

1,1,1,2-TETRACHLOROETHANE: PAST AND FUTURE STATUS

1,1,1,2-Tetrachloroethane has recently been synthesized in the Solvents Laboratories of the Texas Division, and a supply is present in Midland in the Toxicology Department.

Some of its physical properties are listed in Table 1.

TABLE 1

SOME PHYSICAL PROPERTIES OF 1,1,1,2-TETRACHLOROETHANE

Physical State	Colorless Liquid
Molecular Weight	167.86
Boiling Point	130.5°C
Specific Gravity	1.5465
Flash Point	None

There is a need for a degreaser or cleaning solvent with a high boiling point.

In comparison with other chlorinated solvents that are sold by Dow (Table 2), it is apparent that 1,1,1,2-tetrachloroethane has a higher boiling point than all of the compounds listed, particularly 1,1,1-trichloroethane (a widely used industrial cleaner and degreaser), and trichloroethylene (a widely used vapor degreaser).

1,1,1,2-Tetrachloroethane has the potential of becoming a new product in the Dow chlorinated solvent area, providing it has a low toxicity.

TABLE 2

1968 SALES, THRESHOLD LIMIT VALUES (TLV), FLASH POINTS,
AND BOILING POINTS OF SOME DOW CHLORINATED SOLVENTS

Common Name	IUPAC ^a Name	Dow 1968 Sales (\$)	TLV (PPM)	Flash ^b Point °F	Boiling Point °C
Methylene Chloride	Dichloromethane	10 Million	500	None	40.1
Chloroform	Trichloromethane	4 Million	50	None	61.3
Carbon Tetrachloride	Tetrachloromethane	13 Million	10	None	76.8
Ethyl Chloride	1-Chloroethane	983 Thousand	1000	45	12.2
Ethylidene Dichloride	1,1-Dichloroethane	8 Thousand	100	10	57.3
Ethylene Dichloride	1,2-Dichloroethane	10 Million	50	60	83.5
Methyl Chloroform	1,1,1-Trichloroethane	24 Million	350	None	74.1
Vinyl Trichloride	1,1,2-Trichloroethane	269 Thousand	10	None	113.5
Acetylene Dichloride (1,2-Dichloroethylene)	1,2-Dichloroethene (Mixed Isomers)	2 Thousand	200	30	46-64
Acetylene Trichloride (Trichloroethylene)	1,1,2-Trichloroethene	8 Million	100	None	87.0
Perchloroethylene (Tetrachloroethylene)	1,1,2,2-Tetrachloroethene	11 Million	100	None	121.2

^a International Union of Pure and Applied Chemistry

^b Tag Open Cup

Few toxicological or metabolic investigations of 1,1,1,2-tetrachloroethane have been conducted. Van Dyke (1) has completed some in vitro dechlorination experiments, and Ferguson (2) has exposed adult female rats (200 - 220 g) to concentrations of 10,000 and 500 ppm vapor.

In vitro dechlorination. From Van Dyke's data (Table 3), it appears that enzymatic dechlorination may correlate with toxicity. For example, 1,1,2-trichloroethane, 1,1,2,2-tetrachloroethane, and 1,1-dichloroethane are dechlorinated and are known to produce pathological alterations in the liver; whereas ethyl chloride and 1,1,1-trichloroethane do not undergo extensive dechlorination and are of a different order of toxicity.

Since 1,1,1,2-tetrachloroethane is not dechlorinated, it may be a relatively non-toxic compound and should be evaluated.

TABLE 3
ENZYMATIC DECHLORINATION OF CHLOROETHANES

<u>Common Name</u>	<u>IUPAC Name</u>	<u>% Enzymatically Dechlorinated</u>
<u>Group I: Dechlorinated</u>		
Ethylidene Dichloride	1,1-Dichloroethane	13.5
Vinyl Trichloride	1,1,2-Trichloroethane	9.8
Acetylene Tetrachloride	1,1,2,2-Tetrachloroethane	6.0
<u>Group II: Non-Dechlorinated</u>		
Ethyl Chloride	Chloroethane	<0.5
Methyl Chloroform	1,1,1-Trichloroethane	<0.5
- - - - -	1,1,1,2-Tetrachloroethane	0.8

Exposure of rats to 1,1,1,2-tetrachloroethane. Female rats were exposed for four hours per day, four days per week, for two weeks by Ferguson (2).

