Iodo-DBP Formation from the Reaction of Chlorinated Oxidants with X-Ray Contrast Media in the Presence of Natural Organic Matter

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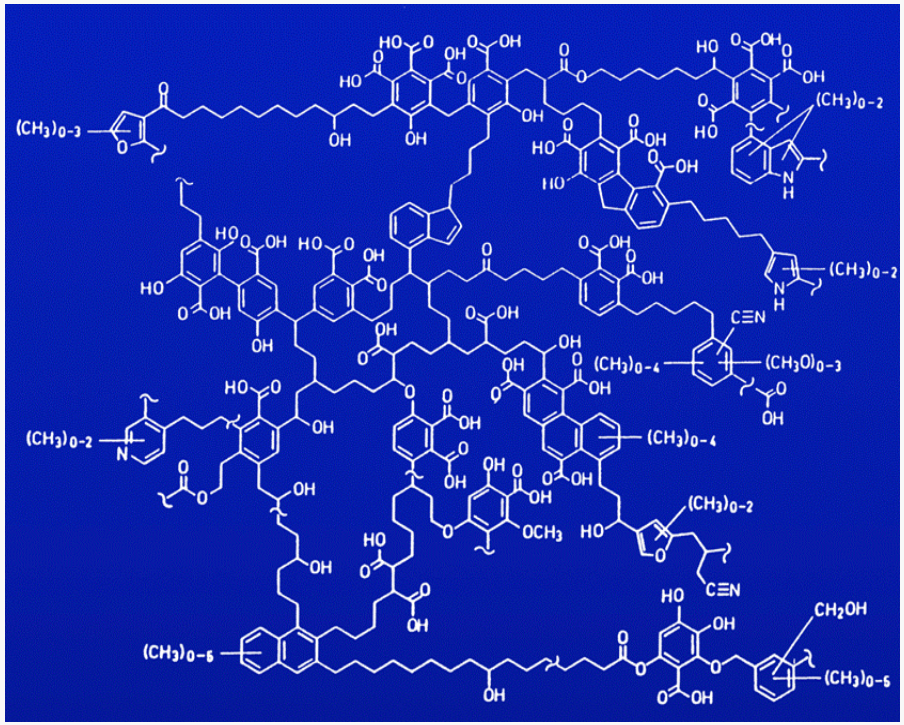
Iodo-DBP Occurrence Study

	Iodide (µg/L)	Sum iodo-acids (µg/L)	Sum iodo-THMs (µg/L)
Plant 2	1.0	0.37	4.9
Plant 4	ND	0.10	1.2
Plant 11	1.5	0.21	2.3
Plant 15	ND	0.17	2.4

Detection limit = 0.13 µg/L

Richardson et al., *Environ. Sci. Technol.* 2008, 42, 8330-8338.

Typically, DBPs formed by reaction of disinfectants with NOM and Br/I



NOM

$$+\ I^- \xrightarrow[NH_2Cl]{HOCl} \text{Iodo-DBPs}$$

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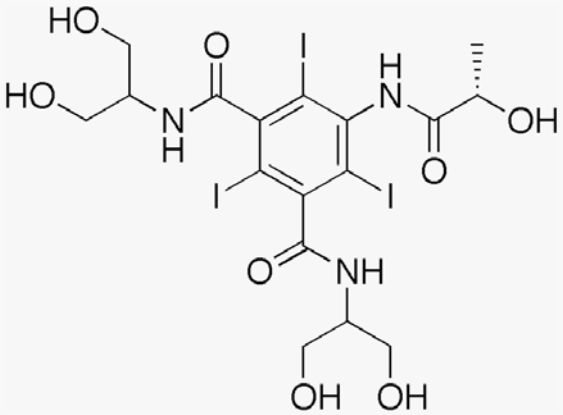
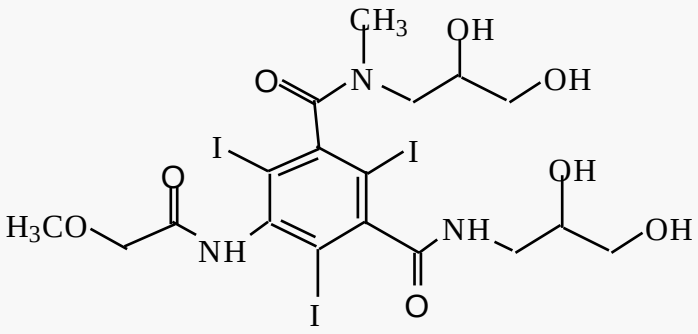
What about other sources of iodine?

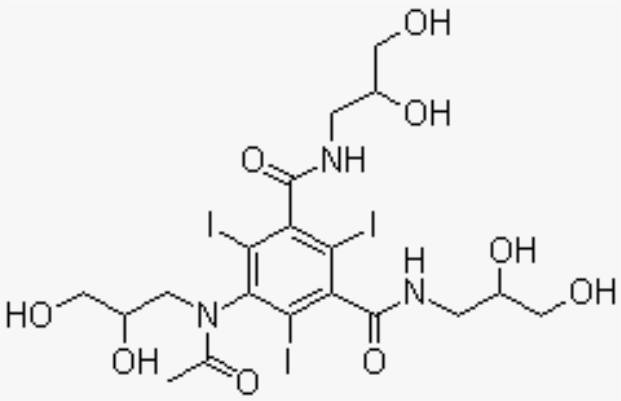
Iodinated X-ray Contrast Media (ICM)



Iopamidol

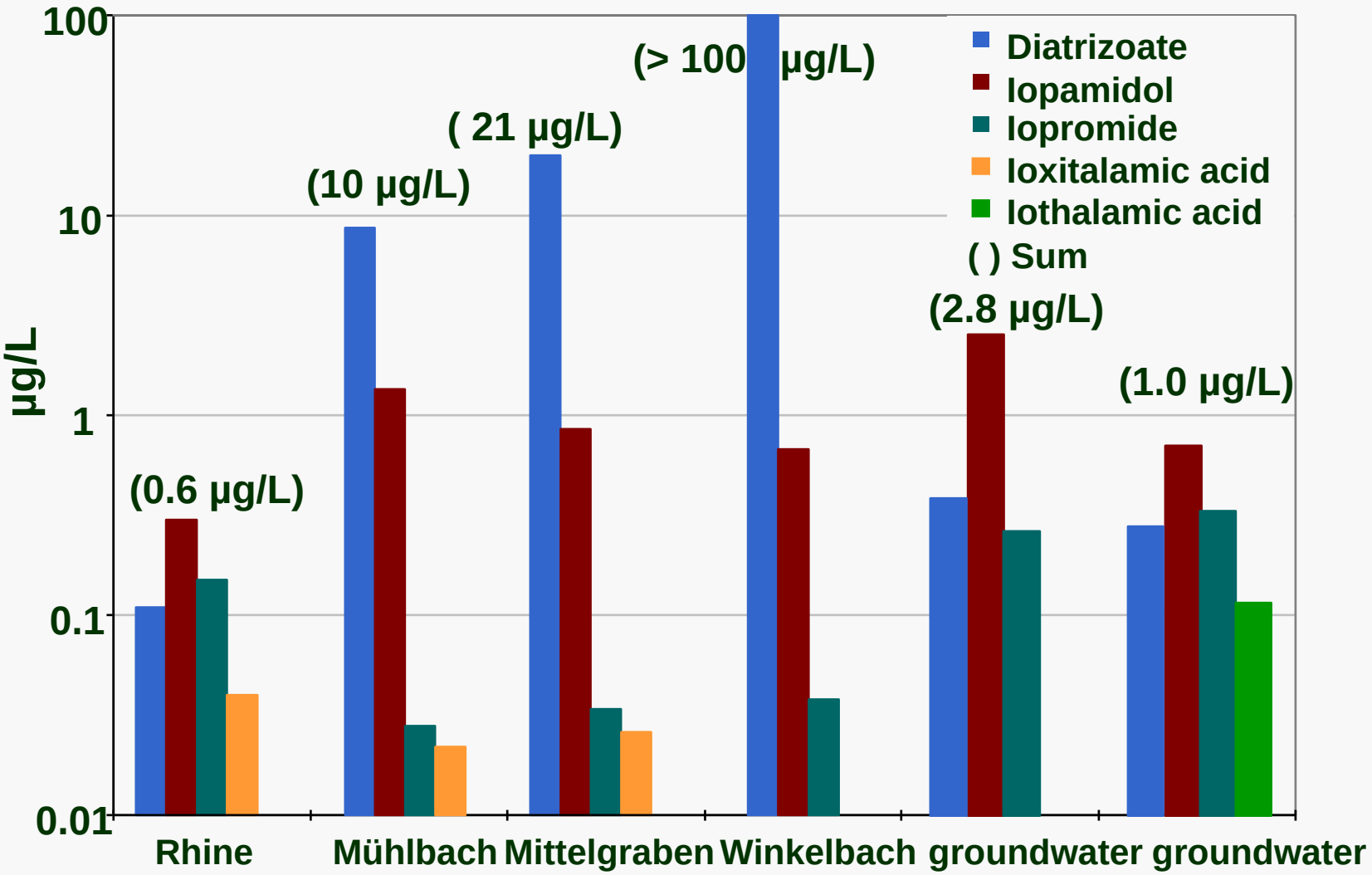


Iopromide



Iohexol

ICM concentrations: rivers, creeks and ground water



Ternes & Hirsch, *Environ. Sci. Technol*. (2000) 34, 2741-2748

ICM in U.S. Drinking Water Sources (ng/L)

