Inorganic and organic halamine formation mechanisms and reactivity in water disinfection: recent developments

Kumudu H. Rathnayake[†], Julia E. Stroud[†], Susana Y. Kimura[*]

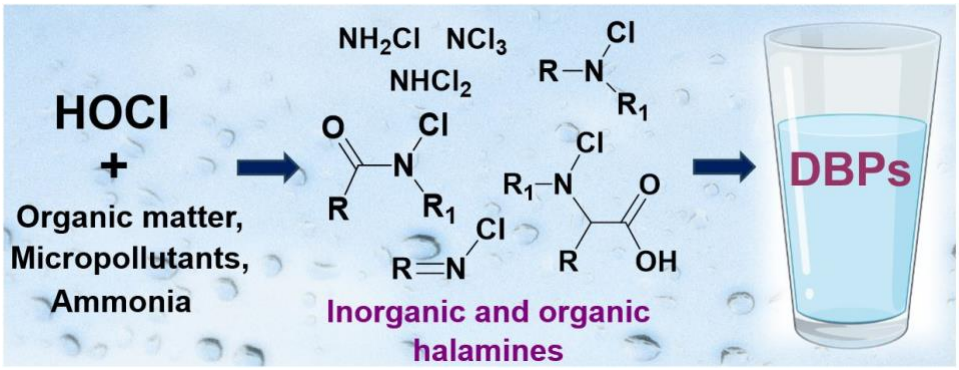
Department of Chemistry, University of Calgary, Calgary, Alberta, T2N 1N4, Canada

[†]co-principal authors

[*]corresponding author

Abstract

Inorganic and organic halamines, characterized by a minimum of one nitrogen-halogen (N–X) bond, have received increased attention in water treatment due to their formation during disinfection, limited understanding of their reactivity, and potential taste and odour impacts on drinking water. Understanding the formation mechanisms of *N*-halamines and their role in toxic disinfection by-product (DBP) formation is crucial for devising DBP control strategies. This review highlights recent studies (2021-2025) that investigated formation mechanisms and reactivity of inorganic and organic halamines, including inorganic chloramines, *N*-halamines, *N*-halamides, and *N*-halamino acids.



Keywords: organic halamines, disinfection by-products, formation mechanisms, chloramines, *N*-halamino acids, *N*-halamides.

1. Introduction

Water disinfection is a critical step in drinking water treatment aimed at inactivating pathogens and inhibiting regrowth in disinfected water. Chlorine (HOCl) and inorganic chloramines (NH_2Cl, $NHCl_2$, NCl_3) are the most applied chemical disinfectants due to their disinfection efficacy and ability to maintain a residual throughout distribution systems. However, chemical disinfectants can react with organic matter and other components in source waters to unintentionally form disinfection by-products (DBPs). Consumption of chlorinated water have been associated with adverse health effects, including bladder cancer and adverse birth outcomes,[1] prompting investigation into DBP precursors and formation mechanisms[1-3].

The role that halamines have on DBP formation is of interest partly because they can act as nitrogen sources for nitrogenous DBPs (N-DBPs), which are significantly more toxic than their carbon-only counterparts[3]. For example, inorganic chloramines are a nitrogen source for haloacetonitriles, and *N*-haloacetamides,[4,5] and their reactions have led to *N*-nitrosodimethylamine (NDMA) formation, a probable carcinogen[6,7]. Organic halamines are formed via reactions between chlorine-based disinfectants with nitrogen-containing precursors including amino acids and amides. Therefore, "organic halamines" is a collective term for *N*-halamines, *N*-halamides, *N*-halamino acids, and *N*-halaldimines[2]. Early findings on organic chloramines were reviewed by How *et al.*[2] and Kimura and Ortega-Hernandez[3]. As such, this

review focuses on recent advances of inorganic and organic halamine formation and reactivity mechanisms, emphasizing their roles as key intermediates in DBP formation, and speciation.

Table 1. Glossary of abbreviations and associated specialized terminology referenced herein.

Abbreviation	Description
DBPs	disinfection by-products
N-DBPs	nitrogenous disinfection by-products
HOCl	hypochlorous acid
NH_2Cl	monochloramine
$NHCl_2$	dichloramine
NCl_3	trichloramine
NDMA	*N*-nitrosodimethylamine
HNO	nitroxyl
NO^-	nitroxyl anion
ONOOH	peroxynitrous acid
$ONOO^-$	peroxynitrite anion
'UP'	'unidentified product'
$Cl–N–NO_2^-$	chloronitramide ion
ClNO	nitrosyl chloride
UV	ultraviolet
HCl	hydrochloric acid
OCl^-	hypochlorite
EAS	electrophilic aromatic substitution
FAAs	free amino acids
Cl_2O	dichlorine monoxide

2. Inorganic chloramines

Chloramine chemistry was unified by Jafvert and Valentine, outlining 14 reactions that accurately model the formation and degradation of chloramines[8]. However, mechanisms

governing dichloramine ($NHCl_2$) decomposition remained unresolved for more than three decades [8, 9]. Recent work by the Fairey group (Figure 1a) demonstrated that $NHCl_2$ hydrolysis produces nitroxyl anion (HNO/NO^-), which subsequently reacts with dissolved oxygen to generate peroxynitrous acid/peroxynitrite anion ($ONOOH/ONOO^-$)−a key intermediate in NDMA formation[7]. The authors reported the formation of an "unidentified product" (UP) whose yield depended on dissolved oxygen[10]. A follow-up study revealed that NO_2^+ reacts with NH_2Cl or $NHCl_2$, followed by hydrolysis to form chloronitramide anion ($Cl–N–NO_2^-$)—the UP, resolving the long-standing mystery[9]. $Cl–N–NO_2^-$ was detected in 40 chloraminated U.S. drinking water samples at concentrations (1.3-92 µg/L; median 23 µg/L) comparable to regulated DBPs, highlighting its widespread occurrence and relevance[9].

