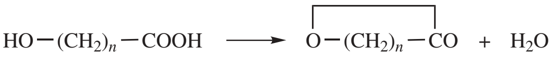
ESTERS, ORGANIC

1. Introduction

Organic carboxylic esters are compounds that are formed by a condensation reaction between a molecule of carboxylic acid and a molecule of alcohol or phenol with elimination of water as depicted in the following equation.

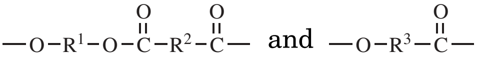
$$R^1COOH + R^2OH \rightleftharpoons R^1COOR^2 + H_2O$$

where R^1 and R^2 are the same or different hydrocarbon radicals including unsaturated ones. The reverse reaction, ester hydrolysis, is one of the widely studied reactions. When R^1 and R^2 are bonded together, the resultant cyclic ester is called a lactone. Lactones can be produced from molecules containing both carboxyl and hydroxyl groups.



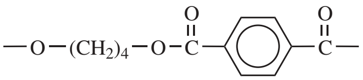
$$HO-(CH_2)_n-COOH \longrightarrow \overline{O-(CH_2)_n-CO} + H_2O$$

Polyesters are polymers with basic structural units:

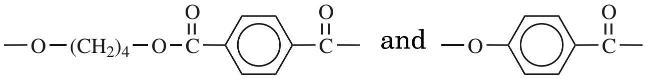


$$-O-R^1-O-\overset{O}{\overset{\|}{C}}-R^2-\overset{O}{\overset{\|}{C}}- \text{ and } -O-R^3-\overset{O}{\overset{\|}{C}}-$$

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:



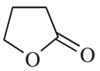
Orthoesters, $RC(OR^1)_3$ (1), thioesters, $RCSOR^1$ (2,3) (see SULFUR COMPOUNDS; THIOLS), and carbamates, H_2NCOOR, are not covered in this article.

2. 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, $CH_3CH_2COOCH_3$, the methyl ester of propanoic acid is called methyl propanoate [554-12-1] (or methyl propionate, if the trivial name, propionic acid, is 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, $CH_3OCOCH_2CH_2COOH$, is called methyl hydrogen succinate or more systematically methyl hydrogen butanedioate [3878-55-5]. In fully esterified polybasic acids, the names of alkyl or aryl groups are cited in alphabetical order, eg, Ethyl methyl malonate.

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].

Intramolecular esters of hydroxy carboxylic acids are generally known as lactones and are named as heterocycles or by substituting "-olactone" for the "-ic acid" ending of a trivial name of a hydroxyl acid or "-lactone" for the "-ic acid" ending of a systematic "-oic acid" name for the nonhydroxylated parent acid, and inserting a locant designating the position of the hydroxyl group between the "o" and "lactone".



Tetrahydrofuran-2-one or dihydro-2(3*H*)-furanone [96-48-0]. Butano-2-lactone (traditional name is γ-Butyrolactone).

When, in an ester with the general structure $R{-}CO{-}O{-}R^1$, another group is present that has priority for citation as a suffix, or when all ester groups cannot be described by the common methods, an ester is indicated by prefixes such as "alkoxycarbonyl-" or "aryloxycarbonyl-" for the group $-CO-OR^1$, or "acyloxy-" for the group $R{-}CO{-}O{-}$, eg,

$$C_2H_5-O-CO-CH_2-CH_2-Cl$$

2-(Ethoxycarbonyl)ethyl chloride

$$C_6H_5-CO-O-CH_2-CH_2-COOH$$

3-(Benzoyloxy)propanoic acid

In naming esters containing one or more substituents, it is necessary to indicate specifically in which portion of the molecule the substituents occur, eg, $ClCH_2COOCH_2CH_3$ is ethyl chloroacetate [105-39-5] and $CH_3COOCH_2CH_2Cl$ is 2-chloroethyl acetate [542-58-5].

Orthoesters are trivially named as derivatives of ortho acids such as triethyl orthoformate [122-51-0], $HC(OC_2H_5)_3$, or named systematically as ethers, 1,1,1-triethoxymethane.

3. Occurrence and Preparation

3.1. Occurrence. Currently, most of the simple esters used commercially are of synthetic origin, although esters occur naturally in large quantities in oils, fats, and waxes. Oils and fats from plants and animals consist mainly of glycerol esters of stearic, palmitic, and oleic acids (6). 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 possess antibacterial properties.

Essential oils are obtained from fruits and flowers (7,8). 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.

3.2. Preparation. 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 ion-exchange resins of the sulfonic acid type. The reaction, known as the *Fischer esterification*, is a simple route to esters from readily available starting materials. Equilibrium constants for esterification are often relatively small in magnitude. To shift the equilibrium favorably, an azeotropic agent such as benzene, toluene, or cyclohexane can be used to remove water and force the reaction to completion.

It is often desirable to convert the carboxylic acid to a reactive acyl halide so that reaction with alcohol becomes an irreversible process. A base, usually a tertiary amine, is generally employed to neutralize the liberated hydrogen halide. Anhydrides, though less reactive than acyl chlorides, are often suitable for the preparation of esters. One portion of the molecule acylates the alcohol, and the other one-half of the anhydride is recovered as carboxylic acid. When the anhydride is part of a cyclic structure, reaction with one mole of alcohol opens the ring and forms a half-ester.

