



Science for Diplomats

Schedule 1 and 2 chemicals as captive intermediates and unintended by-products

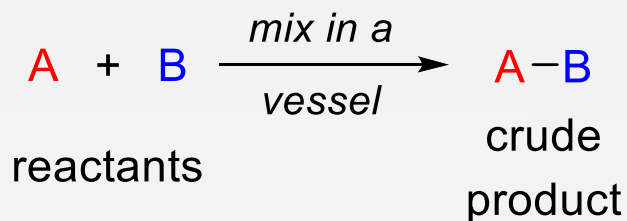
Dr. Christopher M. Timperley



Chemical production

The deliberate encouragement of chemical reactions to obtain one or more products by physical manipulations

What is a chemical reaction?

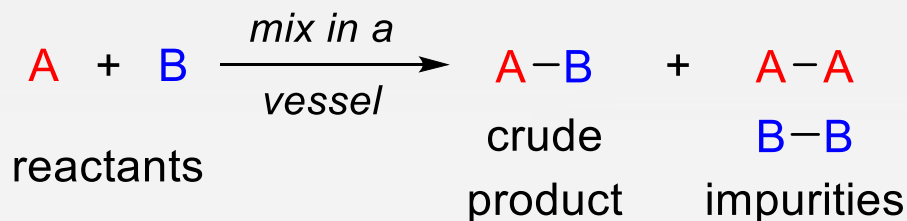




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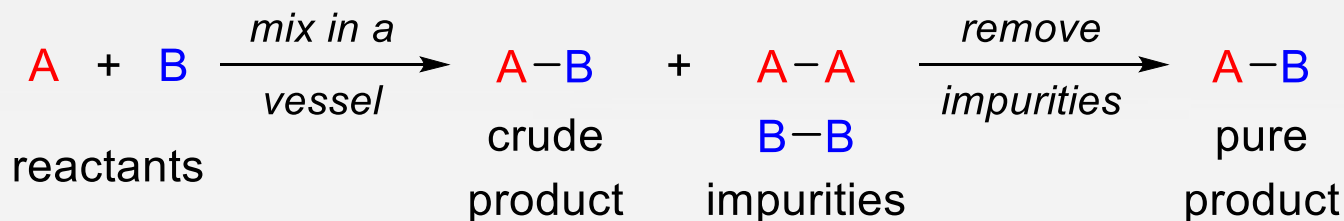




Chemical production

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What is a chemical reaction?

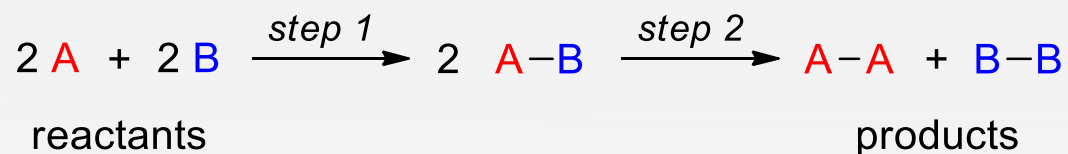




Chemical production

The deliberate encouragement of chemical reactions in a stepwise sequence to obtain one or more target products

An example of two step reaction sequence :

