

# **Valorisation of industrial hemp residue from essential oil production by recovery of cannabidiol and chemo-enzymatic conversion to cannabielsoin**

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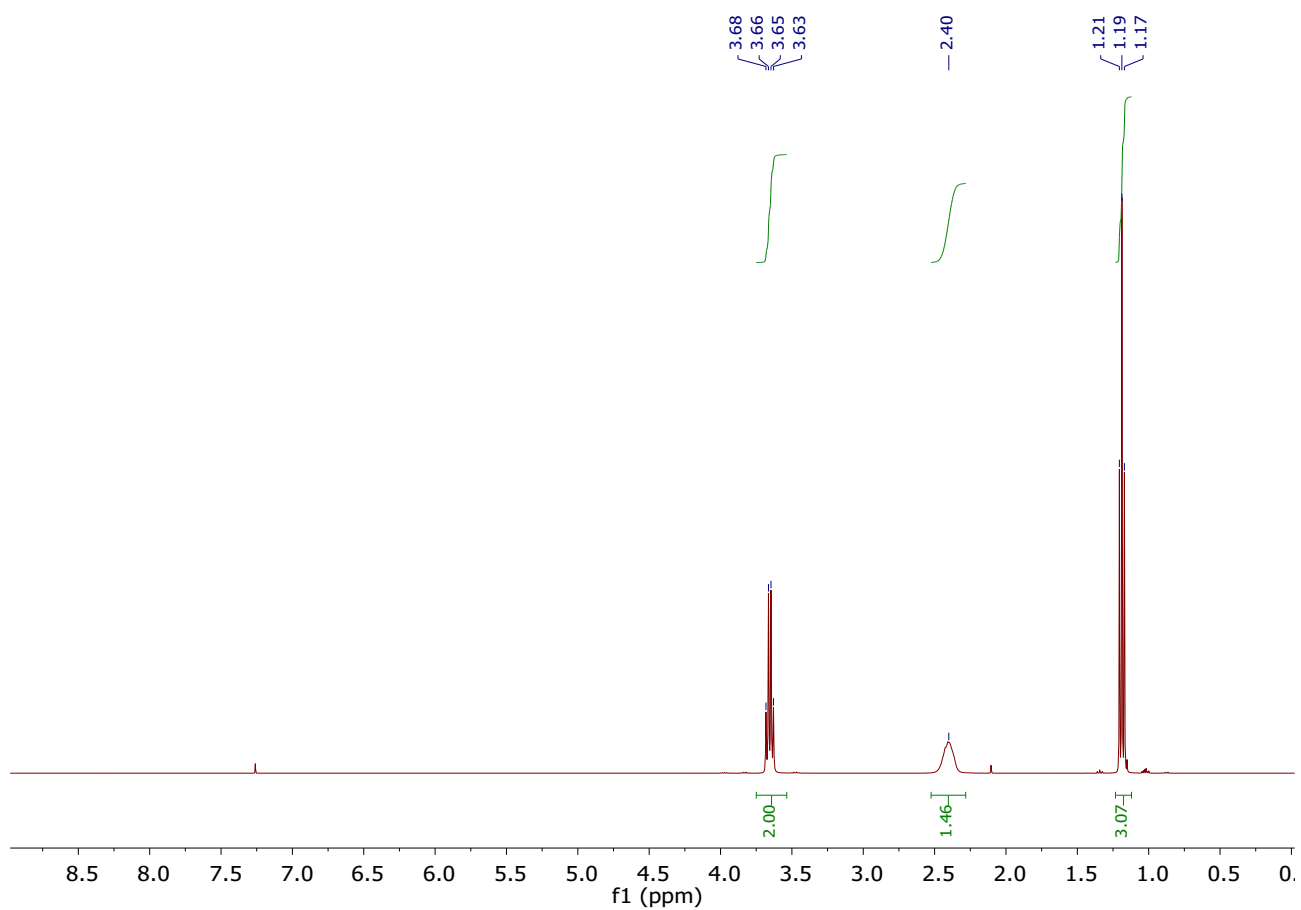
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<sup>#</sup> Equal contribution

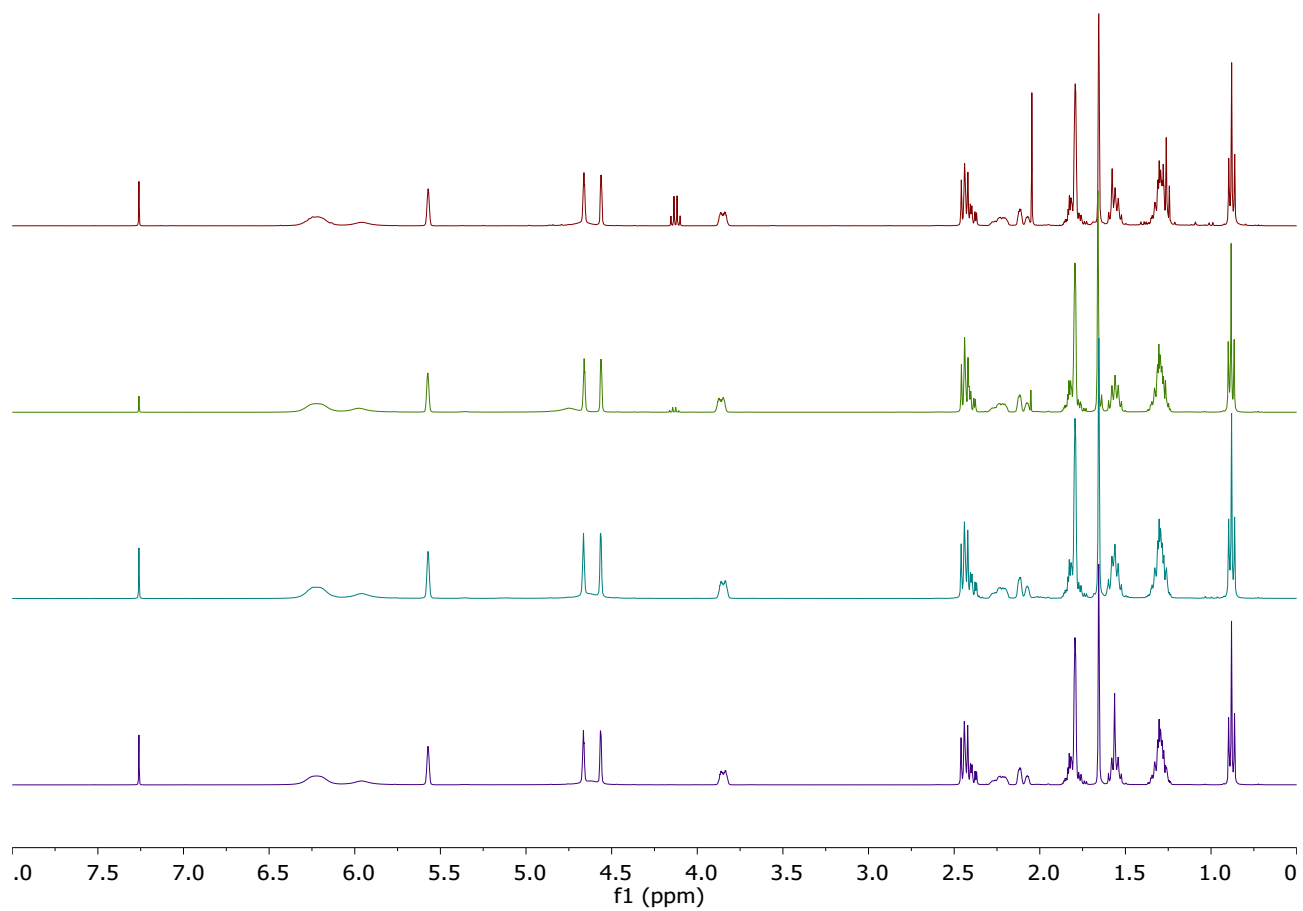
**Electronic supplementary information (ESI)**

