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Chemistry and Toxicity of Tear Gases

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ABSTRACT

The article presents a historical background on the use of tear gases in war and civilian riot control activity. The classification of chemical compounds used as irritants, and their structure – activity relationship established through different studies has been examined. A review of toxic effects which is different from irritancy of Adamsite, ω- chloroacetophenone (CN), o-chlorobenzylidene malononitrile (CS) and Dibenz (b,f), [1, 4] – oxazepine (CR) has been presented.

1. INTRODUCTION

Tear gas compounds are used by Defence services in many countries and law-enforcing agencies in all the countries of the world. These compounds bring about temporary incapacitation by the irritation of eyes, nose, respiratory tract and skin with consequent production of profuse tears and mucous. The effect last a little longer than the duration of exposure.

Toxicity studies of tear-gases are important from two view points - (a) from the occupational health view point to assess the risk to all involved in production and handling of tear gas munitions and (b) to those who are occasionally exposed to it in training manoeuvres and general public in actual use.

All the tear gas compounds in low concentrations produce instantaneous physiological response and activation of the lacrimal glands. Some of these have more severe and punishing physiological effects, like pain in the eyes accompanied by involuntary reflexes and secretion of viscous fluids. The mucous membrane of the nose, throat and lungs are particularly susceptible. In low concentrations, short exposures causes only irritation of the nose and throat, producing sneezing, coughing,

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lacrimation, viscous discharge from the nose and severe headache. In higher concentrations or prolonged exposure the symptoms increase in severity accompanied by an acute pain in the chest, difficulty in breathing, cramps, nausea, vomiting and stinging sensation of the skin.

Immediately after the out break of the first World War, use of eye irritants were reported to by the Germans and the French. These were well known organic compounds, synthesised in the laboratory during the preceeding century and hardly has been exploited industrially. The first use of tear gas during civil disturbances has been attributed to the Paris Police, who used 'Hand bombs' filled with ethylbromoacetate[1] (EBA) in 1912. A rapid expansion in the use of chemicals for peace keeping occurred in the U.S. following a marked increase in the crime rate in the 20s. Since then, the use of tear gases to restore law and order during violent demonstrations have increased on world wide scale. ω- Chloroacetophenone (CAP or CN) and Diphenylaminechloroarsine (Adamsite or DM) were the chemicals favoured upto the 1940's, and CAP is still in use in our country.[2] Then o-chlorobenzalmalononitrile (CS) was introduced by the British in the 50's initially in Malaya for fighting the Communists in the dense forests. This is in use with most of the police forces abroad. The more recent innovation in the 70's is Dibenz (b,f), [1, 4] – oxazepine (CR) a British discovery, is slowly getting acceptance abroad as a riot control agent.

2. CLASSIFICATION

Dixon,[3] Dixon and Needham,[4] Mackworth[5] and Bacq[6-7] have proposed the following classification on the basis of irritant chemical's interaction with SH groups of the receptor protein associated with the nerve ending. ω-Chloroacetophenone initially was utilised to classify 'thio-enzyme' depending on whether or not these are inhibited.[8] A similar behaviour with vesicant has already been reported earlier by Peters[9] et al. 1963.

The compounds used so far are listed in Table 1 along with their toxicity data. They can be grouped as given follows :

Group I : Compounds possessing a positive halogen.

Group II : Compounds possessing ethylenic double bond.

Group III : Compounds possessing $>C=N$ linkage.

Group IV : Compounds possessiong trivalent arsenic.

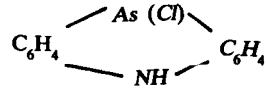
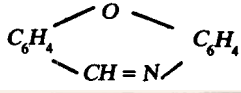
The structural formulae and physical characteristic of some of these tear gas compounds are given in Table 1.

