Electronic Supplementary Material (ESI) for CrystEngComm.

SUPPORTING INFORMATION

Polymorph prediction through observed structural isomorphism leading to a new crystalline form of cannabidiol

Hannah Straker, Lynn McMillan, Lina Mardiana, Glen R Hebberd, Elle Watson, Paul G Waddell, Michael R Probert and Michael J Hall

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General Experimental Information

Melting points were measured using Stuart SMP3 melting point apparatus. Crystallisation experiments were completed using a TTP LabTech mosquito® liquid handling robot using SwissSCI Modular LCP 96 well glass plates with a 100 micron spacer and sealed with a glass cover slip. Visualisation of experiments was carried out with a Nikon SMZ1000 microscope fitted with a cross polariser, with photographs were taken with a GXCAM-U3-5 5.1MP camera. Single crystal X-ray diffraction experiments were performed using an in-house diffractometers (Rigaku Oxford Diffraction Gemini ultra with an Atlas detector and Cu sealed tube source with focussing optics, or a Bruker D8 Venture with a Photon 2 detector and an Incoatec IμS (Cu) both equipped with an Oxford Cryosystems Cryostream cryostream with data recorded at 150 K).

Crystalisation of CBD Form 1 by Classical Methods - Slow Solvent Evaporation

5 mg of CBD was placed into straight sided glass sample tubes, into which was added 0.5 – 1 mL of an organic solvent (pentane, *n*-hexane, *n*-heptane, dichloromethane and chloroform) until no solid remained. Glass sample tubes were then sealed with a plastic lid, into which two-three small holes had been made, and left to crystallise at room temperature in the dark. Visual examination, by cross-polarised optical microscopy, for the presence of CBD crystals was performed every few days.

Single crystals of CBD were subsequently observed after 1-2 weeks from *n*-pentane, *n*-hexane, *n*-heptane and dichloromethane. Single crystals suitable for SCXRD were analysed on an in-house X-ray diffractometer. Full SCXRD analysis was performed on a crystal obtained from *n*-pentane by Dr Paul Waddell, to give an X-ray structure consistent with known CBD Form 1 (CANDOM01, CANDOM10 and CANDOM11). Unit cell analysis was also carried out on CBD crystals obtained from *n*-hexane, *n*-heptane, and dichloromethane, showing that they all had the same unit cell parameters as CBD Form 1.

ENaCt Experiments: Crystalisation of CBD Form 1 by ENaCt

Approximately, 50 mg of CBD was dissolved in a minimum of 50 μL of solvent, with additional solvent added as required to dissolve the sample, resulting CBD stock solutions in *n*-pentane [0.11 g/mL], *n*-hexane [0.084 g/mL], *n*-heptane [0.063 g/mL], chloroform [1.00 g/mL], 1,2-dichloroethane [1.00 g/mL], toluene [1.02 g/mL], fluorobenzene [1.00 g/mL], chlorobenzene [1.01 g/mL], and hexafluorobenzene [0.20 g/mL]. These stock solutions, labelled as high concentration (H), were also diluted by two fold, medium concentration (M), and four fold, low concentration (L), to provide three different sample concentrations for our ENaCt experiments. Next, using a SPT LabTech mosquito® liquid-handling robot, 200 nL of each inert oil (PDMSO, FC-40, FY and mineral oil) were dispensed into each well of a Laminex™ 96-well glass plate, followed by injection of 50 nL of the appropriate CBD solution into each oil droplet. The 96-well glass plates were then sealed with a glass cover slip and stored in the dark at room temperature for up to 14 days (Figure S1).

Oils		50 nL of CBD stock solutions											
		no oils			with 200 nL oils								
		H	M	L	H			M			L		
		1	2	3	4	5	6	7	8	9	10	11	12
PDMSO	A												
	B												
FC-40	C												
	D												
FY	E												
	F												
Mineral oil	G												
	H												

Oils Used for ENaCt Experiments

ENaCt Oils	
PDMSO	poly(dimethylsiloxane); CAS: 63148-62-9; supplier: Sigma Aldrich
FC-40	Fluorinert FC-40; CAS: 51142-49-5; supplier: Fluorochem
FY	Fomblin YR-1800; CAS: 69991-67-9; supplier: Alfa Aesar
MO	Mineral oil; CAS: 8042-47-5; supplier: Sigma Aldrich

Figure S1. A typical arrangement of a 96-well glass plate containing inert oils and CBD solutions. H = high concentration (100% stock solution), M = medium concentration (50% stock solution), L = low concentration (25% stock solution). Oils used in ENaCt.

Plates were checked for the presence of crystals by cross-polarised optical microscopy at day 1, 7 and 14. Each experimental outcome was categorized as either: (F) failed; (1) in solution; (2) oiled-out or non-crystalline solid; (3) microcrystalline solid and (4) single crystals suitable for SCXRD (**Figure S2**).

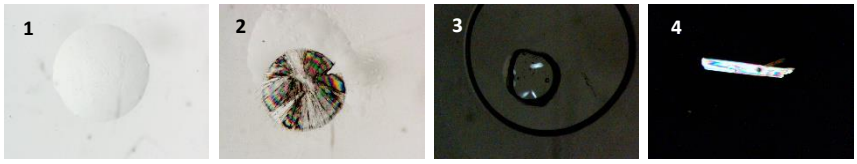


Figure S2. Examples of ENaCt outcome of CBD crystallisations: (1) in solution; (2) oiled-out or non-crystalline solid; (3) microcrystalline solid and (4) single crystals suitable for SCXRD.

