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Missione 4 Istruzione e Ricerca

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Photochemical behavior and degradation products of natural cannabinoids

2° Congresso Intersocietà sui Prodotti Vegetali Per La Salute: Il Ruolo Delle Piante Medicinali Nella Medicina Moderna

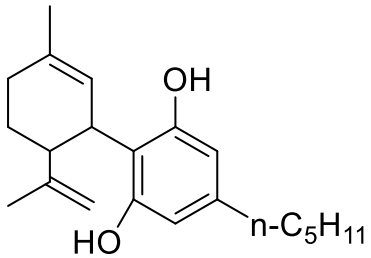
Napoli, 10-12 aprile 2025

Introduction

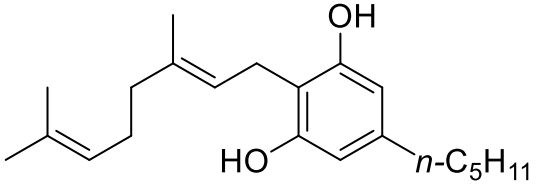
Cannabinoids have recently gathered significant attention due to their potential applications, ranging from medical use to cosmetics.

While an impressive number of compounds have been discovered, only the thermal and biological inspired transformations of the main cannabinoids (cannabidiol and Δ^9-tetrahydrocannabinol) have been investigated. Moreover, available data on their photoreactivity are scarce, outdated and, in some cases, conflicting.

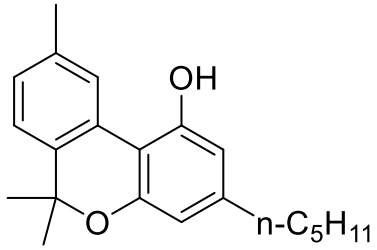
Our studies focused on the photochemistry of cannabinoids, both in solution and in a vegetable matrix, in order to investigate the chemical paths involved in the photodegradation processes and the nature of the obtained products.



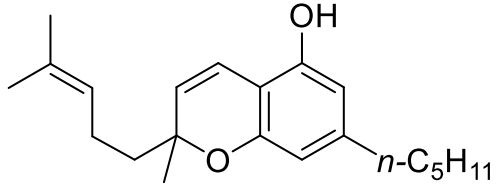
Cannabidiol (CBD)



Cannabigerol (CBG)



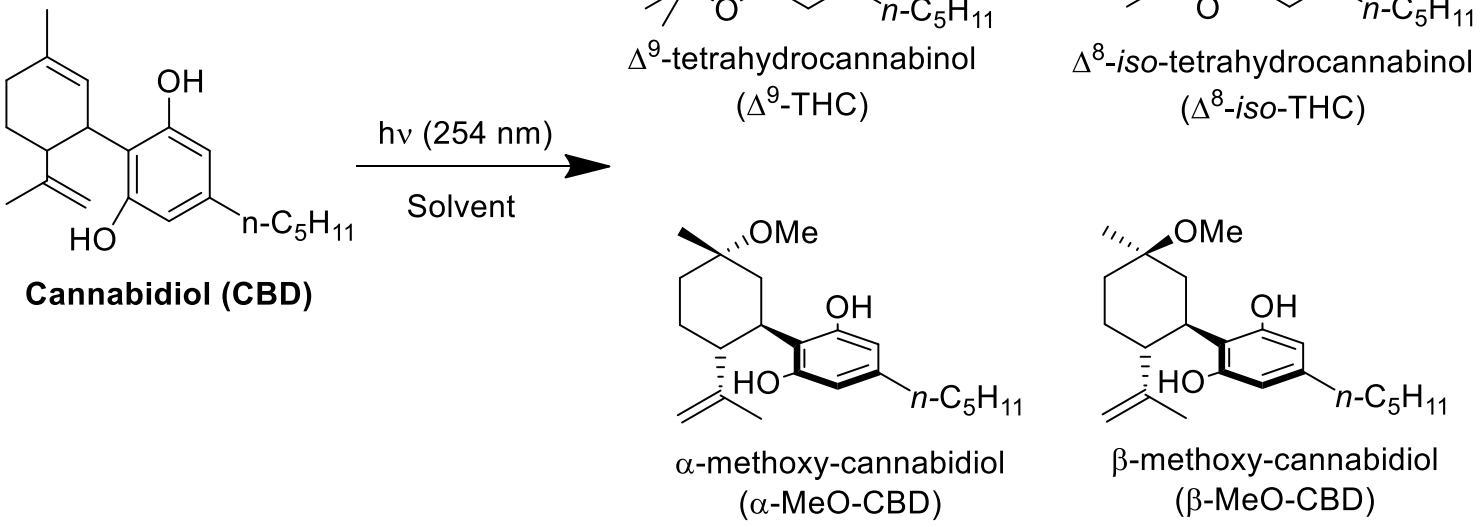
Cannabinol (CBN)

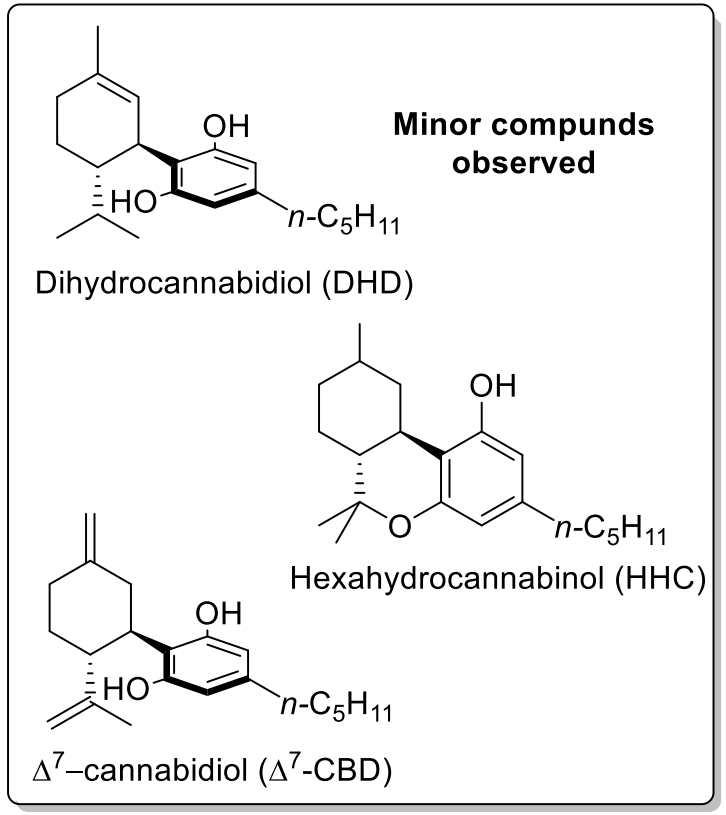


Cannabichromene (CBC)

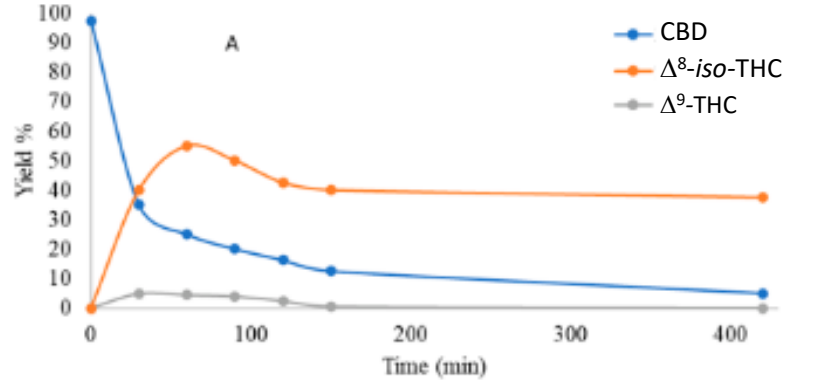
Cannabidiol (CBD)

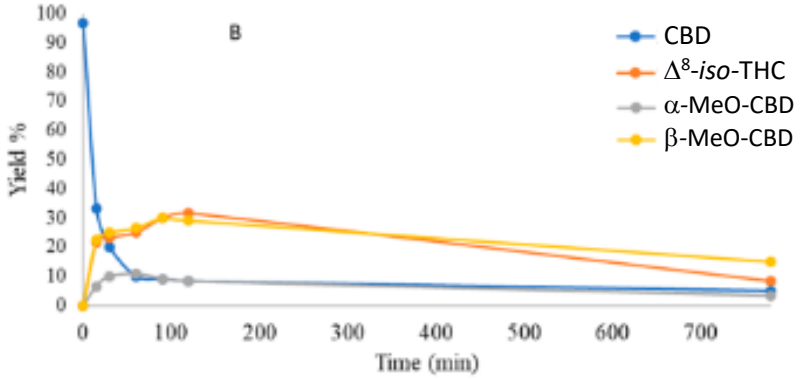
Cannabidiol (**CBD**) is the main exponent of the non-psychotropic cannabinoids, and one of the most abundant found in most *C. Sativa* chemotypes.

