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Using model compounds to show how a change in thinking is required for regulation of brominated haloacetic acids in drinking water

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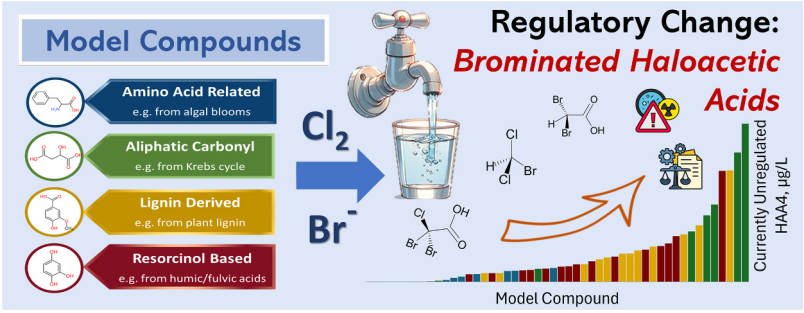
HIGHLIGHTS

- Unregulated brominated HAAs form from compounds within all the groups studied.
- Current proxy measures (DOC, UV) do not inform on potential for unregulated HAAs.
- Regulated DBPs (THM, HAA5) are poor predictors for unregulated HAAs.
- Aromatic precursors predominately form Br-TXAAs within the unregulated species.
- Aliphatic precursors form the most unregulated HAAs on a mass basis.

GRAPHICAL ABSTRACT



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ABSTRACT

Brominated disinfection by-products (Br-DBPs) are formed during the chlorination of drinking water where sufficient organic precursor molecules and bromide are present. They are of heightened concern due to their enhanced toxicity over the chlorinated analogues, yet despite this Br-DBPs are not as widely studied so their prevalence and capacity for formation is less well understood. Importantly, four brominated haloacetic acids (Br-HAAs) currently sit outside of regulatory standards. This raises the question of how thinking about DBPs will change if regulation expands to include all nine chlorinated and brominated HAAs (HAA9). The current work explored this question by utilising model compounds to establish the impacts associated with different groups of organic molecules and varying functional group on the ability to form Br-HAAs. This identified that high formation of unregulated HAAs was associated to precursors within all groups, with BDCAA (bromodichloroacetic acid) forming from the aromatic and amino acid-based groups, and BCAA (bromochloroacetic acid) forming from within the aliphatic, amino acid-based and lignin-derived groups. Critical structural insight was related to the balance of TXAA (tri-halogenated acetic acids) and DXAA (di-halogenated acetic acids) which was associated with stabilisation of the di-halogenated intermediates. Consequently, thinking about formation of the currently unregulated brominated HAAs needs to consider both hydrophobic and hydrophilic precursor types, appreciating that enhanced formation propensity can originate from small changes in molecular structure. Furthermore,

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variation in formation pathways and bromination preference between the THMs, DXAAs and TXAAs dictates that monitoring and management of the HAA9 will require divergence from current DBP strategies.

1. Introduction

The potential for toxic disinfection by-products (DBPs) to be formed unintentionally during the chlorination of drinking water was identified in the 1970s and extensive research since has highlighted both the breadth of compounds formed and the potential risk they pose to human health [1,2]. Consequently, two of the major groups of DBPs formed by mass, the trihalomethanes (THMs) and haloacetic acids (HAAs), are widely regulated and controlled in drinking water. Brominated DBPs (Br-DBPs) are formed when bromide is present during chlorine-based disinfection and are receiving increased attention due to their enhanced cyto- and geno-toxicity over their chlorinated analogues [3], with indications that some brominated haloacetic acids (Br-HAAs) are of particular concern [4–6]. Guideline Values (GVs) have been established by the World Health Organisation (WHO) to indicate the potential for harm from chlorinated HAAs (Cl-HAAs), with these set at 20 μg/L for monochloroacetic acid (MCAA), 50 μg/L for dichloroacetic acid (DCAA) and 200 μg/L for trichloroacetic acid (TCAA), where lower values indicate greater risk. A recent report has proposed additional GVs for brominated HAAs (Br-HAAs) of 333 μg/L for monobromoacetic acid (MBAA), 100 μg/L for bromochloroacetic acid (BCAA), 3 μg/L for DBAA, 73 μg/L for bromodichloroacetic acid (BDCAA), 50 μg/L for dibromochloroacetic acid (DBCAA) and 1 μg/L for tribromoacetic acid (TBAA) [7]. Consequently, the formation of Br-HAAs, and particularly the fully brominated DBAA and TBAA, is of increasing concern.

Although all four chlorinated and brominated THMs (THM4) are commonly regulated, the equivalent standards for HAAs are sporadic. For instance, the Cl-HAAs (MCAA, DCAA and TCAA) are regulated in Japan and Australia (<20, <30, <30 and <150, <100, <100 μg/L, respectively) while DCAA and TCAA are regulated in China (<50 and <100 μg/L). In the EU, US, Scotland and Singapore, HAA regulation has been extended to add two of the Br-HAAs (MBAA and DBAA) such that five HAAs (HAA5) are regulated to < 60 μg/L, and likewise HAA5 < 80 μg/L is the guideline in Canada. This focus on smaller, Cl-HAAs has left a gap in our understanding of the more toxic Br-HAAs, and there is increasing concern that this needs to be addressed by monitoring all nine chlorinated and brominated HAAs (HAA9). Consequently, in England and Wales it has recently been proposed that regulations are expanded to include HAA9 < 80 μg/L, adding the four currently unregulated Br-HAAs ($HAA4_{unreg}$ = BCAA, BDCAA, DBCAA and TBAA) [8,9]. This warrants investigation into the types of precursors that are key to the formation of HAAs and particularly the currently unregulated $HAA4_{unreg}$. The insights generated from such research translate to improved understanding of the potential to monitor and manage precursors in relation to the risk they pose, especially concerning the generation of $HAA4_{unreg}$. In turn this enables discussion of whether a switch to HAA9 requires a change in thinking compared to the current approach where just THMs are regulated, or where the scope of regulation would extend from HAA5 to HAA9.

High levels of bromide may arise in some source waters both naturally, from geogenic sources or saline intrusion, or from anthropogenic activity such as fracking or industrial discharges. A maximum level of 4130 μg/L has been reported in saline impacted waters in Australia [10], while observed levels in the UK range from 14 μg/L to 310 μg/L [11]. The average levels measured in US surface and ground water during Fourth Unregulated Contaminant Monitoring Rule (UCMR4) were 307 μg/L and 149 μg/L, respectively [12]. Conventional water treatment processes do not readily remove bromide [13], and pre-treatment processes may not remove all organic precursors of DBPs [14], with the risk that treatment of source waters including by chlorination may increase levels of smaller aromatic compounds, both halogenated and non-halogenated, which can be intermediates in the formation of the regulated, aliphatic DBPs [15]. Importantly, an understanding of the nature of organic precursors that preferentially form the more toxic brominated disinfection by-products is missing, especially in relation to the currently unregulated $HAA4_{unreg}$. Consequently, as increased demand forces reliance on poorer quality source water, the potential risk associated with Br-HAAs, including the $HAA4_{unreg}$, will increase [16,17].

Current understanding of DBP formation pathways asserts that the key mechanistic steps are: the formation of hypohalous acid; activation of α-carbon by keto-enol tautomerism; halogenation by electrophilic substitution; and formation of DBPs by hydrolysis and/or cleavage [18–21] (illustrations of the pathways are included in Supplementary Material Figure S1). Although the formation behaviour of the hypohalous acids has been investigated [22,23], the subsequent complex and competing three-way interaction between organic precursor compounds and active chlorine and bromine (defined as including the hypohalous acid and equivalent free base) is rarely reported.

