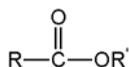


ESTERIFICATION

This article describes methods for the production of carboxylic esters:



For the properties of these compounds, see [ESTERS, ORGANIC](#). For esters of inorganic acids, see the articles on nitric acid, phosphoric acids, sulfuric acid, etc.

Esters are most commonly prepared by the reaction of a carboxylic acid and an alcohol with the elimination of water. Esters are also formed by a number of other reactions utilizing acid anhydrides, acid chlorides, amides, nitriles, unsaturated hydrocarbons, ethers, aldehydes, ketones, alcohols, and esters (via ester interchange). Detailed reviews of esterification are given in References 1–9.

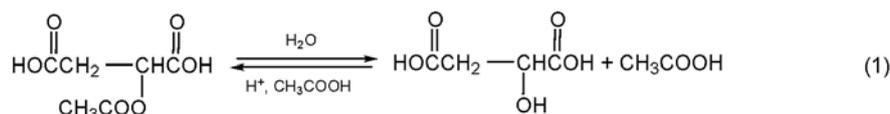
On the basis of bulk production (10), poly(ethylene terephthalate) manufacture is the most important ester producing process. This polymer is produced by either the direct esterification of terephthalic acid and ethylene glycol, or by the transesterification of dimethyl terephthalate with ethylene glycol. In 1990, poly(ethylene terephthalate) manufacture exceeded 3.47×10^6 t/yr (see [POLYESTERS](#)). Dimethyl terephthalate is produced by the direct esterification of terephthalic acid and methanol.

Other large-volume esters are vinyl acetate [108-05-4] (VAM, 1.15×10^6 t/yr), methyl methacrylate [80-62-6] (MMA, 0.54×10^6 t/yr), and dioctyl phthalate [117-81-7] (DOP, 0.14×10^6 t/yr). VAM (see [VINYL POLYMERS](#)) is produced for the most part by the vapor-phase oxidative acetoxylation of ethylene. MMA (see [METHACRYLIC POLYMERS](#)) and DOP (see [PHTHALIC ACIDS](#)) are produced by direct esterification techniques involving methacrylic acid and phthalic anhydride, respectively.

The acetates of most alcohols are also commercially available and have diverse uses. Because of their high solvent power, ethyl, isopropyl, butyl, isobutyl, amyl, and isoamyl acetates are used in cellulose nitrate and other lacquer-type coatings (see [CELLULOSE, ESTERS](#)). Butyl and hexyl acetates are excellent solvents for polyurethane coating systems (see [COATINGS; URETHANE POLYMERS](#)). Ethyl, isobutyl, amyl, and isoamyl acetates are frequently used as components in flavoring (see [FLAVORS AND SPICES](#)), and isopropyl, benzyl, octyl, geranyl, linalyl, and methyl acetates are important additives in [perfumes](#) (qv).

Reactions Between Organic Acids and Alcohols

In the esterification of organic acids with alcohols, it has been shown that in most cases under acid catalysis, the union is between acyl and alkoxy groups. Acid hydrolysis of acetoxy succinic acid gives malic acid with retention of configuration at the asymmetric carbon atom (11):



n-Amyl alcohol produced by basic hydrolysis of *n*-amyl acetate with ^{18}O -enriched water does not contain ^{18}O (12).

Effect of Structure. The rate at which different alcohols and acids are esterified as well as the extent of the equilibrium reaction are dependent on the structure of the molecule and types of functional substituents of the alcohols and acids. Specific data on rates of reaction, mechanisms, and extent of reaction are discussed in the following. More details concerning structural effects are given in References 6, 13–15.

In making acetate esters, the primary alcohols are esterified most rapidly and completely, ie, methanol gives the highest yield and the most rapid reaction. Ethyl, *n*-propyl, and *n*-butyl alcohols react with about equal velocities and conversions. Under the same conditions, the secondary alcohols react much more slowly and afford lower conversions to ester products; however, wide variations are observed among the different members of this series. The tertiary alcohols react slowly, and the conversions are generally low (1–10% conversion at equilibrium). With isobutyl alcohol at 155°C, acids containing a straight-chain (acetic, propionic, and butyric) and phenylacetic and β -phenylpropionic acids are esterified readily. Formic acid has the highest initial rate of reaction. The introduction of a branched chain in the acid decreases the rate of esterification, and two branches cause a still greater retarding effect. However, the conversions to ester products from these substituted acids is higher than for the normal straight-chain acids. Similarly, aromatic acids, benzoic and *p*-toluic, react slowly but have high equilibrium conversions.

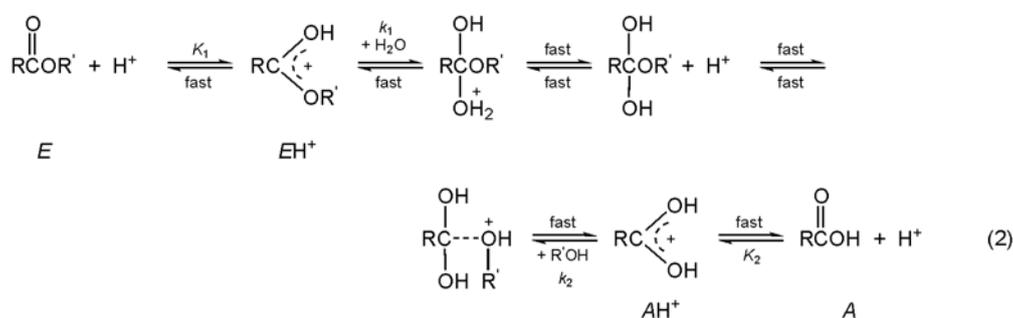
The introduction of a nitrile group on an aliphatic acid has a pronounced inhibiting effect on the rate of esterification. With the chloroacetic acids, the velocity decreases with increased chlorination. Double bonds also have a retarding influence on the rate of esterification. Tests on substituted acrylic acids have shown that α,β -unsaturated acids are esterified much less easily than the saturated analogues. A triple bond in the α,β position has about the same effect as a double bond. A β,γ -double bond has less of a

retarding action. If the double bond is sufficiently removed, as in erucic and brassidic acids (see [CARBOXYLIC ACIDS](#)), no effect is noted. Conjugated double bonds, when one is in the α,β -position, afford a great retarding effect. Cis-substituted unsaturated acids esterify more slowly than the trans isomers.

In the preparation of ethyl esters using anhydrous ethyl alcohol and hydrogen chloride catalyst, the rate of esterification of straight-chain fatty acids from propionic through stearic is substantially constant: branching of the fatty acid chain causes retardation. In the saturated dibasic acids, the rate of esterification is a maximum at glutaric acid. The ease of esterification of the cycloparaffin monocarboxylic acids increases in the order C3, C7, C6, C5, and C4 rings; with the exception of cyclopropanecarboxylic acid, these are esterified more rapidly than the corresponding open-chain acids.

Substitutions that displace electrons toward the carboxyl group of aromatic acids diminish the rate of the reaction (16). The substitution of fluoromethoxy or ethoxy groups in the ortho position has an accelerating action, whereas iodo, bromo, nitro, or methyl groups produce retardation. The influence of groups in the meta and para positions is not nearly so marked (17).

Kinetic Considerations. Extensive kinetic and mechanistic studies have been made on the esterification of carboxylic acids since Berthelot and Saint-Gilles first studied the esterification of acetic acid (18). Although ester hydrolysis is catalyzed by both hydrogen and hydroxide ions (19,20), a base-catalyzed esterification is not known. A number of mechanisms for acid- and base-catalyzed esterification have been proposed (4). One possible mechanism for the bimolecular acid-catalyzed ester hydrolysis and esterification is shown in equation 2 (6).



This mechanism leads to the rate equation (eq. 3) for hydrolysis and to an analogous expression for the esterification (13):

$$-\frac{d[E]}{dt} = \frac{k_1 K_1 [E] [H_2O] [H^+]}{1 + \alpha} - \frac{k_2 K_2 [A] [R'OH] [H^+]}{1 + 1/\alpha} \quad (3)$$

In this expression, α depends on those rate coefficients in the above mechanism whose values are assumed to be high. Other mechanisms for the acid hydrolysis and esterification differ mainly with respect to the number of participating water molecules and possible intermediates (21–23).

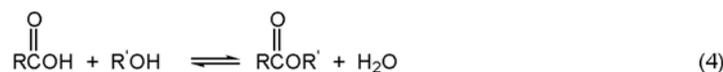
Applications of kinetic principles to industrial reactions are often useful. Initial kinetic studies of the esterification reaction are usually conducted on a small scale in a well stirred batch reactor (24). In many cases, results from batch studies can be used in the evaluation of the esterification reaction in a continuous operating configuration. Generally, the rate of esterification with acid catalyst is proportional to the acid or hydrogen ion concentration as well as the concentration of the alcohols and organic acid. The effect of temperature on the reaction rate is given by the well known Arrhenius equation. These factors are interrelated, and may be used to predict optimum operational conditions for the production of a given ester if the necessary data are available, ie, the order of the reaction under the conditions to be used, a mathematical relation describing the yield with time, and an empirical equation relating the reaction rate constant with temperature, catalyst concentration, and proportions of reactants.

With these kinetic data and a knowledge of the reactor configuration, the development of a computer simulation model of the esterification reaction is invaluable for optimizing esterification reaction operation (25–28). However, all esterification reactions do not necessarily permit straightforward mathematical treatment. In a study of the esterification of 2,3-butanediol and acetic acid using sulfuric acid catalyst, it was found that the reaction occurs through two pairs of consecutive reversible reactions of approximately equal speeds. These reactions do not conform to any simple first-, second-, or third-order equation, even in the early stages (29).

In a study of the kinetics of the reaction of 1-butanol with acetic acid at 0–120°C, an empirical equation was developed that permits estimation of the value of the rate constant with a deviation of 15.3% from the molar ratio of reactants, catalyst concentration, and temperature (30). This study was conducted using sulfuric acid as catalyst with a mole ratio of 1-butanol to acetic acid of 3:19.6, and a catalyst concentration of 0–0.14 wt %.

Similar studies have been performed on the formation of mono *n*-butyl phthalate at 80–150°C with sulfuric acid catalyst (31). The reaction of phthalic anhydride with mono *n*-butyl phthalate to afford di *n*-butyl phthalate is complete in 10 min at 100°C with 1 wt % catalyst.

Equilibrium Constants. The reaction between an organic acid and an alcohol to produce an ester and water is expressed in equation 4:



This was first demonstrated in 1862 by Berthelot and Saint-Gilles (32), who found that when equivalent quantities of ethyl alcohol and acetic acid were allowed to react, the esterification stopped when two-thirds of the acid had reacted. Similarly, when equal molar proportions of ethyl acetate and water were heated together, hydrolysis of the ester stopped when about one-third of the ester was hydrolyzed. By varying the molar ratios of alcohol to acid, yields of ester >66% were obtained by displacement of the equilibrium. The results of these tests were in accordance with the mass action law shown in equation 5.

$$K = [\text{ester}] [\text{water}] / [\text{acid}] [\text{alcohol}] \quad (5)$$

However, in many cases the equilibrium constant is affected by the proportion of reactants (7,33,34). The temperature as well as the presence of salts may also affect the value of the equilibrium constant (35,36).

The effect of water on the equilibrium constant for the reaction of 1 mol of ethanol, 1 mol of acetic acid, and 23 moles of water has been investigated. This mixture has an equilibrium constant of 3.56, compared with 3.79 for the reaction with anhydrous materials (7,37).

Theoretical yields of ester obtainable with proportions of reactants are shown in Figure 1 for four values of the equilibrium constant. Thus when K equals 10 (esters of *p*-toluic acid with primary alcohols), with equivalent amounts of acid and alcohol, a yield of about 76% may be expected.

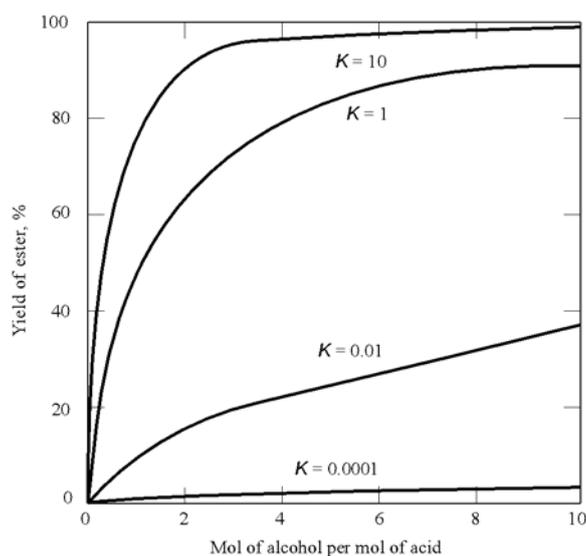


Fig. 1. Theoretical yields of ester obtainable with varying proportions of reactants for different values of equilibrium constant.

In general, esters having equilibrium constants below unity are not prepared by direct interaction of alcohol and acid; in these cases, the acid anhydrides or acid chlorides are used, since the equilibrium favors the ester product.

Completion of Esterification. Because the esterification of an alcohol and an organic acid involves a reversible equilibrium, these reactions usually do not go to completion. Conversions approaching 100% can often be achieved by removing one of the products formed, either the ester or the water, provided the esterification reaction is equilibrium limited and not rate limited. A variety of distillation methods can be applied to afford ester and water product removal from the esterification reaction (see **DISTILLATION**). Other methods such as reactive extraction and reverse osmosis can be used to remove the esterification products to maximize the reaction conversion (38). In general, esterifications are divided into three broad classes, depending on the volatility of the esters:

- (1) Esters of high volatility, such as methyl formate, methyl acetate, and ethyl formate, have lower boiling points than those of the corresponding alcohols, and therefore can be readily removed from the reaction mixture by distillation.
- (2) Esters of medium volatility are capable of removing the water formed by distillation. Examples are propyl, butyl, and amyl formates, ethyl, propyl, butyl, and amyl acetates, and the methyl and ethyl esters of propionic, butyric, and valeric acids. In some cases, ternary azeotropic mixtures of alcohol, ester, and water are formed. This group is capable of further subdivision: with ethyl acetate, all of the ester is removed as a vapor mixture with alcohol and part of the water, while the balance of the water accumulates in the system. With butyl acetate, on the other hand, all of the water formed is removed overhead with part of the ester and alcohol, and the balance of the ester accumulates as a high boiler in the system.

(3) Esters of low volatility are accessible via several types of esterification. In the case of esters of butyl and amyl alcohols, water is removed as a binary azeotropic mixture with the alcohol. To produce esters of the lower alcohols (methyl, ethyl, propyl), it may be necessary to add a hydrocarbon such as benzene or toluene to increase the amount of distilled water. With high boiling alcohols, ie, benzyl, furfuryl, and β -phenylethyl, an accessory azeotroping liquid is useful to eliminate the water by distillation.

Use of Azeotropes to Remove Water. With the aliphatic alcohols and esters of medium volatility, a variety of azeotropes is encountered on distillation (see [DISTILLATION, AZEOTROPIC AND EXTRACTIVE](#)). Removal of these azeotropes from the esterification reaction mixture drives the equilibrium in favor of the ester product (39).

Binary azeotropes may be formed between the alcohol and water, the alcohol and ester, and the ester and water. Ternary azeotropes involving the alcohol, ester, and water are also possible. In general, the ternary azeotropes have the lowest boiling points, but the differences between the boiling points of the various combinations in some instances are very small. The ester–water binaries have boiling points close to those of the ternary mixtures. An extremely efficient fractionating column is usually required to obtain a pure ternary azeotrope. Binary azeotropes of the alcohol and water may be utilized in the preparation of the higher boiling, nonvolatile esters for completion of the reaction (39). Almost all of the alcohols (up to C₂₀-alcohols) except methanol form binary azeotropes with water. The azeotropes formed by water with ethyl, *n*-propyl, isopropyl, allyl, and *tert*-butyl alcohols are single phase, ie, on condensation of the vapor, the components are completely miscible. Other means to eliminate water are often necessary: extraction of the ester with a water-insoluble solvent, eg, benzene, cyclohexane, or carbon tetrachloride; reactive distillation; drying with potassium carbonate; or salting out. The higher alcohols form azeotropes that on condensation separate into two liquid phases; in such a case, the alcohol-rich phase can be separated by further distillation into azeotrope and pure alcohol, and the water-rich phase into azeotrope and water. Under certain conditions, entraining gases are used to facilitate the removal of water (40).

Use of Desiccants and Chemical Means to Remove Water. Another means to remove the water of esterification is calcium carbide supported in a thimble of a continuous extractor through which the condensed vapor from the esterification mixture is percolated (41) (see [CARBIDES](#)). A column of activated bauxite (Florite) mounted over the reaction vessel has been used to remove the water of reaction from the vapor by adsorption (42).

Catalysts. The choice of the proper catalyst for an esterification reaction is dependent on several factors (43–46). The most common catalysts used are strong mineral acids such as sulfuric and hydrochloric acids. Lewis acids such as boron trifluoride, tin and zinc salts, aluminum halides, and organo–titanates have been used. Cation-exchange resins and zeolites are often employed also.

In laboratory preparations, sulfuric acid and hydrochloric acid have classically been used as esterification catalysts. However, formation of alkyl chlorides or dehydration, isomerization, or polymerization side reactions may result. Sulfonic acids, such as benzenesulfonic acid, *p*-toluenesulfonic acid, or methanesulfonic acid, are widely used in plant operations because of their less corrosive nature. Phosphoric acid is sometimes employed, but it leads to rather slow reactions. Soluble or supported metal salts minimize side reactions but usually require higher temperatures than strong acids.

