

That's Dope: A Novel Approach for the Differentiation of Δ^9 -THC Isomers in Cannabis

Alleigh N. Couch^{a,*}, Emma K. Hardwick^a, Christany Liggins^a, Christopher M. Zall^b, J. Tyler Davidson^a

^a Department of Forensic Science, Sam Houston State University, Huntsville, Texas, USA

^b Department of Chemistry, Sam Houston State University, Huntsville, Texas, USA



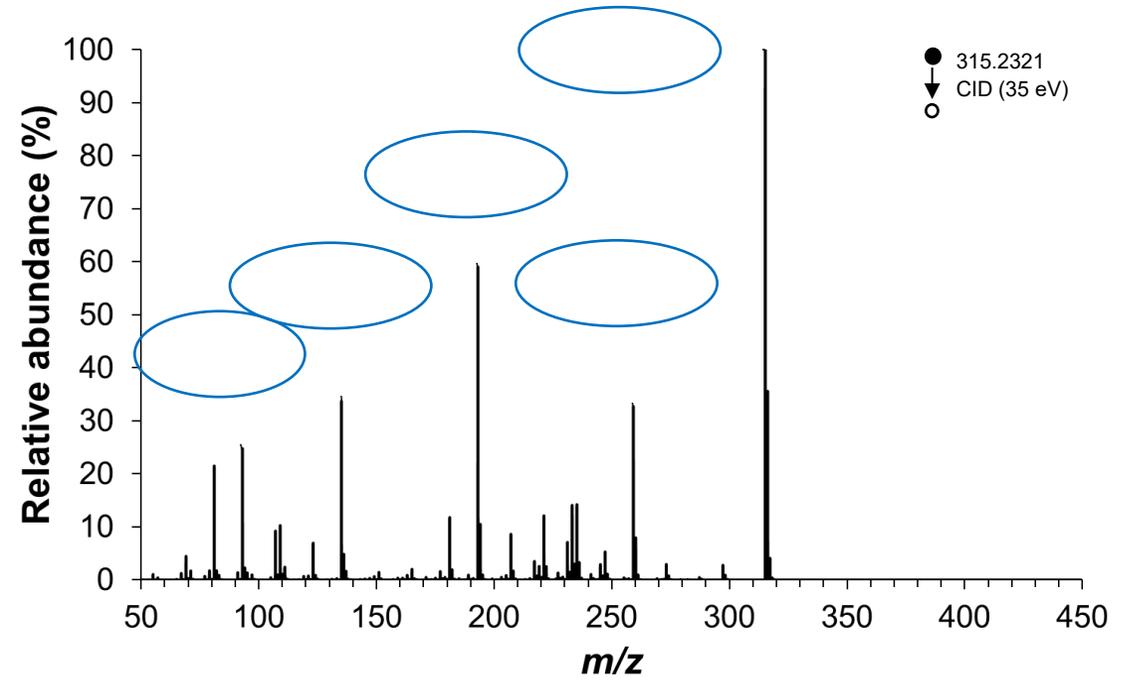
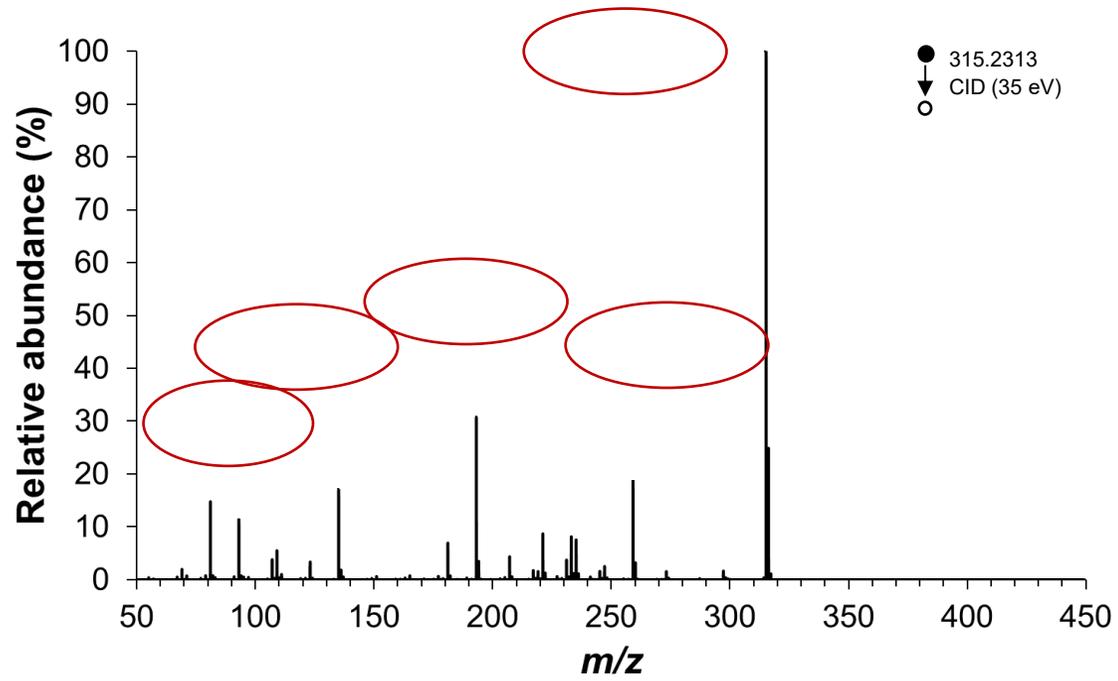
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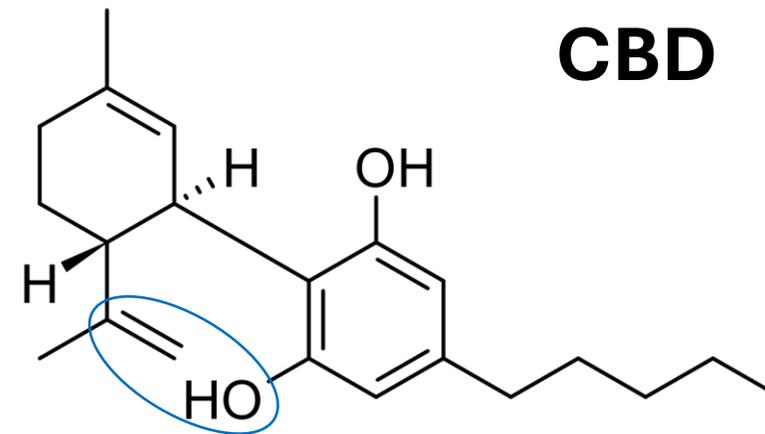
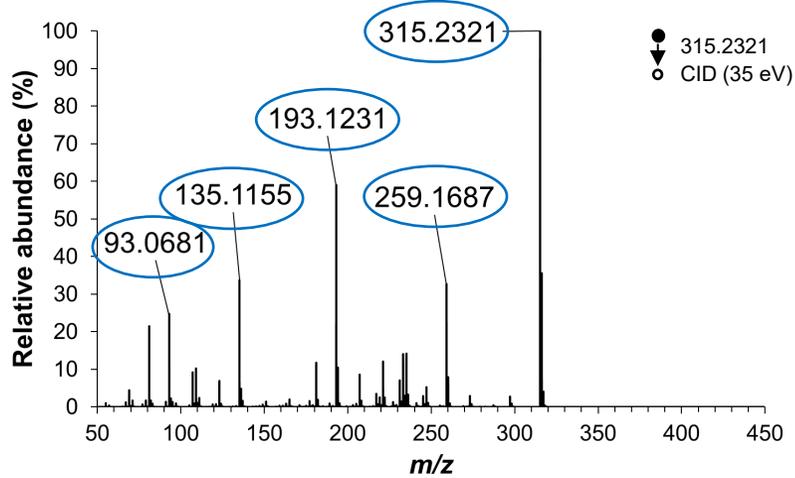
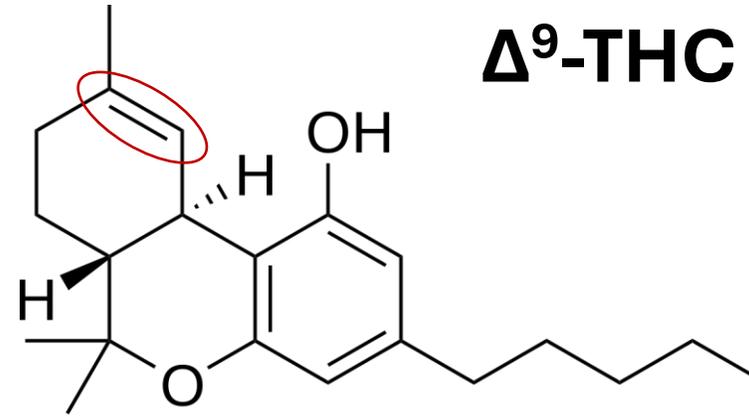
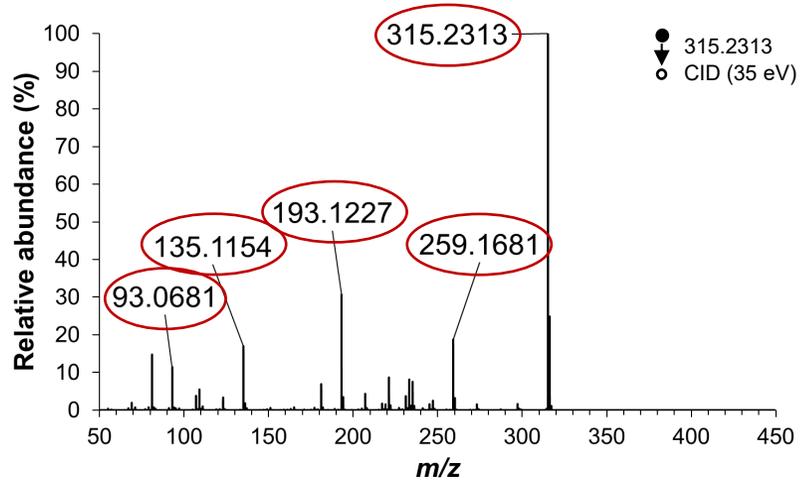
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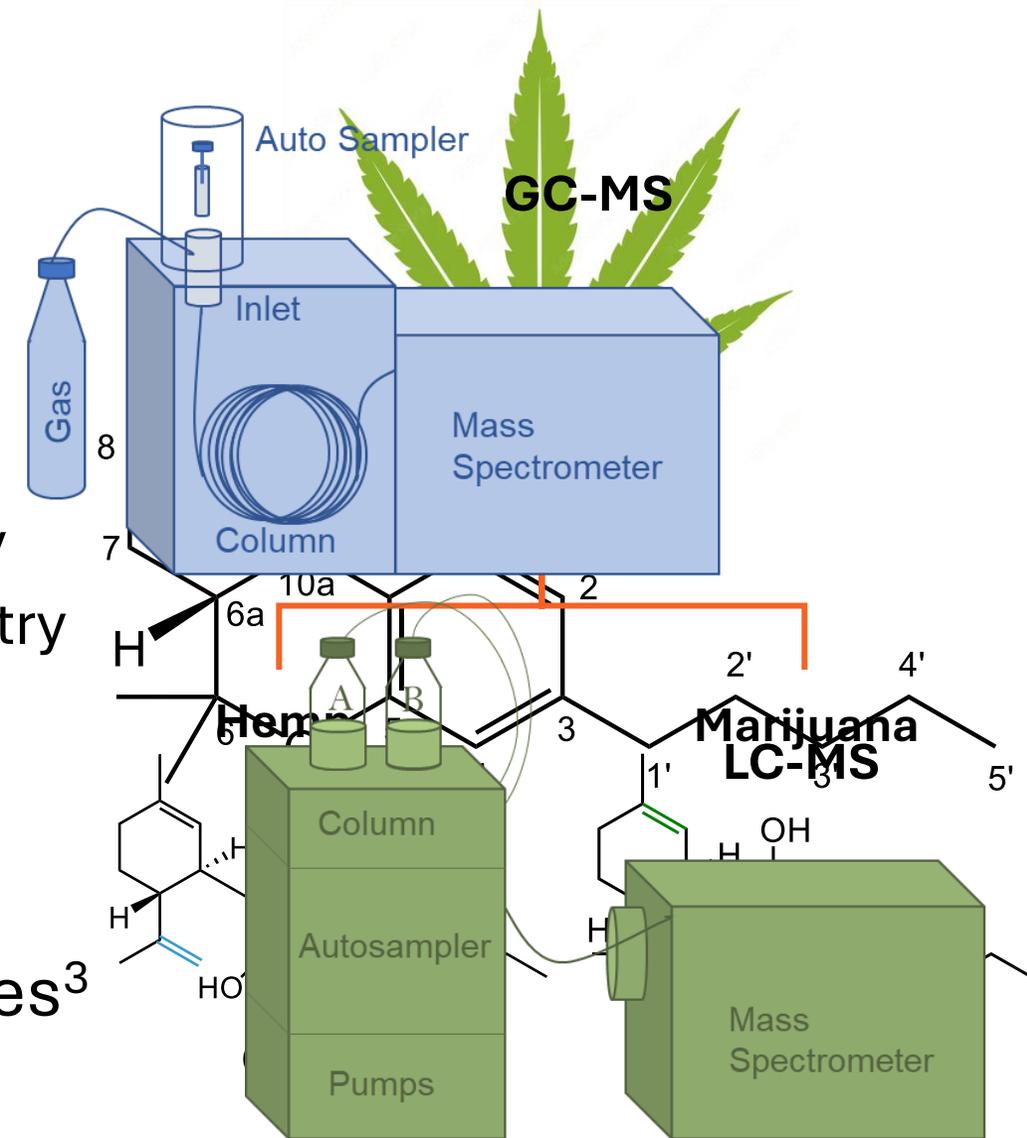
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Hemp vs. Marijuana