From the 864 ENaCt experiments undertaken, 18 (2.1%) gave single crystals suitable for SCXRD after 14 days (3 from chloroform, 4 from 1,2-dichloroethane, 6 from toluene, and 5 from fluorobenzene). 11 of 18 of the single crystals observed were formed from high concentration (H) solutions of CBD, whilst the majority 16 of 18 was formed from experiments containing mineral oil. Control experiments, without the presence of inert oils, gave no suitable single crystals (**Figure S3**).

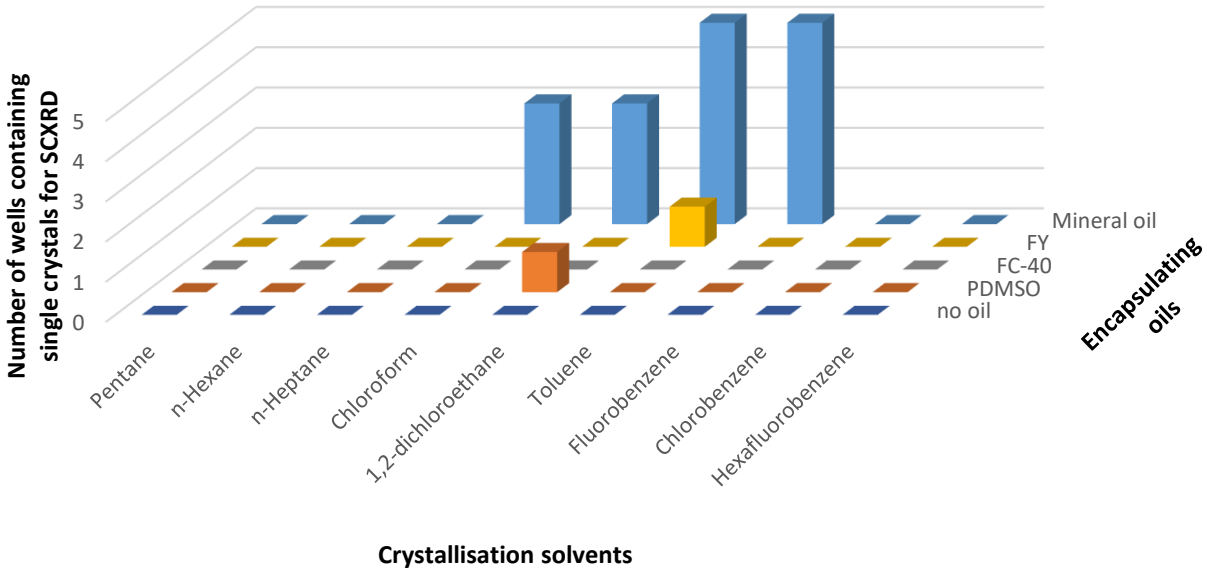


Figure S3. CBD single crystals suitable for SCXRD observed from different solvents and oils using ENaCt.

Single crystals of CBD grown via ENaCt showed a needle-like morphology, similar to those grown under classical conditions. Therefore, we examined four single crystals of CBD grown via ENaCt from chloroform, toluene, and fluorobenzene using in-house X-ray analysis (**Figure S4**).

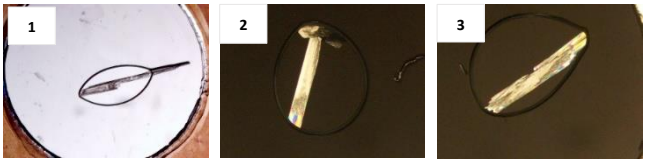


Figure S4. Single crystals of CBD grown using ENaCt, with encapsulation by mineral oil, showing needle-like morphology: (**1**) chloroform; (**2**) toluene; (**3**) fluorobenzene.

X-ray analysis was undertaken for all three of the single crystals selected, all of which gave unit cell data that matched the known crystal structure of CBD. A complete X-ray crystal structure was determined for a CBD crystal grown from toluene and mineral oil using Cu Kα radiation. This gave an excellent data set showing a monoclinic $P2_1$ space group with unit cell dimensions which aligned well with the structural data available from the CCDC (CANDOM01, CANDOM10 and CANDOM11), with measurement of the absolute stereochemistry of CBD also possible (**Figure S5**).