3. STRUCTURE-ACTIVITY RELATIONSHIP OF IRRITANTS

3.1 Group I : Compounds with a Positive Halogen

The main characteristic of halogenated compounds is the positive halogen from electron displacement under the influence of neighbouring groups, such as, carbonyl

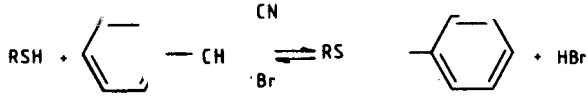
Table 1. Structural formulae and physical characteristic of tear gas compounds

S. No.	Compounds	Structural formulae	Code	Specific gravity	Minimum Lacrimatory Conc. (mg/l.)	Minimum Lethal Conc. (mg/l.)
	Ethylbromoacetate	$BrCH_2COOC_2H_5$	EBA	1.50	0.0030	2.30
	Ethyl iodoacetate	$ICH_2COOC_2H_5$	EIA	1.80	0.0014	1.50
	Chloroacetone	$ClCH_2COCH_3$	A-Stoff	1.80	0.0180	2.30
4	Iodoacetone	ICH_2COCH_3		1.43	0.0120	1.90
5	Bromomethylethyl ketone	$BrCH_2COCH_2CH_3$			0.0126	2.00
6.	Benzyl iodide	$C_6H_5CH_2I$		1.70	0.0020	3.00
7	Cyanogen bromide	$CNBr$	CNBr	2.00		
	Phenyl Carbylamine chloride	$C_6H_5CNCl_2$		1.35	0.0030	0.50
9.	Bromobenzyl cyanide	$C_6H_4(CN)Br$	CA or BBC		0.0015	0.35
10.	Bromoacetone	$BrCH_2COCH_3$	BA	1.60	0.0015	3.20
11.	Benzyl bromide	$C_6H_5CH_2Br$	-	1.49	0.0040	4.50
12.	Chloropicrin	CCl_3NO_2	PS	1.66	0.0020	2.00
13.	Xylyl bromide	$C_6H_4(CH_2)_2Br$	T-Stoff	1.40	0.0018	5.60
14.	o-Chloroacetophenone	$ClCH_2COC_6H_5$	CN/CAP	1.32	0.0003	0.85
15.	Acrolein	$CH_2=CH-CHO$	-	0.84	0.0070	0.35
16	o-Chlorobenzylidene-malononitrile	$C_6H_4(Cl)CH=(CN)_2$	CS	mp 94°C		
17.	Diphenyl chloroarsine	$(C_6H_5)_2AsCl$	DA	38°C		
18	Diphenyl cyanoarsine	$(C_6H_5)_2AsCN$	DC	19°C		
19.	Adamsite		DM	195°C		
20.	Dibenz (b,f) [1,4]- oxazepine		CR	72°C		

in esters, ketones, aldehyde, amide etc.

$$RSH + RCOCH_2Cl \rightleftharpoons R\text{-}S\text{-}CH_2\text{-}\underset{\underset{O}{\|}}{C}\text{-}R + HCl$$

Receptor Protein



The chemicals of group I have not been extensively tested on the animals except chloroacetophenone (CN). Moncrief[10] has given the general rules to correlate the structure of these compounds with their biological activity :

(i) If the halogen is present in the β-position, sensory irritation is more intense than in the α-position e.g. ethyl β-chloropropionate > ethyl α-chloropropionate.

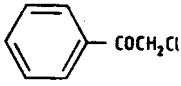
(ii) One halogen atom often confers more lacrimatory properties than 2 or 3-halogen atoms. Monochloromethyl chloroformate is predominantly lacrimator but trichloromethyl chloroformate is not a lacrimator but an asphyxiant.

(iii) Activity also depends on the atomic weight of the halogen atom in the order F< Cl< Br< I; thus bromoacetone is 18 times more irritating than chloroacetone; benzyl iodide is a more powerful irritant than the corresponding bromo-derivatives.

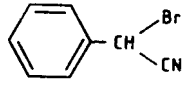
(iv) In aromatic series, chlorine in a side chain increases irritancy but not in the nucleus e.g. ω-chloroacetophenone is a very powerful lacrimator, while 2-chloroacetophenone a non-irritant. Xylyl bromide is a lacrimator but bromoxylene is not. Symmetrical compounds are usually more lacrimatory than unsymmetrical.

(v) The introduction of nitro group into the molecule has been found to increase lacrimatory properties.

Amongst the intensively active compounds in Group I used as tear gas compounds are the compounds having chlorine or cyanide in the side chain.