When the carboxylic acid and hydroxy groups are present in the same molecule, a lactone (cyclic ester) may form. Lactonization occurs readily with γ- and δ-hydroxy acids that form unstrained five- and six- membered rings.

Esters are also produced by a number of other reactions starting from amides, nitriles, unsaturated hydrocarbons, ethers, aldehydes and ketones and by dehydrogenation of alcohols. For detailed description of these methods see ESTERIFICATION.

Equilibration of an alcohol with an ester containing a different alkoxy group is a method for converting one ester to another (alcoholysis). Similarly, new esters can be made by equilibration of an acid with an ester having different carboxylic acid moiety (acidolysis). The process, known as transesterification, is normally catalyzed by an acid.

4. Physical Properties

The physical properties of organic esters vary according to the molecular weight of each component (9–13). 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 solvents. 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^{20}_{D}	d^{20}_{20}	bp, °C[a]	Freezing point, °C	Flash point, °C[b]
methyl formate	[107-31-3]	60.05	1.344	0.0975	32	−99.8	−19
ethyl formate	[109-94-4]	74.08	1.3598	0.9236	54.3	−80	−20
butyl formate	[592-84-7]	102.13	1.3889	0.8885[c]	106	−91.9	−18
methyl acetate	[79-20-9]	74.08	1.3594	0.933	57	−98.1	−10
ethyl acetate	[141-78-6]	88.1	1.3723	0.0902	77.1	−83.6	−4
vinyl acetate	[108-05-4]	86.1	1.3959	0.932	72.2	−93.2	−8
propyl acetate	[109-60-4]	102.13	1.3844	0.887	101.6	−92.5	13
isopropyl acetate	[108-21-4]	102.13	1.3773	0.872	90	−73.4	2
butyl acetate	[123-86-4]	116.16	1.3951	0.882	126	−73.5	22
isobutyl acetate	[110-19-0]	116.16	1.3902	0.871	117.2	−98.6	18
sec-butyl acetate	[105-46-4]	116.16	1.3877	0.8758[d]	112		31.1[e]
tert-butyl acetate	[540-88-5]	116.16	1.3855	0.8665[c]	97		
pentyl acetate	[628-63-7]	130.18	1.4023	0.876	149.3	−70.8	25
isoamyl acetate	[123-92-2]	130.18	1.4000	0.872	142	−78	25
sec-hexyl acetate	[108-84-9]	144.22	1.4014[f]	0.8651[g]	157	0	
2-ethylhexyl acetate	[103-09-3]	172.26	1.4204	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	1.4019	1.0067	145	−65.1	44
2-ethoxyethyl acetate	[111-15-9]	132.16	1.4058	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	1.4265	0.981	247	−32.2	110
benzyl acetate	[140-11-4]	150.18	1.5232	1.055	215.5	−51.5	90
glyceryl triacetate	[102-76-1]	218.23	1.4296	1.161	258	−78	138
ethyl 3-ethoxypropionate	[763-69-9]	146.19		0.95	165–172	−50	58

Table 1 (*Continued*)

Ester	CAS Registry number	Mol wt	n^{20}_{D}	d^{20}_{20}	bp, °C[a]	Freezing point, °C	Flash point, °C[b]
glyceryl tripropionate	[139-45-7]	260.3	1.4318	1.100[h]	176	−58	167[e]
methyl acrylate	[96-33-3]	86.09	1.4040	0.953	80.5	<−75	−3
ethyl acrylate	[140-88-5]	100.11	1.4068	0.923	99.8	<−72	10
butyl acrylate	[141-32-2]	128.17	1.4185	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	1.4119	0.944	100	−48	10[e]
methyl butyrate	[623-42-7]	102.13	1.3878	0.898	102.3	−84.8	14
ethyl butyrate	[105-54-4]	116.16	1.4000	0.878	121.6	−100.8	24
butyl butyrate	[109-21-7]	144.22	1.4075	0.871	166.6	−91.5	53
methyl isobutyrate	[547-63-7]	102.13	1.3840	0.891	92.6	−84.7	
ethyl isobutyrate	[97-62-1]	116.16	1.3870	0.869	110	−88	<21
isobutyl isobutyrate	[97-85-8]	144.22	1.3999	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	213–215	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	1.4409	1.152	204		91
dimethyl oxalate	[95-92-1]	111.09	1.4096	1.148	185	−41	76
dimethyl adipate	[627-93-0]	174.2	1.4283	1.0600	115	10.3	
diethyl adipate	[141-28-6]	202.25	1.4372	1.008	245	−19.8	
di(2-ethylhexyl) adipate	[103-23-1]	370.58	1.4472	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	1.4911	1.0465	340	−35	157
di(2-ethylhexyl) phthalate	[117-81-7]	390.56	1.486	0.9861	231[j]	−50	218.3
dimethyl isophthalate	[1459-93-4]	194.19	1.5168	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	1.3682	1.0694[c]	90	3	19[e]
diethyl carbonate	[105-58-8]	118.13	1.3854	0.9752[c]	127	−43	25

[a] At 101.3 kPa (760 mm Hg) unless otherwise stated.

