PRESENTERS

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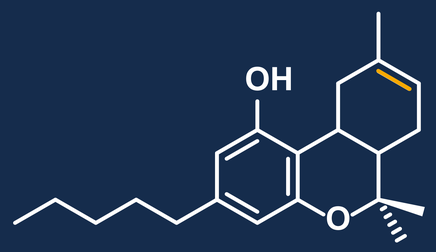
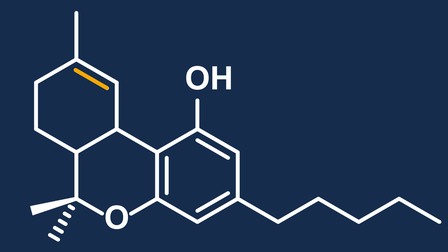
Separate Δ8 from Δ9

(and isolate other cannabinoids)





Background

Legislation has long been a point of conflict for the cannabis industry. With the legalization of hemp-derived products in 2018, the industry quickly realized the accessibility (and inadvertent legality) of Δ8-THC synthesized from CBD. However, many methods for the conversion of CBD into Δ8-THC also produce Δ9-THC, a substance still controlled under federal law. The significant similarity in their structures has established a challenge for the resolution of the two compounds. Here we demonstrate the preparative scale separation (2.2 grams) of the two compounds using a CPC 250 / PLC 2050 Lab System. The techniques developed herein can be adapted to CPC 1000 Pilot and CPC Process systems for higher throughput and legal compliance.

Methods

Both Δ8- and Δ9-THC were synthesized from CBD to provide a mixed injection sample for demonstrating the separation. The resulting solutions were worked up with typical filtration and aqueous washing to remove the acid followed by rotary evaporation to remove solvent.

A suitable solvent system was identified for Δ9- and Δ8-THC with log(K_p) values of -0.31 and -0.41 respectively.

The solvents were pre-mixed in a separatory funnel and the resulting layers were isolated from each other. Separation was first conducted as a simple batch mode elution-extrusion run on 0.8 grams of material.

The second separation was conducted as a Multiple Dual Mode run with 2.2 grams of material.

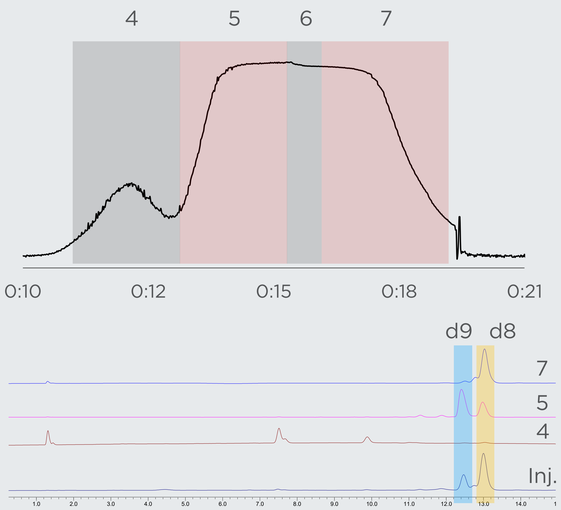
Fractions were independently concentrated by rotary evaporation and analyzed by HPLC.

Discussion

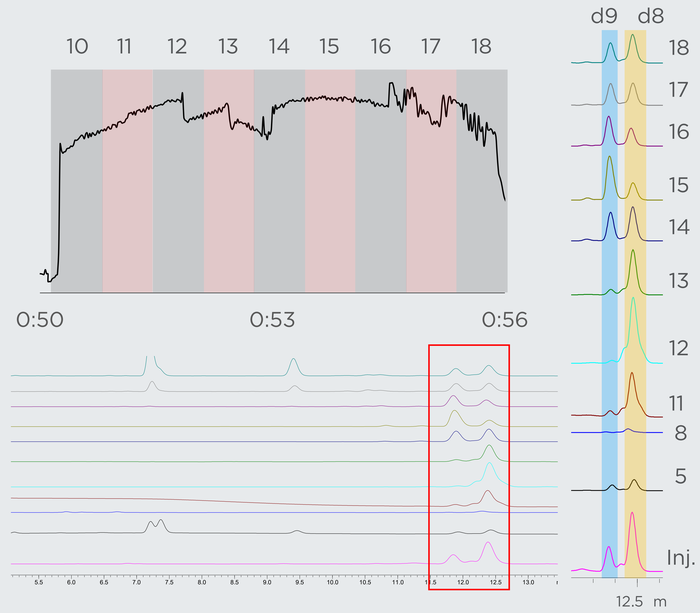
The batch mode injection provided two peaks, one that was a leading impurity for the main THC peak. HPLC analysis of this impurity peak showed a majority peak with a retention time and UV profile similar to that of CBN. The following major CPC peak corresponded to the two THC isomers with a small degree of separation, with fraction 5 being enriched in Δ9-THC and fraction 7 almost exclusively comprising Δ8-THC.

To further improve the resolution between the two compounds, the same separation was carried out in Multiple Dual Mode (MDM) where the direction of flow through the column and the roles of the stationary/mobile phases are reversed. Each iteration of reversal increases the resolution between the compounds. Despite injecting nearly triple the quantity of material, fractions 11, 12, and 13 show significant enrichment of Δ8-THC with subsequent fractions showing a greater proportion of Δ9-THC. Fractions 12 and 13 also represent most of the recovered mass.

Batch Mode Injection:

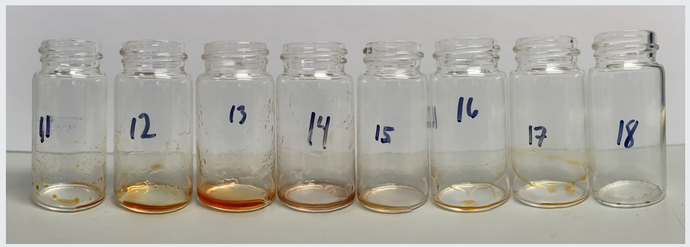


Multiple Dual Mode Injection:



Δ9 Synthetic Scheme

Δ8 Synthetic Scheme



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