Kirk-Othmer Encyclopedia of Chemical Technology.

KETENES, KETENE DIMERS, AND RELATED SUBSTANCES

Ketenes are oxo compounds with cumulated carbonyl and carbon–carbon double bonds of the general structure $R_1R_2C{—}C{—}O$, where R_1 and R_2 may be any combination of hydrogen, alkyl, aryl, acyl, halogen, and many other functional groups. Ketenes with $R_1 = H, R_2 \neq H$ are sometimes called aldoketenes, those with $R_1, R_2 \neq H$, ketoketenes. The S– and N– analogues of ketenes are called thioketenes ($R_1R_2C{—}C{—}S$) and ketenimines ($R_1R_2C{—}C{—}NR$), respectively.

The parent substance, ketene itself [463-51-4] is the only ketene to be manufactured in very large industrial quantities. Its principal applications are for the manufacture of acetic anhydride [108-24-7] and diketene [674-82-8]. The latter is an important organic intermediate used as the source of acetoacetic esters, amides, and anilides, which are widely used in the preparation of fine chemicals, pigments, drugs, and agrochemicals. Dimeric long-chain alkylketenes (C_{12}–C_{20}) are used in industrial quantities as paper sizing agents.

The chemistry of ketenes is dominated by their high reactivity: most of them are not stable under normal conditions, many exist only as transient species. Nucleophilic attack at the *sp*-carbon, $[2+2]$ cycloadditions, and ketene insertion into single bonds are the most important and widely used reactions of such compounds.

Ketenes and related compounds have been reviewed extensively (1–9). For the synthesis and synthetic uses of conjugated ketenes see Reference 10. Ketenes with three or more cumulated double bonds have been prepared (11, 12). The best known is carbon suboxide [504-64-3], C_3O_2, which has preparative uses and has been reviewed (13–16). Thioketenes (17, 18), ketenimines (19–21), and their dimers show interesting reactivity, but they have not achieved industrial importance to date.

1. Monomeric Ketenes

1.1. Physical Properties

Ketenes range in their properties from colorless gases such as ketene and methylketene [6004-44-0] to deep colored liquids such as diphenylketene [525-06-4] and carbon subsulfide [627-34-9]. Table 1 lists the physical state mp, and bp for certain ketenes, thioketenes, and ketenimines.

Other important physical properties of the parent compound ketene are as follows. Density is $0.65\ \mathrm{g/mL}$ at $-60°\mathrm{C}$, whereas vapor density, compared to theoretical, air $= 1$, is 1.45. Free energy of formation $\Delta G_f^\circ = -49.6 \pm 1.6\ \mathrm{kJ/mol}$ and enthalpy of formation $\Delta H_f^\circ = -47.7\ \mathrm{kJ/mol}\,(-11.4\ \mathrm{kcal/mol})$. The dipole moment is $4.7 \times 10^{-30}\ \mathrm{C{\cdot}m}$ (1.41 D).

Vapor pressure data from -71 to 90°C has been given:

vapor pressure, *t*, °C	−71°C	20°C	30°C	40°C	50°C	90°C
vapor pressure, MPa	0.02	2.0	2.64	3.41	4.35	10.03

Table 1. Properties of Some Ketenes, Thioketenes, and Ketenimines

Name	CAS Registry Number	Physical state	Mp or bp, °C[a]
ketene	[463-51-4]	colorless gas	mp −134.1, bp −41 (22)
diphenylketene	[525-06-4]	orange liquid	mp 9–10, bp 96–99 (2.67 Pa) (23)
carbon suboxide	[504-64-3]	colorless gas	mp −112.2 (24), bp 6.8 (25)
dichloroketene	[4591-28-0]	not isolated	
dimethylketene	[598-26-5]	yellow liquid	mp −97.5, bp 34 (26)
bis(trifluoromethyl)ketene	[684-22-0]	colorless gas	bp 5 (27)
methylketene	[6004-44-0]	colorless gas	−23 (28)
tert-butylcyanoketene	[29342-22-1]	isolated in solution only (29)	
(trimethylsilyl)ketene	[4071-85-6]	colorless oily liquid	bp 81–82 (30)
methylphenylketene	[3156-07-8]	liquid	mp −7, bp 76 (1.86 kPa) (31)
carbon subsulfide	[627-34-9]	dark red liquid	bp 60–40 (1.6 kPa)
thioketene	[18282-77-4]	detected, not isolated (32)	
bis(*tert*-butyl)thioketene	[16797-75-4]	purple liquid	bp 64–65 (0.8 kPa) (33)
N-(4-methylphenyl)-ketenimine	[5110-45-2]	yellow crystals	mp 82–83 (34)
triphenylketeneimine	[14181-84-1]	yellow crystals	mp 55–56 (35)
etheneimine	[17619-22-6]	not isolated	
(2-methyl-prop-1-enyliden)aniline	[14016-34-3]	liquid	bp 99–100 (1.6 kPa) (36)

[a] At 101.3 kPa unless otherwise stated; to convert kPa to mm Hg, multiply by 7.5.

To convert MPa to mm Hg, multiply by 7500.

1.2. Chemical Properties

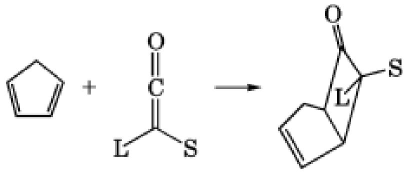
The chemistry of ketenes is dominated by the strongly electrophilic *sp*-hybridized carbon atom and a low energy lowest unoccupied molecular orbital (LUMO). Therefore, ketenes are especially prone to nucleophilic attack at C1 and to $[2+2]$ cycloadditions. Less frequent reactions are the so-called ketene insertion, a special case of addition to substances with strongly polarized or polarizable single bonds (37), and the addition of electrophiles at C2. For a review of addition reactions of ketenes see Reference 8.

1.2.1. Nucleophilic Addition

Reagents with labile hydrogen atoms, such as alcohols, thiols, phenols, carboxylic acids and amines, add to ketenes giving the corresponding carboxylic acid derivatives (**1**) as shown in Figure 1 (38). Not many are of practical importance, as there are better ways to such compounds. A notable exception is the manufacture of acetic anhydride from ketene and acetic acid [64-19-7], which is still of importance even though a new industrial process based on carbonylation of methyl acetate [79-20-9] appeared in the 1980s (39).

1.2.2. $2+2$ Cycloaddition

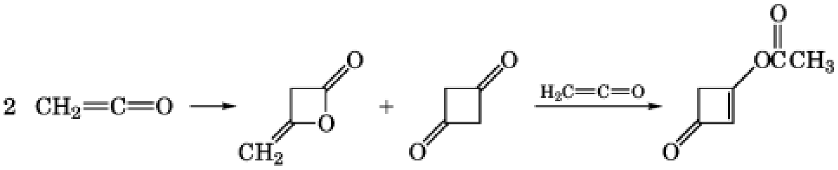
Ketenes are ideal components in $[2+2]$ cycloadditions for additions to the opposite sides of a π-system as shown in the cyclobutane product (**2**) in Figure 1. Electron-rich double bonds react readily with ketenes, even at room temperature and without catalysts. In conjugated systems, ketenes add in a $[2+2]$ fashion. This is illustrated in the reaction following, where the preferential orientation of L (large substituent) and S (small substituent) is seen (40). This reaction has been used in the synthesis of tropolone [533-75-5].