- 2018 Agriculture Improvement Act¹
 - Marijuana > 0.3% Δ^9 -THC \leq hemp
- Current instrumentation²
 - Gas chromatography-mass spectrometry
 - Liquid chromatography-mass spectrometry
- Analysis complicated by cannabinoid interferences
 - Δ^9 -THC positional isomers
- Prevalence of potential marijuana cases³



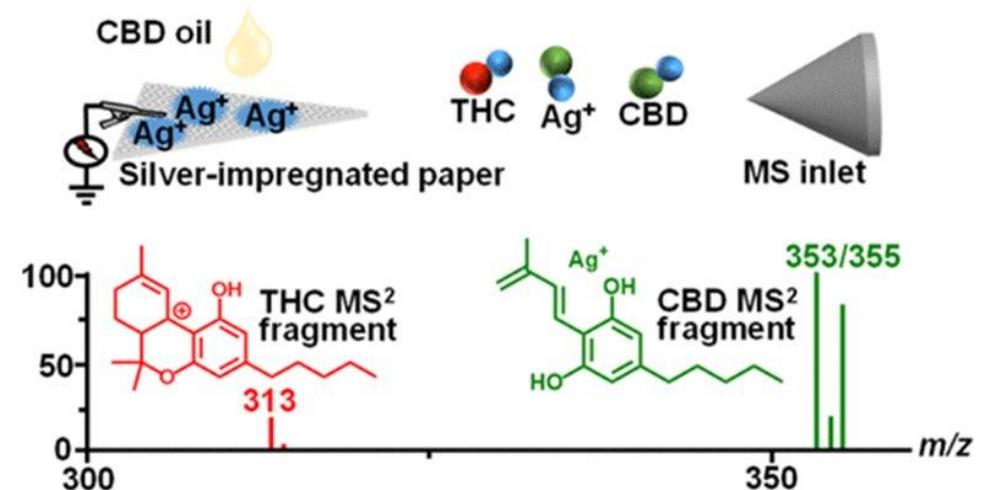
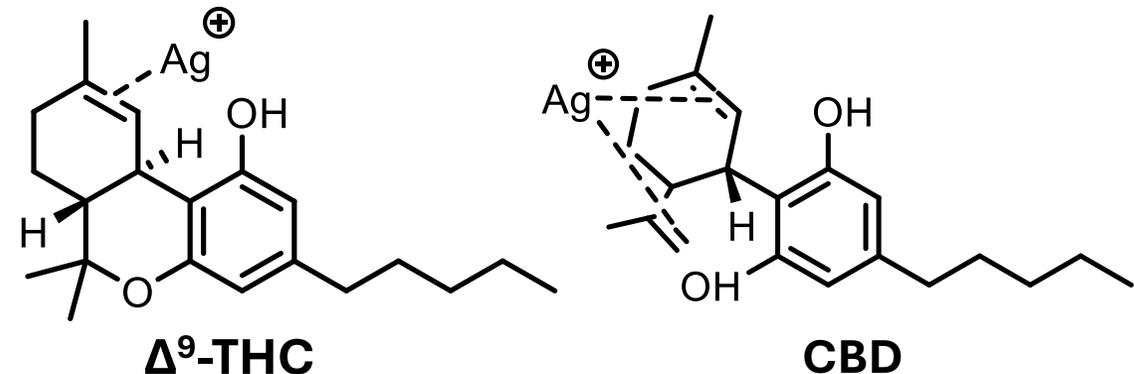
1. H.R.2-115th Congress: Agriculture Improvement Act of 2018.