Acid-Regenerated Cation Exchangers. The use of acid-regenerated cation resin exchangers (see [ION EXCHANGE](#)) as catalysts for effecting esterification offers distinct advantages over conventional methods. Several types of cation-exchange resins can be used as solid catalysts for esterification (47,48). In general, the strongly acidic sulfonated resins comprised of copolymers of styrene, ethylvinylbenzene, and divinylbenzene are used most widely. With the continued improvement of ion-exchange resins, such as the macroporous sulfonated resins, esterification has become one of the most fertile areas for use of these solid catalysts. With low molecular weight acids and alcohols, in most cases the resin structure has minimal effect on the yield or kinetics of the esterification as long as the catalyst contains strongly acidic groups. The kinetics in batch and tubular reactors of the esterification of 1-butanol with acetic acid catalyzed by a macroporous sulfonated polystyrene exchange resin have been studied. The catalytic activity was dependent on the water content of the resin and the rate determining step is the surface reaction of the chemisorbed acid and adsorbed alcohol (49).

Despite the higher cost compared with ordinary catalysts, such as sulfuric or hydrochloric acid, the cation exchangers present several features that make their use economical. The ability to use these agents in a fixed-bed reactor operation makes them attractive for a continuous process (50,51). Cation-exchange catalysts can be used also in continuous stirred tank reactor (CSTR) operation.

The resin (Amberlite IR-116 and Amberlite IR-120B) catalyzed continuous esterification of butanol or 2-ethylhexanol with acrylic acid is a novel example. High conversion and selectivity to the acrylate ester are accomplished. The CSTR in this application has advantage over a fixed-bed configuration since water separation from the higher boiling ester product in the reactor is more rapid, and this leads to a higher conversion with fewer by-products. The type of exchange resin also affects the esterification. The degree of cross-linking, porosity, and surface area of the strongly acid cation-exchange resin in combination with the back-mixed reactor design are critical factors to minimize secondary by-product formation and polymeric fouling of the resin catalyst (46).

The esterification of *n*-butyl alcohol and oleic acid with a phenol–formaldehydesulfonic acid resin (similar to amberlite IR-100) is essentially second order after an initial slow period (52). The velocity constant is directly proportional to the surface area of the catalyst per unit weight of reactants.

A series of tests using Amberlite IR-12 (sulfonated polystyrene resin) to esterify diethylene glycol (DEG) using toluene as the entrainer for removal of water gave the results in Table 1 (53).

Table 1. Tests Using Amberlite IR-120 to Esterify Diethylene Glycol (DEG)

Acid	DEG, mol/mol acid	IR-120, g/100 g acid	Temp, °C	Reaction time, h	Monoester, % conv	Diester, % conv
lauric	1	7.5	140	18	24	71
lauric	4	15.5	130	10	71	21
lauric	6	7.5	140	18	86	11
lauric	12	15.0	132	18	100	
oleic	12	10.6	140	18	100	
stearic	12	8.9	150	18	100	
benzoic	2	24.6	140	4	75	

Recovery of dilute acetic acid is achieved by esterification with methanol using a sulfonated resin (Dowex 50w) in a packed distillation column (54). Pure methyl acetate is obtained. This reaction is second order in acetic acid, zero order in methanol, and partially diffusion controlled.

Batch Esterification

Ethyl Acetate. A typical plant configuration for production of ethyl acetate [141-78-6] as a low boiling overhead product relative to water is shown in Figure 2 (2). The esterification reactor is a cylindrical tank, or still pot, heated by a closed-coil steam pipe. The reactor is charged with acetic acid, 95% ethanol, and concentrated sulfuric acid. The temperature at the top of the fractionating column is maintained at ca 70°C to give a ternary azeotropic mixture of ca 83% ethyl acetate, 9% alcohol, and 8% water. The vapor is condensed, part of it is returned to the top plate of the column as reflux, and the remainder is drawn off to storage. The ternary azeotrope (production-grade ethyl acetate) is satisfactory for many commercial purposes, but for an alcohol-free and water-free ester, further purification is needed.

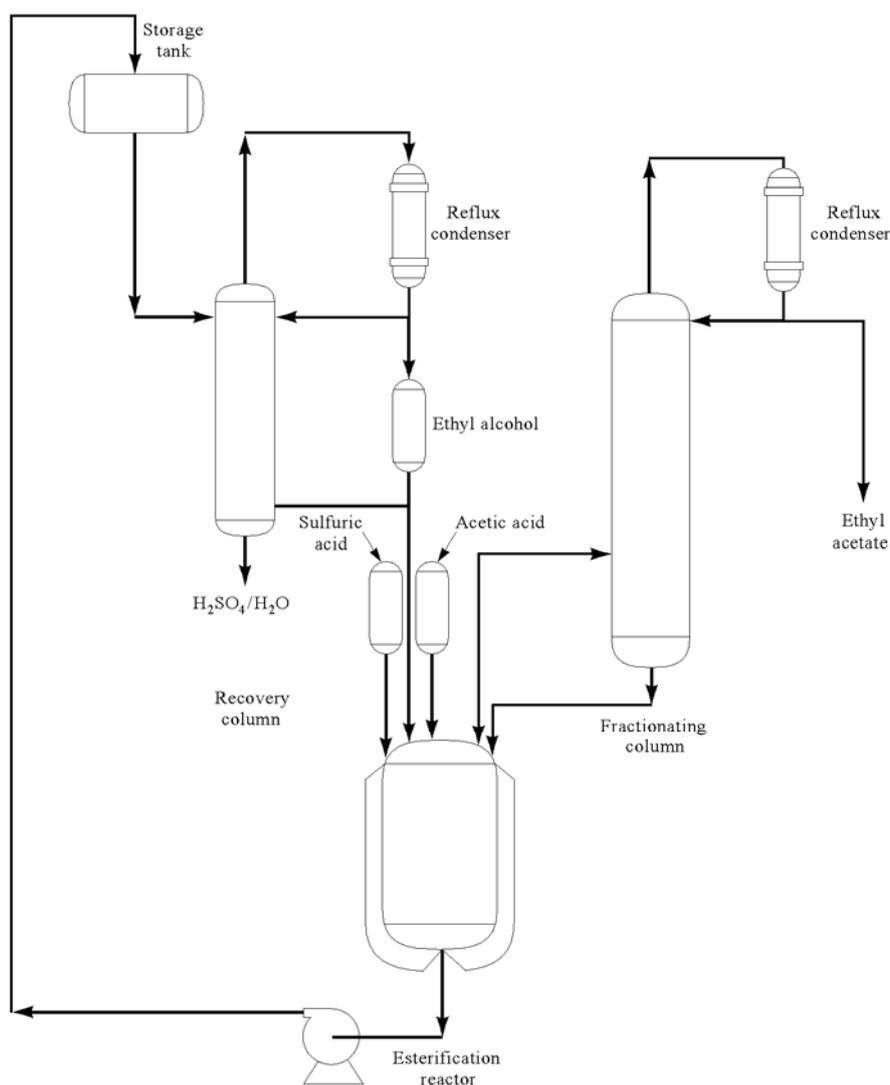
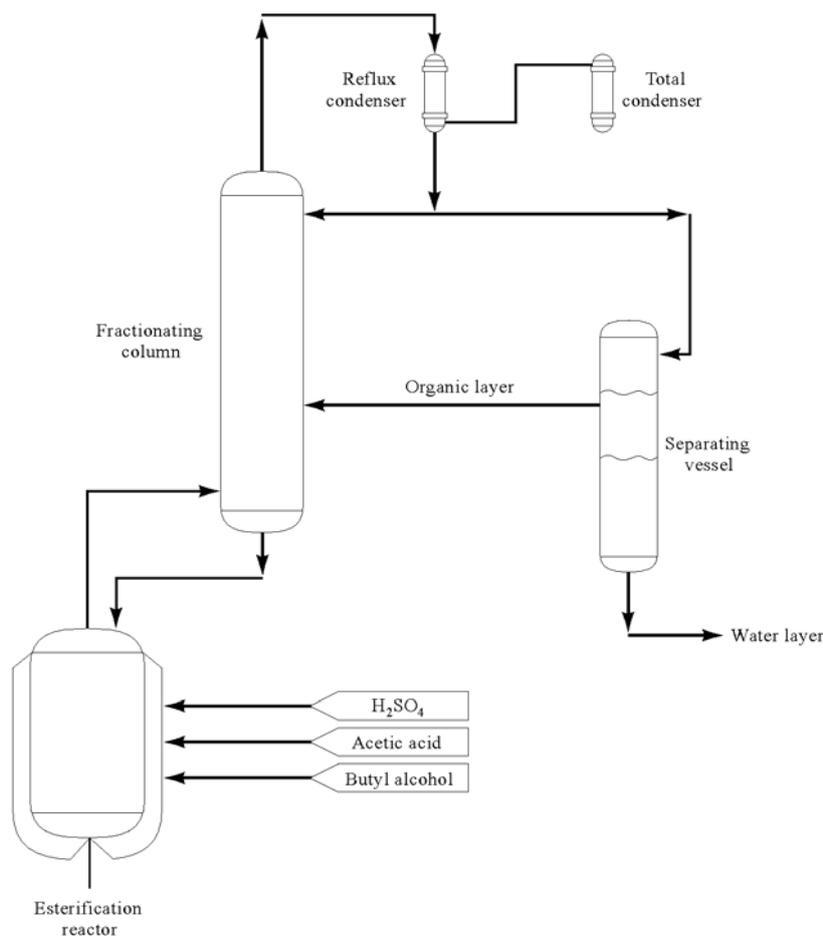


Fig. 2. Batch ethyl acetate process (2).

***n*-Butyl Acetate.** Equipment used for the batch esterification to give butyl acetate [123-86-4] is shown in Figure 3. Glacial acetic acid is mixed with an excess of butyl alcohol and a small amount of concentrated sulfuric acid in the esterification reactor. The mixture is heated for several hours by means of a steam jacket to give esterification equilibrium. After the preliminary heating, slow rectification is permitted to remove the water already formed and thus increase the yield. The esterification is continued until no more water separates. At this point, the temperature at the top of the column rises, and the percentage of acetic acid in the distillate increases. It is necessary to neutralize the small amount of acid remaining in the esterification reactor before further distillation. A solution of sodium hydroxide is added to the esterification reactor, and the mixture is allowed to stand to form a water layer that is removed. The organic ester layer (upper layer) is then washed with water and distilled to obtain an overhead butyl acetate product of 75–85% purity; the remainder is butyl alcohol.

Fig. 3. Batch *n*-butyl acetate process (2).

Continuous Esterification

The law of mass action, the laws of kinetics, and the laws of distillation all operate simultaneously in a process of this type. Esterification can occur only when the concentrations of the acid and alcohol are in excess of equilibrium values; otherwise, hydrolysis must occur. The equations governing the rate of the reaction and the variation of the rate constant (as a function of such variables as temperature, catalyst strength, and proportion of reactants) describe the kinetics of the liquid-phase reaction. The usual distillation laws must be modified, since most esterifications are somewhat exothermic and reaction is occurring on each plate. Since these kinetic considerations are superimposed on distillation operations, each plate must be treated separately by successive calculations after the extent of conversion has been determined (see [DISTILLATION](#)).

Continuous esterification of acetic acid in an excess of *n*-butyl alcohol with sulfuric acid catalyst using a four-plate single bubblecap column with reboiler has been studied (55). The rate constant and the theoretical extent of reaction were calculated for each plate, based on plate composition and on the total incoming material to the plate. Good agreement with the analytical data was obtained.

A continuous distillation process has been studied for the production of high boiling esters from intermediate boiling polyhydric alcohols and low boiling monocarboxylic aliphatic or aromatic acids (56). The water of reaction and some of the organic acid were continuously removed from the base of the column.

Methyl Acetate. High purity methyl acetate [79-20-9] is required for the rhodium catalyzed carbonylation process to produce acetic anhydride (57). In the most recently developed commercial process for the manufacture of high purity methyl acetate, acetic acid functions both as a reactant and as an extractant in a countercurrent reactive distillation column (58,59), thereby alleviating the problem of azeotrope formation. This methyl acetate purification process obviates the use of additional vacuum or extractive distillation means to separate methyl acetate from its low boiling water and methanol azeotropes (60,61). As shown in Figure 4, this process uniquely demonstrates the use of reactive distillation as a means to produce essentially dry methyl acetate. The esterification reaction catalyzed by sulfuric acid occurs in the middle of the column. Acetic acid is fed to the top portion of the reactor section, and the methanol is fed to the lower portion of the reactor section. The countercurrent flow of acetic acid and methyl acetate with its azeotropes is used to remove water and by-products from methyl acetate. Below the acetic acid feed and above the reaction section, water and some methanol are extracted from methyl acetate using acetic acid. Acetic acid and methyl acetate are then separated above the acetic acid feed in the rectification portion of the column. High purity methyl acetate (at least 99.5 wt % methyl acetate) is isolated from the column overhead. The catalyst and impurities (primarily methyl propionate and isopropyl acetate) are removed from the reactor section by a sidedraw. Methanol in turn is stripped from the water in the lower portion of the column below the methanol feed. The impurities are further concentrated and removed from the process in two distillation columns with catalyst and acetic acid being recycled back to the reactive distillation column.

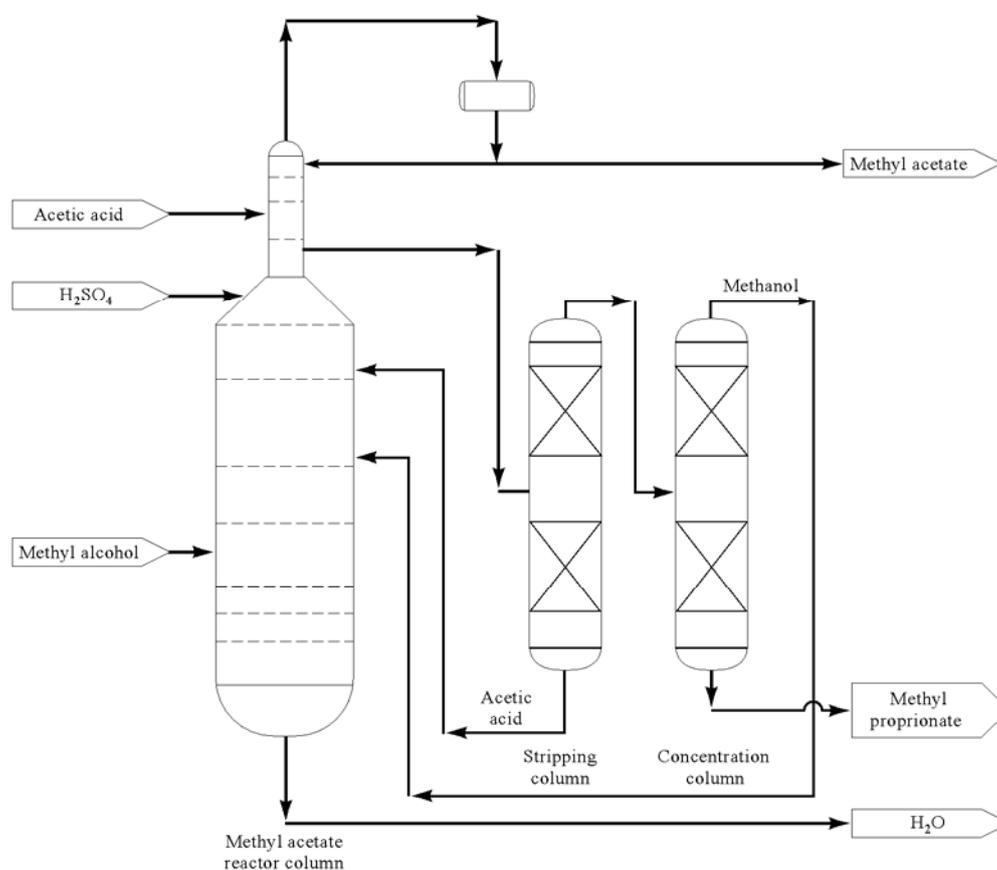


Fig. 4. Continuous methyl acetate process (59).

Ethyl Acetate. The production of ethyl acetate by continuous esterification is an excellent example of the use of azeotropic principles to obtain a high yield of ester (2). The acetic acid, concentrated sulfuric acid, and an excess of 95% ethyl alcohol are mixed in reaction tanks provided with agitators. After esterification equilibrium is reached in the mixture, it is pumped into a receiving tank and through a preheater into the upper section of a bubblecap plate column (Fig. 5). The temperature at the top of this column is maintained at ca 80°C and its vapor (alcohol with the ester formed and ca 10% water) is passed to a condenser. The first recovery column is operated with a top temperature of 70°C, producing a ternary azeotrope of 83% ester, 9% alcohol, and 8% water. The ternary mixture is fed to a static mixer where water is added in order to form two layers and allowed to separate in a decanter. The upper layer contains ca 93% ethyl acetate, 5% water, and 2% alcohol, and is sent to a second recovery or ester-drying column. The overhead from this column is 95–100% ethyl acetate which is sent to a cooler and then to a storage tank. This process also applies to methyl butyrate.

