

Electronic Supplementary Material for

Imaging deposition-dependent supramolecular chiral organisation

by

C. Elizabeth Killalea,^{a,b} Mario Samperi,^{a*} Giuliano Siligardi,^{*c} and David B. Amabilino^{*a}

^a School of Chemistry and GSK Carbon Neutral Laboratories for Sustainable Chemistry,
University of Nottingham, Triumph Road, Nottingham, NG7 2TU, UK.

^b School of Physics and Astronomy, The University of Nottingham, University Park, Nottingham, NG7 2RD

^c Diamond Light Source, Harwell Science and Innovation Campus, Didcot, Oxfordshire OX11 0DE, UK

^{*} Present address: Istituto di Tecnologie Avanzate per l'Energia "Nicola Giordano" - CNR-ITAE, Messina, Italy.

^o New address: Institut de Ciència de Materials de Barcelona (ICMAB-CSIC), Campus Universitari de Cerdanyola, 08193 Spain.

Materials

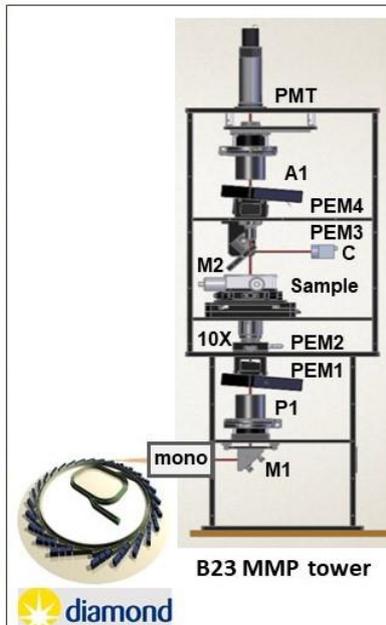
The starting material ethyl 5-oxo-2-(thiophene-2-yl)-4,5-dihydro-1H-pyrrole-3-carboxylate was prepared according to published procedure.¹ All other starting materials were purchased from standard chemical suppliers and used without further purification: Acros (4-cyanophenol 99%, 3,4-dihydro-2H-pyran 99%); Aldrich (cesium carbonate 99%, (S)-(+)-citronellyl bromide 95%, sodium 99.9%); Chromatography purifications were performed using Sigma-Aldrich Silica Gel (pore size 60Å, particle size 40- 63 µm) and thin-layer chromatography (TLC) was carried out on E. Merck silica gel plates, irradiated using UV light (365 nm).

General methods

¹H-NMR and ¹³C-NMR spectra were recorded on a Bruker Ascend 400 (400MHz) nuclear magnetic resonance spectrometer. FTIR spectra were recorded on a Bruker Alpha Platinum ATR. Solution circular dichroism spectra were recorded on an Applied Photophysics Chirascan plus spectrometer.

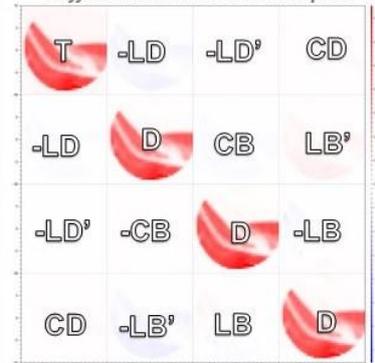
Films of **1** prepared by drop casting a chloroform solution (2 µL 1.7 mM and 2 µL 34 mM) onto a substrate heated to 90 °C, and repeated 10 times per sample to increase the film thickness and spot size. Spun cast films were deposited onto a substrate at room temperature (40 µL, 34 mM, 550 rpm, 30 seconds) and dried by further spinning (3000 rpm, 30 seconds). For CD measurements, the films (prepared using a POLOS spin150i spin coater) were cast onto quartz for spectroscopy, and for Atomic Force Microscopy (AFM) they were cast onto freshly exfoliated mica. AFM was performed with a Bruker FastScan Bio Icon. Height and adhesion data were collected in Tapping Mode using a NuNano Scout 70 type tip with a cantilever spring constant of 2 N/m and a resonant frequency of approximately 70 kHz. The film thickness estimated from the absorption of the films, using the extinction coefficient of the 280 nm band (6500 M⁻¹cm⁻¹) in the aggregates, which gives values of approximately 600 nm for the spun coated film and 250-1600 nm for the drop coated film.

UVi and CDi measurements. UVi and CDi experiments of thin films were recorded using Module B spectrophotometer at B23 beamline for Synchrotron Radiation CD (SRCS) of Diamond Light Source (see photograph and illustration below). Module B employs an Olis DSM20 Monochromator and Photomultiplier tube detector. The beam light was positioned in a vertical measurement chamber using a motorized XY stage and temperature variation was achieved with a Linkam hot stage. UV and CD spectra were recorded simultaneously in the range of 250 to 650 nm with 100 increments (which is equal to 4nm steps) over this range.

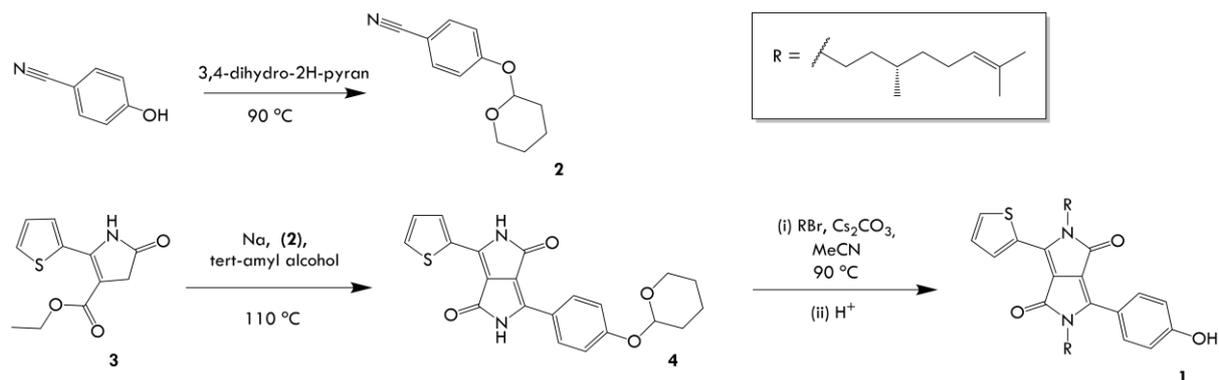


- CD** = Circular Dichroism
- CB** = Circular Birefringence
- LD** = Linear Dichroism
- LD'** = 45° Linear Dichroism
- LB** = Linear Birefringence
- LB'** = 45° Linear Birefringence
- T** = Transmittance
- D** = Degree of Depolarization

Differential Mueller Matrix plot.

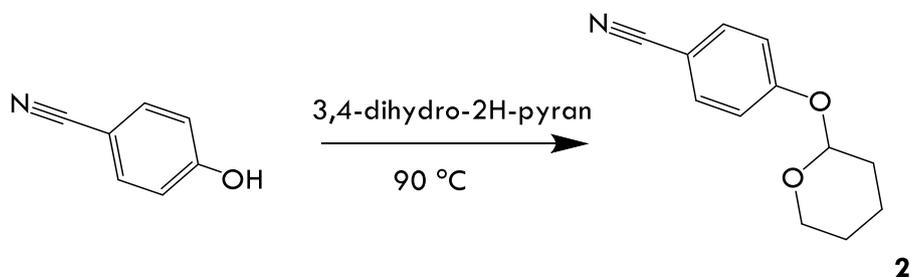


Overall synthetic route:



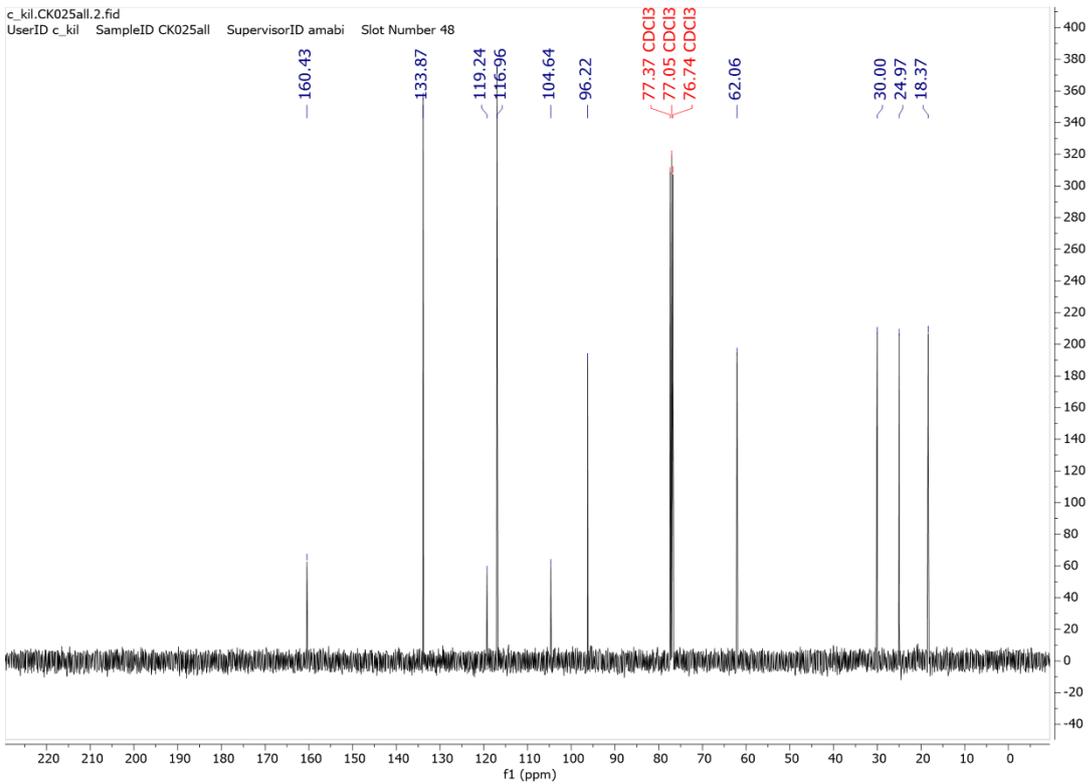
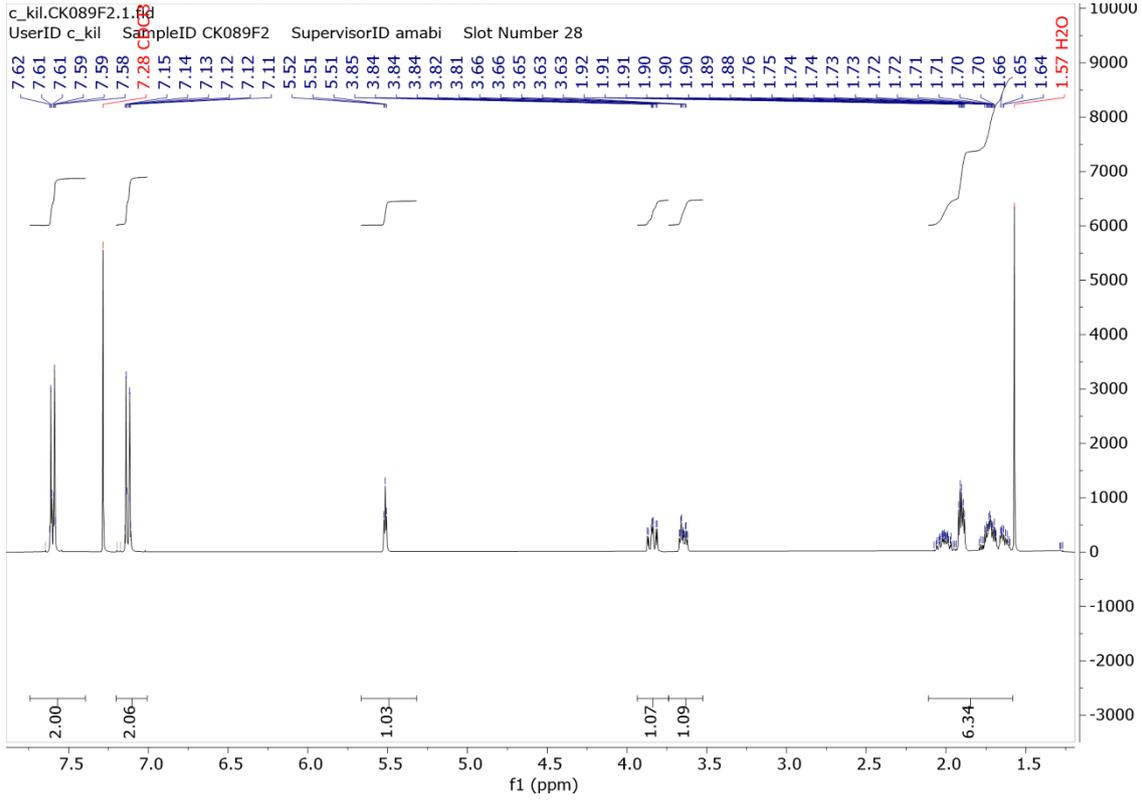
Scheme S1: The convergent synthesis of **1**.