2. Capriotti, A.L., et al. Recent applications of mass spectrometry for the characterization of cannabis and hemp phytocannabinoids: From targeted to untargeted analysis. *J. Chromatogr. A*, **2021**. 1655: 462492.

3. NFLIS-DRUG 2022 Annual Report. **2022**, U.S. Department of Justice Drug Enforcement Administration: Diversion Control Division.

Metal-Ion Complexation

- Transition metals: Ag or Cu
 - Reversibly bind to carbon-carbon π -bonds⁴
 - Number and location of alkene(s) influence binding affinity
- Cannabinoid-metal adducts⁵⁻⁷
 - Δ^9 -THC and CBD differentiation using characteristic MS/MS product ions

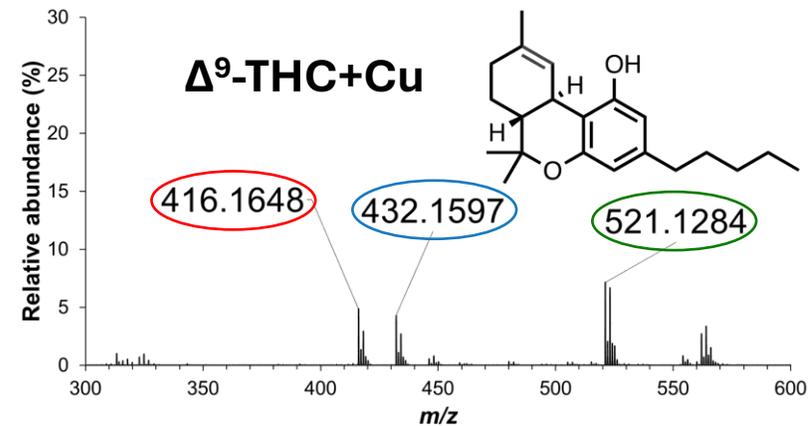




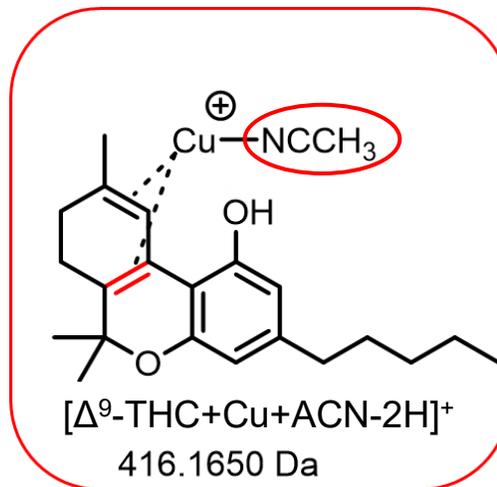
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Cu-Ion Complexation

- Copper salts → Oxygen activation⁸
 - Reactive oxygen species
- Δ^9 -THC fortified with $[\text{Cu}(\text{ACN})_4]\text{BF}_4$ in ACN
 - Formation of various Δ^9 -THC Cu-complexes
- Limitations of metal salts
 - Selectivity, solubility, and stability in solution

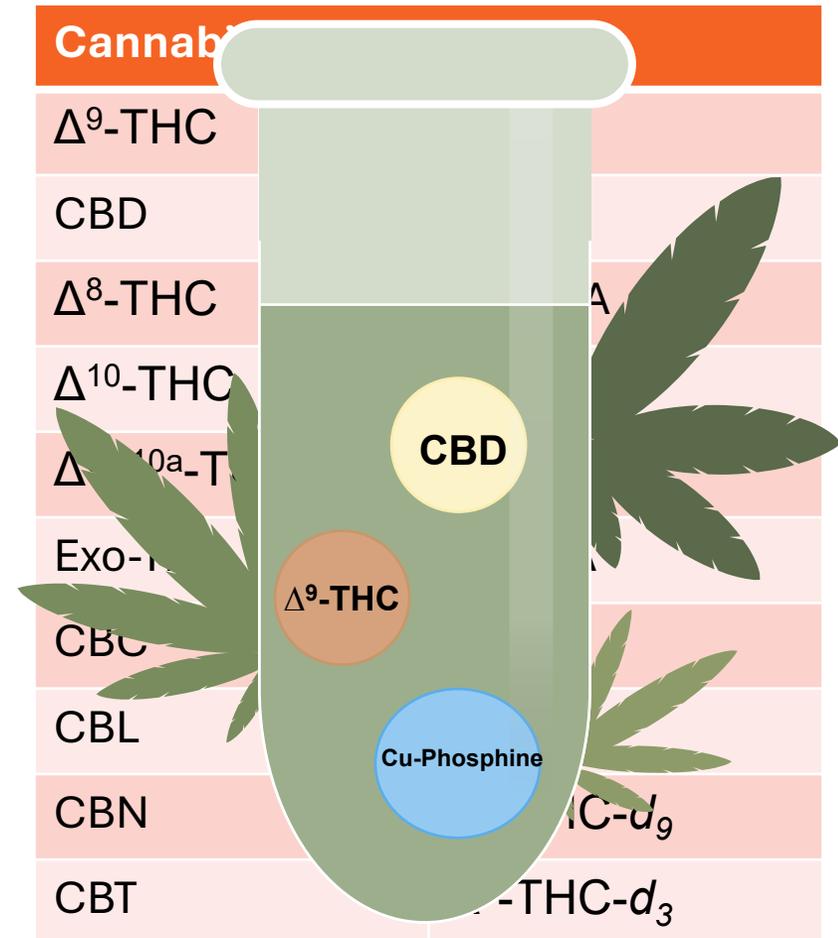


Hydrogen Abstraction



Cu-Phosphine Ion Complexation

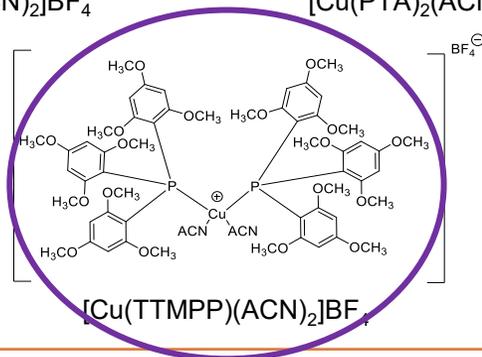
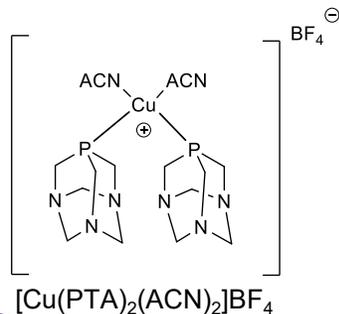
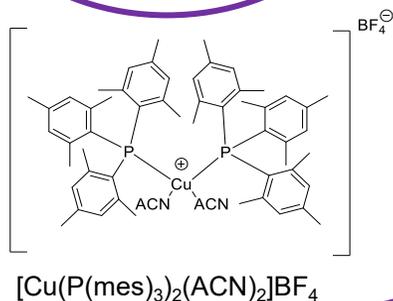
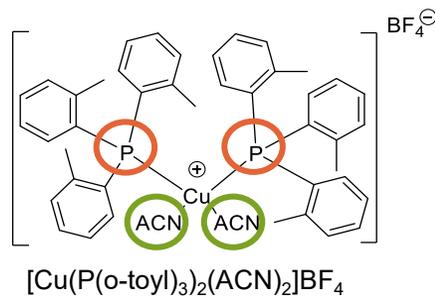
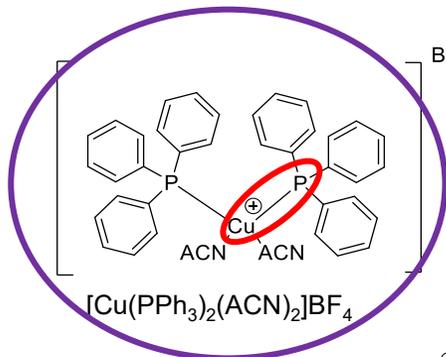
- Instrumentation
 - Agilent Technologies 6530 Q-TOF
 - Direct injection: 18 $\mu\text{L}/\text{min}$
 - MS/MS CID activation energies: 15-45 eV
- Characterization of 11 Cu-phosphine complexes in the presence of 20 cannabinoids
 - 50 ppm cannabinoid:15 μM Cu-phosphine
- Stepwise evaluation to determine optimal Cu-phosphine complex
- Methanolic extracts of cannabis plant material



