SCIENCE FOR DIPLOMATS

Tuesday 12 March 2019
Ooms Room 13:30 - 14:45
Light Lunch Available at 13:00

The Expanding Chemical Universe: From C1 to C10 and beyond

A lunch time mission to boldly go where no delegation has gone before...
The Expanding Chemical Universe:
From C1 to C10 and Beyond

Science for Diplomats at EC-90
The Hague, 12 March 2019

Starring:
Mr Cheng Tang, SAB Chair
Dr Jonathan E. Forman, Science Policy Adviser and SAB Secretary
Mr Peter Brud, Ms Maria Hemme, and Ms Giovanna Pontes
Office of Strategy and Policy

With special guest star Ms Andrea Dymytrova
Let us Know You are Here!

In Honour of the International Year of the Periodic Table of Chemical Elements 2019

Colour in your “element” on the Periodic Table of States Parties outside the Ooms Room
Scheduled Chemicals under the Chemical Weapons Convention (CWC)

**Schedule 1**

**Guidelines for Schedule 1**

The following criteria shall be taken into account in considering whether a toxic chemical or precursor should be included in Schedule 1:

(a) It has been developed, produced, stockpiled or used as a chemical weapon as defined in Article 1;

(b) It poses otherwise a high risk to the object and purpose of this Convention by virtue of its high potential for use in activities prohibited under this Convention because one or more of the following conditions are met:

(i) It possesses a chemical structure closely related to that of other toxic chemicals listed in Schedule 1, and has, or can be expected to have, comparable properties;

(ii) It possesses such lethal or incapacitating toxicity as well as other properties that would enable it to be used as a chemical weapon;

(iii) It may be used as a precursor in the final single technological stage of production of a toxic chemical listed in Schedule 1, regardless of whether this stage takes place in facilities, munitions or elsewhere;

(c) It has little or no use for purposes not prohibited under this Convention.

**Schedule 2**

**Guidelines for Schedule 2**

The following criteria shall be taken into account in considering whether a toxic chemical not listed in Schedule 1, or a precursor to a chemical listed in Schedule 1, or a chemical listed in Schedule 2, part A or to a chemical in Schedule 2, part A, should be included in Schedule 2:

(a) It possesses a significant risk to the object and purpose of this Convention because it possesses such lethal or incapacitating toxicity as well as other properties that could enable it to be used as a chemical weapon;

(b) It may be used as a precursor in one of the chemical reactions at the final stage of formation of a chemical listed in Schedule 1 or Schedule 2, part A;

(c) It possesses a significant risk to the object and purpose of this Convention by virtue of its importance in the production of a chemical listed in Schedule 1 or Schedule 2, part A;

(d) It is not produced in large commercial quantities for purposes not prohibited under this Convention.

**Schedule 3**

**Guidelines for Schedule 3**

The following criteria shall be taken into account in considering whether a toxic chemical or precursor, not listed in other Schedules, should be included in Schedule 3:

(a) It has been developed, produced, stockpiled or used as a chemical weapon;

(b) It poses otherwise a high risk to the object and purpose of this Convention because it possesses such lethal or incapacitating toxicity as well as other properties that might enable it to be used as a chemical weapon;

(c) It may be used as a precursor in the final single technological stage of production of a toxic chemical listed in Schedule 1 and Schedule 2, part B;

(d) It may be produced in large commercial quantities for purposes not prohibited under this Convention.

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**ORGANISATION FOR THE PROHIBITION OF CHEMICAL WEAPONS**

Working Together for a World Free of Chemical Weapons
Scheduled Chemicals under the Chemical Weapons Convention (CWC)

“Given the substantial changes in chemistry and chemical industry since the schedules were finalised a quarter century ago, a review of the schedules should be considered to assess whether: (a) the chemicals currently listed are in the appropriate Schedule, and (b) any toxic chemicals or specific precursors should be added to or removed from the Schedules.”
Given the substantial changes in chemistry and chemical industry since the schedules were finalised a quarter century ago, a review of the schedules should be considered to assess whether:

(a) the chemicals currently listed are in the appropriate Schedule, and
(b) any toxic chemicals or specific precursors should be added to or removed from the Schedules.

The Director-General has received a joint proposal from Canada, the Netherlands, and the United States of America for a change to Schedule 1 of the Annex to the Chemical Weapons Convention for the consideration of the Conference of the States Parties to the Convention.
Before We Begin...

- Listen to the Science Adviser
- **Stamp words as you hear them!**
- A stamped horizontal, vertical or diagonal row of 5 “wins”
- 1<sup>st</sup> person to get a Bingo wins “acetylcholinesterase”
- Next prizes are “Schedule 1” Key Chains
- After 1<sup>st</sup> Bingo, 1<sup>st</sup> Bingo in a chair wins a model kit
Before We Begin...

- Listen to the Science Adviser
- **Stamp words as you hear**

And horizontal, vertical or diagonal row of 5 “wins”

- 1st person to get a Bingo wins “acetylcholinesterase”
- Next prizes are “Schedule 1” Key Chains
- After 1st Bingo, 1st Bingo in a chair wins a model kit
Science for Diplomats at EC-88

The Chemical Universe: Scheduled and Unscheduled

Tuesday, 10 July 2018
Ooms Room, OPCW
13:30 - 14:45
Light lunch served at 13:00
What Do You Remember?
Lets Quickly Review Where we left off from July

How are chemicals organized in the Schedules?
### How are chemicals organized in the Schedules?

<table>
<thead>
<tr>
<th>Family</th>
<th>No idea</th>
<th>Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Three Scheduled Chemicals</td>
<td>Me neither</td>
<td>Toxicity</td>
</tr>
<tr>
<td>You tell me</td>
<td>Groups</td>
<td>by threat to the convention and industrial relevance</td>
</tr>
<tr>
<td>Toxicity</td>
<td>Schedule 2</td>
<td>Gangnam style</td>
</tr>
<tr>
<td>Precursors</td>
<td>Bonds</td>
<td>Used as CW</td>
</tr>
<tr>
<td>Toxicity</td>
<td>Prohibited use</td>
<td>Common use</td>
</tr>
<tr>
<td>Commercial uses</td>
<td>Toxicity</td>
<td>Different use and toxicity</td>
</tr>
<tr>
<td>Millions</td>
<td>Tsousands</td>
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</tbody>
</table>

**OPCW**
Scheduled Chemicals under the Chemical Weapons Convention (CWC)

Schedule 1

Guidelines for Schedule 1
The following criteria shall be taken into account in considering whether a toxic chemical or precursor should be included in Schedule 1:

(a) It has been developed, produced, stockpiled or used as a chemical weapon as defined in Article II;
(b) It poses otherwise a high risk to the object and purpose of this Convention because of its high potential for use in activities prohibited under this Convention because one or more of the following conditions are met:
(i) It possesses such lethal or incapacitating toxicity as well as other properties that would enable it to be used as a chemical weapon;
(ii) It may be used as a precursor in the final single technological stage of production of a chemical listed in Schedule 3, regardless of whether this stage takes place in facilities, in munitions or elsewhere;
(c) It has little or no use for purposes not prohibited under this Convention.