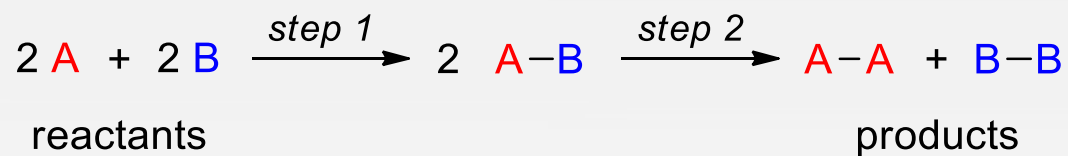




Chemical production

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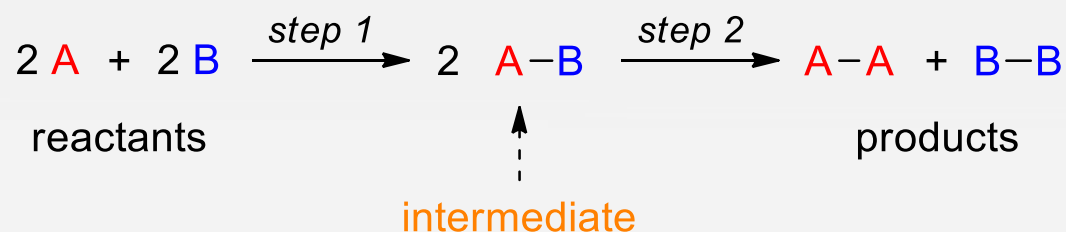




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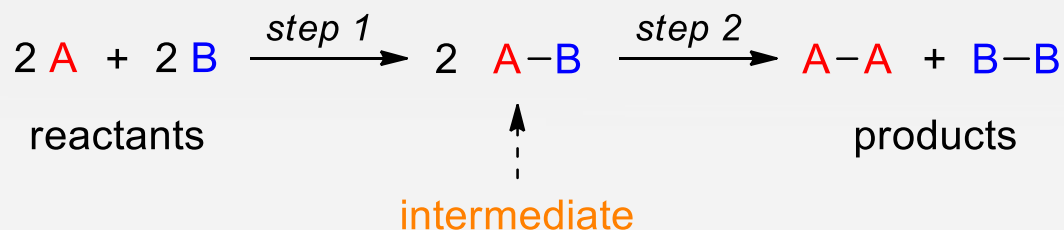




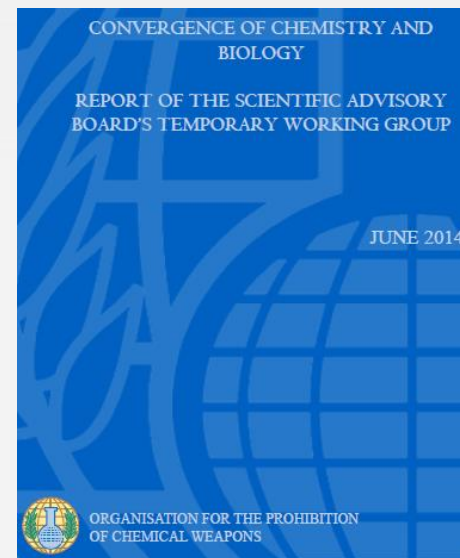
Chemical production

The deliberate encouragement of chemical reactions in a stepwise sequence to obtain one or more target products

An example of two step reaction sequence :



Some intermediates can be made biologically





Schedules of Chemicals

Schedule 1

- Developed, produced, stockpiled or used as a chemical weapon
- Pose otherwise a high risk to the object and purpose of the CWC
- Have little or no use for purposes not prohibited under the CWC

Schedule 2

- Possesses lethal or incapacitating toxicity and other properties that could enable them to be used as chemical weapons or to obtain Sch. 1
- Not produced in large commercial quantities in chemical industry

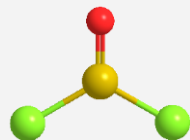
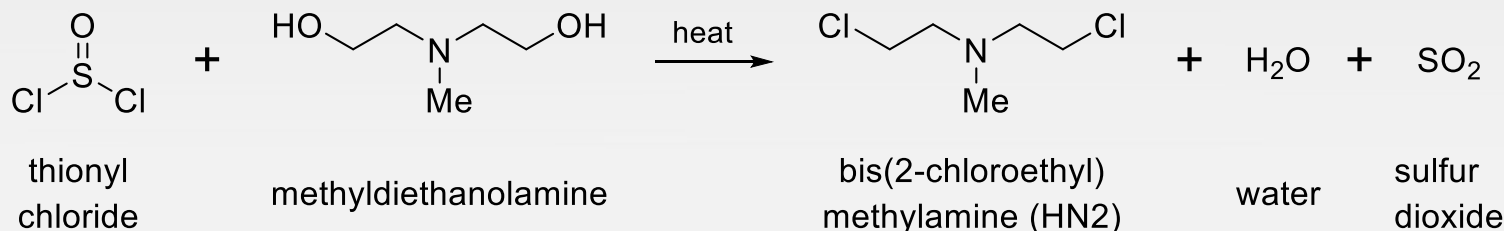
Schedule 3