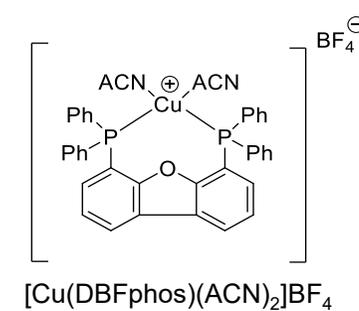
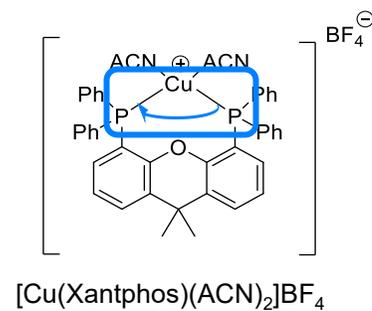
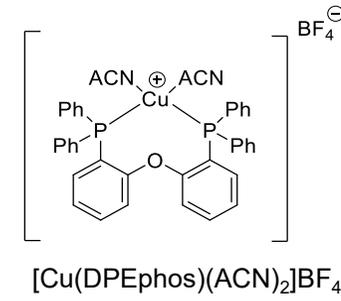
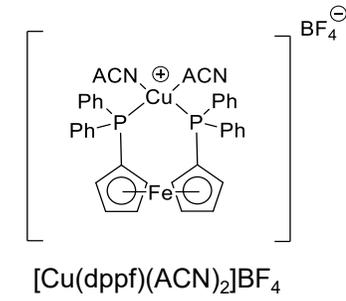
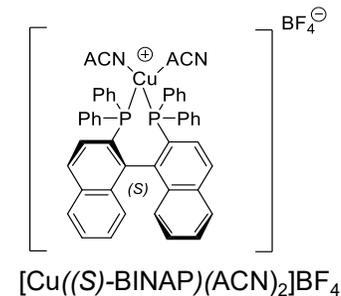
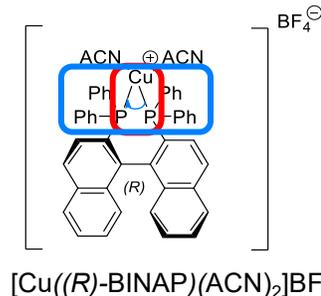