Synthetic procedures and characterization

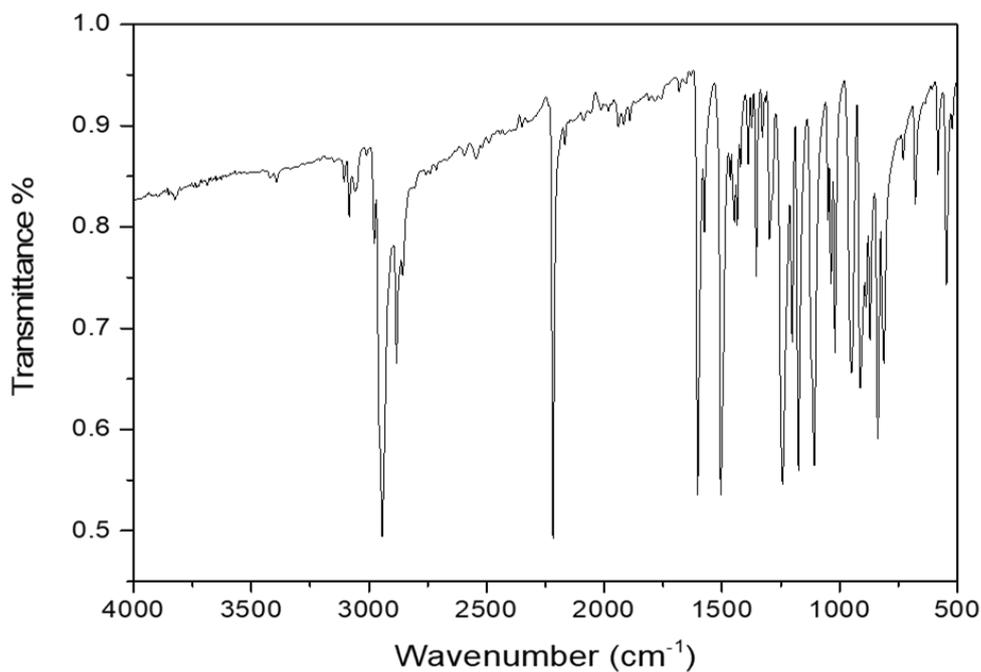


4-((Tetrahydro-2H-pyran-2-yl)oxy)benzonitrile (2) 4-cyanophenol (11.1 g, 92.9 mmol) was added to 3,4 dihyrdopyran (45 mL, 493 mmol). The reaction mixture was stirred at 85 °C for 96 h. Excess 3,4 dihyrdopyran was removed under reduced pressure to give white crystals coated in a viscous yellow oil. The product was recrystallized from a water / ethanol solution (50:50) to give white crystals which were then filtered and washed with water and cold methanol to give the desired product (8.90 g, 43.8 mmol, 47%). lit mp: 68.5-70 °C;² mp 70-72 °C ¹H NMR (400 MHz, CDCl₃) δ 7.59 (d, *J* = 8.9, 2H), 7.11 (d, *J* = 8.9, 2H), 5.51 (t, *J* = 3.1 Hz, 1H), 3.84 (ddd, *J* = 11.4, 9.8, 3.1 Hz, 1H), 3.64 (dtd, *J* = 11.4, 4.1, 1.5 Hz, 1H), 2.11 – 1.54 (m, 6H) ppm; ¹³C NMR (101 MHz, CDCl₃) δ 160.4, 133.8, 119.2, 116.9, 104.6, 96.2, 62.0, 29.9, 24.9, 18.3 ppm; ν_{\max} (ATR-IR) 2943 (CH stretch), 2283 (CH stretch), 2218 (CN stretch), 1603, 1504, 1243, 1175, 1107, 1037, 1020, 951, 911, 870, 837, 812, 545; , *m/z*, calc. 201.08, found MS-ESI [M+Na] 226.08 (100%).

NMR Spectra for 4-((Tetrahydro-2H-pyran-2-yl)oxy)benzointrile



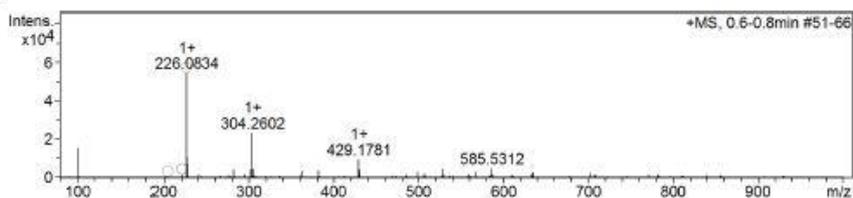
IR Spectrum for 4-((Tetrahydro-2H-pyran-2-yl)oxy)benzotrile



Mass Spectrum for 4-((Tetrahydro-2H-pyran-2-yl)oxy)benzotrile

Analysis Name: c_kil_CNPhOPr_584070_40_01_18833.d Acquisition Date: 4/3/2019 4:17:34 PM
 Ionisation Mode: ESI Positive Instrument: Bruker MicroTOF

+MS, 0.6-0.8min #51-66



| # | m/z | I % |
|----|----------|-------|
| 1 | 79.0210 | 6.6 |
| 2 | 101.0030 | 28.5 |
| 3 | 226.0834 | 100.0 |
| 4 | 226.9510 | 19.8 |
| 5 | 227.0865 | 13.3 |
| 6 | 282.2782 | 7.5 |
| 7 | 302.2446 | 7.9 |
| 8 | 304.0972 | 14.1 |
| 9 | 304.2602 | 42.8 |
| 10 | 305.2636 | 8.7 |
| 11 | 362.9257 | 6.6 |
| 12 | 382.2740 | 7.4 |
| 13 | 429.1781 | 17.5 |
| 14 | 430.1815 | 4.7 |
| 15 | 430.9127 | 8.2 |
| 16 | 498.9000 | 5.7 |
| 17 | 528.5101 | 8.2 |
| 18 | 566.8878 | 5.9 |
| 19 | 585.5312 | 9.2 |
| 20 | 634.8744 | 4.8 |

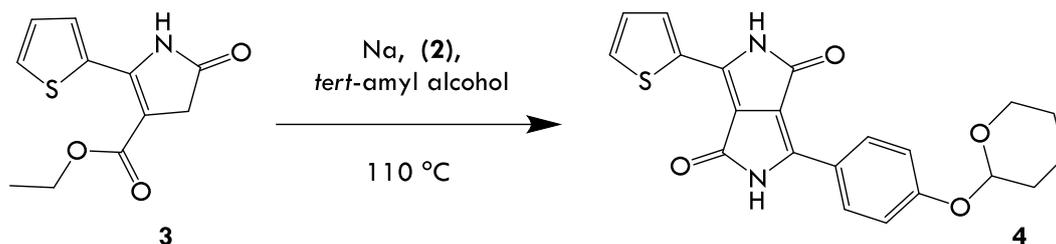
Generate Molecular Formula Parameters

| Charge | Tolerance | sigma limit | H/C Ratio | Electron Conf. | Nitrogen Rule | Chrom.BackGround | Calibration |
|--------|-----------|-------------|-----------|----------------|---------------|------------------|-------------|
| +1 | 6 ppm | 0.08 | 3 - 0 | both | false | false | TRUE |

Expected Formula: C12 H13 N1 O2 Adduct(s): H, Na, NH4, C3H5N2, radical

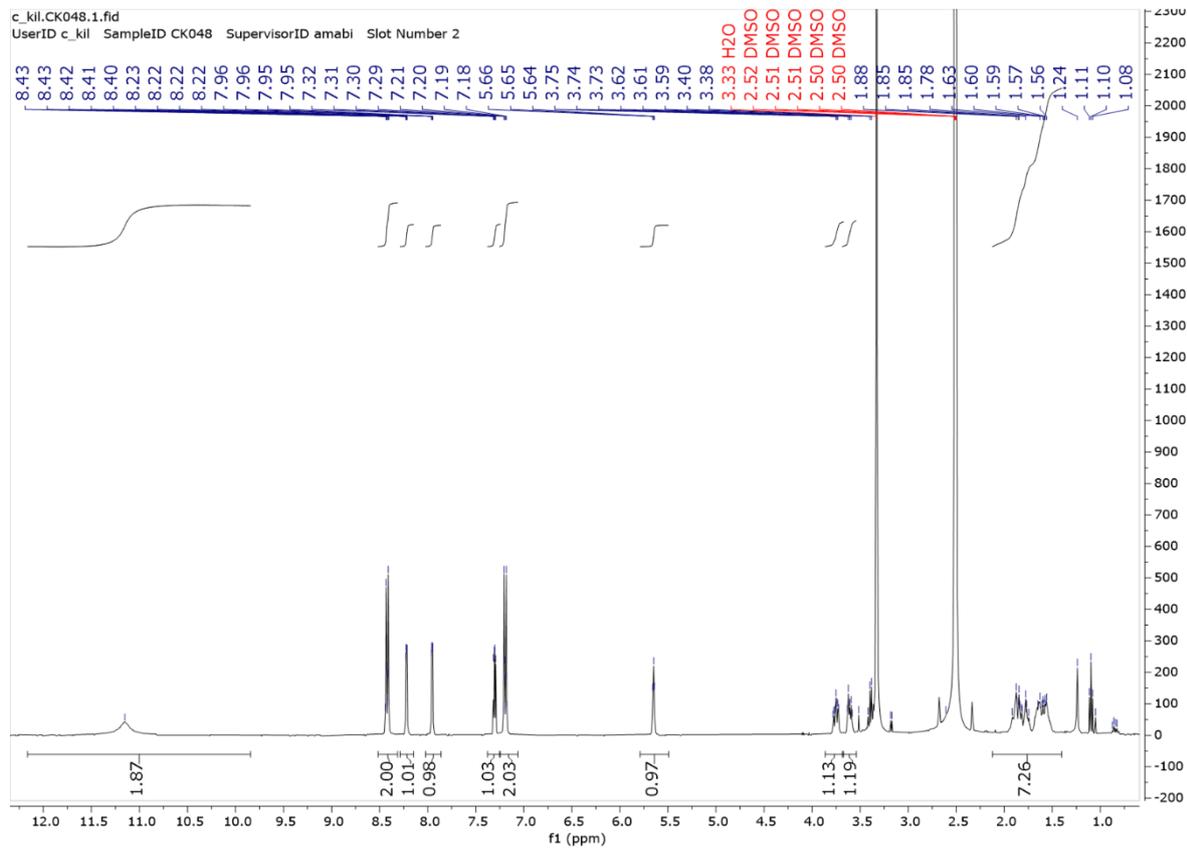
| # | meas. m/z | theo. m/z | [Err][ppm] | Sigma | Formula | Adduct | Adduct Mass |
|---|-----------|-----------|------------|--------|-------------|--------|-------------|
| 1 | 226.0834 | 226.0838 | 2.10 | 0.0018 | C12H13NNaO2 | M+Na | 22.9898 |

Note: Sigma fits < 0.05 indicates high probability of correct MF

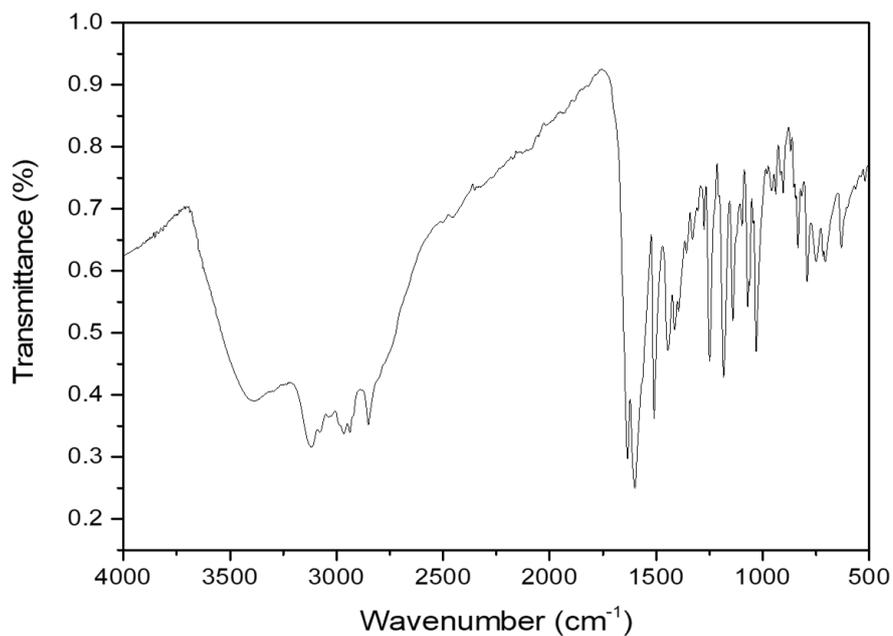


3-((Tetrahydro-2H-pyran-2-yl)oxy)phenyl-6-(thiophen-2-yl)-2,5-dihydropyrrole[3,4-c]pyrrole-1,4-dione (4) In a flame dried flask, sodium (0.41 g, 17.84 mmol) was stirred in tert-amyl alcohol (40 mL) at 100 °C for 2 h until dissolved. The reaction mixture was cooled to room temperature, then ethyl 5-oxo-2-(thiophene-2-yl)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3**) (3.00 g, 12.6 mmol) and 4-((tetrahydro-2H-pyran-2-yl)oxy)benzotrile (**3**) (2.83 g, 14.0 mmol) were added. The reaction mixture was stirred at 100 °C for 7 h. The reaction mixture was poured into water (ca. 100 mL) and precipitation occurred. The solid was filtered and washed with water, methanol and diethyl ether to produce the desired product as a deep red solid (2.07 g, 5.23 mmol, 42 %). mp > 300 °C ^1H NMR (400 MHz, DMSO) δ ^1H NMR (400 MHz, DMSO- d_6) δ 11.25 (s, 1H), 11.16 (s, 1H), 8.53 – 8.35 m, 2H), 8.22 (dd, J = 3.8, 1.2 Hz, 1H), 7.95 (dd, J = 5.0, 1.2 Hz, 1H), 7.30 (dd, J = 5.0, 3.8 Hz, 1H), 7.19 (m, 2H), 5.72 – 5.56 (m, 1H), 3.86 – 3.47 (m, 2H), 2.11 – 1.34 (m, 6H); ν_{max} (ATR-IR) 3108 (NH stretch), 2960 (CH stretch), 2840 (CH stretch), 1632 (CO stretch), 1596, 1503, 1432, 1403, 1241, 1176, 1132, 1063, 1024, 946, 899, 830, 784, 737, 711, 621, 514, 478, 425; m/z , calc. 394.10, found MS-MALDI-TOF [M- H] 585.31. Elemental analysis: calcd. for $\text{C}_{21}\text{H}_{18}\text{N}_2\text{O}_4\text{S}$: C, 63.95; H, 4.60; N, 7.10%; found: C, 63.58; H, 4.97; N, 6.82%

¹H NMR Spectrum for 3-(-(tetrahydro-2H-pyran-2-yl)oxy)phenyl-6-(thiophen-2-yl)-2,5-dihydropyrrole[3,4-c]pyrrole-1,4-dione



IR Spectra for 3-(-(tetrahydro-2H-pyran-2-yl)oxy)phenyl-6-(thiophen-2-yl)-2,5-dihydropyrrole[3,4-c]pyrrole-1,4-dione