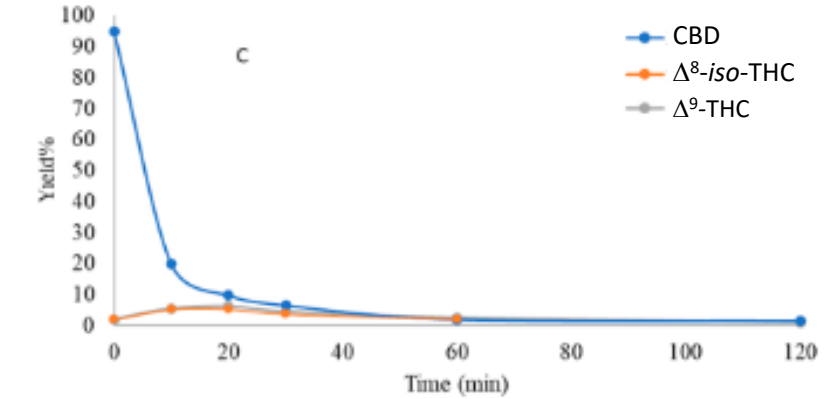


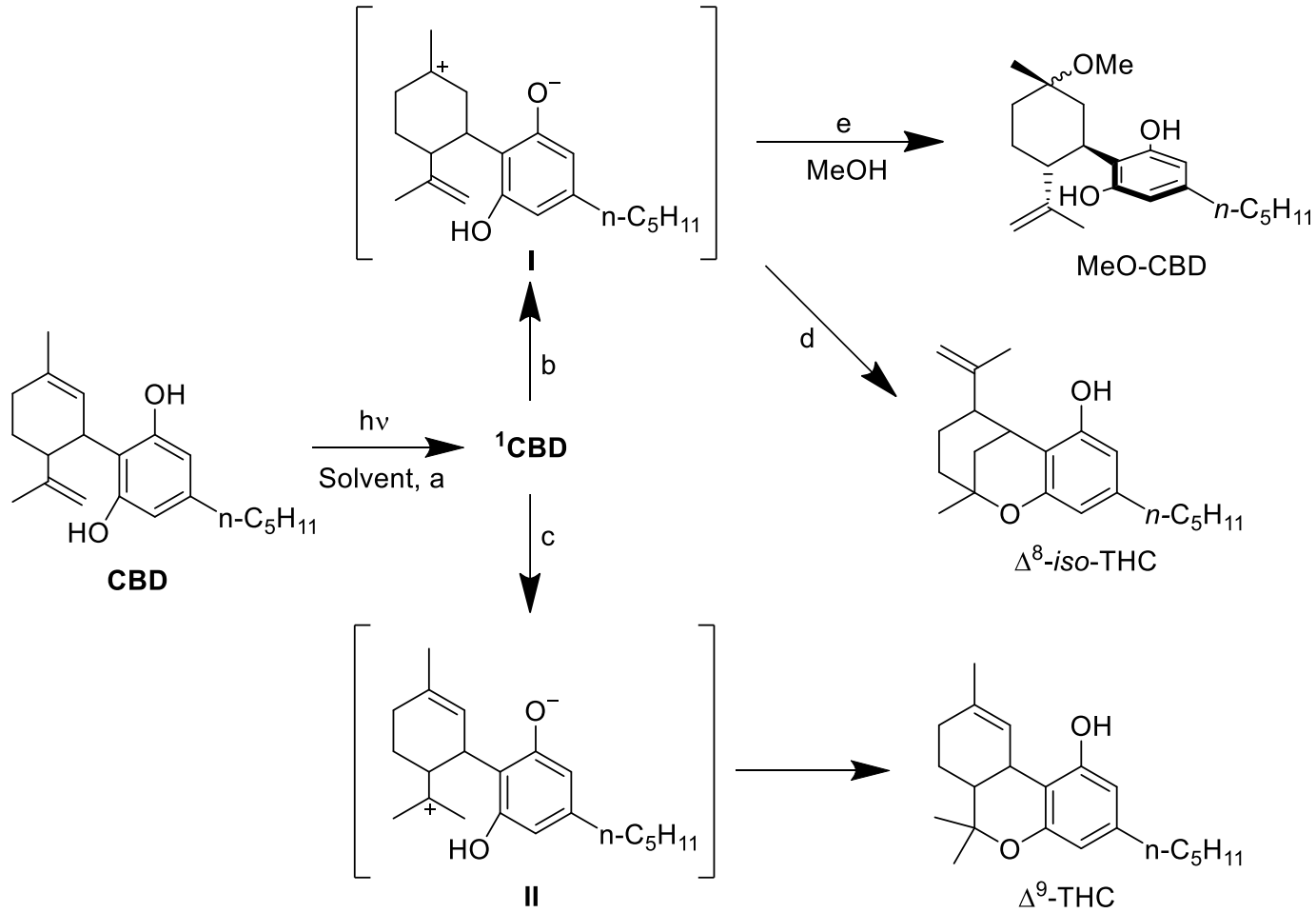


Cannabidiol: suggested mechanism





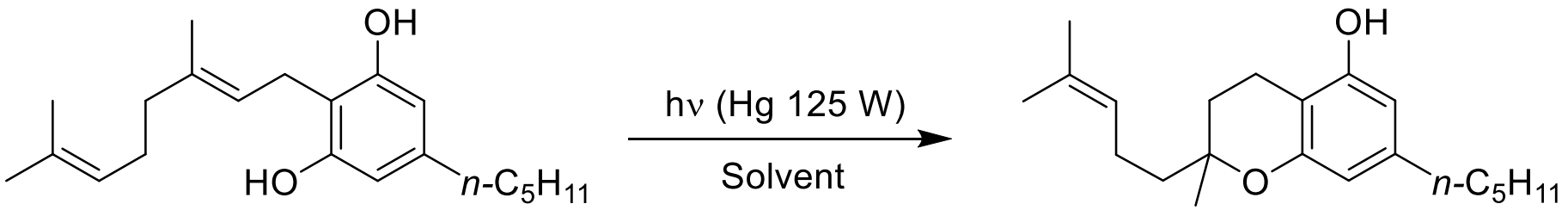




[1] P. Seccamani et al, J. Nat. Prod. 84 (2021) 2858–2865.

Cannabigerol (CBG)

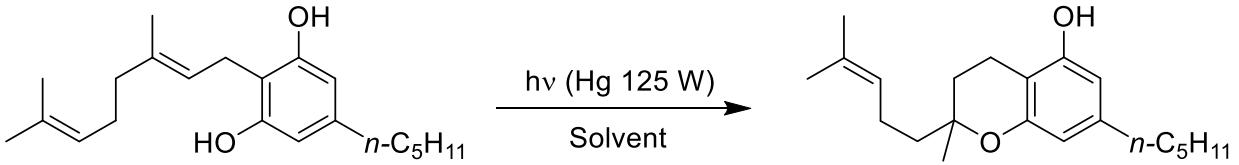
Cannabigerol (**CBG**) is obtained through decarboxilation of its acidic precursor, **CBGA**, naturally found in *C. Sativa* (chemotype IV).