Exploration of how molecular structure influences the competing pathways for chlorination and bromination to alter the balance between Br- and Cl-DBPs is currently pauce. Although the use of model compounds to explore DBP formation in laboratory experiments is common, and resorcinol has been particularly well studied, a systematic approach to identifying influences on Br-DBP formation potential (FP) is missing. Further, the majority of previous research has focused on THMs and Cl-HAAs and often does not include bromide in the trials, despite research demonstrating that brominated aromatic compounds formed during chlorination are key intermediates in the formation of regulated DBPs [24]. To illustrate, of seventy-two model compound studies identified in the literature, only six included bromide and analysed for THM4 and HAA9, accounting for only 49 (6.2 %) of the 789 compounds studied to date (Supplementary Material S1). These studies demonstrated an increase in Br-DBPFP when bromide is present, with variability observed across hydrophilic, hydrophobic and nitrogenous fractions of organic matter [25,26], as well as identifying the significant catalytic influence of metals and amines [27–29]. However, poor correlation between the physical characteristics of the surrogates and their DBP formation was noted, warranting more detailed investigation [25]. Further, existing literature considering the mechanistic routes for the formation of HAAs often relies on the pathways from hypochlorous and hypobromous acids being the same [30–32], despite the known faster kinetics of bromination than chlorination [23] (Supplementary Material Sections S2.2 and S8). Where different formation pathways are proposed for bromination, which could account for increased formation of unregulated Br-HAAs, this has been linked to formation of different electrophiles [33,34] or alternate mechanistic steps such as 'ipso' substitution decreasing bromine incorporation into aromatic intermediates [35, 36]. Insight into the possible mechanistic pathways for Br-HAA formation during chlorination also demonstrated the importance of the reactive components of precursor compounds such as humic acid and the catalytic effect of bromide, which promote increased formation of THMs and HAAs [37].

The aim of this study was to generate a unique framework linking the attributes of organic molecules to high Br-DBP yields and use this knowledge to examine how our current understanding of DBP mitigation strategies would change with the expansion of regulation to include the four currently unregulated brominated $HAA4_{unreg}$. In so doing this will inform a re-assessment of the potential significance of Br-HAAs as well as the role of currently used surrogate precursor monitoring strategies. A key question for the current work relates to how molecular structure impacts the competition between chlorine and bromide under environmentally relevant conditions, given the chlorine is in excess but

bromination exhibits faster reaction kinetics [38].

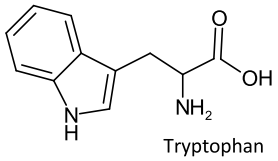
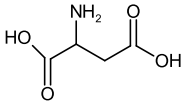
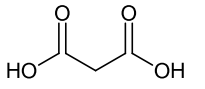
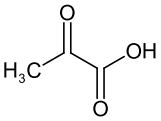
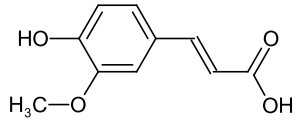
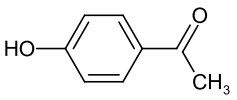
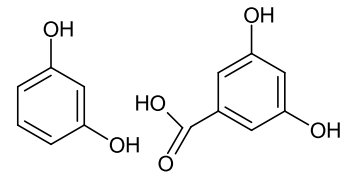
The novelty of the current work lies in exploring this dynamic across a broad range of compounds to examine the impact of changing molecular structure across acidic, basic and neutral fractions as well as aromatic and aliphatic components. By utilising such a range of definitive model compounds under controlled conditions the compound characteristics that are favourable from bromination to occur are isolated. The current study includes thirty-seven compounds that have never been studied in terms of their risk of Br-HAA formation (detailed Table S2 Supplementary Material). From the resorcinol based group, only resorcinol itself has previously been studied for HAA9 with bromide and chlorine present together. From the lignin derived group, three compounds (coumaric, ferulic and sinapic acids) have been tested this way, from the aliphatic carbonyls four compounds (3-oxopentanedioic, malonic, citric and pyruvic acid), and from the amino acid related group five compounds (tryptophan, tyrosine, aspartic acid, asparagine and alanine). This study therefore provides the most complete investigation to date into the individual molecular features that are significant for preferential bromination to occur, work which can only be conducted with model compounds and could not be resolved by conducting studies on real waters containing mixed and variable organic components. Instead, the current work compliments such studies and provides an updated framework from which to interpret the observations. Similarly, the current work juxtaposes previous kinetic studies which generally occur on a limited number of compounds and often focus on THM and chlorinated systems, providing a basis for selection of future kinetic experiments.

2. Materials and methods

2.1. Chemicals and reagents

The model compounds were selected, within the constraints of commercial availability, to demonstrate the impact of systematically

Table 1
Selected model compound groups with examples.

Group	Rationale for Selection	Examples	Proposed Key Features of Functional Groups
Amino Acid Related	Activated amino acids known to form higher levels of target DBPs [41]. Additional related compounds (not previously tested) were selected to demonstrate proposed mechanism and assess FP of potential intermediates. May be present at high levels in source water due to biological activity such as algal blooms.	 Tryptophan  Aspartic Acid	Proposed to primarily chlorinate at amino group with nitrogenous DBPs formed. When THMs and HAAs form it is suggested this may be from the side group, where structure will influence formation potential and bromine incorporation. The amino acid group is zwitterionic. Activated substituted aromatic amino acids: known to form higher THMs and HAAs. Smaller aliphatic amino acids: proposed to form HAAs [41].
Aliphatic Carbonyls	Short chain carboxylic acids with multiple carbonyl groups, proposed as precursor molecular structure for HAAs and representative of hydrophilic organic matter [21]. Most are included within the Krebs (citric acid) cycle of energy release in cells and present in plants. Potential to form by oxidation of larger molecules and relatively recalcitrant to coagulation.	 Malonic acid  Pyruvic acid	Location of carbonyl groups are α (1,2), β (1,3) or γ (1,4) to each other with this expected to influence HAA formation. Acids will be dissociated at pH 7 (pK_a ~2–4) but acetoacetate esters will not (pK_a>9). Known to form keto-enol tautomers which will direct for electrophilic substitution at the α carbon via the enol tautomer. The influences on bromination are predicted to relate to this step.
Lignin Derived	Lignin monomers are hydrophobic organic matter, proposed to be derived from breakdown of plant lignin, and known to form THMs and HAAs [42]. Monomer structure varies with plant type, with hardwoods forming vanillyls and syringyls and herbaceous crops forming p-hydroxybenzenes. Likely to be present in organic matter leaching from forested areas or where impacted by wastewater from paper industry.	 Ferulic acid  p-Hydroxyacetophenone	Methoxy groups (OCH_3) are located ortho to the hydroxy group either once (vanillyl), twice (syringyl) or not at all (p-hydroxy), thus potentially inhibiting halogenation at the α carbon to the phenol group (pK_a ~8–9). Para to the hydroxy are carboxylic acid (pK_a ~4), aldehyde, methyl ketone (acetyl) or cinnamyl (acrylic acid, pK_a ~4.3) group which are systematically varied. Relative position and oxidation/conjugation of functional group predicted to impact on type of DBP formed and extent of bromination.
Resorcinol-Based	Compounds based around resorcinol (1,3-dihydroxybenzene) are well studied and known to form THMs [38]. Related compounds available with a variety of functional group types and locations (4- or 5-), including previously unstudied with specific characteristics. Aromatic alcohols and acids are potential breakdowns products of humic and fulvic acid type organic matter likely present in natural organic matter.	 Resorcinol 3,5-dihydroxybenzoic acid	Functional groups are selected to be electron donating (and therefore activating for electrophilic substitution) or electron withdrawing (and therefore stabilising for phenol dissociation pK_a ~ 8–9). They can direct to the ortho/para (1-,3-,5-) or meta (2-,4-) locations and/or provide resonance stability (via lone pair or aromaticity) and/or form tautomers (keto-enol, imine-enamine, nitrile-ketenimine). These functionalities predicted to influence DBP formation levels, type and extent of bromination.

varying functional groups which were predicted to influence DBP outcomes through altering the pathways or shifting the kinetic behaviours. Fifty model compounds were selected within four main groups (amino acids, aliphatic compounds, lignin derived and resorcinol-based) to represent the predominant types of organic matter proposed to be present in treated waters and to form the target DBPs (Table 1), detailed individually in Supplementary Material Table S3). These include compounds which could be formed during water treatment such as aromatic halogenated and non-halogenated compounds from breakdown of natural organic matter such as humic acids and lignin polymers [39], and oxidised aliphatic compounds from oxidative treatment processes [40]. Chemicals were purchased at reagent grade or higher. Ultra-pure (UP) water (18.2 MΩ·cm) was provided by an Elga Purelab Ultra Genetic system.

2.2. Formation potential experiments

Experiments were performed in triplicate on 15 μM of model compound prepared individually in ultrapure water with 5 μM of bromide (400 μg/L) and buffered to pH 7 with 5 mM of phosphate. Chlorination blanks were prepared as samples from UP water. Chlorination was conducted using 10.7 mgCl_2/L which is equivalent to a 10:1 molar ratio of chlorine (as Cl_2) to model compound. Chlorination solution was prepared from a ≈ 14 % sodium hypochlorite solution and standardised before use (Hach Pocket Colorimeter II, Method 8021). Experiments were maintained at 20°C in the dark for 24 ± 1 h. After 24 h samples were quenched using sodium sulphite for THMs or ammonium chloride for HAAs (with each at 100 mg/L in the final vial in line with US EPA procedures 551.1 and 557) and stored in a fridge prior to DBP analysis within one week. As chlorine was added at a fixed level, and consistent with experimental practice when using model compounds [43], measurement of residual chlorine was not required to assess the dose, and the 100 mg/L of quenching agent was sufficient to prevent further chlorination reactions.

