CEE 690K
ENVIRONMENTAL REACTION KINETICS

Lecture #16

Case Study: Nitrogenous Disinfection Byproducts
Primary Literature as noted

PROTEINS AS IMPORTANT REACTIVE COMPOUNDS IN DRINKING WATER TREATMENT

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MA WRCC 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

Trihaloacetic 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
  - Cyanogen Halides
  - Haloacetonitriles
  - Halonitromethanes

- Major types:
  - Cyanogen Halides
  - Haloacetonitriles
  - Halonitromethanes

- Special focus on these compounds because of large data set

HCN & CNBr

Dichloroacetonitrile (DCAN)

Bromochloroacetonitrile (BCAN)

Dibromoacetonitrile (DBAN)

Chloropicrin (CHP)

Trichloroacetonitrile (TCAN)

9 species
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

**CHO Cell Cytotoxicity as %C½ Values (~LC50)**

Log Molar Concentration (72 h Exposure)
Quantitative Structure-Toxicity Models

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

![Bar chart showing the distribution of estimated chronic LOAELs, mg/kg day⁻¹ for halogenated DBPs and halonitriles.]

Distribution of estimated chronic LOAELs, mg/kg day⁻¹

Chemistry of the end products

**DCAN**

![Graph showing the chemistry of DCAN over time with different chlorine doses.]

Surface Water

Dichloroacetamide (μg/L)

Chlorine Dose:
- 2.5 mg/L
- 5 mg/L
- 10 mg/L
DHAN

- Key intermediate
- Concentrations are well known

Proposed Rate Law for DCAN

- Hydrolysis and oxidation

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

- $k_1 = 1.78 \times 10^{-7}$ ± $0.35 \times 10^{-7}$ (s$^{-1}$)
- $k_2 = 3.42$ ± $0.31$ (M$^{-1}$s$^{-1}$)
- $k_3 = 1.30 \times 10^{-1}$ ± $0.08 \times 10^{-1}$ (M$^{-1}$s$^{-1}$)
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:
  - Measureable by GC
  - Haloacetonitriles $\Rightarrow$ Haloacetamides $\Rightarrow$ Haloacetic Acids

**Haloacetamides**

Chlorine $\rightarrow$ N-Halogenated Forms $\rightarrow$ Combined (c) $\rightarrow$ Total (t)

**DCAD Stability**

- Chlorine Residual (mg/L)
- pH

**DCAD Half-life**

- 10 Minutes
- 1 Hour
- 8 Hours
- 1 Day
- 3 Days
- 1 Week
- 3 Weeks

**Stable**

- HOCl

**Reducing Conditions**

- OH$^-$
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

[Diagram of the pathway to NDMA showing the interactions between dichloramine, oxygen, and the formation of nitrosodimethylamine (NDMA).]
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?

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### Reaction of UDMH

- **Abbreviations**
  - 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

THMs, THAAs

DHAAs

ICR Compounds

50 MWDSC DBPs

~700 Known DBPs

Halogenated Compounds

Non-halogenated Compounds

Organic Nitrogen Abundance

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

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)

<table>
<thead>
<tr>
<th>Classification</th>
<th>50thile</th>
<th>90thile</th>
<th>99thile</th>
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<tbody>
<tr>
<td>DON</td>
<td>350</td>
<td>800</td>
<td>2000</td>
</tr>
<tr>
<td>Free AA</td>
<td>20</td>
<td>50</td>
<td>200</td>
</tr>
<tr>
<td>Combined AA</td>
<td>40</td>
<td>100</td>
<td>400</td>
</tr>
<tr>
<td>Nucleic acids</td>
<td>20</td>
<td>50</td>
<td>200</td>
</tr>
<tr>
<td>Amino Sugars</td>
<td>40</td>
<td>100</td>
<td>400</td>
</tr>
<tr>
<td>Humic–N</td>
<td>25</td>
<td>200</td>
<td>1000</td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
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</table>

Amino Acids and Proteins

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

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

![Alanine](image1)