Mass Spectra for 3-((tetrahydro-2H-pyran-2-yl)oxy)phenyl-6-(thiophen-2-yl)-2,5-dihydropyrrole[3,4-c]pyrrole-1,4-dione



The University of
Nottingham

UNITED KINGDOM · CHINA · MALAYSIA

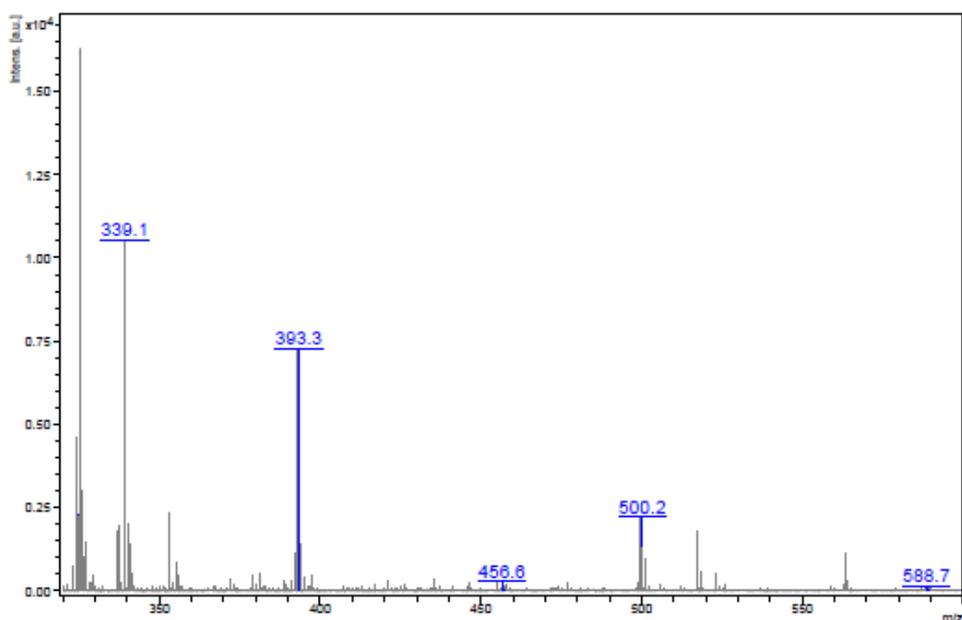
Mass Spectrometry
Analytical Services
School of Chemistry

D:\DATA\c_kill\Core DPP\ThPHOPrDPPNHnegativenarrow\0_J16\1

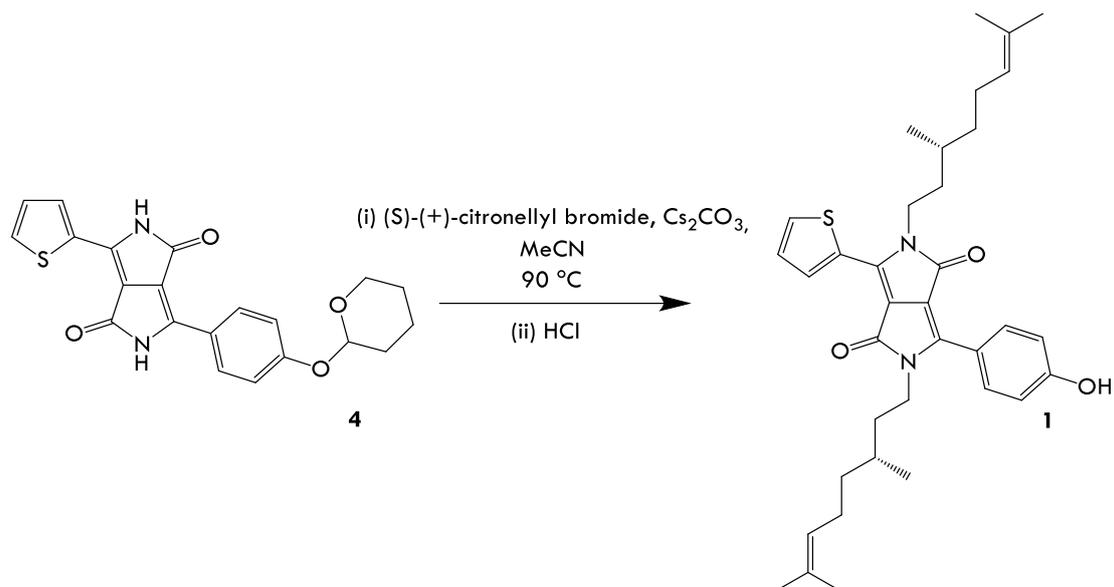
Print date: 5/24/2021 4:27:21 PM

Instrument: MALDI

Sample: ThPHOPrDPPNHnegativenarrow\0_J16\1

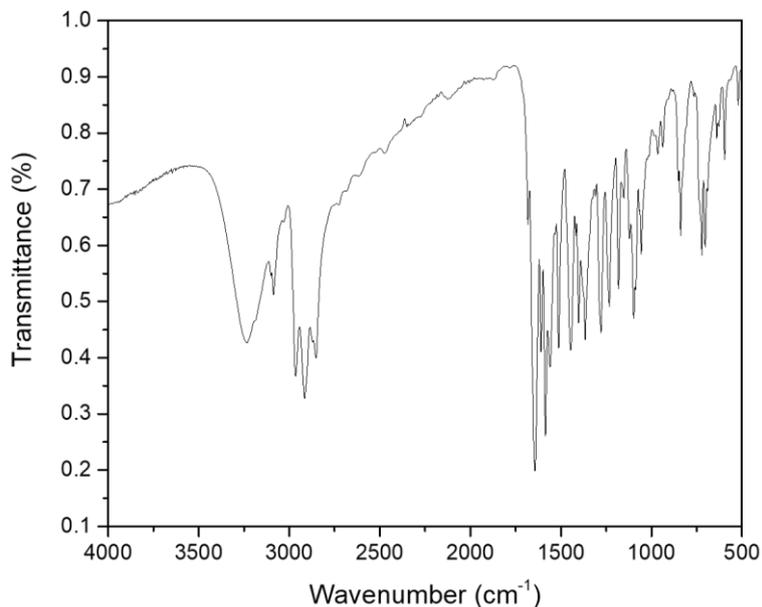


| m/z | Rel. Intens. |
|---------|--------------|
| 324.966 | 20 |
| 339.148 | 100 |
| 393.307 | 69 |
| 456.579 | 2 |
| 457.355 | 2 |
| 500.238 | 13 |
| 588.674 | 1 |
| 589.518 | 1 |

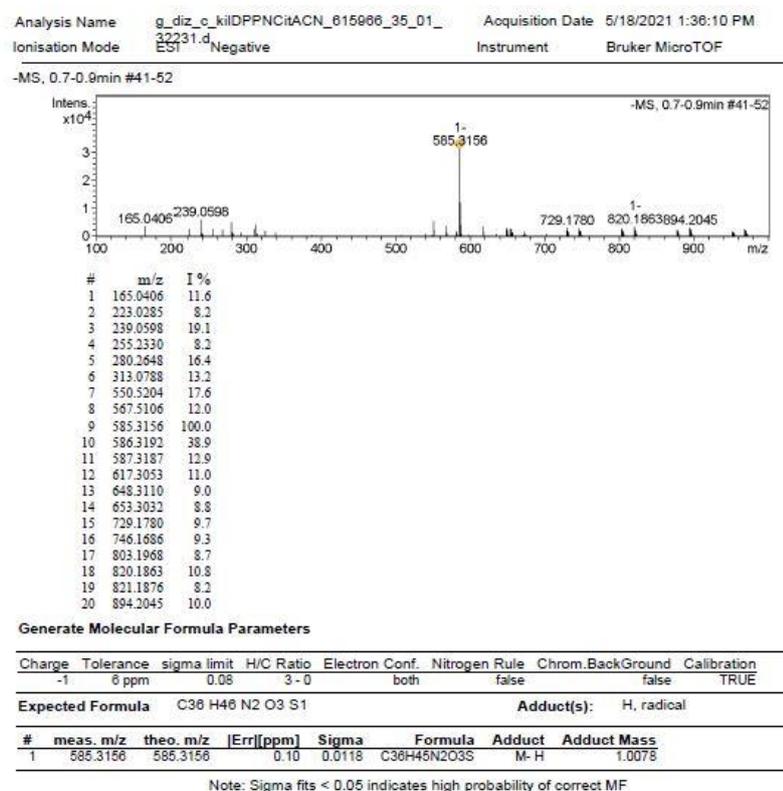


5-((S)-3,7-dimethyloct-6-en-1-yl)-2-((S)-3,7-dimethyloct-6-en-1-yl)-3-(4-hydroxyphenyl)-6-(thiophen-2-yl)-2,5-dihydropyrrolo[3,3-c]pyrrole-1,4-dione (1) 3-(4-((Tetrahydro-2H-pyran-2-yl)oxy)phenyl)-6-(thiophene-2-yl)-2,5-dihydropyrrolo[3,3-c]pyrrole-1,4-dione (**4**) (1.00 g, 2.51 mmol) and caesium carbonate (3.26 g, 10.00 mmol) were stirred at 90 °C in acetonitrile (40 mL) for 15 min. (S)-(+)-citronellyl bromide (1.97 mL, 10.00 mmol) was then added to the reaction mixture, which was stirred at 90 °C for 24 h. The reaction mixture was cooled to room temperature and stirred in 6 M HCl until precipitation occurred. The solid was filtered and washed with water, methanol and diethyl ether. After drying *in vacuo*, the crude product was purified by column chromatography (silica gel) to afford **1** as a red powder (411 mg, 0.70 mmol, 28%). mp 181-184 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.84 (dd, *J* = 4.1, 1.1 Hz, 1H), 7.96 (s, 1H), 7.75 (d, *J* = 8.8 Hz, 2H), 7.66 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.31 ppm (dd, *J* = 5.0/4.1 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 2H), 5.11 (tt, *J* = 7.0, 1.4 Hz, 1H), 5.05 (tt, *J* = 7.0, 1.4 Hz, 1H), 4.09 (m, 2H), 3.86 (m, 2H), 1.61 - 2.10 (m, 13H), 1.11 - 1.55 (m, 13H). 1.04 (d, *J* = 6.4 Hz, 3H), 0.90 ppm (d, *J* = 6.3 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 162.38, 162.29, 160.07, 149.77, 134.83, 131.39, 131.35, 130.88, 130.48, 129.67, 128.60, 124.59, 124.47, 119.43, 116.38, 77.34, 77.22, 77.02, 76.70, 40.88, 40.64, 36.94, 36.77, 36.62, 36.34, 30.91, 30.54, 25.73, 25.71, 25.45, 25.36, 19.40, 19.29, 17.70, 17.67 δ ppm; ν_{\max} (ATR-IR) 3226 (OH stretch), 3174 (CH stretch), 3083 (CH stretch), 2960 (CH stretch), 2908 (CH stretch), 2843 (CH stretch), 1640 (C=O stretch), 1607, 1578, 1555, 1511, 1442, 1397, 1364, 1274, 1229, 1181, 1054, 834, 723, 702, 595 cm⁻¹; *m/z*, calc, 586.32, found MS-ESI [M-H]⁻ 585.31 (100%). Elemental analysis: calcd. for C₂₈H₃₄N₂O₃S: C, 70.26; H, 7.16; N, 5.85%; found: C, 70.89; H, 7.36; N, 6.01 %.

IR Spectrum 5-((S)-3,7-dimethyloct-6-en-1-yl)-2-((S)-3,7-dimethyloct-6-en-1-yl)-3-(4-hydroxyphenol)-6-(thiophen-2-yl)-2,5-dihydropyrrolo[3,3-c]pytrole-1,4-dione



Mass Spectrum 5-((S)-3,7-dimethyloct-6-en-1-yl)-2-((S)-3,7-dimethyloct-6-en-1-yl)-3-(4-hydroxyphenol)-6-(thiophen-2-yl)-2,5-dihydropyrrolo[3,3-c]pytrole-1,4-dione



Supplementary Figures

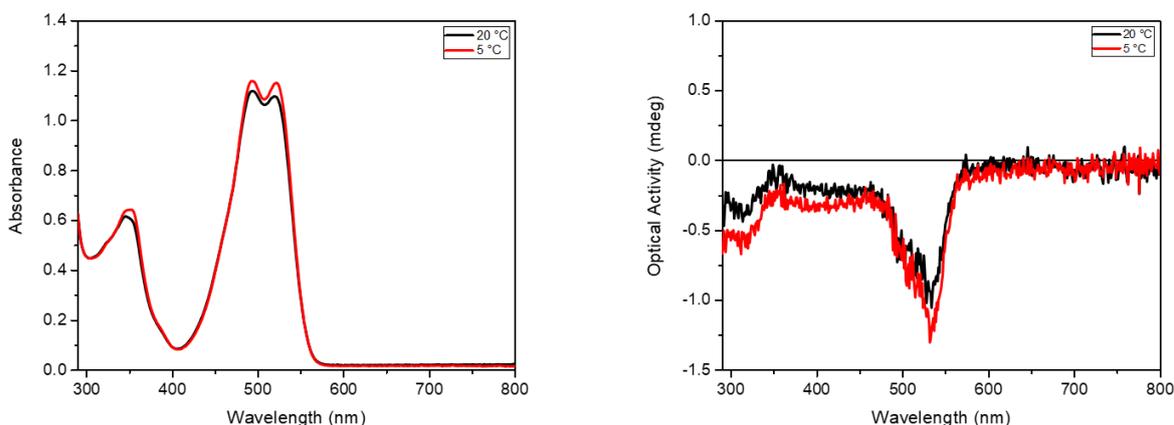


Figure S1: CD spectra (right) and corresponding absorbance spectra (left) of a molecular solution (3.41 mM in a 0.1 mm pathlength quartz cell) of **1** in toluene at 5 (red) and 20 °C (black).