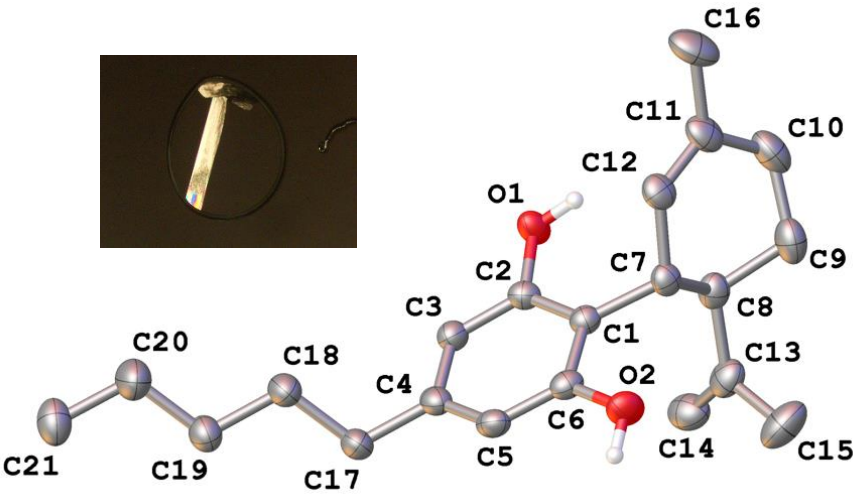


Figure S5. Structure of CBD derived from X-ray diffraction data, crystal obtained from ENaCt protocol (solvent: toluene, encapsulation: mineral oil). Hydrogen atoms bound to carbon have been removed for clarity. Anisotropic displacements have been plotted at the 50% probability level.

ENaCt Experiments: Crystalisation of CBD Form 2 by ENaCt with Seeding with CBD-3 and CBD-4

Preparation of Stock Solutions for ENaCt

Stock solutions were prepared as follows: into 1.5 mL screw top glass vials was weighed 25 - 50 mg of CBD, and solvent was added portionwise until the sample fully dissolved at room temperature.

Stock Solutions for Plates GW001 to GW005

Vial	Solvent	Concentration of substrate / mg mL^{-1}
1	Chloroform ($CHCl_3$)	1888
2	1,2-Dichloroethane (DCE)	1700
3	1,1,2,2-Tetrachloroethane (TeCE)	926
4	Toluene	1042
5	4-Fluorotoluene	1042

Stock Solutions for Plates GW006 to GW010

Vial	Solvent	Concentration of substrate / mg mL^{-1}
6	Chloroform ($CHCl_3$)	1852
7	1,2-Dichloroethane (DCE)	1852
8	1,1,2,2-Tetrachloroethane (TeCE)	694
9	Toluene	1042
10	4-Fluorotoluene	1042

Seeding of Plates

Seed crystals were prepared starting from classically recrystallized material or commercially supplied crystalline material and were crushed using a spatula to provide a stock of seed crystals. Seeding of ENaCt plates was completed via use of a Hampton micro-tool. This was used to pick up a small quantity of crushed seed crystals which were then manually placed in each well.

ENaCt Experimental Setup

Using a STP Labtech mosquito liquid handling robot, 250 nL of one of four oils (PDMSO, FC-40, FY and mineral oil) were dispensed into each well of a 96 well SWISSCI LCP plate with a 100 micron spacer. Following which 100 nL of each stock solution containing CBD was collected from the parent plate and dispensed into each of the oil droplets within the wells. The plates were sealed with a glass cover slip and were stored in the dark at room temperature and after 1 week, evaluation of crystals growth was carried out visually by a cross-polarised optical microscopy.

Key for Outcomes of ENaCt Experiments for the Formation of CBD Form 1 and Form 2 Crystals

Sample's code													
Vial	Standard Method		Volume of Oil = 250 nL										
	Volume of Solvent		100 nL										
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
x	Solvent used to dissolve sample	A	1											
		B												
		C			2									
		D					3							
		E							3*					
		F									4			
		G											4*	
		H												

1	remained in solution
2	oiled out/amorphous solids
3	microcrystals (needle-like, Form 1)
3*	microcrystals (block-like, Form 2)
4	crystals (needle-like, Form 1)
4*	crystals (block-like, Form 2)

Crystallisation of CBD Form 2 by ENaCt with Seeding with CBD-3

GW001

Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
1	$CHCl_3$	A	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO	
	$CHCl_3$	B	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO	
	$CHCl_3$	C	No oil		FC-40		No oil		FC-40		No oil		FC-40	
	$CHCl_3$	D	No oil		FC-40		No oil		FC-40		No oil		FC-40	
	$CHCl_3$	E	No oil		FY		No oil		FY		No oil		FY	
	$CHCl_3$	F	No oil		FY		No oil		FY		No oil		FY	
	$CHCl_3$	G	No oil		MO		No oil		MO		No oil		MO	
	$CHCl_3$	H	No oil		MO		No oil		MO		No oil		MO	
			No seed				CBD seed				CBDv seed			

GW001

Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
1	$CHCl_3$	A	1	2	2	2	3	4	4	1	4*	4*	4*	4*
	$CHCl_3$	B	1	2	2	2	3	4	4	1	4*	4*	4*	4*
	$CHCl_3$	C	1	1	1	1	3	3	3	4	4	3	3	3
	$CHCl_3$	D	1	1	1	1	3	3	3	4	4	3	3	3*
	$CHCl_3$	E	1	1	1	1	3	3	3	4	4*	4	4	2
	$CHCl_3$	F	1	1	1	1	3	3	3	4	4	4	4*	4*
	$CHCl_3$	G	1	2	2	2	3	4	4	4	4	4*	4*	1
	$CHCl_3$	H	1	2	2	2	3	4	4	4	4*	4*	4*	2

