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Exotic Electrophiles in Chlorinated and Chloraminated Water: When Conventional Kinetic Models and Reaction Pathways Fall Short

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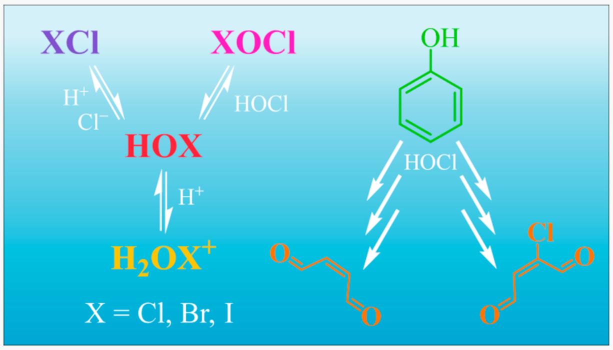
ABSTRACT: Halogenation and oxidation of organic matter in chlorinated and chloraminated water are typically attributed to the most abundant electrophiles present. This interpretation sometimes fails to explain laboratory observations, including halogenation kinetics and product distributions. Exotic electrophiles, species commonly overlooked in the environmental literature, can help to resolve these discrepancies. Herein, we review evidence demonstrating the significance of lesser-studied electrophilic chlorinating (Cl_2 and Cl_2O), brominating (BrCl, BrOCl, and Br_2O), and iodinating (H_2OI^+ and ICl) agents in chlor(am)inated water. The evidence includes reaction rate dependencies on [Cl^-], [H^+], and [HOCl] that cannot be attributed to the reactivity of hypohalous acids or hypohalites alone. For example, enhancement of chlorination and bromination rates by Cl^- implicates Cl_2 and BrCl, respectively, as active halogenating agents. Herein, we discuss a new method for quantifying the sensitivity of halogenation to rate enhancement by Cl^-. We also discuss complexities that Cl^- can impart on iodination kinetics. In addition, we highlight recent insights into radical-mediated reaction pathways and unexpected organic electrophiles in chlorinated water. Finally, we discuss practical implications, identify research needs, and offer recommendations to improve the design of future halogenation experiments. Overall, this review aims to spur new research into underappreciated electrophiles in chlor(am)inated water.



INTRODUCTION

The ubiquitous water disinfectants free chlorine (i.e., HOCl + OCl^-) and monochloramine (NH_2Cl) induce oxidation reactions that can transform contaminants and produce disinfection byproducts (DBPs).[1] HOCl and NH_2Cl quickly oxidize Br^- and I^- to produce other electrophilic halogen species (e.g., HOBr and HOI).[2,3] Researchers examining electrophilic substitution often focus on reactions directly involving the most abundant halogen species [e.g., hypohalous acids (HOX), where X = Cl, Br, or I].[4,5] However, reaction models that include only the electrophiles that are prevalent in chlor(am)inated water sometimes fail to accurately predict product distributions[6] and the effects of halide ion concentration, disinfectant concentration, and pH on reaction rates (see examples in Figures S1−S3).[7−16]

The chemistry and consequences of the less abundant halogenating agents [e.g., Cl_2O, BrCl, and H_2OI^+ (Figure S4)] have garnered increased attention in the past decade.[7−16] Nevertheless, much about their influence on disinfection efficacy, disinfectant consumption rates, total organic halogen (TOX) formation rates, product distributions, reaction pathways, and toxicity remains unknown. We use the term exotic electrophiles to describe these less abundant halogenating agents because they are commonly overlooked in the environmental literature. This article focuses primarily on exotic halogenating agents that are known to react via electrophilic addition and substitution.[7−16] We also discuss recent discoveries of radical-mediated reaction pathways and novel organic electrophiles (e.g., 2-butene-1,4-dial and phenoxy radicals).[6,17] Finally, we offer recommendations for future research directions and practical advice for improving halogenation experiments.

With the exception of Cl_2,[18] direct observations of exotic electrophiles in chlor(am)ination experiments have not been reported, likely due to low concentrations, instability, and drowning of spectroscopic signatures by predominant species (e.g., HOX). The influence of exotic electrophiles can, however, be inferred by examining the effects of solution conditions (e.g., pH, [Cl^-], and chlorine dose) that are known to influence electrophile speciation on measured halogenation rates. Exotic electrophiles are expected to exert appreciable influence under conditions that increase their concentrations,

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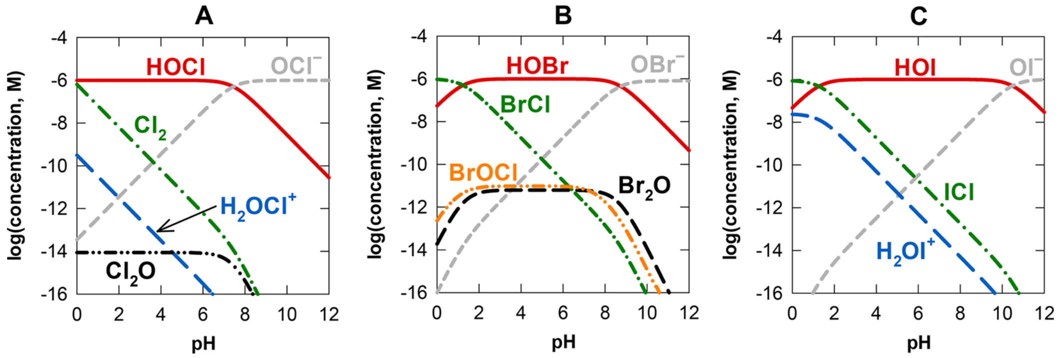