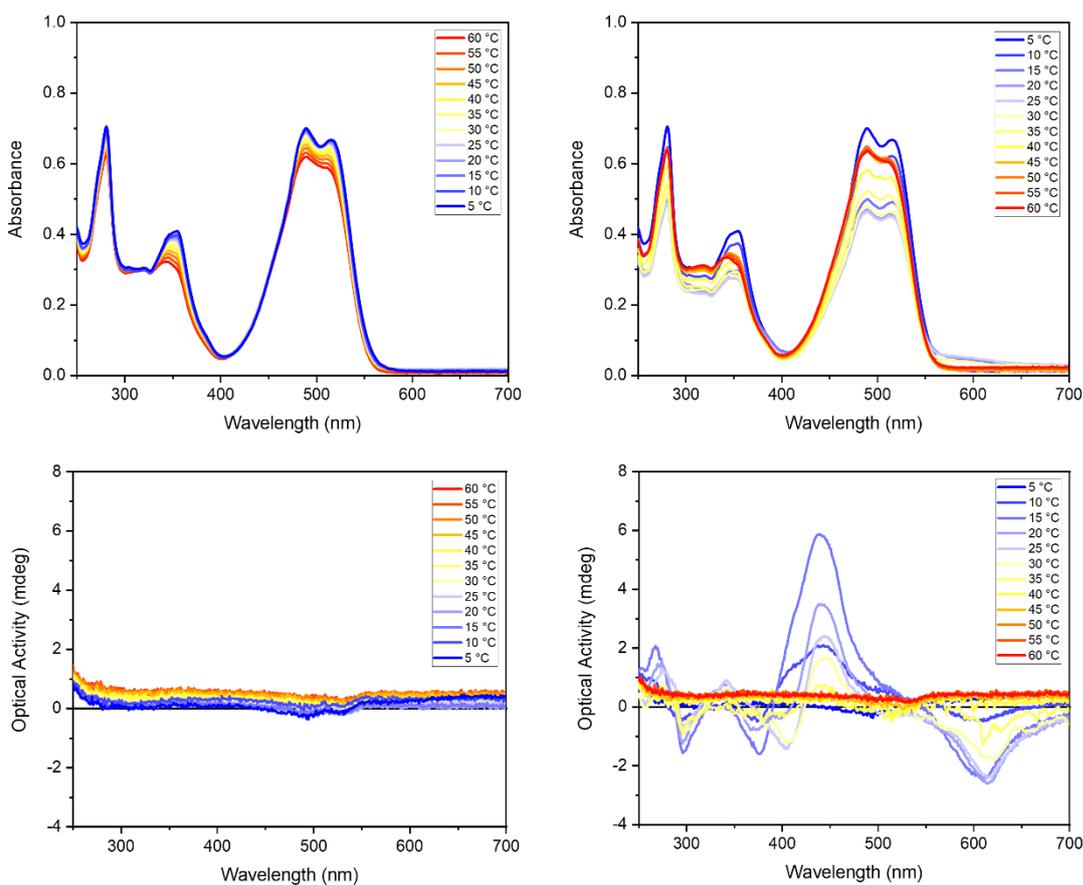


Figure S2: Temperature dependent CD spectra (bottom) and their corresponding absorbance spectra (top) of 0.46 mM solution of **1** in cyclohexane (in a 2 mm pathlength quartz cell). Left: Spectra as solution is cooled from 60 °C to 5 °C. Right: Spectra as solution is reheated from 5 °C to 60 °C.

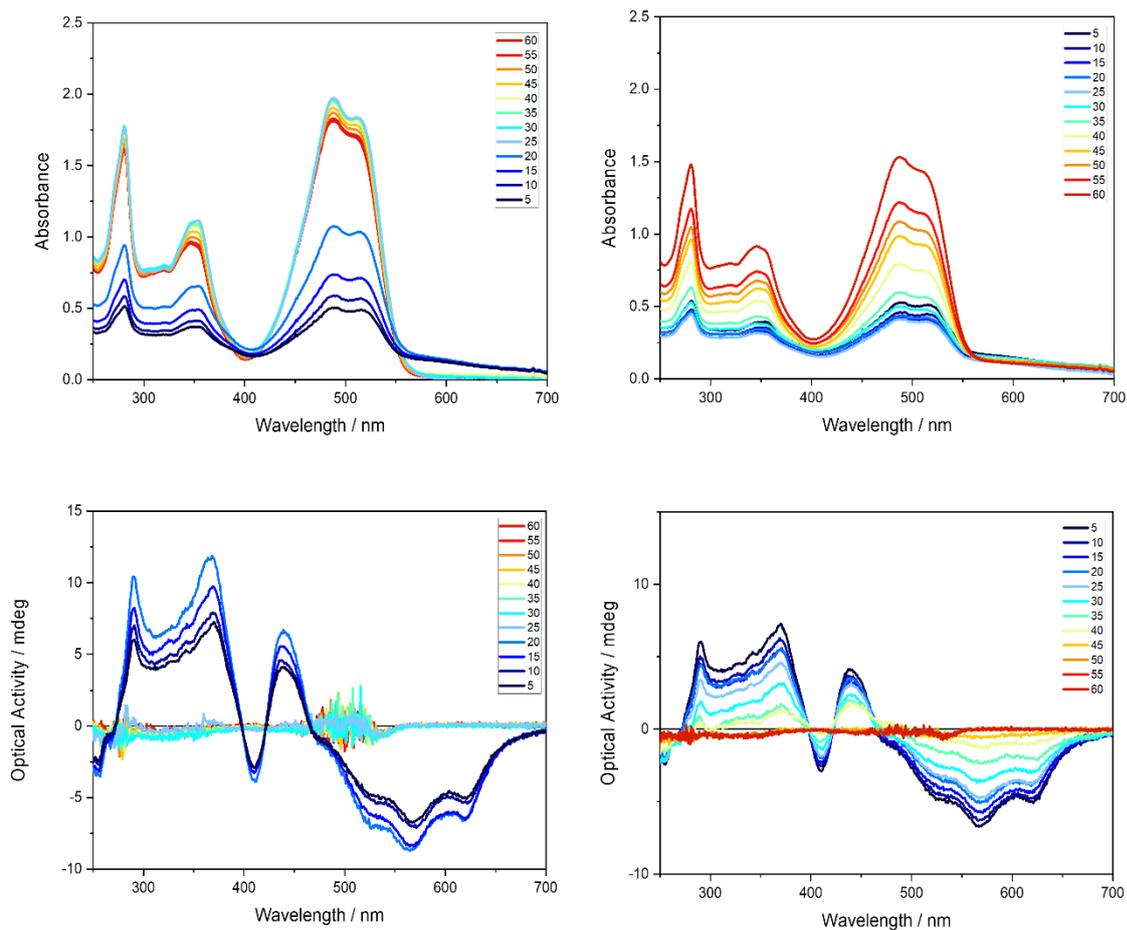


Figure S3: Temperature dependent CD spectra (bottom) and their corresponding absorbance spectra (top) of 0.46 mM solution of **1** in cyclohexane (in a 1 mm pathlength quartz cell). Left: Spectra as solution is cooled from 60 °C to 5 °C. Right: Spectra as solution is reheated from 5 °C to 60 °C.

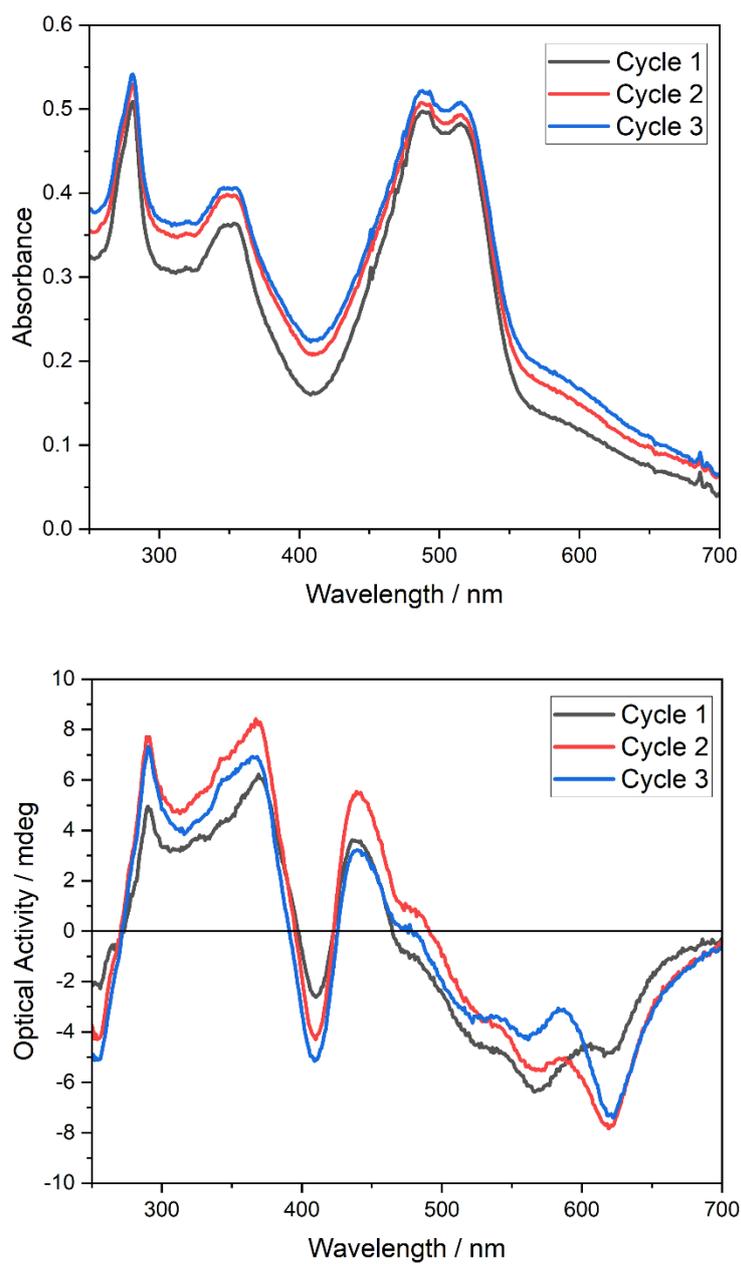


Figure S4: Absorption (top) and optical activity (bottom) of **1** in a 0.46 mM solution of cyclohexane at 5 °C after cooling from 60 degrees on three consecutive cycles.

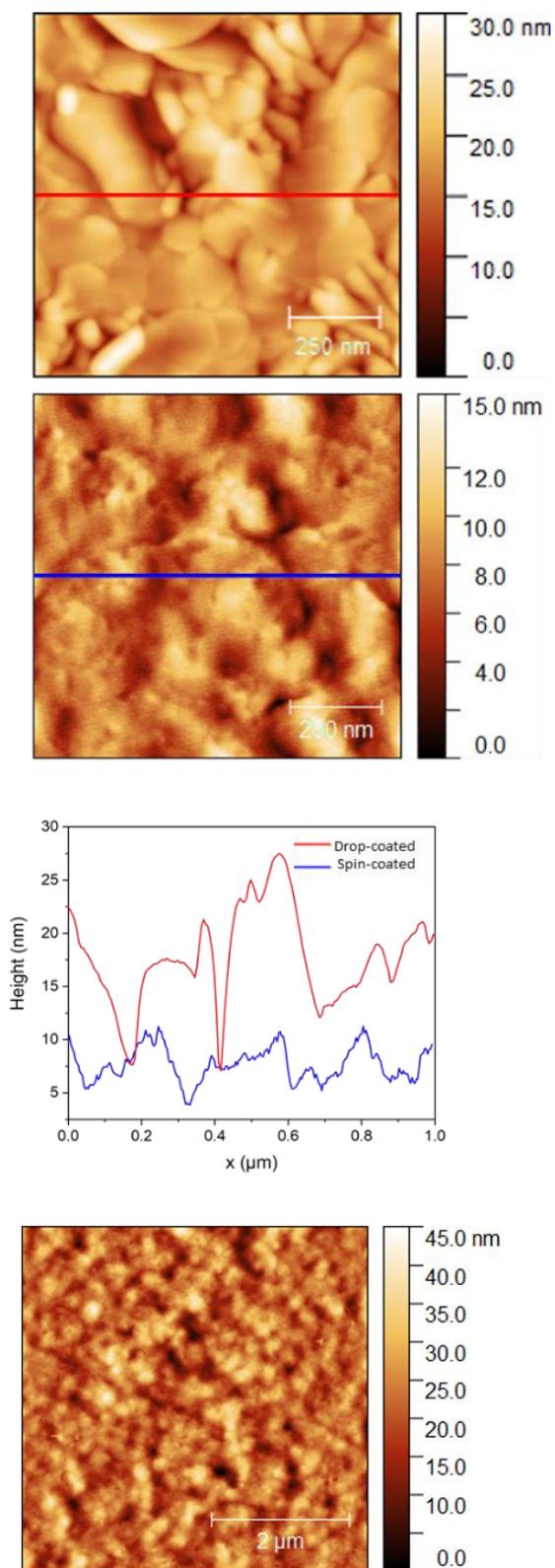


Figure S5: Atomic Force Micrographs of a $1 \mu\text{m}^2$ area of drop-coated (top) and spin-coated (second down) films of **1**. Note the z scales on each micrograph are different from each other. Roughness: drop-coated 2.3 nm; spun-coated: 1.7 nm. Bottom: Topographical Atomic Force Micrograph of a $5 \mu\text{m}^2$ area of a spin coated film of **1**. Roughness: 4.4 nm.

