Carrier gas: Helium
Linear velocity: 35 cm/s
Injection type: Split ratio, 20:1
Injection size: 1 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times for methyl alcohol, acetone, and acetonitrile are 1.0, about 1.6, and about 1.8, respectively.]
Suitability requirements
Resolution: NLT 15 between methyl alcohol and acetone, *System suitability solution*
Tailing factor: NLT 1.5 for methyl alcohol, *System suitability solution*
Relative standard deviation: NMT 2.0% for the ratio of the peak area of methyl alcohol to acetonitrile, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of methyl alcohol (CH_3OH) in the portion of Methyl Alcohol taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

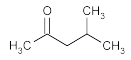
R_U = peak area ratio from the *Sample solution*
R_S = peak area ratio from the *Standard solution*
C_S = concentration of USP Methyl Alcohol RS in the *Standard solution* (mg/mL)
C_U = concentration of Methyl Alcohol in the *Sample solution* (mg/mL)
Acceptance criteria: NLT 99.5%

IMPURITIES
- **NONVOLATILE RESIDUE**
Sample: 250 mL of Methyl Alcohol
Analysis: Evaporate the *Sample* in a 600-mL beaker on a steam bath, in a well-ventilated hood, until the volume is reduced to about 100 mL. Cool, transfer a portion of the liquid to a suitable, tared 50-mL platinum dish on a steam bath, and evaporate. Repeat the process until all of the liquid has been transferred, and then evaporate to dryness. Dry at 105° for 30 min, cool, and weigh.
Acceptance criteria: The weight of the residue does not exceed 2 mg, corresponding to NMT 0.001% (w/w).
- **ACETONE AND ALDEHYDES** (as acetone)
Standard solution: Dilute 1.9 mL (1.5 g) of acetone with water to 1000 mL, then dilute 1.0 mL of this solution with water to 100 mL. Dilute 2 mL of the resulting solution with water to 5 mL. The *Standard solution* contains 30 µg of acetone and is freshly prepared.
Sample solution: Dilute 1.25 mL (1 g) of Methyl Alcohol with water to 5 mL.
Analysis: Adjust to and maintain each solution at 20°. Add 5 mL of alkaline mercuric–potassium iodide TS to each of the *Standard solution* and *Sample solution.*
Acceptance criteria: Any turbidity produced in the *Sample solution* is not greater than that produced in the *Standard solution* (NMT 0.003%).
- **READILY CARBONIZABLE SUBSTANCES** ⟨**271**⟩
Sample: 5 mL
Analysis: Cool 5 mL of sulfuric acid, contained in a small conical flask, to 10°, and add the *Sample* dropwise with constant mixing, maintaining the temperature below 20° throughout the test.
Acceptance criteria: No discoloration develops.
- **READILY OXIDIZABLE SUBSTANCES**
Sample: 20 mL of Methyl Alcohol
Analysis: Cool the *Sample* to 15°, add 0.1 mL of 0.1 N potassium permanganate, and allow to stand at 15°.
Acceptance criteria: The pink color does not completely disappear within 5 min.

SPECIFIC TESTS
- **ACIDITY**
Sample solution: Mix 25 mL of water with 10 mL of alcohol and 0.5 mL of phenolphthalein TS, and add 0.02 N sodium hydroxide until a slight pink color persists after shaking for 30 s. Taking precautions to avoid absorption of carbon dioxide, add 19 mL (15 g) of Methyl Alcohol.
Analysis: Titrate the *Sample solution* with 0.020 N sodium hydroxide.
Acceptance criteria: NMT 0.45 mL of 0.020 N sodium hydroxide is required to produce a pink color.
- **ALKALINITY** (as ammonia)
Sample: 28.6 mL (22.6 g) of Methyl Alcohol
Analysis: Mix the *Sample* with 25 mL of water, add 1 drop of methyl red TS, and titrate with 0.020 N sulfuric acid.
Acceptance criteria: NMT 0.20 mL of 0.020 N sulfuric acid is required to produce a pink color (3 ppm).
- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 0.1%

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in tight containers, remote from heat, sparks, and open flames.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Acetone RS
USP Methyl Alcohol RS

Methyl Isobutyl Ketone

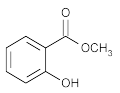


$C_6H_{12}O$ 100.16
2-Pentanone, 4-methyl-.
4-Methyl-2-pentanone [108-10-1].

