

# Focus on Cannabinoids

## Chemical Analysis & Conversions

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CHEM 422 – Chemistry of Hemp & Cannabis

Department of Chemistry

Colorado State University

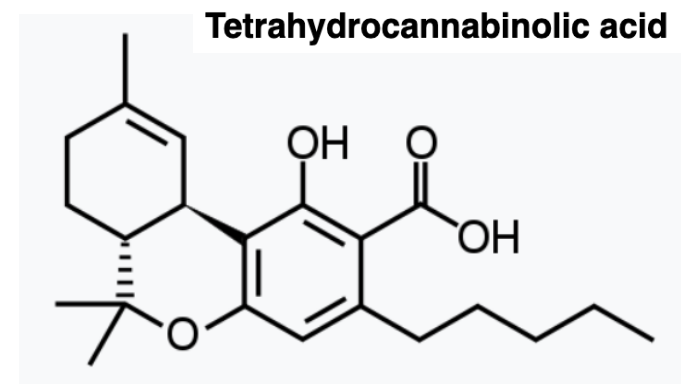
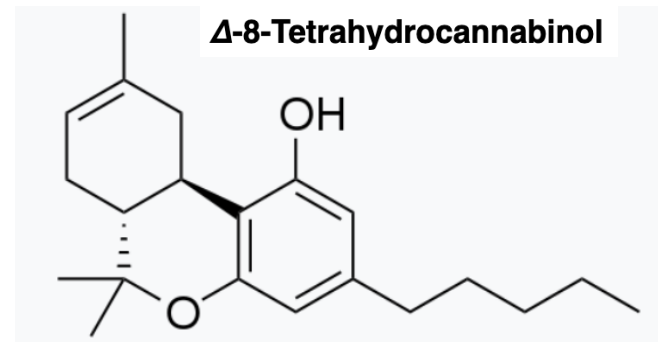
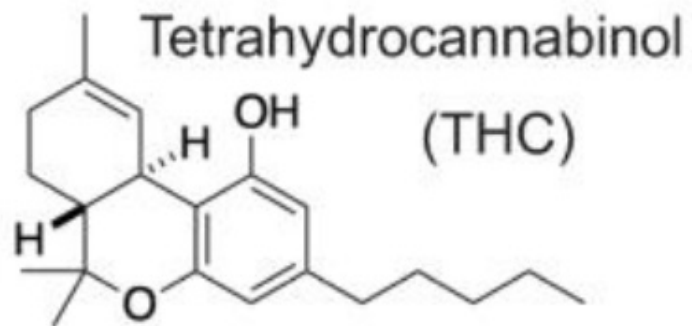
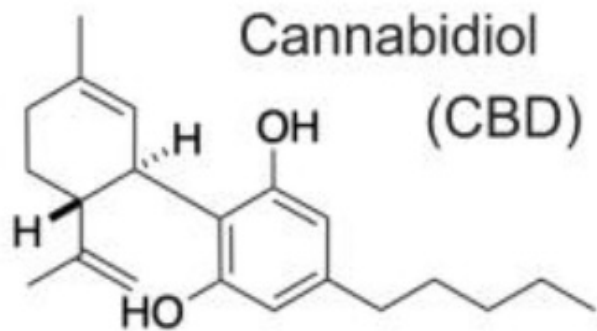
Fort Collins, CO USA