Simple olefins do not usually add well to ketenes except to ketoketenes and halogenated ketenes. Mild Lewis acids as well as bases often increase the rate of the cycloaddition. The cycloaddition of ketenes to acetylenes yields cyclobutenones. The cycloaddition of ketenes to aldehydes and ketones yields oxetanones. The reaction can also be base-catalyzed if the reactant contains electron-poor carbonyl bonds. Optically active bases lead to chiral lactones (41–43). The dimerization of the ketene itself is the main competing reaction. This process precludes the parent compound ketene from many $[2+2]$ cycloadditions. Intramolecular cycloaddition reactions of ketenes are known and have been reviewed (7).

1.2.3. Dimerization

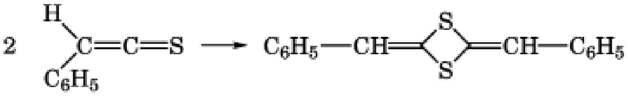
A special case of the $[2+2]$ cycloadditions is the dimerization of ketenes. Of the six possible isomeric structures, only the 1,3-cyclobutanediones and the 2-oxetanones (β-lactones) are usually formed. Ketene itself gives predominantly (80–90%) the lactone dimer, 4-methylene-2-oxetanone (**3**), called diketene [674-82-8]; approximately 5% is converted to the symmetrical dimer, 1,3-cyclobutanedione [15506-53-3] (**4**) which undergoes enol-acetylation to so-called triketene [38425-52-4] (**5**) (44).



(3) **(4)** **(5)**

Aldoketenes also form predominantly the lactone dimers, although the ratio of isomers can be influenced by base catalysis. Ketoketenes dimerize symmetrically, and at a slower rate, to 1,3-cyclobutanediones, unless acidic or basic catalysts are present.

Sterically hindered or very electrophilic substituted ketenes, such as diphenylketene, di-*tert*-butylketene [19824-34-1], and bis(trifluoromethyl)ketene, are quite stable as monomers. Ketenimines tend to polymerize. The dimerization of thioketenes results in 1,3-dithiacyclobutanones (**6**) (45), a type of dimer not observed with ketenes.



(6)

1.2.4. Ketene Insertions

Ketenes insert into strongly polarized or polarizable single bonds, such as reactive carbon–halogen bonds, giving acid halides (**7**) and into active acid halides giving halides of β-ketoacids (**8**) (46). Phosgene [77-44-5] (47) and thiophosgene [463-71-8] (48) also react with ketenes.

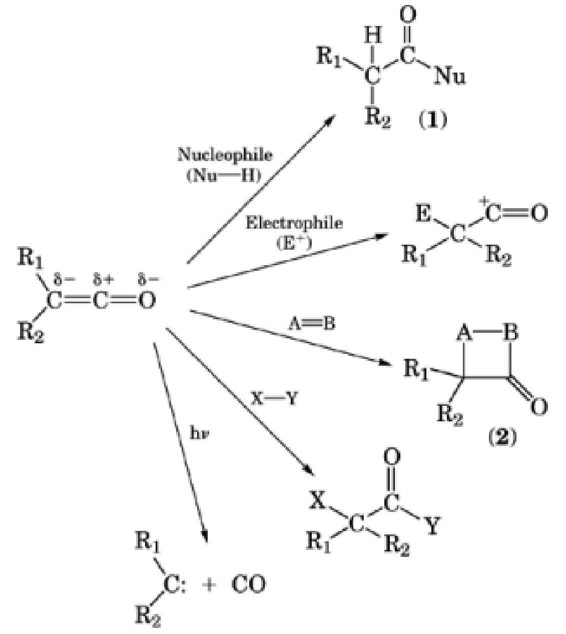
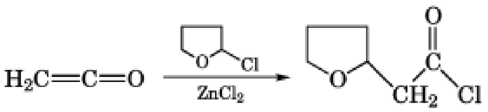


Fig. 1. Reactions of ketenes.



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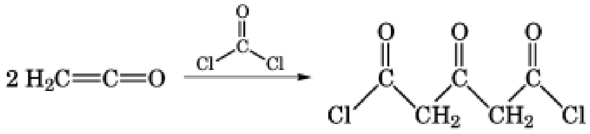
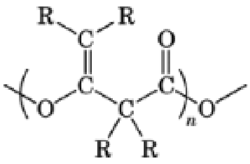
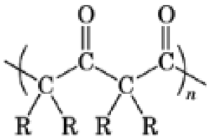


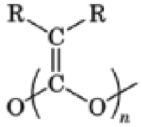
(8)

1.2.5. Other Reactions

The photolysis of ketenes results in carbenes. The polymerization of ketenes has been reviewed (49). It can lead to polyesters and polyketones (50). The polymerization of higher ketenes results in polyacetals depending on catalysts and conditions. Catalysts such as sodium alkoxides (polyesters), aluminum tribromide (polyketones), and tertiary amines (polyacetals) are used. Polymers from R_2C—C—O may be represented as follows.







Ketenes can react in several ways with organometallic compounds and complexes. They can add as ligands to coordinated metals forming stable ketene, ketenyl, and ketenylidene complexes. Ketenes can be inserted into metal–hydride, metal–alkyl, metal–OR, and metal–NR_2 bonds, react with metal–oxide complexes, and with coordinated ligands. This chemistry has been reviewed (9, 51).

1.3. Manufacture

Ketenes can be considered the internal anhydrides of the corresponding carboxylic acids, and as such can be made by removing a molecule of water from these acids, either directly or indirectly. Numerous methods to convert a carboxylic acid or derivative to the corresponding ketene have been described (1–4).

Commercially and industrially most important, ketene itself, H_2C—C—O, is produced by pyrolysis of acetic acid [64-19-7]. In this process, high quality acetic acid is evaporated and the vapor passed continuously through a radiant coil under reduced pressure at 740–760°C.

The materials of construction of the radiant coil are highly heat-resistant steel alloys, such as Sicromal containing 25% Cr, 20% Ni, and 2% Si. Triethyl phosphate [78-40-0] catalyst is injected into the acetic acid vapor. Ammonia [7664-41-7] is added to the gas mixture leaving the furnace to neutralize the catalyst and thus prevent ketene and water from recombining. The crude ketene obtained from this process contains water, acetic acid, acetic anhydride, and 7 vol % other gases (mainly carbon monoxide [630-08-0], carbon dioxide [124-38-9], ethylene [74-85-1], and methane [74-82-8]). The gas mixture is chilled to less than 100°C to remove water, unconverted acetic acid, and the acetic anhydride formed as a liquid phase (52, 53).

The production of ketene by this method has no significant environmental impact. The off-gases from the ketene furnace are either circulated to the furnace and burned to save energy or led to a flare system. The reaction can also be carried out at 350–550°C in the presence of alkali-exchanged zeolite catalysts (54). Small quantities of ketene are prepared by pyrolysis of acetone [67-64-1] at 500–700°C in a commercially available ketene lamp (55, 56).

For the two most important industrial uses, the gaseous ketene is immediately treated with acetic acid to form acetic anhydride or dimerized to diketene.

The manufacture of the highly pure ketene required for ketenization and acetylation reactions is based on the pyrolysis of diketene, a method which has been employed in industrial manufacture. Conversion of diketene to monomeric ketene is accomplished on an industrial scale by passing diketene vapor through a tube heated to 350–600°C. Thus, a convenient and technically feasible process for producing ketene uncontaminated by methane, other hydrocarbons, and carbon oxides, is available. Based on the feasibility of this process, diketene can be considered a more stable form of the unstable ketene.

