HYDROXYCARBOXYLIC ACIDS

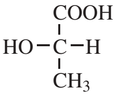
1. Lactic Acid

Lactic acid [50-21-5] (2-hydroxypropanoic acid), $CH_3CHOHCOOH$, is the most widely occurring hydroxycarboxylic acid and thus is the principal topic of this article. It was first discovered in 1780 by the Swedish chemist Scheele. Lactic acid is a naturally occurring organic acid that can be produced by fermentation or chemical synthesis. It is present in many foods both naturally or as a product of *in situ* microbial fermentation, as in sauerkraut, yogurt, buttermilk, sourdough breads, and many other fermented foods. Lactic acid is also a principal metabolic intermediate in most living organisms, from anaerobic prokaryotes to humans.

Although lactic acid is ubiquitous in nature and has been produced as a fermentation by-product in many industries (eg, corn steep liquor, a principal by-product of the multimillion-ton per year corn wet-milling industry, contains ~25 wt% lactic acid), it has not been a large-volume chemical. By 1990, its worldwide production volume had grown to ~40,000 t/year with two significant producers, CCA Biochem bv of the Netherlands, with subsidiaries in Brazil and Spain, and Sterling Chemicals, Inc. in Texas City, Texas, as the primary manufacturers (1). CCA used carbohydrate feedstocks and fermentation technology, and Sterling used a chemical technology. Thus lactic acid has been considered a relatively mature fine chemical in that only its use in new applications, eg, as a monomer in plastics or as an intermediate in the synthesis of high volume oxygenated chemicals, would cause a significant increase in its anticipated demand (1). By 2003, several major changes had occurred in the United States. Sterling exited the lactic acid business and two new manufacturers based on carbohydate fermentation technology, Archer Daniels Midland (ADM) and Cargill Dow (a joint venture between Dow Chemical company and Cargill corporation), entered the business. ADMs focus has been on lactic acid and its derivatives for conventional and other uses whereas Cargill Dow has been the primary leader in the lactic based polymer business. In the far east Mushashino has been reportedly manufacturing lactic acid by carbohydrate fermentation technology with Chinese partners. The current worldwide production (including polymer uses) is estimated to be ~100,000 t/year. Thus, in the last decade the lactic acid production has grown considerably, mainly due to the development of new uses, and the production technology is now primarily based on carbohydrate fermentation.

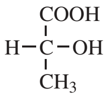
1.1. Physical Properties. Pure, anhydrous lactic acid is a white, crystalline solid with a low melting point. However, it is difficult to prepare the pure anhydrous form of lactic acid; generally, it is available as a dilute or concentrated aqueous solution. The properties of lactic acid and its derivatives have been reviewed (2). A few important physical and thermodynamic properties from this reference are summarized in Table 1.

Lactic acid is also the simplest hydroxy acid that is optically active. L (+)-Lactic acid [79-33-4] (**1**) occurs naturally in blood and in many fermentation products (3). The chemically produced lactic acid is a racemic mixture and some fermentations also produce the racemic mixture or an enantiomeric excess of D (−)-lactic acid [10326-41-7] (**2**) (4).



$$HO-\overset{\overset{\large COOH}{|}}{\underset{\underset{\large CH_3}{|}}{C}}-H$$

(1)



$$H-\overset{\overset{\large COOH}{|}}{\underset{\underset{\large CH_3}{|}}{C}}-OH$$

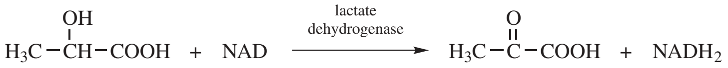
(2)

Many of the physical properties are not affected by the optical composition, with the important exception of the melting point of the crystalline acid, which is estimated to be 52.7–52.8°C for either optically pure isomer, whereas the reported melting point of the racemic mixture ranges from 17 to 33°C (2). The boiling point of anhydrous lactic acid has been reported by several authors; it was primarily obtained during fractionation of lactic acid from its self-esterification product, the dimer lactoyllactic acid [26811-96-1]. The difference between the boiling points of racemic and optically active isomers of lactic acid is probably very small (2). The uv spectra of lactic acid and dilactide [95-96-5], which is the cyclic anhydride from two lactic acid molecules, as expected show no chromophores at wavelengths >250 nm, and lactic acid and dilactide have extinction coefficients of 28 and 111 at 215 and 225 nm, respectively (5,6). The infrared (ir) spectra of lactic acid and its derivatives have been extensively studied and a summary is available (2).

1.2. Chemical Properties. Its two functional groups permit a wide variety of chemical reactions for lactic acid. The primary classes of these reactions are oxidation, reduction, condensation, and substitution at the alcohol group.

Oxidation. Lactic acid oxidation by strong oxidizing agents such as permanganate, chromate, hydrogen peroxide, or halogens under photochemical activation leads to the formation of a multitude of decomposition products, including varying amounts of pyruvate, acetaldehyde, acetate, carbon dioxide, etc . The yield and specificity of the products depend on the type of the oxidant and the reaction mechanism. The production of these oxidized products using lactic acid as a feedstock is not of potential commercial or synthetic interest.

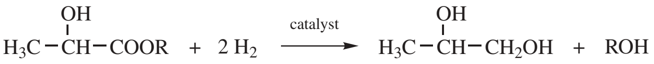
Biochemical oxidation of lactate to pyruvate by lactate dehydrogenase is a well-known enzymatic reaction in metabolic pathways.



$$H_3C-\overset{\overset{OH}{|}}{CH}-COOH + NAD \xrightarrow[\text{}]{\substack{\text{lactate}\\ \text{dehydrogenase}}} H_3C-\overset{\overset{O}{\|}}{C}-COOH + NADH_2$$

Reduction. Lactic acid has been reduced with hydrogen iodide to propionic acid (11). The carboxyl group can be reduced to an alcohol group by catalytic hydrogenolysis or by reduction with hydrogenating chemicals such as lithium aluminium hydride or sodium borohydride. Usually the esters of lactic acid have been converted to propylene glycol by reduction. When hydrogenating chemicals were used with optically active ester, the optical configuration was retained in the propylene glycol (12). Reportedly, in catalytic hydrogenolysis using copper chromite or Raney nickel, racemization occurred (13) and the propylene glycol was optically inactive.

Advances in catalysts and process engineering development have enabled the conversion of organic acids to corresponding alcohols with high selectivity and rates under moderate temperatures and pressure, thus improving the process economics (14,15). Using such processes for the conversion of lactate to propylene glycol [57-55-6] (**3**) could be an important industrial process in the future in the manufacture of large-volume industrial chemicals from fermentation of renewable carbohydrates (1,16).

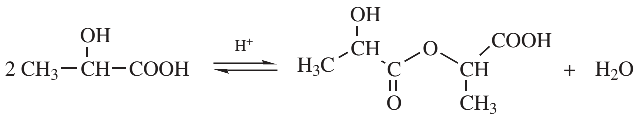


$$H_3C-\overset{OH}{CH}-COOR + 2\,H_2 \xrightarrow{\text{catalyst}} H_3C-\overset{OH}{CH}-CH_2OH + ROH$$

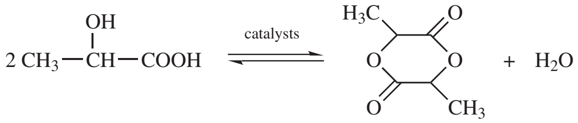
(**3**)

Condensation. A variety of condensation reactions involving the hydroxyl or the carboxyl or both groups occur with lactic acid. The important reactions where products can be obtained in high yields are esterification (both intramolecular and with another alcohol or acid), dehydration, and aminolysis.