At 10,000 ppm, 10/10 rats died after two hours exposure. At 500 ppm, gross examination of livers, lungs, and kidneys indicated the presence of several pale livers. The serum glutamic acid-pyruvic acid transaminases (SGPT) were normal. Microscopic histology of the lungs and kidneys appeared to be normal. A diffuse, minimal fatty metamorphosis was present in the livers.

The effects of vapor exposure to rats of 1-chloroethane, 1,1- and 1,2-dichloroethane, 1,1,1- and 1,1,2-trichloroethane and 1,1,2,2-tetrachloroethane are listed in Table 4. The absence of pathological and histological changes in the livers of rats exposed to 10,000 ppm of 1,1-dichloroethane conflicts with previous vapor work. Smyth (3) has quoted unpublished results that repeated inhalation by rats produced liver injury, and rats were killed at 16,000 ppm.

PROPOSED FUTURE TOXICOLOGICAL INVESTIGATIONS
OF 1,1,1,2-TETRACHLOROETHANE

It is proposed that six adult male and six adult female rats (200 - 250 g) be exposed to each vapor concentration (5,000, 1,000, and 200 ppm) for two weeks, six hours per day for five days the first week and six hours per day for four days the second week. Six male and six female rats will be used as controls and exposed to air under the same conditions. Rats from each vapor

TABLE 4

THE RESULTS OF INHALATION EXPOSURE OF FEMALE RATS
TO SEVERAL CHLOROETHANES (2)

Compound	Gross Pathology		Histology		SGPT Level	Organ Wt/100 g Body Wt	
	Liver	Kidney	Liver	Kidney		Liver	Kidney
	<u>100 PPM</u>						
1,2-Dichloroethane	0	0	0	0	0	2	2
1,1,2-Trichloroethane	0	0	0	0	0	0	0
1,1,2,2-Tetrachloroethane	2	0	1	0	0	0	0
	<u>500 PPM</u>						
1,2-Dichloroethane	0	0	1	0	0	0	2
1,1,2-Trichloroethane	1	0	1	1	1	2	0
	<u>10,000 PPM</u>						
1-Chloroethane	0	0	1	0	0	0	0
1,1-Dichloroethane	0	0	0	0	0	1	0
1,1,1-Trichloroethane	0	0	0	0	0	2	2

Gross Pathology	Histology		SGPT Level and Organ Weight/ 100 g Body Weight
	Liver	Kidney	
0 No visual lesions	0 No changes	0 No changes	0 No significant difference between means, Student's t test
1 Slightly pale	1 Slight fatty meta- morphosis, tissue necrosis	1 Slight tissue degeneration	1 Significant change at high doses, 95% confidence
2 Slightly pale with lobular markings	2 Moderate fatty meta- morphosis, tissue necrosis	2 Moderate tissue degeneration	2 Significant change at high and low doses, 95% confidence

concentration group will be withdrawn on the ninth day, fasted overnight, sacrificed by decapitation, and blood collected for SGPT analyses.

Livers and kidneys will be weighed. Weight of rats will be recorded at the beginning and end of the experiment, and liver and kidney weight per 100 g body weight will be calculated. Livers, lungs, and kidneys will be examined for gross pathology, and sections prepared for histological examination.

The results of this investigation should provide valuable information on the toxicity of 1,1,1,2-tetrachloroethane, and should indicate whether it holds promise as a new addition to the chlorinated solvent product line.

REFERENCES

1. R. A. Van Dyke and C. G. Wineman, "Enzymatic Dechlorination: In Vitro Dechlorination of Chloroethanes and Propanes", BC R-529, January 2, 1969.
2. J. Ferguson, P. B. Conran, and M. B. Chenoweth, Work completed, paper in preparation.
3. H. F. Smyth, D. E. Cummings Memorial Lecture, Amer. Ind. Hyg. Assoc. Quart., 17:129 (1956).