Figure 1. Speciation of (A) chlorine(+1), (B) bromine(+1), and (C) iodine(+1) in water as a function of pH. All species shown are potential electrophilic halogenating agents, except those colored gray. Concentrations were computed using the equilibrium constants listed in Table 1 (corrected to an ionic strength of 10 mM using the Davies equation). To permit comparisons across each system, all calculations assume [halogen(+1)] = 1.0 μM and [Cl^-] = 1.0 mM. These concentrations are similar to those employed in laboratory studies (e.g., refs 13, 14, and 16) seeking to elucidate organic compound halogenation rates and mechanisms. Frame B assumes 28.0 μM (2.0 mg/L as Cl_2) chlorine(+1) co-occurs with 1.0 μM bromine(+1).

Table 1. Equilibrium (K_{eq}) and Forward Reaction Rate Constants (k_+) for Free Halogen Species at 25 °C[a]

reaction	log K_{eq}	k_+	μ[b] (M)	ref
$2HOCl(aq) \rightleftharpoons Cl_2O(aq) + H_2O$ (1)	−2.06[c]	undetermined	0	35
$HOCl(aq) + Cl^- + H^+ \rightleftharpoons Cl_2(aq) + H_2O$ (2)	2.98	2.14×10^4 M^{-2} s^{-1}	0.5	36
$HOCl(aq) + Br^- + H^+ \rightleftharpoons BrCl(aq) + H_2O$ (3)	9.06	1.32×10^6 M^{-2} s^{-1}	1.0	37
$BrCl(aq) + H_2O \rightleftharpoons HOBr(aq) + Cl^- + H^+$ (4)	−3.89	3.0×10^6 s^{-1}	1.0	37
$HOCl(aq) + Br^- \rightleftharpoons HOBr(aq) + Cl^-$ (5)	5.17	1.6−6.8 × 10^3 M^{-1} s^{-1}	1.0	37−40
$Br_2(aq) + H_2O \rightleftharpoons HOBr(aq) + Br^- + H^+$ (6)	−8.21	97 s^{-1}	0.5	41
$2HOBr(aq) \rightleftharpoons Br_2O(aq) + H_2O$ (7)	0.80	undetermined	0	11
$HOCl(aq) + HOBr(aq) \rightleftharpoons BrOCl(aq) + H_2O$ (8)	−0.46	undetermined	0	11
$H_2OI^+ \rightleftharpoons HOI(aq) + H^+$ (9)	0.3	undetermined	0.2	42
$HOI(aq) + Cl^- + H^+ \rightleftharpoons ICl(aq) + H_2O$ (10)	4.09	2.4×10^6 s^{-1}	0.5	43

[a] Anionic halogen species (e.g., Cl_3^-, Br_2Cl^-, and ICl_2^-) are not shown as they are unlikely to contribute appreciably as electrophilic halogenating agents (see refs 3 and 12). [b] μ is the ionic strength. [c] Corrected to 25 °C according to ref 9.

including a high disinfectant dose, low pH, and high [Cl^-].[6−16] Such conditions are particularly relevant for laboratory experiments, in which disinfectant doses often exceed those used in actual water treatment and in which Cl^- can be introduced unintentionally by adjusting the pH with HCl. In drinking water treatment, the coagulant ferric chloride ($FeCl_3$) increases the [Cl^-] and lowers the pH.[9] In comparison to drinking water, lower pH, higher [Cl^-], and higher disinfectant doses are common during treatment of nonpotable water, including wastewater, ballast water, industrial cooling water, and hydraulic fracturing waste.

Less nucleophilic moieties (e.g., aromatic ethers) are more susceptible to halogenation by exotic electrophiles,[12,13,15] whereas more nucleophilic moieties (e.g., phenolates) react less selectively with the most abundant electrophiles (e.g., HOX).[13,19] In a drinking water distribution system, halogenation of moderately nucleophilic moieties by exotic electrophiles should become more important as water travels away from the treatment facility after the reactivity of the most nucleophilic moieties has been attenuated by halogenation or other oxidation reactions (i.e., during the "slow" phase of DBP formation[20]). Similarly, exotic electrophiles are anticipated to influence halogenation processes in systems containing preoxidized organic matter for which the fast-reacting fraction of nucleophilic sites has been consumed; such systems include recreational waters (particularly seawater pools) and water reuse scenarios.