Because lactic acid has both hydroxyl and carboxyl functional groups, it undergoes intramolecular or self-esterification and forms linear polyesters, lactoyllactic acid (**4**) and higher poly(lactic acid)s, or the cyclic dimer 3,6-dimethyl-*p*-dioxane-2,5-dione [95-96-5] (dilactide) (**5**). Whereas the linear polyesters, lactoyllactic acid and poly(lactic acid)s, are produced under typical condensation conditions such as by removal of water in the presence of acidic catalysts, the formation of dilactide with high yield and selectivity requires the use of special catalysts that are primarily weakly basic. The use of tin and zinc oxides and organostannates and -titanates has been reported (2,17–19).



(**4**)



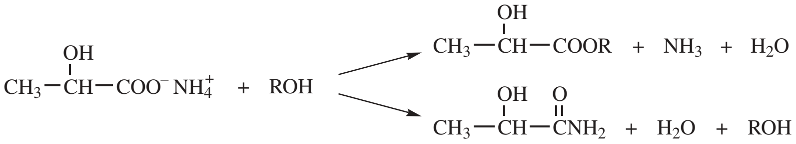
(**5**)

Dilactide exists as three stereoisomers, depending on the configurations of the lactic acid monomer used. The enantiomeric forms wherein the methyl groups are cis are formed from two identical lactic acid molecules, D- or L-, whereas the dilactide formed from a racemic mixture of lactic acid is the optically inactive meso form, with methyl groups trans. The physical properties of the enantiomeric dilactide differ from those of the meso form (2), as do the properties of the polymers and copolymers produced from the respective dilactide (19–21).

Polylactide is the generally accepted term for highly polymeric poly(lactic acid)s. Such polymers are usually produced by polymerization of dilactide; the polymerization of lactic acid as such does not produce high molecular weight polymers. The polymers produced from the enantiomeric lactides are highly crystalline, whereas those from the meso lactide are generally amorphous. Usually dilactide from L-lactic acid is preferred as a polymerization feedstock because of the availability of L-lactic acid by fermentation and for the desirable properties of the polymers for various applications (1,19,22).

Esterification of the carboxyl group is another important reaction that is used either to recover and purify lactic acid from impure solutions or to produce the ester as the desired end product. Several methods can be used to prepare lactic acid esters; the important ones are direct reaction with an alcohol, transesterification of one ester into another with alcohol, alcoholysis of ammonium lactate solution, and reaction of a metal lactate with an alkyl halide. Direct esterification is usually catalyzed by mineral acids such as sulfuric, hydrochloric, or phosphoric acids or *p*-toluenesulfonic acid/lactic acid reacts with excess alcohol under reflux and the water formed in the reaction is removed. With lower alcohols this method does not give satisfactory yields because the alcohol volatilizes instead of reacting. A more effective method has been to pass the vapors of alcohol through lactic acid previously heated to a temperature above the boiling point of the alcohol. This method is more efficient than the reflux still method and has been used for purification of lactic acid from impure streams such as fermentation broths (23,24). Transesterification is often used to prepare higher alcohol esters from methyl or ethyl lactate. Generally good yields ranging from 65 to 90% are obtained (2,25).

Ammonium lactate [34302-65-3] in concentrated aqueous solutions has been converted to ammonia and the ester by alcoholysis at temperatures ranging from 100–200°C using a variety of alcohols and water entrainers, such as toluene. Ester yields ranging from 50–60% were obtained. This method has also been suggested as a recovery and purification method from impure solutions of lactate (26). However, a considerable amount of the lactate is not converted to the recoverable ester and is lost as lactamide (**6**). In a recent patent, a process based on pervaporation assisted esterification of ammonium lactate to ethyl lactate is described. This process is being further developed with membranes that selectively permeate water vapor and ammonia over ethanol and the ester and thus provide good selectivity and yield (27).



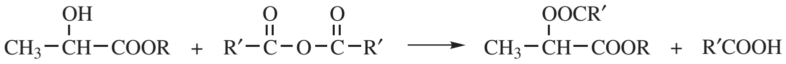
$$CH_3-\overset{OH}{\overset{|}{C}H}-COO^-NH_4^+ + ROH \rightarrow CH_3-\overset{OH}{\overset{|}{C}H}-COOR + NH_3 + H_2O$$

$$CH_3-\overset{OH}{\overset{|}{C}H}-C\overset{O}{\overset{\|}{}}NH_2 + H_2O + ROH$$

(**6**)

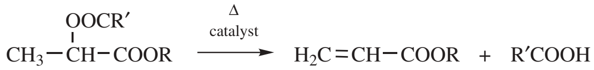
Reaction of a metal lactate (such as silver lactate) with an alkyl halide is a classic method of preparation of the ester, but it is too expensive to be of commercial relevance. Lactamide [2043-43-8] is another high yielding condensation product from lactic acid. It can be produced by aminolysis of dilactide or lactate ester such as methyl or ethyl lactate.

Substitution at the Alcohol Group. Acylation of the OH group by acylating agents such as acid chlorides or anhydrides is one of the important high yielding substitution reactions at the OH group of lactic acid and its functional derivatives. Aliphatic, aromatic, and other substituted derivatives can be produced.



$$CH_3-\overset{OH}{\overset{|}{C}H}-COOR + R'-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-R' \longrightarrow CH_3-\overset{OOCR'}{\overset{|}{C}H}-COOR + R'COOH$$

Several emulsifiers used in bakery and other food processing applications, such as stearoyl-2-lactylic acid and mono- and diglyceride derivatives are important commercial products produced by substitution reactions at the OH group. Upon pyrolysis of acylated esters, the corresponding acrylic acid ester (**7**) is produced with the simultaneous elimination of the acylating acid molecule. This reaction, when further developed and integrated with economical lactic acid production technology, could lead to economical process for acrylic acid manufacture (1,16).



$$CH_3-\overset{OOCR'}{\overset{|}{C}H}-COOR \xrightarrow{\overset{\Delta}{\text{catalyst}}} H_2C{=}CH-COOR + R'COOH$$

(**7**)

1.3. Manufacturing and Processing.

Lactic acid can be manufactured either by chemical synthesis or by carbohydrate fermentation; both are used for commercial production. In the United States, lactic acid was manufactured synthetically by Sterling Chemicals, Inc. using the lactonitrile route, but Sterling exited the business. In the far east, Musashino Chemical Co. uses this technology for some of its production. CCA Biochemical bv of the Netherlands uses carbohydrate fermentation technology in plants in Europe and Brazil and markets worldwide. Prior to 1991, the annual U.S. consumption of lactic acid was estimated at 18,500 t, with domestic production of ~8600 t by Sterling Chemical and the rest imported from Europe and Brazil. Worldwide consumption was estimated at ~40,000 t/year. By 2003, two new manufacturers based on carbohydate fermentation technology, Archer Daniels Midland (ADM) and Cargill Dow (a joint venture between Dow Chemical company and Cargill corporation), entered the business. ADMs focus has been on lactic acid and its derivatives for conventional and other uses, whereas Cargill Dow has been the primary leader in the lactic based polymer business. In the far east Mushashino has been reportedly manufacturing lactic acid by carbohydrate fermentation technology with Chinese partners. The current worldwide production (including polymer uses) is estimated to be ~100,000 t/year. Thus, in the last decade the lactic acid production has grown considerably, mainly due to the development of new uses, and the production technology is now primarily based on carbohydrate fermentation.