» Methyl Isobutyl Ketone contains not less than 99.0 percent of $C_6H_{12}O$.

Packaging and storage—Preserve in tight containers.
Identification—The IR absorption spectrum of a thin film of it between sodium chloride crystals exhibits maxima, among others, at the following wavelengths, in µm: 5.81 (*vs*), 6.80 (*m*), 7.00 (*m*), 7.09 (*m*), 7.29 (*vs*), 7.72 (*m*), 8.06 (*m*), 8.31 (*sh*), 8.53 (*s*), and 8.91 (*m*).
Specific gravity ⟨841⟩: not more than 0.799, indicating not less than 99.0% of $C_6H_{12}O$.
Distilling range, *Method I* ⟨721⟩: between 114° and 117°, a correction factor of 0.046° per mm being applied as necessary.
Acidity—Mix 15.0 mL with 15 mL of neutralized alcohol, add phenolphthalein TS, and titrate with 0.050 N sodium hydroxide: not more than 0.40 mL is required for neutralization.
Limit of nonvolatile residue—Evaporate 50 mL in a tared porcelain dish on a steam bath, and dry at 105° for 1 hour: the weight of the residue does not exceed 4 mg (0.008%).

Methyl Salicylate



$C_8H_8O_3$ 152.15
Benzoic acid, 2-hydroxy-, methyl ester;
Methyl salicylate [119-36-8].

DEFINITION

Methyl Salicylate is produced synthetically or is obtained by maceration and subsequent distillation with steam from the leaves of *Gaultheria procumbens* Linné (Fam. Ericaceae) or from the bark of *Betula lenta* Linné (Fam. Betulaceae). It contains NLT 98.0% and NMT 100.5% of methyl salicylate ($C_8H_8O_3$).

IDENTIFICATION

- **A.**

Sample: 1 drop of Methyl Salicylate

Analysis: Shake the *Sample* with 5 mL of water, and add 1 drop of ferric chloride TS.

Acceptance criteria: The resulting mixture has a deep violet color.

ASSAY

- **PROCEDURE**

Sample: 2 g of Methyl Salicylate

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Residual titration

Titrant: 1 N sodium hydroxide VS

Endpoint detection: Colorimetric

Analysis: Place the *Sample* in a flask, and add 40.0 mL of 1 N sodium hydroxide VS. Boil gently under a reflux condenser for 2 h. Cool, rinse the condenser and the sides of the flask with a few mL of water, and add phenolphthalein TS. Titrate the excess alkali with 1 N sulfuric acid VS. Perform a blank determination. Each mL of 1 N sodium hydroxide corresponds to 152.2 mg of methyl salicylate ($C_8H_8O_3$).

Acceptance criteria: 98.0%–100.5%

IMPURITIES

- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 20 ppm

SPECIFIC TESTS

- **SOLUBILITY IN 70% ALCOHOL:** One volume of synthetic Methyl Salicylate dissolves in 7 volumes of 70% alcohol. One volume of natural Methyl Salicylate dissolves in 7 volumes of 70% alcohol, the solution having NMT a slight cloudiness.
- **SPECIFIC GRAVITY** ⟨**841**⟩**:** 1.180–1.185 for the synthetic variety; 1.176–1.182 for the natural variety
- **OPTICAL ROTATION,** *Angular Rotation* ⟨**781A**⟩**:** Synthetic Methyl Salicylate and that from *Betula* are optically inactive. Methyl Salicylate from *Gaultheria* is slightly levorotatory, the angular rotation not exceeding –1.5° in a 100-mm tube.
- **REFRACTIVE INDEX** ⟨**831**⟩**:** 1.535–1.538 at 20°

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers.
- **LABELING:** Label it to indicate whether it was made synthetically or distilled from either of the plants of *Gaultheria procumbens* or *Betula lenta*.