CHLORINE SPECIES

In free chlorine solutions, HOCl (pK_a = 7.54; 25 °C)[21] and OCl^- are the most abundant chlorine species present (Figure 1A). Thus, [free chlorine] is typically approximated as [HOCl] + [OCl^-]. As HOCl is more reactive than OCl^- toward most organic compounds,[22] conventional wisdom dictates that HOCl is the predominant chlorinating agent under conditions relevant to drinking water treatment. Rate constants for reactions with HOCl have been reported for numerous compounds.[22] To compare results across different reaction conditions, experimentally determined pseudo-first-order rate constants (k_{obs}) are often divided by the initial [free chlorine] (i.e., [HOCl] + [OCl^-]) to obtain apparent second-order rate constants (k_{app}) or divided by [HOCl] or [OCl^-] to obtain second-order rate constants that are specific for HOCl (k_{HOCl}) or OCl^- (k_{OCl^-}), respectively. These calculations assume that chlorination reactions are first-order in [free chlorine] or that HOCl (or OCl^-) is the sole chlorinating agent under the experimental conditions employed, respectively.

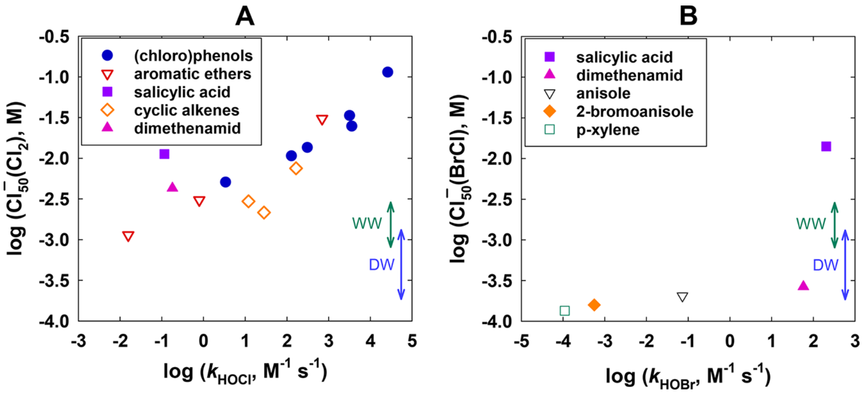

Figure 2. (A) Extent of chlorination rate enhancement by Cl^- [represented by $Cl^-_{50}(Cl_2)$, the $[Cl^-]$ required such that Cl_2 contributes 50% to the overall chlorination rate] as a function of the reactivities of organic compounds toward HOCl (k_{HOCl}). $Cl^-_{50}(Cl_2)$ values were computed from second-order rate constants for reactions of Cl_2, Cl_2O, and HOCl; values shown for (chloro)phenols were calculated using second-order rate constants for both the phenol and phenolate forms. (B) Extent of bromination rate enhancement by Cl^- [represented by Cl^-_{50}(BrCl), the $[Cl^-]$ required such that BrCl contributes 50% to the overall bromination rate] as a function of the reactivities of organic compounds toward HOBr (k_{HOBr}). Cl^-_{50}(BrCl) values were computed from previously reported second-order rate constants for BrCl, BrOCl, and HOBr. Conditions applicable to both frames: pH 7.0, [free chlorine] = 28 μM (2 mg/L as Cl_2), and ionic strength = 0.1 M. For organic compounds capable of reacting with free chlorine or free bromine at more than one position, data shown represent the net reactivity of all reactive positions. Only rate constants from the aforementioned references were included because they were obtained under similar experimental conditions. WW and DW denote typical $[Cl^-]$ in municipal wastewater[47] and drinking water,[48] respectively. Derivations of $Cl^-_{50}(Cl_2)$ and Cl^-_{50}(BrCl) and the complete list of organic compounds are provided in Text S1 and Table S1, respectively. The extent of iodination rate enhancement by Cl^- is not illustrated because sufficient data do not exist.

Findings from multiple studies have challenged the assumption that HOCl is the predominant chlorinating agent in free chlorine solutions. The chlorination rates of allyl alcohol,[23] crotonic acid,[24] anisole,[25] biphenyl,[26] *p*-xylene,[7,8] naphthalene,[27] and fluoranthene[27] show a second-order dependence on [HOCl]; most of these studies[7,8,23−26] attribute this observation to Cl_2O being the primary chlorinating agent because $[Cl_2O]$ has a second-order dependence on [HOCl] (Table 1, eq 1). Cl_2, which is present in free chlorine solutions containing Cl^- (eq 2), has long been acknowledged as a potent chlorinating agent[7,27−33] and oxidant,[18,34] especially at pH <6. Both Cl_2O and Cl_2 are anticipated to be stronger electrophiles than HOCl because OCl^- and Cl^- (from Cl_2O and Cl_2, respectively) are better leaving groups compared with OH^- (from HOCl).[9,10] Nonetheless, Cl_2O and Cl_2 have largely been overlooked in the environmental literature, perhaps due to their concentrations being lower (by approximately 6 orders of magnitude) than that of HOCl under conditions typical of drinking water chlorination (Figure 1A).