[b] Closed cup determination unless otherwise stated.

[c] d^{20}_{2}.

[d] d^{16}_{4}.

[e] Open cup determination.

[f] n^{25}_{D}.

[g] d^{15}_{15}.

[h] d^{20}_{18}.

[i] At 6.7 kPa (50 mm Hg).

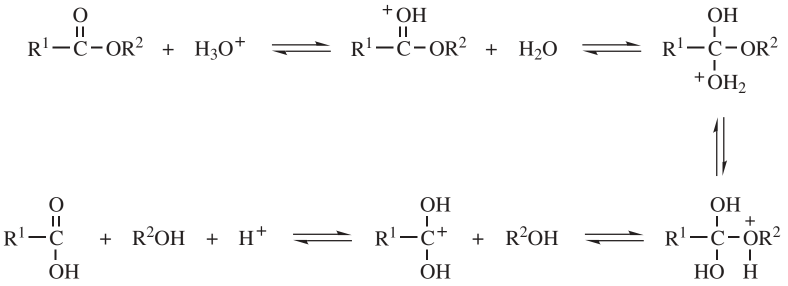
[j] At 0.67 kPa (5 mm Hg).

5. Chemical Properties

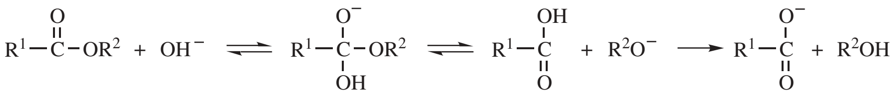
The reactions of esters have extensively been reviewed (14–18). The chemical properties of esters may differ considerably as they are composed of a large number and variety of acid and alcohol moieties. Only typical reactions relevant to the majority of esters are described in the following sections.

5.1. Hydrolysis. Esters are cleaved (hydrolyzed) into their parent acid and alcohol in the presence of water. This hydrolysis is catalyzed by acids or bases. The mechanistic aspects of ester hydrolysis have received considerable attention and have been reviewed (19). 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. As expected, higher temperatures also accelerate the reaction.

The catalysis of ester hydrolysis by other groups within the ester molecule (intramolecular catalysis) has been extensively studied (20,21). These reactions are important because they simulate catalysis by enzymes. Intramolecular catalysis of esters has been used as a model in drug discovery efforts (22).

Acidic Hydrolysis. Hydrolysis of esters catalyzed by 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.

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.

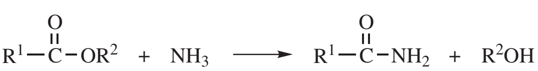
Hydrolysis by Steam. High pressure steam, 4.5–5.0 MPa (650–725 psi), at 250°C in the absence of a catalyst hydrolyzes oils and fats to the fatty acids and glycerol (23). The reaction is commonly carried out continuously in a countercurrent method. The glycerol produced during the reaction is continuously 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 (24–27). 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 (28). 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 (29).

5.2. Transesterification. When esters are heated with alcohols, acids, or other esters in the presence of a catalyst, the alcohol or acid groups are exchanged. The reaction 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 types 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 (30). Enzymes can be used as asymmetric catalysts in these reactions to prepare optically active alcohols and esters (31).

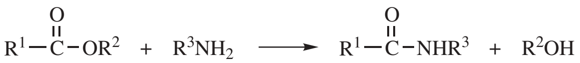
Transesterification has a number of important commercial uses. Methyl esters of fatty acids are produced from fats and oils. Transesterification is also the basis of recycling technology to break up poly(ethylene terephthalate) [25038-59-9] to monomer for reuse (32) (see Recycling, plastics). Because 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].

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



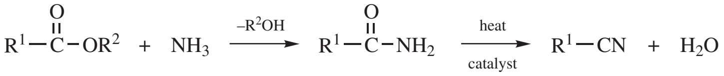
$$R^1-\overset{\displaystyle O}{\overset{\|}{C}}-OR^2 + NH_3 \longrightarrow R^1-\overset{\displaystyle O}{\overset{\|}{C}}-NH_2 + R^2OH$$

This reaction can be carried out in aqueous or alcoholic ammonia. Low molecular weight esters give good yields even at room temperature; high molecular weight esters require higher temperature and pressure. If primary or secondary amines are used, *N*-substituted amides are formed. This reaction is called aminolysis.



$$R^1{-}\overset{O}{\overset{\|}{C}}{-}OR^2 + R^3NH_2 \longrightarrow R^1{-}\overset{O}{\overset{\|}{C}}{-}NHR^3 + R^2OH$$

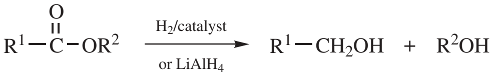
Hydrazines yield the corresponding hydrazides, which can then be treated with nitrous acid to form the azides used in the Curtius rearrangement. Hydroxylamines give hydroxamic acids. When esters are passed with ammonia over a contact catalyst such as alumina or thoria at 400–500°C, nitriles are obtained via dehydration of the intermediate amides:



$$R^1{-}\overset{O}{\overset{\|}{C}}{-}OR^2 + NH_3 \xrightarrow{-R^2OH} R^1{-}\overset{O}{\overset{\|}{C}}{-}NH_2 \xrightarrow[\text{catalyst}]{\text{heat}} R^1{-}CN + H_2O$$

Thus fats are converted to the fatty nitriles (33).

