Proteins as Important Reactive Compounds in Drinking Water Treatment

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MA WRRC Conference
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Outline

- Formation of N-DBPs from NOM
  - Occurrence
  - Characteristics
- Chemistry of selected End Products
  - DHAN
  - DHAD
  - NDMA
- Reactivity of Specific Nitrogenous Constituents
  - Amino Acids
  - Proteins & others
- Key N-DBPs and Methods to be developed

Reactions with Chlorine

The Precursors!

HOCl

+ natural organics (NOM)

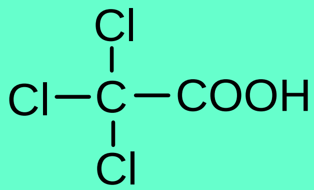
Oxidized NOM
and inorganic chloride
- Aldehydes

Chlorinated Organics
- TOX
- THMs
- HAAs

The THMs

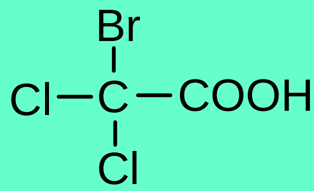
Chloroform | Bromodichloromethane | Chlorodibromomethane | Bromoform

The Haloacetic Acids

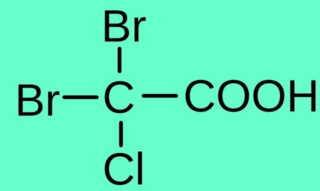


Trichloroacetic Acid

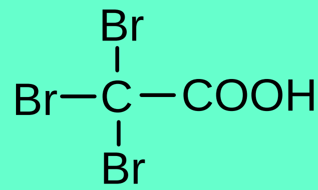
(TCAA)



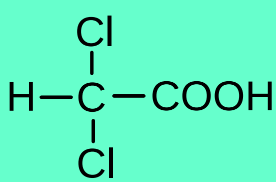
Bromodichloroacetic Acid



Chlorodibromoacetic Acid

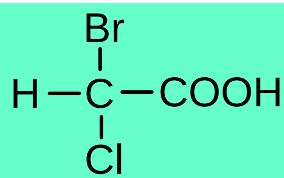


Tribromoacetic Acid

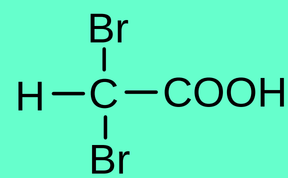


Dichloroacetic Acid

(DCAA)



Bromochloroacetic Acid

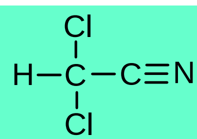


Dibromoacetic Acid

N-DBPs we know about: end products

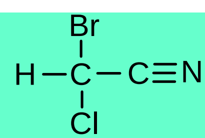
- Certain to come from N-organics when using free chlorine
- Major types:
  - Cyanogen Halides
  - Haloacetonitriles
  - Halonitromethanes

CNCl & CNBr



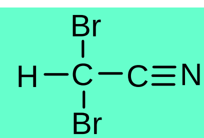
Dichloroacetonitrile

(DCAN)



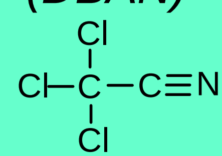
Bromochloroacetonitrile

(BCAN)



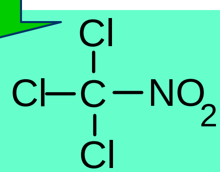
Dibromoacetonitrile

(DBAN)



Trichloroacetonitrile

(TCAN)



Chloropicrin

(CHP)

9 species

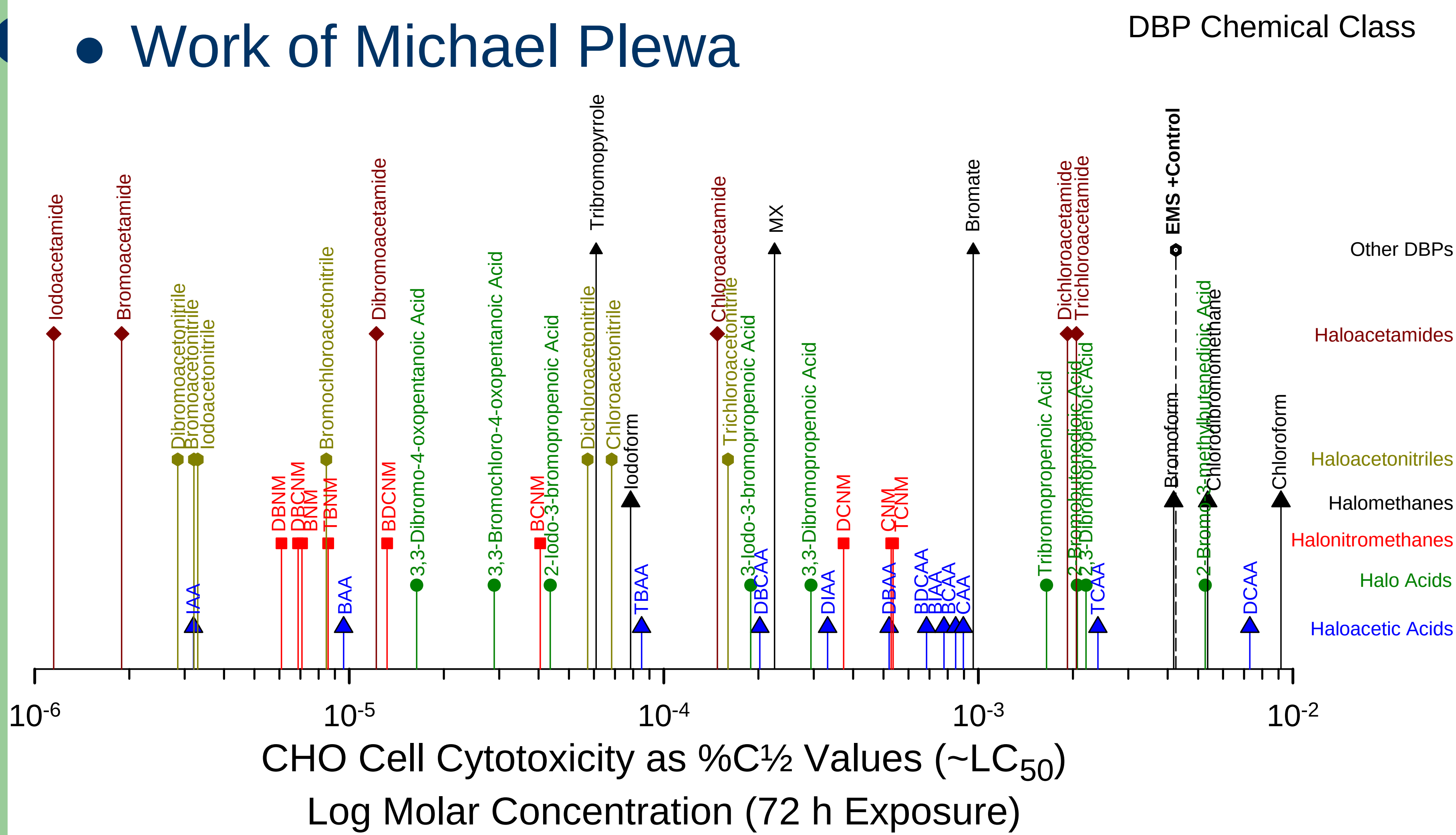
Special focus on these compounds because of large data set

Why N-DBPs?

- Nitrogenous organics are generally quite reactive
- Can be enhanced by chloramination
- Some evidence that they are major contributors to adverse human health effects of DBPs
- Very little is known about N-DBPs
- Analytical chemistry is more complicated