Chemical Synthesis. The commercial process is based on lactonitrile [78-97-7], which used to be a by-product of acrylonitrile synthesis. It involves base-catalyzed addition of hydrogen cyanide to acetaldehyde to produce lactonitrile (**8**). This is a liquid-phase reaction and occurs at atmospheric pressures. The crude lactonitrile is then recovered and purified by distillation and is hydrolyzed to lactic acid using either concentrated hydrochloric or sulfuric acid, producing the corresponding ammonium salt as a by-product. This crude lactic acid is esterified with methanol, producing methyl lactate. The latter is recovered and purified by distillation and hydrolyzed by water under acid catalysts to produce lactic acid, which is further concentrated, purified, and shipped under different product classifications, and methanol, which is recycled.

$$\mathrm{CH_3CHO} + \mathrm{HCN} \xrightarrow{\text{catalyst}} \mathrm{CH_3{-}CHOH{-}CN} \qquad (\mathbf{8})$$

$$\mathrm{CH_3CHOHCN} + 2\,\mathrm{H_2O} + 1/2\,\mathrm{H_2SO_4} \longrightarrow \mathrm{CH_3CHOHCOOH} + 1/2\,\mathrm{(NH_4)_2SO_4}$$

$$\mathrm{CH_3CHOHCOOH} + \mathrm{CH_3OH} \longrightarrow \mathrm{CH_3CHOHCOOCH_3} + \mathrm{H_2O}$$

$$\mathrm{CH_3CHOHCOOCH_3} + \mathrm{H_2O} \longrightarrow \mathrm{CH_3CHOHCOOH} + \mathrm{CH_3OH}$$

Other possible chemical synthesis routes for lactic acid include base-catalyzed degradation of sugars; oxidation of propylene glycol; reaction of acetaldehyde, carbon monoxide, and water at elevated temperatures and pressures; hydrolysis of chloropropionic acid (prepared by chlorination of propionic acid); nitric acid oxidation of propylene; etc. None of these routes has led to a technically and economically viable process (2).

Carbohydrate Fermentation. The existing commercial production processes use homolactic organisms such as *Lactobacillus delbrueckii, L. bulgaricus, and L. leichmanii*. Mutant fungal strains of *Aspergilus Niger* are also allegedly used. A wide variety of carbohydrate sources, eg, molasses, corn syrup, whey, dextrose, and cane or beet sugar, can be used. The use of a specific carbohydrate feedstock depends on the price, availability, and its purity. Proteinaceous and other complex nutrients required by the organisms are provided by corn steep liquor, yeast extract, soy hydrolysate, etc. Excess calcium hydroxide/carbonate is added to the fermenters to neutralize the acid maintaining the pH ~5 to 6, and produce a calcium salt of the acid in the broth. The fermentation is conducted batch or fedbatch wise, taking 2–4 days to complete, and lactate yields of ~90 wt% from a dextrose equivalent of carbohydrate are obtained. It is usually desired to keep the calcium lactate in solution so that it can be easily handled with the cell biomass and other insolubles, and the final concentration is 10 wt%. The calcium lactate-containing broth is filtered to remove cells, carbon-treated, evaporated, and acidified with sulfuric acid to convert the salt into lactic acid and insoluble calcium sulfate, which is removed by filtration. The filtrate can be further purified by carbon columns and ion exchange and evaporated to produce technical- grade lactic acid, but not a high purity, heat-stable product, which is required for the stearoyl lactylates, polymers, solvents and other value-added applications. For the high purity product, the technical grade lactic acid is esterified with methanol or ethanol and the ester is recovered by distillation, hydrolyzed by water, evaporated, and the alcohol recycled. This separation process produces a highly pure product which, like the synthetic product, is water-white and heat stable.

$$\mathrm{C_6H_{12}O_6} + \mathrm{Ca(OH)_2} \xrightarrow{\text{fermentation}} \mathrm{(CH_3CHOHCOO^-)_2Ca^{2+}} + 2\,\mathrm{H_2O}$$

$$\mathrm{(CH_3CHOHCOO^-)_2Ca^{2+}} + \mathrm{H_2SO_4} \longrightarrow 2\,\mathrm{CH_3CHOHCOOH} + \mathrm{CaSO_4}$$

Some of the economic hurdles and process cost centers of this conventional carbohydrate fermentation process, schematically shown in Figure , are in the complex separation steps that are needed to recover and purify the product from the crude fermentation broths. Furthermore, approximately a ton of crude gypsum, $CaSO_4$, a waste by-product is produced and needs to be disposed of for every ton of lactic acid produced by the conventional fermentation and recovery process . These factors have made large-scale production by this conventional route economically and ecologically unattractive.

The utilization of the purified lactic acid to produce polymers and other chemical intermediates requires the development and integration of catalytic chemical conversion process steps with the lactic acid production processes. In the past, little effort was devoted to developing efficient and potentially economical processes for such integrations because only small-volume, high margin specialty polymers for biomedical applications or specialty chemicals were the target products. Currently, several alternative process are being developed and process demonstrations are being attempted, to overcome this difficult technical and economic hurdle of the salt waste problem.

Advances in membrane-based separation and purification technologies, particularly in micro- and ultrafiltration and electrodialysis, have led to the inception of new processes for lactic acid production. These processes should, when developed and commercialized, lead to low cost production of lactic acid with reduction of nutrient needs, and without creating the by-product gypsum problem (29–33). Desalting electrodialysis requires low amounts of energy to recover, purify, and concentrate lactate salts from crude fermentation broths (29,30). Advances in water-splitting electrodialysis membranes enable the efficient production of protons and hydroxyl ions from water and can thus produce acid and base from a salt solution (31). Patents (29,30) describe an efficient and potentially economical process for lactic acid production and purification. Using an osmotolerant strain of lactic acid bacteria and a configuration of desalting electrodialysis, water-splitting electrodialysis, and ion-exchange purification steps, a concentrated lactic acid product containing $<0.1\%$ of proteinaceous impurities could be produced from a carbohydrate fermentation. The electric power requirement for the electrodialysis steps was approximately $1\text{kW}\cdot\text{h/kg}$ lactic acid. The process produces no by-product gypsum and only a small amount of by-product salt from the ion-exchange regeneration.

Ecochem, Inc., a Du Pont-Conagra partnership, had developed a recovery and purification process that produced a by-product ammonium salt instead of insoluble gypsum cake, and the company intended to sell this as a low cost fertilizer. A demonstration-scale plant based on whey feedstock had been completed to prove the process but the process was not successful due to several separations problems.

