A85 Synthesis of Fluoromethcathinones

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After attending this presentation, attendees will have learned how to synthesize fluoromethcathinones and will be familiar with the supporting analytical data for all three structural isomers of the fluoromethcathinones.

This presentation will impact the forensic science community by providing information on the synthesis of 2'-, 3'- and 4'- fluoromethcathinone along with analytical data by GC/MS, ATR-FTIR, 1H-NMR, LC-MS/MS, solubility, and other physical chemical data.

Fluoromethcathinone is an amphetamine-like drug of abuse surfacing in the world of illicit drugs. This emerging cathinone derivative has been seen in both pill and powder form. It is being advertised as a "legal alternative to ecstasy" in online marketplaces in the United Kingdom. Fluoromethcathinone, methcathinone, 4'-methylmethcathinone and 3, 4-methlenedioxymethcathinone are analogs of cathinone that are being used as recreational drugs.[1] These analogs of cathinone have been popularized by their ease of synthesis. Cathinone is the primary central nervous system stimulating component of *Catha edulis,* better known as the khat plant. When the plant matures, cathinone is converted into cathine and norephedrine, which also have stimulating effects. The khat plant is grown mainly in Yemen, Somalia and Kenya and its roots and buds are commonly chewed to obtain euphoric effects.[2] When the leaves dry, they can be used in a tea called Arabian or Abyssinian tea. The khat plant is believed to be brought to the United States by immigrants to help cope with being away from their homelands and families. Internationally, cathinone is a schedule I drug under the Convention of Psycotropic Subtanaces and it is also a schedule I drug under the DEA Controlled Substances Act of 1993.

The fluorine in fluoromethcathinone can be arranged in the 2'-, 3'- or 4'- position of the methcathinone structure. The 4'- fluoromethcathinone is also called "flephedrone". Synthesis of fluoromethcathinones has been done previously with the following yields: 27% of 4'-fluoromethcathinone, 20% of 2'-fluoromethcathinone and 8% of 3'-fluoromethcathinone.[1] In an attempt to increase yields of fluoromethcathinone, sodium carbonate, lithium carbonate or cesium hydroxide were added in equimolar amounts before addition of the methylamine. Sodium carbonate proved to be most beneficial in the synthesis of 4'-fluoromethcathinone with a yield of 73.9%. Yields of 17.4% and 11.6% were obtained with the addition of sodium carbonate for 3'-fluoromethcathinone and 2'-fluoromethcathinone respectively. Lithium carbonate was used in the synthesis of 2'-fluoromethcathinone and produced yields of only 4.5%. Since lithium carbonate was not advantageous in the 2'-fluoromethcathinone synthesis, it was no longer used in further synthesis of fluormethcathinones.

Confirmation of the presence of the fluoromethcathinones was done by ATR-FTIR and gas chromatography/mass spectroscopy and compared to previous results.[1] A 30 meter methylsilicone (0.25 mm x 0.025 um) capillary column was used which yielded retention times of the compounds as follows: 10.123 minutes – 4'-fluoromethcathinone;
10.197 minutes – 3'-fluoromethcathinone; 10.264 minutes – 2'- fluoromethcathinone. Major fragmentation of fluoromethcathinone includes the ions *m/z* 58, *m/z, 95* and *m/z* 123. In 2'-fluoromethcathinone *m/z* 56 is present instead of *m/z* 58 which correlates with previous data from R.P. Archer.[1]

H-NMR, LC-MS/MS, solubility, and other physical chemical data will be presented.

References:

1 Archer RP. Fluoromethcahinone, a new substance of abuse. Forensic Sci Int 2009;185:10-20.

2 Feyissa AM, Kelly JP. A review of the neuropharmacological properties of khat. Progress in Neuro-Psychopharmacology and Biological Psychiatry 2008;32:1147-1166.

Fluoromethcathinone, Cathinone, Gas Chromatography/Mass Spectroscopy

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