GW002

Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
2	DCE	A	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO	
	DCE	B	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO	
	DCE	C	No oil		FC-40		No oil		FC-40		No oil		FC-40	
	DCE	D	No oil		FC-40		No oil		FC-40		No oil		FC-40	
	DCE	E	No oil		FY		No oil		FY		No oil		FY	
	DCE	F	No oil		FY		No oil		FY		No oil		FY	
	DCE	G	No oil		MO		No oil		MO		No oil		MO	
	DCE	H	No oil		MO		No oil		MO		No oil		MO	
			No seed				CBD seed				CBDv seed			

GW002

Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
2	DCE	A	1	2	2	2	3	4	4	2	4*	4*	4*	4*
	DCE	B	1	4	2	2	3	2	2	4	4*	4*	4*	4*
	DCE	C	1	1	1	1	3	4	4	4	4	3	3	4*
	DCE	D	1	1	1	1	3	4	4	4	4*	3	3	2
	DCE	E	1	1	1	1	3	4	4	4	4*	4	4	4*
	DCE	F	1	1	1	1	3	4	4	4	4*	4	4	4
	DCE	G	1	2	2	1	3	4	4	4	4	4*	4*	4*
	DCE	H	1	2	2	2	3	4	4	4	4	4*	4*	4*

GW003

Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
3	TeCE	A	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO	
	TeCE	B	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO	
	TeCE	C	No oil		FC-40		No oil		FC-40		No oil		FC-40	
	TeCE	D	No oil		FC-40		No oil		FC-40		No oil		FC-40	
	TeCE	E	No oil		FY		No oil		FY		No oil		FY	
	TeCE	F	No oil		FY		No oil		FY		No oil		FY	
	TeCE	G	No oil		MO		No oil		MO		No oil		MO	
	TeCE	H	No oil		MO		No oil		MO		No oil		MO	
			No seed				CBD seed				CBDv seed			

GW003

Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
3	TeCE	A	2	2	2	2	4	4	4	4	4*	3	4*	3
	TeCE	B	2	2	2	2	F	4	4	4	2	4*	4*	3
	TeCE	C	2	1	1	1	4	4	4	4	4*	4*	4*	3
	TeCE	D	2	1	1	1	4	4	4	4	2	3	4*	2
	TeCE	E	1	1	1	1	4	1	1	4	4*	4*	4*	2
	TeCE	F	1	1	1	1	4	4	4	4	4	4	2	2
	TeCE	G	1	2	2	2	4	4	4	4	2	4*	4*	4*
	TeCE	H	1	2	2	2	4	4	4	4	4	4*	4*	4*

GW004

Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
4	Toluene	A	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO	
	Toluene	B	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO	
	Toluene	C	No oil		FC-40		No oil		FC-40		No oil		FC-40	
	Toluene	D	No oil		FC-40		No oil		FC-40		No oil		FC-40	
	Toluene	E	No oil		FY		No oil		FY		No oil		FY	
	Toluene	F	No oil		FY		No oil		FY		No oil		FY	
	Toluene	G	No oil		MO		No oil		MO		No oil		MO	
	Toluene	H	No oil		MO		No oil		MO		No oil		MO	
			No seed				CBD seed				CBDv seed			

GW004

Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
4	Toluene	A	1	2	2	2	4	2	2	2	4*	2	2	2
	Toluene	B	1	2	2	2	4	4	4	4	4*	2	4*	4
	Toluene	C	1	1	1	1	4	4	4	4	4*	4	4*	3
	Toluene	D	1	1	1	1	4	4	4	4	4*	4	2	2
	Toluene	E	1	1	1	1	4	4	4	4	4*	4	4*	4*
	Toluene	F	1	1	1	1	4	4	4	4	4*	4	4	4*
	Toluene	G	1	2	2	2	4	4	4	4	4*	4*	4*	2
	Toluene	H	1	2	2	2	4	4	4	4	4*	2	2	2

GW005																
Vial	Standard Method		Volume of Oil = 250 nL													
	Volume of Solvent		100 nL													
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12		
5	4-Fluorotoluene	A	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO			
	4-Fluorotoluene	B	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO			
	4-Fluorotoluene	C	No oil		FC-40		No oil		FC-40		No oil		FC-40			
	4-Fluorotoluene	D	No oil		FC-40		No oil		FC-40		No oil		FC-40			
	4-Fluorotoluene	E	No oil		FY		No oil		FY		No oil		FY			
	4-Fluorotoluene	F	No oil		FY		No oil		FY		No oil		FY			
	4-Fluorotoluene	G	No oil		MO		No oil		MO		No oil		MO			
	4-Fluorotoluene	H	No oil		MO		No oil		MO		No oil		MO			
			No seed				CBD seed				CBDv seed					

GW005														
Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
5	4-Fluorotoluene	A	1	2	2	2	4	4	4	4	4*	4*	4*	4*
	4-Fluorotoluene	B	1	2	2	2	4	2	4	4	4*	2	4*	2
	4-Fluorotoluene	C	1	2	1	1	4	4	4	4	4*	4*	4*	4*
	4-Fluorotoluene	D	1	2	1	1	4	4	4	4	4*	4*	4	4*
	4-Fluorotoluene	E	1	1	1	1	4	4	4	4	4*	4	4	4*
	4-Fluorotoluene	F	1	1	1	1	4	4	4	4	4*	4	4	2
	4-Fluorotoluene	G	1	2	2	2	4	4	4	4	4*	4*	4*	2
	4-Fluorotoluene	H	1	2	2	2	4	4	4	4	4*	4*	4*	2

