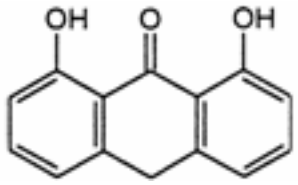
Dithranol (Dithranolum)



$C_{14}H_{10}O_3$

Relative molecular mass. 226.2

Chemical name. 1,8,9-Anthratriol; CAS Reg. No. 1143-38-0.

Other name. Anthralin.

Description. A yellow or brownish yellow, crystalline powder.

Solubility. Practically insoluble in water; soluble in dichloromethane R; sparingly soluble in acetone R; slightly soluble in ethanol (~750 g/l) TS and ether R.

Category. Keratolytic agent.

Storage. Dithranol should be kept in a tightly closed container, protected from light.

Requirements

Dithranol contains not less than **98.5%** and not more than **101.0%** of $C_{14}H_{10}O_3$, calculated with reference to the dried substance.

Identity tests

• Either tests A and D or tests B, C, and D may be applied.

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from dithranol RS or with the *reference spectrum* of dithranol.

B. The absorption spectrum of a 10µg/mL solution in dichloromethane R, when observed between 250nm and 450nm, exhibits 3 maxima at about 256nm, 288nm, and 356 nm. The absorbance of a 1-cm layer at the maximum wavelength at 356 nm is about 0.46 and at 288 nm about 0.49.

C. Carry out the test as described under 1.14.1 Thin-layer chromatography, using silica gel R3 as the coating substance and a mixture of equal volumes of hexane R and dichloromethane R as the mobile phase. Apply separately to the plate 10µl of each of 3 solutions in dichloromethane R containing (A) 1.0 mg of Dithranol per mL, (B) 1.0 mg of dithranol RS, and for solution (C) dissolve 5 mg of dantron R in 5 mL of solution B. After removing the plate from the chromatographic chamber, allow it to dry in air. Place the plate in a chamber saturated with ammonia vapour until the spots appear. Examine the chromatogram in daylight.

The principal spot obtained with solution A corresponds in position, appearance, and intensity with that obtained with solution B. The test is not valid unless the chromatogram obtained with solution C shows two clearly separated spots.

D. Melting temperature, about 180 °C.

Chlorides. Dissolve 2.5 g in a mixture of 2.0 mL of nitric acid (~130 g/l) TS and 30 mL of water, and proceed as described under 2.2.1 Limit test for chlorides; the chloride content is not more than 0.1 mg/g.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry to constant mass at 105 °C; it loses not more than 5mg/g.

pH value. Shake 1.5 g with 30 mL of carbon-dioxide-free water R for 1 minute and filter; pH of the filtrate, 6.0-7.6.

Related substances

A. Carry out the test as described under 1.14.4 High-performance liquid chromatography, using a stainless steel column (25cm × 4.6mm) packed with particles of porous silica (5µm). As the mobile phase, use a mixture of 82 volumes of hexane R, 5 volumes of dichloromethane R, and 1 volume of glacial acetic acid R.

Prepare the following solutions. For solution (A) dissolve 0.20g of Dithranol in 20ml of dichloromethane R, add 1.0ml of glacial acetic acid R, and dilute to 100 mL with hexane R. For solution (B) dissolve 10.0 mg of each of

anthrone R, dantron R, 9,9'-bisanthracene-10,10'(9*H*,9'*H*)- dione RS, and dithranol RS in dichloromethane R, and dilute to 10.0ml with the same solvent. To 1.0ml of this solution add 19ml of dichloromethane R and 1.0 mL of glacial acetic acid R, and dilute to 50ml with hexane R.

Operate with a flow rate of 2.0 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of 260nm.

Inject 20µl each of solutions A and B. Continue the chromatography for 1.5 times the retention time of the peak due to 9,9'-bisanthracene-10,10'(9*H*,9'*H*)-dione obtained with solution B. Adjust the sensitivity of the system so that the height of the peak due to dithranol in the chromatogram obtained with solution B is about 70% of the full scale of the recorder. The peaks are eluted in the following order: dithranol, dantron, anthrone and 9,9'-bisanthracene-10,10'(9*H*,9'*H*)-dione. The test is not valid unless, in the chromatogram obtained with solution B, the resolution between the peaks due to dithranol and dantron is greater than 2.0.

Measure the areas of the peak responses obtained in the chromatograms from solutions A and B, and calculate the content of the related substances as a percentage. In the chromatogram obtained with solution A, the area of any peak corresponding to anthrone, dantron or 9,9'-bisanthracene-10,10'(9*H*,9'*H*)-dione is not greater than that of the corresponding peak in the chromatogram obtained with solution B (1.0%). The area of any peak, other than the principal peak and any peaks due to anthrone, dantron or 9,9'-bisanthracene-10,10'(9*H*,9'*H*)-dione, is not greater than that of the peak due to dithranol in the chromatogram obtained with solution B (1.0%).

B. Carry out the test as described under 1.14.4 High-performance liquid chromatography, using a stainless steel column (20cm × 4.6mm) packed with particles of silica gel, the surface of which has been modified with chemically bonded octadecylsilyl groups (5µm). As the mobile phase, use a mixture of 60 volumes of water, 40 volumes of tetrahydrofuran R, and 2.5 volumes of glacial acetic acid R.

Prepare the following solutions in the mobile phase: solution (A) 1.0mg of Dithranol per mL; and for solution (B) dissolve 0.5mg of 1-hydroxy-9- anthrone RS and 0.5 mg of dithranol RS per mL, and dilute 1.0 mL of this solution to 20 mL with the mobile phase.

Operate with a flow rate of about 0.9 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of 254nm.

Inject 20µl each of solutions A and B. Continue the chromatography for 3 times the retention time of the peak due to dithranol. The test is not valid unless, in the chromatogram obtained with solution B, the resolution between the peaks due to 1-hydroxy-9-anthrone and dithranol is greater than 2.5.

Measure the areas of the peak responses obtained in the chromatograms from solutions A and B, and calculate the content of the related substances as a percentage. In the chromatogram obtained with solution A, the area of any peak corresponding to 1-hydroxy-9-anthrone is not greater than that of the corresponding peak in the chromatogram obtained with solution B (2.5%).

The total content of related substances as determined in tests A and B is not more than 3.0%.

Assay. Dissolve about 0.2 g, accurately weighed, in 50 mL of anhydrous pyridine R and titrate under an atmosphere of nitrogen with tetrabutylammonium hydroxide (0.1 mol/l) VS as described under 2.6 Non-aqueous titration, Method B, determining the end-point potentiometrically.

Each mL of tetrabutylammonium hydroxide (0.1 mol/l) VS is equivalent to 22.62mg of $C_{14}H_{10}O_3$.