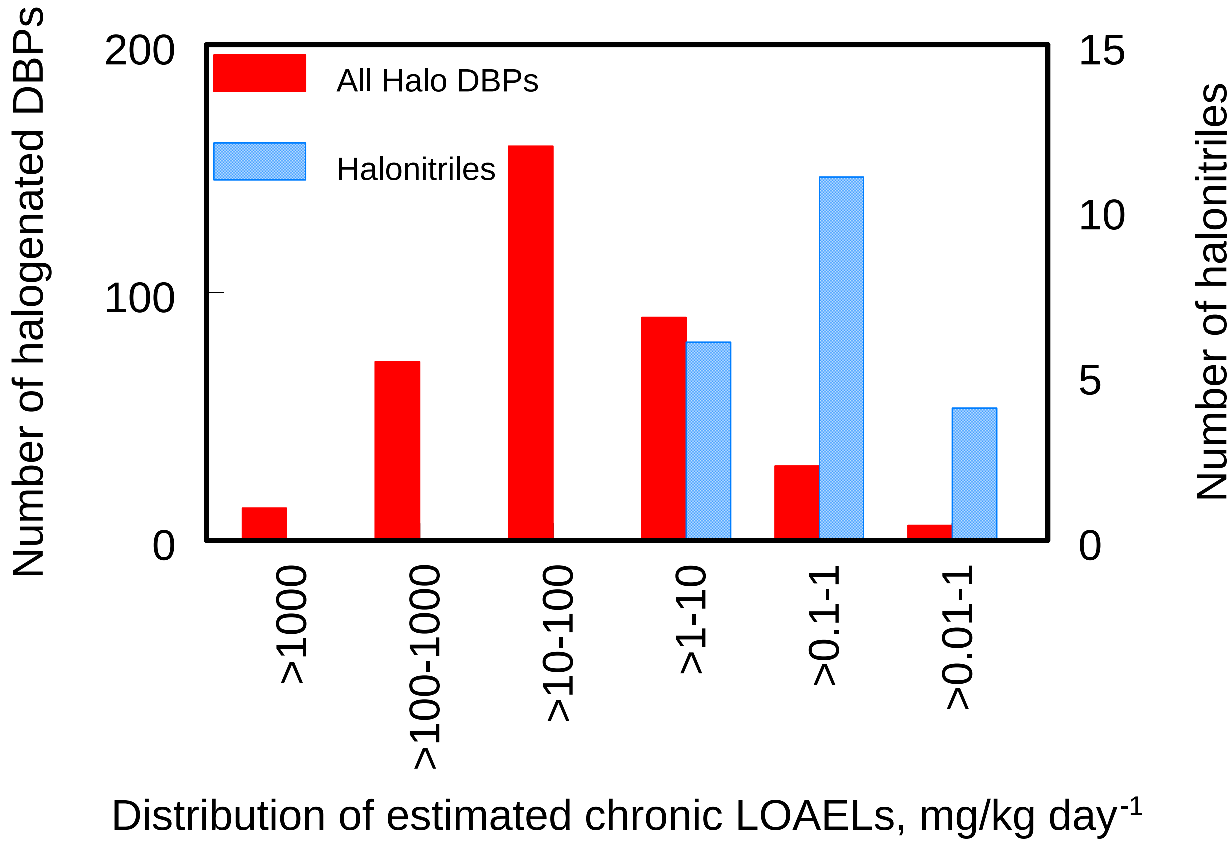
CHO Cytotoxicity

- Work of Michael Plewa



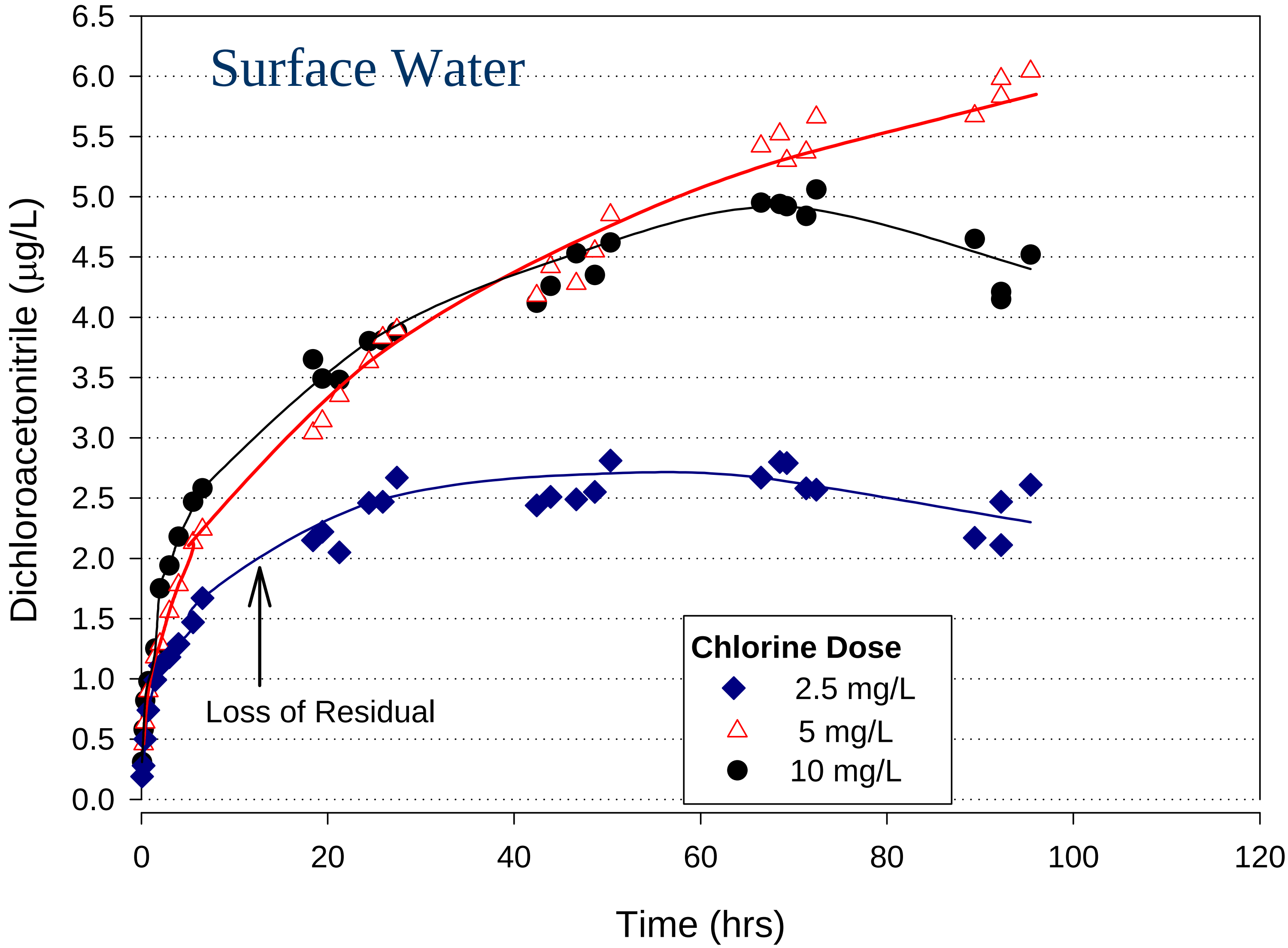
Quantitative Structure-Toxicity Models

- Lowest Observed Adverse Effect Level
  - AWWARF report by Bull et al., 2007



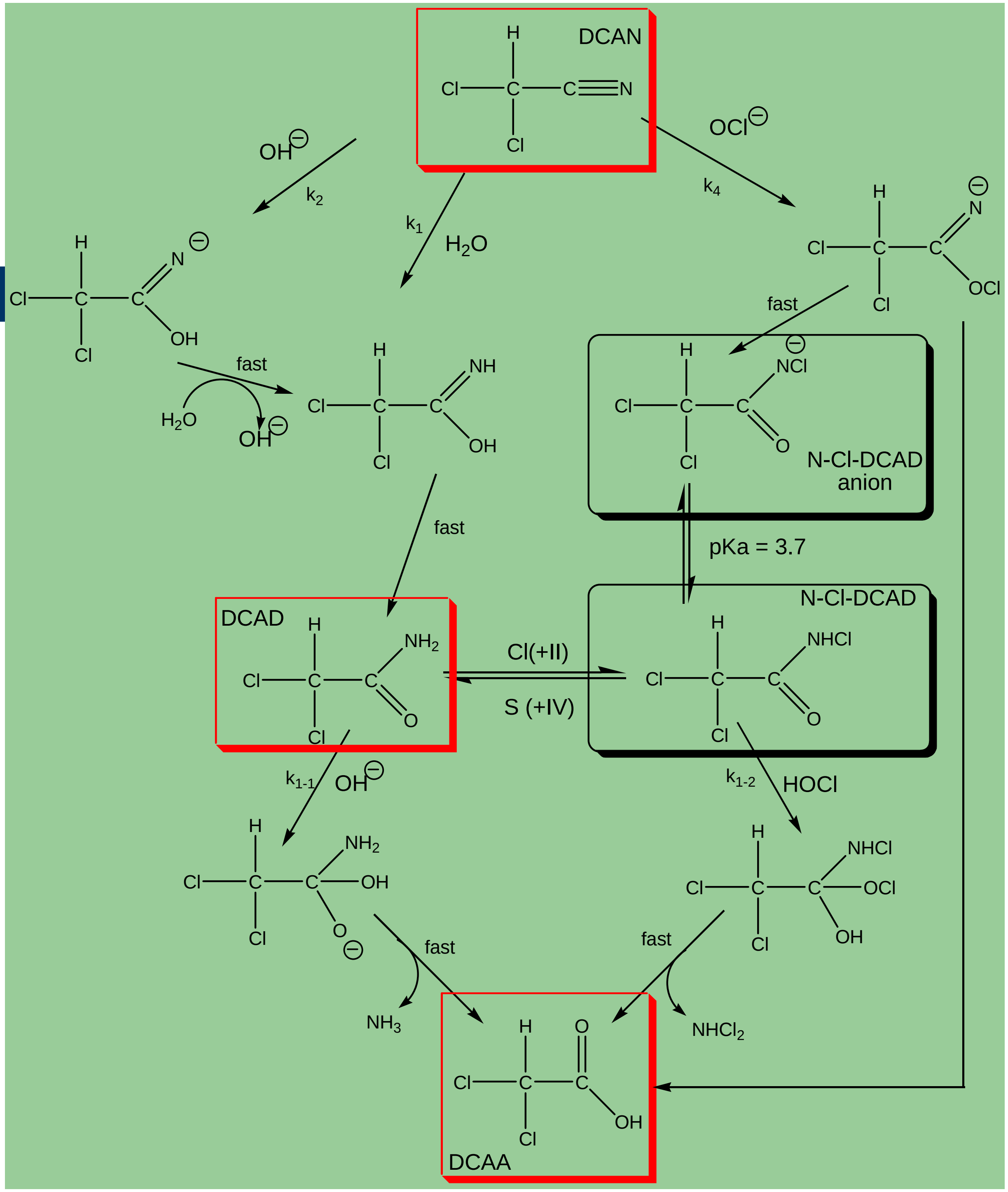
Chemistry of the end products

DCAN



DHAN

- Key intermediate
- Concentrations are well known



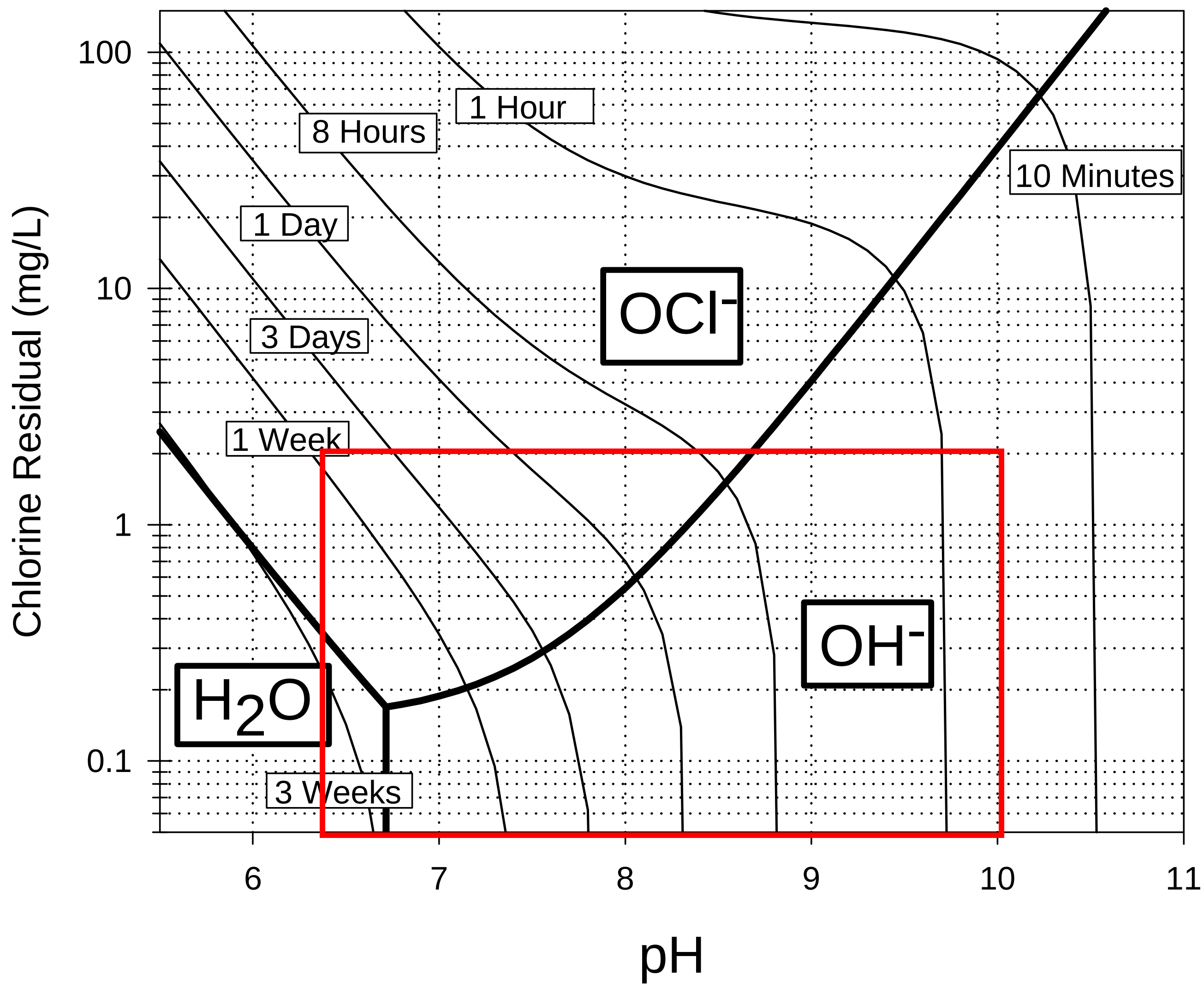
Proposed Rate Law for DCAN

- Hydrolysis and oxidation

$$\frac{dC}{dt} = -\{k_1 + k_2[OH^-] + k_3[Cl(+I)]\}C$$

k1 = 1.78 x10-7 ±0.35 x10-7 (s-1)
k2 = 3.42 ±0.31 (M-1s-1)
k3 = 1.30 x 10-1 ±0.08 x 10-1 (M-1s-1)

