The Halogenated Hydrocarbons Toxicity & Potential Dangers
U.S. Dept. of HEW
1955ed

:ORIDE

luene,

ecular weight 162.90 and is a
ity of 1.25445 13° which boils
what hygroscopic.
.7 to 1.0 mM (114 to 163 mg.)
causing paralysis without in-
tability, and convulsions.

nzer, Berlin, 1931, p. 340.
o, 1928.
35, 375, 1808.

: DERIVATIVES

ly *bromoxylene* has been in-
pure product has not been
at a mixture of $C_6H_4CH_3Br$-
s lacrimator in chemical war-
which has a boiling range of
(1937), a specific gravity 1.31.
imals severe irritation of the
s. High concentrations will
pulmonary edema, and, after
d death.
.° per m.° (0.56 mg./liter) for
r (1925), concentrations of
ght. As stated by Uttermark
r are intolerable and such of
g irritation.

zer, Berlin, 1931, p. 340.
ntriegifte, O. Meissner, Hamburg.

warfare, Williams and Wilkins.

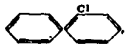
L DERIVATIVES

nyl Derivatives

TL

forms, depending upon the
bon rings.

o-Chlorodiphenyl,



has the molecular weight 188.65 and forms crystals which melt at 34° and boil at 267° to 268° C. and which are insoluble in water but very soluble in ligroine.

m-Chlorodiphenyl,



has the molecular weight 188.65 and forms crystals which melt at 89° and boil at 284° to 285° C.

p-Chlorodiphenyl,



has the molecular weight 188.65 and forms leaflets which melt at 77.5° C. and boil at 282° C., and which are insoluble in water but soluble in ligroine.

Smyth (1931) studied the toxicity of the ortho- and para-compounds in rabbits and guinea pigs and found that the former killed animals within 20 to 40 hours with doses of 2.5 gm. per kg., causing mild convulsions, whereas the latter was fatal in 40 hours in doses of 3.5 gm. per kg. without causing convulsions.

REFERENCE

Smyth, H. F., J. Ind. Hyg., *13*, 87, 1931.

B. Dihalogenated Diphenyl Derivatives

Of the dihalogenated diphenyl derivatives only difluorodiphenyl has been studied to some extent. It exists in two isomeric forms, of which only the p,p′ derivative has been studied toxicologically.

p,p′-Difluorodiphenyl,



has the molecular weight 190.18. It forms monoclinic columns of the specific gravity 1.336 25°/4° which melt at 90° to 95° C., and boil at 254 to 255° C., and which are insoluble in water and soluble in alcohol, ether, and chloroform.

Kempf, Greenwood, and Nelson (1937) reported that rats kept on a diet containing 0.05 percent of this material (calculated as fluorine) developed neither mottled enamel of the teeth nor changes of the red blood cell count or of the hemoglobin.

REFERENCE

Kempf, C. A., D. A. Greenwood, and V. E. Nelson, J. Lab. Clin. Med., *22*, 1133, 1937.

MONS 046925

C. Polychlorinated Diphenyl Derivatives

Polychlorinated diphenyl derivatives are of considerable toxicological interest because they are constituents, together with chloronaphthalenes, of certain synthetic waxes used extensively in industry as for the insulation of electrical equipment.

Penning (1930) described the process by which these products are prepared. In the course of this procedure first a mixture of 2- and 4-chlorodiphenyl is formed, and as the chlorination proceeds the mixture becomes more and more viscous and finally solid. These products are marketed under the name of "Aroclor" and represent mixtures of different isomers. "Aroclor" is insoluble in water and glycerol, not very soluble in lower alcohols, but very soluble in oils and other organic solvents. The "Aroclors" are solvents for sulfur, rubber, asphalt, paraffin, and natural waxes, and are used for protective coating, waterproofing of wood, and for electric insulation.

The toxicological evaluation of these products is difficult because of their variable composition. Drinker, Warren, and Bennett (1937) used a preparation which contained 65 percent of chlorine and Miller (1944) used a viscous, almost white material of the empirical formula $C_{12}H_4Cl_6$ of a specific gravity 1.374 to 1.383.

The *toxicity of chlorodiphenyl for experimental animals* was first studied by Smyth and Smyth (1931) who found that their product proved nontoxic by oral administration to guinea pigs and rabbits in doses of 4 gm. per kg. given as a paste. Drinker, Warren, and Bennett (1937) and Bennett, Drinker, and Warren (1938) found that feeding rats about 0.8 gm. daily was highly toxic when given over a period of 6 days, and that even 0.05 gm. per rat was definitely toxic, causing injury to the liver, although no yellow atrophy of the liver was observed. Miller (1944) found that feeding guinea pigs 2 doses of 69 mg. 1 week apart was fatal in 11 to 29 days after the first dose, and that the animals showed marked liver changes.