2.3. DBP analysis

THMs and HAAs were selected as they can be individually quantified and so the extent of DBP bromination can be compared between model compounds. HAA analysis was performed by Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS). In brief, samples were adjusted to pH 2 prior to direct aqueous injection analysis using reverse phase chromatography and negative Electrospray Ionisation Multiple Reaction Monitoring (ESI-MRM) [44]. Method validation demonstrated acceptable linearity (r^2>0.995), sensitivity (<0.8 μg/L), precision (<7 %) and bias (<10 %). THM analysis was performed as per US EPA 551.1 with methyl tert-butyl ether (MTBE) as the extraction solvent and analysis by Gas Chromatography Electron Capture Detection (GC-ECD) [45]. Method validation demonstrated acceptable linearity (r^2>0.995), sensitivity (<1 μg/L), precision (<8 %) and bias (<5 %). Further details are provided in Supplementary Material.

2.4. Additional bromide experiments

Calculations were performed to establish the proportion of bromine available which had been incorporated into measured DBPs, reported as the Bromine Utilisation Factor (BUF), where:

$$BUF = \frac{[MBAA] + [BCAA] + [BDCAA] + BDCM] + 2([DBAA] + [DBCAA] + [DBCM]) + 3([TBAA] + [TBM])}{[Br^-]}$$

and BDCM is bromodichloromethane, DBCM is dibromochloromethane, TBM is tribromomethane (bromoform) and Br^- is initial bromide (all as molar concentrations). Where it was identified that all available bromide had been incorporated into the measured DBPs (BUF≈1.0, Table S7), additional experiments were conducted to establish the full potential for bromine incorporation in compounds which favour it. For these, bromide levels were increased to 12.5 μM and 62.5 μM (1 mg/L and 5 mg/L) while all other experimental parameters were maintained. Although such levels are rarely observed in drinking water, by shifting the equilibrium towards bromination this allows improved understanding of the limiting factors on bromine incorporation and further confirmation of the molecular level features which are most amenable to high levels of bromine incorporation.

3. Results and discussion

3.1. Influence of compound group on DBP formation

Comparison across the groups of precursor compounds revealed differences in the relative formation potential (FP) of DBPs and the balance between THMFP and HAAFP, with FP expressed as μM of DBP formed per mM of model compound (μM/mM) (Fig. 1). For instance, the aromatic, resorcinol-based precursor compounds formed high levels of THMs and moderate levels of HAAs with median THMFP of 891 (range 149–1290) μM/mM and HAAFP of 103 (range 1.35–1710) μM/mM. By contrast, the aliphatic based precursors formed more HAAs than THMs. In addition, clear separation was observed within the aliphatic group between the β-dicarbonyls and the α- and γ- dicarbonyls. The β-dicarbonyls formed median THMFP of 1.09 (range 0.604–881) μM/mM and HAAFP of 965 (range 709–996) μM/mM. While similarly low THMFP was observed from α- and γ-dicarbonyls with median THMFP of 0.766 (range 0.477–6.62) μM/mM across both groups, the HAAFP was notably lower for α- and γ- than β-dicarbonyls, with median HAAFP of 0.926 (range 0.490–2.89) μM/mM. This contrasting formation behaviour has been attributed the formation of THMs from resorcinol type compounds via a pathway of halogenation by electrophilic substitution, cleavage, further halogenation and base catalysed haloform reaction (Supplementary Material Figure S1c [20]). The differing propensity of β-dicarbonyls to form HAAs has been attributed to simpler formation pathway of halogenation by electrophilic substitution and hydrolysis (Supplementary Material Figure S1d [21]). The other two groups within this study formed substantially lower levels of both THMs and HAAs with lignin derived compounds exhibiting THMFP between 13.7 and 180 μM/mM (median 88) and HAAFP between 34.6 and 404 μM/mM (median 113). The equivalent for the amino acid compounds was a range of 0.436–61.4 μM/mM for THMFP and 0.681–61.7 μM/mM for HAAFP. Importantly, $HAA4_{unreg}$ formation potential also demonstrates significant variability across the groups, with the highest relative formation from the aliphatic β-dicarbonyls (median 23.0, range 0.181–282 μM$HAA4_{unreg}$ /mM) and the lignin derived compounds (median 41.4, range 12.5–196 and μM$HAA4_{unreg}$ /mM). Resorcinol based compounds formed significant amounts of $HAA4_{unreg}$ from some compounds (median 24.4, range 0.684–166 μM$HAA4_{unreg}$ /mM), but amino acid compounds were lower forming, consistent with their lower overall DBPFP (median 6.06, range 0.239–20.5 μM$HAA4_{unreg}$ /mM). The most significant group exhibiting a consistent propensity for $HAA4_{unreg}$ formation were the aliphatic β-dicarbonyls (range of 90.0–282 with median 138 μM$HAA4_{unreg}$ /mM), showing their potential importance when moving from a HAA5 to a HAA9 regulation.

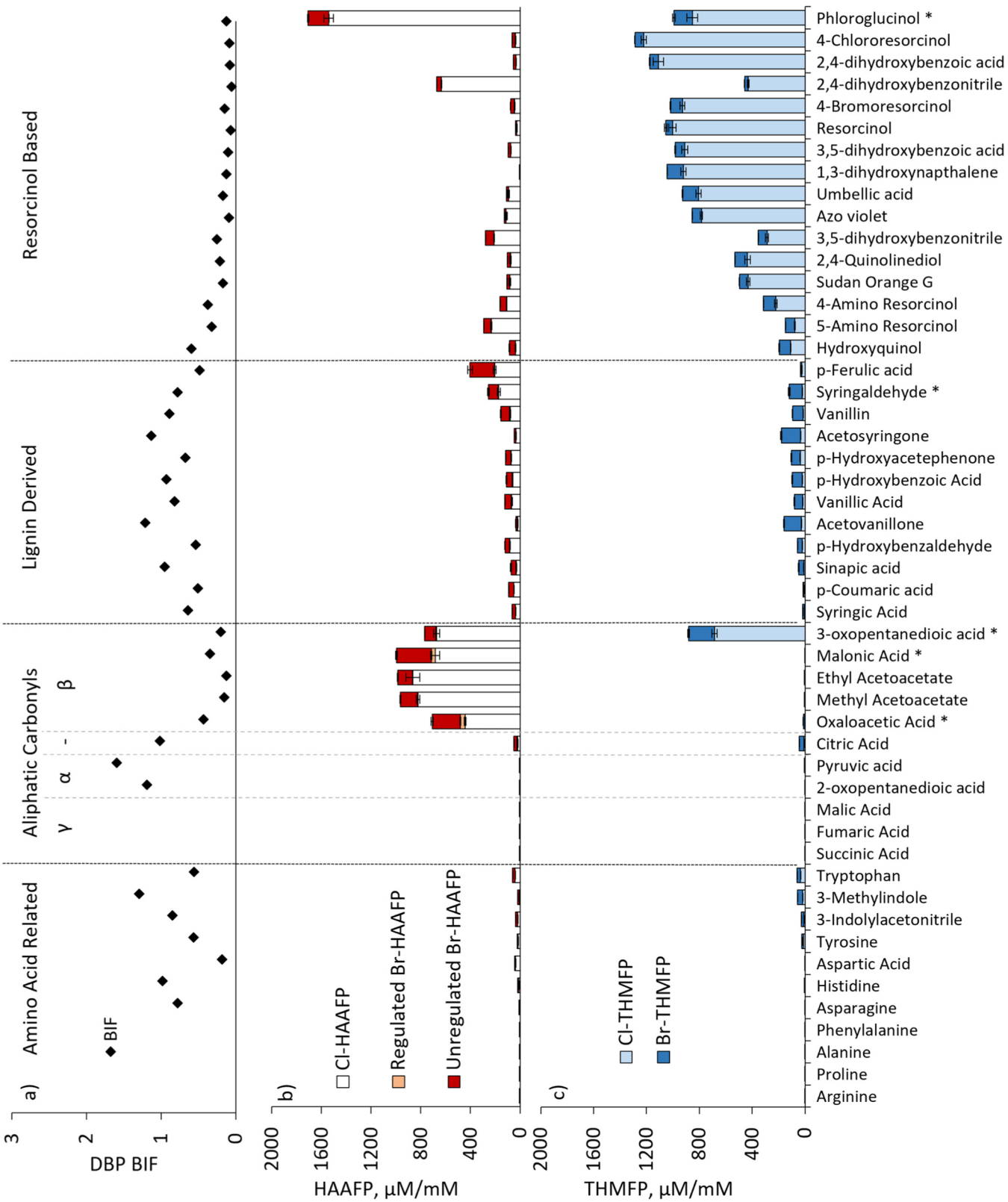


Fig. 1. DBP results for model compounds for a) bromine incorporation factor b) HAA formation potential and c) THM formation potential, where error bars represent standard deviation and * compounds where BUF ≈ 1.0.