Complementary work by the Chuang group (Figure 1b) has expanded the understanding of reactions involved in breakpoint chlorination, revealing their pivotal role in NDMA formation and micropollutant degradation[6, 11]. They investigated the reaction between NCl_3 and $NHCl_2$ and identified *N,N*-tetrachloro hydrazine as a transient intermediate that can hydrolyze to form nitrosyl chloride (ClNO)−a potent nitrosating agent implicated in NDMA formation[6]−and/or decompose to 1,1-dichlorodiazine and hydroxyl radicals (•OH), particularly at acidic pH[11]. Together, these discoveries demonstrate that chloramine chemistry extends far beyond simple inorganic equilibria; rather it involves a complex system of nitrosating, oxidative, and radical pathways that control DBP formation. Future work could clarify how bromide and bromamines participate in these halamine reaction systems, potentially revealing additional transformation pathways.

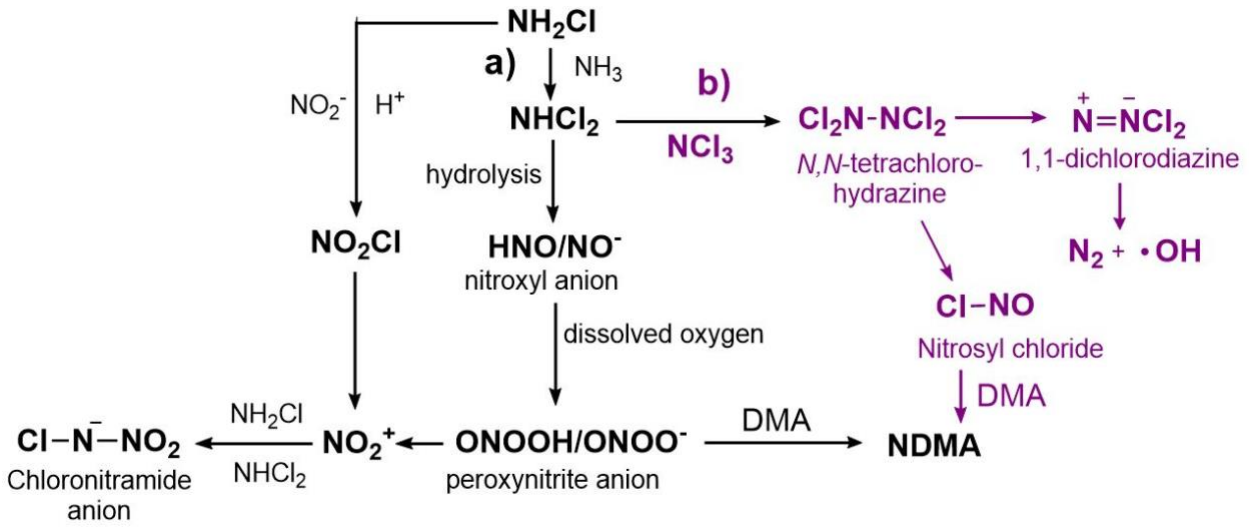


Figure 1. Chloramine chemistry characterized by the a) Fairey group and b) the Chuang group [6-7, 9-11].

3. *N*-halamines

N-halamines are formed via the halogenation of primary or secondary amines,[2] and from the reaction of inorganic chloramines with dissolved organic nitrogen/carbon[2, 12]. Algal organic matter is also an important *N*-halamine precursor during chlorination[13]. Recently, *N*-halamines have been identified as key intermediates in the formation of high-molecular-weight DBPs,[14, 16] and haloacetonitriles[15, 16], as well as during chlorination of pollutant precursors such as sulfonamides,[17] and benzotriazole[18,19]. Chlorine/sunlight treatment of benzotriazole produces higher yields of *N*-chlorobenzotriazole compared to chlorination alone[18]. Recently, our group revealed that *N*-chlorobenzotriazole acts as a persistent free-chlorine reservoir that drives unexpectedly high and pH-dependent DBP formation across diverse water matrices[19].

Photolysis of *N*-halamines generates reactive radicals that promote micropollutant degradation and DBP formation[20-26]. A unifying mechanism has emerged: UV cleavage of

N–Cl or N–Br bonds generate •OH, •Cl, •Br and nitrogen-containing radicals, that undergo hydrogen/alkyl shifts, β-scission, intramolecular rearrangements, and halogenation reactions. For example, UV activation of chlorinated atenolol generates nitrogen-containing radicals that undergo 1,2-hydrogen shifts, β-scission, intramolecular addition[20]. UV activation of *N*-chlorosarcosine generates •OH, •Cl, and nitrogen-containing radicals that accelerate micropollutant (metoprolol) degradation and trihalomethane and haloketone formation [21]. The Zhou group showed that UV-activation of both organic *N*-chloramines and *N*-bromamines enhanced haloacetonitrile and halonitromethane formation, with *N*-bromamines photolyzing more rapidly and producing higher •OH levels [22-24]. In bromide-containing waters, *N*-bromamines enhances brominated haloacetonitrile formation, whereas NH_2Cl suppresses these pathways by inhibiting *N*-bromamine formation[24]. Additional studies showed that UV/chlorination in bromide-containing waters enhances halonitromethane yields and bromine incorporation[25], and that aliphatic *N*-chloramines contribute to halonitromethane formation through •OH and •Cl mediated pathways[26]. Collectively, these findings identify N-halamine photolysis as a radical-generation mechanism that links micropollutant transformation with shifts in DBP formation and speciation. However, major knowledge gaps remain, including limited quantification of radical yields across different *N*-halamine structures and poor understanding of the stability of *N*-halamine intermediates.