Schedule 2

Guidelines for Schedule 2
The following criteria shall be taken into account in considering whether a toxic chemical not listed in Schedule 1 or a precursor to a Schedule 1 chemical or to a chemical listed in Schedule 2, part A, should be included in Schedule 2:

(a) It poses a significant risk to the object and purpose of this Convention because of its lethal or incapacitating property as well as other properties that would enable it to be used as a chemical weapon;
(b) It may be used as a precursor in the final single technological stage of production of a chemical listed in Schedule 1 or Schedule 2, part A;
(c) It poses a significant risk to the object and purpose of this Convention by virtue of its importance in the production of a chemical listed in Schedule 1 or Schedule 2, part A;
(d) It is not produced in large commercial quantities for purposes not prohibited under this Convention.

Schedule 3

Guidelines for Schedule 3
The following criteria shall be taken into account in considering whether a toxic chemical or precursor, not listed in other Schedules, should be included in Schedule 3:

(a) It has been produced, stockpiled or used as a chemical weapon;
(b) It poses otherwise a high risk to the object and purpose of this Convention because of its high potential for use in activities prohibited under this Convention because one or more of the following conditions are met:
(i) It possesses such lethal or incapacitating toxicity as well as other properties that would enable it to be used as a chemical weapon;
(ii) It may be used as a precursor in the final single technological stage of production of a chemical listed in Schedule 3, regardless of whether this stage takes place in facilities, in munitions or elsewhere;
(c) It has little or no use for purposes not prohibited under this Convention.

ORGANISATION FOR THE PROHIBITION OF CHEMICAL WEAPONS

Working Together for a World Free of Chemical Weapons

Schedule 2 Part A, Toxics Chemicals

Schedule 2 Part B, Precursors

Schedule 3 Part A, Toxics Chemicals

Schedule 3 Part B, Precursors

Relationship between Schedules, illustrated with sulfur mustard.
Scheduled Chemicals under the Chemical Weapons Convention (CWC)

### Schedule 1

**Guidelines for Schedule 1**
The following criteria shall be taken into account in considering whether a toxic chemical or precursor should be included in Schedule 1:

1. It has been developed, produced, stockpiled or used as a chemical weapon as defined in Article I.
2. It poses a significant risk to life or health, including through exposure that could enable it to be used.
3. It may be used as a precursor in the production of a chemical listed in Schedule 2 or Schedule 3, part A.
4. It is not produced in large commercial quantities for purposes not prohibited under this Convention.

### Schedule 2

**Guidelines for Schedule 2**
The following criteria shall be taken into account in considering whether a chemical not listed in Schedule 1 or a precursor to a chemical listed in Schedule 2, part A, should be included in Schedule 2:

1. It has been developed, produced, stockpiled or used as a chemical weapon as defined in Article I.
2. It poses a significant risk to life or health, including through exposure that could enable it to be used.
3. It may be used as a precursor in the production of a chemical listed in Schedule 1 or Schedule 2, part A.
4. It is not produced in large commercial quantities for purposes not prohibited under this Convention.

### Schedule 3

29 Single chemical substances

Chemicals, as precursors, not listed in other Schedules, should be included in Schedule 3:

1. It has been developed, produced, stockpiled or used as a chemical weapon as defined in Article I.
2. It poses a significant risk to life or health, including through exposure that could enable it to be used.
3. It may be used as a precursor in the production of a chemical listed in Schedule 1 or Schedule 2, part A.
4. It is not produced in large commercial quantities for purposes not prohibited under this Convention.

#### 3 Groups of chemicals

(15 total chemical substances)

- **Type of Chemicals**
  - Sulfur analogs (15)
  - Oxime analogs (4)
  - Other analogs (2)

#### Shown here as pairs of stereoisomers

Schedule 1: Part A, Toxins and Chemicals

Schedule 2: Part B, Precursors

Schedule 3: Used in the production of Schedule 1 chemicals

**Relationship between Schedules, illustrated with sulfur mustard.**

**Organisation for the Prohibition of Chemical Weapons**

Working together for a world free of chemical weapons.

 OGow on Twitter | OGow on Facebook | OGow on LinkedIn | OGow on Instagram | OGow on YouTube

**Scheduled chemicals, including those in schedules 1 and 2, can have scientifically and economically important uses. This chart captures the number of yearly scientific publications that refer to them.**
and 11 “families” of chemical weapons agents and precursors
5 in Schedule 1, 6 in Schedule 2

All 11 families cover organophosphorus chemicals (8) or amines (3)
These types of chemicals are also Scheduled as specific chemicals and in groups
Let's quickly review where we left off from July.

How are chemicals organized in the Schedules?

How many actual chemicals are listed in the Schedules?
How many actual chemicals are listed in the Schedules?

- trillions
- infinity plus 1
- with the additions
- infinity
- millions
- infinite
- to infinity and beyond
- 150 possible millions
- infinity - 3
- hundreds

Answers from Participants
How Many Actual Chemicals are in the Schedules?

<table>
<thead>
<tr>
<th>Schedule 3</th>
<th>Schedule 1</th>
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</thead>
</table>

**A. Toxic chemicals:**

<table>
<thead>
<tr>
<th>Number</th>
<th>Name of Chemical</th>
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<tbody>
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<td>1</td>
<td>Acetone</td>
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<tr>
<td>2</td>
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<td>3</td>
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<tr>
<td>100</td>
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</table>

**B. Preservatives:**

- (1) Acetic acid
- (2) Acetic ester
- (3) Acetic anhydride
- (4) Acetic acid
- (5) Acetic ester
- (6) Acetic anhydride
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- (98) Acetic ester
- (99) Acetic anhydride
- (100) Acetic acid

**Guidelines for Schedule 3:**

- (a) It has been produced, stockpiled, or used as a chemical weapon.
- (b) It poses a risk to the object and purpose of this Convention because it possesses such lethal or incapacitating toxicities as well as other properties that might enable it to be used as a chemical weapon.
- (c) It may be produced in large commercial quantities for purposes not prohibited under this Convention.
How Many Actual Chemicals are in the Schedules?

All the listed specific chemicals have a Chemical Abstracts Service (CAS) Registry Number.

Specific chemicals

<table>
<thead>
<tr>
<th>Schedule 1</th>
<th>(CAS registry number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Phosgene</td>
<td>(75-47-8)</td>
</tr>
<tr>
<td>(2) Cyanogen chloride</td>
<td>(506-77-4)</td>
</tr>
<tr>
<td>(3) Hydrogen cyanide</td>
<td>(140-08-3)</td>
</tr>
<tr>
<td>(4) Chloroform</td>
<td>(68-12-2)</td>
</tr>
</tbody>
</table>

B. Pesticides

- A.
  - Toxic chemicals:
    - Aminonitrosamines: N,N-Diethyl-1,3-Diarylureas
    - Methyl parathion-methyl
    - Sequenax: 1,3,5-Trichloro-1,1,1-trifluorobenzene
    - Ethion: (S)-3-Quinuclidine benzenesulfonate
  - Pesticides:
    - Aminonitrosamines: N,N-Diethyl-1,3-Diarylureas
    - Methyl parathion-methyl
  - Exemption:
    - Monocrotophos (p-ethyl-5-phenylloxazin-2-one)
    - Chlorpyrifos (4,4',5,5'-Tetrachlorobiphenyl-2,2'-pentachlorophenyl)
- C. Miscellaneous:
  - 2,2-Dichloro-1,1-Dihydroxyethane (76-85-7)
  - Methyl parathion-methyl (888-83-9)
  - Diethyl phosphates (724-36-0)
  - Methyl parathion-methyl (724-36-0)
  - Dichloroacetic acid (112-87-5)
  - Ethylene dibromide (107-71-8)

ORGANISATION FOR THE PROHIBITION OF CHEMICAL WEAPONS

Working together for a world free of chemical weapons.