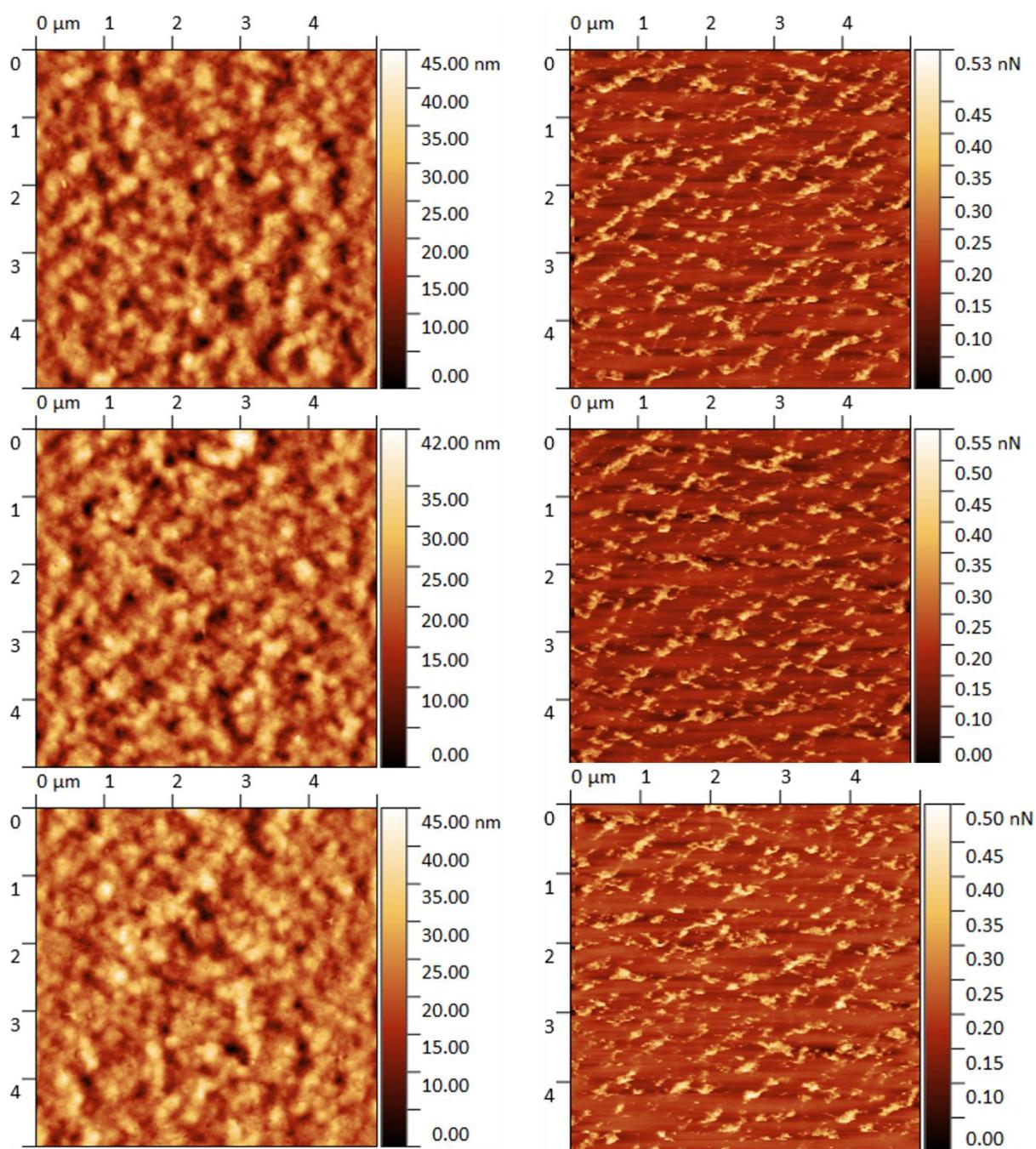


Figure S6: Atomic Force Micrographs of three 5 x 5 μm areas of a spun coated film of ThPhOHDPPN(Cit) showing topography (left) and the corresponding adhesion image (right) of each area. Area 1 (top) roughness: 4.9 nm; Area 2 (middle) roughness: 4.6 nm; Area 3 (bottom) roughness: 4.4 nm.

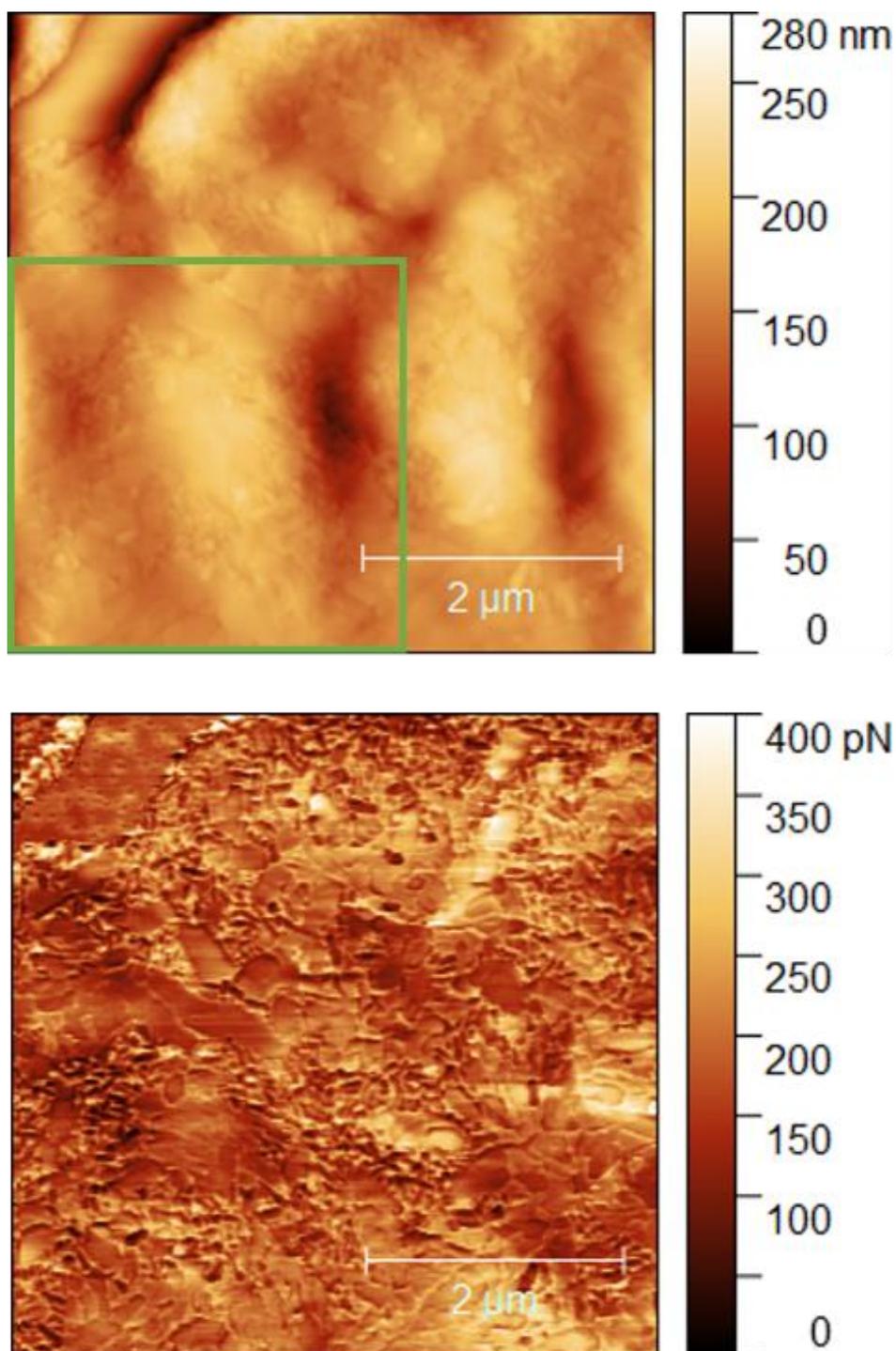


Figure S7: Atomic Force Micrographs of a $5 \mu\text{m}^2$ area of a drop coated film of **1** showing topography (top) and corresponding adhesion image (bottom). Roughness: 23.1 nm, green $3 \times 3 \mu\text{m}$ roughness: 22.6 nm.

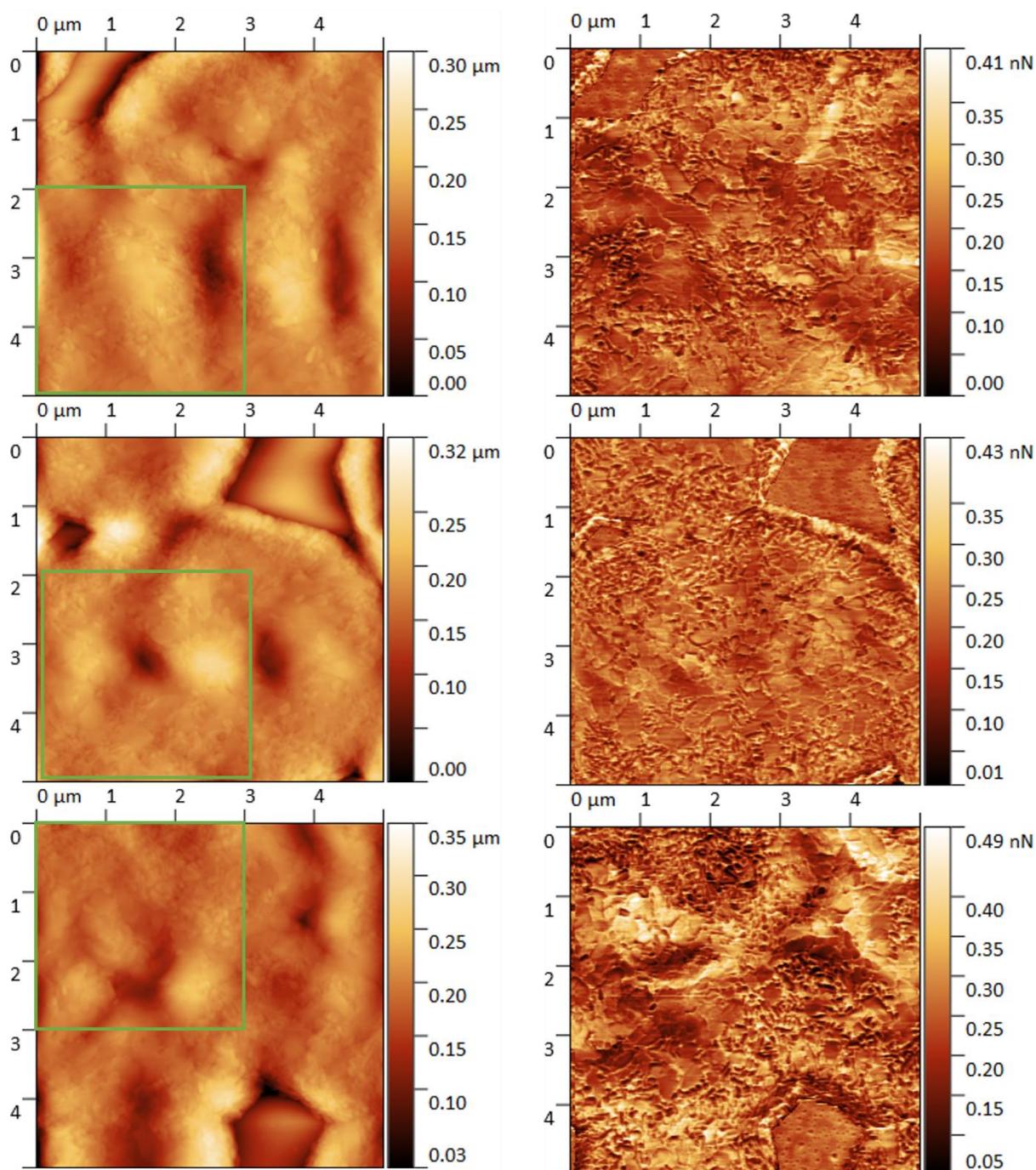


Figure S8: Atomic Force Micrographs of three $5 \times 5 \mu\text{m}$ areas of a drop coated film of **1** showing topography (left) and the corresponding adhesion image (right) of each area. Area 1 (top) $5 \times 5 \mu\text{m}$ roughness: 23.1 nm, green $3 \times 3 \mu\text{m}$ roughness: 22.6 nm; Area 2 (middle) $5 \times 5 \mu\text{m}$ roughness: 25.3 nm, green $3 \times 3 \mu\text{m}$ roughness: 20.1 nm; Area 3 (bottom) $5 \times 5 \mu\text{m}$ roughness: 25.6 nm, green $3 \times 3 \mu\text{m}$ roughness: 18.3 nm.

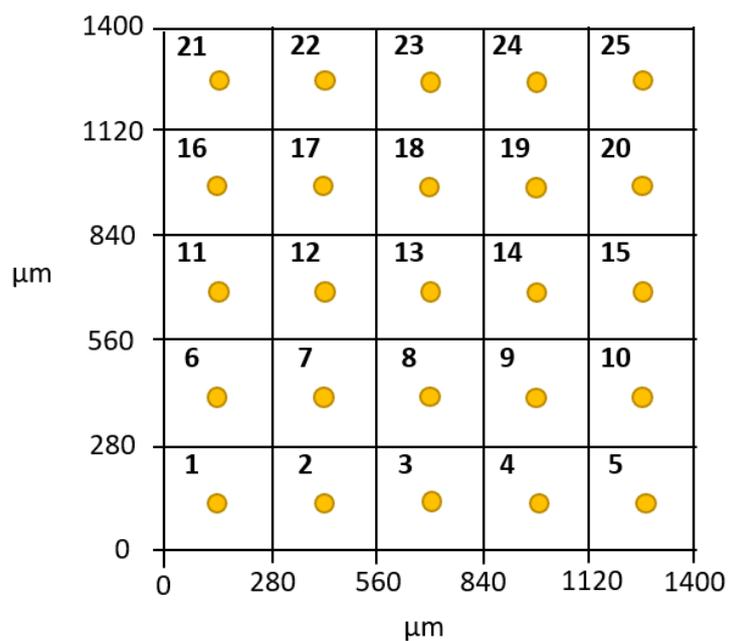


Figure S9: Illustration of 5 x5 grid array used when scanning films of **1**, showing a step size of 280 μm and the area illuminated using the 50 μm beam as yellow dots.