4. *N*-chloramides

N-chloramides form in disinfected waters from the 1) chloramination of aldehydes[4,5], 2) chlorination/chloramination of amides[27, 28], and 3) chlorination of haloacetonitriles[29]. The Mariñas group confirmed the “aldehyde pathway” is a significant pathway for haloacetonitrile and *N*-haloacetamide formation in drinking water via carbinolamine dehydration, and oxidation by

NH_2Cl (Figure 2a-b)[4]. In a recent computational study, Xue *et al.*[5] proposed that the carbinolamine intermediate undergoes HCl elimination to form an iminol that leads to *N*-haloacetamides (Figure 2c). Moreover, aldehydes substituted with electron-donating or withdrawing groups or can enhance haloacetonitrile or *N*-haloacetamide formation, respectively. However, aldehydes substituted with conjugated groups are favorable for both[5].

Zhang *et al.*[27] investigated the chlorination of seven aliphatic and cyclic amides and found that they react primarily through hypochlorite (OCl^-)-mediated pathways to form mono- and di-substituted *N*-chloramides. These intermediates subsequently react with phenolic compounds via electrophilic aromatic substitution (EAS) or electron transfer, generating chlorinated phenols while partially regenerating the parent amide[27]. Similarly, Lim *et al.*[28] studied six nitrogen heterocycle amides and showed that structural differences strongly influence subsequent reactions after initial *N*-chloramide formation. For example, the *N*-chloramide intermediate of 2-piperidone remained stable for days under excess chlorine, whereas saturated heterocyclic imides hydrolyzed to ring-opened acids. In uracil derivatives, chlorine addition across double bonds produced 5-chlorouracil, which fragmentated to trichloroacetaldehyde; however, *N*-substitution in uridine and 1,3-dimethyluracil suppressed fragmentation, leading to stable chlorinated or ring-opened products[28].

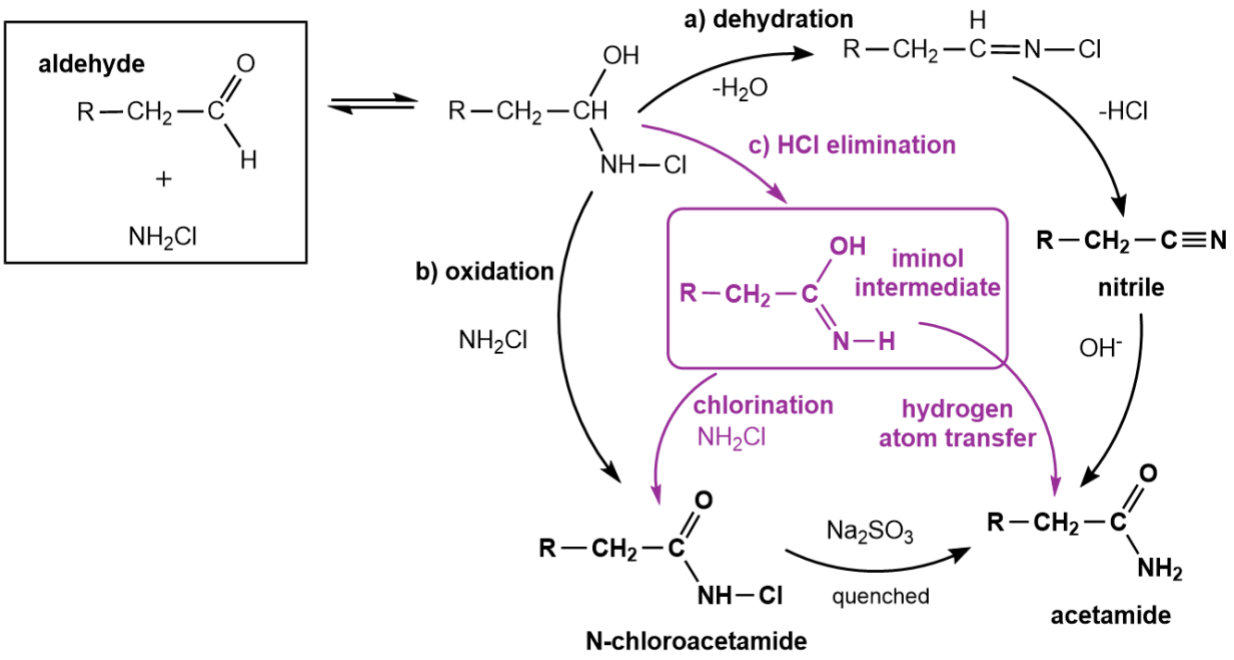


Figure 2. Aldehyde transformation pathway to nitrile and *N*-chloroacetamide[4-5]

5. *N*-halamino acids

Amino acids are major DBP precursors in disinfected waters and important contributors to dissolved organic nitrogen[30]. They occur as free amino acids (FAAs) in ng-µg/L levels or as either short -or long chain peptides in mg/L levels in surface waters[31-33]. Although present at lower concentrations, FAAs have been observed to form more N-DBPs and are less effectively removed through conventional drinking water treatment methods due to their size and behaviour [33-35].