Cu-Phosphine Complexes

Monodentate

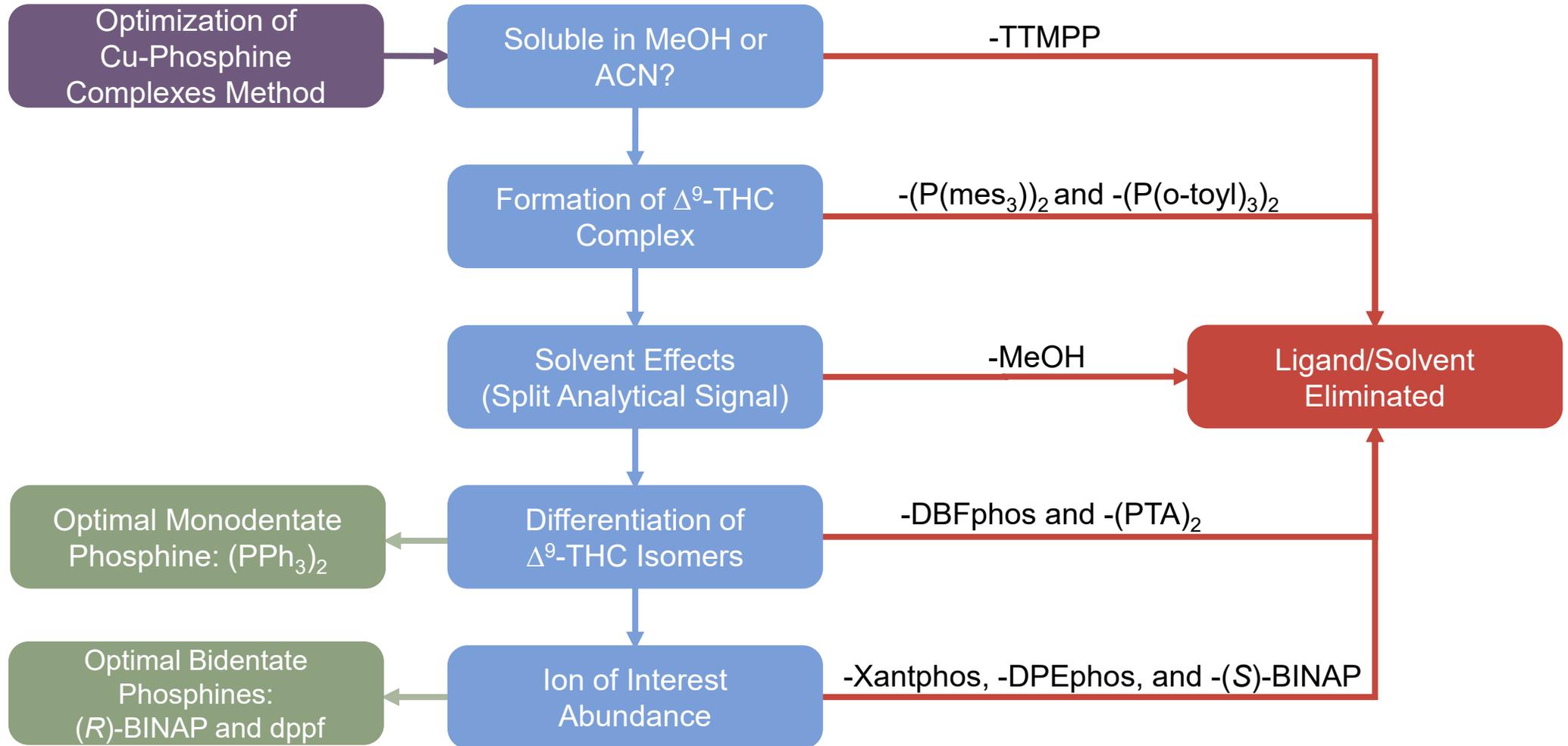


Bidentate



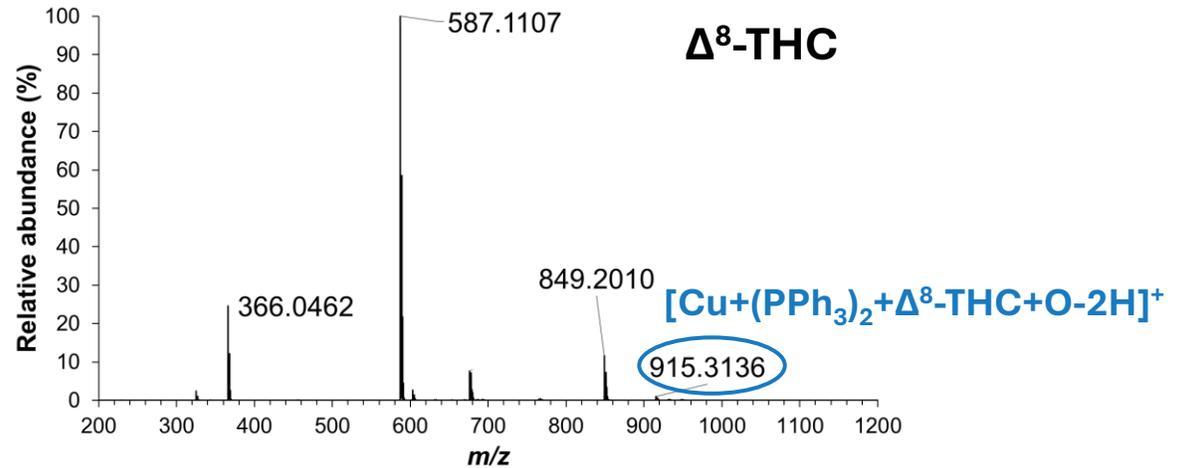
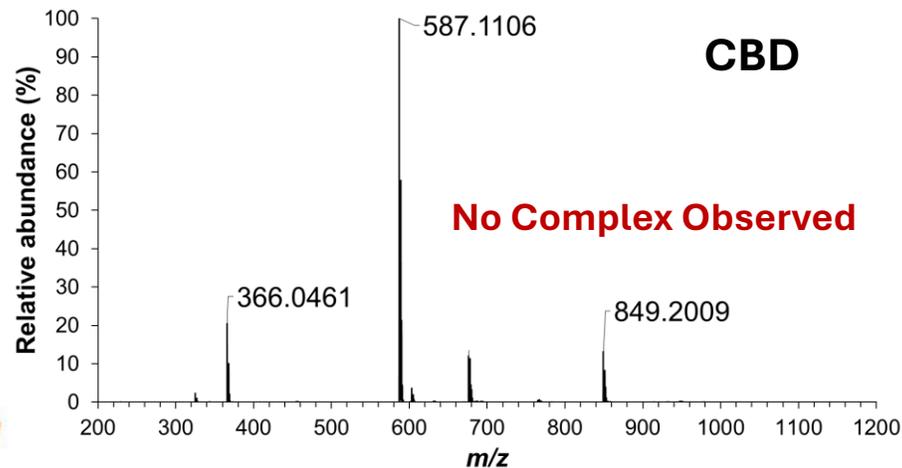
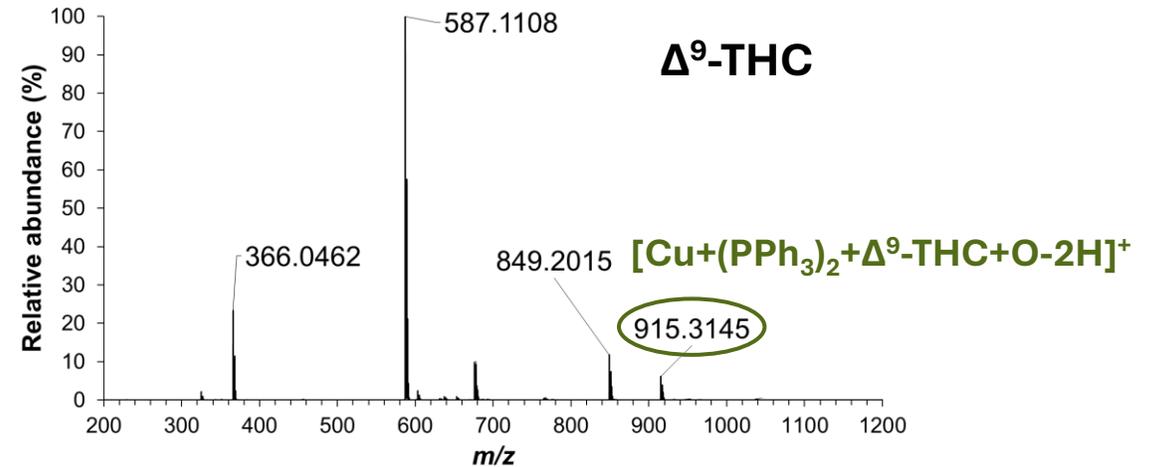
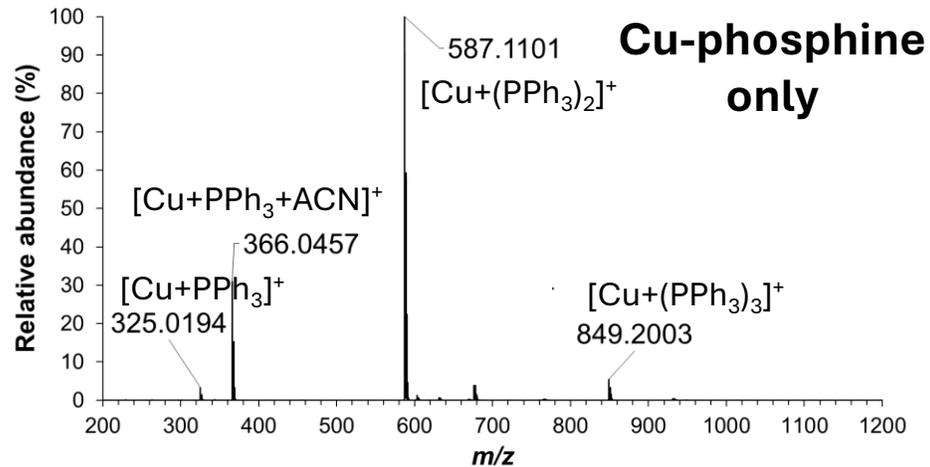


Evaluation of Optimal Phosphine Ligands

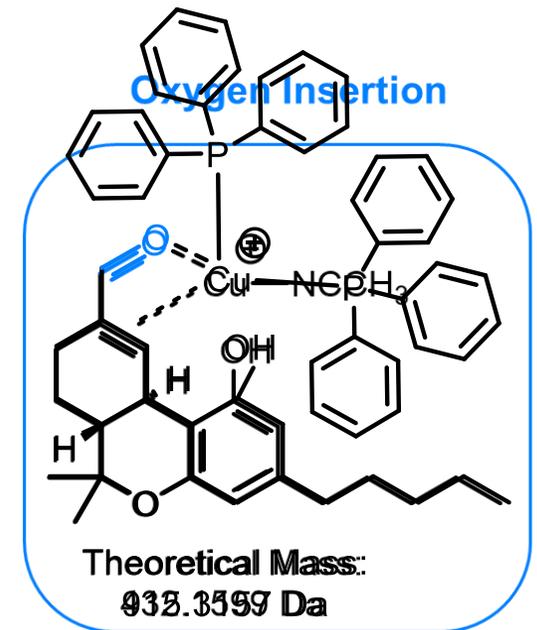
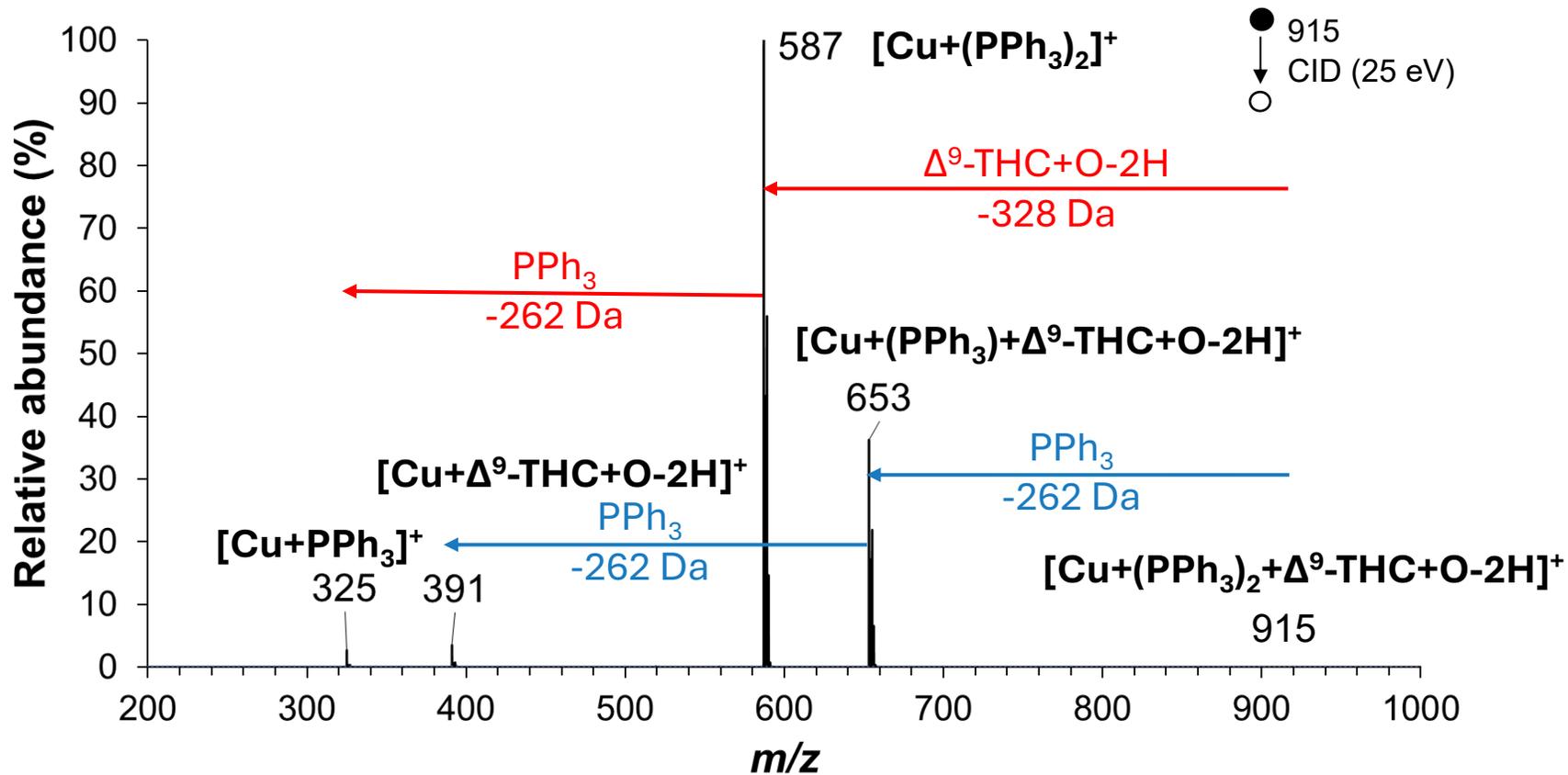




