MUSTARD GAS

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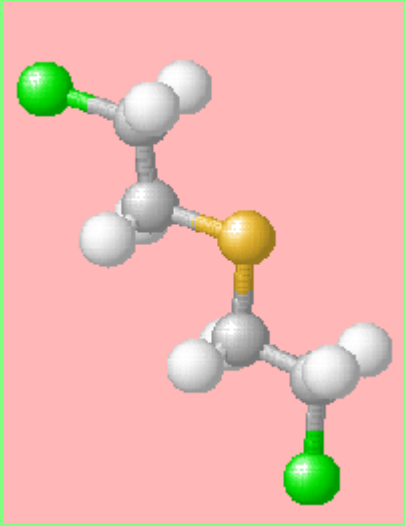

Molecule of the Month - June 1998
Also available: JSMol version.

Mustard gas is the common name given to 1,1-thiobis(2-chloroethane), a chemical warfare agent that is believed to have first been used near Ypres in Flanders on 12th July 1917. Its chemical formula is Cl-CH_2-CH_2-S-CH_2-CH_2-Cl

Its other names include **H, yprite, sulfur mustard** and **Kampstoff Lost**, but the name mustard gas became more widely used, because the impure "agent quality" is said to have an odour similar to that of mustard, garlic or horseradish. (8) When pure, it is in fact both odourless and colourless. (6)

It was synthesised much earlier than its first reported use, by a man named Frederick Guthrie in 1860, who reacted ethylene with Cl_2, and noticed the toxic effects it had on his own skin. (1) The effects of mustard gas exposure include the reddening and blistering of skin, and, if inhaled, will also cause blistering to the lining of the lungs, causing chronic impairment, or at worst, death. Exposure to high concentrations will attack the corneas of the eyes, eventually rendering the victim blind. (6)

Any area of the body which is moist is particularly susceptible to attack by mustard gas, because although it is only slightly soluble in water, which makes it difficult to wash off, hydrolysis (the splitting of a compund by water) is rapid, and occurs freely.

The reaction proceeds via this pathway:

```
          mustard gas
              |       nucleophilic attack of the carbon
              |       by the sulfide
              v
intermediate sulfonium salt
              |       attack by water
              |
              v
  hemi-mustard + HCl
              |       attack by water
              |
              v
  thiodiglycol + HCl
              |       internal displacement
              |
              v
  1,4 thioxane + HCl
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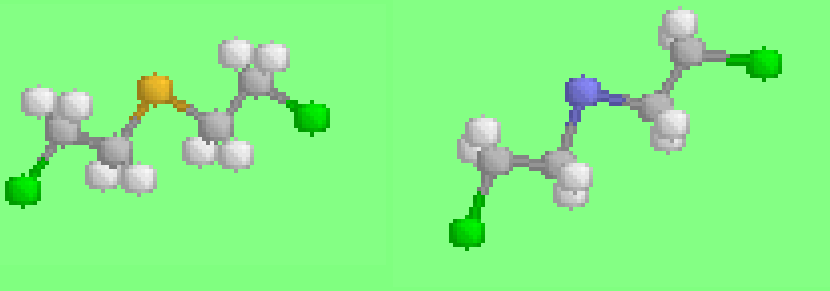
It is important to note here that not only are mustard gas and hemi-mustard both vesicants (blister skin), but the hydrolysis reaction also produces three molecules of HCl, which in itself is a skin irritant.

Despite the ease of hydrolysis, mustard gas in its solid form has been found to last underground for up to ten years. This is because, in an environment where the concentration of water is relatively low, the reaction pathway is able to proceed once, thiodiglycol is formed using most of the water available at the solid surface, but then the sulfonium intermediate reacts with this instead of another molecule of water, as the concentration of water molecules at the bulk surface is now

lower than the concentration of thiodiglycol. This produces stable, non-reactive sulfonium salts, which form a protective layer around the bulk material, and therefore prevent further reaction. (8)

Mustard Gas **N-mustard**



Mustard gas is a paticularly deadly and dehabilitating poison, but its real danger when it was first used in WW1, compared to other chemical warfare agents at the time, was the fact that it could penetrate all protective materials and masks that they had available at the time. (5) In more recent years, urethane was discovered to be resistant to mustard gas, and also to have the advantages of being tough, resistant to cut growth, and to be stable at a wide range of temperatures. (9)

One of the reasons that exposure to mustard gas must be prevented, rather than cured, is that detoxification is quite difficult due to its insolublity, and that the effects of mustard gas are devastating - essentially if the inhalation of the mustard gas itself does not kill you, it is very likely to cause cancer later in life. (7) During WW1, doctors were fairly helpless for treating victims, as the only means of detoxification was by oxidation with hypochlorite bleaches - $NaOCl^-$ and $(CaCOCl^-)_2$ (a super-chlorinated bleach) were most commonly used. (8)

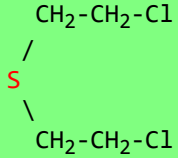
Detoxification is no longer such a problem, as there are several methods developed in recent years which are quite efficient. Both sulphur amines (sulphur dissolved in amines) (4) and magnesium monoperoxyphthalate (10) have been found to quite good decontaminants, but, the best method is the use of peroxy acids (RC(O)OOH, where R=C_7H_{15}, C_9H_{19}, $C_{11}H_{23}$, $C_{13}H_{27}$), as they react within a few seconds, and this rate of reaction can be enhanced further by use of a catalyst. (11)

Mustard Gas as an Anti-Cancer Agent

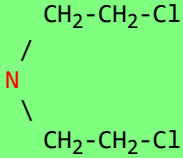
Mustard gas has always been seen as a particularly nasty poison, resulting in a painful and often slow death, and, ironically, whilst it causes cancer, it has also been used to help cure it. It was in 1919, not long after the first usage of mustard gas, that it was noted that victims had a low blood cell count, because the mustard gas attacked white blood cells, and bone marrow aplasia (breakdown).

Research then began in 1946 to show that nitrogen mustards (differing only from mustard gas due to the presence of a nitrogen atom, not a sulphur atom) reduced tumor growth in mice, via a mechanism whereby 2 strands of DNA are linked by a molecule of nitrogen mustard.

Mustard gas (sulphur mustard)



Nitrogen Mustard



It had already been shown that the sensitivity of the bone marrow of mice to mustard gas is similar to that of humans, and therefore resarch lead to clinical trials, and nitrogen mustards became part of modern chemotherapy treatment, being mainly used as a cure for cancer of the lmyph glands - Hodgkin's Disease. (3)

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