N-halamino acids from FAAs. *N*-halamino acid formation from FAAs is driven by electrophilic substitution by HOCl at amino-group nitrogen atoms, influenced by molecular structure and halogen identity. Aliphatic FAAs follow straightforward *N*-chlorination and deamination pathways (Figure 3a-b), while aromatic FAAs undergo additional oxidative transformations

(Figure 3c)[2-3,31,37-40]. A recent review highlighted *N*-chlorination as an essential first step when aliphatic FAAs are exposed to chlorinating agents, producing *N*-halamino acids that act as intermediates in the formation of N-DBPs including dichloroacetonitrile, trichloroacetontrile, trichloronitromethane, and dichloroacetamide [2-3,30]. More detailed mechanistic studies have observed that *N*-halamino acid formation from glycine, α-alanine, and branched chain amino acids begins with rapid electrophilic substitution by HOCl at the terminal amino group, followed by pH-dependent pathways. Under alkaline conditions, *N*-chloramino acids undergo base-catalyzed deprotonation at the α-carbon generating carbanion intermediates that rapidly eliminate chloride and decompose, producing nitriles and aldehydes (Figure 3a). At neutral or slightly acidic pH, Cl_2O/HOCl act as dominant chlorinating agents, promoting sequential *N*-chlorination to yield *N,N*-dichlorinated amino acids, which can rearrange or dehydrohalogenate—forming *N*-chloraldimines (Figure 3b)[2,36-39]. Recent studies have shown that *N*-chloraldimines are key reactive intermediates that can undergo further *N*-halogenation and dehydrochlorination to generate haloacetonitriles, and halonitromethanes, corroborating and extending the framework proposed by How et al.(Figure 2d)[2,40-41]. This aligns with findings that UV254-induced homolytic cleavage of N-Cl bonds in *N*-chlorinated α-amino acids generates nitrogen-centered radicals (e.g., •NHCl) that undergo C-C or C-N bond cleavage followed by chlorination or oxidation to form dichloroacetonitrile and trichloronitromethane, with low pH enhancing these processes due to increased HOCl reactivity[42,43].

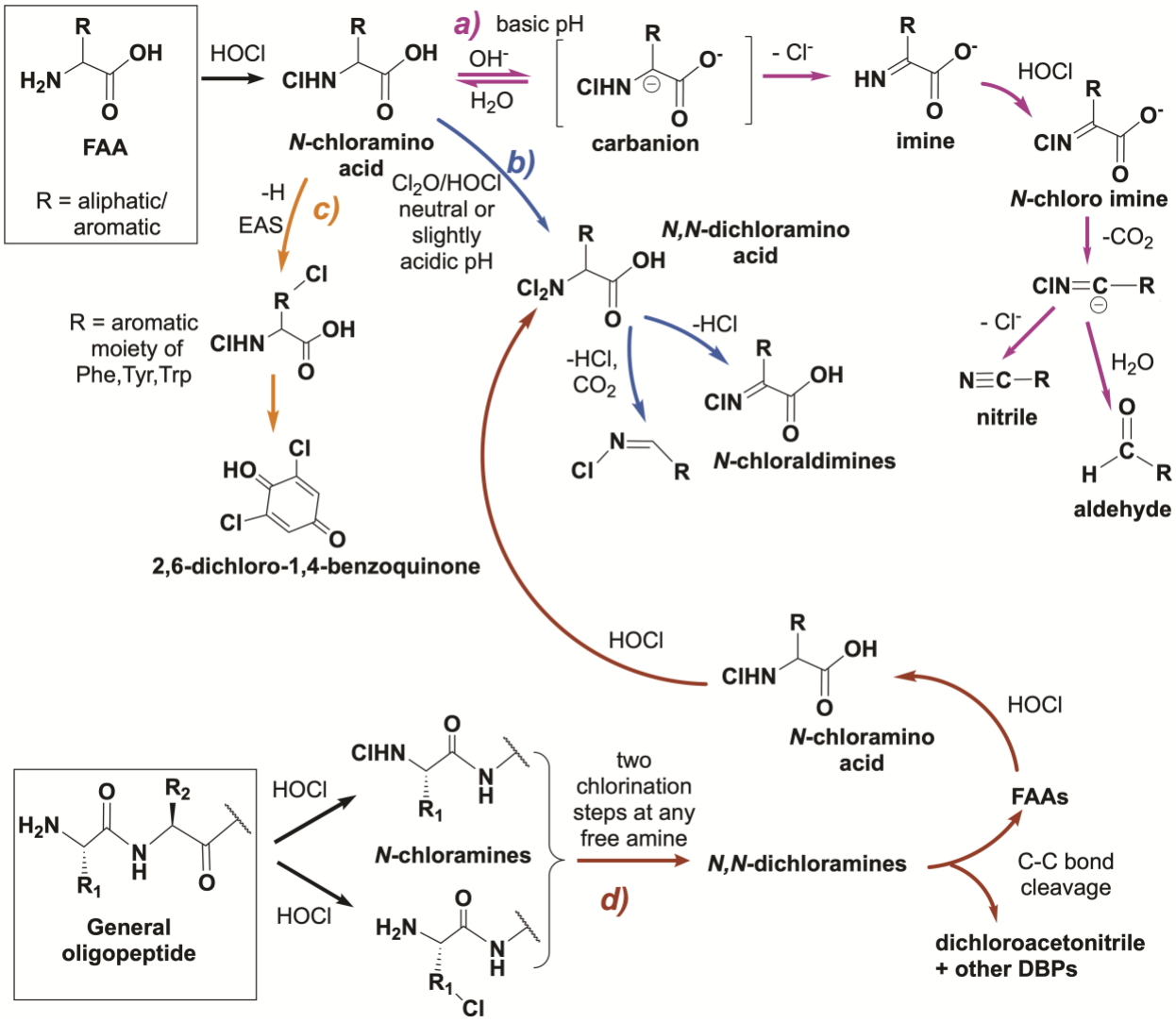


Figure 3. Summary of general mechanisms for *N*-chloramino acid and *N*-chloraldimine formation from both FAAs and peptide-bound amino acids[2-3,31,37-40,40-41,44-47]. Formation mechanisms from FAAs with aliphatic side chains at basic **(a)** and neutral/slightly acidic **(b)** pH as well as aromatic **(c)** side chains are shown. DBP and *N*-chloraldimine formation mechanisms from peptide-bound amino acids **(d)** are shown as well. Phe=phenylalanine, Tyr=tyrosine, Trp=tryptophan.