OPCW
There is an infinite (indeterminate) number of Scheduled Chemicals (with three exemptions: "infinity minus three")
To Make Sense of all of this Requires a Discussion of Chemistry (Atoms, Molecules and Math!)
What do Scheduled Chemicals Look Like?

Guidelines for Schedule 1
The following criteria shall be taken into account in considering whether a toxic chemical or precursor should be included in Schedule 1:
(a) It has been developed, produced, stockpiled or used as a chemical weapon as defined in Article II;
(b) It poses otherwise a high risk to the object and purpose of this Convention because of its high potential for use in activities prohibited under this Convention because or one or more of the following conditions are met:
(i) It possesses a chemical structure closely related to that of other toxic chemicals listed in Schedule 1, and has, or can be expected to have, comparable properties;
(ii) It possesses such lethal or incapacitating toxicity as well as other properties that would enable it to be used as a chemical weapon;
(iii) It may be used as a precursor in the final single technological stage of production of a toxic chemical listed in Schedule 1, regardless of whether this stage takes place in facilities, in munitions or elsewhere;
(c) It has little or no use for purposes not prohibited under this Convention.

Guidelines for Schedule 2
The following criteria shall be taken into account in considering whether a toxic chemical not listed in Schedule 1 or a precursor to a chemical listed in Schedule 1, or a chemical in Schedule 2, part A, should be included in Schedule 2:
(a) It poses a significant risk to the object and purpose of this Convention because it possesses such lethal or incapacitating toxicity as well as other properties that could enable it to be used as a chemical weapon;
(b) It may be used as a precursor in one of the chemical reactions at the final stage of formation of a chemical listed in Schedule 1 or Schedule 2, part A;
(c) It poses a significant risk to the object and purpose of this Convention by virtue of its importance in the production of a chemical listed in Schedule 1 or Schedule 2, part A;
(d) It is not produced in large commercial quantities for purposes not prohibited under this Convention.

Guidelines for Schedule 3
The following criteria shall be taken into account in considering whether a toxic chemical or precursor, not listed in other Schedules, should be included in Schedule 3:
(a) It has been developed, produced, stockpiled or used as a chemical weapon;
(b) It poses otherwise a risk to the object and purpose of this Convention because it possesses such lethal or incapacitating toxicity as well as other properties that might enable it to be used as a chemical weapon;
(c) It poses a risk to the object and purpose of this Convention by virtue of its importance in the production of one or more chemicals listed in Schedule 1 or Schedule 2, part B;
(d) It may be produced in large commercial quantities for purposes not prohibited under this Convention.

Schedule 2 Part A. Toxic Chemicals

Schedule 2 Part B. Precursors

Schedule 3 Part A. Toxic Chemicals

Schedule 3 Part B. Precursors

Relationship between Schedules, illustrated with sulfur mustard.
What do Scheduled Chemicals Look Like?

Schedule 2

Guidelines for Schedule 3
The following criteria shall be taken into account in considering whether a toxic chemical or precursor, not listed in other Schedules, should be included in Schedule 3:
(a) It has been produced, stockpiled or used as a chemical weapon;
(b) It poses otherwise a risk to the object and purpose of this Convention because it possesses such lethal or incapacitating toxicity as well as other properties that might enable it to be used as a chemical weapon;
(c) It poses a risk to the object and purpose of this Convention by virtue of its importance in the production of one or more chemicals listed in Schedule 1 or Schedule 3, part B;
(d) It may be produced in large commercial quantities for purposes not prohibited under this Convention.

Schedule 3 Part A. Toxic Chemicals

Schedule 3 Part B. Precursors

ORGANISATION FOR THE PROHIBITION OF CHEMICAL WEAPONS
Working Together for a World Free of Chemical Weapons

Relationship between Schedules, illustrated with sulfur mustard.

Important note: This chart captures the number of yearly scientific publications that refer to these.
What do Scheduled Chemicals Look Like?

Water molecules!

DOI: 10.1038/ncomms14313

What distinguishes liquid water from liquid sarin? VERY different molecular structures!
Recognizing How a Chemical “Behaves” is all About the Atoms!

Atom Models in History

The last 200 years have seen ideas about the atom develop from Dalton’s “indivisible atom” where it is the smallest thing possible; to the discovery of sub-atomic particles (electrons, protons & neutrons); to sophisticated understandings about where these particles are found and how they behave.

Each model has allowed hypotheses to be made & predictions tested. This has lead to the development of our knowledge as the technology has improved.

video link
Recognizing How a Chemical “Behaves” is all About the Atoms!

When Niels Bohr won the Nobel Prize in 1922, the Carlsberg brewery gave him a free house. That house was right next door to the brewery and had unlimited free beer on tap.

Each model has allowed hypotheses to be made & predictions tested. This has lead to the development of our knowledge as the technology has improved.
Recognizing How a Chemical “Behaves” is all About the Atoms!
There are 118 Types of Atoms (at least for now...)

### THE PERIODIC TABLE OF ELEMENTS

<table>
<thead>
<tr>
<th>Symbol Key</th>
<th>Groups of elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atomic number</td>
<td>Element symbol</td>
</tr>
<tr>
<td>Atomic number</td>
<td>Element symbol</td>
</tr>
</tbody>
</table>

- **s block elements**
- **p block elements**
- **d block elements**
- **f block elements**

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There are 118 Types of Atoms (at least for now…)

THE PERIODIC TABLE OF ELEMENTS

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<td></td>
<td>f block elements</td>
</tr>
</tbody>
</table>

Atoms found in chemical weapon agents

Additional atoms (halogens) that might be found in Schedule 2B.05 chemicals
There are 118 Types of Atoms (at least for now...)

**THE PERIODIC TABLE OF ELEMENTS**

**Schedule 2B.04:** All atoms are theoretically possible! ("X" can be anything except Carbon)

Chemicals, except for those listed in Schedule 1, containing a phosphorus atom to which is bonded one methyl, ethyl or propyl (normal or iso) group but not further carbon atoms

An indeterminate number of possibilities...

**Additional atoms (halogens) that might be found in Schedule 2B.05 chemicals**
Chemicals are Defined by the Types of Atoms and Bonds

**FUNCTIONAL GROUPS IN ORGANIC CHEMISTRY**

Functional groups are groups of atoms in organic molecules that are responsible for the characteristic chemical reactions of those molecules. In the general formulae shown below for each functional group, 'R' represents the rest of the molecule, and 'X' represents any halogen atom.