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



$$R^1{-}\overset{O}{\overset{\|}{C}}{-}OR^2 \xrightarrow[\text{or LiAlH}_4]{H_2\text{/catalyst}} R^1{-}CH_2OH + R^2OH$$

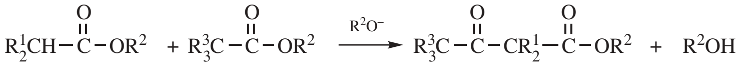
Catalytic Hydrogenation. Esters can be hydrogenated to primary alcohols using a transition-metal catalyst (34–36) such as copper chromite, copper oxide, Raney nickel, nickel–copper– aluminum–rhenium oxides, or related species. The catalyst of choice is copper chromite. Conditions are stringent: 10–30 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 (36,37). 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 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 (36). 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–C_2H_5OH, Li or Na–NH_3, $LiAlH_4$, $LiBH_4$, or $NaBH_4$ to give alcohols in excellent yield (38,39). Carbon–carbon double bonds are usually preserved using these reducing reagents.

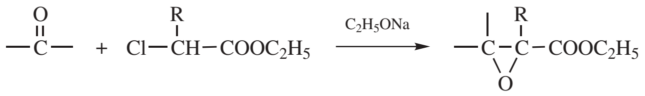
The reduction of esters to aldehydes is carried out with hydrides such as $NaH_2Al(OCH_2CH_2OCH_3)_2$, $(i\text{-}C_4H_9)_2AlH$, $NaAlH_4$, or $LiAlH_4$–$(C_2H_5)_2NH$. The use of BH_3 or $LiAlH_4{-}BF_3{\cdot}O(C_2H_5)_2$ as a reducing agent converts esters to ethers. Thus, reduction of esters can be manipulated by the judicious selection of metal-containing reducing reagents.

5.5. Reaction of Enolate Anions. In the presence of certain bases, eg, sodium alkoxide, an ester having 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 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:



$$R^1_2CH-\overset{\mathrm{O}}{\overset{\|}{C}}-OR^2 + R^3_3C-\overset{\mathrm{O}}{\overset{\|}{C}}-OR^2 \xrightarrow{R^2O^-} R^3_3C-\overset{\mathrm{O}}{\overset{\|}{C}}-CR^1_2-\overset{\mathrm{O}}{\overset{\|}{C}}-OR^2 + R^2OH$$

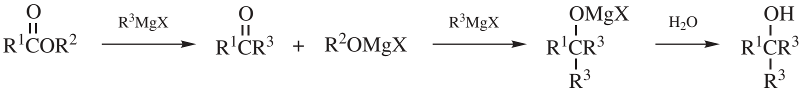
The intramolecular Claisen condensation of diesters, or Dieckman reaction, occurs readily to give five- or six-membered rings, and it has been extensively used for cyclopentanone and cyclohexanone derivatives. Condensations of aldehydes or ketones with α-halo esters give α,β-epoxy esters. This is called the Darzens condensation.



$$-\overset{\mathrm{O}}{\overset{\|}{C}}- + Cl-\overset{R}{\overset{|}{C}}H-COOC_2H_5 \xrightarrow{C_2H_5ONa} -\underset{\underset{\mathrm{O}}{\backslash\,/}}{\overset{|}{C}-\overset{R}{\overset{|}{C}}}-COOC_2H_5$$

Enolizable compounds react with non-nucleophilic strong bases, eg, lithium diisopropylamide [4111-54-0] to generate stable enolate anions. Reactions of these enolates with compounds such as alkyl halides are useful in synthetic organic chemistry (40). In the quest for improved stereospecificity, enolates with different cations such as silicon, aluminum, boron, and zinc have also been used (41). In group-transfer polymerization, ketene silyl acetals, eg, $(CH_3)_2C{=}C[OSi(CH_3)_3](OCH_3)$ are employed as initiators (42).

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

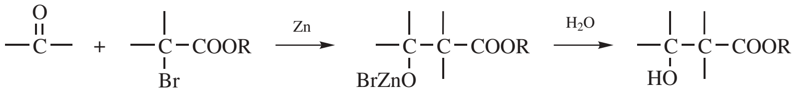


$$R^1\overset{\mathrm{O}}{\overset{\|}{C}}OR^2 \xrightarrow{R^3MgX} R^1\overset{\mathrm{O}}{\overset{\|}{C}}R^3 + R^2OMgX \xrightarrow{R^3MgX} R^1\underset{\underset{R^3}{|}}{\overset{OMgX}{\overset{|}{C}}}R^3 \xrightarrow{H_2O} R^1\underset{\underset{R^3}{|}}{\overset{OH}{\overset{|}{C}}}R^3$$

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 cyclopentanols (43). 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 (44). Tebbe's reagent, $Cp_2TiCH_2AlCl(CH_3)_2$, where Cp is cyclopentadienyl, and other metal carbene complexes can convert the C=O of esters to $C{=}CR_2$ (45,46).