Bromination of FAAs produce both more and different types of DBPs than chlorination via bromine attack to the backbone primary amine, followed by downstream C-C bond cleavage

between the α- and β-carbons[30]. However, chlorination of iodotyrosine promotes iodoacetonitrile formation via aromatic substitution and oxidative side-chain transformation where chlorine replaces the iodine in the amino acid molecule[44]—a process involving *ipso* substitution and halogen exchange, which has been reported for brominated aromatics in chlorinated waters[45]. Thus, the chlorination of FAAs has been well elucidated and while some recent studies appear to investigate other forms of halogenation, reports of bromination and iodination mechanisms are lacking.

Recently, DBP formation from aromatic FAAs has also been reported. Chlorination of phenylalanine, tyrosine, and tryptophan, after initial backbone-amine chlorination, proceeds via EAS, introducing chlorine atom(s) to the aromatic ring (Figure 3c)[46-47]. Subsequent side chain transformations—highly dependent on FAA structure—may include hydroxylation, oxidative side-chain degradation, and ring-cleavage, leading to the formation of chlorinated benzoquinones such as 2,6-dichloro-1,4-benzoquinone (Figure 3c)[46].

N-halamino acids from peptides. Recent studies have reported that peptides also undergo *N*-chlorination through similar electrophilic pathways to FAAs (Figure 3), but their larger size, modified termini, and functional side chains lead to more diverse and persistent *N*-halamino intermediates[48-49]. Shi and Mitch[49] showed that short lysine- and arginine-containing peptides undergo *N*-chlorination at both α- and ε-amino groups, forming stable *N*-halo-peptide intermediates that can transform into cyclic chlorinated products and aldehydes depending on peptide structure and chlorine dose(Figure 3d). Zhou *et al.*[48] similarly found that dipeptides undergo *N*-chlorination followed by C–C bond cleavage, contributing to dichloroacetonitrile formation. It was recently reported that aromatic and functionalized peptides, or peptide analogues such as tyrosyl dipeptides, can undergo EAS on their side chains, generating halogenated aromatic

by-products including iodinated aromatic rings; as well, computational studies suggest that amino groups may also undergo *N*-halogenation [50-51]. Under oxidative conditions—particularly post UV chlorination—these peptides show enhanced reactivity compared to FAAs, resulting in elevated levels of aromatic DBPs including 2,6-dichloro-4-nitrophenol and 2,6-dichloro-1,4-benzoquinone (Figure 3c)[52,53]. Although the mechanisms of *N*-chlorination and decomposition of FAAs are well characterized, the analogous pathways in peptides remain less clear; it appears to not yet be well understood when *N*-chlorination remains on the peptide backbone versus when it leads to peptide bond cleavage and subsequent release of FAAs. Bromination and iodination mechanisms are also not well understood.

5. Conclusion

Recent advances have greatly expanded our understanding of *N*-halamine chemistry, revealing that both inorganic and organic halamines act as critical intermediates in the formation of toxic N-DBPs. Mechanistic studies have clarified long-standing uncertainties in chloramine decomposition and NDMA formation, including the discovery of the Cl–N–NO_2^- arising from $NHCl_2$ hydrolysis, and the identification of potent oxidants such as ClNO and •OH generated during breakpoint chlorination. Parallel research on UV cleavage of N-Cl and N-Br bonds in N-chlorinated α-amino acids and halamines, particularly bromamines, has shown that photolysis promotes micropollutant degradation but also elevates DBP formation through radical-centered pathways involving •OH, •Cl, •Br, and nitrogen-containing radicals. Additional work has uncovered iodine-specific halogen-exchange pathways during iodotyrosine chlorination and established *N*-halaldimines—formed through sequential chlorination and dehydrohalogenation—as important intermediates from free amino acids and peptide precursors. Collectively, these studies highlight that reactive nitrogen species and radical-centered intermediates are generated

not only from UV activation but also from water disinfection reactions which are central to N-DBP formation[54]. Their characterization however, is constrained by the need of specialized analytical methods capable of detecting short-lived nitrogen species and radicals. Recent work has mostly focused on inorganic and organic chloramines—and, to a lesser extent, bromamines, iodamines and mixed halide systems—as key contributors to DBP formation, yet the influence of bromide/iodide and bromamine/iodamine chemistry remains poorly understood and warrants further investigation. Together, these findings underscore the need for a holistic and mechanistic approach to anticipate and mitigate toxic DBP formation in disinfected waters.

Statement of Competing Interests

The authors declare that they have no competing financial, personal, or other interests that would have influenced the work herein.

6. Acknowledgements

Support for this work was provided by the Natural Sciences and Engineering Research Council (NSERC), Canada Research Chair and the University of Calgary.

7. Author contributions

KR, JS, and SYK contributed to the conceptualization, literature review, writing, and editing of this work.

References

[1] Li X-F, Mitch WA. Drinking Water Disinfection Byproducts (DBPs) and Human Health Effects: Multidisciplinary Challenges and Opportunities. Environmental Science & Technology. 2018, 52(4):1681-9 https://doi.org/10.1021/acs.est.7b05440.

[2] How ZT, Kristiana I, Busetti F, Linge KL, Joll CA. Organic chloramines in chlorine-based disinfected water systems: A critical review. Journal of Environmental Sciences. 2017, 58:2-18 https://doi.org/10.1016/j.jes.2017.05.025.

[3] Kimura SY, Ortega-Hernandez A. Formation mechanisms of disinfection byproducts: Recent developments. Current Opinion in Environmental Science & Health. 2019, 7:61-8 https://doi.org/10.1016/j.coesh.2018.11.002.