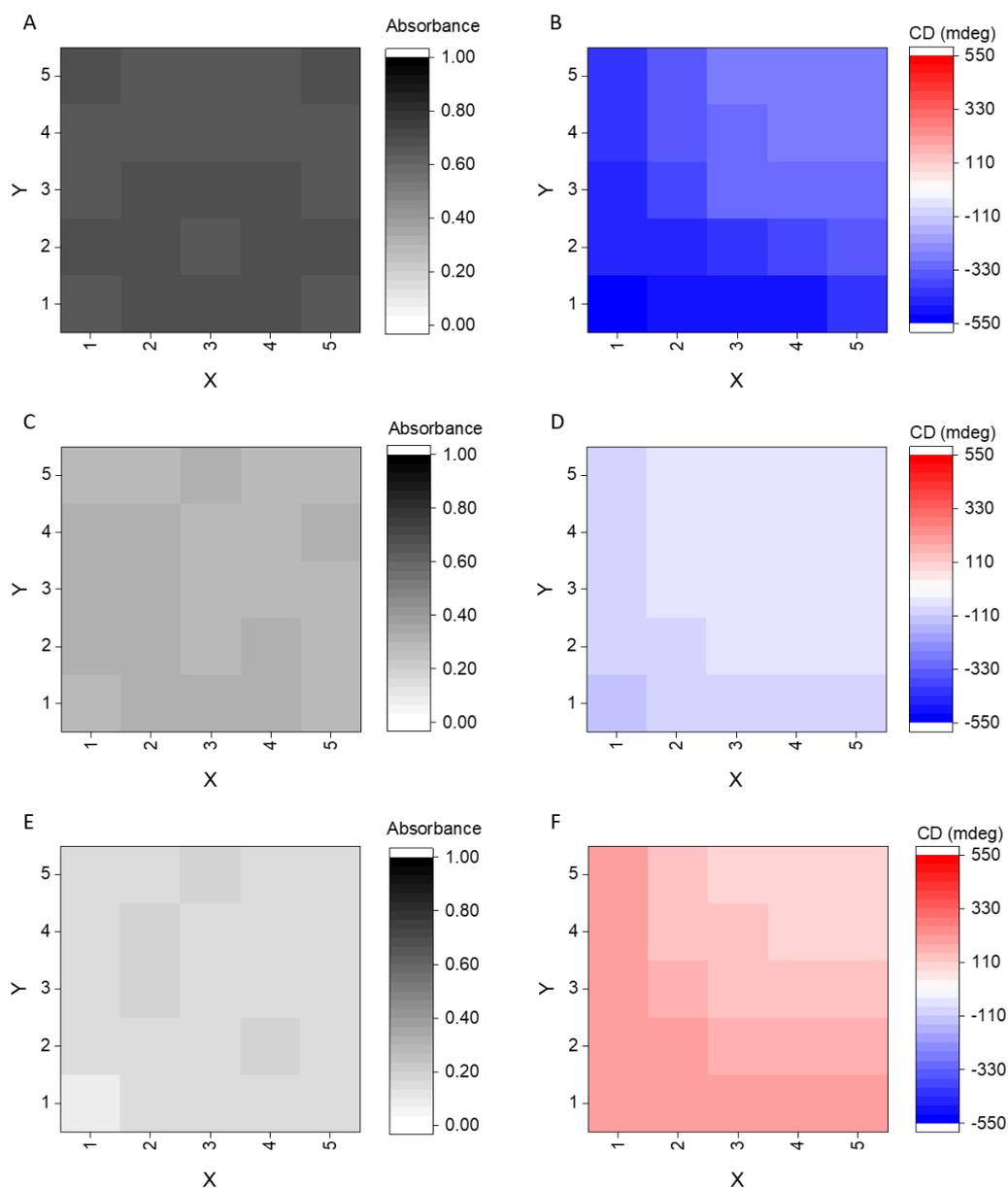


Figure S10: 2D maps of a spin-coated film of **1** at 20 °C before annealing: Absorbance vs X-Y (grey hues) and CD intensity vs X-Y (red and blue hues for positive and negative signals, respectively) for each of the wavelengths that had the most intense optical activity 282 nm (A and B), 350 nm (C and D) and 382 nm (E and F); each square represents a 280 μm^2 area of which a 50 μm^2 area in the centre was illuminated.

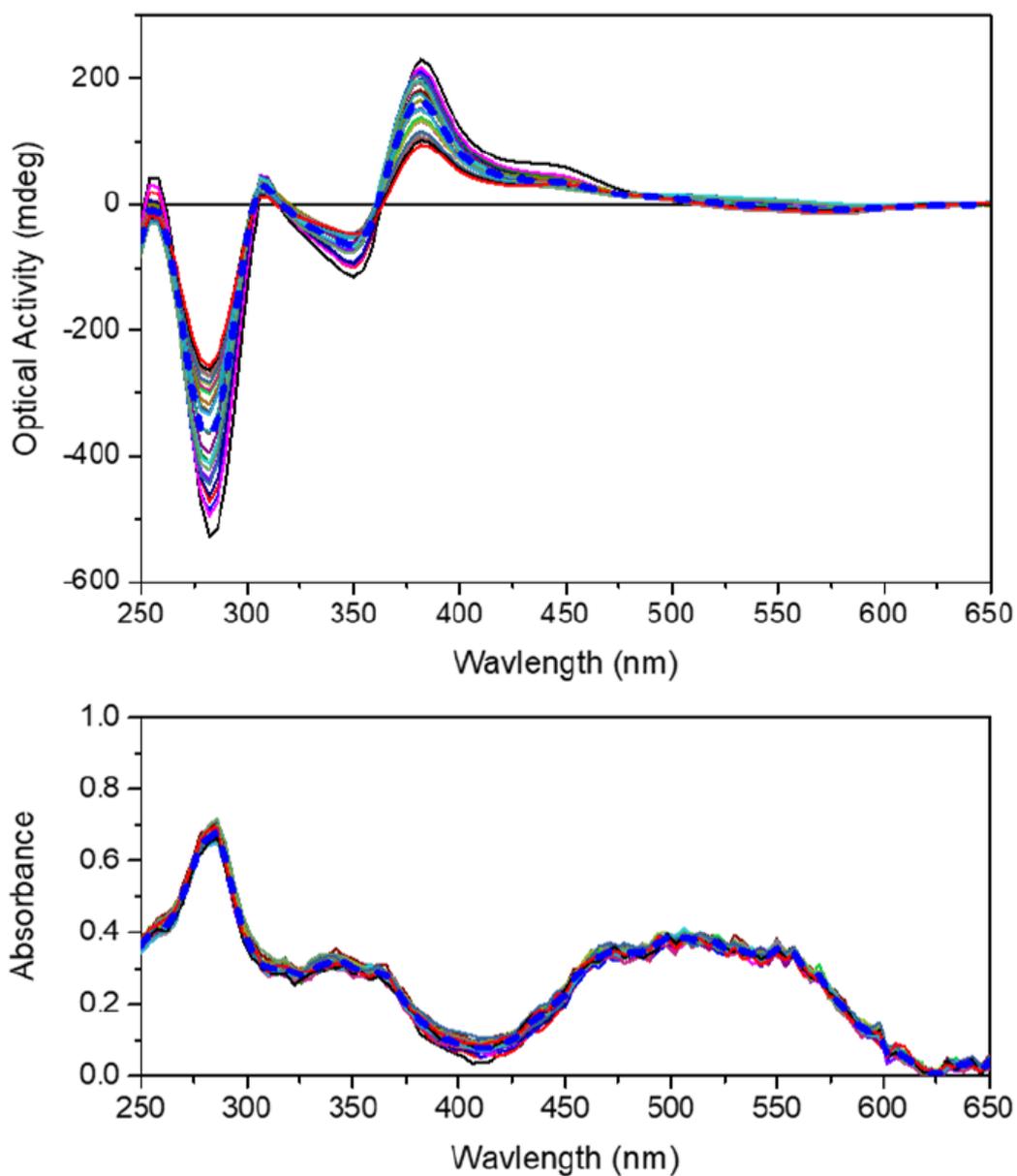


Figure S11: Absorbance spectra (top) and Optical Activity spectra (bottom) of the 25 scans that make up the 5 x5 grid array (Figure S10) and their averages (blue dotted lines) at 20 °C of a spin-coated film of **1**.

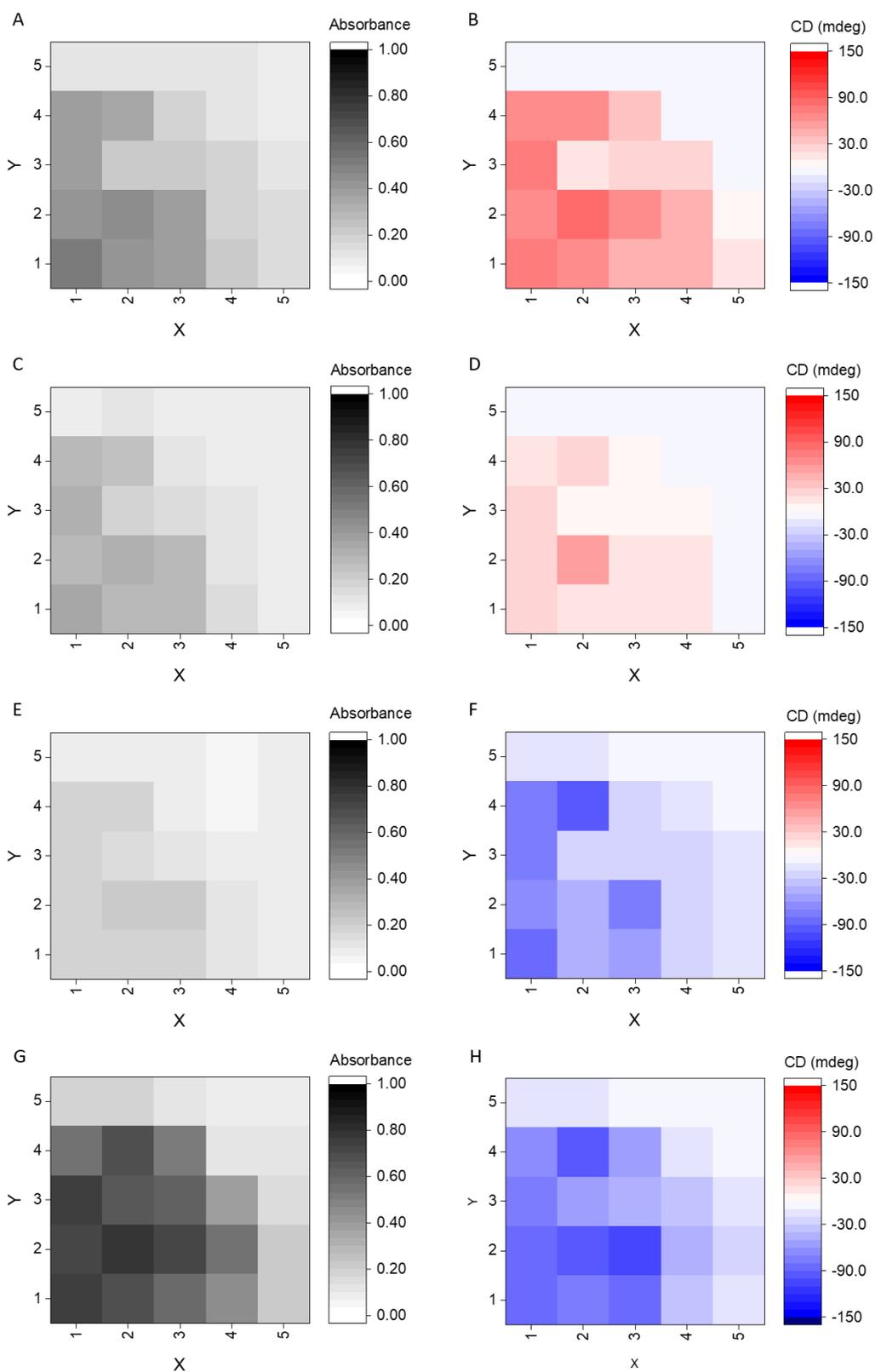


Figure S12: 2D maps of a drop-coated film of **1** at 20 °C before annealing Absorbance vs X-Y (grey hues) and CD intensity vs X-Y (red and blue hues) for each of the wavelengths that had the most intense optical activity 274 nm (A and B), 334 nm (C and D), 390 nm (E and F) and 534 nm (G and H); each square represents a 280 μm^2 area of which a 50 μm^2 area in the centre was illuminated.

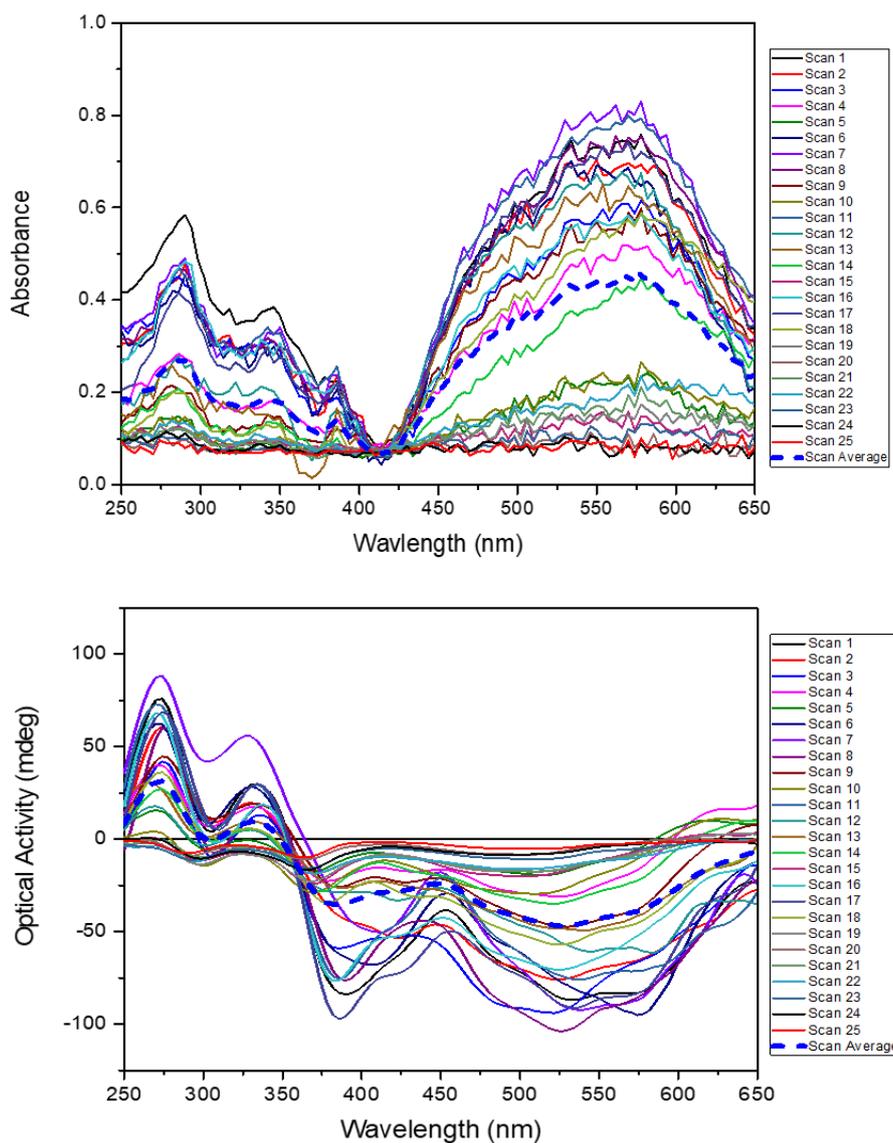


Figure S13: Absorbance spectra (top) and Optical Activity spectra (bottom) of the 25 scans that make up the 5 x5 grid array (Figure S12) and their averages (blue dotted lines) at 20 °C of a drop-coated film of **1**.