Full Scan Differentiation: $[\text{Cu}(\text{PPh}_3)_2(\text{ACN})_2]\text{BF}_4$

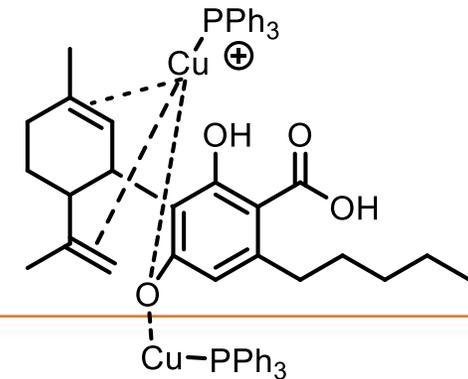
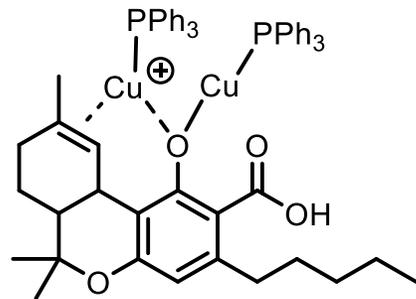
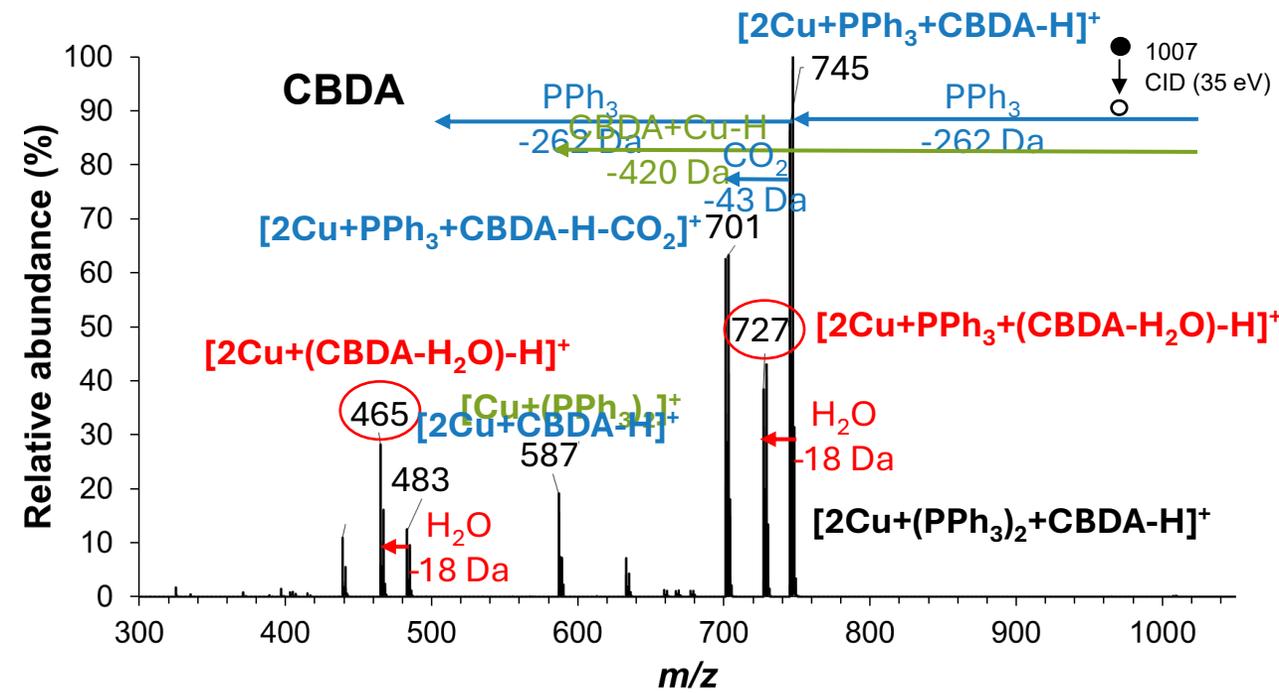
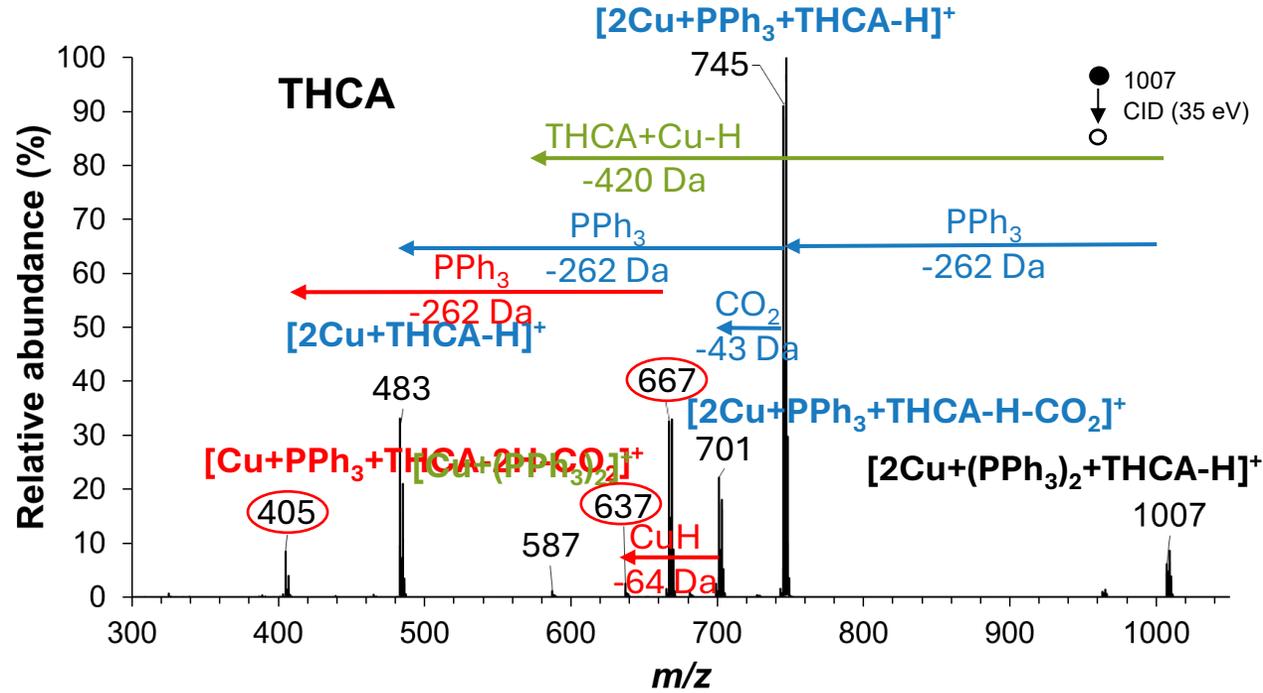