Cannabigerol (CBG) **Cannabichromane (CBCa)**

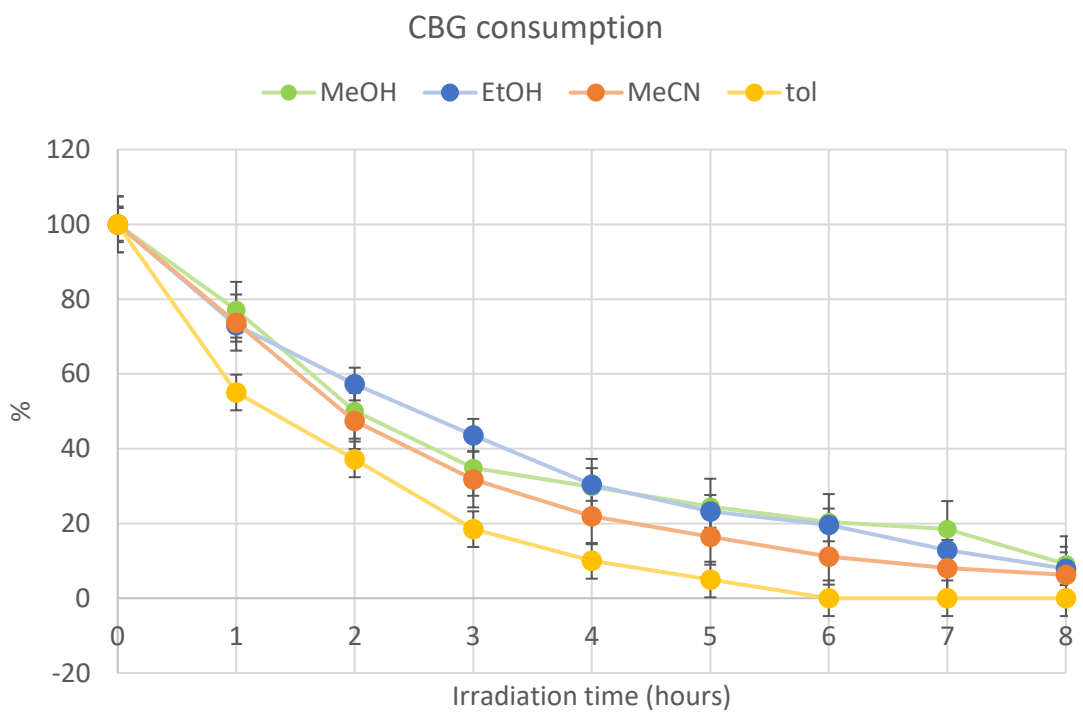
Photodecomposition of CBG resulted in the selective formation of a single product in all examined solvents, showcasing an unexpected selectivity.

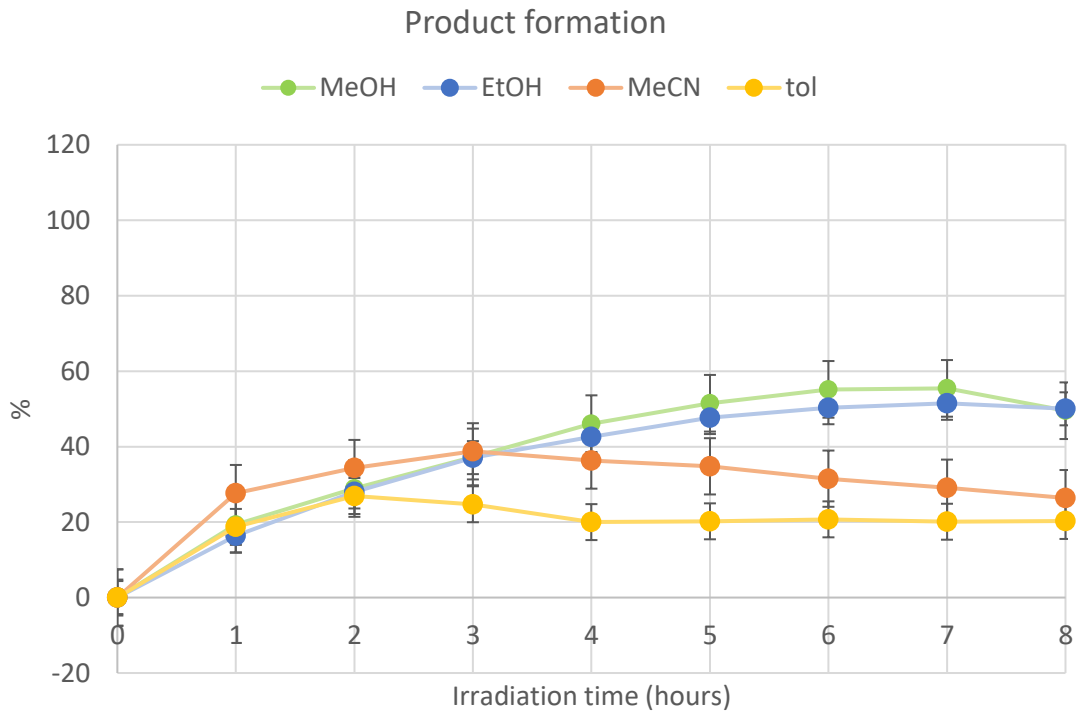
Cannabigerol (CBG)



Cannabigerol (CBG) **Cannabichromane (CBCa)**

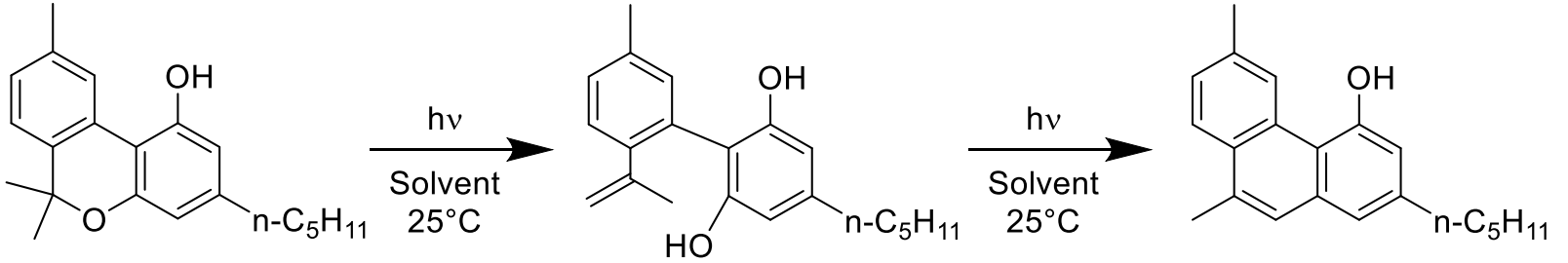
	Solvent	CBCa, yield (%)
1	MeOH	55
2	EtOH	50
3	MeCN	32
4	Toluene	21





Cannabinol (CBN)

Irradiation experiments have been carried out overnight in a multilamp reactor equipped with 10 x 15 W low pressure Hg lamps, using two different set of lamps (emission at 254 nm and emission centered at 310 nm)