Acetone and acetic anhydride can be used as alternative raw materials to acetic acid in the industrial production of ketene. However, the use of acetone as a raw material is only interesting when the price is low. It is believed that acetone is still used in the former Soviet Union for the production of ketene.

Other methods for the preparation of aldo- and ketoketenes (57) are the pyrolysis or photolysis of ketones, pyrolysis of carboxylic acids and anhydrides, (especially malonic acid mixed anhydrides) (58), thermolysis or photolysis of α-diazoketones via a carbene intermediate and dehalogenation of α-halogen acid chlorides with zinc [7440-66-6] (59). The method of dehydrohalogenation of carboxylic acid chlorides with a base, usually a trialkylamine (60) in producing ketenes, is used for the only other ketenes which are produced industrially, the long-chain (C10–C20) monoalkylketenes (aldoketenes). The starting material in these syntheses are fatty acid chlorides, in particular, stearoyl chloride [112-76-5]. Their lactone dimers have been used for paper sizing for many years. The intermediate, reactive ketenes dimerize to the lactone dimers in the presence of acidic catalysts (61, 62).

Thioketenes can be prepared in several ways, from carboxylic acid chlorides by thionation with phosphorus pentasulfide [1314-80-3], P_2S_5, from ketene dithioacetals by β-elimination, from 1,2,3-thiadiazoles with flash pyrolysis, and from alkynyl sulfides (thioacetylenes). The dimerization of thioketenes to 2,4-bis(alkylidene)-1,3-dithietane compounds occurs quickly. They can be cleaved back pyrolytically (63). For a review see Reference 18.

Ketenimines are usually prepared from carboxylic acid derivatives such as amides and imino chlorides via elimination and from nitriles via alkylation with alkyl halides under strong basic conditions (21, 64).

1.4. Shipping and Storage

Most ketenes are extremely reactive and unstable so they cannot be stored or transported. Some have been isolated only in solution, or have not been isolated at all, but are used *in situ*. Ketene itself is stable for some hours at $-80°\text{C}$, but dimerizes within minutes at 0°C. It cannot even be transferred through a pipe for any significant distance, even within the same plant, and has to be used *in situ* immediately. All reactions with ketene on an industrial scale have been performed either directly in the ketene manufacturing plant or by transporting diketene and cracking it back to ketene immediately next to the reaction vessel (65). Information on emergency procedures in some safety data sheets (66) give the misleading impression that ketene is stored in cylinders, which is simply not feasible. Some sterically hindered ketoketenes are reasonably stable at room temperature.

1.5. Economic Aspects

Due to the physical nature and instability of these materials, all ketene production is used captively and production figures are not readily available. The economic aspects of the products made from ketenes will be addressed later.

1.6. Analytical and Test Methods

For a review of detection, determination, and identification of ketenes see Reference 67. Typical properties are the strong ir absorption bands at $2151\ \text{cm}^{-1}$ (C—O) and at $1120\ \text{cm}^{-1}$ as well as a very low field signal of the *sp*-hybridized carbon at approximately 194 to 206 ppm and a very high field signal of the sp^2 hybridized carbon at approximately 2.5 to 27 ppm in^{13}C-nmr spectroscopy.

1.7. Health and Safety Factors

Ketene itself is a highly poisonous gas, strongly irritating to the eye, the respiratory tract, and the skin (66, 68). Different, sometimes conflicting values for its toxicity are found in the literature (69, 70), mainly due to the difficulty in maintaining accurately and measuring low levels of the unstable ketene over hours. Its toxicity is estimated to be of the same order of magnitude as that of phosgene (71), and like the latter it can cause latent damage of the respiratory tract which may become acute only several hours after exposure (pulmonary edema). Repeated or high exposure may cause permanent lung damage.

The LC_{LO} (lowest possible lethal concentration) has been reported to be 23 ppm for a 30 min exposure time (mouse), 53 ppm for an exposure time of 100 min (rat, rabbit, and guinea pig), and 200 ppm for an exposure time of 10 min (monkey). No toxic effects were reported upon exposure to 1 ppm for $7\ \mathrm{h/d}$ over 55 days. The oral LD_{50} (rat) of ketene is $1300\ \mathrm{mg/kg}$, the low level of toxicity probably being due to the almost immediate formation of acetic acid and other acetates in the digestive tract.

The OSHA PEL and NIOSH REL $(\text{recommended exposure limit})/10\ \mathrm{h{-}TWA}$ exposure limit for ketene is 0.5 ppm $(0.9\ \mathrm{mg/m^3})$ (72). This is also the MAK (maximum allowable concentration) value in Germany (73) and Switzerland (74). The NIOSH maximal allowable short-time exposure concentration (TLV-STEL) is 1.5 ppm in the United States, and in Germany 1 ppm for no longer than 5 min and no more than 8 times a day. According to Reference 66, exposure to 25 ppm is immediately dangerous to life and health. Inhalation of even small quantities of ketene leave a characteristic, long lasting unpleasant taste; smokers seem to be particularly sensitive to this. No carcinogenic effects of ketene have been reported. Ketene is listed in the EPA TSCA chemical inventory (1990) and in the EPA TSCA Test Submission (TSCATS) Data Base and the 1992 NHOS Hazard Code 41840.

Practically nothing is known about the toxicity of higher ketenes, thioketenes, and ketenimines, but it is prudent to consider them at least as toxic and hazardous as ketene itself. Ketenes and related compounds are highly reactive with a wide variety of substances. They can polymerize violently or even explosively especially in the presence of bases or strong acids. Ketoketenes are somewhat more stable than aldoketenes but they are prone to oxidation by air, forming highly explosive peroxides (75), and should be handled under nitrogen or argon. Ketene itself is stable in dry air and oxygen [7782-44-7]. Like most volatile organic compounds, most ketenes are flammable and form explosive mixtures with air. Contrary to the statement in Reference 66 under "Emergency Information," ketene itself is a flammable gas which forms explosive mixtures with air in the range 5.5–18 vol %. The liquid has a flash point of $-107°\mathrm{C}$. In case of fire, water or extinguishing powder should be used (76).

1.8. Uses

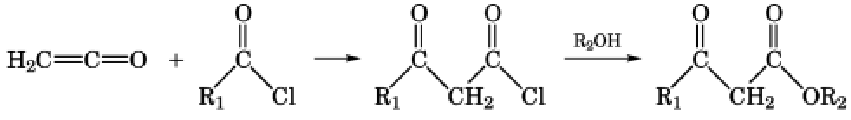
The lowest member of this class, ketene itself, is a powerful acetylating agent, reacting with compounds containing a labile hydrogen atom to give acetyl derivatives. This reaction is used only when the standard acetylation methods with acetic anhydride or acetyl chloride [75-36-5] do not work well. Most of the ketene produced worldwide is used in the production of acetic anhydride. Acetic anhydride is prepared from the reaction of ketene and acetic acid.

This process is one of the three commercially practiced processes for the production of acetic anhydride. The other two are the oxidation of acetaldehyde [75-07-0] and the carbonylation of methyl acetate [79-20-9] in the presence of a rhodium catalyst (coal gasification technology, Halcon process) (77). The latter process was put into operation by Tennessee Eastman in 1983. In the United States the total acetic anhydride production has been reported to be in the order of 1000 metric tons.

The second most important use of ketene is in the production of diketene [674-82-8] (**3**) by controlled dimerization. Diketene has wide utility in the manufacture of pharmaceutical and agricultural chemicals, dyes, pigments and fine chemicals.