DCAN half-life based on pH & HOCl



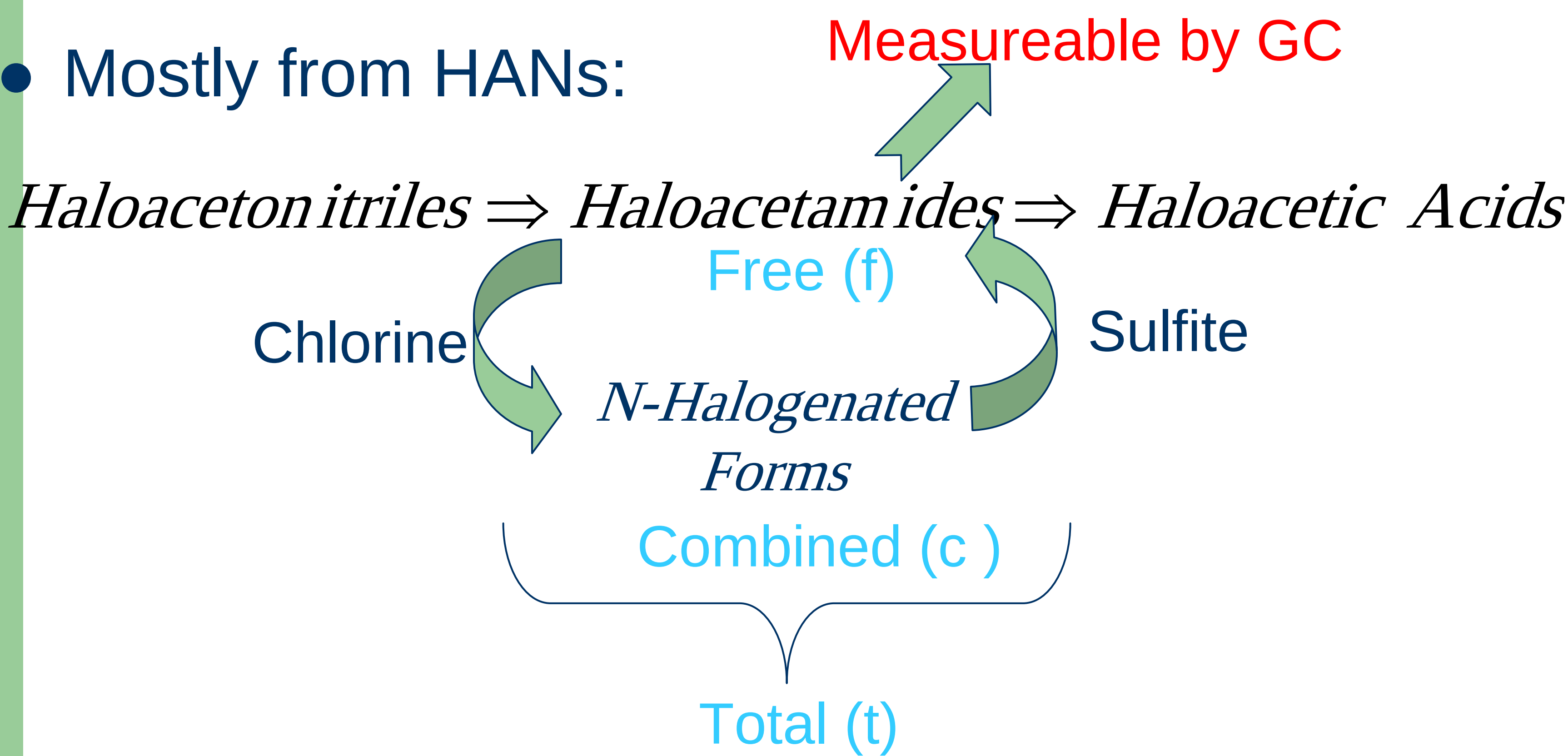
- At 20 C
- From Reckhow, Platt, MacNeill & McClellan, 2001
  - Aqua 50:1:1-13
- Degradation in DS observed to increase with increasing pH
  - ICR data: Obolensky & Frey, 2002

Halamides

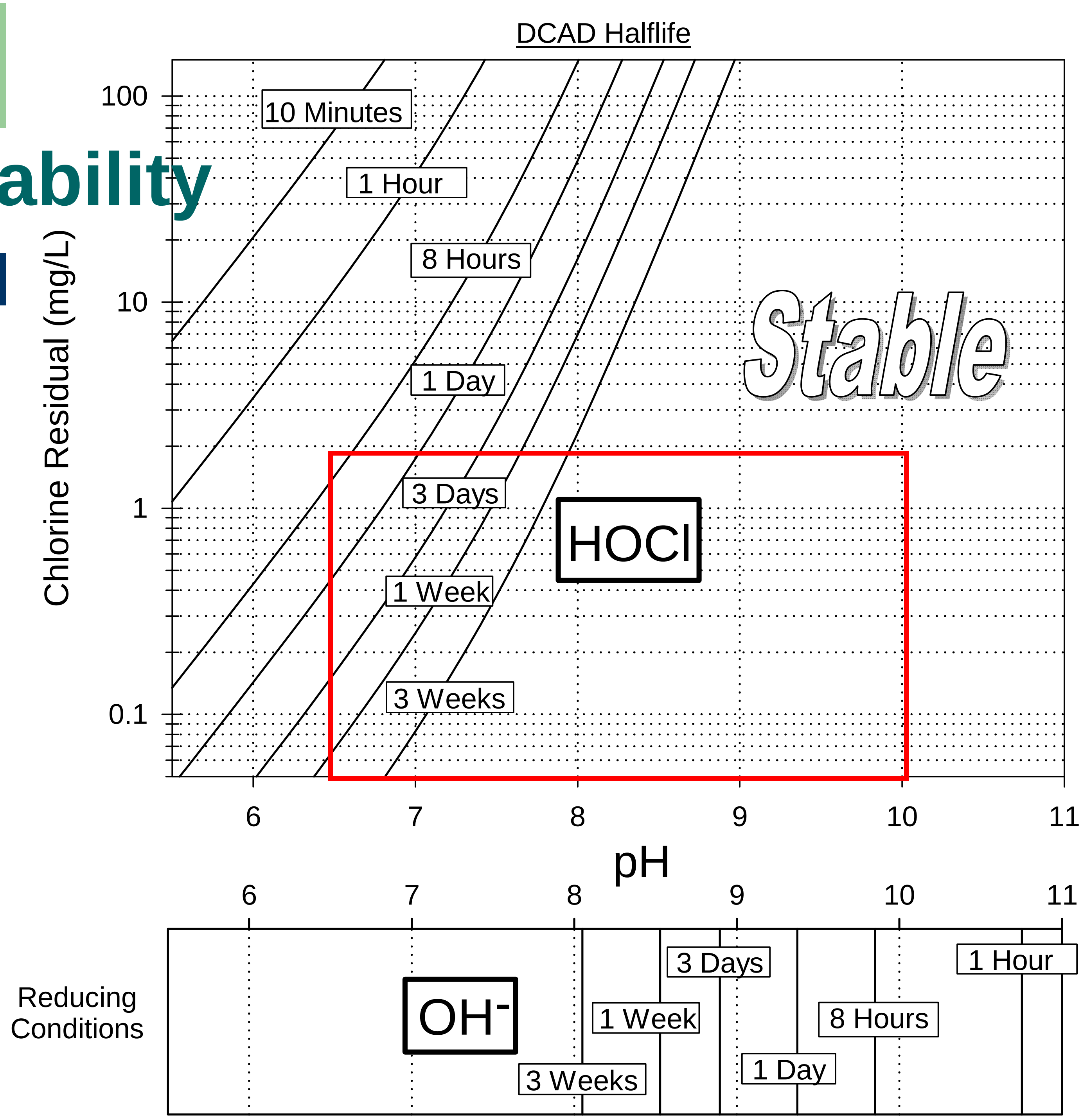
- Compounds
  - Monohaloacetamides
    - Chloroacetamide, Bromoacetamide
  - Dihaloacetamides
    - Dichloroacetamide (DCAD)
    - Bromochloracetamide (BCAD)
    - Dibromoacetamide (DBAD)
  - Trihaloacetamides
    - trichloroacetamide & analogues
- Chlorination byproducts
  - Probably a bit less prevalent with chloramines
  - Pre-oxidation will probably reduce subsequent formation

Haloacetamides

- Mostly from HANs:



