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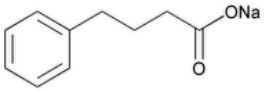
Sodium Phenylbutyrate



$C_{10}H_{11}NaO_2$ 186.18
Benzenebutanoic acid, sodium salt;
Sodium 4-phenylbutyrate;
Sodium 4-phenylbutanoate. CAS RN®: 1716-12-7; UNII: NT6K61736T.

DEFINITION

Sodium Phenylbutyrate contains NLT 99.0% and NMT 101.0% of sodium phenylbutyrate ($C_{10}H_{11}NaO_2$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

• **B.** **Identification Tests—General ⟨191⟩, *Sodium***

Sample solution: Dissolve 150 mg in 2 mL of water.

Acceptance criteria: Meets the requirements of test *A*

ASSAY

• **Procedure**

Sample: 150 mg

Analysis: Disperse the *Sample* in 50 mL of anhydrous acetic acid. [Note—The opalescence of the solution disappears during the titration.] Titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Each mL of 0.1 N perchloric acid is equivalent to 18.62 mg of sodium phenylbutyrate ($C_{10}H_{11}NaO_2$).

Acceptance criteria: 99.0%–101.0% on the anhydrous basis

IMPURITIES

• **Limit of Phenylbutyrate Related Compound C**

Silylation solution: To 2 mL of bis(trimethylsilyl)trifluoroacetamide add 0.04 mL of chlorotrimethylsilane, and mix.

Sample solution: Dissolve 50.0 mg of Sodium Phenylbutyrate in 3 mL of water, and add 0.5 mL of hydrochloric acid. Extract with 2 quantities, each of 5 mL, of methylene chloride. Evaporate the combined methylene chloride extracts to dryness in a vial with a screw cap, and add 0.5 mL of the *Silylation solution*. Seal the vial, and heat at 70 ± 5° for 20 min.

Standard stock solution: 0.5 mg/mL of USP Phenylbutyrate Related Compound C RS in methylene chloride

Diluted standard stock solution: 0.05 mg/mL of USP Phenylbutyrate Related Compound C RS in methylene chloride from *Standard stock solution*

Standard solution: Place an amount of the *Diluted standard stock solution,* equivalent to 0.05 mg, in a vial with a screw cap, evaporate to dryness, and add 0.5 mL of the *Silylation solution.* Seal the vial, and heat at 70 ± 5° for 20 min.

System suitability solution: Prepare a solution containing 0.4 mg/mL of USP Sodium Phenylbutyrate RS in water. To 3 mL of this solution add 0.1 mL of hydrochloric acid. Extract with 2 quantities, each of 5 mL, of methylene chloride. Combine the methylene chloride extracts in a vial with a screw cap, and add 2 mL of *Standard stock solution.* Evaporate to dryness, and add 0.5 mL of the *Silylation solution.* Seal the vial, and heat at 70 ± 5° for 20 min.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

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Column: 25-m × 0.25-mm fused silica capillary; coated with a 1.0-µm film of phase G27

Temperatures

Injector: 270°

Detector: 270°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	0	50	5
50	10	270	5

Carrier gas: Helium

Flow rate: 0.9 mL/min

Injection volume: 1 µL

Split ratio: 1:100

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for phenylbutyrate related compound C and phenylbutyrate are about 0.98 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between the phenylbutyrate related compound C and phenylbutyrate peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phenylbutyrate related compound C in the portion of Sodium Phenylbutyrate taken:

$$\text{Result} = (r_U/r_S) \times (W_S/W_U) \times 100$$

r_U = peak response of phenylbutyrate related compound C from the *Sample solution*

r_S = peak response of phenylbutyrate related compound C from the *Standard solution*

W_S = amount of USP Phenylbutyrate Related Compound C RS taken to prepare the *Standard solution* (mg)

W_U = amount of Sodium Phenylbutyrate taken to prepare the *Sample solution* (mg)

Acceptance criteria: NMT 0.1%

• **ORGANIC IMPURITIES**

Mobile phase: Methanol, glacial acetic acid, and water (49:1:50)

Impurity stock solution A: 0.1 mg/mL of USP Phenylbutyrate Related Compound A RS in methanol

Impurity standard solution A: Dilute 1.0 mL of *Impurity stock solution A* with water to 50.0 mL. This solution contains 2 µg/mL of USP Phenylbutyrate Related Compound A RS.