Chlorine adds to ketene to form chloroacetyl chloride [79-04-9] (78). Chloroacetyl chloride (CAC) is used in large volume in the manufacture of the pre-emergence herbicides alachlor [15972-60-8] and butachlor [23184-66-9]. It is estimated that the CAC requirement for this application was in excess of 45,000 metric tons in 1992. Significant volumes of CAC are also used in pharmaceutical manufacture, such as anesthetics of the lidocaine type, and in the production of the tear gas chloroacetophenone [532-27-4]. Other commercial methods for the manufacture of CAC have been described (79).

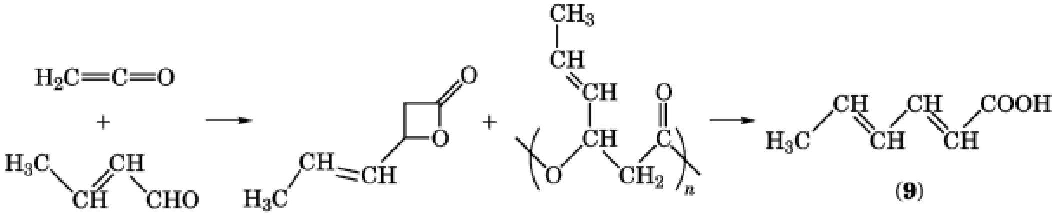
In the presence of strong acid, such as boron trifluoride [7637-07-2], appropriately substituted acyl chlorides (**7**, $R_1 = CF_3$, CCl_3) add to ketene to form the corresponding acetoacetyl chlorides, which can further react with alcohols to form the corresponding acetoacetates.



(7)

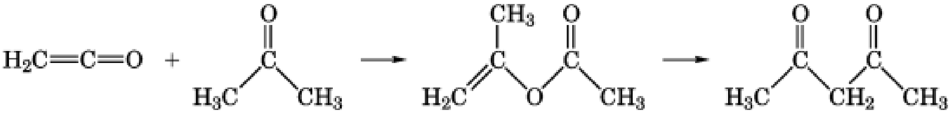
Of industrial significance are ethyl 4,4,4-trifluoroacetoacetate [372-31-6], methyl 4,4,4-trifluoroacetoacetate, and isopropyl 4,4,4-trifluoroacetoacetate for the production of herbicides (eg, Monsanto's Dimension) and antimalarial agents such as Roche's Mefloquin [51773-92-3], as well as ethyl 4,4,4-trichloroacetoacetate [3702-98-5] for the production of pharmaceuticals.

Another principal use of ketene is in the production of sorbic acid [110-44-1] (80, 81). In this process, which requires an acidic or manganese(II) catalyst, ketene adds to crotonaldehyde [123-73-9] **(8)** with subsequent conversion of the *β*-lactone and the polyester to sorbic acid (qv) **(9)**.



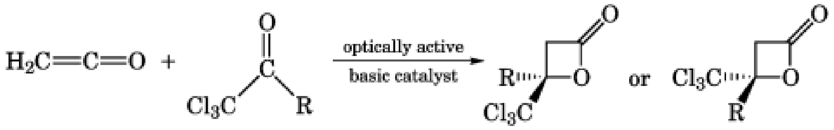
(8) **(9)**

Ketones with labile hydrogen atoms undergo enol acetylation on reaction with ketene. Strong acid catalysis is required. If acetone is used, isopropenyl acetate [108-22-5] **(10)** is formed (82–85). Isopropenyl acetate is the starting material for the production of 2,4-pentanedione (acetylacetone) [123-54-6] **(11)**.



(10) **(11)**

Ketene can also be added to trihalosubstituted aldehydes or ketones **(12)** to form 4-trihalomethyloxetanones. If this addition is performed in the presence of optically active bases such as quinine [130-95-0] chiral lactones are obtained (41, 42).



(12)

Table 2. Dimeric Ketenes

Name	CAS Registry Number	Physical properties	Mp or bp,[a] °C
diketene	[674-82-8]	colorless liquid	mp −7.5, bp 127 (101.3 kPa), bp 69–71 (13.3 kPa), bp 38.5 (3.1 kPa)
hexadecylketene dimer	[10126-68-8]	colorless crystals	mp 64 (88),also 81 (89)
dimethylketene dimer	[3173-79-3]	lachrimatory liquid[b]	bp 170 (97.6 kPa) (90), bp 83–85 (5.3 kPa)
octadecylketene dimer	[24430-01-1]	crystals	mp 80 (91)
tetradecylketene dimer	[42272-70-8]	crystals	mp 57–58 (89)
dimethylketene dimer	[933-52-8]	white crystals, sublimes at 95°C	mp 108–111 (92)
dimethylthioketene dimer	[10181-56-3]	crystals	mp 123.5–125 (93)
cyclobutane-1,3-dione	[15506-53-3]	white crystals	mp 119–120 dec (94)
dispiro(5.1.5.1)tetra-decane-7,14-dione	[950-21-0]	crystals	mp 164–165 (95)

[a] At 101.3 kPa unless otherwise stated; to convert kPa to torr, multiply by 7.5.

[b] Density = 1.88 g/mL; $n_D = 1.4381$.

Ketene has also been used on a large scale for C-acetylation in the synthesis of the carbapenem antibiotic thienamycin [59995-64-1] (86, 87).

2. Dimeric Ketenes

2.1. Physical Properties

Dimeric ketenes are colorless to dark brown liquids or crystalline solids with a broad range of melting and boiling points. Table 2 lists examples of dimeric ketenes and thioketenes.

2.2. Chemical Properties

Diketene is a reactive and versatile compound which can undergo reaction with a large variety of compounds. These reactions have been reviewed comprehensively (1, 5, 6, 96).

In most reactions diketene appears to react as acetylketene or one of its tautomeric forms. This is one of the reasons for the correct structure of diketene being firmly established only in 1952, 45 years after its discovery (97, 98).

Diketene usually reacts either at the carbonyl group (nucleophilic attack), or at the olefinic bond (electrophilic attack), either process resulting almost always in an exothermic reaction and in the opening of the strained diketene ring (Fig. 2). The strain energy is = 94.2 kJ/mol (22.5 kcal/mol). The so-formed 1,3-dicarbonyl compounds can react further if other functional groups are present often forming heterocyclic compounds. Acetoacetylations and the formation of five- and six-membered heterocyclic rings are the very heart of diketene chemistry.

It is, however, possible to perform reactions such as hydrogenation, halogenation, polymerization, and $[2+2]$ cycloadditions with the exocyclic double bond of diketene without opening the β-lactone ring.

2.2.1. Acetoacetylation Reactions

The best known and commercially most important reaction of diketene is the acetoacetylation of nucleophiles to give derivatives of acetoacetic acid (Fig. 2) (1, 5, 6). A wide variety of substances with acidic hydrogens can be acetoacetylated. This includes alcohols, amines, phenols, thiols, carboxylic acids, amides, ureas, thioureas,

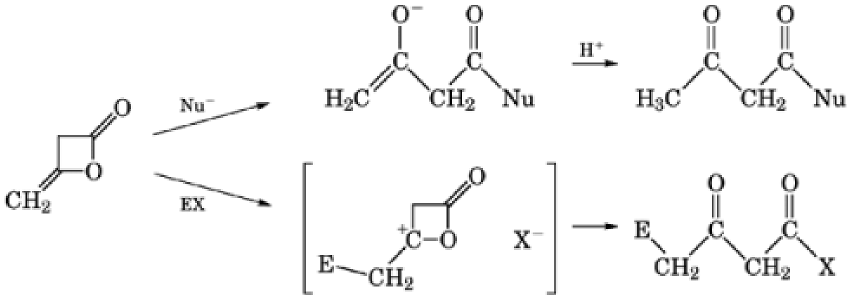


Fig. 2. The reactions of diketene with nucleophiles (Nu^-) and electrophiles (EX).

