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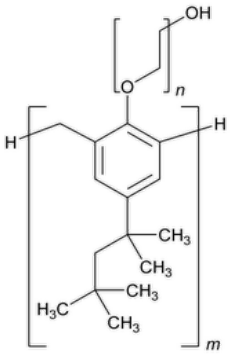
Tyloxapol



Phenol, 4-(1,1,3,3-tetramethylbutyl)-, polymer with formaldehyde and oxirane;
p-(1,1,3,3-Tetramethylbutyl)phenol polymer with ethylene oxide and formaldehyde
CAS RN®: 25301-02-4.

DEFINITION

Tyloxapol is a nonionic liquid polymer of the alkyl aryl polyether alcohol type. [Note—Precautions should be exercised to prevent contact of Tyloxapol with metals.]

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197F** ▲(CN 1-May-2020)

Analysis: On the undried specimen

Acceptance criteria: Meets the requirements

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 1.0%

• **Limit of Anionic Detergents**

Standard solution: Transfer 50 mL of water and 1 mL of a solution of sodium lauryl sulfate containing 150 µg/mL to a 125-mL separator.

Sample solution: Mix 20 mL of a solution containing 10 mg/mL of Tyloxapol with 30 mL of water in a 125-mL separator.

Analysis: To both separators add 2 drops of 3 N hydrochloric acid, 1 drop of methylene blue solution (1 in 25), and 25 mL of chloroform. Shake both separators gently for 2 min, allow to stand for 10 min, and transfer the chloroform layers to individual separators. Wash the chloroform extracts with separate 25-mL portions of water, transfer the chloroform solutions to matched 50-mL color-comparison tubes, and view downward over a white surface.

Acceptance criteria: The chloroform solution from the *Sample solution* is not darker than that from the *Standard solution*, corresponding to NMT 0.075% of anionic detergents (as sodium lauryl sulfate).

• **Limit of Ethylene Oxide**

Standard solution

[Caution—Ethylene oxide is toxic and flammable. Prepare in a well-ventilated hood, using great care.]

Transfer 25 mL of dimethylformamide to a 50-mL volumetric flask and weigh. Add 0.5 mL of ethylene oxide. Reweigh to obtain the weight of ethylene oxide by difference. Dilute with dimethylformamide to volume. Dilute a portion of this solution with dimethylformamide to obtain a solution having a concentration of 10 µg/g of ethylene oxide.

Sample solution: Transfer 1 g of Tyloxapol into a glass- stoppered, 5-mL graduated cylinder. Dilute with dimethylformamide to 2.0 mL.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: GC

Detector: Flame ionization

Column: 1.8-m × 2-mm glass column containing 5% phase G16 on support S12

Temperatures

Injection port: 200°

Detector: 250°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold at Final Temperature (min)
50	0	50	3
50	25	200	5

Carrier gas: Helium

Flow rate: 25 mL/min

Injection volume: 3 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 10%

Analysis

Samples: *Standard solution and Sample solution*

Calculate the quantity of ethylene oxide in the portion of Tyloxapol taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U)$$

r_U = peak response of ethylene oxide from the *Sample solution*

r_S = peak response of ethylene oxide from the *Standard solution*

C_S = concentration of ethylene oxide in the *Standard solution* (µg/mL)

C_U = concentration of Tyloxapol taken in the *Sample solution* (g/mL)

Acceptance criteria: NMT 10 µg/g

- **Limit of Formaldehyde**

Diluent: Isopropyl alcohol and water (4 in 10)

Standard solution: Transfer 750 µL of a solution containing 27 µg/mL of formaldehyde to a 25-mL volumetric flask containing 5 mL of *Diluent*.

Sample solution: Prepare a solution containing 200 mg/mL of Tyloxapol in *Diluent*. Transfer 500 µL of this solution to a 25-mL volumetric flask containing 5 mL of *Diluent*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: Vis

Analytical wavelength: 520 nm

Cell: 1 cm

Analysis

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

To the *Standard solution*, the *Sample solution*, and a blank (prepared by placing 5 mL of *Diluent* in a 25-mL volumetric flask) add 500 µL of phenylhydrazine hydrochloride solution (7.5 in 100). Mix, and allow to stand for 10 ± 1 min. Add 300 µL of potassium ferricyanide solution (50 mg/mL) to each flask, mix, and allow to stand for 5 min ± 30 s. Then add 2.0 mL of 2.5 N sodium hydroxide to each. Mix, and allow to stand for 4 ± 1 min. Dilute each flask with *Diluent* to volume, mix, and read the absorbances after 10 ± 3 min.

Acceptance criteria: NMT 0.0075%; the absorbance of the *Sample solution* does not exceed that of the *Standard solution*.

- **Free Phenol**

Sample solution: 10 mg/mL

Analysis: To 10 mL of *Sample solution* add 1 mL of bromine TS, and mix.

Acceptance criteria: No cloudiness or precipitation is observed immediately.

- **Absence of Cationic Detergents**

Sample solution: 10 mg/mL

Analysis: Place 10 mL of the *Sample solution* in a glass-stoppered, 50-mL graduated cylinder, and make distinctly alkaline to litmus with sodium carbonate TS (about 1 mL). Add 4 mL of aqueous bromophenol blue solution (0.4 mg/mL), mix, and add 10 mL of a 1-in-10 solvent mixture of ethylene dichloride in toluene. Shake gently, and allow the layers to separate.

Acceptance criteria: No blue color is observed in the organic solvent layer.

SPECIFIC TESTS

- **Cloud Point**

Sample solution: Transfer 1.0 g of Tyloxapol, previously mixed, to a 150-mL beaker. Add 100.0 mL of water, and mix until dissolved. Warm the solution while mixing.

Analysis: Transient turbidity may be observed as the solution is warmed. Determine the temperature at which the mixture becomes completely turbid.

Acceptance criteria: The cloud point is between 92° and 97°.

- **pH** ⟨791⟩

Sample solution: 50 mg/mL

Acceptance criteria: 4.0–7.0

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.
- **USP Reference Standards** ⟨11⟩

USP Tyloxapol RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
TYLOXAPOL	Documentary Standards Support	CE2020 Complex Excipients
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

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