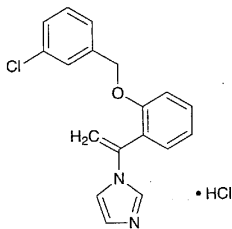


Croconazole Hydrochloride

塩酸クロコナゾール



$C_{18}H_{15}ClN_2O \cdot HCl$: 347.24
1-{1-[2-(3-Chlorobenzyloxy)phenyl]vinyl}-1*H*-imidazole
monohydrochloride [77174-66-4]

Croconazole Hydrochloride, when dried, contains not less than 98.5% of $C_{18}H_{15}ClN_2O \cdot HCl$.

Description Croconazole Hydrochloride occurs as white to pale yellowish white crystals or crystalline powder.

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

Identification (1) Determine the absorption spectrum of a solution of Croconazole Hydrochloride in methanol (1 in 20,000) 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.

(2) Determine the infrared absorption spectrum of Croconazole Hydrochloride, previously dried, as directed in the potassium chloride 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.

(3) Dissolve 0.05 g of Croconazole Hydrochloride in 10 mL of water, add 2 mL of sodium hydroxide TS and 20 mL of diethyl ether, and shake. Wash the separated aqueous layer with two 10-mL portions of diethyl ether, and acidify the solution with 2 mL of dilute nitric acid: the solution responds to the Qualitative Tests for chloride.

Melting point 148 – 153°C

Purity (1) Heavy metals—Proceed with 1.0 g of Croconazole Hydrochloride according to Method 4, and perform the test. Prepare the control solution with 1.0 mL of Standard Lead Solution (not more than 10 ppm).

(2) Related substances—Dissolve 0.050 g of Croconazole Hydrochloride in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add methanol to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μ 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 ethyl acetate, hexane, methanol and ammonia solution (28) (30:15:5:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot

and other than the spot of the starting point from the sample solution are not more intense than the spot from the standard solution.

Loss on drying Not more than 0.5% (1 g, 60°C, 4 hours).

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

Assay Weigh accurately about 0.6 g of Croconazole Hydrochloride, previously dried, dissolve in 10 mL of acetic acid (100), add 40 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS [indicator: 1 to 2 drops of a solution of malachite green oxalate in acetic acid (100) (1 in 100)] until the color of the solution changes from blue-green through green to yellow-green. Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 34.724 mg of $C_{18}H_{15}ClN_2O \cdot HCl$

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Cyanamide

シアナミド

H_2N-CN

CH_2N_2 : 42.04
Aminonitrile [420-04-2]

Cyanamide contains not less than 97.0% of CH_2N_2 , calculated on the anhydrous basis.

Description Cyanamide occurs as white crystals or crystalline powder. It has a faint, characteristic odor.

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

The pH of a solution of Cyanamide (1 in 100) is between 5.0 and 6.5.

It is hygroscopic.

Melting point: about 46°C

Identification (1) To 5 mL of a solution of Cyanamide (1 in 100) add 2 mL of a solution of sodium pentacyanoamine ferroate (II) *n*-hydrate (1 in 100): a red-purple color develops.

(2) To 1 mL of a solution of Cyanamide (1 in 100) add 1 mL of potassium 1,2-naphthoquinone-4-sulfonate TS and 0.2 mL of sodium hydroxide TS: a deep red color develops.

(3) To 5 mL of a solution of Cyanamide (1 in 100) add 1 mL of ammonia TS and 1 mL of silver nitrate TS: a yellow precipitate is formed.

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

(2) Sulfate—Perform the test with 0.5 g of Cyanamide. Prepare the control solution with 0.40 mL of 0.005 mol/L sulfuric acid VS (not more than 0.038%).

(3) Heavy metals—Proceed with 2.0 g of Cyanamide 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).

(4) Calcium—Dissolve 0.2 g of Cyanamide in 20 mL of water, add 2 mL of ammonia TS and 2 mL of ammonium oxalate TS, and allow to stand for 5 minutes: no turbidity is produced.

(5) Diethyl ether-insoluble substances—Dissolve 1.0 g of Cyanamide in 3.0 mL of diethyl ether by shaking, allow to stand for 10 minutes, and shake again: the solution is clear.

Water Not more than 1.0% (1 g, direct titration).