![Tyrosine](image2)
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

From: Perdue & Ritchie, 2004
<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>AA conc. (µM/mg-C)</th>
<th>Cl₂ Cons. (mg/mg-C)</th>
<th>DBP Formation (µg/mg-C)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>TOX</td>
</tr>
<tr>
<td>Glycine</td>
<td>0.030</td>
<td>0.0072</td>
<td>0.002</td>
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<tr>
<td>Alanine</td>
<td>0.030</td>
<td>0.0046</td>
<td>0.007</td>
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<tr>
<td>Valine</td>
<td>0.013</td>
<td>0.0022</td>
<td>0.009</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>0.011</td>
<td>0.0018</td>
<td>0.004</td>
</tr>
<tr>
<td>Leucine</td>
<td>0.015</td>
<td>0.0022</td>
<td>0.000</td>
</tr>
<tr>
<td>Serine</td>
<td>0.028</td>
<td>0.0063</td>
<td>0.001</td>
</tr>
<tr>
<td>Threonine</td>
<td>0.018</td>
<td>0.0068</td>
<td>0.012</td>
</tr>
<tr>
<td>Methionine</td>
<td>0.003</td>
<td>0.0010</td>
<td>0.004</td>
</tr>
<tr>
<td>Aspartic acid</td>
<td>0.026</td>
<td>0.0083</td>
<td>0.849</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td>0.026</td>
<td>0.0036</td>
<td>0.004</td>
</tr>
<tr>
<td>Lysine</td>
<td>0.004</td>
<td>0.0013</td>
<td>0.011</td>
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<tr>
<td>Ornithine</td>
<td>0.005</td>
<td>0.0017</td>
<td>0.011</td>
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<tr>
<td>Arginine</td>
<td>0.019</td>
<td>0.0104</td>
<td>0.032</td>
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<tr>
<td>Histidine</td>
<td>0.007</td>
<td>0.0040</td>
<td>0.153</td>
</tr>
<tr>
<td>Asparagine</td>
<td>0.001</td>
<td>0.0004</td>
<td>0.012</td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.001</td>
<td>0.0004</td>
<td>0.000</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>0.006</td>
<td>0.0068</td>
<td>0.432</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>0.009</td>
<td>0.0017</td>
<td>0.000</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>0.006</td>
<td>0.0053</td>
<td>0.257</td>
</tr>
<tr>
<td>Total FAA</td>
<td>0.259</td>
<td>0.0780</td>
<td>1.789</td>
</tr>
<tr>
<td>Whole Waters</td>
<td>1.69</td>
<td>185</td>
<td>48.2</td>
</tr>
<tr>
<td>Total FAA</td>
<td>4.1%</td>
<td>1.0%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Upper Limit</td>
<td>55.0%</td>
<td>12.9%</td>
<td>5.6%</td>
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</table>

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
  - Secondary amines

  \[ R - NH_2 \rightarrow R - NHCl \rightarrow R - NCl_2 \]

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

LFERs

- Relationship between basicity and 2nd 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

<table>
<thead>
<tr>
<th>Parent Amine</th>
<th>$k_{obs}$ ($s^{-1}$)</th>
<th>$t_1/2$ (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine</td>
<td>1.3E-04</td>
<td>86</td>
</tr>
<tr>
<td>Glycine</td>
<td>1.4E-06</td>
<td>8400</td>
</tr>
<tr>
<td>Histidine</td>
<td>2.7E-04</td>
<td>43</td>
</tr>
<tr>
<td>Leucine</td>
<td>1.6E-04</td>
<td>72</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>2.2E-04</td>
<td>52</td>
</tr>
<tr>
<td>Serine</td>
<td>2.4E-04</td>
<td>49</td>
</tr>
<tr>
<td>Creatinine</td>
<td>3.5E-06</td>
<td>3300</td>
</tr>
<tr>
<td>Glycine N acetyl</td>
<td>6.0E-07</td>
<td>19000</td>
</tr>
<tr>
<td>Glycine ethyl ester</td>
<td>2.3E-04</td>
<td>50</td>
</tr>
<tr>
<td>Glycylglycine</td>
<td>1.0E-05</td>
<td>1100</td>
</tr>
<tr>
<td>Sarcosine</td>
<td>5.3E-05</td>
<td>210</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Group</th>
<th>Example</th>
<th>Occurrence</th>
<th>Toxicology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloquinones</td>
<td>2,6-dichloro-3-methyl-1,2-benzoquinone (DMBQ)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Organic N-haloamines</td>
<td>Prioritize on range of stabilities and mutagenic activity</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Alkaloidal nitrosamines</td>
<td>N-nitrosonomicotine 1-N-oxide</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Cyclopentenonic acids &amp; MX-related</td>
<td>3,5-dichloro—1-hydroxy-4-ketocyclopent-2-enoic acid CMCF</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Halonitriles</td>
<td>2,3-Dichloropropenal (Carc)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2,3-dibromopropionitrile (DTC)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

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
☐ To next lecture