A135 Analysis of Fluoro-Phenethylamine Regioisomers Using Electrospray Ionization-Mass Spectrometry and Capillary Electrophoresis

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After attending this presentation, attendees will become aware of how ESI-MS and CE techniques can be used to distinguish between 2-, 3-, and 4-fluoroamphetamine and 2-, 3-, and 4-fluoromethamphetamine.

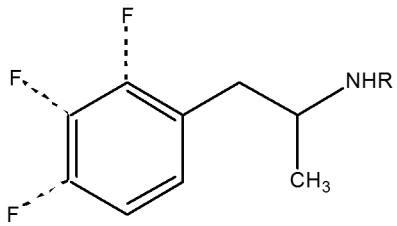
This presentation will impact the forensic science community by providing awareness of alternative methods for analyzing ring regioisomers of controlled substances.

During the past couple of years, local, state, and federal forensic chemistry laboratories have encountered a great array of new designer chemicals. The new compounds are available through the clandestine drug market and have been designed with the intention of circumventing legal regulations. Laboratory submissions containing these new compounds present significant challenges to analysts and laboratory managers due to both the lack of reliable sources of reference materials and the inability to use routine laboratory techniques like gas chromatography-mass spectrometry (GC/MS) to unambiguously distinguish potential chemical variations in the structure of the compounds.

Two types of new designer compounds recently encountered are fluoroamphetamine (FA) and fluoromethamphetamine (FMA), which may be considered structural analogues of controlled phenethylamines. As observed in the structures below, there are three possible phenyl ring regioisomers for each one of these compounds, depending on the location of the fluorine atom. When the fluorine atom is located in position two, three, or four, the resulting compounds are the *ortho*, *meta*, or *para*-fluoro-phenethylamines, respectively. It is believed that replacement of the hydrogen atom by fluorine facilitates passage through the blood-brain barrier, as the substitute atom increases the lipophilicity of the compound.[1]

Analysis of FA and FMA using routine GC/MS conditions results in similar retention times and electron ionization (EI) fragmentation patterns for all three positional isomers of each compound. That is, the unequivocal distinction between 2-FA, 3-FA, and 4-FA, and between 2-FMA, 3-FMA, and 4-FMA cannot be accomplished solely by GC/MS analysis. This presentation will describe application of the techniques of electrospray ionization mass spectrometry (ESI-MS) and capillary electrophoresis (CE) to the analysis of FA and FMA regioisomers.

Analysis of 2-FA, 3-FA, and 4-FA using ESI-MS results in protonated pseudomolecular ions at m/z 154, consistent with the molecular weight of 153 Da. The analogous ions at m/z 168 were observed during analysis of the FMA regioisomers. Collision-induced dissociation (CID) experiments were designed in order to investigate the possibility for distinguishing the regioisomers from each other. To achieve this, the CID conditions were methodically varied between 20% and 30% collision energy, and MS^2 and MS^3 fragmentation data were collected for each of the six regioisomers. Based on the fragmentation patterns observed, it can be concluded that 2-FA and 3-FA cannot be distinguished from each other. However, the fragmentation pattern observed for these two regioisomers can be clearly differentiated from that obtained for 4-FA. This pattern of distinction is statistically reproducible and also repeated within the FMA regioisomer series. That is, 2-FMA and 3-FMA result in similar MS^n fragmentation spectra, which then can be distinguished from that of 4-FMA.



R = H (amphetamine) R = CH_3 (methamphetamine)

Analysis of FA and FMA regioisomers using routine non-chiral CE experimental conditions resulted in similar migration times for all six regioisomers. Under chiral analysis conditions, the migration times observed changed, but are only slightly distinguishable. However, the use of 2-OH-β-cyclodextrin as a buffer additive did result in noticeable differences between the enantiomeric pairs of each compound. A reproducible pattern of separation is observed which can be used to distinguish between the *ortho*-, *meta*-, and *para*-phenethylamines. The resolution between the *d*- and *l*- enantiomer peaks is observed to increase as the position of the fluorine is changed from four to three to two; that is, as the fluorine atom moves closer to the alkyl chain. For 4-FA and 4-FMA, the enantiomers are practically co-migrating; for 3-FA and 3-FMA the peak separation increases and the presence of 2 enantiomers is evident, although baseline separation is not complete. For 4-FA and 4-FMA, the resolution values measured are twice those observed for 3-FA and 3-FMA, respectively.

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This presentation will also include application of the above described ESI-MS and CE techniques during the analysis of multiple unknown case samples. This material included in this presentation is expected to be of interest to other forensic chemistry analysts and laboratory personnel involved in the analysis and evaluation of controlled substance analogues.

Reference:

1. Fyaz I. Important fluorinated drugs in experimental and clinical uses. Journal of Fluorine Chemistry 2002;118: 27-33.

Regioisomer, Analogues, Controlled Substance

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