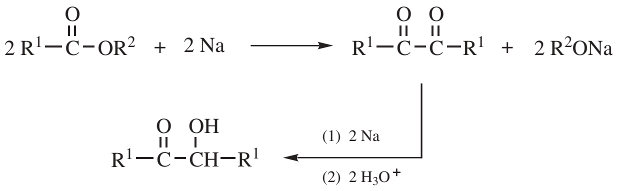
α-Halo esters react with aldehydes or ketones in the presence of zinc to form β-hydroxy esters. This is known as the Reformatsky reaction (47).



$$-\overset{O}{\overset{\|}{C}}- \; + \; -\underset{Br}{\underset{|}{\overset{|}{C}}}-COOR \xrightarrow{Zn} -\underset{BrZnO}{\underset{|}{\overset{|}{C}}}-\underset{|}{\overset{|}{C}}-COOR \xrightarrow{H_2O} -\underset{HO}{\underset{|}{\overset{|}{C}}}-\underset{|}{\overset{|}{C}}-COOR$$

5.7. 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 (48):



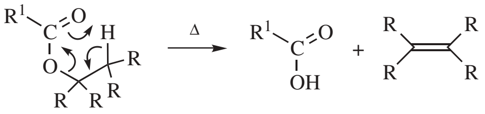
$$2\,R^1-\overset{O}{\overset{\|}{C}}-OR^2 + 2\,Na \longrightarrow R^1-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-R^1 + 2\,R^2ONa$$

$$R^1-\overset{O}{\overset{\|}{C}}-\overset{OH}{\overset{|}{C}}H-R^1 \xleftarrow[(2)\ 2\,H_3O^+]{(1)\ 2\,Na}$$

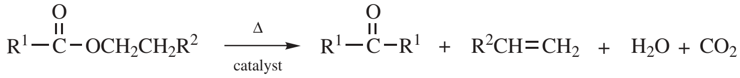
This reaction is used in the synthesis of large-ring compounds.

5.8. Pyrolysis.

The pyrolysis of simple esters of the formula R^1COOCR_2-CHR_2 to form the free acid and an alkene is a general reaction that is used for producing olefins:



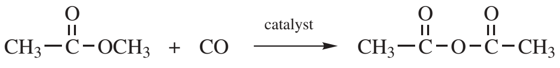
The pyrolysis is generally carried out at 300–500°C over an inert heat-transfer agent such as Pyrex glass or 96% silica glass chips. Esters of tertiary alcohols are pyrolyzed more readily than esters of secondary alcohols, and esters of primary alcohols are the most difficult to pyrolyze. A detailed review on this reaction has been given (49). 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 (50):



$$R^1-\overset{O}{\overset{\|}{C}}-OCH_2CH_2R^2 \xrightarrow[\text{catalyst}]{\Delta} R^1-\overset{O}{\overset{\|}{C}}-R^1 + R^2CH{=}CH_2 + H_2O + CO_2$$

5.9. Carbonylation Reaction.

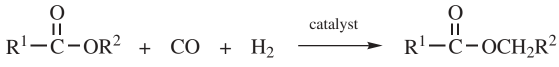
The carbonylation of methyl acetate is an important industrial reaction for producing acetic anhydride:



$$CH_3-\overset{O}{\overset{\|}{C}}-OCH_3 + CO \xrightarrow{\text{catalyst}} CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3$$

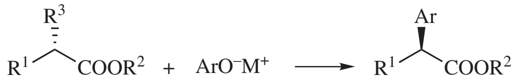
Earlier catalysts were based on cobalt, iron, and nickel. However, recent catalytic systems involve rhodium compounds promoted by methyl iodide and lithium iodide (51,52). Higher molecular weight alkyl esters do not show any particular ability to undergo carbonylation to anhydrides.

Ruthenium complexes have been used in the hydrocarbonylation of simple esters to produce the corresponding homologous esters (53). The hydrocarbonylation affects the alkyl moiety rather than the carboxylate group:



$$R^1-\overset{\overset{O}{\parallel}}{C}-OR^2 + CO + H_2 \xrightarrow{\text{catalyst}} R^1-\overset{\overset{O}{\parallel}}{C}-OCH_2R^2$$

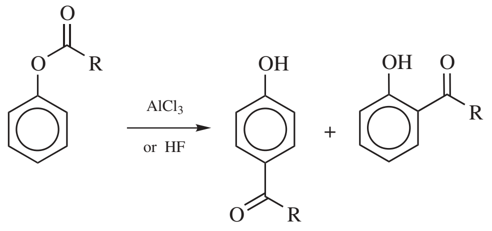
5.10. Substitution, Alkylation, and Rearrangement. The reaction of alkaline phenoxides with alkyl (*S*)-2-(chloro)- or (*S*)-2-(mesyloxy)propionate gives optically active (*R*)-2-aryloxyalkanoic acid esters in good chemical and optical yields (>97% ee) (54–56):



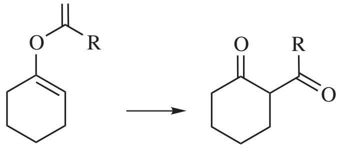
The reaction is utilized in the synthesis of several phenoxy herbicides.