- **Hydrocarbons**
- **Simple Oxygen Heteroatoms**
- **Halogen Heteroatoms**
- **Carbonyl Compounds**
- **Nitrogen-Based**
- **Sulfur-Based**
- **Aromatic**

### Examples

- **Alkane**
  - Naming: -ane
  - E.g.: ethane

- **Alkene**
  - Naming: -ene
  - E.g.: ethene

- **Alkyne**
  - Naming: -yne
  - E.g.: ethyne

- **Alcohol**
  - Naming: -ol
  - E.g.: ethanol

- **Ether**
  - Naming: -ene oxide
  - E.g.: ethene oxide

- **Epoxyde**
  - Naming: -ene oxide
  - E.g.: ethene oxide

- **Haloalkane**
  - Naming: halo-
  - E.g.: chloroethene

- **Aldehyde**
  - Naming: -al
  - E.g.: ethanal

- **Ketone**
  - Naming: -one
  - E.g.: propanone

- **Carboxylic Acid**
  - Naming: -oic acid
  - E.g.: ethanoic acid

- **Acid Anhydride**
  - Naming: -oic anhydride
  - E.g.: ethanoic anhydride

- **Ester**
  - Naming: -oate
  - E.g.: ethanoate

- **Amide**
  - Naming: -amide
  - E.g.: ethanamide

- **Acyl Halide**
  - Naming: -yl halide
  - E.g.: ethanoyl chloride

- **Amine**
  - Naming: -amine
  - E.g.: ethanamine

- **Nitrile**
  - Naming: -nitrile
  - E.g.: ethanenitrile

- **Imine**
  - Naming: -imine
  - E.g.: ethanimine

- **Isocyanate**
  - Naming: -yl isocyanate
  - E.g.: ethyl isocyanate

- **Azo Compound**
  - Naming: azo-
  - E.g.: azoethane

- **Thiol**
  - Naming: -thiol
  - E.g.: methanethiol

- **Arene**
  - Naming: -yl benzene
  - E.g.: ethyl benzene

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Chemicals are Defined by the Types of Atoms and Bonds

Specific examples listed in the Schedules (Possible to have the others in scheduled chemicals as well)
Chemical Behavior is Dictated by the Types of Atoms and Bonds

**ORGANIC FUNCTIONAL GROUP INTERCONVERSIONS**

**ALKANE**
- Cracking (variety of products)
- H₂, Ni cat., 150°C, 5 atm

**ALKENE**
- Polymerisation
  - Addition Polymer
- CONC. H₂O₂, 20°C, 30 min, conc. H₂O₂ cat.
- H₂SO₄, heat (1° alcohol only)
- HOT, CONC. KOH, alcoholic solution

**EPOXIDE**
- Polymerisation

**HALOALKANE**
- R–X
- H₂, Ni cat., 250–300°C, 10–20 atm (ethene only)
- Other alkenes: RCO₂H in CH₂Cl₂
- H₂, Ni cat., 150°C, 5 atm
- H₂O, warm
- H₂O₂, 20°C, 30 min, conc. H₂O₂ cat.
- H₂SO₄, heat (1° alcohol only)
- HOT, CONC. KOH, alcoholic solution

**HETEROALKANE**
- R–X
- CONC. H₂O₂, 20°C, 30 min, conc. H₂O₂ cat.

**ALCOHOL**
- R–OH
- R–OH, reflux
- NaOH (aq), reflux
- KON, ethanolic solution, reflux
- CONC. NH₃ heat in sealed tube

**ACID ANHYDRIDE**
- R–CO₂R₂
- C₆H₅CO₂H, H₂O, reflux

**ALKYL HYDROXISULFATE**
- R–OSO₃H
- H₂O, warm

**ALDEHYDE**
- R–CHO
- R–CHO, reflux

**EPHER**
- R–O–R₂

**AMIDE**
- R–CONH₂
- R–CONH₂, reflux

**ACYL CHLORIDE**
- R–COCl
- SO₃, PO₃, or PO₄, reflux

**AMINE**
- R–NH₂
- R–NH₂, reflux (gives 1° amide)

**ACYL CHLORIDE**
- R–COCl
- SO₃, PO₃, or PO₄, reflux

**ESTER**
- R–CO₂R₂
- ROH, room temp.

**KETONE**
- R–C–O–R₂
- R–C–O–R₂, reflux (gives 2° amide)

**NITRILE**
- R–C≡N
- R–C≡N, reflux

**CARBOXYLIC ACID**
- R–CO₂H
- R–CO₂H, reflux, H₂O or OH⁻

**REACTIONS KEY**
- ADDITION
- SUBSTITUTION
- OXIDATION
- REDUCTION
- ELIMINATION
- HYDROLYSIS
- ACYLATION
- ESTERIFICATION
- OTHER

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What do Scheduled Chemicals Look Like?

“Double Bond”

“Single Bond”

“Triple Bond”

Guidelines for Schedule 3
The following criteria shall be taken into account in considering whether a toxic chemical or precursor, not listed in other Schedules, should be included in Schedule 3:
(a) It has been produced, stockpiled or used as a chemical weapon;
(b) It poses otherwise a risk to the object and purpose of this Convention because it possesses such lethal or incapacitating toxicity as well as other properties that might enable it to be used as a chemical weapon;
(c) It poses a risk to the object and purpose of this Convention by virtue of its importance in the production of one or more chemicals listed in Schedule 1 or Schedule 2 part B;
(d) It may be produced in large commercial quantities for purposes not prohibited under this Convention.

Schedule 3 Part A. Toxic Chemicals

Schedule 3 Part B. Precursors

“Triple Bond”

“Single Bond”
Colour scheme of your model kit

<table>
<thead>
<tr>
<th>Colour Code for Chemical Elements typically used in models</th>
<th>In the Structures of Relevance to the Annex on Chemicals:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon (C) ●</td>
<td>Carbon atoms (C) have four bonds</td>
</tr>
<tr>
<td>Hydrogen (H) ○</td>
<td>If less than four bonds are shown in shorthand, the missing bonds are always C to H</td>
</tr>
<tr>
<td>Nitrogen (N) ●</td>
<td>Chlorine and Fluorine atoms (Cl and F) have one bond</td>
</tr>
<tr>
<td>Phosphorus (P) ●</td>
<td>Hydrogen atoms (H) have one bond</td>
</tr>
<tr>
<td>Arsenic (As) ●</td>
<td>Nitrogen atoms (N) have three or four bonds</td>
</tr>
<tr>
<td>Chlorine (Cl) ●</td>
<td>○ four bonds are only for the “salt” form</td>
</tr>
<tr>
<td>Fluorine (F) ●</td>
<td>○ Oxygen atoms (O) have two bonds</td>
</tr>
<tr>
<td>Sulfur (S) ●</td>
<td>○ Phosphorus and Arsenic atoms (P and As) can have three, four, five or six bonds</td>
</tr>
<tr>
<td>Oxygen (O) ●</td>
<td>○ In the form of a nerve agent P has five bonds - three single bonds and one double bond</td>
</tr>
</tbody>
</table>

Double bond

Sarin

Single bond

Nitrogen mustard (HN-3)

Models

Translation

“Shorthand” structures

Graphical representation. These pictures translate the colour of the atoms into the chemical element associated to it, and illustrate the connection between the atoms. This is an intermediate representation to the “shorthand” used by chemists.

This is a format often used by chemists. It allows bonds between carbon atoms (C) to be shown as connected lines: C atoms that are located at each point where a line connects to other lines or where a line terminates. Additionally, bonds between C and H are not shown for easier visualisation of the structure. Only C-H bonds are hidden, all other bonds are shown.
Colour scheme of your model kit

Molecular structure = Connected atoms

Sarin

It’s ok to be lazy and not use the letter “C” and not show the H atoms
Molecular structure = Connected atoms

It’s ok to be lazy and not use the letter “C” and not show the H atoms

Simple rules:
Point where a line ends or intersects with other lines = a “C” (carbon)
“C” always is connected to 4 “lines”
The missing lines are single bonds to “H” (hydrogen)
The Problem with Lazy...

The same or different?
The Problem with Lazy...

The same!