Spring 2022

# Structures & Species

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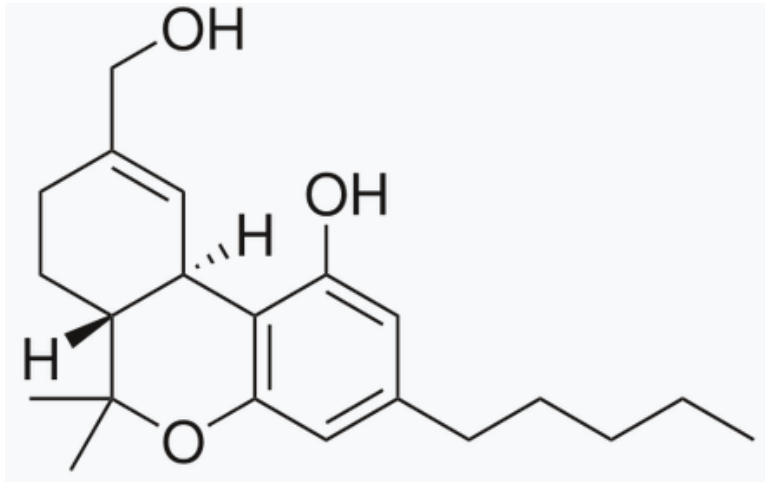
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# Metabolites of THC

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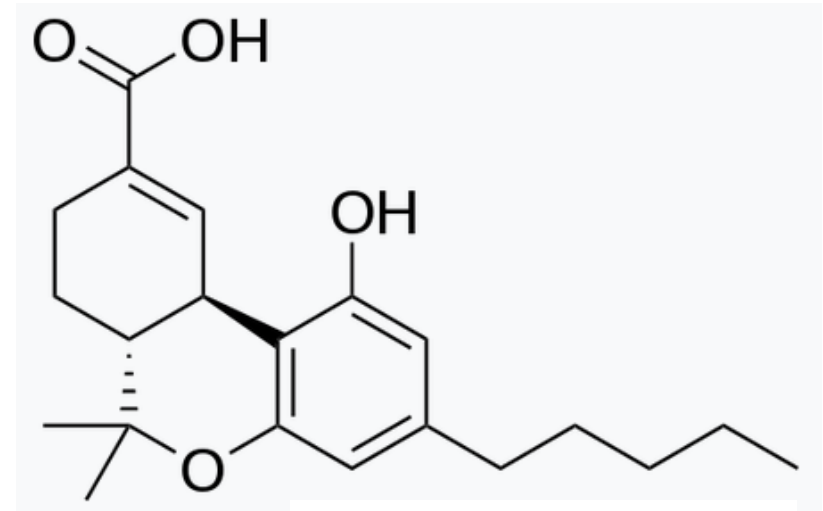
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**11-Hydroxy-THC**

main primary  
metabolite of  
tetrahydrocannabinol

Has a comparable  
psychoactive effect to  
THC but with a faster  
onset of effect



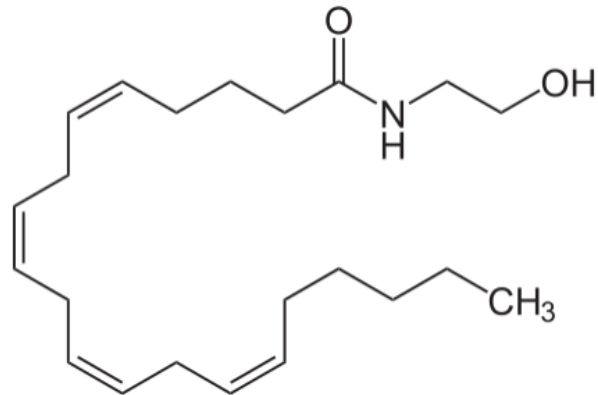
**11-Nor-9-carboxy-THC**

main secondary  
metabolite of  
tetrahydrocannabinol

# Endogenous Cannabinoids

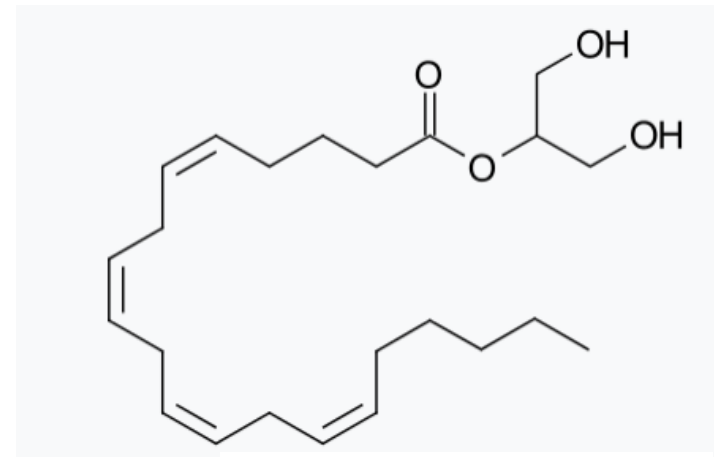
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**Anandamide**

