



Machine Learning Collision Cross Sections using Differential Mobility Spectrometry

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INTRODUCTION

Differential mobility spectrometry (DMS) is a recently developed technique that enables the separation of gas-phase ions based upon differences in structure and interaction potential. Inside the DMS cell (See Figure 1), an asymmetric oscillating electric field called the separation voltage (SV) influences ion motion due to differing mobilities under high- and low-field conditions. The selectivity of DMS can be further improved by adding solvent modifiers (e.g. acetonitrile, water, etc.), which enhance separation of isomers,² tautomers,⁴ etc. through differences in dynamic clustering propensities.¹

The collision cross section (CCS) is a property that is commonly used to assign molecular structure. While CCS can be readily obtained via traditional ion mobility measurements, to date it has not been measured via DMS. Here we employ machine learning to treat DMS data for a variety of molecular ions and extract CCS values along with other molecular properties.

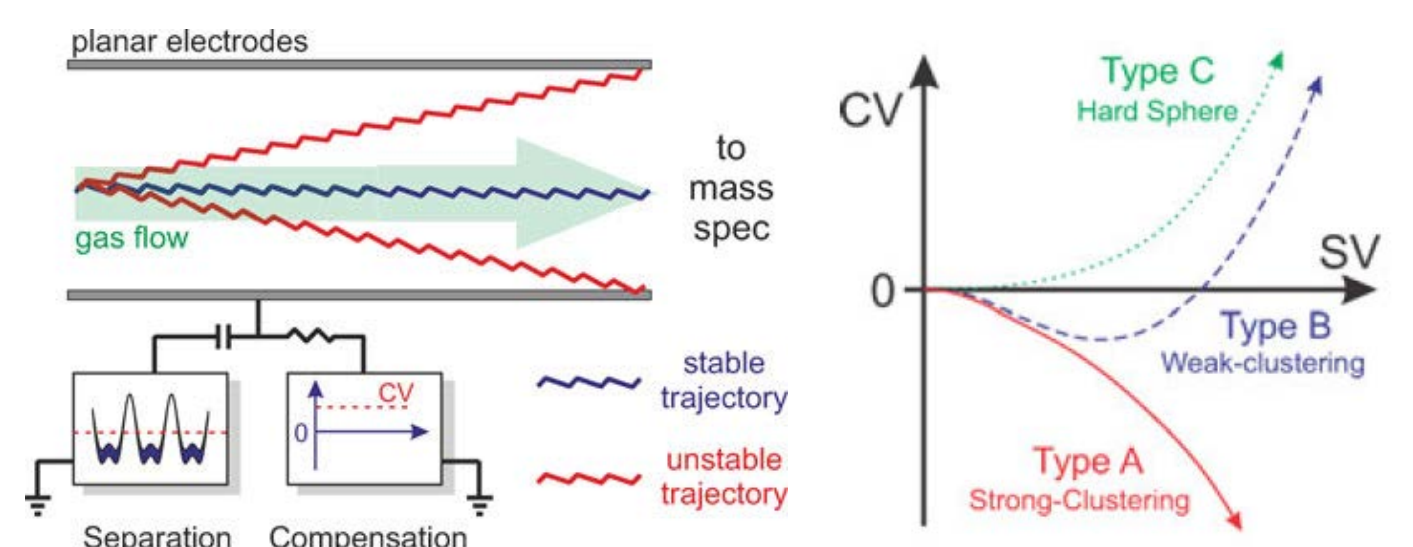


Figure 1. (Left) Schematic diagram of the DMS cell. (Right) Different types of DMS behaviour observed as analytes move through the DMS cell.¹

MATERIALS AND METHODS

Sample Preparation:

- ~200 compounds have been combined into a mixture and diluted to a 100 ng/ml solution using a 50:50 mix of methanol and water along with 0.1% v/v formic acid.

Computational Methods:

- Initial optimizations performed using the semi-empirical PM7 theory/
- further optimizations and energy calculations performed at the DFT/B3LYP with 6-31++G(d,p) basis set.
- CCSs were calculated for each compound using modified MOBCAL software
- See Figure 2 below for a visual explanation of the process.