Cargill Dow, the primary developer of lactic polymer technology and products, has been developing an alternative process based on tertiary amine–carbonate technology (34). In this process sodium lactate is produced by fermentation and the broth is concentrated and extracted by a tertiary amine solvent mixture under CO_2 pressure to produce and precipitate a sodium bicarbonate salt and an amine lactic acid extract. This is back extracted with hot water at 140°C and 100 psig to produce a lactic acid solution and a regenerated amine solvent mixture that is recycled. The lactic acid can be further purified and converted to the dilactide for the polymer manufacture. The sodium bicarbonate is further heated to produce sodium carbonate and CO_2, which are recycled into the process. Cargill Dow has recently built a manufacturing plant for lactic polymers with a carbohydrate front end, but how much of this alternative lactic acid production technology is being used is not clear.

In a recent patent, a process based on pervaporation assisted esterification of ammonium lactate to ethyl lactate is described. This process is being further developed with membranes that selectively permeate water vapor and ammonia over ethanol and the ester, and thus provide good selectivity and yield (27). The aqueous ammonia can be recycled to the fermentor for neutralization of the acid produced, and the ester can be further purified by distillation. If successful, this technology could lead to an efficient and economical process to make purified lactate esters such as ethyl lactate that are useful an solvents and solvent blends and also make purified lactic acid for its variety of applications.

For the production of polymers or other derivatives, several advances in catalysts and process improvements have occurred, and proprietary technologies have been developed that may enable the commercialization of integrated processes for large-scale production in the future. In many patents issued to Cargill Inc. (19), the development of continuous processes for manufacture of lactide polymers with controlled optical purity from purified lactic acid is described. The processes use a configuration of multistage evaporation followed by polymerization to low molecular weight prepolymer which is then catalytically converted to dilactide and the purified dilactide is recovered in a distillation system with partial condensation and recycling. The dilactide can be used to make high mol wt polymers and copolymers. The process has been able to use fermentation-derived lactic acid, and the claimed ability to recycle and reuse the acid and prepolymers could make such a process very efficient and economical (19). In patents issued to Du Pont (35), processes to make cyclic esters, dilactide, and glycolide from their corresponding acid or prepolymer are described. This process uses an inert gas such as nitrogen to sweep away the cyclic esters from the reaction mass and then recovers and purifies the volatilized cyclic ester by scrubbing with an appropriate organic liquid, and separates the cyclic ester from the liquid by precipitation or crystallization and filtration of the solids. High purity lactide with minimal losses due to racemization has been claimed as a product in this process. Recycling and reuse of the lactic moiety in the various process streams have been claimed to be feasible (35). Currently, Cargill Dow is the leader in the lactic polymer technology and markets.

Hydrogenolysis reaction technology designed to produce alcohol from organic acids or esters has also advanced recently; new catalysts and processes give high selectivity and rates and operate at moderate pressures (14,15,36). This technology has been commercialized to produce 1,4-butanediol, tetrahydrofuran (THF), and other four-carbon chemical intermediates from maleic anhydride. In the future such technologies could be integrated with low cost lactic acid production processes to make propylene glycol and other intermediate chemicals (16).

1.4. Economic Aspects. The annual U.S. production of lactic acid in the decade spanning 1980–1990 ranged between 8000 and 9000 t, with only one producer, Sterling Chemicals Inc., manufacturing by chemical synthesis. The annual consumption increased from ~12,000 to ~18,500 t during this period. Thus, imports, primarily of fermentation-derived product from Europe or Brazil, supplied ~50% of the demand. The worldwide demand and production for the year 1990 was estimated to be ~40,000 t. The principal manufacturers were Sterling (synthetic, the United States), Musashino (synthetic, Japan), and CCA (fermentation: CSM (Holland); IQSF (Brazil); Ayuso (Spain)). Croda (fermentation, U.K.) and Benkeiser (fermentation, Germany) had discontinued their production. The price, which depended on the product grade, ranged from $2200 to $2500/t. Thus, since the early 1980s, lactic acid had been a mature fine chemical with growing but established markets and a few producers manufacturing in small plants with old technology.

By 2003, Sterling has exited the business and, two new manufacturers based on carbohydate fermentation technology, Archer Daniels Midland (ADM) and Cargill Dow (a joint venture between Dow Chemical company and Cargill corporation), entered the business. ADMs focus has been on lactic acid and its derivatives for conventional and other uses whereas Cargill Dow has been the primary leader in the lactic based polymer business. In the far east, Mushashino has been reportedly manufacturing lactic acid by carbohydrate fermentation technology with Chinese partners. The current worldwide production (including polymer uses) is estimated to be ~100,000 t/year. Thus, in the last decade the lactic acid production has grown considerably, mainly due to the development of new uses, and the production technology is now primarily based on carbohydrate fermentation and the current prices are ~$1500 ton.

In the future, the incentive for economical production of lactic acid will continue to come from the development of new, large-volume uses of lactic acid, particularly as feedstocks for biodegradable polymers, “Green” solvents and oxygenated chemicals (1,16). To meet these potential opportunities, efficiently integrated processes have to be developed and commercialized and integrated with large low cost production facilities for carbohydrate feedstocks.

1.5. Specifications, Quality Control, and Analytical Methods. Lactic acid is primarily sold as a *heat-stable fermentation product:* a highly refined, heat-stable product from esterification of fermentation-derived lactic acid, followed by hydrolysis of the recovered ester to produce the acid; Other categories include: *food grade fermentation,* which has been handled with food grade standards; *synthetic:* a highly purified product from a chemical synthesis process. It is water-white, has excellent heat stability, and can be used in both food and industrial applications; and *technical:* a crude product from either a synthetic or fermentation process, used in industrial applications where high purity is not required.

The products are generally sold in 50 and 88% concentrations. The food-grade product meets the *Food Chemicals Codex III* and the pharmaceutical grade meets the FCC and the *United States Pharmacopoeia XX* specifications (3). Other lactic acid derivatives such as salts and esters are also available in well-established product specifications. Standard analytical methods such as titration and liquid chromatography can be used to determine lactic acid, and other gravimetric and specific tests are used to detect impurities for the product specifications. A standard titration method neutralizes the acid with sodium hydroxide and then back-titrates the acid. An older standard quantitative method for determination of lactic acid was based on oxidation by potassium permanganate to acetaldehyde, which is absorbed in sodium bisulfite and titrated iodometrically.

Lactic acid is generally recognized as safe (GRAS) for multipurpose food use. Lactate salts such as calcium and sodium lactates and esters such as ethyl lactate used in pharmaceutical preparations are also considered safe and nontoxic (3). The U.S. Food and Drug Administration (FDA) lists lactic acid (all isomers) as GRAS and sets no limitations on its use in food other than current good manufacturing practice (37).

1.6. Uses. Traditionally, the principal use of lactic acid is in food and food-related applications, which in the United States accounted for ~85% of the demand. The rest (~15%) of the uses are for nonfood industrial applications. Currently, with the development and commercialization of the biopolymers lactic acid use has increased considerably and 20–30% of the 2003 production is estimated to be in these new applications. In the future, the growth of lactic acid is expected to continue to come from the development of new, large-volume uses of lactic acid, particularly as feedstocks for biodegradable polymers, ‘Green’ solvents and oxygenated chemicals.

