This preliminary result is considered as a valuable new development in the range of immunochemical detection techniques. Probably, the detection limit can be significantly improved.

d. Attempts to detect protein adducts

As described earlier, there are clearcut advantages in the use of protein adducts for retrospective detection of exposure to sulfur mustard. The adducts are longer-lived than those with DNA, which are usually removed by cellular repair systems. Moreover, ca. 10^3 x larger amounts of sulfur mustard are bound to protein than to DNA in human blood. Presumably, this is probably also the case in skin biopsies. On the other hand, the adducts with proteins are less defined and concentrated than those with DNA. It is difficult to find out which amino acid in proteins would form adducts preferentially with sulfur mustard (32). Therefore, it is also difficult to define which hapten should be synthesized for generation of antibodies.

In order to elucidate the structure of the products resulting from alkylation with sulfur mustard, simple model compounds (Figure 6) were synthesized of those amino acids

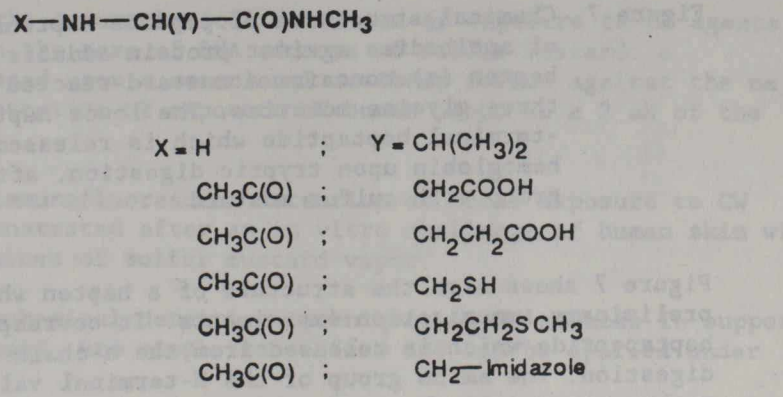

Figure 6 Chemical structures of model compounds used to elucidate the structures of sulfur mustard adducts with amino acids in proteins.

which are potential substrates for alkylation by sulfur mustard. Except for the α-amino group of valine (vide infra), the α-amino and α-carboxylic groups of the amino acids were acylated and amidated, respectively, as they are in proteins. The primary reaction products with sulfur mustard were identified by means of thermospray LC-MS. It was shown that the free carboxylic acid functions of glutamic and aspartic acid are alkylated, whereas cysteine and methionine react with mustard at the sulfur atom. Both ring nitrogens of histidine and the α-amino group of valine are alkylated.
A start was also made with the measurement of the relative rates of alkylation of the model peptides. One result of these measurements stands out quite clearly: the cysteine model compound reacts several orders of magnitude faster than the other model compounds. Since cysteine is reactive in various blood proteins and is also present in skin proteins, work is in progress on the