(CN)



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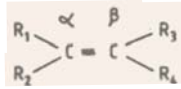
3.2 Group II : Compounds with Ethylenic Bonds

The compounds of the group II contain ethylenic double bond, which is polarised in the presence of electron withdrawing groups. These groups can be ester carbonyl, keto carbonyl, amide, nitrile, nitro or halogens.

Tarantino and Sass[11, 12] have investigated the reactivity of Group II compounds towards -SH groups using diethylaminoethyl mercaptan (DEAEM) as substrate. Using fall in respiratory rates as an index in mice, a series of benzalmalononitriles were evaluated as sensory irritants.[13] A few rules on the molecular feature of these compounds needed for irritancy could be worked out. The general structure of this series is



(i) Where R_1 is H and R_2 is Aryl or Alkyl, Nitroalkyl. The compounds having nitro group are more irritant.

(ii) R_3 and R_4 are essentially those capable of polarizing the adjacent double bond so that nucleophilic reagents can react easily.

(iii) R_1 must be *H* on a *α*–carbon atom, as it is a prime requirement of this series of compounds. Since replacement of *H* by any group, such as, phenyl, CH_3 or *CN* yield completely inactive compounds.

(iv) The substitution on benzene ring in R_2 by halogen will increase the irritancy of Benzalmalononitriles.

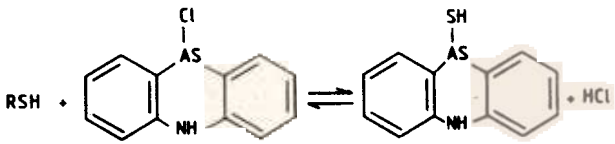
$$RSH + RCH = C \begin{matrix} CN \\ CN \end{matrix} \rightleftharpoons R\text{-}\underset{\displaystyle RS}{\underset{|}{CH}}\text{-}\underset{\displaystyle H}{\underset{|}{C}} \begin{matrix} \nearrow \\ \searrow \end{matrix}$$

3.3 Group III – Compounds Possessing > *C=N* Linkage

Compounds containing > *C=N* are very potent sensory irritants[14] but there is very little information on any correlation of activity with structure. These compounds are more susceptible to nucleophilic attack in presence of electron withdrawing group attached to the phenyl group e.g., Dibenz (b, f), [1, 4] –oxazepine (CR) and halogenated oximes. The 11–methyl derivative of Dibenz (b, f), [1, 4] –oxazepine is a non–irritant, whereas 3–methyl and 9–methyl retained some irritancy, but both are less potent[15] than CR.

3.4 Group IV – Compounds with Trivalent Arsenic

By the reaction of organic trivalent arsenicals with SH group of the receptor proteins the mercaptides are formed e.g. DM, DA and DC.



Influence of various halogen atoms on the physiological effect in case of organic compounds of arsenic is the reverse of that found for the eye irritants. The effect is in the order $I < Br < Cl$, the presence of a *CN* group increases the irritant effect and the toxicity. Thus diphenyl cyanoarsine (DC) is more toxic than diphenyl chloroarsine (DA).

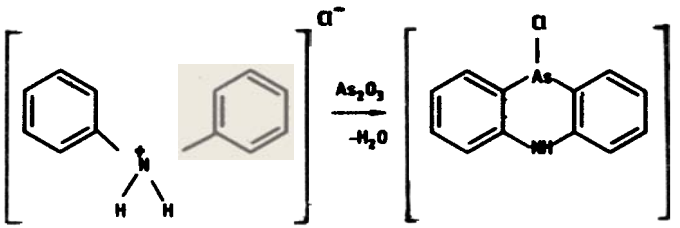
$$\begin{matrix} C_6H_5 \\ C_6H_5 \end{matrix} \begin{matrix} \nearrow \\ \searrow \end{matrix} ASCl \quad \text{(DA) Lower threshold } 10^{-4} \text{ mg/l}$$

$$\begin{matrix} C_6H_5 \\ C_6H_5 \end{matrix} \begin{matrix} \nearrow \\ \searrow \end{matrix} ASCN \quad \text{(DC) Lower threshold } 10^{-5} \text{ mg/l}$$