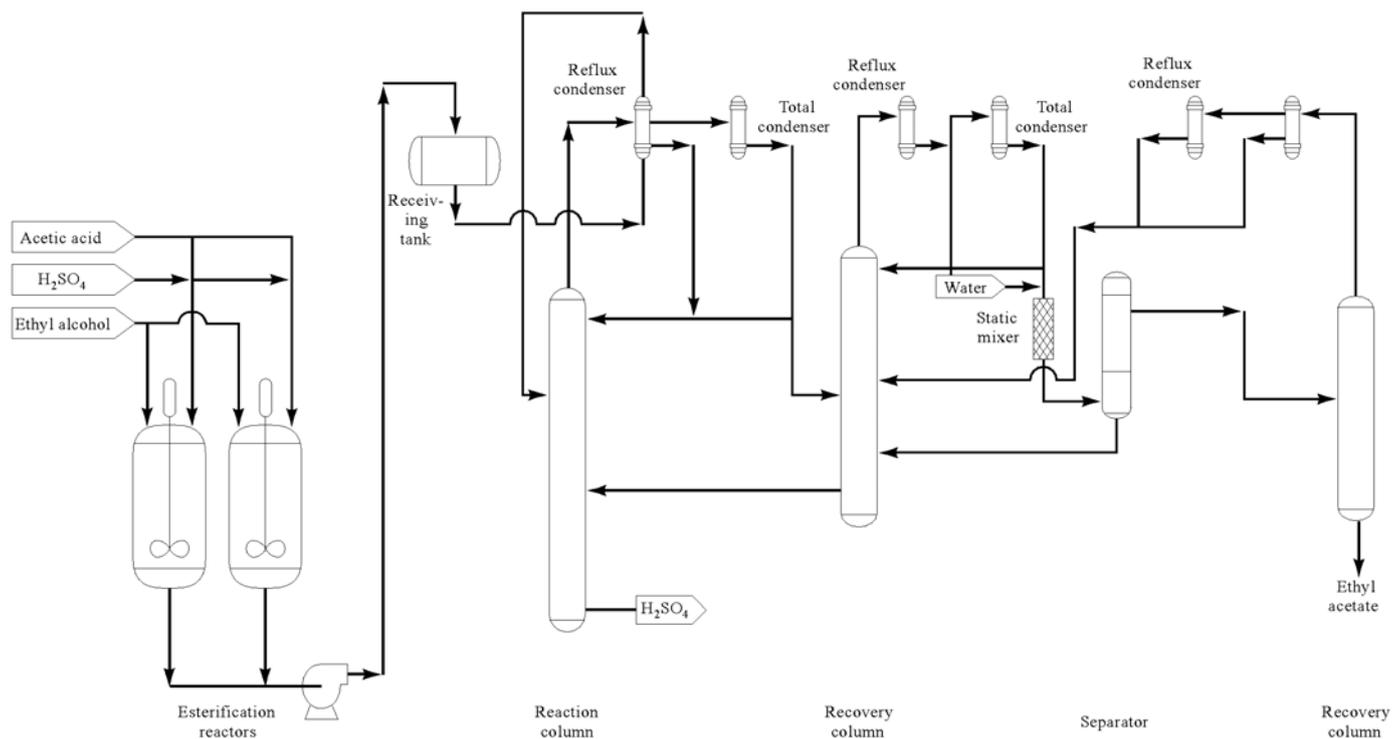


Fig. 5. Continuous ethyl acetate process (2).

Vapor-Phase Esterification

Catalytic esterification of alcohols and acids in the vapor phase has received attention because the conversions obtained are generally higher than in the corresponding liquid-phase reactions (7).

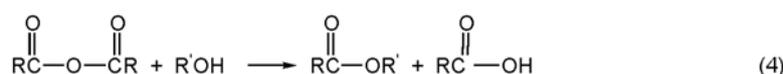
Physicochemical Considerations. The determination of the equilibrium constant K_C for the reaction $C_2H_5OH + CH_3COOH = C_2H_5OOCCH_3 + H_2O$ has been the subject of a number of investigations over the temperature range of 40–300°C (62). The values of the equilibrium constant range from 6–559 (63) with 71–95% ester as the equilibrium concentration from an equimolar mixture of ethyl alcohol and acetic acid, depending on the technique used. A study of the reaction mechanism indicates that adsorption of acetic acid is the rate-controlling step; the molecularly adsorbed acetic acid then reacts with alcohol in the vapor phase. The rate of esterification of acetic acid and ethyl alcohol in equimolar quantities has been studied in a dynamic system using silica gel catalyst at 150–270°C (64).

Ethyl Acetate. Catalysts proposed for the vapor-phase production of ethyl acetate include silica gel, zirconium dioxide, activated charcoal, and potassium hydrogen sulfate. More recently, phosphoric-acid-treated coal (65) and calcium phosphate (66) catalysts have been described.

Other Esters. The esterification of acetic acid with various alcohols in the vapor phase has been studied using several catalysts precipitated on pumice (67).

Esterification of Other Compounds

Acid Anhydrides. Acid anhydrides react with alcohols to form esters (in high yields in many cases) with a carboxylic acid formed as by-product:

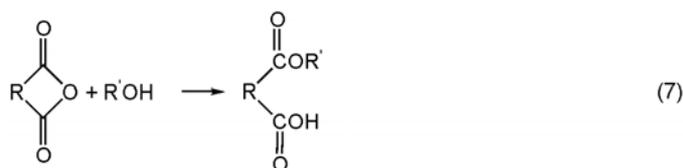


However, this method is applied only when esterification cannot be effected by the usual acid–alcohol reaction because of the higher cost of the anhydrides. The production of cellulose acetate (see [FIBERS, CELLULOSE ESTERS](#)), phenyl acetate (used in acetaminophen production), and aspirin (acetylsalicylic acid) (see [SALICYLIC ACID](#)) are examples of the large-scale use of acetic anhydride. The speed of acylation is greatly increased by the use of catalysts (68) such as sulfuric acid, perchloric acid, trifluoroacetic acid, phosphorus pentoxide, zinc chloride, ferric chloride, sodium acetate, and tertiary amines, eg, 4-dimethylaminopyridine.

Formic anhydride is not stable. However, formate esters of alcohols and phenolics can be prepared using formic–acetic

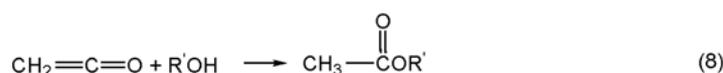
anhydride (69,70). Anhydrides can also be incorporated into polystyrene backbones which can then be treated with alcohols to afford the corresponding esters and carboxypolystyrene for recycle (71).

Dibasic acid anhydrides such as phthalic anhydride and maleic anhydride readily react with alcohols to form the monoalkyl ester:



This reaction can be used for identification of individual alcohols because of the wide variations noted in the melting points of monoalkyl esters up to the dodecyl derivatives. The reaction can be used to separate alcohols of various classes. Monoesters are converted into the normal diesters by heating with an excess of alcohol and a catalyst; however, diesters are generally formed directly from the corresponding diacids.

Ketene, like acid anhydrides, reacts with alcohols to form (acetate) esters:

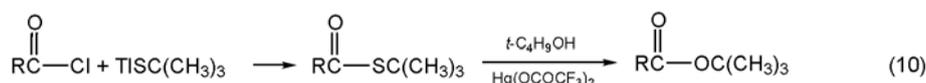


Ketene is an efficient acetylating agent with some alcohols, but in the absence of catalysts may be either nonreactive or sluggish with others, especially phenols and tertiary alcohols (72) (see [KETENES AND RELATED SUBSTANCES](#)).

Acid Chlorides. Acid chlorides react with alcohols to form esters:



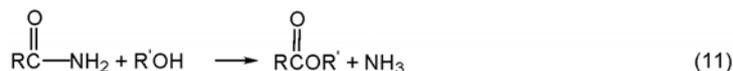
The acid chlorides are generally more reactive than the corresponding acid anhydrides. In fact, the alcoholysis of acid chlorides is probably the best laboratory method for preparing esters. Frequently, basic materials are added during the course of the reaction to neutralize by-product hydrochloric acid. When the basic material is aqueous caustic, the procedure is referred to as the Schotten-Baumann procedure (73). Esterification of tertiary alcohols by acid chlorides is described in Reference 74. Esters of tertiary alcohols can also be formed through an intermediate *t*-butyl thioate group (75):



Acid chlorides are used for the quantitative determination of hydroxyl groups and for acylation of sugars. Industrial applications include the formation of the alkyl or aryl carbonates from **phosgene** (see [CARBONIC AND CHLOROFORMIC ESTERS](#)) and phosphate esters such as triethyl, triphenyl, tricresyl, and tritoyl phosphates from phosphorus oxychloride.

The reaction of alcohols and acid chlorides in the presence of magnesium has been described (68). With primary and secondary alcohols the reaction is very smooth, and affords high and sometimes quantitative yields. Difficulty esterifiable hydroxy compounds such as tertiary alcohols and phenols can be esterified by this method. The reaction carried out in ether or benzene is usually very vigorous with evolution of hydrogen.

Amides. Alcoholysis of amides provides another method for synthesizing esters:



In order to produce high yields of ester in this manner it is necessary to remove the by-product ammonia (or amine) either by heating or combining with mineral acid, eg, H₂SO₄ or HCl. Recent work has shown that acidic ion-exchange resins can be used in place of mineral acids for converting sensitive unsubstituted amides (76). The structural relationships involved in esterification of amides are shown in Table 2 (77).

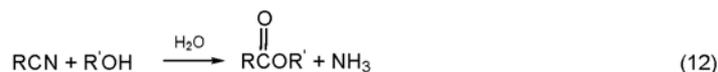
Table 2. Comparative Yields of Esters from Amides or Acids

Methyl ester	Yield of ester, %	
	From amide	From acid

formate	34	
acetate	70	56
monochloroacetate	64	65
dichloroacetate	57	70
trichloroacetate	53	73
phenylacetate	50	86
propionate	80	44
benzoate	15	37

Other methods of converting amides to esters have been described (78). Alkyl halides can be treated with amides to give esters (79). Also, esters can be synthesized from *N*-alkyl-*N*-nitrosoamides, which are derived from the corresponding amides (80).

Nitriles. Alcoholysis of nitriles offers a convenient way to produce esters without isolating the acid:



Acids are used to combine with the ammonia formed. A large excess of alcohol is used, but the amount of water is generally kept small. Catalysts such as hydrogen chloride, hydrogen bromide, and sulfuric acid have been employed (71).

One of the most important applications of this process is that of methyl methacrylate manufacture. In this process (81), acetone cyanohydrin is treated with sulfuric acid at 100°C, affording the corresponding methacrylamide sulfate which is esterified with methanol. After purification, methyl methacrylate (99.8% purity) is obtained in a yield of ca 85%.

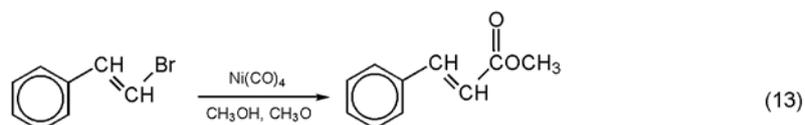
Unsaturated Hydrocarbons. Olefins from ethylene through octene have been converted into esters via acid-catalyzed nucleophilic addition. With ethylene and propylene, only a single ester is produced using acetic acid, ethyl acetate and isopropyl acetate, respectively. With the butylenes, two products are possible: *sec*-butyl esters result from 1- and 2-butynes, whereas *tert*-butyl esters are obtained from isobutylene. The C5 olefins give rise to three *sec*-amyl esters and one *t*-amyl ester. As the carbon chain is lengthened, the reactivity of the olefin with organic acids increases.

In the case of ethylene, it is necessary to use high temperatures and pressures as well as active catalyst to effect esterification (82). Yields of 40–50% based on ethylene were obtained with boron trifluoride–hydrogen fluoride mixtures as catalysts at 150°C. 2-Butene under pressure at 115–120°C with an excess of glacial acetic acid containing 10% H₂SO₄ gave as much as a 60% yield of *sec*-butyl acetate (83).

tert-Butyl acetate [540-88-5] was prepared by passing isobutylene and acetic acid (2:1 mol ratio) in the liquid phase over a silica catalyst impregnated with vanadium pentoxide and potassium sulfate at 1.7 MPa (250 psi). Conversion of isobutylene to ester increased with increasing temperature and ranged from 10% at 52°C to 24% at 93°C. Based on the acetic acid charged, yields of 31–43% of *t*-butyl acetate resulted at 93°C (84).

Most of the vinyl acetate produced in the United States is made by the vapor-phase ethylene process. In this process, a vapor-phase mixture of ethylene, acetic acid, and oxygen is passed at elevated temperature and pressures over a fixed-bed catalyst consisting of supported palladium (85). Less than 70% oxygen, acetic acid, and ethylene conversion is realized per pass. Therefore, these components have to be recovered and returned to the reaction zone. The vinyl acetate yield using this process is typically in the 91–95% range (86). Vinyl acetate can be manufactured also from acetylene, acetaldehyde, and the liquid-phase ethylene process (see VINYL POLYMERS).

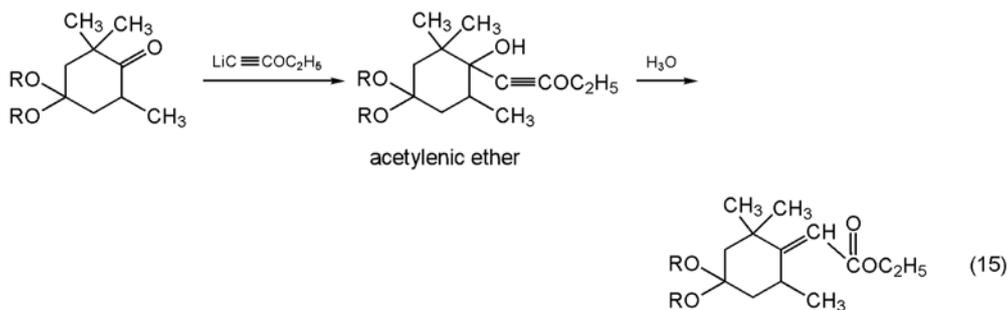
Esters can be obtained from halogenated olefins using a metal carbonyl catalyst (87), eg, *trans*-1-bromo-2-phenylethylene is treated with nickel carbonyl in the presence of methanol to afford the corresponding methyl cinnamate (see CINNAMIC ACID).



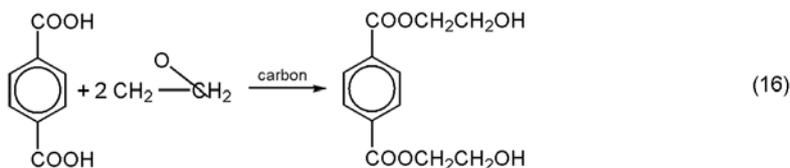
Ethers. In the presence of anhydrous agents such as ferric chloride (88), hydrogen bromide, and acid chlorides, ethers react to form esters (see ETHERS). Esters can also be prepared from ethers by an oxidative process (89). With mixed sulfonic–carboxylic anhydrides, ethers are converted to a mixture of the corresponding carboxylate and sulfonate esters (90):



Unsaturated esters can be prepared from the corresponding acetylenic ethers with yields in most cases of >50% (91) as in the following example:



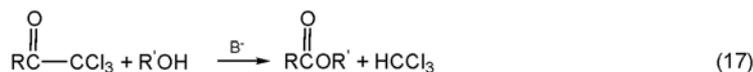
β -hydroxyethyl esters can be prepared from carboxylic acids and ethylene oxide:



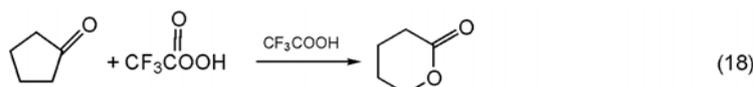
Bis-(β -hydroxyethyl) terephthalate and related compounds can be produced in this manner using finely divided carbon catalyst (92). The carbon functions not only as a catalyst but also helps to remove color from the reaction mixture upon removal of the carbon by hot filtration.

Aldehydes and Ketones. Esters are obtained readily by condensation of aldehydes in the presence of alcoholate catalysts such as aluminum ethylate, $\text{Al}(\text{OC}_2\text{H}_5)_3$, by the Tishchenko reaction. The alcoholate catalysts may be prepared from commercial aluminum and *n*-butyl or isobutyl alcohol in the presence of 2–5% aluminum chloride (93).

Trihalomethyl ketones react with alcohols in the presence of alkaline catalysts even at room temperature (94):

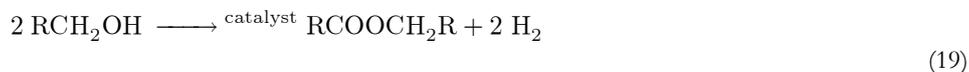


A variety of esters can be prepared from the corresponding ketones using peracids in a process usually referred to as the Baeyer-Villiger reaction (95); i.e., cyclopentanone is converted to δ -valerolactone upon treatment of the ketone with peroxytrifluoroacetic acid:



This conversion can be carried out, in many cases, with >80% yield.

Alcohols. The direct synthesis of esters by dehydrogenation or oxidative hydrogenation of alcohols offers a simple method for the preparation of certain types of esters, such as ethyl acetate (96–98):



The reaction is catalyzed by copper with various promoters or activators, and is carried out in the vapor phase at 200–300°C.

Technical Preparation of Esters

Esterification is generally carried out by refluxing the reaction mixture until the carboxylic acid has reacted with the alcohol and the water has been split off. The water or the ester is removed from the equilibrium by distillation. The choice of the esterification process to obtain a maximum yield is dependent on many factors, i.e., no single process has universal applicability. Although extensive preparative techniques have been reviewed elsewhere (7,68), the methods given in this section are representative of both laboratory and plant-scale techniques used in batch esterifications.