DMS Experimental Conditions:

- DMS experiments run using multi reaction monitoring mode, allowing for the examination of multiple compounds at once.
- Compounds observed using N₂ and H₂O modifiers and observed at 150/225/300°C

Machine Learning Methods:

- CCSs are predicted by using molecule and experimental DMS parameters:
 - m/z, calculated CCS, temperature, SV and corresponding CV values, gas modifier used, etc.
- Leave one out method is then applied to this data - All compounds, save one, used as training set to attempt to predict the CCS of the remaining compound.
- Random forest algorithm with 500 trees is used to make predictions.

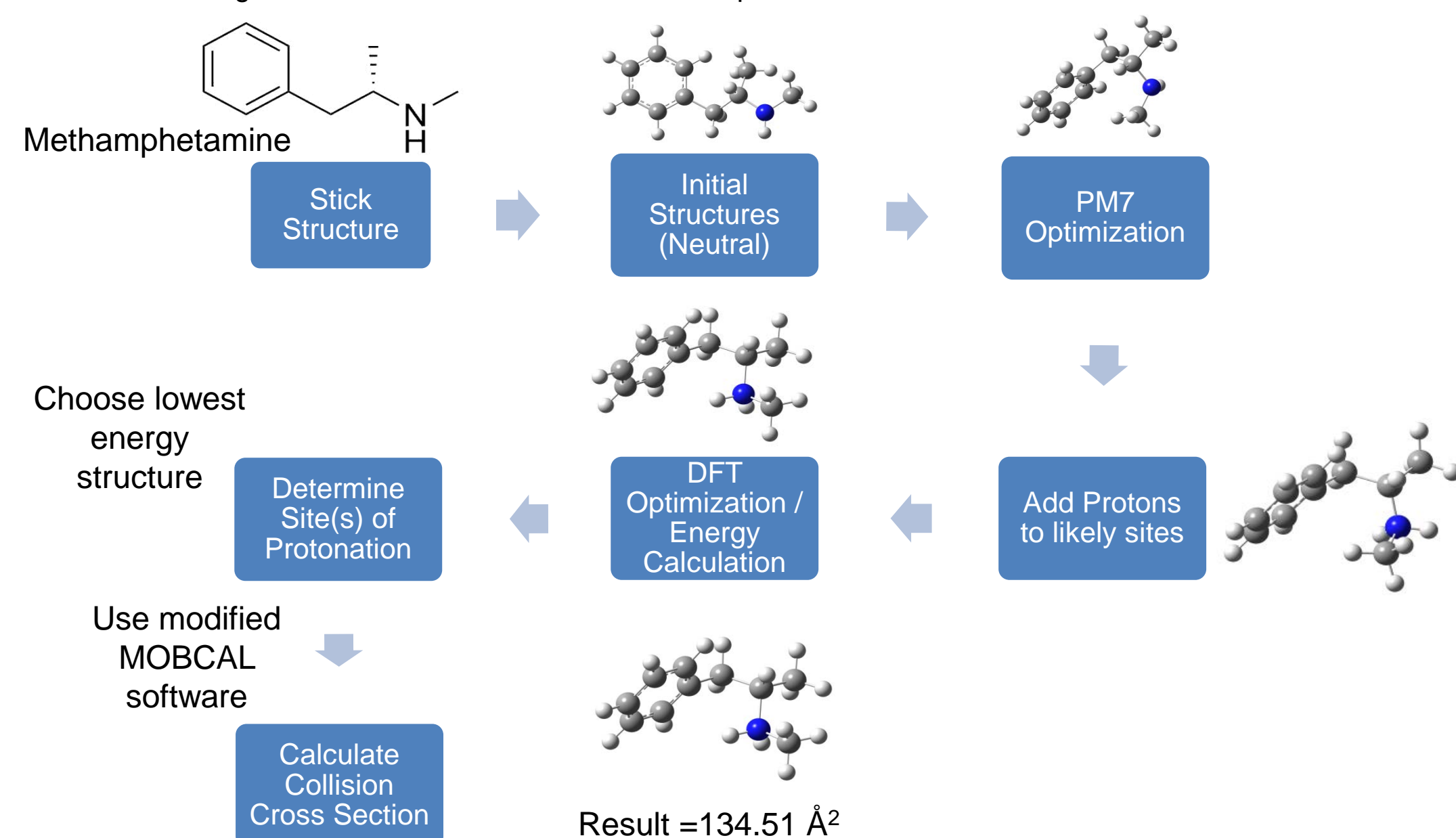


Figure 2. Example workflow for determining the CCS of a given analyte compound.