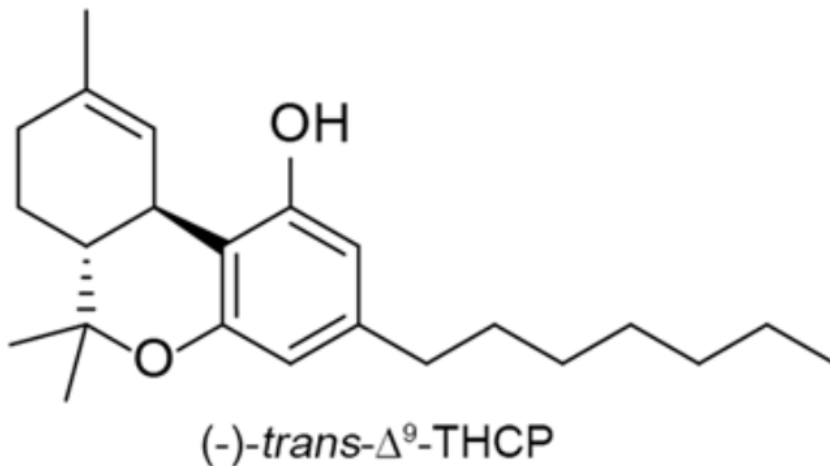
an endogenous agonist of  
the CB<sub>1</sub> receptor and the  
primary endogenous ligand  
for the CB<sub>2</sub> receptor



**2-Arachidonoylglycerol**

an endogenous agonist of  
the CB<sub>1</sub> receptor and the  
primary endogenous  
ligand for the CB<sub>2</sub> receptor

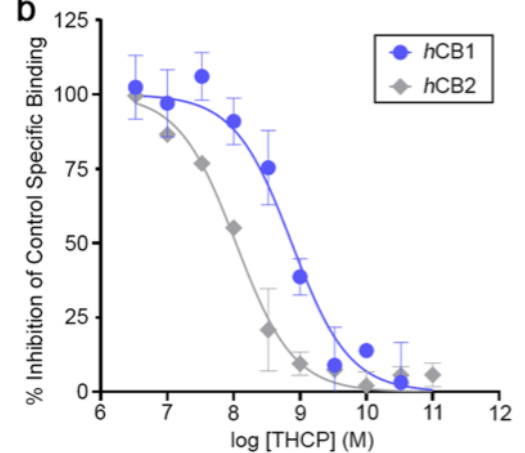
A novel phytocannabinoid isolated from *Cannabis sativa* L. with an *in vivo* cannabimimetic activity higher than  $\Delta^9$ -tetrahydrocannabinol:  $\Delta^9$ -Tetrahydrocannabiphorol



a

	R	hCB1 $K_i$ (nM)	hCB2 $K_i$ (nM)
(-)- <i>trans</i> - $\Delta^9$ -THCV	-propyl	75.4	62.8
(-)- <i>trans</i> - $\Delta^9$ -THCB	-butyl	15	51
(-)- <i>trans</i> - $\Delta^9$ -THC	-pentyl	40	36
(-)- <i>trans</i> - $\Delta^9$ -THCP	-heptyl	1.2	6.2