[4] Vu TN, Kimura SY, Plewa MJ, Richardson SD, Mariñas BJ. Predominant N-Haloacetamide and Haloacetonitrile Formation in Drinking Water via the Aldehyde Reaction Pathway. Environmental Science & Technology. 2019, 53(2):850-9 https://doi.org/10.1021/acs.est.8b02862.

[5] Xue J, Zhou Y, Liu YD, Zhong R. Transformation mechanisms of acetaldehyde and its substituted aldehydes into the corresponding nitriles and (N-chloro)amides during chloramination: A computational study. Science of The Total Environment. 2022, 836:155592 https://doi.org/10.1016/j.scitotenv.2022.155592.

**[6] Chuang Y-H, Chen T-Y, Chou C-S, Chu L-K, Hou C-Y, Szczuka A. Critical Role of Trichloramine Interaction with Dichloramine for N-Nitrosamine Formation during Breakpoint

Chlorination. Environmental Science & Technology. 2023, 57(40):15232-42 https://doi.org/10.1021/acs.est.3c03326.

This study revealed the critical role of NCl_3-$NHCl_2$ interaction in N-nitrosamine formation, indetifying nitrosyl chloride(ClNO) as a key intermediate and characterized distinct reaction kinetics and pathways that explain elevated NDMA yields under chloraminated conditions.

[7] Pham HT, Wahman DG, Fairey JL. Updated Reaction Pathway for Dichloramine Decomposition: Formation of Reactive Nitrogen Species and N-Nitrosodimethylamine. Environmental Science & Technology. 2021, 55(3):1740-1749. https://doi.org/10.1021/acs.est.0c06456

[8] Jafvert CT, Valentine RL. Reaction scheme for the chlorination of ammoniacal water. Environmental Science & Technology. 1992, 26(3):577-86 https://doi.org/10.1021/es00027a022.

**[9] Fairey JL, Laszakovits JR, Pham HT, Do TD, Hodges SD, McNeill K, Wahman DG. Chloronitramide anion is a decomposition product of inorganic chloramines. Science. 2024, 386(6724):882-7 https://doi.org/10.1126/science.adk6749.

This study identified chloronitramide anion ($Cl–N–NO_2^-$) as the long-elusive decomposition product of inorganic chloramines, resolving a decades-old mystery in drinking water chemistry.

[10] Pham HT, Wahman DG, Fairey JL. Closing Dichloramine Decomposition Nitrogen and Oxygen Mass Balances: Relative Importance of End-Products from the Reactive Nitrogen

Species Pathway. Environmental Science & Technology. 2024, 58(4):2048-57 https://doi.org/10.1021/acs.est.3c08088.

*[11] Chuang Y-H, Chou C-S, Chu Y-L. Unveiling the Critical Pathways of Hydroxyl Radical Formation in Breakpoint Chlorination: The Role of Trichloramine and Dichloramine Interactions. Environmental Science & Technology. 2024, 58(47):21086-96 https://doi.org/10.1021/acs.est.4c08403.

This study investigated the key pathways of •OH formation during breakpoint chlorination, highlighting that interactions between NCl_3 and $NHCl_2$ are the primary drivers of •OH generation and significantly influence radical-mediated DBP formation.

[12] Guo Y, Yang Q, Xu J, Bai X, Han Q, Nie J, Zhang L, Li H, Gao H, Zhou W, Li J.. Formation of organic chloramines during chlorination of 18 compounds. Water Research. 2021, 204:117570. https://doi.org/10.1016/j.watres.2021.117570.

[13] Li X, Zhai H, Luo J, Hou R. A new concern raised from algal bloom: Organic chloramines in chlorination. Water Research. 2024, 260:121894. https://doi.org/10.1016/j.watres.2024.121894

[14] Wang P, Ye B, Nomura Y, Fujiwara T. Revisiting the chloramination of phenolic compounds: Formation of novel high-molecular-weight nitrogenous disinfection byproducts. Water Research. 2024, 266:122335. https://doi.org/10.1016/j.watres.2024.122335

*[15] Kralles ZT, Werner CA, Dai N. Overlooked Contribution of the Indole Moiety to the Formation of Haloacetonitrile Disinfection Byproducts. Environmental Science & Technology. 2023, 57(17):7074-85 https://doi.org/10.1021/acs.est.3c01080.

This study investigated the previously overlooked role of the indole moiety in promoting haloacetonitrile formation during disinfection, highlighting its significance as a precursor in nitrogenous DBP pathways and showing that *N*-halamines are formed as key intermediates in this process.

[16] Kralles ZT, Deherikar PK, Werner CA, Hu X, Kolodziej EP, Dai N. Halogenation of Anilines: Formation of Haloacetonitriles and Large-Molecule Disinfection Byproducts. Environmental Science & Technology. 2024, 58(39):17497-509 https://doi.org/10.1021/acs.est.4c05434.

[17] Xia D, Liu H, Lu Y, Liu Y, Liang J, Xie D, Lu G, Qiu J, Wang R. Utility of a non-target screening method to explore the chlorination of similar sulfonamide antibiotics: Pathways and NCl intermediates. Science of The Total Environment. 2023, 858:160042 https://doi.org/10.1016/j.scitotenv.2022.160042.

[18] Choo Z-S, Hsieh M-C, Lin HH-H, Yang J-S, Lin AY-C. Reactive chlorine species in the enhanced degradation of UV stabilizers during the sunlight/free chlorine process. Chemosphere. 2022, 309:136677 https://doi.org/10.1016/j.chemosphere.2022.136677

[19] Rathnayake KH, Hossain MF, Brown A, Kimura SY. From Micropollutant to DBP Driver: The Unexpected Reactivity of 1-Chlorobenzotriazole in Water Disinfection. ChemRxiv. 2025; doi:10.26434/chemrxiv-2025-9tc0l (accessed 2025-11-19).