RESULTS - EXPERIMENTAL

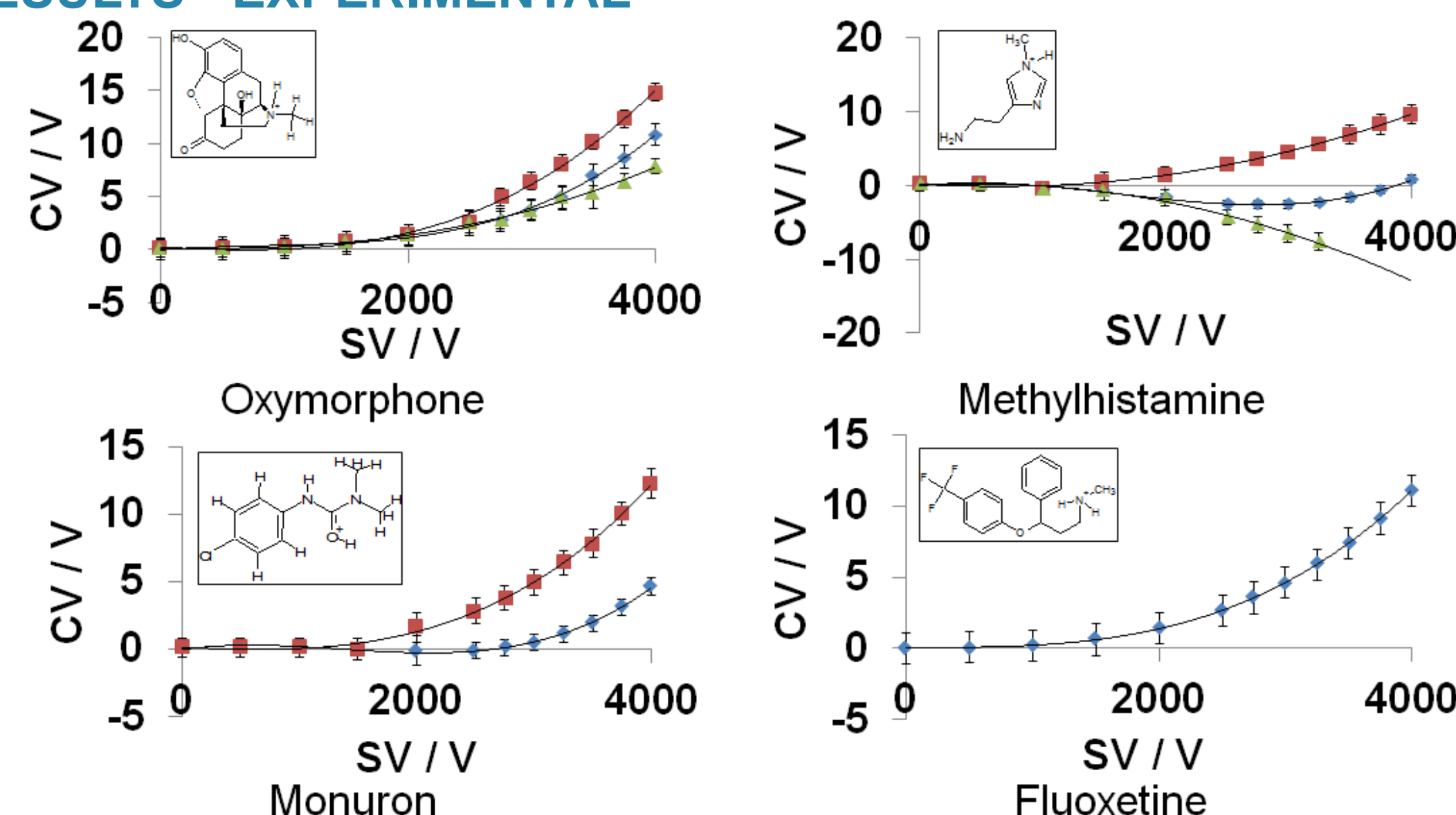


Figure 3. Sample dispersion plots (SV vs. CV) taken from the DMS experiments. Each point is generated by taking the CV values of peak maximums that are generated from plots of CV vs. intensity (ionograms) that are outputted by the DMS. Ionograms are taken at multiple different SV values in order to display how compounds behave in increasing electric field. Different colours represent different peaks in the ionograms, with blue representing the peaks of highest intensity.