**Supplementary figures and tables**

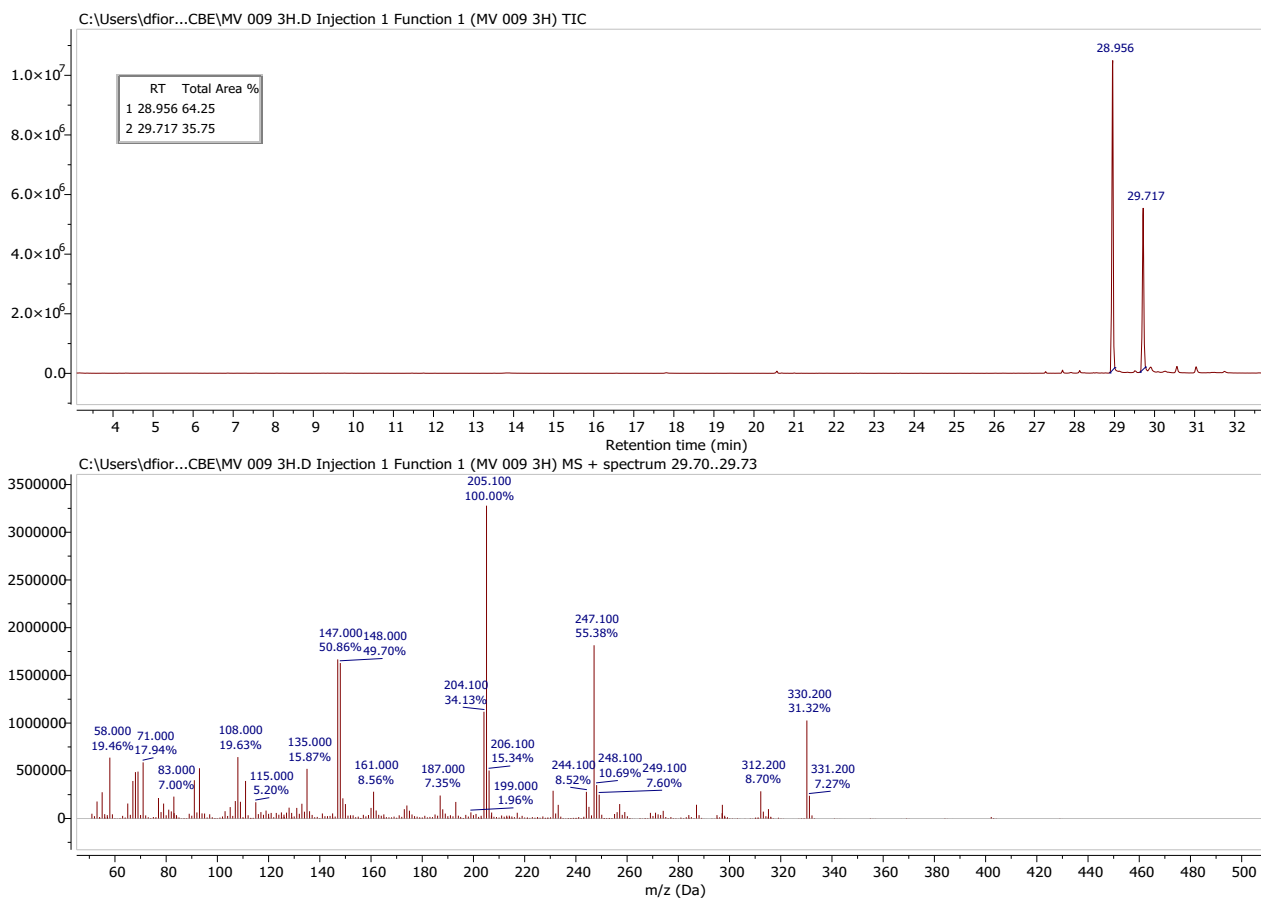
**Figure S1.**  $^1\text{H}$  NMR spectra of commercial bioethanol.



**Figure S2.** Comparison of  $^1\text{H}$  NMR spectra of different samples of CBD recovered from waste by chromatography (a,b) or by vacuum distillation (c,d).



**Figure S3.** Representative GC-MS trace for the chemo-enzymatic one-step synthesis of CBE from CBD.



**Table S1.** Screening of the conditions for lipase-mediated chemo-enzymatic oxidation of CBD.<sup>a</sup>

Entry	T [°C]	Enz. loading [% w/w]	H <sub>2</sub> O <sub>2</sub> [equiv.]	t [h] <sup>b</sup>	Conv. to CBE [%] <sup>c</sup>
1a	4	5	1.1	2	9
1b				4	29
1c				6	35
2a	4	10	1.1	2	18
2b				4	22
2c				6	31
3a	30	5	1.1	2	34
3b				4	<b>53</b>
3c				6	51
4a	30	10	1.1	2	26
4b				4	38
4c				6	31
5a	4	5	4.0	2	15
5b				4	38
5c				6	39
6a	4	10	4.0	2	38
6b				4	47
6c				6	43
7a	30	5	4.0	2	43
7b				4	47
7c				6	17
8a	30	10	4.0	2	33
8b				4	41
8c				6	28

<sup>a</sup> Conditions: 50 mg CBD, 15 mL EtOAc (working conc. 10 mM), 1.1-4.0 equiv. H<sub>2</sub>O<sub>2</sub> (3.5% w/w aq. sol.), 5-10% w/w immobilised Novozym<sup>®</sup> 435, 4-30°C, 2-24 h.

<sup>b</sup> Datapoints for longer reaction times (18-24 h) are not shown due to extremely low or no CBE contents in all cases, as a consequence of oxidative decomposition.

<sup>c</sup> Determined by quantification of CBE formed (by GC-MS, using *n*-decane as internal standard). Note: direct calculation of the conversion by comparison of CBD and CBE peaks is unreliable due to the formation of other polar products not detected by GC-MS.

## Details of the calculations of simplified E-factor (sEF) for the processes considered

The simplified E-factor values have been calculated according to Roschangar *et al.*, *Green Chem.* **2015**, *17*, 752-768. This metric considers all waste originated from reagents, co-substrates and catalysts, and does not take into account water and solvents and recyclable materials. For literature procedures, the data has been collected from the descriptions of the experimental procedures available. Due to its definition, this metric should only be used for the purpose of comparison, and not to draw conclusions on the actual amounts of waste produced.

Chemical via silylated CBD (3 steps)	
CBD	37
BSTFA	200
mCPBA	30
Reagents	267
Product	23,9
Waste	243,1
sEF	10,17

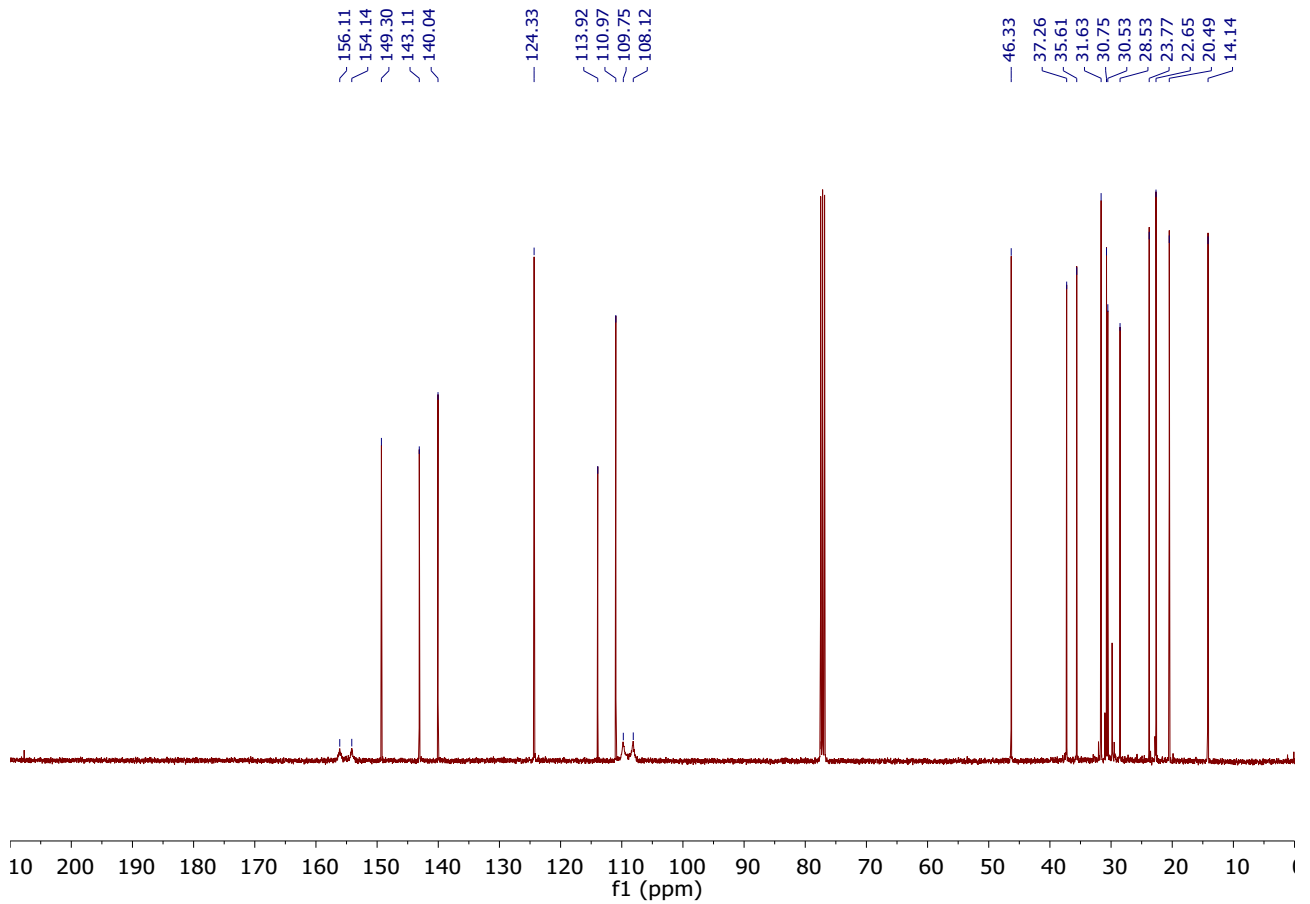
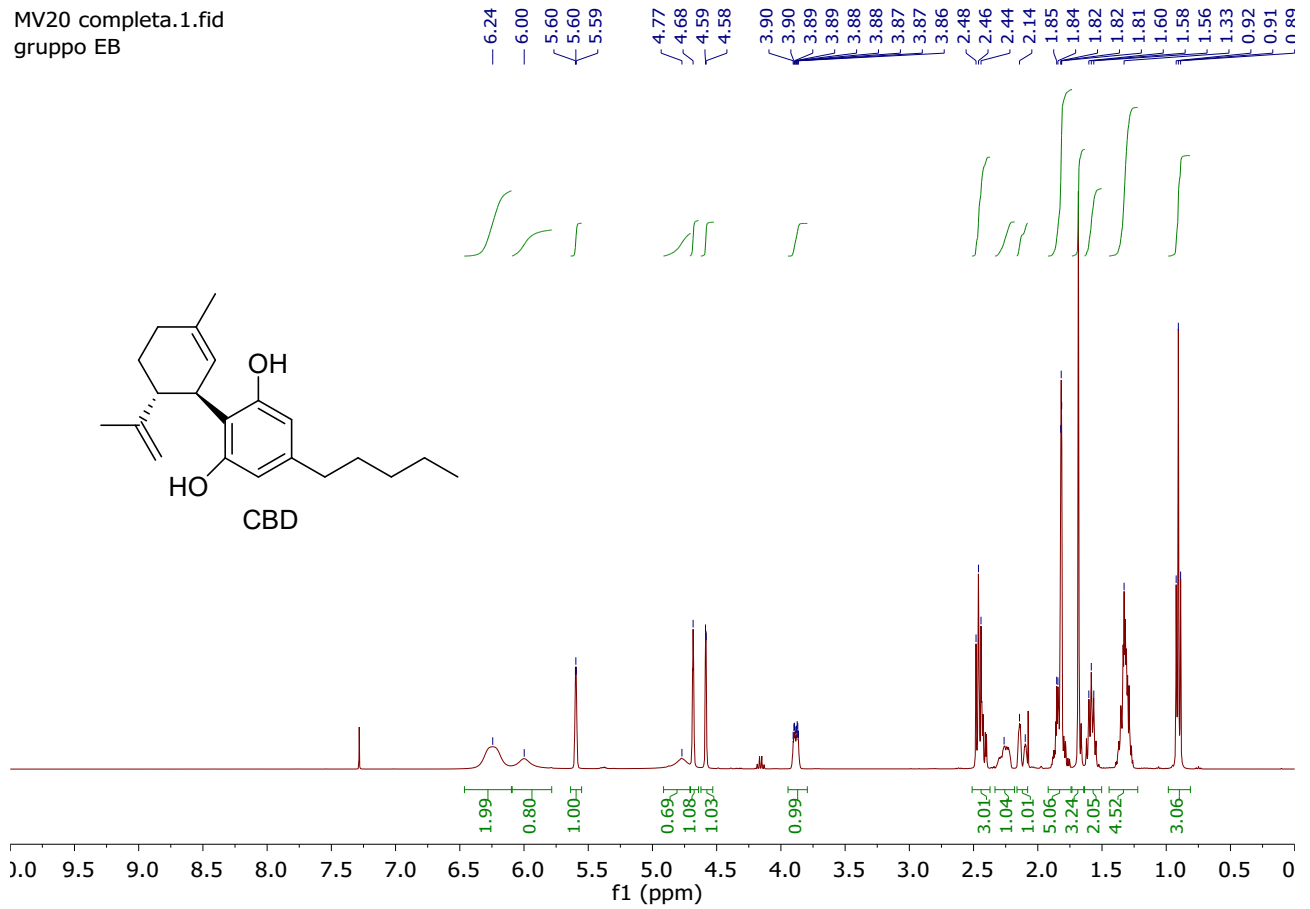
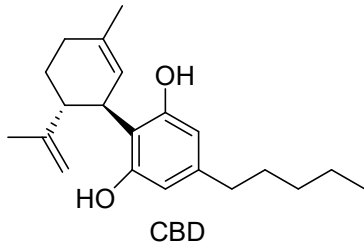
Chemical via CBD diacetate (3 steps)					
Step 1		Step 2		Step3	
CBD	3,27	CBD-diAc	2,66	CBDO-diAc	2,57
Ac2O	3,9	NaHCO3	0,617	K2CO3	4,28
Et3N	5,8	mCPBA	1,54		
DMAP	0,25				
Reagents	13,22	Reagents	4,817	Reagents	6,85
Product	4,05	Product	2,02	Product	1,54
Waste	9,17	Waste	2,797	Waste	5,31
sEF	2,26	sEF	1,38	sEF	3,45
				sEF tot	7,10