Δ^9 -THC: MS/MS of m/z 915

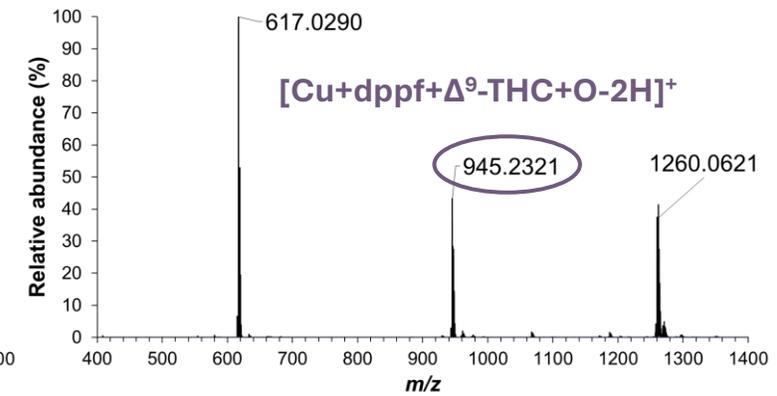
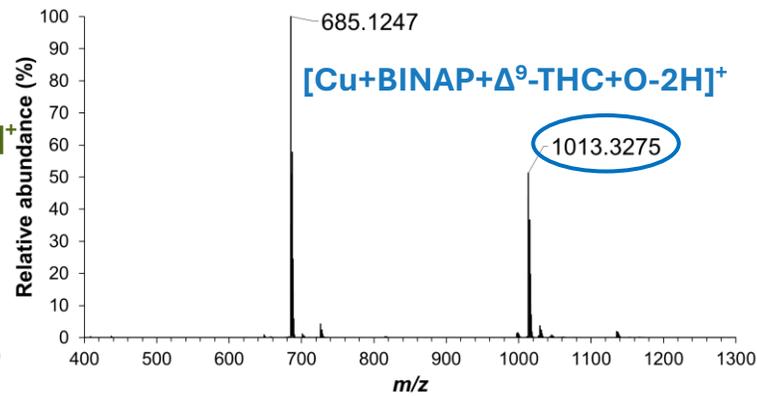
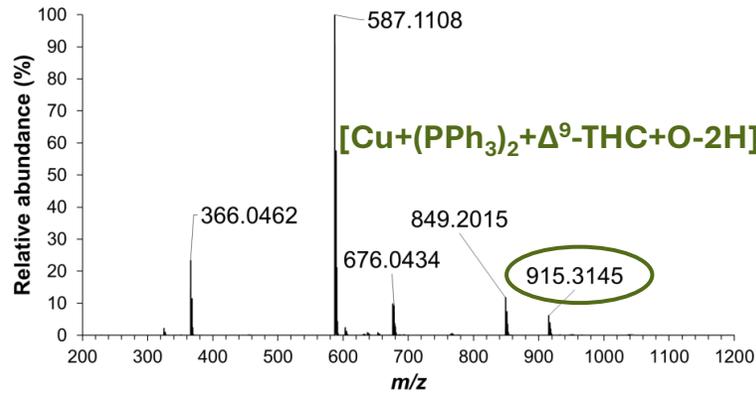
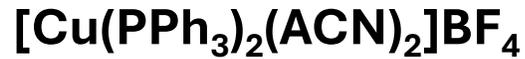




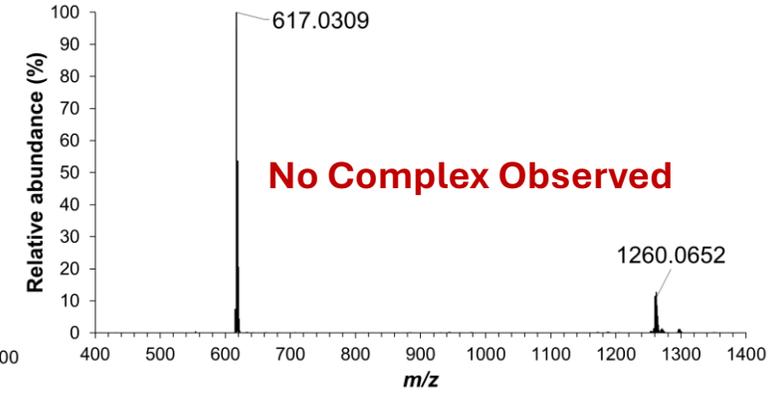
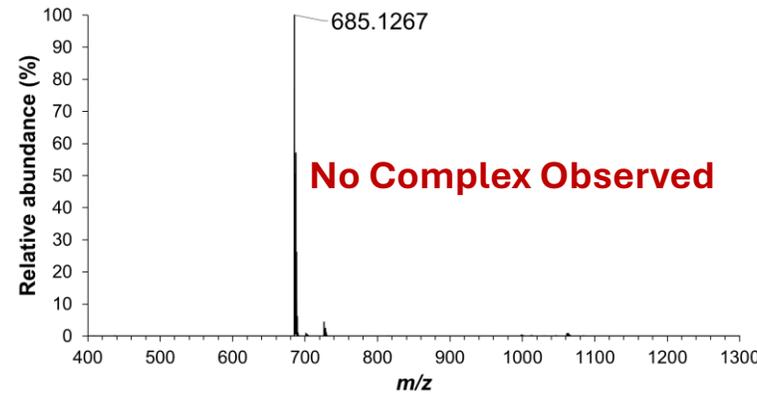
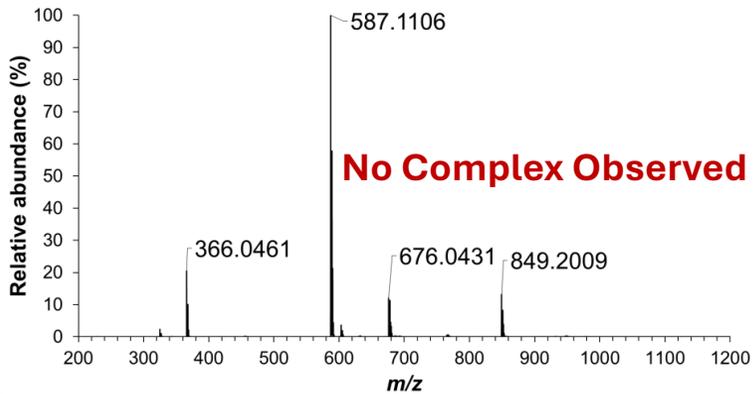
MS/MS Differentiation: THCA vs. CBDA