	Iopamidol	Iomeprol	Iopromide	Iohexol	Diatrizoate
Plant 1	11	ND	ND	ND	ND
Plant 2	510	ND	24	120	93
Plant 4	110	ND	6	49	ND
Plant 10	ND	ND	ND	ND	ND
Plant 11	100	ND	ND	85	ND
Plant 12	280	ND	ND	120	ND
Plant 13	ND	ND	ND	ND	ND
Plant 15	2700	ND	25	ND	ND
Plant 17	ND	ND	ND	ND	ND
Plant 19	ND	ND	ND	ND	ND

Courtesy of Thomas Ternes, Federal Institute of Hydrology, Germany
ICM measured using LC/ESI-MS/MS; DLs = 5-20 ng/L

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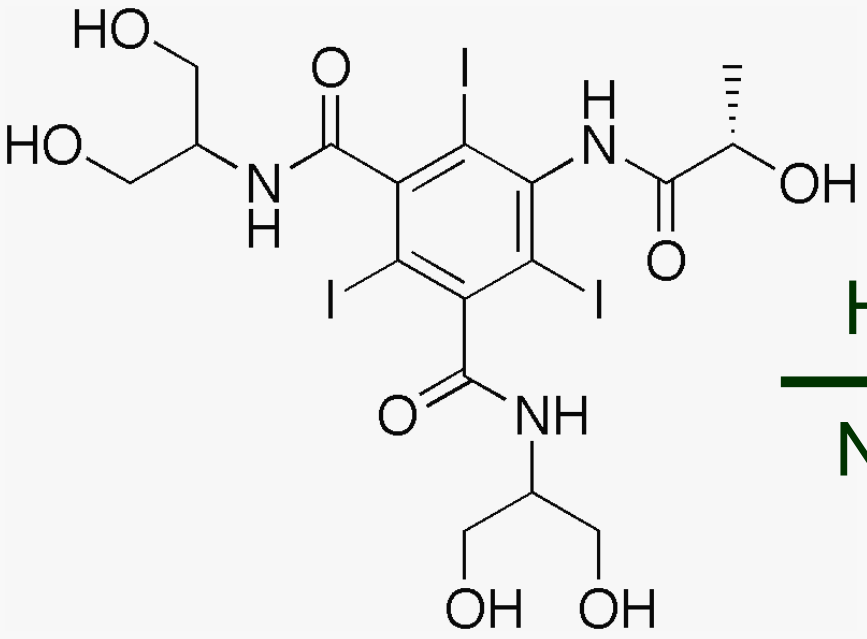
Do iodinated X-ray contrast media form iodo-DBPs?



Iopamidol

HOCl

NH_2Cl

Iodo-DBPs

??

Controlled Laboratory Reactions

Experiments

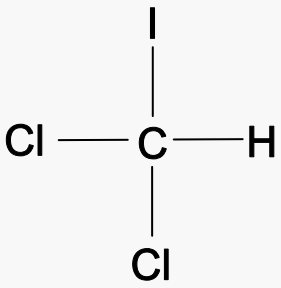
- React ICM with HOCl, NH_2Cl (with and without NOM)
- 3 pHs
- Follow formation of iodo-DBPs
- Follow decay of ICM and identify reaction products and intermediates
- Compare ICM reactions to reactions with native iodide
- Measure genotoxicity of chlorinated water containing ICM and compare to chlorinated water without ICM and untreated source water containing ICM

Methods

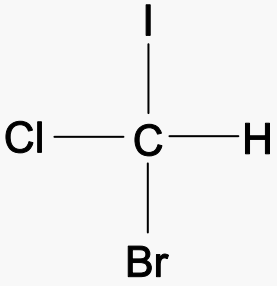
- Iodo-THMs: GC/EI-MS
- Iodo-Acids: GC/NCI-MS (with derivatization)
- Iodate: IC
- Iopamidol (and other ICM): LC, LC/MS/MS
- Larger MW products and intermediates: LC/MS/MS
- Chlorine: DPD-FAS titration
- Genotoxicity: Chinese hamster ovary cells, single cell gel electrophoresis