Chemo-enzymatic direct (1 step)	
CBD	200
H2O2	12
Lipase	5
Reagents	217
Product	65
Waste	152
sEF	2,34

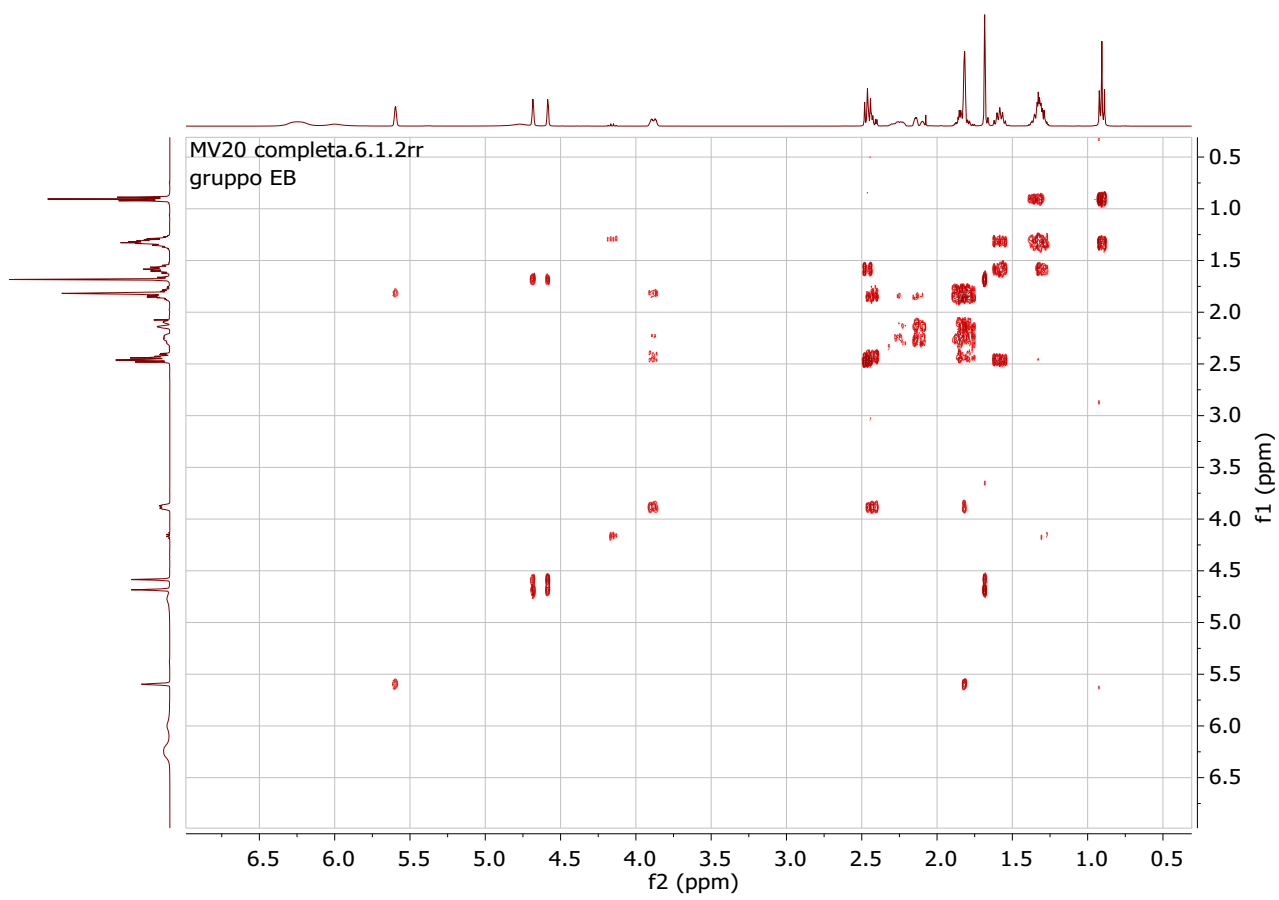
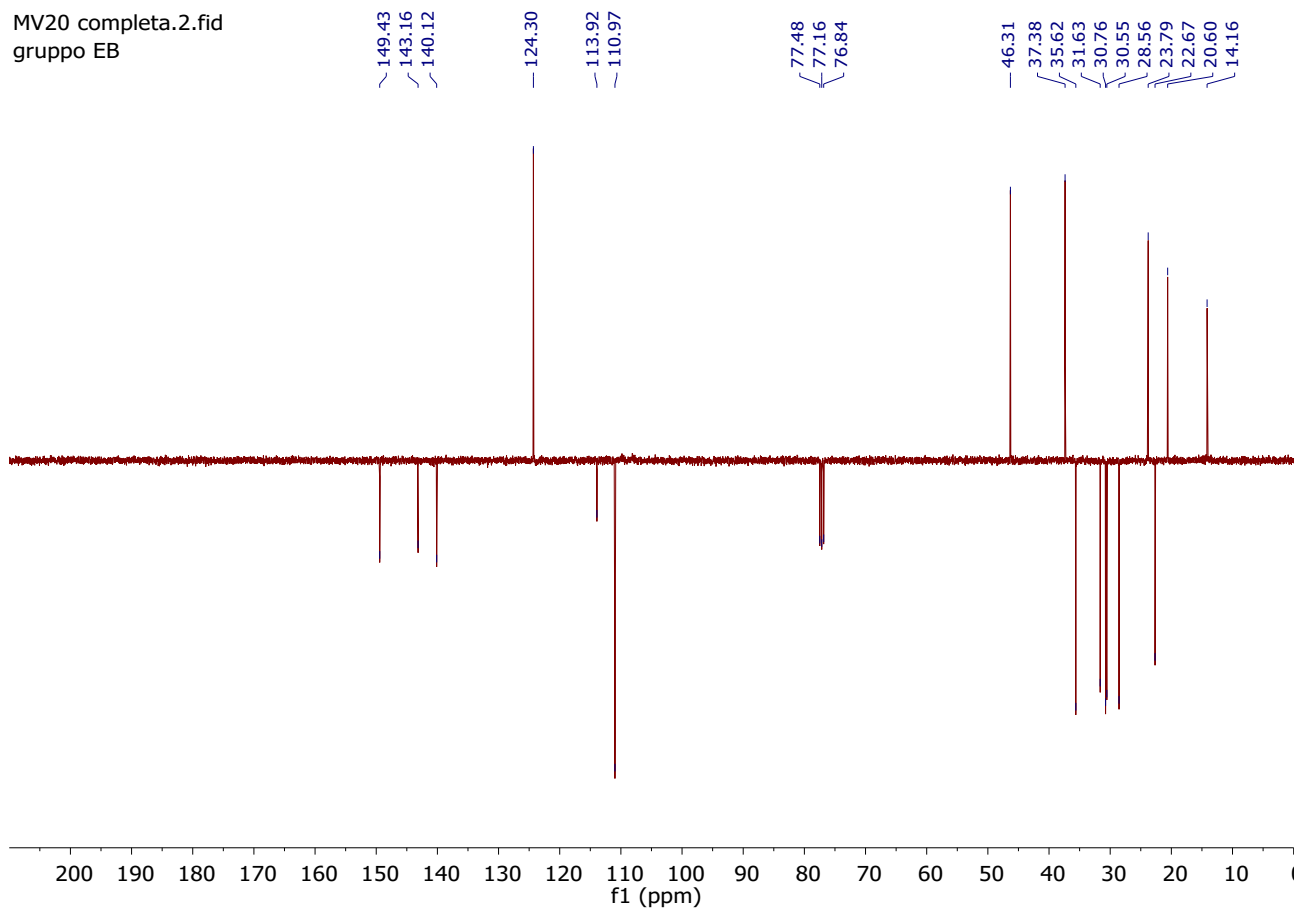
Chemo-enzymatic via CBD diacetate (3 steps)					
Step 1		Step 2		Step 3	
CBD	300	CBD-diAc	240	CBDO-diAc	140
Ac2O	340	Lipase	12	K2CO3	234
Et3N	500	H2O2	24		
DMAP	22				
Reagents	1162	Reagents	276	Reagents	374
Product	290	Product	174	Product	101
Waste	872	Waste	102	Waste	273
sEF	3,01	sEF	0,59	sEF	2,70
				sEF tot	6,30

