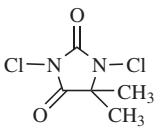
N-HALAMINES

1. Introduction

N-Halamines are inorganic and organic compounds in which oxidative halogen is attached to nitrogen. They have both research and industrial importance. The *N*-halamine bond is formed by reaction of an amine, imine, amide, or imide with halogen, hypohalous acid, or hypohalite. Numerous *N*-fluoramines have been prepared and are used as selective fluorinating agents. Iodamines are the least stable and least studied. Only the chloro and bromo derivatives are of commercial importance, particularly for disinfection and free-halogen stabilization applications. The chemistry of chloramines and bromamines is diversified not only because nitrogen and halogen act as reaction sites, but also because of the different modes by which these functionalities react. In aqueous solution, chloramines and bromamines undergo hydrolysis to varying degrees forming HOCl and HOBr. Thus generally the *N*-halamines can be considered as halogen release agents, and many find use in bleaching, disinfecting, and sanitizing applications. Others, such as the halogen derivatives of ammonia, are important because they are industrial process intermediates (monochloramine) or of significance in water treatment (mono-, di-, and trichloramine). Very recent developments concern the covalent attachment of *N*-halamine moieties to insoluble polymers creating materials with considerable commercial potential for water disinfection and biocidal coatings.

2. Properties

2.1. Available Halogen. The available halogen in an *N*-halamine is the percent N−X halogen expressed in terms of equivalent molecular halogen, ie, it is a measure of the oxidizing capacity in terms of elemental halogen. For example, the available chlorine (av Cl_2) in trichloroisocyanuric acid (TCCA) is 91.5%. The following equation illustrates the concept of available halogen, wherein halamines liberate free halogen upon acidification, 1 mol of halogen being liberated for each N−Cl or N−Br bond: $RR'NX + HX \rightarrow RR'NH + X_2$. In water treatment, a distinction is made between free available chlorine (FAC) and combined available Cl_2 (CAC). Historically, FAC has referred to $HOCl + ClO^-$, and CAC to ammonia chloramines and other slightly hydrolyzed N−Cl compounds. FAC reacts with *N,N*-dimethyl-*p*-phenylenediamine (DPD), whereas CAC requires the presence of acidic KI. Although TCCA exists predominately in the form of chloroisocyanurates in aqueous media, it analyzes essentially as FAC because the hydrolysis reactions are so rapid. Thus TCCA is a reservoir of HOCl, representing potential FAC. By contrast to TCCA, the first chlorine of 1,3-dichloro-5,5-dimethylhydantoin (**1**) analyzes as FAC, but the second as CAC.



(**1**)

2.2. Hydrolysis. Halogen in *N*-halamines is formally positive, ie, the oxidation state is + 1. *N*-Halamines hydrolyze yielding hypohalous acid, which ionizes to hypohalite ion depending on pH.

$$RR'NX + H_2O \rightleftharpoons RR'NH + HOX \rightleftharpoons RR'NH + H^+ + XO^- \quad (1)$$

The extent of hydrolysis is a function of the polarity of the N–X bond, which is determined by the electronegativity of X and the nature of the other substituents; the lower the polarity, the lower the extent of hydrolysis. In general, electron-donating groups retard hydrolysis, whereas electron-withdrawing groups enhance it. Presence of charges and steric and resonance effects also influence the extent of hydrolysis. Bromo compounds hydrolyze to a greater extent than do chloro compounds.

The equilibrium expressions for the hydrolysis reactions (eq. 1) follow; K_a and K_w are the ionization constants of HOX and water, respectively. Equation 2 rearranged for the

$$K_{HOX} = [RR'NH]\,[HOX]/[RR'NX] \quad (2)$$

$$K_{OX^-} = [RR'NH]\,[OX^-]/[RR'NX]\,[HO^-] = K_{HOX}K_a/K_w \quad (3)$$

Concentration of HOX, shows that the percent hydrolysis increases with decreasing concentration of *N*-halamine. However, as HOX is consumed, hydrolysis is retarded

$$[HOX] = K_{HOX}[RR'NX]/[RR'NH]$$

because of build-up of free amine. Consumption of hypohalous acid through reaction with HX can result in formation of elemental halogen: $HOX + H^+ + X^- \rightarrow X_2 + H_2O$ (1–3). The tendency for halogen formation is much greater for HOBr and becomes significant at moderately acidic pH.

In the case of multiple halogen atoms, the hydrolysis constant K_h decreases significantly for successive halogens. For example, in the case of trichloroisocyanuric acid, K_h ranges from 1.6×10^{-2} to 8.5×10^{-4} for the first to the third chlorines (4). The presence of negative charge also reduces K_h significantly, eg, 1.2×10^{-3} and 3.2×10^{-4} for dichloroisocyanuric acid and ion, respectively.

2.3. Bleaching. A K_h of 10^{-4} is sufficient to provide acceptable performance, which approaches that of hypochlorite bleaches. Commercial products such as bleaches, dishwasher detergents, and hard surface cleaners are formulated with alkaline ingredients such as polyphosphates, silicates, etc, so that chloramines initially hydrolyze to hypochlorite during use. Consumption of hypochlorite forms acidic compounds by reaction with soil causing the pH to drop, resulting in formation of some HOCl, which increases the bleaching rate. In laundry bleaching this can result in lowering of the tensile strength of the fabric. In bleaching applications, four variables are important including pH, temperature, contact time, and concentration. In commercial laundries, optimum pH, and temperature are in the 10.2–11.0 and 66–71°C ranges, respectively.

2.4. Disinfection. The disinfection efficacy of *N*-halamines is generally related to the extent of hydrolysis to hypohalous acid. For example, NH_2Cl ($K_h \sim 10^{-12}$) is a poor bactericide compared to HOCl (5). By contrast, monochloroisocyanurate ($K_h \sim 10^{-6}$) exhibits good bactericidal properties (6). Since hypohalous acid is a much more effective disinfectant than hypohalite, pH affects the disinfection efficiency. The fraction of hypohalous acid for aqueous chlorine and bromine is $HOX/(HOX + XO^-) = 1 - ([H^+]/K_a + 1)^{-1}$, where the pK_a values of HOCl and HOBr at 25°C are 7.54 (2) and 8.70, respectively (7). The pK_a values indicate that significant fractions of HOBr acid exist at higher pH compared to HOCl, with 50% neutralization pH of 8.7 and 7.54, respectively. Increasing the temperature increases the extent of dissociation of hypohalous acids. For HOCl, pK_a varies with temperature (K) as follows: $pK_a = 0.0253T + 3000/T - 10.0686$ (2).

For optimum disinfection in swimming pools, the pH is maintained in the 7.2–7.6 range, where HOCl represents 69–47% of the FAC. By contrast, the HOBr fraction varies from 97 to 93%. Nevertheless, the bactericidal effectiveness of HOCl is greater than that of HOBr below pH 8 on a molar basis (8). However, above pH 8 the superiority of HOCl is overcome by the fact that the concentration of ClO^- exceeds that of HOCl above pH 7.5, whereas the concentration of HOBr still exceeds that of BrO^- up to pH 8.7. Hypochlorous acid is a superior virucide to HOBr, but HOBr is more effective against certain algae (9).

Although pH determines the ratio of hypohalous acid to hypohalite ion, the fraction of the total available halogen present as HOX is dependent on K_h of the halamine as well as the concentration of excess amine. In the case of chloroisocyanurates, which are the most widely used *N*-chloramine disinfectants in swimming pools and spas, the extent of hydrolysis at 1 ppm av Cl_2 (as monochloroisocyanurate) is ~34%, but only ~1% when 25 ppm cyanuric acid is added (4). Nevertheless, effective disinfection can still occur with chloroisocyanurates if a sufficient FAC is maintained, eg, 1–3 ppm. The observed reduction in disinfection rate because of cyanuric acid (6) has been shown to be directly related to the concentration of HOCl formed by hydrolysis of chloroisocyanurates (10).

