Supplementary Information (SI)

Exploration of how the molecular structure surrounding the β-dicarbonyl group impacts formation of brominated haloacetic acids

Data supporting this study are openly available from CORD at DOI 10.57996/cran.ceres-2745.

This Supplementary Information (SI) consists of:

1 Materials and Methods

1.1 Reagents

Ammonium chloride (reagent grade), N,N Diethyl-1,4 Phenylenediamine (DPD, Hach Lange™ Free Chlorine Reagent Powder Pillows), formic acid (LCMS grade), methanol (HPLC and LCMS grade), methyl tert-butyl ether (MTBE, extra pure), potassium bromide (extra pure), potassium phosphate monobasic (extra pure), sodium hydroxide (1M, NIST standard), sodium hypochlorite (technical ~14%), sodium phosphate dibasic (reagent grade), sodium sulphate (anhydrous, extra pure), sulfuric acid (concentrated, reagent grade) and model compounds (other than the exceptions detailed below) were purchased from Fisher Scientific (Pittsburgh, USA).

2,3-dibromopropionic acid (2,3-DBPA), standard solutions of 4-bromofluorobenzene (4-BFB, 2000 µg/ml in methanol) and Trihalomethanes (THM4, 2000 µg/ml in methanol) and model compounds 3-oxobutanoic acid (as lithium salt), 3-aminobutanoic acid, trichloroacetoacetate, ethyl 4-bromoacetoacetate and 3-oxopentanedioic acid were purchased from Merck (Darmstadt, Germany). Diethyl malonate-2-^{13}C and 3-oxohexanedioic acid were purchased from LGC Standards (London, UK). Methyl 3,5-dioxohexanoate was purchased from Key Organics (Camelford, UK). Malonamic acid was purchased from Apollo Scientific (Cheshire, UK). Haloacetic acids (HAA9, 1000 µg/ml in MTBE) standard solution was purchased from Restek (Buckinghamshire, UK).

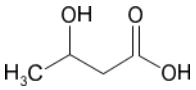
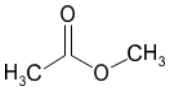
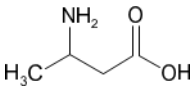
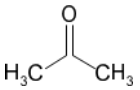
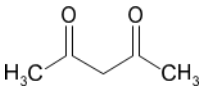
THM4 comprises chloroform (trichloromethane, TCM), bromodichloromethane (BDCM), dibromochloromethane (DBCM) and bromoform (tribromomethane, TBM). HAA9 comprises monochloroacetic acid (MCAA), monobromoacetic acid (MBAA), dichloroacetic acid (DCAA), bromochloroacetic acid (BCAA), dibromoacetic acid (DBAA), trichloroacetic acid (TCAA), dichlorobromoacetic acid (DCBAA), chlorodibromoacetic acid (CDBAA) and tribromoacetic acid (TBAA).

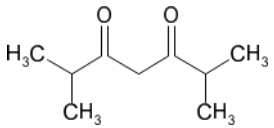
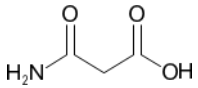
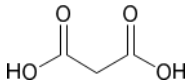
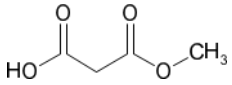
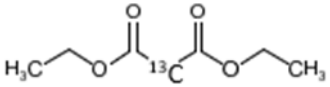
Stock solutions of model compounds were prepared in methanol. Appropriate adjustments were made for salts or purity where required.

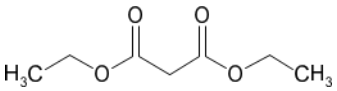
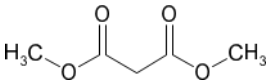
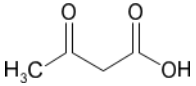
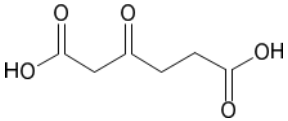
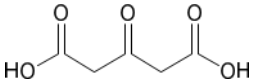
Ultra-pure (UP) water (18.2 MΩ·cm) was provided by an Elga (Woodridge, IL USA) Purelab Ultra Genetic system.

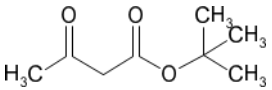
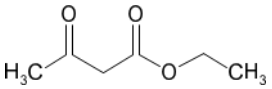
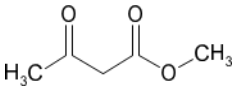
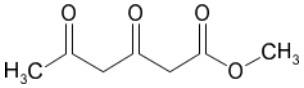
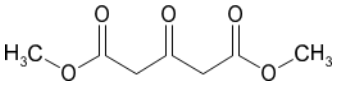
1.2 Model Compounds

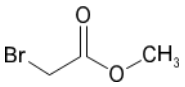
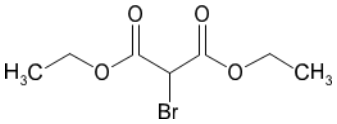
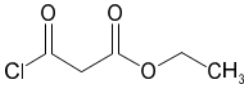
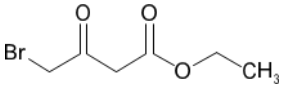
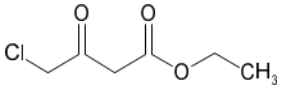
Table S1 Details of aliphatic carbonyl model compounds

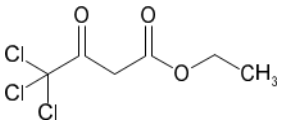
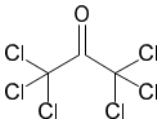
#	Model Compound; Synonyms; CAS	Structure; Group	Proposed Key Influences	Comparisons Within this Study
1	3-Hydroxybutanoic acid; 300-85-6	 No β-ketone	No β-dicarbonyl so no double enol activation at α carbon - halogenation by electrophilic substitution less likely. Cleavage by decarboxylation would not give target DBPs. pK_a ~4.4 so will be dissociated at acid.	Hydroxy equivalent of 3-aminobutanoic acid or 3-oxobutanoic acid. Potential for 6-membered H-bonded stabilised intermediate but not as enol for electrophilic substitution.
2	Methyl acetate; 79-20-9	 No β-ketone	No β-dicarbonyl so α halogenation less likely. Not dissociated. No β-dicarbonyl.	Decarboxylation product of methyl malonate, if decarboxylation was first step. Non-halogenated equivalent of methyl 2-bromoacetate.
3	3-Aminobutanoic acid; 541-48-0	 No β-ketone	No β-dicarbonyl so α halogenation less likely. pK_a ~4.2 and 10.5 so partially dissociated. No β-dicarbonyl.	Amino equivalent of 3-hydroxybutanoic acid or 3-oxobutanoic acid. Potential for 6-membered H-bonded stabilised intermediate but not enol for electrophilic substitution.
4	Acetone; Propan-2-one; 67-64-1	 No β-ketone	No β-dicarbonyl so α halogenation less likely. Not dissociated. No β-dicarbonyl.	Non-halogenated equivalent of hexachloroacetone.
5	Acetylacetone; Pentane-2,4-dione; 123-54-6	 β-ketone only	β- dicarbonyl so likely halogenate at α carbon. Also has terminal (non-substituted) carbons. pK_a ~8.6 so not dissociated. Decarboxylation not possible. Steric factor V(vdW)[¥] = 49.06 Å^3	Two terminal carbons compared to one for 3-oxobutanoic acid and none for malonic acid. Non-substituted terminal carbons compared to 2,6-Dimethyl-3,5-heptanedione.

#	Model Compound; Synonyms; CAS	Structure; Group	Proposed Key Influences	Comparisons Within this Study
6	2,6-Dimethyl-3,5-heptanedione; 18362-64-6	 β-ketone only	β- dicarbonyl so likely halogenate at α carbon. Terminal carbons substituted and sterically hindered. pK_a ~8.5 so not dissociated. Decarboxylation not possible. Steric factor V(vdW) = 118.26 Å^3	Substitution of terminal carbons compared to acetylacetone.
7	Malonamic acid; 3-amino-3-oxopropanoic acid; 2345-56-4	 3 carbon β-ketone acid	β- dicarbonyl so likely halogenate at α carbon. Decarboxylation will not give HAAs. pK_a ~3.7 so will be dissociated. Steric factor V(vdW) = 32.94 Å^3	Amino equivalent of malonic acid, with potential for 6-membered H-bonded stabilised intermediate retained. Terminal nitrogen instead of carbon compared to 3-oxobutanoic acid.
8	Malonic acid; Propanedioic acid 141-82-2	 3 carbon β-ketone acid	β- dicarbonyl so likely halogenate at α carbon. Decarboxylation possible. pK_a ~2.4 and 5.9 so will be doubly dissociated. Steric factor V(vdW) = 29.42 Å^3	Hydroxy equivalent of malonamic acid. Acid equivalent of methyl and dimethyl malonate esters. One acetate unit shorter than 3-oxopentanedioic acid. Terminal hydroxy equivalent of terminal carbon on 3-oxobutanoic acid and acetylacetone.
9	Methyl malonate; 3-methoxy-3-oxopropanoic acid; 16695-14-0	 3 carbon β-ketone ester	β- dicarbonyl so likely halogenate at α carbon. Decarboxylation possible at one acid. pK_a ~3.7 so will be dissociated at acid. Steric factor V(vdW) = 48.03 Å^3	Single methyl ester of malonic acid. Could undergo ester hydrolysis and/or decarboxylation. Terminal hydroxy equivalent of methyl acetoacetate.
10	Diethyl malonate-2-^{13}C; Diethyl propanedioate-2-^{13}C; 67035-94-3	 3 carbon β-ketone ester	β- dicarbonyl so likely halogenate at α carbon. Decarboxylation not possible. pK_a ~13.4 so will not be dissociated. Steric factor V(vdW) = 101.24 Å^3 (assumes physical properties similar for ^{13}C).	Labelled diethyl malonate at α carbon to demonstrate the source of carbon in HAAs formed.

#	Model Compound; Synonyms; CAS	Structure; Group	Proposed Key Influences	Comparisons Within this Study
11	Diethyl malonate; diethyl propanedioate; 105-53-3	 3 carbon β-ketone ester	β- dicarbonyl so likely halogenate at α carbon. Decarboxylation not possible. pK_a ~13.4 so will not be dissociated. May be influence of larger ethyl ester. Steric factor V(vdW) = 101.24 Å^3	Double ethyl ester of malonic acid. Could undergo ester hydrolysis, then decarboxylation. Ethyl equivalent of dimethyl malonate. Non halogenated equivalent of diethyl bromomalonate.
12	Dimethyl malonate; dimethyl propanedioate; 108-59-8	 3 carbon β-ketone ester	β- dicarbonyl so likely halogenate at α carbon. Decarboxylation not possible. pK_a ~13.9 so will not be dissociated. May be influence of smaller methyl ester. Steric factor V(vdW) = 66.64 Å^3	Double methyl ester of malonic acid and methyl malonate. Could undergo ester hydrolysis, then decarboxylation. Methyl equivalent of diethyl malonate.
13	3-oxobutanoic acid; Acetoacetic acid; 541-50-4 3483-11-2 Li salt	 >3 carbon β-ketone acid	β- dicarbonyl so likely halogenate at α carbon. Decarboxylation possible at acid. pK_a ~4 so will be dissociated at acid. Steric factor V(vdW) = 39.24 Å^3	Terminal carbon (longer chain) compared to malonic acid, but one less carbon on chain than acetylacetone. Acid equivalent of acetoacetate esters. Hydroxy equivalent of 3-hydroxybutanoic acid.
14	3-oxohexanedioic acid; 689-31-6	 >3 carbon β-ketone acid	β- dicarbonyl so likely halogenate at α carbon. Decarboxylation possible only at acid where intermediate carbanion supported. pK_a ~4 so will be dissociated (at 1 hydroxy). Steric factor V(vdW) = 87.46 Å^3	Single carbon longer chain compared to 3-oxopentanedioic acid.
15	3-oxopentanedioic acid; 542-05-2	 >3 carbon β-ketone acid	Double β- dicarbonyl so likely halogenate at both α carbons. Decarboxylation possible at acids. pK_a ~3.2, 4 so both acids dissociated. Steric factor V(vdW) = 70.17 Å^3	Acetate unit longer than malonic acid. Single carbon shorter chain compared to 3-oxohexanedioic acid. Acid equivalent of the dimethyl ester.

#	Model Compound; Synonyms; CAS	Structure; Group	Proposed Key Influences	Comparisons Within this Study
16	t-Butyl acetoacetate; tert-butyl 3-oxobutanoate; 1694-31-1	 >3 carbon β-ketone ester	β- dicarbonyl so likely halogenate at α carbon. Decarboxylation not possible and will not be dissociated (pK_a ~10). Ester hydrolysis predicted easier due to larger ester. Steric factor V(vdW) = 111.06 Å^3	Butyl ester of 3-oxobutanoic acid. Butyl equivalent of methyl and ethyl esters (acetoacetates).
17	Ethyl acetoacetate; ethyl 3-oxobutanoate; 141-97-9	 >3 carbon β-ketone ester	β- dicarbonyl so likely halogenate at α carbon. Decarboxylation not possible and will not be dissociated (pK_a ~10.5). Steric factor V(vdW) = 75.15 Å^3	Ethyl ester of 3-oxobutanoic acid. Ethyl equivalent of butyl and methyl esters (acetoacetates).
18	Methyl acetoacetate; methyl 3-oxobutanoate; 105-45-3	 >3 carbon β-ketone ester	β- dicarbonyl so likely halogenate at α carbon. Decarboxylation not possible and will not be dissociated (pK_a ~10.9). Steric factor V(vdW) = 57.85 Å^3	Methyl ester of 3-oxobutanoic acid. Methyl equivalent of methyl and butyl esters (acetoacetates).
19	Methyl 3,5-dioxohexanoate; 29736-80-9	 >3 carbon β-ketone ester	Double β- dicarbonyl so likely halogenate at both α carbons. Decarboxylation not possible and will not be dissociated (pK_a ~8.6). Ester hydrolysis possible. Steric factor V(vdW) = 98.6 Å^3	Single terminal carbon equivalent to dimethyl ester of 3-oxopentanedioic acid.
20	Dimethyl 3-oxopentanedioate; 3-Oxo-pentanedioic acid 1,5-dimethyl ester; 1830-54-2	 >3 carbon β-ketone ester	Double β- dicarbonyl so likely halogenate at both α carbons. Decarboxylation not possible and will not be dissociated (pK_a ~10.6). Ester hydrolysis possible. Steric factor V(vdW) = 107.39 Å^3	Single acetate unit longer than dimethyl malonate. Dimethyl ester of 3-oxopentanedioic acid.

#	Model Compound; Synonyms; CAS	Structure; Group	Proposed Key Influences	Comparisons Within this Study
21	Methyl 2-bromoacetate; 96-32-2	 Single halogenation	No β-dicarbonyl so α halogenation less likely but initial halogenation may promote further halogenation or cleavage. Not dissociated. Ester hydrolysis possible. No β-dicarbonyl	Halogenated equivalent of methyl acetate.
22	Diethyl bromomalonate; diethyl 2-bromopropanedioate; 685-87-0	 Single halogenation	β-dicarbonyl so α halogenation likely but initial α halogenation may promote or hinder further halogenation or cleavage. pK_a 12.3 so not dissociated. Ester hydrolysis possible. Steric factor V(vdW) = 127.76 Å^3 (note Br is included in this value but likely has a promotional effect on halogenation as well as steric hinderance)	Halogenated at α carbon equivalent of diethyl malonate.
23	Ethyl malonate chloride; ethyl 3-chloro-3-oxopropanoate; 36239-09-5	 Single halogenation	β-dicarbonyl so α halogenation likely but existing halogenation may promote or hinder further halogenation or cleavage pK_a 8.7 so not dissociated. Ester hydrolysis possible. Steric factor V(vdW) = 77.14 Å^3	Terminal chlorine equivalent of ethyl acetoacetate.
24	Ethyl 4-bromooacetoacetate; ethyl 4-bromo-3-oxobutanoate; 13176-46-0	 Single halogenation	β-dicarbonyl so α halogenation likely but existing terminal halogenation may promote or hinder further halogenation or cleavage. pK_a 10.8 so not dissociated. Ester hydrolysis possible. Steric factor V(vdW) = 94.44 Å^3	Brominated terminal carbon equivalent of ethyl acetoacetate. Brominated of ethyl 4-chloroacetoacetate.
25	Ethyl 4-chloroacetoacetate; ethyl 4-chloro-3-oxobutanoate; 638-07-3	 Single halogenation	β-dicarbonyl so α halogenation likely but existing terminal halogenation may promote or hinder further halogenation or cleavage. pK_a 9.7 so not dissociated. Ester hydrolysis possible. Steric factor V(vdW) = 90.37 Å^3	Chlorinated terminal carbon equivalent of ethyl acetoacetate. Chlorinated of ethyl 4-bromooacetoacetate.