- Have been produced, used or stockpiled as a chemical weapon
- Possess lethal or incapacitating toxicity and other properties that could enable them to be used as a chemical weapon or to obtain Sch. 1 or 2
- Produced in large commercial quantities in the chemical industry

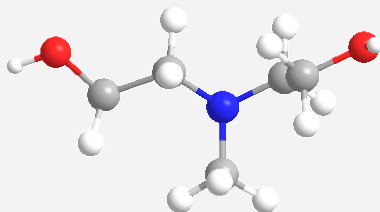


Nitrogen mustard HN2

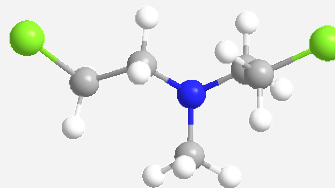
Moving through the Schedules to make a chemical warfare agent :



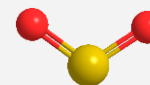
Schedule 3B14



Schedule 3B16



Schedule 1A6



Not scheduled



Schedule 1 captive intermediate in production of a pharmaceutical

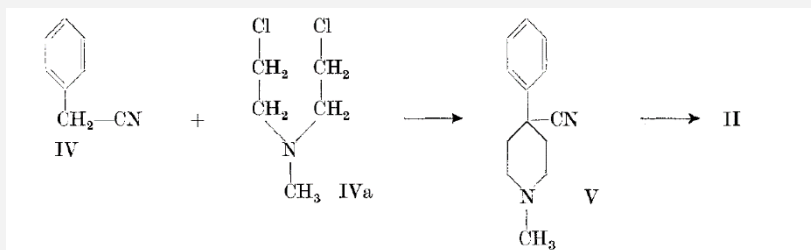
HN2 can be used to make the anti-cancer drug ketobemidone, a pain-killer for children with cancer that are allergic to morphine

Volumen XXXII, Fasciculus VII (1949) – No. 323.

2489

**323. Über eine neue Synthese morphinähnlich wirkender
4-Phenylpiperidin-4-alkylketone und verwandter Verbindungen**
von H. Kägi und K. Miescher.

stehenden und unter dem Namen „Nitrogen mustard“ bekannt gewordenen sehr giftigen Amins IVa zu vermeiden, beschriften wir einen

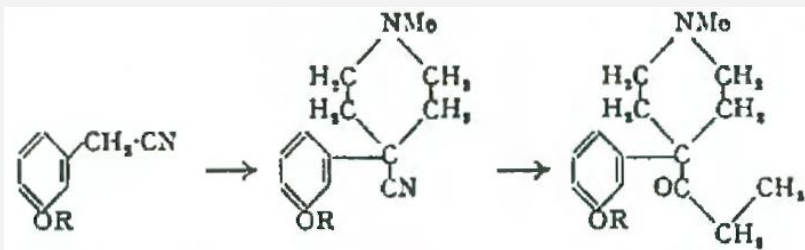


Helv. Chim. Acta 1949, 32, 2489

303. Synthetic Analgesics. Part VI. The Synthesis of Ketobemidone

By A. W. D. AVISON and A. L. MORRISON.

Ketobemidone (Hoechst 10720) has been prepared from *m*-methoxybenzyl cyanide by condensing it with methyl-di-(2-chloroethyl)amine in the presence of sodamide, submitting the resulting cyanopiperidine derivative to a Grignard reaction, and demethylating the product with hydrobromic acid.