DCAD Stability

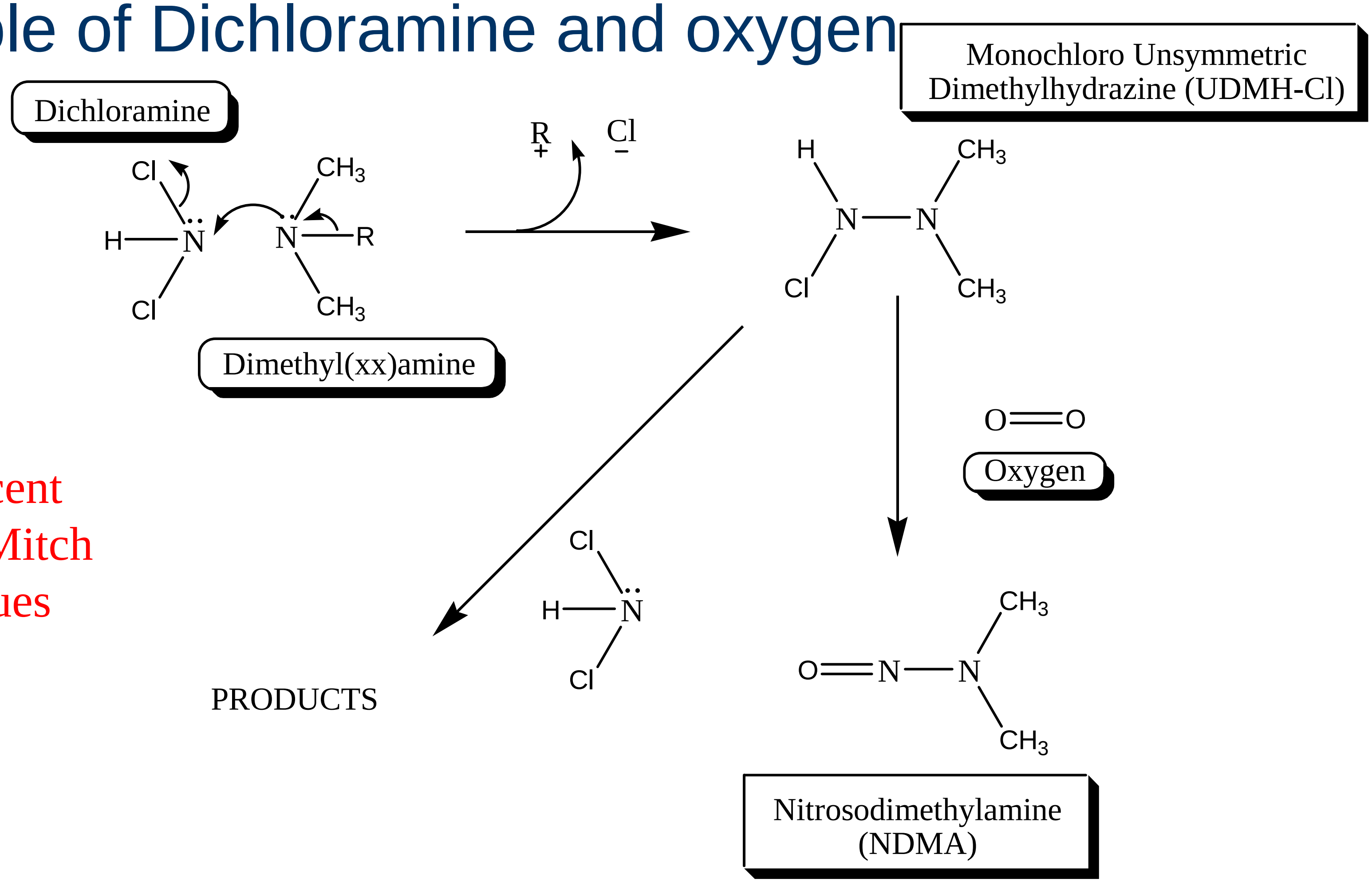


Nitrosamines

- NDMA: typically formed at greater levels with chloramination than with chlorination
  - Continues to form across DS?
- other nitrosamines (beyond NDMA) have been reported in chloraminated water
- Levels and mechanisms
  - Earlier work: Valentine & Weinberg
  - New mechanism: Mitch

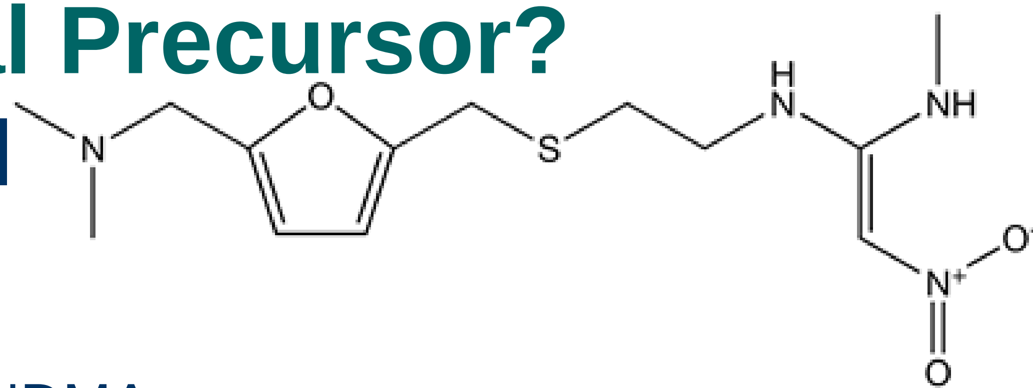
Pathway to NDMA

- Role of Dichloramine and oxygen



Based on recent work by Bill Mitch and colleagues

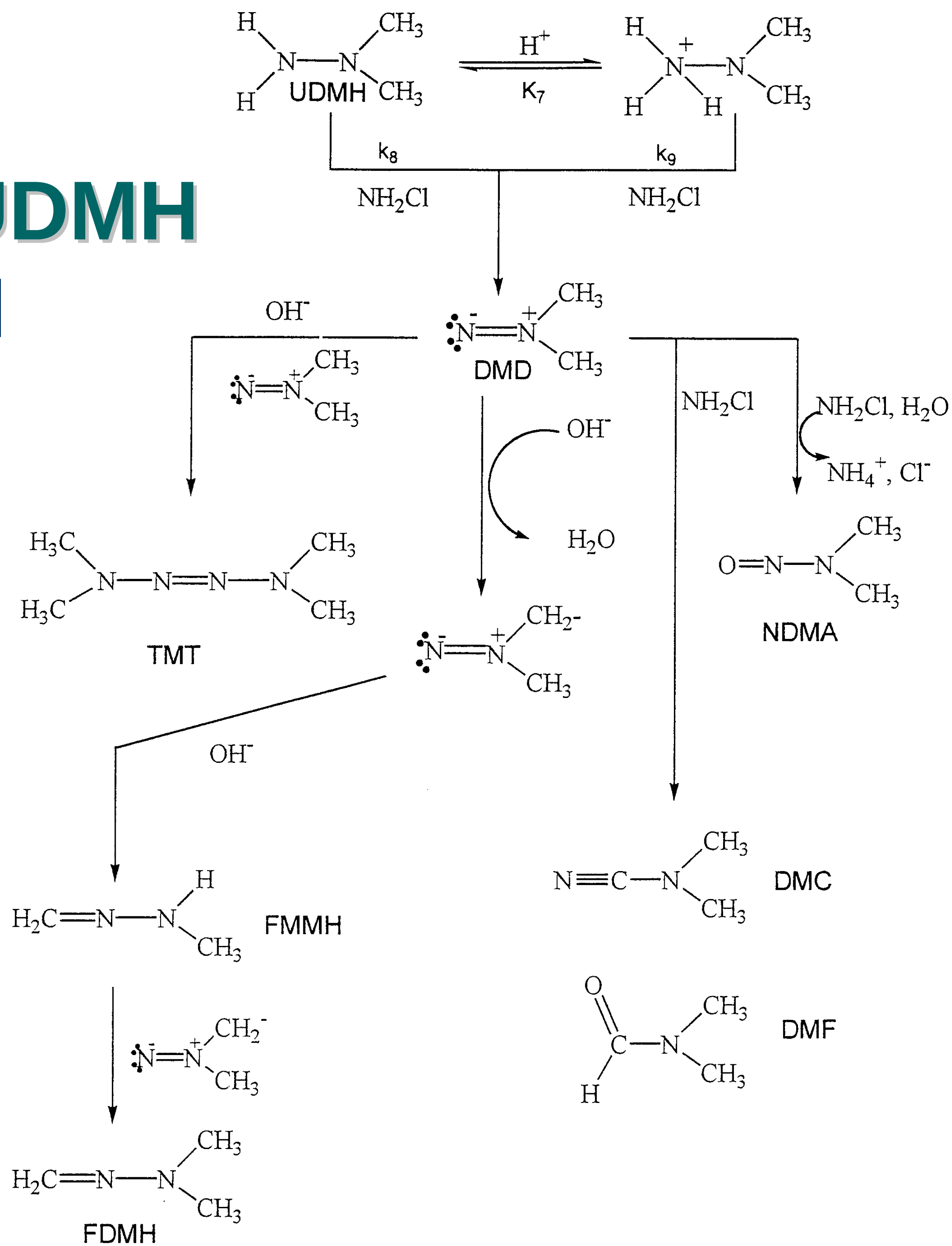
The Unnatural Precursor?



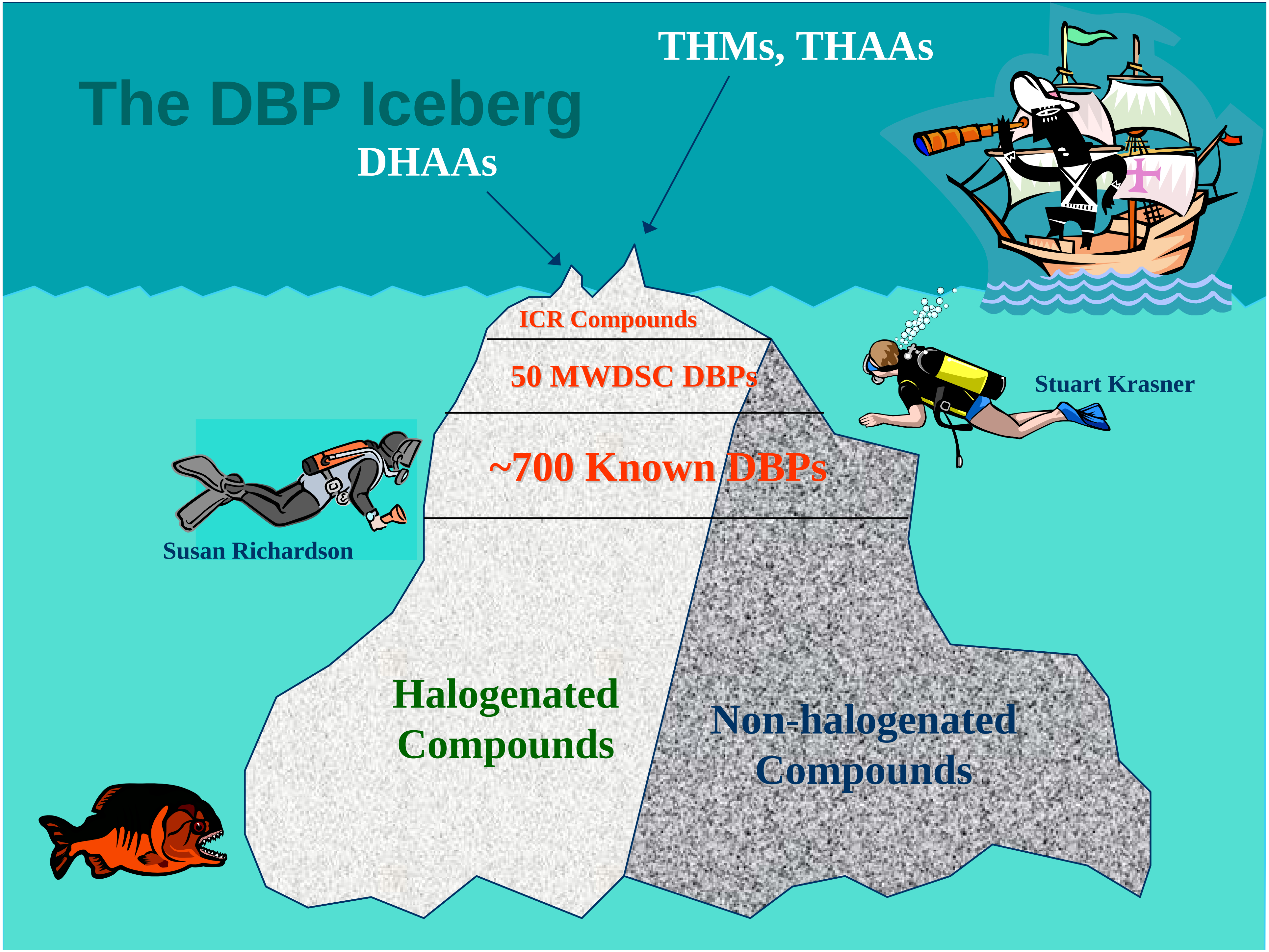
- Ranitidine (Zantac)
  - 63% conversion to NDMA
    - Schmidt et al., 2006 [WQTC]
  - Introduced in 1981, largest selling prescription drug by 1988
    - Stomach ulcers and esophageal reflux
  - Mean concentration of 3000 ng/L estimated for raw municipal WW (national average)
    - Sedlak 2005 AWWARF report
  - 450 ng/L formation in raw WW expected
  - Unknowns: how much does this persist in treatment and in the environment?