This variability in DBPFP aligns with previous studies, where, for example, resorcinol was identified as forming high levels of DBPs (~1250 µM/mM in the presence of bromide, comparable to 1090 µm/mM in this study, although DBP speciation varied under the differing chlorination conditions [25]). Proposed mechanisms to enable this capability suggested a pathway for the formation of THMs and HAAs from resorcinol compounds relying on the stability of the carbanion intermediate and subsequent hydrolytic or oxidative fission to

trichloromethane or Cl-HAAs [46], with more recent stable isotope studies providing evidence for four key pathways including for HAA formation from phenolic compounds [47]. The variation between α- and β-dicarbonyls has been also observed in previous research where a notably lower formation of HAAs was observed from the α-dicarbonyl 2-oxopentanedioic acid when compared to β-dicarbonyls ethyl acetoacetate and 3-oxopentanedioic acid (70 μM/mM compared to 910 μM/mM and 816 μM/mM, respectively) [48]. Although the values for the HAAFP are different for the equivalent compounds in this study, attributed to the different chlorination conditions and the presence of bromide, a similar pattern is observed with lower formation from the α-dicarbonyl (1.19 μM/mM compared to 986 μM/mM and 769 μM/mM, respectively from the β-dicarbonyls). New insight is provided in the range of aromatic compounds considered, as no resorcinol-based compounds other than resorcinol have been previously studied for THM4 and HAA9. Accordingly, the current work provides new insight into compounds within the group such as phloroglucinol and 2,4-dihydroxybenzonitrile which formed significant levels of both THMs and HAAs. In the presence of bromide, these compounds exhibited high THMFP and HAAFP: 993 and 1710 μM/mM (for phloroglucinol) versus 457 and 673 μm/mM (for 2,4-dihydroxybenzonitrile), respectively. This demonstrates that although THM and HAA precursors are often different, when high concentrations of both groups of DBPs are formed this does not dictate that there were different precursors.

Further, this is the first time the bromine incorporation factor (BIF) has been reported for a large range of model compounds and reveals a substantial divergence between the groups with BIF values ranging from 0.059 to 1.6 (Fig. 1a). BIF is the number of moles of bromine per mole of DBP formed, therefore having a maximum value of 1.0 for monohalogenated HAAs (MXAAs), 2.0 for di-halogenated HAAs (DXAAs) and 3.0 for tri-halogenated HAAs (TXAAs) or THMs. To illustrate:

$$DBP\ BIF = \frac{[MBAA] + [BCAA] + [BDCAA] + [BDCM] + 2([DBAA] + [DBCAA] + [DBCM]) + 3([TBAA] + [TBM])}{[HAA] + [THM]}$$

$$HAA\ BIF = \frac{[MBAA] + [BCAA] + [BDCAA] + 2([DBAA] + [DBCAA]) + 3[TBAA]}{[HAA]}$$

$$THM\ BIF = \frac{[BDCM] + 2[DBCM] + 3[TBM]}{[THM]}$$

High median BIF values of 0.78 and 0.80 were observed for the precursor compounds within the amino acid and lignin derived groups and hence high BIF can occur across both aromatic and aliphatic groups. A much lower BIF of 0.14 was recorded for the resorcinol-based compounds, where a maximum value of 0.59 was observed for hydroxyquinol. The β-dicarbonyls presented a more complex pattern with a BIF range of 0.13–0.44 and a median value of 0.20. However, in some cases (labelled * in Fig. 1) all available bromide was incorporated (BUF≈1.0), thus limiting the extent of bromination. Bromine incorporation into the DBPs is generally viewed to be favoured due to the fact that apparent rate constants for bromination are up to three orders of magnitude higher than for chlorination [19,49]. However, despite this kinetic preference, it was observed that in the competing environment of this study, bromine incorporation over chlorine was not complete (average BIF<<3.0) and was significantly lower in the resorcinol-based compounds and for the aliphatic acetoacetate esters (BIF 0.15 and 0.13). Factors that are proposed to be responsible for limiting the formation of more brominated DBPs include kinetic variability and steric hinderance, with the larger van der Waals radius of bromide (1.85 Å) compared to chloride (1.76 Å) [50] proposed to limit multiple bromine substitution, and the possibility of 'ipso' substitution of bromine for chlorine on aromatic compounds [35] (Supplementary Material Table S8).

Importantly, both amino acid related and lignin derived precursor compounds displayed high propensity for the DBPs formed to be brominated, with an average 57 % and 50 % of DBPs formed as Br-DBPs respectively, compared to 16 % for resorcinol based compounds. The implication here is that the presence of substantial absolute amounts of amino acids or lignin derived compounds, for example through algal blooms or extreme rainfall events, retains the potential to form high levels of brominated DBPs, despite low relative DBP formation potential. This is an area where future kinetics studies would provide important insights into the relative competition between precursor compounds as a means to understand DBP formation in bromide rich waters, and thus a window into potential routes to their mitigation.

3.2. Influence of molecular structure on formation potential

The results for resorcinol-based compounds presented here establish that electron-withdrawing functional groups (e.g. halogenated resorcinols) favour THM formation whereas those with lone pairs of electrons (e.g. amino resorcinols) and the ability to stabilise as resonance structures, show increased HAA formation (Supplementary Material Figure S2d). For example, halogenated resorcinols such as 4-chloro and 4-bromo resorcinols formed 1290 and 1020 μM/mM THMs and 64.1 and 75.4 μM/mM HAAs respectively, whereas amino resorcinols such as 4- and 5- amino resorcinol form only 315 and 149 μM/mM THMs but 163 and 294 μM/mM HAAs. This translated into higher formation of $HAA4_{unreg}$ from the amino resorcinols (52.7 and 60.7 μM/mM compared to 25.7 and 29.2 μM/mM from the halogenated equivalents) and also represents a general preference for bromination with 31 % and 30 % of DBPs by mole being brominated from the amino resorcinols compared to 7.0 and 11 % from the halogenated resorcinols, despite the initial bromination of 4-bromoresorcinol. This demonstrated that when functional groups on resorcinol type compounds contain a lone pair this can promote $HAA4_{unreg}$ formation through higher HAAFP and bromine incorporation into DBPs, thus such compounds may represent an overlooked source of risk given their lower THMFP. It is also noteworthy that all resorcinol-based compounds, other than 1,3-dihydroxynapthalene, formed more $HAA4_{unreg}$ than resorcinol itself which formed 10.7 μM/mM compared to median 24.4 μM/mM and a range of 0.684–166 μM/mM for the group. This demonstrates that future model compound studies should not use resorcinol as a representative compound when

investigating the cause of difference between HAA5FP and HAA9FP.

A key observation across these studies was that minor changes in the molecular structure of precursor compounds led to significant changes in the DBP formation potential. To illustrate, phloroglucinol formed a combined HAA9 and THM4 level of 2700 μM/mM whereas hydroxyquinol formed an order of magnitude less at 280 μM/mM. The difference in their structures is the location of the third hydroxy group, moving from 1,3,5- to 1,3,4-trihydroxybenzene respectively, with neither compound dissociated (pK_a>8) thus negating this as a cause. Consequently, it is proposed that electron transfer oxidation to the quinone group is the key differentiating pathway, with this mechanistic pathway option previously explored for humic acid and determined to involve an intermediate brominated quinone [24]. For phloroglucinol the regenerated bromide from electron transfer forms more hypobromous acid which rapidly undertakes electrophilic substitution leading to significant DBP formation, whereas for hydroxyquinol it is proposed that the ortho-quinone formed is unstable and degrades before significant halogenation occurs. The relative proportion of $HAA4_{unreg}$ to regulated HAAs is 9.7 % for phloroglucinol and 55 % for hydroxyquinol, revealing the pathways that impact the levels of DBPs formed do not necessarily govern the relative distribution of regulated and unregulated HAAs.