As a food acidulant, lactic acid has a mild acidic taste, in contrast to other food acids. It is nonvolatile, odorless, and is classified GRAS for general-purpose food additives by the FDA in the United States and by other regulatory agencies elsewhere. It is a good preservative and pickling agent for sauerkraut, olives, and pickled vegetables. It is used as acidulant, flavoring, pH buffering agent, or inhibitor of bacterial spoilage in a wide variety of processed foods such as candy, breads and bakery products, soft drinks, soups, sherbets, dairy products, beer, jams and jellies, mayonnaise, processed eggs, and many other processed foods, often in conjunction with other acidulants (3). An emerging new use for lactic acid or its salts is in the disinfection and packaging of carcasses, particularly those of poultry and fish, where the addition of aqueous solutions of lactic acid and its salts during processing increase shelf life and reduce the growth of anaerobic spoilage organisms such as *Clostridium botulinum* (38,39).

A large fraction (>50%) of the lactic acid for food-related uses goes to produce emulsifying agents used in foods, particularly for bakery goods. The emulsifying agents are esters of lactate salts with longer chain fatty acids. Four important products are calcium and sodium stearoyl-2-lactylate [25383-99-7], glyceryl lactostearate [1338-10-9], and glyceryl lactopalmitate [1335-49-5]. Of the stearoyl lactylates, the calcium salt [5793-94-2] is a good dough conditioner and the sodium salt is both a conditioner and an emulsifier for yeast-leavened bakery products. The glycerates and palmitates are used in prepared cake mixes and other bakery products and in liquid shortenings. In prepared cake mixes, the palmitate improves cake texture, whereas the stearate increases cake volume and permits mixing tolerances (3). The manufacture of these emulsifiers requires heat-stable lactic acid; hence only the heat-stable fermentation grade is used for this application.

Technical-grade lactic acid has long been in use in the leather tanning industry as an acidulant for deliming hides and in vegetable tanning. In various textile-finishing operations and acid dying of wool, technical-grade lactic acid was used extensively. Cheaper inorganic acids are now more commonly used in these applications. The future availability of lower cost lactic acid and the increasing environmental restrictions on waste salt disposal may reopen these markets for lactic acid.

Traditionally, lactic acid is used in a wide variety of small-scale, specialized industrial applications where the functional speciality of the molecule is desirable. Examples include pH adjustment of hardening baths for cellophane used in food packaging, terminating agent for phenol–formaldehyde resins, alkyd resin modifier, solder flux, lithographic and textile printing developers, adhesive formulations, electroplating and electropolishing baths, and detergent builders (with maleic anhydride to form carboxymethoxysuccinic acid-type compounds). Owing to the high cost and low volume of production, these applications accounted for only 5–10% of the consumption of lactic acid (3).

Lactic acid and ethyl lactate [97-64-3] have long been used in pharmaceutical and cosmetic applications and formulations, particularly in topical ointments, lotions, parenteral solutions, and biodegradable polymers for medical applications such as surgical sutures (qv), controlled-release drugs, and prostheses. A substantial part of pharmaceutical lactic acid is used as the sodium salt [16595-31-6] for parenteral and dialysis applications. The calcium salt [5743-48-6] is widely used for calcium deficiency therapy and as an effective anticarries agent. As humectants in cosmetic applications, the lactates are often superior as natural products and more effective than polyols (3). Ethyl lactate is the active ingredient in many antiacne preparations. The use of the chirality of lactic acid for synthesis of drugs and agrochemicals is an opportunity for new applications for optically active lactic acid or its esters. The chiral synthesis routes to (*R*)-(+)-phenoxypropionic acid [1129-46-0] and its derivatives using (*S*)-(−)-lactate ester as a chiral synthon have been described (3). These compounds are used in herbicide production. Another use, as an optically active liquid crystal using lactic acid as a chiral synthon, has been described (40). These advances open new small-volume specialty chemical opportunities for optically active lactic acid and its derivatives.

Polymers of lactic acids are biodegradable thermoplastics that can be made from a variety of renewable carbohydrate resources. A fairly wide range of properties is obtainable by copolymerization with other functional monomers such as glycolide, caprolactone, polyether polyols, etc. The polymers are transparent, which is important for packaging applications. They offer good shelf life because they degrade slowly by hydrolysis that can be controlled by adjusting the composition and molecular weight. The properties of lactic copolymers which approach that of large-volume petroleum-derived polymers such as poly-styrene, flexible poly(vinyl chloride) (PVC), vinylidene chloride, etc, have been summarized (1). There are numerous patents and articles on lactic acid polymers and copolymers, their properties, potential uses, and processes, dating back to the early work by Carothers at Du Pont (1,41–44). Currently, Cargill Dow is the primary developer and commercializer of lactic acid based polymers and products,and a recent patent search showed that >100 U.S. patents in this area were assigned to this company.

Large-volume oxygenated chemicals such as propylene glycol (2000 U.S. production, 500,000 t), propylene oxide (2000 U.S. production, 2×10^6 t), acrylic acid and acrylate esters (2000 U.S. production, 700,000 t), and other chemical intermediates such as lactate ester plasticizers can potentially be made from lactic acid (1,16). The advances made in hydrogenolysis technology can be further developed and integrated to make propylene glycol from lactic acid in the future. Advances in catalysis and process technologies are needed for efficient conversion of lactate to acrylate, or propylene glycol to propylene oxide (qv), even though some of the early patents show the technical feasibility of such conversions (45–48).

Environmentally friendly 'Green' solvents is another growing area for lactic acid derivatives particularly lactate esters of low molecular weight alcohols such as ethyl, propyl, and butyl lactates. These esters and their blends with other biologically derived solvents such as fatty acid methyl esters or *d*-limonene can have a wide range of solvating and cleaning properties and significant future markets for a wide range of agricultural and industrial applications (49,50). The U.S. Environmental Protection Agency (EPA) recently Classified lactate esters, namely ethyl and butyl lactate as Class 4A inert ingredient for use in formulation of pesticides and other bioactive compounds. Class 4A designation is given to compounds that have demonstrated negligible toxicity and excellent environmental profile. Low molecular weight polymers of L-lactic acid having a degree of polymerization (DP) $2-10$ have plant growth promotion activity for a variety of crops and fruits when applied at a low level (51,52). These findings may lead to products and formulations that would incorporate L-poly(lactic acid) as or into controlled-release or degradable mulch films for large-scale agricultural applications. Thus in addition to its current applications lactic acid and its derivatives may also be used as a very large-volume polymer feedstock, 'green' solvents and chemical intermediate as new products and production technologies are deployed.

2. Hydroxyacetic Acid

Hydroxyacetic acid [79-14-1] (glycolic acid), $HOCH_2COOH$, is the first and simplest member of the family of hydroxycarboxylic acids. It occurs naturally as the chief acidic constituent of sugar-cane juice and also occurs in sugar beets and unripe grape juice. It was first synthesized in 1848 by reaction of glycine with nitrous acid, and it was characterized in 1851. It is widely used as a cleaning agent for a variety of industrial applications, and also as a specialty chemical and biodegradable copolymer feedstock (28,44).