#	Model Compound; Synonyms; CAS	Structure; Group	Proposed Key Influences	Comparisons Within this Study
26	Ethyl-4,4,4-trichloroacetoacetate; ethyl 4,4,4-trichloro-3-oxobutanoate; 3702-98-5	 Triple halogenation	β-dicarbonyl so α halogenation likely but existing fully halogenated terminal carbon may promote or hinder further halogenation or cleavage. pK_a 8.5 so not dissociated. Ester hydrolysis possible. Steric factor V(vdW) = 120.79 $Å^3$	Fully chlorinated terminal carbon equivalent of ethyl acetoacetate. Fully chlorinated of ethyl 4-chlorooacetoacetate.
27	Hexachloroacetone; 1,1,1,3,3,3-hexachloropropan-2-one; 116-16-5	 Triple halogenation	No further halogenation possible. Chlorine promotes dipole on carbonyl carbon and subsequent cleavage. Not dissociated. No β-dicarbonyl.	Fully chlorinated equivalent of acetone.

Notes: All pK_a values were obtained from Chemicalize, October 2024, https://chemicalize.com/, developed by ChemAxon.

[¥] Steric factor V(vdW) – for the purpose of comparison of steric effects between β-dicarbonyl compounds a steric factor was obtained based on the Van der Waals volume (V(vdW). This simple estimate of functional group volume was calculated using the method described by Zhao *et al. (*2003)[1] for each group either side of the β-dicarbonyls and summed to represent the influence on the α-carbon where halogenation occurs. Where two enolisable carbons are present then the value is calculated for each and the lowest value selected, although note for the compounds here they are symmetric so the value used is the same. Where no β-dicarbonyl is present no value was calculated as the effect of the 1,3-dicarbonyl itself is presumed to dominate due to the double activation to electrophilic substitution at the α-carbon.

1.3 Determination of Hypochlorite Concentration

Chlorination solution was prepared by dilution of ≈14% sodium hypochlorite and standardised before use to establish the exact free chlorine concentration at the time of use. Standardisation was performed using Hach Pocket Colorimeter II (Cat. 58700-00) and DPD (N,N-diethyl-p-phenylenediamine) in Hach Lange Free Chlorine Reagent Powder Pillows for 10ml samples. This procedure is based on a method adapted from Standard Method 4500-Cl G for drinking water[2] as described in Hach Method 8021.

1.4 HAA9 by LC-MS/MS

The method was developed in-house and fully validated in line with ISO:17025 and NS30 guidelines as reported previously[3].

1.4.1 Sample Preparation

Samples were adjusted to pH 2±0.5 using 10% sulfuric acid and 2,3-Dibromopropionic acid (2,3-DBPA) was added as an internal standard. Where necessary, samples were diluted into the range of the method with pH 2 water containing internal standard (levels adjusted as appropriate) prior to re-analysis.

1.4.2 Liquid Chromatography Conditions

The chromatography instrument used was a SCIEX (Framingham, MA, USA) ExionLC Ultra High Pressure Liquid Chromatography (UHPLC) system with temperature controlled autosampler and column compartment. The chromatography column was a Waters (Milford, MA, USA) Acquity HSS T3 Premier 100 x 2.1 mm 1.8 µm with associated Vanguard column. The mobile phase comprised A: 0.2 mM formic acid in water and B: 0.2 mM formic acid in methanol. Initial conditions were 1% B for 1 minute, followed by a gradient to 70% B at 5 minutes, then holding for 2 minutes before re-equilibration, with a total run time of 10 minutes. The flow was 0.2 ml/min, injection volume was 20 µL, column temperature 50°C and autosampler temperature 7°C.

1.4.3 Mass Spectrometry Conditions

The mass spectrometer instrument used was a SCIEX (Framingham, MA, USA) QTrap 6500+ system with Electrospray Ionization (ESI) source. It was operated in negative ionization Multiple Reaction Monitoring (MRM) mode. Curtain gas (CUR, nitrogen) was set to 25 psi, ion source temperature (TEM) 350°C, ion source gas 1 (GS1, air) 50 psi, ion source gas 2 (GS2, air) 60 psi, Collisionally Activated Dissociation (CAD, nitrogen) gas 'High', ion spray voltage (IS) -4500 V. The instrument was controlled with SCIEX Analyst version 1.6.3 software and the quantification was performed with SCIEX MultiQuant version 3.0.2. The acquisition parameters and observed retention times for individual compounds are summarised in Table S2.

Table S2 LC-MS/MS acquisition parameters

Compound	Retention time (mins)	Q1[a] (Da)	Q3[b] (Da)	Dwell[c] (ms)	DP[d] (V)	EP[e] (V)	CE[f] (V)	CXP[g] (V)
MCAA	2.8	92.98	34.97	15	-5	-3	-15	-15
MCAA	2.8	94.98	36.97	15	-5	-3	-15	-10
MBAA	3.45	136.92	78.92	15	-10	-9	-15	-10
MBAA	3.45	138.92	80.92	15	-10	-3	-15	-10
DCAA	4.12	126.94	34.97	15	-5	-3	-30	-15
DCAA	4.12	126.94	82.95	15	-5	-9	-15	-10
BCAA	4.48	126.9	78.92	15	-30	-9	-20	-10
BCAA	4.48	170.88	126.9	15	-5	-9	-15	-10
DBAA	4.85	216.83	172.84	15	-5	-6	-15	-10
DBAA	4.85	216.83	78.92	15	-5	-12	-40	-10
TCAA	6	116.91	34.97	15	-5	-3	-20	-15
TCAA	6	118.91	36.97	15	0	-3	-20	-10
BDCAA	6.18	160.86	78.92	15	-10	-3	-15	-10
BDCAA	6.18	162.86	80.92	15	-20	-3	-20	-15
DBCAA	6.34	206.8	78.92	15	-5	-12	-20	-10
DBCAA	6.34	208.8	80.92	15	-5	-12	-20	-10
TBAA	6.5	252.75	80.92	15	-20	-6	-20	-10
TBAA	6.5	250.75	78.92	15	-10	-6	-25	-10
2,3-DBPA‡	5.76	80.9	80.9	15	-30	-6	-10	-10
2,3-DBPA‡	5.76	78.9	78.9	15	-30	-6	-10	-10

[a] Mass to charge ratio of precursor ion [b] Mass to charge ratio of product ion [c] Dwell time [d] Declustering Potential [e] Entrance Potential [f] Collision Energy [g] Collision cell Exit Potential ‡ Internal Standard (IS)

1.4.4 Semi-Quantitative Analysis of ^{13}C-HAAs

LC-MS/MS analysis of the HAAs formed from diethyl malonate-2-^{13}C was performed using the same conditions as for non-labelled HAAs except that additional mass transitions as detailed in Table S3 were included to cover the ^{13}C-HAAs produced. The area from these additional transitions were used to obtain a relative response to the internal standard area which was then quantified against the calibration curve from the non-labelled haloacetic acids. These results are therefore considered semi-quantitative as they assume a similar response between labelled and unlabelled HAAs.

GC-ECD analysis is unable to distinguish between the labelled and unlabelled outcome for THMs as ECD is not mass selective. However, for both labelled and non-labelled diethyl malonate the THM results were less that the detection limit of the method.

Table S3 Additional LC-MS/MS acquisition parameters for ^{13}C-HAAs

Compound	Retention time (mins)	Q1[a] (Da)	Q3[b] (Da)	Dwell[c] (ms)	DP[d] (V)	EP[e] (V)	CE[f] (V)	CXP[g] (V)
^{13}C-MCAA	2.80	94.0	35.0	15	-5	-3	-15	-15
^{13}C-MCAA	2.80	96.0	37.0	15	-5	-3	-15	-10
^{13}C-MBAA	3.45	137.9	78.9	15	-10	-9	-15	-10
^{13}C-MBAA	3.45	139.9	80.9	15	-10	-3	-15	-10
^{13}C-DCAA	4.12	127.9	35.0	15	-5	-3	-30	-15
^{13}C-DCAA	4.12	127.9	84.0	15	-5	-9	-15	-10
^{13}C-BCAA	4.48	127.9	78.9	15	-30	-9	-20	-10
^{13}C-BCAA	4.48	171.9	127.9	15	-5	-9	-15	-10
^{13}C-DBAA	4.85	217.8	78.9	15	-5	-6	-15	-10
^{13}C-DBAA	4.85	217.8	173.9	15	-5	-12	-40	-10
^{13}C-TCAA	6.00	117.9	35.0	15	-5	-3	-20	-15
^{13}C-TCAA	6.00	119.9	37.0	15	0	-3	-20	-10
^{13}C-BDCAA	6.18	161.9	78.9	15	-10	-3	-15	-10
^{13}C-BDCAA	6.18	163.9	80.9	15	-20	-3	-20	-15
^{13}C-DBCAA	6.34	207.8	78.9	15	-5	-12	-20	-10
^{13}C-DBCAA	6.34	209.8	80.9	15	-5	-12	-20	-10
^{13}C-TBAA	6.50	253.8	80.9	15	-20	-6	-20	-10
^{13}C-TBAA	6.50	251.8	78.9	15	-10	-6	-25	-10
2,3-DBPA‡	5.76	80.9	80.9	15	-30	-6	-10	-10
2,3-DBPA‡	5.76	78.9	78.9	15	-30	-6	-10	-10

[a] Mass to charge ratio of precursor ion [b] Mass to charge ratio of product ion [c] Dwell time [d] Declustering Potential [e] Entrance Potential [f] Collision Energy [g] Collision cell Exit Potential ‡ Internal Standard (IS)

1.5 THM Analysis by GC-ECD

THM analysis followed the published US EPA Method 551.1 Revision 1.0[4] using an HP/Agilent (Santa-Clara, CA, USA) 6890 GC-ECD. The instrument was controlled and quantitation performed with OpenLab CDS ChemStation version C.01.07 SR4 software.

1.5.1 Sample Preparation

Samples were buffered at pH 5 with phosphate buffer prior to liquid-liquid extraction with methyl tert-butyl ether (MTBE) extraction solvent and internal standard 4-bromofluorobenzene (4-BFB). Where necessary, samples were diluted into the range of the method with MTBE containing internal standard prior to re-analysis.

1.5.2 Gas Chromatography Conditions

The injection volume was 1 µL and the injector was run in split mode at 200°C 13 psi with split ratio 10:1. The initial oven temperature was 35°C with hold time of 22 min followed by ramp at 10°C/min to 145°C then hold for 2 mins before ramping at 20°C/min to 225°C then hold time of 5 min followed by ramp at 10°C/min to 260°C

then hold for 5 mins before returning to 40°C for post run time of 5 min. The column used was a Restek Rtx-1 30 m, 250 µm diameter, 1 µm thickness. The carrier gas was helium with an initial pressure of 13 psi and flow of 1.2 ml/min.

1.5.3 Electron-Capture Detection Conditions

The ECD was operated at temperature 290°C with nitrogen at 30 ml/min.

2 Results

2.1 Results from Chlorination of Aliphatic Carbonyls

Table S4 Results from chlorination of aliphatic carbonyls at 15 µM

	THM Results at 15 µM							HAA Results at 15 µM					
Compound	**Chloroform**	**BDCM**	**DBCM**	**Bromoform**	**MCAA**	**MBAA**	**DCAA**	**BCAA**	**DBAA**	**TCAA**	**BDCAA**	**DBCAA**	**TBAA**
Units	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l
3-Hydroxybutanoic acid	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~
Methyl acetate	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~
3-Aminobutanoic acid	~~0.1~~	~~0.2~~	~~0.3~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~
Acetone	~~0.3~~	1.3	2.3	~~0.4~~	~~0.3~~	~~0.3~~	0.5	0.6	0.9	~~0.2~~	~~0.3~~	~~0.4~~	~~0.2~~
Acetylacetone	299.2	206.8	26.1	0.7	48.6	3.9	75.4	29.4	0.9	1.0	~~0.2~~	~~0.0~~	~~0.0~~
2,6-Dimethyl-3,5-heptanedione	810.6	222.5	14.3	~~0.3~~	~~0.0~~	~~0.0~~	1.7	~~0.1~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~
Malonamic acid	~~0.0~~	~~0.0~~	~~0.1~~	~~0.1~~	~~0.2~~	~~0.0~~	327.1	208.6	33.0	4.9	1.1	~~0.0~~	~~0.0~~
Malonic acid	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	0.7	~~0.1~~	950.0	595.3	55.9	3.3	1.0	~~0.3~~	~~0.0~~
Methyl malonate	~~0.0~~	~~0.2~~	~~0.2~~	~~0.1~~	~~0.4~~	~~0.1~~	329.3	113.9	19.3	0.6	~~0.4~~	~~0.2~~	~~0.0~~
Diethyl malonate-2-13C	~~0.4~~	~~0.1~~	~~0.1~~	~~0.0~~	~~0.1~~	~~0.2~~	1219.9	81.2	2.3	1.4	0.6	~~0.1~~	~~0.0~~
Diethyl malonate	~~0.1~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.1~~	1480.9	96.7	1.1	2.2	~~0.5~~	~~0.2~~	~~0.0~~
Dimethyl malonate	~~0.0~~	~~0.1~~	~~0.0~~	~~0.0~~	~~0.1~~	~~0.0~~	1641.7	193.5	4.1	1.9	~~0.3~~	~~0.0~~	~~0.0~~
3-oxobutanoic acid	246.5	327.8	45.5	0.7	43.3	0.8	135.3	6.6	~~0.0~~	0.8	~~0.1~~	~~0.0~~	~~0.0~~
3-oxohexanedioic acid	1336.4	518.7	105.3	3.6	~~0.1~~	~~0.0~~	32.0	6.8	~~0.1~~	3.5	~~0.1~~	~~0.0~~	~~0.0~~
3-oxopentanedioic acid	1110.7	345.8	61.4	3.5	103.9	0.9	1749.0	239.0	13.9	9.1	1.1	~~0.1~~	~~0.0~~
t-Butyl acetoacetate	22.2	15.1	2.3	~~0.1~~	11.0	2.3	1611.2	257.7	7.4	2.7	0.6	~~0.2~~	~~0.0~~
Ethyl acetoacetate	~~0.4~~	~~0.3~~	~~0.1~~	~~0.0~~	1.8	0.6	1656.7	337.2	9.8	2.6	0.6	~~0.2~~	~~0.0~~
Methyl acetoacetate	~~0.4~~	0.5	~~0.1~~	~~0.0~~	1.4	0.6	1699.4	370.8	13.4	2.1	~~0.5~~	~~0.2~~	~~0.0~~
Methyl 3,5-dioxohexanoate	281.6	50.5	9.7	0.8	26.9	2.6	1653.4	302.5	13.7	66.2	22.8	4.2	~~0.2~~
Dimethyl 3-oxopentanedioate	~~0.4~~	~~0.0~~	~~0.0~~	~~0.1~~	0.7	~~0.0~~	3111.7	746.2	34.6	7.0	3.6	~~0.2~~	~~0.0~~
Methyl bromoacetate	~~0.1~~	~~0.2~~	~~0.3~~	~~0.4~~	~~0.1~~	666.8	~~0.0~~	~~0.1~~	6.4	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~
Diethyl bromomalonate	~~0.0~~	~~0.0~~	~~0.0~~	0.8	~~0.4~~	~~0.1~~	8.4	904.8	22.2	~~0.0~~	1.1	~~0.1~~	15.3
Ethyl malonate chloride	0.7	0.8	0.9	~~0.4~~	~~0.3~~	~~0.0~~	1664.2	136.5	2.0	3.5	1.5	0.6	~~0.1~~
Ethyl 4-bromooacetoacetate	3.9	174.8	166.2	18.0	7.6	1087.2	785.5	575.3	144.0	2.5	8.8	9.5	2.9
Ethyl 4-chloroacetoacetate	14.7	7.6	1.4	~~0.0~~	1475.4	~~0.2~~	1688.4	478.9	17.8	5.2	1.4	~~0.1~~	~~0.0~~
Ethyl-4,4,4-trichloroacetoacetate	899.1	71.3	~~0.3~~	~~0.0~~	7.3	~~0.1~~	279.3	468.0	26.8	1289.5	83.1	~~0.2~~	~~0.0~~
Hexachloroacetone	1795.5	~~0.2~~	~~0.0~~	~~0.0~~	~~0.1~~	~~0.0~~	7.7	~~0.3~~	~~0.3~~	2561.6	~~0.1~~	~~0.2~~	~~0.1~~