b



# Decarboxylation

H. Perrotin-Brunel et al./Journal of Molecular Structure 987 (2011) 67–73

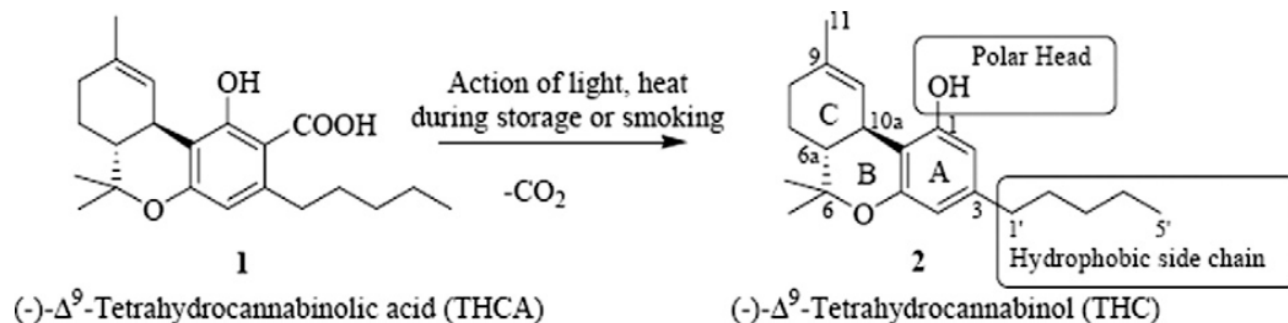


Fig. 1. Model of the decarboxylation reaction of  $\Delta^9$ -THCA.

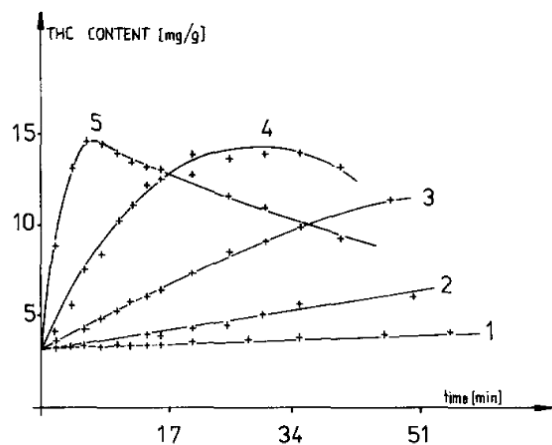
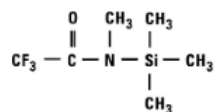
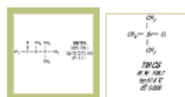


Fig. 3. Effect of heating time and temperature on the THC content of an *n*-hexane marijuana extract after heating on the glass surface in an open reactor. Curves: 1 = 80°C; 2 = 94°C; 3 = 106°C; 4 = 122°C; 5 = 145°C.



**MSTFA**  
MW 199.1  
bp 70°C/75 mm  
d<sub>4</sub><sup>20</sup> 1.11



Gallery (2) >

## MSTFA and MSTFA + 1% TMCS Silylation Reagent

Use Thermo Scientific™ MSTFA and MSTFA + 1% TMCS Silylation Reagent for GC analyses of early eluting compounds that would otherwise be obscured in the chromatogram. Use Thermo Scientific™ MSTFA and MSTFA + 1% TMCS Silylation Reagent for GC analyses of early eluting compounds that would otherwise be obscured in the chromatogram. MSTFA, the most volatile TMS-amide available, and its byproduct N-methyltrifluoroacetamide typically elute with the solvent front, allowing TMS derivatives of small molecules to be analyzed. Addition of Thermo Scientific™ TMCS aids derivatization of amides, secondary amines, and hindered hydroxyls not derivatized by MSTFA alone.