Methylcellulose—*see Methylcellulose General Monographs*

Methylene Chloride

CH_2Cl_2 84.93

Methane, dichloro-.

Dichloromethane [75-09-2].

» Methylene Chloride contains not less than 99.0 percent of CH_2Cl_2.

Caution— Perform all steps involving evaporation of methylene chloride in a well-ventilated fume hood.

Packaging and storage —Preserve in tight containers.

Identification—Place about 5 mL into a glass-stoppered, 10-mL conical flask, and shake for several minutes. Remove the stopper, quickly withdraw a portion of the vapor into a 50-mL syringe that is not fitted with a needle, and inject the vapor into a suitable evacuated gas cell: the IR absorption spectrum of the vapor shows strong doublet peaks at 7.8 μm and 7.9 μm and at 13.2 μm and 13.4 μm, and relatively few minor peaks.

Specific gravity ⟨841⟩**:** between 1.318 and 1.322.

Water, *Method I* ⟨921⟩**:** not more than 0.02%.

Limit of hydrogen chloride—Into each of 2 glass-stoppered, 50-mL color-comparison cylinders having an internal diameter of 20 mm place 10 mL of water, 2 drops of phenolphthalein TS, and sufficient 0.010 N sodium hydroxide to produce a pink color that persists after vigorous shaking for 30 seconds, and is of equal intensity in each cylinder. [NOTE—In the following steps, take special care to avoid contamination with carbon dioxide.] Into one of the cylinders place 20.0 mL of Methylene Chloride and 0.70 mL of 0.010 N sodium hydroxide, and shake again. The pink color in the test cylinder is at least as intense as that in the comparison cylinder, and the color persists for not less than 15 minutes (0.001%).

Limit of nonvolatile residue—Evaporate 50 g in a platinum or porcelain dish on a steam bath, and dry at 105° for 30 minutes: the weight of the residue does not exceed 1 mg (0.002%).

Heavy metals, *Method I* ⟨231⟩**—**Evaporate 15 mL (20 g) in a glass evaporating dish on a steam bath to dryness. Cool, add 2 mL of hydrochloric acid, and slowly evaporate again on a steam bath to dryness. Dissolve the residue in 1 mL of 1 N acetic acid, add 24 mL of water, and mix: the limit is 1 ppm.

Free chlorine—To 10 mL add 10 mL of water and 0.1 mL of potassium iodide TS, shake for 2 minutes, and allow the liquids to separate: the lower layer does not show a violet tint.

Assay—

Chromatographic system—Under typical conditions, the instrument is equipped with a thermal conductivity detector, and contains a 4-mm × 1.8-m column packed with 15% liquid phase G18 on 30- to 60-mesh S1C unsilanized support. The temperatures of the column, the injection port, and the detector are maintained at 60°, 200°, and 250°, respectively; and helium is used as the carrier gas, at a flow rate of about 20 mL per minute.

System suitability—Chromatograph five 1-μL injections of a mixture of 3 mL of methylene chloride with 7 mL of chloroform. The relative standard deviation of the peak response ratio does not exceed 2%, the resolution factor is not less than 4.0, and the tailing factor is not more than 1.4 (see *Chromatography* ⟨621⟩).

Procedure—Inject about 1 μL of Methylene Chloride, and determine the peak responses by any convenient means. The order of elution is amylenes (5 or 6 peaks), if present, and then methylene chloride. Calculate the percentage of CH_2Cl_2 in the Methylene Chloride by dividing the response due to the methylene chloride by the sum of the responses for all the peaks and multiplying by 100.