Studies quantifying the influence of Cl_2O, Cl_2, and HOCl on reaction kinetics are scarce. Voudrias and Reinhard[7,8] computed second-order rate constants for reactions of *p*-xylene with Cl_2O and Cl_2 (i.e., k_{Cl_2O} and k_{Cl_2}, respectively), but *p*-xylene reacted sufficiently slowly with free chlorine that it was not possible to obtain a second-order rate constant for HOCl (i.e., k_{HOCl}), precluding quantitative comparisons of the reactivities of Cl_2O, Cl_2, and HOCl. Unless otherwise indicated, all second-order rate constants herein are specific to the halogenating agent. Sivey et al.[9] systematically varied the pH, chlorine dose, and $[Cl^-]$ when examining the reaction kinetics of the herbicide dimethenamid and obtained estimates of k_{Cl_2O} and k_{Cl_2} that are 7 orders of magnitude larger than k_{HOCl}. Subsequent investigations of aromatic ethers,[10] antipyrine,[44] carbamazepine,[45] tramadol,[46] phenols,[13] salicylic acid,[14] and cyclic alkenes[15] similarly showed that Cl_2O and Cl_2 are more potent electrophiles than HOCl, with k_{Cl_2} and k_{Cl_2O} estimated to be 10^2−10^7 times greater than k_{HOCl} depending on the organic nucleophile.

The relative importance of Cl_2O, Cl_2, and HOCl depends on several factors. As $[Cl_2O]$ is proportional to $[HOCl]^2$, the influence of Cl_2O will increase with an increase in the chlorine dose at a given pH. At a fixed chlorine dose, Cl_2 will become more important as the pH decreases and as $[Cl^-]$ increases. The inherent nucleophilicity of organic compounds also affects the likelihood of reactions with Cl_2O and Cl_2. To illustrate, we used the second-order rate constants for Cl_2, Cl_2O, and HOCl (i.e., k_{Cl_2}, k_{Cl_2O}, and k_{HOCl}) reported in the literature to compute values of the chloride concentration such that Cl_2 contributes 50% to overall chlorination rates (assuming pH 7.0 and [free chlorine] = 28 μM = 2 mg/L as Cl_2, conditions representative of a drinking water treatment chlorine contactor); we abbreviate this chloride concentration as $Cl^-_{50}(Cl_2)$. The calculations are shown in Text S1. Compounds that are more sensitive to rate enhancement of chlorination by Cl^- are associated with lower $Cl^-_{50}(Cl_2)$ values. Figure 2A shows the relationship between log $Cl^-_{50}(Cl_2)$ and log(k_{HOCl}), which represents a compound's inherent reactivity toward HOCl. A lower value of k_{HOCl} is associated with a lower $Cl^-_{50}(Cl_2)$ value, indicating that the influence of Cl_2 generally increases as reactivity toward free chlorine decreases, even for cyclic alkenes that do not react via electrophilic aromatic substitution. These results suggest that rate enhancement of chlorination by Cl^- is potentially substantial in drinking water and wastewater for organic compounds with a k_{HOCl} of <100 M^{-1} s^{-1}. A similar conclusion can be drawn regarding the reactivities of organic compounds that are likely to react with Cl_2O (see Text S2).[10,13,15]

A number of publications (e.g., refs 49−53) have attributed the reactivities of organic compounds at low pH to H_2OCl^+. However, evidence from Raman spectroscopy indicates that Cl_2, rather than H_2OCl^+, is the predominant oxidant at low pH.[18] It was also unnecessary to include a term for $k_{\mathrm{H_2OCl^+}}$ in the kinetic models to fit the experimental data for dimethenamid,[9] aromatic ethers,[10] phenols,[13] salicylic acid,[14] and cyclic alkenes.[15] The estimates of $k_{\mathrm{Cl_2}}$ reported in the literature[9,10,13−15] were obtained using data from experiments in which ≥1 mM NaCl was added to the reaction solution, thus promoting the influence of Cl_2 over the potential influence of H_2OCl^+. Nevertheless, as chloride was ostensibly present in all reactors even without added chloride, it is unclear whether the compounds examined would have similar reactivities in chloride-free solutions (i.e., free chlorine solutions that contain H_2OCl^+ but not Cl_2).

BROMINE SPECIES

Bromide (Br^-) is ubiquitous in natural waters, with median concentrations ranging from the low micrograms per liter range in precipitation[54] to 65 mg/L in seawater.[55] In potable water and in wastewater, $[Br^-]$ values of ∼0.1 and ∼0.2 mg/L, respectively, are typical;[47,56] however, $[Br^-]$ values of >1 mg/L have been reported in some locations.[57−60] Free chlorine can oxidize Br^- to BrCl (Table 1, eq 3), which readily hydrolyzes to HOBr (eq 4).[38,40] Oxidation of Br^- to HOBr (eq 5) is fast (half-life of seconds) under conditions typically encountered in chlorinated drinking water.[40] The sum of all aqueous bromine(+1) species (plus Br_2, excluding bromamines) is termed free bromine.[12] In environmental systems, HOBr (pK_a = 8.8; 25 °C)[61] is usually the most abundant free bromine species. With few exceptions,[7,11,62] HOBr is generally assumed to be "the" reactive bromine(+1) species in solutions of free bromine.