Glycolic acid is a colorless, translucent solid; $mp = 10^\circ C$; $bp = 112^\circ C$; d at $25^\circ C = 1.26$ g/mL; K_a at $25^\circ C = 1.5 \times 10^{-4}$; pH at $25^\circ C = 0.5$; heat of combustion $= 697.1$ kJ/mol (166.6 kcal/mol); heat of solution $= -11.55$ kJ/mol; and flash point $>300^\circ$ C (53). Crystalline glycolic acid has unit space cell dimensions of $a = 0.8965$ nm, $b = 1.0563$ nm, $c = 0.7826$ nm, and $Z = 8$ with unit cell of $P2./c$. The crystal structure consists of a loose, three-dimensional (3D) H-bonded network of two closely similar but crystallographically distinct types of molecules.

Glycolic acid is soluble in water, methanol, ethanol, acetone, acetic acid, and ethyl acetate. It is slightly soluble in ethyl ether and sparingly soluble in hydrocarbon solvents.

Because it contains both a carboxyl and a primary hydroxyl group, glycolic acid can react as an acid or an alcohol or both. Thus some of the important reactions it can undergo are esterification, amidation, salt formation, and complexation with metal ions, which lead to many of its uses. As a fairly strong acid it can liberate gases (often toxic) when it reacts with the corresponding salts, eg, carbon dioxide from carbonates; hydrogen cyanide from cyanide salts; hydrogen sulfide from metal sulfides; chlorine from some active chlorine compounds such as hypochlorites, chlorinated isocyanurates, and chlorinated hydantoins; and hydrogen from some metals.

Direct esterification of the free acid or poly(glycolic acid) or transesterification of the methyl ester leads to the facile formation of alkyl esters. Esters of the hydroxyl group are readily prepared by reaction with the corresponding acid chloride. Self-esterification or dehydration is another important reaction; it occurs upon heating in concentrated solution with loss of water to form a mixture of the linear dimer carboxymethyl hydroxyacetate, $HOCH_2COOCH_2COOH$; cyclic dimer diglycolide (glycolide [502-97-6]); and polymeric polyglycolide (poly(hydroxyacetic acid) [26124-68-5]). Di- and polyglycolides are useful, low molecular weight, biodegradable polymers with several applications, and they are also copolymers with lactic acid polymers for biomedical applications and have potential for large-volume usage as biodegradable packaging polymers (1,53). *N*-Hydroxyacetamide can be prepared by reaction of ammonia with the polyacid or by reaction of an ester of glycolic acid with aqueous ammonium hydroxide. Substituted amines are prepared by the reaction of an amine with the acid.

Glycolic acid also undergoes reduction or hydrogenation with certain metals to form acetic acid, and oxidation by hydrogen peroxide in the presence of ferrous salts to form glyoxylic acid [298-12-4], HCOCOOH, and in the presence of ferric salts in neutral solution to form oxalic acid, HOOCCOOH; formic acid, HCOOH; and liberate CO_2 and H_2O. These reduction and oxidation reactions are not commercially significant.

Hydroxyacetic acid is produced commercially in the United States as an intermediate by the reaction of formaldehyde with carbon monoxide and water.

$$\mathrm{HCHO} + \mathrm{CO} + \mathrm{H_2O} \xrightarrow{\text{Catalyst}} \mathrm{HOCH_2{-}COOH}$$

Du Pont Chemicals is the primary manufacturer in the United States and Hoechst in Europe. Annual production is estimated to be ~10,000 t and selling prices range between \$1.40 and \$1.60/kg, depending on the product grade. Formaldehyde reacts with carbon monoxide in the presence of water and an acid catalyst such as HF; other mineral acids such as sulfuric, phosphoric, or hydrochloric; or acidic ion-exchange resins. The pressures and temperatures are believed to range between 10 and 50 MPa (100 and 500 atm) and 50 and 100°C, respectively; the actual conditions used in the process are not disclosed. The reaction mixture is purified by ion exchange, carbon treatment, and steam stripping to remove ionic, color, and volatile impurities, respectively.

From 1940 to ~1968, Du Pont produced ethylene glycol by a multistep glycolic acid, methanol, and formaldehyde route. Glycolic acid as the intermediate was esterified by methanol, methyl glycolate was then hydrogenated to produce ethylene glycol, and the methanol was recycled. This process was thought to be run at a 75,000-t/year scale but the advent of inexpensive ethylene and improved ethylene oxide processes made this process economically unattractive for ethylene glycol manufacture. Glycolic acid, however, is made by this route and prior manufacturing experience suggests that large-scale production of glycolic acid by this route is feasible should the demand for glycolic acid rise.

Other methods of production include hydrolysis of glycolonitrile [107-16-4] with an acid (eg, H_3PO_3 or H_2SO_3) having a pK_a of ~1.5–2.5 at temperatures between 100 and 150°C; glycolonitrile produced by reaction of formaldehyde with hydrogen cyanide; recovery from sugar juices; and hydrolysis of monohalogenated acetic acid. None of these has been commercially and economically attractive.

Hydroxyacetic acid is available in three grades: as a 70% technical aqueous solution; a 70% low sodium aqueous solution; or, in smaller quantities, in a 99+% pure crystalline form. The aqueous solutions are a clear, light amber liquid with a mild odor resembling burnt sugar. The specifications have been provided (53). The acid and the dimer (glycolide) are not regulated as hazardous materials, and the primary safety and handling precautions are based on their acidic nature. They are only slightly toxic by ingestion. The approximate oral LD_{50} is 4240 mg/kg for glycolic acid, and the approximate lethal dose for glycolide is 3400 mg/kg (oral, rats) (53).

The primary uses of hydroxyacetic acid are in cleaning and metal processing, with many other specialized applications in a variety of industries. It has many properties which make it an ideal hard-surface cleaner. It is nonvolatile and biodegradable, for safe, environmentally friendly use. Its hard water salts and iron oxide dissolution ability give it excellent cleaning characteristics. Its metal complexes are water soluble, providing superior rinsibility. Its use is compatible with most other acids and with cleansing compounds (eg, surfactants, glycol ethers, scents, and dyes), which leads to its use in a variety of cleaning formulations for superior performance.

In applications as hard surface cleaners of stainless steel boilers and process equipment, glycolic acid and formic acid mixtures are particularly advantageous because of effective removal of operational and preoperational deposits, absence of chlorides, low corrosion, freedom from organic iron precipitations, economy, and volatile decomposition products. Ammoniated glycolic acid in mixture with citric acid shows excellent dissolution of the oxides and salts and the corrosion rates are low.

Other cleaning applications are in cooling tower–heat exchanger scale build-up removal, well water light iron and carbonate scale removal, dairy equipment milkstone and other deposit removal, nonferrous metal cleaning formulations, food processing equipment, masonry, paper felt, and as a laundry sour in detergent formulations. Details of some of these cleaning applications are available (35). In metal processing, glycolic acid is used in a variety of applications in pickling, etching, electroplating, electropolishing, and brightening. In pickling operations, it is used to replace volatile organic acids and reduces losses and emissions at elevated temperatures. In etching, the soluble nature of its metal complexes is useful for prevention of unwanted precipitates. In electroplating (qv), the sodium and potassium glycolates are excellent substitutes for Rochelle salts in bath additives, and because glycolic acid forms complexes with virtually all multivalent metals, its salts are used in many electroplating baths, eg, chrome, lead, copper, nickel, cobalt, and tin. Electropolishing of stainless steel utilizes glycolic acid in combination with either phosphoric or sulfuric acids. The mixture gives a bath with long life and reduced sludging characteristics. Brightening of copper and copper alloys utilizes glycolic acid baths to enhance and retain luster.