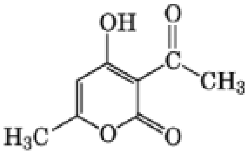
urethanes, and sulfonamides. Where more than one functional group is present, ring closure often follows acetoacetylation, giving access to a variety of heterocyclic compounds. These reactions often require catalysts in the form of tertiary amines, acids, and mercury salts. Acetoacetate esters and acetoacetamides are the most important industrial intermediates prepared from diketene.

Diketene is used to C-acetoacetylate aromatic compounds in the presence of aluminum trichloride [7446-70-0]. Benzene [71-43-2] and diketene react to produce acetoacetylbenzene [93-91-4]. Pyrrole [109-97-7] and diketene react to produce 2-acetoacetylpyrrole [22441-25-4]. The C-acetoacetyl derivatives of active methylene compounds such as cyanoacetates, malonodinitrile [109-77-3], and Meldrum's acid [2033-24-1], and olefins can be prepared using diketene.

Water hydrolyzes pure diketene only slowly to give acetoacetic acid [541-50-4] which quickly decomposes to acetone and carbon dioxide, but increasing the pH or adding catalysts (amines, palladium compounds) increases the rate of hydrolysis. The solvolysis of diketene in ammonia results in acetoacetamide [5977-14-0] if used in stoichiometric amounts (99), and β-aminocrotonamide [15846-25-0] if used in excess (100).

2.2.2. Six-Membered Heterocycle Ring Formation

Heterocycle formation involving diketene usually involves acetoacetylation of a substrate, followed by intramolecular condensation. Diketene itself readily dimerizes through self-condensation forming mainly dehydroacetic acid [771-03-9] (DHA) (**13**). Dehydroacetic acid and sodium dehydroacetate [4418-26-2] are used as preservatives for foods and cosmetics. DHA is found as an unwanted by-product in many diketene reactions, but can be obtained intentionally by dimerizing diketene in the presence of pyridine [110-86-1] in benzene, diazabicyclo[2.2.2]octane [280-57-9] (DABCO), and other basic catalysts.



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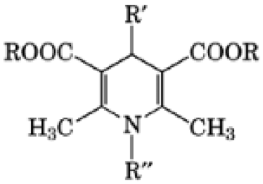
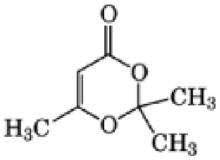


(14)

Another important reaction of diketene derivatives is the Hantzsch pyridine synthesis (101). This synthesis is the preparation of 1,4-dihydropyridines (**14**) starting either from two acetoacetic esters, which react with an aldehyde and ammonia or a primary amine or from 3-aminocrotonates and 2-alkylidene acetoacetic esters, both diketene derivatives. Several such dihydropyridines such as nifedipine [21829-25-4] (102), nimodipine [66085-59-4], and nicardipine [55985-32-5] exhibit interesting pharmaceutical activity as vasodilators (blood vessel dilation) and antihypertensives (see Cardiovascular agents).

Six-membered heterocycles with two heteroatoms are prepared by reaction of diketene with a substrate containing a C—O or C—N multiple bond. With carbonyl compounds diketene reacts in the presence of acids to give 1,3-dioxin-4-ones. The best known is 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one [5394-63-8] (**15**), the so-called diketene–acetone adduct, often used as a diketene replacement that is safer to handle and to transport, albeit somewhat less reactive than diketene itself (103, 104), forming acetylketene upon heating.



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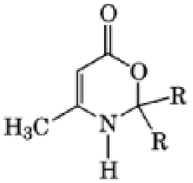


(16)

Diketene reacts with imines to give 1,3-oxazinones (**16**) (105). This reaction has been used in the synthesis of the tranquilizer Ketazolam [27223-35-4] from diazepam [439-14-5] (106).

Other six-membered rings with two heteroatoms are also obtained from reaction of diketene with imidates, cyanamides, carbodiimides, isocyanates, oxazolines, or other multifunctional compounds.

2.2.3. Five-Membered Heterocycle Ring Formation

Diketene reacts with a variety of bifunctional compounds to give five-membered heterocycles, usually through acetoacetylation followed by intramolecular condensation. Thus hydrazines give pyrazolones (107), important dyestuff intermediates, hydrazones give pyrazolin-3-ones, hydroxylamines afford 3-methylisoxazol-5-ones or isomers depending on conditions (108), hydroxamic acids give oxazoles, α-hydroxyketones can give butenolides (109), and α-hydroxy acids give furanones (110). Several of these five-membered heterocycles are intermediates for pharmaceuticals and agrochemicals. A variety of five- and six-membered heterocycles are also obtained indirectly from diketene via 2- and 4-chloroacetoacetates.

2.3. Other Reactions of Diketene

Diketene reacts with elemental chlorine to give 4-chloroacetoacetyl chloride [41295-64-1], which can further react to the corresponding esters (111).

4-Chloroacetoacetic esters are important industrial intermediates used especially for the synthesis of the aminothiazolylacetic acid side chain of modern cephalosporins (see Antibiotics, β-lactams–cephalosporins). For a review of the chemistry of 4-chloroacetoacetates see Reference 112.

Diketene can be hydrogenated to β-butyrolactone [3068-88-0]. In the presence of 2,2′-bis(diphenylphosphino)-1,1′-binaphthylruthenium(II) complexes the reaction is stereoselective (113).

Ozonolysis of diketene affords formaldehyde [50-00-0] and the very un-stable malonic anhydride [15159-48-5] (114), which readily decomposes to CO_2 and ketene, but can be converted at low temperature to malonic acid monoesters or Meldrum's acid (115) (see Malonic acid and derivatives).

Pyrolysis of diketene at temperatures greater than 400°C gives two molecules of ketene. This method has been used industrially. At present there is no method to convert diketene efficiently into allene [463-49-0] and CO_2, the thermodynamic products.

Grignard reagents add to diketene in the presence of cobalt iodide [15238-00-3], CoI_2, or palladium [440-05-3] to give 3-methylenecarboxylic acids, used in terpenoid and hormone syntheses, as well as monomers for radical copolymers (116, 117) (see Hormones; Terpenoids).

Diketene also reacts with organometallic compounds including organoboron, organosilicon, organoaluminum, and organotin compounds to afford acetoacetate complexes (118). Diketene can be polymerized with various catalysts such as boron trifluoride, mercury(II) chloride [7847-94-7], $HgCl_2$, and ion-exchange resins to low molecular weight polymers containing unconjugated methylene groups (119, 120). Diketene can also be copolymerized under radical conditions with monomers such as vinyl chloride [75-01-4], vinyl acetate [108-05-4], and acrylonitrile [107-13-1], giving polymers containing the β-lactone ring in the monomer units (121). The lactone ring can further react with nucleophiles to produce elaborately functionalized polymers.