Although often overlooked, BrCl, Br_2, BrOCl, and Br_2O can also form in solutions of free bromine and can serve as brominating agents of organic compounds[7,11,12,63] and as oxidants of Mn(II).[64] Indeed, BrCl, Br_2, BrOCl, and Br_2O were determined to be more inherently reactive (often by several orders of magnitude) compared to HOBr in reactions with dimethenamid,[11] anisoles,[12] Mn(II),[64] and salicylic acid.[14] In these studies, several lines of evidence suggested species other than HOBr were serving as active brominating agents, including observations that bromination rates were (1) first-order in chloride, implicating BrCl, whose concentration is proportional to $[Cl^-]$ (eq 4); (2) first-order in bromide in the absence of residual free chlorine, implicating Br_2, whose concentration is proportional to $[Br^-]$ (eq 6); (3) greater than first-order in HOBr, implicating Br_2O, whose concentration has a second-order dependence on [HOBr] (eq 7); and (4) first-order in HOCl, implicating BrOCl, whose concentration is proportional to [HOCl] (eq 8). These findings corroborate a previous examination of *p*-xylene, in which Br_2 and BrCl proved to be several orders of magnitude more reactive than HOBr.[7,8]

The extent to which exotic free bromine species influence bromination rates is of practical importance, and the potential ramifications for water treatment are significant. For example, when BrCl contributes to bromination rates, $[Cl^-]$ will be a key variable (eq 4).[7,8,65] Consider, for instance, the use of $FeCl_3$ as a coagulant during drinking water treatment. The increase in $[Cl^-]$ upon addition of typical doses of $FeCl_3$ at pH 7 is sufficient to increase the bromination rate of dimethenamid by a factor of 9.[11] During ultraviolet/chlorine treatment of bromide-containing water at pH 7, transformation rates of nalidixic acid (a quinolone antibiotic) increased by ∼10-fold in the presence of 0.54 M Cl^- compared to experiments conducted in the absence of added Cl^-; the difference in reactivity was ascribed to BrCl.[66] Effects of chloride may be particularly significant in drinking water impacted by road salt,[67−71] seawater intrusion,[72,73] and oil/gas exploration.[59,74−76] Chloride in municipal wastewater,[47] saline sewage,[77] salt water swimming pools,[78,79] ballast water,[80,81] and desalination plants[82−85] is also likely to enhance bromination rates.

The susceptibility of bromination reactions to rate enhancement by Cl^- can be described by Cl^-_{50}(BrCl), the $[Cl^-]$ required at pH 7.0 and 28 μM free chlorine (2 mg/L as Cl_2) such that BrCl contributes 50% to the overall bromination rate. As Cl^-_{50}(BrCl) decreases, the sensitivity of a bromination reaction to rate enhancement by Cl^- increases. Of the five Cl^-_{50}(BrCl) values depicted in Figure 2B, four correspond to Cl^- concentrations typical of drinking water. For salicylic acid, $\mathrm{Cl}^-_{50}(\mathrm{Cl_2}) \approx \mathrm{Cl}^-_{50}(\mathrm{BrCl})$, indicating that chlorination and bromination of salicylic acid are comparably catalyzed by Cl^-. For dimethenamid, $\mathrm{Cl}^-_{50}(\mathrm{Cl_2}) > \mathrm{Cl}^-_{50}(\mathrm{BrCl})$ indicating that chlorination of dimethenamid is less sensitive to Cl^- catalysis than is bromination.

Few previous studies have addressed the possible role of exotic bromine(+1) species in more complex systems (e.g., drinking water, wastewater, and pool water). In their examination of the effects of seawater intrusion on DBP formation in chlorinated groundwater, Ged and Boyer[86] observed increases in molar concentrations of trihalomethanes (THMs) with increasing seawater content at pH 8.0 and noted that reactions involving BrCl could account for their observations.[86] Liu et al.[87] quantified THMs in synthetic brackish water ($[Cl^-]$ = 0.27 M) amended with free bromine (generated from NaOCl + 10% excess Br^-) and phenol or *β*-dicarbonyl acid. The unexpected formation of chlorine-containing THMs (e.g., $CHBr_2Cl$) was attributed to reactions involving BrCl.[87] At high $[Cl^-]$ values, formation of C−Cl bonds could occur via nucleophilic attack of Cl^- at carbocation intermediates. BrCl is not, however, anticipated to serve as a chlorinating agent due to the partial positive charge on Br.[88,89]

Residual free chlorine can also influence bromination reactions by promoting formation of BrOCl (eq 8), which is anticipated to serve as a brominating agent because bromine is the least electronegative atom in BrOCl. In chlorinated groundwater, Amy et al.[90] discovered that the fraction of brominated THMs increased with increasing chlorine dose (in which bromide was the limiting reagent). In such systems, the possible influence of BrOCl cannot be ruled out. We note, however, that additional factors may be at play, including (1) generation of mixed Cl/Br-DBPs,[87] (2) Br^-/HOBr redox cycles involving HOCl,[91] and (3) HOCl-mediated transformations (e.g., oxidation) of organic compounds that do not involve C−Cl bond formation.[6,92]