Cristal and Steve

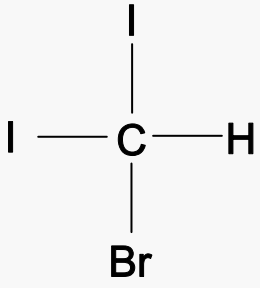
Iodo-DBPs



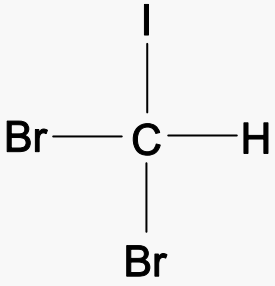
Dichloroiodo-methane



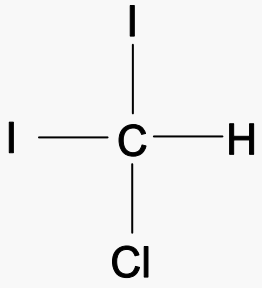
Bromochloroiodo-methane



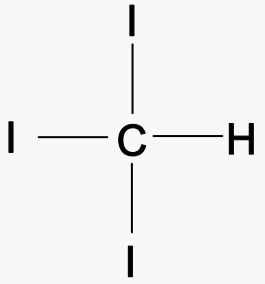
Bromodiiodo-methane



Dibromoiodo-methane

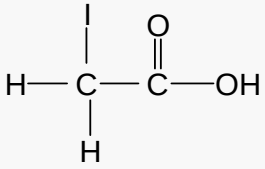


Chlorodiiodo-methane

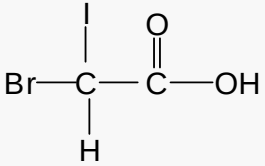


Iodoform

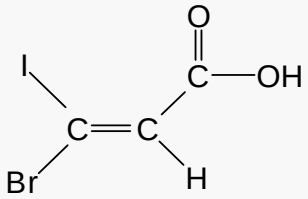
Iodo-THMs



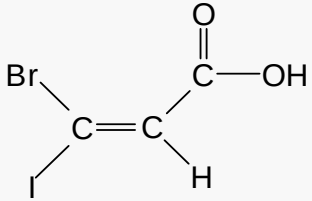
Iodoacetic acid



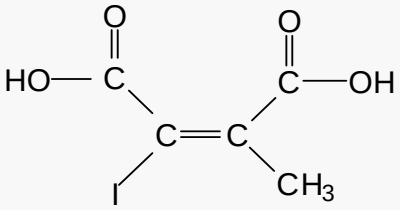
Bromoiodoacetic acid



(*Z*)-3-Bromo-3-iodopropenoic acid



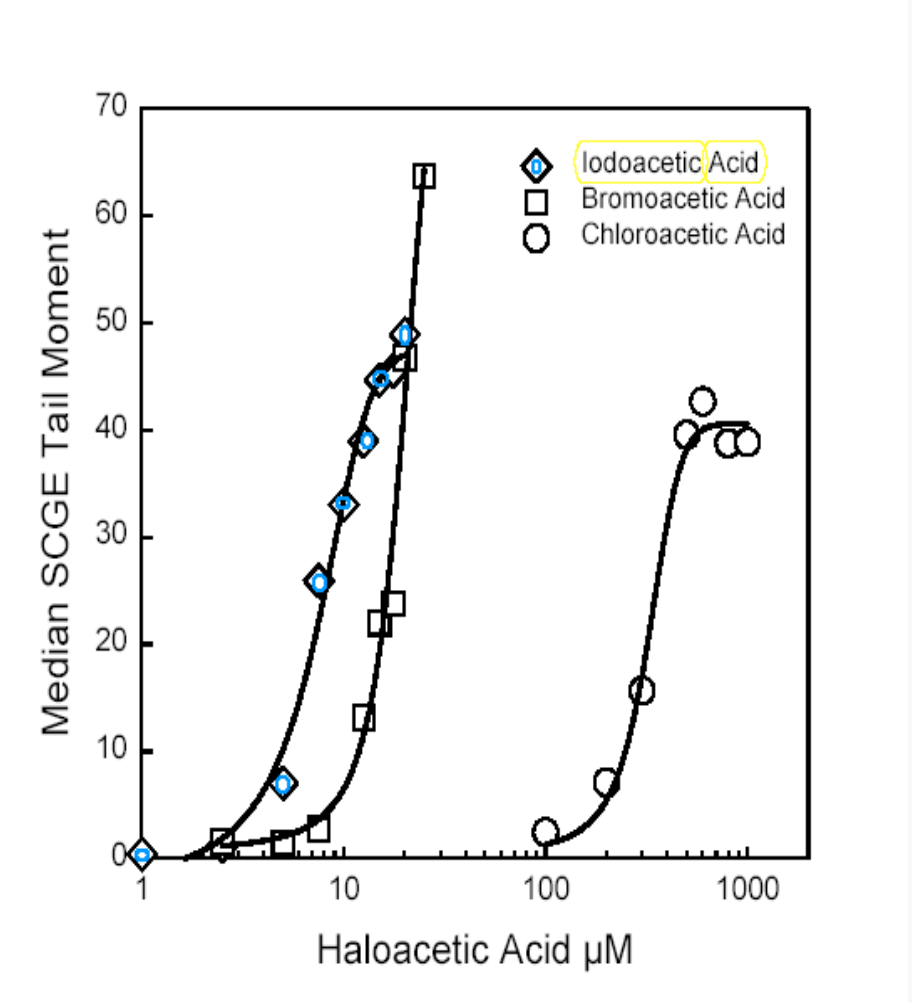
(*E*)-3-Bromo-3-iodopropenoic acid



(*E*)-2-Iodo-3-methylbutenedioic acid

Iodo-Acids

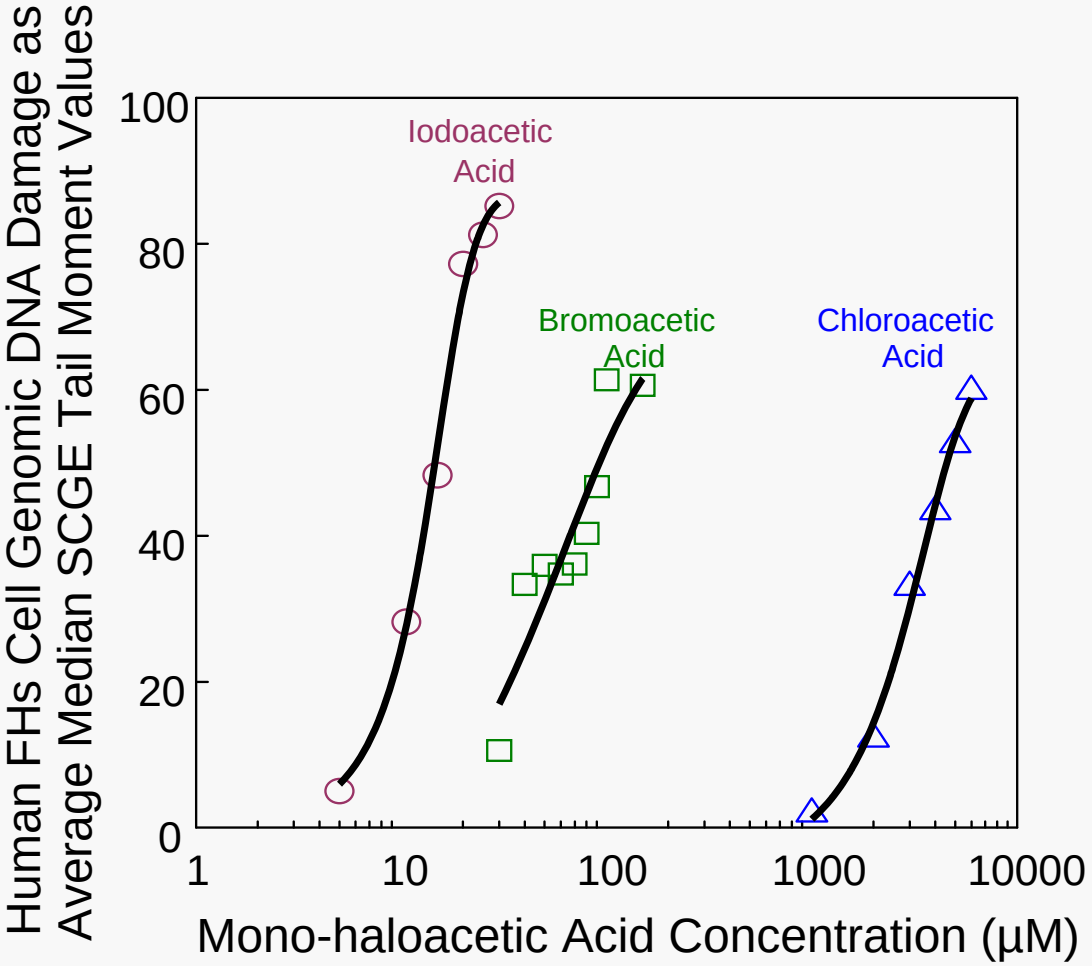
Genotoxicity of Iodoacetic Acid



Plewa et al., *Environ. Sci. Technol*. 2004

IA also caused developmental effects in mouse embryos (Hunter et al., 1995)

Genomic DNA Damage in Normal, Non-Transformed Human Fetal Intestinal Cells



Courtesy of Michael Plewa, Univ. Illinois

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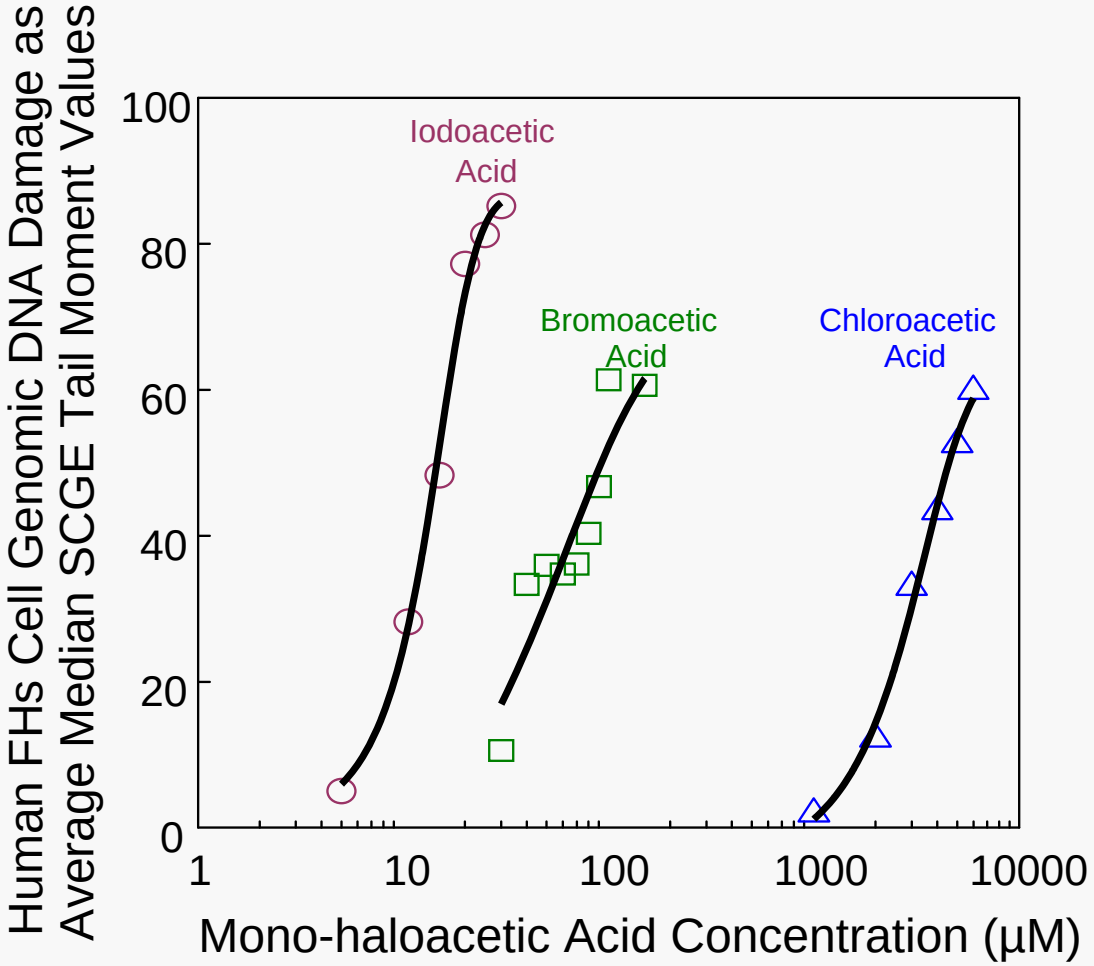
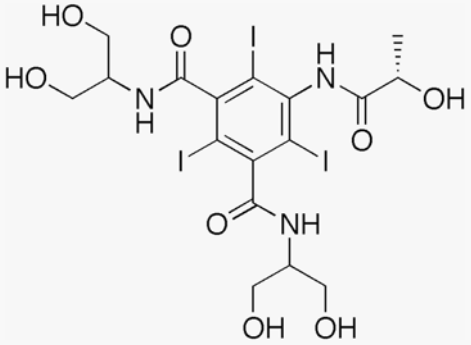


In addition, iodo-THMs are cytotoxic
Only one iodo-THM (chlorodiiodomethane) genotoxic

