LACHRYMATORS

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Many chemical compounds possess more or less lachrymatory properties varying in intensity from mild irritation to severe, with a flow of tears so copious as to blind the victim temporarily. Some of these compounds, like chloropicrin, are also toxic. The lachrymatory property seems to be connected with the halogen group, and all lachrymators contain one of the halogens. In general, those compounds containing iodine have the strongest lachrymatory effect; bromine compounds are less powerful and chlorine compounds still less effective (304). The comparative rarity and expense of iodine makes the use of this element impractical. Most of the lachrymators used during the World War contained bromine and some, like bromobenzyl cyanide, were extremely effective. But bromine is quite expensive as compared with chlorine, and the development of the lachrymator chloroacetophenone, which is as effective as bromobenzyl cyanide, makes it appear probable that in the future no other lachrymatory gas will be manufactured. It is an interesting fact that even as early as 1887 Prof. Bayer, in his lectures to advanced students, included a reference to the military value of lachrymators (180). When tear gas is referred to by the general public, chloroacetophenone is usually meant.

The chemical agents introduced during the World War proved very effective, as shown by the reports of the War Departments of the countries involved and the increased number of gas shells fired during the latter part of the war. Despite these facts, there is still an unholy fear of such agents on the part of the average citizen, owing to the mass of war propaganda against the use of gas and the lack of accurate information concerning same. Men fear the unknown; it is easier for them to maintain morale in the face of bullets, naked bayonets, and the sword's edge than in the presence of invisible gas; likewise a mob has less fear of the fire hose, night clubs, and bullets than of gas. There is always the uncertainty in their minds as to the effects of the gas, and more especially if there be a little smoke mixed with it, for they know not what may be behind it. The only real danger of serious injury from using non-toxic tear gas is from the possibility that members of the crowd may be trampled upon in attempts to escape.

In this paper we have studied the several lachrymatory agents which have proved effective, paying particular attention to the methods of their preparation, their physical, chemical, and physiological properties, their peace time uses, etc.

BENZYL BROMIDE, 1-BROMOTOLUENE, 1-BROMOMETHYLBENZENE, $C_6H_5CH_2Br$

Benzyl bromide has been prepared by the saturation of benzyl alcohol with hydrobromic acid (161, 302), by the action of bromine on boiling toluene (25), and by dropping bromine on toluene in the sunlight (250). If the last reaction is carried out in the dark, it has been found that a rise in temperature increases the amount of benzyl bromide, that carriers (aluminum bromide, ferric bromide, and aluminum amalgam) favor the introduction into the benzene nucleus, and that red phosphorus favors introduction into the side chain. The action of sunlight or diffused daylight, even at 25°C., results in the formation of benzyl bromide quantitatively, but the addition of 0.5 g. of aluminum to 3 cc. of bromine causes all the bromine to enter the nucleus even in the sunlight (302). Upon treating toluene with carbon tetrabromide (155) the following reaction takes place:

$$C_6H_5CH_3 + CBr_4 \rightarrow C_6H_5CH_2Br + CHBr_3$$

Carbon tetrabromide brominates selectively the side chains of the benzene hydrocarbons instead of attacking the ring, exchanging a bromine atom for a hydrogen; bromoform is always the by-product of such bromination. Benzyl bromide is prepared by heating a mixture of benzyl benzamide with phosphorus pentabromide (49), according to the following reaction:

$$C_6H_5CH_2CONHC_6H_5 + PBr_5 \rightarrow C_6H_5CH_2Br + C_6H_5CN + POBr_3 + HBr$$

Holleman and Polak (150) treated toluene with bromine according to van der Laan's method (302) until all the bromine was used up; the influence of concentration and temperature on the relative amounts of benzyl bromide formed was determined as follows:

Moles of toluene : 1 mole of bromine		*Per cent of benzyl bromide formed*
At 25°C.	4.7	7.9
	8.0	10.6
	16.6	20.1
	25.5	36.5
At 50°C.	4.26	24.1
	8.0	42.3
	8.47	45.3
	10.47	56.2
	13.4	67.0
	20.6	82.5
	28.55	95.3

Ferric bromide, antimony bromide, or bromine do not transform benzyl bromide into bromotoluene, so the large amounts of this product obtained when the bromine concentration is large cannot be due to an autocatalysis of benzyl bromide formed as a primary product. The experiments of Cohen, Dawson, and Crosland (69), who electrolyzed concentrated hydrochloric acid under toluene, were repeated with hydrobromic acid, and it was found that, contrary to their statements, benzyl bromide was formed. This and theoretical considerations make improbable the theories of Bruner and Dluska (52) and of Bancroft (20) that bromination in the side chain is effected by bromine molecules and in the nucleus by bromine atoms. Holleman and Polak believe that free bromine molecules attack the methyl group, and that substitution in the nucleus is effected by hydrogen bromide aggregates. Hydrogen bromide decreases the volume of formation of benzyl bromide enormously. The Société Chimique des Usines du Rhône (269) received French patent 483,622 on July 26, 1917 for the preparation of benzyl bromide by the action of bromine on toluene in the presence of chlorates.

The experiments of LeBlanc and Andrich (178) on the photobromination of toluene showed the yield of benzyl bromide to be independent of the intensity of the light and constant throughout the entire portion of the spectrum investigated. The speed of the reaction decreases with decrease of wave length and is practically zero for wave lengths shorter than 300 $\mu\mu$. Experiments on bromine in carbon tetrachloride and hexane indicate that the increased reactivity of bromine in the light is not due to the splitting-off of electrons.

A later work by Andrich and LeBlanc (5) was conducted with special reference to the influence of light of varying wave lengths on the yield of benzyl bromide. The relative proportions of benzyl bromide and bromotoluene formed during the photobromination of toluene depend upon the oxygen content of the reaction mixture; the larger the quantity of oxygen the more benzyl bromide formed. The yield of the latter substance is constant between 579$\mu\mu$ and 325$\mu\mu$, and independent of small changes in bromine concentration and light intensity, but it decreases slightly with decrease in temperature. The yield of benzyl bromide was found to depend on the presence of oxygen in the reaction mixture, the yield increasing with the amount of oxygen. This had been traced to the oxidation of the hydrogen bromide, whereby bromine is regenerated. Comparative bromination experiments in the presence of hexane and ethyl acetate indicate that the free bromine molecules are photosensitive, whereas the solvated molecules are not. This relation affords an explanation of the fact that photosensitiveness of the reaction between bromine and toluene diminishes rapidly as the wave length of the incident radiation decreases. The rate

of photobromination of toluene decreases rapidly below 400$\mu\mu$; the reaction is not light sensitive from 300$\mu\mu$ to 202$\mu\mu$. The addition of water to the reaction mixture reduces the velocity considerably in the presence of pure oxygen, but the effect is small in the presence of air.

Benzyl bromide is a colorless liquid, with the following constants: b.p., 127°C. at 80 mm. (302), 197–198°C. (101), 198–199°C. (161), 199°C. at 749 mm. (19). Melting point, −3.9°C. (302). Density: 22°/0°, 1.4380 (161); 17°/17°, 1.4430; 64°/64°, 1.3886 (302). It exhibits very little conductivity in liquid sulfur dioxide (306).

The following reaction velocity measurements of benzyl bromide have been made: with pyridine at 30.5°C., 4.4 (19), at 55.6°C., 5.118 (63); with aniline at 30.5°C., 35 (269); with dimethylaniline at 30.5°C., 6.34; with methylacetanilide at 30.5°C., 0.134; with dimethyl-*o*-toluidine at

TABLE 1

Refractivity and spectral dispersion of benzyl bromide at 20°C.

BENZYL BROMIDE	n_D^t	BENZYL BROMIDE	C/D	D/F	F/G
per cent		*per cent*			
00.0000	1.52505	00.0000	502	1207	1017
18.8772	1.53165	18.8772	511	1245	1085
23.3439	1.53347	23.3439	519	1250	1094
33.0428	1.53669	33.0428	512	1274	1087
48.0849	1.54197	48.0849	513	1301	1117
65.3828	1.54820	65.3828	530	1319	1136
73.9944	1.55130	73.9944	538	1329	1143
78.9757	1.55295	78.9757	532	1348	1150
100.0000	1.56042	100.0000	552	1366	1180

30.5°C., 0.235; with *p*-bromodimethylaniline at 30.5°C., 1.93; with acetylpiperidine at 30.5°., 0.136 (291); with sodium sulfite at 40°C., 5.86; at 30°C., 18.6 (274). For the reaction of pyridine and triethylamine, respectively, with benzyl bromide in various solvents (205) the following results have been obtained: at 29°C., in ethyl alcohol, 17.0, 39.0; in nitrobenzene, 32.3, 171.0; in benzene, 0.73, 3.70; at 45°C., in ethyl alcohol, 56.7, 127.5; in nitrobenzene, 65.5, 369.3; in benzene, 2.26, 9.20.

The capillary constant of benzyl bromide at 110°C. is 4.54 sq. mm.; at 156°C., 3.81 sq. mm. (84).

Morguleva (203) determined the refractivity and spectral dispersion of benzyl bromide at 20°C., as shown in table 1.

Alekseevskii and Alekseev (2) found benzyl bromide to be not very destructive on smooth metallic surfaces at room temperature in either dry or humid atmospheres, since the metals gradually acquire passivity.

Benzyl bromide is destroyed very slowly by water (103); the presence of small quantities of water accelerates the velocity of the reaction with organic hydroxyl groups; at 65°C. the presence of 0.44 mole of water per liter increases the velocity of the reaction 1.16 times, while the presence of 5.96 moles increases it over 2.5 times the value in absolute alcohol (131). Shoesmith and Rubli (261) carried out the hydrolysis of benzyl bromide in dilute alcohol at 25°C. and determined the value of K as 125. Benzyl bromide in water at 60°C. hydrolyzes as follows (262): at the end of 30 minutes, 22 per cent; 60 minutes, 37 per cent; 120 minutes, 59 per cent; 180 minutes, 71 per cent.

The copper–zinc couple acts vigorously on benzyl bromide with evolution of hydrogen bromide and formation of two isomers of benzylene (119), the ether-soluble modification known as α-benzylene and the ether-insoluble one as β-benzylene. In the presence of anhydrous ether the reaction is very vigorous; no hydrogen bromide is formed but instead dibenzyl, $C_6H_5CH_2CH_2C_6H_5$, as shown in the following equation:

$$3C_6H_5CH_2Br + 2Zn\text{–}Cu \rightarrow C_6H_5CH_2CH_2C_6H_5 + ZnBr_2 + C_6H_5CH_2ZnBr + 2Cu$$

Alcoholic ammonia reacts with benzyl bromide even in the cold to form tribenzylamine, $(C_6H_5CH_2)_3N$ (161).

By oxidation of benzyl bromide with nitric acid (density, 1.52), Flürscheim and Holmes (101) prepared, besides benzoic acid, tribromoaniline and tribromoaminobenzoic acid.

When chlorine is passed into boiling benzyl bromide in direct sunlight p-bromobenzyl bromide, $BrC_6H_4CHBr_2$, is obtained (92, 273).

Upon boiling benzyl bromide with dilute alcohol for two hours the respective ethers are formed (47): with methyl alcohol, benzyl methyl ether, $C_6H_5CH_2OCH_3$ b.p. 174°C.; with ethyl alcohol, benzyl ethyl ether, $C_6H_5CH_2OC_2H_5$, b.p. 189°C.; with allyl alcohol, benzyl allyl ether, $C_6H_5CH_2OC_3H_5$, a liquid with a pleasant ethereal odor, b.p. 204–205°C.

When benzyl bromide is treated with bromoform there is formed benzal bromide or benzotribromide, depending on the ratio of materials used (155).

Dufraisse and Bongrand (83) defined the threshold of concentration as the lowest concentration which the organs can detect during an exposure of 30 seconds, and took benzyl bromide as the standard with a value of unity.

Bertrand and Rosenblatt (29), experimenting upon the larvae of *Bombix neustria*, *Polychrosis botrana*, and *Eudemis botrana*, found that benzyl bromide should be placed between carbon disulfide and chloroacetone in its toxicity.

Bellay and Houdard (26), experimenting on the absorptive powers of moist garden soil, garden soil dried at 100°C., moist river sand, gravelly

sand, and vegetable humus, found that the absorptive power, which was very slight for sand, increased with the quality of vegetable humus. The action is chemical and exothermic, the soil showing a sharp change of color and an elevation of temperature, sensible to the touch. Moisture facilitates the fixation of the gas; but humus dried at 100°C. still retains 67 per cent of its absorptive power.

Bishopp, Roark, Parman, and Laake (33) found that all the species of flies under their observation were strongly repelled by benzyl bromide.

BROMOACETONE, BROMOPROPANONE, $CH_2BrCOCH_3$

Bromoacetone has only been prepared by the action of bromine, or a compound of the halide, on acetone. Several modified methods have been introduced but they differ only in details: by steam distilling the oily product formed by allowing bromine and acetone to stand with 10 volumes of water (270); by conducting 1.38 parts of bromine into 1 part of well-cooled acetone by means of a current of air (50, 89, 214); by introducing 1 part of bromine into 4 parts of acetone in which 1 part of marble is suspended and gradually pouring into the mixture 2.5 parts of water at 28–31°C. (248); by treating a mixture of 1 part of acetone, 1 part of glacial acetic acid, and 4 parts of water with 2.76 parts of bromine under a reflux at 70°C. (209). Lapworth (175) prepared bromoacetone by the action of bromine on acetone in the presence of various acids and bases. It has also been prepared as follows: by the action of bromine on a mixture of acetone and dilute hydrochloric acid (154); by the electrolysis of a mixture of hydrobromic acid and acetone at 35–40°C. (239); by allowing a dilute methyl alcohol solution of chloroacetone and potassium bromide to stand for several days (248); by the action of phosphorus pentabromide in petroleum ether on acetone in the cold (96); by the action of bromine and sodium bromate on a water solution of acetone in the presence of sulfuric acid (60); by the action of bromine on a dilute acetic acid solution of acetone (184).