Crystallisation of CBD Form 2 by ENaCt with Seeding with CBD-4

GW006																
Vial	Standard Method		Volume of Oil = 250 nL													
	Volume of Solvent		100 nL													
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12		
6	$CHCl_3$	A	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO			
	$CHCl_3$	B	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO			
	$CHCl_3$	C	No oil		FC-40		No oil		FC-40		No oil		FC-40			
	$CHCl_3$	D	No oil		FC-40		No oil		FC-40		No oil		FC-40			
	$CHCl_3$	E	No oil		FY		No oil		FY		No oil		FY			
	$CHCl_3$	F	No oil		FY		No oil		FY		No oil		FY			
	$CHCl_3$	G	No oil		MO		No oil		MO		No oil		MO			
	$CHCl_3$	H	No oil		MO		No oil		MO		No oil		MO			
			No seed				CBD seed				CBD4 seed					

GW006														
Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
6	$CHCl_3$	A	1	2	2	3	3	3	3	3	4*	4*	4*	4*
	$CHCl_3$	B	1	1	2	1	3	3	3	3	3	4*	4*	4*
	$CHCl_3$	C	3	1	1	1	3	3	3	3	4*	4*	4*	4*
	$CHCl_3$	D	1	1	1	1	3	3	3	3	4*	3	4*	4*
	$CHCl_3$	E	1	1	1	1	3	3	3	3	4*	3	3*	3*
	$CHCl_3$	F	1	2	1	1	3	3	3	3	3	3	3*	3*
	$CHCl_3$	G	1	2	2	2	3	3	3	3	1	3	4*	4*
	$CHCl_3$	H	1	2	4	4	3	3	3	3	3	3	3*	3*

GW007																
Vial	Standard Method		Volume of Oil = 250 nL													
	Volume of Solvent		100 nL													
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12		
7	DCE	A	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO			
	DCE	B	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO			
	DCE	C	No oil		FC-40		No oil		FC-40		No oil		FC-40			
	DCE	D	No oil		FC-40		No oil		FC-40		No oil		FC-40			
	DCE	E	No oil		FY		No oil		FY		No oil		FY			
	DCE	F	No oil		FY		No oil		FY		No oil		FY			
	DCE	G	No oil		MO		No oil		MO		No oil		MO			
	DCE	H	No oil		MO		No oil		MO		No oil		MO			
			No seed				CBD seed				CBD4 seed					

GW007														
Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
7	DCE	A	1	2	2	2	3	3	2	2	4	3	1	4*
	DCE	B	1	2	2	2	3	2	3	3	1	2	1	4*
	DCE	C	1	2	1	1	3	3	3	3	3*	2	3*	2
	DCE	D	1	1	1	1	3	3	3	3	4*	4*	4*	3
	DCE	E	1	1	1	1	1	3	4	3	4*	3	3	4*
	DCE	F	1	1	1	1	3	2	4	1	4*	3	4*	4*
	DCE	G	3	2	2	2	3	4	4	1	4*	4*	4*	4*
	DCE	H	1	2	2	2	3	4	4	4	4*	4*	4*	4*

GW008																
Vial	Standard Method		Volume of Oil = 250 nL													
	Volume of Solvent		100 nL													
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12		
8	TCE	A	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO			
	TCE	B	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO			
	TCE	C	No oil		FC-40		No oil		FC-40		No oil		FC-40			
	TCE	D	No oil		FC-40		No oil		FC-40		No oil		FC-40			
	TCE	E	No oil		FY		No oil		FY		No oil		FY			
	TCE	F	No oil		FY		No oil		FY		No oil		FY			
	TCE	G	No oil		MO		No oil		MO		No oil		MO			
	TCE	H	No oil		MO		No oil		MO		No oil		MO			
			No seed				CBD seed				CBD4 seed					

GW008														
Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
8	TCE	A	1	2	2	2	3	2	4	2	4*	1	4*	2
	TCE	B	1	2	2	2	3	3	3	2	4*	4*	2	2
	TCE	C	1	1	1	1	3	1	3	3	1	4*	4*	4*
	TCE	D	1	2	2	1	1	1	3	3	4*	4*	4*	4*
	TCE	E	1	1	2	2	1	1	3	3	4*	1	1	1
	TCE	F	1	1	1	1	3	1	4	1	1	4*	4	4*
	TCE	G	1	2	2	2	3	4	4	4	4	4*	3	1
	TCE	H	1	2	2	2	3	4	4	4	1	4*	4*	4*

GW009																
Vial	Standard Method		Volume of Oil = 250 nL													
	Volume of Solvent		100 nL													
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12		
9	Toluene	A	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO			
	Toluene	B	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO			
	Toluene	C	No oil		FC-40		No oil		FC-40		No oil		FC-40			
	Toluene	D	No oil		FC-40		No oil		FC-40		No oil		FC-40			
	Toluene	E	No oil		FY		No oil		FY		No oil		FY			
	Toluene	F	No oil		FY		No oil		FY		No oil		FY			
	Toluene	G	No oil		MO		No oil		MO		No oil		MO			
	Toluene	H	No oil		MO		No oil		MO		No oil		MO			
			No seed				CBD seed				CBD4 seed					