### NMR characterisation of CBD

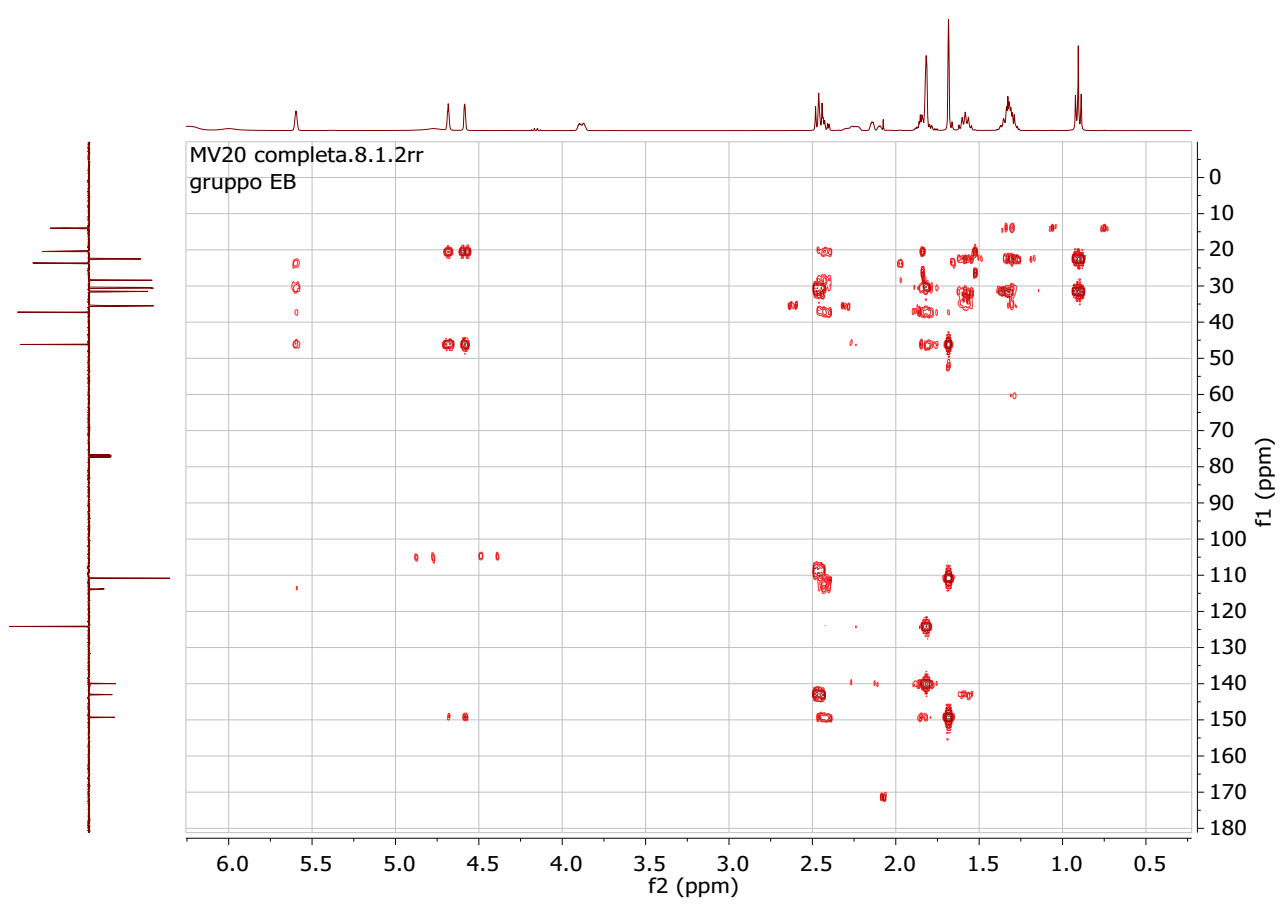
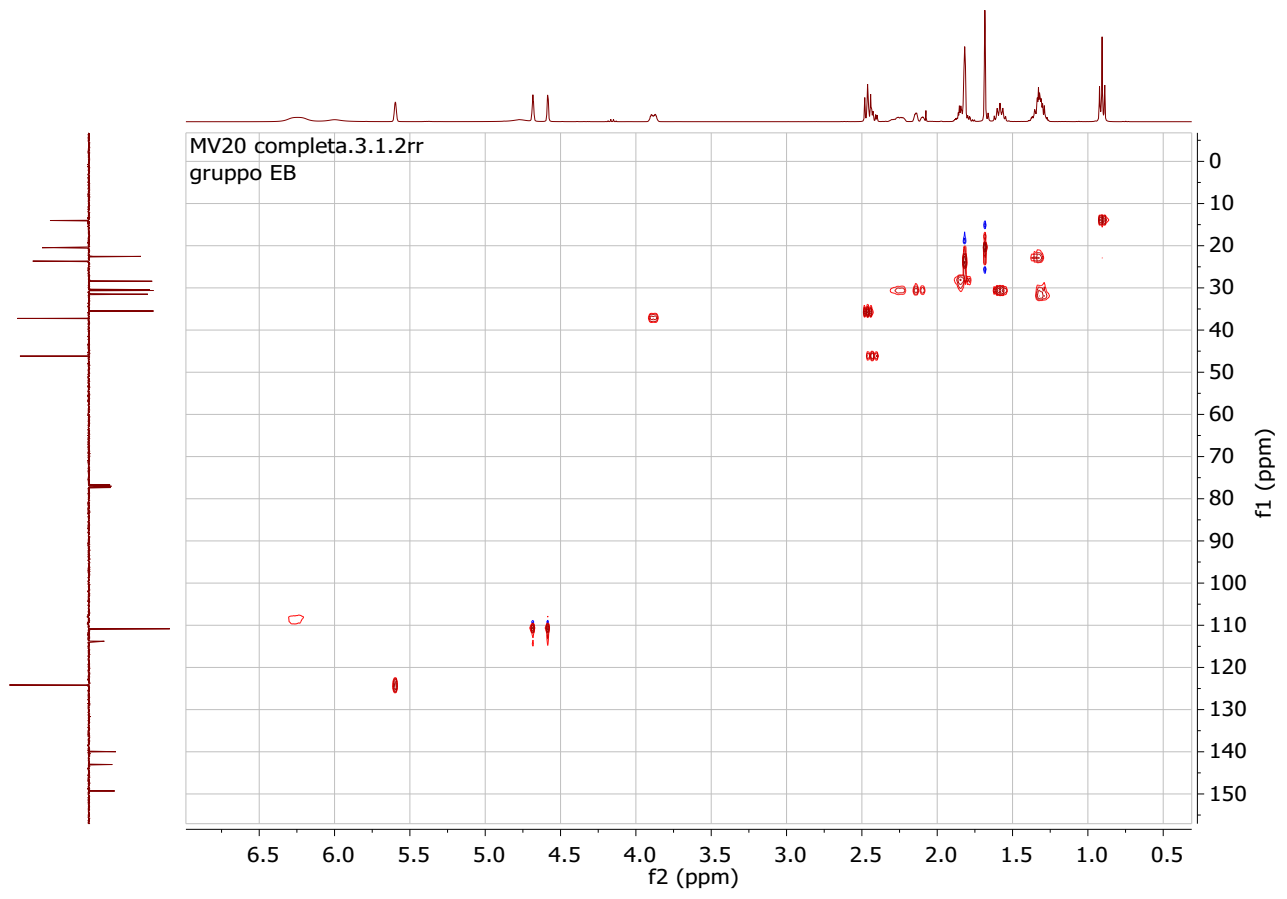
MV20 completa.1.fid  
gruppo EB