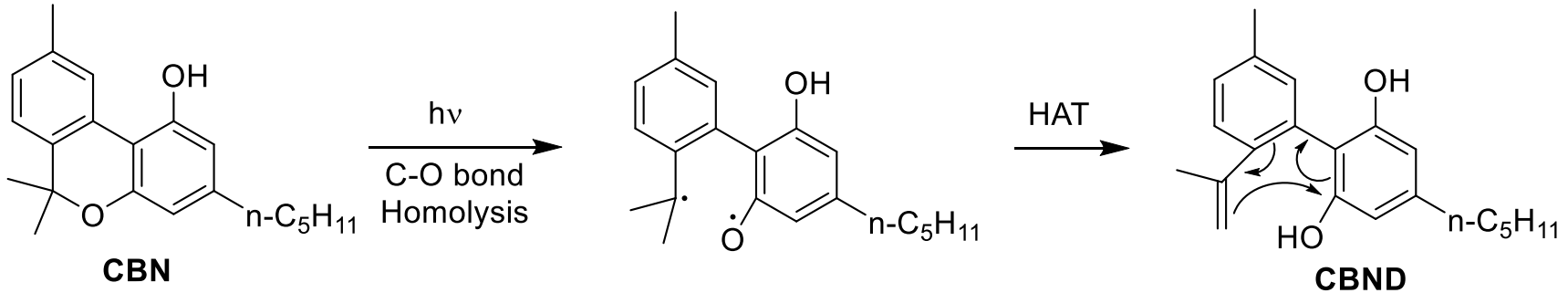
Cannabinol (CBN) **Cannabinodiol (CBND)** **Cannabiphenanthrene (CBP)**

λ_{exc} (nm)	Solvent	CBP, yield (%)
254	Cyclohexane	> 99
	MeCN	> 99
	MeOH	> 99
310	Cyclohexane	> 99
	MeCN	> 99
	MeOH	> 99

CBND can be achieved upon excitation with light of 310 nm and using a Pyrex tube as the reaction vessel.

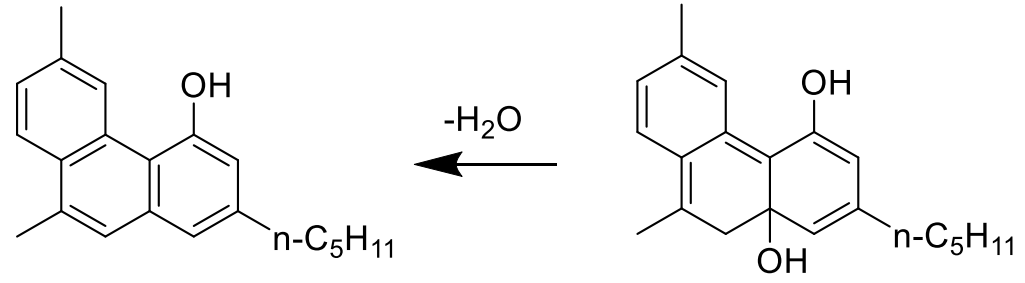
[3] A. Bowd et al, J. Chem. Soc. Chem. Commun. 310 (1975) 797–798.

Cannabinol: suggested mechanism



CBN

CBND
Isolated and characterized
by MS and NMR analyses



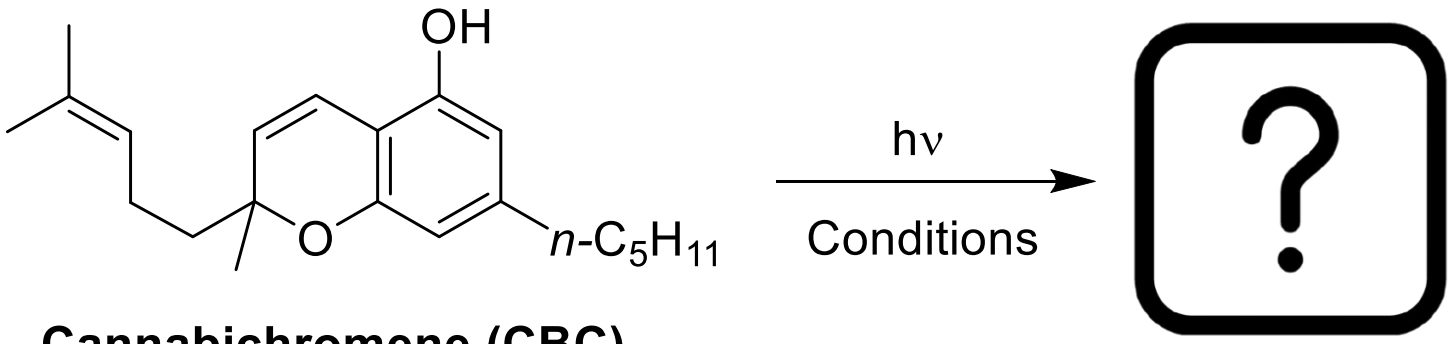
CBP
Isolated and characterized
by MS and NMR analyses

Work in progress: photoreactivity of CBC

Irradiation experiments are being carried out in a multilamp reactor equipped with 10 x 15 W low pressure Hg lamps (emission centered at 310 nm).

Chosen solvents:

- Cyclohexane
- Acetonitrile
- Methanol



Cannabichromene (CBC)

→ Preliminary data indicate the incorporation of methanol in the observed photoproducts.

Work in progress: photoreactivity of CBC

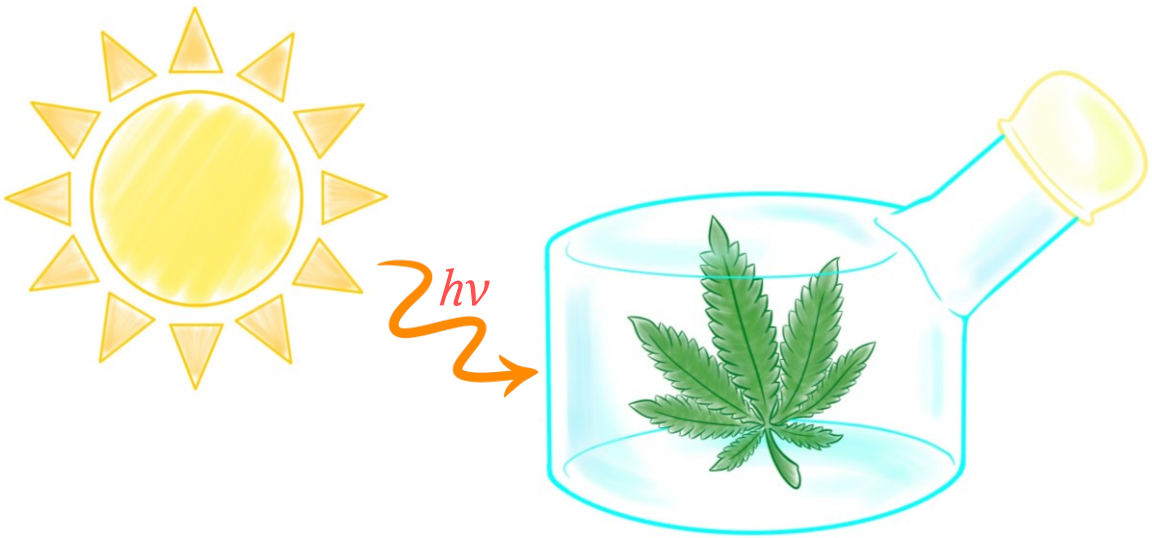
The sensitivity of CBC to UV light in the chosen media is being investigated by the measured consumption quantum yield (Φ_{-1})

λ_{exc} (nm)	Solvent	Φ_{-1}
254	*n*-hexane	0.074
	MeCN	0.068
	MeOH	0.053

4-Chloroanisole has been used as an actinometer.

Plant material: three chemotypes of *C. Sativa*

Irradiation was performed in a Solar Box equipped with a xenon lamp (spectral field from 290 to 800 nm, colour temperature 6000 K) and a power set up at 500 W/m^2.



- *c-I:* Δ^9-THC 2.50 $\%_{w/w}$, CBN, 0.88$\%_{w/w}$.