Both are C10 with identical connectivity between atoms

- Molecules are not “rigid” and can exist and be illustrated in a variety of configurations!
Tuesday 12 March 2019
Ooms Room 13:30 - 14:45
Light Lunch Available at 13:00

The Expanding Chemical Universe: From C1 to C10 and beyond

A lunch time mission to boldly go where no delegation has gone before...
Example of a Specific Chemical: Schedule 3B.14

Thionyl chloride
CAS 7719-09-7

From OPCW Handbook on Chemicals

From chemspider.com
Understanding Scheduled Chemicals

- Example of a Group of Related Chemicals: Schedule 1A.04

**Sulfur mustards:**

- 2-Chloroethylchloromethylsulfide
- Bis(2-chloroethyl)sulfide
- Bis(2-chloroethylthio)methane
- Bis(2-chloroethylthio)ethane
- 1,3-Bis(2-chloroethylthio)-n-propane
- 1,4-Bis(2-chloroethylthio)-n-butane
- 1,5-Bis(2-chloroethylthio)-n-pentane
- Bis(2-chloroethylthiomethyl)ether
- O-Mustard: Bis(2-chloroethylthioethyl)ether

**Chemical Structures:**

![Chemical Structures of Sulfur Mustards](image-url)
Understanding Scheduled Chemicals

- Example of a Group of Related Chemicals: Schedule 1A.04

**Sulfur mustards:**

- 2-Chloroethyl chloromethyl sulfide
- Mustard gas: Bis(2-chloroethyl)sulfide
- Bis(2-chloroethylthio)methane
- Sesquimustard: 1,2-Bis(2-chloroethylthio)ethylene
- 1,3-Bis(2-chloroethylthio)-n-propane
- 1,4-Bis(2-chloroethylthio)-n-butane
- 1,5-Bis(2-chloroethylthio)-n-pentane
- Bis(2-chloroethylthiomethyl)ether
- O-Mustard: Bis(2-chloroethylthioethyl)ether

 tuần

(2625-76-5)
(505-60-2)
(63869-13-6)
(3563-36-8)
(63905-10-2)
(142868-93-7)
(142868-94-8)
(63918-90-1)
(63918-89-8)
Understanding Scheduled Chemicals

Example of a Group of Related Chemicals: Schedule 1A.04

Sulfur mustards:
- 2-Chloroethylchloromethyl sulfide (2625-76-5)
- Mustard gas: Bis(2-chloroethyl)sulfide (505-60-2)
- Bis(2-chloroethylthio)methane (63869-13-6)
- Sesquimustard: 1,2-Bis(2-chloroethylthio)ethane (3563-36-8)
- 1,3-Bis(2-chloroethylthio)-n-propane (63905-10-2)
- 1,4-Bis(2-chloroethylthio)-n-butane (142868-93-7)
- 1,5-Bis(2-chloroethylthio)-n-pentane (142868-94-8)
- Bis(2-chloroethylthiomethyl)ether (63918-90-1)
- O-Mustard: Bis(2-chloroethylthioethyl)ether (63918-89-8)

Cross-link between two guanine bases
Understanding Scheduled Chemicals

- Example of a Group of Related Chemicals: Schedule 1A.04

Sulfur mustards:
- Mustard gas: Bis(2-chloroethyl)sulfide
- 2-Chloroethylchloromethylsulfide (2625-76-5)
- Bis(2-chloroethylthio)methane (505-60-2)
- Sesquimustard: 1,2-Bis(2-chloroethylthio)ethane (3563-36-8)
- 1,3-Bis(2-chloroethylthio)-n-propane (63905-10-2)
- 1,4-Bis(2-chloroethylthio)-n-butane (142868-93-7)
- 1,5-Bis(2-chloroethylthio)-n-pentane (142868-94-8)
- Bis(2-chloroethylthio)methyl ether (63918-90-1)
- O-Mustard: Bis(2-chloroethylthioethyl)ether (63918-89-8)

Cross-link between two guanine bases
Understanding Scheduled Chemicals

- Example of a Group of Related Chemicals: Schedule 1A.04

Sulfur mustards:

- 2-Chloroethylchloromethylsulfide
- Mustard gas: Bis(2-chloroethyl)sulfide
- Bis(2-chloroethylthio)methane
- Sesquiumustard: 1,2-Bis(2-chloroethylthio)ethane
- 1,3-Bis(2-chloroethylthio)-n-propane
- 1,4-Bis(2-chloroethylthio)-n-butane
- 1,5-Bis(2-chloroethylthio)-n-pentane
- Bis(2-chloroethylthiomethyl)ether
- O-Mustard: Bis(2-chloroethylthioethyl)ether

Cross-link between two guanine bases
What About Families?

Expand your Chemical Universe
Construct a Molecule!

You are in possession of the
“O-Alkyl (≤ C10, incl. cycloalkyl) alkyl (Me, Et, n-Pr or i-Pr)-phosphonofluoridate” Construction Kit.

Instructions:

Your kit contains:
- 3 phosphonofluoridate moieties, this is a phosphorus center (P) bonded to two substituents
- Atoms (P, O) and one functional atom (O-)
- ≤ 2 carbon atoms (C), ≥ 3 carbon atoms (C)
- ≤ 6 hydrogen atoms (H), ≥ 7 hydrogen atoms (H)
- ≥ 2 C-C length bonds
- ≤ 2 C-O length bonds
- ≥ 2 C-N length bonds

Your task is to construct alkyl and/or cycloalkyl groups and build a member of the “O- Alkyl (≤ C10, incl. cycloalkyl) alkyl (Me, Et, n-Pr or i-Pr)-phosphonofluoridate” family of chemicals. To do so, you must construct alkyl and/or cycloalkyl groups and attach them to the two free pegs of the O and P atoms of the phosphonofluoridate moiety. Following the rules outlined in the instruction handout, points will be rewarded based on the type of structures assembled for each group, as shown on the score sheet. Prices will be given for those with the highest scores and for getting the structures right.

What is an “O-Alkyl (≤ C10, incl. cycloalkyl) alkyl (Me, Et, n-Pr or i-Pr)-phosphonofluoridate”?
What is an O-alkyl (=/< C10, incl. cycloalkyl) alkyl (Me, Et, n-Pr or i-Pr)-phophonoflouridate"?

schedule 1a01 warfare agent
“O - Alkyl (≤ C10, incl. cycloalkyl) alkyl (Me, Et, n-Pr or i-Pr) phosphonofluoridate”

A: “phosphonofluoridate”

B: the “carbon atom” is part of an alkyl group... which is Me, Et, n-Pr or i-Pr

C: There is one other alkyl group : “≤ C10, incl. cycloalkyl” attached to the “O” with the single bond...

(Me, Et, n-Pr, or i-Pr) (≤ C10, alkyl, including cycloalkyl”)
There is an Easier Way...

R = “the rest of the molecule” (a “moiety”)

R$^1 \leq C_{10}$ alkyl, including cycloalkyl

R$^2 = \text{Me, Et, n-Pr, i-Pr}$

Me, Et, i-Pr, n-Pr and alkyl/cycloalkyl...

Do you know what to do?
“Alkyl” is a Substructure of an “Alkane”

- An alkane is a molecule that is composed of carbon (C) and hydrogen (H) atoms
  - Each carbon atom has four single bonds – to four other atoms (can be carbon or hydrogen)
  - Each hydrogen atom has one single bond to a carbon atom

- Alkanes are a type of hydrocarbon

PART IX (Verification Annex)

ACTIVITIES NOT PROHIBITED UNDER THIS CONVENTION IN ACCORDANCE WITH ARTICLE VI

REGIME FOR OTHER CHEMICAL PRODUCTION FACILITIES

A. DECLARATIONS

List of other chemical production facilities

1. The initial declaration to be provided by each State Party pursuant to Article VI, paragraph 7, shall include a list of all plant sites that:

   (a) Produced by synthesis during the previous calendar year more than 200 tonnes of unscheduled discrete organic chemicals; or

   (b) Comprise one or more plants which produced by synthesis during the previous calendar year more than 30 tonnes of an unscheduled discrete organic chemical containing the elements phosphorus, sulfur or fluorine (hereinafter referred to as “PSF-plants” and “PSF-chemical”).