RESULTS - COMPUTATIONAL

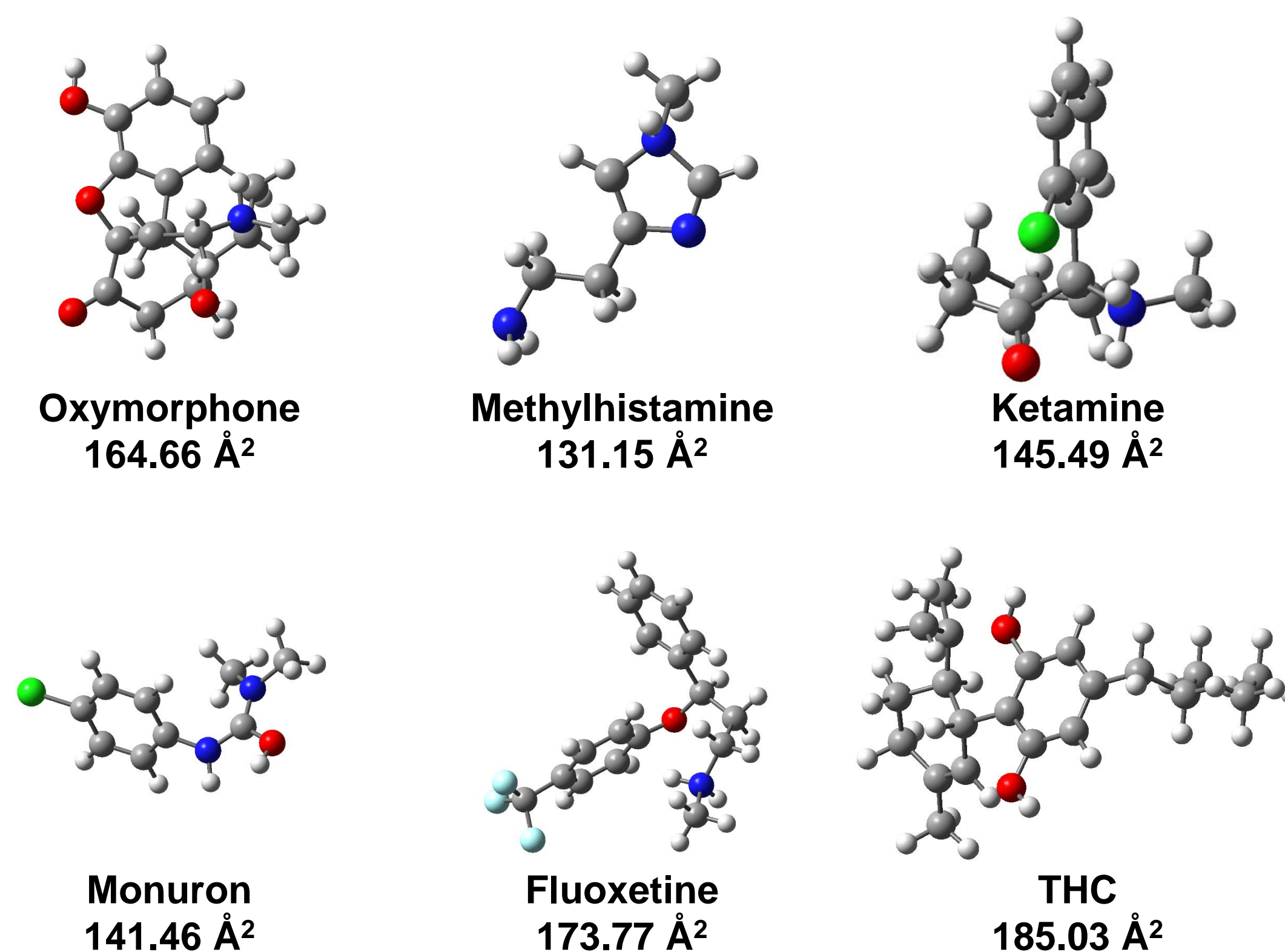


Figure 4. Examples of the studied compounds.