Table S5 Results from chlorination of aliphatic carbonyls at 1.5 µM

	THM Results at 1.5 µM						HAA Results at 1.5 µM						
Compound	**Chloroform**	**BDCM**	**DBCM**	**Bromoform**	**MCAA**	**MBAA**	**DCAA**	**BCAA**	**DBAA**	**TCAA**	**BDCAA**	**DBCAA**	**TBAA**
Units	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l
3-Hydroxybutanoic acid	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.1~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~
Methyl acetate	~~0.0~~	~~0.0~~	~~0.0~~	~~0.1~~	~~0.1~~	~~0.0~~	~~0.1~~	~~0.2~~	0.9	~~0.1~~	~~0.1~~	~~0.1~~	~~0.2~~
3-Aminobutanoic acid	~~0.0~~	~~0.0~~	~~0.2~~	~~0.4~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~
Acetone	~~0.0~~	~~0.0~~	~~0.3~~	0.8	~~0.0~~	~~0.3~~	~~0.0~~	~~0.1~~	1.0	~~0.0~~	~~0.0~~	~~0.1~~	~~0.2~~
Acetylacetone	9.7	34.7	38.8	8.2	1.8	3.7	~~0.3~~	2.1	1.8	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~
2,6-Dimethyl-3,5-heptanedione	21.1	62.0	42.9	7.4	~~0.0~~	~~0.0~~	~~0.1~~	~~0.1~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~
Malonamic acid	~~0.1~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	0.7	9.5	32.3	~~0.0~~	~~0.0~~	~~0.1~~	~~0.0~~
Malonic acid	~~0.5~~	~~0.0~~	~~0.1~~	~~0.2~~	~~0.1~~	~~0.3~~	4.0	62.3	204.3	~~0.0~~	~~0.0~~	~~0.1~~	~~0.2~~
Methyl malonate	~~0.1~~	~~0.0~~	~~0.0~~	~~0.1~~	~~0.0~~	~~0.1~~	7.3	22.4	22.8	~~0.1~~	~~0.0~~	~~0.1~~	~~0.1~~
Diethyl malonate-2-13C	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.1~~	~~0.0~~	41.0	39.4	7.5	~~0.0~~	~~0.0~~	~~0.1~~	~~0.1~~
Diethyl malonate	~~0.1~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.1~~	38.0	30.6	7.9	~~0.1~~	~~0.0~~	~~0.1~~	~~0.1~~
Dimethyl malonate	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.1~~	70.9	115.7	39.3	~~0.1~~	~~0.0~~	~~0.1~~	~~0.1~~
3-oxobutanoic acid	~~0.2~~	10.7	147.6	86.4	2.9	3.4	~~0.5~~	1.9	2.4	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~
3-oxohexanedioic acid	2.0	14.3	116.9	166.0	~~0.1~~	~~0.0~~	0.6	1.1	1.0	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~
3-oxopentanedioic acid	1.5	17.8	97.9	123.5	13.2	11.7	8.6	49.1	85.7	~~0.0~~	~~0.1~~	~~0.2~~	~~0.1~~
t-Butyl acetoacetate	~~0.4~~	4.2	10.2	5.7	~~0.5~~	1.1	67.3	108.3	47.6	~~0.1~~	~~0.0~~	~~0.1~~	~~0.1~~
Ethyl acetoacetate	~~0.0~~	~~0.0~~	~~0.1~~	~~0.1~~	~~0.1~~	~~0.4~~	81.2	107.3	29.6	~~0.0~~	~~0.0~~	~~0.0~~	~~0.1~~
Methyl acetoacetate	~~0.1~~	~~0.1~~	~~0.2~~	~~0.2~~	~~0.1~~	~~0.3~~	86.0	104.7	29.6	~~0.0~~	~~0.0~~	~~0.0~~	~~0.1~~
Methyl 3,5-dioxohexanoate	11.8	17.2	11.8	6.6	1.0	2.6	81.0	77.8	20.4	4.1	4.4	2.4	1.3
Dimethyl 3-oxopentanedioate	~~0.1~~	~~0.1~~	~~0.0~~	~~0.2~~	~~0.2~~	~~0.0~~	231.5	153.7	51.0	~~0.1~~	0.6	~~0.3~~	~~0.4~~
Methyl bromoacetate	~~0.1~~	~~0.0~~	~~0.1~~	~~0.1~~	~~0.0~~	58.1	~~0.0~~	~~0.0~~	0.6	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~
Diethyl bromomalonate	~~0.0~~	~~0.0~~	~~0.0~~	~~0.1~~	~~0.0~~	~~0.0~~	~~0.4~~	39.6	9.9	~~0.0~~	~~0.0~~	~~0.0~~	1.6
Ethyl malonate chloride	~~0.0~~	~~0.0~~	~~0.1~~	~~0.1~~	~~0.1~~	~~0.0~~	66.4	72.5	12.4	~~0.0~~	~~0.1~~	~~0.1~~	~~0.0~~
Ethyl 4-bromooacetoacetate	~~0.0~~	2.1	18.0	26.9	~~0.4~~	102.5	40.6	62.5	31.3	~~0.0~~	~~0.1~~	~~0.4~~	0.6
Ethyl 4-chloroacetoacetate	~~0.1~~	0.6	1.5	1.1	133.5	~~0.2~~	88.4	98.0	24.7	~~0.0~~	~~0.1~~	~~0.1~~	~~0.0~~
Ethyl-4,4,4-trichloroacetoacetate	96.8	62.2	0.8	~~0.1~~	~~0.5~~	~~0.0~~	2.3	23.6	3.5	38.5	13.3	~~0.0~~	~~0.0~~
Hexachloroacetone	192.0	~~0.0~~	~~0.0~~	~~0.0~~	~~0.0~~	~~0.1~~	0.8	~~0.1~~	~~0.3~~	228.1	~~0.0~~	~~0.1~~	~~0.1~~

Note: where results are less than the reporting limit of the method they are given for information only and are crossed through

Table S6 Calculated results from chlorination of aliphatic carbonyls at 15 µM

	THM				HAA				DBP			
Compound	**THMFP**	**THM BIF**	**MXAA**	**DXAA**	**TXAA**	**HAAFP**	**HAA BIF**	**DBPFP**	**DBPFP**	**CUF**	**BIF**	**BUF**
Units	µM/mM		%	%	%	µM/mM		µM/mM	µg/mg C			
3-Hydroxybutanoic acid	0.0					0.0		0.0	0.0	0.0		0.0
Methyl acetate	0.0					0.0		0.0	0.1	0.0		0.0
3-Aminobutanoic acid	0.2					0.0		0.3	0.9	0.0		0.0
Acetone	1.5	1.5				1.4		3.0	14.7	0.0	1.2	0.0
Acetylacetone	259.8	0.4	41.4	58.0	0.6	87.2	0.2	347.0	769.3	0.1	0.3	0.3
2,6-Dimethyl-3,5-heptanedione	547.9	0.2	0.0	100.0	0.0	0.9		548.8	647.8	0.1	0.2	0.3
Malonamic acid	0.1		0.0	99.1	0.9	261.9	0.4	262.0	1064.9	0.2	0.4	0.3
Malonic acid	0.0		0.1	99.7	0.2	739.6	0.4	739.7	2975.4	0.5	0.4	0.8
Methyl malonate	0.2		0.2	99.6	0.2	220.8	0.3	221.0	645.6	0.1	0.3	0.2
Diethyl malonate-2-13C	0.3		0.0	99.9	0.1	663.8	0.0	664.1	1036.8	0.2	0.0	0.1
Diethyl malonate	0.1		0.0	99.9	0.1	804.6	0.0	804.7	1255.5	0.2	0.0	0.1
Dimethyl malonate	0.0		0.0	99.9	0.1	925.7	0.1	925.7	2046.4	0.4	0.1	0.2
3-oxobutanoic acid	285.8	0.6	29.8	69.9	0.4	103.8	0.0	389.5	1121.1	0.1	0.4	0.5
3-oxohexanedioic acid	992.1	0.3	0.3	92.6	7.1	20.7	0.1	1012.8	1858.1	0.2	0.3	0.9
3-oxopentanedioic acid	781.6	0.2	6.8	92.8	0.4	1078.6	0.1	1860.2	4042.9	0.6	0.2	0.9
t-Butyl acetoacetate	19.3	0.4	0.9	98.9	0.1	944.9	0.1	964.1	1342.2	0.2	0.1	0.3
Ethyl acetoacetate	0.4		0.2	99.7	0.1	992.3	0.1	992.7	1861.4	0.3	0.1	0.4
Methyl acetoacetate	0.5		0.1	99.8	0.1	1027.9	0.1	1028.4	2321.5	0.4	0.1	0.5
Methyl 3,5-dioxohexanoate	181.2	0.2	2.0	94.6	3.4	1031.3	0.1	1212.5	1932.6	0.3	0.1	0.5
Dimethyl 3-oxopentanedioate	0.2		0.0	99.8	0.2	1911.4	0.2	1911.6	3098.7	0.5	0.2	0.9
Methyl bromoacetate	0.3		99.4	0.6	0.0	322.1	1.0	322.4	1248.8	0.2	1.0	1.0
Diethyl bromomalonate	0.2		0.1	98.9	1.1	363.2	1.0	363.4	756.6	0.1	1.0	1.1
Ethyl malonate chloride	1.1	1.1	0.0	99.8	0.2	916.0	0.1	917.2	2012.6	0.4	0.1	0.2
Ethyl 4-bromooacetoacetate	131.3	1.5	43.7	55.7	0.6	1205.7	0.7	1337.0	2765.1	0.4	0.8	3.1
Ethyl 4-chloroacetoacetate	11.7	0.3	49.4	50.5	0.1	2106.3	0.1	2118.1	3417.7	0.7	0.1	0.6
Ethyl-4,4,4-trichloroacetoacetate	531.2	0.1	0.6	37.3	62.1	890.6	0.3	1421.8	2893.6	0.4	0.2	0.8
Hexachloroacetone	1002.7	0.0	0.0	0.4	99.6	1049.5	0.0	2052.2	8085.1	1.0	0.0	0.0

FP – formation potential; MXAA/DXAA/TXAA – mono-, di-, tri-halogenated HAAs; BIF – bromide incorporation factor (moles of bromine per mole of DBP formed, 0-3); CUF/BUF – carbon/bromide utilisation factor (proportion of carbon/bromide available which is incorporated into measured DBPs, 0-1)

Table S7 Calculated results from chlorination of aliphatic carbonyls at 1.5 µM

	THM				HAA				DBP			
Compound	**THMFP**	**THM BIF**	**MXAA**	**DXAA**	**TXAA**	**HAAFP**	**HAA BIF**	**DBPFP**	**DBPFP**	**CUF**	**BIF**	**BUF**
Units	µM/mM		%	%	%	µM/mM		µM/mM	µg/mg C			
3-Hydroxybutanoic acid	0.0					0.7		0.7	1.8	0.0		0.0
Methyl acetate	0.7					6.3		7.0	37.3	0.0		0.0
3-Aminobutanoic acid	1.7					0.3		2.0	9.0	0.0		0.0
Acetone	3.3					5.8		9.2	54.1	0.0		0.0
Acetylacetone	341.5	1.3	66.2	33.6	0.2	45.6	0.8	387.1	1124.1	0.1	1.3	0.1
2,6-Dimethyl-3,5-heptanedione	527.1	1.1				0.8		527.9	824.7	0.1	1.1	0.2
Malonamic acid	0.7		0.0	99.7	0.3	139.6	1.7	140.3	792.8	0.1	1.7	0.1
Malonic acid	3.5		0.2	99.7	0.1	888.7	1.7	892.2	5040.4	0.6	1.7	0.4
Methyl malonate	0.9		0.5	99.2	0.3	195.3	1.2	196.1	738.3	0.1	1.2	0.1
Diethyl malonate-2-13C	0.2		0.3	99.6	0.2	388.2	0.5	388.4	701.1	0.1	0.5	0.1
Diethyl malonate	0.5		0.2	99.7	0.2	339.5	0.5	340.0	610.3	0.1	0.5	0.1
Dimethyl malonate	0.0		0.1	99.9	0.1	932.9	0.7	932.9	2513.2	0.4	0.7	0.2
3-oxobutanoic acid	744.8	2.2	68.4	31.6	0.0	53.3	0.7	798.1	3552.7	0.2	2.1	0.5
3-oxohexanedioic acid	881.4	2.4				11.0		892.4	2796.0	0.2	2.4	0.6
3-oxopentanedioic acid	719.7	2.3	23.1	76.7	0.2	646.0	1.2	1365.7	4548.3	0.4	1.8	0.7
t-Butyl acetoacetate	67.1	1.9	1.0	99.0	0.1	919.4	0.8	986.6	1705.0	0.2	0.9	0.3
Ethyl acetoacetate	0.5		0.3	99.7	0.0	925.5	0.6	926.0	2025.9	0.3	0.6	0.2
Methyl acetoacetate	1.7		0.2	99.7	0.0	940.0	0.6	941.7	2458.4	0.4	0.6	0.2
Methyl 3,5-dioxohexanoate	191.3	1.0	2.3	92.9	4.8	839.9	0.6	1031.2	1924.0	0.3	0.6	0.2
Dimethyl 3-oxopentanedioate	1.0		0.1	99.7	0.2	1950.0	0.5	1951.0	3477.4	0.6	0.5	0.3
Methyl bromoacetate	1.1		99.4	0.6	0.0	280.7	1.0	281.8	1092.4	0.2	1.0	0.1
Diethyl bromomalonate	0.5		0.2	97.9	2.0	188.4	1.2	188.9	410.5	0.1	1.2	0.1
Ethyl malonate chloride	0.9		0.1	99.8	0.1	661.7	0.5	662.6	1688.3	0.3	0.5	0.1
Ethyl 4-bromooacetoacetate	137.3	2.5	47.4	52.3	0.3	1042.9	0.9	1180.2	2641.7	0.4	1.1	0.2
Ethyl 4-chloroacetoacetate	10.6	1.9	50.9	49.1	0.0	1852.4	0.3	1862.9	3223.2	0.6	0.3	0.1
Ethyl-4,4,4-trichloroacetoacetate	796.2	0.3	1.2	35.8	63.1	316.7	0.5	1113.0	2236.8	0.2	0.4	0.1
Hexachloroacetone	1072.4	0.0	0.1	0.6	99.3	937.1	0.0	2009.5	7808.4	1.0	0.0	0.0

Note: Where results are less than the reporting limit of the method then proportional or relative calculated results are not given