MV20 completa.2.fid  
gruppo EB

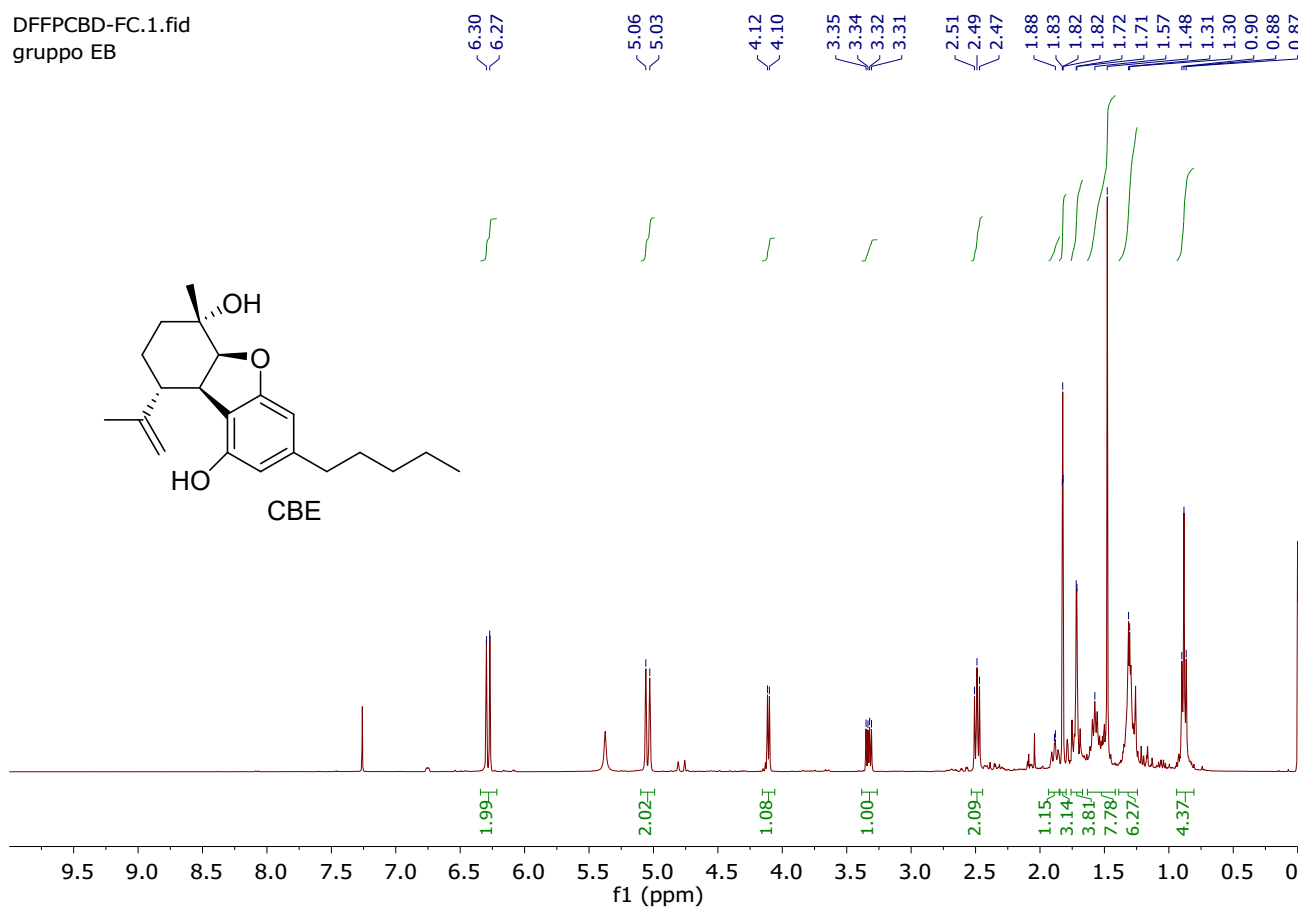




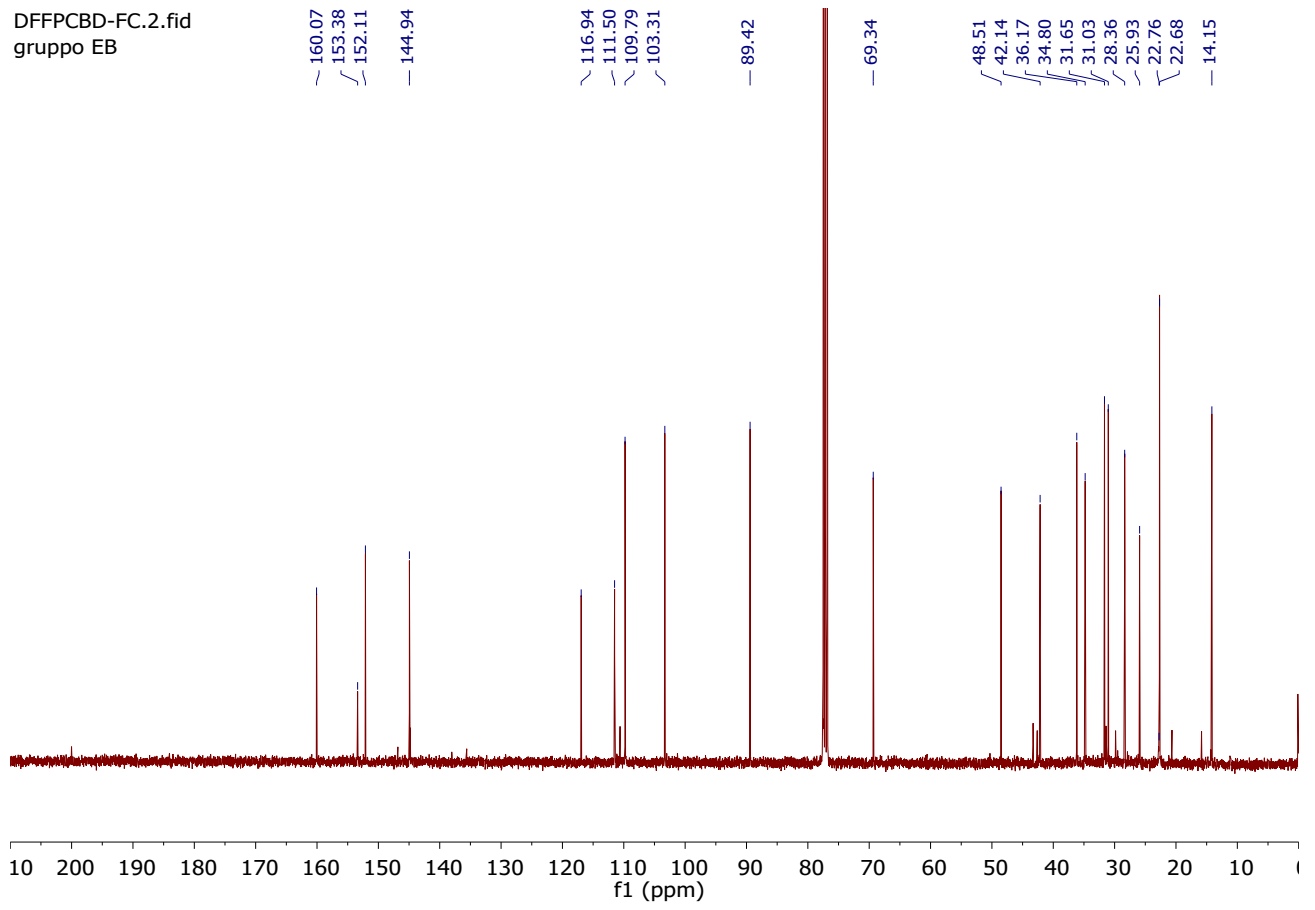