In studies with organic *N*-chloramines, the following factors were shown to significantly influence antimicrobial activity: *(1)* the aliphatic chain length; *(2)* the degree of chlorination of the N atom; and *(3)* the nature of a positive charge (11).

2.5. Thermal and Photostability. Some chloramines and bromamines exhibit the lack of stability expected of compounds with bonds between two strongly electronegative elements. Decomposition kinetics can be rapid, energetic, and explosive in many cases, eg, NCl_3 and NBr_3. However, these compounds can be handled safely in dilute organic or aqueous solution. In general, bromamines are less stable than are chloramines. A significant factor responsible for degradation of *N*-haloorganics is dehydrohalogenation across the carbon–nitrogen bond. Therefore, it is essential to stability to replace hydrogen atoms on the carbon adjacent to nitrogen with alkyl or other functional groups. Commercial organic *N*-bromamines and *N*-chloramines have good stability, which is a function of temperature, moisture, and impurities. For example, sodium dichloroisocyanurate and trichloroisocyanuric acid lose substantially less than 1% of their av Cl_2 in a year when stored at moderate temperature and rh.

When chlorine is employed for outdoor swimming pool sanitation, it is relatively rapidly decomposed by sunlight. Isocyanuric acid stabilizes chlorine by formation of photostable chloroisocyanurates (12). By contrast, bromine is not effectively stabilized by isocyanuric acid.

3. Inorganic Chloramines and Bromamines

Inorganic chloramines are formed by electrophilic attack on ammonia nitrogen via a series of bimolecular reactions, where k ($M^{-1}s^{-1}$) and K (M^{-1}) are the formation and equilibrium constants at 25°C and $\mu = 0.50\ M$ (13–18). The lack of dependence on ionic strength in

$$NH_3 + HOCl \rightleftharpoons NH_2Cl + H_2O, \quad k = 2.9 \times 10^6, \quad K = 1.5 \times 10^{11}$$

$$NH_2Cl + HOCl \rightleftharpoons NHCl_2 + H_2O, \quad k = 150, \quad K = 2.3 \times 10^8$$

$$NHCl_2 + HOCl \rightleftharpoons NCl_3 + H_2O, \quad k = 4.0, \quad K = 1.3 \times 10^6$$

the first reaction indicates that it occurs between neutral species. Mono- and dichloramine react much slower than does ammonia because of their lower basicities. The reaction is faster with Cl_2 because it is a stronger electrophile than is HOCl. The degree of chlorination increases with decreasing pH and increasing $HOCl/NH_3$ mole ratio. Since chlorination rates exceed hydrolysis rates, initial product distribution is determined by formation kinetics. The chloramines hydrolyze very slowly and only to a slight extent and are an example of CAC.

Similar reactions occur with ammonia and HOBr (19–25), but since HOBr is a stronger electrophile than is HOCl, formation rates are faster. Because of rapid bromine transfer between bromamines, equilibrium concentrations of the respective bromamines are obtained rapidly. Monobromamine predominates at basic pH at high N/Br ratios. Below pH 8.5, $NHBr_2$ and NBr_3 predominate. Tribromamine formation is favored at lower pH and higher Br/N ratios. The bromamines are less stable than are the chloramines but are better disinfectants.

At environmental pH 6–9, ammonia is oxidized to nitrogen by the following overall reaction (26,27). Some nitrate is also formed; thus the $HOCl/NH_3$ stoichiometry is greater than

$$2\,NH_3 + 3\,HOCl \longrightarrow N_2 + 3\,H^+ + 3\,Cl^- + 3\,H_2O$$

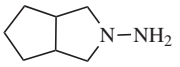
theoretical, ie, ~1.7. This reaction, commonly called breakpoint chlorination, involves intermediate formation of unstable dichloramine and has been modeled kinetically (28). Hypobromous acid also oxidizes ammonia via the breakpoint reaction (29). The reaction is virtually quantitative in the presence of excess HOBr. In the case of chlorine, little or no decomposition of NH_3 occurs until essentially complete conversion to monochloramine. In contrast, oxidation of NH_3 commences immediately with HOBr because equilibrium concentrations of NH_2Br and $NHBr_2$ are formed initially. As a result, the typical hump in the breakpoint curve is much lower than in the case of chlorine.

3.1. Monochloramine. The most important of the ammonia halamines, monochloramine [10559-90-3], is prepared by reaction of equimolar solutions of NH_3 and ClO^- (30). The pure compound decomposes even at low temperatures (31). Concentrated aqueous NH_2Cl (~70 mol%) is a colorless liquid with a strong pungent odor that decomposes at $-50°C$ to N_2, Cl_2, and NCl_3 (32). However, it is relatively stable when employed in dilute solutions of ether or water. For kinetic studies, stable aqueous chloramine solutions are formed quantitatively under efficient mixing conditions if NH_3 is in slight excess and pH $\geq$ 8.5 (15). Monochloramine is the least odorous of the chloramines; the odor and taste threshold is 5 ppm. Chloramination, ie, *in situ* NH_2Cl formation, is increasingly employed to disinfect public water supplies to reduce trihalomethane (THM) formation (33). Since direct transfer of Cl from NH_2Cl to organonitrogen compounds can occur (34–36), this can cause a problem in nonnitrified effluents from wastewater that contain significant amounts of amino acids because *N*-chloroamino acids are even poorer disinfectants than chloramines from ammonia (37).

The chemistry of NH_2Cl involves chlorination, amination, addition, condensation, redox, acid–base, and decomposition reactions. Monochloramine adds to ketones forming vicinal chloroamines and condenses with aldehydes giving *N*-chloroimines. Excess base decomposes NH_2Cl to NH_3 and N_2. Reaction of equimolar amounts of NH_2Cl and caustic with excess NH_3 is the basis of the industrial scale production of hydrazine [302-01-2].

$$NH_3 + ClO^- \longrightarrow NH_2Cl + OH^- \xrightarrow{NH_3} NH_2NH_2 + Cl^- + H_2O$$

Monochloramine is also used in organic synthesis for preparation of amines, substituted hydrazines, etc. For example, reaction of NH_2Cl with 3-azabicyclo [3.3.0]octane [5661-03-0] yields *N*-amino-3-azabicyclo[3.3.0]octane [54528-00-6], a pharmaceutical intermediate (38). Recent studies concerning monochloramine include a kinetic study of its



decomposition (39), factors affecting disinfectant-by-product formation during chloramination (40), formation of nitrosodimethylamine from it (41), kinetics of its reduction with sodium borohydride (42), and studies of its inactivation of poliovirus (43).

3.2. Dichloramine. The least stable inorganic chloramine, dichloramine [3400-09-7], has not been prepared in pure form. However, it has sufficient stability in dilute organic or aqueous solutions for determination of some physical and chemical properties. It has a pungent odor and can impart an odor or off-taste to water at concentrations >0.8 ppm. Dichloramine can be produced by reaction of HOCl with a slight excess of NH_3 in the pH range 4–7 or by disproportionation of NH_2Cl at pH 3.5–4.0:

$$2\,NH_2Cl + H^+ \rightleftharpoons NHCl_2 + NH_4^+ \qquad K_{eq}^{25°C} = 4.3 \times 10^6\ M^{-1}$$

Prepared by the latter route, decomposition is ~10% in 24 h. This reaction involves direct Cl transfer to NH_2Cl via the intermediate NH_3Cl^+, NH_2Cl hydrolysis playing little or no role. The presence of NH_4^+ improves stability by reacting with HOCl, which tends to increase decomposition (44). Trichloramine also increases decomposition, whereas NH_2Cl has little effect. Dichloramine is useful for preparation of diazirine (45). The formation of nitrosodimethylamine from it during chlorination has also been recently studied (46).