Results

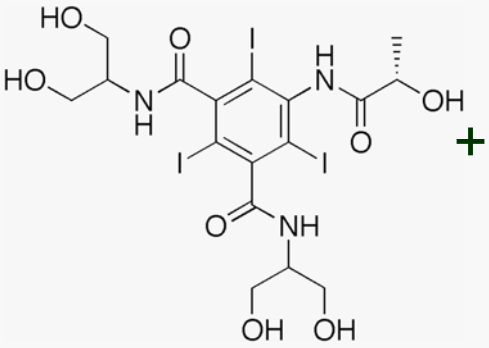


Iopamidol

HOCl

NH_2Cl

Iodo-DBPs



Iopamidol + NOM

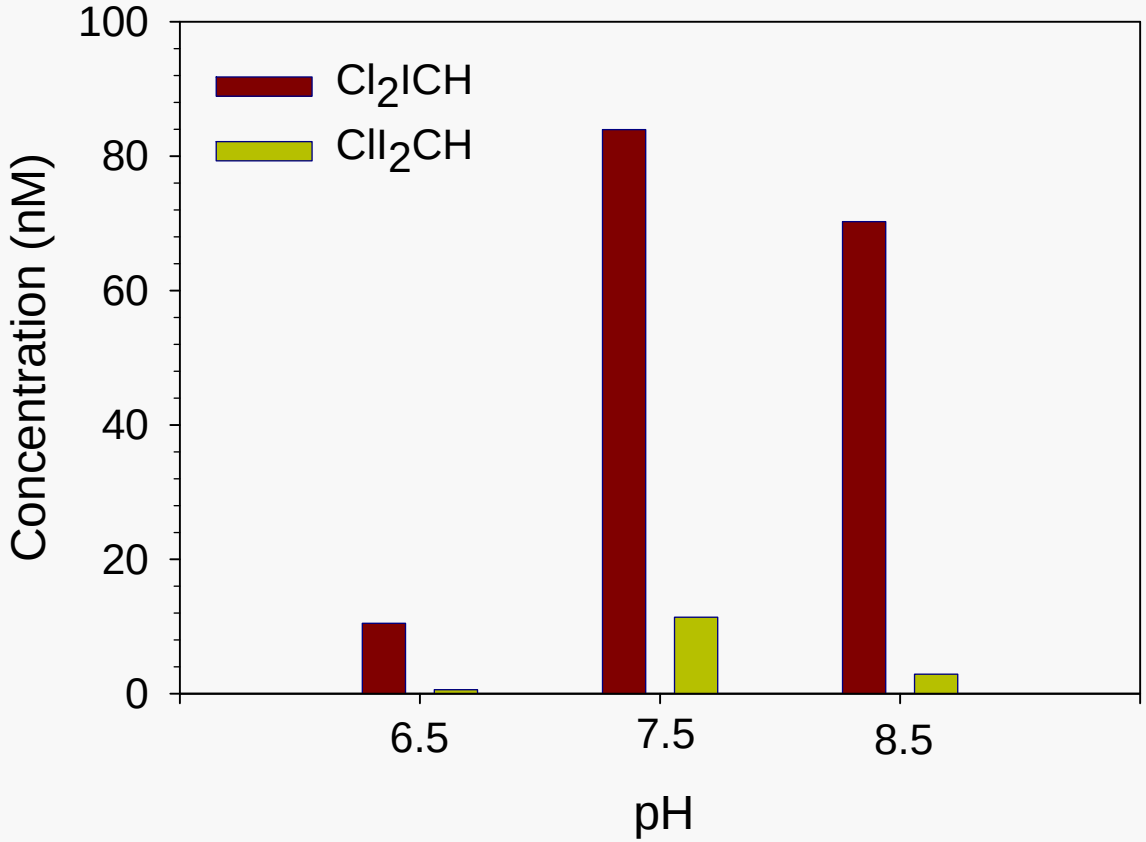
HOCl

NH_2Cl

Iodo-DBPs ✓

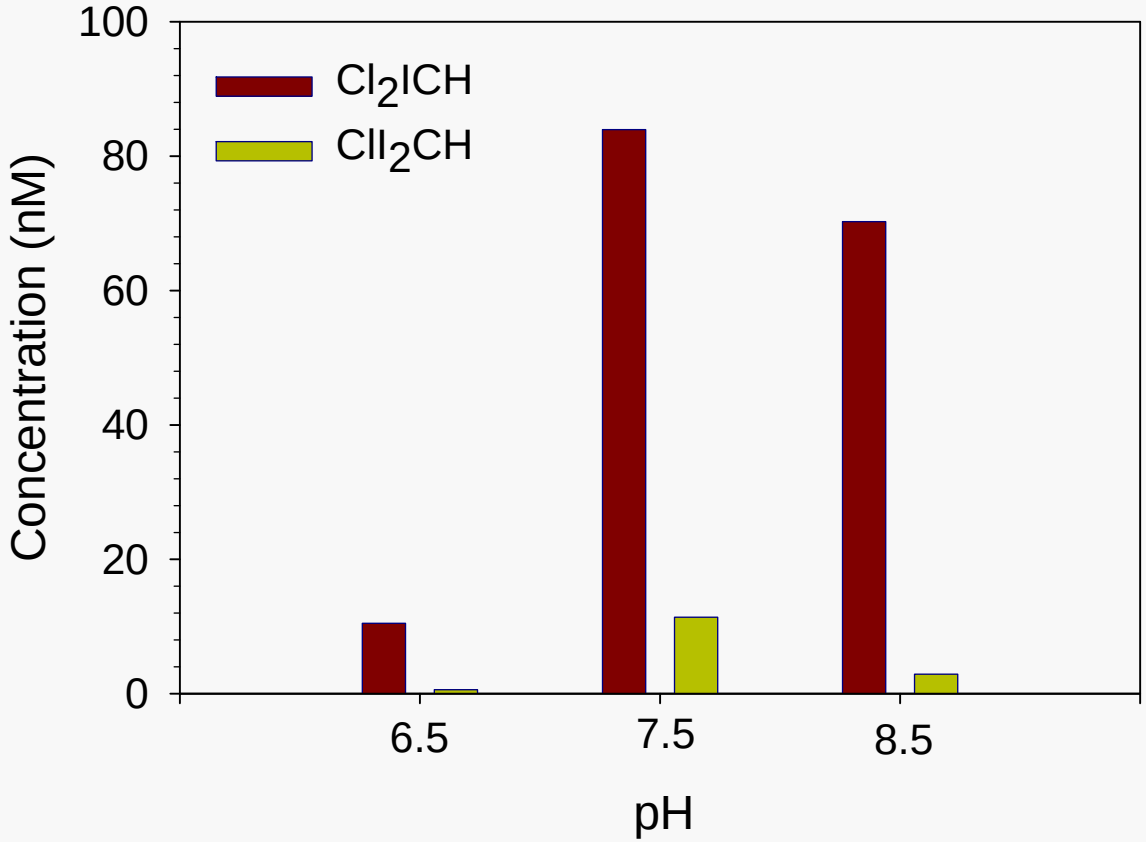
Iodo-THMs
&
Iodo-Acids

Iodo-THM Formation at 72 hr: Chlorine



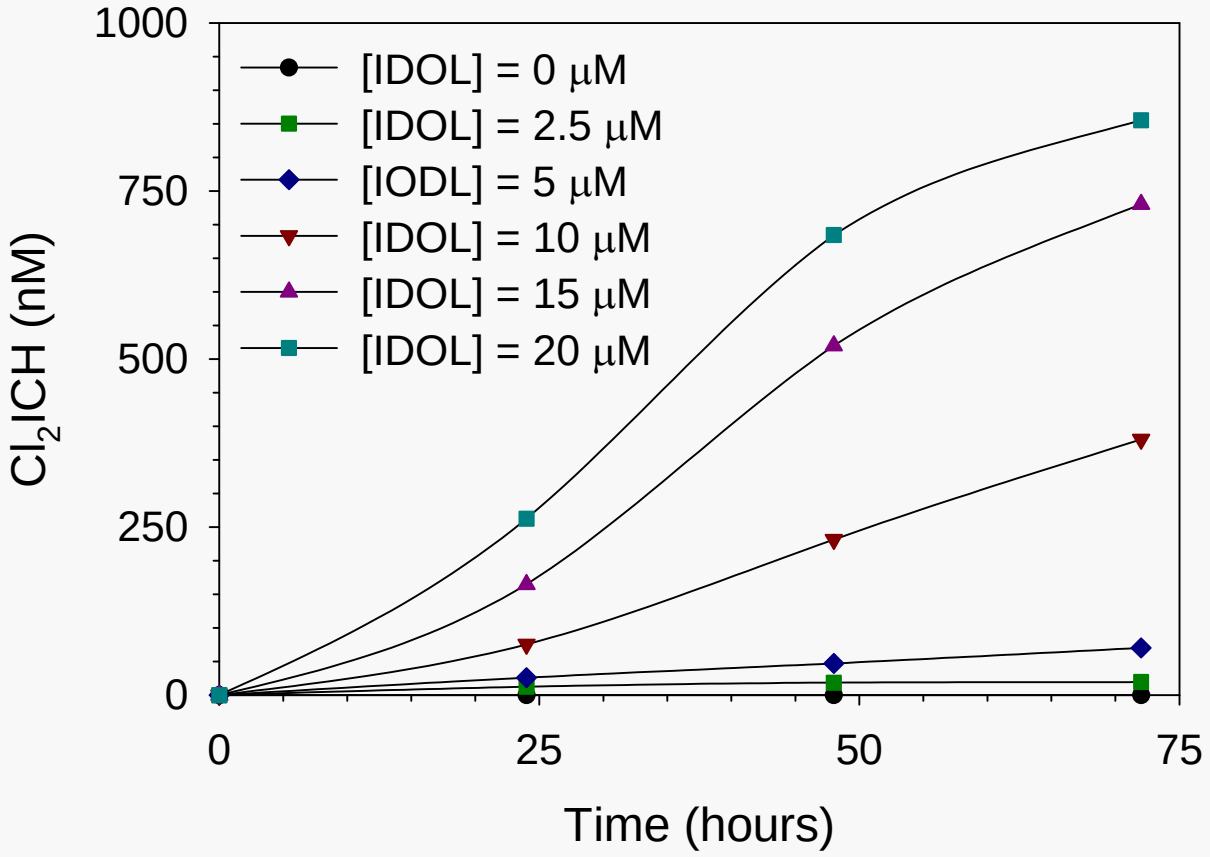
Conditions: HOCl = 100 μM (7.1 mg/L), IDOL = 5 μM (3.1 mg/L)
Buffer = 10 mM, Temperature = 25 °C, TOC= 2.1 mg/L