2. The list of other chemical production facilities to be submitted pursuant to paragraph 1 shall not include plant sites that exclusively produced explosives or hydrocarbons.
“Alkyl” is a Substructure of an “Alkane”

- An alkane is a molecule that is composed of carbon (C) and hydrogen (H) atoms
  - Each carbon atom has four single bonds – to four other atoms (can be carbon or hydrogen)
  - Each hydrogen atom has one single bond to a carbon atom

- Alkanes are a type of hydrocarbon
From C1 to C3...

- Does your C1 Alkane look like this?
  Methane, CH₄

- Now build a C2 alkane
  Ethane, C₂H₆

- And finally, build a C3 alkane
  Propane, C₃H₈
From C1 to C3...

- Does your C1 Alkane look like this?
  - Methane, CH₄

- Now build a C2 alkane
  - Ethane, C₂H₆

- And finally, build a C3 alkane
  - Propane, C₃H₈

Did anyone build one of these?

- Cyclopropane, C₃H₆
  - The smallest “cycloalkane”
Cycloalkanes

“Strained Bonds”

Six-membered ring allows for more optimal bonding geometry

Still ways to strain larger cycloalkanes!

“Cubane”
Cycloalkanes

CAS Registry Number: 13172-14-0
Formula: C₇H₁₂FO₂P
CA Index Name: Phosphonofluoridic acid, methyl-, bicyclo[2.2.0]hex-2-yl ester (7Cl,8Cl)

Other Names
Bicyclo[2.2.0]hexan-2-ol, methylphosphonofluoridate

Number of References
~1

Document Types
Journal

Properties
Predicted

Commercial Sources
Not Available

All connections that meet the “rules” for an alkane are allowed! (and some strained molecules may be unstable)
From “Alkanes” to “Alkyls”

- Remove one hydrogen atom (and the short bond to which is attached)
- Attach the “alkyl group” to another molecular structure through one of the free bonds in your kit!

From Methane to “Methyl”
\[
\text{CH}_4 \text{ to CH}_3\text{X}
\]

From Ethane to “Ethyl”
\[
\text{C}_2\text{H}_6 \text{ to CH}_3\text{CH}_2\text{X}
\]
What About Propane?

2 Isomers: “n-Pr” “i-Pr”
## Significance of Carbon Atoms: Additional Molecular Possibilities

<table>
<thead>
<tr>
<th>Number of Alkyl Carbon Atoms</th>
<th>Parent Alkane Structures</th>
<th>Alkyl Group Structures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>C = 1</strong></td>
<td>CH₄</td>
<td>H₃C─X (&quot;methyl&quot; or &quot;Me&quot;)</td>
</tr>
<tr>
<td><strong>C = 2</strong></td>
<td>H₃C─CH₃</td>
<td>H₃C─X (&quot;ethyl&quot; or &quot;Et&quot;)</td>
</tr>
<tr>
<td><strong>C = 3</strong></td>
<td></td>
<td>H₃C─X (&quot;iso-propyl&quot; or &quot;i-Pr&quot;)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H₃C─X (&quot;n-propyl&quot; or &quot;n-Pr&quot;)</td>
</tr>
</tbody>
</table>

### For C = 1 to C = 4:

- **R² alkyl groups!**
- **From C1 to C4:**
  - 10 Alkanes provide 15 possible alkyl groups
  - All possibilities allowed for R¹ from C1 to C10!
Are these “O - Alkyl (≤ C10, incl. cycloalkyl) alkyl (Me, Et, n-Pr or i-Pr)-phosphonofluoridates”?

- **R² = Me, Et, n-Pr, i-Pr**
- **R¹ ≤ C₁₀ alkyl, including cycloalkyl**

<table>
<thead>
<tr>
<th>R¹</th>
<th>R²</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>C7</td>
<td>Et</td>
<td>Yes</td>
</tr>
<tr>
<td>C7</td>
<td>Me</td>
<td>Yes</td>
</tr>
<tr>
<td>C₁₀</td>
<td>i-Pr</td>
<td>Yes</td>
</tr>
<tr>
<td>C₁₀</td>
<td>C₄</td>
<td>No</td>
</tr>
<tr>
<td>C₁₁</td>
<td>C₄</td>
<td>No</td>
</tr>
</tbody>
</table>

(both are the same)
Your Turn to Explore “Chemical Space”

Expand your Chemical Universe
Construct a Molecule!
You are in possession of the
“O-Alkyl (≤ C10, incl. cycloalkyl) alkyl (Me, Et, n-Pr or i-Pr) phosphonofluoridate” Construction Kit.

Instructions:
Your kit contains:
- 1 phosphonofluoridate molecule, this is a phosphorus-centric (P) bound to two oxygen.
- 15 carbon atoms (C), one bonded to P.
- 13 carbon atoms (C), eight without bonds.
- 28 hydrogen atoms (H), each attached to a 2 cm length bar(s).
- 23 bar(s) 2.5 cm length bonds.

Your task is to construct alkyl and/or cycloalkyl groups and build a member of the “O-Alkyl (≤ C10, incl. cycloalkyl) alkyl (Me, Et, n-Pr or i-Pr) phosphonofluoridate” family of chemicals. To do so, you must construct alkyl and/or cycloalkyl groups and link them to the two free pegs of the O and P atoms of the phosphonofluoridate moiety. Following the rules outlined in the instruction handout, points will be awarded based on the type of structures assembled for each group, as shown on the score sheet. Points will be given for those with the highest scores and for getting the structures right.

Construct a Molecule
Score Sheet

Name: _______________________
Delegation: _________________

Your task is to construct a member of the “O-Alkyl (≤ C10, incl. cycloalkyl) alkyl (Me, Et, n-Pr or i-Pr) phosphonofluoridate” family of chemicals. To do so, you must construct alkyl and/or cycloalkyl groups and link them to the two free pegs of the O and P atoms of the phosphonofluoridate moiety. Following the rules outlined in the instruction handout, points will be awarded based on the type of structures assembled for each group, as shown on the score sheet. Points will be given for those with the highest scores and for getting the structures right.

<table>
<thead>
<tr>
<th>Chemical Structure</th>
<th>Points</th>
<th>Your Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear chain of carbon atoms</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Branched chain of carbon atoms</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Cyclic (a ring) (per ring)</td>
<td>+1</td>
<td></td>
</tr>
<tr>
<td>Fused ring</td>
<td>+2</td>
<td></td>
</tr>
<tr>
<td>Tertiary carbon atom (per C atom)</td>
<td>+2</td>
<td></td>
</tr>
<tr>
<td>Quaternary carbon atom (per C atom)</td>
<td>+3</td>
<td></td>
</tr>
<tr>
<td>Bicyclic</td>
<td>+3</td>
<td>Total:</td>
</tr>
</tbody>
</table>

Beginner Level

Intermediate Level

Expert Level

OPCW
### How Many Ways Can the Carbon and Hydrogen Atoms be Arranged?

