Thermal Degradation of Synthetic Cannabinoids Containing a Cyclopropyl Group

David Eckre, BSa; Lee Badness, BSb; J. Graham Rankin, PhDb; Candice Bridge, PhDb

a) Marshall University, 1401 Forensic Science Drive, Huntington, WV 25701
b) United States Army Criminal Investigation Laboratory, 4930 N 31st St, Forest Park, GA 30297

Abstract

The newest wave of synthetic cannabinoids, e.g. UB-144 and XLR-11, contain cyclopropyl rings and therefore circumvent the new S.3187 law. The analysis of cyclopropyl containing molecules can be challenging because the chromatograms of the standards (and casework) contain multiple related peaks. Standards of UB-144 and XLR-11 were heated and then both the Unheated and the Heated samples were analyzed using GC-MS, LC-MS, solid-phase GC-IR, FT-IR, Raman, and pyrolysis GC-MS. It was concluded that the first peak was the original molecule and the second was a thermodynamic product where the cyclopropyl ring was formally opened. This research provided methods to identify cyclopropyl-containing synthetic cannabinoids, as well as answer what was happening to create two peaks in the chromatogram.

Disclaimers

This study was conducted because many samples that involve compounds containing cyclopropyl rings have multiple peaks in the chromatogram and analysis is questioning what is causing the extra peaks. It was previously reported that two cyclopropyl ketones do thermally rearrange to homoallylic ketones.1 The Dea temporarily placed SW-1, SW-7, SW-8, SW-13, and SW-122. Several European countries enacted generic bans that controlled synthetic cannabinoids based on general chemical structures.3

Introduction

The first wave of synthetic cannabinoids was detected in herbal smoking packages in late 2008 and included JWH-018, JWH-073, and CP-47,497. In 2009, JWH-018, JWH-073, and CP-47,497 were explicitly controlled in several European countries.3

A second wave of synthetic cannabinoids hit the market in 2010 and included JWH-081, AM-2201, JWH-210, and JWH-122. Several European countries enacted generic bans that controlled synthetic cannabinoids based on general chemical structures.3

In March 2011, the DEA temporarily placed JWH-018, JWH-073, JWH-200, CP-47,497, and cannabicyclohexanol and their salts, isomers, and salts of isomers into Schedule I of the Controlled Substances Act for twelve months. The ban was later extended an additional six months.6

On July 9, 2011 Senate bill S.3187 was signed into law. This bill classified cannabimimetic agents as Schedule I controlled substances and defined them as "any substance that was a cannabimimetic receptor type 1 (CB1 receptor) agonist as demonstrated by binding studies and functional assays within any of the following structural classes" (Fig. 1). The bill also listed 16 synthetic cannabinoids by name, making them Schedule I controlled substances including the five temporarily scheduled in 2011.7

Materials and Methods

- Heated standards: • Heated to 300°C • 1 min standard into well of a spot well plate (SWP) • Placed SWP onto hot plate (~10 min) • Re-analyzed both Unheated and Heated synthetic cannabinoids using:
  - Gas Chromatography – Mass Spectrometry (GC-MS)
  - Liquid Chromatography – Mass Spectrometry (LC-MS)
- Extracts were analyzed both Unheated and Heated using GC-IR
- XLR-11 4-Fluoropentyl Isomer (1-(4-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl) methanone)
- XLR-11 4-Pentenyl Analog (1-(pent-4-en-1-yl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl) methanone) (

Results and Discussion

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The following spectra are for UR-144. Similar spectra were observed for XLR-11, 4-PA, and 4-FPI standards.

Materials and Methods

- Purchased following standards from Cayman Chemical:
  - UR-144 (4-pentyl-1-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl) methanone
  - XLR-11 (1-(4-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl methanone)
  - XLR-11 4-Fluoropentyl Isomer (1-(4-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl) methanone)
  - XLR-11 4-Pentenyl Analog (1-(pent-4-en-1-yl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl methanone)
  - UB-144 (1-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl) methanone (Fig. 2)
  - CP-47,497 (Fig. 3-8)

References

2) Pyrolysis GC-MS (PGC-MS) and therefore very efficient.
4) Results and Discussion

Figure 1. The three general structures in the five classes of genetically controlled structures that are new Schedule I drugs.

Figure 2. Structures of (A) UR-144, (B) XLR-11, (C) XLR-11 4-Fluoropentyl Isomer (1-(4-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl) methanone)

Figure 3. The closed cyclopropyl ring (A) can form 3 possible structures: (B) 2,3,3-trimethyl-1-butene (TMB), (C) 3,3,4-trimethyl-1-pentene.

Figure 4. Comparing the solid-phase GC-IR spectra of the Unheated and Heated UB-144. Chromatography (A) Standard Rt = 1.765 min and Standard Rt = 2.225 min.

Figure 5. Comparing the solid-phase GC-IR spectra of the Unheated and Heated UR-144. (A) Standard Rt = 2.212 min, (B) Product 1 Rt = 9.765 min, (C) Unheated Standard Rt = 2.225 min, and (D) Heated Product 1 Rt = 9.765 min.

Figure 6. Comparing the solid-phase GC-IR spectra of the Unheated and Heated XLR-11. (A) Standard Rt = 2.125 min, (B) Product 1 Rt = 2.225 min.