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

Assay Weigh accurately about 1 g of Cyanamide, and dissolve in water to make exactly 250 mL. Pipet 15 mL of this solution, add 2 to 3 drops of dilute nitric acid, 10 mL of ammonia TS and exactly 50 mL of 0.1 mol/L silver nitrate VS, and allow to stand for 15 minutes with occasional shaking. Add water to make exactly 100 mL, filter, discard the first 20 mL of the filtrate, and pipet the subsequent 50 mL. After neutralizing this solution with dilute nitric acid, add 3 mL of dilute nitric acid, and titrate the excess silver nitrate with 0.1 mol/L ammonium thiocyanate VS (indicator: 2 mL of ammonium iron (III) sulfate TS). Perform a blank determination.

$$\begin{aligned} \text{Each mL of 0.1 mol/L silver nitrate VS} \\ = 2.1020 \text{ mg of } \text{CH}_2\text{N}_2 \end{aligned}$$

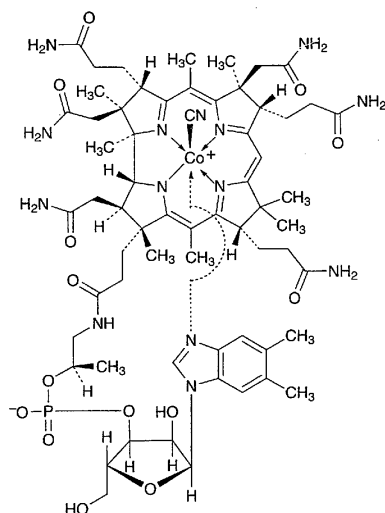
Containers and storage Containers—Tight containers.

Storage—In a cold place.

Cyanocobalamin

Vitamin B₁₂

シアノコバラミン



$\text{C}_{63}\text{H}_{88}\text{CoN}_{14}\text{O}_{14}\text{P}$: 1355.37

*Co*α-[α-(5,6-Dimethylbenz-1*H*-imidazol-1-yl)]-*Co*β-cyanocobamide [68-19-9]

Cyanocobalamin contains not less than 95.0% of $\text{C}_{63}\text{H}_{88}\text{CoN}_{14}\text{O}_{14}\text{P}$, calculated on the dried basis.

Description Cyanocobalamin occurs as dark red crystals or powder.

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

It is hygroscopic.

Identification (1) Determine the absorption spectrum of the sample solution obtained in the Assay as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Cyanocobalamin Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Mix 1 mg of Cyanocobalamin with 0.05 g of potassium hydrogen sulfate, and fuse by igniting. Cool, break up the mass with a glass rod, add 3 mL of water, and dissolve by boiling. Add 1 drop of phenolphthalein TS, then add dropwise sodium hydroxide TS until a light red color just develops. Add 0.5 g of sodium acetate trihydrate, 0.5 mL of dilute acetic acid and 0.5 mL of a solution of disodium 1-nitroso-2-naphthol-3,6-disulfonate (1 in 500): a red to orange-red color is immediately produced. Then add 0.5 mL of hydrochloric acid, and boil for 1 minute: the red color does not disappear.

(3) Transfer 5 mg of Cyanocobalamin to a 50-mL distilling flask, dissolve in 5 mL of water, and add 2.5 mL of hypophosphorous acid. Connect the flask with a short condenser, and dips its tip into a test tube containing 1 mL of a solution of sodium hydroxide (1 in 50). Heat gently for 10 minutes, then distil 1 mL into a test tube. To the test tube add 4 drops of a saturated solution of ammonium iron (II) sulfate hexahydrate, shake gently, then add about 0.03 g of sodium fluoride, and heat the contents to boil. Immediately add dropwise diluted sulfuric acid (1 in 7) until a clear solution results, then add 3 to 5 drops more of diluted sulfuric acid (1 in 7): a blue to blue-green color develops.

pH Dissolve 0.10 g of Cyanocobalamin in 20 mL of water: the pH of this solution is between 4.2 and 7.0.

Purity (1) Clarity and color of solution—Dissolve 0.020 g of Cyanocobalamin in 10 mL of water: the solution is clear and red in color.

(2) Pseudocyanocobalamin—Dissolve 1.0 mg of Cyanocobalamin in 20 mL of water, transfer the solution to a separator, add 5 mL of a mixture of *m*-cresol and carbon tetrachloride (1:1), and shake vigorously for 1 minute. Allow to separate, draw off the lower layer into another separator, add 5 mL of diluted sulfuric acid (1 in 7), shake vigorously, and allow to separate completely. If necessary, centrifuge the mixture: the supernatant liquid is colorless or has no more color than the following control solution.

Control solution: Dilute 0.6 mL of 0.02 mol/L potassium permanganate VS with water to make 1000 mL.

Loss on drying Not more than 12% (0.05 g, in vacuum at a pressure not exceeding 0.67 kPa, phosphorus (V) oxide, 100°C, 4 hours).

Assay Weigh accurately about 0.02 g each of Cyanocobalamin and Cyanocobalamin Reference Standard (previously determine the loss on drying in the same manner as Cyanocobalamin), dissolve in water to make exactly 1000 mL, respectively, and use these solutions as the sample solution and the standard solution. Determine the absorbances,