<table>
<thead>
<tr>
<th>Carbon Atoms</th>
<th>Acyclic Isomers</th>
<th>Attachment Possibilities for R-X</th>
<th>Isomers with cycles</th>
<th>Attachment Possibilities for R-X</th>
<th>C1 to Cn Possibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
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<td>10</td>
<td>39</td>
<td>63</td>
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<tr>
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<td>5</td>
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<td>26</td>
<td>84</td>
<td>164</td>
</tr>
<tr>
<td>7</td>
<td>9</td>
<td>39</td>
<td>71</td>
<td>374</td>
<td>577</td>
</tr>
<tr>
<td>8</td>
<td>18</td>
<td>89</td>
<td>?</td>
<td>?</td>
<td>&gt; 666</td>
</tr>
<tr>
<td>9</td>
<td>35</td>
<td>211</td>
<td>?</td>
<td>?</td>
<td>&gt; 877</td>
</tr>
<tr>
<td>10</td>
<td>75</td>
<td>507</td>
<td>?</td>
<td>?</td>
<td>&gt; 1384</td>
</tr>
</tbody>
</table>

For C8 to C10 cycloalkyls: a computational study is required to find the possibilities!

> 1384 possible alkyl groups

R¹ ≤ C¹₀ alkyl, including cycloalkyl

R² = Me, Et, n-Pr, i-Pr

4 possible alkyl groups

> (4 X 1384 =) 5536

Schedule 1A.01

Parent Structures!
From C1 to Cn...

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<tr>
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<th>Attachment Possibilities</th>
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How Many Ways Can the Carbon and Hydrogen Atoms be Arranged?

For C8 to C10 cycloalkyls: a computational study is required to find the possibilities!

$R_1 \leq C_{10}$ alkyl, including cycloalkyl

$R_2 = \text{Me, Et, n-Pr, i-Pr}$

> 1384 possible alkyl groups

4 possible alkyl groups

4 x 1384 = 5536

Schedule 1A.01

Parent Structures!
“Parent Structures” are Far From the Whole Story...

- Molecules have 3-Dimensional Spatial Orientations

  “Mirror images” Cannot rotate and convert one for to the other!
“Parent Structures” are Far From the Whole Story...

- Molecules have 3-dimensional spatial orientations.

"Mirror images" cannot rotate and convert one into the other!
Stereoisomers Occur Whenever an Atom has Four Non-Equivalent Connections (“Chirality”)

Mirror Images

Cannot rotate and convert one for to the other!
Every 1A.01 parent structure has 2 stereoisomers for the spatial orientation around the phosphorus atom.

Every “chiral” center in an alkyl group generates additional stereoisomers.

Cannot rotate and convert one for to the other!
From C1 to C10, >> 5536!
(estimate does not reflect stereoisomers or C8-C10 cycloalkyls)
Thousands Possible, How Many Are Actually Known?

- CAS Database: **472 1A.01 chemical substances**
- OPCW handbook on chemicals: **376 1A.01 chemicals**
- OCAD V21: **569 1A.01 Mass Spectra**
The Most Famous Member of the
“O - Alkyl (≤ C10, incl. cycloalkyl) alkyl (Me, Et, n-Pr or i-Pr)-phosphonofluoridate” Family?
The Most Famous Member of the
“O - Alkyl (≤ C10, incl. cycloalkyl) alkyl (Me, Et, n-Pr or i-Pr)-phosphonofluoridate” Family?

Sarin: 17 CAS numbers!
- Stereoisomers
- Isotopic labels
- Specific combinations with other chemicals
The Most Famous Member of the "O - Alkyl (≤ C10, incl. cycloalkyl) alkyl (Me, Et, n-Pr or i-Pr)-phosphonofluoridate" Family?

Conference paper


Advice from the Scientific Advisory Board of the Organisation for the Prohibition of Chemical Weapons on isotopically labelled chemicals and stereoisomers in relation to the Chemical Weapons Convention

https://doi.org/10.1515/pac-2018-0803

Article note: A special issue containing invited papers on Innovative Technologies for Chemical Security, based on work done within the framework of the Chemical Weapons Convention.
Acetylcholinesterase Inhibition

created by Sofia Sola Sancho and Maria Hemme

Acetylcholinesterase

The primary toxicity of organophosphorus nerve agents results from the inhibition of the enzyme Acetylcholinesterase (AChE).

AChE is responsible for breaking down the neurotransmitter acetylcholine (ACh). This switches a nerve signal from on to off. If the enzyme is inhibited, ACh accumulates in the synapse and the signal continues to transmit.

Effects and Symptoms

Inhibition of AChE in muscarinic synapses (neuromuscular system) induces cholinergic crisis. Nicotinic synapses (central nervous system, e.g. brain) are also affected.

Symptoms include sweating, salivation, miosis (pinpoint pupils), paralysis, respiratory failure, seizures and eventually death.

Treatment

Atropine blocks the action of AChE at muscarinic receptors and treats SLUDGE.

Oximes such as 2-PAM (pyridostigmine) can reactivate inhibited AChE, but only before the aging process. (Fig. 3, Step 3)

Nerve Agent Molecular Shape and Size

Toxicity of an organophosphorus nerve agent depends on the ability to access the AChE binding site. Size, shape and hydrophobicity of the nerve agent exerts an effect. As alkyl substituents increase in size and degrees of freedom, toxicity decreases.

The spatial orientation (shape) of the molecule also matters, as illustrated by toxicity differences across the four stereoisomers of Soman.
Broad Coverage Under a Schedule? What Does it Accomplish?
How Many 1A.01 Chemicals can Inhibit Acetylcholinesterase?

From PDB Molecule of the Month, 2004
https://pdb101.rcsb.org/motm/54
How Many 1A.01 Chemical can Inhibit Acetylcholinesterase?

Sarin

$LD_{50} = 0.015 \text{ mg/kg (i.v. rabbit)}$*

larger than sarin, cyclo & branched alkyls
similar toxicity

C3/C1

C6/C1

C4/C1

C6/C1

Cyclo-Sarin

$LD_{50} = 0.018 \text{ mg/kg (i.v. rabbit)}$*

Butyl-Sarin

$LD_{50} = 0.012 \text{ mg/kg (i.v. rabbit)}$*

Hexyl-Sarin

$LD_{50} = 0.145 \text{ mg/kg (i.v. rabbit)}$*
Defining the Cn limit is all about capturing “Chemical Space”

All possible structures for $R = H/C\ell$ to $C^{\infty}$
Can You Accurately Define Cn?

All possible structures for $R = \frac{H}{C_1}$ to $C_\infty$

“ Toxic Portion”
(toxic family)

$R \leq C_n$ overlaps but does not fully contain “Toxic Portion”
Do the Schedules Provide Guidance?
Both approaches have their own merits and disadvantages.
Other Families?

1A.02: O-Alkyl (≤ C10, incl. cycloalkyl) N,N-dialkyl (Me, Et, n-Pr or i-Pr)-phosphoramidocyanidates

R¹ ≤ C₁₀ alkyl, including cycloalkyl, R², R³ = Me, Et, n-Pr, i-Pr

“Phosphoro” not “Phosphono”
(no alkyl group connected to P atom)

“Dialkylamino” group (phosphoramido)

<table>
<thead>
<tr>
<th></th>
<th>Me</th>
<th>Et</th>
<th>n-Pr</th>
<th>i-Pr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>Me Me</td>
<td>Me Et</td>
<td>Duplicates of other asymmetric set</td>
<td></td>
</tr>
<tr>
<td>Et</td>
<td>Et Me</td>
<td>Et Et</td>
<td>Et n-Pr</td>
<td>Et i-Pr</td>
</tr>
<tr>
<td>n-Pr</td>
<td>n-Pr Me</td>
<td>n-Pr Et</td>
<td>n-Pr n-Pr</td>
<td>n-Pr i-Pr</td>
</tr>
<tr>
<td>i-Pr</td>
<td>i-Pr Me</td>
<td>i-Pr Et</td>
<td>i-Pr n-Pr</td>
<td>i-Pr i-Pr</td>
</tr>
</tbody>
</table>

10 possibilities for dialkylamino group

10 (dialkylamino) X (> 1384 C1 to C10) > 13,840 parent structures
Your Turn!