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### Silylation

If THCA has to be analysed separately, i.e. without decarboxylation, 1.5 ml aliquots of the above (non-thermally decarboxylated) extract has to be derivatized before GC analysis. Derivatizing agents frequently used are:

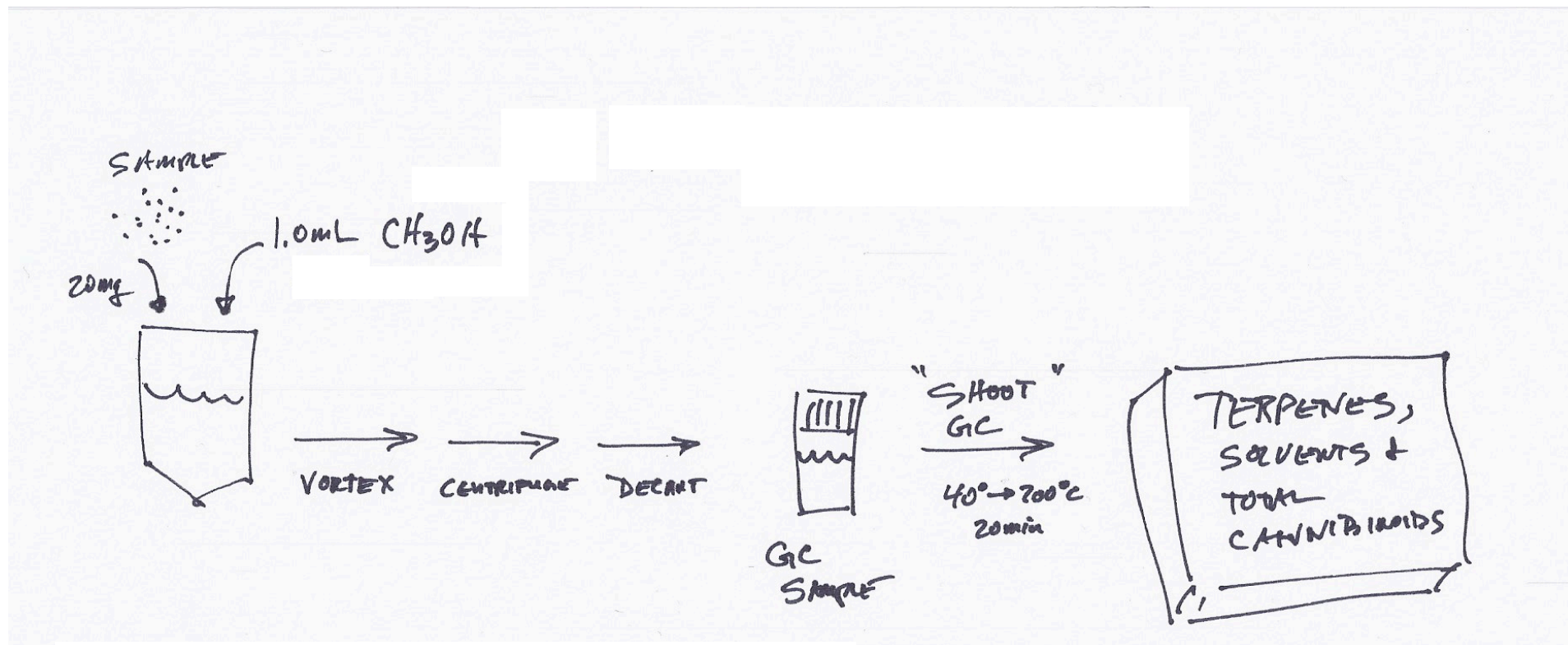
MSTFA: N-methyl-N-trimethylsilyltrifluoroacetamide

BSTFA/TMCS: N,O-bis(trimethylsilyl)trifluoroacetamide/Trimethylchlorosilane (1 per cent)

Silylizable solvents such as ethanol have to be removed, usually by a gentle stream of nitrogen. The residue is taken up in 1.5 ml chloroform. 100 µl MSTFA are added and heated for 30 min at 70°C. The resulting solution can be analysed directly.