2.2 Results from Three Targeted Compounds with Changing Concentrations

Table S8 Results from malonic acid at varying concentrations

		THM Results				HAA Results								
Concentration Bromide	**Concentration Compound**	**Chloroform**	**BDCM**	**DBCM**	**Bromoform**	**MCAA**	**MBAA**	**DCAA**	**BCAA**	**DBAA**	**TCAA**	**BDCAA**	**DBCAA**	**TBAA**
µM	µM	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l
0	2	0.54	~~0.08~~	~~0.12~~	~~0.09~~	~~0.19~~	~~0.00~~	68.78	~~0.11~~	~~0.02~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~
1.25	2	~~0.50~~	~~0.11~~	~~0.17~~	~~0.14~~	~~0.00~~	~~0.00~~	42.91	55.01	14.92	~~0.00~~	~~0.04~~	~~0.02~~	~~0.00~~
2.5	2	~~0.00~~	~~0.04~~	~~0.07~~	~~0.01~~	~~0.00~~	~~0.04~~	25.39	125.79	80.17	~~0.00~~	~~0.11~~	~~0.12~~	~~0.00~~
3.75	2	~~0.00~~	~~0.04~~	~~0.08~~	~~0.06~~	~~0.00~~	~~0.09~~	17.69	128.65	142.63	~~0.00~~	~~0.12~~	~~0.26~~	~~0.07~~
5	2	~~0.00~~	~~0.00~~	~~0.00~~	~~0.04~~	~~0.00~~	~~0.00~~	8.05	106.62	192.01	~~0.02~~	~~0.07~~	~~0.23~~	~~0.13~~
6.25	2	~~0.01~~	~~0.03~~	~~0.08~~	~~0.07~~	~~0.00~~	~~0.13~~	7.46	100.38	255.32	~~0.00~~	~~0.06~~	~~0.34~~	~~0.27~~
7.5	2	~~0.01~~	~~0.03~~	~~0.07~~	~~0.18~~	~~0.00~~	~~0.13~~	4.21	87.66	291.92	~~0.00~~	~~0.03~~	~~0.33~~	~~0.46~~
8.75	2	0.50	~~0.11~~	~~0.19~~	~~0.40~~	~~0.00~~	~~0.13~~	2.79	71.69	315.06	~~0.00~~	~~0.02~~	~~0.41~~	0.57
10	2	~~0.02~~	~~0.03~~	~~0.07~~	~~0.27~~	~~0.00~~	~~0.12~~	1.89	59.48	322.23	~~0.00~~	~~0.02~~	~~0.46~~	0.78
5	0	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.02~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~
5	1	~~0.00~~	~~0.00~~	~~0.00~~	~~0.13~~	~~0.00~~	~~0.00~~	0.63	15.60	66.25	~~0.01~~	~~0.00~~	~~0.04~~	~~0.09~~
5	2	~~0.00~~	~~0.00~~	~~0.00~~	~~0.04~~	~~0.00~~	~~0.00~~	8.05	106.62	192.01	~~0.02~~	~~0.07~~	~~0.23~~	~~0.13~~
5	3	~~0.00~~	~~0.00~~	~~0.01~~	~~0.03~~	~~0.11~~	~~0.19~~	53.93	199.16	208.81	~~0.05~~	~~0.25~~	~~0.42~~	~~0.14~~
5	4	~~0.00~~	~~0.00~~	~~0.01~~	~~0.00~~	~~0.07~~	~~0.16~~	117.55	279.46	202.31	~~0.10~~	~~0.46~~	0.57	~~0.12~~
5	5	~~0.01~~	~~0.00~~	~~0.02~~	~~0.00~~	~~0.12~~	~~0.16~~	194.36	338.61	183.47	~~0.20~~	0.77	0.68	~~0.09~~
5	6	~~0.03~~	~~0.01~~	~~0.03~~	~~0.00~~	~~0.13~~	~~0.15~~	286.85	372.32	183.62	~~0.22~~	0.77	0.56	~~0.06~~
5	7	~~0.05~~	~~0.01~~	~~0.04~~	~~0.00~~	~~0.15~~	~~0.16~~	381.08	405.25	161.98	~~0.35~~	0.96	0.58	~~0.05~~
5	8	~~0.09~~	~~0.02~~	~~0.05~~	~~0.00~~	~~0.18~~	~~0.16~~	506.25	446.80	152.89	~~0.48~~	1.26	0.64	~~0.04~~

Table S9 Results from 3-oxobutanoic acid at varying concentrations

		THM Results				HAA Results								
Concentration Bromide	**Concentration Compound**	**Chloroform**	**BDCM**	**DBCM**	**Bromoform**	**MCAA**	**MBAA**	**DCAA**	**BCAA**	**DBAA**	**TCAA**	**BDCAA**	**DBCAA**	**TBAA**
µM	µM	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l
0	2	39.49	~~0.16~~	~~0.00~~	~~0.00~~	2.66	~~0.00~~	13.24	~~0.02~~	~~0.06~~	~~0.19~~	~~0.00~~	~~0.00~~	~~0.00~~
1.25	2	18.20	62.75	19.37	0.53	5.86	~~0.21~~	8.44	1.45	~~0.19~~	~~0.07~~	~~0.00~~	~~0.00~~	~~0.00~~
2.5	2	6.57	76.90	89.12	7.33	7.08	0.80	4.93	2.83	0.62	~~0.04~~	~~0.00~~	~~0.03~~	~~0.00~~
3.75	2	2.65	60.92	165.26	26.92	6.75	1.91	2.57	3.56	1.33	~~0.01~~	~~0.00~~	~~0.04~~	~~0.00~~
5	2	1.20	47.04	225.33	60.22	5.73	3.04	1.62	3.47	1.94	~~0.04~~	~~0.00~~	~~0.03~~	~~0.00~~
6.25	2	0.60	31.27	232.12	98.35	4.38	3.81	0.77	2.97	2.63	~~0.02~~	~~0.00~~	~~0.05~~	~~0.02~~
7.5	2	~~0.35~~	22.45	226.40	137.35	3.62	4.56	0.51	2.43	2.96	~~0.00~~	~~0.00~~	~~0.05~~	~~0.03~~
8.75	2	~~0.17~~	14.56	209.57	177.40	2.72	4.94	~~0.33~~	1.87	3.24	~~0.01~~	~~0.00~~	~~0.04~~	~~0.05~~
10	2	~~0.13~~	11.22	199.90	218.60	2.15	5.19	~~0.22~~	1.65	3.52	~~0.00~~	~~0.00~~	~~0.04~~	~~0.07~~
5	0	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.04~~	~~0.00~~	~~0.00~~	~~0.00~~
5	1	~~0.02~~	4.72	89.00	105.84	1.15	2.95	~~0.15~~	0.98	2.29	~~0.03~~	~~0.00~~	~~0.03~~	~~0.03~~
5	2	1.20	47.04	225.33	60.22	5.73	3.04	1.62	3.47	1.94	~~0.04~~	~~0.00~~	~~0.03~~	~~0.00~~
5	3	5.92	124.72	258.49	30.99	11.74	2.25	5.04	5.55	1.45	~~0.07~~	~~0.01~~	~~0.04~~	~~0.00~~
5	4	16.04	208.26	219.15	15.42	17.31	1.50	11.95	6.06	0.94	~~0.09~~	~~0.02~~	~~0.05~~	~~0.00~~
5	5	28.94	273.18	177.32	8.97	22.39	1.13	20.57	6.34	0.72	~~0.15~~	~~0.03~~	~~0.05~~	~~0.00~~
5	6	46.97	319.29	144.80	5.97	26.59	0.92	31.28	6.33	0.59	~~0.23~~	~~0.05~~	~~0.05~~	~~0.00~~
5	7	69.98	356.68	119.64	4.11	29.90	0.83	41.58	6.87	0.54	~~0.33~~	~~0.06~~	~~0.05~~	~~0.00~~
5	8	97.54	343.64	100.83	3.08	33.05	0.75	54.14	7.34	0.51	~~0.45~~	~~0.09~~	~~0.05~~	~~0.00~~

Table S10 Results from 3-oxopentanedioic acid at varying concentrations

		THM Results				HAA Results								
Concentration Bromide	**Concentration Compound**	**Chloroform**	**BDCM**	**DBCM**	**Bromoform**	**MCAA**	**MBAA**	**DCAA**	**BCAA**	**DBAA**	**TCAA**	**BDCAA**	**DBCAA**	**TBAA**
µM	µM	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l	µg/l
0	2	192.88	~~0.27~~	~~0.00~~	~~0.02~~	11.61	~~0.00~~	180.44	~~0.29~~	~~0.00~~	0.84	~~0.00~~	~~0.00~~	~~0.00~~
1.25	2	87.55	72.95	22.63	~~0.32~~	20.02	0.77	112.86	45.18	5.94	~~0.47~~	~~0.17~~	~~0.00~~	~~0.00~~
2.5	2	42.79	89.29	72.68	15.65	25.12	2.45	58.75	66.17	24.24	~~0.27~~	~~0.19~~	~~0.02~~	~~0.00~~
3.75	2	18.90	78.05	124.79	49.99	25.39	5.12	32.72	75.68	53.10	~~0.16~~	~~0.20~~	~~0.09~~	~~0.00~~
5	2	7.33	53.66	157.50	107.74	25.45	10.11	18.60	73.91	81.96	~~0.07~~	~~0.18~~	~~0.16~~	~~0.00~~
6.25	2	2.56	30.25	151.10	165.84	21.73	15.80	10.15	68.50	114.59	~~0.03~~	~~0.15~~	~~0.20~~	~~0.08~~
7.5	2	0.91	16.76	136.63	224.33	18.67	21.74	6.11	48.89	131.12	~~0.03~~	~~0.12~~	~~0.24~~	~~0.18~~
8.75	2	~~0.30~~	9.50	116.28	266.90	15.65	27.18	3.75	41.19	147.25	~~0.03~~	~~0.09~~	~~0.25~~	~~0.29~~
10	2	~~0.15~~	5.58	96.31	300.77	12.15	31.68	2.14	32.27	163.01	~~0.01~~	~~0.09~~	~~0.24~~	~~0.41~~
5	0	~~0.03~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~	~~0.00~~
5	1	~~0.23~~	2.69	43.71	153.98	5.12	15.03	0.98	15.51	81.39	~~0.00~~	~~0.00~~	~~0.05~~	~~0.11~~
5	2	7.33	53.66	157.50	107.74	25.45	10.11	18.60	73.91	81.96	~~0.07~~	~~0.18~~	~~0.16~~	~~0.00~~
5	3	41.87	140.31	179.96	59.19	42.74	5.74	72.02	123.76	63.02	~~0.34~~	~~0.30~~	~~0.13~~	~~0.00~~
5	4	96.93	205.12	167.67	36.86	56.05	3.87	145.71	148.02	48.67	0.91	~~0.46~~	~~0.13~~	~~0.00~~
5	5	159.70	227.77	156.25	26.05	60.73	3.24	222.48	160.86	40.00	1.29	0.59	~~0.14~~	~~0.00~~
5	6	274.15	259.51	141.73	18.51	66.43	2.36	316.20	180.43	35.81	1.73	0.63	~~0.10~~	~~0.00~~
5	7	377.43	290.08	129.09	14.13	71.75	2.07	405.09	188.38	30.40	2.47	0.75	~~0.11~~	~~0.00~~
5	8	484.21	329.12	110.89	10.05	74.84	1.69	535.44	197.78	27.41	3.00	0.84	~~0.09~~	~~0.00~~

Note: where results are less than the reporting limit of the method they are given for information only and are crossed through

2.3 Graphical Representations of Results from Targeted Compounds

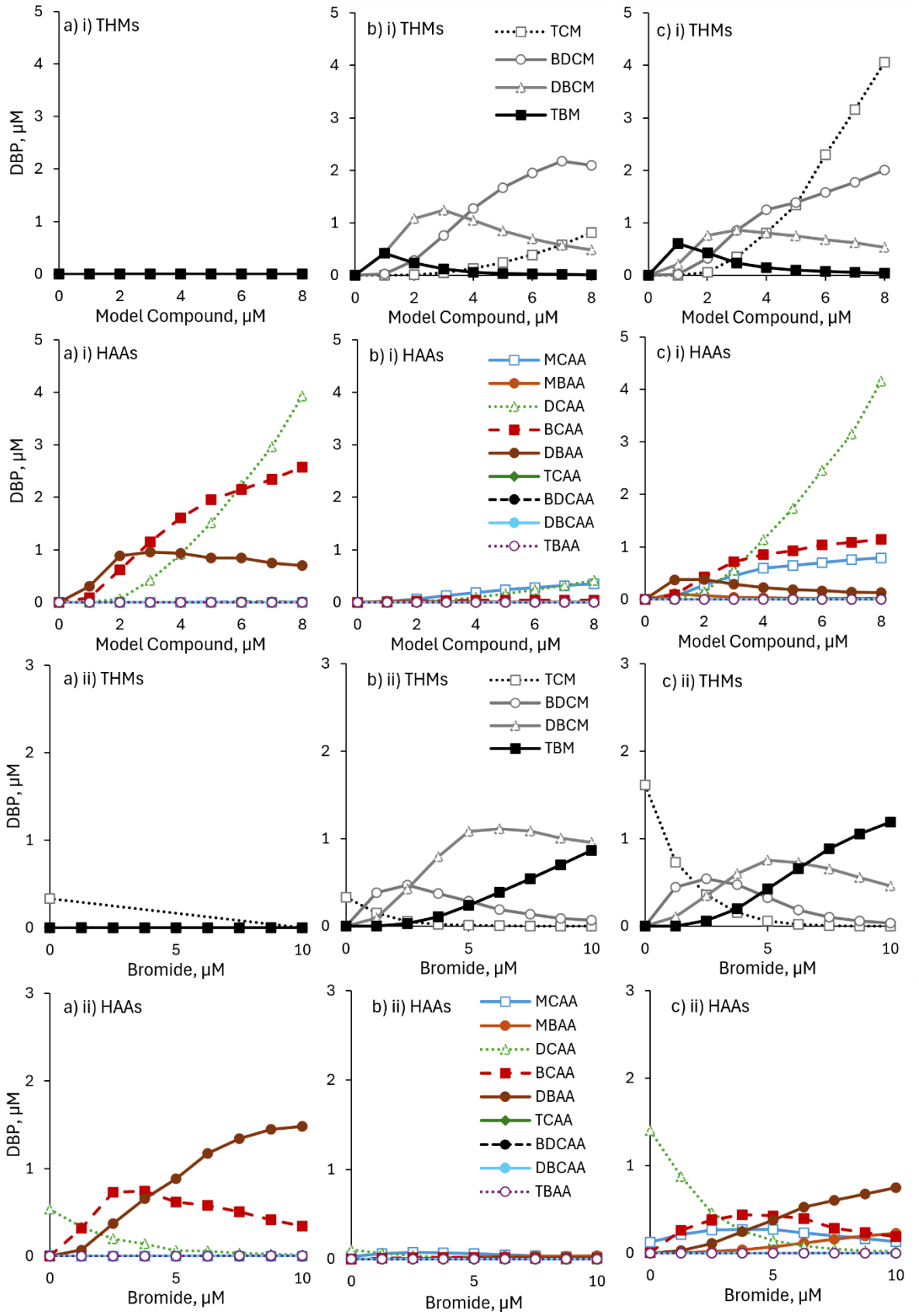


Figure S1 DBP formation patterns for a) Malonic acid b) 3-Oxobutanoic acid c) 3-Oxopentanedioic acid with changing concentration of i) model compound and ii) bromide

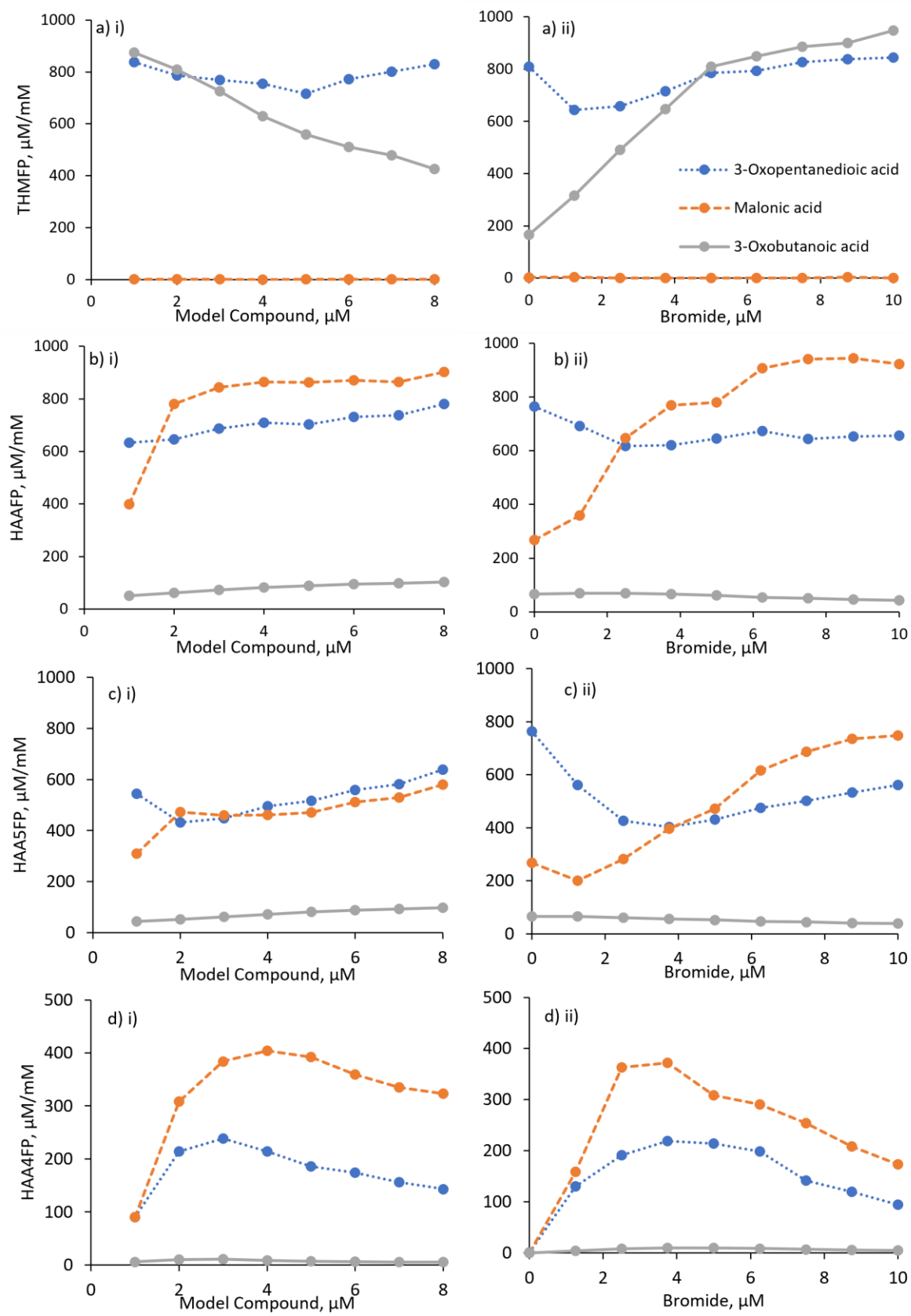


Figure S2 Results from changing concentration experiments for a) THMFP b) HAA9FP c) HAA5FP d) HAA4FP from i) changing model compound and ii) changing bromide