Other specialized applications include biomedical uses, printed wire board flux, adhesives, textiles, hydrogen sulfide abatement, tanning, oil well acidification, and biodegradable polymers and copolymers (53). For biomedical applications, highly pure polymers of glycolic acid and lactic acid derived from the condensation polymerization of glycolide and lactide are used to manufacture bioabsorbable surgical sutures (qv), staples, and clips, sustained-release drug delivery systems, and implantable prosthetic devices. Some of the future applications of these polymers may be in the manufacture of larger volume biodegradable polymers for commercial consumer use as the production processes and economics become favorable (1,17,35). The low sodium grade of the acid is used as an intermediate flux in the electronic industry, as well as for cleaning and deoxidizing circuit boards before soldering.

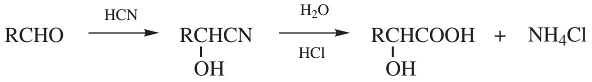
The ability of glycolic acid to react with casein to form cationic casein has been utilized in the manufacture of adhesives and textile sizing compounds. The FDA has given clearance for its use in food packaging adhesives (54). In the textile applications, glycolic acid has been used to acidify dye baths; complex metal ions present in bath water, rinse, etc; in dyeing of chrome colors; solvation of liquid cationic dye products; neutralization of fabric following alkaline treatments; and many other applications where the low volatility of the acid is useful. In the tanning process, glycolic acid is used to replace mineral acids where high quality leather is desired. It is used in the deliming operation to provide pH adjustment of the tanning liquor, where glycolic acid prevents staining of leather caused by the highly colored metal tanning salts.

A complex of glycolic acid with ferrous ion can catalyze the oxidation of hydrogen sulfide. This ability is used in the abatement of dissolved hydrogen sulfide in steam condensates from geothermal power generators. Glycolic acid and its low molecular weight polymers are used for oil well acidification, complexing with metals (especially iron) during cleaning operations, or water flooding. The easy degradability is advantageous for these applications.

3. Other Hydroxy Acids

Apart from lactic and hydroxyacetic acids, other α- and β-hydroxy acids have been small-volume specialty products produced in a variety of methods for specialized uses. γ-Butyrolactone [96-48-0], which is the monomeric inner ester of γ-hydroxybutyric acid [591-81-1], is a large-volume chemical derived from 1,4-butanediol (see ACETYLENE-DERIVED CHEMICALS) (1).

The general preparation of α-*hydroxy acids* is by the hydrolysis of an α-halo acid or by the acid hydrolysis of the cyanohydrins of an aldehyde or a ketone.

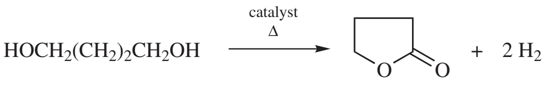


$$\mathrm{RCHO} \xrightarrow{\mathrm{HCN}} \underset{\mathrm{OH}}{\mathrm{RCHCN}} \xrightarrow[\mathrm{HCl}]{\mathrm{H_2O}} \underset{\mathrm{OH}}{\mathrm{RCHCOOH}} + \mathrm{NH_4Cl}$$

Aliphatic α-hydroxy acids that do not have side chains can be prepared in good yields by the hydrolysis of α-nitrato acids with aqueous sulfite solutions. The α-nitrato acids are obtained by the reaction of olefins and N_2O_4 in the presence of oxygen. The α-hydroxy acids that are obtained can be esterified or acylated directly to yield anhydro ester acids which, in turn, give the α-hydroxy acid on saponification. For example, 2-nitrooxyoctanoic acid, $C_6H_{13}CH(ONO_2)COOH$ (from 1-octene), is added to a solution of sodium sulfite (2.5mol/mol acid) at 60−90°C; it is then cooled and acidified. The organic layer yields 95% 2-hydroxyoctanoic acid [617-73-2], C_6H_{13} CHOHCOOH (mp, 55−65°C, saponification no. 354 and acid no. 320) (55).

β-*Hydroxy acids* may be made by catalytic reduction of β-keto esters followed by hydrolysis. β-Hydroxy acids can also be prepared by the Reformatsky reaction. This reaction is analogous to the Grignard reaction (qv). An aldehyde or ketone reacts with an α-haloester in the presence of activated zinc in anhydrous ethyl ether (56). Though ether is the commonly used solvent, benzene, toluene, xylene, or mixtures of these with ether, depending on the temperature of the reaction, may also be used. The reaction product is treated with an aqueous acid to hydrolyze the organozinc complex to produce the β-hydroxy ester. The organozinc compounds are considerably less reactive toward the carbonyl group than Grignard reagents. Thus the carbonyl groups that may be used include saturated and unsaturated aliphatic aldehydes, aromatic aldehydes, and aliphatic, aromatic, alicyclic, saturated, and unsaturated *ketones*. Among the halo esters, the α-bromo esters generally give the best results; α-chloro esters react slowly or not at all and the α-iodo esters are not commonly available. β-Hydroxypropionic acid [503-66-2] can be formed by the reaction of formaldehyde and lead tetraacetate trihydrate with catalytic amounts of pyridine and hydroquinone under pressure at 175°C for 2 h. After acidification with excess HCl, the reaction yields lead chloride and a red solution which, when extracted with a suitable solvent, produces the desired β-hydroxy acid (57).

γ-*Hydroxy acids* are seldom obtained in the free state because of the ease with which they form monomeric inner esters, which form stable five-membered rings. Thus the lactones of these acids are the common chemical forms and among these lactones γ-butyrolactone (**9**) is one of the larger volume specialty chemicals derived from dehydrogenation of 1,4-butanediol.



(**9**)

γ-Butyrolactone production in 1992 in the United States was estimated to be ~45,000 t/year; GAF Corp. and Du Pont were the primary manufacturers in their integrated acetylenic chemical manufacturing plants.

The common reactions that α-hydroxy acids undergo such as self- or bimolecular esterification to oligomers or cyclic esters, hydrogenation, oxidation, etc, have been discussed in connection with lactic and hydroxyacetic acid. A reaction that is of value for the synthesis of higher aldehydes is decarbonylation under boiling sulfuric acid with loss of water. Since one carbon atom is lost in the process, the series of reactions may be used for stepwise degradation of a carbon chain.