# Derivitization

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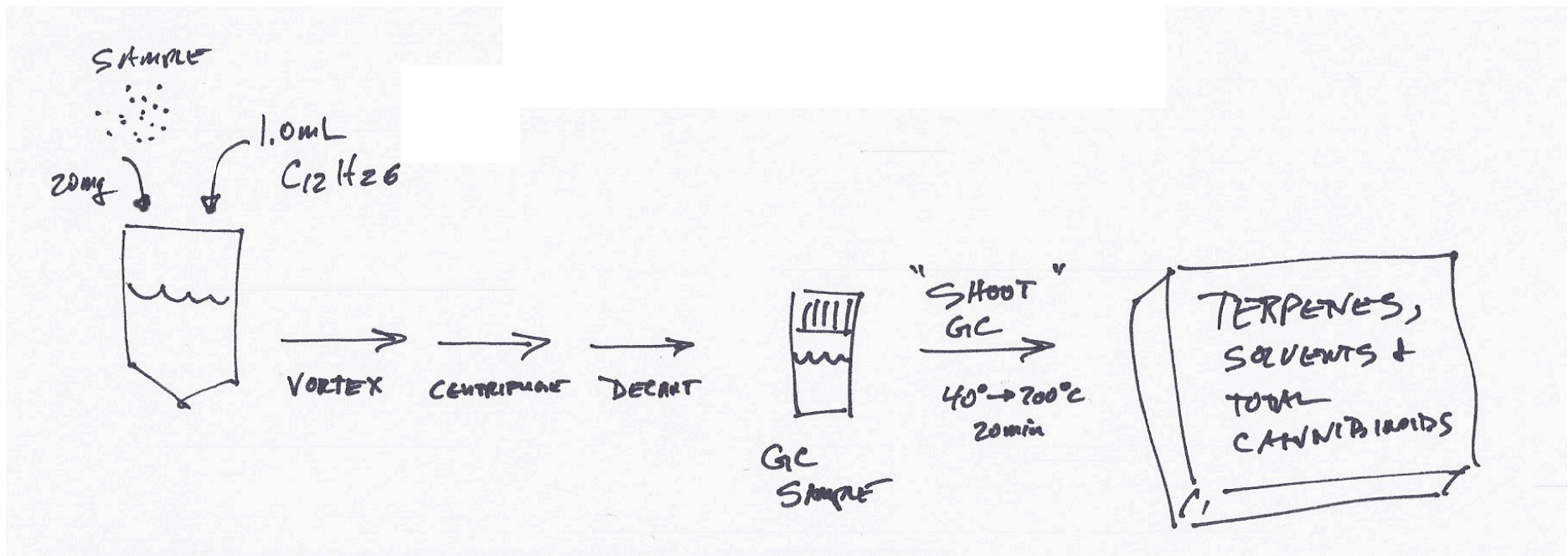


j\_chromat\_b\_2011\_v879\_p3059.pdf

5  $\mu$ l of THCA solution (100  $\mu$ g/mL in methanol) were evaporated and derivitized by silylation with 25  $\mu$ l MSTFA and 25  $\mu$ l ethyl acetate for 45 min at 90 °C. 1  $\mu$ l was finally injected into the GC-MS system.