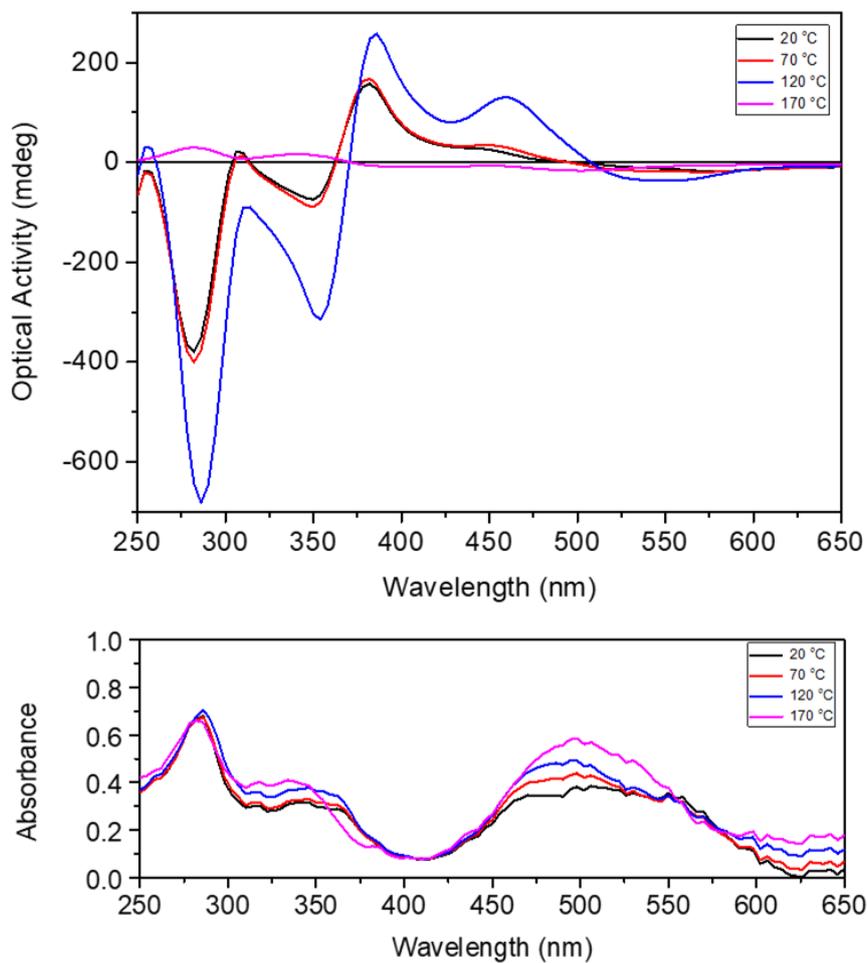


Figure S14a: Averages of 25 absorbance spectra (top) and corresponding averaged of 25 Optical activity spectra (bottom) at a variety of temperatures of a spin-coated film of **1**.

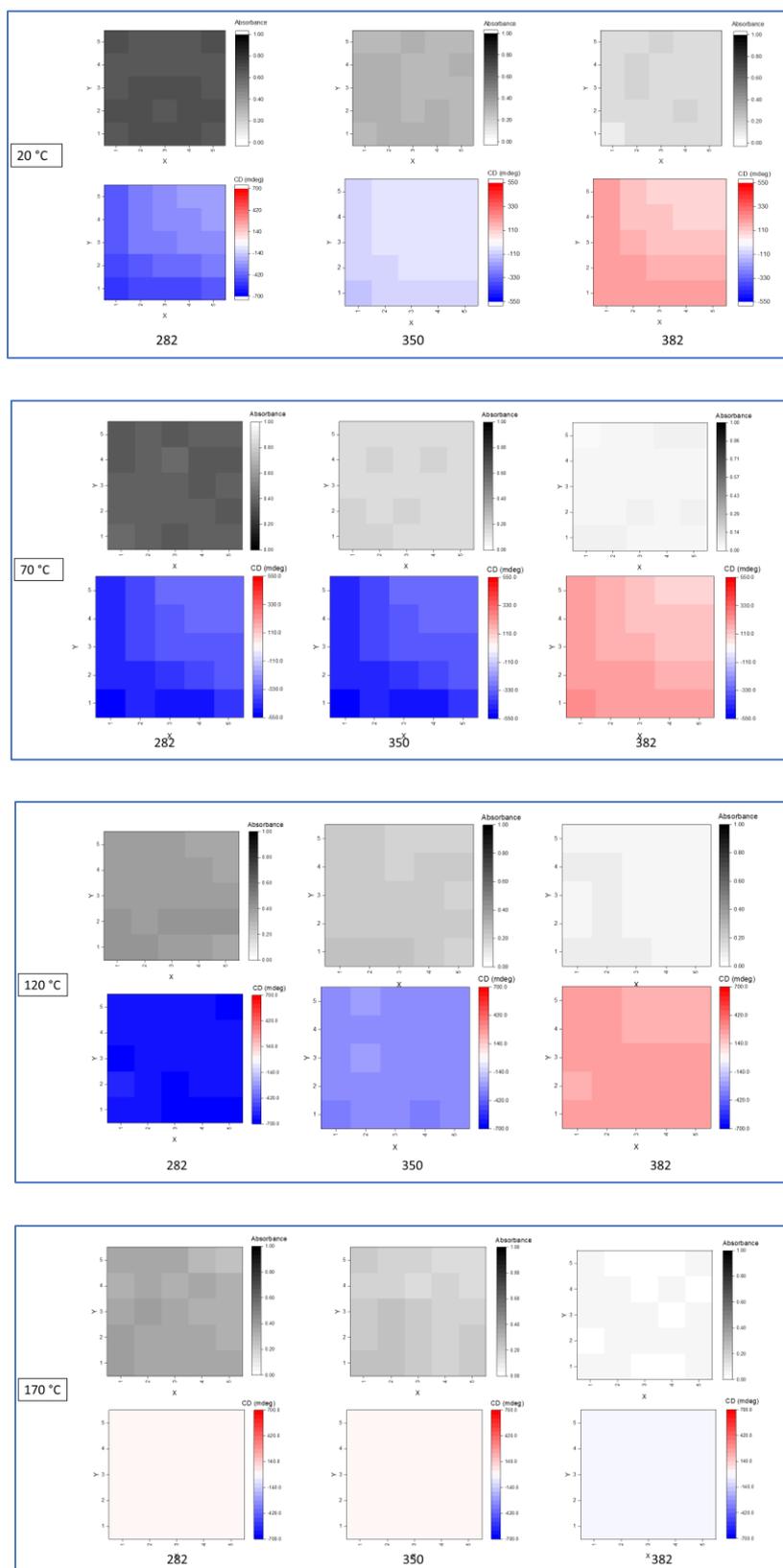


Figure S14b: Absorption and CD maps at a variety of temperatures corresponding to the spectra in Figure 14a, at 282, 350 and 382 nm, of a spin-coated film of **1**.

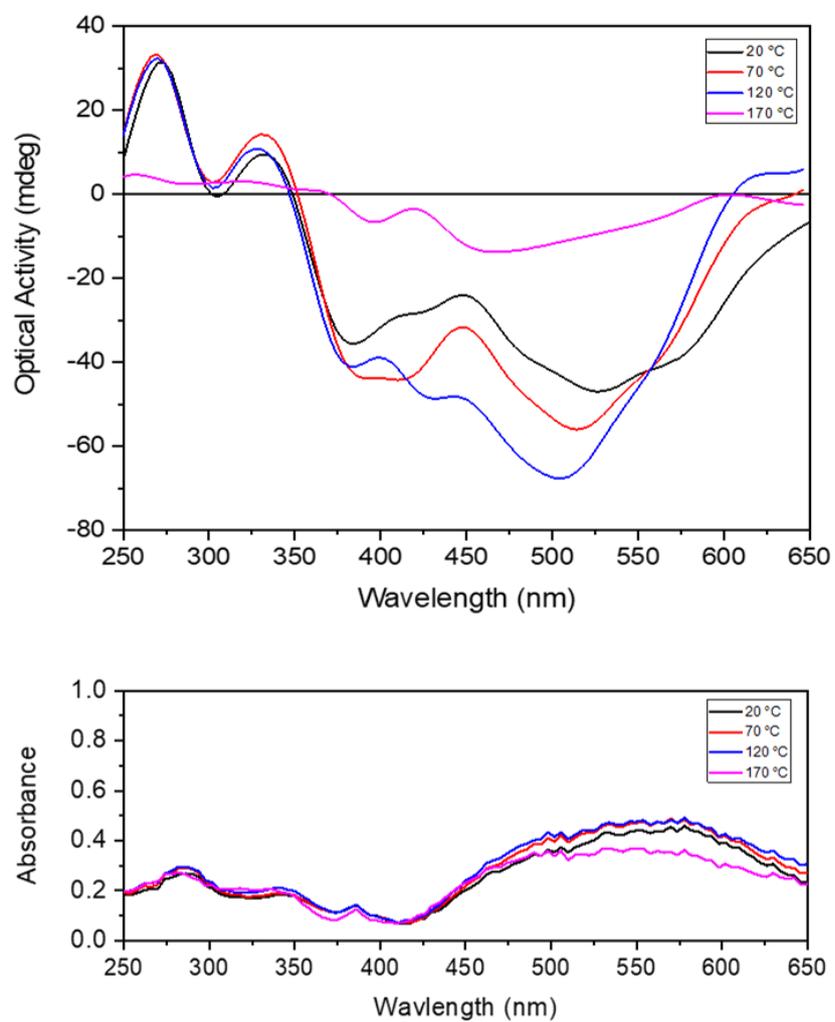


Figure S15a: Averages of 25 absorbance spectra (top) and corresponding averaged of 25 Optical activity spectra (bottom) at a variety of temperatures of a drop-coated film of **1**

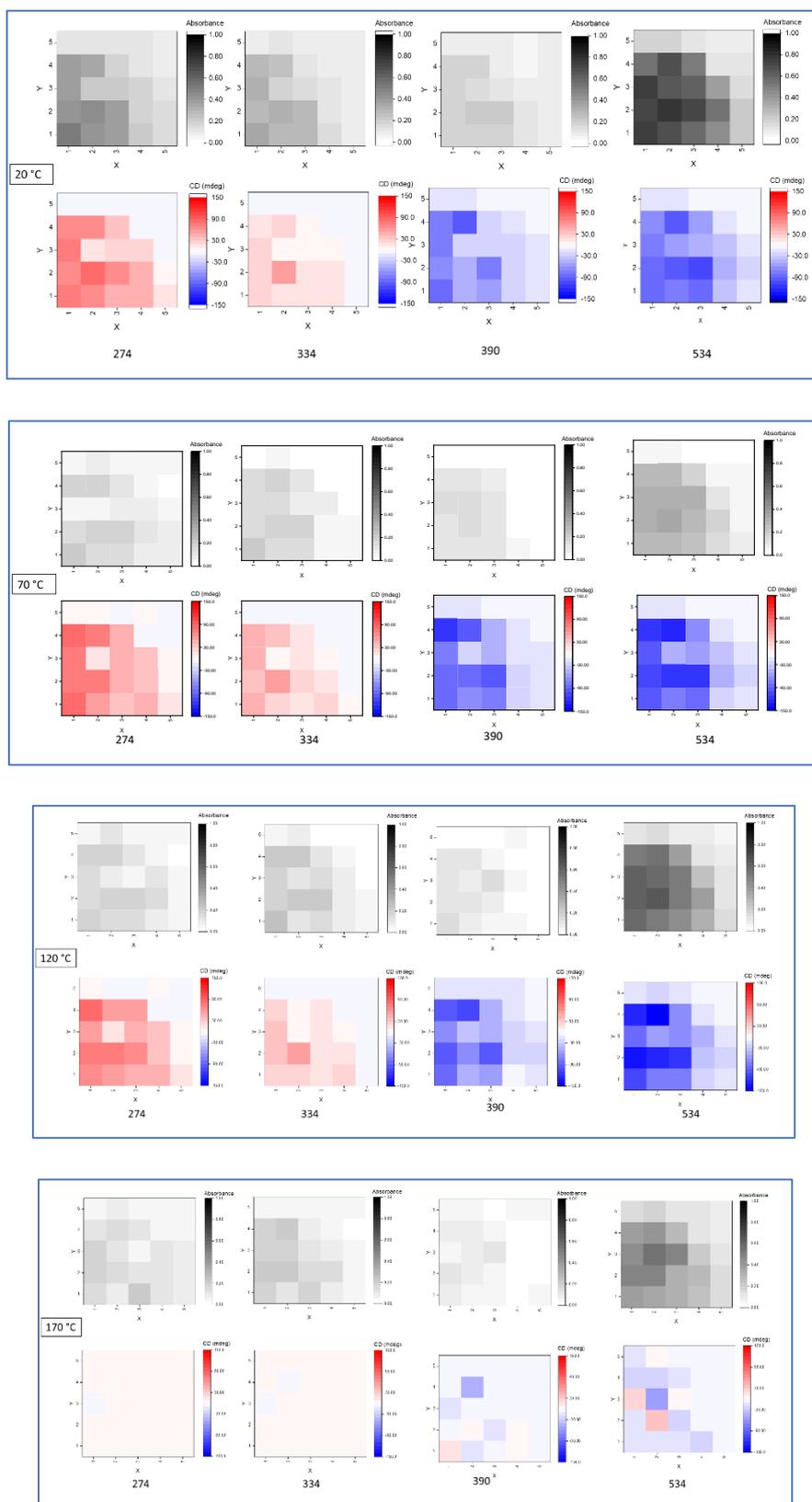


Figure S15b: Absorption and CD maps at a variety of temperatures corresponding to the spectra in Figure 15a, at 274, 334, 390 and 534 nm, of a drop-coated film of **1**.