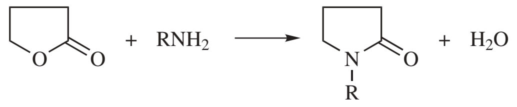
$$\mathrm{RCHOHCOOH} \xrightarrow{H^+} \mathrm{RCHOHC(OH)_2} \xrightarrow{-H_2O} \mathrm{RCHOHC^{+}O} \xrightarrow{-CO} \xrightarrow{H^+} \mathrm{RCHO}$$

β-Hydroxy acids lose water, especially in the presence of an acid catalyst, to give α,β-unsaturated acids, and frequently β,γ-unsaturated acids. β-Hydroxy acids do not form lactones readily because of the difficulty of four-membered ring formation. The simplest β-lactone, β-propiolactone, can be made from ketene and formaldehyde in the presence of methyl borate, but not from β-hydroxypropionic acid. β-Propiolactone [57-57-8] is a useful intermediate for organic synthesis but caution should be exercised when handling this lactone because it is a known carcinogen.

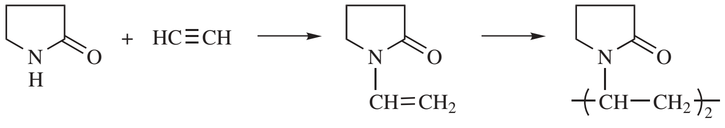
γ-Hydroxybutyric acid and its derivatives, particularly its sodium salt, have been studied and used as anesthetics, tranquilizers, sedatives, and hypnotics in surgery and general obstetrics. Some of the physicochemical properties, metabolism, toxicity, pharmacological and clinical aspects, and uses of γ-hydroxybutyric acid have been reviewed (58).

Certain bacterial species produce polymers of γ-hydroxybutyric acid and other hydroxyalkanoic acids as storage polymers. These are biodegradable polymers with some desirable properties for manufacture of biodegradable packaging materials, and considerable effort was devoted by ICI Ltd. and others to the development of bacterial fermentation processes to produce these polymers at a high molecular weight (59).

γ-Butyrolactone (**9**) undergoes amination reactions with methylamine or ammonia to produce *N*-methyl-2-pyrrolidinone [872-50-4] (NMP) (**10**, $R=CH_3$) or 2-pyrrolidinone [616-45-5] (PDO) (**10**, R=H), respectively, both of which are commercially important derivatives: NMP is a commercially important solvent used in lube oil and other solvent extractions and reaction solvents in the electronics industry; PDO reacts with acetylene to make *N*-vinylpyrrolidinone [88-12-0] (**11**), which is used to make poly(vinylpyrrolidinone) polymers (**12**) and copolymers for a number of commercial uses in cosmetics, hair spray, pharmaceutical formulations, germicides, and other consumer and industrial products (60).

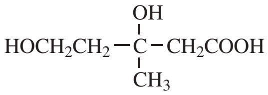


(**9**) (**10**)



(**11**) (**12**)

Other multifunctional hydroxycarboxylic acids are mevalonic and aldonic acids which can be prepared for specialized uses as aldol reaction products {mevalonic acid [150-97-0] (**13**)} and mild oxidation of aldoses (aldonic acids).



$$HOCH_2CH_2-\overset{\displaystyle OH}{\underset{\displaystyle CH_3}{C}}-CH_2COOH$$

(**13**)

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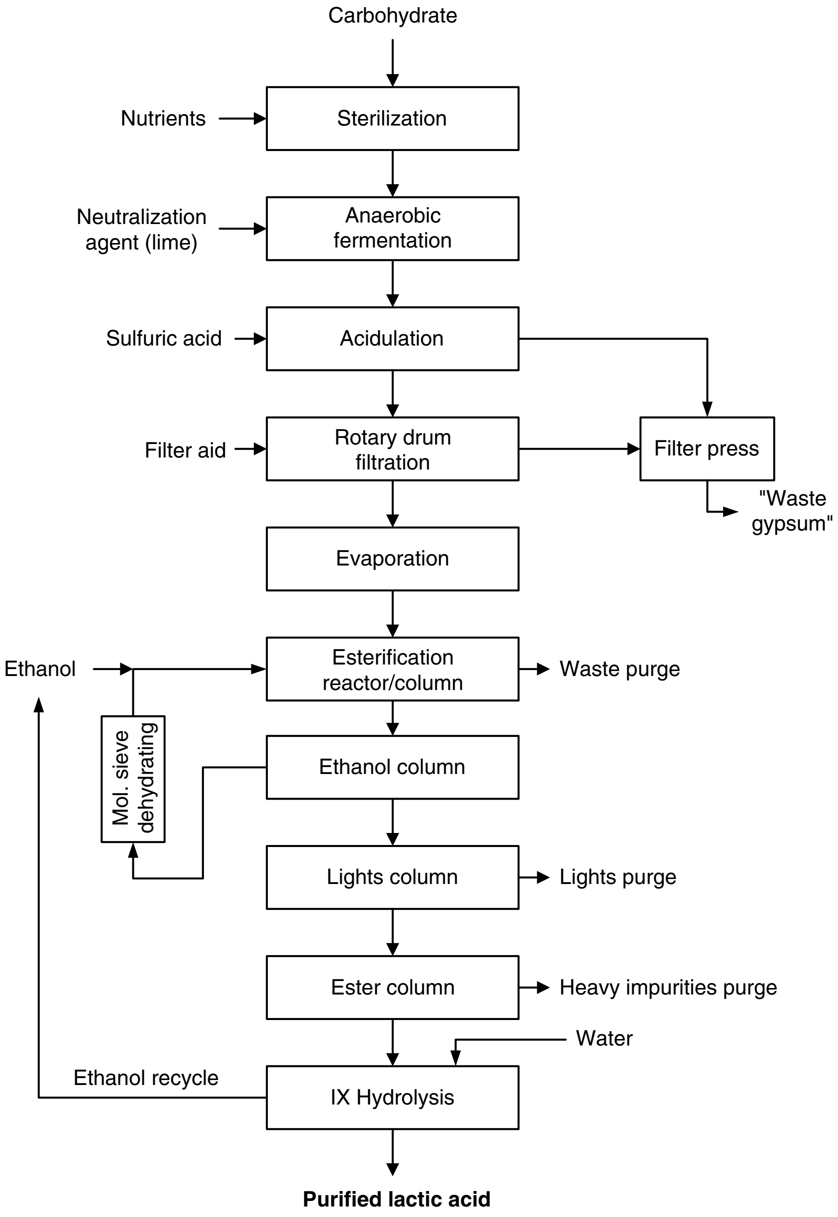

Fig. 1. Conventional process for lactic acid production from carbohydrate.

Table 1. **Physical and Thermodynamic Properties of Lactic Acid**

Property	Value
density, g/mL at 20°C	1.2243
viscosity,[a] mPa(=cP)	36.9
dissociation constant, pK_a at 25°C	3.862
heat capacity, J/(gK)[b]	
crystalline	1.41
liquid, 25°C	2.34
heat of dissociation at 25°C, J/mol[b]	−263
free energy of dissociation, kJ/mol[b]	20.9
heat of solution, L(+) at 25°C, kJ/mol[b]	7.79
heat of fusion, kJ/mol[b]	
racemic	11.33
L(+)	16.86
heat of combustion, MJ/mol[b]	
racemic	−1.355
L(+)	−1.343
heat of formation, MJ/mol[b]	
crystalline L(+)	−0.693
dilute solution	−0.686
free energy of formation, MJ/mol[b]	
crystalline L(+)	−0.522
liquid racemic	−0.529

[a] 88.6 wt% solution at 25°C.

[b] To convert J to cal, divide by 4.184.