3.3. Trichloramine. Nitrogen trichloride, trichloramine [10025-85-1], the only stable pure ammonia halamine, is a shock-sensitive dense yellow liquid (bp 71°C) with a volatility similar to chloroform. In the gas phase it can be completely decomposed to N_2 and Cl_2 by spark initiation at concentrations of only a few percent in air. At higher concentrations, the decomposition is propagated by flame, exhibiting the characteristics of explosion, and eventually detonation. Trichloramine has a pungent odor and is a lachrymator. Its solubility in water at room temperature is ~2000 ppm (12). It is the most irritating of the chloramines and can impart an odor or off-taste to water at concentrations above only 0.02 ppm. Trichloramine is prepared by reaction of $(NH_4)_2SO_4$ with Cl_2 (47) or HOCl with ammonia in a 3:1 M ratio at pH 3–4. Dilute solutions are relatively stable when protected from light and volatilization (48). It decomposes in basic solution to N_2 and ClO^- via intermediate formation of dichloramine: $2NCl_3 + 6HO^- \rightarrow N_2 + 3ClO^- + 3Cl^- + 3H_2O$. Reaction of NCl_3 with olefins gives high yields of vicinal dichlorides via a radical mechanism (49). When catalyzed with $AlCl_3$, trichloramine acts as an aminating agent towards various organic substrates (50). Trichloramine has been used as a bleaching agent for flour, in manufacture of paper, and as a fungicide for treatment of fruit.

3.4. Monobromamine. In organic solvents monobromamine [14519-10-9] is dark violet. It is formed rapidly and quantitatively by reaction of NH_3 and Br_2 in organic or aqueous media; $k(H_2O\ /HOBr) = 7.4 \times 10^7 M^{-1}s^{-1}$ at 25°C. The solutions are relatively unstable, decomposing as follows: $2NH_2Br + 4HO^- \rightarrow N_2 + 2Br^- + 4H_2O$ (19). In aqueous media, the decomposition increases with pH and Br/N mol ratio. For example, at pH 9 and Br/N = 0.02, the decomposition rate is ~30%/h, whereas at Br/N = 0.002 the decomposition rate is 5%/h. Monobromamine disproportionates to dibromamine.

$$2\,NH_2Br + H^+ \rightleftharpoons NHBr_2 + NH_4^+$$

$$K^{25°C} = 2.4 \times 10^8\ M^{-2}S^{-1}, \qquad K_{eq}^{25°C} = 4.9 \times 10^9\ M^{-1}$$

3.5. Dibromamine. Dibromamine [14519-03-0] can be prepared in ether by reaction of Br_2 with a slight excess of NH_3 (51). The solution has a strawberry-yellow color and a sharp irritating odor. Although stable at −70°C, it decomposes rapidly at ≥0°C. In aqueous media, $k(HOBr) = 7.0 \times 10^5 M^{-1}s^{-1}$ at 25°C. Best yields are obtained in the 5.5–6.3 pH range and a Br/N mol ratio of ~0.05 (19). Dibromamine is less stable than NH_2Br, eg, at pH 7.2 and Br/N = 0.34, ≥90% decomposition occurs in <5 min.

3.6. Tribromamine. Pure solid nitrogen tribromide [15162-90-0] is deep red and explodes even at −100°C (52). Formation of NBr_3 in aqueous media is

favored by lower pH and an excess of Br to N (19,29). At pH 4.5 and a Br/N molar ratio of 2.5, essentially complete conversion of Br to NBr_3 occurs. Tribromamine is more stable than dibromamine. At pH 4.5 it decomposes at 5%/h.

3.7. Sulfamates and Imidosulfonates. Sodium, potassium, and bromine analogues of *N*-chlorosulfamic acid [17172-27-9], $ClHNSO_3H$, and *N,N*-dichlorosulfamic acid [17085-87-9], Cl_2NSO_3H, have been prepared, and the kinetics of chlorination of sulfamic acid have been studied (13). Dichlorosulfamate is relatively stable in dilute buffered aqueous solution (53), but is decomposed by excess av Cl_2 forming NCl_3 and H_2SO_4 (54). Sulfamic acid was once used as a stabilizer for av Cl_2 in swimming pools (55). However, its use was discontinued because of the poor bactericidal properties of mono- and dichlorosulfamate (56). *N*-Chlorosulfamates are useful in dishwashing compositions (57,58), textile bleaching (53,59,60), and vat or sulfur dyeing (61). *N,N*-Dichlorosulfamate can be used as a bleach (57,61) and disinfectant (53,60,62). *N*-Chloroimidodisulfonates, eg, sodium *N*-chloro-imidodisulfonate [6700-32-7], $ClN(SO_3Na)_2$, can be used for fabric bleaching and stain removal (63,64).

3.8. Other Inorganic Compounds. The cyclic sodium trichloroimidometaphosphamate [67651-15-4], $NaH_2(ClNPO_2)_3$, 52% av Cl_2, was once employed as a bleaching and sanitizing agent (65). *N*-Halosulfinylamines, O=S=NX, can be prepared by reaction of SOX_2 with $[(CH_3)_3Si]_2NI$ (66). They are thermally stable liquids at room temperature but react explosively with water. *N*-Halo-*S,S*-diflurosulfilimines, $F_2S{=}NX$, are formed when SF_4 and $[(CH_3)_3Si]_2NX$ react in a 1:1 mol ratio; whereas, a 1:2 mol ratio yields *N,N′*-dihalosulfurdiimides, XN=S=NX (67). *N,N′*-Dibromosulfurdiimide is shock sensitive. *N*-Chloroimidodisulfuryl fluoride [15588-41-7], $(FSO_2)_2NCl$, rearranges photochemically to a tetrasubstituted hydrazine and adds to unsaturated molecules such as olefins, CO, and cyanogen halides (68). *N*-Chloroimidosulfuryl fluoride [13816-63-2], $F_2S(O){=}NCl$, prepared by chlorination of $(CH_3)_3SiN{=}SOF_2$, adds photochemically to olefins (69). Pentafluorosulfanyl-*N,N*-dichloramine [22650-46-0], SF_5NCl_2, bp 64°C, formed by reaction of ClF with $N{=}SF_3$, is shock sensitive, unstable at 80°C, and hydrolyzes slowly (70). In the presence of SF_5Cl it photolyzes to the novel hydrazine $(SF_5)_2NN(SF_5)_2$ (71).

4. Organic Chloramines and Bromamines

Organic chloramines and bromamines can be broadly classified as aliphatic, aromatic, and heterocyclic. Monohalo derivatives of primary amides, carbamates, and sulfonamides are sufficiently acidic to form metal salts. As with ammonia halamines, organo *N*-halamines disproportionate to *N,N*-dihalamines. *N*-Halamines can rearrange under the influence of heat, catalysts, or light; eg, *N*-chloroaniline rearranges to ring chlorinated anilines (72). *N*-Halamines are versatile reagents that react with a variety of substrates via radical and polar pathways. They add to olefins and acetylenes providing routes to cyclic compounds (73) and can also cleave certain C−C, C−N, and C−O bonds. They act as aminating, halogenating, dehydrohalogenating, and oxidizing agents, and are useful in the preparation of many types of compounds (74–77).