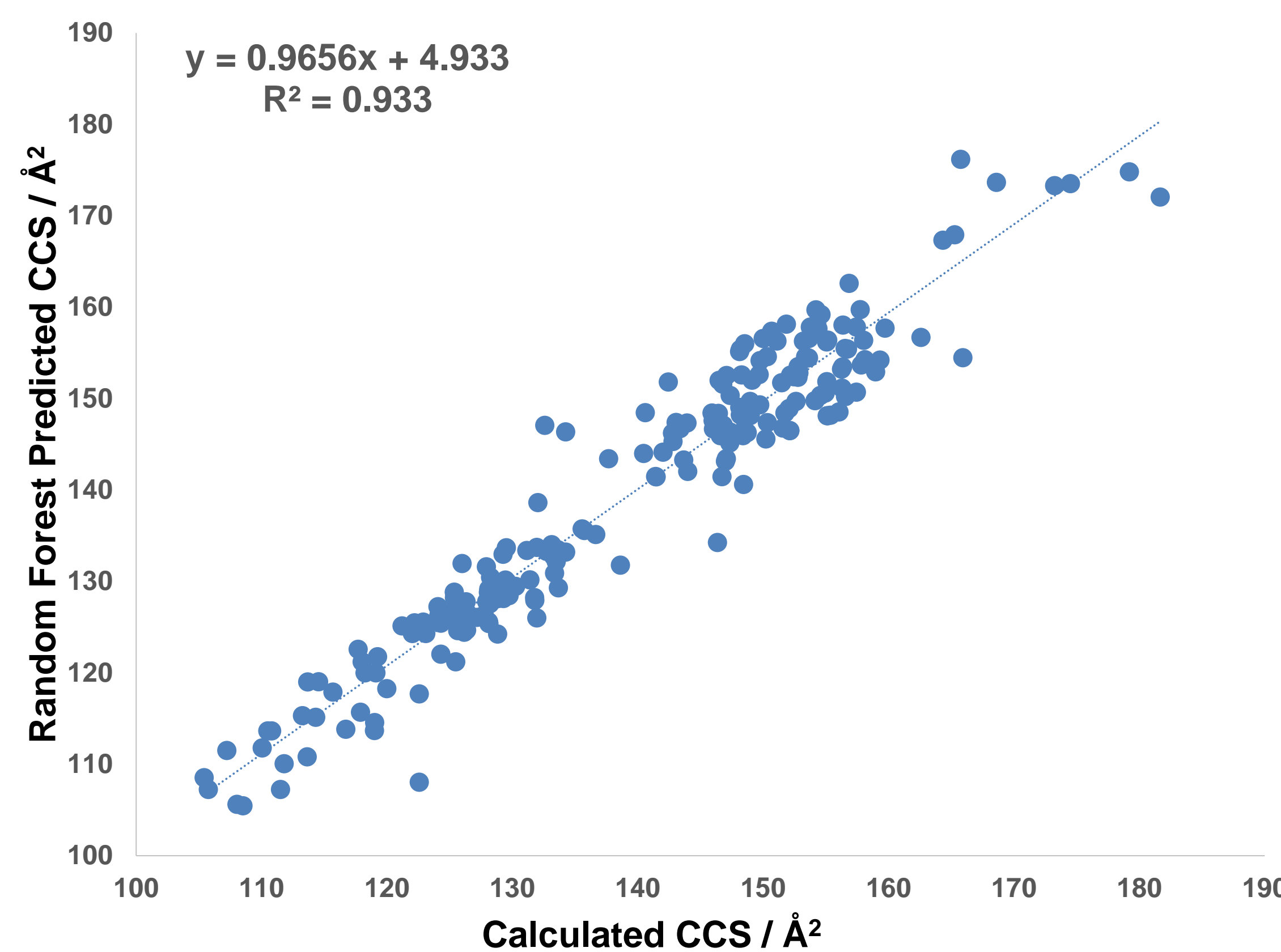


Figure 5. Comparison of MOBCAL calculated CCS and ML predicted CCS for ~200 compounds from our machine learning database of chemical information. The MAE for this data set was 3.08 Å²