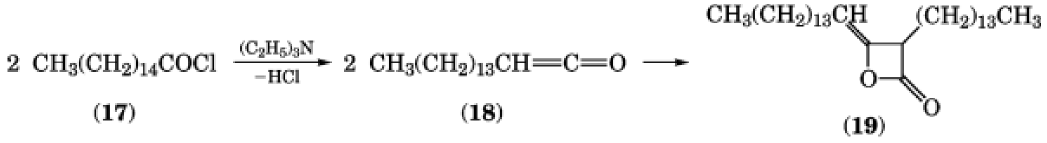
Dimeric aldoketenes and ketoketenes of β-lactone structure show a chemical behavior which is not much different to that of diketene. Thus nucleophiles add in similar fashion to give derivatives of 3-ketoacids which are mono- or dialkylated at C-2 (aldo- and ketoketene dimers, respectively), but the reaction can often be slower than with the parent compound and, in case of long-chain or bulky substituents, may not proceed at all. Other reactions can proceed differently than those with diketene. For an overview of important reactions of aldoketene and ketoketene dimers see Reference 122.

2.4. Manufacture

Of the industrially used ketene dimers, the first member of the group, diketene itself, is by far the most significant. The only other ketene dimers used on an industrial scale are the long-chain alkylketene dimers (AKDs) (usually C-12 to C-20) which are made by Hercules for paper sizing applications. Diketene is made industrially by controlled dimerization of ketene. The gaseous ketene from the ketene furnace, dried and cooled and at a pressure of 20–30 kPa before entering the dimerization unit, is dimerized in a liquid ring pump. The dimerization is preferably carried out in diketene itself (52, 123), and gives yields up to 85% based on acetic acid.

Crude diketene obtained from the dimerization of ketene is dark brown and contains up to 10% higher ketene oligomers but can be used without further purification. In the crude form, however, diketene has only limited stability. Therefore, especially if it has to be stored for some time, the crude diketene is distilled to $>99.5\%$ purity (124). The tarry distillation residue, containing triketene (**5**) and other oligomers, tends to undergo violent spontaneous decomposition and is neutralized immediately with water or a low alcohol. Ultrapure diketene (99.99%) can be obtained by crystallization (125, 126). Diketene can be stabilized to some extent with agents such as alcohols and even small quantities of water [7732-18-5] (127), phenols, boron oxides, sulfur [7704-34-9] (128) and sulfate salts, eg, anhydrous copper sulfate [7758-98-7].

Long-chain alkylketene dimers are also produced from their corresponding monomers by controlled dimerization (58, 59). The starting materials are mixed fatty acids (C_{12}–C_{22}, mostly C_{16}–C_{20}), which are converted to the acid chlorides **(17)** using phosphorus trichloride [7719-12-2], and then to the ketenes **(18)** through the removal of hydrogen chloride [7647-01-0] with triethylamine [121-44-8]. These intermediary long-chain aldoketenes combine to the unsymmetrical dimers **(19)** (β-lactones), with a dione dimer content of $<1\%$. The raw product of AKDs is 80–85% pure as β-lactone. The rest is free acids, their anhydrides, and some pyrones.



(17) **(18)** **(19)**

This purity is adequate for conversion into aqueous emulsions which are supplied to the paper industry.

2.5. Shipping and Storage

Because of its extreme reactivity and hazardous properties, diketene is now generally consumed at the site of production. Regulations still allow the transport of diketene by road and ship (transport by plane has recently been forbidden) but the two largest producers in the United States, Lonza Inc. and Tennessee Eastman, several years ago voluntarily agreed to no longer ship diketene. Diketene, however, was shipped in refrigerated tank cars for many years without incident when it was still sold on the merchant market (129).

Pure diketene is stable for several weeks if stored at or below 0°C in an aluminum or stainless steel container. Glass should be avoided because of its inherent basicity which favors slow polymerization. Above 15°C slow decomposition occurs and the color becomes progressively darker. Pressure build-up upon prolonged exposure to heat is possible. Heating and contamination of the container, especially by acids, bases, and water, should be avoided. Residual vapors in empty containers are hazardous and may explode on ignition.

A shippable but somewhat less reactive form of diketene is its acetone adduct, 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (**15**) (103, 104). Thermolysis of this safer to handle compound provides acetylketene, a reactive intermediate that can be used for acetoacetylation and cycloaddition reactions. The diketene–acetone adduct as well as *tert*-butylacetoacetate [1694-31-1] (also used for acetoacetylations by the transacetoacetylation reaction) (130), are offered commercially.

The higher, long-chain dimers as well as the tetramer dehydroacetic acid are far more stable and can be handled safely. The alkylketene dimers (AKDs) are shipped to the paper industry in tank trucks in the form of ready-to-use aqueous emulsions with a total solids content of 12–25% and a guaranteed shelf life of 30 days, as they have good hydrolytic stability. In this form they are not combustible liquids, and are listed in the Canadian Domestic Substances List.

2.6. Economic Aspects

All diketene production is used captively and, therefore, production figures can only be estimated by the volume of derivatives output on the merchant market. World production of diketene is probably close to 100,000 metric tons, approximately 20% of that production in the United States. Before the discontinuation of all shipment in the United States, diketene was sold for less than \$2.20/kg.

The world production of the alkylketene dimers is believed to be around 15,000 metric tons, equally split between the United States and the rest of the world. The value of the AKDs (80–85% assay) is $\$4.00 - 4.40/\mathrm{kg}$.

2.7. Analytical and Test Methods

Colorimetric qualitative tests for diketene are known but seldom used (131). Identification is by spectrometric methods. Diketene has typical ir absorption bands at ~ 1880, 1855, and 1685 cm^{-1}, and signals at 3.92 (t), 4.51 (m), and 4.87 (m) ppm in the ^{1}H-nmr spectrum ($CDCl_3$). Purity is routinely monitored by gc. Alternatively, diketene is quantitatively converted to acetoacetic derivatives which are assayed by standard methods.

3. Health and Safety Factors

Good ventilation, eye and skin protection, and an approved organic vapor respirator should be used when handling diketene.

Diketene is a strongly irritating, powerfully lachrimatory, poisonous liquid, but is considerably less toxic than ketene (68). The eye and respiratory tract are especially endangered, as diketene quickly damages the tissue of the cornea and lung. Lung edema may occur even up to two days after inhalation. Exposure causes a burning sensation in eyes, nose, and throat, as well as respiration difficulties and coughing. At higher levels, loss of consciousness and death can occur. Absorption of liquid diketene by the skin is possible, with local itching and severe burning of the skin (131). Ingestion causes irritation of the gastrointestinal tract.

Chronic effects are not known and diketene was not found to be carcinogenic on skin application, injection beneath the skin, or gastric feeding in mice and rats (132–134). It is not listed as a carcinogen by International Agency for Research on Cancer (IARC), the National Toxicology Program (U.S.), OSHA, and ACGIH.

Since diketene is a strong eye irritant even at low levels, it has a strong warning effect. Diketene becomes unbearable before acute toxic levels are reached. Due to the risk of delayed lung edema, a physician should be consulted and the patient monitored carefully after exposure.

Rat LD_{50} is $560\ \mathrm{mg/kg}$ (rat) and the lowest lethal dose, LD_{LO} is $800\ \mathrm{mg/kg}$ (mouse). By inhalation, the LC_{50} is $3\ \mathrm{g/m^3}$ for a 2 h period which is approximately 860 ppm (guinea pig) and the LC_{LO} is $20,000\ \mathrm{ppm/1\ h}$ (rat). By skin application, the LD_{50} is $2830\ \mathrm{mg/kg}$ (rabbit). The DOT skin irritation index is 5.0 (strongly irritating). No ACGIH threshold limit values or OSHA permissible exposure limits have been established. No odor threshold is available.