4.1. Preparation. Substituted *N*-halamines are usually prepared by reaction of RR′NH with halogen, hypohalous acid, or hypohalite, where R is an organic substituent, and R′ is either an organic substituent or H. They are generally produced in neutral to slightly acid solution.

$$RR'NH + X_2 \longrightarrow RR'NX + HX \xrightarrow{OH^-} RR'NX + X^- + H_2O \quad (4)$$

$$RR'NH + HOX \longrightarrow RR'NX + H_2O \quad (5)$$

$$RR'NH + XO^- \longrightarrow RR'NX + OH^- \xrightarrow{H^+} RR'NX + H_2O \quad (6)$$

$$RR'NH + XO^- \longrightarrow RR'NX + OH^- \xrightarrow[RR'NH]{X_2} 2\,RR'NX + X^- + H_2O \quad (7)$$

N-Halo-*N*-sodioamidates, *N*-halo-*N*-sodiocarbamadiates, and *N*-halo-*N*-sodiosulfonamidates are exceptions, being prepared at moderately basic pH.

N-Chloramines and *N*-bromamines are unstable to excess av Cl_2 or base, which can cleave the C–N bond forming potentially explosive compounds, eg, NCl_3 and NBr_3. In some cases, the acid or base by-product must be neutralized as it is formed, since acid may prevent formation of halamine, and base may cause decomposition. The reaction with halogen (eq. 4) is employed in commercial processes such as production of chloroisocyanurates; the base is added initially in the form of mono-, di-, or trisodium cyanurate. Other sources of electropositive halogen have also been used, eg, *N*-halamines (78), Cl_2O (79), *t*-C_4H_9OCl (80), *t*-C_4H_9OBr (81), and $CH_3C(O)OBr$ (82). Sodium acetate has been used as an acid acceptor (83). In some cases, eg, in preparation of hexachloromelamine, an HCl acceptor may not be necessary if the reaction is carried out in dilute solution (84). *N*-Halocarbamidates and *N*-halosulfonamidates are formed directly by reaction of a carbamate or sulfonamide with hypohalite (85,86). Neutralization of the Na salts offers a convenient route to *N*-halocarbamates and *N*-halosulfonamides (85). In the preparation of a bromamine, a combination of Cl_2 or an *N*-chloramine and Br^- or Cl_2 plus Br_2 can be employed in order to eliminate the more expensive Br^- as a by-product: $RR'NH + Cl_2 + Br^- + HO^- \rightarrow RR'NBr + 2Cl^- + H_2O$ (87,88). *N*-Bromo-*N*-chloramines can be prepared from equimolar quantities of the respective halamines: $RNBr_2 + RNCl_2 \rightarrow 2RNBrCl$ (89).

4.2. Aliphatic Compounds. *Amines.* Although the chlorination of aqueous alkylamines is analogous to that of ammonia, mono- and di-alkylamines generally chlorinate faster because of their higher basicities (13). Bromination rates are significantly faster than chlorination rates, and in some cases, eg, $(CH_3)_2NH$ ($k \sim 3 \times 10^9 M^{-1}s^{-1}$ at 25°C), become diffusion, rather than chemically controlled (21). Cleavage of the Si–N bond in trimethylsilyalkylamines by halogen in chloroform is a convenient route to primary and secondary *N*-haloalkylamines (90). Pure lower molecular weight *N,N*-dichloroalkylamines are volatile oils that are fairly stable at room temperature but unstable or explosive upon heating. The stability of *N,N*-dibromamines is variable; tertiary compounds are more stable than secondary (91) ones. Mixtures of *N,N*-dibromomethylamine

[10218-83-4] and *N,N*-dichloromethylamine [7651-91-4], CH_3NCl_2, rapidly equilibrate under the influence of uv light to form *N*-bromo-*N*-chloromethylamine [76019-33-5] (92). *N,N*-Dichloramines are rapidly converted to *N,N*-dibromamines by reaction with Br^- in acetonitrile (93). *N*-Chloroalkylamines are useful for the preparation of substituted hydrazines by reaction with excess amine in the presence of base. *Uns*-dimethylhydrazine is employed as a fuel in space applications.

$$RNH_2 + ClO^- \longrightarrow RNHCl + HO^- \xrightarrow{R'NH_2} RHN{-}NHR' + Cl^- + H_2O$$

N,N-Dichloroalkylamines can be converted to nitriles in basic media or by treatment with CsF in acetonitrile (75). Protonated *N*-chloroalkylamines under the influence of heat or uv

$$RCH_2NCl_2 + 2\,HO^- \longrightarrow RC{\equiv}N + 2\,H_2O + 2\,Cl^-$$

light rearrange to piperidines or pyrrolidines (Hofmann-Löffler reaction) (94). The free-radical addition of alkyl and dialkyl-*N*-chloramines to olefins and acetylenes yields β-chloroalkyl-, β-chloroalkenyl-, and δ-chloroalkenylamines (95). Various *N*-bromo- and *N*-chloropolyfluoroalkylamines have been synthesized whose addition products to olefinic double bonds can be photolyzed to fluoroazaalkenes (96).

Amides. Because amides are less basic, they chlorinate less rapidly than amines. *N*-Halamides are converted to amines in basic solution via intermediate formation of an isocyanate (Hofmann degradation reaction) (97). By contrast, base cleaves the C–N bond

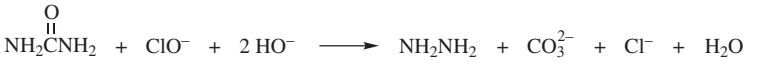
$$RC(=O){-}NHX + HO^- \longrightarrow RNCO + H_2O + X^- \longrightarrow RNH_2 + CO_2 + X^-$$

$$RC(=O){-}NX_2 + 2\,HO^- \longrightarrow RCOO^- + 0.5\,N_2 + 1.5\,X^- + 0.5\,HOX + 0.5\,H_2O$$

in *N,N*-dihalamides (98). The Cr(II) catalyzed addition of *N*-bromamides and *N*-chloramides to olefins yields primarily *N*-(2-haloalkyl)amides, which can be cyclized to oxazolines with alkoxide (99). *N*-Halamides are photochemically rearranged to 4-halamides, which can be cyclized to γ-iminolactones and γ-lactones (81). *N*-Bromoacetamide [79-15-2], mp 102–105°C, is unstable to light and heat. Nevertheless, it is useful in organic synthesis as a brominating and oxidizing agent. It selectively oxidizes allylic alcohols, and in the presence of HF and ether, it reacts with olefins forming bromofluoro compounds, and it has been used in synthesis of steroids (100) and fluorosteroids (101).

Ureas. Chlorination of aqueous urea yields unstable *N*-chloro compounds. With excess ClO^- decomposition yields CO_2, N_2O, and NCl_3; the latter decomposes further to NO_3^- (102). Only two solid derivatives have been isolated: *N*-chlorourea [3135-74-8], mp 74–76°C, and *N,N′*-dichlorourea [2959-01-5], which decomposes at its mp of 83°C with evolution of NCl_3. As an amide, urea also

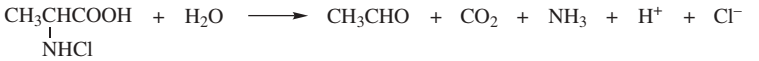
undergoes the Hofmann degradation reaction yielding hydrazine. This route to hydrazine was once employed commercially.



Various substituted *N*-bromo- and *N*-chloroureas have also been prepared (103). These compounds are useful for synthesis of oxazolidinones, and also hydrazine, hydrazo, and azo compounds. *N*-Bromourea [51918-81-1] is useful for selective oxidation of sugar derivatives (104).