Iodo-THM Formation at 72 hr: Chlorine



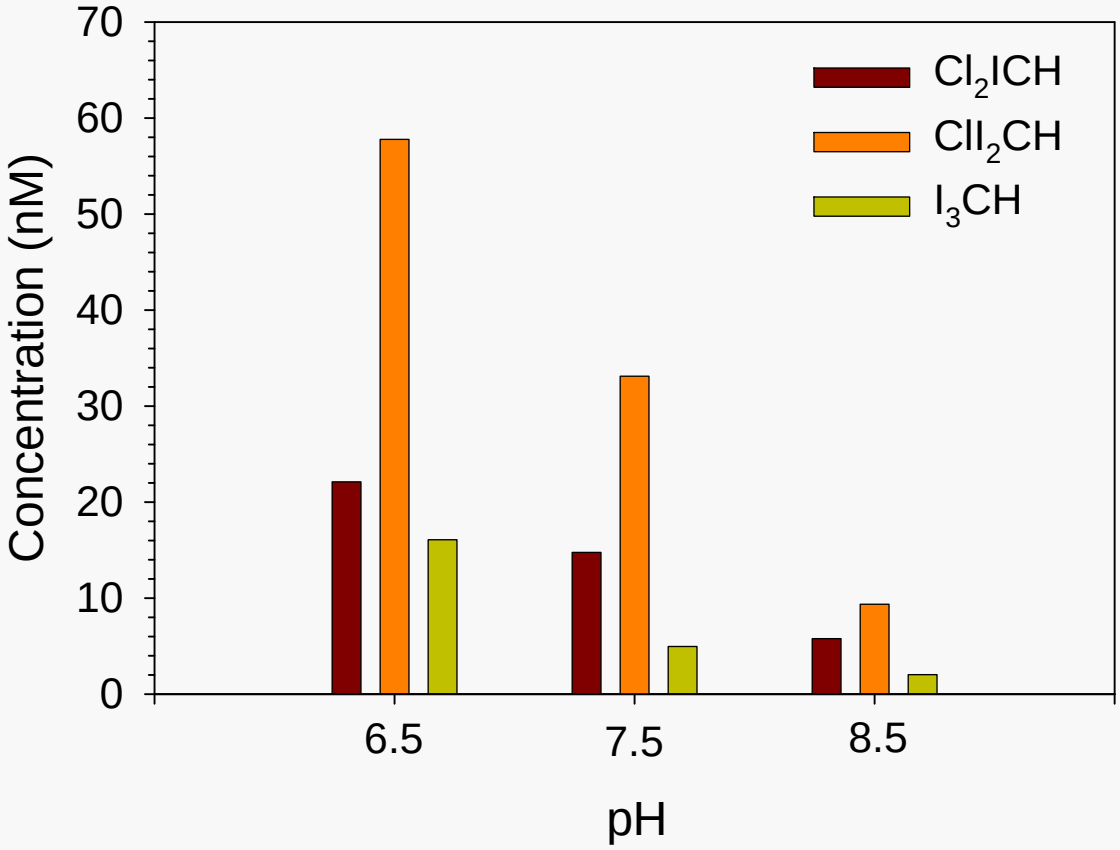
Note: Because no Br^- added for these experiments, no bromo species formed (and minimal Br- present in Athens, GA raw source waters)

Cl_2ICH Formation at pH 8.5



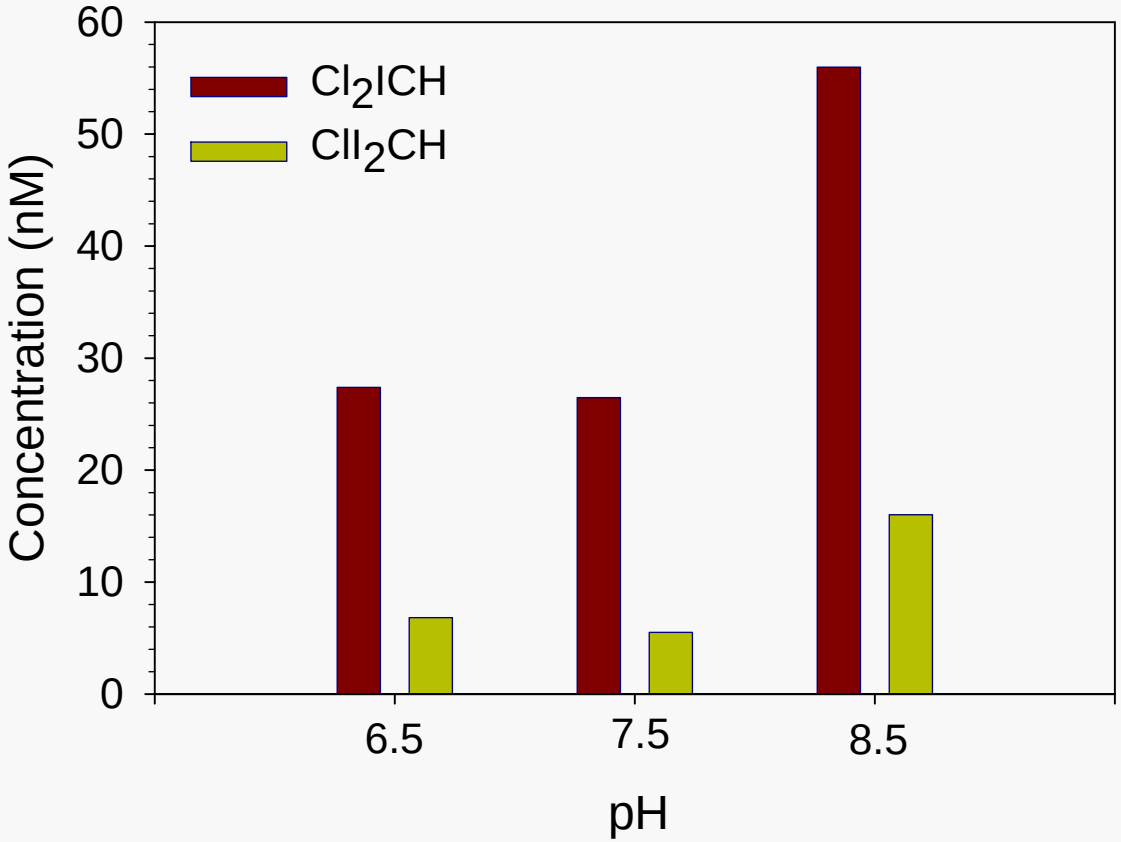
Conditions: HOCl = 100 μM (7.1 mg/L), IDOL = 0-20 μM, Buffer = 10 mM
Temperature = 25 °C, TOC = 2.1 mg/L

Iodo-THM Formation at 72 hr: Monochloramine



Conditions: NH_2Cl = 100 μM, IDOL = 5 μM, Buffer = 10 mM, Cl/N = 0.7
Temperature = 25 °C, and TOC = 2.1 mg/L

Iodo-THM Formation from Iodide at 24 hr: Chlorine



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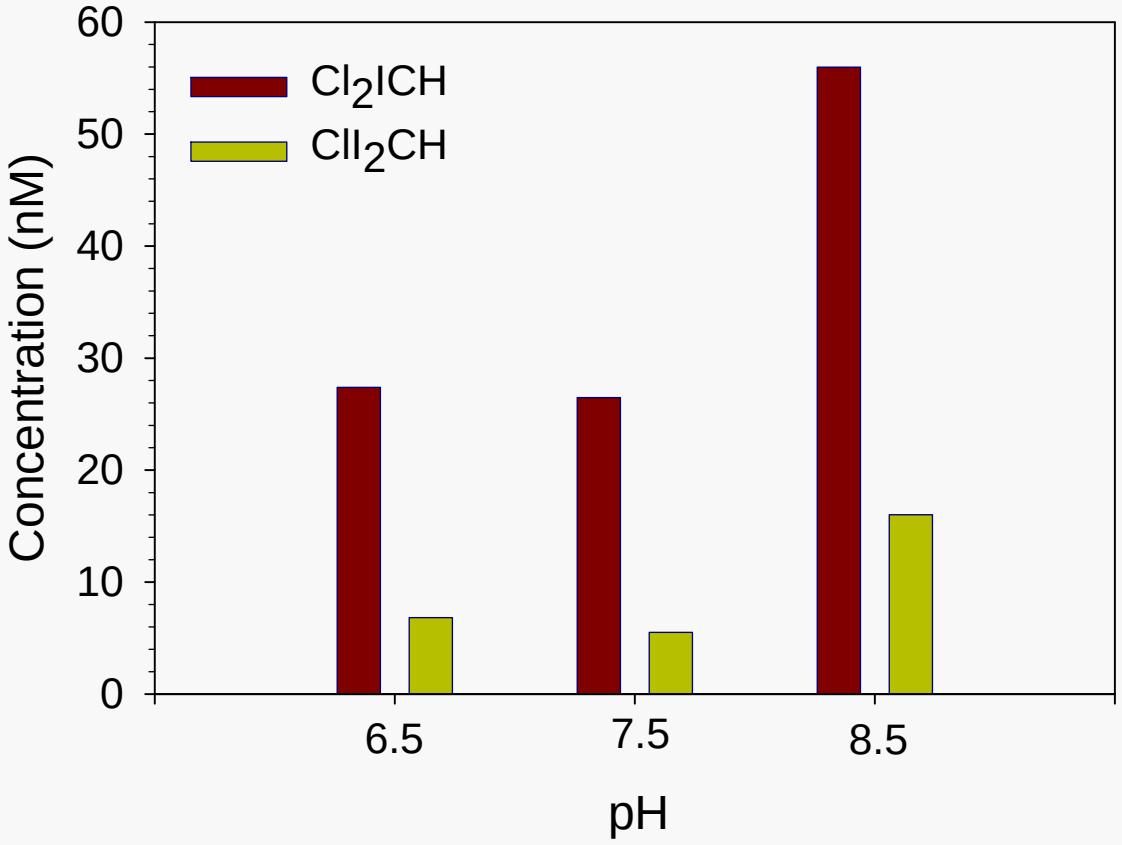