Optimized Ligands: Complex Formation Pattern

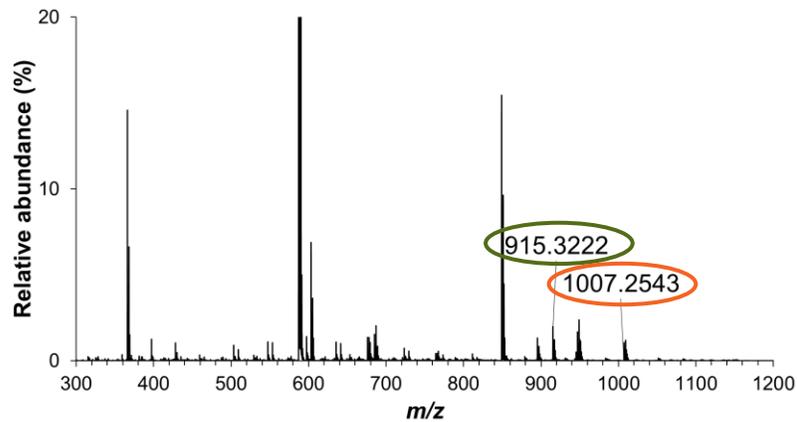


CBD

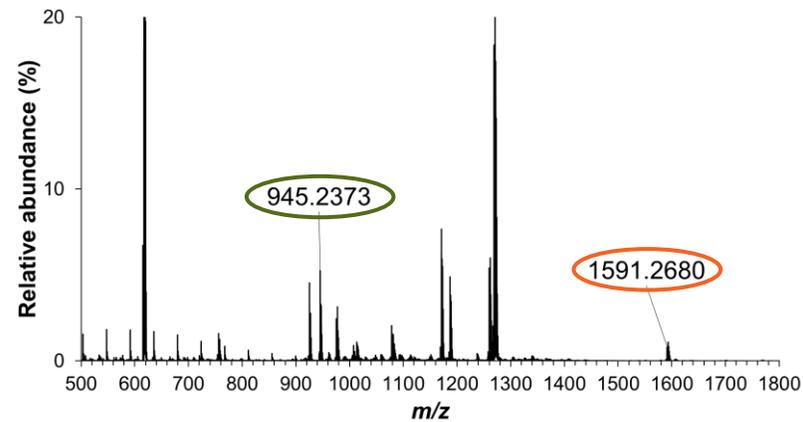


Authentic Samples

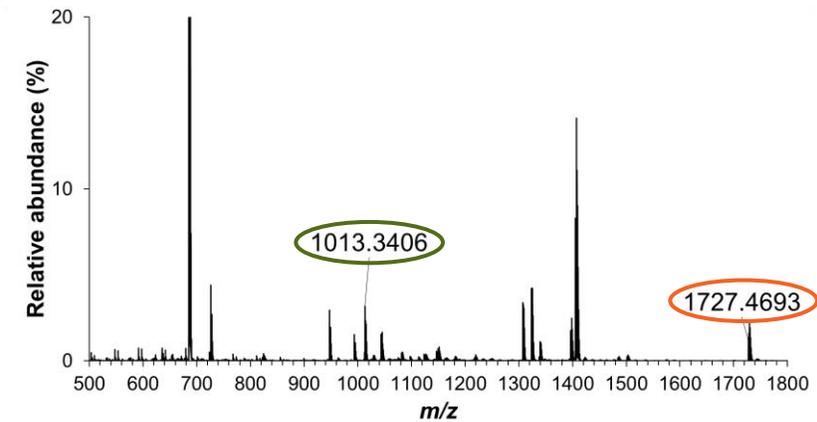
$[\text{Cu}(\text{PPh}_3)_2(\text{ACN})_2]\text{BF}_4$



$[\text{Cu}(\text{dppf})(\text{ACN})_2]\text{BF}_4$



$[\text{Cu}((R)\text{-BINAP})(\text{ACN})_2]\text{BF}_4$



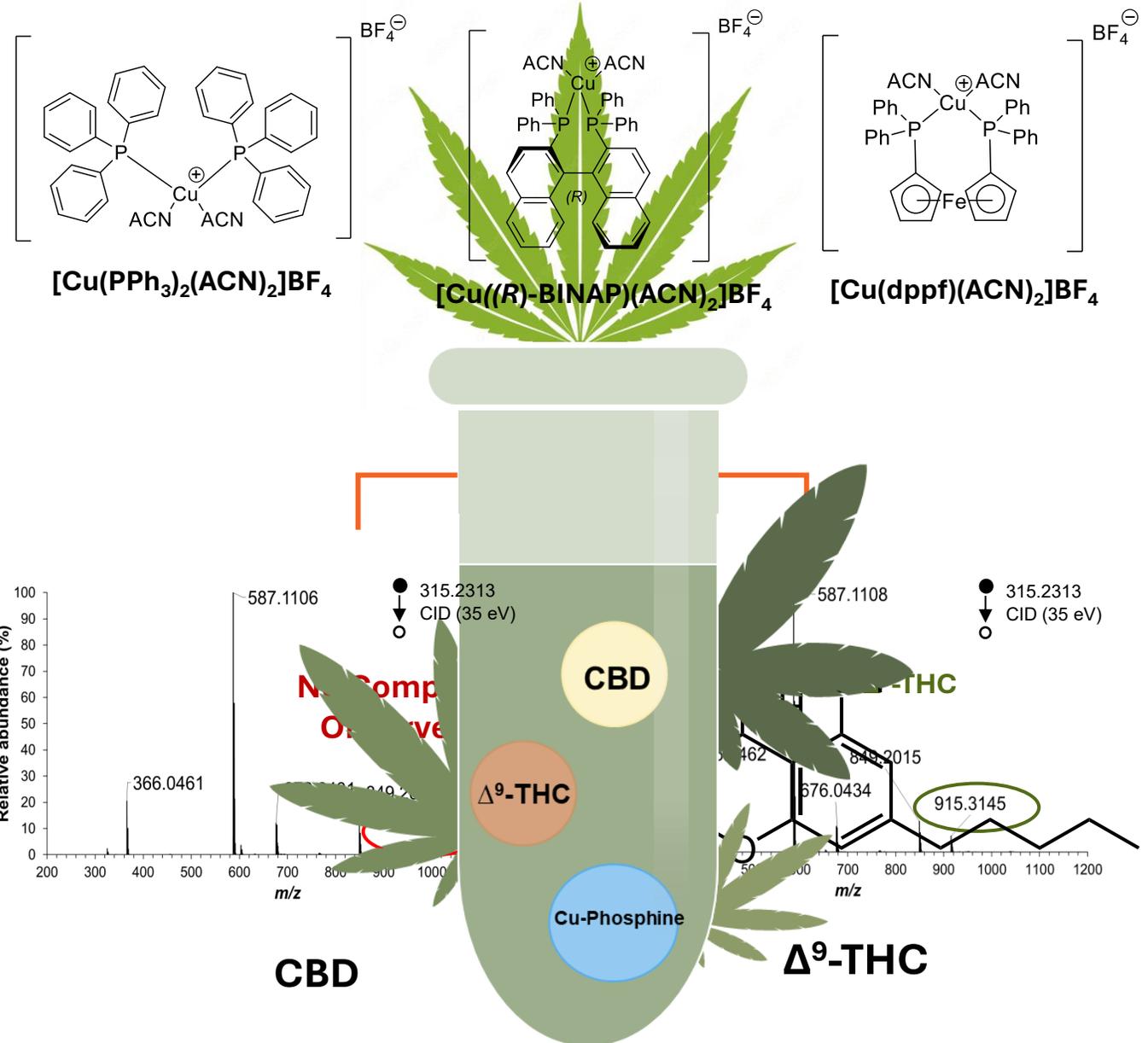
Δ^9 -THC

THCA/CBDA



Conclusion

- 20 cannabinoids with 10 Cu-phosphine complexes
- Optimized Cu-phosphine complexes for full scan differentiation
- Applied to authentic cannabis extracts
- Novel solution
- Next steps:
 - Hemp vs marijuana



Acknowledgments

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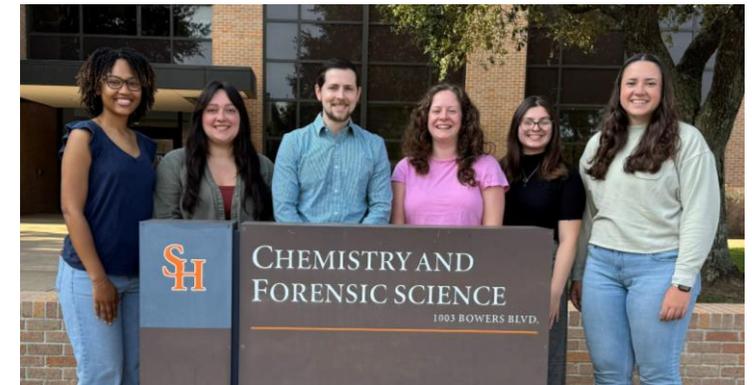
- Davidson Group

- Dr. J. Tyler Davidson
- Emma Hardwick
- Christany Liggins



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Questions

Speaker Name: Alleigh Couch

Email Address: alleigh.couch@shsu.edu



Ag-Ligand
Qualitative



Ag-Phosphine
Semi-Quant



Cu-Ion
Complexation



Molecular Ion
Formation