Optically active 2-arylalkanoic acid esters have been prepared by Friedel-Crafts alkylation of arenes with optically active esters, such as methyl (*S*)-2-(chlorosulfonoxy)- or (*S*)-2-(mesyloxy)propionate, in the presence of aluminum chloride (57,58).

The Fries rearrangement of phenol esters gives a mixture of 2- and 4-acylphenols (59). The reaction is catalyzed by Lewis acids such as aluminum chloride or by Bronsted 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] (60):



Similarly, enol esters undergo rearrangement to give the corresponding 1,3-diketones. This reaction can be accomplished thermally (500°C) or with a catalyst (61,62):



6. 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 oils and fats, 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, acidity, color, nonvolatile material, odor, purity, and water and alcohol content.

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 chromatography and gas chromatography coupled with mass spectrometric techniques are required by the United States Government for monitoring and detection of some organic esters (69).

Esters are usually readily identified using molecular spectroscopy (70). Among these, Fourier Transform Infrared Spectroscopy (FT–IR) is especially useful for identifying the carbonyl of the ester group that has characteristic absorption bands. The carbonyl absorption is very strong in the IR at 1750–1735 cm^{-1}; in addition, C–O stretching bands are observed in the range 1100–1300 cm^{-1}. Another spectroscopic method used in identifying organic esters is nuclear magnetic resonance (nmr). The ^{1}H 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 ~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. Yet another useful method for ester determination is mass spectrometry. The mass spectrometry of esters (73) has been extensively investigated. Commercial mass spectral reference libraries are very useful in identification of organic esters by spectrum matching.

7. 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.

If an organic ester is released, then appropriate action must be taken. The U.S. 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, CO_2, water spray, or alcohol-resistant foam extinguishing media should be used (77).

8. Health and Safety Factors

8.1. Toxicity.

The degree of toxicity of organic esters covers a wide range (78). These toxicities are usually described in terms of threshold limit 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,

Table 2. **Flammability and Toxicity of Organic Esters**

				NFPA[c] hazard information toxicity data						
Ester	Autoignition temp, °C[a]	Upper flammable limit, vol% in air[b]	Lower flammable limit, vol% in air[b]	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
sec-butyl acetate	422	9.8	1.7	1	3	0			200	950
tert-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
sec-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)				mouse	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	mouse	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	mouse	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	mouse	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	mouse	8.5		

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[a] ASTM D286 and D2155.

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

[c] See Ref. 11.

[d] Permissible exposure limit; see Ref. 76.

[e] Threshold limit value–time-weighted average.

[f] Intraperitoneal.

[g] LD_{100}.

although OSHA uses the PEL values (Table 2). The lethal dosages for 50% of the exposed animals, LD_{50}s, are also used as an indicator of the relative toxicity. An accumulation of the LD_{50} data of organic esters for rabbits, rats, and mice can also be found in Table 2. The LD_{50}s 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 size of alcohol moiety increases. For example, the LD_{50} (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 vinyl and allyl 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 LD_{50}s (rat) ranging between 2.5 and 1.6 g/kg for phenyl and benzyl acetate compared to LD_{50}s (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 LD_{50} (rat, oral) for ethyl nonanoate [123-29-5] is >43 g/kg, and the LD_{50} (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 LD_{50}s 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 LD_{50} rat of 9.1 g/kg, and di(2-ethylhexyl) succinate [117-81-7], which has an oral LD_{50} 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 sodium and calcium salts of malonic acid 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 LD_{50}s (mouse) for methyl- to butyl hydroxybenzoates 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 molecular weight of alcohol group increases. For example, dimethyl phthalate has an oral LD_{50} (mouse) of 7.2 g/kg, whereas di(2-ethylhexyl) phthalate shows an oral LD_{50} (rat) of >26 g/kg.

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

8.2. Exposure Limits. The Occupational Safety and Health Act (OSHA) 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.

9. 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).

10. Uses

Organic esters find use in wide range of fields encompassing solvents, extractants, diluents, plasticizing agents, lubricants, perfumes, medicinals, herbicides and pesticides and photoresists. Uses of some specific esters are also given in Table 3.

10.1. 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 (95). 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.

10.2. Plasticizers. Plasticizers are materials that soften and flexibilize inherently rigid, and even brittle polymers. Organic esters are widely used as plasticizers in polymers (96,97). 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] 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 (C_6–C_{11}) 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.