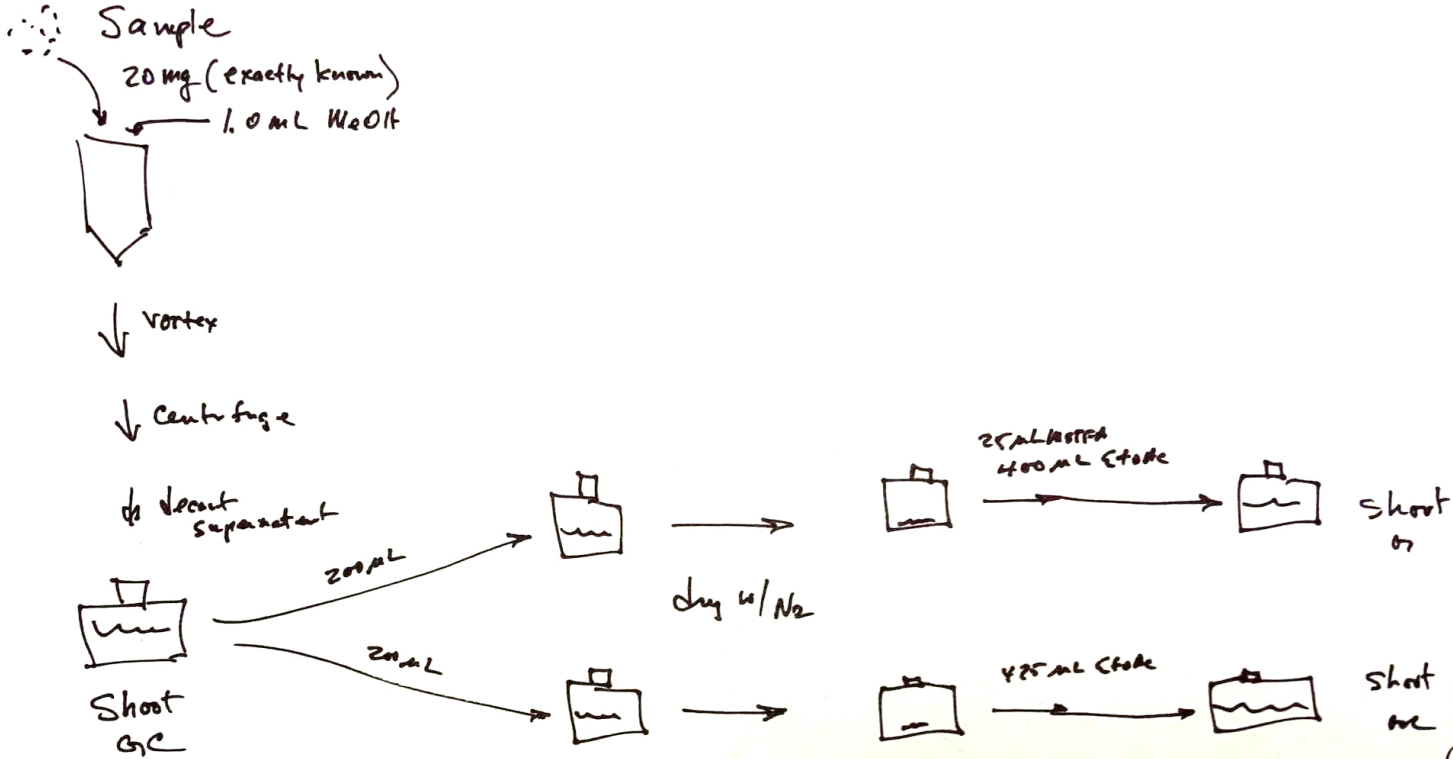
# Derivatization



j\_chromat\_b\_2011\_v879\_p3059.pdf

5  $\mu$ l of THCA solution (100  $\mu$ g/mL in methanol) were evaporated and derivatized by silylation with 25  $\mu$ l MSTFA and 25  $\mu$ l ethyl acetate for 45 min at 90 °C. 1  $\mu$ l was finally injected into the GC-MS system.

# Combination Derivatization & Analysis



types of  
total  
cannabinoids

Derivatized &  
Understand Cannabinoids

Cannabis and Cannabinoid Research  
Volume 4, Number 3, 2019  
Mary Ann Liebert, Inc.  
DOI: 10.1089/can.2019.0016

## ORIGINAL RESEARCH

# Absence of Entourage: Terpenoids Commonly Found in *Cannabis sativa* Do Not Modulate the Functional Activity of $\Delta^9$ -THC at Human CB<sub>1</sub> and CB<sub>2</sub> Receptors

Marina Santiago,<sup>1,\*</sup> Shivani Sachdev,<sup>1</sup> Jonathon C. Arnold,<sup>2,3</sup> Iain S. McGregor,<sup>2,4</sup> and Mark Connor<sup>1</sup>