4. TOXICITY STUDIES OF IRRITANTS

4.1 Adamsite (DM, Diphenylaminechloroarsine)

Adamsite was the American answer to the German tear gas DA (Diphenyl chloroarsine), first prepared by Major Rodger Adams in 1918 (and called Adamsite after him) by heating arsenic (III) chloride with diphenylamine or arsenic (III) oxide with diphenyl ammonium chloride.[16]



In pure state, it is bright canary-yellow crystalline solid, sp. gr. 1.65 and m.p. 195°C. DM is practically odourless with low vapour pressure. When it is dispersed by burning type munitions, it forms a yellow particulate cloud that has characteristic 'smoky odour'. DM is stable on storage and is not affected by the water or moisture in solid state. However, in aerosol form it is hydrolysed slowly by water or moisture to hydrogen chloride and diphenyl amino arsenious oxide. The oxide is more poisonous. When DM is used during riots or for training purposes, the oxide is capable of poisoning open foodstuffs and water supplies. It has a persistency less than 10 minutes.

Exposure to DM produces acute pain in the nose and paranasal air sinuses with a burning sensation in the throat, tightness and pain in the chest, accompanied by sneezing violent coughing, eye pain, lacrimation, blepharospasm, rhinorrhoea, excess salivation, nausea and vomiting. There is usually a delay of some minutes between the exposure and onset of symptoms; recovery is normally complete within 1 to 2 hours after exposure. Compared with CN and CS, DM could be absorbed before warning symptoms occur.[17] It irritates the eyes and mucous membrane after one to two minutes in concentration around 0.00038 mg/l of air, producing sneezing and coughing. Highest intensity of irritation is around 0.0005 mg/l. The concentration 0.65 mg/l is reported to be lethal after about thirty minutes and 3.0 mg/l after 10 minutes. Death from severe pulmonary damage on exposure to higher concentrations of DM has been reported.[18] Heavy exposure to DM may produce necrosis of corneal epithelium.[19] In humans, acute inhalation dose[20] L $(Ct)_{50}$ estimated is 11000–25000 mg/min/m.[3]

4.2 ω-Chloroacetophenone (CN)

ω-Chloroacetophenone or CN was discovered in 1871 by the German Chemist Graebe[21] and was introduced in the military during first world war. CN can be prepared

Table 2. Physico-chemical properties and acute mammalian toxicity data of commonly used tear gases

		DN	CN	CS	CR
	Structural formula	10-chloro 5,10-dihydro phenarsazine	1-chloro acetophenone	2-chloro benzylidene malononitrile	Dibenz (b,f) [1,4]–oxazepine
2.	Physical state	Green-yellow solid	White solid	White solid	Pale-yellow solid
3.	Melting point(°C)	195	59	94	72
4	Mol. weight	277.5	154.5	188.6	195.1
5	Vapour pressure at 20°C (mm Hg)	2×10^{-13}	5.4×10^{-3}	3.4×10^{-5}	5.9×10^{-5}
6.	Water solubility at 20°C (moles/ litre)	Insoluble	4.4×10^{-3}	2.0×10^{-4}	3.5×10^{-4}
7	TC_{50} for aerosol (mg/m^3) respiration	0.5	0.4	23×10^{-3}	2×10^{-3}
8.	Acute mammalian toxicity : Rat				
	(i) LD_{50} mg/kg				
	(a) Intravenous *	26	35-41	28-35	68
	(b) Intraperitoneal	164	36-56	48-66	166-817
	(c) Oral	563	52-258	178-1366	13000*
	(ii) $L(Ct)_{50}$				
	(a) Inhalation: Pure material	3700-12710	3700-18800	88480	425000
	(b) Inhalation: Smoke	48217	23330	68000	139000

