Inhalation Toxicity of Some Aliphatic Thiiranes

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Introduction

In recent years, the aliphatic episulfides, or thiiranes, have shown promise in various phases of polymer technology. In the presence of a suitable catalyst, ethylene sulfide may be polymerized and molded to form plastic articles. In addition, when incorporated as the monomer and polymerized, the episulfides are known to impart exceptional hardening and anti-ozonant properties to substances such as rubber. The three thiiranes of greatest interest to industry are ethylene, propylene and chloropropylene sulfides. They may be prepared by interaction of the appropriate epoxide with potassium thiocyanate, as follows:

where R = H for ethylene,
CH_3 for propylene, and
$CH_2 \cdot Cl$ for chloropropylene

The acute oral, intraperitoneal and inhalation toxicities of these three episulfides have been determined in rats and some observations were also made on their potential for skin and eye irritation in rabbits (1). The inhalation studies were performed under static conditions, in 30-minute trials with small groups of rats. Because of continued interest in the vapor toxicities of these compounds, a more critical estimation of the vapor toxicities has been undertaken, utilizing dynamic gassing equipment and larger groups of animals in exposure periods of 1 and 6 hours.

Materials and Methods

Chemical Samples

The three episulfides are colorless, volatile liquids (see reference (1) for physical

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properties). The samples employed were synthetized and distilled by the manufacturer and were of at least 98% purity. They were preserved in the dark under refrigeration. Despite this, some precipitate from polymer formation developed in the ethylene sulfide sample and this was removed by filtration immediately prior to use in the inhalation studies. Polymer formation was not seen in the propylene and chloropropylene samples and filtration was unnecessary.

Inhalation Equipment

Each episulfide was delivered at a constant rate from a precision, dual-syringe liquid metering pump into an evaporation flask assembly, immersed either in a water or oil bath maintained at a temperature equal to the boiling point of the episulfide under test. Preheated air at the same temperature was pumped into the evaporation flask above the liquid at a rate of approximately 15 l./min. to facilitate volatilization. The episulfide vapor, diluted with air, was then conducted to the inlet pipe of the exposure chamber, where additional make-up air was introduced to yield a final overall flow rate of 250 l./min. through the chamber. The chamber was of standard design, with pyramidal top and bottom, constructed of stainless steel and glass, and having a volume of 1 cu.m.

Exposure Procedures

Male rats of the Wistar strain, weighing 225-275 g., were used for this study. An average of 6 runs, each employing 10 rats housed in a compartmented exposure basket, were required to determine the 1-hour and 6-hour LC50 for each episulfide. The nominal concentration of episulfide was determined for each run from the flow rate of air through the chamber and the rate of episulfide volatilization. The animals were observed during and after exposure for signs of toxicity and death. Animals that succumbed were necropsied promptly and survivors, kept under observation for 2 weeks, were sacrificed and necropsied. Observations of gross pathological changes were made in all cases and the trachea, lung, heart, liver, adrenal and kidney from a representative number of animals were preserved in formalin. The tissues were stained with H and E and examined microscopically. From the mortality records, the LC50 for the 1-hour and 6-hour exposure periods was determined by the method of Miller and Tainter (2).

Results

Mortality

The calculated LC50 values for the three episulfides for the two exposure durations are presented in Table 1.

TABLE 1

1-hour and 6-hour LC50 Values of Episulfides in Rats

	1-hour LC50	6-hour LC50
Ethylene Sulfide	2800 ± 117	690 ± 15
Propylene Sulfide	2750 ± 160	660 ± 4.5
Chloropropylene Sulfide	1350 ± 47	305 ± 2.5

Concentration ± Standard Error in ppm.

Histopathological Findings

Rats exposed to the three episulfides showed marked similarities in the lesions found in tissues. In the lungs, congestion ranging from slight to severe was a common finding. Edema and slight to moderate hemorrhage were seen. A moderate to severe degree of cuffing was noted. A few instances of pneumonia and bronchitis were recorded. Degenerative changes in the trachea were slight or absent. No striking alterations were noted in the heart or liver. Kidney changes afforded some evidence of a differemce in the action of chloropropylene sulfide as compared with the non-halogenated episulfides. Protein casts were seen in the cortex and the medullary region, with degeneration and necrosis, in animals exposed to chloropropylene sulfide; these changes were not conspicuous in rats exposed to ethylene and propylene sulfides.

Discussion

The present data shows that ethylene and propylene sulfides are of about equal toxicity when

administered as vapors by the respiratory route in 1-hour and 6-hour acute exposures. Chloropropylene sulfide is approximately twice as toxic as the non-halogenated episulfides under these conditions. A consistent departure from Haber's rule (Ct = constant) is evident for all three episulfides when the results from the two exposure durations are compared. This renders comparison with the earlier work of Brown and Mastromatteo (1) uncertain. However, there is an acceptable degree of agreement between their results and those found in the present study with respect to ethylene and propylene sulfides, but there is a noticeable discrepancy in the case of the respective results on chloropropylene sulfide.

It should be mentioned that Eizengart and his associates have performed a series of toxicological investigations on ethylene sulfide (3,4,5). They believe that the compound affects the neurosecretory function of the hypothalamus and causes alterations in brain and skin histamine content. On the basis of chronic inhalation studies in rats, Pugaeva et al. (5) recommended a rather stringent maximum concentration of 0.1 mg/m^3 (0.04 ppm) in the industrial workplace.

References

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