Reaction Complete in 24 hr

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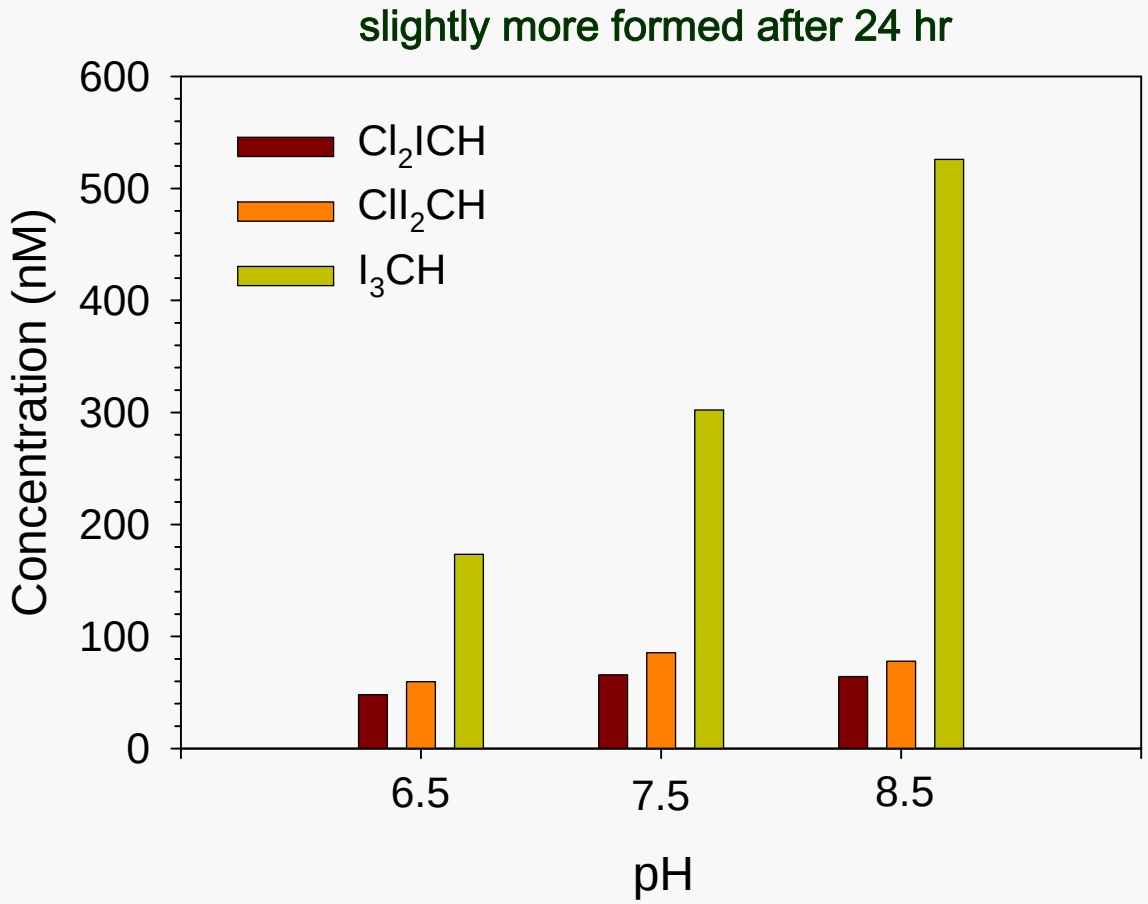
Iodo-THM Formation from Iodide at 72 hr: Monochloramine



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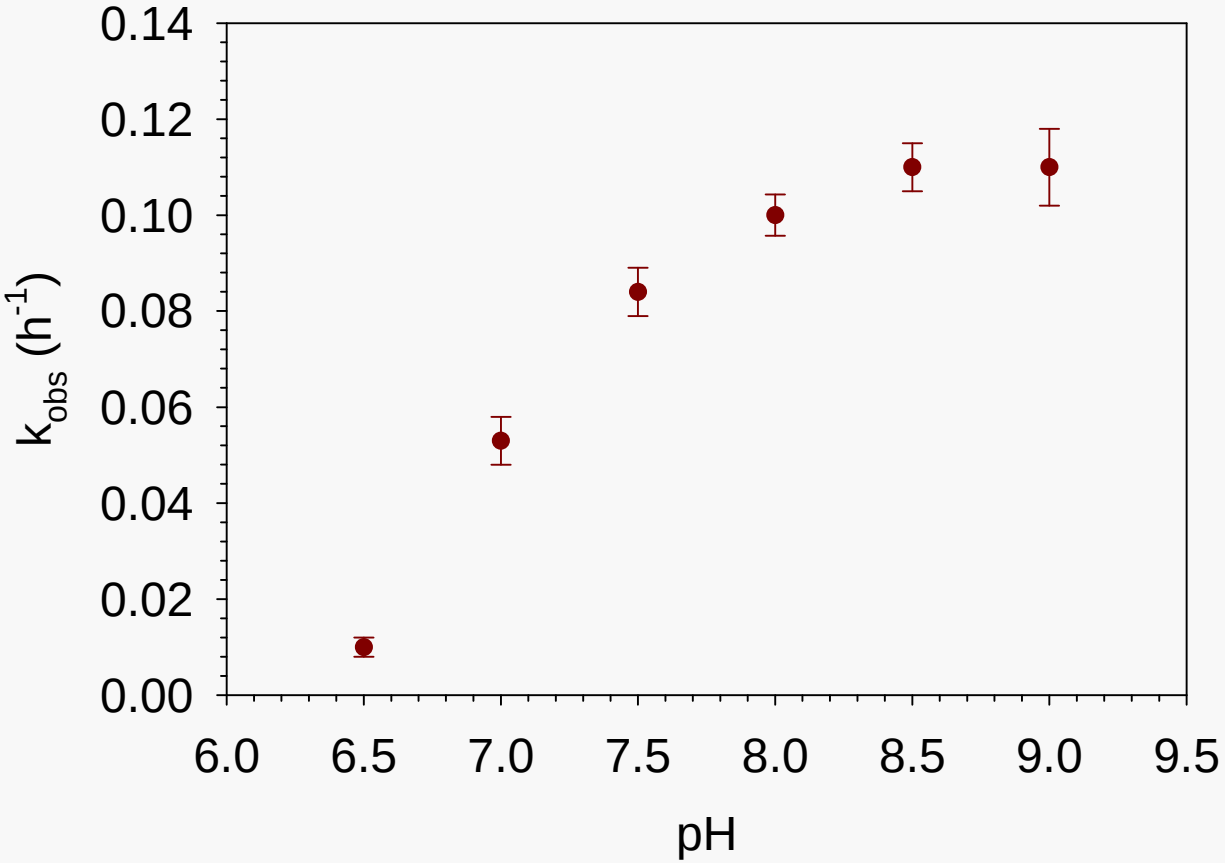
Temperature = 25 °C, TOC = 2.1 mg/L