Fill in the blank:

**Phosphono Thiolate**
Your Turn!

Fill in the blank:
Phos____ Thiolate

R\(^1\) ≤ C\(_{10}\) alkyl, including cycloalkyl, alkyl

R\(^2\), R\(^3\), R\(^4\) = Me, Et, n-Pr, i-Pr
How Many Parent Structures?

10 dialkylamino possibilities

R\(^1\) ≤ C\(_{10}\) alkyl, including cycloalkyl, alkyl

R\(^2\), R\(^3\), R\(^4\) = Me, Et, n-Pr, i-Pr

> 1384 possibilities

10 (dialkylamino) X 4 X (> 1384 C\(_{1}\) to C\(_{10}\))

> 53,360 parent structures
And Just to Complicate Things, What Does Schedule 1A.03 Actually Say?

1 protonated salt for every parent structure, > 110,720 possibilities

How many possible alkyl groups and anions?

1000? 10,000? 100,000?

If 1000, > 110 billion possibilities
If 10,000, > 110 trillion possibilities
If 100,000, > 110,000 quadrillion

0-Alkyl (H or ≤C10, incl. cycloalkyl) S-2-dialkyl (Me, Et, n-Pr or i-Pr)-aminoethyl alkyl (Me, Et, n-Pr or i-Pr) phosphonothiolates and corresponding alkylated or protonated salts.
How Many 1A.03 Chemicals Are Actually Known?

- CAS Database: **161** chemical substances
- OPCW handbook on chemicals: **715** chemicals
- OCAD V21: **772** Mass Spectra
Take the Quiz!

Download the Quiz
Download the Answer Sheets
Download the Answer Key

Test your knowledge of the Schedules of the Chemical Weapons Convention with an Augmented Reality Schedules quiz!
Why Does All of This Matter?

- Technical issues require sound technical inputs
- All of the nuances required to understand what Schedules and their content represent in terms of chemistry came up in the recent Article XV discussions and evaluations
- Don’t let the technical jargon be a hindrance!
- *Ice-cream and prizes*
Making Helpful Information More Accessible!

ORGANISATION FOR THE PROHIBITION OF CHEMICAL WEAPONS

"THE SCIENCE FOR DIPLOMATS" ANNEX ON CHEMICALS

A user friendly and scientifically annotated version of the Chemical Weapons Convention Annex on Chemicals

C. SCHEDULES OF CHEMICALS

The following Schedules list toxic chemicals and their precursors. Implementing the Convention, these Schedules identify chemicals of verification measures according to the provisions of the V. Paragraph to Article II, subparagraph 1 (a), these Schedules do not constitute a list of chemical weapons.

Individual Schedules are defined by a general formula for a class of specific chemical compounds. Annotated chemical names and Service (CAS) numbers are also included. Some of the chemicals have an "augmented reality" that can be viewed by scanning a QR code. This code is identified by "(A)".

Whenever reference is made to groups of similar chemicals, for example in parentheses, all chemicals possible by all possible combinations are included. The chemicals listed in the parentheses are considered as listed in the group, even if they are not explicitly exempted. A chemical marked "(A)" is subject to special thresholds for declaration and verification, VII of the Verification Annex.

Scientific Advisory Board Recommendations:

Chemical Abstract Service (CAS) numbers should not solely be used to identify chemicals covered by the schedules. Although relevant in some cases, they are not the only means to identify whether a chemical is included or excluded in the schedule.

Schedule 1 (CAS registry number)

A. Toxic chemicals:

(1) O-Alkyl-O=C₂H₅ (incl. cyclic alkyl) alkyl (Me, Et, n-Pr or i-Pr) phosphonodithioates

R¹ = C₂H₅, including cyclic alkyl, alkyl (Me, Et, n-Pr or i-Pr)

e.g. S(methyl)methylphosphonodithioate

(167-44-4)

(2) O-Alkyl-O=C₂H₅ (incl. cyclic alkyl) N,N-diethyl

Me, Et, n-Pr or i-Pr phosphoramidocyanates

R² = C₂H₅, including cyclic alkyl, alkyl (Me, Et, n-Pr or i-Pr)

e.g. Tolmethyl N,N-diethylphosphoramidocyanate

(77-81-4)

OPCW

For further information see: "Advice from the Scientific Advisory Board of the OPCW on Schedules of Chemicals and their Precursors as Provision of the Chemical Weapons Convention (CWC)" OPCW/2016.90E.
Making Helpful Information More Accessible!

What would be helpful to have in it?
Help us build a glossary!

- soman
- tabun
- toxicity
- exemptions
- nomenclature
- protonated salts
- CNS-acting
- alkyl
- iso-propyl
- mole
- guanadine
- ethyl
- amidine
- n-propyl
Where do We Go from Here?
Where do We Go from Here?

- **SAB** will meet from 11 – 14 June
- **TWG** will meet in April, September (TBC) and November (TBC)
Look for Continued Technical Secretariat Engagement in 2019 as Well!

Science for Diplomats at EC-89
Suitability for Fieldwork: The Science and Technology of Physical Protection

Are you as agile as an OPCW Inspector?
Join us to find out!

Tuesday 9 October
13:30 – 14:45
Ooms Room
Light lunch available at 13:00
Science Advice, Science Diplomacy and Science Communication at the Organisation for the Prohibition of Chemical Weapons

Scientific Advisory Board

The Chemical Weapons Convention is built on a scientific foundation, requiring technical expertise for effective implementation, and scientific literacy for decision making.

Scientific principles provide the foundation for what is, and what can be a chemical weapons convention to become comprehensive. Determinations guarantee the robustness of sampling and analysis and other verification methods. The Chemical Weapons Convention requires technical expertise and methods used for verification, investigations and destruction, which approaches to assurance, protection and broader outreach to scientific communities.

The Scientific Advisory Board (SAB) is an independent body of the OPCW serving as an independent science advisory mechanism to provide advice to inform the work and position the OPCW, and to develop scientific literacy for the implementing process. The SAB was established in accordance with the Chemical Weapons Convention to enable the Director General to render specialized advice in areas of science and technology relevant to the Convention, in State Parties, the Conference of States Parties, and the Executive Council.

So the basis of the SAB to the Chemical Weapons Convention, see Article VIII, Paragraph 21 (b).

Scientific Diplomacy in Support of the Convention

The SAB is made up of 25 experts from OPCW Member States, nominated on the basis of their technical and scientific expertise. The SAB meets once a year to communicate and share views. The SAB also interacts with advisory bodies.

Scientists from more than 50 States have served on the SAB and its working groups since the Convention was established in 1997. The SAB promotes the implementation of the Convention.

International scientific collaboration is essential to the implementation of the Chemical Weapons Convention. The SAB plays an important role in supporting the implementation of the Convention.

The SAB reports to the Director General, who provides responses and recommendations to States Parties. The SAB also comments on the reports and recommendations of the OPCW.

Reports, Infographics and More

Available from the “Science and Technology” section of OPCW.org