10.3. Resins, Plastics, and Coatings. Unsaturated and bifunctional 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

Table 3. **Uses of Some Specific Esters**

Name and structure	Use
methyl formate, $HCOOCH_3$	raw material for production of formamide, dimethylformamide (DMF), and formic acid
methyl acetate, CH_3COOCH_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 carbonylation
ethyl acetate, $CH_3COOC_2H_5$	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, $CH_3COOCH_2CH_2CH_3$	good solvent for cellulose nitrate, chlorinated rubber, and heat-reactive phenolics; principal use is as a printing ink solvent[b]
isopropyl acetate, $CH_3COOCH(CH_3)_2$	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, $CH_3COO-(CH_2)_3CH_3$	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, pine-apple, grenadine, butterscotch, and raspberry; also a cleaning solvent for silicon wafers
isobutyl acetate, $CH_3COOCH_2CH(CH_3)_2$	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, $CH_3COOC_5H_{11}$	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 *sec*-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

Table 3 (*Continued*)

Name and structure	Use
2-ethylhexyl acetate, $CH_3COOCH_2CH(C_2H_5)-(CH_2)_3CH_3$	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, $CH_3COOCH_2CH_2OC_4H_9$	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)ethylacetate, $CH_3CO(OCH_2CH_2)_2-OC_4H_9$	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] $CH_3CH(OCOCH_3)-CH_2OCH_3$	solvent in inks, ink remover, paints, automotive coatings, and photoresist; also a substitute for 2-ethoxyethyl acetate in many applications
benzyl acetate, $CH_3COOCH_2C_6H_5$	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, $C_2H_5OCH_2CH_2COOC_2H_5$	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, $(CH_3)_2-CHCOOCH_2CH(CH_3)_2$	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 distinct odor and flavor make it an interesting material for the formulation of perfumes, and as a bulk component of flavor essences
2,2,4-trimethyl-1,3-pentanediol[d] monoisobutyrate	widely used as a coalescing aid in latex paints, effective with a broad range of latex emulsion systems; retarder solvent for high solid coatings, and a sweetener in letterpress and lithographic inks to improve solvent activity of ink's solvent system
butyl stearate, $CH_3(CH_2)_{16}-COO(CH_2)_3CH_3$	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, ointments, 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, $[CH_2CH_2COOCH_2CH-(C_2H_5)C_4H_9]_2$	plasticizer to impart low temperature flexibility to PVC formulations, particularly in vinyl meat-wrapping film

Table 3 (*Continued*)

Name and structure	Use
benzyl benzoate, $C_6H_5COOCH_2C_6H_5$	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 repellent, and dye carrier
methyl salicylate, $2{-}HOC_6H_4COOCH_3$	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 inertness; used as preservative in cosmetic formulations, general-purpose cleaners, disinfectants, and mouth wash and contact lens cleaning solutions; also used as food additive and pharmaceutical preservative
methyl cinnamate, $C_6H_5CH{=}CHCOOCH_3$	fragrance in soaps, perfumes, and confectioneries
2-ethylhexyl 4-methoxycinnamate	absorbs uv rays effectively; thus about 75% of all sunscreen formulations use it; usually nonallergenic and nonstaining
dimethyl phthalate	raw material for polyesters; also used as plasticizer, 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 pressure-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 that promote improved flow and leveling characteristics in a variety of coating formulations.

[c] Propylene glycol methyl ether acetate.

[d] $(CH_3)_2CHCOOCH_2C(CH_3)_2CH(OH)CH(CH_3)_2$.

[e] Dioctyl phthalate (DOP).

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]. 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 under hood 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 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 (98).

10.4. Lubricants. Monohydric alcohol esters of dibasic acids and polyol esters of monobasic acids are synthetic lubricants (99). They are generally prepared from the following alcohols and acids: (*1*) C_8–C_{13} monohydric alcohols such as 2-ethylhexyl, isooctyl, isodecyl, and isotridecyl alcohols; (*2*) polymethylol compounds such as trimethylolpropane, pentaerythritol, and dipentaerythritol; (*3*) C_6–C_{10} monobasic acids such as heptanoic and nonanoic acids; and (*4*) C_6–C_{10} 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.

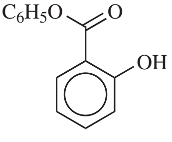
10.5. Perfumes, Flavors, Cosmetics, and Soap. Many naturally occurring esters in essential oils and some synthetic esters are important fragrance and flavor compounds (7,8). They are used in perfumes, flavors, cosmetics, soaps, detergents, and air fresheners. Benzyl, butyl, ethyl, methyl, and phenyl 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 (100). 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 (101).

Benzyldiethyl[(2,6-xylylcarbamoyl)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 oils and fats from tallow and plants such as soybean, cottonseed, linseed, and castor bean are important raw materials for soap, paints, and food industries.

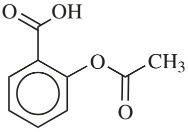
10.6. Surface-Active Agents. Polyol (eg, glycerol, sorbitol, and propylene glycol) or poly(ethylene oxide) esters of long-chain fatty acids are nonionic surfactants (qv) used in foods, pharmaceuticals, cosmetics, textiles, cleaning compounds, and many other applications (102,103). Those that are most widely used are included in Table 3.

10.7. Medicinals. In recent years, esters as protecting groups have played an increasing role in modulating efficacy and bioavailability of pharmaceuticals. As a result, many esters are used as pharmaceuticals (104,105). 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.



(**1**)

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 vice versa) detoxifies it by decreasing the concentration of active compound present. The active compound is released gradually in the body by hydrolysis of the ester (106). 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.