J. Chem. Soc. 1950, 1469-1471



Schedule 1 captive intermediate in production of a pharmaceutical

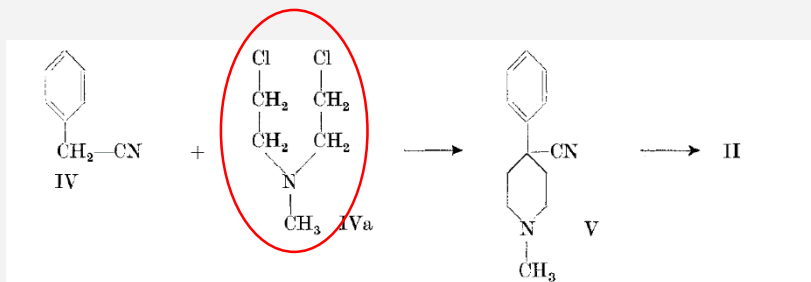
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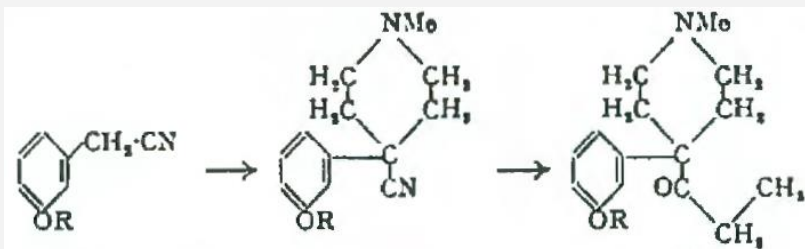


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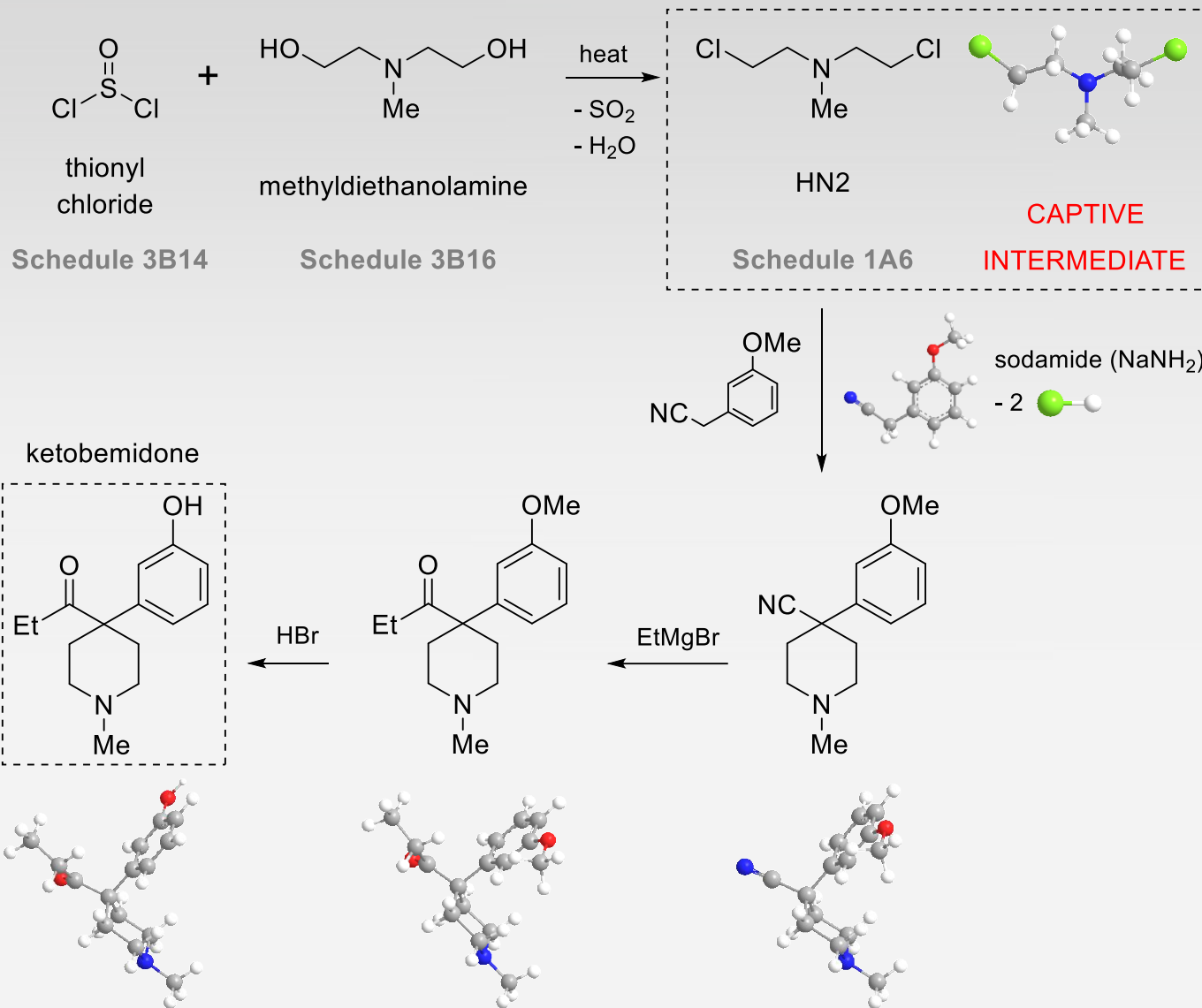
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Production of Schedule 1 chemical