RESULTS – OTHER INFLUENCES ON DMS BEHAVIOUR

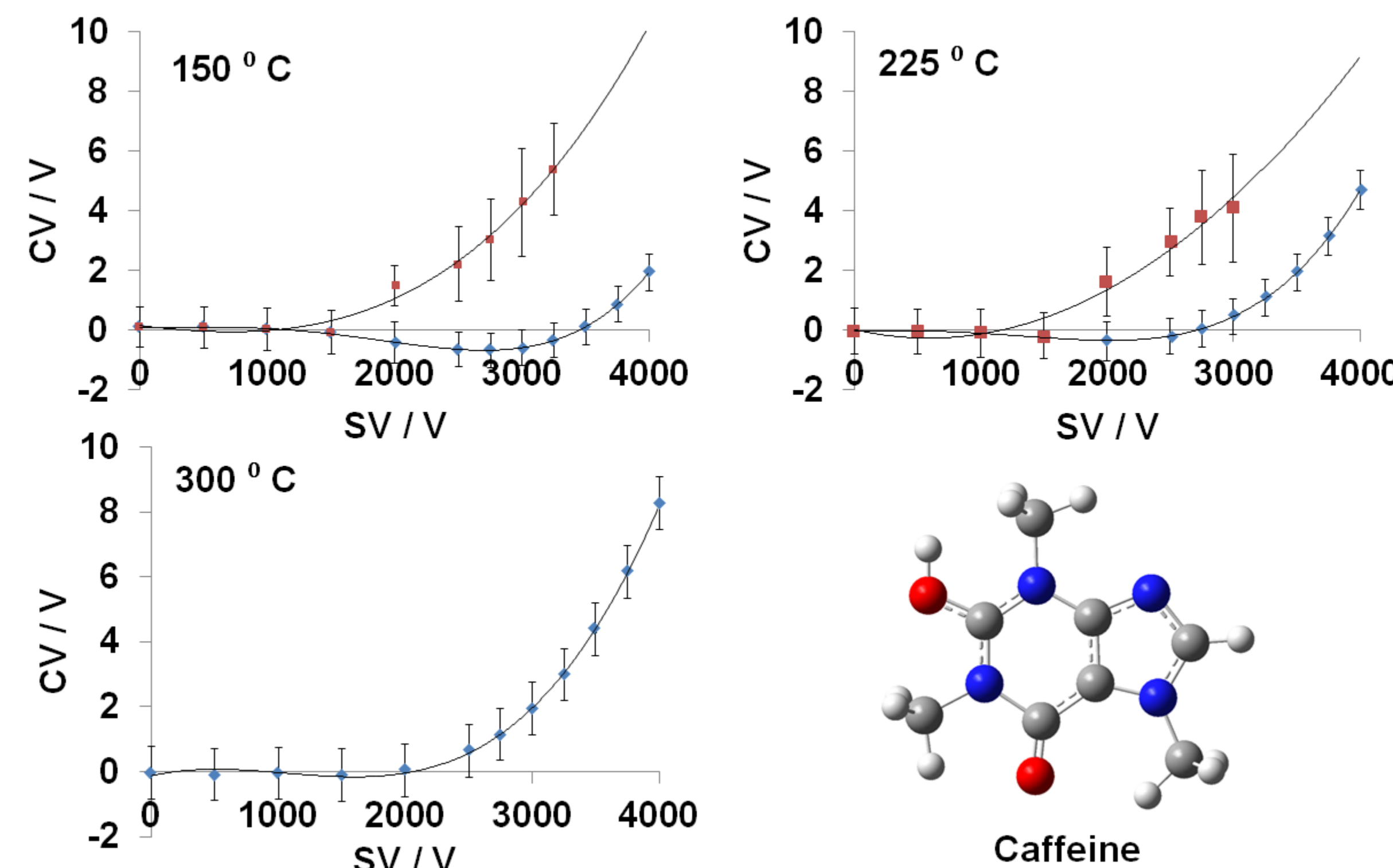


Figure 6. Dispersion plots showing the differences in DMS temperature. (using N₂ modifier) The increase in Gibbs' free energy disrupts clustering interactions (Type A/B behavior) and causes the analyte compounds to undergo more hard sphere type interactions. (Type C behavior).