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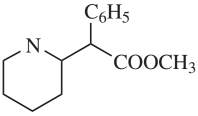
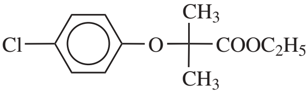
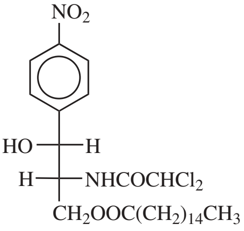


(**3**)



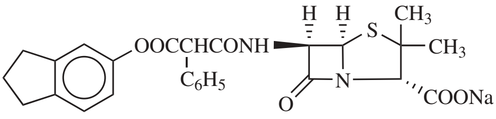
(**4**)

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] (**5**) and clindamycin [18323-44-9] have been derivatized as their palmitate esters in order to minimize their bitter taste.

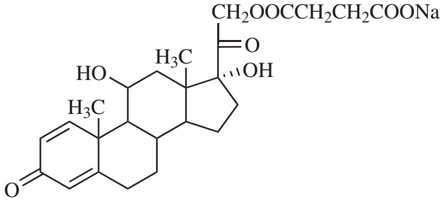


(**5**)

In order to improve the poor oral absorption of carbenicillin [4697-36-3], a lipophilic indanyl ester has been formulated, Geocillin [35531-88-5] (**6**). Prednisolone [50-24-8], a steroid, is derivatized to its C-21 hemisuccinate sodium salt (**7**) to make it extremely water soluble (107).



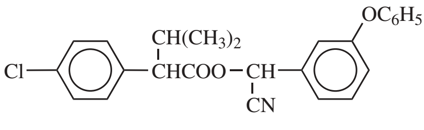
(**6**)



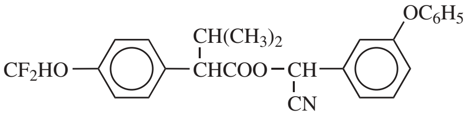
(**7**)

10.8. Herbicides and Pesticides. Several esters are used as herbicides and pesticides (108–110). 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.

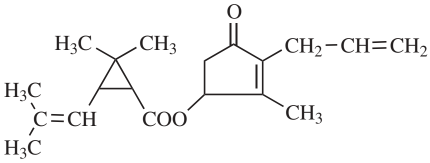
Pyrethroids are synthetic esters produced to imitate or improve the activity of biological principles of the pyrethrum plant. They are powerful contact insecticides causing rapid knockdown of treated insects. The pyrethroids are extensively used in controlling insect pests on fruit trees, vegetables, 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] (**8**), flucythrinate [70124-77-5] (**9**), allethrin [584-79-2] (**10**), tetramethrin [7696-12-0] (**11**), cyfluthrin [68359-37-5] (**12**), cypermethrin [52315-07-8] (**13**), deltamethrin [52918-63-5] (**14**), and permethrin [52645-53-1] (**15**).



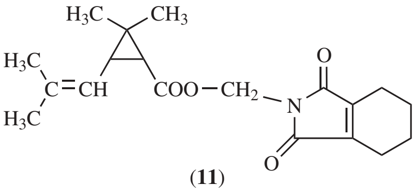
(**8**)



(**9**)

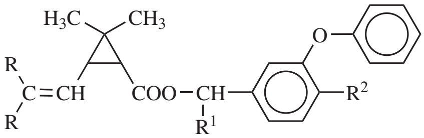


(**10**)



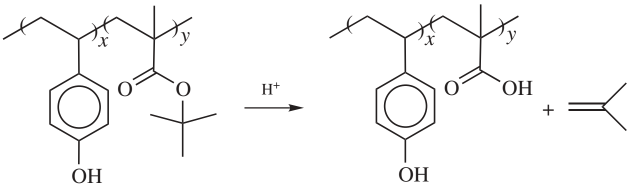
(**11**)

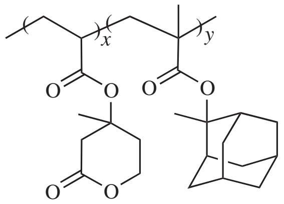
10.9. Photoresists. Chemically amplified photoresists have proven to be very useful for advanced microlithography, which plays a prominent role in making integrated circuits. The base soluble sites of the resin in photoresist (usually carboxylic acids) are capped with protecting groups such as *tert*-butyl making them insoluble in aqueous base. Under lithographic conditions wherein excimer laser light is shone on the resist through a mask, these protecting groups can be catalytically removed to return the solubility in aqueous base, thereby a mask pattern on the resist is created after development. The acid catalyst necessary for the deprotection reaction is produced by photochemical reaction of photoacid generator (PAG). The mechanism of deprotection involves protonation of the ester group by acid, liberating a tertiary carbocation that undergoes beta-proton elimination to reproduce an acidic proton and volatile isobutylene (111) (see LITHOGRAPHIC RESISTS).



(**12**) R = Cl; R^1 = CN; R^2 = F
(**13**) R = Cl; R^1 = CN; R^2 = H
(**14**) R = Br; R^1 = CN; R^2 = H
(**15**) R = Cl; R^1 = H; R^2 = H

Tertiary esters having other functional properties have been developed for lithography, eg, 2-methyl-2-adamantyl ester (112).





10.10. Miscellaneous Uses. Since esters can be made and hydrolyzed with ease, they are used as protecting groups for hydroxyl and carboxylic acid groups (113). 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 *tert*-butyl, benzyl, and substituted benzyl esters (114,115). 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 (116).

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