Bromoacetone is a colorless liquid; b.p., 23.5–24.5°C. at 3.5 mm. (60), 31.4°C. at 8 mm. (248), 38–46°C. at 13 mm. (184, 209), 39.5°C. at 18 mm. (154), 40–42°C. at 13 mm. (184, 209), 48–53°C. at 25–6 mm. (50), 72–77°C. at 40 mm. (264), 136°C. (284), 136.5°C. at 725 mm. (248), 136.5°C. (7). It freezes to a colorless solid at −54°C. (7, 284). Density: 23°/23°, 1.6340 (209). It is slightly soluble in water, and easily soluble in alcohol and acetone and other organic solvents (89). It has a penetrating odor; its vapor is quickly irritating to the eyes. Bromoacetone quickly becomes violet colored in the presence of light and air (50, 89). Its vapor pressure is 1 mm. at 10°C. and 9 mm. at 20°C. (284). One cubic meter of air at 10°C. becomes saturated with 75 g. of bromoacetone in the vapor form (7).

Lapworth (175) suggests that the characteristic replacement by halogens of the α-hydrogen atom in carbonyl compounds might involve a preliminary change of the compound to its enolic form

$$CH_2{:}O \rightarrow CH{-}OH$$

The suggestion was based on his discovery that bromine reacts with acetone in dilute aqueous solution (to give monobromoacetone) at a rate which is proportional to the concentration of the ketone, but independent of that of the halogen; the reaction, moreover, is accelerated to a very marked extent by mineral acids (174, 176, 199). These observations led Lapworth to suggest that a slow change to the enolic form is followed by a very rapid reaction of the latter with bromine.

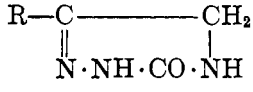
$$CH_3COCH_3 \xrightarrow{(slow)} CH_2{:}C(OH)CH_3 \xrightarrow{Br\ (rapid)} CH_2BrCOCH_3 + HBr$$

According to Sokolowsky (271) the reaction of bromoacetone with 1 mole of bromine leads to *as*-dibromoacetone, but Hughes, Watson, and Yates (154) found the mechanism of bromination of bromoacetone to be similar to that established for acetone; in water and in the absence of a catalyst bromoacetone reacts with bromine more quickly than does acetone. The autocatalytic influence of the hydrogen bromide is vastly different in the two cases: the bromination of acetone is accelerated very markedly as halogen acid accumulates in the system, but there is no appreciable autocatalysis in the case of bromoacetone. Among other products of the bromination of bromoacetone are to be found *s*-dibromoacetone, m.p. 24.1°C., b.p. 57–58°C. at 4 mm., and *as*-dibromoacetone, b.p. 38–40°C. at 7 mm.

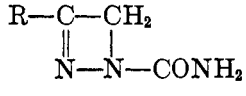
By the action of silver oxide or the alkaline carbonates on bromoacetone, an alcohol of acetone is produced, namely, acetol (acetyl carbinol), CH_3COCH_2OH (89). By the action of freshly precipitated silver oxide in the presence of water, bromoacetone is converted into a liquid having a sweet taste, which appeared (88) to be an alcohol of pyruvic acid; owing to its decomposition upon dehydration it could not be obtained pure. Using the oxide of mercury on bromoacetone and treating the products of the reaction with sodium amalgam, Linnemann (188) was able to obtain only acetic acid. Acetylcarbinyl acetate was prepared (51, 226) by adding bromoacetone to a warm solution of anhydrous potassium acetate in alcohol. Sokolowsky (270) obtained a crystalline compound with sodium hydrogen sulfite, and a crystalline, but unstable, compound with dry ammonia. Aqueous ammonia converts bromoacetone into basic compounds. The addition product with α-picoline melts at 196°C. (185). The cyanohydrin boils at 94.5–95.5°C. at 5.5 mm. (60). The action of monobromoacetone on ammonium sulfocyanide in an alcoholic solution forms sul-

focyanide of sulfocyanpropimine, $CH_2SCN \cdot CNH \cdot HSCN \cdot CH_3$ (214). Linnemann (185) formed the unstable addition product with bromine at 0°C., $C_3H_6O \cdot Br_2$, along with epibromohydrin and acrolein.

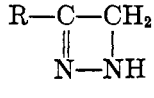
The semicarbazone of bromoacetone is easily prepared by stirring an aqueous solution of semicarbazide hydrochloride, the ketone, and sodium bicarbonate together; it melts at 135°C. It is very unstable and is decomposed by boiling water or alcohol with the formation of halogen-free compounds. Such a reaction may give rise to the formation of: (1) the six-membered ring



(2) the four-membered ring



which may pass into



by splitting off the $CONH_2$ group; (3) $(N:CRCH_2Br)_2$, together with $(NHCONH_2)_2$; (4) $HOCH_2C(:NNH_2)CH_3$ (153).

The diethyl acetal of bromoacetone, α-bromo-β,β-diethoxypropane, a liquid with a camphor-like odor, density 0°/0°, 1.1075, was prepared by Evlampiev (93) by distilling the product resulting from the action of bromoacetone and ethyl formate in a sulfuric acid solution of ethyl alcohol.

In the presence of metals, acids, or even light, bromoacetone liberates hydrogen bromide and resinifies (284), the product being a dark mass, melting above 350°C., not reacting with phenylhydrazine or hydroxylamine but dissolving in fuming nitric acid; on dilution of this solution with water, a yellow infusible product separates which is not hydrolyzed when boiled with 50 per cent potassium hydroxide (118).

Dow (81) on April 4, 1922 received U. S. patent 1,411,422 for a lachrymatory gas composed of 40 parts of bromoacetone, 10 parts of alcohol, 10 parts of tetrachloroethylene, and 40 parts of carbon tetrachloride.

Knoll (166) found bromoacetone to be an excellent irritant with hydrocyanic acid in fumigation, but it was difficult to remove from gassed compartments.

It is impossible to remain in an atmosphere containing 30 mg. of bromoacetone per cubic meter; upon inhalation of 32 mg. per minute death ensues

(284). The most practical method of purifying a confined space containing bromoacetone is to neutralize by spraying with an aqueous solution of sodium polysulfide and soap lye (79).

Guérin and Lormand (129) exposed several species of house plants to bromoacetone for periods of 30, 60, and 120 minutes. Most of the plants exposed for from 60 to 120 minutes in an atmosphere of 1 to 2000 parts by weight of the gas survived the toxic action. The plants lost their leaves, in consequence of plasmolysis or protoplasmic contraction (128), but new leaves grew and the plants resumed their normal vegetation.

The lachrymatory value of bromoacetone, compared with benzyl bromide taken as a standard with a value of unity, is 1.8 (83).

BROMOBENZYL CYANIDE, PHENYLBROMOACETONITRILE, α-BROMO-α-TOLUNITRILE, $C_6H_5CHBrCN$

Bromobenzyl cyanide was first prepared by Reiner (238) as the principal product from the action of bromine on benzyl cyanide at 120–130°C. Cyanogen bromide reacts with an alcoholic solution of benzyl cyanide in the presence of sodium ethoxide to form bromobenzyl cyanide (45):

$$C_6H_5CH_2CN + BrCN + NaOC_2H_5 \rightarrow C_6H_5CHBrCN + NaBr + C_2H_5OH$$

Steinkopf, Mieg, and Herold (281) prepared bromobenzyl cyanide by the action of bromine vapor on phenylacetonitrile at 105°C. illuminated with a 1000-candle power Ostram-Azo lamp; Nekrasov (210) prepared it by the bromination of benzyl cyanide.

Phenylbromoacetonitrile is a yellow oil, boiling at 130°C. at 12 mm. (7), 132–134°C. at 12 mm. (281), 137–139°C. at 15 mm. (210), 231.7°C. (200), 232°C. (7). It solidifies to yellow crystals melting at 25.4°C. (210), 29°C. (7, 210, 284). Its density is 1.54 (7, 200). It is very stable, and does not appreciably decompose in air and in the presence of water at ordinary temperatures (284). It cannot be distilled even in high vacuum; it has a low vapor pressure and is thus highly persistent. It is about as toxic as chlorine, but is many times more effective as a lachrymator than any of the halogenated ketones, excepting chloroacetophenone, or aromatic halides studied. An atmosphere containing as little as 0.3 mg. per cubic meter is uninhabitable (201, 284), and 60 mg. inhaled per minute leads to death (284). It has a pleasant odor and produces a burning sensation on the mucous membrane. One cubic meter of air at 20°C. becomes saturated with 0.75 g. of bromobenzyl cyanide in the vapor form (7).

Bromobenzyl cyanide is easily converted into stilbene dicyanide by the action of an alcoholic solution of potassium cyanide; if an excess of potassium cyanide is used the product contains some dibenzylene dicyanide and a mixture of the stereoisomeric forms (57). It is converted into potassium

stilbenedicarboxylate by alcoholic potassium hydroxide and if the reaction takes place in the cold then stilbenedicarbonimide is obtained (238).

BROMOETHYL METHYL KETONE, 3-BROMOBUTANONE-2, METHYL α-BROMOETHYL KETONE, $CH_3CHBrCOCH_3$

With phosphorus pentabromide or bromine all ketones having hydrogen in the α-position give α-monobromoketones, as in $CH_3CHBrCOCH_3$. The formation of the latter is supposed to be preceded by enolization caused by the halogen used or arising from the dissociation of the pentahalide. Further bromination of the bromine compound introduces another bromine at the same carbon atom as the first, giving unsymmetrical dibromo derivatives as in $CH_3CBr_2COC(CH_3)_3$. With ethyl acetate, phosphorus pentabromide yields the bromide, $CH_3CHBrCOCH_3$, a liquid of a caustic odor, and reducing Fehling's solution in the cold. It boils at 35–38°C. at 12 mm.;

TABLE 2

The comparative value of the various lachrymators

LACHRYMATOR	QUANTITY NECESSARY TO PRODUCE LACHRYMATION (108)
	mg. per liter
Bromobenzyl cyanide	0.0003
Chloroacetophenone	0.0003
Ethyl iodoacetate	0.0014
Bromoacetone	0.0015
Xylyl bromide	0.0018
Benzyl bromide	0.0040
Chloroacetone	0.0180
Chloropicrin	0.0190

its density, 20°/20°, is 1.4380. It is converted by barium carbonate into $CH_3CHOHCOCH_3$. With 1 mole of bromine, ethyl acetate yields $CH_3CHBrCOCH_3$, while with an excess of bromine α,α-dibromoethyl methyl ketone is produced (95).

The product of the action of 1 mole of bromine or of sulfuryl bromide on ethyl methyl ketone consists of more than 67 per cent of the secondary bromo derivative, $CH_3CHBrCOCH_3$, b.p. 134–135°C. (143), 133–134°C. (303), and of nearly 33 per cent of bromomethyl ethyl ketone, $CH_2BrCOC_2H_5$, b.p. 144–145°C. (143), 145–146°C. (303). Both are nearly colorless, tear-exciting liquids which become colored in the light.

On December 15, 1926 Schering and Kahlbaum received British patent 282, 412 for the preparation of bromoethyl methyl ketone from ethylene and acetyl bromide in the presence of aluminum chloride; it boils at 55–60°C. at 15 mm. (246).

CHLOROACETONE, ACETYLMETHYL CHLORIDE, CH_3COCH_2Cl

Riche (240, 241) first prepared monochloroacetone by electrolyzing a mixture of hydrochloric acid and acetone; this same method has been subsequently employed by Bischoff (30), Szper (286), and Richard (239). The passage of chlorine into well-cooled, dry acetone is far a more popular method for its preparation. The following have employed this means: Glutz and Fischer (121), Kriwasin (173), Mulder (206), Barbaglia (21), Bischoff (31), Cloëz (68), and Fritsch (109, 110). Kling (162, 162a) and Mulder (206) prepared monochloroacetone by the action of hypochlorous acid on acetone. Tcherniac (287) prepared it by distilling thiocyanoacetone with water in a vacuum; Linnemann (187) by distillation of monobromo(chloro)propylene with mercuric oxide and hypochlorous acid; Markownikow (193) by the action of chromic acid on chloroisopropyl alcohol; Morley and Green (204) by the oxidation of propylene chlorohydrin with chromic or nitric acid; Henry (141) by distilling a concentrated sulfuric acid solution of chloropropylene; Béhal and Detouef (24) by allowing chlorocarbamide to act on the calculated amount of an aliphatic ketone in aqueous solution.