Further demonstration that presence of specific functional group will not identify high formation of $HAA4_{unreg}$ comes from the lignin derived compound ferulic acid, which forms 196 μM/mM $HAA4_{unreg}$ from a total 404 μM/mM HAA9. The suggestion from previous research [42] that high HAAFP relates primarily to the cinnamyl group is not supported by the lower HAA formation observed from sinapic and coumaric acids (72.3 and 90.5 μM/mM of which 40.9 and 39.1 μM/mM are $HAA4_{unreg}$, respectively) which also contain the cinnamyl group. A mechanistic explanation for increased HAA formation from ferulic acid was proposed to included nucleophilic addition across the cinnamyl group (Supplementary Material Figure S2c) [25, 51], but does not differentiate by secondary functional group on the phenol ring.

Similarly, in terms of the aliphatic carbonyl precursor compounds, changing from a hydroxy to a carbonyl group in malic acid (2-hydroxybutanedioic acid) and oxaloacetic acid (2-oxobutanedioic acid) reveals an even more significant difference in HAA formation with 0.926 (0.398 as $HAA4_{unreg}$) μM/mM for malic acid and 709 (229 as $HAA4_{unreg}$) μM/mM for oxaloacetic acid. This highlights the significance of the β-dicarbonyl where the α carbon is doubly activated for electrophilic substitution by the keto-enol equilibrium and promoted for bromination by the faster kinetics (Supplementary Material S2 and Table S8).

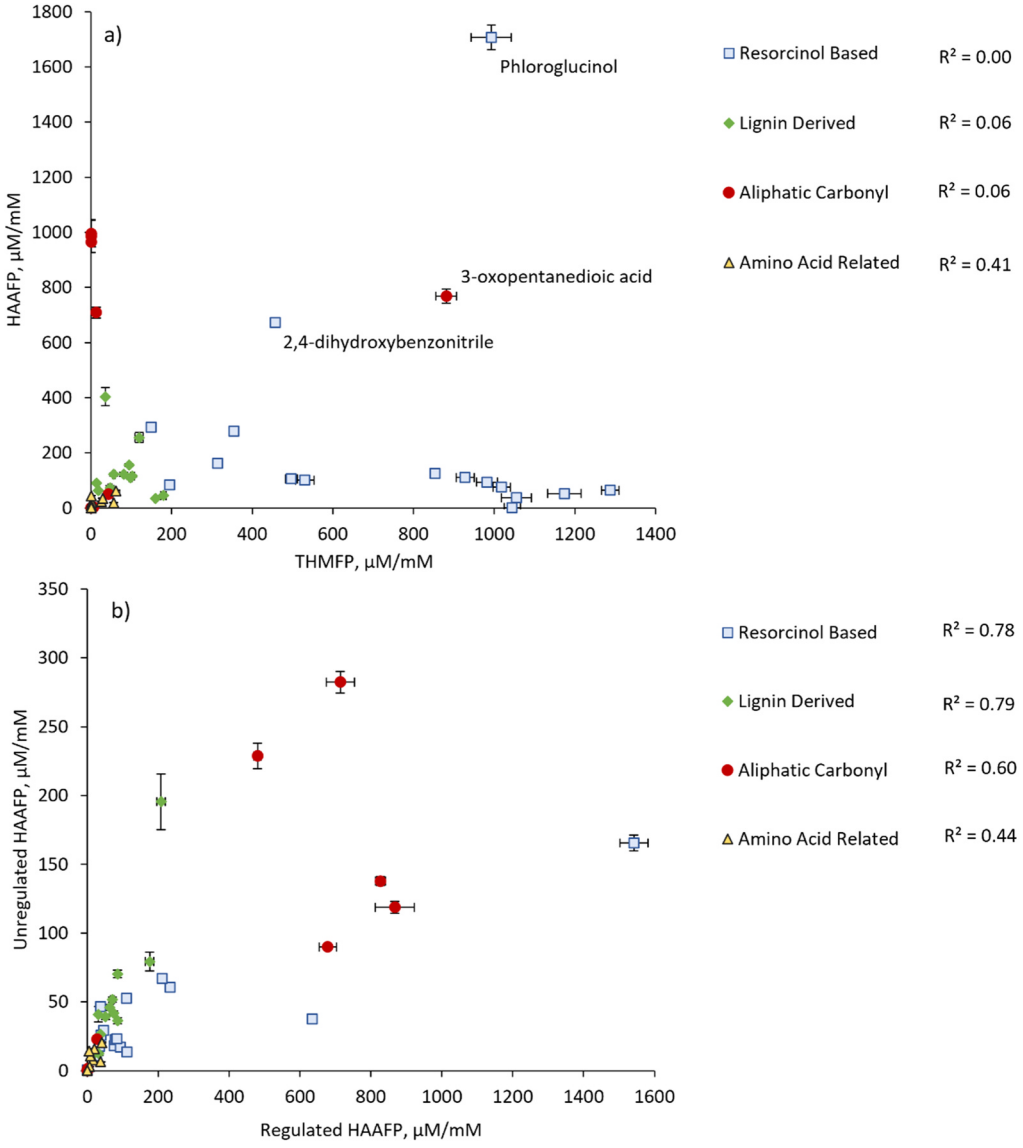


Fig. 2. Comparison of model compound formation potentials for a) THM and HAA and b) regulated HAA5 and unregulated $HAA4_{unreg}$, where error bars represent standard deviation.

Conversely, α- and γ-dicarbonyls are unable to form these more stable conjugated enol structures and so halogenation by electrophilic substitution is minimised. Importantly, unlike phenolic compounds, β-dicarbonyls do not appear to require dissociation to form HAAs with, for instance, the undissociated esters methyl and ethyl acetoacetate forming 965 μM/mM and 986 μM/mM respectively. However, when $HAA4_{unreg}$ formation is considered, these esters form notably lower levels than similar acidic compounds such as malonic and oxaloacetic acid (14 % and 12 % of HAAs as $HAA4_{unreg}$ compared to 28 % and 32 % for the acids respectively). Interestingly, given the maximum bromine utilisation of the acid compounds (calculating the proportion of the initial bromide included within DBPs measured demonstrates BUF of 1.0 and 0.94, respectively), it is proposed their formation of $HAA4_{unreg}$ would decrease with further available bromide, forming increased levels of DBAA which is within the regulated HAA5 group. This highlights the particular complexity of differentiating the formation of regulated and unregulated HAAs from aliphatic β-dicarbonyls where DXAA formation is predominant. The underlying reasons for this different formation pattern are proposed to include both the steric hinderance of the ester group, as observed during ester hydrolysis reactions [52], and the faster rate of bromination for the dissociated enolate ion formed from the β-keto acids [53].

3.3. Use of THMs and HAA5 to inform on the unregulated HAA4

Comparison of formation potentials for all fifty model compounds reveals no overall correlation between THMFP and HAAFP (correlation coefficient $R^2 = 0.02$), congruent with previous reports suggesting that the two DBP groups form through different pathways [31] (Fig. 2). This is also consistent with findings from real waters that link hydrophobic organic content to THM and TXAA formation, and hydrophilic organic content to DXAAs and brominated DBPs [54]. An analysis to evaluate the predictability of unregulated HAAs from measured HAA5 levels revealed correlation remains low ($R^2 = 0.51$) and consequently HAA5 does not offer reliable information on the formation of $HAA4_{unreg}$ when bromide is present (Fig. 2b). To illustrate, compounds with high HAA5FP of over 500 μM/mM are observed to form significantly varied levels of $HAA4_{unreg}$, ranging from 37.5 to 282 μM/mM (2,4-dihydroxybenzonitrile and malonic acid respectively). This has significance as historically HAA5 has been more widely measured and studied, but HAA5 results should not be extrapolated to give predictions for HAA9 formation. This also implies that aromaticity indicators (such as UV_{254}) and THM levels may not be suitable proxies for risk, due to poor correlation with the formation of the more toxic Br-HAAs, a finding reflected in real water results [55–57].