Loss of Iopamidol

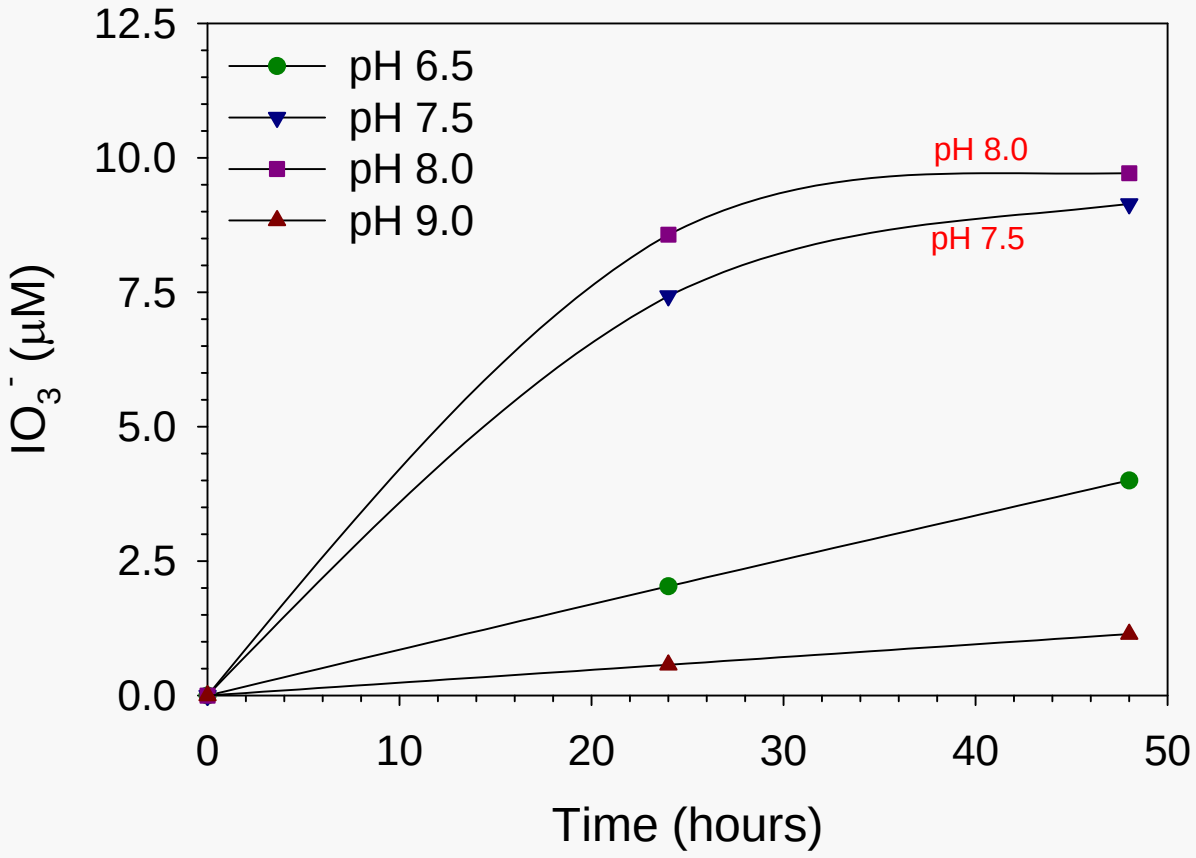


$$HOCl \rightleftharpoons OCl^- + H^+$$

$$pK_a = 7.5$$

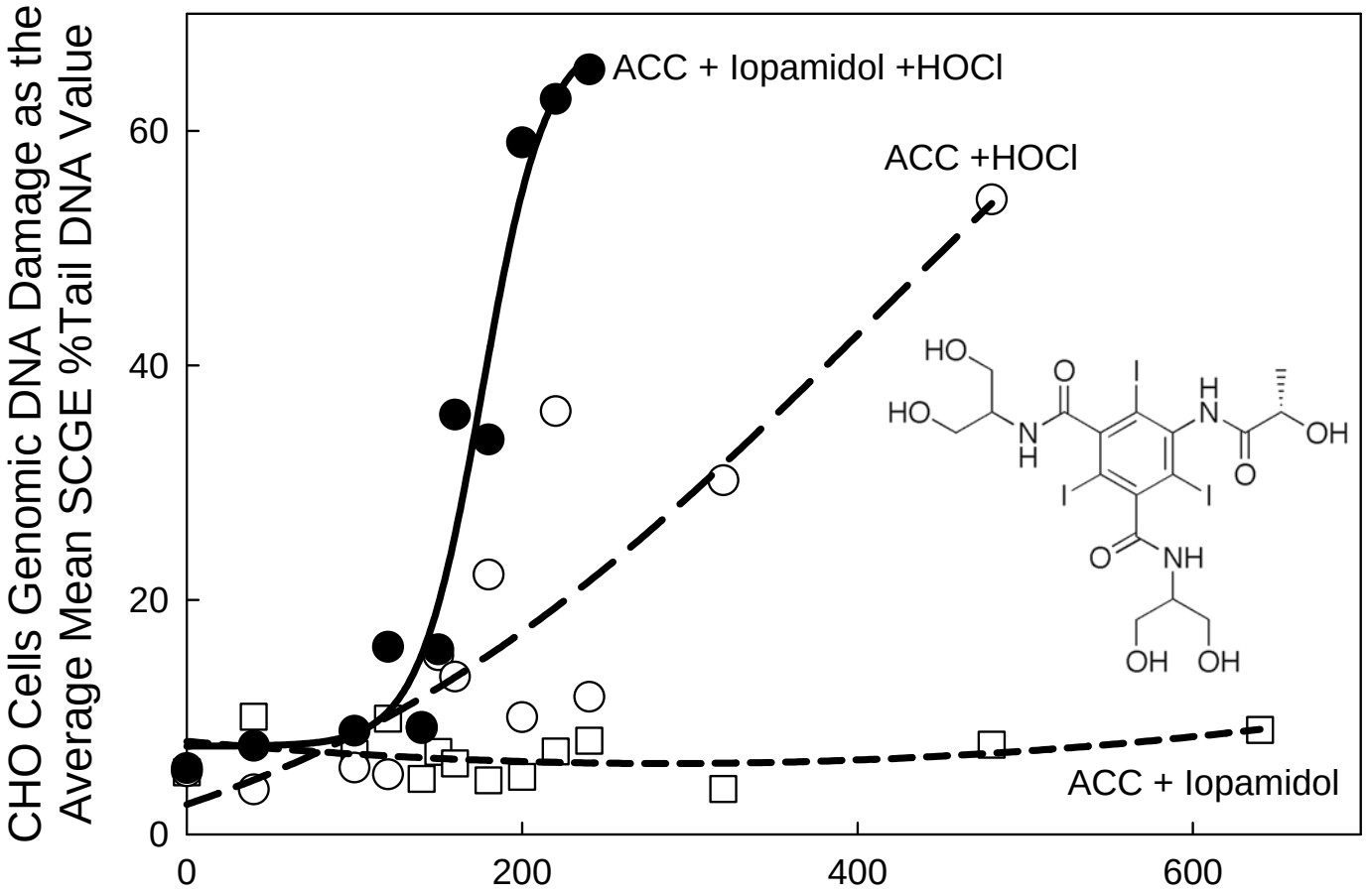
Conditions: HOCl = 100 μM, IDOL = 5 μM, Buffer = 10 mM, Temperature = 25 °C

IO_3^- Formation: Chlorination of Iopamidol

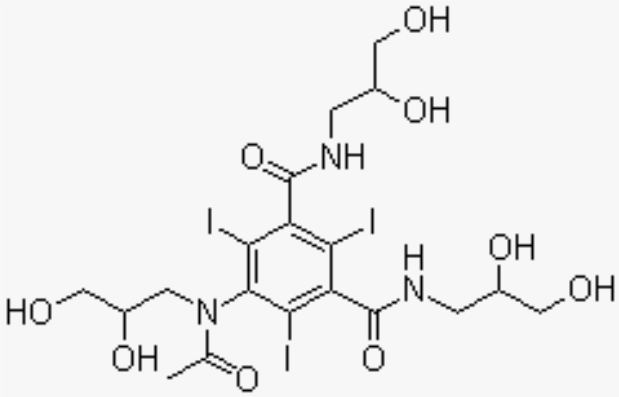


Conditions: HOCl = 100 μM, IDOL = 5 μM, Buffer = 10 mM, Temperature = 25 °C

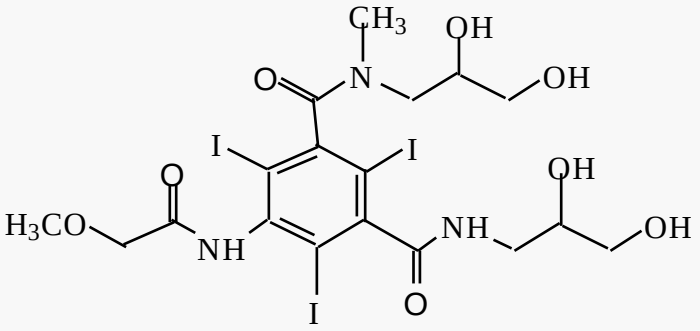
Gentoxicity of Chlorinated Waters Containing Iopamidol



What about other ICM?