Chloroacetone is a colorless, heavy liquid; it is slightly soluble in water but dissolves in all proportions in alcohol, ether, and chloroform. It does not form a crystalline hydrate; it volatilizes readily in water vapor. When freshly prepared it has no irritating odor, but after exposure to the air for some days it gives off irritating vapors. It is neutral to helianthin and monobasic towards phenolphthalein and Poirrier's blue (13). It is colored carmine by potassium hydroxide (206). Its boiling point is given as 117°C. (240), 117–118°C. (68), 118–120°C. (109, 110, 141, 187), 118–121°C. (30), 119°C. (21), 119°C. at 735 mm. (186), 119.7°C. (179), 120–125°C. (172). Values given for its specific gravity are 1.158 at 13°C. (68), 1.154 at 15°C. (110), 1.18 at 16°C. (187), 1.162 at 16°C. (186). Density at 17.5°/15° is 1.164 (80).

The velocity coefficient for the reaction of pyridine and chloroacetone at 55.6°C. was determined as 0.0686 (63). The dielectric constant at 19.1°C. is 29.75 (λ = 60 cm.) (80). The value for the electric moment obtained in units of 10^{18} E.S.U. is 2.17 (314). If the magnetic susceptibility, $S^M = -K \times 10^{-7}$, the value for K was determined experimentally by Pascal (221, 222, 223) as 530 as compared with 531.5, the calculated value. The absorption spectrum of the vapor of chloroacetone at various temperatures and pressures in a 200-mm. tube is described by Purvis and McCleland (234) in table 3. The vapor thus shows one very strong band, which becomes wider and stronger as the temperature and pressure increase. $N/10$ alcoholic solution showed a very large band (see figure 1).

When chloroacetophenone is conducted through a tube heated to 450°C. it forms a mixture of acetaldehyde, acetone, and crotonaldehyde (214). When it is acted upon by nitric acid (density, 1.48), oxalic acid and chloromethylnitrolic acid, $CCl(NO_2):NOH$, are formed (231).

Fritsch (110) found that when acetone is chlorinated in the usual way, the first product obtained has the boiling point ascribed to monochloroacetone, but contains about 4 per cent less of chlorine than is required for this substance, the deficiency being probably due to the presence of mesityl oxide, $(CH_3)_2C:CHCOCH_3$, formed by the action of the accumu-

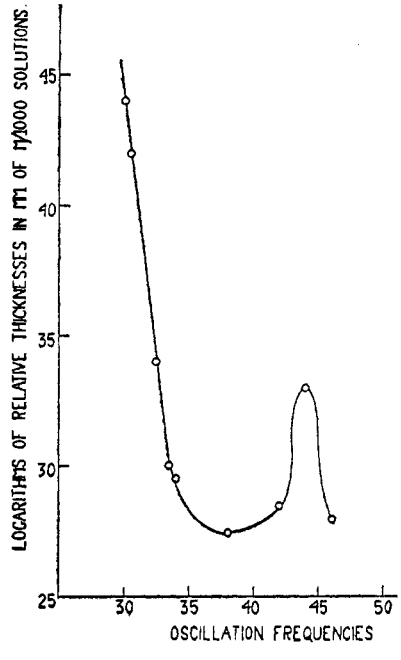


FIG. 1

lated hydrochloric acid on the excess of acetone; this conclusion is in agreement with that of Tcherniac (287). This impurity may be avoided and pure monochloroacetone formed by introducing marble into the chlorinating flask. Further chlorination of acetone, carried out in the same manner in diffused daylight, gave a product consisting of monochloroacetone mixed with both *as*-dichloroacetone, $CH_3COCHCl_2$, and *s*-dichloroacetone, $CH_2ClCOCH_2Cl$. The latter, which has not been recognized previously among the products of the direct chlorination of acetone (21, 192), is found in the fraction which boils at 167–172°C., and is formed to the extent of about 10 per cent of the whole. When monochloroacetone is treated with

chlorine at 100°C. in sunlight as long as the gas is absorbed, the principal product is pentachloroacetone, $CHCl_2COCCl_3$ (109).

Bromine has very little effect on chloroacetone in the cold, but at 100°C. energetic reaction takes place with the formation of chlorotribromoacetone (68). The velocity of the autocatalyzed bromination of chloroacetone reaches its minimum value when the concentration of hydrobromic acid formed is 0.002 *M* (134).

Monochloroacetone is reduced by hydrochloric acid and zinc to acetone (187).

Monochloroacetone reacts with a concentrated solution of potassium cyanide (215) to form β-methyl-β-hydroxy-γ-cyano-γ-acetobutyronitrile,

$$CH_3COCH(CN)-C(CH_3)(OH)CH_2CN$$

TABLE 3

Absorption spectrum of vapor of chloroacetone

TEMPERATURE	PRESSURE	RESULTS
°C.	*mm.*	
19	762	The rays were transmitted to λ2150
30	806	The rays were transmitted to λ2155
45	832	The rays were transmitted to λ2160
60	862	The rays were transmitted to λ2180, but they were weak between λ3080–λ2750
75	891	The rays were absorbed between λ3100–λ2750 and then transmitted to λ2270
90	922	The rays were absorbed between λ3180–λ2580 and then weakly transmitted to λ2340

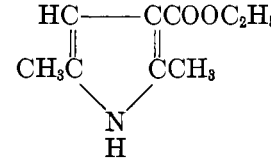
An energetic reaction sets in when chloroacetone is poured into an aqueous solution of potassium cyanide. There is formed a complicated condensation product, crystallizing from alcohol, in which it is readily soluble, in small needles, and melting at 176°C.; it has the composition, $C_{10}H_{13}N_3O$. It is tasteless and odorless, and only moderately soluble in hot water and ether. It is doubtless identical with the "cyanaceton" described by Glutz (120), but its chemical behavior indicates a high molecular weight; it cannot be readily decomposed into acetone or acetic acid and carbon dioxide, and when treated with acids and alkalies yields a complex compound, melting at 65°C. When potassium cyanide is treated with chloroacetone in alcoholic solution a dark oil, boiling above 120°C., is obtained in very small quantities, together with considerable quantities of non-volatile substances. By heating chloroacetone with a strong hydrocyanic acid–alcohol solution for twenty-four hours and evaporating the liquid, the

compound, α-hydroxy-α-chloromethylpropionitrile, $CH_3C(CH_2Cl)(OH)CN$, is left behind as a thin, oily liquid, which, when heated with hydrochloric acid yields α-hydroxy-α-chloromethylpropionic acid, $CH_3C(CH_2Cl)(OH)COOH$ (30).

Acetylcarbinol, CH_3COCH_2OH, is best prepared by boiling chloroacetone with anhydrous potassium or sodium formate in methyl alcohol under a reflux (209). Acetylcarbinol acetate, $CH_3COOCH_2COCH_3$, a limpid liquid having a refreshing smell and bitter taste, is prepared by treating chloroacetone with potassium acetate (51, 142, 162, 226).

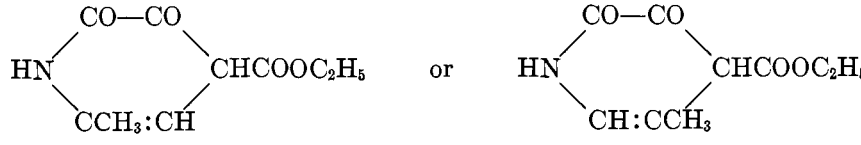
By passing dry ammonia into monochloroacetone, aminoacetone, $CH_3COCH_2NH_2$, is prepared (114).

Hantzsch (135) prepared ethyl 2,5-dimethylpyrrole-3-carboxylate,



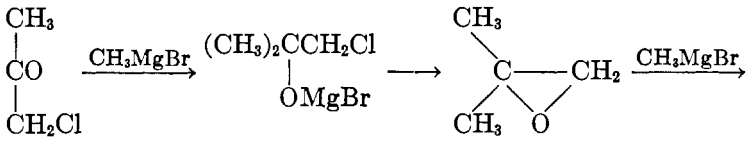
m.p. 116.7°C., by adding concentrated ammonia to a mixture of chloroacetone and ethyl acetoacetate. Feist (99), on condensation of ethyl acetoacetate with chloroacetone and ammonia, obtained, in addition to ethyl 2,5-dimethylpyrrole-3-carboxylate, ethyl 2,4-dimethylfurfurane-3-carboxylate, which is an oil, b.p. 97°C. at 10 mm. Korschun (168) prepared methyl 2,5-dimethylpyrrole-3-carboxylate from methyl acetoacetate, chloroacetone, and dilute ammonia in the manner employed by Hantzsch for the preparation of the ethyl ester. It crystallizes from dilute alcohol, melts at 119.5°C., and boils at 170° at 15 mm. The reaction was explained by Hantzsch as being due to the intermediate formation of ethyl β-aminocrotonate. It is not possible to prepare the ester directly from ethyl β-aminocrotonate and chloroacetone, and the reaction is better explained by Korschun by the formation of an ester of diacetopropionic acid, which then condenses with ammonia to form the pyrrole derivative.

When ammonia is passed into an ethereal solution of ethyl oxalate and chloroacetone, condensation ensues with the formation of oxamide and ethyl oxymethylpyridonecarboxylate (99):



Methylmagnesium bromide in ethereal solution reacts with chloroacetone giving the compound, $CH_2ClC(CH_3)_2OMgBr$, which, on heating in ethereal

solution, forms magnesium chlorobromide and isobutylene oxide; the latter, when again treated with the organomagnesium halide, forms methylisopropylcarbinol (146):



$(CH_3)_2CHCHOHCH_3$

Fourneau and Tiffeneau (104) obtained the chlorohydrin of methylethylglycol, $C_2H_5C(CH_3)OHCH_2Cl$, b.p. 152–153°C., density 1.068 at 0°C., and the alcohol, $(C_2H_5)(CH_3)CHCHOHC_2H_5$, b.p. 149–151°C., density 0.8518 at 0°C., as the result of the action of methylmagnesium bromide on chloroacetone.

By the interaction of chloroacetone and dimagnesiumdibromoacetylene, there is obtained the product, $CH_3C(CH_2Cl)(OH)C{\equiv}CC(OH)(CH_2Cl)CH_3$, an oil (density: 0°/4°, 1.277; 20°/4°, 1.257); it does not distil at 6 mm. and does not crystallize (313).

When phenylmagnesium bromide in ether reacts on chloroacetone, the reaction mixture being kept cold, there is formed methylchlorostyrolene, $C_6H_5(CH_3)C{:}CHCl$, diphenyl, $C_6H_5C_6H_5$, methylstilbene, $C_6H_5C(CH_3){:}CHC_6H_5$, and the alcohol, $C_6H_5CH(CH_3)CHOHC_6H_5$ (296). After the organomagnesium halide is allowed to react on chloroacetone, the reaction mixture is cooled to room temperature and the complex magnesium compound heated to 130–140°C.; upon decomposing the resulting product with dilute sulfuric acid phenylacetone, $C_6H_5CH_2COCH_3$, is formed (294, 297).

The action of chloroacetone on phenylmagnesium bromide yields the chlorohydrin $HOC(C_6H_5)(CH_3)CH_2Cl$; on methylmagnesium iodide the chlorohydrin, $HOC(CH_3)_2CH_2Cl$; on ethylmagnesium bromide the chlorohydrin, $HOC(CH_3)(C_2H_5)CH_2Cl$ (293). These results are regarded as supporting Krassusky's (171) conclusion that when hypochlorous acid combines with ethylenic hydrocarbons the hydroxyl group always attaches itself to the carbon atom combined with the smallest number of hydrogen atoms.

Hexamethylenetetramine forms with chloroacetone a crystalline additive product, which is obtained as lustrous needles melting at 122°C. (191).

By the action of trimethylamine on monochloroacetone, trimethylacetonylammonium chloride, $CH_3COCH_2N(CH_3)_3Cl$, is produced as a crystalline, very deliquescent mass (111, 213, 247).

Dimethylaminoacetone, $N(CH_3)_2CH_2COCH_3$, is prepared by adding

chloroacetone to an aqueous 30 per cent solution of dimethylamine. It is a colorless oil, miscible with water, alcohol, and ether in all proportions, and becomes brown on exposure to air; it boils at 123°C. (282).

Upon heating chloroacetone, ethyl orthoformate, alcohol, and a drop or two of concentrated sulfuric acid there is formed monochloroacetone ethylacetal, $ClCH_2C(CH_3)(OC_2H_5)_2$ (a colorless liquid with a pleasant odor, b.p. 162–163°C., b.p. 57°C. at 12 mm., density 14°/0°, 1.0002 (8)), and α-chloro-β,β-diethoxypropane, b.p. 52–53°C. at 14 mm. (93).

Scholl and Matthaiopoulos (248) prepared chloroacetoxime, $CH_2ClC(CH_3):NOH$, by treating chloroacetone with less than the theoretical amount of hydroxylamine hydrochloride and sodium carbonate; the substance boils at 71.2°C. at 9 mm., 84.5°C. at 21 mm., 98°C. at 45 mm., 171°C. at 727 mm. Methylglyoxime (acetoximic acid) $CH(:NOH)—C(:NOH)CH_3$, m.p. 156°C. is also formed at the same time, but it is the only product if about three times the theoretical amount of hydroxylamine is used (136).