  Weight ratio of the two cannabinoids approximately about 3:1 (Δ^9-THC:CBN);

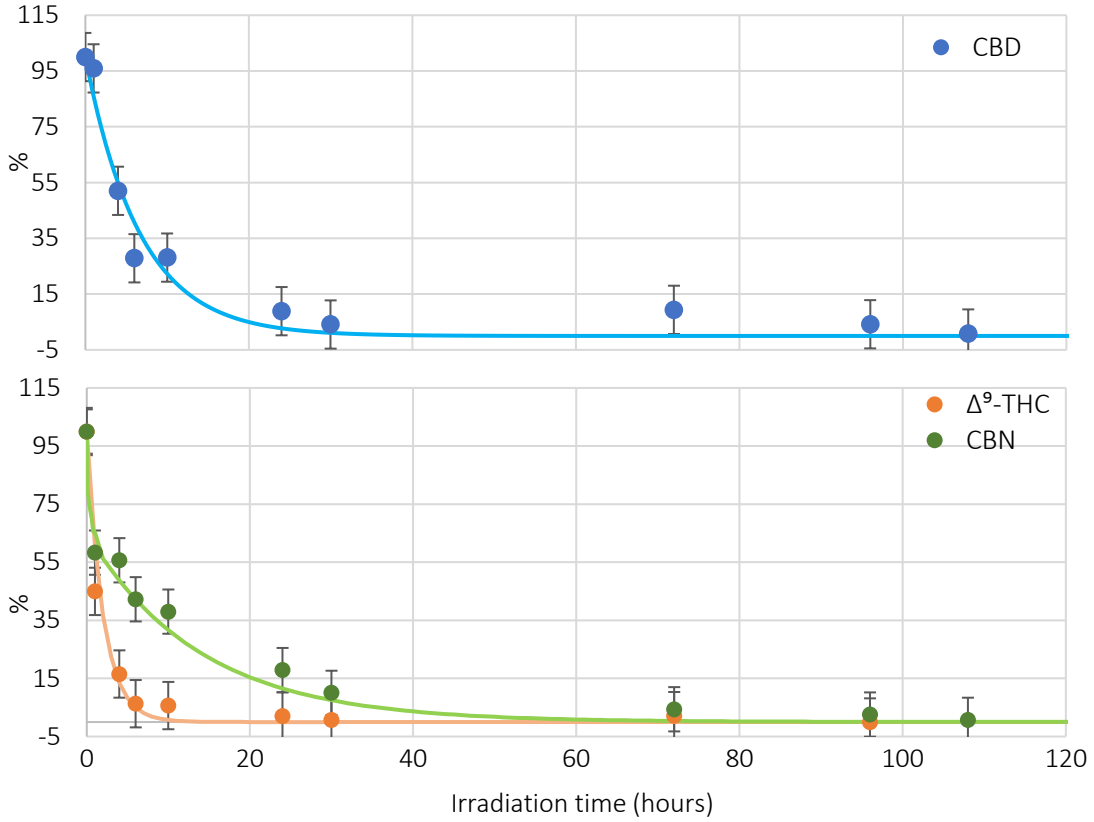
- *c-II:* CBD, 5.82$\%_{w/w}$, Δ^9-THC 3.19$\%_{w/w}$, CBN 2.34$\%_{w/w}$.

  Weight ratio of the three cannabinoids approximately about 6:3:2 (CBD:Δ^9-THC:CBN);

