Chem Factsheet

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An Interesting Molecule

This Chem Factsheet is concerned with applying structural principles and other chemical priciples to the Sarin molecule.

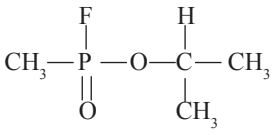
Sarin (also called GB) is a notorious organophosphorus compound which has been used during various worldwide conflicts as a weapon of mass destruction, even though its manufacture, storage and use was banned by the 1993 Chemical Weapons Convention. Ironically, it was discovered during research designed to develop new pesticides and so benefit mankind!

It is a colourless, odourless liquid. It is lethal, even at very low concentrations (e.g. 0.00007 g per kg of bodyweight) , with death following within a minute after exposure due to suffocation because of lung muscle paralysis. Furthermore, it is quite volatile and, when vapourised, it becomes far quicker acting.

Structure and synthesis

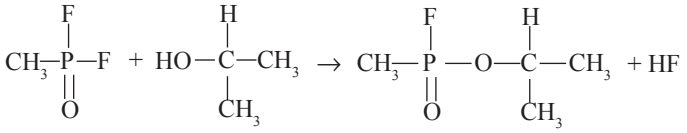
The structure of sarin is shown in Fig.1.

Figure 1



It is made by reacting methylphosphonyl difluoride [CH_3POF_2] with propan-2-ol as shown in Fig. 2.

Figure 2



This is a **condensation** reaction.

1. Why is this reaction classified as a condensation reaction?

Hyrogen fluoride is also formed. This is a very toxic substance and is removed from the reaction mixture by including 2-aminopropane [$CH_3CH(NH_2)CH_3$] (also called 2-propylamine or iso-propylamine) in the reaction mixture. The reaction converts the HF to a salt.

$CH_3CH(NH_2)CH_3 + HF \rightarrow [CH_3CH(NH_3^+)CH_3]F^-$

2. What type of reaction occurs between HF and the amine?
3. Does the HF act as an acid or a base? Explain.
4. Does the amine act as an acid or a base? Explain.

The inclusion of the amine also improves the yield of sarin obtained by the reaction shown in Fig. 2.

5. In terms of Le Chatelier's Principle, explain why the yield of sarin is increased by the presence of the amine.

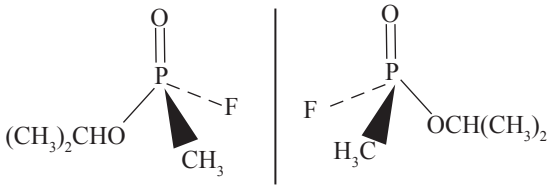
The synthesis of sarin can also be classified as a **nucleophilic substitution**.

6. Which of the reacting particles is the nucleophile? Explain why.
7. Which atom is attacked by the nucleophile? Explain why.
8. During the production of sarin, if a significant excess of propan-2-ol is used, a by-product with molecular formula $C_7H_{17}PO_3$ is formed. Explain the production of this molecule and draw its structure.

Chirality of sarin

Sarin exhibits **stereoisomerism**. It exists as a pair of **optical isomers** (enantiomers) because the molecule, as shown in Fig. 3, is **chiral**.

Figure 3



9. What are stereoisomers?
10. What general feature of the molecule's structure allows it to occur as two distinct isomers?
11. By what technique can the 2 optical isomers be distinguished?

An equimolar mixture of the 2 isomers is produced during the synthesis reaction. This is called a **racemic mixture** (or **racemate**) and shows zero optical activity.

12. Why does a racemic mixture show zero optical activity?
13. What sort of intermediate must be involved in the mechanism for the synthesis of sarin, in order to produce a racemic mixture? Explain.

When racemic mixtures are formed during the industrial synthesis of a drug in the pharmaceutical industry, great trouble in terms of time and money is taken to separate (**resolve**) the optical isomers in order to maximise the effectiveness of the required isomer and avoid harmful side effects caused by the other isomer.

14. Why, after manufacture, is sarin's racemic mixture ***not*** separated?

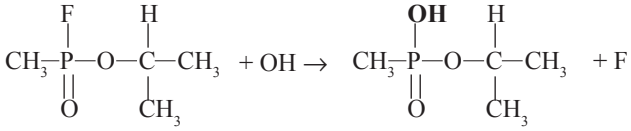
Destruction of sarin

According to the 1993 Chemical Weapons Convention any stockpiles of sarin must be destroyed to avoid their use as a weapon. Fortunately, because of the chemical nature of the molecule, this is *relatively* simple in principle.