Reaction of UDMH

- DMD: dimethyldiazene
- TMT: tetramethyltetrazene
- FMMH: formaldehyde monomethylhydrazone
- FDMH: formaldehyde dimethylhydrazone
- DMC: dimethylcyanamide
- DMF: dimethylformamide

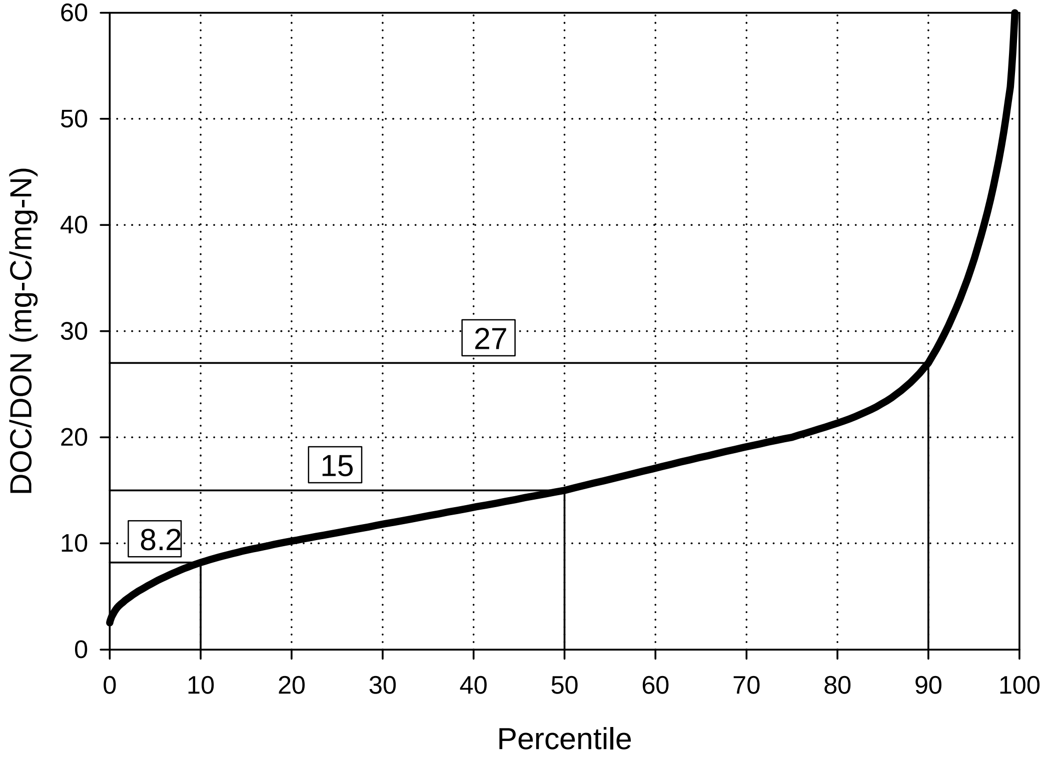


From: Mitch & Sedlak, 2002 [ES&T, 36:588]


The DBP Iceberg
THHMs, THAAs
DHAAs
ICR Compounds
50 MWDSC DBPs
~700 Known DBPs
Stuart Krasner
Susan Richardson
Halogenated Compounds
Non-halogenated Compounds

Organic Nitrogen Abundance

- Ratio to carbon
  - *Redrawn from Westerhoff & Mash, 2002*



Ranges of Org-N by types

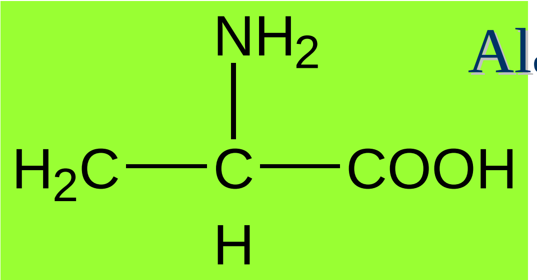
- Estimates from literature surveys

Order of magnitude estimates for organic nitrogen in surface waters (all values in µg-N/L)

Classification	50%ile	90%ile	99%ile
DON	350	800	2000
Free AA	20	50	200
Combined AA	40	100	400
Nucleic acids	20	50	200
Amino Sugars	40	100	400
Humic-N	25	200	1000
Others			

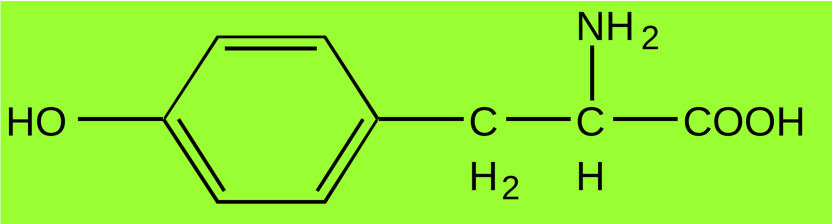
Amino Acids and Proteins

- Simple Amino Acids
  - some form THMs and HANs
  - Highest reactivity for activated AAs
    - Tyrosine & Tryptophan: activated aromatic
    - Cysteine: sulfhydryl group



Alanine

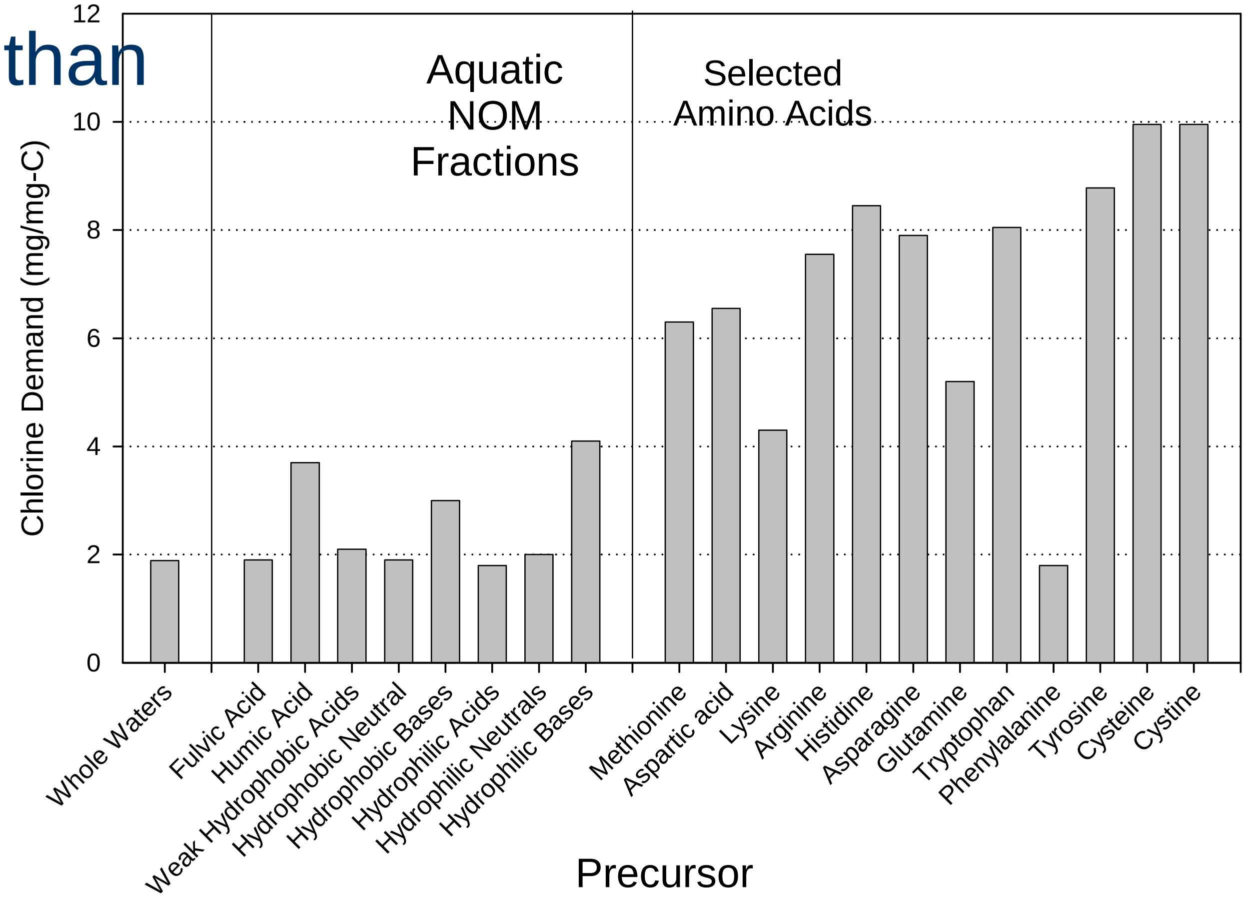
- Proteins
  - many linked AAs; relatively unreactive polypeptide bonds
  - Reactions with proteins occurs most readily on AA side chains