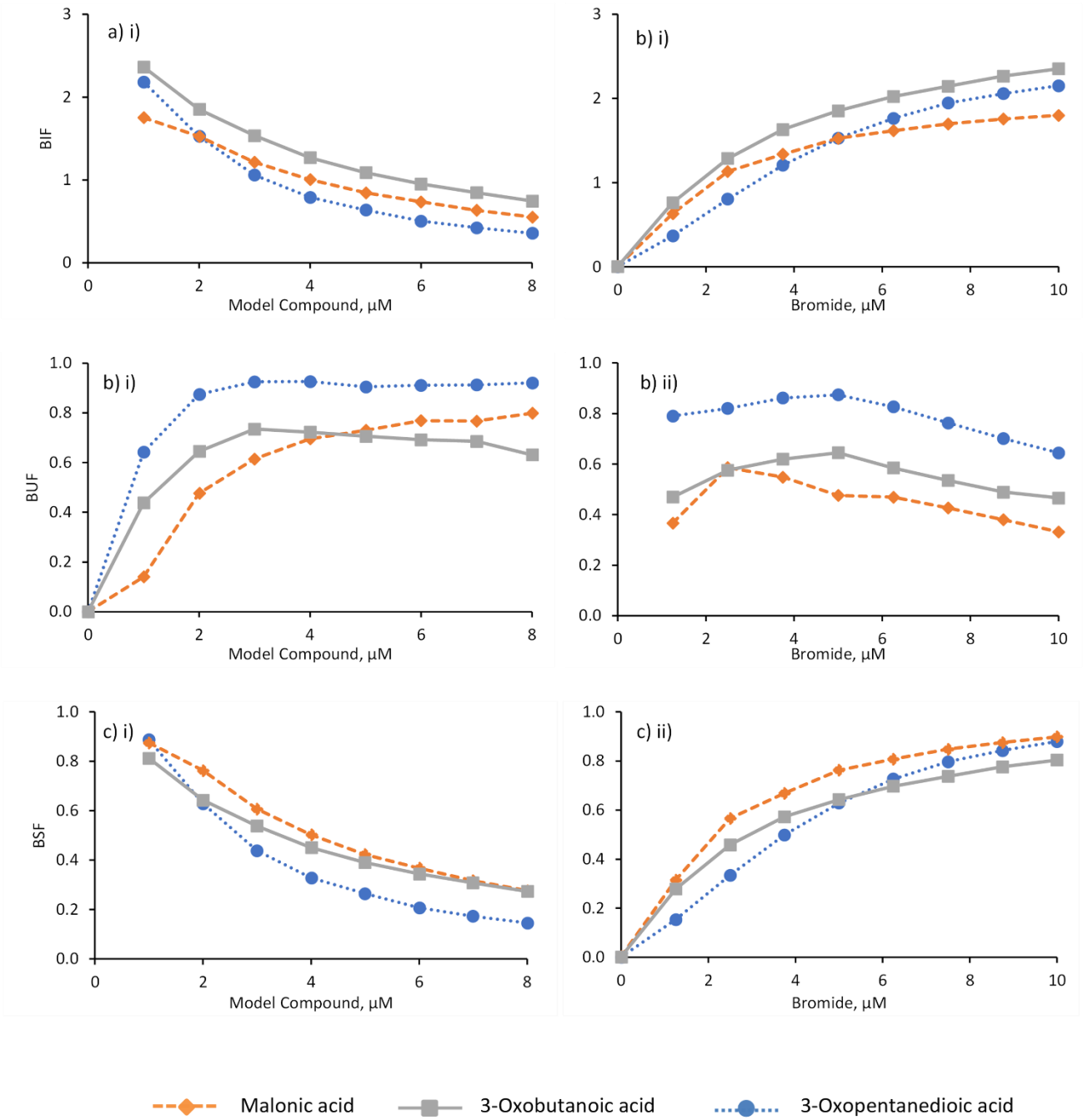


Figure S3 Bromine incorporation results from changing concentration experiments for a) BIF b) BUF c) BSF from i) changing model compound and ii) changing bromide

BIF – Bromine Incorporation Factor – moles bromide incorporated per mole DBP (0-3)

BUF – Bromide Utilisation Factor – proportion of available bromide incorporated into measured DBPs (0-1)

BSF – Bromine Substitution Factor – moles bromide incorporated per mole of halogen in DBP (0-1)

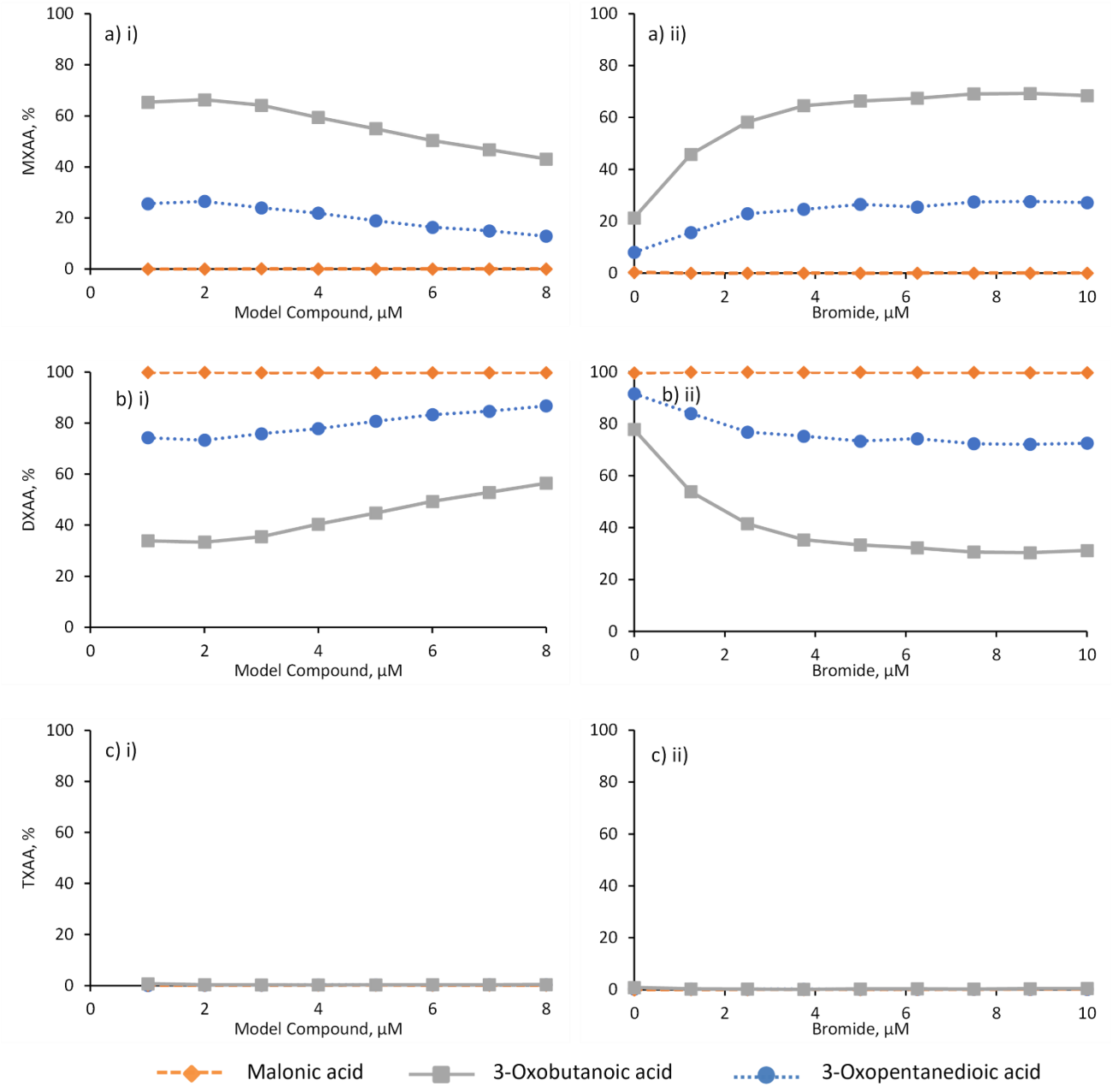


Figure S4 HAA speciation results from changing concentration experiments for a) MXAA b) DXAA c) TXAA from i) changing model compound and ii) changing bromide

3 Discussion

3.1 Background Chemistry

This work utilises existing model compound research which identified that aliphatic β-dicarbonyls form high levels of DBPs [5]. This high formation potential is proposed due to the keto-enol equilibrium which enhances the potential for electrophilic substitution at the α-carbon and subsequent cleavage to DBPs (Figure S5).

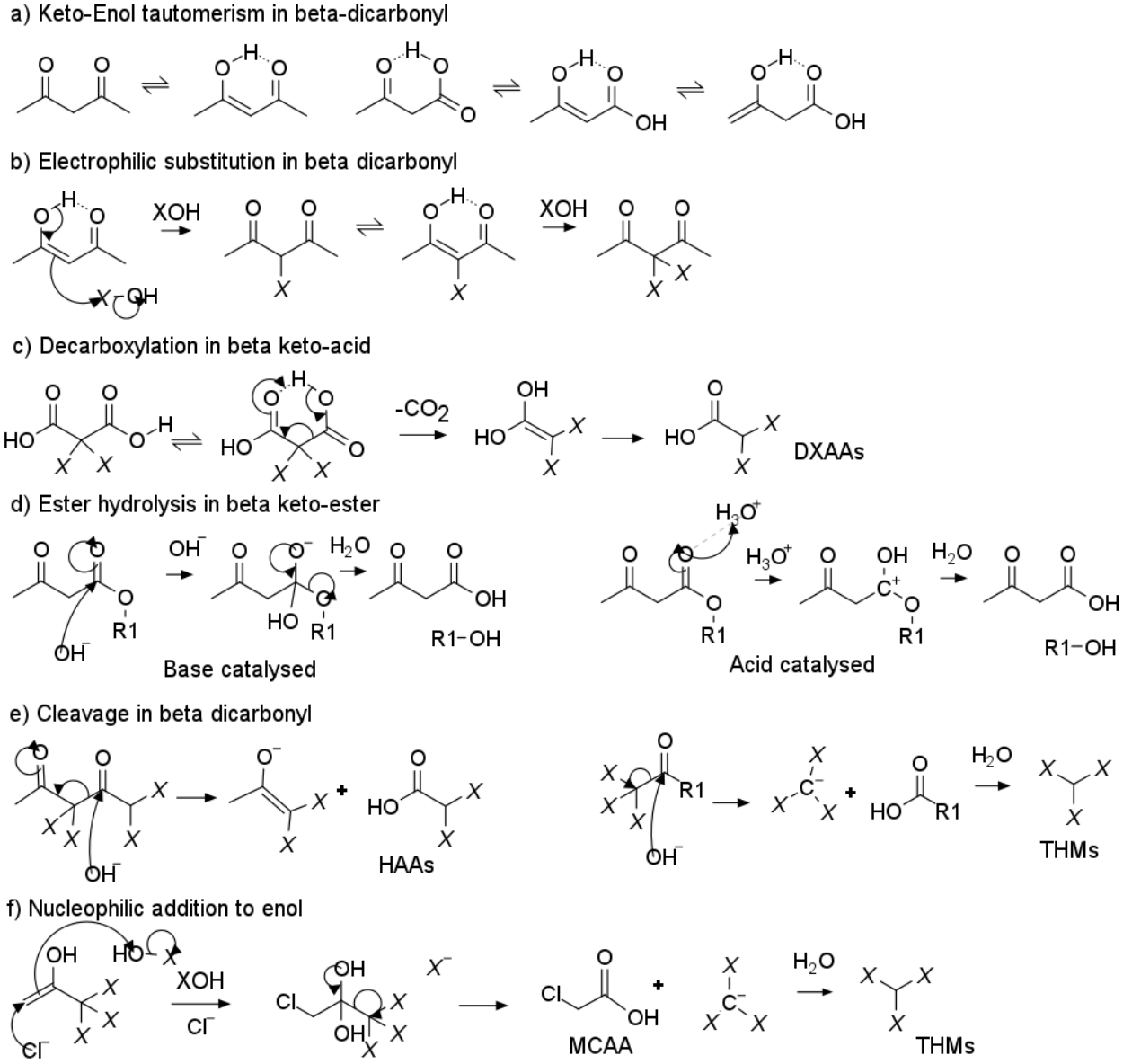


Figure S5 Proposed key pathways in DBP formation from aliphatic carbonyls with example a) keto enol tautomerism b) electrophilic substitution c) decarboxylation d) ester hydrolysis e) cleavage f) nucleophilic addition (where X = halogen)

This bromination preference is crucial for understanding the risk presented by the DBPs formed and is proposed due to several competing factors. The first of these is the very fast reaction of hypochlorous acid (HOCl) with bromide to form hypobromous acid (HOBr) (k = 1550 $M^{-1}s^{-1}$) [6]. At the pH of most water treatments (~6-8), hypochlorous acid is formed from aqueous hypochlorite, with both the hypohalous acids mainly existing in their non-dissociated forms at pH 7 (HOCl pK_a = 7.5, HOBr pK_a = 8.8). Kinetics plays a further role due to the enhanced electrophilicity of HOBr (bromine

electronegativity 2.96 is lower than chlorine 3.16), ensuring the reaction by electrophilic substitution will be faster for bromination than for chlorination [7]. For example, in aromatic compounds the ratio of bromine to chlorine species-specific rate constants of phenolic compounds is about 3000 [8]. However, as halogenation kinetics is generally observed to be first order and chlorine levels are much higher than bromide in real treatment processes, the competition between these chlorination and bromination pathways will influence the final extent of bromination. Additionally, although bromination by electrophilic substitution is generally faster, in some compounds the rate determining step will be formation of the enol and consequently the rate of the reaction between model compound and bromine will be independent of the bromide concentration [9]. The comparative reaction rate of the enol and the enolate conjugate base may also be significant for the outcome from halogenation by electrophilic substitution [10], with the equilibrium between the two being conditional on the pK_a of the model compound. Further factors proposed likely to influence the extent of bromination include steric hindrance due to the difference in size of the halides (van der Waals atomic radii 1.85 and 1.76Å for bromine and chlorine respectively [11]), so bromination being more restricted at hindered carbons or within the chain. Also, the inverse influence of the differing electronegativity of the halides has the potential to affect nucleophilic reactions, with nucleophilic addition or substitution proposed to favour chlorination, though often observed to be a minor pathway [12,13]. Note that nucleophilic reactions are expected to be a minor pathway in the reactions considered in this study due to the conditions under which it was performed and the nature of the compounds studied. At pH 7 and with a substantial level of bromide present (5 µM, 400 µg/L), the predominant forms present will be the hypochlorous acid and hypobromous acid which are stronger electrophiles, while the nucleophilic hypochlorite will be at lower levels and hypobromite at very low levels[6]. Thus stronger electrophiles will be the predominant forms present. Further, the β-dicarbonyl compounds which are the majority of this study are proposed to promote electrophilic substitution over nucleophilic addition due to their double activation of the α-carbon to electrophilic substitution by the enols formed and by the stabilisation of intermediates by hydrogen bonding between the carbonyls, which also promotes decarboxylation (Figure S5). Where nucleophilic reactions may have a minor role this would be expected to increase relative chlorine incorporation and could involve nucleophilic attack on the unsaturated bond of terminal enols (Figure S7, Figure S10).

