B139 The Importance of Detailed Mechanistic Fragmentation Analysis for Interpretation of GC/MS-derived Spectra and its Application to Methamphetamine and Regioisomers

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The goal of this presentation is to challenge the controlled substances analyst to think about mass spectrometry (MS) fragmentation mechanisms of organic molecules in general and apply these rules to regioisomers of methamphetamine. The ultimate goal is to approach spectral interpretation in a mechanistic fashion allowing the analyst to assign most peaks in a spectrum to a chemically reasonable and specifically identified structure.

This presentation will impact the forensic community and/or humanity by allowing the analyst to 1) discount a spectral library sug- gestion as inaccurate, thus lowering the chance of a misidentification, 2) verify that the compound in question has been correctly identified leaving no major peaks in a MS-derived spectrum unexplained or 3) construct a reasonable chemical structure based on logical losses of an unknown that possesses an unusual spectrum; for example, when a non-routine com- pound is encountered.

An overview of the primary decomposition routes giving rise to many of the molecular fragments observed as *m/z* peaks in MS-derived spectra will be presented. Examples of these routes include: induction, α-cleavage, benzylic cleavage and rearrangements. Each of these routes will be defined and illustrated. In addition to these primary decompositions, another important analysis is to determine whether or not molecular fragments undergo secondary decompositions, which include internal rearrangements and further fragmentation. While admittedly more difficult to perform, the capability to propose chemically viable mechanisms for secondary decom- position analysis is an important skill which will be highlighted in the remainder of this work.

It is important to recognize that several sites of ionization are possible in a molecule depending on the type of functional groups present and how large the molecule is. The proportion of the entire analyte population with a given radical cation site from any of the several ionization sites available in the molecule is dependent upon the ionization potential of the site. This means that several mechanistic pathways are occurring simultaneously within the analyte population necessitating a full account of all possible fragmentations in order to assign structures to each of the spectral peaks. It should be noted that while multiple ionizations within one molecule are possible, the energy required to accomplish this is prohibitive thus effec- tively rendering any resultant peaks arising from this process to extremely small relative abundances within the spectrum. The work presented here was performed on an electron impact (EI) quadrupole mass-spectrometer. Upon evaluation and comparison with ion-trap mass-spectrometer data, no significant differences were found.

A full fragmentation scheme for methamphetamine will be presented. This scheme will be used as an example for a deconstructive-style analysis of MS-derived spectra showing examples of each of the primary decompo- sition routes, namely, induction, α and benzylic cleavage and rearrange- ments described above. Generalizations from this specific example will provide insight into fragmentation mechanisms for molecules containing amine groups and phenyl rings as these functional groups are virtually omnipresent in routine controlled substance analyses. Also shown will be an empirically derived procedure to easily determine the geometry of dimethyl- or ethyl-substituted imine fragments (RRC=NRR where *m/z*=58) by simple spectral peak pattern recognition. Comparison of quadrupole data with ion trap and spectral library data shows that this imine secondary fragmentation analysis is indeed platform independent.

Skills from this analytical approach will be showcased by studying a previously unreported regioisomer of methamphetamine: N,α,4-trimethyl phenmethylamine, or TMPMA. The authors synthesized this novel ring-substituted methamphetamine regioisomer with the sole intent of testing *a priori* analysis of expected spectral peaks. It will be shown that the mech- anistic chemistry detailed above provided a correct explanation for all of the peaks above 10% relative abundance of the base peak. Certainly this predictive skill is useful in some casework; however, the converse may be more useful: when an unexpected or unusual peak pattern arises in a spectrum, analyzing it to determine structure of the molecule. However infrequently the need arises to analyze an unusual compound in casework, reliance solely on the spectral library may not yield useful results, necessi- tating alternative methods such as those proposed here.

Methamphetamine, Fragmentation, Gas Chromatography/Mass Spectrometry (GC/MS)

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