Cyanamides and Derivatives. *N*-Chloro-*tert*-alkylcyanamides, RN(Cl)CN, are oils that have medicinal and other applications (105). Primary and secondary alkyl-*N*-chlorocyanamides add photochemically to olefins yielding 1:1 adducts. By contrast, *N*-chloro-*N*-*tert*-butylcyanamide initially rearranges photochemically to *N*-chloro-*N*-*tert*-butylcarbodiimide, $(CH_3)_3CN{=}C{=}NCl$, prior to addition to olefins giving carbodiimides (73,106). *N,N′*-Dichlorocarbodiimide is useful in preparation of photothermographic materials (107). Chlorinated guanylurea (av Cl_2 85%), prepared from dicyanamide, is useful as a bleach for synthetic fabrics (108). Chlorazodin, dichloroazodicarbonamidine, $NH_2C(=NCl)N{=}NC(=NCl)NH_2$ [502-98-7], prepared from guanidine, is a pale yellow solid that is stable at room temperature but decomposes at 155°C (109). Once used as a surgical antiseptic, it finds use in vulcanization of rubber (110). *N*-Chloroamidines, eg, $RNHC(CN){=}NCl$ and $CCl_2[C(NHR){=}NCl]_2$, exhibit fungicidal properties (111). *N*-Chloroamidines are useful for preparation of biocidal imidazoles (112) and thiadiazolines (113). *N*-Chloroguanidines, $RNHC(=NCl)NHR'$, serve as starting materials for synthesis of imidazoles, oxadiazoles, and thiadiazoles (114,115).

Amino Acids. The formation of *N*-halo-α-amino acids involves halogenation of the acid anion (13). *N*-Chloro-α-amino acids decompose to aldehydes and nitriles, the selectivity depending on pH and stoichiometry (116). For example, *N*-chloroalanine decomposes in the 6.5–10 pH range. In addition to aldehydes, nitriles are also formed either at lower



pH (≤5) or at higher pH by decomposition of *N,N*-dichloroalanine. When excess av Cl_2 is employed, the ammonia by-product is oxidized to nitrogen. The oxidation of amino acids by excess av Cl_2 is similar to breakpoint chlorination of ammonia, but slower (26). *N*-Chloroamino acids are poorer disinfectants than ammonia chloramines (37). Glycine is useful as a stabilizer for av halogen in cooling towers, providing reduced corrosion (117). Esters of *N*-chloro- and *N,N*-dichloro-α-amino acids are stable and can be isolated in pure form. A large number of *N*-chloro- derivatives of α-aminobutyrates have been prepared and evaluated as disinfectants (11). The chlorination of lysine in municipal wastewaters has recently been studied (118).

Carbamates. Lower alkyl *N*-halo- and *N,N*-dihalocarbamates are distillable liquids (76,119). *N*-Halo-*N*-metallocarbamates are crystalline hygroscopic solids. *N*-Chloro-*N*-sodiourethane [17510-52-0], $C_2H_5OCONClNa$, does not decompose on heating to 250°C (120), but violent decompositions have occurred at room temperature (121). *N*-Halocarbamates react with a variety of organic substrates, eg, the free-radical addition of *N*-chlorourethane [16844-21-6], $C_2H_5OCONHCl$, and *N,N*-dichlorourethane [13698-16-3], $C_2H_5OCONCl_2$, to olefins provides a convenient route to β-chlorocarbamates, which can be converted to aziridines and alkyloxazolidones (99,122). *N*-Chloro-*N*-sodiourethane reacts with organoboranes forming *N*-alkylcarbamates (121), and with olefins, catalyzed by Os, forming vicinal hydroxy carbamates (123).

Sulfonamides. *N*-Halo-*N*-alkylsulfonamides, $RSO_2NR'X$, are relatively stable distillable liquids. Under the influence of uv light they form 1:1 adducts with olefins (73,106). *N*-*tert*-Butyl derivatives rearrange forming precursors to cyclopropanes and sultams. *N*-Halo-*N*-sodioalkylsulfonamidates, RSO_2NClNa, have been less extensively studied than their aromatic counterparts (76). The stability of these compounds approaches that of the aromatic sulfonamides (86). The dodecyl compound exhibits properties of both a disinfectant and a surfactant.

Other Aliphatic Compounds. Sodium *N*-chloro-*N*-alkylsulfamates have been patented as bleaching and disinfecting agents (124). *N,N*-Dichloro-1,8-diformamido-*p*-menthane [67700-31-6] can be used to prepare polyisocyanate-based resins (125). *N*-Bromo-*S,S*-dimethyl sulfoximine, $(CH_3)_2S(O)NBr$, undergoes nucleophilic substitution with phosphines and thioethers forming interesting salts (126). *N,N*′-Dibromo-*S,S*-dimethylsulfur diimide, $(CH_3)_2S(NBr)_2$, reacts similarly, also forming cyclic compounds (127). *N,N*(-Dichloro-*S,S*-dialkylsulfur diimides explode violently when heated. *O,O*-Diethyl-*N,N*-dichlorophosphoramidate, $(C_2H_5O)_2P(O)NCl_2$, is a distillable oil that adds to olefins forming 1:1 adducts that can be reduced to *N*-(β-chloroalkyl)phosphoramidates (128). *N*-Bromotriphenylphosphine imine, $(C_6H_5)_3P{=}NBr$, (mp 170–172°C), is useful for synthesis of organically substituted compounds with PN/P, PN/S, and PN/As linkages (129). *N*-Chloro-(bis-trimethylsilyl)amine [4148-01-0], $[(CH_3)_3Si]_2NCl$, a yellow liquid (bp 149°C), reacts with NaN_3 forming a tetraazadiene and with BCl_3 to give hexachloroborazene (130).

4.3. Aromatic Compounds. *Sulfonamidates and Sulfonamides.* Chloramine-T, *N*-chloro-*N*-sodiomethylbenzenesulfonamidate trihydrate [127-65-1], $CH_3C_6H_4SO_2NClNa \cdot 3H_2O$, a white to slightly yellow solid, effloresces in air losing chlorine, becoming less soluble in water (77). It has a mp of 175°C, an av Cl_2 of 25%, and is moderately soluble in cold water giving pH ∼9. Heating >130°C may lead to explosion. The anhydrous product may explode at lower temperatures. Chloramine-T can be prepared by reaction of the amide with NaOCl. It was originally introduced in 1916 as a germicide. Mustard gas, $(ClC_2H_4)_2S$, is rendered ineffective by oxidation with chloramine-T (77). Chloramine-T is used in analysis and organic synthesis (76,77). Other uses include instrument sterilization (131), its use in radiolabeling techniques (132), its use in kinetics and mechanistic studies of chlorine exchange between it and secondary amines (133) and oxidation of nitrite (134), triethanolamine (135), and aminoacids (136), in desulfurization of light oils to form sulfimides (137), and in

reaction with araldoximes (138). Bromine analogues are also known, ie, bromamine-T [41085-71-6] and *N*-bromo-*N*-sodio-4-nitrobenzenesulfonamidate [41085-73-8]. The bromo derivatives are also used in organic synthesis (76), eg, in the Ru (IV) catalyzed oxidation of secondary alcohols (139).

Chloramine-B, *N*-chloro-*N*-sodiobenzenesulfonamidate [127-52-6], is prepared similarly to chloramine-T. It has been used as a disinfectant in dairies (140). A bromine equivalent, bromamine-B [16917-09-2], has also been prepared. The chloro and bromo compounds are used in analytical chemistry and in organic synthesis, eg, in the Os(IV) catalyzed oxidation of indole (141), in the oxidation of acetylcholine (142), and in the oxidation of primary amines (143).