Very little is known about the toxicology of other dimeric ketenes. For the dimeric dimethylketene there is equivocal evidence of tumors resulting from massive exposure in rats reported for the β-lactone form (3,3-dimethyl-4-isopropylidene-2-oxetanone), whereas the symmetric form (2,2,4,4 tetramethylcyclobutane-1,3-dione) induces tumors in mice after lengthy skin applications.

Diketene is a flammable liquid with a flash point of 33°C and an autoignition temperature of 275°C. It decomposes rapidly above 98°C with slow decomposition occurring even at RT. The vapors are denser than air (relative density 2.9, air $\mathrm{air} = 1$). The explosive limits in air are 2–11.7 vol % (135). In case of fire, water mist, light and stabilized foam, as well as powder of the potassium or ammonium sulfate-type should be used. Do not use basic extinguisher powders and do not add water to a closed container.

The greatest hazard is violent exothermic polymerization with quick pressure build-up and rupture of the vessel. Pressure increases of $12.1\ \mathrm{MPa/min}$ have been measured. Polymerization can take place on heating or through contact with even catalytic amounts of bases, mineral acids, strong oxidants, Friedels-Crafts catalysts, and other substances. On addition of 1 drop of an amine to 1 g of diketene, the hot reaction mixture is violently projected out of the test tube within a few seconds. Water decomposes diketene slowly. Acids react slower than bases; storage vessels should therefore be thoroughly clean and free of contaminants. In chemical reactions diketene should be added slowly to the other reagents, not vice-versa, making sure that there is no build-up of unreacted diketene.

Higher dimeric ketenes are flammable but have higher flash points and are less reactive than diketene. Almost no data are available. Diketene can be disposed of by incineration, preferably after dilution with an inert solvent such as toluene. Higher ketene dimers can also be incinerated.

3.1. Uses

Diketene is described as having bactericidal activity (136, 137). It also raises the octane rating of gasoline (138) but is not used for these purposes in the Western world.

As the most reactive and economical source of the acetoacetyl moiety, diketene is used as a valuable synthetic intermediate in the manufacture of acetoacetic acid derivatives and heterocyclic compounds which are used as intermediates in the manufacture of dyestuffs, agrochemicals, pharmaceuticals, and polymers.

The AKDs are used in paper sizing applications. Paper sizing chemicals provide paper and paperboard with resistance to wetting by liquids, especially water repellency in paper cups, milk cartons, photographic paper, coatings, and packaging paper (139) (see Paper; Papermaking additives).

Ketene trimer can be recovered from the tarry residue of diketene distillation and converted into valuable building blocks like 1,3-cyclobutanedione and squaric acid [2892-51-5] (140, 141), an important intermediate in the synthesis of pharmaceuticals and squarylium dyes used in photostatic reproduction (142, 143).

4. Acetoacetic Acid Derivatives

The most important use of diketene is for the preparation of derivatives of acetoacetic acid, such as acetoacetate esters, acetoacetamides, and chloroacetoacetates, which have found many uses in life sciences, dyestuffs, adhesives, and coatings.

4.1. Physical Properties

Acetoacetic esters are high boiling liquids with pleasant odors. Lower N-alkylamides are water-soluble liquids; acetoacetamide and acetoacetarylides are solids. 4-Chloroacetoacetates are high boiling lachrymatory liquids. Some physical properties are listed in Tables 3 and 4.

4.2. Chemical Properties

The acetoacetyl moiety is highly functionalized and can undergo many transformations. At the active methylene group, condensation reactions with other carbonyl compounds, halogenation, alkylation, and nitrosation can occur. At the ester or amide group, decarboxylation and trans-esterification can occur. At the ketone carbonyl group, reduction and addition of nucleophiles can occur. Combination of such reactions gives access to a broad spectrum of different types of compounds. For a general overview on the chemistry of acetoacetates see References (96, 144–146); of 4-haloacetoacetates see Reference 112; of acetoacetarylides and pyrazolones in azo dyes and pigment uses see Azo dyes.

4.3. Manufacture and Uses

Acetoacetic esters are generally made from diketene and the corresponding alcohol as a solvent in the presence of a catalyst. In the case of liquid alcohols, manufacturing is carried out by continuous reaction in a tubular reactor with carefully adjusted feeds of diketene, alcohol, and catalyst, or alcohol–catalyst blend followed by

Table 3. First Generation Diketene Derivatives

Diketene derivative	CAS Registry Number	Mp or bp,[a] °C	Principal uses
methyl acetoacetate	[105-45-3]	bp 169–170, bp 69–71 (1.8 kPa)	herbicides, pesticides, chemical synthesis, protection of NH_2 groups
ethyl acetoacetate	[141-97-9]	bp 181, bp 74 (1.9 kPa)	antibiotics, protection of NH_2 groups, chemical synthesis
tert-butyl acetoacetate	[1694-31-1]	bp 76–78 (2.0 kPa)	acetoacetylations
2-acetoacetoxyethyl methacrylate	[21282-97-3]	bp 100 (0.1 kPa)	acetoacetylated polymers, coatings
methyl 4-chloro- acetoacetate	[32807-28-6]	mp 14, bp 50 (0.133 kPa)	L-carnitine amino-thiazole–acetic acid derivatives
ethyl 4-chloro- acetoacetate	[638-07-3]	mp −8.5, bp 95 (1.33 kPa)	coumarins, aminothiazole–acetic acid deriva-tives
acetoacetamide	[5977-14-0]	mp 54	methylpyrazolones
N-methyl- acetoacetamide	[20306-75-6]	bp 96–98 (13 kPa)	insecticides, polyester curing
N,N-dimethyl-acetoacetamide	[2044-64-6]	bp 75–77 (0.2 kPa)	insecticides, polyester curing
N-(β-hydroxy)ethyl-acetoacetamide	[24309-97-5]	mp 35–40	animal feed additive
diethylacetoacetamide	[2235-46-3]	bp 123–124 (1.2 kPa)	insecticides
acetoacetanilide	[101-01-2]	mp 84–85	yellow pigments, fungicides
o-acetoacetotoluidide	[93-68-5]	mp 104	orange pigments
o-acetoacetoaniside	[92-15-9]	mp 87	yellow dyes
N-(2,4-dimethyl-phenyl)-3-oxo-butyramide	[97-36-9]	mp 89	orange and yellow pigments
N-acetoacet-*p*-phenetidide[b]	[122-82-7]	mp 103.5	yellow road pigment
dehydroacetic acid	[520-45-6]	mp 109–111	antimicrobials
diketene–acetone adduct	[5394-63-8]	bp 65–67 (15 kPa)	diketene substitute
6-methyluracil	[626-48-2]	mp 270–280 (dec)	dipyridamole

[a] At 101.3 kPa, unless otherwise stated; to convert kPa to torr, multiply by 7.5.