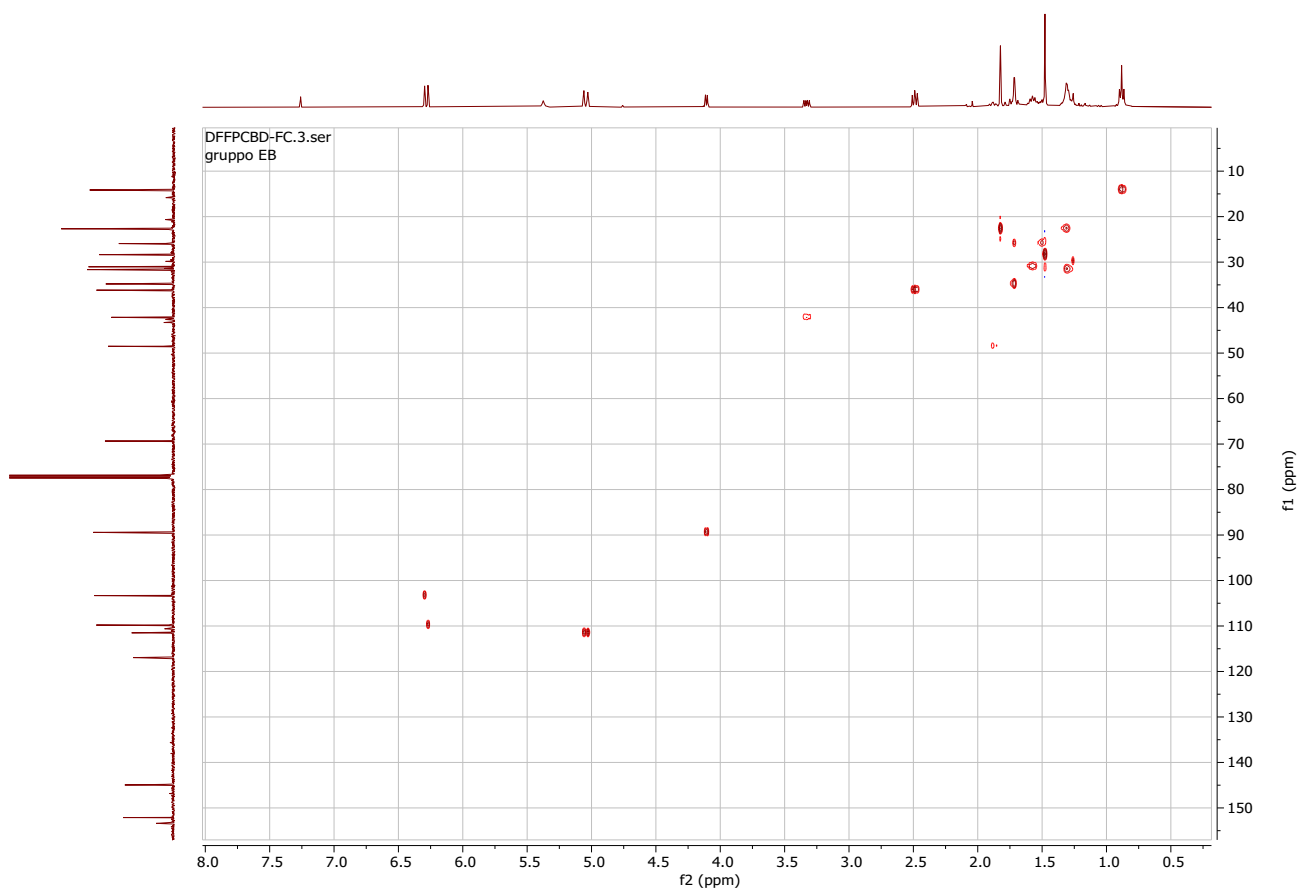
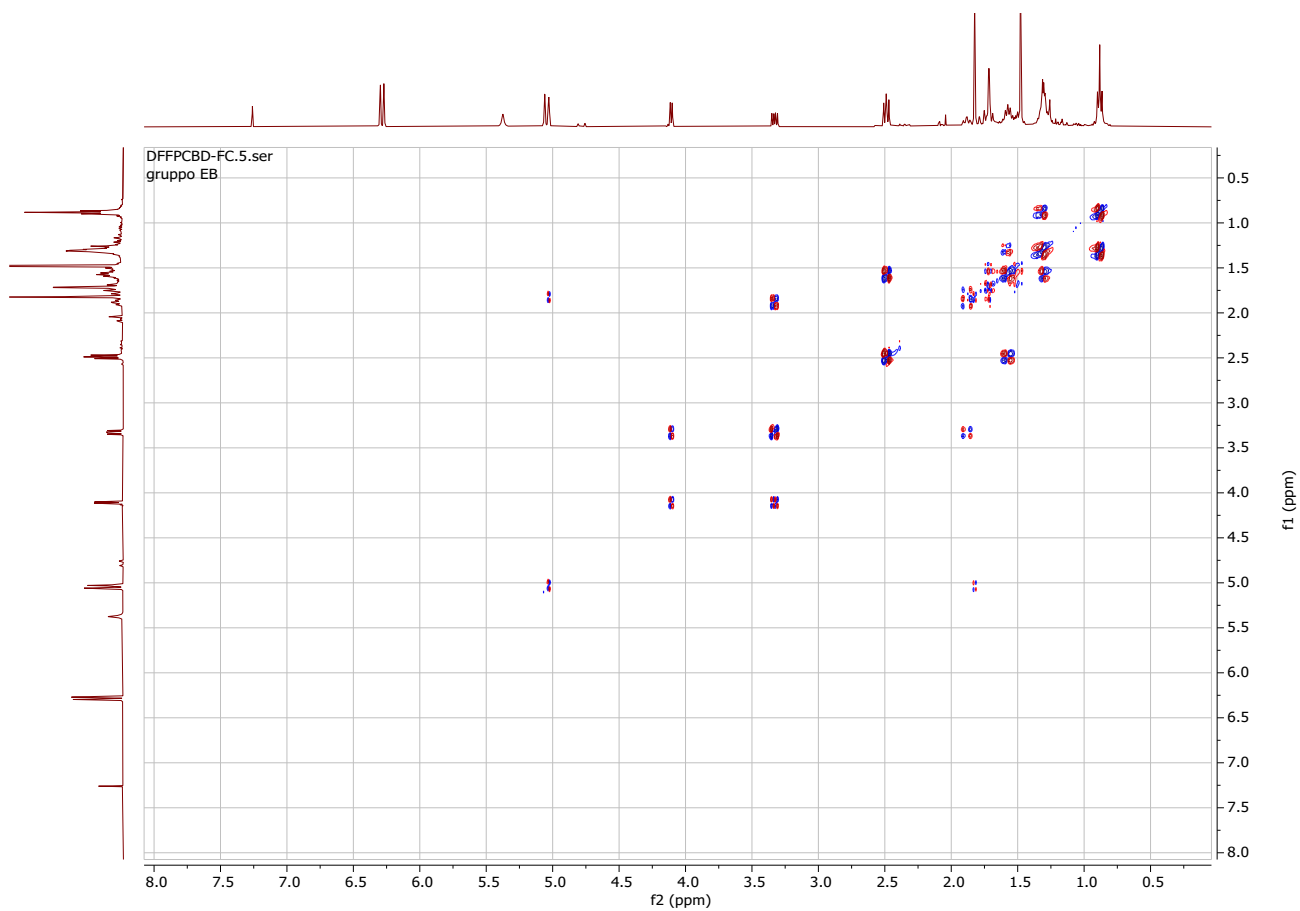
### NMR characterisation of CBE (chemo-enzymatic one-step)