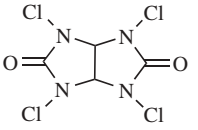
Polymer-bound *N*-chloro-*N*-sodiobenzenesulfonamidate, prepared via functionalization of poly(styrene-*co*-divinylbenzene), and its derivatives are useful in water disinfection and in removal of cyanide from water (144–151). They have also been used in kinetic and mechanistic studies of the oxidation of pentoses (152) and phenylethyl alcohols (153).

Dichloramine-T, *N,N*-dichloro-4-methylbenzenesulfonamide [473-34-7], $CH_3C_6H_4SO_2NCl_2$, mp 80°C, can be prepared by chlorination of the free amine or chloramine-T. It is also formed via disproportionation of chloramine-T (154). It is almost insoluble in water and has been used as a topical dressing and an antivesicant ointment (155). It is also used in organic synthesis. Dichloramine-B, *N,N*-dichlorobenzenesulfonamide [473-29-0], $C_6H_5SO_2NCl_2$, has been used as a deodorant and bleach for certain oils. Bromine analogues, ie, dibromamine-B [938-05-6], dibromamine-T [21849-4-1], and bromochloramine-T [27824-67-5], have also been prepared. Halazone, *p*-(*N,N*-dichlorosulfamoyl)benzoic acid [80-13-7], $HOOCC_6H_4SO_2NCl_2$, is a white solid that decomposes at ~195°C and is slightly soluble in water. It was used for emergency disinfection of water prior to, during, and after World War II (156). The homologue 3-(dichlorosulfamoyl)phthalic acid [67700-34-9], $(HOOC)_2C_6H_3SO_2NCl_2$, is also a useful disinfectant (157).

Other Aromatic Compounds. *N*-Chloro-*N*-substituted-*p*-nitroanilides, and other similar compounds, serve as sources of hypochlorite when mixed with alkaline materials (158). *N*-Chlorophenyldiguanidino compounds were once used as laundry bleaches (159,160). Sodium *N*-chloro-*N*-arylsulfamates have been patented as bleaches and disinfectants (125). *N*-Halophthalimides and *N*-haloquinolimides are converted under alkaline conditions to isatoic and 3-azaisatoic anhydrides, respectively, which are useful in production of pharmaceuticals and agrochemicals (161). *N*-Bromo derivatives of amides, imides, and sulfonamides are prepared in near quantitative yield using $CH_3C(O)OBr$ (82). *N*-Bromophthalimide [2439-85-2] and *N*-bromosaccharin [35812-01-2], a derivative of *o*-sulfamoylbenzoic acid, are useful brominating agents in analytical chemistry (162). Numerous *N*-halo derivatives of aromatically substituted amines, such as ureas, cyanamides, carbamates, and amino acids, have also been prepared.

4.4. Heterocyclic Compounds. *Glycolurils.* Chlorinated glycolurils were developed in the 1950s–1960s for protection against chemical agents and as bleaches, disinfectants, and foliage protectants (163–166). The most important is 2,4,6,8-tetrachloro-2,4,6,8-tetrazobicyclo[3.3.0]octane-3,7-dione [776-19-2] (**2**). The parent compound, glycoluril, is readily prepared by condensation of

urea and glyoxal. Substituted glycolurils are prepared by reaction of urea with the appropriate diketone (167). Like the chlorinated hydantoins, the chlorinated glycolurils are sparingly soluble in water. Tetrachloroglycoluril, eg, has a solubility of 77 ppm at 25°C. Although it has a theoretical av Cl_2 of 101.6%, only 10–20% titrates as FAC. It was once used in swimming pool disinfection. It has been employed in wastewater disinfection as a component of $Ca(OCl)_2$ tablets called Sanuril (168). 1,3,4,6-Tetrachloro-3α,6α-diphenyl-glycoluril [51592-06-4] (**3**), Iodogen, is useful as a disinfectant (169) and is widely used in radioimmunoassay as an oxidizing agent for preparation of ^{125}I labeled proteins, glycoproteins, and peptides (170). Bromo and bromochloro analogues have also been prepared (87,160,163).



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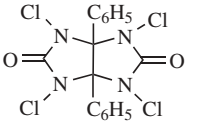
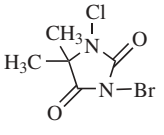


(**3**)

Hydantoins. Chlorinated hydantoins, first introduced in the 1930s, did not find wide use because of low dissolution rate. An additional disadvantage was the fact that hydrolysis of the second chlorine required a temperature of ~70°C. 1,3-Dichloro-5,5-dimethyl hydantoin [118-52-5] (DCDMH, Halane) (**1**) (171) was once used as a chemical warfare decontaminating agent (172). It has been used as a chlorinating agent, disinfectant, industrial deodorant, and as a laundry bleach. It is no longer used in home laundering because of changing needs of synthetic fabrics, but it is used to a small extent in commercial laundries where temperatures of ~70°C can be used. At pH 9 it decomposes to $(CH_3)_2CHNCl$, Cl^-, N_2, and CO_2 (173). 1-Bromo-3-chloro-5,5-dimethylhydantoin [16079-88-2] (BCDMH) (**4**) (87,89,160,174) is used in industrial water treatment and in sanitizing spas and hot tubs. Its use in outdoor swimming pools is limited because of cost, a very slow dissolution rate, and the fact that bromine is not stabilized against photolytic decomposition by dimethylhydantoin. The bactericidal properties of BCDMH have been studied in detail (175). The bromine hydrolyzes to a greater extent than the chlorine. Since excess bromide is normally present, it reacts rapidly with any HOCl or ClO^- formed by hydrolysis of BCDMH to generate av Br_2, eg, $HOCl + Br^- \rightarrow HOBr + Cl^-$, $k = 2.95 \times 10^3 M^{-1}s^{-1}$ at 25°C. Typical commercial products are based on BCDMH. However, one product is a mixture of DCDMH, BCDMH, and 1,3-dichloro-5-ethyl-5-methylhydantoin [89415-87-2] (176). BCDMH is also useful in control of biofouling in water recirculating systems (177), in toilet bowl cleaning (178), in metal recovery (179), and in laundry bleaching (180). 1,3-Dibromo-5,5-dimethylhydantoin [77-48-5] (87,88,171) is employed in organic synthesis (181–184).



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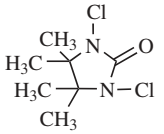

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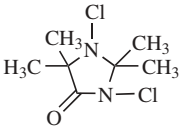
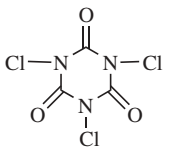


(**6**)

Imidazolidinones. Several mono and dichloro isomers have been prepared and tested as disinfectants (185): 1-chloro-4,4,5,5-tetramethylimidazolidin-2-one [58816-19-6]; 1,3-dichloro-4,4,5,5-tetramethylimidazolidin-2-one [58816-20-9] (**5**), mp 102–104°C; 1-chloro-2,2,5,5-tetramethylimidazolidin-4-one [38951-95-8], mp 157–158°C; and 1,3-dichloro-2,2,5,5-tetramethylimidazolidin-4-one [128780-87-0] (**6**), mp 69–71°C (186). In water, these compounds are extremely stable and better disinfectants than the oxazolidinones. They have potential for water disinfection and in hard surface cleaners. 1-Bromo-3-chloro- [108602-19-3], mp 102–104°C, and 1,3-dibromo- [108602-18-2], mp 119–121°C, derivatives of 4,4,5,5-tetramethylimidazolidin-2-one have also been prepared. The derivative 1-chloro-2,2,5,5-tetramethylimidazolidin-4-one is particularly stable having a K_h of $\leq 10^{-10}$. It is being tested for a variety of possible commercial applications for which long shelflife is necessary for a disinfectant. It has also been shown to have use potential for the aquaculture industry (187). Spirocycloalkyl derivatives of the *N*-chloroimidazolidinones, which may find application as disinfectants for nonpolar media, have also been reported (188).