Across the trial, three compounds exhibited an ability to form high THMs and high HAAs, namely phloroglucinol and 2,4-dihydroxybenzonitrile, both resorcinol-based precursors, and 3-oxopentanedioic acid, an aliphatic carbonyl (Fig. 2a). This is of interest as most high DBP forming compounds favour either THM or HAA formation, not both, so this finding implies that simplifying DBP formation to specific molecular types is not always appropriate. There is limited corroborative evidence in literature for these findings, with 2,4-dihydroxybenzonitrile not previously studied and phloroglucinol only considered for THMs and limited HAAs [58]. 3-oxopentanedioic acid has been more widely studied [21,25,59], with Dickenson et al. (2008) also finding similar molar formations for THMs and HAAs when chlorinated (710 and 694 μM/mM respectively) but lower formation for HAAs when brominated (810 and 312 μM/mM), compared to 881 and 769 μM/mM in this study when bromide and chlorine are present concurrently. Conversely, Bond et al. (2009) identified a lower THMFP (≈150 μM/mM) and significantly lower HAAFP (≈20 μM/mM) for chlorination of 3-oxopentanedioic acid in the presence of bromide, with the significant experimental difference being in the 35 M/M ratio of chlorine, compared to 10 M/M used in this study (other experimental parameters were consistent at 15 μM compound, 24 h chlorination time, 20ºC, pH 7 phosphate buffer and a similar bromide concentration of 450 μg/L). However, when considering how to identify or target the removal of such key precursors, little commonality is observed in these three compounds. Both aromatic and aliphatic structures are represented, there is variation in functional group (OH and CN) and location (1,3,5 and 1,3,4) within the resorcinol-based compounds and levels of dissociation are also varied (phloroglucinol minimally dissociated (pK_a 8.0, 9.2, 14.0), 2,4-dihydroxybenzonitrile partially dissociated (pK_a 7.0) and 3-oxopentanedioic acid fully dissociated (pK_a 3.3)). This variability in molecular features precludes a single mechanistic step which accounts for formation of both DBP groups from the same molecule. Proposals for the mechanistic pathways for formation (Supplementary Material Section S7) suggest that the halo-decarboxylation to a tri-halogenated terminal carbon may be an important mechanistic step, when combined with β-dicarbonyl and δ-functional group with a lone pair to promote a stabilised carbanion intermediate. However, this key structural feature can be within the precursor itself or the intermediate, and so the variability in physical characteristics of the precursors will make it difficult to target such compounds for removal or identification of DBP risk.

3.4. Significance of HAA speciation

A key observed impact of molecular structure is in relation to the balance of levels of halogenation that occur (mono-, di- or tri- halogenated HAAs; MXAA, DXAA or TXAA) (Fig. 3). Importantly, three of the four unregulated HAAs belong to the TXAA group (BDCAA, CDBAA, TBAA) with only BCAA belonging to the DXAA group. Overall, aliphatic carbonyls almost exclusively formed DXAA (>95 %) and resorcinol-based compounds predominantly formed TXAA (most >70 %). MXAAs were rarely formed, an observation that aligns with results from real waters [60], and is explained by the promotion of further electrophilic substitution and low preference for hydrolysis from singly halogenated intermediates [61].

The predominate TXAA formed within the aromatic precursor compounds were the regulated species TCAA and the currently unregulated BDCAA (Fig. 3). To illustrate, within the resorcinol group 60 % (range 18–91 %) were TCAA and 16 % (range 4.8–29 %) were BDCAA. Similarly, for the lignin derived group the equivalent numbers were 44 % (range 11–62 %) and 24 % (range 3.9–36 %) respectively. In contrast, within the β-dicarbonyls, the predominate species was the regulated DCAA forming a median level of 78 % (range 62–87 %) of the total, followed by unregulated BCAA with a median of 14 % (range 12–31 %).

The formation of tri-halogenated DBPs (THMs and TXAAs) over DXAAs is posited to occur when the di-halogenated intermediate is stabilised sufficiently for further electrophilic substitution (Supplementary Material S2 and S7). To illustrate, in resorcinol-based compounds it is proposed that this stability is conferred by resonance and charge distribution onto electronegative atoms such as oxygen and can be observed in the lower pK_a values for such compounds, where the enhanced acidity indicates a more stable anionic free base (Supplementary Material Table S3, Figure S7). For instance, the nitro group on the azo violet molecule stabilises the carbanion formed at cleavage leading to formation of 925 μM/mM tri-halogenated DBPs (71.3 μM/mM of TXAA and 854 μM/mM of THMs) and 53.9 μM/mM of DXAA. Conversely, where this stability is not provided and an alternative 6-membered intermediate is supported by hydrogen bonding, DXAAs are observed to be the primary HAA formed (Supplementary Material Figure S10). For example, small β-keto acids and esters, such as malonic acid and acetoacetate esters, form on average 95 % DXAAs, and aspartic acid, where the amino is also β, forms 98 % DXAAs. It is noteworthy that for these β-dicarbonyl compounds the HAAFP is observed to be similar for acids and esters (average HAAFP 975 and 825 μM/mM for β-keto acids and β-keto esters, respectively) and so does not link to the pK_a of the compound or whether it is present as an enol or enolate at pH 7.

In total, $HAA4_{unreg}$ contributed a median formation potential of 41.4 (range 12.5–196) μM/mM within the lignin derived group, 24.4 (range

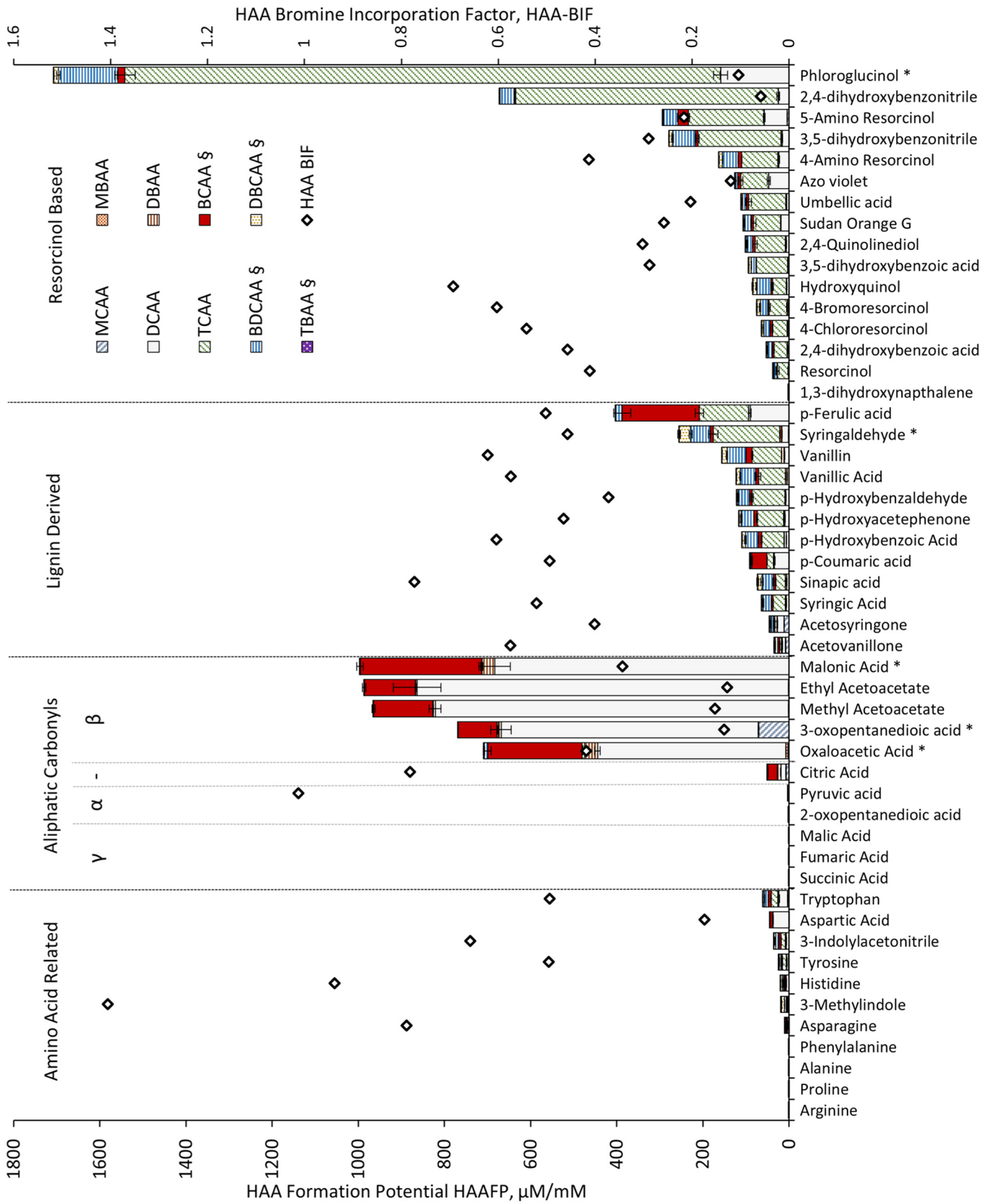


Fig. 3. HAA formation potential and HAA BIF for model compounds, where error bars represent standard deviation, * BUF ≈ 1, § identifies the unregulated $HAA4_{unreg}$.

