Kirk-Othmer Encyclopedia of Chemical Technology.

ACETYL CHLORIDE

Acetyl chloride [75-36-5], C_2H_3OCl, mol wt 78.50, is a colorless, corrosive, irritating liquid that fumes in air. It has a stifling odor and reacts very rapidly with water, readily hydrolyzing to acetic acid and hydrochloric acid. As little as 0.5 ppm activate the flow of tears, and often provoke a burning sensation in the eyes, nose, and throat. Acetyl chloride is toxic. Its high reactivity with hydroxyl, sulfhydryl, and amine groups leads to modifications that block the action of many important enzymes needed by living tissue.

1. Physical and Chemical Properties

The common physical properties of acetyl chloride are given in Table 1. The vapor pressure has been measured (2,7), but the experimental difficulties are considerable. An equation has been worked out to represent the heat capacity (8), and the thermodynamic ideal gas properties have been conveniently organized (9).

The important chemical properties of acetyl chloride, CH_3COCl, were described in the 1850s (10). Acetyl chloride was prepared by distilling a mixture of anhydrous sodium acetate [127-09-3], $C_2H_3O_2Na$, and phosphorous oxychloride [10025-87-3], $POCl_3$, and used it to interact with acetic acid yielding acetic anhydride. Acetyl chloride's violent reaction with water has been used to model liquid-phase reactions.

$$CH_3COCl + H_2O \longrightarrow CH_3COOH + HCl$$

A fixed-bed reactor for this hydrolysis that uses feed-forward control has been described (11); the reaction, which is first order in both reactants, has also been studied kinetically (12–14). Hydrogen peroxide interacts with acetyl chloride to yield both peroxyacetic acid [79-21-0], $C_2H_4O_3$, and acetyl peroxide [110-22-5], $C_4H_6O_4$ (15). The latter is a very dangerous explosive.

Reactions of acetyl chloride that are formally analogous to hydrolysis occur with alcohols, mercaptans, and amines: primary or secondary compounds form corresponding acetates or amides; tertiary alcohols generally yield the tertiary alkyl chlorides. Acetyl chloride can split the ether linkages of many ordinary ethers and acetals. It equilibrates with fatty acids to provide measureable amounts of the mixed acetic–alkylcarboxylic anhydride or acyl chloride, either of which may be employed in esterifications. For example, lauric acid [143-07-7], $C_{12}H_{24}O_2$, and acetyl chloride undergo the reactions

$$CH_3\,(CH_2)_{10}\,COOH + CH_3COCl \longrightarrow CH_3\,(CH_2)_{10}\,COCl + CH_3COOH$$

$$CH_3\,(CH_2)_{10}\,COCl + CH_3\,(CH_2)_{10}\,COOH \longrightarrow (CH_3\,(CH_2)_{10}\,CO)_2\,O + HCl$$

Table 1. Physical Properties of Acetyl Chloride

Property	Value	Reference
freezing point, °C	−112.0	1
boiling point, °C at 101.3 kPa[a]	50.2	2
density, g/mL		3
4°C	1.1358	4
20°C	1.1051	3
25°C	1.0982	4
heat of formation, ΔH_f, kJ/mol[b]	−243.93	5
heat of vaporization at bp, ΔH_v, kJ/g[b]	0.36459	6
refractive index, n_D^{20}	1.38976	3

[a] To convert kPa to atm, divide by 101.3.
[b] To convert kJ to kcal, divide by 4.184.

Acetyl chloride reacts with aromatic hydrocarbons and olefins in suitably inert solvents, such as carbon disulfide or petroleum ether, to furnish ketones (16). These reactions are catalyzed by anhydrous aluminum chloride and by other inorganic chlorides (17). The order of catalytic activity increases in the order

$$ZnCl_2 < BiCl_3 < TeCl_4 < TiCl_4 < SnCl_4 < TeCl_2 < FeCl_3 < SbCl_5 < AlCl_3$$

Acetyl chloride is reduced by various organometallic compounds, eg, $LiAlH_4$ (18). *tert*-Butyl alcohol lessens the activity of $LiAlH_4$ to form lithium tri-*tert*-butoxyalumium hydride [17476-04-9], $C_{12}H_{28}AlO_3Li$, that can convert acetyl chloride to acetaldehyde [75-07-0] (19). Triphenyltin hydride also reduces acetyl chloride (20). Acetyl chloride in the presence of Pt(II) or Rh(I) complexes, can cleave tetrahydrofuran [109-99-9], C_4H_8O, to form chlorobutyl acetate [13398-04-4] in $\sim$ 72% yield (21). Although catalytic hydrogenation of acetyl chloride in the Rosenmund reaction is not very satisfactory, it is catalytically possible to reduce acetic anhydride to ethylidene diacetate [542-10-9] in the presence of acetyl chloride over palladium complexes (22). Rhodium trichloride, methyl iodide, and triphenylphosphine combine into a complex that is active in reducing acetyl chloride (23).

2. Manufacture

Acetyl chloride is manufactured commercially in Europe and the Far East. Some acetyl chloride is produced in the United States for captive applications such as acetylation of pharmaceuticals.