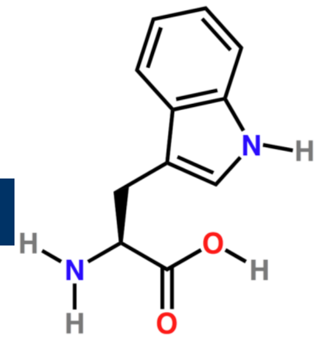
Tyrosine

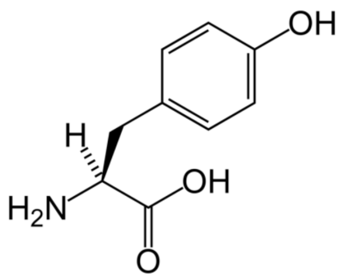
Chlorine Demand

- More reactive than most NOM

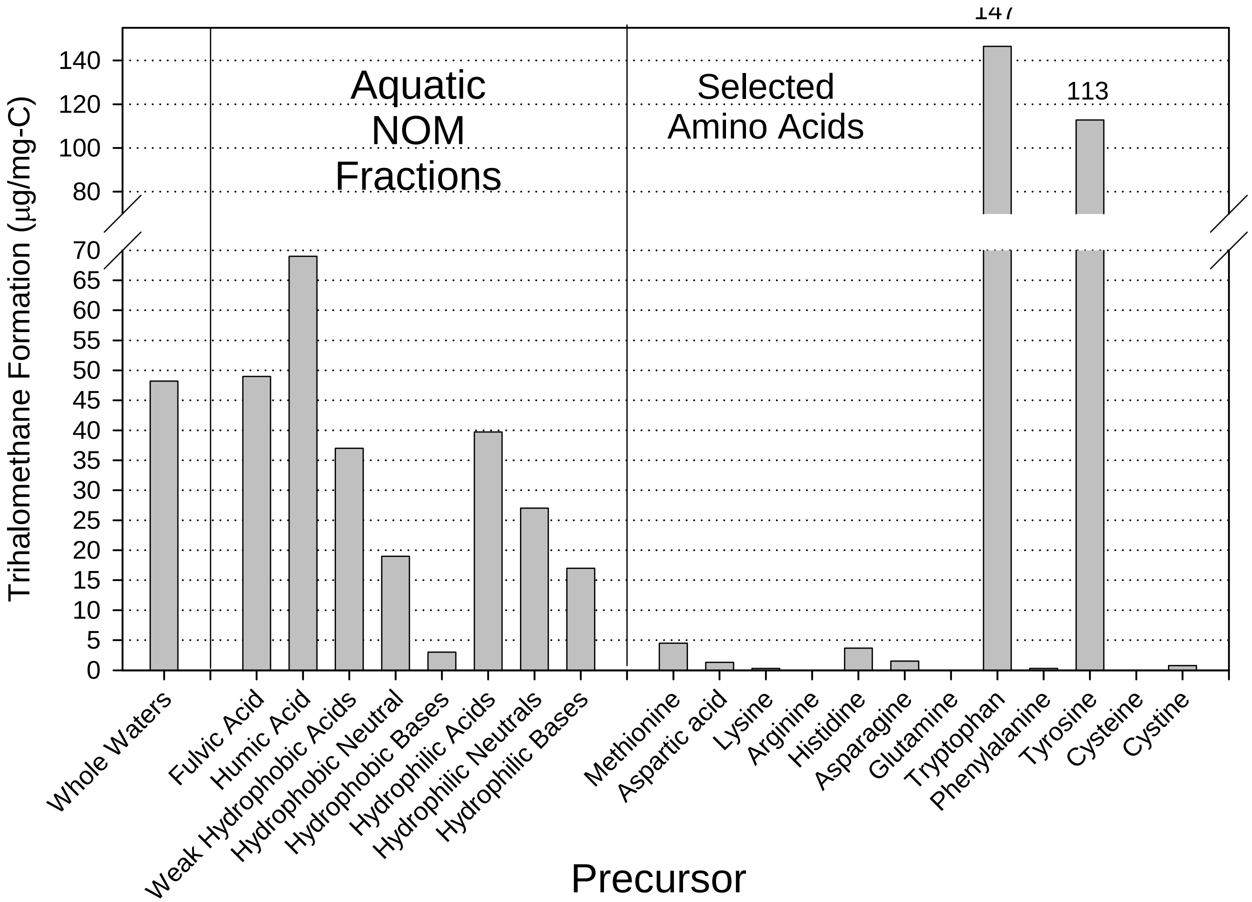


THM formation



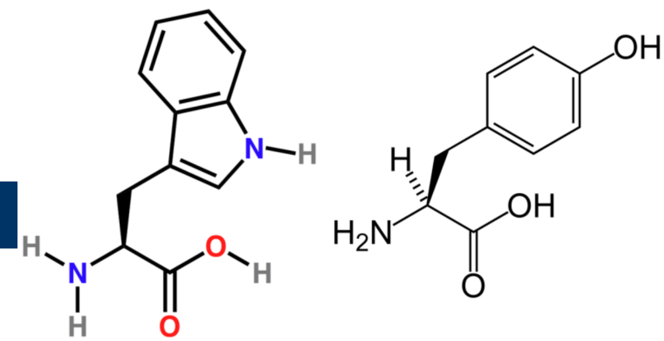


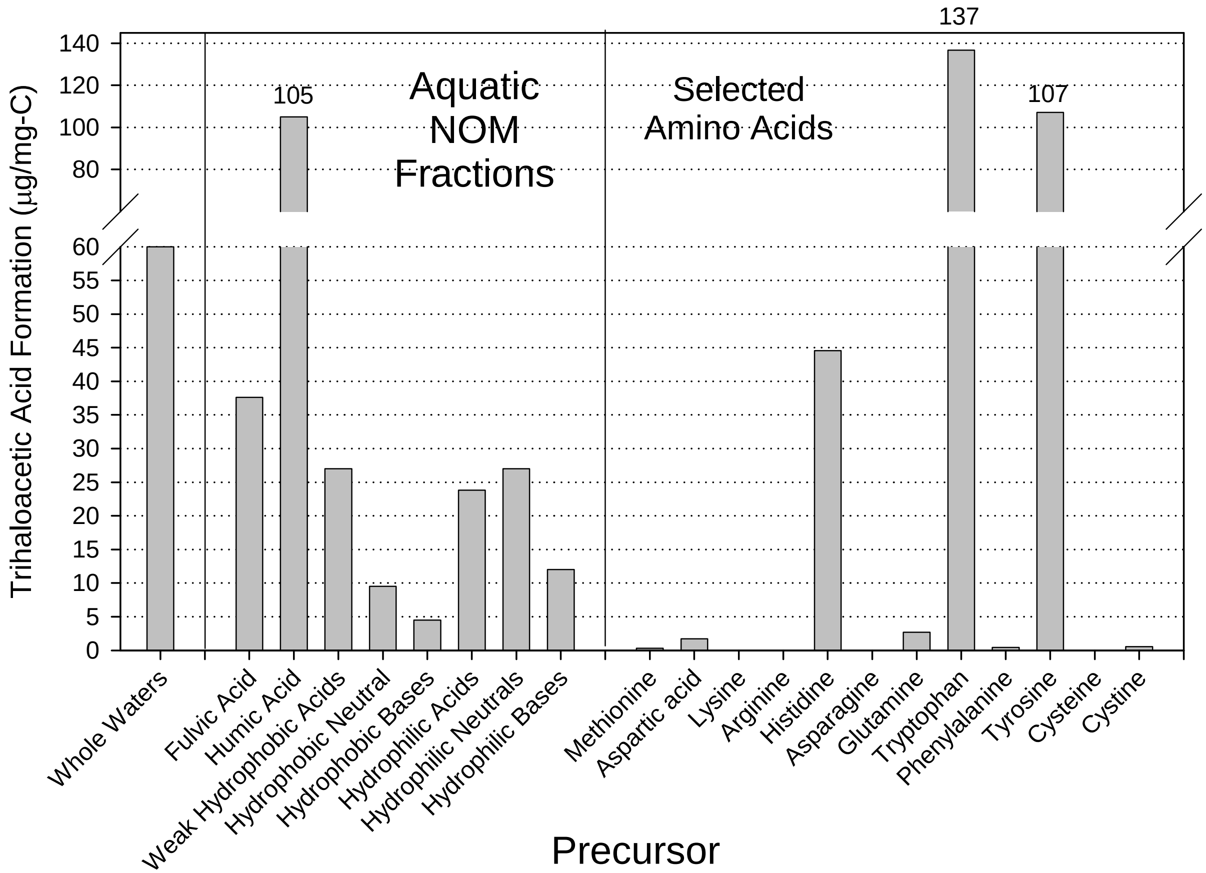
- Minor except for two
  - Tryptophan
  - Tyrosine