By stirring a mixture of chloroacetone and a solution of sodium thiocyanate, Tcherniac (288) obtained thiocyanoacetate, CH_3COCH_2SCN. This was first obtained by the action of chloroacetone on barium thiocyanate in alcoholic solution (139), but later it was found that the reaction takes place in the absence of alcohol when the crystalline barium salt is intimately mixed with the ketone. Tcherniac and Norton (289, 290) found that when ammonium thiocyanate acts on chloroacetone in alcohol solution, thiocyanoacetone is formed, but that it reacts with the excess of the ammonium salt to produce the thiocyanate of a new base which they named thiocyanopropimine. These changes may be expressed thus:

$$CH_3COCH_2Cl \xrightarrow{NH_4SCN} CH_3COCH_2SCN \xrightarrow{NH_4SCN} (SCNCH_2C(:NH)(CH_3)HSCN$$

When chloroacetone and phenylhydrazine, both dissolved in absolute alcohol, were mixed and allowed to stand in a freezing mixture, a yellow crystalline mass separated which melted at 162.5°C. and which proved to be the phenylhydrazone of phenylhydrazinoacetate, $NHC_6H_5NHCH_2C(CH_3):NNHC_6H_5$ (27, 35).

In the presence of metals, acids, or even light, monochloroacetone resinifies, the product being a dark mass, melting above 350°C., which liberates hydrogen chloride in air. It does not react with phenylhydrazine, hydroxylamine, or oleum. It dissolves in fuming nitric acid, and on dilution with water a yellow infusible product separates. Boiling with 50 per cent potassium hydroxide does not hydrolyze the product (118).

1,2,2-Tri(hydroxyphenyl)propane, $CH_3C(C_6H_4OH)_2CH_2C_6H_4OH$ is prepared by heating chloroacetone with 3 moles of phenol and fuming hy-

drochloric acid. It decomposes at 175°C. 1,2,2-Tri(dihydroxyphenyl)-propane, $CH_3C[C_6H_3(OH)_2]_2CH_2[C_6H_4(OH)_2]$, prepared in a similar manner from resorcinol, gives a colorless or faintly red colored substance, m.p. 180°C. (189).

Lecat (179), using 71.5 per cent toluene (b.p., 110.75°C.) and chloroacetone (b.p., 119.7°C.), formed an azetope boiling at 109.2°C.

Slator and Twiss (267) found chloroacetone to react rapidly with sodium thiosulfate, the velocity constant being 0.134 at 15°C. and 0.375 at 25°C.

Chloroacetone and diazomethane react to form chloroisobutylene oxide,

$$CH_2C(CH_3)CH_2Cl$$
$$\diagdown\diagup$$
$$O$$

b.p. 124°C., and a mixture of higher oxides (10).

Chloroacetone 4-*m*-nitrophenylsemicarbazone, $CH_2ClC(CH_3)C{=}NNHCONHC_6H_4NO_2$, prepared by mixing chloroacetone with *m*-nitrophenylsemicarbazide hydrochloride, forms pale yellow needles melting to a semi-solid at 223°C. and to a dark brown liquid at 238°C. (309).

Chloroacetone semicarbazone, m.p. about 150°C., is prepared by stirring aqueous semicarbazide hydrochloride, chloroacetone, and sodium bicarbonate together (153).

The *p*-bromophenyl-4-semicarbazone of chloroacetone is prepared by heating an alcoholic solution of the semicarbazide with an excess of the ketone; upon cooling beautiful crystals separate, which decompose upon melting at 182°C. (308).

Monochloroacetone is not as easily reduced as the dichloroacetone, since it tends to inhibit fermentation, yet a 25 per cent yield of monochloroisopropyl alcohol, $CH_3CH(OH)CH_2Cl$, is obtained when an alcoholic solution of monochloroacetone is added over a period of several hours to a mixture of pressed beer yeast and starch or cane sugar dissolved in water and allowed to stand for some hours at 35°C. (257).

An aqueous solution of benzenediazonium chloride at 0°C. in the presence of sodium acetate gives with chloroacetone a reddish yellow precipitate, probably the azo derivative, $CH_3COCHClN{:}NC_6H_5$, which is rapidly transformed into the phenylhydrazone of pyruvyl chloride, $CH_3COCCl{:}NNHC_6H_5$, melting at 136–137°C. (97).

When monochloroacetone reacts with a solution of mercuric sulfate and mercuric oxide, the following reaction takes place:

$$2HgSO_4 + 3HgO + CH_3COCH_2Cl \longrightarrow \begin{matrix} Hg{-}O{-}HgO \\ SO_4 \\ \rangle Hg \\ SO_4 \\ Hg{-}O{-}HgO \end{matrix} \begin{matrix} \diagdown \\ \diagup \\ C \\ \diagdown \\ \diagup \end{matrix} \begin{matrix} CH_2Cl \\ \\ \\ \\ CH_3 \end{matrix}$$

The resulting product is an insoluble solid which dissolves in hydrochloric acid and decomposes explosively when heated to about 133°C. (78).

Sodium ethylate and chloroacetone react very rapidly (138), so much

$$CH_3COCH_2Cl + NaOC_2H_5 \rightarrow CH_3COCH_2OC_2H_5 + NaCl$$

so that the equilibrium constant has not been determined, but when equivalent quantities of sodium ethylate and chloroacetone of concentration 0.05 N were used at 0°C. the course of the reaction could be followed graphically from the following data:

TIME	CLEAVAGE	1000 K
minutes	*per cent*	
1	31.4	965
2	40.9	705
6	52.4	379
15	60.7	184

This is further illustrated in figure 2.

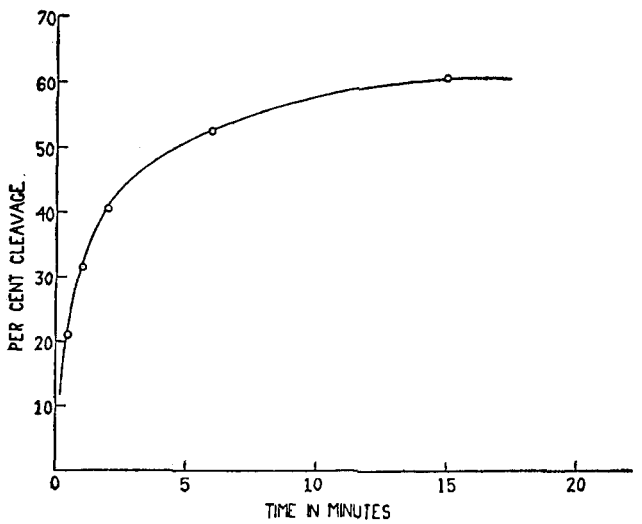


FIG. 2

The condensation of chloroacetone with 2,4-dinitrophenylhydrazine first gives chloroacetone 2,4-dinitrophenylhydrazone, $(NO_2)_2C_6H_3NHN{:}C(CH_3)CH_2Cl$, yellow needles, m.p. 124–125.5°C. Prolonged boiling in alcoholic solution converts it into the corresponding osazone, $(NO_2)_2C_6H_3NHN{:}CHC(CH_3){:}NNHC_6H_3(NO_2)_2$, dark red crystals, m.p. 298°C. (53).

Two cases have been reported where small colorless bottles containing monochloroacetone have exploded. The contents had polymerized to a black rubber-like substance without lachrymatory properties and smelling strongly of hydrogen chloride but free from chlorine (3, 94).

Dufraisse and Bongrand (83) compared the activity of chloroacetone with that of benzyl bromide by determining the concentration in atmospheres necessary to produce the same lachrymogenic effect. The power of the substance studied will be inversely as its concentration thus determined. The "concentration de seuil" of chloroacetone was determined as 0.125. Bertrand (28), commenting on the work of Dufraisse and Bongrand, shows that the minimum concentration of a lachrymatory substance which is perceptible depends not only on the observer, but also on the duration of the exposure. Thus chloropicrin acts suddenly, and but slowly increases its intensity on prolonged contact; monochloroacetone acts with progressively increasing intensity. The different actions of these agents is ascribed to their varying solubility in the aqueous liquids of the eye. Thus the method of Dufraisse and Bongrand does not give a correct comparison between different lachrymatory substances.

Bertrand and Rosenblatt (29) performed experiments on the larvae of *Bombix neustria*, *Polychrosis botrana*, and *Eudemis botrana*. The insects were subjected to the action of measured amounts of air and poisonous vapor from several chemicals; chloroacetone was found to be much more effective than ether, chloroform, carbon disulfide, or carbon tetrachloride.

CHLOROACETOPHENONE, PHENACYL CHLORIDE, BENZOYLCARBINOL CHLORIDE, $C_6H_5COCH_2Cl$

Chloroacetophenone was first prepared by Graebe (124) in 1871 by passing a stream of chlorine into boiling acetophenone; since that time Staedel (276), Dyckerhoff (86), Gautier (117), and Korner and Scholl (169) have prepared the chlorinated acetophenone in a similar manner. By dissolving chloroacetyl chloride in benzene and adding aluminum chloride, Friedel and Crafts (106) and Tutin (300) prepared chloroacetophenone. It is also prepared by the oxidation of diphenacyltelluride dichloride with potassium permanganate (243); by the action of monochlorourea on an aqueous solution of acetophenone (24); by treating an ethereal solution of aromatic acyl chlorides with diazomethane (67, 280); by the electrolysis of hydrochloric acid in an aqueous solution of acetophenone and acetic acid at 5.6–6.5 volts and 0.6 ampere per square decimeter (286).

Chloroacetophenone crystallizes from dilute alcohol in rhombic plates (107) whose axial ratios ($a:b:c$), were determined by Aminoff (4) as 0.9957:1:0.4270 and by Staedel (276) as 0.9957:1:0.2135. Its melting point has been given as 41°C. (124), 55–59°C. (284), 56°C. (18, 106),

58.5°C. (7), 58–59°C. (67, 243, 276), 59°C. (300); its boiling point as 113°C. at 18 mm. (16), 139–141°C. at 14 mm. (67), 241–242°C. (106), 244–245°C. (276), 244.5°C. (7), 245°C. (284), 246°C. (124). Density: 15°/4°, 1.3240 (4, 117); 16.6°/4°, 1.2016; 20°/4°, 1.198 (16). It is practically insoluble in water (about 1 g. per liter at room temperature) (284), but is easily soluble in alcohol, ether, and benzene. It has an agreeable aromatic odor but its vapor acts very strongly on the eyes (117, 124, 276). Its vapor pressure is 0.0028 at 0°C. (284, 304). One cubic meter of air at 0°C. is saturated with 30 mg. and at 20°C. with 105 mg. of chloroacetophenone (7).

The following reaction velocity measurements of chloroacetophenone have been made: with sodium thiosulfate in dilute alcohol at 15°C., 0.65 (267); with pyridine in absolute alcohol at 55.6°C., 0.1339 (63); with pyridine in 90 per cent alcohol at 30.5°C., 0.11 (18); with 1 mole of acetone solution of potassium iodide with 5 moles of the chloroacetophenone at 0°C. is 22.4 (72). With equimolecular quantities of chloroacetophenone and aniline in absolute alcohol at 40°C. it was found that no reaction occurred, but with 2 moles of the chloroacetophenone and 5 moles of the aniline the reaction was rapid, the value of $k \times 10$ being 0.67 (194).

Exposed to light, chloroacetophenone rapidly turns green. Upon oxidation it yields benzoic acid entirely free of chlorine, which proves conclusively that the chlorine is contained in the methyl group. It is unchanged by boiling water, but on heating with water in sealed tubes hydrogen chloride is formed and also a solid of very high boiling point (124).

If, during the preparation of chloroacetophenone, more chlorine is passed into the vapor of acetophenone than is necessary for taking up 1 atom of chlorine, the product obtained is essentially different from the ordinary one. On fractional distillation a liquid passes over at 250–255°C., which consists chiefly of the dichloride. By the continued action of chlorine, a dark, thick mass is obtained, which, on distillation, yields a small quantity of a liquid which consists chiefly of benzoyl chloride. That portion with highest boiling point contains products poorer in chlorine. Analysis gave numbers pointing to the formula $C_{16}H_{11}O_2Cl$. Possibly this substance was formed in a similar way to the chlorides obtained by Staedel (275) by the removal of 1 mole of hydrogen chloride from 2 moles of chloroacetophenone. At a temperature above 360°C. a substance passed over which solidified in amorphous masses on cooling, and emitted a smell of oil of bitter almonds. The occurrence of benzoic acid was also noted. The formation of benzoyl chloride and benzoic acid may be explained in two ways: (1) It may be supposed that chlorine was gradually substituted for the hydrogen atoms of the methyl group, and finally split off, the $—CCl_3$ residue taking its place, and forming benzoyl chloride. Carbon tetrachloride must have been formed at the same time, though it could not be

detected. In the preparation of chloroacetophenone, water is always formed, and it may possibly convert the benzoyl chloride partly into benzoic acid. (2) The water formed from the acetophenone may, in the presence of the chlorine, exercise an oxidizing influence, so that from a small part of the acetophenone benzaldehyde may be first formed, which may then be partly converted, by further oxidation, into benzoic acid, while another part passes, under the influence of the chlorine, into benzoyl chloride (86).

When an ethereal solution of chloroacetophenone is treated with ammonia two isomeric substances, α- and β-chlorodiphenacyl, are formed; one is readily soluble in alcohol and ether and crystallizes in needles melting at 117°C., while the other is much less soluble and forms prisms melting at 154–155°C. (277, 279). Chlorodiphenacyls were also prepared by the action of sodium ethoxide on chloroacetophenone in absolute alcohol (220). It was later found (219) that the mother liquor after the crystallization of α- and β-chlorodiphenacyls contained a small quantity of a compound, $C_{16}H_{13}O_2C$, which crystallized from alcohol in white needles melting at 189°C., and which is an isomer of the chlorodiphenacyls but yields no diphenacyl on reduction.