[b] 4-Ethoxyacetoacteanilide

Table 4. Second Generation Diketene Derivatives

Diketene derivative	CAS Registry Number	Mp or bp,[a] °C	Principal uses
1-phenyl-3-methyl-5-pyrazolone	[89-25-8]	mp 127.5	yellow, orange, and red pigments
1-(*p*-tolyl)-3-methyl-5-pyrazolone	[86-92-0]	mp 133	orange and red pigments
3-methyl-5-pyrazolone	[108-26-9]	mp 217	yellow and orange dyes
4-hydroxy-6-methyl-pyrone	[675-10-5]	mp 185–187	chemical synthesis
5-aminoorotic acid	[7164-43-4]	mp 250 dec	dipyridamole
ethyl 2-chloroacetoacetate	[609-15-4]	bp 107 (1.87 kPa)	chemical synthesis, imidazoles, vitamin B_6
methyl 2-chloro-acetoacetate	[4755-81-1]	bp 137	chemical synthesis, imidazoles, vitamin B_6
methyl 3-aminocrotonate	[14205-39-1]	mp 81–84, bp 112 (55 kPa)	dihydropyridine calcium-channel blockers
methyl 3-oxopentanoate	[30414-53-0]	bp 180.7	ethyl substituted pyrimidines, non-steroidal anti-inflammatories
ethyl 2-(2-aminothiazole-4-yl)-acetate	[53266-94-7]	mp 92–94	side chains of third generation cephalosporins
L-carnitine	[541-15-1]	mp 210–212 dec	dietary supplement
1,4-cyclohexanedione	[637-88-7]	mp 76–79	chemical building block
tetronic acid	[4791-56-6]	mp 141–143 dec	chemical building block, vitamins

[a] At 101.3 kPa, unless otherwise stated; to convert kPa to torr, multiply by 7.5.

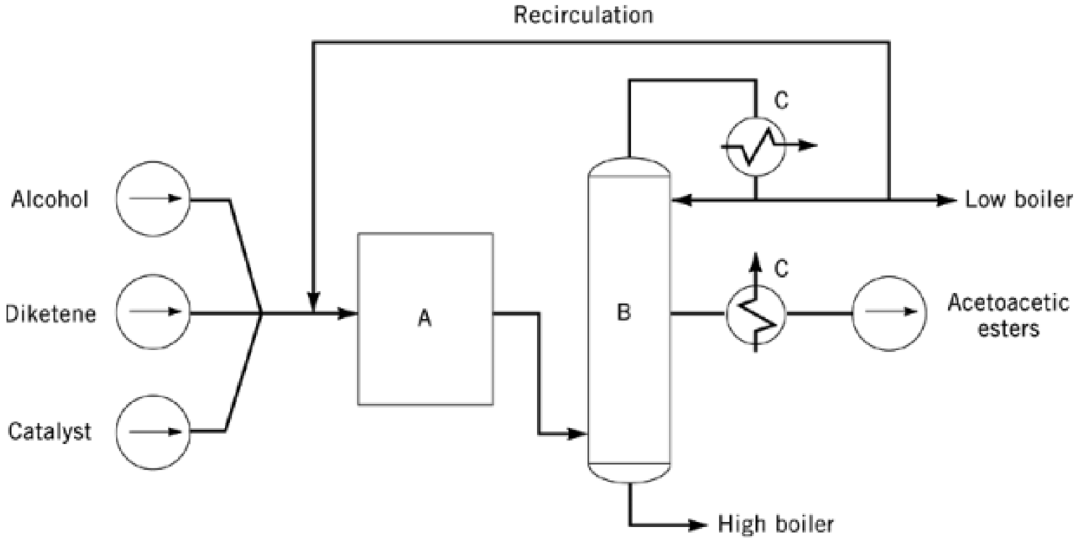


Fig. 3. Flow sheet for the preparation of acetoacetic esters (Lonza). A, reactor; B, rectification column; C, condensor.

continuous purification (Fig. 3). For solid alcohols, an inert solvent is used. Catalysts used include strong acids, tertiary amines, salts such as sodium acetate [127-09-3], organophosphorus compounds, and organometallic compounds (5).

Methyl acetoacetate (MAA) and ethyl acetoacetate (EAA) are the most widely used esters; they are found in the pharmaceutical, agricultural, and allied industries. Both esters are used extensively as amine protecting agents in the manufacture of antibiotics and synthetic sweeteners (Dane Salts) (147). Principal outlets for MAA are the manufacture of the organophosphorus insecticide diazinon [333-41-5] (148, 149) and the uracil herbicides bromacil [314-40-9] and terbacil [5902-51-2] (150, 151) (see Insect control technology; Herbicides).

Hydroxyalkyl acrylates and polyols are acetoacetylated with diketene to give comonomers used in adhesives, polymers, and coatings, especially the new low solvent coatings, and for emulsion polymerization. The most widely used compound is 2-acetoacetoxyethyl methacrylate (AAEMA) (152).

Alkylacetoacetamides are often made by reaction of diketene and the corresponding alkylamines in aqueous solutions. They are traded mostly as aqueous solutions, which in the case of the *N*-monoalkyl derivatives have limited stability and require refrigeration for prolonged storage. The acetoacetamides produced from small-chain aliphatic amines are used in the manufacture of systemic insecticides such as monocrotophos (Azodrin) [6923-22-4] (153) and dicrotophos (Bidrin) [141-66-2] (153), phosphamidon (Dimecron) [13171-21-6] (154), and oxamyl (Vydate) [23135-22-0]. With the exception of oxamyl, these insecticides are no longer produced in the United States (see Insect control technology). *N*-Hydroxyethylacetoacetamide [24309-97-5] is used in the manufacture of the animal feed additive olaquindox [23696-28-8] (155) (see Feeds and feed additives). Lower aliphatic acetoacetamides are also used as copromoters in the curing of unsaturated polyesters and alkyd coatings (156).

The acetoacetarylides, are produced in a similar way from diketene and aromatic amines, either in water, butyl acetate [123-86-4] or water–organic solvent mixture. These derivatives are widely used in dyes and pigments. These applications involve the coupling of the acetoacetarylide with a diazonium salt (Japp-Klingemann reaction) to produce the corresponding diazo compound. CI Pigment Yellow 12 [6358-85-6], one of the largest volume pigments sold in the United States, is produced in this fashion by reaction of acetoacetanilide [102-01-2] (AAA) and the bis(diazo) salt of 3,3′-dichlorobenzidine. Other color pigments are produced from differently substituted arylides and differently substituted coupling components (see Azo dyes). AAA itself is also used in the manufacture of carboxin [5234-68-4], a widely used seed treatment (157).

5. Shipping and Storage

MAA and EAA are stable liquids, and are shipped in nonreturnable 208-L (55-gal) polyethylene-lined drums. For bulk shipments, insulated stainless steel tank containers and trucks provide secure protection. 2-Acetoacetoxyethyl methacrylate is a liquid stabilized with radical inhibitors such as BHT [128-37-0] and has a shelf life of approximately three months. Shipment is in 60- or 208-L polyethylene-lined drums. Acetoacetarylides are nicely crystalline, stable solids and are shipped in 208-L drums with polyethylene liners.

6. Economic Aspects

Total U.S. annual production of MAA and EAA combined is estimated to be 6000–7000 metric tons. The list prices at the end of 1992 for large volumes were \$2.75/kg for MAA and \$3.00/kg for EAA. There are only two U.S. producers of these esters at this time, Tennessee Eastman Co. in Kingsport, Tennessee, and Lonza Inc. in Bayport, Texas.

Total U.S. annual production of all arylides combined is estimated to be 12,000–13,000 metric tons. The largest volume arylide is AAA (acetoacetanilide) for Pigment Yellow 12 as well as for carboxin. The list price of AAA at the end of 1992 was \$3.40/kg.

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