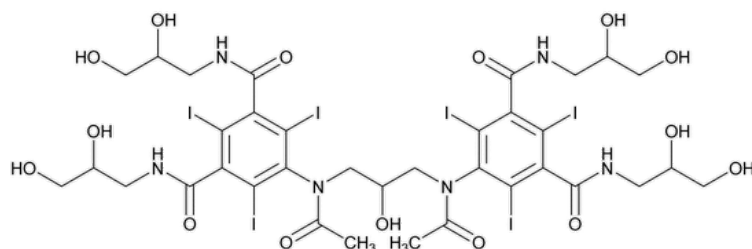


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Iodixanol



$C_{35}H_{44}I_6N_6O_{15}$ 1550.18

1,3-Benzenedicarboxamide, 5,5'-[(2-hydroxy-1,3-propanediyl)bis(acetylimino)]bis[*N,N'*-bis(2,3-dihydroxypropyl)-2,4,6-triiodo-;

5,5'-[(2-Hydroxytrimethylene)bis(acetylimino)]bis[*N,N'*-bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophthalamide] CAS RN®: 92339-11-2; UNII: HW8W27HTXX.

DEFINITION

Iodixanol contains NLT 98.6% and NMT 101.0% of iodixanol ($C_{35}H_{44}I_6N_6O_{15}$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 197K**
- **B.** The retention times of the three principal peaks of the *Sample solution* correspond to those of the *Identification solution*, as obtained in the test for *Limit of Iodixanol Related Compound E and Iodixanol Impurity H*. [NOTE—A third isomer may appear as a minor peak.]

ASSAY

PROCEDURE

Sample solution: Transfer 500 mg of Iodixanol to a glass-stoppered, 125-mL conical flask. Add 25 mL of 1.25 N sodium hydroxide and 500 mg of powdered zinc. Connect the flask to a reflux condenser, and reflux for 1 h. Cool the flask to room temperature, rinse the condenser with 20 mL of water, disconnect the flask from the condenser, and pass the mixture through a filter. Rinse the flask and the filter thoroughly with small portions of water, adding the rinsings to the filtrate. Add 5 mL of glacial acetic acid.

Titrimetric system

(See [Titrimetry \(541\)](#).)

Mode: Direct titration

Titrant: 0.1 N silver nitrate VS

Endpoint detection: Potentiometric

Analysis

Sample: *Sample solution*

Titrate the *Sample solution* with the *Titrant*.

Calculate the percentage of iodixanol ($C_{35}H_{44}I_6N_6O_{15}$) in the portion of Iodixanol taken:

$$\text{Result} = [(V \times N \times F)/W] \times 100$$

V = sample titrant volume (mL)

N = *Titrant* normality (meq/mL)

F = equivalent weight of iodixanol, 258.4 mg/meq

W = weight of iodixanol (mg)

Acceptance criteria: 98.6%–101.0% on the anhydrous basis

IMPURITIES• **LIMIT OF FREE IODIDE**

Sample solution: 5 g of Iodixanol in 30 mL of water

Titrimetric system

(See [Titrimetry \(541\)](#).)

Mode: Direct titration

Titrant: 0.001 N silver nitrate VS

Endpoint detection: Potentiometric

Analysis

Calculate the percentage of free iodide in the portion of Iodixanol taken:

$$\text{Result} = [(V \times N \times F)/W] \times 100$$

V = sample titrant volume (mL)

N = Titrant normality (meq/mL)

F = equivalent weight of iodide, 0.1269 mg/meq

W = weight of Iodixanol (mg)

Acceptance criteria: NMT 0.001%

• **LIMIT OF IONIC COMPOUNDS**

[NOTE—Rinse all glassware with water.]

Standard solution: 4 µg/mL of sodium chloride in water

Sample solution: 2 g of Iodixanol in 100 mL of water

Acceptance criteria: The specific conductance in the *Sample solution* is NMT that of the *Standard solution* (equivalent to NMT 0.02% of ionic compounds, as sodium chloride).

• **LIMIT OF FREE AROMATIC AMINE**

Solution A: 3 mg/mL of *N*-(1-naphthyl)ethylenediamine dihydrochloride in a mixture of propylene glycol and water (70:30)

Blank solution: Add 15 mL of water to a 25-mL volumetric flask.

Standard stock solution: 10 µg/mL of [USP Iohexol Related Compound B RS](#) in water

Standard solution: Transfer 10.0 mL of the *Standard stock solution* and 5 mL of water to a 25-mL volumetric flask.

Sample solution: Transfer 200 mg of Iodixanol to a 25-mL volumetric flask, and add 15 mL of water.

Instrumental conditions

Mode: UV-Vis

Analytical wavelength: 495 nm

Cell: 5 cm

Analysis

Samples: *Blank solution*, *Standard solution*, and *Sample solution*

Treat the *Samples* as follows. Place the flask in an ice bath for 5 min. Add 1.5 mL of 6 N hydrochloric acid, and mix by swirling. Add 1.0 mL of sodium nitrite solution (20 mg/mL), and allow to stand in the ice bath for 4 min. Remove the flask from the ice bath, add 1.0 mL of sulfamic acid solution (40 mg/mL), and swirl gently until gas evolution ceases. [**CAUTION**—Considerable pressure is produced.] Add 1.0 mL of *Solution A*, dilute with water to volume, and allow to stand for 5 min.

Measure the absorbance of the *Standard solution* and the *Sample solution* against the *Blank solution*.

Acceptance criteria: The absorbance of the *Sample solution* is NMT that of the *Standard solution* (NMT 0.05% of free aromatic amine).

Change to read:• **LIMIT OF 2-METHOXYETHANOL**

Internal standard solution: 0.01 mg/mL of secondary butyl alcohol in water

Standard stock solution: 0.005 mg/mL of methanol and 0.01 mg/mL (ERR 1-Mar-2022) each of isopropyl alcohol, secondary butyl alcohol, and 2-methoxyethanol in *Internal standard solution*

Standard solution: Transfer about 0.25 g of [USP Iodixanol RS](#) and 1.0 mL of *Standard stock solution* to a headspace vial and seal the vial with a septum and crimp cap.

Sample solution: Transfer about 0.25 g of Iodixanol and 1.0 mL of *Internal standard solution* to a headspace vial and seal the vial with a septum and crimp cap.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: GC with suitable headspace autosampler