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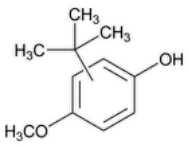
Butylated Hydroxyanisole



$C_{11}H_{16}O_2$ 180.24

Phenol, (1,1-dimethylethyl)-4-methoxy-;

tert-Butyl-4-methoxyphenol CAS RN®: 25013-16-5.

DEFINITION

Butylated Hydroxyanisole is predominantly 3-*tert*-butyl-4-hydroxyanisole, with varying amounts of 2-*tert*-butyl-4-hydroxyanisole. It contains NLT 98.5% of butylated hydroxyanisole ($C_{11}H_{16}O_2$) as a sum of the two isomers.

IDENTIFICATION

Change to read:

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

Analysis: Determine the position of the most intense 3-*tert*-butyl-4-hydroxyanisole peaks within 10 cm^{-1} of 682, 815, 855, 914, 1031, 1196, 1413, and 1504 cm^{-1} in a spectrum of USP 3-*tert*-Butyl-4-hydroxyanisole RS. Compare the peak positions of Butylated Hydroxyanisole to those of USP 3-*tert*-Butyl-4-hydroxyanisole RS.

Acceptance criteria: All peak positions determined from Butylated Hydroxyanisole are within 5 cm^{-1} of those determined from USP 3-*tert*-Butyl-4-hydroxyanisole RS.

• **B.**

Solution A: 5% acetic acid, prepared by diluting 50 mL of glacial acetic acid in a 1-L flask with water to volume

Mobile phase: Acetonitrile and *Solution A* (65:35)

Standard solution: 0.4 mg/mL of USP 3-*tert*-Butyl-4-hydroxyanisole RS and 0.1 mg/mL of USP 2-*tert*-Butyl-4-hydroxyanisole RS in *Mobile phase*

Sample solution: 0.5 mg/mL of Butylated Hydroxyanisole in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 275 nm

Column: 3.0-mm × 15-cm; 3-µm packing L1

Column temperature: 40°

Flow rate: 0.75 mL/min

Injection volume: 10 µL

Run time: NLT 15 min

Analysis

Samples: *Standard solution* and *Sample solution*

[Note—2-*tert*-Butyl-4-hydroxyanisole and 3-*tert*-butyl-4-hydroxyanisole coelute under these chromatographic conditions. However, a small shoulder of 2-*tert*-butyl-4-hydroxyanisole may be seen on the left-hand side of the 3-*tert*-butyl-4-hydroxyanisole peak. The retention time of the 3-*tert*-butyl-4-hydroxyanisole peak is about 2.1 min.]

Acceptance criteria: The retention time of the main peak of the *Sample solution* corresponds to that of the *Standard solution*. The chromatographic profile of the *Sample solution* should be similar to that of the *Standard solution* and exhibit only 1 major peak corresponding to butylated hydroxyanisole.

ASSAY

Change to read:

• **Procedure**

Solution A: Prepare as directed in *Identification B*.

Mobile phase: Acetonitrile and *Solution A* (45:55)

▲**System suitability solution:**▲ (NF 1-May-2019) 90 µg/mL of USP 3-*tert*-Butyl-4-hydroxyanisole RS and 10 µg/mL of USP 2-*tert*-Butyl-4-hydroxyanisole RS in *Mobile phase*

▲**Standard solution A:** 90 µg/mL of USP 3-*tert*-Butyl-4-hydroxyanisole RS in *Mobile phase*

Standard solution B: 10 µg/mL of USP 2-*tert*-Butyl-4-hydroxyanisole RS in *Mobile phase*▲ (NF 1-May-2019)

Sample solution: 100 µg/mL of Butylated Hydroxyanisole in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 290 nm

Column: 4.6-mm × 75-mm; 3.5-µm packing L1

Column temperature: 30°

Flow rate: 1.2 mL/min

Injection volume: 20 µL

System suitability

Samples: ▲*System suitability solution*, *Standard solution A*, and *Standard solution B*▲ (NF 1-May-2019)

[NOTE—The retention times of 2-*tert*-butyl-4-hydroxyanisole and 3-*tert*-butyl-4-hydroxyanisole are about 4.2 and 4.6 min, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the 3-*tert*-butyl-4-hydroxyanisole isomer and 2-*tert*-butyl-4-hydroxyanisole isomer peaks, ▲*System suitability solution*▲ (NF 1-May-2019)

Tailing factor: NMT 1.5, ▲*Standard solution A* and *Standard solution B*▲ (NF 1-May-2019)

Relative standard deviation: NMT 2.0% for the 3-*tert*-butyl-4-hydroxyanisole isomer and 2-*tert*-butyl-4-hydroxyanisole isomer peaks, ▲*Standard solution A* and *Standard solution B*▲ (NF 1-May-2019)

Analysis

Samples: ▲*Standard solution A*, *Standard solution B*,▲ (NF 1-May-2019) and *Sample solution*

Measure the peak areas for each isomer.

Calculate the percentage of each isomer in the portion of Butylated Hydroxyanisole taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak area of the corresponding isomer from the *Sample solution*

r_S = peak area of the corresponding isomer from ▲*Standard solution A* or *Standard solution B*▲ (NF 1-May-2019)

C_S = concentration of the appropriate Reference Standard in ▲*Standard solution A* or *Standard solution B*▲ (NF 1-May-2019) (µg/mL)

C_U = concentration of Butylated Hydroxyanisole in the *Sample solution* (µg/mL)

[NOTE—Calculate the percentage of butylated hydroxyanisole ($C_{11}H_{16}O_2$) in the portion of Butylated Hydroxyanisole taken by adding the quantities of the two isomers.]

Acceptance criteria: NLT 98.5%

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩**

Sample: 10 g

Acceptance criteria: NMT 0.01%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers.

• **USP REFERENCE STANDARDS ⟨11⟩**

USP 2-*tert*-Butyl-4-hydroxyanisole RS	$C_{11}H_{16}O_2$	180.25
USP 3-*tert*-Butyl-4-hydroxyanisole RS	$C_{11}H_{16}O_2$	180.25

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

Topic/Question	Contact	Expert Committee
BUTYLATED HYDROXYANISOLE	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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