3.2 DBP Formation Pathways

3.2.1 Example of 3-oxopentanedioic acid

The major pathway for the formation of DBPs from 3-oxopentanedioic acid is proposed to be via electrophilic substitution followed by cleavage to malonic acid and THMs, with the malonic acid decarboxylating to give DXAAs via a 6-membered hydrogen bonded intermediate (Figure S6). Evidence is from the formation of 1M of DXAAs and 0.78M of THMs from 1M of this compound, and 0.74M of DXAAs from malonic acid, the proposed intermediate. Consequently 96% of the carbon in 3-oxopentanedioic acid and 83% from malonic acid is accounted for in the DBPs formed.

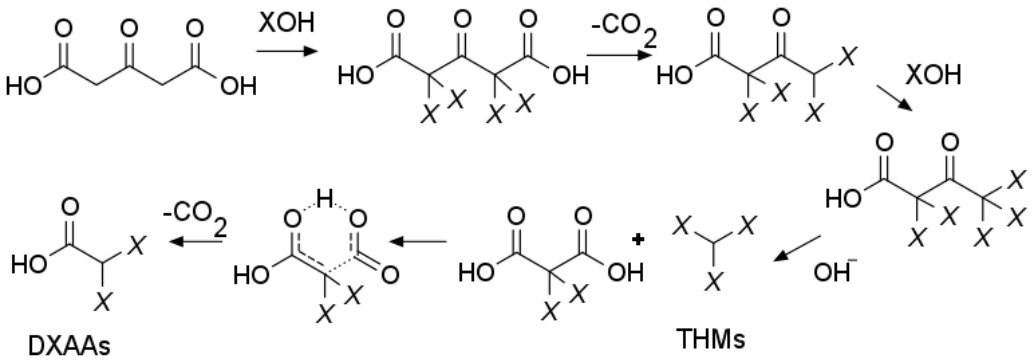


Figure S6 Proposed mechanism for formation of THMs and DXAAs from 3-oxopentanedioic acid

Such high forming mechanisms allows for aliphatic carbonyls to make a significant contribution to the DBP formation from treated water, with this example of 3-oxopentanedioic acid forming over 4 mg of DBPs per mg of carbon. This capacity of hydrophilic organic matter, which is poorly removed by coagulation, to form DBPs is therefore demonstrated and is particularly significant for the proposed incoming legislation for HAA9. Notably, given the propensity for brominated HAA formation from acidic aliphatic carbonyls, it is posited that such compounds present a significant risk for forming the currently unregulated HAA4 and, as many form low levels of THMs, they will historically have been disregarded for DBP risk. For example, malonic acid formed the highest relative levels of the unregulated HAA4, generating 596.6 µg/L of HAA4 but negligible THMs from 1.56 mg/L of compound.

3.2.2 Utilising pre-halogenated model compounds

This research also takes a novel approach in using pre-halogenated aliphatic model compounds to elucidate formation pathways. For example, the results from the ethyl 4-haloacetoacetates demonstrate that a singly halogenated terminal carbon cleaves to the corresponding MXAA rather than undergoing further terminal electrophilic substitution, this occurring almost completely for the chlorinated terminal compound whereas only half the time for the brominated equivalent. Thus 1041 µM/mM of MCAA comes from ethyl 4-chloroacetoacetate and 522 µM/mM MBAA from ethyl 4-bromoacetoacetate. However, the bromo- compound forms more THMs than the chloro-, at THMFP 336 and 22 µM/mM respectively, with the higher BIF (1.46 vs 0.34) suggesting the THMs were derived from the terminal carbon. This pathway divergence is proposed due to the increased electronegativity of the chlorine which induces a more significant dipole on the carbonyl and therefore encourages cleavage over further halogenation. Further evidence for this cleavage mechanism is provided by the ~1:1 conversion of hexachloroacetone to TCAA and chloroform.

3.2.3 Identification of influences on DBP formation

The results from this study data, including the pre-halogenated compounds, can therefore be utilised to understand both the important molecular level features and the significant pathways for the formation of THMs and HAAs. The interaction of these factors is proposed to drive DBP formation and, importantly in the current context, Br-HAA outcome (Table S11).

Table S11 Linking key pathways for DBP formation with molecular features identified as significant

Mechanism / Feature	No β-ketone	β-ketone only	3 Carbon chain, acid	3 Carbon chain, ester	>3 Carbon chain, acid	>3 Carbon chain, ester	Single halogenation	Triple halogenation
Acid-base dissociation	Acids dissociated, ketones, esters not dissociated	Not dissociated	Dissociated	Not dissociated	Dissociated. Enolate stabilised.	Not dissociated	These are esters so not dissociated	These are esters so not dissociated
Keto-enol equilibrium	Low enol formation - no hydrogen bond promoting enolization.	Double activation α carbon by enol. H-bond intermediate only with enol.	Double activation α carbon by enol. H-bond intermediate with and without enol.	Double activation α carbon by enol. H-bond intermediate only with enol.	Double activation α carbon by enol. H-bond intermediate with and without enol.	Double activation α carbon by enol. H-bond intermediate only with enol.	Substituted enols more stable. Halogen can stabilise enolate.	Enolization at tri-halogenated carbon not possible.
Electrophilic Substitution (SE)	Without enolization, SE not promoted	SE promoted at α carbon and lesser extent at terminal carbon.	SE promoted at α carbon, fast kinetics as dissociated. Steric hinderance if multiple bromination.	SE promoted at α carbon, slow kinetics as not dissociated. Steric hinderance of ester and/or bromine.	SE promoted at α carbon, fast kinetics as dissociated. Steric hinderance if multiple Br substituted. If stabilised intermediate get terminal SE.	SE promoted at α carbon, slow kinetics as not dissociated. Steric hinderance of ester and/or bromine. If stabilised intermediate get terminal SE.	Bromination at α likely to restrict further halogenation sterically, lesser effect at terminal where may promote via enol.	Already fully substituted. Some further SE at α carbon may occur.
Decarboxy-lation	Only acids with stable leaving group to distribute charge.	Not applicable	Stabilised by H-bonded intermediate to DXAAs. After halogenation.	Not applicable until after ester hydrolysis.	Stabilised by H-bonded intermediate to DXAAs. After halogenation or simultaneous (halo-decarboxylation)	Not applicable until after ester hydrolysis.	Not applicable until after ester hydrolysis. Halogenation will promote by stabilising the carbanion formed.	Not applicable until after ester hydrolysis. Halogenation will promote by stabilising the carbanion from decarboxylation.
Ester Hydrolysis	Potentially for methyl acetate, but without SE would not result in target DBPs.	Not applicable	Not applicable.	Ethyl esters more stable to hydrolysis than methyl.	Not applicable	Ethyl esters more stable than methyl but butyl hydrolyses more readily.	Ethyl esters more stable than methyl. Halogenation may induce dipole and/or sterically restrict.	Halogenation may induce dipole and/or sterically restrict.
Cleavage	Without halogenation less stability for carbanions. Cleavage products may not be targets.	Halogenation promotes δ positive at carbonyl, OH-attack, stabilises carbanion including terminal.	Will decarboxylate in preference to cleavage - hydroxide attack on carboxylic acid group unlikely.	Will hydrolyse and decarboxylate in preference to cleavage - hydroxide attack on ester group unlikely.	Cleavage depends on stability of leaving group/carbanion, with CX_3^- stabilised to form THMs.	Cleavage depends on stability of leaving group/carbanion, with CX_3^- stabilised to form THMs.	Halogen promotes cleavage by inducing dipole on carbonyl.	CX_3^- stabilised so cleavage promoted. Halogens will induce dipole on carbonyl.
Nucleophilic Addition	Maybe to a very low level but not significant influence.	May be at terminal enol in acetylacetone which then cleaves. Low levels.	Likely SE will dominate - as observed in high BIF.	Likely electrophilic substitution will dominate as doubly activated α carbon.	Likely SE will dominate - as observed in high BIF. May be at terminal enol which then cleaves. Low levels.	Likely SE will dominate as doubly activated α carbon. May be at terminal enol which then cleaves. Low levels.	Halogenation unlikely to promote nucleophilic addition.	Tri-halogenation may promote - leaving group adjacent to conjugate (e.g. in intermediate). Low levels.

3.2.4 Mechanism Suggestions

The results from this study can be used to propose possible pathways for DBP formation from aliphatic carbonyls.

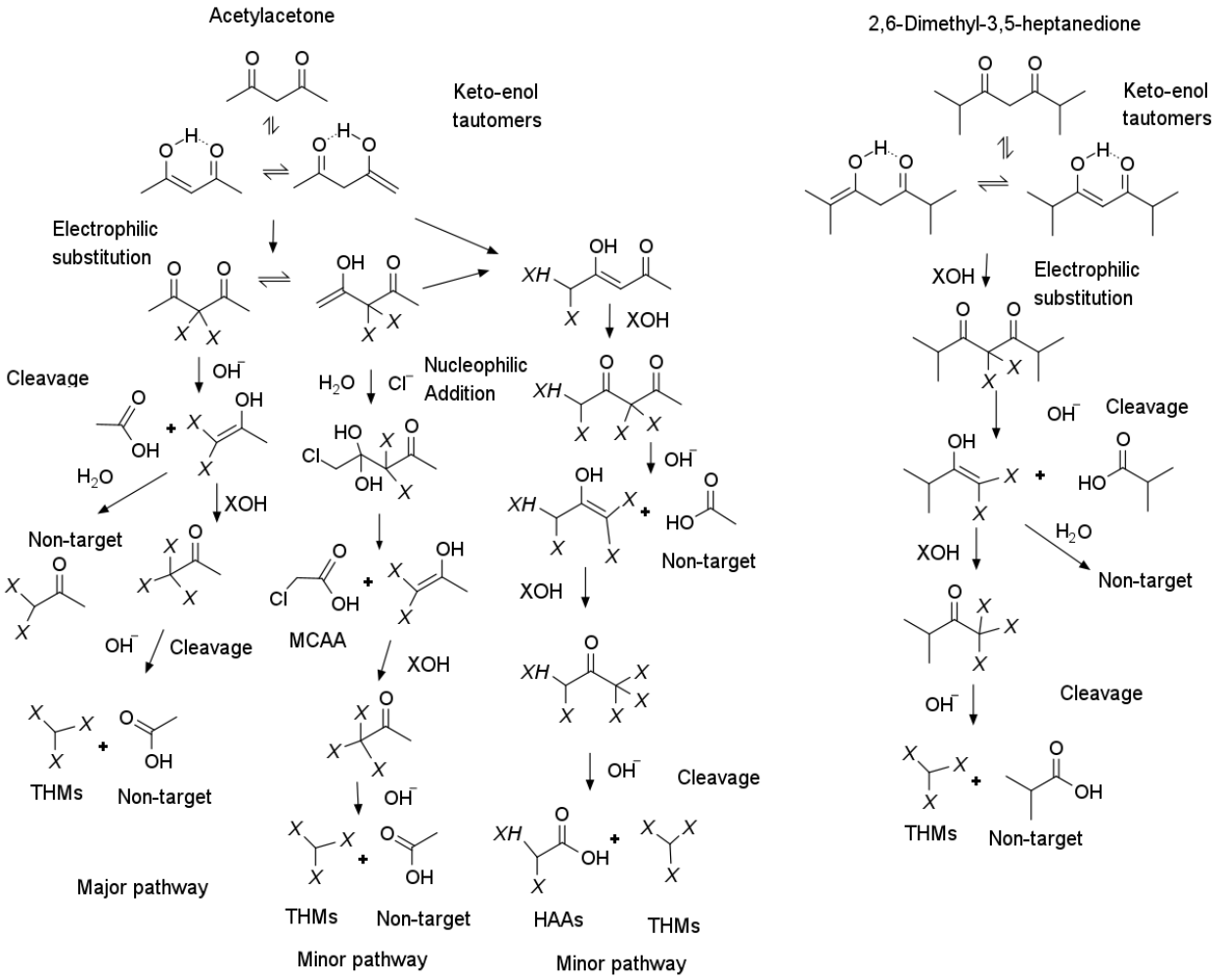


Figure S7 Possible mechanisms for the formation of THMs and HAAs from β-ketone aliphatic carbonyls

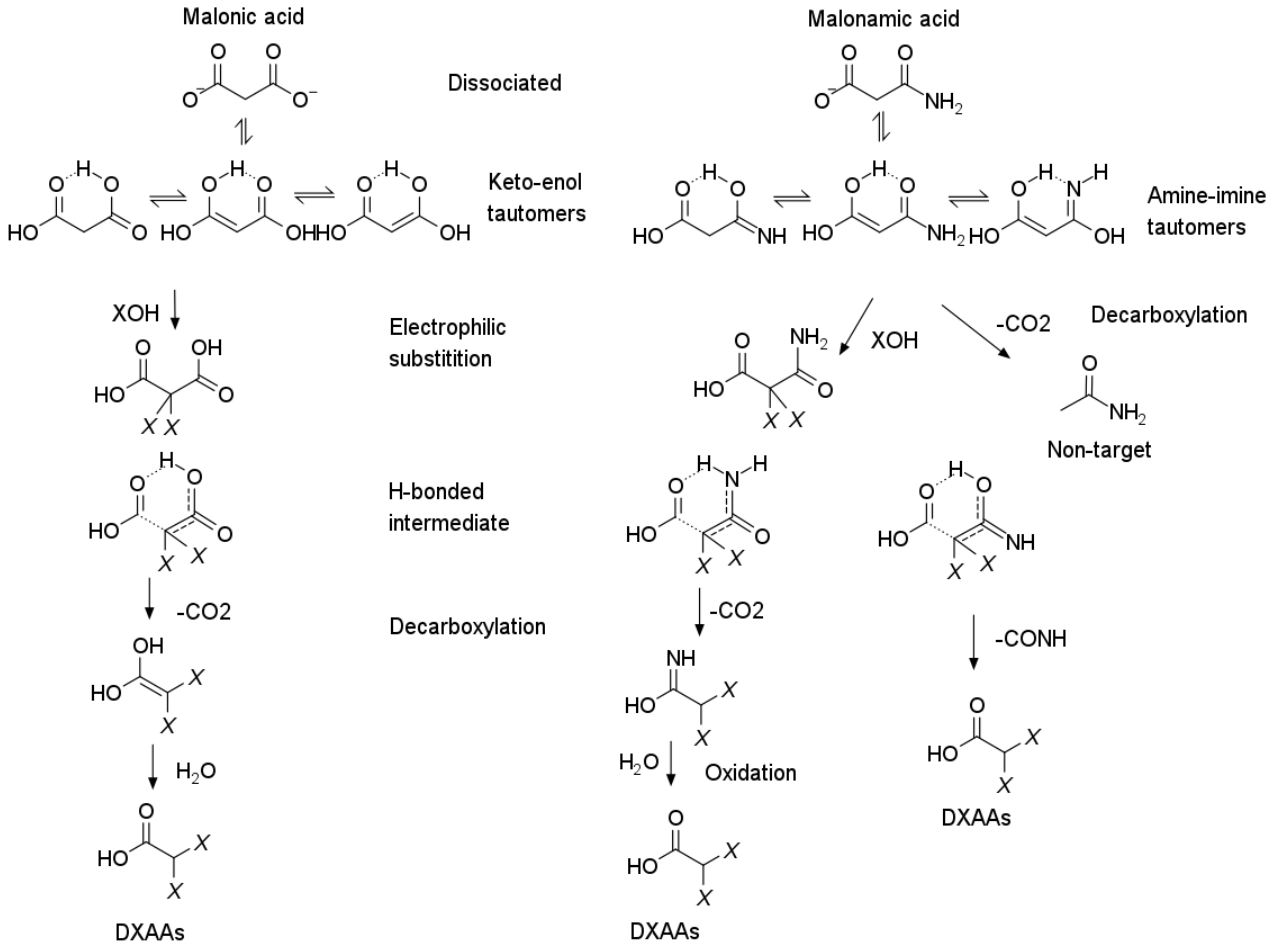


Figure S8 Possible mechanisms for the formation of THMs and HAAs from 3-carbon β-keto acid aliphatic carbonyls