Methyl Esters. Methyl esters are obtained in good yield using methylene dichloride or ethylene dichloride as solvent (99). The latter is generally preferred, but the choice of the solvent depends to some extent on the boiling point of the desired ester. Also, the toxicity of these solvents should be considered prior to using them (see [CHLOROCARBONS AND CHLOROHYDROCARBONS](#)). The general procedure is as follows: for each mole of aliphatic carboxyl group, 96 g (3 mol) of methanol, 300 mL of ethylene dichloride, and 3 mL of concentrated H_2SO_4 are used. With aromatic acids, the amount of H_2SO_4 is increased to 15 mL/mol of carboxyl group. The mixture is refluxed for 6–15 h, although in some cases the time may be as short as 30 minutes. Progress of esterification is usually

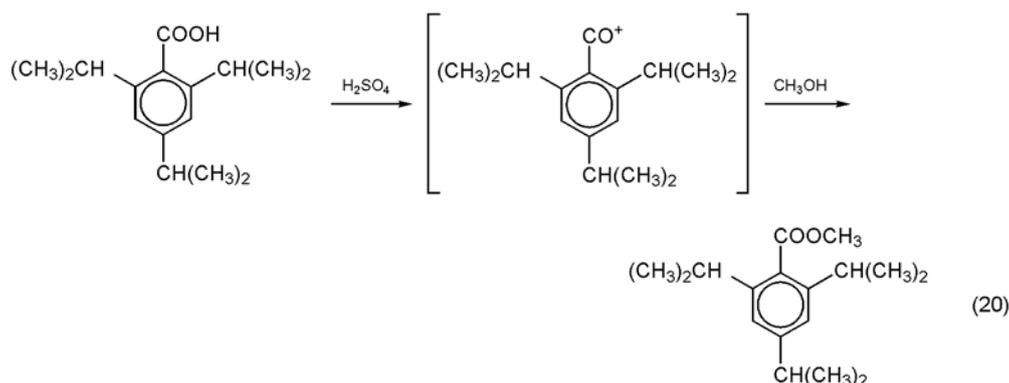
indicated by the development of cloudiness and separation of an upper layer containing water, methanol, and sulfuric acid. After the reaction is completed, the cooled mixture is washed successively with water, sodium bicarbonate solution, and again with water. The ethylene chloride layer is then distilled at atmospheric or reduced pressure, and the residual methyl ester is purified by distillation or crystallization.

The manufacture of high purity methyl acetate by a reactive distillation process has been accomplished; high conversion of one reactant can be achieved only with a large excess of the other reactant. Because the reaction is reversible, the rate of reaction in the liquid phase is increased by removing methyl acetate preferentially to the other components in the reaction mixture (100).

Medium Boiling Esters. Esterification of ethyl and propyl alcohols, ethylene glycol, and glycerol with various acids, eg, chloro- or bromoacetic, or pyruvic, by the use of a third component such as benzene, toluene, hexane, cyclohexane, or carbon tetrachloride to remove the water produced is quite common. Benzene has been used as a co-solvent in the preparation of methyl pyruvate from pyruvic acid (101). The preparation of ethyl lactate is described as an example of the general procedure (102). A mixture of 1 mol 80% lactic acid and 2.3 mol 95% ethyl alcohol is added to a volume of benzene equal to half that of the alcohol (ca 43 mL), and the resulting mixture is refluxed for several hours. When distilled, the overhead condensate separates into layers. The lower layer is extracted to recover the benzene and alcohol, and the water is discarded. The upper layer is returned to the column for reflux. After all the water is removed from the reaction mixture, the excess of alcohol and benzene is removed by distillation, and the ester is fractionated to isolate the pure ester.

High Boiling Esters. The following procedure can be used for making diethyl phthalate and other high boiling esters (103). Phthalic anhydride (1 equiv) and 2.5 equivalents of ethanol are refluxed for 2 h in the presence of 1% of concentrated H_2SO_4 . To produce the monoester, the excess of alcohol is distilled at $<100^\circ\text{C}$. For the diester, a mixture of 67% benzene and 33% alcohol is introduced continuously below the surface of the reaction mixture and the resulting alcohol–water–benzene ternary is distilled and condensed. A yield of diester of $>99\%$ is obtained by passing 3.4–7 equivalents of alcohol through the mixture in 4.5–7 hours. In another continuous process for the production of diesters, the mixture of alcohol, acid, and the catalyst is introduced into the upper part of a distillation column and an excess of the alcohol is introduced into the bottom. The column is heated so that the ester, water, and excess alcohol are distilled off (104). Organotitanates, zirconates, or organotin compounds are effective catalysts for the esterification of carboxylic acids or anhydrides with higher boiling monohydroxy alcohols at temperatures that permit the continuous distillation of the water formed (105). Refluxing 1 mol phthalic anhydride with 3 mol 2-ethyl-2-hexanol with stirring using these agents, then removing the water by a trap separator gives the corresponding esters in $\sim 99\%$ yields (see **PHTHALIC ACID**). Phthalic anhydride has been esterified with $>99\%$ conversion with 10–30% excess alcohol in the presence of 0.8–1.5 mol % alkyl titanate containing 0.08–0.2% activating agent in a vertical, multistage reactor connected to a devolatilization column and filter (106).

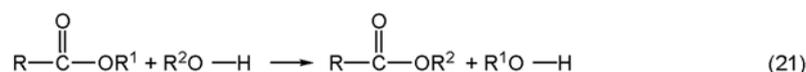
Difficulty Esterifiable Acids. The sterically hindered acids, such as 2,6-disubstituted benzoic acids, cannot usually be esterified by conventional means. Several esters of sterically hindered acids such as 2,4,6-triisopropylbenzoic acid [49623-71-4] have been prepared by dissolving 2 g of the acid in 14–20 mL of 100% H_2SO_4 (107). After standing a few minutes at room temperature, when presumably the acylium cation is formed (eq. 20), the solution is poured into an excess of cold absolute methanol. Most of the alcohol is removed under reduced pressure, about 50 mL of water is added, and the distillation is continued under reduced pressure to remove the remainder of the methanol. The organic matter is extracted with ether and treated with sodium carbonate solution. The ester is then distilled. Yields of esters made in this manner are 57–81%.



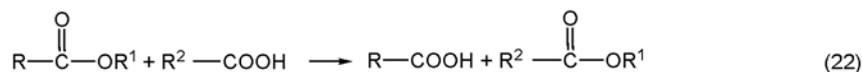
Ester Interchange

Ester interchange (transesterification) is a reaction between an ester and another compound, characterized by an exchange of alkoxy groups or of acyl groups, and resulting in the formation of a different ester. The process of transesterification is accelerated in the presence of a small amount of an acid or a base.

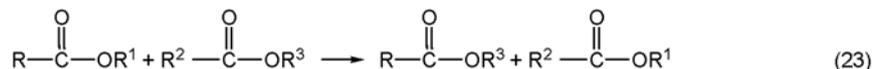
Three types of transesterification are known: (1) exchange of alcohol groups, commonly known as alcoholysis. In this process the compound with which an ester reacts is an alcohol:



(2) exchange of acid groups, acidolysis. In this process the compound with which an ester reacts is an acid:



(3) ester-ester interchange. In this process an exchange takes place between two esters:



These reactions are reversible and ordinarily do not involve large energy changes.

ESTER-ALCOHOL INTERCHANGE

Reaction Conditions. Alcoholysis commonly takes place in one liquid phase, sometimes with one of the reactants being only partially soluble and going into solution gradually as the reaction proceeds. Unless an excess of one of the reactants is used, or unless one of the products is withdrawn from the reaction phase by vaporization or precipitation, the reaction does not proceed to completion but comes to a standstill with substantial proportions of both alcohols and both esters in equilibrium. The concentrations present at equilibrium depend on the characteristics of the alcohols and esters involved, but in most practical uses of the reaction, one or both of the devices mentioned are used to force the reaction toward completion.

Temperatures. With alkaline catalysts, the reaction often takes place at RT or even lower temperatures. With acid catalysts, temperatures near 100°C are commonly used. With no catalyst, temperatures ~250°C may be required for a practical reaction rate.

Catalysts. Of the alkaline catalysts, alkali metal alkoxides are the most effective; ordinarily, the sodium or potassium alkoxide of the alcohol entering the reaction is preferred. Various other catalysts of milder alkalinity are preferred in special cases. For example, the use of sodium methyl carbonate as catalyst in the methanolysis of poly(vinyl acetate) is said to yield a poly(vinyl alcohol) having improved color. Aluminum alkoxide has been proposed as a catalyst for the alcoholysis of certain unsaturated esters; other sensitive esters have been made with a Grignard reagent as catalyst. Zinc is reported to be an efficient catalyst in the alcoholysis of ethyl esters of α -halogenated aliphatic acids by allyl and methallyl alcohols; conventional catalysts favor undesirable side reactions. Neutral organic titanates have received much attention (108). Divalent metal salts such as zinc or manganese acetate and organotin compounds such as dibutyltin oxide have been employed.

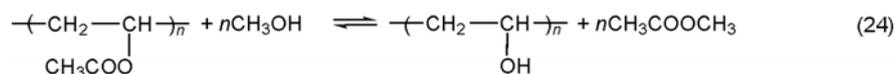
Among the acid catalysts, sulfuric acid, sulfonic acids, and hydrochloric acid are most used. With polyhydric alcohols, sulfuric acid is preferred to hydrochloric acid because of the tendency of hydrochloric acid to form chlorohydrins.

Equilibrium. In general, primary alcohols are more reactive than secondary alcohols (that is, they tend to displace them), and secondary alcohols tend to displace tertiary alcohols, but in addition, there are considerable differences among different members of the same class. Various alcohols have been compared in this way (4,109).

Applications. Transesterifications via alcoholysis play a significant role in industry as well as in laboratory and in analytical chemistry. The reaction can be used to reduce the boiling point of esters by exchanging a long-chain alcohol group with a short one, eg, methanol, in the analysis of fats, oils, and waxes. For more details see References 7 and 68. A few examples are given below.

***n*-Butyl Oleate.** Olive oil, 3 kg, consisting mainly of the glyceryl esters of oleic acid, is refluxed for 20 h with 7 L of *n*-butyl alcohol containing 150 g of concentrated H₂SO₄. The product contains a small proportion of saturated esters (110).

Poly(vinyl alcohol). Poly(vinyl alcohol) (see VINYL POLYMERS) is more easily prepared, in a form that can be filtered and washed in a practical way, by alcoholysis of poly(vinyl acetate), than by its saponification in an aqueous system:



The use of a catalytic quantity of alkali equivalent to only a small fraction of the acetate has the advantage that contamination of the poly(vinyl alcohol) with salts, which are difficult to remove, is minimized. A variant of the process is the use of a mixture of alcohol with the acetate ester produced by the alcoholysis as the alcoholyzing agent. This provides a means of controlling the completeness of removal of the acetate groups from the poly(vinyl acetate) (111).

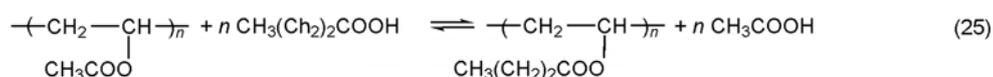
Acrylic Esters. A procedure has been described for preparation of higher esters from methyl acrylate that illustrates the use of an acid catalyst together with the removal of one of the products by azeotropic distillation (112). Another procedure for the preparation of butyl acrylate, secondary alkyl acrylates, and hydroxyalkyl acrylates using *p*-toluenesulfonic acid as a catalyst has been described (113). Aluminum isopropoxide catalyzes the reaction of amino alcohols with methyl acrylate and methyl methacrylate. A review of the synthesis of acrylic esters by transesterification is given in Reference 114 (see ACRYLIC ACID AND DERIVATIVES).

ESTER-ACID INTERCHANGE

Acidolysis requires the use of an elevated temperature, the use of an acid catalyst (7), or both. Like alcoholysis, the reaction is reversible and requires the use of an excess of the replacing acid or removal of one of the products from the reaction if a high degree of replacement of the acid radical of an ester by another acid is to be obtained. This can be accomplished by distilling one of the products from the reaction mixture during the acidolysis.

In a series of organic acids of similar type, not much tendency exists for one acid to be more reactive than another. For example, in the replacement of stearic acid in methyl stearate by acetic acid, the equilibrium constant is 1.0. However, acidolysis in formic acid is usually much faster than in acetic acid, due to higher acidity and better ionizing properties of the former (115). Branched-chain acids, and some aromatic acids, especially sterically hindered acids such as ortho-substituted benzoic acids, would be expected to be less active in replacing other acids. Mixtures of esters are obtained when acidolysis is carried out without forcing the replacement to completion by removing one of the products. The acidolysis equilibrium and mechanism are discussed in detail in Reference 115.

An industrial example of acidolysis is the reaction of poly(vinyl acetate) with butyric acid to form poly(vinyl butyrate). Often a butyric acid-methanol mixture is used and methyl acetate is obtained as a coproduct.



ESTER-ESTER INTERCHANGE

The reaction between two esters to produce two other esters was described by Friedel and Crafts in 1865, but has not been used as much as alcoholysis. The same general principles apply with regard to reversibility of the reaction and the means of driving the reaction to completion (7). In general, the same catalysts are effective as in alcoholysis. Usually the reaction is slower than alcoholysis of the same esters. Without a catalyst, a reaction time of several h at >250°C is required to bring two typical esters to equilibrium. Catalysts are almost essential to bring reaction rates into a practical range so that the use of destructive temperatures can be avoided. Tin compounds, especially stannous hydroxide, have been mentioned frequently as catalysts and do not produce much decomposition or discoloration of the esters (116). More effective at lower temperatures are the acid catalysts, such as sulfuric acid and sulfonic acids, and especially the alkaline catalysts such as sodium alkoxides. With an alkaline catalyst, ester-ester interchange can be carried out at temperatures as low as 0°C.

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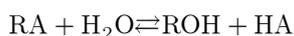
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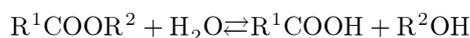
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ESTERS, ORGANIC

Esters are compounds that, on hydrolysis, yield alcohols or phenols and acids according to the equation:



where R is a hydrocarbon fragment and A is the anion portion of an organic acid. For carboxylic acid esters, the reaction can be represented as:

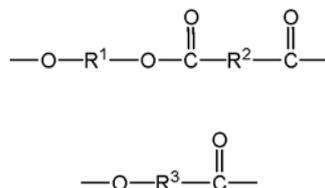


where R¹ and R² are the same or different hydrocarbon radicals. The reverse reaction constitutes the usual method for preparing esters (see [ESTERIFICATION](#)). When R¹ and R² are bonded together, the resultant cyclic ester is called a lactone. Lactones can be

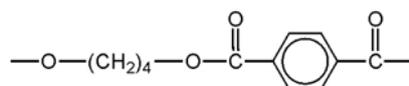
produced from molecules containing both carboxyl and hydroxy groups.



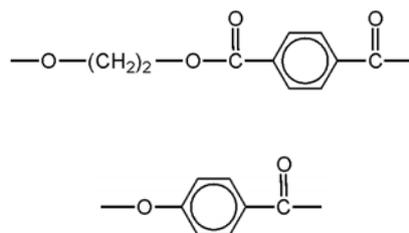
Polyesters are polymers with basic structural units:



where R^1 , R^2 , and R^3 are alkyl, aromatic, or alkyl-aromatic radicals and they may be the same or different. For example, poly(butylene terephthalate) [26062-94-2] has the repeating unit



whereas poly(ethylene terephthalate-*p*-oxybenzoate) [25822-54-2] copolymer consists of the following two repeating units



Orthoesters, $\text{RC(OR}^1\text{)}_3$ (1), thioesters, RCSOR^1 (2,3) (see [SULFUR COMPOUNDS](#); [THIOLS](#)), and carbamates, H_2NCOOR , are not covered in this review.

Nomenclature

The names of esters consist of two words that reflect their formation from an alcohol and a carboxylic acid. According to the IUPAC rule, the alkyl or aryl group of the alcohol is cited first followed by the carboxylate group of the acid with the ending -ate replacing the -ic of the acid (4,5). For example, $\text{CH}_3\text{CH}_2\text{COOCH}_3$, the methyl ester of propanoic acid, is called methyl propanoate [554-12-1] (or methyl propionate, if the trivial name, propionic acid, is used for the carboxylic acid). The monoesters of dibasic acids are named by inserting the word hydrogen between names of the alcohol and the carboxylate. The monomethyl ester of succinic acid, $\text{CH}_3\text{OCOCH}_2\text{CH}_2\text{COOH}$, is called methyl hydrogen succinate or more systematically methyl hydrogen butanedioate [3878-55-5].

Based on the IUPAC rule, esters of polyhydric alcohols with monobasic acids are named analogously to simple esters: 1,2-ethanediyl diacetate for ethylene glycol diacetate [111-55-7], 2-hydroxyethyl acetate for ethylene glycol monoacetate [542-59-6], 1,2,3-propanetriyl triacetate for glycerol triacetate [102-76-1]. Cyclic esters are called lactones, and are named by changing the -ic acid of the hydroxy-acid to -olactone. A Greek letter (α , β , γ , δ , etc) is used to designate the carbon atom that bears the hydroxyl group of the parent acid. Lactones are best named, however, as heterocyclic compounds. For example, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}$, γ -butyrolactone, is dihydro-2(3*H*)-furanone [96-48-0].

When the ester function is named as a substituent, it is indicated by alkoxy-carbonyl or acyloxy depending on the connection to

the ---C=O group: $\text{CH}_3\text{OC---R}$ is a methoxycarbonyl derivative whereas $\text{CH}_3\text{CO---R}$ is the acetoxy derivative. In naming esters containing one or more substituents, it is necessary to indicate specifically in which portion of the molecule the substituents occur, eg, $\text{ClCH}_2\text{COOCH}_2\text{CH}_3$ is ethyl chloroacetate [105-39-5] and $\text{CH}_3\text{COOCH}_2\text{CH}_2\text{Cl}$ is 2-chloroethyl acetate [542-58-5].

Orthoesters are trivially named as derivatives of ortho acids such as triethyl orthoformate [122-51-0], $\text{HC(OC}_2\text{H}_5\text{)}_3$, or named systematically as ethers, 1,1,1-triethoxymethane.

Physical Properties

The physical properties of organic esters vary according to the molecular weight of each component (6–10). Lower molecular weight esters are colorless, mobile, and highly volatile liquids that usually have pleasant odors. As the molecular weight increases, volatility decreases and the consistency becomes waxy, then solid, and eventually even brittle, often with formation of lustrous crystals. The melting point of an ester is generally lower than that of the corresponding carboxylic acid. However, the boiling point depends on the chain length of the alcohol component and eventually exceeds that of the acid. Lower molecular weight esters are relatively stable when dry and can be distilled without decomposition. Organic esters are generally insoluble in water, but soluble in various organic liquids. Lower esters are themselves good solvents for many organic compounds. The physical properties of commercially important aliphatic and aromatic organic esters are listed in Table 1.