* Pravin, K. et al. (1986), Report on toxicity[93] of CR

** B.Ballantyne, Report on riot control agents, Special article[94] (1978).

industrially by two methods, by chlorination of acetophenone or by Friedel and Craft's reaction from benzene and chloroacetyl chloride. It is a colourless crystalline substance which melts at 57-58°C, the volatility at 20°C is 0.11 mg/l. The vapours are 5.2 times heavier than air and does not decompose at its own boiling point (247°C). CN starts decomposing at 450°C and decomposes[22] completely above 1000°C. Other physico-chemical properties and acute mammalian toxicity of this compound is given in Table 2. CN is an alkylating agent which reacts directly with nucleophilic compounds by SN^2 reaction. Toxic effects of CN are probably due to alkylation of -SH containing enzymes.[23,24] The harassing effects of CN occur at concentration around 10 $mg/m.^3$ First symptoms are lacrimation and salivation followed by burning or stinging sensations in the throat, eyes, and nose accompanied by rhinorrhoea, constriction sensation in the chest and difficulty in breathing. CN by all the routes of administration is significantly more toxic than CS or CR (Table 2) but less toxic than DM.[25] The chemical injuries to eye occur more with CN solution than powder. CN may also cause primary contact dermatitis, erythema, oedema, vesication, purpura and necrosis.[26-29] Allergic contact dermatitis has also been described and confirmed by

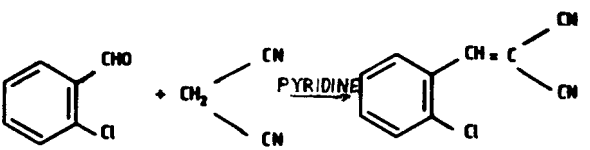
conventional skin patch test in man.[30,31] Most of the sign and symptoms disappear within 20 minutes except conjuctivitis which may persists for 24 hours.

The maximum safe inhaled dose[32] of CN for man is 500 mg/min/m.^{3} Human lethal acute inhalation dosage[20,33] were estimated to be 8500-25000 mg/min/m.^{3} McNamara[34] et al. estimated the $L(Ct)_{50}$ for CN to man as 7000 mg/min/m^3 for pure aerosol and 14000 mg/min/m^3 for commercial grenade. Five deaths have been reported with the high inhalation dose by lung damage following the use of CN grenades in confined spaces.[35,36]

In the United States, military establishments were using various liquid chloroacetophenone formulations which were discontinued due to the long lasting cumulative effects.

4.3 o-Chlorobenzylidene Malononitrile (CS)

Synthesis of o -chlorobenzylidene malononitrile (CS) was first reported by Corson and Stoughton[37] and was introduced as riot control agent in 1958. 2-Chlorobenzylidene malononitrile can be prepared by the condensation of 2-chlorobenzaldehyde and malononitrile in presence of pyridine as base.



It is a white crystalline solid, ten times more potent[38-41] than CN (Table 2). To produce immediate effects on the eyes and respiratory tract, 4 mg/m^3 concentration is sufficient.[17,42] Exposure to CS results in immediate burning sensation in the eye, accompanied by copious flow of tears and involuntary closing of eyes. Irritation of the respiratory tract results in sneezing, tightness of the chest with difficulty in breathing and coughing. In high concentrations CS causes nausea and vomiting. In addition there is severe stinging sensations on the moist surfaces of the exposed skin, which may be followed by erythema.[43] Recovery is usually complete within 30 minutes after the exposure but a few signs and symptoms may persist little longer.[44] Eye damage with CS seems to be significantly[40,45-47] lower than with CN. On the human eye CS grenade smoke cause only irritation.[47] Punte[48] et al. studied the effect of CS on human volunteers at elevated temperature and humidity and found that tolerance to CS could be reduced by exercise, hyperventilation, elevated temperature and humidity. If the whole body is drenched with a solution of CS in concentration range 0.0001-0.005 per cent (10-50 μg/ml) causes almost immediate eye discomfort, blephorospasm and excess lacrimation.[49] The severity and duration of the cutaneous irritant effect of solution of CS are less than that caused by a dilute solution[50,51] of CR. CS is not teratogenic in animal studies[52,53] and epidemiological studies.[39] It is also not embryotoxic and has no adverse effects on human pregnancy.[54] The minimum exposure dose of CS causing fatal lung damage after acute exposure or chronic exposure is hundred times more