GW009														
Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
9	Toluene	A	2	3	2	2	3	2	4	2	3*	4*	2	2
	Toluene	B	1	2	2	2	3	3	4	2	1	2	2	4*
	Toluene	C	1	1	1	2	3	3	3	3	3*	3	3	4*
	Toluene	D	2	1	1	1	3	3	3	3	3*	4*	4*	3*
	Toluene	E	2	1	1	1	3	1	4	1	3*	4*	4*	4*
	Toluene	F	2	1	1	1	3	4	1	3	3*	4*	4*	4*
	Toluene	G	3	2	2	2	3	4	4	4	4*	4*	4*	4*
	Toluene	H	2	2	2	2	3	4	4	4	3*	4*	4*	4*

GW010																
Vial	Standard Method		Volume of Oil = 250 nL													
	Volume of Solvent		100 nL													
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12		
10	4-Fluorotoluene	A	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO			
	4-Fluorotoluene	B	No oil		PDMSO		No oil		PDMSO		No oil		PDMSO			
	4-Fluorotoluene	C	No oil		FC-40		No oil		FC-40		No oil		FC-40			
	4-Fluorotoluene	D	No oil		FC-40		No oil		FC-40		No oil		FC-40			
	4-Fluorotoluene	E	No oil		FY		No oil		FY		No oil		FY			
	4-Fluorotoluene	F	No oil		FY		No oil		FY		No oil		FY			
	4-Fluorotoluene	G	No oil		MO		No oil		MO		No oil		MO			
	4-Fluorotoluene	H	No oil		MO		No oil		MO		No oil		MO			
			No seed				CBD seed				CBD4 seed					

GW010														
Vial	Standard Method		Volume of Oil = 250 nL											
	Volume of Solvent		100 nL											
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
10	4-Fluorotoluene	A	1	2	2	2	4	4	4	4	3*	2	2	2
	4-Fluorotoluene	B	1	2	2	2	3	4	4	4	3*	4*	2	4*
	4-Fluorotoluene	C	1	2	2	2	3	3	3	3	3*	4*	4*	3*
	4-Fluorotoluene	D	1	2	2	2	3	3	3	3	3*	4*	4*	4*
	4-Fluorotoluene	E	1	1	1	1	3	4	3	3	3*	1	1	1
	4-Fluorotoluene	F	1	1	4	1	3	1	3	4	3	3	4*	4*
	4-Fluorotoluene	G	3	2	2	2	3	4	4	4	3	4*	4*	4*
	4-Fluorotoluene	H	1	2	2	4	3	4	4	4	3*	1	4*	4*

Unit Cells for CBD Form 1 and Form 2 formed via ENaCt with Seeding with CBD, CBD-3 and CBD-4

ENaCt Conditions	Description	a/ Å	b/ Å	c/ Å	α	β	γ	Z	Bravais Lattice
GW_002_H7 DCE, MO	CBD seeded w/ CBD	10.59 (3)	10.61 (3)	17.23 (3)	90°	95.25 (3)°	90°	1	Monoclinic *P*
GW_002_H8 DCE, MO	CBD seeded w/ CBD	10.51 (6)	10.53 (7)	10.09 (11)	90°	95.19 (4)°	90°	1	Monoclinic *P*
GW_002_G12 DCE, MO	CBD seeded w/ CBDV	10.88 (3)	12.81 (3)	13.69 (3)	90°	90°	90°	1	Orthorhombic *P*
GW_002_G12 DCE, MO	CBD seeded w/ CBDV	10.89 (15)	12.83 (17)	13.71 (19)	90°	90°	90°	1	Orthorhombic *P*
GW_010_G11 4-fluorotoluene, MO	CBD seeded w/ CBD4	10.868 (13)	12.812 (14)	13.668 (15)	90°	90°	90°	1	Orthorhombic *P*
GW_010_H11 4-fluorotoluene, MO	CBD seeded w/ CBD4	10.869 (14)	12.796 (17)	13.679 (18)	90°	90°	90°	1	Orthorhombic *P*

ENaCt Experiments: Formation of CBD Form 2 Crystals from DCE/MO seeded with CBD-3 for Melting Point Analysis

In order to grow CBD Form 2 crystals for melting point experiment, a stock solution of CBD in DCE was prepared (50 mg of CBD in 96 µL DCE, 521 mg mL^{-1}). Seed crystals of CBD-3 (CBDV) were prepared starting from classically recrystallized material and were crushed using a spatula to provide a stock of seed crystals. Seeding of ENaCt plates was completed via use of a Hampton micro-tool. This was used to pick up a small quantity of crushed CBD-3 seed crystals which were then manually placed in each well. Using a STP Labtech mosquito liquid handling robot, 250 nL of mineral oil was dispensed into each well of a 96 well SWISSCI LCP plate with a 100 micron spacer. Following which, 100 nL of each stock solution containing CBD was dispensed into each of the oil droplets within the wells. A total of 4 plates were used to grow crystals of CBD Form 2 (GW_MP2_P1 to GW_MP2_P4). The plates were sealed with a glass cover slip and were stored in the dark at room temperature and after 1 week, evaluation of crystals growth was carried out visually by cross-polarised optical microscopy. CBD Form 2 crystals were identified by morphology, and wells containing CBD Form 2 were opened and individual crystals transferred onto a glass slide and then packed into a melting point tube. Melting points were then measured using Stuart SMP3 melting point apparatus.