Table 1. Physical Properties of Some Common Esters

Ester	CAS Registry Number	Mol wt	n_D^{20}	d_{20}^{20}	Bp, °C ^a	Freezing point, °C	Flash point, °C ^b
methyl formate	[107-31-3]	60.05	1.344	0.097	32	-99.8	-19
ethyl formate	[109-94-4]	74.08	1.359	0.923	54.3	-80	-20
butyl formate	[592-84-7]	102.13	1.388	0.888	106	-91.9	-18
methyl acetate	[79-20-9]	74.08	1.359	0.933	57	-98.1	-10
ethyl acetate	[141-78-6]	88.1	1.372	0.090	77.1	-83.6	-4
vinyl acetate	[108-05-4]	86.1	1.395	0.932	72.2	-93.2	-8
propyl acetate	[109-60-4]	102.13	1.384	0.887	101.6	-92.5	13
isopropyl acetate	[108-21-4]	102.13	1.377	0.872	90	-73.4	2
butyl acetate	[123-86-4]	116.16	1.395	0.882	126	-73.5	22
isobutyl acetate	[110-19-0]	116.16	1.390	0.871	117.2	-98.6	18
<i>sec</i> -butyl acetate	[105-46-4]	116.16	1.387	0.875	112		31.1 ^e
<i>t</i> -butyl acetate	[540-88-5]	116.16	1.385	0.866	97		
pentyl acetate	[628-63-7]	130.18	1.402	0.876	149.3	-70.8	25
isoamyl acetate	[123-92-2]	130.18	1.400	0.872	142	-78	25
<i>sec</i> -hexyl acetate	[108-84-9]	144.22	1.401	0.865	157	0	
2-ethylhexyl acetate	[103-09-3]	172.26	1.420	0.873	199.3	-93	71
ethylene glycol diacetate	[111-55-7]	146.14	1.415	1.128	191	-31	88
2-methoxyethyl acetate	[110-49-6]	118.13	1.401	1.006	145	-65.1	44
2-ethoxyethyl acetate	[111-15-9]	132.16	1.405	0.975	156.4	-61.7	47
2-butoxyethyl acetate	[112-07-2]	160.12	1.42	0.943	187.8	-32	81
2-(2-ethoxyethoxy)ethyl acetate	[111-90-0]	176.21	1.423	1.011	217.4	-25	107
2-(2-butoxyethoxy)ethyl acetate	[112-34-5]	204.27	1.426	0.981	247	-32.2	110
benzyl acetate	[140-11-4]	150.18	1.523	1.055	215.5	-51.5	90

glyceryl triacetate	[102-76-1]	218.23	1.429 6	1.161	258	-78	138
ethyl 3-ethoxypropionate	[763-69-9]	146.19		0.95	165-17 2	-50	58
glyceryl tripropionate	[139-45-7]	260.3	1.431 8	1.100 ^h	176	-58	167 ^e
methyl acrylate	[96-33-3]	86.09	1.404 0	0.953	80.5	<-75	-3
ethyl acrylate	[140-88-5]	100.11	1.406 8	0.923	99.8	<-72	10
butyl acrylate	[141-32-2]	128.17	1.418 5	0.898	69	-64.6	29
2-ethylhexyl acrylate	[103-11-7]	184.28		0.887	130 ⁱ	-90	82 ^e
methyl methacrylate	[80-62-6]	100.12	1.411 9	0.944	100	-48	10 ^e
methyl butyrate	[623-42-7]	102.13	1.387 8	0.898	102.3	-84.8	14
ethyl butyrate	[105-54-4]	116.16	1.400 0	0.878	121.6	-100.8	24
butyl butyrate	[109-21-7]	144.22	1.407 5	0.871	166.6	-91.5	53
methyl isobutyrate	[547-63-7]	102.13	1.384 0	0.891	92.6	-84.7	
ethyl isobutyrate	[97-62-1]	116.16	1.387 0	0.869	110	-88	<21
isobutyl isobutyrate	[97-85-8]	144.22	1.399 9	0.875	148.7	-80.7	38
methyl stearate	[112-61-8]	298.5	1.457	0.836	215	40	153
ethyl stearate	[111-61-5]	312.52	1.429	1.057	213-21 5	33.7	
butyl stearate	[123-95-5]	340.58		0.855	343	27.5	160
dodecyl stearate	[5303-25-3]	440.8	1.433			28	
hexadecyl stearate	[1190-63-2]	496.91	1.441			57	
dimethyl maleate	[624-48-6]	144.13	1.440 9	1.152	204		91
dimethyl oxalate	[95-92-1]	111.09	1.409 6	1.148	185	-41	76
dimethyl adipate	[627-93-0]	174.2	1.428 3	1.060 0	115	10.3	
diethyl adipate	[141-28-6]	202.25	1.437 2	1.008	245	-19.8	
di(2-ethylhexyl) adipate	[103-23-1]	370.58	1.447 2	0.927	214	-60	206
methyl benzoate	[93-58-3]	136.15	1.517	1.094	199.5	-12.5	83
ethyl benzoate	[93-89-0]	150.18	1.505	1.051	212.9	-34.2	88
methyl salicylate	[119-36-8]	152.15	1.536	1.184	223.3	-8.6	96
ethyl salicylate	[118-61-6]	166.18	1.522	1.137	231.5	1.3	107
dimethyl phthalate	[131-11-3]	194.19	1.515	1.190	282	-2	146
diethyl phthalate	[84-66-2]	222.24	1.499	1.118	295	-33	161
dibutyl phthalate	[84-74-2]	278.35	1.491 1	1.046 5	340	-35	157
di(2-ethylhexyl) phthalate	[117-81-7]	390.56	1.486	0.986 1	231 ^j	-50	218.3
dimethyl isophthalate	[1459-93-4]	194.19	1.516 8	1.194 ^c	124	67	138
dimethyl terephthalate	[120-61-6]	194.19			288	140	153
methyl anthranilate	[134-20-3]	151.17	1.584	1.168	132	24	>100
benzyl cinnamate	[103-41-3]	238.29		1.109 ^g	244 ^j	39	110
dimethyl carbonate	[616-38-6]	90.08	1.368	1.069	90	3	19 ^e

diethyl carbonate	[105-58-8]	118.13	2 1.385 4	4 ^c 0.975 2 ^c	127	-43	25
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^a At 101.3 kPa = 760 mm Hg unless otherwise stated.

^b Closed cup determination unless otherwise stated.

^c d_4^{20}

^d d_4^{16}

^e Open cup determination.

^f n_D^{25}

^g d_{15}^{15}

^h d_{18}^{20}

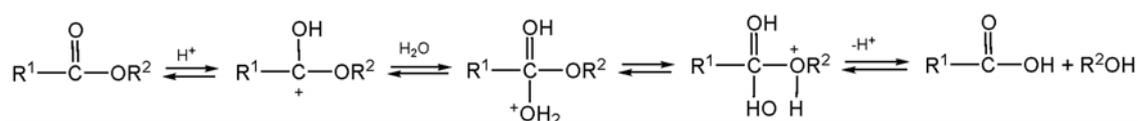
ⁱ At 6.7 kPa (50 mm Hg).

^j At 0.67 kPa (5 mm Hg).

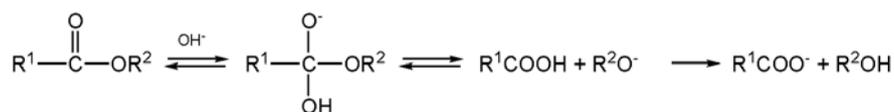
Chemical Properties

The reactions of esters have been reviewed (11–15). Because of the large number of possible acid and alcohol moieties, the chemical properties of esters may differ considerably. Only typical reactions applicable to the majority of esters are described in the following sections.

Hydrolysis. Esters are cleaved (hydrolyzed) into an acid and an alcohol through the action of water. This hydrolysis is catalyzed by acids or bases. The mechanistic aspects of ester hydrolysis have received considerable attention and have been reviewed (16). For most esters only two reaction pathways are important. Both mechanisms involve a tetrahedral intermediate and addition-elimination reactions: *Acid*



Base



Hydrolysis reactions involving tetrahedral intermediates are subject to steric and electronic effects. Electron-withdrawing substituents facilitate, but electron-donating and bulky substituents retard basic hydrolysis. Steric effects in acid-catalyzed hydrolysis are similar to those in base-catalyzed hydrolysis, but electronic effects are much less important in acid-catalyzed reactions. Higher temperatures also accelerate the reaction.

The catalysis of ester hydrolysis by other groups within the ester molecule (intramolecular catalysis) has been extensively studied (17,18). These reactions are important because they simulate catalysis by enzymes. Intramolecular catalysis of esters has been used as a model in drug discovery efforts (19).

Basic Hydrolysis. Throughout most of history, soap was manufactured by boiling an ester with aqueous alkali. In this reaction, known as saponification, the ester is hydrolyzed with a stoichiometric amount of alkali. The irreversible formation of carboxylate anion drives the reaction to completion.

Acidic Hydrolysis. Hydrolysis of esters by use of water and a mineral acid leads to an equilibrium mixture of ester, alcohol, and free carboxylic acid. Complete reaction can only be achieved by removal of alcohol or acid from the equilibrium. Because esters have poor solubility in water, the reaction rate in dilute acids is fairly low. Therefore, emulsifiers such as sulfonated oleic acid or sulfonated aromatic compounds (Twitchell reagent) are added to facilitate the reaction.

Hydrolysis by Steam. High pressure steam, 4.5–5.0 MPa (650–725 psi), at 250°C in the absence of a catalyst hydrolyzes oils and fats to the fatty acids and glycerol (20). The reaction is commonly carried out continuously in a countercurrent method. The glycerol produced during the reaction is continuously extracted from the equilibrium mixture with water. A yield of 98% can be achieved. Currently, the preferred method to produce soaps is steam hydrolysis of fats followed by alkali neutralization of the fatty acids.

Enzymatic Hydrolysis. Enzymatic hydrolysis has received enormous attention (21–24). The enzymes generally employed are lipases from microorganisms, plants, or mammalian liver. They effect hydrolysis below 40°C. However, this temperature limit can be raised by employing the enzymes from thermophilic bacteria. The enzymes may be used as a crude extract, in purified form or entrapped on a solid support. The great advantage of the enzymatic process is its high chemo- and stereoselectivity. Enzymatic hydrolysis has been used to effect partial hydrolysis of triglycerides, chiral separations of racemic esters, and selective production of specific fatty acids from fats (25). For example, lipase from *Candida cylindracea* was employed to resolve racemic mixtures of R- and S- α -methylarylacetic acid esters to yield S- α -methylarylacetic acids (26).

Transesterification. When esters are heated with alcohols, acids, or other esters in the presence of a catalyst, the alcohol or acid groups are exchanged. This process is called transesterification. It is accelerated by the presence of a small amount of acid or alkali. Three types of transesterification are known: (1) exchange of alcohol groups (alcoholysis), (2) exchange of acid groups (acidolysis), and (3) ester–ester interchange (see ESTERIFICATION). Alcoholysis and acidolysis are important for preparative purposes. All three are equilibrium reactions and proceed to completion if one component is removed from the reaction mixture, eg, by distillation. Dispersed alkali metals, mainly sodium, alkali metal oxides, and tin salts, are suitable catalysts for the transesterification of fats. Recently, organic titanates have also been used (27). Enzymes can be used as asymmetric catalysts in these reactions to prepare optically active alcohols and esters (28).

Transesterification has a number of important commercial uses. Methyl esters of fatty acids are produced from fats and oils. Transesterification is also the basis of recycling technology to break up poly(ethylene terephthalate) [25038-59-9] to monomer for reuse (29) (see RECYCLING, PLASTICS). Because vinyl alcohol does not exist, poly(vinyl alcohol) [9002-89-5] is produced commercially by base-catalyzed alcoholysis of poly(vinyl acetate) [9003-20-7] (see VINYL POLYMERS). An industrial example of acidolysis is the reaction of poly(vinyl acetate) with butyric acid to form poly(vinyl butyrate) [24991-31-9].

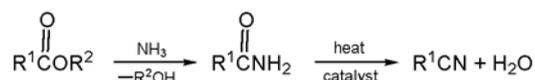
Ammonolysis and Aminolysis. Esters and ammonia react to form amides and alcohols:



This reaction can be carried out in aqueous or alcoholic ammonia. Lower mol wt esters give good yields even at room temperature; higher mol wt esters require higher temperature and pressure.

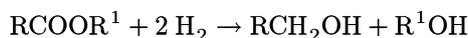
If primary or secondary amines are used, N-substituted amides are formed. This reaction is called aminolysis. Hydrazines yield the corresponding hydrazides, which can then be treated with nitrous acid to form the azides used in the Curtius rearrangement. Hydroxylamines give hydroxamic acids.

When esters are passed with ammonia over a contact catalyst such as alumina or thoria at 400–500°C, nitriles are obtained via dehydration of the intermediate amides:



Thus fats are converted to the fatty nitriles (30).

Reduction. Esters can be reduced to alcohols by catalytic hydrogenation using molecular hydrogen or by chemical reduction:



Catalytic Hydrogenation. Esters can be hydrogenated to primary alcohols using a transition-metal catalyst (31–33) such as copper chromite, copper oxide, Raney nickel, nickel–copper–aluminum–rhenium oxides, or related species. The catalyst of choice is copper chromite. Conditions are stringent: 10–30 MPa (1450–4350 psi) at 150–300°C. Halogens and sulfur are catalyst poisons. When the ester is aliphatic and saturated, the reaction is facile and almost quantitative. Catalysts containing Zn or Cd salts have been developed to convert unsaturated fatty esters into unsaturated fatty alcohols (33,34). The reduction of aromatic carboxylic acid esters proceeds beyond the alcohol in some instances. Benzylic C–O hydrogenolysis, eg, benzyl alcohol to toluene, and aromatic ring hydrogenation upon phenol ester reduction are frequent problems. These problems can be minimized by carrying out the reaction at low temperatures with a high ratio of catalyst to ester.

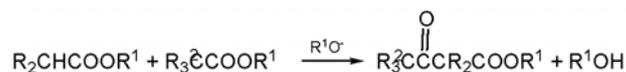
The catalytic hydrogenation of esters is of great commercial importance. It is one of the industrial methods used to produce long-chain fatty alcohols (eg, dodecyl and decyl alcohols) from fatty acid methyl esters (33). The method is also suitable for the conversion of dimethyl 1,4-cyclohexanedicarboxylate [94-60-0] into 1,4-cyclohexanedimethanol [105-08-8], an important intermediate in the manufacturing of polyesters.

Reduction with Metals and Metal Hydrides. Practically any ester can be reduced by Na–C₂H₅OH, Li or Na–NH₃, LiAlH₄, LiBH₄, or NaBH₄ to give alcohols in excellent yield (35,36). Carbon-carbon double bonds are usually preserved using these reducing reagents.

The reduction of esters to aldehydes is carried out with hydrides such as NaH₂Al(OCH₂CH₂OCH₃)₂, (*i*-C₄H₉)₂AlH, NaAlH₄, or LiAlH₄–(C₂H₅)₂NH. The use of BH₃ or LiAlH₄–BF₃·O(C₂H₅)₂ as a reducing reagent converts esters to ethers. Thus, reduction of

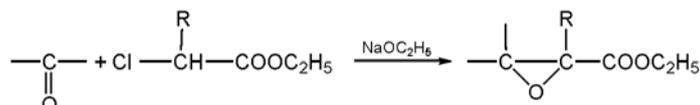
esters can be manipulated by the judicious selection of metal-containing reducing reagents.

Reaction of Enolate Anions. In the presence of certain bases, eg, sodium alkoxide, an ester having a hydrogen on the α -carbon atom undergoes a wide variety of characteristic enolate reactions. Mechanistically, the base removes a proton from the α -carbon, giving an enolate that then can react with an electrophile. Depending on the final product, the base may be consumed stoichiometrically or may function as a catalyst. For example, the sodium alkoxide used in the Claisen condensation is a catalyst:



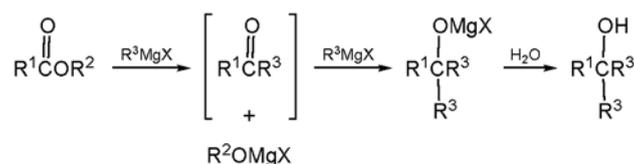
The intramolecular Claisen condensation of diesters, or Dieckman reaction, occurs readily to give five- or six-membered rings, and it has been extensively used for cyclopentanone and cyclohexanone derivatives.

Condensations of aldehydes or ketones with α -halo esters give α,β -epoxy esters. This is called the Darzens condensation.



The lithium enolate generated using lithium diisopropylamide [4111-54-0], lithium 2,2,6,6-tetramethylpiperidide [38227-87-1], or lithium hexamethyldisilazide [4039-32-1] is a chemical reagent that reacts with other reactants to give a variety of products (37). In the quest for improved stereospecificity, enolates with different cations such as silicon, aluminum, boron, and zinc have also been used (38). In group transfer polymerization, ketene silyl acetals, eg, $(\text{CH}_3)_2\text{C}=\text{C}[\text{OSi}(\text{CH}_3)_3](\text{OCH}_3)$ are employed as initiators (39).