0.684–166) μM/mM within the resorcinol group, 23.0 (range 0.181–282) μM/mM within the aliphatic carbonyls group and 6.60 (range 0.239–20.5) μM/mM within the amino acid group. Within the aromatic compound groups $HAA4_{unreg}FP$ comprised 42 % (range 28–57 %) of HAAFP from lignin-derived compounds and 22 % (range 5.5–55 %) of HAAFP from resorcinol based compounds. The higher relative proportion of HAAs as $HAA4_{unreg}$ for the lignin derived group compared to the resorcinol group reflects the higher propensity for bromine incorporation observed for the lignin derived compounds, combined with the fact that all HAAs within $HAA4_{unreg}$ are brominated. This posits that waters rich in lignin type compounds may form higher mass concentrations of HAA9 than waters containing resorcinol like, humic rich waters. This may be true even when the lignin precursor compounds are present at lower absolute concentrations, meaning indicators such UV absorbance (which identifies aromatic compounds) and total carbon may not identify this higher likelihood of HAA9 formation. Importantly, precursors which are lignin derived may form higher mass concentrations of HAA9 even when bromide levels are lower because of their increased propensity to incorporate bromide and the higher mass of bromine than chlorine. In comparison, whilst a low formation of unregulated HAAs was observed within the amino acid group, it represented 33 % (range 15–74 %) of the HAAs formed. The equivalent number for the aliphatic compounds was 28 % (range 12–52 %). Interestingly, the proportion of $HAA4_{unreg}$ within the HAAs was similar between the resorcinol and aliphatic groups, with this likely to be reflected in hydrophobic and hydrophilic organic content of real waters respectively.

The tendency of different precursor groups to form either DXAAs or TXAAs is important for understanding how the HAAs formed distribute between the currently regulated or the currently unregulated (HAA5 or $HAA4_{unreg}$). To illustrate, resorcinol based and lignin-derived compounds form a higher proportion of HAAs as TXAAs and consequently

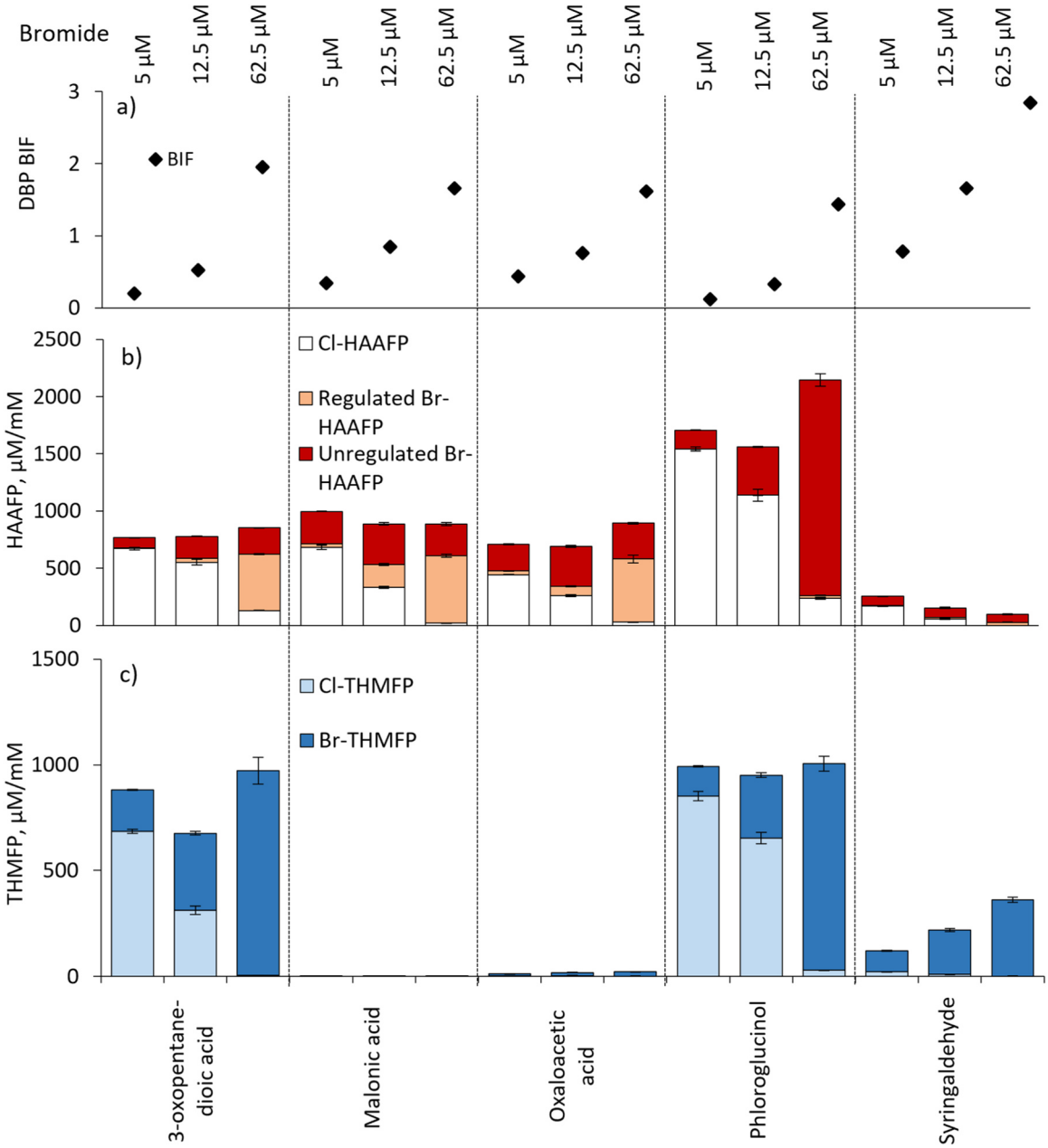


Fig. 4. DBP formation and BIF at elevated bromide concentrations for selected model compounds a) BIF b) HAA formation potential and c) THM formation potential, where error bars represent standard deviation.

these precursor compounds will tend to form Br-TXAAs when bromide is present (81 % and 82 % of the $HAA4_{unreg}$ formed from these compound groups was as Br-TXAAs). All the Br-TXAAs (BDCAA, DBCAA and TBAA) reside within $HAA4_{unreg}$. Conversely, the aliphatic β-dicarbonyls formed almost exclusively DXAAs and consequently 100 % of the $HAA4_{unreg}$ formed from this compound group was as BCAA (the only DXAA within $HAA4_{unreg}$). This becomes significant in a scenario where existing understanding of HAA9 levels are limited and where bromide levels are predicted to increase, for example due to saltwater incursion, blending with desalinated water or changing industrial activity [62]. Water sources containing resorcinol based or lignin derived precursor compounds are posited to increase the proportion of HAAs as $HAA4_{unreg}$ in this scenario, so increasing levels of HAA9 but potentially decreasing HAA5, due to lower formation of TCAA. Contrastingly, aliphatic dicarbonyls would be predicted to show a more varied formation of regulated versus unregulated HAAs, with formation moving from DCAA (HAA5) to BCAA ($HAA4_{unreg}$) then DBAA (HAA5) with increasing bromide. Further research is required to establish these formation patterns, which will have significance for understanding the precursor types and source water characteristics likely to challenge HAA9 standards but not HAA5. Note that the amino acid related compounds (which includes both aliphatic and aromatic components) have median 34 % $HAA4_{unreg}$ as BCAA and 66 % as Br-TXAAs, implying both formation patterns would be observed with increasing bromide from this precursor group.

3.5. The influence of increasing bromide

To explore high bromination preference further, selected compounds where bromide utilisation calculations determined that almost all available bromide had been incorporated into measured DBPs (BUF≈1) were exposed to higher levels of bromide. This did not significantly change the total DBP formation potential but did switch the predominant species formed to more brominated ones, as expected (Fig. 4). However, the level of bromination was structure dependent, with syringaldehyde (lignin derived) becoming fully tri-brominated (BIF 2.9 at 62.5 μM bromide) whereas phloroglucinol (resorcinol based) retained some chlorinated DBP formation (BIF 1.4 at 62.5 μM bromide). For the aliphatic β-dicarbonyl compounds 3-oxopentanedioic acid, malonic acid and oxaloacetic acid the BIF values were 2.0, 1.7 and 1.6 at 62.5 μM bromide, reflecting the high formation of DXAAs (where maximum possible BIF is 2.0).