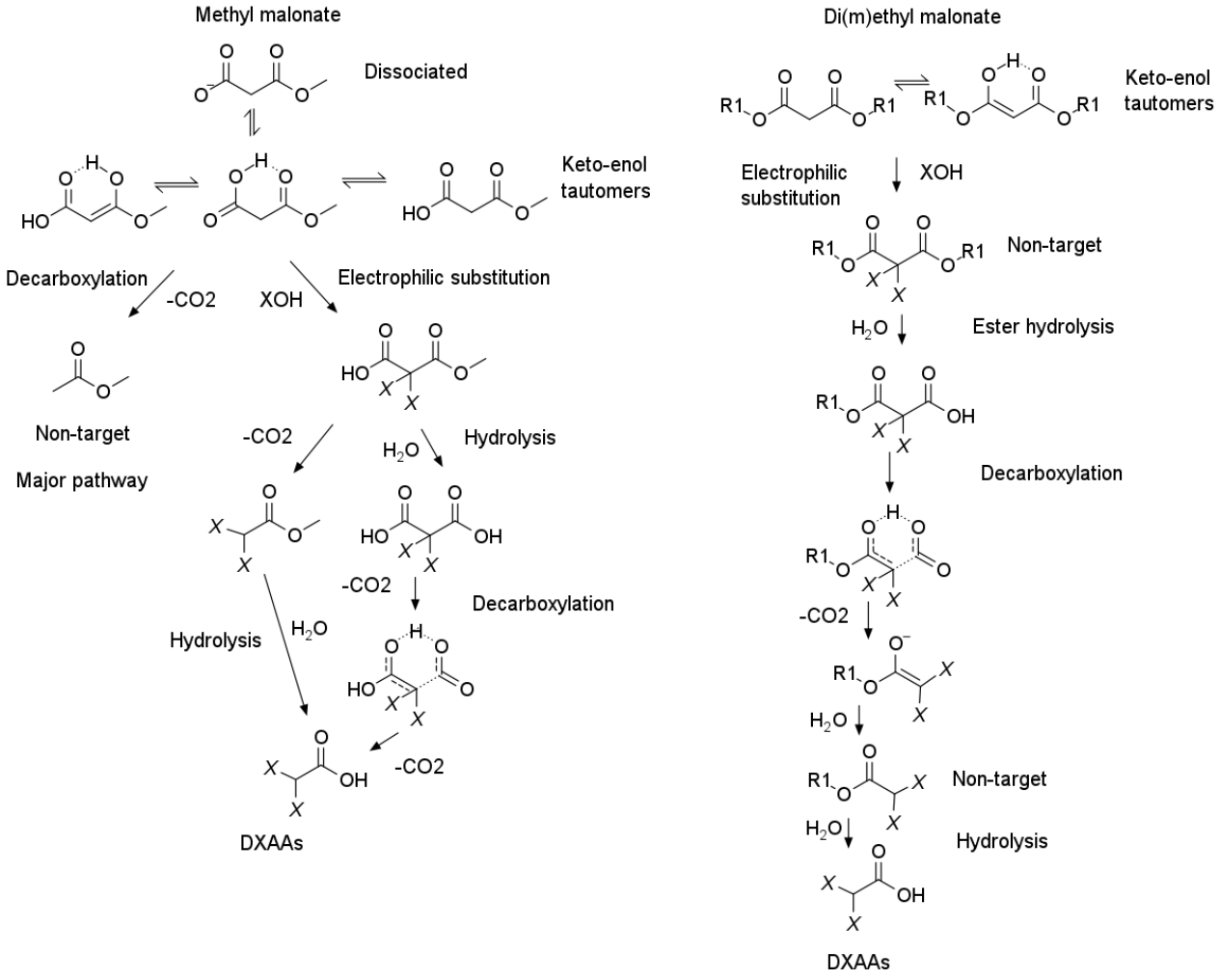


Figure S9 Possible mechanisms for the formation of THMs and HAAs from 3-carbon β-keto ester aliphatic carbonyls

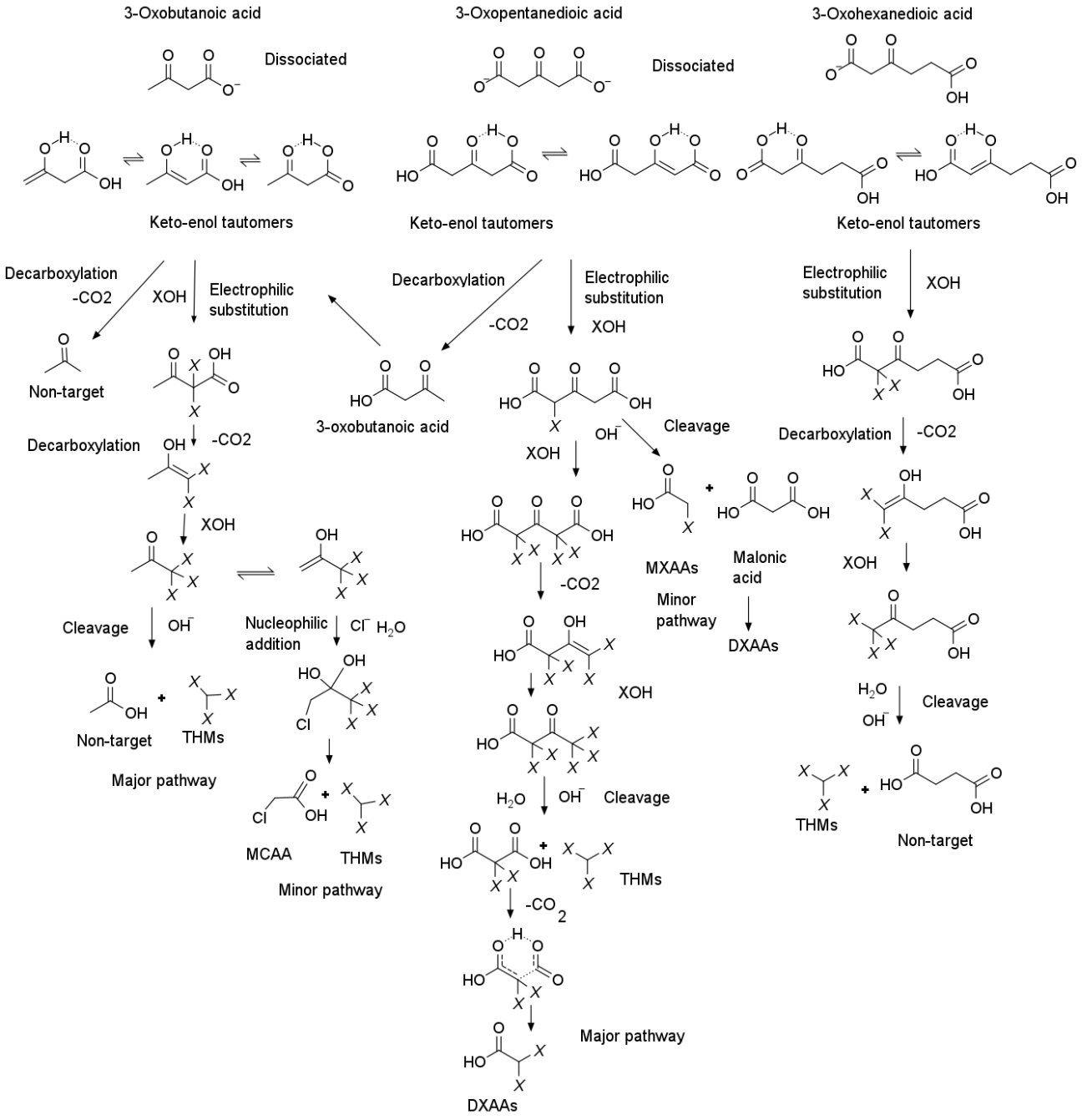


Figure S10 Possible mechanisms for the formation of THMs and HAAs from >3-carbon β-keto acid aliphatic carbonyls

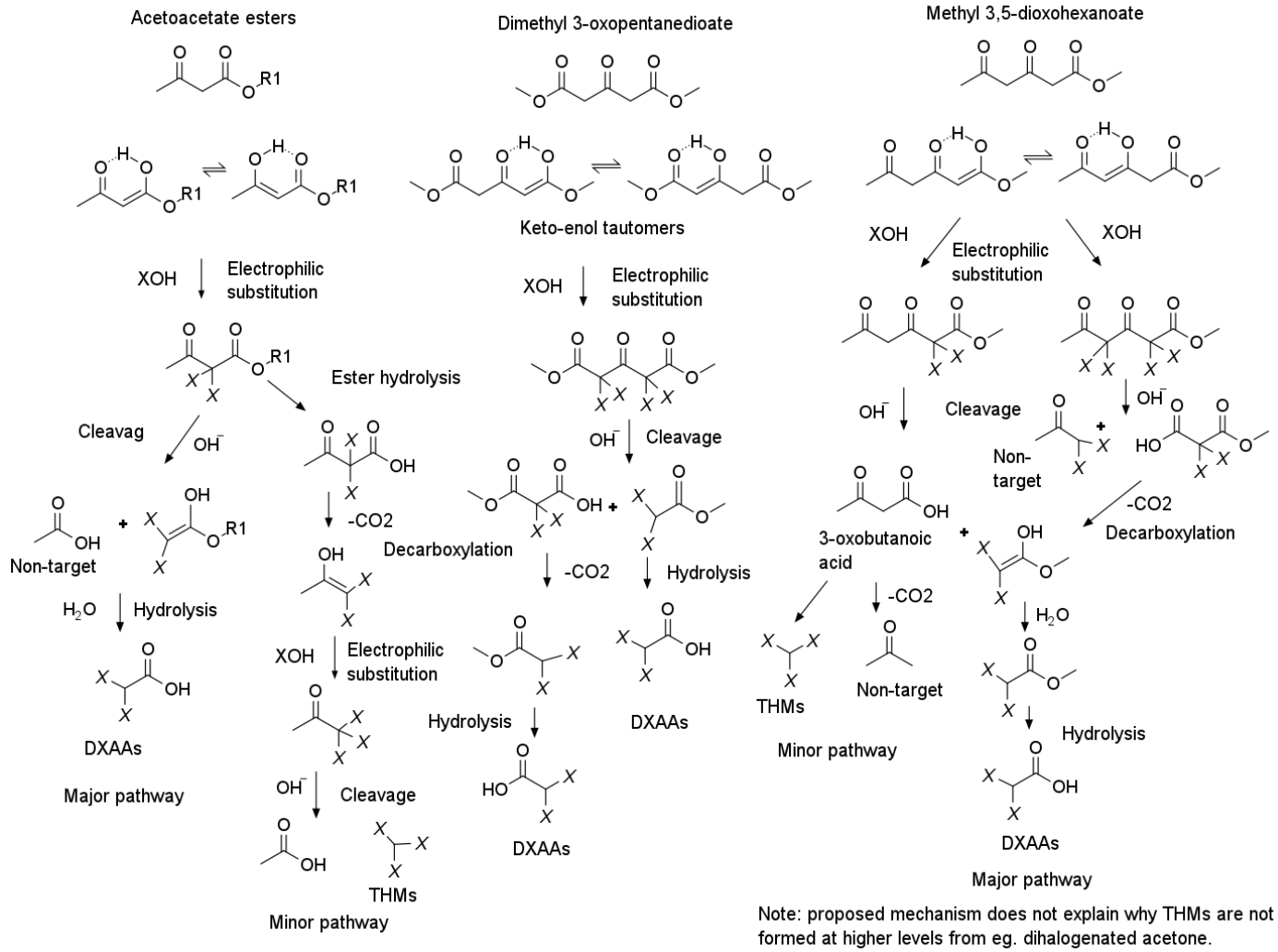


Figure S11 Possible mechanisms for the formation of THMs and HAAs from >3-carbon β-keto ester aliphatic carbonyls (R1 = methyl, ethyl or t-butyl)

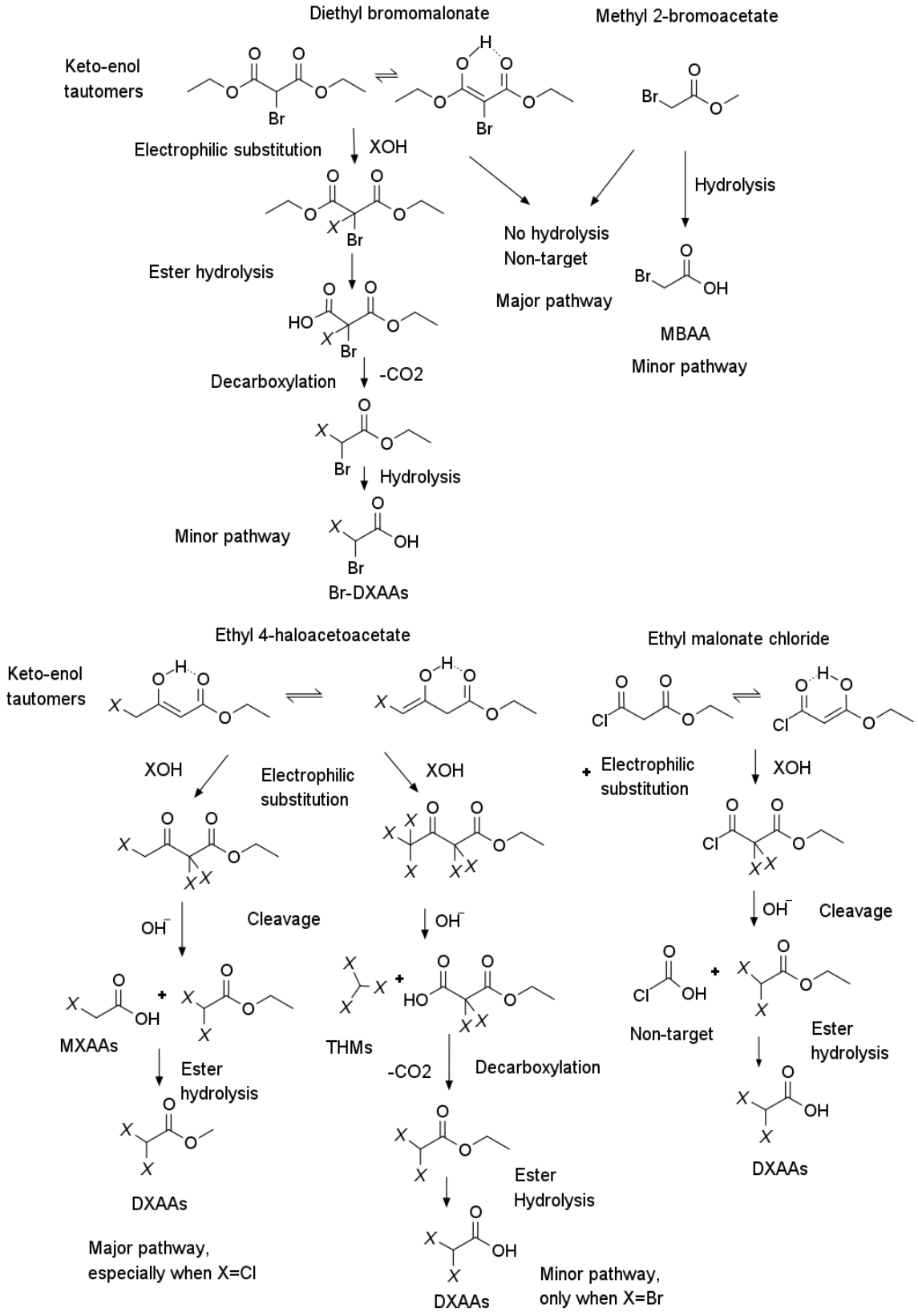


Figure S12 Possible mechanisms for the formation of THMs and HAAs from singly halogenated aliphatic carbonyls