Isocyanurates. Chlorination of cyanuric acid in the presence of base produces dichloroisocyanuric acid (DCCA, HCl_2Cy, where Cy = isocyanurate anion), ie, 1,3-dichloro-*s*-triazine-2,4,6–1*H*,3*H*,5*H*)-trione [2782-57-2] and trichloroisocyanuric acid (TCCA, Cl_3Cy), ie, 1,3,5-trichloro-*s*-triazine-2,4,6–1*H*,3*H*,5*H*)-trione [87-90-1] (**7**). DCCA forms various simple salts, eg, potassium dichloroisocyanurate [2244-21-5] KCl_2Cy, sodium dichloroisocyanurate [2893-78-9] (SDCC), $NaCl_2Cy$, (**8**), and its mono [52671-45-1], $NaCl_2Cy \cdot H_2O$, and dihydrates [51580-86-0], $NaCl_2Cy \cdot 2H_2O$. A number of double salts have also been prepared, eg, $Cl_3Cy \cdot KCl_2Cy$ [30622-37-8] and $Cl_3Cy \cdot 4KCl_2Cy$ [30622-37-8]. Some properties of chloroisocyanurates have been given (12). Bromine and bromochloro derivatives of isocyanuric acid (87) include HBrClCy [89325-49-5], HBr_2Cy [15114-43-9] (72), NaBrClCy [20367-88-8], $NaBr_2Cy$ [15114-34-8], $BrCl_2Cy$ [89696-38-8], Br_2ClCy, and Br_3Cy [17497-85-7] (78). Because of hydrolysis, the tribromo compound can only be prepared in nonaqueous media.



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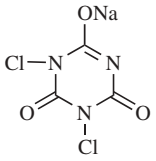

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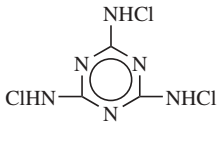
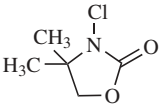


(**9**)

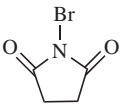
Melamines. Hexachloromelamine [2428-04-8] has a theoretical av Cl_2 of 128% (84,189). It is less stable than the trichloro compound: N^2,N^4,N^6-trichloro-2,4,6 triamino-1,3,5-triazine [12379-38-3] (**9**), av Cl_2 ~93%, mp 175°C, and slightly soluble in water. Several bromo analogues have been prepared (88,189). Trichloromelamine is widely used for sanitation in the food and beverage industry and by the U.S. military kitchen services.

Oxazolidinones. 3-Chloro-4,4-dimethyl-2-oxazolidinone [58629-01-9] (**10**) has been extensively evaluated as a disinfectant (185). It is prepared by phosgenation of $(CH_3)_2CH(NH_2)CH_2OH$ followed by chlorination in the presence of

caustic. It is a white crystalline solid with a theoretical av Cl_2 of 48.1%, a mp of 71–72.5°C, and a solubility of 1.2% in H_2O. It hydrolyzes to only a very slight extent and consequently is very stable in aqueous media relative to other chlorine-based disinfectants. However, disinfection effectiveness is significantly lower than with hypochlorite or chloroisocyanurate. Nevertheless, it may find use in applications for which kill time is not of primary importance, eg, cooling towers. A number of bromine analogues have also been prepared, eg, 3-bromo-4,4-dimethyl-2-oxazolidinone [60491-95-4], which is an orange solid with mp 118–120°C. Because of greater hydrolysis it is less stable in water than the chloro derivative but is a better disinfectant.



(**10**)



(**11**)

Succinimides. *N*-Chlorosuccinimide, 1-chloropyrrolidine-2,5-dione [128-09-6], is a white solid with a slight chlorine odor, a mp of 150–151°C, and a solubility in water of 1.4% at 25°C. It is used in organic synthesis for highly selective oxidation of primary and secondary alcohols to carbonyl compounds, providing improved synthesis of prostaglandins (190), and in conversion of allylic and benzylic alcohols to halides (191). It selectively cleaves tryptophanyl peptide bonds (192) and is useful in fluorometric analysis of proline and hydroxyproline (193). It has recently been used in the oxidation of benzylamine (194). *N*-Bromosuccinimide [128-08-5], (NBS) (**11**) is a solid with mp of 173–175°C and solubility in water of 1.4% at 25°C. It is especially useful in organic synthesis for allylic bromination (Wohl-Ziegler reaction) (195), aromatic ring (196) and side-chain bromination, for oxidation, eg, alcohols to carbonyl compounds, for dehydrohalogenation (74), and is used in the commercial production of cortisone (197) and vitamin D_3.

Other Heterocyclic Compounds. 1,3-Dichlorotetrahydroquinazoline-2,4-dione [23767-45-5] is useful as a laundry bleach. 2-Chloro-4-thiazolines are useful reagents for organic synthesis (198). *N*-Chloropiperidines, *N*-chloropiperidones, and 1,4-dichloro-2,2,5,5-tetrasubstituted-piperazine-3,6-diones have been evaluated as disinfectants (199). 1,3,5-Trichloro-2,4-dioxohexahydrotriazine [67700-33-8] is a useful bactericide (200). *N*-Chloro-2-substituted-imidazolines have been prepared for impregnating clothing for protection against chemical agents such as mustard gas (201). 1-Chlorobenzotriazole [21050-95-3] is useful in organic synthesis for oxidation of alcohols to carbonyl compounds and hydrazo compounds to azo compounds (202). 1,3-Dihalouracils have utility as pesticides, fungicides, bleaching, and sanitizing agents (203). The cyclic amide, *N*-bromo-ε-caprolactam [2439-83-0], mp 64–66°C, functions as an allylic brominating agent similar to *N*-bromosuccinimide, but does not require activation (204). *N*-Chloro- and *N*-bromopolymaleimides are useful as halogenating agents (205).

5. *N*-Halamine Polymers

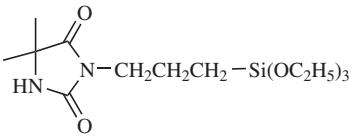
Probably the topic concerning *N*-halamine chemistry which has received the most attention during the past decade, and the one of greatest commercial potential in the areas of water disinfection and biocidal coatings, is the derivatization of polymeric materials with *N*-halamine functional groups. There are three ways in which this could be accomplished. First, an *N*-halamine biocide could simply be blended with a commercial polymeric material. Second, a polymerizable moiety such as a vinyl, an allyl, or an acroyl group could be used to functionalize an *N*-halamine compound followed by polymerization. Third, a commercial polymer could be functionalized by an *N*-halamine moiety. The first method suffers from the limitation that the *N*-halamine biocide could leach out of the polymer matrix over time and could not be replaced *in situ*. The second method is difficult to control, but may find uses in some biocidal coatings. The third method appears to be the most facile approach and has experienced the widest development over the past decade.