Acetyl chloride was formerly manufactured by the action of thionyl chloride [7719-09-7], Cl_2OS, on gray acetate of lime, but this route has been largely supplanted by the reaction of sodium acetate or acetic acid and phosphorus trichloride [7719-12-2] (24). A similar route apparently is still being used in the Soviet Union (25). Both pathways are inherently costly.

Patents on the carbonylation of methyl chloride [74-87-3] using carbon monoxide [630-08-0] in the presence of rhodium, palladium, and iridium complexes, iodo compounds, and phosphonium iodides or phosphine oxides have been obtained (26). In one example, the reaction was conducted for 35 min at 453 K and 8360 kPa (82.5 atm) to furnish a 56% conversion to acetyl chloride. Reactions of this kind are now possible because of improved corrosion-resistant alloys (27, 28). It is not known whether these methods are practiced industrially.

Other acetyl chloride preparations include the reaction of acetic acid and chlorinated ethylenes in the presence of ferric chloride [7705-08-0] (29); a combination of benzyl chloride [100-44-3] and acetic acid at 85%

yield (30); conversion of ethylidene dichloride, in 91% yield (31); and decomposition of ethyl acetate [141-78-6] by the action of phosgene [75-44-5], producing also ethyl chloride [75-00-3] (32). The expense of raw material and capital cost of plant probably make this last route prohibitive. Chlorination of acetic acid to monochloroacetic acid [79-11-8] also generates acetyl chloride as a by-product (33). Because acetyl chloride is costly to recover, it is usually recycled to be converted into monochloroacetic acid. A salvage method in which the mixture of HCl and acetyl chloride is scrubbed with H_2SO_4 to form acetyl sulfate has been patented (33).

A yield of acetyl chloride from the reaction between acetic anhydride and hydrogen chloride is increased by withdrawing acetyl chloride, optionally together with at least some of the acetic acid by-product from the reaction mixture as the reaction proceeds, has been reported in a U.S. Patent (34). The remainder of the reaction mixture is recycled to the reactor for additional reaction with HCl.

3. Shipping

Acetyl chloride must be shipped in polyethylene-lined drums having capacities of only 220 L; it must be labeled as a corrosive substance.

4. Economic Aspects

Little is known of the market for acetyl chloride. The production and sales are believed to be small, but may have potential for very large scale-up. The total U.S. market may amount to only 500 t annually.

Acetyl chloride generated captively from purchased raw materials probably has a unit value of no more than $0.92–0.95/kg. Shipping costs and other factors set the price at about $3/kg for the commercial trade.

5. Analysis and Quality Control

Acetyl chloride frequently contains 1–2% by weight of acetic acid or hydrochloric acid. Phosphorus or sulfur-containing acids may also be present in the commercial material. A simple test for purity involves addition of a few drops of Crystal Violet solution in $CHCl_3$. Pure acetyl chloride will retain the color for as long as 10 min, but hydrochloric, sulfuric, or acetic acid will cause the solution to become first green, then yellow (35).

6. Health and Safety

Acetyl chloride has stifling fumes and an irritating odor. It is highly poisonous. Because of acetyl chloride's combustibility and its high reactivity toward water and many alkalies, extreme caution must be exercised in handling. Provisions must be made for drawing the vapors away from people, and handlers should wear impervious, protective clothing. The large containers ought to be stored in cool, dry areas that are separate from noncorrosive, flammable chemicals.

7. Uses

A small amount of acetyl chloride is consumed in the start-up of acetic acid chlorination to monochloroacetic acid. After initiation, the acetyl chloride by-product provides sufficient catalysis. Acetyl chloride is a powerful acetylating agent. It is used in the manufacture of aspirin, acetaminophen, acetanilide, and acetophenone.

Liquid crystal compositions for optical display and memory devices frequently require acetyl chloride. Reactions that are difficult or lethargic using acetylation agents such as acetic anhydride or acetic acid become facile using acetyl chloride (36, 37). Polymers made by reactions involving acetyl chloride can chelate with metal ions, such as copper, and may be prepared with superior electrical and magnetic properties (38).

Anthralin [1143-38-0] is acetylated using acetyl chloride in toluene and a pyridine catalyst to furnish 1,8-dihydroxy-10-acetylanthrone [3022-61-5], an intermediate in the preparation of medications used in treating skin disorders, such as warts, psoriasis, and acne (39). Sugar esters can be similarly prepared from acetyl chloride under anhydrous conditions (40).

Although acetyl chloride is a convenient reagent for determination of hydroxyl groups, spectroscopic methods have largely replaced this application in organic chemical analysis. Acetyl chloride does form derivatives of phenols, uncomplicated by the presence of strong acid catalysts, however, and it finds some use in acetylating primary and secondary amines.

Acetyl chloride can be used as a substitute for acetic anhydride in many reactions. Whereas the anhydride requires a mineral acid catalyst for acetylation, acetyl chloride does not. Acetyl chloride is utilized in a wide range of reactions wherein its comparatively high price is offset by convenience. Should its nominal cost be lowered, acetyl chloride would be a powerful competitor for acetic anhydride in large scale manufacturing.

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