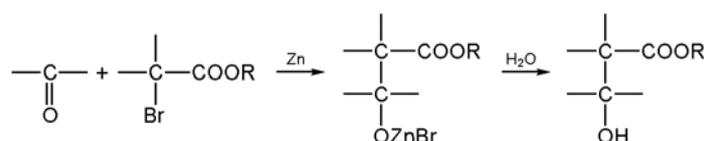
Grignard and Related Reactions. Esters react with alkyl magnesium halides in a two-stage process to give alcohols:



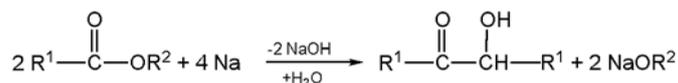
The reaction involves nucleophilic substitution of R^3 for OR^2 and addition of R^3MgX to the carbonyl group. With 1,4-dimagnesium compounds, esters are converted to cyclopentanol (40). Lactones react with Grignard reagents and give diols as products.

Many other organometallic compounds also react with carbonyl groups. Lithium alkyls and aryls add to the ester carbonyl group to give either an alcohol or an olefin. Lithium dimethylcuprate has been used to prepare ketones from esters (41). Tebbe's reagent, $\text{Cp}_2\text{TiCH}_2\text{AlCl}(\text{CH}_3)_2$, where Cp = cyclopentadienyl, and other metal carbene complexes can convert the $\text{C}=\text{O}$ of esters to $\text{C}=\text{CR}_2$ (42,43).

α -Halo esters react with aldehydes or ketones in the presence of zinc to form β -hydroxy esters. This is known as the Reformatsky reaction (44).

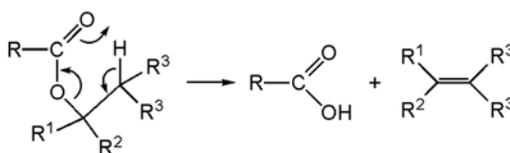


Preparation of Acyloins. When aliphatic esters are allowed to react with metallic sodium, potassium, or sodium-potassium alloy in inert solvents, acyloins (α -hydroxyketones) are formed (45):

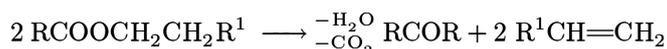


This reaction is used in the synthesis of large-ring compounds.

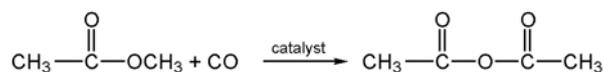
Pyrolysis. The pyrolysis of simple esters of the formula $\text{RCOOCR}^1\text{R}^2\text{CHR}^3$ to form the free acid and an alkene is a general reaction that is used for producing olefins:



The pyrolysis is generally carried out at 300–500°C over an inert heat-transfer agent such as Pyrex glass or 96% silica glass chips. Esters of tertiary alcohols are pyrolyzed more readily than esters of secondary alcohols, and esters of primary alcohols are the most difficult to pyrolyze. A detailed review on this reaction has been given (46). However, when heated to high temperatures in the presence of metal oxides such as thorium oxide, calcium oxide, manganese chromite, or zinc chromite, esters of primary alcohols give high yields of ketones (47):

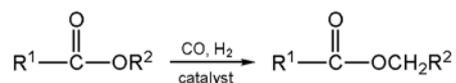


Carbonylation Reaction. The carbonylation of methyl acetate is an important industrial reaction for producing acetic anhydride:

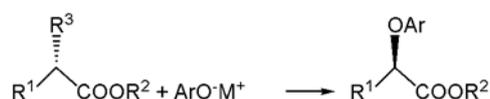


Earlier catalysts were based on cobalt, iron, and nickel. However, recent catalytic systems involve rhodium compounds promoted by methyl iodide and lithium iodide (48,49). Higher mol wt alkyl esters do not show any particular ability to undergo carbonylation to anhydrides.

Ruthenium complexes have been used in the hydrocarbonylation of simple esters to produce the corresponding homologous esters (50). The hydrocarbonylation affects the alkyl moiety rather than the carboxylate group:



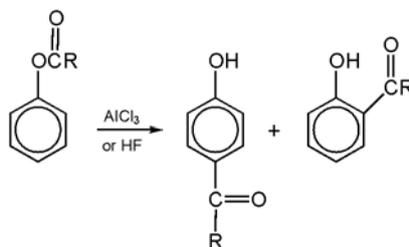
Substitution, Alkylation, and Rearrangement. The reaction of alkaline phenoxides with alkyl *S*-2-(chloro)- or *S*-2-(mesyloxy)propionate gives optically active *R*-2-aryloxyalkanoic acid esters in good chemical and optical yields (>97% ee) (51–53):



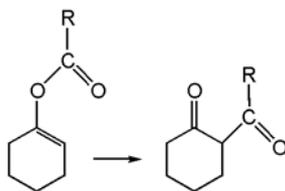
The reaction is utilized in the synthesis of several phenoxy herbicides.

Optically active 2-arylalkanoic acid esters have been prepared by Friedel-Crafts alkylation of arenes with optically active esters, such as methyl *S*-2-(chlorosulfonyl)- or *S*-2-(mesyloxy)propionate, in the presence of aluminum chloride (54,55).

The Fries rearrangement of phenol esters gives a mixture of 2- and 4-acylphenols (56). The reaction is catalyzed by Lewis acids such as aluminum chloride or by Brønsted acids like hydrogen fluoride. This reaction is used in the production of 4-hydroxyacetophenone [99-93-4], a raw material for acetaminophen [103-90-2] (57):



Similarly, enol esters undergo rearrangement to give the corresponding 1,3-diketones. This reaction can be accomplished thermally (500°C) or with a catalyst (58,59):



Occurrence and Preparation Currently, most of the simple esters used commercially are of synthetic origin, although esters occur naturally in large quantities in fats, oils, and waxes. Fats and oils from plants and animals consist mainly of glycerol esters of stearic, palmitic, and oleic acids (60). Natural waxes are esters of monobasic carboxylic acids with higher monohydric and, less commonly, dihydric alcohols. Microorganisms produce a complex array of compounds containing the ester linkage, ranging from simple esters to macrocyclic lactones, such as erythromycin, which are important because of their antibacterial properties.

Essential oils are obtained from fruits and flowers (61,62). Volatile esters of short- and medium-chain carboxylic acids or aromatic carboxylic acids with short- and medium-chain alcohols are primary constituents of essential oils, eg, ethyl acetate in wines, brandy, and in fruits such as pineapple; benzyl acetate in jasmine and gardenia; methyl salicylate in oils of wintergreen and sweet birch. Most of these naturally occurring esters in essential oils have pleasant odors, and either they or their synthetic counterparts are used in the confectionery, beverage, perfume, cosmetic, and soap industries (see OILS, ESSENTIAL).

Recovery of naturally occurring esters is accomplished by steam distillation, extraction, pressing, or by a combination of these processes. Synthetic esters are generally prepared by reaction of an alcohol with an organic acid in the presence of a catalyst such as sulfuric acid, *p*-toluenesulfonic acid, or methanesulfonic acid. Ion-exchange resins of the sulfonic acid type can also be used, and an azeotroping agent such as benzene, toluene, or cyclohexane can be used to remove water and force the reaction to completion (see ESTERIFICATION).

Analysis, Specifications, and Standards

Esters are often characterized by their physical properties. These include boiling point, freezing point, melting point, density, refractive index, residue or ash content, color, odor, and solubility. An overview of the different analytical methods used on organic esters has been written (63). The most common analytical method is the determination of the saponification value, ie, the number of milligrams of KOH necessary to hydrolyze 1.0 g of ester (64,65). Unsaturated esters, eg, natural fats and oils, are often sufficiently characterized by their iodine value. The iodine value is a measure of the number of double bonds in the molecule.

Standard analytical methods and techniques have been developed for the testing of organic esters and determination of specifications. Some of these specifications and the appropriate ASTM methods of analysis include distillation range (ASTM D1078-86), acidity (ASTM D1613-85), color (ASTM D1209-84), nonvolatile material (ASTM D1353-90), odor (ASTM D1296-84), purity (ASTM D3362-84), and water (ASTM D1364-90) and alcohol content (ASTM D3545-90).

Many chromatographic methods are applicable to organic ester analysis. Liquid chromatography, both normal and reverse phase, is used for all types of esters. Thin-layer and gas-liquid chromatography have been used for analysis of long-chain alkyl esters (waxes) and acrylates (66,67). If enantiomeric resolution is desired, then specialized stationary phases can be used with gas or liquid chromatography (68). Gas chromatographic and gas chromatographic-mass spectral methods of detection are required by the United States Government for monitoring and detection of some organic esters (69).

Esters are usually readily identified by their spectroscopic properties (70). Among these, infrared spectroscopy (ir) is especially useful for identifying the carbonyl of the ester group that has characteristic absorption bands. The C=O absorption is very strong in the ir at 1750–1735 cm^{-1} ; in addition, C–O stretching bands are observed in the range of 1100–1300 cm^{-1} . Another spectroscopic method used in identifying organic esters is nuclear magnetic resonance (nmr). The ^1H nmr spectra of esters are characteristic for those protons alpha to the carbonyl group. The peaks for these protons show chemical shifts relative to tetramethylsilane [75-76-3] (TMS) between δ 1.8–2.5 ppm. The peaks for protons alpha to the oxygen function appear between δ 3.3–4.0 ppm relative to TMS. Typical chemical shifts for olefinic protons of α,β -unsaturated esters and enol esters are between 4.5 and 7.5 ppm down field from TMS. The CH proton of formates gives a signal at about 8.0 ppm down field from TMS, and formate esters are therefore easily identified. Another diagnostic method is ^{13}C nmr spectroscopy (71,72) which is effective for the detection of ester groups since the ^{13}C resonance assignable to the carbonyl carbon of the ester group is observable in the range 160–180 ppm downfield from TMS, and is usually distinguishable from other types of carbonyl carbon atoms. Another useful method for ester determination is mass spectroscopy. The mass spectroscopy of esters (73) has been extensively investigated, and a number of general fragmentation processes have been recognized that may be useful for structure determination.

Stability and Storage

All organic esters are unstable in the presence of acid or base and nucleophiles such as water or alcohols. However, if stored anhydrous, they are stable. Storage vessels can be constructed of steel, aluminum, or other metallic materials, but plastic storage tanks are unsuitable because the highly lipophilic esters can sometimes permeate into the container boundary and soften or even dissolve it. When esters are stored in tanks, a nitrogen blanket and vent are necessary because of potential fire hazards. However, acrylates should

be stored in the presence of sufficient oxygen to enable the inhibitor to be effective in preventing polymerization. The esters with high melting points can be stored in paper or wood containers. Proper placarding, packaging, and labeling should always be used before transporting organic esters (74). Sometimes special precautions such as adding inhibitors must be taken before transporting polymerizable esters such as methyl acrylate (75).

The properties of flash point, autoignition temperature, and flammable limit should be considered when an ester is to be handled in any fashion. The flash point is the temperature at which a liquid gives off enough vapor to form an ignitable mixture with air. The flammable limits are the concentrations in air beyond which propagation of flame cannot occur. These limits are usually given as upper and lower concentrations. If the volume percent of the substance is kept above or below these limits, then the mixture will not sustain a flame in oxidizing atmospheres such as air. The autoignition temperature is the temperature required to enable self-sustained combustion of a substance. This information for some selected organic esters is given in Table 2 along with the NFPA ratings of health, flammability, and reactivity. The NFPA ratings are issued on a scale from 1 to 4, the higher value indicating the highest degree of flammability, toxicity, or reactivity.

Table 2. Flammability and Toxicity of Organic Esters

Ester	Auto-ignition temp, °C ^a	Upper flammable limit, vol % in air ^b	Lower flammable limit, vol % in air ^b	NFPA ^c hazard information toxicity data						
				Health	Flammability	Reactivity	Species	Oral LD ₅₀ , g/kg	PEL ^d , ppm	PEL ^d , mg/m ₃
methyl formate	449	23	4.5	2	4	0	rabbit	1.622	100	250
ethyl formate	455	16.0	2.8	2	3	0	rabbit	2.075	100	300
butyl formate	322	8.2	1.7	2	3	0	rabbit	2.66		
methyl acetate	454	16	3.1	1	3	0	rabbit	3.7	200	610
ethyl acetate	426	11.5	2	1	3	0	rabbit	4.97	400	1400
vinyl acetate	402	13.4	2.6	2	3	2	rat	2.92	10	35 ^e
propyl acetate	450	8	1.7(38°C)	1	3	0	rabbit	6.64	200	840
isopropyl acetate	460	8	1.8(38°C)	1	3	0	rabbit	6.95	250	950
butyl acetate	425	7.6	1.7	1	3	0	rat	14	150	710
isobutyl acetate	421	10.5	1.3	1	3	0	rabbit	4.8	150	700
<i>sec</i> -butyl acetate	422	9.8	1.7	1	3	0			200	950
<i>t</i> -butyl acetate		7.3	1.3						200	950
pentyl acetate	360	1.1	7.5	1	3	0	rat	16.6	100	532 ^e
isoamyl acetate	360	7.5	1(100°C)	1	3	0	rabbit	7.42	100	525
<i>sec</i> -hexyl acetate	266	5	0.9				rat	6.16	50	300
2-ethylhexyl acetate	268	8.14	0.76	2	2	0	rat	>3.2		
ethylene glycol diacetate	482	8.4	1.6	1	1	0	rat	6.86		
2-methoxyethyl acetate	394	8.2	1.7	0	2	0	rat	3.39	25	120
2-ethoxyethyl acetate	380	12.7(135°C)	1.7	2	2	0	rat	5.1	5	27 ^e
2-butoxyethyl acetate	340	8.54(135°C)	0.88(93°C)				mou se	1.6		
2-(2-ethoxyethoxy)ethyl acetate	360	23.5(182°C)	0.98(135°C)				rat	8.69		
2-(2-butoxyethoxy)ethyl acetate	290	24.6	0.76(135°C)				rat	11.9		
benzyl acetate	460	6.1	1(189°C)	1	1	0	rat	2.5		
glyceryl triacetate	433	6.4	1.0(189°C)	1	1	0	mou se	1.5 ^f		
glyceryl tripropionate	421		0.8(186°C)	0	1	0	rat	6.4		
ethyl 3-ethoxypropionate	377	8.7	1.05(88°C)				rat	5		
methyl acrylate	468	25	2.8	2	3	2	rat	3	10	35
ethyl acrylate	372	14	1.4	2	3	2	rabbit	1	25	100
butyl acrylate	292	9.9	1.7	2	2	2	rat	3.7	10	52 ^e
2-ethylhexyl acrylate	252	6.4	0.8	2	2	2	rat	5.6		
methyl methacrylate		8.2	1.7	2	3	2	rabbit	6.55	100	410
methyl butyrate		8.8	1.6	2	3	0	rabbit	3.38		
ethyl butyrate	463	7.7	1.3	0	3	0	rabbit	5.23		
butyl butyrate		6.1	1	2	2	0	rabbit	9.52		

methyl isobutyrate		9	1.6				rat	16	
ethyl isobutyrate		7.8	1.3	0	3	0	mou se	0.8 ^f	
isobutyl isobutyrate	432	7.59	0.96	0	2	0	rat	12.8 ^g	
methyl stearate				0	1	0			10 ^e
ethyl stearate									
butyl stearate	355	4.9	0.3	1	1	0	rat	>32	
dodecyl stearate									
hexadecyl stearate									
dimethyl maleate		10.4	1.6	1	1	0	rat	1.41	
dimethyl oxalate		8.4	1.5	0	2	0	rat	0.4–1.6	
dimethyl adipate							rat	1.81 ^f	
diethyl adipate							rat	>1.6	
di(2-ethylhexyl) adipate	377		0.4(242°C)	0	1	0	rat	9.1	
methyl benzoate		6.7	1.2	0	2	0	rabbit	2.17	
ethyl benzoate	490	6.1	1	1	1	0	rabbit	2.63	
methyl salicylate	454	7.2	1.2	1	1	0	rabbit	2.8	
ethyl salicylate							rat	1.32	
dimethyl phthalate	490	5.8	0.9(180°C)	0	1	0	mou se	7.2 ^f	5
diethyl phthalate	457	5.3	0.7(186°C)	0	1	0	rabbit	1	5 ^e
dibutyl phthalate	402	5.3	0.5(235°C)	0	1	0	rat	8	5 ^e
di(2-ethylhexyl) phthalate	390	5.3	0.3(245°C)				rat	>26	5
dimethyl isophthalate		5.8	1	0	1	0	rat	4.39	
dimethyl terephthalate	518	5.5	0.03	1	1	0	rat	>3.2	
methyl anthranilate				0	1	0	rat	2.91	
benzyl cinnamate							rat	5.53	
dimethyl carbonate				2	3	1	rat	13	
diethyl carbonate		12.4	1.7	2	3	1	mou se	8.5	

^c See Ref. 8.

^a ASTM D286 and D2155.

^b ASTM E6181 (temperature at which limit was determined).

^d Permissible exposure limit; see Ref. 76.

^e Threshold limit value–time-weighted average.

^f Intraperitoneal.

^g LD₁₀₀.

If an organic ester is released, then appropriate action must be taken. The United States Department of Transportation has recommendations for responding to such an event. This includes treating the released material as flammable and poisonous if inhaled or absorbed through the skin. Another recommendation is to be aware that combustion may produce irritating or poisonous gases, thus requiring a positive pressure self-contained breathing apparatus to be worn if exposure is possible. Finally, for fighting fires containing organic esters, dry chemical, CO₂, water spray, or alcohol-resistant foam extinguishing media should be used (77).

Health and Safety Factors

Toxicity. The degree of toxicity of organic esters covers a wide range (78). These toxicities are usually described in terms of threshold limiting values (TLV), or permissible exposure limits (PEL). Both the PEL and the TLV describe the average concentration over an 8-h period to which a worker may be exposed without adverse effects (79). The PEL and TLV data are often interchangeable, although OSHA uses the PEL values (Table 2). The lethal dosages for 50% of the exposed animals, LD₅₀s, are also used as an indicator of the relative toxicity. An accumulation of the LD₅₀ data of organic esters for rabbits, rats, and mice can also be found in Table 2. The LD₅₀s of organic esters for small mammals range between 0.4 and 16 g/kg. The TLVs of organic esters range between 5 and 400 ppm.