[20] Ra J, Yoom H, Son H, Hwang T-M, Lee Y. Transformation of an Amine Moiety of Atenolol during Water Treatment with Chlorine/UV: Reaction Kinetics, Products, and

Mechanisms. Environmental Science & Technology. 2019, 53(13):7653-62 https://doi.org/10.1021/acs.est.9b01412.

[21] Wang Y, Dong H, Qin W, Li J, Qiang Z. Activation of organic chloramine by UV photolysis: A non-negligible oxidant for micro-pollutant abatement and disinfection by-product formation. Water Research. 2021, 207:117795. https://doi.org/10.1016/j.watres.2021.117795.

[22] Wu Y, Zhang W, Bu L, Zhu S, Wang J, Zhou S. UV-induced activation of organic chloramine: Radicals generation, transformation pathway and DBP formation. Journal of Hazardous Materials. 2022, 421:126459. https://doi.org/10.1016/j.jhazmat.2021.126459.

[23] Ao J, Bu L, Wu Y, Zhu S, Zhou S. Insights into the fate and properties of organic halamines during ultraviolet irradiation: Implications for drinking water safety. Science of The Total Environment. 2023, 904:165994. https://doi.org/10.1016/j.scitotenv.2023.165994.

[24] Ao J, Bu L, Wu Y, Wu Y, Zhou S. Enhanced formation of haloacetonitriles during chlorination with bromide: Unveiling the important roles of organic bromamines. Science of The Total Environment. 2023, 868:161723 https://doi.org/10.1016/j.scitotenv.2023.161723

[25] Deng L, Luo W, Huang T, Wen L, Singh RP, Zuo Y, Tan C. Formation and transformation of halonitromethanes from dimethylamine in the presence of bromide during the UV/chlorine disinfection. Chemosphere. 2022, 291:132731. https://doi.org/10.1016/j.chemosphere.2021.132731.

[26] Hua Z, Liang J, Wang D, Zhou Z, Fang J. Formation Mechanisms of Nitro Products from Transformation of Aliphatic Amines by UV/Chlorine Treatment. Environmental Science & Technology. 2023, 57(47):18754-64 https://doi.org/10.1021/acs.est.3c00744.

*[27] Zhang T, von Gunten U. Chlorination of amides: Kinetics and mechanisms of formation of N-chloramides and their reactions with phenolic compounds. Water Research. 2023, 242:120131 https://doi.org/10.1016/j.watres.2023.120131.

This study investigated the chlorination kinetics and mechanisms of amides, detailing the formation of N-chloramides and their subsequent reactions with phenolic compounds in water treatment.

[28] Lim S, Wu Y, Mitch WA. Transformation of cyclic amides and uracil-derived nitrogen heterocycles during chlorination. Water Research. 2025, 282:123639 https://doi.org/10.1016/j.watres.2025.123639.

[29] Yu Y, Reckhow D. The Formation and Occurrence of N-chloro-2,2-dichloroacetamide, A Previously Overlooked Nitrogenous Disinfection Byproduct in Chlorinated Drinking Waters. Environmental Science & Technology. 2016, 51(3):1488-1497. https://doi.org/10.1021/acs.est.6b04218.

[30] Li G, Tian C, Karanfil T, Liu C. Comparative formation of chlorinated and brominated disinfection byproducts from chlorination and bromination of amino acids. Chemosphere. 2024, 349:140985. https://doi.org/10.1016/j.chemosphere.2023.140985.

[31] Dotson A, Westerhoff P. Occurrence and removal of amino acids during drinking water treatment. Journal AWWA. 2009, 101(9):101-15 https://doi.org/10.1002/j.1551-8833.2009.tb09963.x.

[32] Chu W, Li D, Gao N, Yin D, Zhang Y, Zhu Y. Comparison of free amino acids and short oligopeptides for the formation of trihalomethanes and haloacetonitriles during chlorination:

Effect of peptide bond and pre-oxidation. Chemical Engineering Journal. 2015, 281:623-31 https://doi.org/10.1016/j.cej.2015.07.005

[33] Li J, Cai Y, Du Z, Zhang Z, Li J. Review of Free Amino Acids in Source Water (River, Lake, and Reservoir): Occurrence, Composition, Molar Yields, Formation Potential, and Contribution to N-DBPs. ACS ES&T Water. 2024, 4(9):3698-712 https://doi.org/10.1021/acsestwater.4c00572.

[34] Yang Y, Yu Q, Zhou R, Feng J, Zhang K, Li X, Ma X, Dietrich AM. Occurrence of Free Amino Acids in the Source Waters of Zhejiang Province, China, and Their Removal and Transformation in Drinking Water Systems. Water. 2020, 12(1). https://doi.org/10.3390/w12010073.

[35] Yu Y, Reckhow DA. Formation of metastable disinfection byproducts during free and combined aspartic acid chlorination: Effect of peptide bonds and impact on toxicity. Water Research. 2020, 168:115131. https://doi.org/10.1016/j.watres.2019.115131.

[36] Simon F, Szabó M, Fábián I. The chlorination of glycine and α-alanine at excess HOCl: Kinetics and mechanism. Journal of Hazardous Materials. 2023, 447:130794. https://doi.org/10.1016/j.jhazmat.2023.130794.

[37] Simon F, Fábián I, Szabó M. Oxidation of branched chain amino acids by HOCl: Kinetics and mechanism. Journal of Hazardous Materials. 2024, 470:134145 https://doi.org/10.1016/j.jhazmat.2024.134145

[38] Szabó M, Baranyai Z, Somsák L, Fábián I. Decomposition of N-Chloroglycine in Alkaline Aqueous Solution: Kinetics and Mechanism. Chemical Research in Toxicology. 2015, 28(6):1282-91. https://doi.org/10.1021/acs.chemrestox.5b00084.