Available reactivity data suggest that among the exotic bromine(+1) species, BrCl and BrOCl are the most likely to influence bromination rates under conditions representative of chlorinated drinking water.[11,12,14] As such, whenever HOBr is assumed to be the only active brominating agent, $[Cl^-]$ and [HOCl] may incorrectly be deemed unimportant. Br_2 may be influential when $[Br^-]$ > [free chlorine] and when bromide-containing waters are ozonated (e.g., disinfected ballast water).[87,93] Compared to other exotic bromine(+1) species, Br_2 is perhaps the most studied. For additional discussions of Br_2, see refs 3 and 94. H_2OBr^+ has also been proposed as a reactive brominating agent in solutions of free bromine,[7,8] but the feasibility of H_2OBr^+ serving as a brominating agent has been debated.[95,96] If H_2OBr^+ were present in solutions containing Cl^-, its contribution to bromination rates could be complicated by the co-occurrence of BrCl (eq 4), whose concentration is also first-order in $[H^+]$ in the absence of Br^-.

IODINE SPECIES

Iodide (I^-) concentrations are low in freshwater (≤ 0.1 mg/L)[97−100] and seawater (0.06 mg/L)[97] but elevated in oil-and-gas-associated brines (0.1−500 mg/L).[59,101] HOCl and NH_2Cl efficiently oxidize I^- to HOI, except for NH_2Cl at high pH [half-life of ≥1 h; pH ≥9.5, 28 μM NH_2Cl (2 mg/L as Cl_2)].[2] HOI (pK_a = 10.4; 25 °C)[102] is the predominant iodine(+1) species in chlor(am)inated water (Figure 1C). HOCl further oxidizes HOI to iodate (IO_3^-),[2] diminishing iodination because IO_3^- is a poor electrophile.[19] In contrast, NH_2Cl does not oxidize HOI appreciably, allowing HOI and other iodine(+1) species to persist and react with organic nucleophiles.[2] Iodamines have not been observed in water,[2] so all aqueous iodine(+1) is ostensibly "free" iodine.

Conventional wisdom designates HOI as the active iodinating agent in chor(am)inated water, although few investigations[16,19] have assessed this rigorously. This interpretation is based upon kinetic analyses of iodination of *para*-substituted phenols,[19,103] α-methyl carbonyl compounds,[19] 3-oxopentanedioc acid,[103] and flavone.[103] Under most circumstances, these iodinations are subject to base catalysis, which indicates that the active nucleophiles are highly reactive, ionized conjugate bases (i.e., phenolates and enolates).[19,103] However, less-reactive nucleophiles (e.g., aniline and anisole) are expected to react predominantly with more-reactive iodinating agents (e.g., H_2OI^+) than HOI.[104−107]

A recent kinetic investigation of iodination in chloraminated water employing dimethenamid, a non-ionizable and moderately nucleophilic aromatic compound, did not detect reaction with HOI and, instead, identified H_2OI^+ and ICl as active iodinating agents.[16] Dimethenamid iodination is first-order in $[H^+]$ throughout a circumneutral pH range (4−9), conditions under which [HOI] is invariant (Figure 1C). Both $[H_2OI^+]$ (eq 9) and [ICl] (eq 10) are directly proportional to $[H^+]$ at pH ≤9. The contribution of ICl (eq 10) was isolated by varying $[Cl^-]$ at a constant pH and a constant ionic strength. Iodination rates increased with $[Cl^-]$ up to ∼20 mM and then plateaued up to 100 mM, indicating a complex mechanism. I_2(aq) has been proposed as an iodinating agent of phenolic compounds in chlorinated water.[108] In contrast, I_2(aq) appears unreactive toward dimethenamid because iodination rates decrease as $[I^-]$ increases above [iodine(+1)], conditions under which I_2(aq) is the predominant iodine(+1) species.[16]

The series of dimethenamid halogenation studies offers the best available comparison of chlorinating,[9] brominating,[11] and iodinating[16] agents in chlor(am)inated water. HOX and X_2 contribute measurably to dimethenamid chlorination and bromination but not to iodination. Exotic electrophiles, primarily Cl_2 (eq 2), BrCl (eq 4), and H_2OI^+ (eq 9), account for the observed increases in dimethenamid halogenation rates as pH decreases below pK_{HOX} values. The varying importance of XCl and H_2OX^+ as halogenating agents could be caused by differences in electrophile concentrations and/or electrophilicity. As halogen size increases (Cl < Br < I), H_2OX^+/HOX and XCl/HOX concentration ratios increase for a given pH and $[Cl^-]$, though variation in $[H_2OX^+]/[HOX]$ is greater than in [XCl]/[HOX].[16] Leaving group ability, a determinant of electrophilicity, may be reflected by bond dissociation energy (BDE; e.g., BDE_{X-Cl} for XCl, BDE_{X-O} for H_2OX^+).[11] A lower BDE should reflect a better leaving group, assuming trends in heterolytic BDEs parallel those in homolytic BDEs. The BDE_{X-Cl}/BDE_{X-O} ratio for iodine (1.15) is greater than unity, unlike those of bromine (0.93) and chlorine (0.90), potentially contributing to the prominence of H_2OI^+, BrCl, and Cl_2 as halogenating agents.[16]