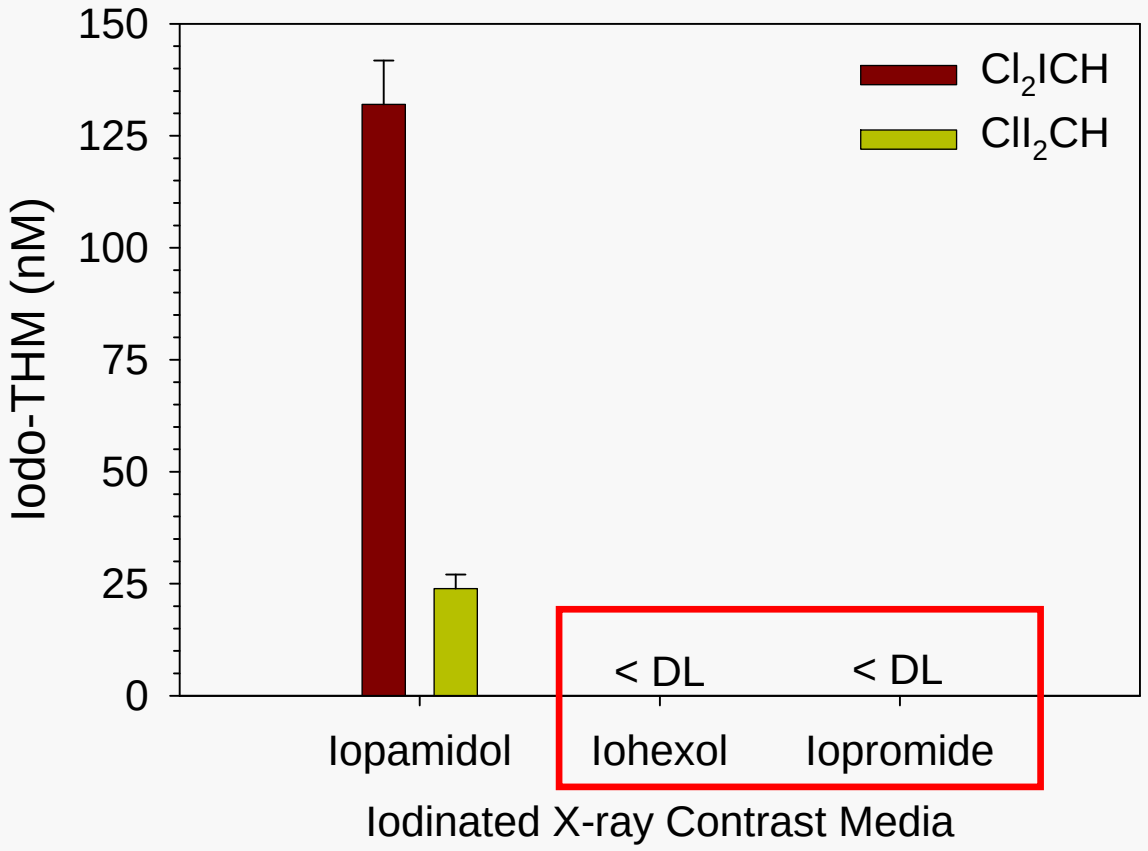
Iohexol



Iopromide

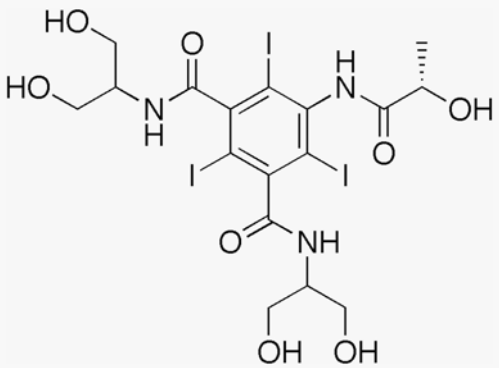
Iodo-THM Formation with other ICM

pH 8.5 after 48 hrs



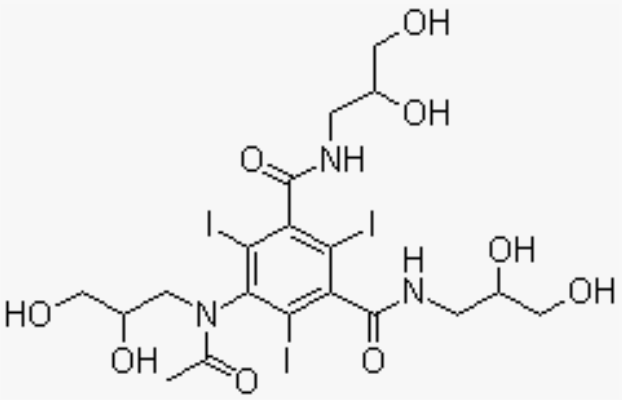
Conditions: HOCl = 100 μM, IDOL = 5 μM, Buffer = 10 mM, Temperature = 25 °C

A Mystery….

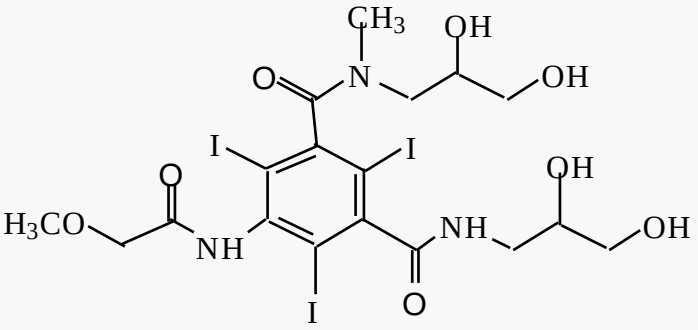


Iopamidol

Why does this one react, but not the others???

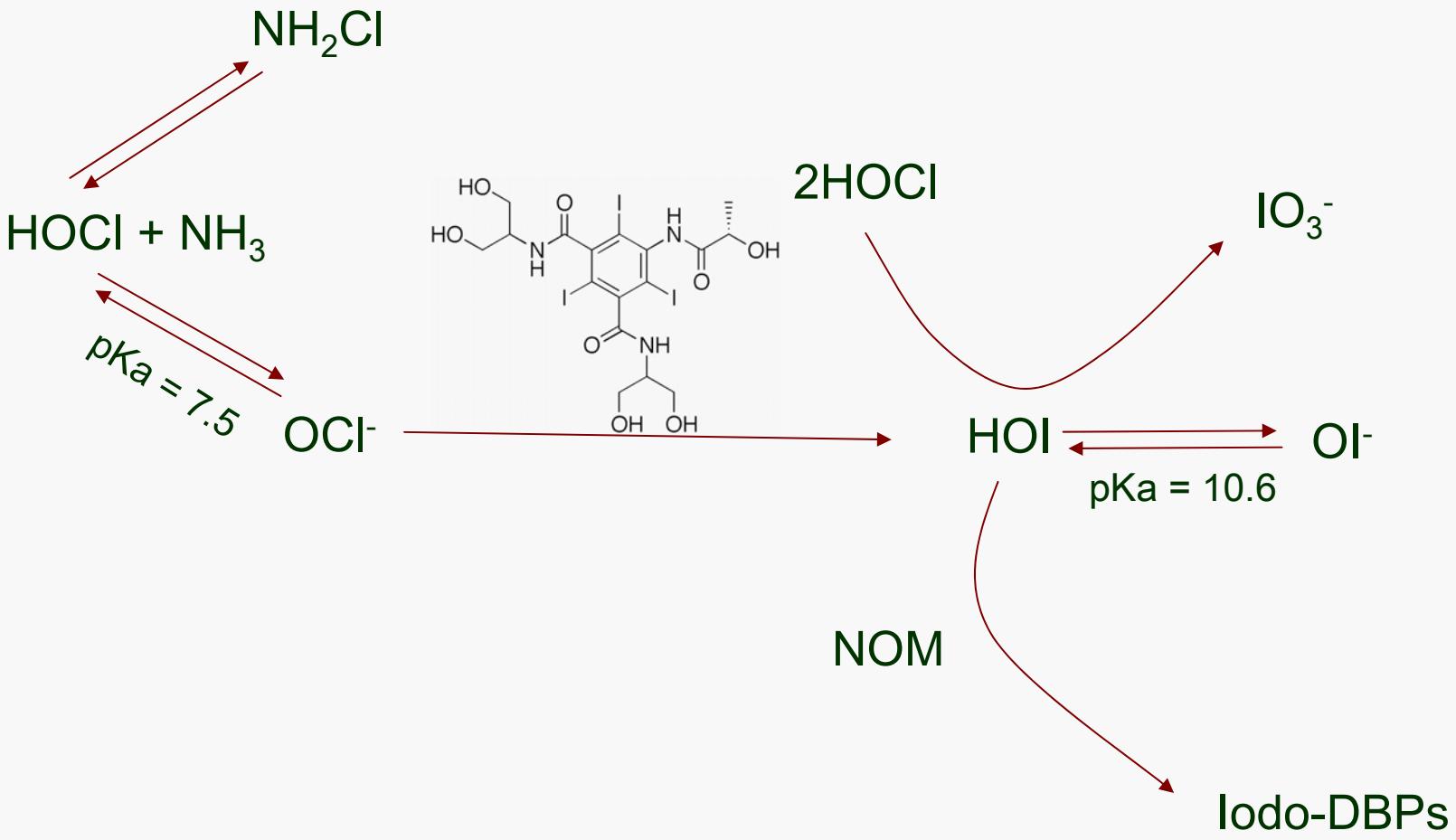


Iohexol



Iopromide

Proposed Pathways



Summary

- Iodo-THMs and Iodo-Acids formed
- Appears OCl^- reacts with iopamidol (increased formation above pK_a of HOCl; and excess NH_3 with Cl_2 to form NH_2Cl → see nothing)
- Chlorinated oxidants react with iopamidol:
  - Chlorine formed Cl_2ICH and ClI_2CH
  - Monochloramine formed Cl_2ICH, ClI_2CH, and I_3CH
  - Preliminary experiments indicate that IAA and (*E*)-2-iodo-3-methylbutenedioic acid also formed
- Chlorine forms somewhat higher levels of iodo-THMs from iopamidol than NH_2Cl
- So far, iohexol and iopromide don't form iodo-DBPs (a mystery…)
- Iodopamidol vs. native iodide:
  - Iodide produces more iodo-THMs with monochloramine vs. chlorine; get more iodine incorporation with iodide (I_3CH)
- Chlorinated iodopamidol in source water containing NOM has higher genotoxicity than source water with iopamidol alone or with chlorine alone

What's Next

- Identify iopamidol degradation products and intermediates (LC/MS/MS)
- Will do minimum energy calculations (3-D structures) of other ICM compounds
- Will try additional experiments with other ICM

Ever wonder what happens when you have to scale things up for toxicity testing ? ? ?

The Land of Extraordinarily Large Lab Equipment

Chris

Toxicity?

20 L → 1 mL

Steve

Cristal