When ingested or absorbed, organic esters are likely to be hydrolyzed to the corresponding alcohols and carboxylic acids. Therefore the toxicities of the hydrolysis products should also be considered (80,81). Some organic esters are highly volatile and can act as asphyxiant or narcotic. Also, skin absorption and inhalation are among the hazards associated with esters that are volatile or have

good solvent action. Because of the high solubility of fats and oils in organic esters, prolonged or repeated exposure to skin can cause drying and irritation.

Formate esters generally become less toxic as the alcohol moiety increases up to C₄. With this increase in alkyl size, the LD₅₀ (oral, rabbit) increases from 1.62 g/kg for methyl formate to 3.0 g/kg for isoamyl formate [110-45-2]. In comparison, both allyl and vinyl formates are more toxic than their saturated analogues.

Acetates generally do not cause any physiological effects unless high exposure occurs since they are usually converted into or occur naturally as metabolites. However, large enough exposure to acetate esters can cause narcotic effects. The aromatic acetate esters cause death more rapidly than aliphatic acetates with oral LD₅₀s (rat) ranging between 2.5 and 1.6 g/kg for phenyl and benzyl acetate compared to LD₅₀s (rat) of 4.8 to 8.3 g/kg for methyl through propyl acetate. Vinyl acetate gives approximately the same level of toxicity as the other acetate esters and less so when it is polymerized.

Propionates and higher aliphatic esters generally become less toxic as the size of the alkyl carboxylate increases. As an example, the LD₅₀ (rat, oral) for ethyl nonanoate [123-29-5] is greater than 43 g/kg, and the LD₅₀ (rat, oral) for ethyl heptanoate [106-30-9] is 34.6 g/kg.

The acrylate esters are more physiologically hazardous than their saturated homologues. They are usually lachrymators and irritants, and their toxicities decrease with increasing molecular weights. The LD₅₀s of acrylates usually fall between 1 and 5 g/kg for rabbits. Methacrylate esters are generally less toxic than their corresponding acrylates. The decreased physiological activity is believed to result from added steric hindrance of the α -methyl group, but the methacrylates are potent sensitizers.

Among adipates, oxalates, malonates, and succinates, the adipates are the least toxic. An example of this can be seen in the comparison between di(2-ethylhexyl) adipate, which has an oral LD₅₀ rat of 9.1 g/kg, and di(2-ethylhexyl) succinate [117-81-7], which has an oral LD₅₀ rat of 4.3 g/kg. The malonates and oxalates are generally more toxic than the adipates. Exposure to diethyl oxalate [95-92-1], the most common oxalate, gives symptoms similar to exposure to oxalic acid [114-62-7], ie, twitching and convulsions. The malonates presumably are less toxic than oxalates because the corresponding malonic acid sodium and calcium salts are much more soluble than calcium oxalates and are thus more easily excreted.

Benzoate esters, like most organic esters, are not very toxic. They are not absorbed through the skin as rapidly as alkyl esters but are more potent physiologically. They are also moderate skin irritants. The oral LD₅₀s (mouse) for methyl- to butylhydroxy benzoates range between 8 and 5 g/kg.

The phthalate esters are one of the most widely used classes of organic esters, and fortunately they exhibit low toxicity (82). Because of the ubiquitous nature of phthalates, many investigations have been conducted to determine their toxicities to marine life as well as in mammals (83–85). Generally, phthalates are not absorbed through the skin and are not very potent when inhaled. The phthalates become less toxic as the alcohol group increases in molecular weight. For example, dimethyl phthalate has an oral LD₅₀ (mouse) of 7.2 g/kg, whereas di(2-ethylhexyl) phthalate shows an oral LD₅₀ (rat) of greater than 26 g/kg.

More information on the toxicities of a range of organic esters is available in the literature (86,87).

Exposure Limits. The Occupational Safety and Health Act (OSHA) of 1990 lists a multitude of acetates, phthalates, formates, and acrylates along with the corresponding permissible exposure limits and threshold limit values (76). The PEL data is listed in Table 2. If there is potential for exposure to an organic ester for which PEL or TLV data has been identified, then an exposure limit lower than that listed is usually selected for working in that environment.

Regulation and Waste

Waste from production of organic esters is usually not a problem since the method of synthesis often involves a carboxylic acid condensation with an alcohol and the only by-product is water. Any organic remnants lost to the process water can usually be biologically degraded. The biochemical oxygen demand (BOD) or chemical oxygen demand (COD) should be measured if biological treatment is used on the process waste from ester production (87). Organic ester vapor emitted in processing usually can be burned.

Extensive federal environmental regulations exist that govern organic esters as well as many other substances (88). These regulations must always be consulted for complete information before using large amounts of organic esters (89). State and local regulations must also be met, which in some cases are more stringent than federal regulations.

Among these federal regulations, the Clean Air Act regulates the amount of an organic ester or other substance that is allowed to be emitted into the atmosphere. Several organic esters are listed as Hazardous Air Pollutants in the Clean Air Act amendments of 1990, and therefore are more tightly regulated (90). If an organic ester is sent to a wastewater treatment facility and subsequently discharged to surface waters, then compliance with the Clean Water Act is required (91). If an organic ester or other substance becomes a solid waste as defined under the Resource Conservation and Recovery Act (RCRA), then specific requirements apply that regulate the treatment, storage, and disposal of that waste. Regulations under RCRA and the Department of Transportation also apply that pertain to the proper labeling, manifesting, and shipping of hazardous wastes (92). The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) provides a list of hazardous substances, some of which are organic esters (93). The organic esters listed in CERCLA must be properly reported if spilled or otherwise released to the environment in amounts exceeding the reportable quantities specified. Note that spills or releases may need to be reported to state agencies even in amounts that do not exceed the CERCLA reportable quantity. The Superfund Amendments and Reauthorization Act (SARA) of 1986 established

regulations requiring facilities to annually report organic esters and other chemicals stored on-site in amounts exceeding reporting thresholds in pure form or as percentages in mixtures. Facilities must also report certain organic esters and other chemicals (listed under SARA 313) that are stored in amounts exceeding reporting thresholds that are released to the environment via air, water, or off-site disposal (94).

Uses

Table 3 lists only those carboxylic acid esters whose 1990 U.S. production, sales quantity, value, and raw materials have been published (95). They are grouped on the basis of their principal use. For a complete list of the organic esters produced and sold in the United States and their manufacturers, the original publication should be consulted. Uses of some specific esters are also given in Table 4.

Table 3. U.S. Production and Sales of Carboxylic Esters, 1990

Material	CAS Registry Number	Production, t	Sales	
			Quantity, t	Value, 10 ³ \$
	<i>Plasticizers</i>			
phthalic anhydride esters, total		573,892	572,137	544,485
dibutyl phthalate (including diisobutyl phthalate)	[84-76-2]	7,917	7,714	7,936
diisononyl phthalate	[28553-12-0]	93,575	93,911	78,011
dimethyl phthalate (including dimethyl isophthalate)	[131-11-3]	5,679	5,194	5,830
dioctyl phthalates		140,649	149,805	119,159
all other phthalic anhydride esters		326,072	315,513	333,549
trimellitic acid esters		22,942	28,631	44,524
adipic acid esters, total		87,020	46,683	79,371
di(2-ethylhexyl) adipate	[103-23-1]	24,228	24,587	30,489
diisodecyl adipate	[1330-86-5]	1,494	732	1,211
all others adipic acid esters		61,298	21,364	47,662
complex linear polyesters and polymeric plasticizers		52,904	28,820	59,484
epoxidized esters		47,456	46,518	54,132
butyl oleate	[142-77-8]	805	775	1,149
sebacic acid esters, total		3,139	2,902	14,995
dibutyl sebacate	[109-43-3]	259	268	1,008
all other sebacic acid esters		2,880	2,634	13,987
stearic acid esters, total		5,093	4,850	8,632
isobutyl stearate	[646-13-9]	3,444	3,406	4,338
all other stearic acid esters		1,649	1,444	4,294
	<i>Surface-active agents</i>			
carboxylic acid esters, total		166,424	129,375	238,044
anhydrosorbitol esters, total		18,986	14,303	24,106
anhydrosorbitol monolaurate	[1338-39-2]	3,744	2,399	4,594
anhydrosorbitol monooleate	[1338-43-8]	4,442	2,493	4,676
anhydrosorbitol monostearate	[1338-41-6]	8,782	7,919	12,170
all other anhydrosorbitol esters		2,018	1,492	2,666
diethylene glycol esters, total		2,857	1,653	3,701
diethylene glycol monolaurate	[141-20-8]	105	105	172
all other diethylene glycol esters		2,752	1,548	3,529
ethoxylated anhydrosorbitol esters, total		14,292	13,117	29,875
ethoxylated anhydrosorbitol monolaurate	[9005-64-5]	3,315	2,991	7,332
ethoxylated anhydrosorbitol monooleate	[9005-65-6]	3,852	3,554	7,486
ethoxylated anhydrosorbitol monostearate	[9005-67-8]	5,117	4,772	10,803
ethoxylated anhydrosorbitol tristearate	[9005-71-4]	273	291	659
all other ethoxylated anhydrosorbitol esters		1,735	1,509	3,595
	<i>Surface-active agents</i>			
ethylene glycol distearate	[627-83-8]	1,483	1,434	2,475
ethylene glycol monostearate	[111-60-4]	2,021	1,907	3,554
glycerol esters, total		47,883	37,518	71,108
glycerol dilaurate	[27638-00-2]	233	176	489
glycerol monooleate	[25496-72-4]	4,802	4,926	8,466
glycerol monostearate	[1319-95-5]	3,828	3,869	7,252

all other glycerol esters		39,020	28,547	54,901
natural fats and oils, ethoxylated, total		26,300	18,239	28,530
castor oil, ethoxylated	[61791-12-6]	10,552	9,025	12,366
hydrogenated castor oil, ethoxylated	[61788-85-0]	1,895	1,671	2,233
lanolin, ethoxylated	[61790-81-6]	215	201	529
all other natural fats and oils, ethoxylated		13,638	7,342	13,402
poly(ethylene glycol) esters, total		27,483	21,503	34,975
poly(ethylene glycol) diester of tall oil acids		3,003	832	844
poly(ethylene glycol) dilaurate	[9005-02-1]	724	643	946
poly(ethylene glycol) dioleate	[9005-07-6]	2	610	1,153
poly(ethylene glycol) distearate	[9005-08-7]	920	821	2,726
poly(ethylene glycol) monolaurate	[9004-81-3]	3,456	3,504	5,309
poly(ethylene glycol) monooleate	[9004-96-0]	1,865	1,752	2,312
poly(ethylene glycol) monopalmitate	[9004-94-8]	792		
poly(ethylene glycol) monostearate	[9004-99-3]	3,158	2,928	5,353
poly(ethylene glycol) sesquiester of tall oil acids	[61791-30-8]	865	873	1,652
all other poly(ethylene glycol) esters		10,971	9,540	14,680
poly(glycerol monooleate)	[9007-48-1]	315	265	829
poly(glycerol monostearate)	[37349-34-1]		26	102
1,2-propanediol monostearate	[1323-39-3]	775	199	812
all other carboxylic acid esters		24,029	19,211	37,977
<i>Flavor and perfume materials</i>				
benzyl benzoate	[120-51-4]	245	255	721
phenethyl isobutyrate	[103-48-0]	10		
2-phenethyl phenylacetate	[102-20-5]	24		
cedryl acetate	[77-54-3]	96	30	424
citronellyl acetate	[150-84-5]	41	22	261
citronellyl formate	[105-85-1]	11	5	109
3,7-dimethyl- <i>cis</i> -2,6-octadienol, acetate (neryl acetate)	[141-12-8]	13	12	129
<i>Miscellaneous chemicals</i>				
esters of monohydric alcohols, total		3,113,090	1,481,937	1,354,300
<i>n</i> -butyl acetate	[123-86-4]	114,530	93,242	70,511
butyl acrylate	[141-32-2]	280,129	108,684	129,733
dilauryl-3,3'-thiodipropionate	[123-28-4]	694	704	2,684
distearyl-3,3'-thiodipropionate	[693-36-7]	2,519	2,456	8,168
ethyl acetate (100% basis)	[141-78-6]	123,522	113,668	76,296
ethyl acrylate	[140-88-5]	136,485	66,442	71,791
2-ethylhexyl acrylate	[103-11-7]	53,348	46,300	55,475
fatty acid esters, not included with plasticizers or surface-active agents, total		5,614	2,955	4,904
methyl esters of tallow	[61788-61-2]	2,526		
myristyl myristate	[3234-85-3]		88	607
all other fatty acid esters not included with plasticizers or surface-active agents		3,088	2,867	4,297
isopropyl acetate	[108-21-4]	20,376	19,299	16,970
methyl methacrylate, monomer	[80-62-6]	536,283		
propyl acetate	[109-60-4]	32,868	30,612	29,968
vinyl acetate, monomer	[108-05-4]	1,206,021	674,970	465,772
all other monohydric alcohol esters		471,306	292,578	357,367
polyhydric alcohol esters, total		145,708	128,357	184,527
2-(2-butoxyethoxy)ethyl acetate	[112-34-5]	4,701	2,957	4,476
2-butoxyethyl acetate	[112-07-2]	8,357	6,492	9,709
glycerides, mixed C14–18 and C16–18, mono- and di-		13,863	13,387	16,993
all other polyhydric alcohol esters		118,787	105,521	153,349

Table 4. Uses of Some Specific Esters

Name and structure	Use
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methyl formate, HCOOCH_3	raw material for production of formamide, dimethylformamide, and formic acid
methyl acetate, $\text{CH}_3\text{COOCH}_3$	solvent for cellulose nitrate, cellulose acetate, and many resins and oils; used in the manufacture of artificial leather; raw material for production of acetic anhydride via carboxylation
ethyl acetate, $\text{CH}_3\text{COOC}_2\text{H}_5$	primarily as a solvent for various resins in protective coatings; also used extensively in formulating printing inks and adhesives; new applications include its uses as a process solvent in the pharmaceutical industry and as an extraction solvent in food processing; as a substitute ^a for methyl ethyl ketone (MEK) in many applications
propyl acetate, $\text{CH}_3\text{COOCH}_2\text{CH}_2\text{CH}_3$	good solvent for cellulose nitrate, chlorinated rubber, and heat-reactive phenolics; principal use is as a printing ink solvent ^b
isopropyl acetate, $\text{CH}_3\text{COOCH}(\text{CH}_3)_2$	active solvent for many synthetic resins, such as ethylcellulose, cellulose acetate butyrate, cellulose nitrate, some vinyl copolymers, polystyrene, and methacrylate resins; as a solvent for printing ink; like propyl acetate, it can also be used in the recovery of acetic acid from dilute aqueous solutions
butyl acetate, $\text{CH}_3\text{COO}(\text{CH}_2)_3\text{CH}_3$	excellent solvent for inks and lacquers because of its high blush resistance and evaporation rate; widely used as solvent in paints, thinner, video tape binders, and extraction of pharmaceuticals; also used as a perfume ingredient and as a component in synthetic flavors such as apricot, banana, butter, pear, quince, pineapple, grenadine, butterscotch, and raspberry; also a cleaning solvent for silicon wafers
isobutyl acetate, $\text{CH}_3\text{COOCH}_2\text{CH}(\text{CH}_3)_2$	resembles butyl acetate and methyl isobutyl ketone (4-methyl-2-pentanone) and can be used interchangeably for these solvents in many formulations; also a component in synthetic flavors of apple, apricot, banana, butter, mirabelle plum, pineapple, rum, and strawberry
amyl acetates, $\text{CH}_3\text{COOC}_5\text{H}_{11}$	amyl acetate and mixed amyl acetates (a mixture of normal, secondary, and isoamyl acetates) are used as lacquer solvents, as extractants in penicillin manufacture, and in the production of photographic film, leather polishes, dry-cleaning preparations, and flavoring agents; mixed <i>sec</i> -amyl acetates are used as solvents for cellulose compounds and in the production of leather finishes, textile sizes, and printing compounds; isoamyl acetates are used as solvents and in flavorings and perfumes
2-ethylhexyl acetate, $\text{CH}_3\text{COOCH}_2\text{CH}(\text{C}_2\text{H}_5)(\text{CH}_2)_3\text{CH}_3$	high boiling retarder solvent with limited water solubility used to promote flow of and retard blushing in lacquers, emulsions, and silk-screen inks, and as a flow-control agent in baking enamels; also used as a dispersant for vinyl organosols, and as a coalescing aid for latex paints
2-butoxyethyl acetate, $\text{CH}_3\text{COOCH}_2\text{CH}_2\text{OC}_4\text{H}_9$	slow-evaporating glycol ether ester useful as a coalescing aid in poly(vinyl acetate) emulsion system; also used as a retarder solvent in lacquers, enamels, and printing inks
2-(2-butoxyethoxy) ethyl acetate, $\text{CH}_3\text{CO}(\text{OCH}_2\text{CH}_2)_2\text{OC}_4\text{H}_9$	solvent in printing inks and high bake enamels; also used as a coalescing aid in latex paints, in silk-screen inks, and as a component in polystyrene coatings for decals
1-methoxy-2-propyl acetate, ^c $\text{CH}_3\text{CH}(\text{OCOCH}_3)\text{CH}_2\text{OCH}_3$	solvent in inks, ink remover, paints, automotive coatings, and photoresist; also a substitute for 2-ethoxyethyl acetate in many applications
benzyl acetate, $\text{CH}_3\text{COOCH}_2\text{C}_6\text{H}_5$	component of the extract of gardenia, hyacinth, and ylang-ylang, and the main component of extract of jasmine; most benzyl acetate is used in soap odors, but it is also popular for other perfumes and is used to a minor extent in flavors
ethyl 3-ethoxypropionate, $\text{C}_2\text{H}_5\text{OCH}_2\text{CH}_2\text{COOC}_2\text{H}_5$	linear ether ester with excellent solvent properties for many of the polymers and resins used in coating industry; provides lower solution viscosity than many other retarder solvents of similar evaporation rate, and it can be a replacement for 2-ethoxyethyl acetate
isobutyl isobutyrate, $(\text{CH}_3)_2\text{CHCOOCH}_2\text{CH}(\text{CH}_3)_2$	a retarder solvent in wood lacquers, automotive coatings, metal coatings, and a variety of thinner blends; also used in high solids coatings because of its low surface tension, which improves surface characteristics; its