EMERGING INSIGHTS INTO REACTION PATHWAYS

In addition to incomplete knowledge of the relevance of exotic electrophiles for halogenation kinetics of organic compounds in drinking water, there is still considerable uncertainty about the identity of the majority of DBPs and the reaction mechanisms and pathways that lead to their formation. Traditionally, the chlorination of organic contaminants has been attributed almost exclusively to reactions with HOCl via electrophilic substitution, addition to unsaturated bonds, and/or oxidation.[22] One of the most extensively investigated groups of DBP precursors consists of phenolic compounds, which react with HOCl via electrophilic aromatic substitution. For phenol, this results in its quantitative transformation to *ortho*- and *para*-substituted chlorophenols, including 2- and 4-chlorophenol, 2,4- and 2,6-dichlorophenol, and 2,4,6-trichlorophenol.[13,28,109] This is followed by conversion of 2,4,6-trichlorophenol into ring-cleavage products, including chloroform and chloroacetic acid.[20,51,110−113]

Similar to the initial reactions of HOCl with phenols, previous studies have attributed ring cleavage to electrophilic substitution reactions of 2,4,6-trichlorophenol and the formation of 2,6-dichloro-*p*-benzoquinone (DCBQ) as an important intermediate. However, while DCBQ has been identified as a major transformation product of 2,4,6-trichlorophenol, these experiments were conducted under acidic conditions (pH <6).[114−116] In contrast, DCBQ yields were found to be negligible (0.2%) in chlorination experiments with 2,4,6-trichlorophenol under circumneutral conditions,[117] suggesting the involvement of other transformation pathways.

With the exception of resorcinol, previously identified ring-cleavage products of phenols generally account for only a small fraction of the total carbon mass balance, indicating the formation of other, unknown DBPs.[51,110,118] These results suggest the relevance of other, so far unknown transformation mechanisms, which are corroborated by the identification of DBPs that cannot be explained by reaction mechanisms postulated previously. For example, a series of publications by Onodera et al., published in the 1980s and 1990s, demonstrated the formation of phenyl-phenols in the reaction of various substituted phenols with HOCl.[119−122] This provides strong evidence for the involvement of radical intermediates that are formed via one-electron transfer reactions. Phenoxy radicals are commonly observed when phenols react with radicals such as hydroxyl radicals ($^\bullet$OH).[123,124] The relevance of radical-mediated mechanisms during chlorination is further supported by the identification of halogenated and nonhalogenated α,β-unsaturated dicarbonyl compounds that have recently been identified in chlorination experiments with phenol, chlorophenols, bromophenols, and alkyl-substituted phenols (Table S2).[6] For example, 2-butene-1,4-dial (BDA) is formed during chlorination of phenol at a maximum yield of 18%;[6] BDA is also generated upon reaction of phenol with $^{\bullet}$OH.[125]

Even though the relevance of free radical intermediates in aqueous chlorination of phenolic compounds has not been studied in detail, formation of BDA could be explained via the reaction of Cl_2O (eq 1) with phenols.[126] Formation of phenoxy radical intermediates in the reaction of Cl_2O with phenols has been attributed to homolysis of Cl_2O into $Cl^{\bullet}$ and $ClO^{\bullet}$.[126] However, the relevance of this mechanism has so far been demonstrated in only organic solvents, while its relevance in aqueous systems remains controversial.[13,126,127] Another potential phenoxy radical formation pathway is a direct oxidation of dihydroxyphenols, in particular catechol and hydroquinone. This reaction can generate quinone species that react further with a second catechol/hydroquinone via comproportionation, yielding phenoxy radical species.[4,128,129] This is supported by the high BDA yields observed for 3,5-dichlorocatechol.[6] Overall, these recent findings indicate that in chlorinated water, reaction mechanisms beyond electrophilic substitution/addition can occur. These emerging insights also challenge the notion of HOCl as the most important electrophile under conditions typically observed in chlorinated systems.

■ FUTURE RESEARCH NEEDS AND RECOMMENDATIONS

Several research gaps exist regarding the chemistry and consequences of exotic electrophiles and understudied reaction pathways in disinfected water. For example, little is known about how exotic electrophiles might influence pathogen inactivation. Data spanning several decades and examining a range of microbes have demonstrated that the disinfection efficacy of free chlorine increases as the pH decreases,[130,131] which implicates HOCl as a more potent disinfectant than ClO^-.[132,133] Nevertheless, the concentrations of Cl_2 and Cl_2O also increase with a decrease in pH (at near-neutral pH). As with HOCl,[131] Cl_2 and Cl_2O are uncharged and are therefore anticipated to more effectively penetrate cell walls compared to OCl^-. These observations raise the possibility that disinfectant potency previously ascribed to HOCl might also encompass the effects of Cl_2 and Cl_2O. Whether differences in selectivity can alter the ability of Cl_2 and Cl_2O (relative to HOCl) to reach biomolecular targets (e.g., proteins and DNA)[134−138] in pathogens merits future investigation.