Crystallisation of CBD Form 2 by ENaCt with Seeding with CBD-3 for Melting Point Analysis

GW_MP2_P1													
Vial	Standard Method		Volume of Oil = 250 nL										
	Volume of Solvent		100 nL										
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
MP2	DCE	A	Mineral oil											
	DCE	B												
	DCE	C												
	DCE	D												
	DCE	E												
	DCE	F												
	DCE	G												
	DCE	H												
			CBDV seed											

GW_MP2_P1													
Vial	Standard Method		Volume of Oil = 250 nL										
	Volume of Solvent		100 nL										
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
MP2	DCE	A	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	1	4*
	DCE	B	4*	4*	4*	4*	2	4*	4*	4*	4*	4*	4*	4*
	DCE	C	4*	4*	4*	4*	4*	4*	4*	2	4*	4*	4*	4*
	DCE	D	4*	4*	4*	4*	4*	2	4*	4*	4*	4*	4*	4*
	DCE	E	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	F	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	G	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	2
	DCE	H	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*

GW_MP2_P2													
Vial	Standard Method		Volume of Oil = 250 nL										
	Volume of Solvent		100 nL										
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
MP2	DCE	A	Mineral oil											
	DCE	B												
	DCE	C												
	DCE	D												
	DCE	E												
	DCE	F												
	DCE	G												
	DCE	H												
			CBDV seed											

GW_MP2_P2													
Vial	Standard Method		Volume of Oil = 250 nL										
	Volume of Solvent		100 nL										
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
MP2	DCE	A	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	1	4*
	DCE	B	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	C	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	2
	DCE	D	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	1
	DCE	E	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	F	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	G	4*	4*	4*	4*	4*	2	2	4*	4*	4*	4*	4*
	DCE	H	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*

GW_MP2_P3													
Vial	Standard Method		Volume of Oil = 250 nL										
	Volume of Solvent		100 nL										
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
MP2	DCE	A	Mineral oil											
	DCE	B												
	DCE	C												
	DCE	D												
	DCE	E												
	DCE	F												
	DCE	G												
	DCE	H												
			CBDV seed											

GW_MP2_P3													
Vial	Standard Method		Volume of Oil = 250 nL										
	Volume of Solvent		100 nL										
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
MP2	DCE	A	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	B	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	C	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	D	2	4*	4*	4*	2	4*	4*	4*	4*	1	4*	4*
	DCE	E	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	F	4*	4*	4*	4*	4*	4*	4*	4*	4*	1	4*	4*
	DCE	G	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	1	4*
	DCE	H	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*

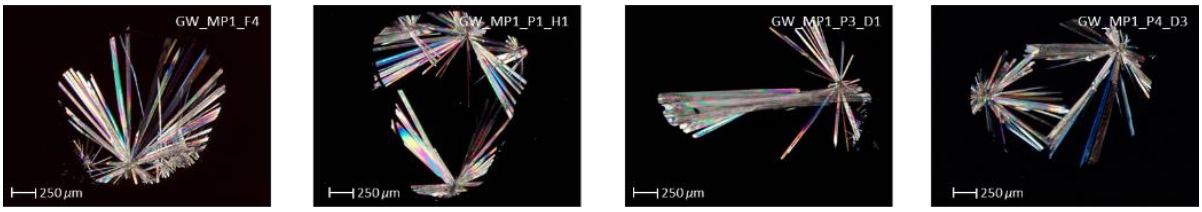
GW_MP2_P4													
Vial	Standard Method		Volume of Oil = 250 nL										
	Volume of Solvent		100 nL										
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
MP2	DCE	A	Mineral oil											
	DCE	B												
	DCE	C												
	DCE	D												
	DCE	E												
	DCE	F												
	DCE	G												
	DCE	H												
			CBDV seed											

GW_MP2_P4													
Vial	Standard Method		Volume of Oil = 250 nL										
	Volume of Solvent		100 nL										
	Solvents		1	2	3	4	5	6	7	8	9	10	11	12
MP2	DCE	A	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	B	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	C	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	D	4*	4*	4*	4*	4*	2	4*	4*	4*	4*	1	2
	DCE	E	4*	4*	4*	4*	4*	1	4*	4*	4*	4*	4*	1
	DCE	F	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*	4*
	DCE	G	4*	4*	4*	4*	4*	2	2	4*	4*	4*	4*	4*
	DCE	H	4*	4*	4*	4*	4*	2	4*	4*	4*	4*	4*	4*

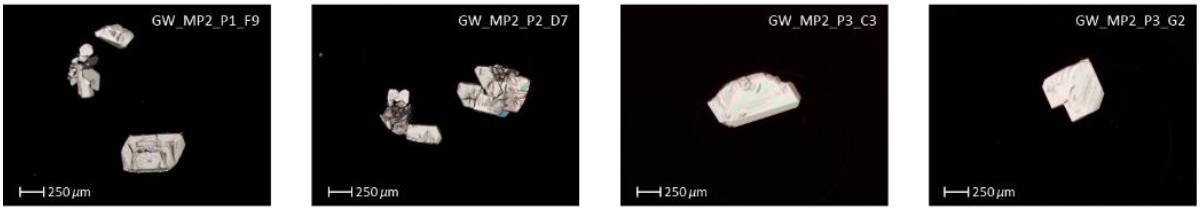
Cross-Polarised Microscopy Images of CBD Crystal