‘is understood for declaration purposes to include intermediates, by-products, or waste products that are *produced and consumed* within a defined chemical manufacturing sequence, where such products are chemically stable and therefore exist for a *sufficient time* to make isolation from the manufacturing stream possible, but where, under normal design or operating conditions, isolation does not occur’

Decision of OPCW CSP (C-10/DEC.12 dated 10 November 2005)



Production of Schedule 1 chemical

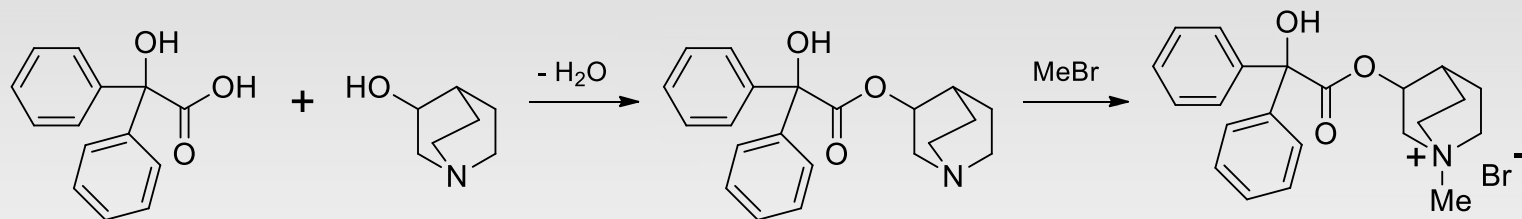
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Expectation to declare a facility consuming a Schedule 1 chemical as an intermediate in production of, for example, a pharmaceutical



BZ as a captive intermediate

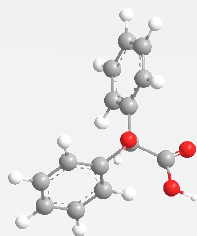


2,2-Diphenyl-2-hydroxyacetic acid

Quinuclidin-3-ol

3-Quinuclidinyl benzilate (BZ)

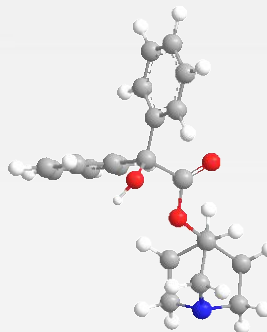
Clinidium bromide (pharmaceutical)