The P-F bond is highly polar because of the extreme electronegativity of the fluorine atom. $\overset{\delta+}{P}\!\!-\!\!\overset{\delta-}{F}$

Hence, the P atom is prone to attack by nucleophiles such as water or hydoxide ions resulting in the nucleophilic substitution of the F atom by an OH group as shown in Fig.4. The P-F bond is said to be **hydrolysed** – literally "split by water".

Figure 4

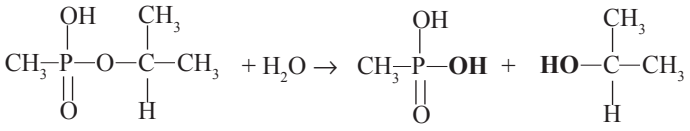


This reaction becomes more likely to occur at a high pH when there is a high concentration of nucleophilic hydroxide ions. Hence, sarin degrades slowly in the presence of water but can be rapidly "destroyed" using sodium hydroxide solution.

15. Earlier in this Chem FactSheet, the use of basic 2-aminopropane to remove HF was discussed. Why is this base *less* likely to cause the degradation of the sarin?

The initial breakdown product of sarin is 2-propyl methylphosphonic acid as shown in Fig. 4. This then degrades into non-toxic methylphosphonic acid and propan-2-ol by further hydrolysis as shown in Fig.5.

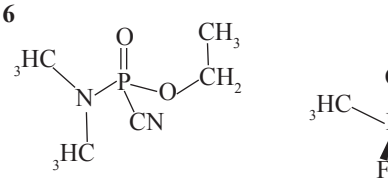
Figure 5



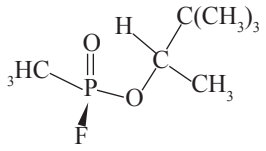
Similar molecules

Sarin is not the only organophosphorus molecule used as a chemical weapon. Tabun, soman and cyclosarin (see Fig. 6) are other closely-related examples which are all lethal, some more and some less than sarin!

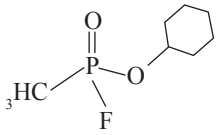
Figure 6



Tabun



Soman

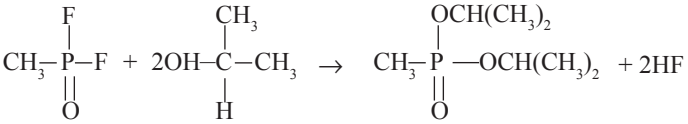


Cyclosarin

16. Remembering these molecules , including sarin, are **all** capable of causing lung muscle paralysis by inhibition of enzymes involved in nerve impulse transmission, by comparing their structures suggest which group of atoms is probably responsible for bonding to the enzyme's active site.

Answers

1. Two molecules are chemically linked to form a larger molecule by elimination of a small molecule (HF).
2. An acid-base reaction to form a salt.
3. Acid. HF donates a proton (H^+) to the amine.
4. Base. The amine accepts a proton (H^+) from HF.
5. The amine removes the HF produced by the sarin production (see Fig. 2). The reaction therefore shifts to the right to replace the HF removed. A shift to the right corresponds an increase in the yeild of sarin.
6. Propan-2-ol. The O atom in the OH group has lone pairs of electrons which it can donate to form a covalent bond.
7. The P atom of CH_3POF_2 which is very electron deficient (δ+) because it is bonded to very electronegative atoms – two F atoms and an O atom.
8. The second F atom is substituted by a propan-2-ol molecule.



9. Molecules with the same structural formula but different arrangements of their groups / atoms in space. Optical and EZ isomers are the two common types.
10. The P atom is bonded to four different groups making the molecule non-superimposeable on its own mirror image.
11. They rotate the plane of plane-polarised light in opposite directions.
12. The rotations of the two isomers cancel.
13. A planar intermediate is involved. This means there is a 50:50 chance of attack by the nucleophile either above or below this plane. Attack "above" the plane produces one optical isomer while attack "below" produces the other optical isomer.
14. Worries about the side effects or reduced efficiency are not very important when the molecule is being used as a weapon of mass destruction!
15. It is a weak base.
16. O=P–O which is common to all.

Acknowledgements: *This Factsheet was researched and written by Mike Hughes.*
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