[39] Szabó M, Bíró V, Simon F, Fábián I. The decomposition of N-chloro amino acids of essential branched-chain amino acids: Kinetics and mechanism. Journal of Hazardous Materials. 2020, 382:120988 https://doi.org/10.1016/j.jhazmat.2019.120988.

[40] How ZT, Linge KL, Busetti F, Joll CA. Chlorination of Amino Acids: Reaction Pathways and Reaction Rates. Environmental Science & Technology. 2017, 51(9):4870-6 https://doi.org/10.1021/acs.est.6b04440.

[41]Wu Y, Huang Y, Zhu S, Wu Y, Bu L, Zhou S, Chu W. Formation and Decomposition of N-Chloroaldimines in Drinking Water Disinfection: An Overlooked Subclass of Organic Chloramines. Environmental Science & Technology. 2025, 59(13):6778-86. https://doi.org/10.1021/acs.est.4c10905.

[42] Ruan X, Zhang X, Lei Y, Lei X, Wang C, Yang X. UV254 irradiation of N-chloro-α-amino acids: Kinetics, mechanisms, and N-DBP formation potentials. Water Research. 2021, 199:117204. https://doi.org/10.1016/j.watres.2021.117204

[43] Hua Z, Li J, Zhou Z, Zheng S, Zhang Y, Fang J. Exploring Pathways and Mechanisms for Dichloroacetonitrile Formation from Typical Amino Compounds during UV/Chlorine Treatment. Environmental Science & Technology. 2022, 56(13):9712-21 https://doi.org/10.1021/acs.est.2c01495.

*[44] Ding S, Du Z, Qu R, Wu M, Xiao R, Wang P, Chen X, & Chu W. Reactivity, Pathways, and Iodinated Disinfection Byproduct Formation during Chlorination of Iodotyrosines Derived from Edible Seaweed. Environmental Science & Technology. 2024, 58(40):17999-8008 https://doi.org/10.1021/acs.est.4c03542.

This study found that the presence of halides in chlorination of free amino acids alters DBP formation mechanisms; specifically, iodine from edible seaweed enhances iodinated DBP and other toxic byproduct formation through a halogen exchange reaction.

**[45] Psoras, A W, McCoy, S W, Reber, K P, McCurry, D L, & Sivey, J D. Ipso Substitution of Aromatic Bromine in Chlorinated Waters: Impacts on Trihalomethane Formation. Environmental Science and Technology, 2023, *57*(47), 18801-18810. https://doi.org/10.1021/acs.est.3c00852

This study revealed the role of *ipso* substitution in promoting halogen exchange during chlorination of brominated aromatics, showing that displaced bromine can be reincorporated into DBPs enhancing brominated trihalomethane formation even in the absence of added bromine.

[46] Chen B, Shen H, Jin Y, Wu Q, Liu J, Wang X, Zhang X, Yu H. Formation mechanisms of chlorinated disinfection byproducts chlorinated benzoquinones from free aromatic amino acids: In vitro and in silico study. Science of The Total Environment. 2025, 966:178685 https://doi.org/10.1016/j.scitotenv.2025.178685.

[47] Yu R, Qian Y, Chen Y, Shi Y, Guo J, An D. Computational-aided analysis of the pathway and mechanism of dichloroacetonitrile formation from phenylalanine upon chloramination.

Science of The Total Environment. 2024, 926:171995. https://doi.org/10.1016/j.scitotenv.2024.171995

[48] Zhou Y, Jiao J-j, Huang H, Liu YD, Zhong R, Yang X. Insights into C–C Bond Cleavage Mechanisms in Dichloroacetonitrile Formation during Chlorination of Long-Chain Primary Amines, Amino Acids, and Dipeptides. Environmental Science & Technology. 2023, 57(47):18834-45. https://doi.org/10.1021/acs.est.2c07779.

[49] Shi JL, Mitch WA. Lysine and Arginine Reactivity and Transformation Products during Peptide Chlorination. Environmental Science & Technology. 2023, 57(14):5852-60. https://doi.org/10.1021/acs.est.2c09556.

[50] Ren Z, Qiu Y, Huan M, Liu YD, Zhong R. Identification of chlorinated products from tyrosine and tyrosyl dipeptides during chlorination: a computational study. Environmental Science: Processes & Impacts. 2022, 24(12):2345-56. https://doi.org/10.1039/d2em00321j.

[51] Qiu Y, Liu YD, Zhong R. New insights into the iodination mechanism of tyrosine and its dipeptides and comparison with chlorination and bromination reactions. Environmental Science: Water Research & Technology. 2024, 10(6):1421-31. https://doi.org/10.1039/d4ew00062e.

[52] Bu L, Chen X, Wu Y, Zhou S. Enhanced formation of 2,6-dichloro-4-nitrophenol during chlorination after UV/chlorine process: Free amino acid versus oligopeptide. Separation and Purification Technology. 2023, 310:123119 https://doi.org/10.1016/j.seppur.2023.123119

*[53] Wawryk NJP, Huang G, Craven C, Qiu J, Jmaiff Blackstock LK, Li X-F. Aspartame-Sweetened Tap Water: Transformation Products and 2,6-Dichloro-1,4-Benzoquinone Formation.

Environmental Science & Technology. 2023, 57(3):1332-41 https://doi.org/10.1021/acs.est.2c07156.

This study investigates the impacts of aspartame sweeteners on DBP formation—a topic gaining significant traction given its relevance in consumer spheres—and observes that aspartame can lead to the formation of toxic benzoquinone DBPs during chlorination. toxic benzoquinone DBPs during chlorination.

[54] Scholes, RC. Emerging investigator series: contributions of reactive nitrogen species to transformations of organic compounds in water: a critical review. Environmental Science: Processes & Impacts, 2022, 24(6):851-869. https://doi.org/10.1039/D2EM00102K