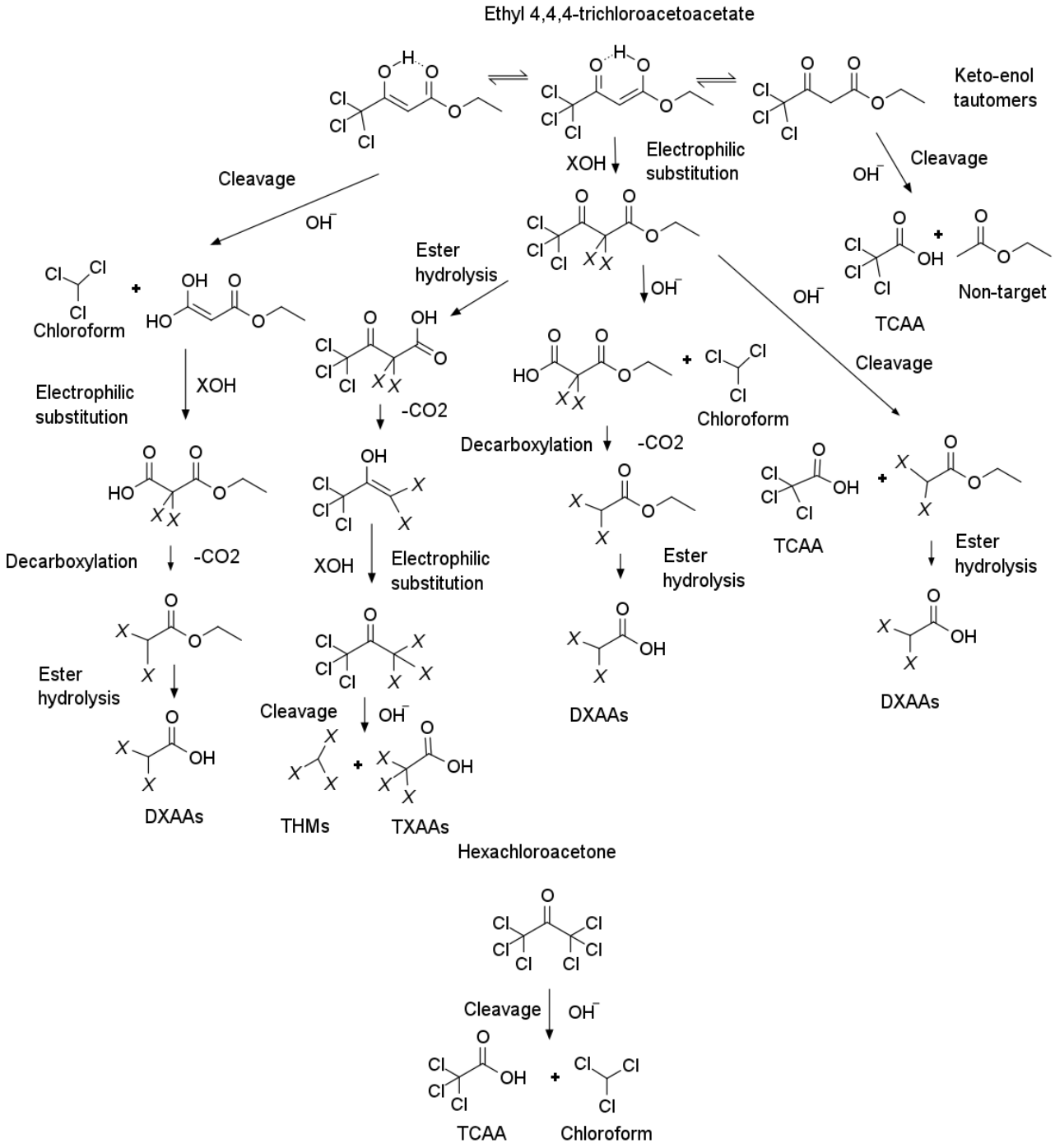


Figure S13 Possible mechanisms for the formation of THMs and HAAs from triple halogenated aliphatic carbonyls

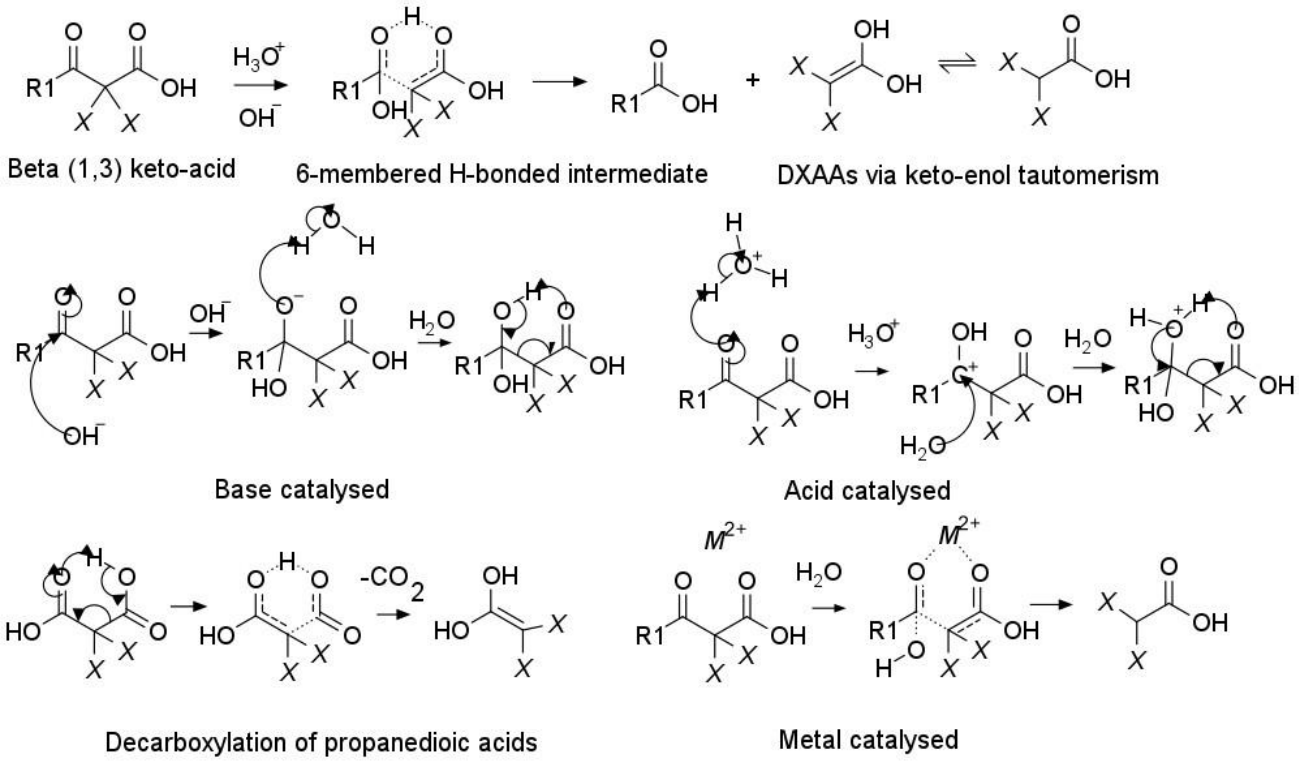


Figure S14 Proposed differentiating mechanism for DXAAs via 6-membered hydrogen bonded intermediate, from Grundy *et al*., (2026), Supplementary Material[14]

3.2.5 Use of kinetic and structural models

Kinetic models have been used to elucidate the key influences on DBP formation from organic matter. Such models were generally observed to establish the following to develop the model:

1. Transformation pathways – the reaction pathways for hypohalous acids with model compounds were established[10]. This included the dissociated or undissociated compound, halogenation by electrophilic substitution, oxidation or electron transfer, any alternative reactions such as decarboxylation or nucleophilic addition, plus the secondary pathways from the intermediates formed (where appropriate for the compound).
2. Acid-base equilibria – reaction rate can be highly dependent on the extent of dissociation, particularly where enol/enolates are involved, and so pK_a was used to establish the proportion of model compound in each state when applying the model[15].
3. Species specific rate constants – for each transformation pathway identified a rate constant was required, which was obtained from literature or if necessary by experimentation within the research[16].
4. Reactions of hypochlorous acid with bromide – this was included in relevant models and is well studied, with the predominant form as hypobromous acid at pH 7. However, previous research has identified that other electrophilic species are formed during chlorination with bromide present, and these can be significant for Br-DBP formation due to their fast reaction kinetics.[17] Consequently, it was proposed that detailed kinetic models should allow for, or discount, the potential role of electrophiles such as BrCl.

Kinetic models act as a complement to molecular structure models which identify the intermediates and final products of the reaction between chlorine and organic matter [18–23]. However, there has been limited research into the kinetic or structural models for formation of DBPs from aliphatic compounds or where both bromide and chlorine are present in competition during Br-HAA formation. This is a complex area given the number of possible transformation pathways possible and the analytical challenge of measuring aliphatic dicarbonyl compounds, but it is potentially significant given incoming regulation and the enhanced toxicity of Br-HAAs. Consequently, this study provides a reference for which future studies can select the most relevant compounds for future detailed studies to better understand formation of the Br-HAAs.

3.2.6 Correlations between molecular structure and BSF

When the values for pK_a and volume of the groups around the β-dicarbonyl group (detailed Table S1) are plotted against the BSF of the DBPs formed then a correlation is observed such that compounds with a lower pK_a (more acidic) were observed to have higher BSF (R^2=0.65 at 15 µM and 0.82 at 1.5 µM compound) while those with larger steric factors around the β-dicarbonyl had a lower BSF (R^2=0.66 at 15 µM and 0.44 at 1.5 µM compound) (Figure S15).

This is proposed due to the balance between kinetic and thermodynamic products at halogenation. Bromination is predicted to have faster kinetics of halogenation for dissociated enolates over enols, which has been demonstrated for phenolates and phenols[8]. However, chlorination is the more thermodynamically stable product due to lower steric hinderance at of the smaller chlorine. Consequently, halogenation is a balance between these factors and more acidic

compounds favour kinetic brominated products but more sterically hindered compounds will form more of the thermodynamic chlorinated products.

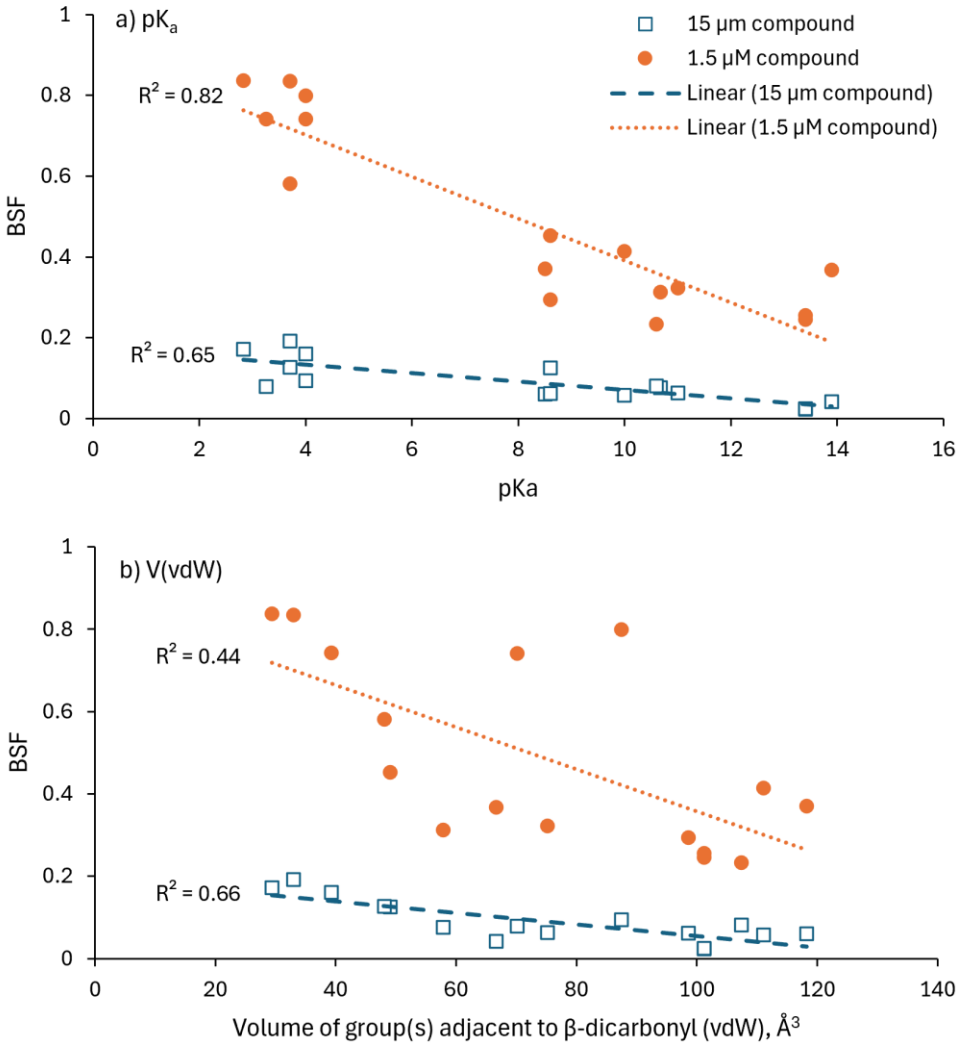


Figure S15 Correlation between BSF and a) pK$_a$ and b) van der Waals volume for functional group adjacent to β-dicarbonyl for non-pre-halogenated compounds at 15 and 1.5 µM concentrations of model compounds, 5 µM bromide

3.3 Consideration of Relative Hazard

When prioritising the challenges for the water industry an alternative and more nuanced approach utilising the Relative Hazard Index (RHI) can be taken. This employs a risk-based assessment to compare outcomes based on the Guideline Values (GVs), and can provide additional insight by allowing comparisons by the risk posed rather than by mass or molar formation [24].

$$Relative\ Hazard\ Index = \sum \frac{Concentration\ DBP\ (\mu g/l)}{Guideline\ Value\ for\ DBP\ (\mu g/l)}$$

Guideline Values are obtained from the World Health Organisation [24] or derived from toxicity data [14,25].

As an example, comparison of the molar RHI for the compounds at 1:3 and 10:3 ratio of bromide to model compound clearly reveals the significant impact of the ratio to bromide on the risk presented by the compounds studied here (Figure S16a). As would be expected from their propensity for bromine incorporation and the higher toxicity of the brominated DPBs, the β-keto acids show particular increase in RHI with increasing ratio of bromide to compound. Further comparison of RHI values demonstrate that for the aliphatic carbonyls in this study the most significant contributor to this risk comes from the HAAs rather than the THMs (Figure S16b). These findings are important for prioritising the strategies to reduce the risk presented by DBPs and highlight that aliphatic dicarbonyls in hydrophilic organic matter could play a significant role in the measured toxicity from chlorination of high bromide waters. Further, these findings suggest that existing measures for identifying risk to consumers such as THMs or HAA5 are not effective in waters containing bromide.

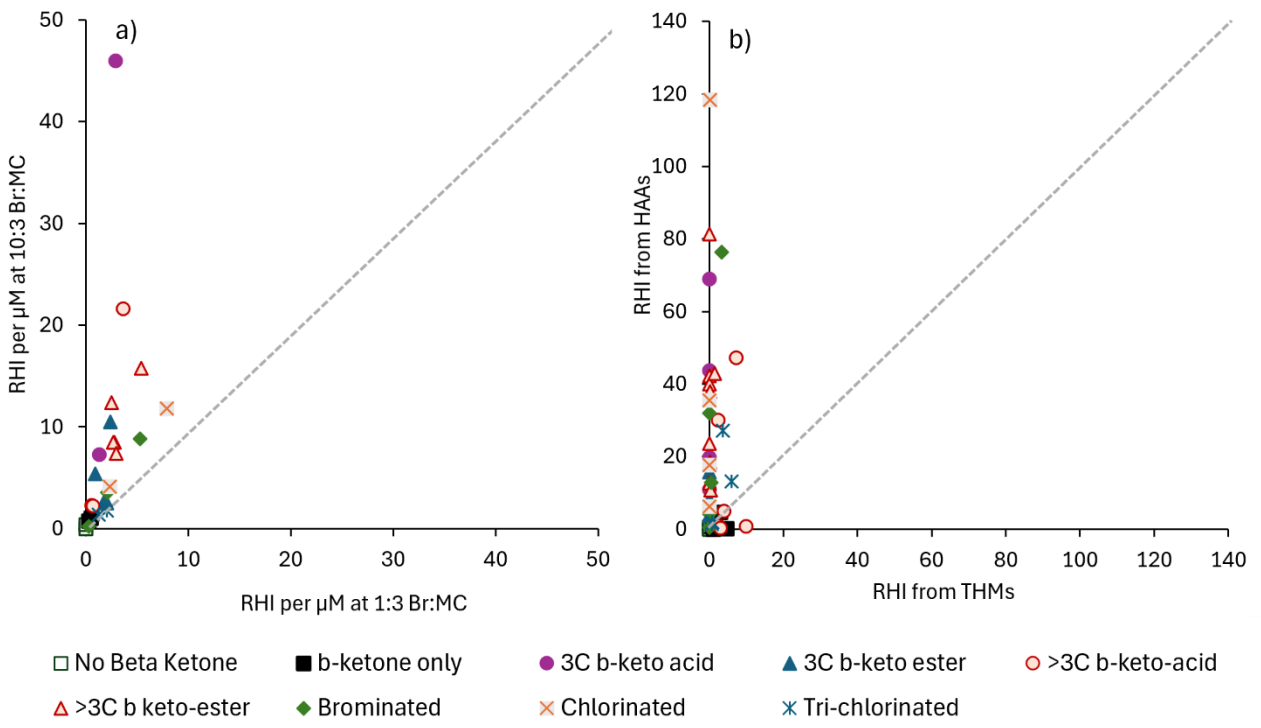


Figure S16 Comparison of RHI for aliphatic carbonyl compounds a) at differing ratio of bromide to model compound (Br:MC) and b) contribution from THMs and HAAs

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