232 North Plaza Drive
Nicholasville, KY 40356

REASSESSMENT OF THE STRUCTURAL ASSIGNMENTS FOR THE DIASTEREOMERS 9R-HHC AND 9S-HHC

Prepared by: Richard A. Sams, Ph.D., Issued May 25, 2022

The catalytic hydrogenation of (-)-*trans*-Δ^8-THC or (-)-*trans*-Δ^9-THC does not alter the stereochemistry at carbon atom 6a and 10a but creates a new stereogenic center at carbon atom 9 resulting in a mixture of substances differing only in the configuration at the new stereogenic center. The resulting mixture contains (6aR,9R,10aR)-HHC and (6aR,9S,10aR)-HHC. For simplicity, these isomers are often written and reported as 9R-HHC and 9S-HHC. The relative abundances of isomers vary depending on the starting materials and reaction and purification steps. The identification of the isomers and their quantification in the mixture is important because the 9R isomer has substantially greater (~20-fold) psychoactivity than the 9S isomer.

KCA Laboratories has used certified reference standards of 9R-HHC (part # C-2540) and 9S-HHC (part # C-2541) from NSI Lab Solutions (https://www.nsilabsolutions.com/contact/) to identify and quantify these two isomers in all HHC samples submitted for analysis through May 13, 2022. However, we have recently obtained reference standards of (6aR,9S,10aR)-HHC (Item No. 27501) and (6aR,9R,10aR)-HHC (Item No. 27500) from Cayman Chemical (https://www.caymanchem.com/contact/cc). Gas chromatographic analysis of the isomers from the two sources indicate that the isomer designated 9R-HHC (Lot# 210825) by NSI and the one designated (6aR,9S,10aR)-HHC by Cayman Chemical are characterized by identical retention times (8.817 and 8.822 min, respectively) and similar relative fragment ion abundances (data available upon request). My review of the supporting documentation in the Certificate of Analysis for the (6aR,9S,10aR)-HHC (Lot#0645988-1) provided by Cayman Chemical indicates that the assignments in the Cayman standard are correct and that the NSI standard is not (6aR,9S,10aR)-HHC but that it may be (6aS,9S,10aS)-HHC which is the enantiomer of (6aR,9R,10aR)-HHC. These conclusions are based in part on the results of NMR data that Cayman obtained for the (6aR,9S,10aR)-HHC isomer. Furthermore, we have observed that the elution order for the 9R-HHC and 9S-HHC isomers as identified by NSI were the opposite of what we have observed for other diastereomers that differ at carbon atom 9.

Based on these considerations, all certificates of analysis for HHC diastereomers issued by KCA are based on the use of the Cayman Chemical reference standards and not those from NSI. Please direct any questions or concerns about this matter to the KCA Laboratories team by using the contact information at the bottom of this document.

Figure 1. GC-MS data for (6aR,9R,10aR)-HHC (Cayman Chemical standard)

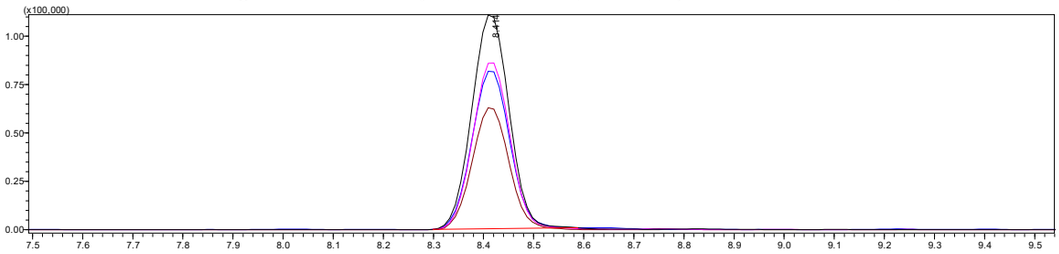

Figure 2. GC-MS data for 9S-HHC (NSI standard)

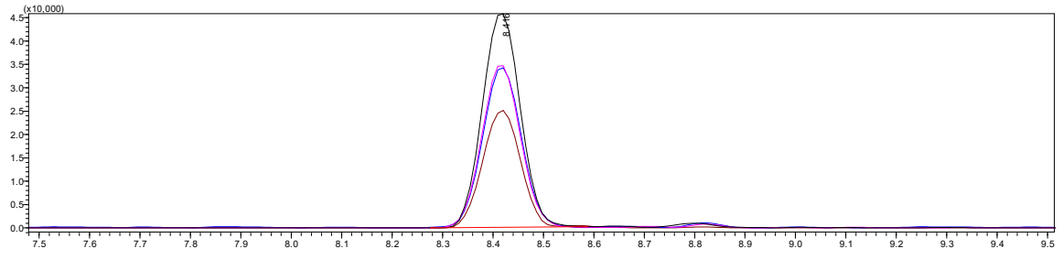

Figure 3. GC-MS data for (6aR,9S,10aR)-HHC (Cayman Chemical standard)

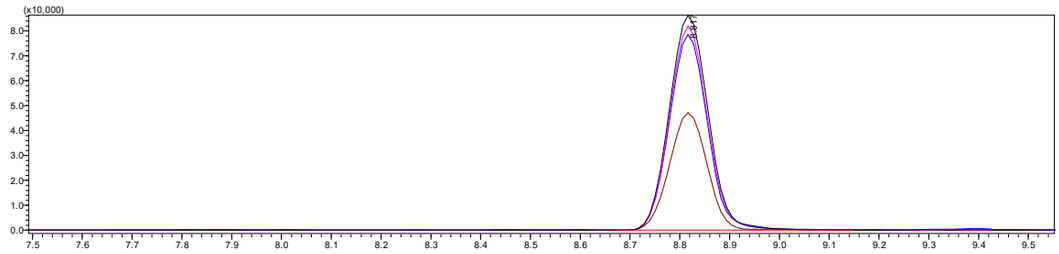

Figure 4. GC-MS data for 9R-HHC (NSI standard)