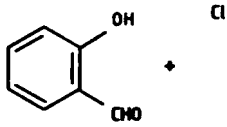
than the intolerable concentration dose in man[39,55,56] it can be said that safety index is very high. The estimate of human acute lethal inhalation dose[33] vary between 25000 and 15000 mg/min/m.^{3} No deaths are reported with CS smoke, the accumulation of an exposure dose of pyrotechnically generated CS smoke of the order of 5000 mg/min/m^3 constitute virtually negligible risk to life.[57] In those with chronic bronchitis there is a possibility of a superimposed acute bronchitis or bronchopneumonia.[58] Likewise CS could trigger asthmatic attack in susceptible persons. Exposure to CS aerosol under controlled conditions results in a transient rise in blood pressure and heart rate, but no significant change in the electrocardiogram, liver function tests, peripheral blood haematology or lymphocyte chromosome morphology.[57,58] There is no significant change in the chest radiograph, peak air flow, tidal volume and vital capacity.[59] Pulmonary gas transfer and alveolar volume are unchanged,[60] but a reduction in exercise ventilation volume occurs[61] possibly due to stimulation of respiratory tract receptors.[62] Primary contact dermatitis and allergic contact dermatitis from CS are less severe[63-65] than from CN, and is less potent as skin sensitizer[66] than CN. The acute exposure of CS causes significant cytochemical changes, both in the cortical and medullary regions of adrenal glands of rats in higher doses.[67,68] The dose dependent inhibition of cytochrome oxidase, sodium pyruvate (pyruvate dehydrogenase complex) and of LDH, SDH, MDH and GDH in the brain of rats *in vivo* were shown by Dube[69] et al. The immuno-suppresive properties in mice were reported by Nagarkatti[70,71] et al.

Both CS and CN are SN^2 alkylating agents that react with sulphydryl (SH) groups of receptor proteins. CS reversibly inhibits lactate dehydrogenase, SH dependent enzyme. The symptoms and time of onset of poisoning by CS and other malononitriles are similar in equimolar dose[72] and urinary thiocyanate excretion is elevated in animals exposed to CS. The lethal toxicity of inhaled CS is by lung damage leading asphyxia and circulatory failure or from bronchopneumonia secondary to respiratory tract damage.[73] In high dosage toxicity is due to the cyhogenic property of the CS like that of other malononitriles.[74,75] The amount of cyanide is negligible from an exposure dose of CS which an individual can tolerate. If both the CN groups were converted to cyanide (there is *in vivo* evidence that only one of the group is effectively cyanogenic) the total amount of cyanide obtained from 1.05 μ mole of CS was equivalent to the cyanide content of two 30 ml puffs from a cigarette. A man exposed to atmospheric concentrations of CS in the range 0.02-6.4 mg/m^3 for 0.05-13 minutes (tolerance time) did not have increased plasma or urinary thiocyanate.[76]

The major metabolites of CS are 2-chlorobenzyl malononitrile (CSH), o-chlorobenzaldehyde (OCB), o-chlorohippuric acid and thiocyanate.[77-79] The reduction of the benzylidene double bond in CS to CSH_2 is catalysed by NADPH dependent erythrocyte enzyme. CS and their metabolites can be detected after respiratory exposure for a long time and CS, CSH_2 and OCB have half lives of 5.5, 9.5 and 4.5 seconds.[80]

4.4 Dibenz (b,f), [1,4] – Oxazepine (CR)

Dibenz (b,f), [1,4] – oxazepine (CR) was first synthesised by Higgnbottom[81] et al. by Bischler-Napieralski type ring closure of o-acylaminodiphenyl ether with PPA. The synthesis of CR was further modified by various workers.[82-84] At DRDE, Gwalior, CR was synthesised by a 2-step procedure involving the formation of Schiff's base by the condensation of salicylaldehyde and orthochloroaniline followed by the ring closure of sodium salt of Schiff's base in the presence[85-87] of DMF.