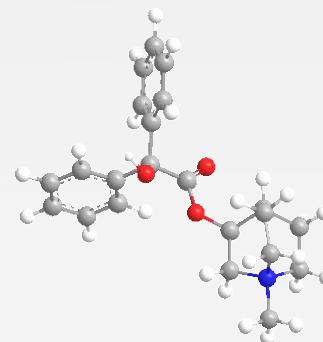
Schedule 2B8



Schedule 2B9



Schedule 2A3



Not scheduled

Clinidium bromide (Librax[®]) is used to treat irritable bowel syndrome



ORGANISATION FOR THE
PROHIBITION OF CHEMICAL WEAPONS

Working together for a world free of chemical weapons

Unintended by-products



Unintended by-products

An unintended by-product is a Schedule 1 or 2 chemical formed unintentionally during a sequence of planned chemical reactions

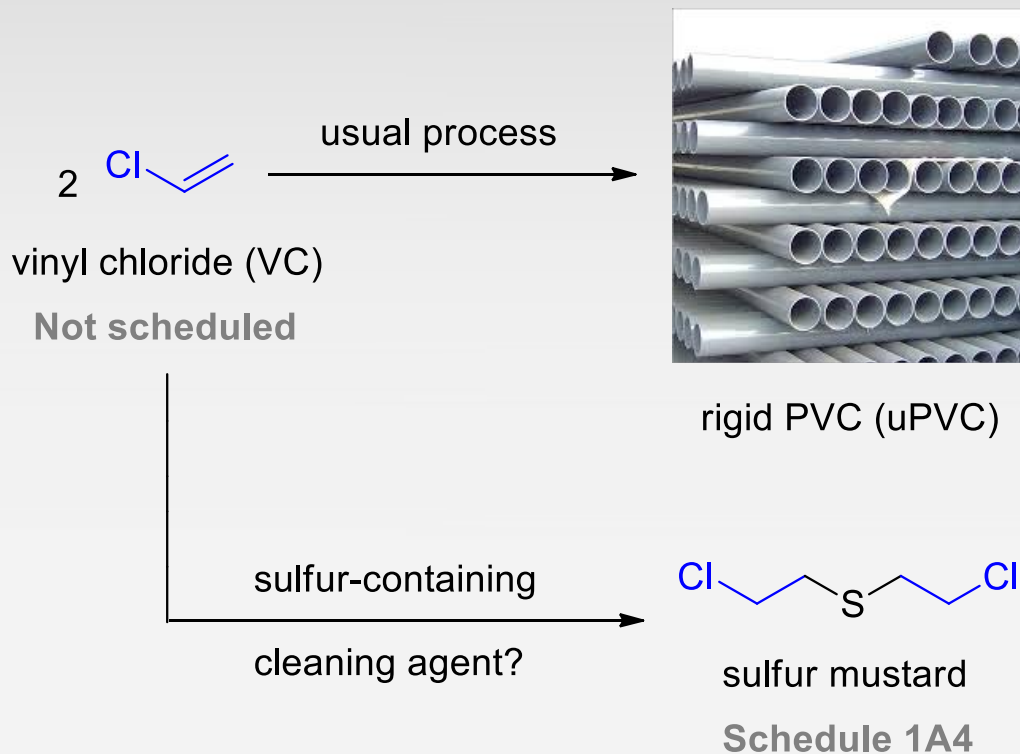
Processes most likely to involve the formation of a blister agent

An accident involving the formation of the Schedule 1 chemical agent sulfur mustard occurred 6 years ago during cleaning of an industrial plant that manufactured polyvinylchloride (PVC) pipes

C Curty, J Ducry, S Mogl. Schedule 1 chemicals as captive intermediates or unavoidable by-products in chemical production: technical feasibility assessment based on literature review, LN 2013-01-CC, Spiez Laboratory, Switzerland, 2013.