The potential influence of exotic free bromine species on disinfection processes is also poorly understood. Similar to free chlorine, in solutions of free bromine, decreases in pH (at near-neutral pH) will favor the formation of HOBr and, concurrently, additional uncharged bromine species [e.g., BrCl, Br_2, and Br_2O (Figure 1B)].[11] Just as the inherent reactivity of HOBr toward some organic compounds has been overestimated by failure to consider the contributions of co-occurring free bromine species,[12,14] it is also possible that the germicidal activity of HOBr reported in the literature may include unrecognized contributions from species such as BrCl, Br_2, and Br_2O. When BrCl served as the free bromine source in industrial cooling water, greater biofouling control was observed relative to that observed with Cl_2.[139] BrCl was also postulated to impart greater germicidal efficiency relative to other free bromine species;[131] however, such investigations are typically based on the identity of the added disinfectant rather than on the equilibrium speciation of the disinfected solutions (e.g., following rapid hydrolysis of BrCl into HOBr), which will vary with conditions such as pH, [Cl^-], and [Br^-]. Consequently, the relative contributions of individual electrophiles to overall disinfection warrant additional research.

Investigations of the reactivity of exotic electrophiles have been largely limited to electrophilic substitution and addition.[9−13] Exotic electrophiles can also serve as oxidizing agents in which halogen species are transformed into halide ions (rather than into organohalides).[4,140] Additional research is needed to better understand how solution conditions influence branching ratios and redox cycles associated with these halogen fate pathways. Moreover, several questions remain regarding the role of radical species in aqueous halogenation processes, particularly for bromination and iodination and for organic nucleophiles other than phenols. Such studies could generate new insights into how electrophile speciation influences active halogen residuals, DBP formation, and redox-active metals in disinfected systems.

The occurrence of exotic electrophiles in disinfected water can complicate the design and execution of halogenation experiments. As such, we conclude this review with recommendations for how the precision and accuracy of halogenation experiments can be enhanced in light of the potential complications arising from the formation of exotic electrophiles. Additional recommendations are provided in Text S3.

(1) Reagent purity is important. For example, Br^- can be unintentionally introduced from lower-purity forms of NaCl and HCl.[9] Dias et al.[141] measured [Br^-] at up to 37 mg/kg in reagent-grade NaCl (≥99.0% purity reported by the manufacturer) and at up to 50 mg/kg in HCl (certified ACS grade). Systematic errors associated with such Br^- contamination will be more pronounced when Cl^- is added in excess of Br^-, as is typical of bromination experiments seeking to mimic environmental chloride/bromide molar ratios.

(2) Carefully control (and quantify) all sources of Cl^-. To accurately determine free halogen speciation, all inputs of Cl^- must be quantified, including Cl^- from NaCl, NaOCl solutions (which are generally equimolar in Cl^-), and (for bromination experiments) oxidation of Br^- by HOCl, for which Cl^- is a product (Table 1). Avoid using HCl to adjust solution pH; consider HNO_3 instead. Recognize that pH electrodes containing KCl/AgCl filling solutions can leach Cl^-.

(3) Quantify active halogen residuals. Consumption of active halogens due to disproportionation or the presence of interfering reductants can complicate halogenation experiments, particularly for iodination and as the duration of such experiments increases. Failure to quantify rates of active halogen consumption can result in erroneous electrophile-specific second-order rate constants. For details about methods of quantifying active halogens, see refs 141−144.

(4) Beware of possible effects of buffers on reaction rates. Buffer catalysis has been reported for chlorination,[13,23,145−147] bromination,[11,148] and iodination.[16,103,149−153] Before a buffer is employed for halogenation experiments, the effects of buffer identity and concentration should be examined.

(5) Determine whether your choice of quenching agent is affecting your results. Some quenchers can adversely affect the stability of DBPs.[143,154] Control experiments that vary the identity and/or concentration of the quencher are wise.

In the environmental literature, conventional kinetic models generally neglect exotic electrophiles, perhaps due to their low concentrations. Herein, we presented evidence challenging such conventional models. We also discussed how recent data are prompting a re-examination of the assumed mechanisms by which free halogens can alter the structures of organic compounds. It is now precarious to assume, for example, that reactions of free chlorine with phenols proceed exclusively via electrophilic aromatic substitutions involving HOCl. Other mechanisms (e.g., involving radical species and organic electrophiles) may be operative. Consequently, the future of aqueous halogenation research is ripe for continued exploration.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.estlett.0c00259.

> Calculation of $Cl^{-}_{50}(Cl_2)$, $Cl^{-}_{50}(BrCl)$, and $HOCl_{50}(Cl_2O)$ values and additional figures and recommendations for halogenation experiments (PDF)

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Notes

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