DFFPCBD-FC.1.fid  
gruppo EB



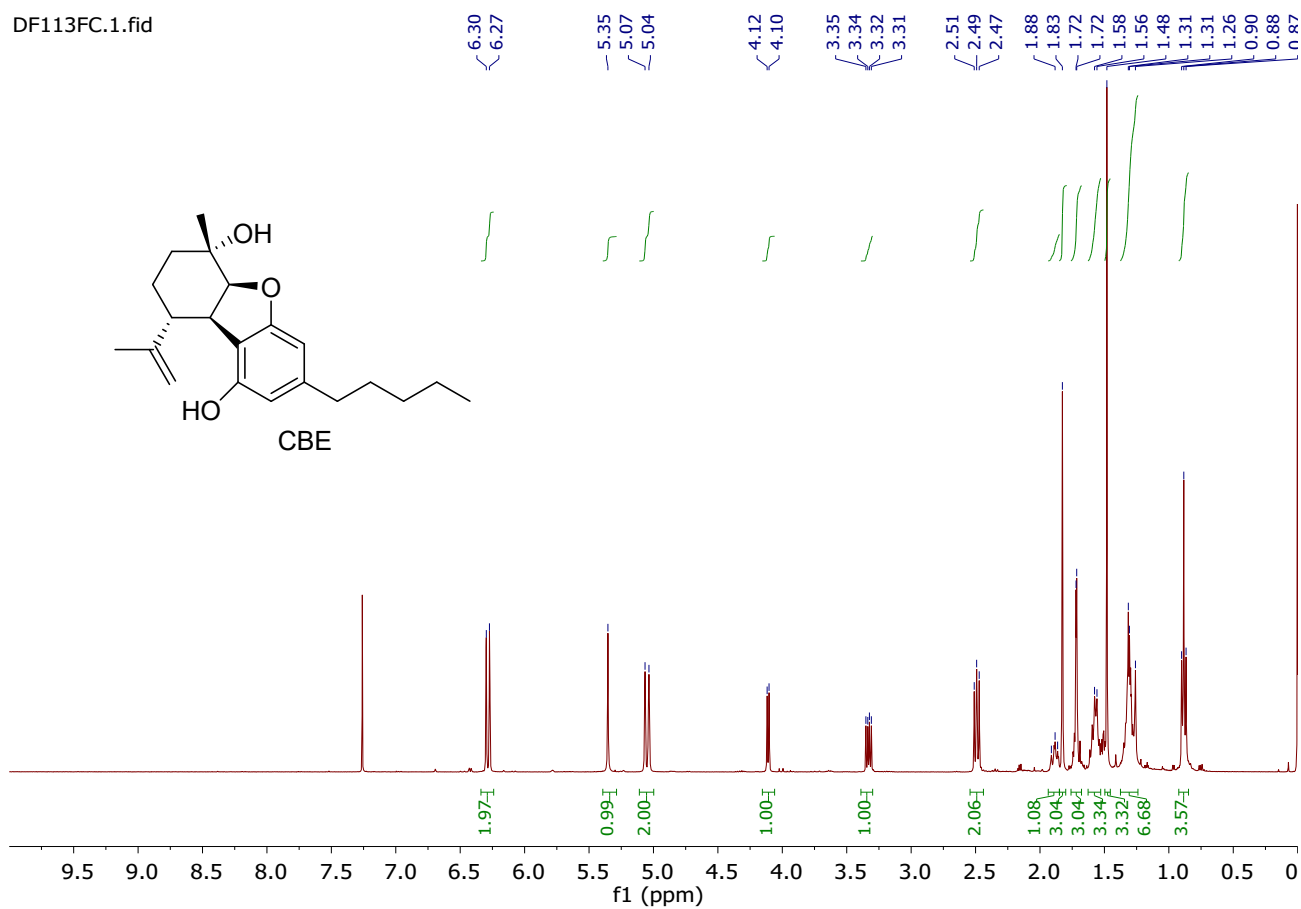
DFFPCBD-FC.2.fid  
gruppo EB



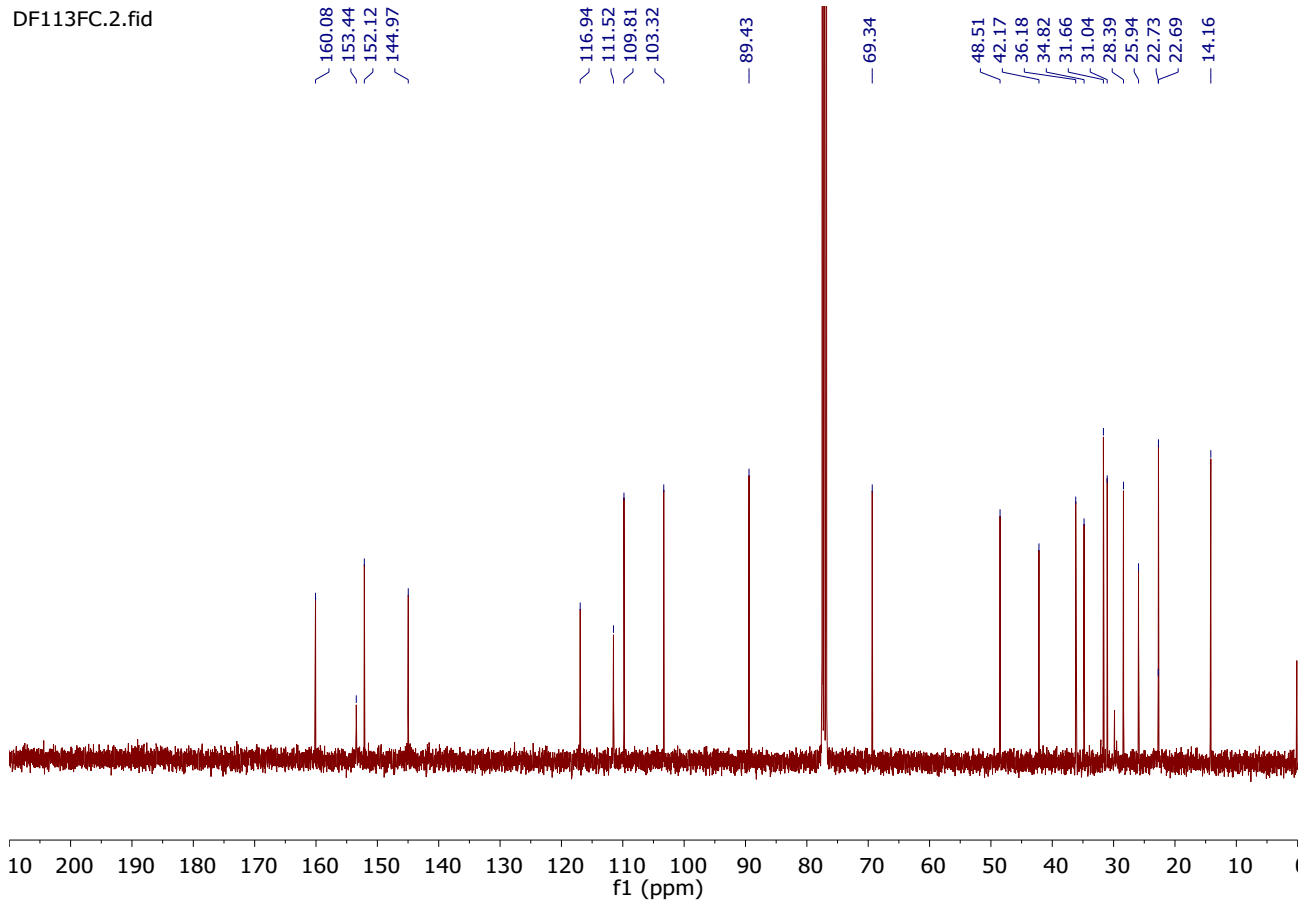


### NMR characterisation of CBE (chemo-enzymatic via CBD diacetate)

DF113FC.1.fid

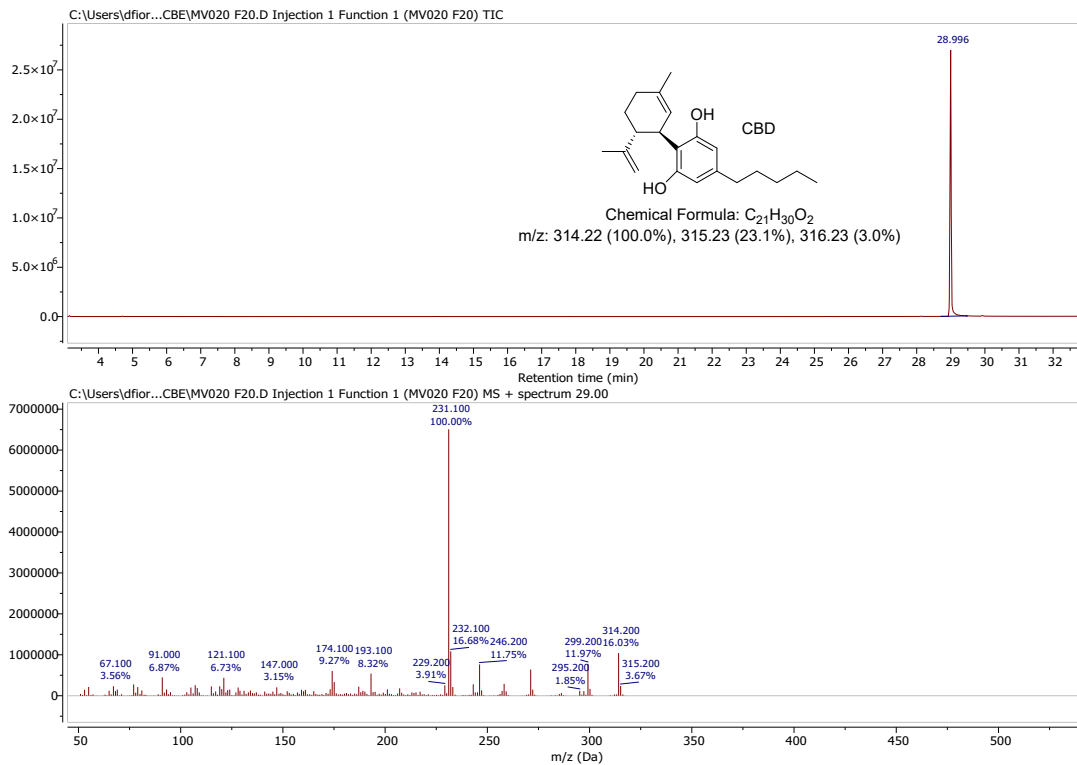


DF113FC.2.fid

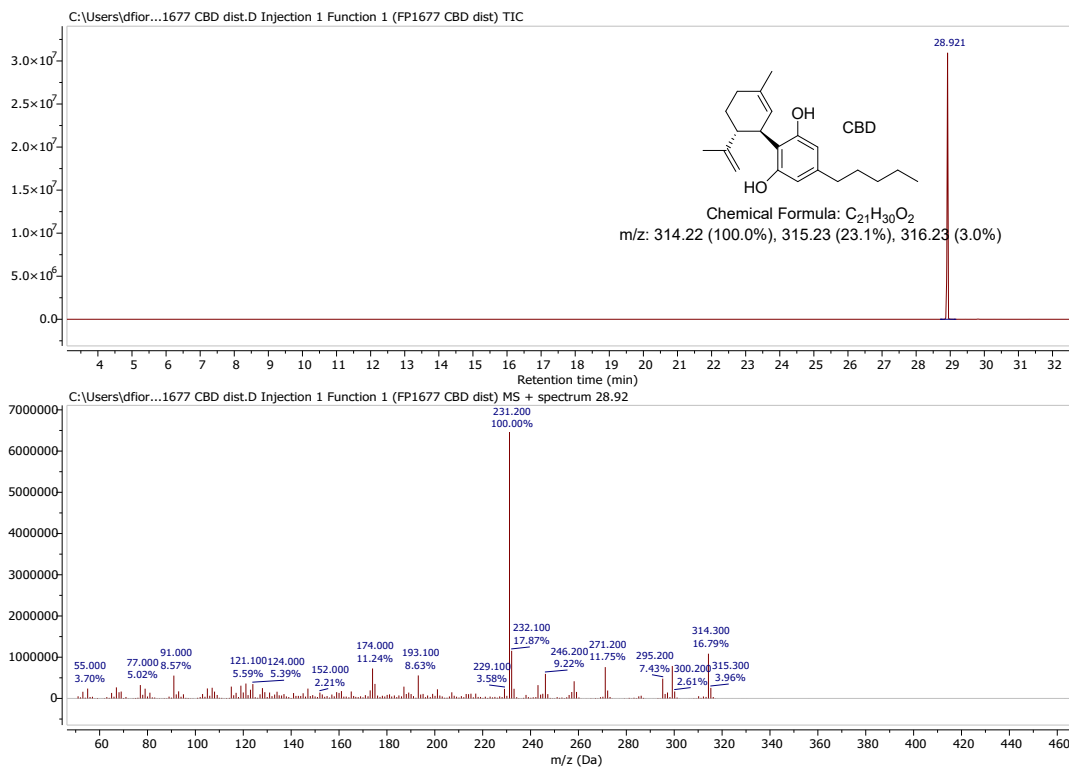


### GC-MS chromatograms and spectra

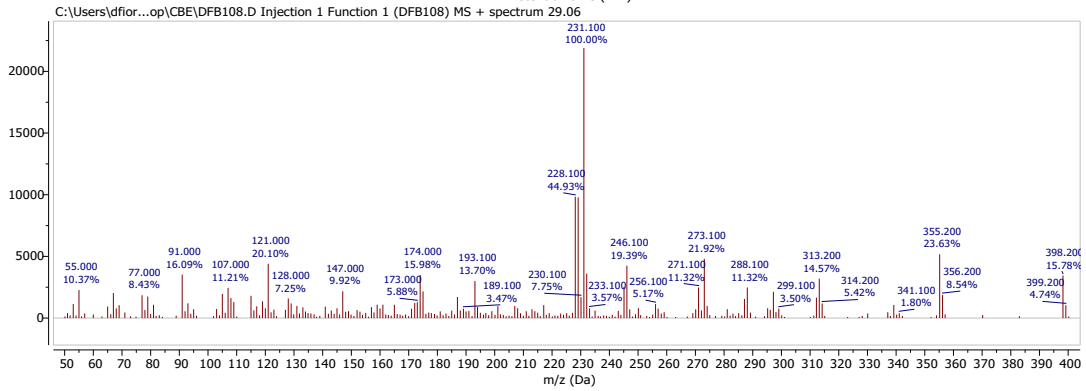