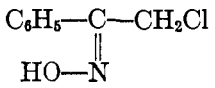
When chloroacetophenone is heated for 1.5 hours at 100°C. in a sealed tube with an excess of alcoholic ammonia, there is obtained a dark bluish green substance which, after purification, crystallizes from xylene in large, colorless plates, melting at 194°C.; it is identified as 2,5-diphenylpyrazine. The original alcoholic filtrate, after further treatment, is found to contain colorless needles, melting at about 189°C. and identified as 2,6-diphenylpyrazine monochloride, which yields 2,6-diphenylpyrazine, colorless needles, melting at 90°C. (300). When chloroacetophenone is heated with dilute ammonia in excess of air 2,5-diphenylpyrazine is formed (276, 278).

Ammonia and chloroacetophenone readily act on each other, even in the cold, more quickly on heating, and yield several products: one of them, with the composition C_8H_7N, crystallizes from hot benzene or glacial acetic acid in glistening, serrated plates, melting at 194–195°C. and subliming in pearly plates; another substance was probably identical with Graebe's (125) benzoylcarbinol, $C_6H_5COCH_2OH$ (278).

The view which has been several times put forward that α-halogen ketones containing the grouping —CO—CHCl are converted by hydroxylamine directly into glyoximes without the formation of intermediate products was shown by Scholl and Mathaiopoulos (248) to be erroneous in the case of aliphatic compounds, while under suitable conditions they yield α-halogen ketoximes. Korten and Scholl (169) find that analogous compounds can be obtained in the aromatic series if the hydroxylamine be made to act in the presence of a mineral acid. In this way, chloroaceto-

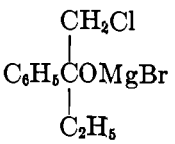
phenone yields aromatic α-halogen ketoximes which are readily crystallizable compounds belonging to the *syn*-phenyl series. When the hydroxylamine is employed in alkaline solution, the glyoxime obtained is accompanied by a small proportion of the *anti*-phenyl ketoxime. The halogen of these α-halogen ketoximes readily reacts with alkalies and ammonia, in the latter case yielding tertiary amines which, under the action of alcoholic hydrochloric acid, are partially deöximated and transformed into paroxazine derivatives.

Syn-phenyl chloromethyl ketoxime,



obtained by the interaction of chloroacetophenone (1 mole) and hydroxylamine hydrochloride (3 moles) in dilute methyl alcohol at ordinary temperature, separates from carbon disulfide in crystals melting at 88.5–89°C. Its vapors are very painful to the eyes; when placed on the skin in either the solid or the dissolved state it produces a very persistent burning sensation (169).

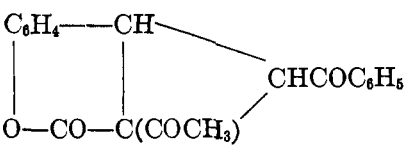
Chloroacetophenone yields on action of ethylmagnesium bromide in ether a complex magnesium compound,



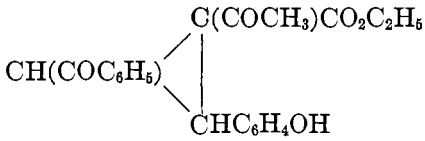
which, upon heating, changes to ethyl benzyl ketone, $C_6H_5CH_2COC_2H_5$, b.p. 221–223°C. Its semicarbazone melts at 146°C. (297).

Upon boiling molecular quantities of chloroacetophenone and potassium sulfocyanide under a reflux for a short time, an ether is obtained which crystallizes from alcohol, ether, and chloroform in long needles having the composition expressed by the formula, $C_6H_5COCH_2SCN$; it melts at 72–73°C. (85).

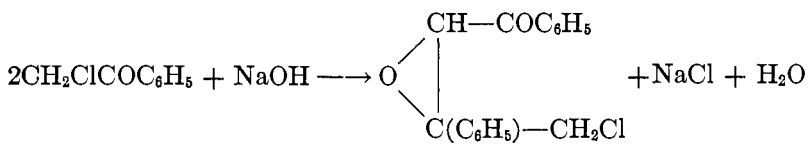
When 3-acetylcoumarin and chloroacetophenone are mixed in cold alcohol and treated with sodium ethylate solution, two products are obtained, the chief one being 3-acetyl-3,4-phenacylidenecoumarin,



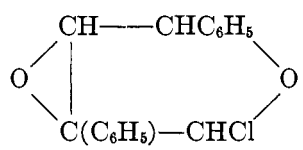
which crystallizes in silky needles, m.p. 184°C.; the other compound, which is the more soluble in alcohol, is ethyl α-acetyl-α,β-phenacylidene-coumarate,



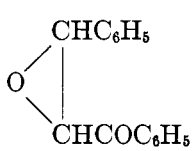
which crystallizes in brilliant quadratic prisms, m.p. 117°C. The condensation must proceed rapidly, as chloroacetophenone gives rise to 2-chloro-3,4-oxido-3,5-diphenyltetrahydrofurane when left with sodium alkyl oxides alone (311). The course of the reaction whereby chloroacetophenone and alcoholic sodium ethoxide yield oxidotetrahydrofurane is, in its first stage, probably analogous to those described by Darzen (75) and by Claisen (62), in which ketones or aldehydes condense with esters of halogenated fatty acids in the presence of sodium ethoxide or of sodamide to form esters of substituted glycidic acids:



The intermediate product then does not yield a four-membered ring by loss of hydrogen chloride, but is converted into a furane derivative



The two suppositions in this explanation are supported by experimental evidence. With regard to the formation of the oxido groups Widman and Almström (312) find that chloroacetophenone and benzaldehyde in the presence of alcoholic sodium ethoxide, in accordance with Darzen's statement that esters of halogenated fatty acids condense preferentially with aldehydes rather than with ketones, yield not a trace of a furane derivative, but a substance (m.p. 89–90°C.) which proves to be α-benzoyl-β-phenyl-ethylene oxide



The second supposition that a ketone containing a halogen atom in the γ-position to the carbonyl group is capable of yielding a furane derivative, is supported by the behavior of a substance described by Perkin (225) as phenyl bromopropyl ketone, $C_6H_5COCH_2CH_2CH_2Br$. This substance, however, does not exhibit the properties of a ketone, and is most probably 2-bromo-5-phenyltetrahydrofurane.

Upon distilling a mixture of chloroacetophenone and phosphorus pentachloride at 225–231°C., α,β-dichlorostyrol, $C_6H_5CCl{:}CHCl$, a colorless, oily liquid, boiling at 221°C. and possessing a pleasant odor, is formed (85).

By saturating a cold glacial acetic acid solution of chloroacetophenone and *m*-nitrobenzaldehyde with hydrogen chloride and allowing to stand for twenty-four hours, then condensing *in vacuo*, there is obtained phenyl α,β-dichloro-β-(*m*-nitrophenyl)ethyl ketone, $C_6H_5COCHClCHClC_6H_4NO_2$, colorless needles melting at 148°C. (34).

Chloroacetophenone and hexamethylenetetramine form a salt-like additive product melting at 145°C. On treatment for three days with hydrochloric acid and alcohol it gives the hydrochloride of aminoacetophenone, m.p. 196–197°C. (191).

Knöpfer (165) prepared the chloroacetophenone semicarbazone, $C_9H_{10}ON_3Cl$, in the form of white crystals melting at 137°C.

When a mixture of benzaldehyde and chloroacetophenone in cold alcohol is treated with sodium ethoxide, benzoylphenyloxidoethane,

$$C_6H_5COCHCHC_6H_5$$
$$\quad\quad\llcorner O \lrcorner$$

is formed, plates, m.p. 89–90°C. (310).

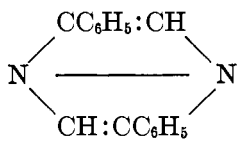
The reaction between chloroacetophenone and phenylhydrazines may take the following course (152): (1) with the formation of a hydrazone; (2) with the formation of compounds of the type

$$C_6H_5C(:NNHC_6H_5)CH_2NHNHC_6H_5$$

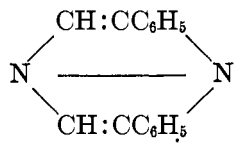
(3) with the formation of compounds of the type

$$\begin{array}{l} \quad\quad N{=}CC_6H_5 \\ \quad\quad\quad | \quad\quad | \\ C_6H_5N{-}CH_2 \end{array}$$

(4) the reaction may take a course similar to the reaction between chloroacetophenone and ammonia, giving 2,5- and 2,6-diphenylpyrazines (112, 113, 278, 300)



and



By the action of an alcoholic solution of potassium acetate, chloroacetophenone is converted into the acetate of acetylbenzene alcohol, $C_6H_5COCH_2OCOCH_3$ which melts at 44°C. and boils at 270°C. On cooling, or by crystallization from alcohol, it is obtained in large rhombic plates, insoluble in water, easily soluble in alcohol and ether; it has a pleasant aromatic odor. The alcohol may be obtained directly from chloroacetophenone by heating with a solution of sodium carbonate or with plumbic hydrate and water, and from the acetate with alcoholic potash solution; in both cases, however, it is mixed with considerable quantities of by-products. In the impure state in which it has hitherto been obtained, it forms a pleasant-smelling body insoluble in water (124).

When chloroacetophenone is heated with benzene and aluminum chloride to 100°C. there is no reaction, but when it is heated with toluene and aluminum chloride to 111°C. (the boiling point of toluene) there is produced methyldeoxybenzoin, $C_6H_5COCH_2C_6H_4CH_3$, small crystals, m.p. 84–85°C. (70).

Chloroacetophenone does not react with sodium bisulfite (117).

Dean and Berchet (76) found that chloroacetophenone reacts with sodium and anhydrous ammonia in the ratio of 1 mole of halide to 2.2 moles of sodium. A reddish oil was obtained which was nitrogen- and halogen-free. There was also separated 0.4 g. of a colorless solid, m.p. 73–74°C., which was unidentified.

Chloroacetophenone is a most effective substance to be used as a warning agent for inflammable and poisonous gases: 0.021 and 0.0083 part per million is all that is required for nasal and eye irritation (159). Hanslian (133) found that lachrymation begins with 0.5 mg. per cubic meter, nasal irritation starts at 1 mg. per cubic meter, irritation of the skin about the face and throat (especially in mouth breathing) occurs at about 2 mg. per cubic meter. It is unbearable to remain in an atmosphere of 5 mg. per cubic meter for more than a few seconds at a time and a concentration of 100 mg. per cubic meter causes burns. Hanzlik and Tarr (137) found chloroacetophenone to be a mild skin irritant as indicated by simple hyperemia without vesication, mild urticarial rash, moderate swelling and edema, and very little or no necrosis.

For the quantitative determination of chloroacetophenone, Chrzasczewska and Chwalinski (59) suggest the use of sodium sulfide.

On December 15, 1925, U. S. patent 1,565,899 was issued to Bradner for a cartridge for the effective dissemination of chloroacetophenone (43) and on September 21, 1926, U. S. patent 1,600,223 was issued to Goss for a cartridge for disseminating chloroacetophenone (122); U. S. patent 16,841 for a means of volatilizing chloroacetophenone (44) was reissued January 3, 1928.

The use of a mixture of chloroacetophenone and hydrocyanic acid in ship fumigation brought out the fact that chloroacetophenone remained long after the hydrocyanic acid and that the two gases tended to form pockets rather than a uniform mixture (6).

Chloroacetophenone has been found to be an effective larvicide for the screwworm and all species of flies under observation (33).

ETHYL BROMOACETATE, $CH_2BrCOOC_2H_5$

Ethyl bromoacetate was first prepared by Perkin and Duppa (228, 229) by heating bromoacetic acid and alcohol in a sealed tube for an hour at 100°C.; from bromoacetic acid anhydride and alcohol (116); by the action of monobromoacetyl bromide and alcohol (207); by heating red phosphorus and bromine with glacial acetic acid on the water bath for six hours and pouring the product into excess alcohol (15); by treating bromoacetyl-chloride in alcohol with red phosphorus (115); from the action of phosphorus pentabromide on ethyl glycolate (140); by the action of bromine on sodium ethylate (256); by the action of cyanogen bromide on diethylamino-acetonitrile (46); by passing gaseous hydrogen bromide into a chloroform solution of ethyl diazoacetate (73). Slimmer (268) upon heating dibromo-phenoxyethylene for seven hours at 110°C. with alcoholic potash obtained ethyl bromoacetate and not phenoxybromoacetylene as stated by Sabaneeff and Dworkowitsch (244). Imbert (156) on October 4, 1906 received German patent 212,592 for the preparation of ethyl bromoacetate from dibromovinyl ether and alcohol, in the absence of water, but in the presence of catalyzers such as aluminum chloride at the ordinary temperature, heating being required in the presence of water. Henry (144, 145) obtained the ester after the method described by DeMole (77), who treated the monoacetin of ethylene glycol with hydrobromic acid.