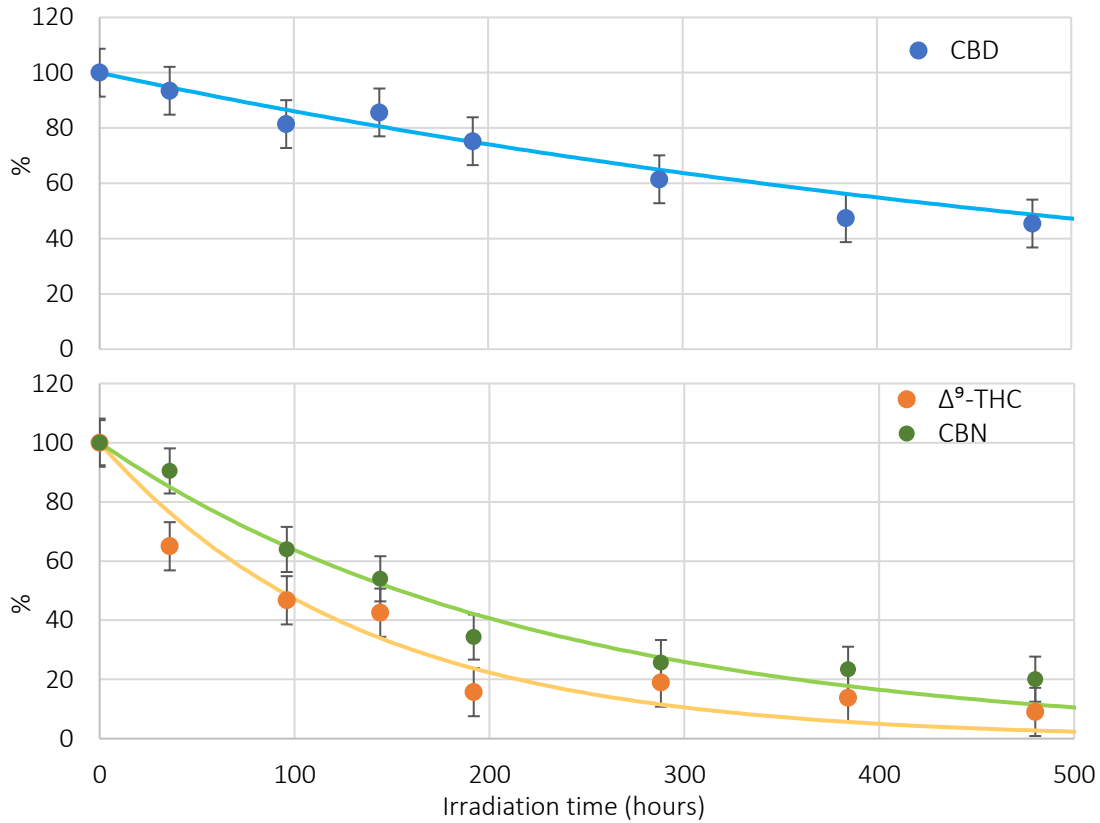
- *c-III*: CBD only, 3.02$\%_{w/w.}$

Photodegradation in *C. Sativa c-II*

Air atmosphere



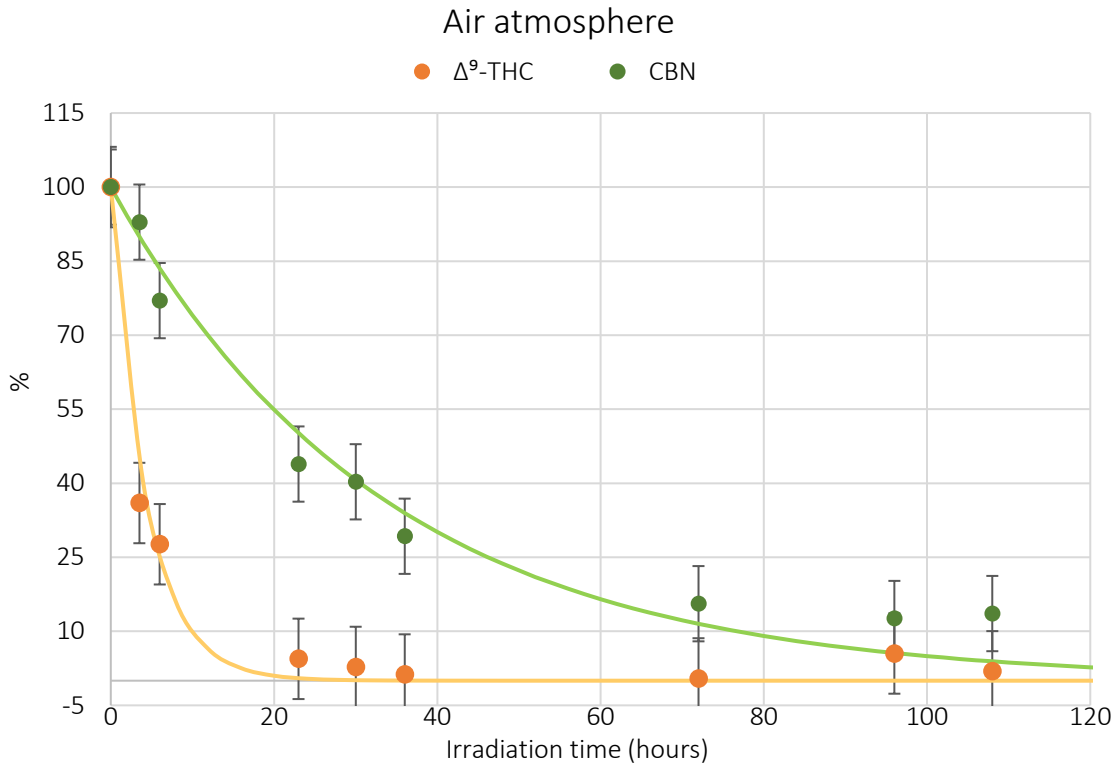
Nitrogen atmosphere

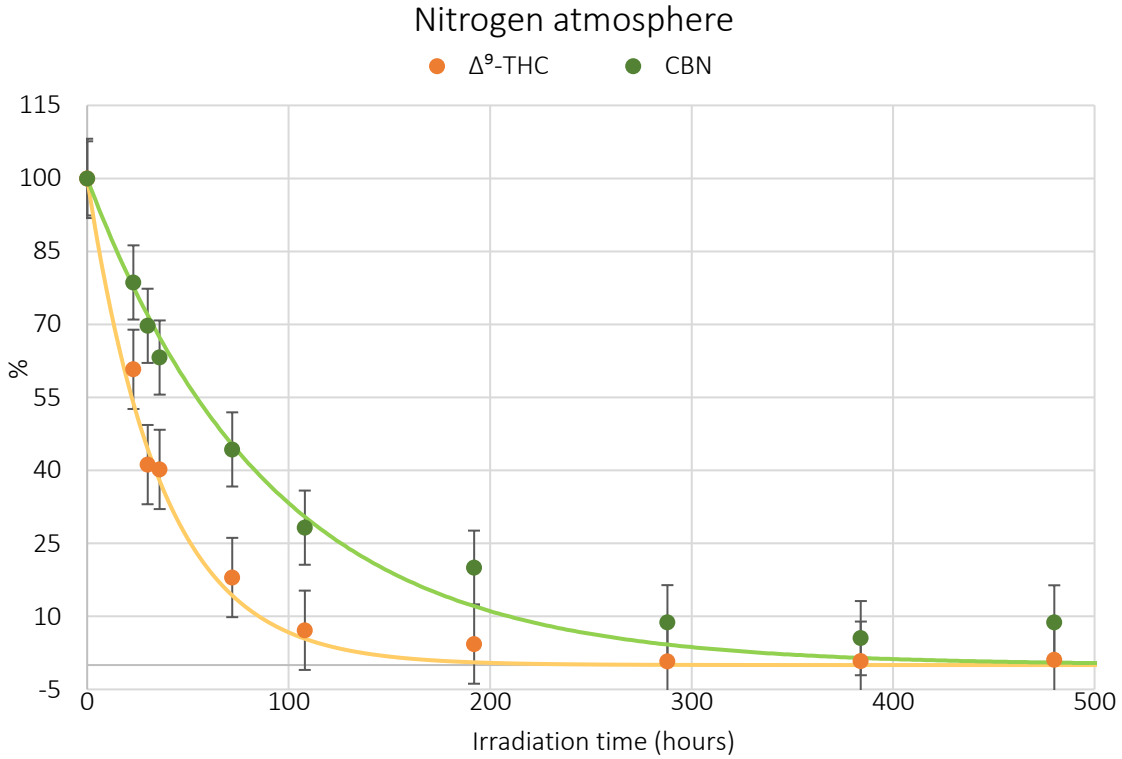


CBD:	100% (5.82%$_{w/w}$) → 0.9% (0.05%$_{w/w}$)	100% (5.82%$_{w/w}$) → 45.4% (2.64%$_{w/w}$)
Δ⁹-THC:	100% (3.19%$_{w/w}$) → < 0.01%	100% (3.19%$_{w/w}$) → 9.0% (0.29%$_{w/w}$)
CBN:	100% (2.34%$_{w/w}$) → 0.7% (0.02%$_{w/w}$)	100% (2.34%$_{w/w}$) → 20.1% (0.47%$_{w/w}$)

[4] A. Bini et al, Photochem. Photobiol. Sci. 23 (2024) 1239–1249.

Photodegradation in *C. Sativa c-I*





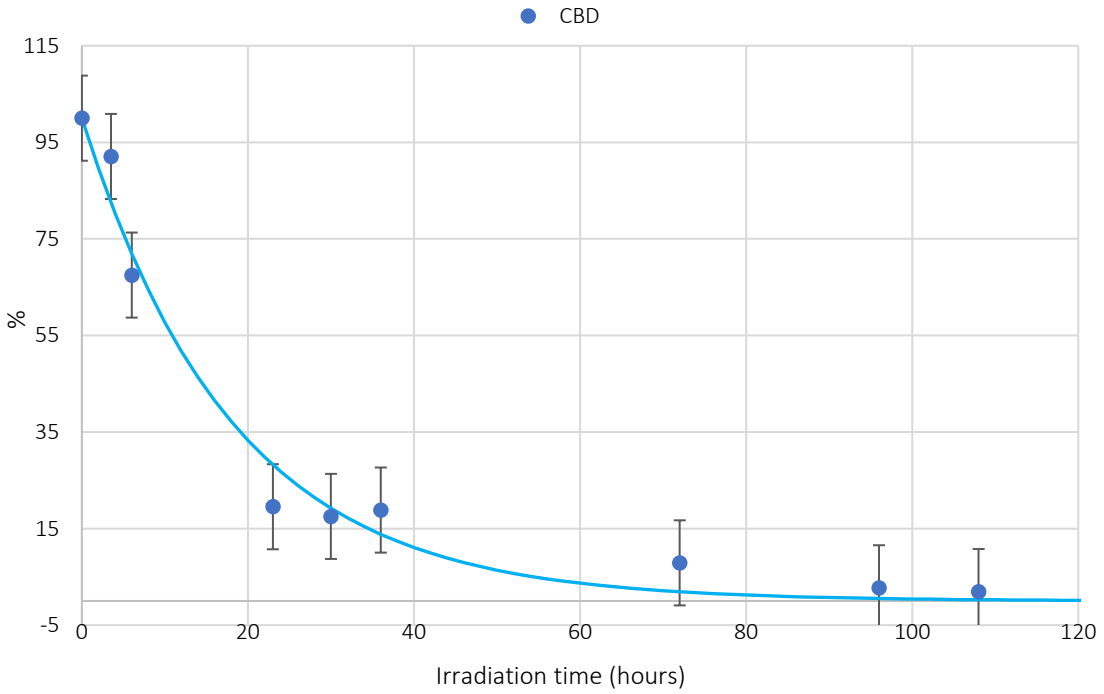
Δ⁹-THC: 100% (2.50%$_{w/w}$) → 1.9% (0.05%$_{w/w}$)
CBN: 100% (0.88%$_{w/w}$) → 19.6% (0.17%$_{w/w}$)

Δ⁹-THC: 100% (2.50%$_{w/w}$) → 1.1% (0.03%$_{w/w}$)
CBN: 100% (0.88%$_{w/w}$) → 8.8% (0.08%$_{w/w}$)

[4] A. Bini et al, Photochem. Photobiol. Sci. 23 (2024) 1239–1249.

