ple solution. To exactly 5 mL of the sample solution add a solution of hydrochloric acid in methanol (1 in 20,000) to make exactly 200 mL, and use this solution as the standard solution (1). Separately, pipet 1 mL of the sample solution, add a solution of hydrochloric acid in methanol (1 in 20,000) to make exactly 50 mL, and use this solution as the standard solution (2). Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL each of the sample solution and the standard solution (1) on a plate of silica gel for thin-layer chromatography (Plate 1), and spot 10 μL each of the sample solution and the standard solution (2) on another plate of silica gel for thin-layer chromatography (Plate 2). Develop the plates with an upper layer of a mixture of water, 1-butanol and acetic acid (100) (5:4:1) to a distance of about 15 cm, and air-dry the plates. Spray evenly a solution of ninhydrin in acetone (1 in 50) on Plate 1, and heat at 100°C for 20 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution (1). Allow Plate 2 to stand in an iodine vapor for 30 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution (2).

(4) Formaldehyde—Dissolve 0.80 g of Ticlopidine Hydrochloride in 19.0 mL of water, add 1.0 mL of 4 mol/L sodium hydroxide TS, shake well, centrifuge, and filter the supernatant liquid. To 5.0 mL of the filtrate add 5.0 mL of acetylacetone TS, mix, and warm at 40°C for 40 minutes: the solution has no more color than the following control solution.

Control solution: Weigh accurately 0.54 g of formaldehyde solution, and add water to make exactly 1000 mL. To exactly 10 mL of this solution add water to make exactly 1000 mL. Prepare before use. To 8.0 mL of this solution add water to make 20.0 mL, and filter. To 5.0 mL of the filtrate add 5.0 mL of acetylacetone TS, and proceed in the same manner.

Water Not more than 1.0% (0.3 g, direct titration).

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

Assay Weigh accurately about 0.4 g of Ticlopidine Hydrochloride, dissolve in 20 mL of acetic acid (100), add 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
= 30.025 mg of $C_{14}H_{14}ClNS.HCl$

Containers and storage Containers—Well-closed containers.

Timepidium Bromide

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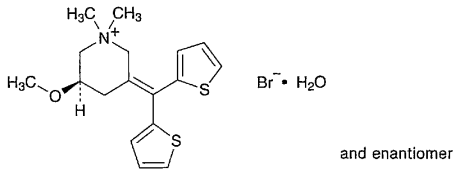

and enantiomer

$C_{17}H_{22}BrNOS_2.H_2O$: 418.41
(*RS*)-3-(Dithien-2-ylmethylene)-5-methoxy-1,1-dimethylpiperidinium bromide monohydrate
[*35035-05-3*, anhydride]

Timepidium Bromide contains not less than 98.5% of $C_{17}H_{22}BrNOS_2$ (mol. wt.: 400.40), calculated on the anhydrous basis.

Description Timepidium Bromide occurs as white crystals or crystalline powder.

It is very soluble in methanol and in acetic acid (100), freely soluble in ethanol (99.5), sparingly soluble in water and in acetic anhydride, and practically insoluble in diethyl ether.

The pH of a solution of Timepidium Bromide in freshly boiled and cooled water (1 in 100) is between 5.3 and 6.3.

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

Identification (1) To 1 mL of a solution of Timepidium Bromide (1 in 100) add 1 mL of ninhydrin-sulfuric acid TS: a red purple color develops.

(2) Determine the absorption spectrum of a solution of Timepidium Bromide (1 in 50,000) 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.

(3) Determine the infrared absorption spectrum of Timepidium Bromide as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhitit similar intensities of absorption at the same wave numbers.

(4) A solution of Timepidium Bromide (1 in 100) responds to the Qualitative Tests (1) for Bromide.

Purity (1) Clarity and color of solution—Dissolve 0.10 g of Timepidium Bromide in 10 mL of water: the solution is clear and colorless.

(2) Heavy metals—Proceed with 1.0 g of Timepidium Bromide 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).

(3) Related substances—Dissolve 0.10 g of Timepidium Bromide in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add methanol to make exactly 100 mL. Pipet 1 mL of this solution, add methanol to make exactly 10 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL 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, methanol, water, acetic acid (100) and ethyl acetate (5:4:1:1:1) to a distance of about 13 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Water 3.5 - 5.0% (0.4 g, direct titration).

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

Assay Weigh accurately about 0.6 g of Timepidium Bromide, dissolve in 60 mL of a mixture of acetic anhydride and acetic acid (100) (2:1), 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
= 40.04 mg of $C_{17}H_{22}BrNOS_2$

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

Tinidazole

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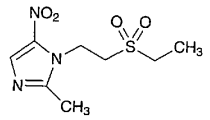


$C_8H_{13}N_3O_4S$: 247.27
Ethyl 2-(2-methyl-5-nitro-1*H*-imidazol-1-yl)ethyl sulfone
[*19387-91-8*]

Tinidazole, when dried, contains not less than 98.5% of $C_8H_{13}N_3O_4S$.

Description Tinidazole occurs as a light yellow, crystalline powder. It is odorless or has a slight, characteristic odor. It has a bitter taste.

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

Identification **(1)** Dissolve 0.01 g of Tinidazole in 2 mL of methanol, and add 1 mL of a solution of *N,N*-dimethylaniline in methanol (1 in 10): a yellow-green color develops.

(2) Determine the absorption spectrum of a solution of Tinidazole in methanol (1 in 50,000) 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.

(3) Determine the infrared absorption spectrum of Tinidazole as directed in the paste 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 125 - 129°C

Purity **(1)** Sulfate—To 2.0 g of Tinidazole add 100 mL of water, boil for 5 minutes, cool, add water to make 100 mL, and filter. Take 25 mL of the filtrate, and add 1 mL of dilute hydrochloric acid and water to make 50 mL. Use this solution as the test solution, and perform the test. Prepare the control solution with 0.45 mL of 0.005 mol/L sulfuric acid VS (not more than 0.043%).

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

(3) Arsenic—Prepare the test solution with 2.0 g of Tinidazole according to Method 3, and perform the test using Apparatus B (not more than 1 ppm).

(4) Related substances—Dissolve 0.050 g of Tinidazole in 2 mL of acetone, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add acetone to make exactly 200 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL 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 and diethylamine (19:1) to a distance of about 10 cm, air-dry the plate, heat at 100°C for 5 minute, and cool. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Loss on drying Not more than 1.0% (1 g, 105°C, 2 hours).

Residue on ignition Not more than 0.1% (1 g).

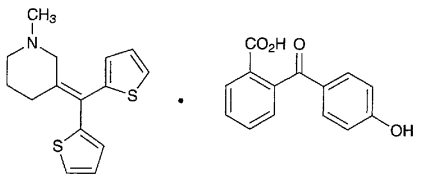
Assay Weigh accurately about 0.35 g of Tinidazole, previously dried, dissolve in 50 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 24.728 mg of $C_8H_{13}N_3O_4S$

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

Tipepidine Hibenzate

ヒベンズ酸チペピジン



$C_{15}H_{17}NS_2.C_{14}H_{10}O_4$: 517.66
3-(Dithien-2-ylmethylene)-1-methylpiperidine mono[2-(4-hydroxybenzoyl)benzoate] [*31139-87-4*]

Tipepidine Hibenzate, when dried, contains not less than 98.5% of $C_{15}H_{17}NS_2.C_{14}H_{10}O_4$.