Ethyl bromoacetate is a not unpleasant smelling, colorless, very mobile liquid of sweetish-caustic taste, which violently attacks the mucous membrane, particularly the eyes. Its boiling point has been given as 122–125°C. at 738 mm. (301), 159°C. (11, 15, 115, 228, 305), 159–160°C. (140, 245), 161–163°C. (77), 162–163°C. (144, 145), 168.7°C. (corrected) (227). It solidifies in freezing mixture of carbon dioxide and ether to colorless needles, melting at −13.8°C. (144, 145). Density: 4°/4°, 1.5282; 10°/10°, 1.5192; 15°/15°, 1.5123; 20°/20°, 1.5059; 25°/25°, 1.5002. Refractive index determinations: density 13°/4°, 1.51414, η 13°/α, 1.45160; η 13°/D, 1.45420; η 13°/γ, 1.46631. The magnetic rotation twice determined (72 readings) gave: t, 16.6°C.; specific rotation, 1.2386; molecular rotation, 7.609 (227). If the magnetic susceptibility, $S^M = -K \times 10^{-7}$, the value of K as determined experimentally by Pascal (222) is 864 and the specific susceptibility, $x_s = -0.496$. Slator (266) and Slator and on Twiss (267) de-

termined the velocity of reaction of ethyl bromoacetate and sodium thiosulfate at 15°C. as 2.36, and at 25°C. as 6.4. Backer and von Mels (17) determined the value of K of ethyl bromoacetate with potassium sulfite at 25°C. in 40 per cent ethyl alcohol as 18.3. Clarke (63) determined the velocity of reaction of ethyl bromoacetate with pyridine at 55°C. as 1.004. Drushel and Hill (82) determined the rate of hydrolysis of ethyl bromoacetate in 0.5 N hydrobromic acid at 25°C. as 23.8. The activity of ethyl bromoacetate by the velocity coefficient of the reaction with silver nitrate at 49.9°C. is $K \times 10^4 = 0.208$ (258).

Clarke (64) derived the values in table 4 when amines were added to an absolute alcoholic solution of ethyl bromoacetate at 0°C.:

$$NR(CH_3)_2 + CH_2BrCO_2C_2H_5 \rightarrow BrNR(CH_3)_2CH_2CO_2C_2H_5$$

Aronstein (11) heated ethyl bromoacetate with ethyl bromide; the principal products were ethylene, hydrobromic acid, and bromoacetic acid.

TABLE 4

Reaction velocity constants

BASE	VALUES OF 10^4k WHEN n IS					
	2	3	4	5	6	7
$C_2H_5(CH_2)_nN(CH_3)_2$	11.4	10.7	10.3	11.2	10.9	
$(CH_3)_2CH(CH_2)_nN(CH_3)_2$	9.7	9.9	10.6	10.6		
$(CH_3)_2N(CH_2)_n(CH_3)_2$	9.5	16.8	24.9	20.8	24.5	27.5
$CH_3O(CH_2)_nN(CH_3)_2$	6.7	9.3	10.6	10.5	11.5	

The ethyl bromide was decomposed into ethylene and hydrobromic acid and this latter acted on the ethyl bromoacetate as follows:

$$HBr + CH_2BrCO_2C_2H_5 \rightarrow C_2H_5Br + CH_2BrCOOH$$

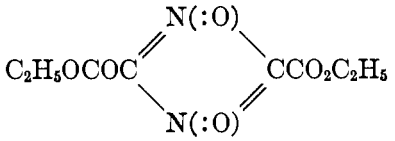
Upon distilling in a vacuum the product resulting from the action of sodium on hot ethyl bromoacetate there results the triethylester of aconitic acid (23).

By means of magnesium iodide in ethereal solution, ethyl bromoacetate is converted into ethyl iodoacetate, $CH_2ICO_2C_2H_5$ (40, 41).

Upon heating an alcoholic solution of ethyl bromoacetate with potassium fluoride in a glass vessel there is formed potassium bromide, silicon tetrafluoride, and glycolic ester (285).

From the interaction of ethyl bromoacetate and silver nitrate the following are obtained: ethyl glycolate, $CH_2(OH)CO_2C_2H_5$; ethyl ethoxyacetate; ethyl glycolate nitrate, $C_2H_5OCOCH_2ONO_2$; ethyl glycolate

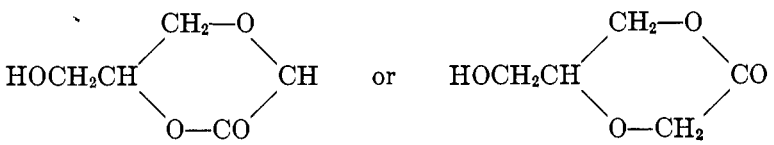
nitrite, $C_2H_5OCOCH_2ONO$; diethyloxalate; ethyloxynitriloformate, $C_2H_5OCOC{\equiv}N{=}O$, crystallizing from hot benzene in colorless needles, melting at 111–111.5°C. and probably formed by the loss of one molecule of water from ethyldioxynitroacetate; ethyldioxydicyanogendicarboxylate a polymeride of the preceding compound, regarded as having the constitution



boiling at 158° (corrected) under 11 mm. and at 233–234°C. at 760 mm. and reduced by tin and hydrochloric acid to aminoacetic acid; and a compound, $C_{12}H_{15}O_8N$, an oil boiling at 188–189°C. at 11 mm., giving an amide by the action of strong ammonia, and regarded as having the constitution $C_3O_2N(CO_2C_2H_5)_3$ (249).

Ethyl bromoacetate reacts with dimethyl sulfide to form the ethyl ester of dimethylthetinbromide, $(CH_3)_2SBrCH_2CO_2C_2H_5$ (181).

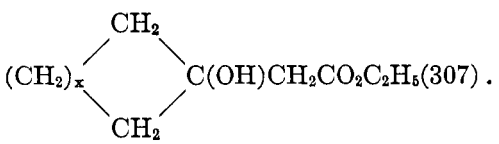
Glyceroloxyacetolacetone,



is obtained from monosodium glycerol and ethyl bromoacetate; it is a viscid yellow oil, boiling at 170–175°C. at 5 mm. (32).

Ethyl bromoacetate, when treated with zinc and methylheptenone, yields the ethyl ester of oxydihydrogeranic acid, $(CH_3)_2C{:}CH(CH_2)_2C(OH)$-$CH_3CH_2CO_2C_2H_5$ (292).

When a cyclic ketone is condensed with ethyl bromoacetate and zinc, an hydroxy ester of the following type results:



Ethyl β-hydroxy-β,β-diphenylpropionate, $HOC(C_6H_5)_2CH_2CO_2C_2H_5$, is readily obtained by the action of dilute acid on the product formed by the condensation of benzophenone, ethyl bromoacetate, and zinc in the presence of benzene. It crystallizes from dilute alcohol in glistening prisms,

m.p. 87°C. Ethyl β-methylcinnamate, $C_6H_5C(CH_3):CHCO_2C_2H_5$, is formed directly from acetophenone, ethyl bromoacetate, and zinc (242).

Ethyl diacetoacetate, $(CH_3CO)_2CHCO_2C_2H_5$, is produced by the interaction of finely divided zinc, acetic anhydride, and ethyl bromoacetate in the presence of ether; ethyldipropionyl acetate, $(C_2H_5CO)_2CHCO_2C_2H_5$, is produced in a similar manner by the use of propionic anhydride; ethyldibutyrylacetate, $(C_2H_5CH_2CO)_2CHCO_2C_2H_5$, from butyric anhydride (190).

The reaction between ethyl bromoacetate and magnesium in ethereal solution leads to the formation of ethyl acetoacetate and of ethyl γ-bromoacetoacetate (283).

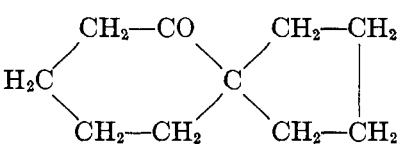
When attempts were made to prepare monobromoacethydroxamic or monoiodoacethydroxamic acids by the action of free hydroxylamine upon ethyl bromoacetate or ethyl iodoacetate unexpected complications arose, owing to the fact that hydroxylamine reacted with the halogen so readily that immediately after mixing the alcoholic solutions of ester and amine, crystalline precipitates formed which were found to be basic hydroxylammonium salts, $NH_2(OH)_2 \cdot HBr$ and $NH_2(OH)_2 \cdot HI$. Various other products, including small amounts of the desired hydroxamic acids, accompanied these salts, among them a crystalline compound, which contained no halogen. It melted at 65°C. and possessed the empirical formula, $C_8H_{15}O_5N$; it is probably a β,β-disubstituted hydroxylamine of the formula $HON:(CH_2COC_2H_5)_2$ (158).

The action of zinc and ethyl bromoacetate on ethyl orthoformate produces a product which, on saponification, results in β-ethoxyacrylic acid, $C_2H_5OCH:CHCOOH$ (299), which crystallizes in colorless prisms, m.p. 110.5°C., and is identical with Otto's ethoxyacrylic acid (218).

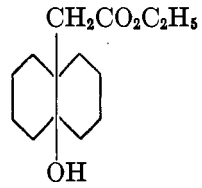
When hydrogen and ethyl bromoacetate are conducted over nickel heated to 250–300°C., there is formed principally ethyl acetate but also hydrogen bromide and a little acetaldehyde (245).

By the action of hydrazine hydrate on ethyl bromoacetate, nitrogen is evolved and the whole of the halogen is obtained in an ionic condition (74).

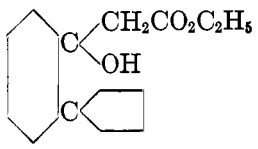
When ethyl bromoacetate is heated with cyclohexene oxide and zinc in benzene for six hours, ethyl 2-hydroxycyclohexylacetate is formed; it boils at 114°C. at 13 mm. The oxide of $\Delta^{9,10}$-octalin, ethyl bromoacetate, and zinc heated for six to seven hours in benzene gives 2-ketocyclohexanespirocyclopentane,



boiling at 95°C. at 14 mm., and the ester,

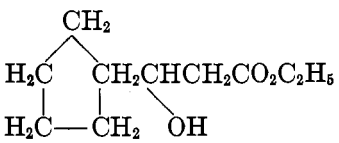


a viscous liquid with a peculiar sweetish smell, boiling at 125°C. at 0.1 mm. When 2-ketocyclohexanespirocyclopentane, ethyl bromoacetate, and zinc are heated in benzene for five hours the compound,

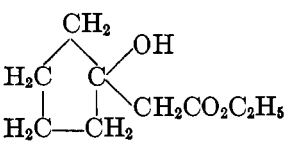


is formed; b.p. 135°C. at 0.25 mm. (65).

When cyclopentane aldehyde, ethyl bromoacetate, and zinc wool are heated in anhydrous benzene on a water bath for three hours the ester, ethyl β-hydroxy-β-cyclopentylpropionate, b.p. 117°C. at 14 mm., is formed



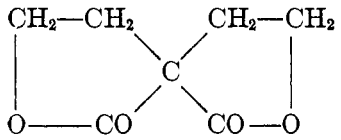
When cyclopentene oxide, ethyl bromoacetate, and zinc wool in dry benzene were heated on a water bath for three hours, a sweet-smelling ester, b.p. 108°C. at 18 mm. resulted, which gave a hydrazide, crystallizing in shining platelets from ethyl acetate, and melting at 143°C. Cyclopentanone, ethyl bromoacetate, and zinc wool in dry benzene when heated on a water bath gave ethyl cyclopentan-1-ol-1-acetate,



boiling at 108°C. at 18 mm.; with hydrazine hydrate, it gave a hydrazine, m.p. 143°C., identical with that obtained above (66).

When sodium ethylate in absolute alcohol at a temperature of 40°C. is treated with ethyl malonate and ethyl bromoacetate, sodium bromide pre-

cipitates and on concentrating the supernatant liquid there is obtained bis-γ-butyrolacetone-α,α-aspiran, in hexagonal plates, melting at 109–110°C. (183).



On heating ethyl bromoacetate to 150°C. for eight hours with mercury diethyl, there is formed ethylmercuric bromide, ethyl acetate, and ethylene (254, 255).

Ethyl bromoacetate has proved an excellent larvicide for screw-worms (33).

When zinc is allowed to react on a *p*-tolyl methyl ketone solution of ethyl bromoacetate the very unstable ethyl β-methyl-*p*-tolylethylenelactate, $C_6H_4(CH_3)C(CH_3)(OH)CH_2CO_2C_2H_5$ is obtained (195).

ETHYL IODOACETATE, $CH_2ICO_2C_2H_5$

Perkin and Duppa (230) first prepared ethyl iodoacetate by treating an alcoholic solution of ethyl bromoacetate with finely powdered potassium iodide and allowing the mixture to stand for several hours at 40–50°C. in the dark. Bodroux and Taboury (41) prepared ethyl iodoacetate in a similar manner; also by treating ethyl chloroacetate with an ethereal solution of magnesiumphenylamine iodide (36, 39, 40). Kekulé prepared the iodoacetate by the action of ethyl chloroacetate on an ethereal solution of potassium iodide (160); Tiemann (292) by the action of ethyl chloroacetate on an ethereal solution of magnesium iodide. By treating orthoiodoethylacetate with nitric acid and by heating an alcoholic solution of diiodoacetylene with excess alcoholic potassium hydroxide at 80–100°C., ethyl iodoacetate is formed (208). When glycol monoacetate or a mixture of glycol and acetic acid is saturated, in the cold, with hydriodic acid, ethyl iodoacetate is formed (265); also when ethyl bromoacetate is treated with sodium iodide for twenty-four hours at room temperature (100). Knoll and Company, on August 26, 1908, received German patent 230,172 for the production of ethyl iodoacetate from sodium iodide–acetone solution (167). Curtius and Hussong (74) prepared ethyl iodoacetate from ethyl diazoacetate by the action of dry hydrogen iodide in absolute ether and also by the action of hydrazine hydrate on ethyl bromoacetate. Perkin (227) prepared it by digesting ethyl chloroacetate with potassium iodide in alcohol. Ethyl chloroacetate reacts with the magnesium iodide derivative of *o*-toluidine in ethereal solution to form iodoaceto-*o*-toluidide but if, as

sometimes happens, the magnesium halogen compound undergoes spontaneous coagulation, the yield of iodoaceto-*o*-toluidide is very small, the chief product being ethyl iodoacetate (37, 38).