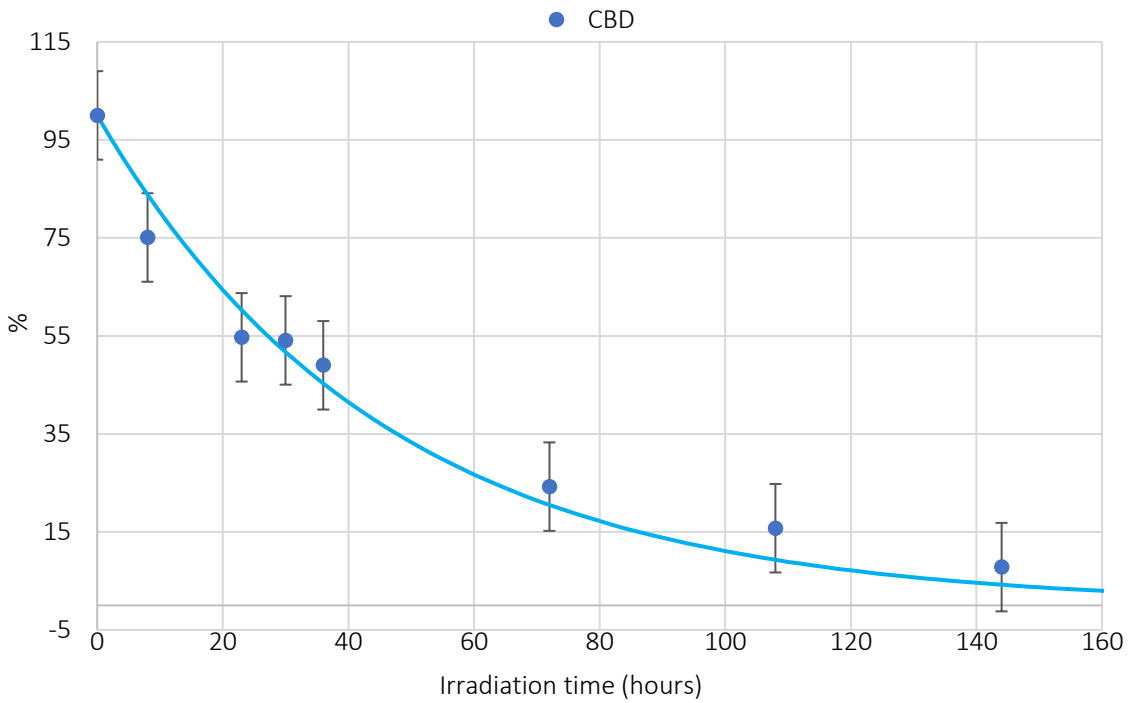
Photodegradation in *C. Sativa c-III*

Air atmosphere



CBD: 100% (3.02%$_{w/w}$) → 1.9% (0.06%$_{w/w}$)

Nitrogen atmosphere



CBD: 100% (3.02%$_{w/w}$) → 7.8% (0.24%$_{w/w}$)

[4] A. Bini et al, Photochem. Photobiol. Sci. 23 (2024) 1239–1249.

Conclusions

- The photochemical behaviour of three pure cannabinoids in different solvents has been investigated, allowing for the evaluation of cannabinoid-containing pharmaceutical and nutraceutical preparations, whose market is continuously gaining attention and growing;

- The behaviour of different decarboxylated chemotypes of cannabis when exposed to simulated sunlight has been investigated, both to assess the possible photochemical conversion of the present cannabinoids into different compounds and to obtain information on the photodegradation profile of the strands studied, thus providing more data on the optimal storage conditions for cannabis;

- The photochemical behaviour of CBC is being investigated.

Thank you for your attention!

Funded by European Union—NextGenerationEU. I punti di vista e le opinioni espresse sono tuttavia solo quelli degli autori e non rifettono necessariamente quelli dell'Unione europea o della Commissione europea. Né l'Unione europea né la Commissione europea possono essere ritenute responsabili per essi—NOrCa—Not Ordinary Cannabis—Exploring the chemical space around hemp (Cannabis sativa L.) waste and by products from a circular economy perspective PRIN: PROGETTI DI RICERCA DI RILEVANTE INTERESSE NAZIONALE—Bando 2022 PNRR Prot. P2022TXJX8.

Cannabigerol (CBG)

Brønsted acids:

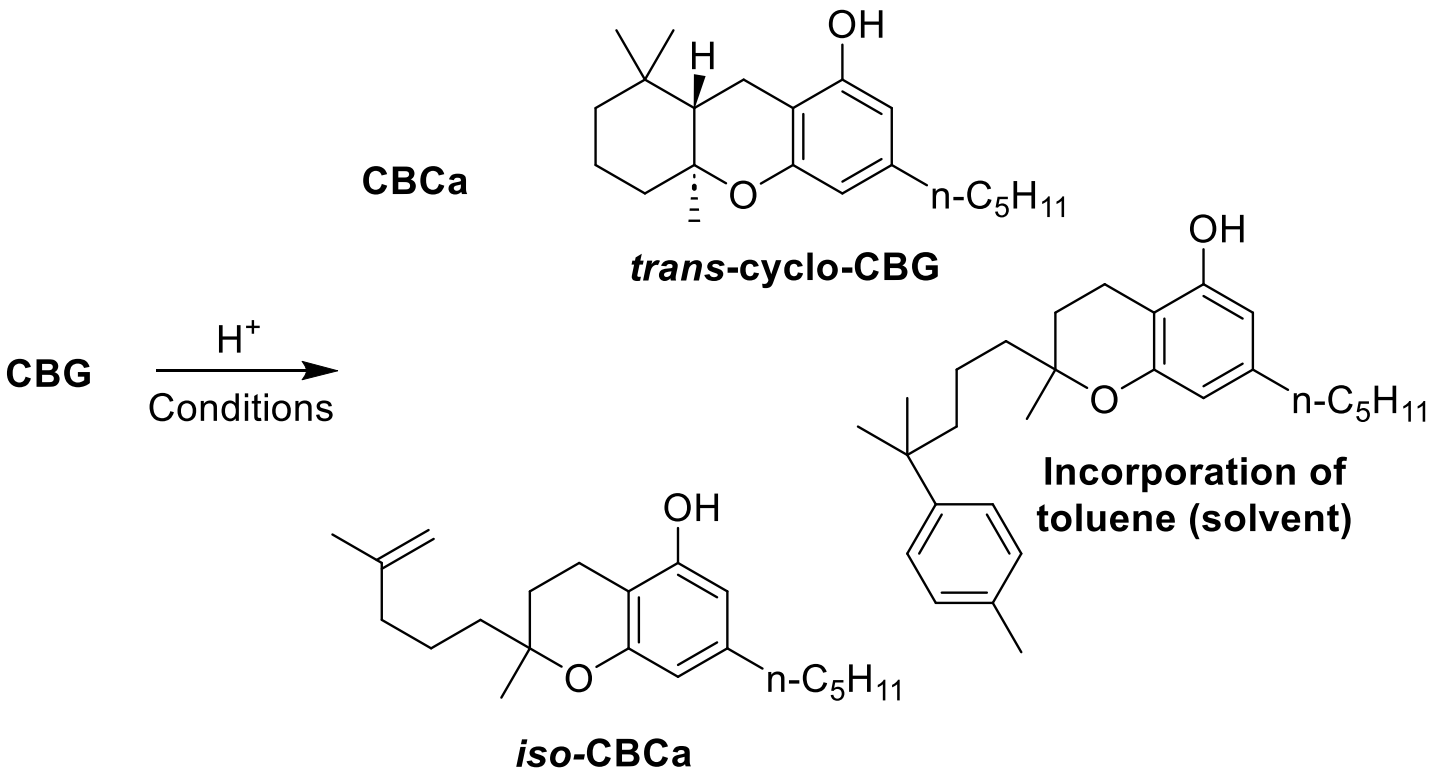
- trifluoroacetic acid (TFA)
- para-toluenesulfonic acid (PTSA)

Lewis acids:

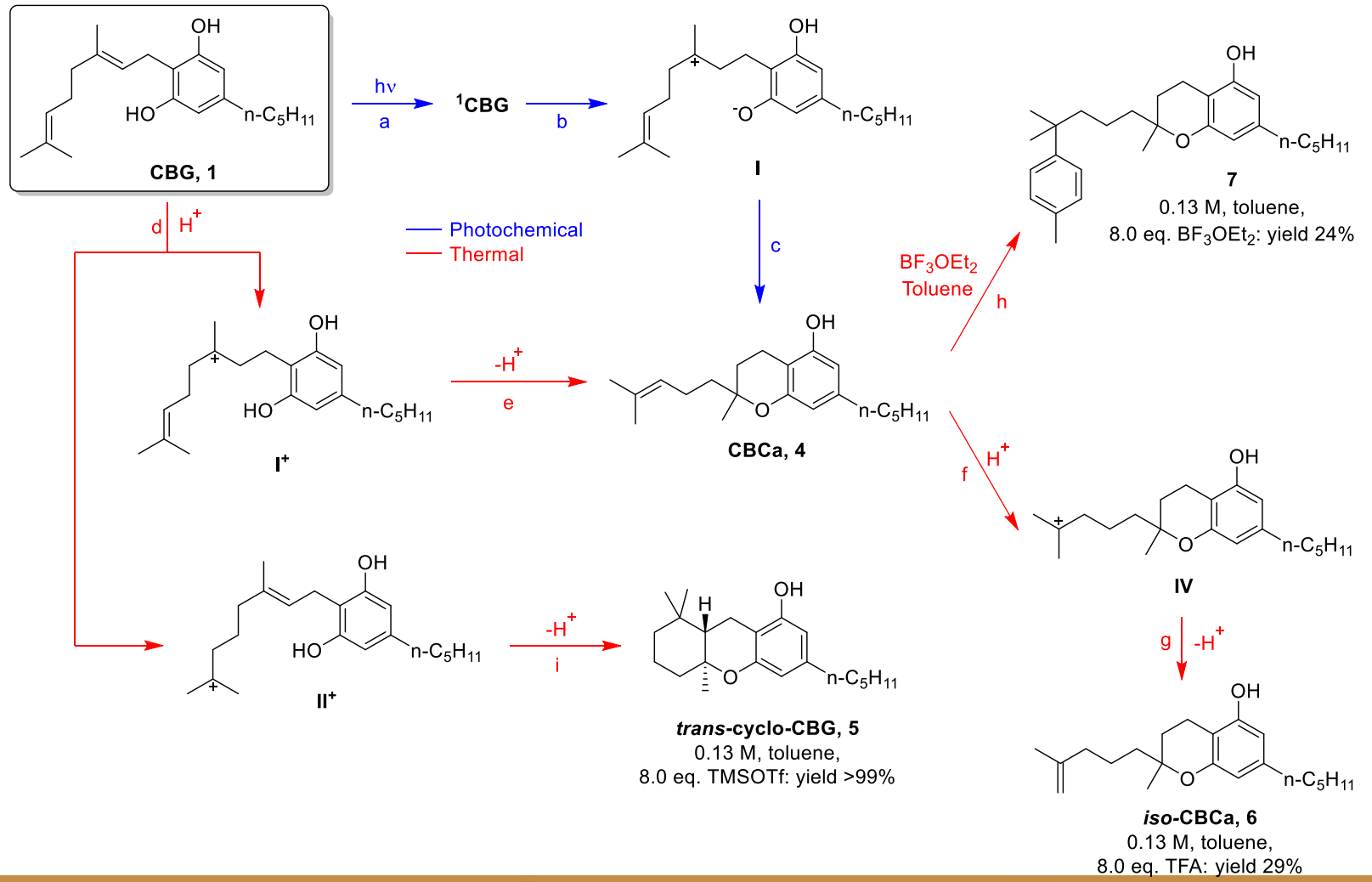
- boron trifluoride diethyletherate (BF_3OEt_2)
- trimethylsilyl trifluoromethanesulfonate (TMSOTf)

Product spread strongly depends on the chosen solvent, followed by the type of acid:

- ✓ MeOH: no reaction
- ✓ MeCN: low yields even after 100 hours
- ✓ Toluene: best solvent for thermal reactions



Cannabigerol: suggested mechanism

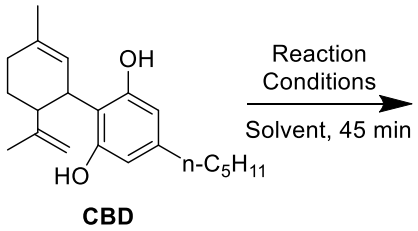


Cannabidiol (CBD)

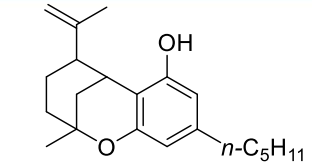
Solvents used:
- *n*-Hexane
- Acetonitrile
- Methanol
- Propylene glycol

Brønsted acids:
- p-toluenesulfonic acid (PTSA)
- methanesulfonic acid (MSA)

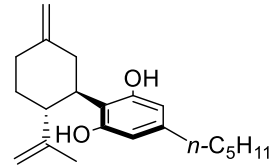
Lewis acids:
- boric acid (BA)
- $ZnCl_2$



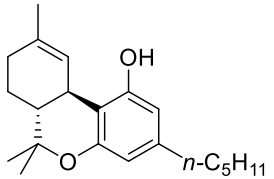
CBD



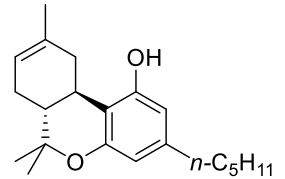
Δ8-*iso*-tetrahydrocannabinol (Δ8-iso-THC)



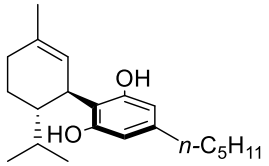
Δ7–cannabidiol (Δ7-CBD)



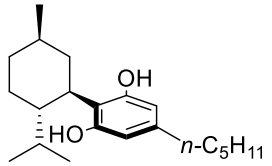
Δ9-tetrahydrocannabinol (Δ9-THC)



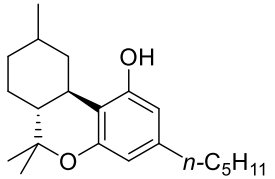
Δ8-tetrahydrocannabinol (Δ8-THC)



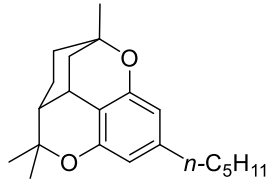
Dihydrocannabidiol (DHD)



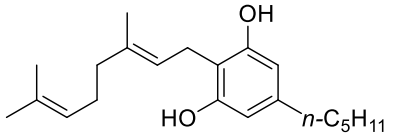
Tetrahydrocannabidiol (THD)



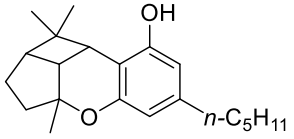
Hexahydrocannabinol (HHC)



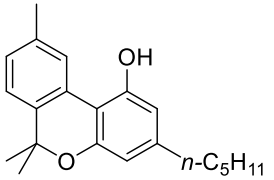
Cannabicitran (CBT)



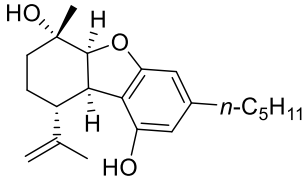
Cannabigerol (CBG)



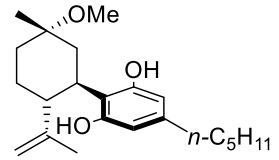
Cannabicyclol (CBL)



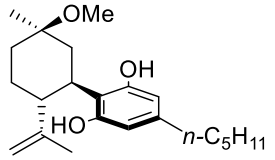
Cannabinol (CBN)



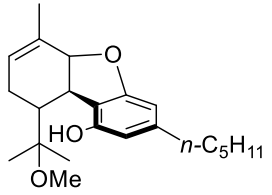
Cannabielsoin (CBE)



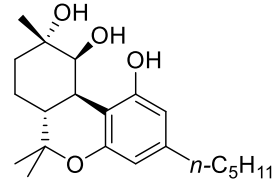
α-methoxy-cannabidiol (α-MeO-CBD)



β-methoxy-cannabidiol (β-MeO-CBD)



Methoxy-cannabielsoin (MeO-CBE)



Hexahydrocannabinol (HHC)