Trihaloacetic Acid

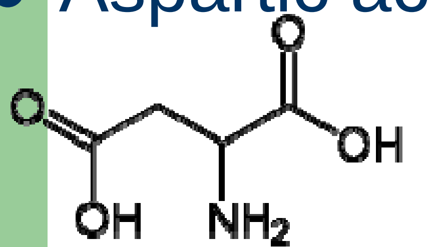
- Like THMs
  - Tryptophan
  - Tyrosine



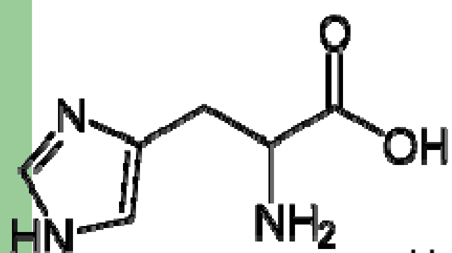


Dihaloacetic Acid

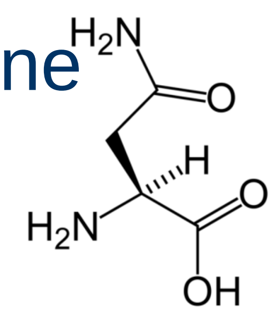
- Aspartic acid

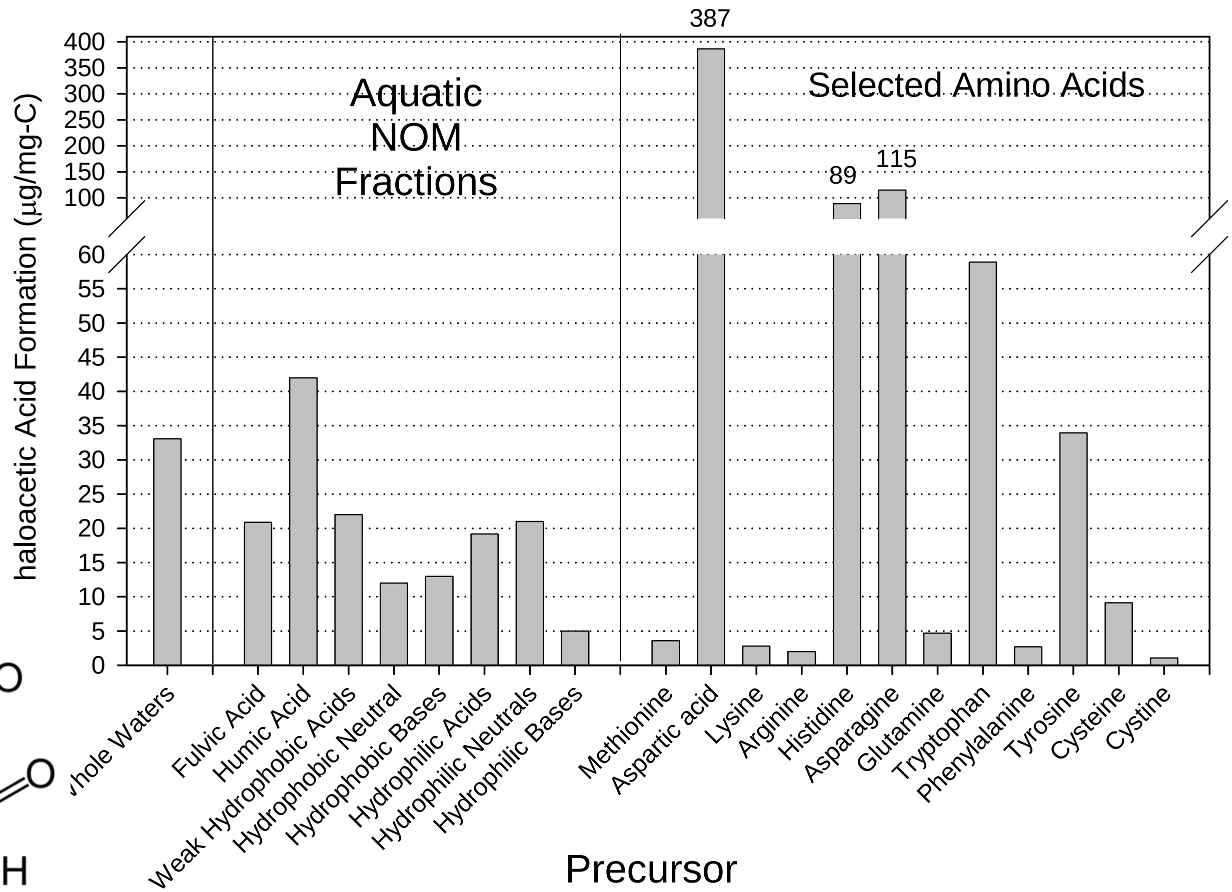


- Histidine



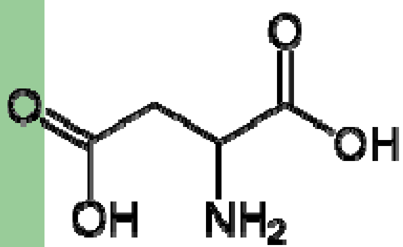
- Asparagine



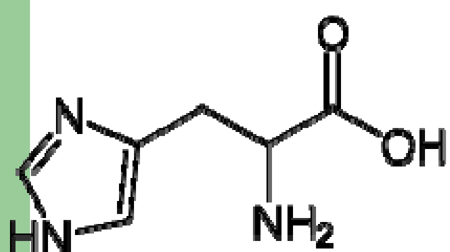


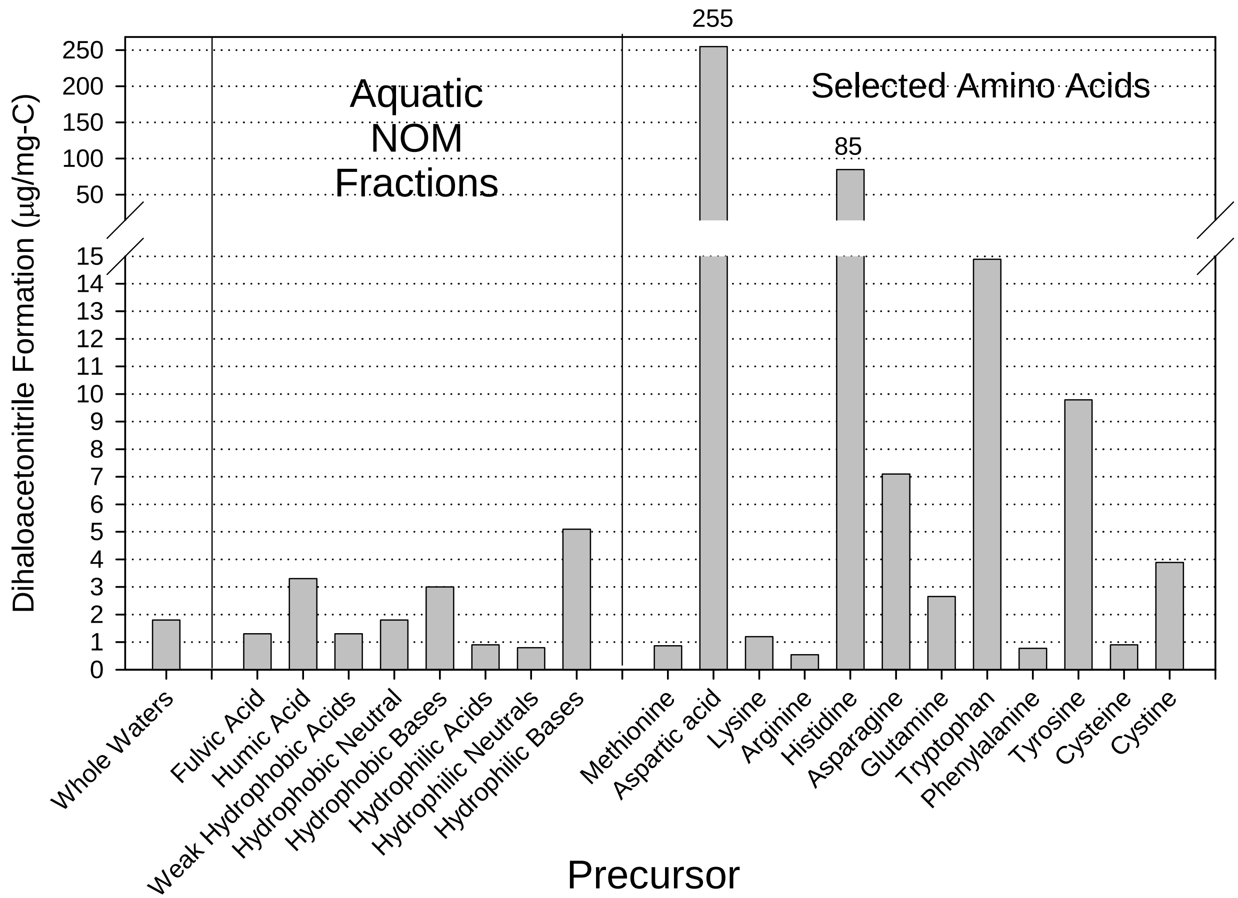
Dihaloacetonitriles

- Aspartic acid

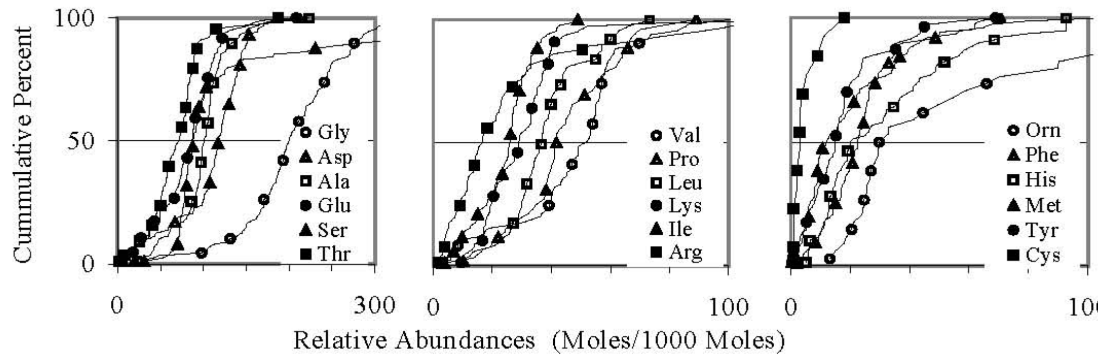


- Histidine





Amino Acids



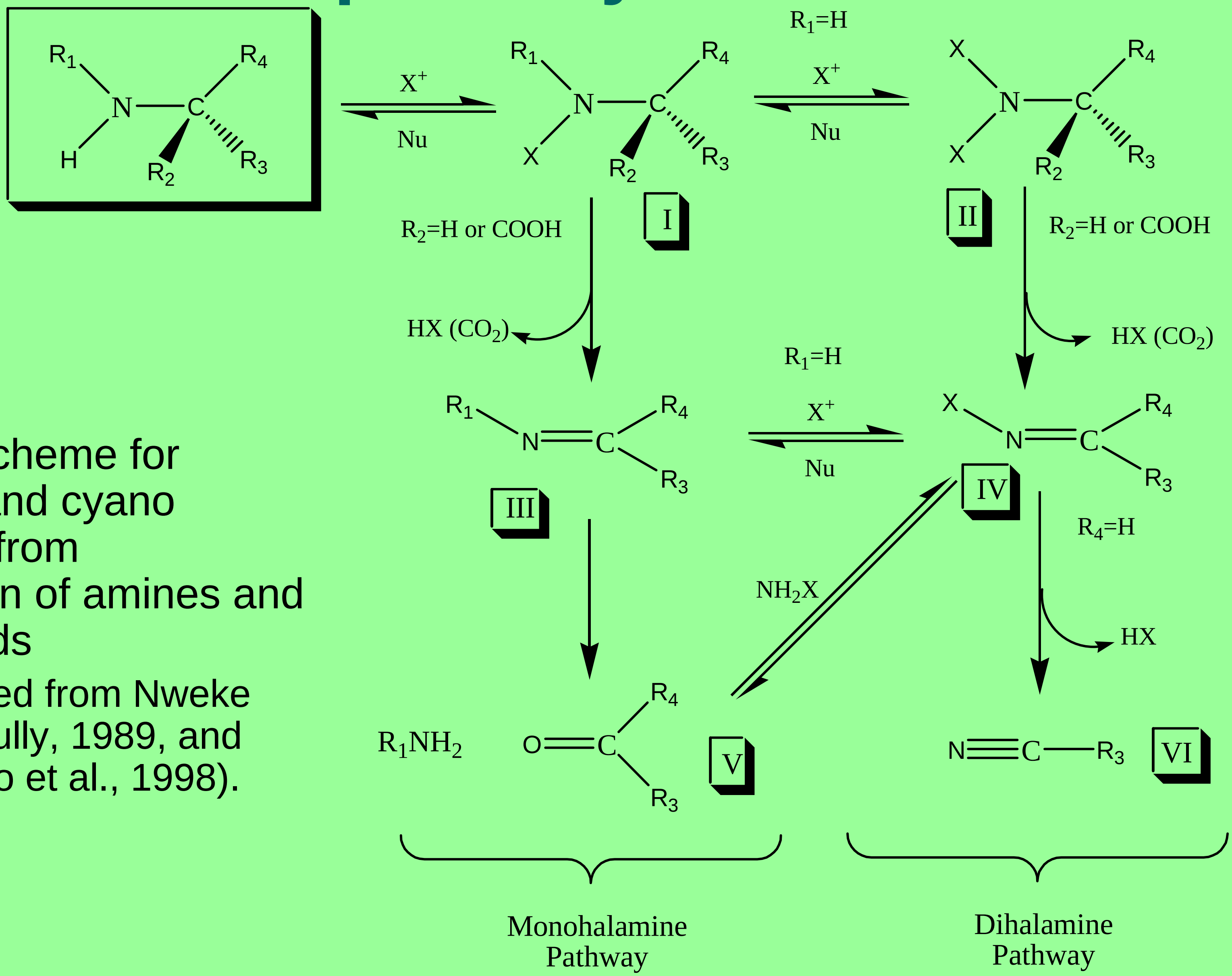
			Relative Abundances (Moles/1000 Moles)			
Amino Acid	THAA[a]	TFAA[a]	Range	Median	Mean	Std. Dev.
Glycine (Glu)	69	19	26 - 450	200	206	64
Aspartic (Asp)	69	19	20 - 212	117	113	38
Alanine (Ala)	69	18	4 - 223	102	98	37
Glutamic (Glu)	69	17	14 - 208	88	84	36
Serine (Ser)	69	19	31 - 483	88	126	94
Threonine (Thr)	69	19	2 - 187	73	70	33
Valine (Val)	69	16	2 - 145	52	49	24
Proline (Pro)	50	2	10 - 89	42	45	17
Leucine (Leu)	68	19	3 - 73	37	38	14
Ornithine (Orn)	25	9	13 - 190	31	55	45
Lysine (Lys)	69	9	9 - 149	29	31	18
Isoleucine (Ile)	67	19	4 - 49	26	24	10
Phenylalanine (Phe)	68	19	2 - 70	23	24	14
Histidine (His)	56	18	5 - 93	20	28	20
Arginine (Arg)	52	15	2 - 117	17	26	25
Tyrosine (Tyr)	61	19	0.5 - 69	15	17	14
Methionine (Met)	60	16	0.2 - 108	12	21	20
Cysteine (Cys)	13	0	1 - 18	3	5	5