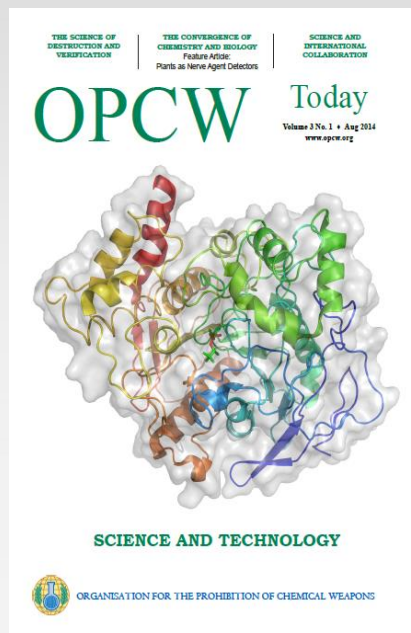
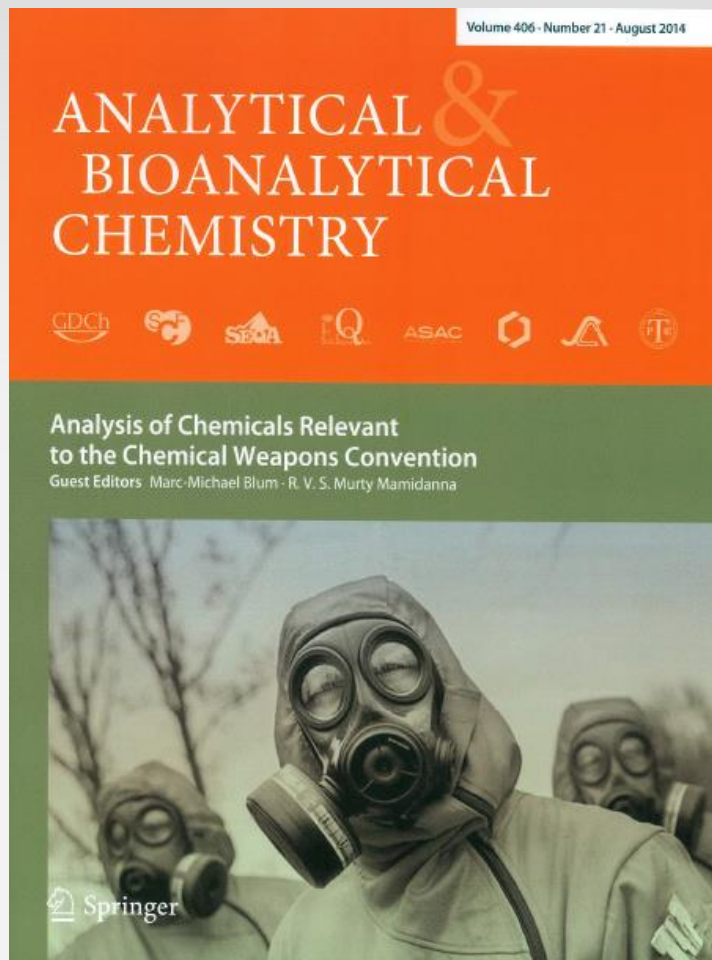
Unintended Schedule 1 production



Employees experienced skin blistering, burns and respiratory problems



Improved analytical capabilities



Over the last decade the power of analytical chemistry techniques has increased hugely

Analysis using mass spectrometers allows detection of minute amounts of chemicals



Practical aspects of isolating Schedule 1 captive intermediates and by-products

Infrastructure of chemical plants that employ a process that involves captive use of a Schedule 1 chemical - or that yields a Schedule 1 chemical as a by-product - would generally be suitable for producing nitrogen or sulfur mustard

Schedule 1 by-products are likely to be present in reaction mixtures as impurities in low concentrations and therefore not suitable for activities prohibited by CWC (i.e. to be used as a toxic agent)

