of about 15 cm, and air-dry the plate. Place the plate in a chamber filled with iodine vapor, and allow to stand for 30 minutes: the number of the spots other than the spot corresponding to that from the standard solution and the principal spot from the sample solution is not more than two, and they are not more intense than the spot from the standard solution.

(4) 1,1'-[3,3'-Dithiobis(2-methyl-1-oxopropyl)]-L-dipropine—Dissolve 0.10 g of Captopril in methanol to make exactly 20 mL, and use this solution as the sample solution. Separately, dissolve 0.025 g of 1,1'-[3,3'-dithiobis(2-methyl-1-oxopropyl)]-L-dipropine in methanol to make exactly 250 mL, and use this solution as the standard solution. Perform the test with 20  $\mu\text{L}$  each of these solutions as directed under the Liquid Chromatography according to the following conditions, and calculate the peak area,  $A_T$  and  $A_S$ , of 1,1'-[3,3'-dithiobis(2-methyl-1-oxopropyl)]-L-dipropine of these solutions:  $A_T$  is not larger than  $A_S$ .

**Operating conditions**—

Detector: An ultraviolet absorption photometer (wavelength: 220 nm).

Column: A stainless steel column 3.9 mm in inside diameter and 30 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10  $\mu\text{m}$  in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: A mixture of water, methanol and phosphoric acid (1000:1000:1).

Flow rate: Adjust the flow rate so that the retention time of 1,1'-[3,3'-dithiobis(2-methyl-1-oxopropyl)]-L-dipropine is about 10 minutes.

**System suitability**—

**System performance:** Dissolve 0.025 g each of Captopril and 1,1'-[3,3'-dithiobis(2-methyl-1-oxopropyl)]-L-dipropine in 200 mL of methanol. When the procedure is run with 20  $\mu\text{L}$  of this solution under the above operating conditions, captopril and 1,1'-[3,3'-dithiobis(2-methyl-1-oxopropyl)]-L-dipropine are eluted in this order with the resolution between these peaks being not less than 3.