II. HALOGENATED OLEFINIC HYDROCARBONS

1. HALOGENATED ETHENE DERIVATIVES

A. Monohalogenated Ethene Derivatives

Vinyl Chloride

Chemistry.—Vinyl chloride, chloroethylene, $CH_2=CHCl$, has the molecular weight 62.50. It is a gas of the specific gravity 0.908 25°/25° which solidifies at −160° C. and boils at −12° C. It is slightly soluble in water, soluble in alcohol, and very soluble in ether. It polymerizes when exposed to light, and its flammability limits are between 4 and 21.7 percent in air (Jones, 1938). It is used in the synthesis of organic compounds such as resins.

Schaumann (1934) determined vinyl chloride in blood by evacuating 5 to 10 cc. of the latter in the Van Slyke apparatus, mixing the liberated blood gases with oxygen, decomposing the chlorinated hydrocarbon over heated platinum, absorbing the liberated hydrochloric acid in Pregl's "sodium carbonate-bisulfite solution" and determining the chlorine titrimetrically by Volhard's method.

Regarding its *absorption, fate, and excretion* it has been shown that it is readily absorbed through the lungs and promptly excreted by this route, 82 percent being eliminated from the blood 10 minutes after discontinuation of the narcosis as shown by Schaumann (1934).

Like other chlorinated hydrocarbons, vinyl chloride has *narcotic properties.* According to Peoples and Leake (1933) the narcotic range for mice is between 3.5 and 5 mM per liter of air. Concentrations of 7 mM per liter of air will cause narcosis in rabbits and dogs after 1 minute, and the recovery is prompt and not followed by untoward effects even after prolonged exposure. Schaumann (1934) determined the vinyl chloride level in the blood of cats anesthetized with 10 to 13 vol. percent as 15 to 17 mg. percent. Oster, Carr, Krantz, Jr., and Sauerwald (1947) used vinyl chloride stabilized with 0.5 percent of p-tert-butyl-catechol for narcosis of dogs, starting with concentrations of 50 vol. percent and reducing the concentration gradually to 7 vol. percent. They found that the induction was rapid, but that "crowing" continued even during deep anesthesia and that there was profuse salivation. During narcosis the relaxation of the abdominal muscles was good but the legs remained rigid showing, throughout the anesthesia, incoordinated movements. The recovery was rapid but associated with violent excitation.

As to the effect of vinyl chloride on the *circulation,* Schaumann (1934) studied its effects in the Starling heart-lung preparation of cats judging the action by the effect on the intra-auricular pressure. He found that

similar effects were produced by 1.3 percent of solaesthin (dichloroethylene), 3 vol. percent of ether, and 18 vol. percent of vinyl chloride. Higher concentrations (20 vol. percent) of vinyl chloride caused a more or less marked relative insufficiency and even 25 to 30 vol. percent were unable to produce complete cardiac failure. Oster, Carr, Krantz, Jr., and Sauerwald (1947) studied the circulatory response in dogs anesthetized with 10 vol. percent of vinyl chloride. They noted a moderate fall of the blood pressure and definite evidence of cardiac irregularities as indicated by intermittent tachycardia, extraventricular systoles and vagal beats. Electrocardiographic studies revealed marked changes of the cardiac rhythm such as tachycardia followed by bradycardia, inversion of the R spike, and in one instance incipient ventricular fibrillation. All records showed abnormalities of the QRS interval varying from sinus arrhythmia and transitory extreme left axis deviation to very serious conditions such as auricular-ventricular block, ventricular tachycardia, ventricular multiform extrasystoles, and inversion of the T wave with elevated ST segment in lead II. As the anesthesia progressed towards respiratory failure most of the QRS abnormalities disappeared but the R amplitude was generally reduced.

As to the *toxicity* of vinyl chloride, Patty, Yant, and Waite (1930) studied this in guinea pigs. They found that exposure to 20 to 40 vol. percent kills the animals in a very short time, that concentrations of 10 vol. percent are dangerous to life with exposures for 30 to 60 minutes, and that 0.5 vol. percent is the maximum allowable concentration for several hours' exposure without causing acute disturbances of severe nature. Animals exposed in this way showed some edema of the lungs and hyperemia of liver and kidneys. They considered vinyl chloride less harmful than chloroform or carbon tetrachloride and of a similar order of toxicity as ethyl chloride. Schaumann (1938) found that mice and rats tolerate repeated light narcosis for 4 hours daily on 5 to 8 consecutive days and for 1 hour daily for 4 weeks without showing kidney or liver injuries. Dogs which had been narcotized for 3 hours with 10 vol. percent on 7 occasions in the course of several weeks showed no considerable changes in kidney and liver. Higher concentrations (20 vol. percent) caused in dogs marked salivation, respiratory arrest, and vomiting after narcosis. Peoples and Leake (1933) determined the lethal range for mice with 10 minutes' exposure as 10 to 12 mM per liter, and Schaumann (1934) determined the vinyl chloride level in the blood at the time of cardiac arrest as <40 mg. percent and at the time of respiratory arrest as 27 to 30 mg. percent, the same value for chloroform being 60 to 70 mg. percent.

Regarding the *toxicity* of vinyl chloride *for man*, Patty, Yant, and Waite (1930) expressed the opinion that the gas does not possess adequate warning properties because of its odor or irritant action, but that it gives warning by producing symptoms of dizziness and disorientation in advance of harm, except when present in exceedingly high concentrations which would cause almost immediately helplessness and unconsciousness. Inhalation of 2.5 percent will soon cause dizziness, disorientation, and a burning sensation in the soles of the feet, which symptoms disappear immediately after discontinuation of the exposure except for a slight headache which may last 30 minutes. These authors suggested the use of

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vinyl chloride for narcosis in man, and Schaumann (1938) considered as narcotic concentrations for man 7 to 10 vol. percent, whereas 12 vol. percent may be dangerous. In the opinion of Oster, Carr, Krantz, Jr., and Sauerwald (1947) it is not suitable for this purpose because of its effects on the circulation. The American Conference of Government Industrial Hygienists (1953) accepted 200 p. p. m. as threshold limit for continued exposure.

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Vinyl Bromide

Vinyl bromide, bromoethylene, $CH_2=CHBr$, has the molecular weight 106.96. It is a liquid of the specific gravity 1.529 11°/4° which solidifies at −137.8° C. and boils at 15.8° C. It is insoluble in water but miscible with alcohol and ether.

According to Abreu, Peoples, and Emerson (1939), the minimal anesthetic concentration for mice is 3.5 mM per liter, and the highest tolerated concentration is 7 mM per liter. Abreu and Emerson (1940) determined the inorganic bromide content of the liver of mice narcotized with vinyl bromide as 0.043 ± 0.0005 mg. per 1 gm. of wet tissue as compared with 0.165 ± 0.006 found in animals narcotized with ethyl bromide, indicating the greater stability of the unsaturated compound.

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Vinyl Fluoride

Vinyl fluoride, fluoroethylene, CH_2-CHF, has the molecular weight 46.044. It is a gas which boils at −51° C.

According to Lester and Greenberg (1950) rats exposed to 60 vol. percent lose their postural reflexes, with 70 vol. percent their righting reflexes, and with 80 vol. percent their corneal reflexes. With the latter concentration the animals became dyspneic, but recovered fully when transferred to fresh air, even after 12½ hours' exposure, without showing evidence of pulmonary irritation.

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