

International Union
of Pure and Applied Chemistry (IUPAC)

Handbook of
Pharmaceutical Salts
Properties, Selection, and Use

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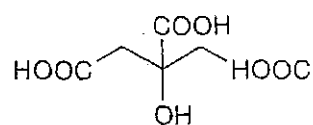


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Safety, Toxicology	<i>Acid</i> : LD_{50} : rat oral, 2500 mg/kg; i.p., 1600 mg/kg; mouse oral, 5 g/kg; i.p., 160 mg/kg; i.v., 380 mg/kg; <i>LDLo</i> : guinea pig oral, > 5 g/kg. <i>Sodium salt</i> : LD_{50} : mouse, i.p., 2 g/kg.
Salt	Cinnamate
Use and Examples	Used for formation of esters.
Remarks	Cinnamic acid has antifungal and antiseptic properties.

Citric Acid



$C_6H_8O_7$, M_r 192.12

pK_a (1) 3.13 (A) (2) 4.76 (A) (3) 6.40 (A)

Properties

Anh.: m.p. 153 °C

Solubility (anh.; H_2O , g/100 g solution (temp. [°C])): 54 (10), 59.2 (20), 64.3 (30), 68.6 (40), 73.5 (60), 78.8 (80), 84.0 (100).

Monohydrate: M_r 210.14, m.p. ~100 °C.

Solubility (g/100 g solution): Et_2O : 2.17, $CHCl_3$: 0.007, $AcOEt$: 5.28; *Solubility* (g/100 g solvent at 19 °C): $MeOH$: 197, $PrOH$: 62.8.

Safety, Toxicology

Acid: LD_{50} : rat oral, 11700 mg/kg; mouse oral, 5040 mg/kg; i.v., 42 mg/kg; rabbit i.v., 330 mg/kg. *Monosodium citrate*: LD_{50} : rat i.p., 1348 mg/kg; mouse i.v., 49 mg/kg; i.p., 1635 mg/kg; rabbit i.v., 379 mg/kg.

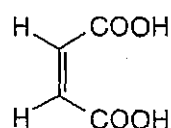
Trisodium citrate: LD_{50} : rat oral, 7200 mg/kg; i.p., 1310 mg/kg; s.c., 1848 mg/kg; i.v., 143 mg/kg; mouse oral, 8954 mg/kg; i.p., 1297 mg/kg; s.c., 1965 mg/kg; i.v., 194 mg/kg; dog oral, > 5 g/kg; i.v., 245 mg/kg; rabbit oral, 4090 mg/kg; i.v., 181 mg/kg.

Salt

Citrate

Examples

Alverine, betaine, butamirate, choline, chlorprothixene, clomifene, depropine, diethylcarbamazine, diphenhydramine,

Maleic Acid*(Z)-Butenedioic acid* $C_4H_4O_4$, M_r 116.07 pK_a

(1) 1.92 (A) (2) 6.23 (A)

Properties

M.p. 131 °C

Solubility (H_2O , g/100 g solution (temp. [°C])):
 28.2 (0), 34.6 (10), 41.1 (20), 44.3 (25), 47.5 (30),
 54.1 (40), 64.0 (60), 73.9 (80).

Safety, Toxicology

Acid: LD_{50} : mouse oral, 2400 mg/kg; rat oral,
 708 mg/kg.

Disodium salt: LD_{50} : rat oral, 3380 mg/kg.

Sodium salt: LD_{50} : i.p., 600 mg/kg; *TDLo*: rat oral,
 9 g/kg in 30 days.

In a drug-maleate study in dogs, acute tubular
 necrosis could be traced back to the maleate moiety
 corresponding to 9 mg/kg maleic acid (see *Remarks*).

Salt

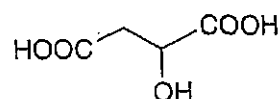
Maleate

Examples

Azatadine, brompheniramine, chlorpheniramine,
 dimetindene, enalapril, levomepromazine, lisuride,
 mepyramine, methylethergometrine, methysergide,
 midazolam, nomifensine, perhexiline, pheniramine,
 pirisudanol, prochlorperazine, thiethylperazine,
 timolol, trimebutine, trimipramine.

Remarks

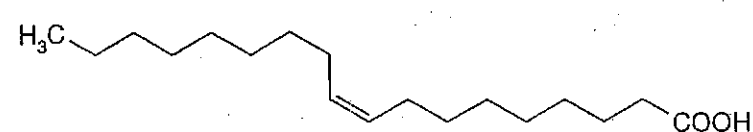
1. May potentially isomerize to fumaric acid.
2. In a recent report [23] maleic acid could be
 made responsible for acute tubular necrosis in
 dogs after a single peroral dose of a test
 substance supplied as a maleate (pravadoline
 maleate) corresponding to a dose of 9 mg/kg
 maleic acid.

(-)-L-Malic Acid $C_4H_6O_5$, M_r 134.09

Octadecanoic Acid (see *Stearic Acid*)

Oleic Acid

(*Z*)-Octadec-9-enoic acid



$C_{18}H_{34}O_2$, M_r 282.45

pK_a ~ 4 (25 °C)

Properties M.p. +4 °C

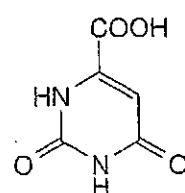
Safety, Toxicology Acid: LD_{50} : rat oral, 74 g/kg; i.v., 2400 mg/kg; mouse i.v., 230 mg/kg; i.p., 282 mg/kg.
Sodium salt: LD_{50} : mouse i.v., 152 mg/kg;
 $LDLo$: rabbit i.v., 150 mg/kg.

Salt, Ester Oleate

Use and Examples For esters. Only one salt known: morphine.

Orotic Acid

1,2,3,6-Tetrahydro-2,6-dioxypyrimidine-4-carboxylic acid, uracil-6-carboxylic acid



$C_5H_4N_2O_4$, M_r 156.10

pK_a (1) ~ 5.85 (A) (2) ~ 8.95 (A)

Properties Anh.: m.p. 345–346 °C.
Monohydrate: m.p. 334 °C.
Solubility: in H_2O : ~ 1.7 mg/ml.

Safety, Toxicology Mono-potassium salt: LD_{50} : rat oral, 10900 mg/kg.

Salt Orotate

Use and Examples Lysine, meclofenoxate.