2,2,4-trimethyl-1,3-pentanediol ^d monoisobutyrate	distinct odor and flavor make it an interesting material for the formulation of perfumes, and as a bulk component of flavor essences widely used as a coalescing aid in latex paints, effective with a broad range of latex emulsion systems; retarder solvent for high solid coat-ings, and a sweetener in letterpress and litho-graphic inks to improve solvent activity of ink's solvent system
butyl stearate, $\text{CH}_3(\text{CH}_2)_{16}\text{COO}(\text{CH}_2)_3\text{CH}_3$	used for compounding lubricating oils, as a lubricant for the textile and molding trade, in special lacquers, and as a waterproofing agent; in the cosmetic and pharmaceutical fields, it is used in vanishing creams, oint-ments, rouges, lipsticks, and nail polishes; its oily characteristics have made it of particular value in polishes and coatings that are to be polished
di(2-ethylhexyl) adipate, $[\text{CH}_2\text{CH}_2\text{COOCH}_2\text{CH}(\text{C}_2\text{H}_5)\text{C}_4\text{H}_9]_2$	plasticizer to impart low temperature flexibility to PVC formulations, particularly in vinyl meat-wrapping film
benzyl benzoate, $\text{C}_6\text{H}_5\text{COOCH}_2\text{C}_6\text{H}_5$	used in perfumery as a fixative, as a solvent for synthetic musks, and in confectionery and chewing gum flavors; also used in medicine and cosmetics and as plasticizer, insect repel-lent, and dye carrier
methyl salicylate, $2\text{-OHC}_6\text{H}_4\text{COOCH}_3$	main component of wintergreen oil and occurs in small quantities in other essential oils and fruit; used primarily for the relief of muscular aches, articular rheumatism, and neuralgia; as a flavor and fragrance agent, it is used in confectionery, dentifrices, cosmetics, and in perfumes; also used as a dye carrier and uv light stabilizer in acrylic resins
benzyl salicylate	widely used in soap and cosmetic industry as fragrance; also effective in absorbing uv light, and can be used in protective sunscreen lotions
methyl 4-hydroxybenzoate	broad spectrum of antimicrobial activity, low levels of toxicity, excellent stability and inert-ness; used as preservative in cosmetic formu-lations, general-purpose cleaners, disinfec-tants, and mouth wash and contact lens cleaning solutions; also used as food additive and pharmaceutical preservative
methyl cinnamate, $\text{C}_6\text{H}_5\text{CH}=\text{CHCOOCH}_3$	fragrance in soaps, perfumes, and confectioneries
2-ethylhexyl 4-methoxycinnamate	absorbs uv rays effectively; thus about 75% of all sunscreen formulations use it; usually nonal-lergenic and nonstaining
dimethyl phthalate	raw material for polyesters; also used as plasti-cizer, mosquito repellent, dye carrier, and in hair sprays
dimethyl terephthalate	raw material for polyesters such as poly(ethylene terephthalate), poly(butylene terephthalate), and unsaturated polyester
di(2-ethylhexyl) phthalate ^e	plasticizer; also used as an insulating fluid in electrical transformers and upressure-sensitive printing

^a Ethyl acetate (exempt solvent) is much less toxic than MEK.

^b Compared with ethyl acetate and isopropyl acetate, propyl acetate has slow evaporation rate and good solvent power which promote improved flow and leveling characteristics in a variety of coating formulations.

^c Propylene glycol methyl ether acetate.

^d $(\text{CH}_3)_2\text{CHCOOCH}_2\text{C}(\text{CH}_3)_2\text{CH}(\text{OH})\text{CH}(\text{CH}_3)_2$.

^e Dioctyl phthalate (DOP).

Solvents. Lower esters are extensively used as solvents in coatings (eg, paints and top coats on automobiles), inks, and adhesives, and in processing other substances (96). They readily dissolve resins or their precursors to become vehicles for application. Because these solvent esters are not on the list of 189 hazardous air pollutants regulated by Section 112 of the Clean Air Act of 1990, they will not face the decline in use in the short term that methyl ethyl ketone and methyl isobutyl ketone will. However, in the long term, environmental concerns enforced by regulations to reduce the amount of volatile organic components (VOCs) in air will gradually decrease the usage of esters in solvent applications.

Plasticizers. Plasticizers are materials that soften and flexibilize inherently rigid, and even brittle polymers. Organic esters are widely used as plasticizers in polymers (97,98). These esters include the benzoates, phthalates, terephthalates, and trimellitates, and aliphatic dibasic acid esters. For example, triethylene glycol bis(2-ethylbutyrate) [95-08-9] is a plasticizer for poly(vinyl butyral) [63148-65-2], which is used in laminated safety glass (see VINYL POLYMERS, POLY(VINYL ACETALS)). Di(2-ethylhexyl)phthalate [117-81-7] (DOP) is a preeminent plasticizer. Variation of acid and/or alcohol component(s) modifies the efficacy of the resultant ester as a plasticizer. In phthalate plasticizers, molecular sizes of the alcohol moiety can be varied from methyl to tridecyl to control permanence, compatibility, and efficiency; branched (eg, 2-ethylhexyl, isodecyl) for rapid absorption and fusion; linear (C6–C11) for

low temperature flexibility and low volatility; and aromatic (benzyl) for solvating. Terephthalates are recognized for their migration resistance, and trimellitates for their low volatility in plasticizer applications.

Resins, Plastics, and Coatings. Unsaturated and difunctional esters are important monomers for the manufacture of many polymers in commercial use. For example, free-radical polymerization of vinyl acetate and methyl methacrylate produces poly(vinyl acetate) [9003-20-7] (PVAc) and poly(methyl methacrylate) [9011-14-7], respectively. Applications of PVAc include latex paint, paper manufacturing, coating for paper board, and adhesives for packaging and labeling (see [VINYL POLYMERS, POLY\(VINYL ACETATE\)](#)). Poly(methyl methacrylate) is used for glazing, lighting fixtures, optical fibers, and surface coatings (see [METHACRYLIC POLYMERS](#)). Another example is dimethyl terephthalate (DMT) which reacts with ethylene glycol to yield poly(ethylene terephthalate) [25038-59-9] (PET). PET is used in fibers, films, and bottles (see [POLYESTERS](#)). Liquid crystal polymers (LCPs) are a class of thermoplastic polyesters with aromatic carbon backbones. Amoco's Xydar resins are based on terephthalic acid, 4,4'-dihydroxybiphenyl [92-88-6], and 4-hydroxybenzoic acid [99-96-7]. Hoechst Celanese's Vectra resins are based on 4-hydroxybenzoic acid and 6-hydroxy-2-naphthoic acid (see [ENGINEERING PLASTICS](#)). LCPs have found application in aviation, electronics (connectors, sockets, chip carriers), automotive underhood parts, and chemical processing. Copolymerization of ethylene with unsaturated esters such as vinyl acetate, methyl acrylate, ethyl acrylate, or butyl acrylate yields polyolefins with special properties. Unsaturated polyesters, produced by condensation of unsaturated dibasic acids (eg, maleic anhydride), and glycols (eg, propylene glycol), are used as thermosets when combined with a cross-linking agent (eg, styrene) in the presence of a free-radical initiator and a promoter. Their applications include boat, automotive exterior parts, cultured marbles, bowling balls, polymeric concrete, and coatings. Polyester polyols are used in polyurethanes (see [URETHANE POLYMERS](#)).

Poly(3-hydroxybutyrate-3-hydroxyvalerate) [80181-31-3] resin, produced from a bacterium during a sugar fermentation process, has been reported to be biodegradable, and its target markets include "flushables" such as feminine hygiene products and disposable diapers (99).

Lubricants. Monohydric alcohol esters of dibasic acids and polyol esters of monobasic acids are synthetic lubricants (100). They are generally prepared from the following alcohols and acids: (1) C₈–C₁₃ monohydric alcohols such as 2-ethylhexyl, isoctyl, isodecyl, and isotridecyl alcohols; (2) polymethylol compounds such as trimethylolpropane, pentaerythritol, and dipentaerythritol; (3) C₆–C₁₀ monobasic acids such as heptanoic and nonanoic acids; and (4) C₆–C₁₀ dibasic acids such as adipic, azelaic and sebacic acids, and phthalic anhydride. These esters are mainly used as base oils in high performance lubricants for automotive (eg, engines), aviation (eg, gas turbines), and machinery (eg, gear, chain, and air compressor) industries. Compared with petroleum oils, ester lubricants exhibit lower pour point, higher thermal and oxidation stability, high viscosity index, lower volatility, and better lubricity. For example, bis(2-ethylhexyl) sebacate [122-62-3] is widely used as base oil for lubricating turbojet engines. Polyol esters are used as textile lubricants because of reduced carbon deposit formation.

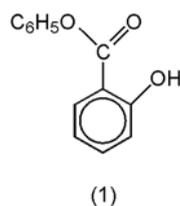
Perfumes, Flavors, Cosmetics, and Soap. Many naturally occurring esters in essential oils and some synthetic esters are important fragrance and flavor compounds (61,62). They are used in perfumes, flavors, cosmetics, soaps, detergents, and air fresheners. Benzyl, butyl, ethyl, methyl, and phenyl esters of benzoic acid are used as flavors, perfumes, and food preservatives. Glyceryl 4-aminobenzoate [136-44-7] and 2-ethylhexyl 4-dimethylaminobenzoate [21245-02-3] are used in cosmetic sunscreen preparations. Alkyl esters of 4-hydroxybenzoic acid, called parabens, have been used under various names for fungus infections of the skin, and as preservatives in lotions and creams (101). Soap and cosmetic fragrances use large amounts of amyl and benzyl salicylate. Benzyl salicylate [118-58-1] is also used in deodorant sprays. 2-Ethylhexyl salicylate [118-60-5] and 2-ethylhexyl 4-methoxycinnamate [5466-77-3] are used in sunscreen formulations (102).

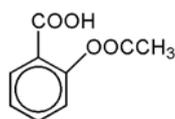
Benzyl diethyl[(2,6-xylylcarbonyl)methyl]ammonium benzoate (denatonium benzoate [3734-33-6], Bitrex) is an extremely bitter tasting, nonirritating, and nonmutagenic compound that has been widely used in many household products such as detergents, nail polish removers, and cleaning agents, to prevent childhood poisoning. It is also used as an alcohol denaturant.

Organic esters in the form of fats and oils from tallow and plants such as soybean, cottonseed, linseed, and castor bean are important raw materials for soap, paints, and food industries.

Surface-Active Agents. Polyol (eg, glycerol, sorbitol, sucrose, and propylene glycol) or poly(ethylene oxide) esters of long-chain fatty acids are nonionic [surfactants](#) (qv) used in foods, pharmaceuticals, cosmetics, textiles, cleaning compounds, and many other applications (103,104). Those that are most widely used are included in Table 3.

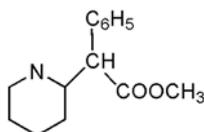
Medicinals. Many esters are used as pharmaceuticals (105,106). Of these, benzocaine, ethyl 4-aminobenzoate [94-09-7] is a topical anesthetic. Phenyl salicylate [118-55-8] (1) has antipyretic, antirheumatic, and antiparasitic properties.



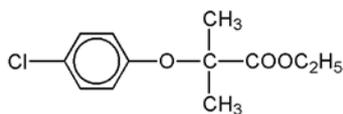


(2)

Some simple benzoates are also used as antiseptic agents. Salicylic acid esters are used as antibacterial agents and pain relievers. Analgesic balms, creams, sprays, and nasal inhalers usually contain various combinations of either methyl or menthyl salicylate and menthol. In general, esterification of a physiologically active alcohol or phenol with aliphatic carboxylic acid or an acid with alcohol detoxifies it by decreasing the concentration of active compound present. The active compound is released gradually in the body by hydrolysis of the ester (107). Examples include aspirin [50-78-2] (2), a common analgesic; methyl phenidate [113-45-1] (3), a central nervous system stimulant; and clofibrate [637-07-0] (4), a antihyperlipoproteinemic.

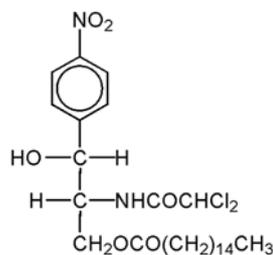


(3)



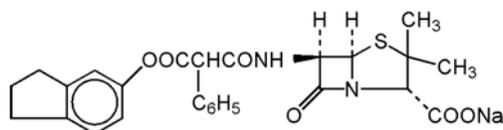
(4)

In recent years, many parent drugs have been converted to esters to generate so-called prodrugs in order to overcome some undesirable property such as bitter taste, poor absorption, poor solubility, and irritation at site of injection. For example, antibiotics such as chloramphenicol [56-75-7] and clindamycin [18323-44-9] have been derivatized as their palmitate esters in order to minimize their bitter taste.

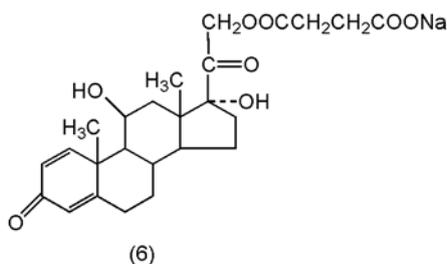


chloramphenicol palmitate

In order to improve the poor oral absorption of carbenicillin [4697-36-3], a lipophilic indanyl ester has been formulated, Geocillin [35531-88-5] (5). Prednisolone [50-24-8], a steroid, is derivatized to its C-21 hemisuccinate sodium salt (6) to make it extremely water-soluble (108).

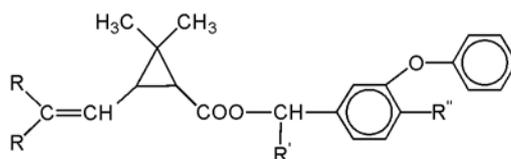
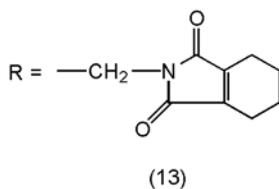
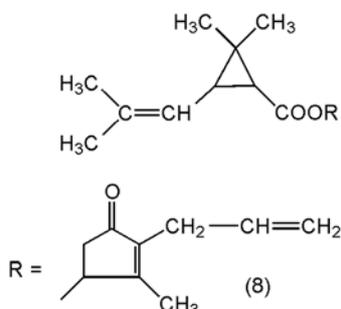
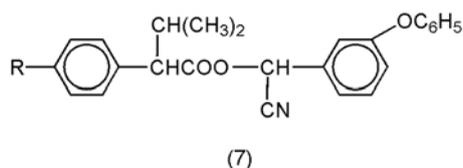


(5)



Herbicides and Pesticides. Several esters are used as herbicides and pesticides (109–111). Many halogenated benzoic acid esters are phytotoxic and are used as herbicides. Dimethyl tetrachloroterephthalate [1861-32-1] and diisopropyl 5-nitroisophthalate [10552-74-6] are used as herbicide and fungicide, respectively. The phenoxy herbicides are primarily propyl, butyl, and isooctyl esters of 2,4-dichlorophenoxyacetic acid [94-75-7], 4-chloro-2-methylphenoxyacetic acid [93-65-2], and methyl, ethyl, or butyl esters of 2-(4-hydroxyphenoxy)propionic acid [67648-61-7]. Because of their low toxicity, high selectivity, and relatively short life in the soil, phenoxy herbicides are widely used. They are used for controlling weeds in a large number of grass crops, ie, corn, small grains, sorghum, rice, sugarcane, pasture, range land, and turf.

Pyrethroids are synthetic esters produced to imitate or improve the activity of biological principles of the pyrethrum plant. They are powerful contact insecticides causing rapid knockdown of treated insects. The pyrethroids are extensively used in controlling insect pests on fruit trees, vegetables, and other field crops; in space sprays and contact sprays to kill insects infesting homes, industrial locations, and nonfood processing areas; and in protection of warehoused food. These compounds include fenvelerate [51630-58-1], (7), R = Cl; flucythrinate [70124-77-5], (7) R = CHF₂O; allethrin [584-79-2] (8); cyfluthrin [68359-37-5] (9); cypermethrin [52315-07-8] (10); deltamethrin [52918-63-5] (11); permethrin [52645-53-1] (12); and tetramethrin [7696-12-0] (13).



- (9) R = Cl; R' = CN; R'' = F
 (10) R = Cl; R' = CN; R'' = H
 (11) R = Br; R' = CN; R'' = H
 (12) R = Cl; R' = H; R'' = H

Miscellaneous Uses. Since esters can be made and hydrolyzed with ease, they are used as protecting groups for hydroxyl and carboxylic acid groups (112). Acetates and benzoates are widely used in carbohydrate, steroid, and nucleoside chemistry, and their cleavage is based on hydrolysis with base, ammonolysis, or methanolysis. Of great importance in peptide chemistry are the *t*-butyl, benzyl, and substituted benzyl esters (113,114). In recent years, esters as protecting groups have played an increasing role in modulating efficacy and bioavailability of pharmaceuticals.

Esters such as benzoates and phthalates are also used in the preparation of high activity catalysts for olefin polymerization. They appear to function as electron donors in the catalyst complex, and play a significant role in catalyst performance (115).

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