

Ethyl Oleate

1 Nonproprietary Names

BP: Ethyl Oleate

PhEur: Ethyl Oleate

USP–NF: Ethyl Oleate

2 Synonyms

Crodamol EO; *DUBCARE OE*; ethylis oleas; ethyl *cis*-9-octadecenoate; ethyl 9-octadecenoate; *Kessco EO*; 9-octadecenoic acid, (*Z*)-, ethyl ester; oleic acid, ethyl ester.

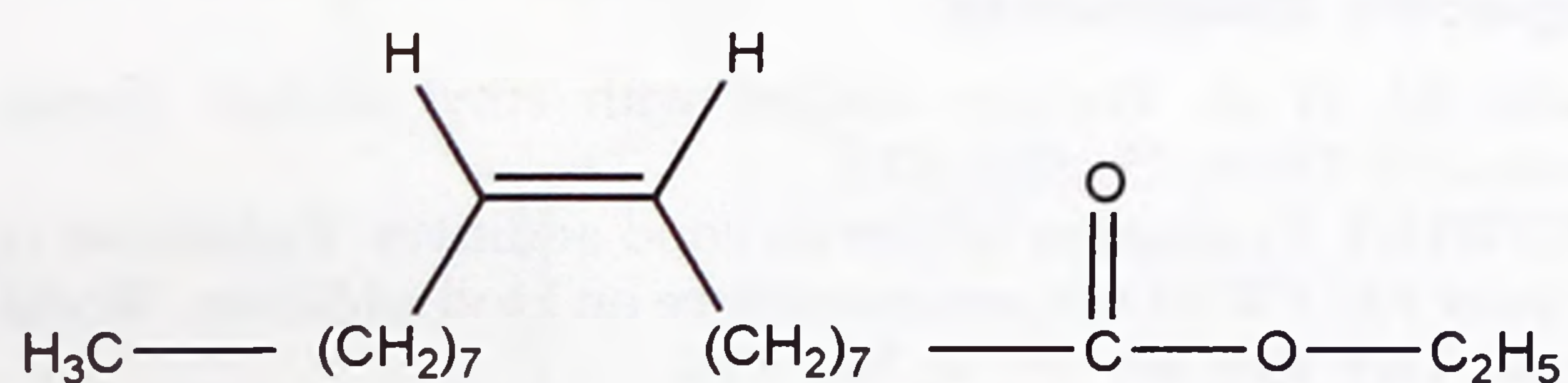
3 Chemical Name and CAS Registry Number

(*Z*)-9-Octadecenoic acid, ethyl ester [111-62-6]

4 Empirical Formula and Molecular Weight

$C_{20}H_{38}O_2$ 310.51

5 Structural Formula



6 Functional Category

Oleaginous vehicle; solvent.

7 Applications in Pharmaceutical Formulation or Technology

Ethyl oleate is primarily used as a vehicle in certain parenteral preparations intended for intramuscular administration. It has also been used as a solvent for drugs formulated as biodegradable capsules for subdermal implantation⁽¹⁾ and in the preparation of microemulsions containing cyclosporin⁽²⁾ and norcantharidin.⁽³⁾ Microemulsion formulations containing ethyl oleate have been investigated,⁽⁴⁾ and have been proposed for topical^(5–8) and ocular⁽⁹⁾ delivery, and for liver targeting following parenteral administration.⁽¹⁰⁾ Ethyl oleate has been used in topical gel formulations,⁽¹¹⁾ and in self-microemulsifying drug delivery systems for oral administration,^(12–15) and intravenous administration.⁽¹⁶⁾

Ethyl oleate is a suitable solvent for steroids and other lipophilic drugs. Its properties are similar to those of almond oil and peanut oil. However, it has the advantage that it is less viscous than fixed oils and is more rapidly absorbed by body tissues.⁽¹⁷⁾

Ethyl oleate has also been evaluated for extended-release injectable formulations,⁽¹⁸⁾ and as a vehicle for subcutaneous injection.⁽¹⁹⁾

8 Description

Ethyl oleate occurs as a pale yellow to almost colorless, mobile, oily liquid with a taste resembling that of olive oil and a slight, but not rancid odor.

Ethyl oleate is described in the USP 40–NF 35 S1 as consisting of esters of ethyl alcohol and high molecular weight fatty acids, principally oleic acid. It contains not less than 65.0% of ethyl (*Z*)-9-octadecenoate ($C_{20}H_{38}O_2$) and may contain suitable stabilizers.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for ethyl oleate.

Test	PhEur 9.2	USP 40–NF 35 S1
Characters	+	—
Identification	+	+
Specific gravity	0.866–0.874	—
Acid value	≤0.5	—
Iodine value	75–90	75–85
Saponification value	177–188	—
Peroxide value	≤10.0	≤10.0
Oleic acid	≥60.0%	—
Water content	≤1.0%	≤1.0%
Total ash	≤0.1%	≤0.1%
Assay	—	+

10 Typical Properties

Boiling point ~205–208°C (some decomposition); also reported as 216–218°C (15 mm)⁽²⁰⁾

Flash point 175.3°C

Freezing point ~–32°C

Moisture content At 20°C and 52% relative humidity, the equilibrium moisture content of ethyl oleate is 0.08%.

Refractive index 1.451

Solubility Miscible with chloroform, ethanol (96%), ether, fixed oils, liquid paraffin, and most other organic solvents; practically insoluble in water.

Surface tension 32.3 mN/m (32.3 dynes/cm) at 25°C⁽¹⁷⁾

Viscosity (dynamic) 3.9 mPa s (3.9 cP) at 25°C⁽¹⁷⁾

Viscosity (kinematic) 0.046 mm²/s (4.6 cSt) at 25°C⁽¹⁷⁾

11 Stability and Storage Conditions

Ethyl oleate should be stored in a cool, dry place in a small, well-filled, well-closed container, protected from light. When a partially filled container is used, the air should be replaced by nitrogen or another inert gas. Ethyl oleate oxidizes on exposure to air, resulting in an increase in the peroxide value. It remains clear at 5°C, but darkens in color on standing. Antioxidants are frequently used to extend the shelf life of ethyl oleate. Protection from oxidation for over 2 years has been achieved by storage in amber glass bottles with the addition of combinations of propyl gallate, butylated hydroxyanisole, butylated hydroxytoluene, and citric or ascorbic acid.^(21,22) A concentration of 0.03% w/v of a mixture of propyl gallate (37.5%), butylated hydroxytoluene (37.5%), and butylated hydroxyanisole (25%) was found to be the best antioxidant for ethyl oleate.⁽²²⁾

Ethyl oleate may be sterilized by heating at 150°C for 1 hour.

12 Incompatibilities

Ethyl oleate dissolves certain types of rubber and causes others to swell.^(23,24) It may also react with oxidizing agents.

13 Method of Manufacture

Ethyl oleate is prepared by the reaction of ethanol with oleoyl chloride in the presence of a suitable hydrogen chloride acceptor.