Already mentioned are the polymer-bound *N*-chloro-*N*-sodiobenzenesulfonamidates, prepared via functionalization of poly(styrene-*co*-divinylbenzene), and its derivatives that are useful in water disinfection and in removal of cyanide from water (144–151). Recently, poly(styrene-*co*-divinylbenzene) has been functionalized with a hydantoin moiety that can be mono- or dichlorinated before use in an *in situ* water disinfection application (206,207). The material can be produced by a heterogeneous synthetic process in the form of microporous beads also, which exhibits the advantage of maintaining rapid flow in a biocidal cartridge water filter (208,209). A few seconds contact time in the filter are sufficient for complete inactivation of pathogenic bacteria, viruses, fungi, and some protozoa, although not the protozoan species *Cryptosporidium*, which is extremely resistant to disinfection by oxidative FAC as well (210). Possibly the most useful feature of the new polymer is that upon loss of the bound oxidative halogen, regeneration is possible numerous times by simply exposing the polymer in its cartridge filter to aqueous free chlorine (dilute bleach).

For the textile industry cellulose has been functionalized with an *N*-chlorohydantoin moiety to render it biocidal (211,212). This was done by direct condensation of 3-hydroxymethyl-5,5-dimethylhydantoin with the cellulose followed by chlorination with dilute bleach that could be accomplished *in situ* during a fabric wash cycle. A similar reacton has been utilized for Nylon 66 following pretreatment with formaldehyde and base (213) and for PET following pretreatment with ammonium hydroxide (214). Grafting techniques are also being employed for cellulose and other fibers to functionalize with a biocidal *N*-halamine moiety (215). The biocidal textiles produced are effective against both Gram positive and Gram negative bacteria in contact times ranging from 2 to 30 min.

In other work, an *N*-halamine-functionalized elastomer has been produced from a poly(styrenebutylene) copolymer for the purpose of creating biocidal rubber gloves and tubing (216). Several *N*-halamine copolymer coating materials have been prepared for use in grafting to surfaces (217) and for polyurethane paints (218). A very recent development is the synthesis of 3-triethoxysilylpro-

pyl-5,5-dimethylhydantoin (**12**), which is soluble in aqueous alcohol solutions, and which can be bonded to a variety of surfaces, such as cellulose, glass, ceramics, and paint (219). Upon chlorination *in situ*, the surfaces become biocidal, inactivating pathogens in minutes of contact time.



(**12**)

6. Economic Aspects

The estimated 1990 worldwide consumption of monochloramine for hydrazine manufacture was 55,000 t. Consumption data on use of monochloramine in water treatment are not available. The U.S. consumption of chloroisocyanurates and halogenated hydantoins in 1986 was 44,045 and 3,409 t, respectively (220). The worldwide capacity for chloroisocyanurates in 2000 was ~180,000 t, with trichloroisocyanuric acid accounting for ~67% of total production, and the U.S. market being the predominant one. In fact, the overall growth in the period 1999–2004 was 3.5%/year (221). The U.S. consumption of bromochloro- and dibromo-dimethylhydantoins, tetrachloroglycoluril, and other specialty *N*-halamines, eg, trichloromelamine, is small. The consumption of polymeric *N*-halamine materials is expected to become significant during the current decade.

7. Analytical Methods

The available halogen in *N*-halamines can be determined by reaction with excess iodide in acid media followed by titration with standard thiosulfate. For mixed bromochloro *N*-halamines, the ratio of av Br_2 to av Cl_2 can be determined by reduction followed by potentiometric titration of Br^- and Cl^-. Standard ir spectra are useful for identification of *N*-halamines (222). A number of instrumental, titrimetric, and colorimetric methods are available for determining various forms of chlorine in dilute aqueous solution, ie, total, free, combined, mono-, di-, and trichloramine (223). Test kits typically based on the Palin or DPD method, employing manual color comparators or spectrophotometers, are available for routine analysis in the laboratory or in the field (224). Hypochlorous acid can be determined directly by sweep voltammetry (225) and amperometry using a membrane electrode (226). Because they undergo hydrolysis to HOCl, inorganic, and organic chloramines can interfere with instrumental and colorimetric FAC measurements (227). The DPD method is also applicable to determination of free and combined av Br_2 (228). Mono-, di-, and trichloramine can also be quantitated by extraction of dilute aqueous solutions with CCl_4 followed by uv spectrophotometry (229). Gas chromatography (GC) can also be used to determine NCl_3 in aqueous solution after extraction with CCl_4. Trichloramine can be determined in the gas phase by uv or gc. Recently, new liquid chromatography techniques

involving postcolumn electrochemical detection have been developed to analyze for *N*-halamines and their decomposition products (230–232); these techniques are particularly useful for detection of short-lived species in wastewater (230,231). Also, it has been shown recently that electrospray and atmospheric pressure–chemical ionization mass spectrometry techniques can be used in organic *N*-chloramine and free chlorine analysis (233).

8. Health and Safety Factors

Chloramines and bromamines react with moisture releasing potentially corrosive, toxic, and explosive gases and should be stored under dry conditions at moderate temperatures, segregated from incompatible materials. Since they are highly reactive, they should not be mixed with other materials such as acids, bases, reducing agents, oxidizing agents, organic compounds, ammonium compounds, etc, since vigorous reactions can occur, accompanied by fire and even explosions, liberating large amounts of heat and potentially toxic gases. *N*-Halamines are irritating to the skin, eyes, and mucous membranes. However, they are nonirritating under use conditions in dilute aqueous solution. Acute oral toxicities, LD_{50} (mg/kg, rat), are TCCA 490, SDCC 735, and BCDMH 600 (234). Even though there have been suggestions that cyanuric acid and the chloroisocyanurates could be carcinogens, recent laboratory studies have alleged to refute these suggestions (235). Monochloramine has been shown to be a weak mutagen, and its use in drinking water is under review by the EPA (33,236). It has been suggested that free chlorine and *N*-chloramines are naturally produced DNA repair inhibitors (237), and the carcinogenic potential of chlorinated water containing free chlorine and chloramines has been discussed (238,239). Finally, there is little published information available concerning the degradation of *N*-halamines in the environment, although an interesting study of the enzymatic degradation of substituted hydantoins to amino acids has been reported (240).

9. Uses

Monochloramine is used in water treatment and as an intermediate in the manufacture of hydrazine (qv). Chloroisocyanurates are employed primarily for sanitation in swimming pools and spas. They are also used in hard surface cleaners, laundry products, as toilet bowl cleaners, eg, TCCA and SDCC/NaBr, and as shrink-proofing agents in wool finishing. Whereas TCCA is the principal product in pool and spa use, SDCC is the main product in nonpool/spa applications. Dichlorodimethylhydantoin is employed as a bleaching agent in industrial and institutional cleaning products. Bromochlorodimethylhydantoin is used primarily as a sanitizer in spas and to a smaller extent in swimming pools. Industrial water treatment applications include cooling towers, air washers, pasteurizers, and paper mills. Small amounts of bromochlorodimethyl hydantoin and tetrachloroglycoluril are used as components of $Ca(OCl)_2$ tablets called Sanuril that are employed in wastewater treatment. *N*-Chlorodimethyloxazolidinone, formed *in situ* from av Cl_2 and dimethyloxazolidinone, is employed as an algistat in

cooling towers and swimming pools. Trichloromelamine is employed as a disinfectant, eg, in restaurants and the U.S. military kitchen services. *N*-Halamines such as *N*-bromo- and *N*-chlorosuccinimide, *N*-bromocaprolactam, *N,N*-dibromo- and *N,N*-dichlorodimethylhydantoin, chloramine-T, *N,N*-dichlorourethane, dibromo- and trichloroisocyanuric acids, etc, are employed as selective reagents for halogenation, oxidation, and other transformations in research, in analysis, and in small-scale production of specialty chemicals, pharmaceuticals, flavors, fragrances, etc. The polymeric *N*-halamines are being used for odor removal in cutting oils and will soon find use in potable water disinfection and in biocidal coatings for a variety of applications.

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