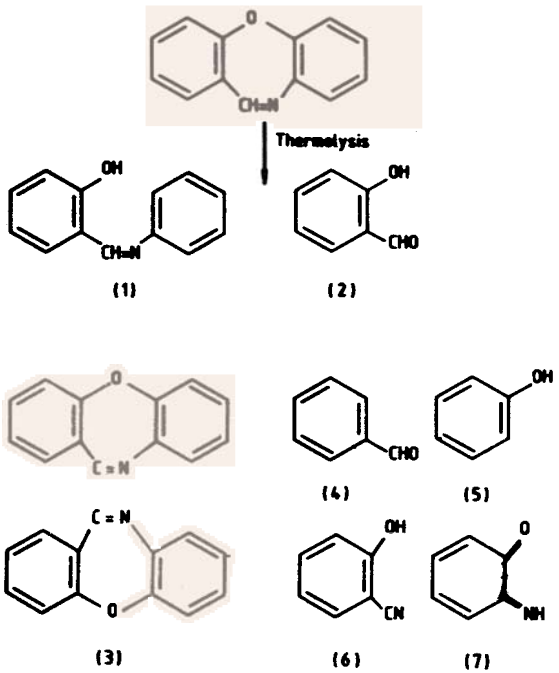


It is a yellow crystalline solid, poorly soluble in water (3.5×10^{-4} mole per litre) but highly soluble in almost all the organic solvents. CR is less toxic[88] than CN, CS and DM. The comparative physico-chemical properties and acute mammalian toxicity data of CN, CS, DM and CR are given in the Table 2. Because of its chemical stability, CR could be used in either aerosol or in the solution form in polyethylene glycol (PEG-300) or dipropylene glycol monoethyl ether (DPM).

The effects produced by solution of CR depend on concentration, formulation, the site and extent of body contamination. The parts of the body affected by CR solution are eyes, skin, mouth and nasal cavity. In the concentration range 0.01-0.1 per cent (0.1-1 mg CR/ml) results in immediate eye pain, blepharospasm and lacrymation, which persists for 15-20 minutes and oedema of lid margins for 3-6 hours. The potential eye damage with CR is significantly less than CN, CS or DM. If the whole body is drenched with a solution of CR (w/v 0.001-0.00025 per cent), it causes irritating effects on the eyes which persists for 3 to 5 minutes. A sharp rise in intraocular pressure is usually present during the acute phase. The lowest concentration of CR in solution causing detectable transient keratitis in animal[89] is 5 per cent. CR effects persist for 20 minutes, but readily reactivated on washing with water.[90,91] CR causes an erythema, restricted to contaminated area of skin which usually subsides within one hour. CR does not induce inflammatory infiltration, vesication or contact sensitisation and does not delay the healing of skin injuries. Daily application of CR solution to skin of mice over 3 months did not lead to any local or systemic long term consequences.

CR causes most unpleasant taste and burning sensations in mouth, accompanied by profuse salivation but there is no serious toxicological hazards. The effect may persist for 10-15 minutes. The splash contamination of the nasal cavity causes nasal irritation, a stuffy sensation and rhinorrhoea.