RESULTS – OTHER INFLUENCES ON DMS BEHAVIOUR - CONTINUED

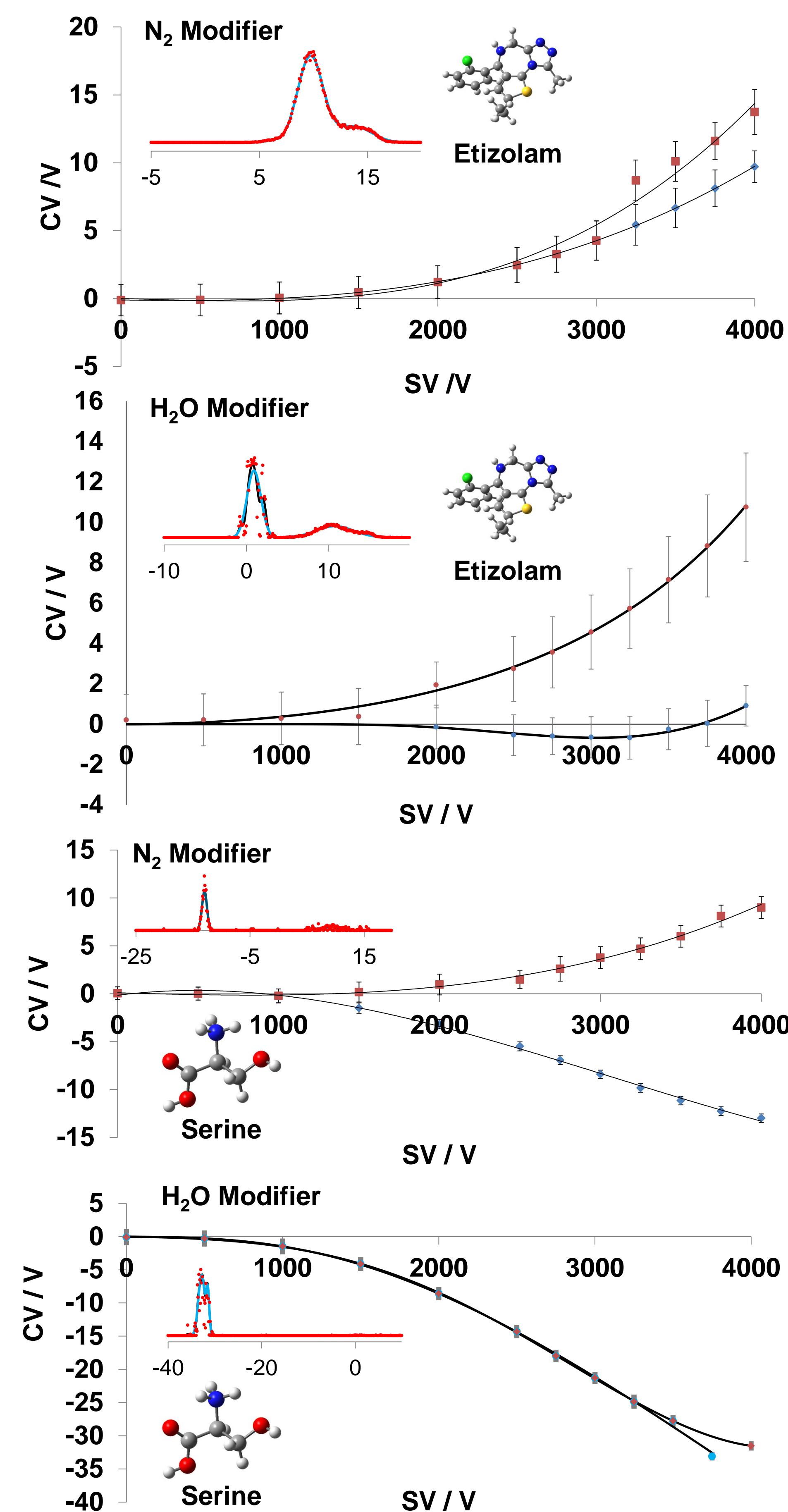


Figure 7. Dispersion plots showing the change in DMS behavior with changing collision partner. In the water-modified environment, compounds exhibit A/B-type behavior, whereas Type-C behavior is observed in pure N₂. (Inlaid) Ionograms at SV = 4000 V.

CONCLUSIONS

The DMS behaviour of ~200 molecules was measured under a variety of temperature and modifier conditions. The increased DMS temperature reduces the Gibbs' energy of binding, thus changing DMS behaviour, while different solvent modifiers alter the DMS behavior by changing the apparent mobility of compounds as they move through the DMS cell. Lastly, machine learning was used to correlate DMS behaviour with molecular CCS.

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