In theory, it is possible to extract a Schedule 1 chemical by-product using an extra purification step or to concentrate it in the reaction mixture, but the cost to isolate a low concentration of pure material would be unreasonably high (versus the ease of deliberate synthesis)

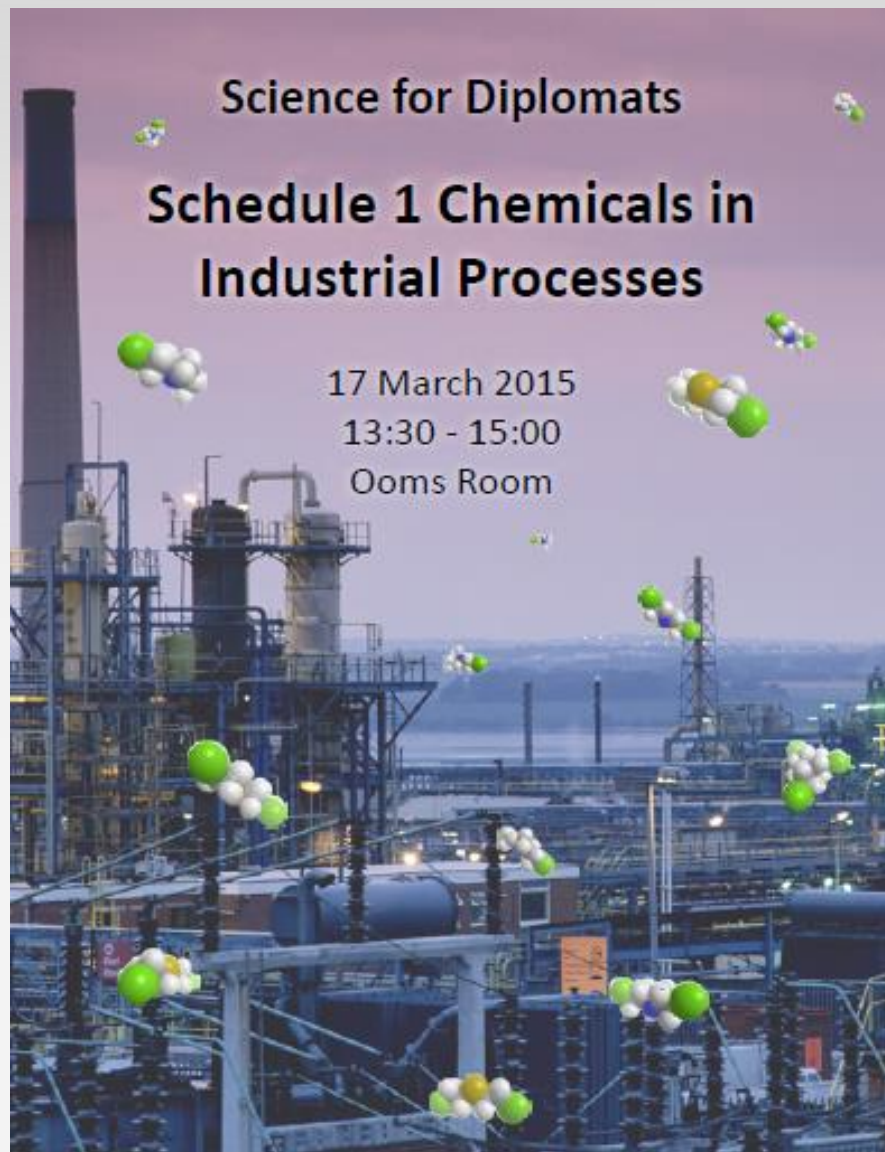


Conclusions

Very few examples of captive use or production as a by-product of Schedule 1 chemicals have been officially reported up to this day

Alternative synthetic methods can be found to avoid this problem

Discussion on the topic of this presentation initiated through the OPCW SAB in 2012: up to the policy making organs and Technical Secretariat to find solutions in cooperation with chemical industry



Questions?