The explanation of the high bromine incorporation for syringaldehyde is equivocal with the proposition that halogenation takes place on a side group where steric restriction is limited and 'ipso' substitution is not possible (Supplementary Material Figure S9). The alternatives are that it involves ring opening via oxidation to 1,5 aliphatic carbonyls prior to contraction by intramolecular nucleophilic substitution [51] or that it involves bromination by 'exotic' electrophiles such as BrCl, rather than hypobromous acid, as these have previously been identified as highly reactive with anisole compounds [34]. In general, further research is needed to conclusively establish the mechanism and understand why lignin derived compounds (such as syringaldehyde) so readily incorporate bromide, whereas resorcinol-based compounds (such as phloroglucinol) retain some chlorine incorporation. Such work would be significant for our understanding of the formation of Br-DBPs from waters with more hydrophobic organic matter. Similarly, the high bromine incorporation of the aliphatic β-dicarbonyl acids in comparison to similar esters is worthy of further attention to inform on formation of Br-HAAs from hydrophilic organic matter.

For these selected model compounds, the impact of increasing the incorporation of bromide was to change the balance of regulated versus unregulated Br-HAAs. For instance, for the aromatic compounds where TXAAs are predominant, the proportion of HAAs which were $HAA4_{unreg}$ moved from 20 % to 41–80 % as bromide increased from 5 to 12.5–62.5 μM. In contrast, for the aliphatic compounds, where DXAAs dominate, this proportion moved from 24 % to 38 % then 31 %. This reflects the inclusion of DBAA in the regulated HAA5, thus decreasing the proportion of $HAA4_{unreg}$ with increasing bromination of DXAAs. Overall, this reveals that when the ratio of bromide to compound increases, the bromination of DBPs formed will increase, with the speciation dependent on molecular structure such that aromatic compounds favour the formation of $HAA4_{unreg}$ through brominated TXAAs. For aliphatic compounds the picture is more nuanced and $HAA4_{unreg}$ may decrease through formation of the regulated DBAA.

3.6. Future work

These model compound studies demonstrate the complexity of DBPFP according to molecular structure and as such provide a useful framework for directing future research into the most significant organic matter precursor types. For instance, this work highlights the potential significance of aliphatic β-dicarbonyl precursors, a finding which becomes more apparent when viewed through the lens of mass of $HAA4_{unreg}$ formed per mass of carbon. Because of the higher by mole formation of $HAA4_{unreg}$ and the higher mass of bromine than chlorine, relatively low carbon concentrations can yield high $HAA4_{unreg}$ from these compounds. To illustrate, the median mass formation potential as μg of DBP formed per mg of precursor carbon was 398 (range 260–1360) $\mu gHAA4_{unreg}$/mgC for the aliphatic β-dicarbonyls compared to 61.6 (range 1.20–477), 89.9 (range 22.0–297) and 14.8 (range 0.680–32.6) $\mu gHAA4_{unreg}$/mgC for the larger resorcinol-based, lignin derived and amino acid related groups respectively. Consequently, water sources containing aliphatic β-dicarbonyl precursor organic matter may give higher formation of HAA9 from lower measured carbon than water sources containing other precursor types. Given smaller, hydrophilic compounds are less amenable to removal by standard coagulation-based processes, and there is some evidence that THM precursors are preferentially removed during treatment [63–65], this has implications for water treatment practice. Importantly, further work is required to understand the real-world concentrations and sources of high forming precursor compounds, particularly those which form high levels of both THMs and HAAs and those which will be present at point of chlorination, with some evidence that THM precursors are preferentially removed during treatment [63–65]. This will then complement research which targets the removal of DBP precursors including the aromatic DBPs which act as intermediates for regulated aliphatic DBP formation [66].

Future work should also consider mixed model compound experiments as these will provide valuable information for identifying high risk water types and better represent real-world scenarios, where multiple precursor compounds and intermediates interact with chlorine and bromide, influencing the level and speciation of DBPS formed. It is important to ask whether the interactions between multiple compounds, chlorine and bromide are synergistic or antagonistic regarding DBP formation and particularly whether the propensity for bromination is retained by the groups of precursors which form high levels of HAAs. To illustrate, an improved understanding of whether the high formation of $HAA4_{unreg}$ observed for aliphatic β-dicarbonyls and lignin derived compounds is maintained when there is competition for the bromide would be informative about the risk such compounds present for HAA9 compliance. Furthermore, the possibility of directing DBP formation away from the more toxic by-products could be explored with research on mixed model compounds. Such studies would also complement a more detailed investigation of the kinetic behaviour of bromide incorporation into DBPs when chlorine is present. Such kinetic studies would have implications for the conditions at chlorination, such as temperature or pH, which influence formation of the regulated or unregulated HAAs.

4. Conclusions

These experiments have demonstrated that formation of the four unregulated HAAs is poorly understood from our knowledge of THM or

HAA5 formation. $HAA4_{unreg}$ form from all the groups of compounds tested but were generated at especially high levels from β-dicarbonyls and high relative percentages from lignin derived compounds. Overall, small changes in precursor chemical structure were shown to make dramatic changes in formation potential, explaining why in some water types the current monitoring approaches (such as UV absorbance or dissolved organic carbon) are unable to inform about potentially significant changes in DBP formation and especially for the currently unregulated species [67]. High formation of BCAA was associated with the β-keto acid group within the aliphatic carbonyls, while BDCAA was associated with the general high bromination propensity and mid-level TXAA formation of the lignin derived compounds.

Importantly, the formation of $HAA4_{unreg}$ was linked to both aromatic and aliphatic precursors, which is key to identifying where compliance with HAA5 regulation deviates from that of HAA9. For the aromatic compounds, formation of $HAA4_{unreg}$ was predominantly through the brominated TXAAs, suggesting hydrophobic aromatic precursors for these DBPs which could be more readily removed by coagulation-based processes. Consequently, focus is needed to ensure maximum removal of treatable hydrophobic material in high bromide waters. Conversely, for aliphatic compounds the picture is more complex. Not only are such hydrophilic compounds more recalcitrant and potentially formed during treatment, but importantly their HAA formation pattern is associated to both $HAA4_{unreg}$ and HAA5 with increasing bromination. Where oxidative treatment processes are in use, care needs to be exercised in relation to DBPs formation from hydrophilic precursors, either by careful process control or effective removal of by-products prior to chlorine disinfection.

Ultimately, the current work contributes two key insights when considering how thinking will need to change if an HAA9 standard is adopted. Both aliphatic and aromatic precursor compounds will need to be scrutinised along with the relative bromide concentration, reflecting the differing formation behaviours and bromination propensity of aromatic and aliphatic precursors. In addition, the current monitoring approaches provide little to no insight in relation to the risk posed by currently unregulated HAAs, and so work is needed to identify suitable techniques for monitoring and control of precursors.

Environmental Implications

As pressure on resources drives the use of lower quality, higher bromide, sources for drinking water production, regulatory attention turns to controlling formation of the more toxic brominated disinfection by-products (DBPs) and expanding existing regulations to include brominated haloacetic acids (Br-HAAs). This study uses model compounds as surrogates to elucidate the impact of molecular structure on the outcomes resulting from the interaction between chlorine, bromide and organic matter during the disinfection process. The findings support the development of strategies to reduce human exposure to hazardous substances and improve understanding of the important precursor types for the four currently unregulated Br-HAAs.

CRediT authorship contribution statement

Bruce Jefferson: Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **John Haley:** Writing – review & editing, Supervision, Conceptualization. **John Fawell:** Writing – review & editing. **Peter Jarvis:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **Emma Goslan:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **Polly Grundy:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation.

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Polly Grundy reports financial support was provided by UK Water Industry Research (UKWIR). Polly Grundy reports financial support was provided by EPSRC Centre for Doctoral Training in Water Infrastructure and Resilience. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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MarvinSketch was used for drawing, displaying and characterising chemical structures and reactions, MarvinSketch 24.1.2, Chemaxon (https://www.chemaxon.com). Icons made by Freepik from www.flaticon.com.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhazmat.2026.141496.

Data Availability

Data supporting this study are openly available from CORD. See DOI: 10.57996/cran.ceres-2667

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