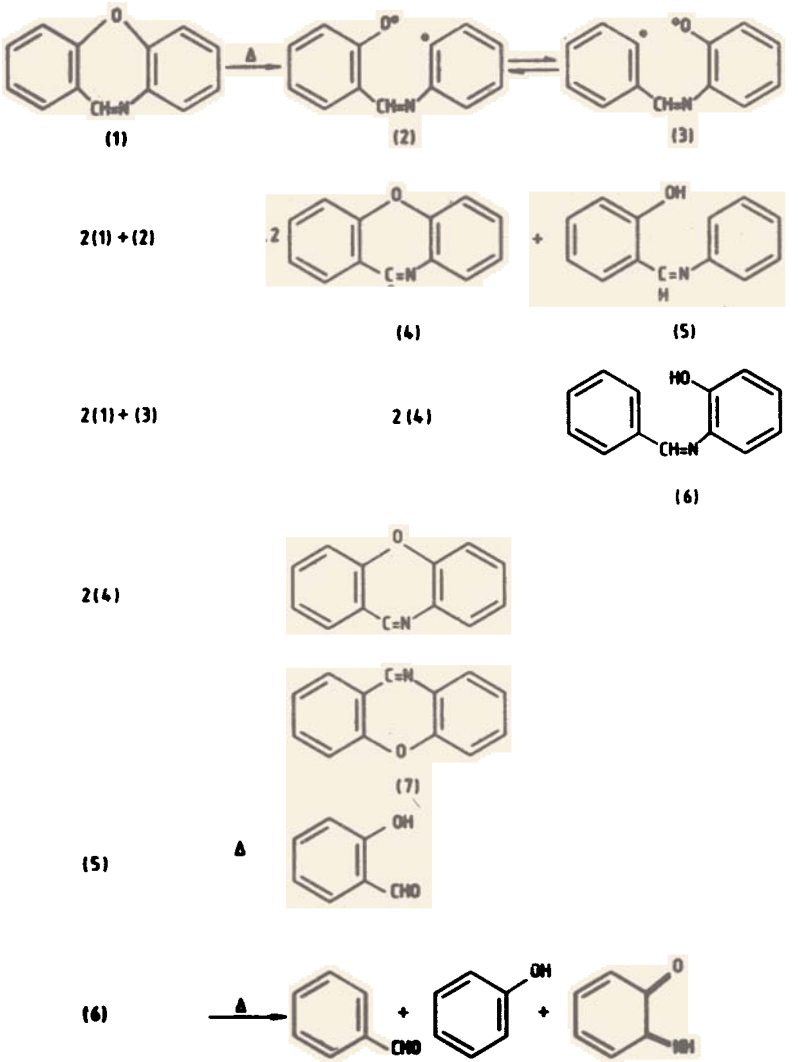
CR is far less toxic than other known irritants, so it has not been possible to obtain an $L(Ct)_{50}$ values for the pure aerosol of CR. The pyrotechnic smoke composition shows acute single dose inhalation toxicity 2-4.6 times less than that of CS containing smoke.[25] The human acute $L(Ct)_{50}$ for pyrotechnically generated CR is probably in excess of 100,000 mg/min/m.[3] The acute inhalation toxicity of pyrotechnically generated CR is more than pure CR which may be due to the formation of other toxic products at higher temperature. Thermolysis studies in this establishment shows that CR is quite stable upto 450°C, above 500°C decomposition starts; some of the products of decomposition are identified by us are the following:



The formation of these products can be explained by the following free radical mechanism.

Some of these products, like salicyl aldehyde (2), phenols (5) and o-aminoquinone (7) have also been reported in the oxidation of CR with dichloroisocyanurate.[92]

Acute toxicity (LD_{50}) studies of CR have also been carried[93] out in mice and rats by oral, intravenous, intraperitoneal and inhalation routes. The values observed were in close agreement with the reported values.[85] Saheb[95] et al. and Alarie[96] have studied the lung mechanics with variety of irritant compounds and found that inhaled chemicals are likely to induce change in the lung surfactant and adversely affect the ventilatory function of the lungs. The detailed lung mechanics and pulmonary dynamic surface tension with pure aerosol of CR (Concentration 2830 mg/m^3) has been carried out in rats and it was observed that lungs were free from pulmonary oedema attributable to CR inhalation. However, other findings like presence of inflammatory reaction at the



level of alveolar septa, mild congestion and increased inflammatory cell in the interstitial spaces, small and scattered foci of patchy areas of emphysema were noticed. No significant changes in the different parameters of pulmonary mechanics or pulmonary dynamic surface tension and in pulmonary phospholipid were observed.

In animal experiment CR is neither teratogenic nor embryotoxic when given as aerosol.[97-98] All biomedical studies show CR to be a potent sensory irritant with a low order of lethal and sub-lethal toxicity.

5. CONCLUSION

For nearly eight decades experiments with irritant compounds as weapons in war and also in peace-keeping operations are being conducted. The lead for using such compounds were probably taken from insects and animals which squirt irritating fluids

on an attacker. However, over the years, these compounds found a firm place with the police forces in peace-keeping and also with some armies. As they are used in war and peace, the tear gases have also become a headache for diplomats in the chemical disarmament talks.

Research has produced a chemical with maximum irritancy or lowest threshold concentration, but the least lethality or very large LD_{50} or $L(Ct)_{50}$ value. In other words, the gap between the two values needed for the safest and the most efficient compound is nearly achieved. Dibenz (b,f), [1,4] – oxazepine should be the most acceptable chemical today.

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