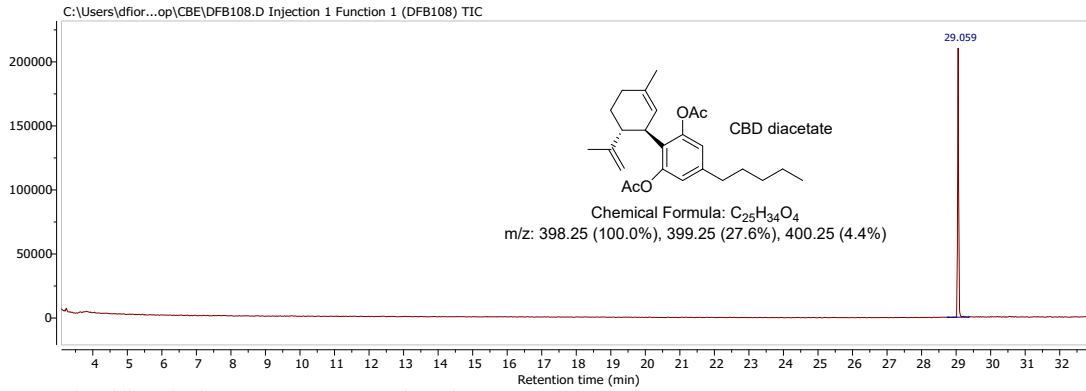
#### CBD (purified by column chromatography)



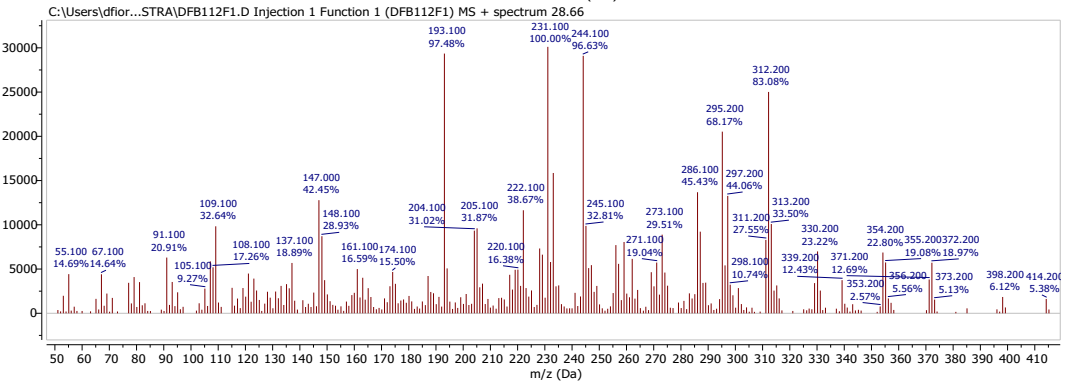
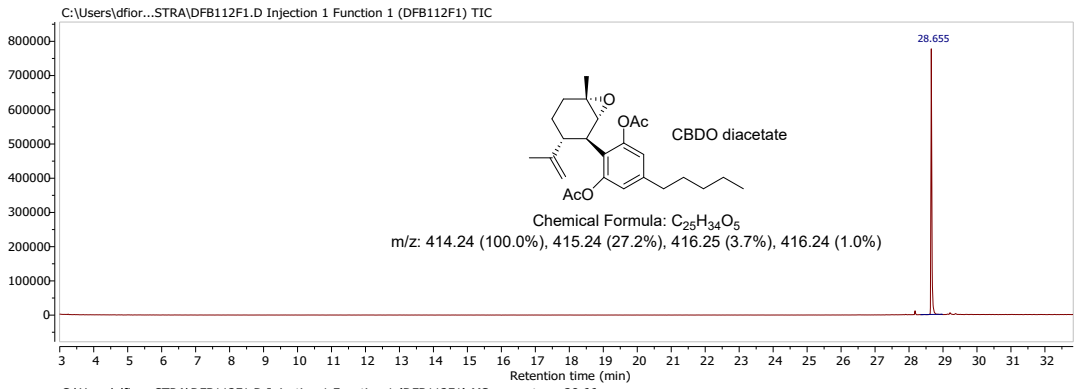
## CBD (purified by vacuum distillation)



## CBD diacetate

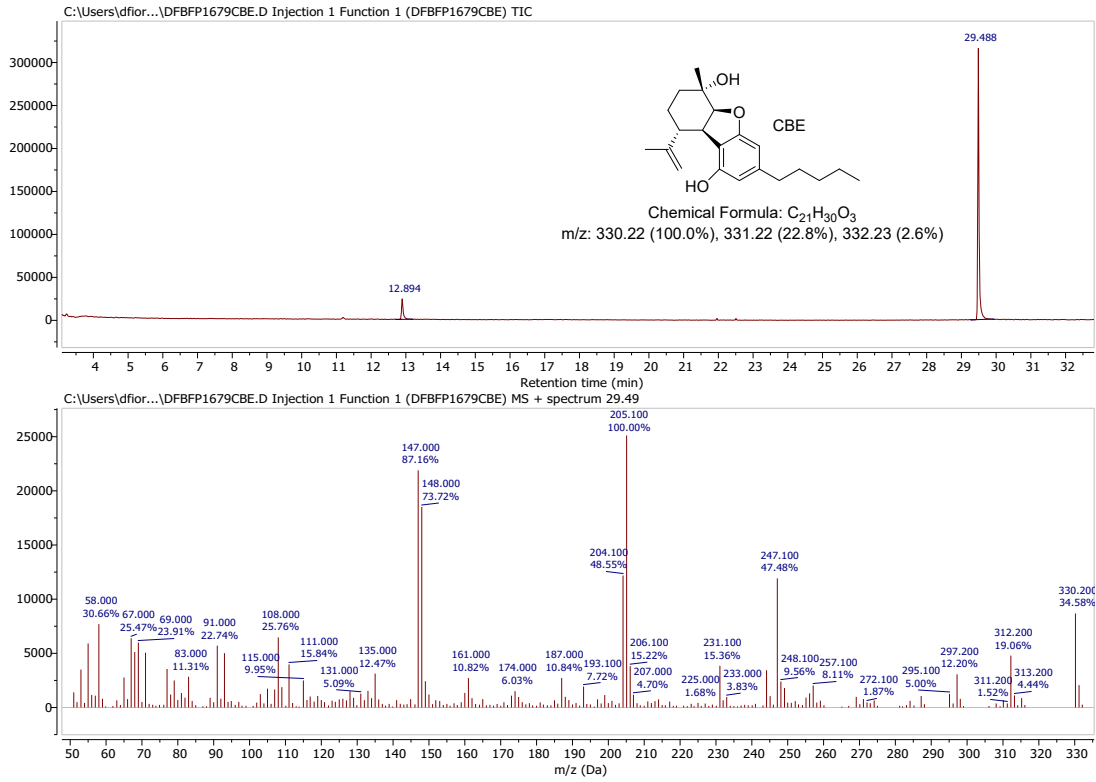


## CBDO diacetate





## CBE (chemo-enzymatic one-step)



## CBE (chemo-enzymatic via CBD diacetate)