Ethyl iodoacetate is a colorless liquid with a pleasant odor but irritating and burning taste; it is practically unaffected by water (103). It boils at 69°C. at 12 mm., 73°C. at 16 mm. (208), 75–78°C. at 16 mm. (292), 85–86°C. at 25 mm. (40, 41), 95–96°C. at 43 mm. (130), 110°C. at 60 mm. (144), 142.5–143.5°C. at 250 mm. (corrected) (227), 178–180°C. (36, 54). Density: 4°/4°, 1.8320; 10°/10°, 1.8224; 15°/15°, 1.8150; 20°/20°, 1.8080; 25°/25°, 1.8013. Refractive index determinations: density, 12.7°/4°, 1.8173; η 12.7°/D = 1.50789; η 12.7°/γ = 1.52683 (227); η 20°/D, 1.5072 (130). Magnetic rotation gave: *t*, 15.4°C.; specific rotation, 1.7784; molecular rotation, 11.652 (227). If the magnetic susceptibility $S^M = -K \times 10^{-7}$, the value of K was determined experimentally by Pascal (221, 222) as 1018 and calculated as 1011.5. Walden (306) found that no measurable electrolytic conductivity was to be observed in liquid sulfur dioxide. The velocity of reaction of ethyl iodoacetate with sodium thiosulfate at 15°C. is 2.55; at 25°C. it is 7.0 (266).

When equimolecular quantities of ethyl iodoacetate and methylethylaniline are mixed, a turbidity appears after about 2.5 hours. No heat of reaction is observed and there is a final contraction of about 6 per cent by volume, the viscosity of the suspended drops increasing as the volume of sirup increases. A periodic stratification of colored zones appears at intervals of twenty-four hours and persists for one or two months unless diffusion gradually renders the interface less sharp. The stratification is intensified when the tube is surrounded with silver. The phenomenon is regarded as due to the nature of the material, in particular to the nitrogen atoms, and not to external factors (105).

Ethyl iodoacetate easily decomposes in light with the liberation of iodine (230), also when warmed with alkalies (54) and when heated with nitric acid (208). With alcoholic sodium ethylate in the cold it gives ethoxyethyl acetate (208). When ethyl iodoacetate is heated to 230°C. with ethyl iodide, ethyl acetate and ethylene iodide (11, 12) are formed. Ethyl iodoacetate is converted by means of ethyl sulfide into ethyl methylthioglycolate, $CH_3SCH_2CO_2C_2H_5$, which with a slight excess of ethyl iodoacetate forms ethyl thiodiglycolate, $S(CH_2CO_2C_2H_5)_2$ (182). When methylheptenone is condensed with ethyl iodoacetate in the presence of zinc, and the product is decomposed by water, a colorless oil of the composition, $C_{10}H_{17}O_3C_2H_5$, is obtained which is ethyl dihydrogeranate (22). Ethyl β-methylcinnamate, $C_6H_5C(CH_3):CHCO_2C_2H_5$, is prepared by condensing acetophenone with ethyl iodoacetate by means of magnesium or zinc (252, 295, 296). This is now a general method for the preparation of β-alkyl-

cinnamic acids (253); ketones interact with ethyl iodoacetate and magnesium in benzene solution according to the equation:

$$ArCOR + IMgCH_2CO_2C_2H_5 \rightarrow ArCR(OMgI)CH_2CO_2C_2H_5$$

The β-arylalkyl hydracrylic acids, $ArCR(OH)CH_2COOH$ are obtained by decomposing the magnesium compound with water and then saponifying the ester; methyl *p*-tolyl ketone forms *p*,β-dimethylcinnamic acid, $C_6H_4(CH_3)C(CH_3):CHCOOH$; propiophenone forms β-phenyl-β-ethylhydracrylic acid, $HOC(C_2H_5)(C_6H_5)CH_2COOH$; butyrophenone forms β-*n*-propylcinnamic acid, $HOC(C_3H_7):CHCOOH$; isovalerophenone forms β-phenyl-β-isobutylhydracrylic acid, $CH(CH_3)_2CH_2C(C_6H_5)(OH)CH_2COOH$; phenyl amyl ketone forms β-*n*-amylcinnamic acid, $C_5H_{11}C(C_6H_5):CHCOOH \cdot H_2O$.

When ethyl iodoacetate is allowed to act on magnesiumaniline iodide, in the presence of sufficient ether to keep the latter in solution, iodoacetanilide is formed (41, 42):

$$CH_2ICO_2C_2H_5 + 2NHC_6H_5MgI \rightarrow CH_2IC(NHC_6H_5)_2OMgI \rightarrow CH_2ICONHC_6H_5$$

When ethyl iodoacetate is heated to 40°C. for several hours in the presence of iodine and zinc the compound, $I_3Zn_2(CH_2CO_2C_2H_5)_3$, is formed (91); tin reacts similarly, so that when ethyl iodoacetate, iodine, and tin are heated to 60–70°C. for several hours the compound, $SnI_2(CH_2CO_2C_2H_5)_2$ is formed (90).

By the action of hydrazine hydrate on ethyl iodoacetate, nitrogen is evolved and the whole of the halogen is obtained in an ionic condition (74).

Chlopin (58) determined ethyl iodoacetate as being 1.3 times more toxic than chlorine.

TRICHLOROMETHYL CHLOROFORMATE, PERCHLOROMETHYL FORMATE, $ClCOOCCl_3$

This is called diphosgene by the British and surpalite by the French.

In the dark chlorine acts only very slightly on methyl formate, even at the boiling point, but in the sunlight action is rapid at ordinary temperatures. If the current of chlorine is continued as long as the gas is absorbed, trichloromethyl chloroformate, $ClCOOCCl_3$, is the main product (147).

Hood and Murdock (151) prepared diphosgene after the method of Hentschel (147) and found that the chlorination took place in steps, methyl formate being formed first and then successively the monochloro-, dichloro-, and trichloromethylchloro derivatives. Methyl formate reacts readily with chlorine in the dark, giving methyl chloroformate; further chlorination

in the dark, without the aid of an accelerating agent, gives some chloromethyl chloroformate, but the reaction velocity is low and the yield poor.

Kling, Florentin, Lassieur, and Schmutz (163) condensed carbonyl chloride with methyl alcohol to give methyl chloroformate which, when acted on by chlorine in sunlight, gives chloromethyl chloroformate, then dichloromethyl chloroformate, and finally the trichloromethyl ester.

Grignard, Rivat, and Urbain (126) found that light exerted a marked influence on the chlorination of methyl chloroformate: in diffused light it is only the chloromethyl ester which is formed, bright sunlight being necessary for the formation of the di- or tri-chloromethyl ester. In ultra-violet light the trichloro ester is easily obtained. The effect of temperature is such that up to 110–112°C. the chlorination proceeds smoothly, but at 113–114°C. it slackens very noticeably, and at 117°C. decomposition begins to take place with the formation of carbonyl chloride.

Trichloromethyl chloroformate is a colorless oily liquid with a fairly pleasant, sweet odor; it boils at 49°C. at 50 mm. (164), 125–126°C. at 748 mm. (127, 284), 127°C. at 750 mm. (7, 164), 127–128°C. (170), 127.5–128°C. (147). Its specific gravity is 1.64 at 14°C. (151), 1.6525 at 14°C. (147), 1.653 at 15°C. (90), 1.644 at 15°C. (127). Its vapor density is 6.636 (air = 1) (147). Its vapor pressure is 2.4 mm. at 0°C., 10.3 mm. at 20°C. (151, 284). One cubic meter of air at 20°C. becomes saturated with 26 g. of trichloromethyl chloroformate (7). Its volatility is 43,000 mg. per cubic meter (284).

The thermal decomposition of diphosgene was studied from 260°C. to 310°C. at pressures of 4 to 17 mm. It is of the first order and homogeneous except for a slight wall effect. The rate constant is given by k as $1.4 \times 10^{13} e^{-14,500/RT}$ (236).

When heated to 300–350°C. diphosgene decomposes, yielding carbon oxychloride in the ratio of 1 mole to 2; but this may be the result of catalytic action. Hentschel (147) states that when it is boiled with refluxing, it breaks down to some extent to phosgene, but Hood and Murdock (151) found practically no loss of weight when a sample of diphosgene was refluxed at the boiling point for fifteen hours. Since diphosgene reacts with alcohol, it is possible that Hentschel's results were due to uncondensed diphosgene vapor passing through the condenser (151).

It is not possible to synthesize diphosgene either from phosgene or from carbon dioxide and carbon tetrachloride by means of alumina or ferric oxide (151).

The solubility of nitrogen peroxide in diphosgene seemed to be of the same order as in tetrachlorodinitroethane, i.e., 30 cc. of dry nitrogen peroxide in 15.7 g. of $C_2Cl_4(NO_2)_2$ at 0°C. (9).

Diphosgene is hydrolyzed slowly by water at ordinary temperature and

fairly rapidly at 100°C., the products being hydrogen chloride and carbon dioxide:

$$ClCOOCCl_3 + 2H_2O \rightarrow 4HCl + 2CO_2$$

Boiling with an aqueous solution of sodium hydroxide for 30 minutes decomposes it completely. It reacts with methyl alcohol in the cold to give trichloromethyl methoxyformate, $CH_3OCO_2CCl_3$,

$$ClCOOCCl_3 + CH_3OH \rightarrow CH_3OCO_2CCl_3 + HCl$$

This reaction evolves heat and at a higher temperature the following reaction is obtained:

$$CH_3OCOOCCl_3 \rightarrow CH_3OCOCl + COCl_2$$

If there is an excess of alcohol, methyl chloroformate is formed,

$$CH_3OCOOCCl_3 + CH_3OH \rightarrow 2ClCOOCH_3 + HCl$$

Ammonia reacts rapidly with diphosgene vapor, forming urea and ammonium chloride,

$$ClCOOCCl_3 + 8NH_3 \rightarrow 2CO(NH_2)_2 + 4NH_4Cl$$

Aniline reacts to form carbanilide, which is insoluble in water,

$$ClCOOCCl_3 + 4C_6H_5NH_2 \rightarrow 2CO(NHC_6H_5)_2 + 4HCl$$

and the carbanilide may react with more diphosgene according to the equation:

$$2CO(NHC_6H_5)_2 + ClCOOCCl_3 \rightarrow 2(CONC_6H_5)_2 + 4HCl$$

Diphosgene does not react directly with benzene but forms triphenylcarbinol chloride in the presence of aluminum chloride when heated to 150° C. in closed tubes:

$$ClCOOCCl_3 + 3C_6H_6 \rightarrow (C_6H_5)_3CCl + 3HCl + CO_2$$

When silver or sodium nitrite is treated with diphosgene, phosgene, nitrogen dioxide, nitrogen tetroxide, carbon dioxide, and the chlorides of the metal are obtained.

The catalytic decompositions of diphosgene are extremely interesting; alumina decomposes it to carbon dioxide and carbon tetrachloride, while ferric oxide splits it into phosgene. Purified charcoal behaves like iron oxide, but is more active. Vanadium oxide causes a slow decomposition, while uranium oxide causes a more rapid decomposition than does iron oxide (151). In the army canister, diphosgene is decomposed to phosgene

by the charcoal and it, in turn, is converted into hydrogen chloride and carbon dioxide; the soda lime decomposes diphosgene also to a very slight extent (151).

With dimethylaniline and benzaldehyde, diphosgene yields a green, with dimethylaniline a violet color-base (147).

With alcohol and phenol, trichloromethyl chloroformate yields trichloromethyl methyl carbonate, $CH_3OCOOCCl_3$, and phenyl chloroformate, $ClCOOC_6H_5$, respectively, while it is practically without action on unsaturated hydrocarbons, such as ethylene and amylene, when heated with them in sealed tubes (148).

Trichloromethyl chloroformate reacts with methyl alcohol to yield methyl trichloromethyl carbonate, and with ethyl and isoamyl alcohols to yield respectively the corresponding ethyl ester, b.p. 78°C. at 19 mm., density 20°/4°, 1.4205; and the isoamyl ester, b.p. 120°C. at 23 mm., density 20°/4°, 1.2644. Sodium phenoxide reacts with trichloromethyl chloroformate to yield phenyl trichloromethyl carbonate, m.p. 70.5°C. (211).

The initial product from equimolecular quantities of trichloromethyl chloroformate and an alcohol is the alkyl trichloromethyl carbonate ($ROCOOCCl_3$). The following have been isolated: *n*-propyl, b.p. 93°C. at 12 mm., density 20°/4°, 1.359, $\eta^{20°}$, 1.4451; isobutyl, b.p. 103°C. at 14 mm., density 20°/4°, 1.302, $\eta^{20°}$, 1.4446; β-chloroethyl, b.p. 110°C. at 12 mm., 115°C. at 16 mm., density 20°/4°, 1.5664, $\eta^{20°}$, 1.4748; allyl, b.p. 89–90°C. at 11 mm., density 20°/4°, 1.4015, $\eta^{20°}$, 1.4590 (212).

