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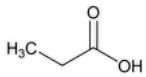
Propionic Acid

Change to read:



▲$C_3H_6O_2$ 74.08

Propanoic acid;

Propionic acid CAS RN®: 79-09-4.▲ (NF 1-Dec-2022)

Change to read:

DEFINITION

Propionic Acid contains ▲NLT 97.0% and NMT 102.0%▲ (NF 1-Dec-2022) of propionic acid ($C_3H_6O_2$).

Add the following:

▲IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197F
- **B. Chromatographic Identity**

Analysis: Examine the chromatograms obtained in the *Assay*.

Acceptance criteria: The retention time of major peak of the *Sample solution* corresponds to that of the *Standard solution*.▲ (NF 1-Dec-2022)

ASSAY

Change to read:

- **Procedure**

▲Solution A: 10 mM potassium phosphate, monobasic, with the pH adjusted to 2.5 using phosphoric acid

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
3.0	100	0
15.0	70	30
25.0	50	50
26.0	100	0
35.0	100	0

Diluent: 2% (v/v) phosphoric acid in water

System suitability solution: 2.0 mg/mL of USP Propionic Acid RS and 0.008 mg/mL of acrylic acid in *Diluent*

Standard solution: 2.0 mg/mL of USP Propionic Acid RS in *Diluent*

Sample solution: 2.0 mg/mL of Propionic Acid in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 45°

Flow rate: 1.0 mL/min

Injection volume: 20 µL

Run time: 35 min

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The approximate relative retention times for related substances are listed in *Table 2*.]

Suitability requirements

Resolution: NLT 1.5 between the propionic acid peak and the acrylic acid peak, *System suitability solution*

Tailing factor: NMT 2, determined from the propionic acid peak, *Standard solution*

Relative standard deviation: NMT 1%, determined from the propionic acid peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the Propionic Acid in the portion of sample taken:

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

r_U = peak area of propionic acid from the *Sample solution*

r_S = peak area of propionic acid from the *Standard solution*

C_S = concentration of USP Propionic Acid RS in the *Standard solution* (mg/mL)

C_U = concentration of Propionic Acid in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–102.0%▲ (NF 1-Dec-2022)

IMPURITIES

Add the following:

▲• Organic Impurities

Mobile phase, Diluent, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 0.008 mg/mL of USP Propionic Acid RS in *Diluent*

Standard solution: 0.016 mg/mL of USP Propionic Acid RS in *Diluent*

Sample solution: 16 mg/mL of Propionic Acid in *Diluent*

System suitability

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

[NOTE—The approximate relative retention times for related substances are listed in *Table 2*.]

Table 2

Name	Relative Retention Time
Acetic acid	0.5
Acrylic acid	0.95
Propionic acid	1.0

Suitability requirements

Resolution: NLT 1.5 between the propionic acid peak and the acrylic acid peak, *System suitability solution*

Relative standard deviation: NMT 5.0%, determined from the propionic acid peak, *Standard solution*

Signal-to-noise ratio: NLT 10, determined from the propionic acid peak, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of sample taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*

r_S = peak area of propionic acid from the *Standard solution*

C_S = concentration of USP Propionic Acid RS in the *Standard solution* (mg/mL)

C_U = concentration of Propionic Acid in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Response Factor	Acceptance Criteria, NMT (%)
Acetic acid	1.0	0.2
Acrylic acid	90.0	0.1
Propionic acid	—	—
Any unidentified individual impurity	1.0	0.2
Total impurities	—	1.0▲ (NF 1-Dec-2022)

• **Limit of Nonvolatile Residue:** Evaporate 20 g of Propionic Acid in a tared dish, and dry at 105° for 1 h: the weight of the residue does not exceed 2.0 mg.

• **Limit of Aldehydes**

Sample solution: Transfer 10.0 mL of Propionic Acid to a glass-stoppered 250-mL conical flask containing 50 mL of water and 10.0 mL of sodium bisulfite solution (1 in 80), insert the stopper, and shake vigorously. Allow the mixture to stand for 30 min.

Blank: Add 50 mL of water and 10.0 mL of sodium bisulfite solution (1 in 80) to a glass-stoppered 250-mL conical flask, insert the stopper, and shake vigorously. Allow the mixture to stand for 30 min.

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Residual titration

Titrant: 0.1 N iodine VS

Endpoint detection: Visual

Analysis: Titrate the *Sample solution* and the *Blank* with *Titrant* to the same brownish-yellow endpoint.

Acceptance criteria: The difference between the volume of 0.1 N iodine required for the *Blank* and that required for the *Sample solution* is NMT 1.75 mL.

SPECIFIC TESTS

• **Distilling Range ⟨721⟩, *Method I*:** 138.5°–142.5°

• **Specific Gravity ⟨841⟩:** 0.988–0.993

• **Readily Oxidizable Substances**

Sample solution: Dissolve 15 g of sodium hydroxide in 50 mL of water. Cool, add 6 mL of bromine, stirring to effect complete solution, and dilute with water to 2000 mL. Transfer 25.0 mL of this solution to a glass-stoppered 250-mL conical flask containing 100 mL of water, and add 10 mL of sodium acetate solution (1 in 5) and 10.0 mL of Propionic Acid. Allow to stand for 15 min, and add 5 mL of potassium iodide solution (1 in 4) and 10 mL of hydrochloric acid.

Blank: Dissolve 15 g of sodium hydroxide in 50 mL of water. Cool, add 6 mL of bromine, stirring to effect complete solution, and dilute with water to 2000 mL. Transfer 25.0 mL of this solution to a glass-stoppered 250-mL conical flask containing 100 mL of water, and add 10 mL of sodium acetate solution (1 in 5). Allow to stand for 15 min, and add 5 mL of potassium iodide solution (1 in 4) and 10 mL of hydrochloric acid.

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Residual titration

Titrant: 0.1 N sodium thiosulfate VS

Endpoint detection: Visual

Analysis: Titrate the *Sample solution* and the *Blank* with *Titrant* just to the disappearance of the brown color.

Acceptance criteria: The difference between the volume of 0.1 N sodium thiosulfate required for the *Blank* and that required for the *Sample solution* is NMT 2.2 mL.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

Add the following:

▲• **USP Reference Standards ⟨11⟩**

USP Propionic Acid RS▲ (NF 1-Dec-2022)

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

Topic/Question	Contact	Expert Committee
PROPIONIC ACID	Documentary Standards Support	SE2020 Simple Excipients
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

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