Miller (1944) reported that the *subcutaneous injection* of a single dose of 0.5 cc. (69 mg.) caused in guinea pigs local necroses at the site of injection, followed by encapsulation, and after 8 days fatty infiltration of the liver, moderate central atrophy and, rarely, focal necroses and some congestion of the kidneys. These injuries were more severe after doses of 0.1 to 0.5 cc. (138 to 690 mg.) and, when given as a 50 percent solution in oil, 345 mg. killed all animals within 13 days. The subcutaneous injection of 63 mg. into rabbits produces fatty infiltration of the liver earlier than observed in guinea pigs but with less marked central atrophy. On the other hand, congestion of the spleen was seen more frequently and often there was a myelosis of the pulp. Doses of 690 mg. produced marked fatty changes in the liver and considerable hypertrophy of the spleen. With *repeated administration* 10 doses of 69 mg. gave definite pathologic changes in the liver, and 10 doses of 690 mg. and of 1380 mg. given on consecutive days caused delayed death and marked *fatty infiltration and sometimes focal necroses of the liver.*

With *cutaneous application* Miller (1944) found that in guinea pigs daily doses of 34.5 mg. for 11 days were fatal after various intervals

up to 21 days, the an
changes in liver and ot
tion. The skin at the si
tion of the capillaries, t
surrounding the blood
struction of the epiderm
The *topical applicati*
caused no local changes
cavernous venous congest
The *toxicity of chloro*
Warren, and Bennett (19
rats. They found that
concentration of 0.57 mg
for a prolonged period o
but when the animals w
showed pale, slightly ye
tion of the liver cells, in
increased vacuolization.
is more toxic than chlori
totoxic action of chlorodi
in the molecule.
There are no reports
phenyl alone, although n
ture with chlorinated na
ernment Industrial Hygi
per m.³ as threshold limit

Am. Conf. Gov. Ind. Hygienis
296, 1938.
Bennett, G. A., C. K. Drinker,
Drinker, C. K., M. F. Warren
Miller, J. W., Pub. Health Rep
Penning, C. H., Ind. Eng. Che
Smyth, H. F. and H. F. Smyth

6. HALOGENA

A. *Monohalo*

M

Monochloronaphthalene
chloronaphthalene, depen
double ring.
Alphachloronaphthalen

MONS 046926

yl Derivatives

of considerable toxicological
ther with chloronaphthalenes,
in industry as for the insula-

which these products are pre-
first a mixture of 2- and 4-
rination proceeds the mixture
ly solid. These products are
represent mixtures of differ-
er and glycerol, not very solu-
ils and other organic solvents.
er, asphalt, paraffin, and natu-
ating, waterproofing of wood,

ucts is difficult because of their
d Bennett (1937) used a prepa-
ine and Miller (1944) used a
pirical formula $C_{12}H_7Cl_5$ of a

perimental animals was first
he found that their product
o guinea pigs and rabbits in
Drinker, Warren, and Bennett
n (1938) found that feeding
n given over a period of 6 days,
ly toxic, causing injury to the
r was observed. Miller (1944)
60 mg. 1 week apart was fatal
at the animals showed marked

eous injection of a single dose
ocal necroses at the site of in-
fter 8 days fatty infiltration
d, rarely, focal necroses and
juries were more severe after
d, when given as a 50 percent
ls within 13 days. The sub-
produces fatty infiltration of
s but with less marked central
of the spleen was seen more
of the pulp. Doses of 600 mg.
and considerable hypertrophy
tion 10 doses of 60 mg. gave
al 10 doses of 600 mg. and of
d delayed death and marked
ses of the liver.
4) found that in guinea pigs
fatal after various intervals

up to 21 days, the animals showing essentially the same pathologic changes in liver and other organs as observed with subcutaneous injection. The skin at the site of the application showed occasionally congestion of the capillaries, thickening of the epidermis, edema of the dermis surrounding the blood vessels, and with prolonged administration destruction of the epidermis.

The *topical application to the cornea* of rats on 25 consecutive days caused no local changes but slight central atrophy of the liver and slight cavernous venous congestion of the spleen.

The *toxicity of chlorodiphenyl by inhalation* was studied by Drinker, Warren, and Bennett (1937) and Bennett, Drinker, and Warren (1938) in rats. They found that exposure of rats for 16 hours daily to an average concentration of 0.57 mg. per m.^{3} or for 8 hours daily to 0.93 mg. per m.^{3} for a prolonged period of time caused no apparent ill effects during life, but when the animals were killed after various periods of exposure they showed pale, slightly yellow, somewhat mottled livers, hyaline degeneration of the liver cells, increased prominence of cytoplasmic granules, and increased vacuolization. The same authors thought that chlorodiphenyl is more toxic than chlorinated naphthalenes and believed that the hepatotoxic action of chlorodiphenyl increased with the percentage of chlorine in the molecule.

There are no reports on human poisoning from exposure to chlorodiphenyl alone, although numerous poisonings have resulted from its mixture with chlorinated naphthalenes. The American Conference of Government Industrial Hygienists (1953) accepted a concentration of 1 mg. per m.^{3} as threshold limit for continued exposure.

BIBLIOGRAPHY

Am. Conf. Gov. Ind. Hygienists, Los Angeles (1953), Arch. Ind. Hyg. Occ. Med., *8*, 296, 1953.
Bennett, G. A., C. K. Drinker, and M. F. Warren, J. Ind. Hyg. Toxicol., *20*, 97, 1938.
Drinker, C. K., M. F. Warren, and G. A. Bennett, J. Ind. Hyg. Toxicol., *19*, 283, 1937.
Miller, J. W., Pub. Health Rep., *59*, 1065, 1944.
Penning, C. H., Ind. Eng. Chem., *22*, 1180, 1930.
Smyth, H. F. and H. F. Smyth, Jr., J. Ind. Hyg., *13*, 87, 1931.

6. HALOGENATED NAPHTHALENE DERIVATIVES

A. Monohalogenated Naphthalene Derivatives

Monochloronaphthalene

Monochloronaphthalene exists in 2 isomeric forms, alpha- and beta-chloronaphthalene, depending on the position of the chlorine atom in the double ring.

Alphachloronaphthalene, α-naphthyl chloride,



MONS 046927