Trichloromethyl chloroformate and the compounds containing the $OCCl_3$ group react with amines as do alcohols and phenols, giving the same end products as in the reaction with phosgene:

$$ClCOOCCl_3 + 8RNH_2 \rightarrow 2CO(NHR)_2 + 4RNH_2 \cdot HCl$$

The mechanism of the reaction without formation of intermediate products is not clear and is being investigated. An ester solution of diphosgene with cooling and shaking was added to an ethereal solution of *p*-nitroaniline with the formation of *sym*-dinitrophenylcarbamide, $CO(NHC_6H_4NO_2)_2$, and the unstable trichloromethyl-*p*-nitrophenylurethan

$$Cl_3COCONHC_6H_4NO_2$$

yellow crystals evolving phosgene. An ether solution of perchloromethylformate was added to an ethereal solution of diphenylamine with the formation of trichloromethyldiphenylphenylurethan, $CO(OCCl_3)N(C_6H_5)_2$, m.p. 61°C. (198).

The action of trichloromethyl chloroformate on carbonic and alkyl-

sulfuric acids gives the corresponding chloroanhydrides, the reaction proceeding possibly thus:

$$CH_3HSO_4 + ClCOOCCl_3 \rightarrow CH_3SO_4CCl_3 + HCl + CO_2$$

and

$$CH_3SO_4CCl_3 \rightarrow CH_3SO_3Cl + COCl_2$$

When a cold mixture of diphosgene and methyl sulfate was heated to 65°C., the turbulent reaction regulated at 20–25°C., the mixture then heated again 4 hours on a boiling water bath, then distilled *in vacuo* with anhydrous Na_2SO_4, methyl chlorosulfonate, $ClSO_3CH_3$ was produced. A mixture of benzoic acid and diphosgene heated eight hours at 95–105°C. produces benzoyl chloride (170).

Hood and Murdock (151) found the lethal concentration of diphosgene for dogs as 0.25 mg. per liter (40 parts per million) for 30 minute exposure.

The toxic effect of the different chloromethyl carbonates and chloroformates on rabbits, guinea pigs, and dogs was examined, the animals inhaling the vapors diluted with air. The chloromethyl chloroformates become more and more toxic as the number of chlorine atoms introduced increases. For the same number of chlorine atoms present in the molecule the chloroformates are more toxic than the carbonates (197). The relative toxicity, compared to chlorine, taken as unity, is 27 (58).

When diphosgene is introduced into the lungs of dogs, polypnea results (98).

XYLYL BROMIDE, BROMODIMETHYLBENZENE, TOLYL BROMIDE, $CH_3C_6H_4CH_2Br$

Xylyl bromide is prepared by the action of bromine on boiling xylene (*o*-, *m*-, or *p*-) (14, 235), or by the action of bromine on the three xylenes in sunlight (251). Haller and Bauer (132) prepared the *o*- and *m*-xylyl bromides by treating the vapor of *o*- and *m*-xylenes with bromine. Pavlovskii (224) prepared the *o*- and *p*-xylyl bromides and Zeltner and Tarassow (315) the latter by boiling the corresponding ditolubenzyl ethers, $(CH_3C_6H_4CH_2)_2O$, with excess hydrobromic acid (density, 1.49) in tubes. Emde (87) prepared *o*-xylyl bromide by treating *o*-xylene with bromine. Colson (71) prepared *o*- and *m*-xylyl bromides by treating the corresponding xylene glycol, $CH_3C_6H_4CH_2OH$, with bromine. Titley (298) prepared *m*- and *p*-xylyl bromides by treating the corresponding hydrocarbons with dry bromine for six hours at 130°C. *m*-Xylyl bromide was prepared by treating a carbon tetrachloride solution of *m*-xylene with a bromine–carbon tetrachloride solution and keeping the mixture cold (196). Hoch (149) prepared *o*-xylyl bromide by treating the corresponding ethyl ether with hydrobromic acid (density, 1.48).

All forms are soluble in alcohol, ether, and chloroform but insoluble in water.

Properties of o-xylyl bromide

Prisms; m.p. 20°C. (262), 21°C. (235); b.p. 102°C. at 11 mm. (262), 108°C. at 16 mm. (132), 215–218°C. (14), 215–220°C. (224), 216–217°C. at 742 mm. (235), 220°C. (71), 223–224°C. (corrected) at 761 mm. (87). Density: 1.3811 at 23°C. (235). The rate of reaction with dimethylaniline at 40°C. is 1.315×10^{1}, and with triisoamylamine at 40°C. is 3.4×10^{0} (233).

On boiling with alcohol there is formed ethyl-*o*-xylyl ether, $CH_3C_6H_4CH_2OC_2H_5$, a liquid with a peppermint-like odor, b.p. 208–210°C. (47). On addition of magnesium in ether there is formed principally the product *sym*-di-*o*-tolylethane (55, 56). On treatment of alcoholic potassium cyanide, *o*-xylyl bromide is converted into the corresponding nitrile (14).

Properties of m-xylyl bromide

Colorless liquid with a penetrating odor (132); b.p. 97–99°C. at 8 mm. (262), 100–101°C. at 14 mm. (298), 105°C. at 13 mm. (132), 110–115°C. at 20 mm. (298), 185°C. at 340 mm. (232), 200–205°C. (196), 212°C. (71), 212–215°C. (14, 235). Density: 1.3711 at 23° (235). The rate of reaction with dimethylaniline at 40° is 8.625×10^{1}; with triisoamylamine at 40°C. is 2.7×10^{0} (233).

On addition of magnesium in ether the principal product is α,β-di-*m*-tolyl ethane (55, 56). When treated with potassium cyanide in dilute alcohol, m-tolylacetonitrile is formed (14, 196, 298).

Properties of p-xylyl bromide

Needles; m.p. 31°C. (61), 35°C. (132, 224, 315), 35.5°C. (14, 235, 251, 262, 298); b.p. 100°C. at 9 mm. (262), 100°C. at 10 mm. (132), 216–224°C. (224), 218–220°C. at 740 mm. (235, 251). Density: 1.3237 at 20°C. (235). The rate of reaction with dimethylaniline at 40°C. is 2.325×10^{1}; with triisoamylamine at 40°C. is 6.6×10^{0} (233); with aniline at 30.5°C. is 87; with pyridine at 30.5°C. is 9.5 (19).

On addition of magnesium in ether to xylyl bromide there is formed principally 4,4′-dimethyldibenzene (55, 56). When xylyl bromide is boiled with potassium cyanide dissolved in dilute alcohol, *p*-tolylacetonitrile is formed (14). By heating for 1.5 hours under reflux with acetic acid and potassium acetate the resulting *p*-tolylcarbinyl acetate is formed, and when boiled with 10 per cent sodium hydroxide it is converted into *p*-tolylcarbinol (157). By heating an acetic anhydride solution of *p*-xylyl bromide

with fuming nitric acid in acetic anhydride there is formed ω-bromo-3-nitro-*p*-xylene (157).

It was anticipated by Shoesmith and Slater (262) as the result of the study by Lapworth and Shoesmith (177), Shoesmith (259), and Shoesmith, Hetherington, and Slater (260) on the influence which oxygen exerts on halogen atoms in various benzoid compounds that the monobromoxylenes in the case of hydrolysis should be $p>o>m$ and of reduction by hydriodic acid should be $m>o>p$. Table 5 substantiates the former prediction. The three xylyl bromides combine directly with hexamethylenetetramine in chloroform solution to give the additive compounds, $C_6H_{12}N_4BrCH_2C_6H_4CH_3$, having melting points, respectively, as follows: *o*-, 198°C.; *m*-, 215°C.; *p*-, 216°C. Each of these is similarly decomposed by boiling with water, giving the corresponding tolualdehydes. The course of this decomposition reaction is not clear, but the relatively abundant production of methylamine points to the possible primary production

TABLE 5

Hydrolysis of bromoxylenes at 60°C. (262)

t	PERCENTAGE CHANGE		
	ortho	meta	para
minutes			
30	55	25	66
60	77	42	87
120	89	64	96
180	94	77	100

of benzylmethyleneamine, which undergoes isomerization to benzylidenemethylamine (272).

$$C_6H_5CH_2N:CH_2 \longrightarrow C_6H_5CH:NCH_3$$

Treatment of the sodium derivative of phenyl isopropyl ketone with xylyl bromides gives the corresponding xylyldimethylacetophenones, $C_6H_5COC(CH_3)_2CH_2C_6H_4CH_3$. Boiling points: *o*-, 199–200°C. at 15 mm.; *m*-, 196–197°C. at 12 mm.; *p*-, 200–202°C. at 13 mm. (132).

Upon saponifying *o*- or *m*-xylyl bromide with a large excess of potassium carbonate solution, tolylcarbinol, $C_6H_4(CH_3)CH_2OH$, is obtained: *o*-, white crystals, m.p. 34.2°C., soluble in 100 parts water at 12°C., b.p. 216–217.5°C.; *m*-, liquid, b.p. 216–217.5°C. at 758 mm., density 1.028 at 12°C., soluble in 80 to 100 parts water at 12°C. (71).

Xylyl bromides are destroyed very slowly by water (103).

p-Xylyl bromide reacts with benzyl-*p*-methylbenzylmethylamine to form

the additive compound, *p*-methylbenzyltrimethylammonium bromide, m.p. 184°C. (48).

All species of flies under observation were strongly repelled by xylyl bromides (33).

PHYSIOLOGICAL ACTION AND PATHOLOGY

Men exposed to the action of chloroacetophenone (the physiological action of other non-toxic lachrymators is practically the same) exhibit the following symptoms: irritation of the eyes, lachrymation, and burning of the more tender portions of the skin. In some cases there is a tendency toward increased salivation and irritation of the throat. Following exposure there may be some discomfort, but this is of relatively short duration, except in the case of exposure to very high concentration or to low concentrations for prolonged periods. In these latter cases it may require twenty-four hours for the eyes to feel normal again. Men exposed experimentally to high concentrations for short periods of time were unable to open their eyes for several minutes after exposure. In some cases a conjunctivitis was observed which lasted several hours.

Chloroacetophenone has comparatively little effect on the skin of either man or animals. When applied in excess to the human skin, there is a burning sensation, slight rubefaction, and sometimes small vesicles appear. This inflammation subsides in about seven days. In vapor form the inflammation produced is very mild and is usually quite unimportant, although in exceptionally sensitive individuals it may prove quite harassing. Chloroacetophenone has no effect on the lungs of man in any concentration that will be met with in the field.

Dogs exposed to the toxic action of chloroacetophenone exhibit great excitement, irritation of the eyes, nose, and throat, lachrymation, salivation, nasal discharge, and dyspnea. Vomiting, trembling, and twitching of the limbs may occur. Following exposure, there is usually a decided corneal involvement—varying from a slight opacity to ulceration and blindness—soreness of the throat, and coughing. A few dogs that died showed congestion and edema of the lungs, a true membranous tracheitis, and decided corneal opacity. It is quite impossible that the concentrations used on these animals should ever be encountered in the field. It is stated that horses are quite resistant to chloroacetophenone and show no evidence of irritation or lachrymation.

Two fatal cases of poisoning by a lachrymator have been recorded. Shufflebotham (263) reports the case of a workman who was gassed by the explosion of a shell containing ethyl iodoacetate and died on the same day from severe inflammation of the trachea and lungs. In this case edema was not marked, but in parts of the lungs the alveoli were packed with

extravasated red corpuscles. A second fatal case of ethyl iodoacetate poisoning occurred in France to a member of a trench mortar crew owing to the premature explosion of a bomb (216). The post-mortem examination showed pulmonary edema with multiple small hemorrhages in the lungs.

TREATMENT

Treatment consists in merely washing the eyes with a solution of boric acid or sodium bicarbonate. As these lachrymators cause no permanent damage to the eyes, and only transient discomfort, even this treatment is generally unnecessary. The mask affords perfect protection against these lachrymators, and with the mask properly adjusted a man can go through the densest fumes in perfect comfort. However, the effect of lachrymators is practically instantaneous, and some discomfort may be experienced before the mask can be adjusted. The natural instinct when a lachrymator is felt is to turn and run. This is what makes these agents so very effective against mobs and for other police purposes. The first instinct of a soldier with a mask should be to put it on; this is only acquired by training, and when that training has been effective the mask should be on and properly adjusted in 7 seconds after the first warning of gas.

PATENTS

Numerous patents have been issued for the means of dispersing lachrymatory gases: Oglesby and Ehrenfeld on February 14, 1926 received U. S. patent 1,659,158 for a device for dispersing lachrymatory irritants by heat from associated combustible material (217); Ranken and Nobel Industries, Ltd., on February 13, 1926 received British patent 275,830 for a lachrymatory torch (237); Ranken and Nobel Industries, Ltd., on February 13, 1926 received British patent 276,279 for a device for producing lachrymatory and like gases for military purposes (237); Flury received U. S. patent 1,712,917 for a fumigant comprising hydrocyanic acid and some lachrymatory warning substance (102); Alden (1) received U. S. patent 1,735,522 for a tear gas projectile; Goss (123) U. S. patent 1,750,101 for a formula for lachrymatory gas; Minto (202) U. S. patent 1,877,773 for a tear gas cartridge.

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