

Interrogating the Extensive Gas-Phase Clustering of Organophosphonate Species via Atmospheric Flow Tube-Mass Spectrometry

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Clowers Research Group



Overview

- Chemical warfare agents (CWAs)
 - Compound classes common to CWAs
- Atmospheric flow tube-mass spectrometry system
 - Ion source and flow tube
 - Gas-phase ion chemistry and kinetics
- Preliminary surface residue analysis of CWA simulants
- Evaluating stability of dimeric phosphonate cluster
- Implications for further research



CWAs and Their Simulants

- Type of chemical warfare agent, nerve agents, includes a large range of organophosphorus compounds
- Common nerve agent classes:
 - G class: fluorine-containing
 - V class: sulfur-containing





CWAs and Their Simulants

- Hazard of CWAs precludes their use in routine method development
- Need to find close analogs to mimic their attributes
- Organophosphorus CWAs decompose largely through hydrolysis
- Hydrolysis products and compounds related in structure are ideal targets



Munro et al. The sources, fate, and toxicity of chemical warfare agent degradation products. *Environmental Health Perspectives, 107*, **1999**, 933-974.



- Non-contact sampling technique
- Reactant ions produced by dielectric barrier discharge sources while transit time down tube promotes cluster formation with analyte
- Surface analysis sampling methods here included sample deposited on woven glass

1) Ewing et al. *Analytical Chemistry, 85,* **2013**, 389-397. 2) Morrison and Clowers. Characterization of Alkylphosphonic Acid Vapors Using Atmospheric Flow Tube-Ion Trap Mass Spectrometry. *Rapid Comm. Mass Spectrom.*, **2018**. Ahead of print.







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- Assuming excess of reactant ions, analyte ion quantity can be maximized by increasing t
- Simplest way to increase t is by using flow tube

$$[A^-] = [R^-]_0 [A]kt$$

- **k** = reaction rate constant ($\sim 10^{-9}$ cm³ molecule⁻¹ s⁻¹)
- t = reaction time in seconds
- **[A]** = analyte concentration
- [A⁻] = analyte ion concentration (measured signal)
- $[R^-]_0$ = initial reactant ion concentration (measured signal)

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- Both positive and negative analyte ion clusters formed
- Predominant analyte species in negative mode consist of nitrate adducts
- Proton-bound adducts are most common for positive mass spectra, generally no specific reactant ion visible



Morrison and Clowers. Characterization of Alkylphosphonic Acid Vapors Using Atmospheric Flow Tube-Ion Trap Mass Spectrometry. *Rapid Comm. Mass Spectrom.*, **2018**. Ahead of print.



Dialkyl Alkylphosphonates Assessed



Longer Chain Alkoxy Groups



Other Organophosphorus Species Analyzed

- Pinacolyl methylphosphonate (PMP) was included to assess the impact of the free hydroxyl on cluster behavior
- Also useful to include due to high degree of similarity in structure to GD





Simple Quantitative Evaluation: P-C Alkyl Chain

- DMMP, DMEP, and DMPP
- Linear signal gains for 0.1 to 10 µg samples
- Ion current trends upward with increasing alkyl group size.
 - Likely result from change in proton affinity; better able to grab charge





Simple Quantitative Evaluation: Alkoxy Chain



- DEMP monomer and dimer:
 - Quantitatively tractable ion current changes with sample quantity





Simple Quantitative Evaluation: Alkoxy Chain



- In contrast, DIMP showed linear signal increases only for monomer
- Also produced quite low SNR for 0.1 µg sample





Simple Quantitative Evaluation: Lengthen Both Chains

- DEEP structure:
 - All three alkyl chains longer vs DMMP
- Low SNR for 0.1 µg sample compared to all others besides DIMP





Simple Quantitative Evaluation: Influence of OH



- Minimum amount of PMP necessary for even slight signal ~50x greater than for others
 - Lower vapor pressure
 - Hydrogen bonding through OH

Homodimer-H⁺





Some Qualitative Notes: Influence of OH

- PMP capable of forming multimers beyond dimers
 - Three or more in one cluster
 - Singly charged
- Can complicate quantitation by splitting signal





Some Observations from Simple Quantitative Work

- Some species demonstrated favorable signals from both monomers and dimers
- Others worked well from only one ion or ion adduct





Some Observations from Simple Quantitative Work

- Although not all homodimers showed linear signal gains, judicious use of dopants can enhance analysis
 - Selectivity around interferences
 - Select for specific ion chemistry
 - Introduce known mass shift





Some Observations from Simple Quantitative Work

- A first metric is to assess the relative stability of a range of both homodimeric and heterodimeric adducts
 - Catalog structure and stability trends
 - See if more vs less stable functions well as dopant





Why Evaluate Cluster Stability?

- Broad trends in complex stability have been characterized by Meot-Ner for amines and simple organics, but not organophosphorus species
 - Higher bond dissociation energies when the difference in proton affinity between both components is minimized
 - For $-O \cdot H + \cdot O -$ type bonds,

$$\Delta H = 127 - 0.4 \Delta PA \text{ (kJ/mol)}$$



M.M. Meot-Ner, The Ionic Hydrogen Bond and Ion Solvation. 1. NH+•••O, NH+•••O, and OH+•••O Bonds. Correlations with Proton Affinity. Deviations due to Structural Effects, J. Am. Chem. Soc. 106 (1984) 1257–1264.



Using Survival Yield Analysis on Clusters

- Survival yield analysis
 - Energy-resolved fragmentation mass spectra
 - Metric of *relative* cluster stability
 - Stability of cluster at each collision energy:

100*precursor

precursor+fragments



Holmes, Huizen, and Burgers. Proton affinities and ion enthalpies. European Journal of Mass Spectrometry, doi: 10.1177/1469066717728451



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Homodimer Trends: Dialkyl Alkylphosphonates





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Homodimer Trends: Dialkyl Alkylphosphonates





Heterodimer Trends: Impact of Alkyl Chain





Heterodimer Trends: Impact of Alkyl Chain





Heterodimer Trends: Impact of Alkyl Chain





Forming Heterodimers with PMP

 Use of PMP in heterodimer clustering tends to slightly enhance the dimers' stability in SY analysis







Findings Summary

- Microgram and sub-microgram quantities of dried phosphonate samples elicit largely linear signal changes with increase in analyte amount
- Using alkyl chain length as an approximation of proton affinity, apparent trend is greater homodimer stability for higher PA dialkyl alkylphosphonate species
- Greater differences in assumed relative PA tended to yield less stable clusters
- Presence of hydroxyl appears to strengthen cluster interactions



Future Directions

- Perform SY analysis on phosphonate species as heterodimers with compounds of known proton affinity
 - Apply kinetic method to obtain tentative proton affinity estimates
- Assess linearity and sensitivity for phosphonate quantitation by monitoring the dopant-analyte signal
- Pursue AFT-MS analysis of additional compound classes