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Gas chromatography of sulfur mustard and its analogs

Vesicants such as bis(2-chloroethyl) sulfide (sulfur mustard) and 2-hydroxyethyl-2'-chloroethyl sulfide (sulfur half-mustard) have been studied extensively as clinically useful anti-tumor agents[1–3] and as alkylating agents in studies of the mechanism of cytotoxicity with DNA *in vitro* and *in vivo*[4–7]. A recent review on the chromatography of alkylating agents[8] discussed the paper and thin-layer chromatography of sulfur mustard and its analogs, but there appears to be no established procedure for gas chromatographic determination of these compounds. The present report concerns the development of a gas chromatographic method for the analysis of sulfur mustard, half-mustard, and a major hydrolysis product of both, bis(2-hydroxyethyl) sulfide (thiodiglycol).

Bis (2-chloroethyl) sulfide and thiodiglycol were obtained from K & K Laboratories, Inc., Plainview, N.Y. 2-Hydroxyethyl-2-chloroethyl sulfide was synthesized by the reaction of ethylene dichloride with sodium mercaptoethanol as described by SELIGMAN *et al.*[3]. The final product was purified by distillation at 48°, 0.08 mm; its naphthyl urethan derivative melted at 96.5–97.5° (ref. 9).

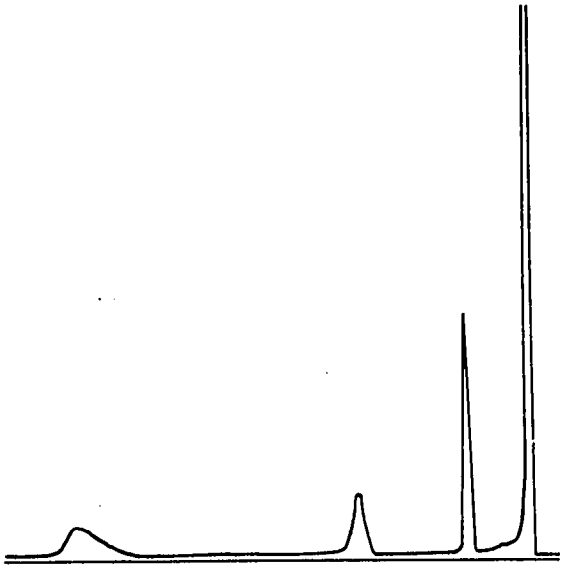

Fig. 1. Isothermal separation of sulfides. Elution order: (first) sulfur mustard, half-mustard, thiodiglycol. The initial off-scale peak is methylene chloride.

Glass columns, 1.5 meter by 0.2 cm (I.D.), were packed with 100–120 mesh Gas-Chrom Q coated with 3% cyclohexanedimethanol succinate (Hi-Eff 8bp, Applied Sciences) and cured overnight at 240° with a low helium flow. Isothermal analyses were made using an Aerograph 600-B gas chromatograph with a hydrogen flame ionization detector and a glass inlet port liner. The column and inlet temperatures were 120° and 170°, respectively, with a helium flow rate of 35 ml/min. Samples were injected as dilute solutions in methylene chloride; the separation obtained is shown in Fig. 1. A linear relationship between peak area and sample size was obtained, as illustrated for sulfur mustard in Fig. 2.

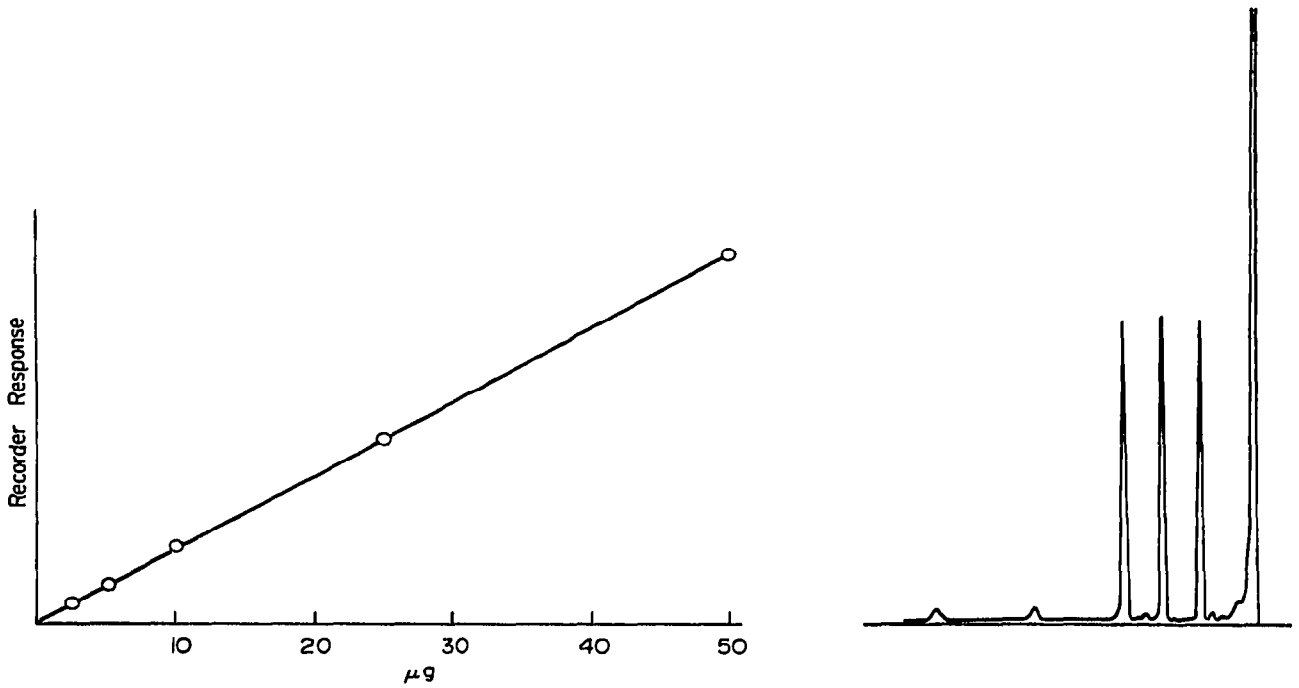

Fig. 2. Standard curve for sulfur mustard. Peak area response is plotted against amount injected.

Fig. 3. Programmed-temperature separation of sulfides. Elution order the same as in Fig. 1 (main peaks). Late-eluting components are impurities.

Temperature programming both shortened the analysis time and eliminated the peak distortion observed with thiodiglycol in Fig. 1. Fig. 3 shows the results obtained using a Perkin-Elmer Model 900 gas chromatograph, injection port and detector temperatures of 240° and 260°, respectively, and a column temperature linearly programmed from 110° to 230° at 8°/min. The helium flow rate was 40 ml/min.

There was no indication of a need to "saturate" these columns with the sample materials. The detector responses per microgram of sulfide injected was the same for the first run in the morning as for the tenth subsequent run.

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