Impurity stock solution B: 0.02 mg/mL of USP Phenylbutyrate Related Compound B RS in methanol

Impurity standard solution B: Dilute 1.0 mL of *Impurity stock solution B* with water to 50.0 mL. This solution contains 0.4 µg/mL of USP Phenylbutyrate Related Compound B RS.

System suitability solution: Prepare a solution containing 20 mg/mL of USP Sodium Phenylbutyrate RS in methanol. Transfer 10 mL of this solution to a 50-mL volumetric flask, add 1.0 mL of *Impurity stock solution B,* and dilute with water to volume.

Sensitivity solution: Dilute 6.0 mL of *Impurity standard solution A* with water to 10.0 mL. This solution contains 1.2 µg/mL of USP Phenylbutyrate Related Compound A RS.

Sample solution: 4.0 mg/mL of Sodium Phenylbutyrate, prepared as follows. Dissolve it first in methanol, using 20% of the final volume, and dilute with water to volume.

Chromatographic system

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

Mode: LC

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Detector: UV 245 nm

Column: 4.6-mm × 25-cm; 5-µm base-deactivated end-capped packing L1

Flow rate: 1.3 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Sensitivity solution*

Suitability requirements

Resolution: NLT 6 between phenylbutyrate and phenylbutyrate related compound B, *System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Impurity standard solution A*, *Impurity standard solution B*, and *Sample solution*

Calculate the percentage of phenylbutyrate related compound A or phenylbutyrate related compound B in the portion of Sodium Phenylbutyrate taken:

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

r_U = peak response of respective impurity in the *Sample solution*

r_S = peak response of phenylbutyrate related compound A or phenylbutyrate related compound B in the respective *Impurity standard solution*

C_S = concentration of USP Phenylbutyrate Related Compound A RS or USP Phenylbutyrate Related Compound B RS in the respective *Impurity standard solution* (mg/mL)

C_U = concentration of Sodium Phenylbutyrate in the *Sample solution* (mg/mL)

Calculate the percentage of any individual unspecified impurity in the portion of Sodium Phenylbutyrate taken:

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

r_U = peak response of each unspecified impurity in the *Sample solution*

r_S = peak response of phenylbutyrate related compound A in *Impurity standard solution A*

C_S = concentration of USP Phenylbutyrate Related Compound A RS in *Impurity standard solution A* (mg/mL)

C_U = concentration of Sodium Phenylbutyrate in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard any peak below 0.03%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Phenylbutyrate related compound A	0.3	0.1
Phenylbutyrate related compound B	0.7	0.01
Sodium phenylbutyrate	1.0	—
Any individual unspecified Impurity	—	0.05
Total impurities	—	0.1

SPECIFIC TESTS

- **Water Determination,** *Method Ia*⟨921⟩**:** NMT 0.5%
- **pH** ⟨791⟩

Sample solution: 20 mg/mL in carbon dioxide-free water

Acceptance criteria: 6.5–7.5

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ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve under argon in tight containers. Store at room temperature.
- **USP Reference Standards** ⟨11⟩

USP Sodium Phenylbutyrate RS

USP Phenylbutyrate Related Compound A RS

3-Benzoylpropionic acid;
4-Oxo-4-phenylbutanoic acid.
$C_{10}H_{10}O_3$ 178.18

USP Phenylbutyrate Related Compound B RS

α-Tetralone;
3,4-Dihydronaphthalen-1(2*H*)-one.
$C_{10}H_{10}O$ 146.19

USP Phenylbutyrate Related Compound C RS

4-Cyclohexylbutanoic acid.
$C_{10}H_{18}O_2$ 170.25

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

Topic/Question	Contact	Expert Committee
SODIUM PHENYLBUTYRATE	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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