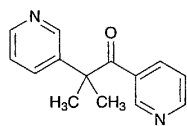


## Metyrapone

メチラポン



$C_{14}H_{14}N_2O$ : 226.27

2-Methyl-1,2-di(pyridin-3-yl)propan-1-one [54-36-4]

Metyrapone, when dried, contains not less than 98.0% of  $C_{14}H_{14}N_2O$ .

**Description** Metyrapone occurs as a white to pale yellow, crystalline powder. It has a characteristic odor and a bitter taste.

It is very soluble in methanol, in ethanol (95), in acetic anhydride, in chloroform, in diethyl ether and in nitrobenzene, and sparingly soluble in water.

It dissolves in 0.5 mol/L sulfuric acid TS.

**Identification (1)** Mix 5 mg of Metyrapone with 0.01 g of 1-chloro-2,4-dinitrobenzene, melt by gently heating for 5 to 6 seconds, cool, and add 4 mL of potassium hydroxide-ethanol TS: a dark red color develops.

(2) Determine the absorption spectrum of a solution of Metyrapone in 0.5 mol/L sulfuric acid TS (1 in 100,000) 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** 50 – 54°C

**Purity (1)** Clarity and color of solution—Dissolve 0.5 g of Metyrapone in 5 mL of methanol: the solution is clear and colorless to pale yellow.

(2) Heavy metals—Proceed with 2.0 g of Metyrapone 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 Metyrapone, according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.25 g of Metyrapone in 5 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add methanol to make exactly 50 mL. Pipet 5 mL of this solution, add methanol to make exactly 50 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 2  $\mu$ L each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of chloroform and methanol (15:1) to a distance of about 10 cm, and air-dry the plate for about 15 minutes. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution is not more intense than the spot from the standard solution.

**Loss on drying** Not more than 0.5% (1 g, in vacuum, silica gel, 24 hours).

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

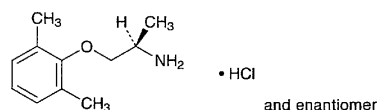
**Assay** Weigh accurately about 0.2 g of Metyrapone, previously dried, dissolve in 10 mL of nitrobenzene and 40 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS  
= 11.314 mg of  $C_{14}H_{14}N_2O$

**Containers and storage** Containers—Tight containers.  
Storage—Light-resistant.

## Mexiletine Hydrochloride

塩酸メキシレチン



$C_{11}H_{17}NO \cdot HCl$ : 215.72

(*RS*)-2-(2,6-Dimethylphenoxy)-1-methylethylamine monohydrochloride [5370-01-4]

Mexiletine Hydrochloride, when dried, contains not less than 98.0% and not more than 102.0% of  $C_{11}H_{17}NO \cdot HCl$ .

**Description** Mexiletine Hydrochloride occurs as a white powder.

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

A solution of Mexiletine Hydrochloride (1 in 20) shows no optical rotation.

**Identification (1)** Determine the absorption spectrum of a solution of Mexiletine Hydrochloride in 0.01 mol/L hydrochloric acid TS (1 in 2000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Mexiletine Hydrochloride Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Mexiletine Hydrochloride, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of dried Mexiletine Hydrochloride Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers. If any difference appears between the spectra, recrystallize the sample from ethanol (95), filter, dry the crystals, and repeat the test on the crystals.

(3) A solution of Mexiletine Hydrochloride (1 in 100) responds to the Qualitative tests (2) for chloride.

**pH** Dissolve 1.0 g of Mexiletine Hydrochloride in 10 mL of water: the pH of this solution is between 3.8 and 5.8.

**Melting point** 200 – 204°C

**Purity (1)** Clarity and color of solution—Dissolve 1.0 g of Mexiletine Hydrochloride in 10 mL of water: the solution is clear and colorless.

(2) Heavy Metals—Proceed with 2.0 g of Mexiletine Hydrochloride according to Method 1, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(3) Related substances—Dissolve 0.020 g of Mexiletine Hydrochloride in 20 mL of the mobile phase, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase to make exactly 250 mL, and use this solution as the standard solution. Perform the test with 20  $\mu$ L each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area of both solutions by the automatic integration method: each peak area of the peaks other than the peak of mexiletine from the sample solution is not larger than the peak area of mexiletine from the standard solution.

**Operating conditions—**

Detector, column, column temperature, mobile phase, flow rate, and selection of column: Proceed as directed in the operating conditions in the Assay.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of mexiletine obtained from 20  $\mu$ L of the standard solution is between 5 mm and 10 mm.

Time span of measurement: About 3 times as long as the retention time of mexiletine after peaks of the solvent.

**Loss on drying** Not more than 0.5% (1 g, 105°C, 3 hours).

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

**Assay** Weigh accurately about 0.02 g each of Mexiletine Hydrochloride and Mexiletine Hydrochloride Reference Standard, each previously dried, and dissolve each in the mobile phase to make exactly 20 mL. Pipet 5 mL each of these solutions, add exactly 5 mL of the internal standard solution, then add the mobile phase to make 100 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 20  $\mu$ L each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios,  $Q_T$  and  $Q_S$ , of the peak area of mexiletine to that of the internal standard, respectively.

$$\begin{aligned} & \text{Amount (mg) of } C_{11}H_{17}NO \cdot HCl \\ &= \text{amount (mg) of Mexiletine Hydrochloride} \\ & \quad \text{Reference Standard} \\ & \quad \times \frac{Q_T}{Q_S} \end{aligned}$$

**Internal standard solution—**A solution of phenethylamine hydrochloride in the mobile phase (3 in 5000).

**Operating conditions—**

Detector: An ultraviolet absorption photometer (wavelength: 210 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 15 cm in length, packed with octylsilylanized silica gel for liquid chromatography (about 7  $\mu$ m in particle diameter).

Column temperature: A constant temperature of about 30°C.

Mobile phase: Dissolve 2.5 g of sodium lauryl sulfate and 3 g of sodium dihydrogenphosphate dihydrate in 600 mL of water, and add 420 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of mexiletine is about 6 minutes.

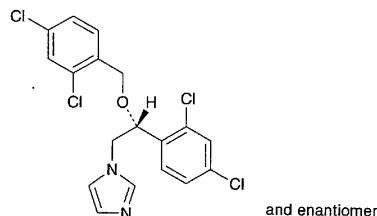
Selection of column: Proceed with 20  $\mu$ L of the standard solution under the above conditions, and calculate the resolution. Use a column giving elution of the internal standard and mexiletine in this order with the resolution between these peaks being not less than 9.

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

Storage—Light-resistant.

## Miconazole

ミコナゾール



$C_{18}H_{14}Cl_4N_2O$ : 416.13

1-[(*RS*)-2-(2,4-Dichlorobenzoyloxy)-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole [22916-47-8]

Miconazole, when dried, contains not less than 98.5% of  $C_{18}H_{14}Cl_4N_2O$ .

**Description** Miconazole occurs as a white to pale yellowish white, crystalline powder.

It is freely soluble in methanol, in ethanol (95) and in acetic acid (100), soluble in diethyl ether, and practically insoluble in water.

A solution of Miconazole in methanol (1 in 20) shows no optical rotation.

**Identification (1)** Determine the absorption spectrum of a solution of Miconazole in methanol (1 in 2500) 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.

(2) Determine the infrared absorption spectrum of Miconazole, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

**Melting point** 84 – 87°C

**Purity (1)** Heavy metals—Proceed with 1.0 g of Miconazole according to Method 2, and perform the test. Prepare the control solution with 1.0 mL of Standard Lead Solution (not more than 10 ppm).