Comparison of CBD Form 1 and Form 2 Crystals Grown via ENaCt with CBD or CBD-3 Seeding

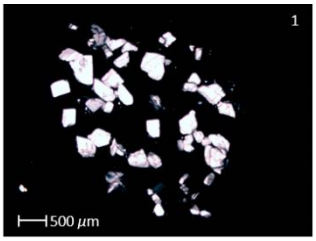
CBD crystals grown with CBD seeds in mineral oil



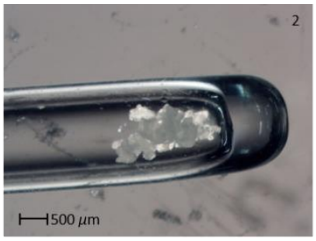
CBD crystals grown with CBDV seeds in mineral oil



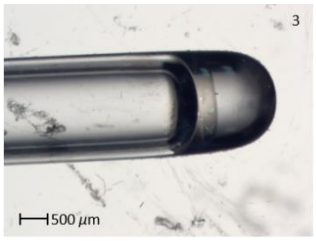
CBD Form 2 Crystals Grown via ENaCt with CBD-3 Seeding for Melting Point Measurements



CBD Form 2 crystals retrieved from plates



CBD Form 2 crystals in a melting point tube



CBD Form 2 crystals after melting point experiment

Crystal Data and Structure Refinement for Additional Strucutres

CBD Form 1 with CBD Seeding

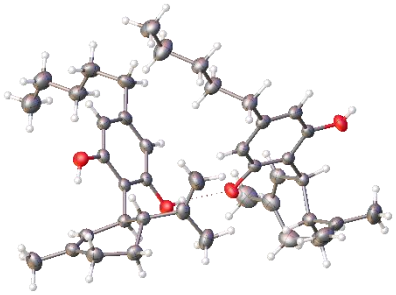


Table 1 Crystal data and structure refinement for CBD_seeded_CBD

Identification code	CBD_seeded_CBD
Empirical formula	$C_{21}H_{30}O_2$
Formula weight	314.45
Temperature/K	150.00
Crystal system	monoclinic
Space group	$P2_1$
a/Å	10.4346(3)
b/Å	10.8763(3)
c/Å	16.7922(5)
α/°	90
β/°	95.4500(10)
γ/°	90
Volume/Å^3	1897.13(9)
Z	4
ρ_{calc}g/cm^3	1.101
μ/mm^{-1}	0.530
F(000)	688.0
Crystal size/mm^3	0.2 × 0.13 × 0.11
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	5.286 to 133.344
Index ranges	-12 ≤ h ≤ 12, -12 ≤ k ≤ 12, -20 ≤ l ≤ 19
Reflections collected	29162
Independent reflections	6688 [R_{int} = 0.0199, R_{sigma} = 0.0140]
Data/restraints/parameters	6688/1/437
Goodness-of-fit on F^2	1.059
Final R indexes [I>=2σ (I)]	R_1 = 0.0281, wR_2 = 0.0734
Final R indexes [all data]	R_1 = 0.0284, wR_2 = 0.0737
Largest diff. peak/hole / e Å^{-3}	0.19/-0.13
Flack parameter	0.02(3)

CBD Form 2 with CBD-3 Seeding

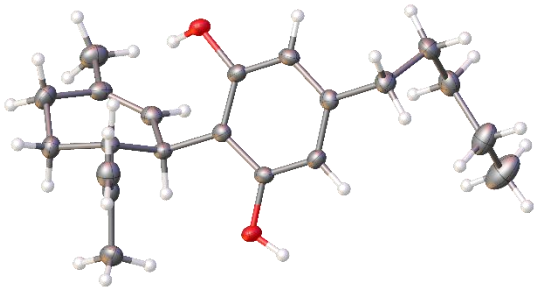


Table 1 Crystal data and structure refinement for CBD_form2_seeded_CBDV.

Identification code	CBD_form2_seeded_CBDV
Empirical formula	$C_{21}H_{30}O_2$
Formula weight	314.45
Temperature/K	150.00
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	10.1971(6)
b/Å	13.0846(8)
c/Å	13.6747(8)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1824.55(19)
Z	4
ρ_{calc}g/cm^3	1.145
μ/mm^{-1}	0.551
F(000)	688.0
Crystal size/mm^3	0.176 × 0.145 × 0.116
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	9.354 to 133.12
Index ranges	-12 ≤ h ≤ 12, -15 ≤ k ≤ 14, -16 ≤ l ≤ 16
Reflections collected	10534
Independent reflections	3188 [R_{int} = 0.0169, R_{sigma} = 0.0145]
Data/restraints/parameters	3188/0/219
Goodness-of-fit on F^2	1.034
Final R indexes [I>=2σ (I)]	R_1 = 0.0250, wR_2 = 0.0644
Final R indexes [all data]	R_1 = 0.0252, wR_2 = 0.0645
Largest diff. peak/hole / e Å^{-3}	0.11/-0.14
Flack parameter	0.06(3)