			Concentration		
	Obs.	Range	Median	Mean	Std. Dev.
THAA (μmol L^{-1})	51	0.12 - 23.2	1.3	4.1	6.2
TFAA (μmol L^{-1})	21	0.05 - 1.8	0.3	0.6	0.5
% DOC as THAA	59	0.42 - 10.4	1.8	2.2	1.8
% DOC as TFAA	14	0.02 - 1.2	0.1	0.3	0.4

From:
Perdue & Ritchie, 2004

Amino Acid	AA conc (μM/mg-C)	Cl_2 Cons. (mg/mg-C)	DBP Formation (μg/mg-C)					
			TOX	THM	TCAA	DCAA	HANs	Unkn TOX
Glycine	0.030	0.0072	0.002	0.000	0.000	0.000	0.000	0.001
Alanine	0.030	0.0046	0.007	0.000	0.000	0.002	0.000	0.006
Valine	0.013	0.0022	0.009	0.002	0.001	0.002	0.000	0.005
Isoleucine	0.011	0.0018	0.004	0.000	0.000	0.002	0.000	0.001
Leucine	0.015	0.0022	0.000	0.000	0.000	0.002	0.000	-0.001
Serine	0.028	0.0083	0.001	0.000	0.000	0.000	0.000	0.001
Threonine	0.018	0.0068	0.012	0.000	0.000	0.000	0.000	0.011
Methionine	0.003	0.0010	0.004	0.001	0.000	0.001	0.000	0.003
Aspartic acid	0.026	0.0083	0.849	0.002	0.002	0.491	0.323	0.367
Glutamic acid	0.026	0.0036	0.004	0.000	0.002	0.002	0.000	0.001
Lysine	0.004	0.0013	0.001	0.000	0.000	0.001	0.000	0.000
Ornithine	0.005	0.0017	0.011	0.002	0.000	0.000	0.000	0.009
Arginine	0.019	0.0104	0.032	0.000	0.000	0.003	0.001	0.030
Histidine	0.007	0.0040	0.153	0.002	0.021	0.042	0.040	0.084
Asparagine	0.001	0.0004	0.012	0.000	0.000	0.005	0.000	0.009
Glutamine	0.001	0.0004	0.000	0.000	0.000	0.000	0.000	0.000
Tryptophan	0.006	0.0068	0.432	0.124	0.115	0.050	0.013	0.193
Phenylalanine	0.009	0.0017	0.000	0.000	0.000	0.003	0.001	-0.002
Tyrosine	0.006	0.0053	0.257	0.069	0.065	0.021	0.006	0.138
Total FAA	**0.259**	**0.0780**	**1.789**	**0.201**	**0.207**	**0.626**	**0.385**	**0.856**
Upper Limit	**3.454**	**1.0403**	**23.855**	**2.677**	**2.765**	**8.340**	**5.131**	**11.418**
Whole Waters		1.89	185	48.2	60	33.1	1.8	129.7
Total FAA		**4.1%**	**1.0%**	**0.4%**	**0.3%**	**1.9%**	**21.4%**	**0.7%**
Upper Limit		**55.0%**	**12.9%**	**5.6%**	**4.6%**	**25.2%**	**285.0%**	**8.8%**

Degradation pathways



- General scheme for carbonyl and cyano formation from chlorination of amines and amino acids
  - (adapted from Nweke and Scully, 1989, and Armesto et al., 1998).

N-chloro-organics

- Reactions of chlorine with organic amines
  - Primary amines

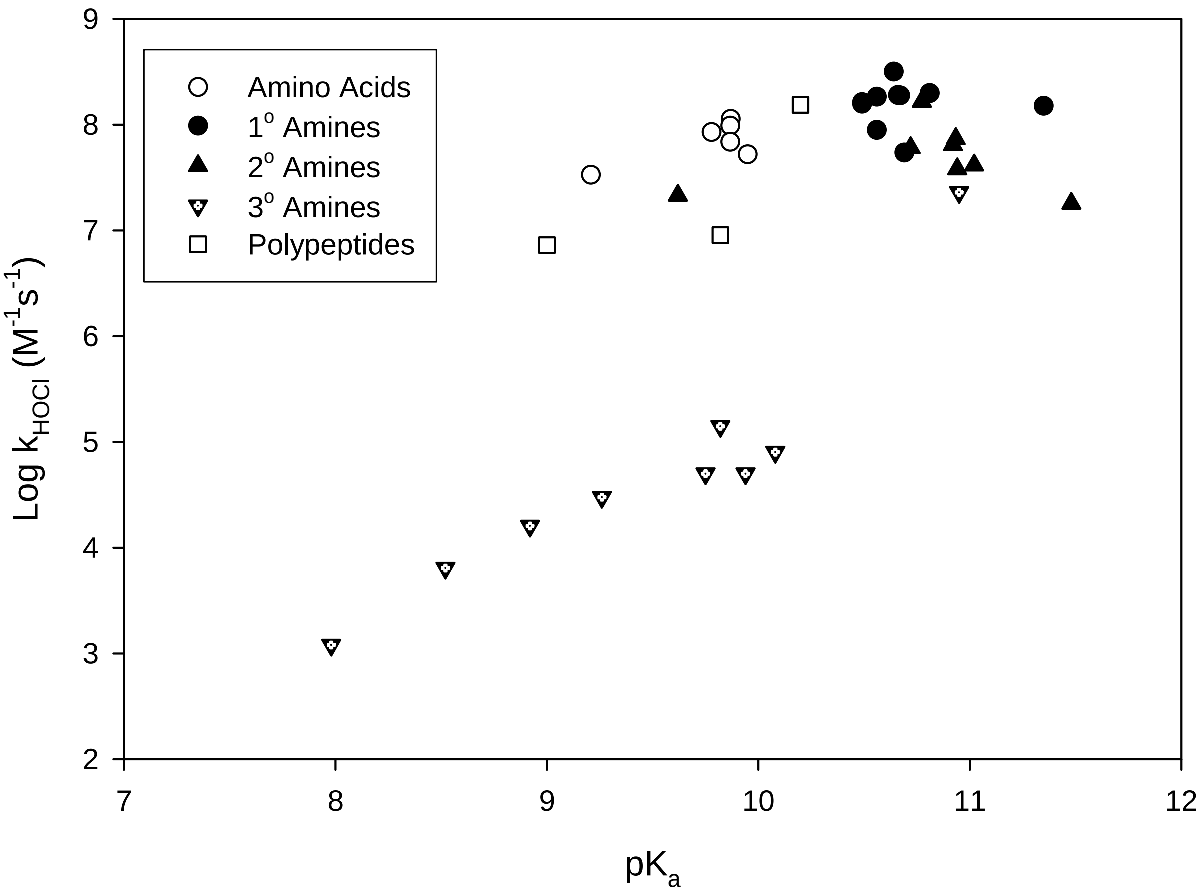
$$R-NH_2 \xrightarrow{HOCl} R-NHCl \xrightarrow{HOCl} R-NCl_2$$

  - Secondary amines

$$R_2-NH \xrightarrow{HOCl} R_2-NCl$$

- Inorganic chloramines can transfer their active chlorine in a similar fashion

LFERs



- **Relationship between basicity and 2^nd order rate constants for reaction of HOCl with N-compounds**
  - ***Data Sources:*** Friend, 1956; Hussain et al., 1972; Isaac et al., 1983; Armesto et al., 1993; Armesto et al., 1994; Antelo et al., 1995; Abia et al., 1998

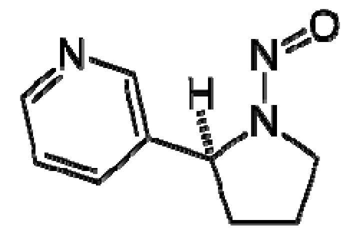
Degradation of Organic Chloramines

Parent Amine	k_{obs} (s^{-1})	$t_{½}$ (min)
Alanine	1.3E-04	86
Glycine	1.4E-06	8400
Histidine	2.7E-04	43
Leucine	1.6E-04	72
Phenylalanine	2.2E-04	52
Serine	2.4E-04	49
Creatinine	3.5E-06	3300
Glycine N acetyl	6.0E-07	19000
Glycine ethyl ester	2.3E-04	50
Glycylglycine	1.0E-05	1100
Sarcosine	5.3E-05	210

Analysis of Organic N-chloramines

- Approach
  - Seems well suited to LC
  - Prior efforts with GC were not very successful
    - e.g., tosyl derivatization
- Proposal
  - Fast analysis with UPLC
  - Parallel detection and analysis by
    - Post-column reaction with I and absorbance
    - LC/MS/MS

Conclusions: from QSTR



		Research needs	
Group	**Example**	**Occurrence**	**Toxicology**
Haloquinones	2,6-dichloro-3-methyl-1,2-benzoquinone (DMBQ)	1	2
Organic N-haloamines	**Prioritize on range of stabilities and mutagenic activity**	**2**	**1**
Alkaloidal nitrosamines	**N-nitrosonornicotine 1-N-oxide**	**1**	**2**
Cyclopentenoic acids & MX-related	3,5-dichloro—1-hydroxy-4-ketocyclopent-2-enoic acid CMCF	1 2	2 1
Halonitriles	**2,3-Dichloropropenal (Carc)** **2,3-dibromopropionitrile (DT)**	**1**	**1**

Summary

- There is a broad range of nitrogenous organic compounds in natural waters that are reactive with chlorine and produce both regulated and non-regulated DBPs
- Amino acids are generally reactive
  - High Chlorine demand
  - Very high DHAN formation
  - Moderate to high DiHAAs; low to moderate THMs & TriHAAs
- Proteins
  - Rapid degradation at reactive sites
  - Then slow degradation, leading to similar DBP profiles
- Toxic compounds that may be regulated could include
  - Organic chloramines
  - Halonitriles
  - Alkaloidal nitrosamines

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The End

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