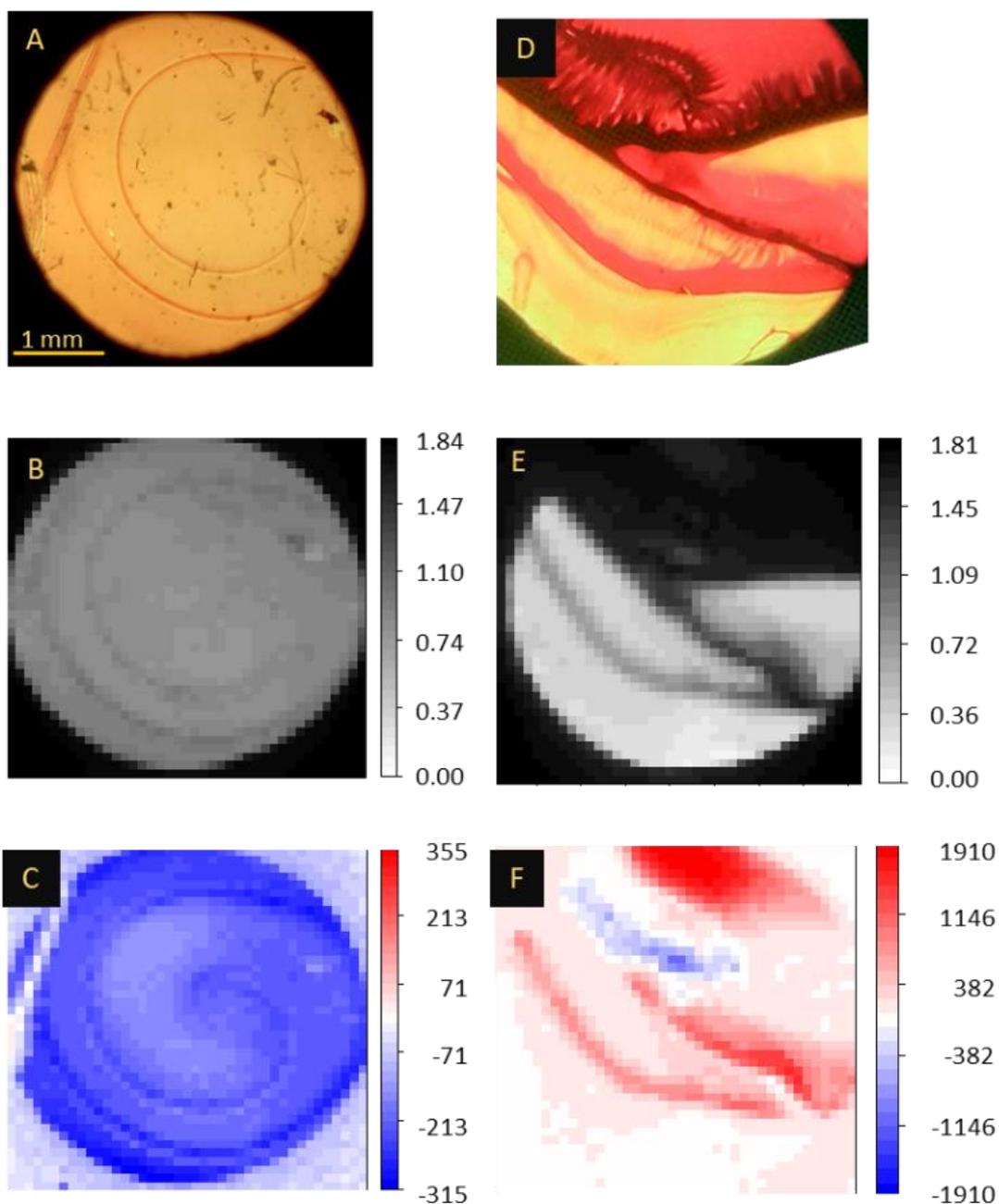


Figure S16: Optical micrographs (top), absorption maps (middle) and CD maps (bottom) for spin-coated (left, A-C) and drop-coated (right, D-F) films, of 1 from the MMP measurements where homogeneous and heterogeneous regions are scanned. Images B and C were registered at 284 nm while E and F are shown for the 408 nm signal. The 2D maps were the result of raster scanned 41 x 41 grids at 100 μm interval steps.

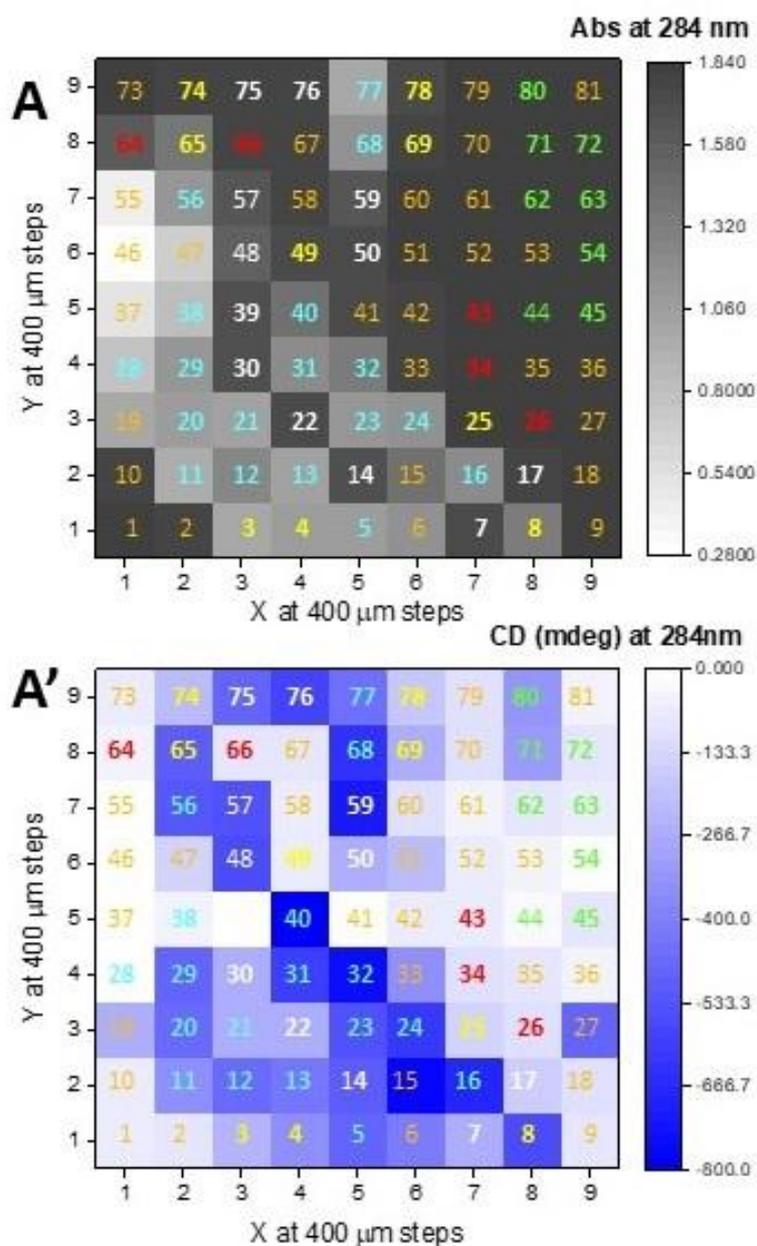


Figure S17: 2D UV(A) and CD (A') maps from MMP data measured at 284nm of **1** drop-coated thin film from chloroform solution. The numbers represent the coordinate of the 81 spots of the 9 x9 grid measured at 400 μm steps. The colour scheme of the coordinates is that of figure S17 whereas those of the maps are white to black for the Abs intensity magnitude and white to blue for the negative CD intensity magnitude at 284 nm.

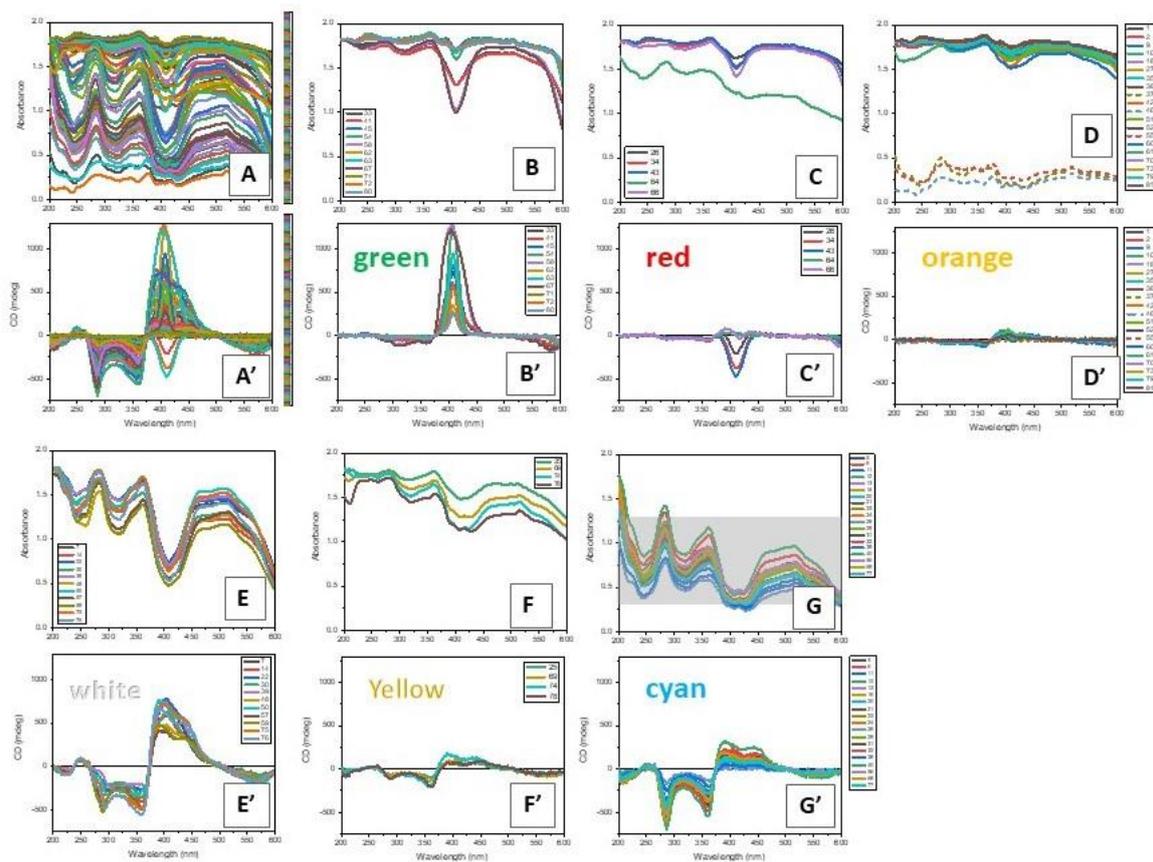


Figure S18: Absorption, Abs (A) and CD (A') spectra of the drop-coated thin film of **1** from chloroform of 9 x 9 grid at 100 mm steps of which 2D maps at 284 nm are illustrated in figure 6. The figures B-B' to G-G' are the spectra grouped in terms of Abs and CD similarities with the colour labels used to identify the spots coordinates of figure S16.

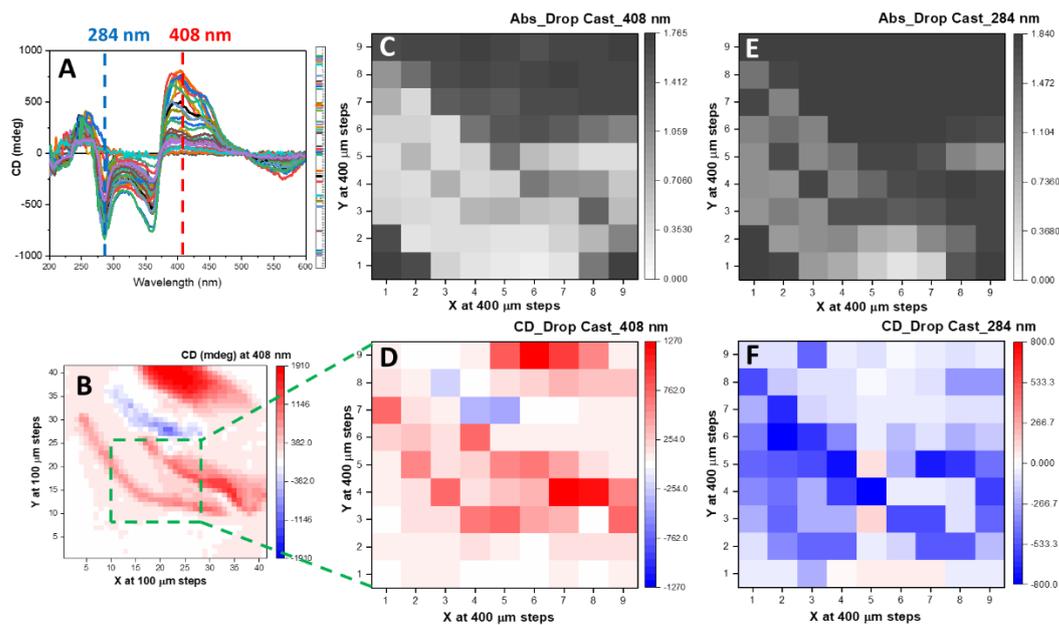


Figure S19: A) 31 CD spectra selected with optimal transmission out of the 81 spectra of the 9x9 grid smaller area at 400 nm interval steps scanned from the initial larger area (B) of the drop coated film of **1**. From these spectra, 2D maps of absorption and CD at 408nm (C and D) and 284nm (E and F) were generated illustrating and confirming the chiroptical homogeneity of the film.

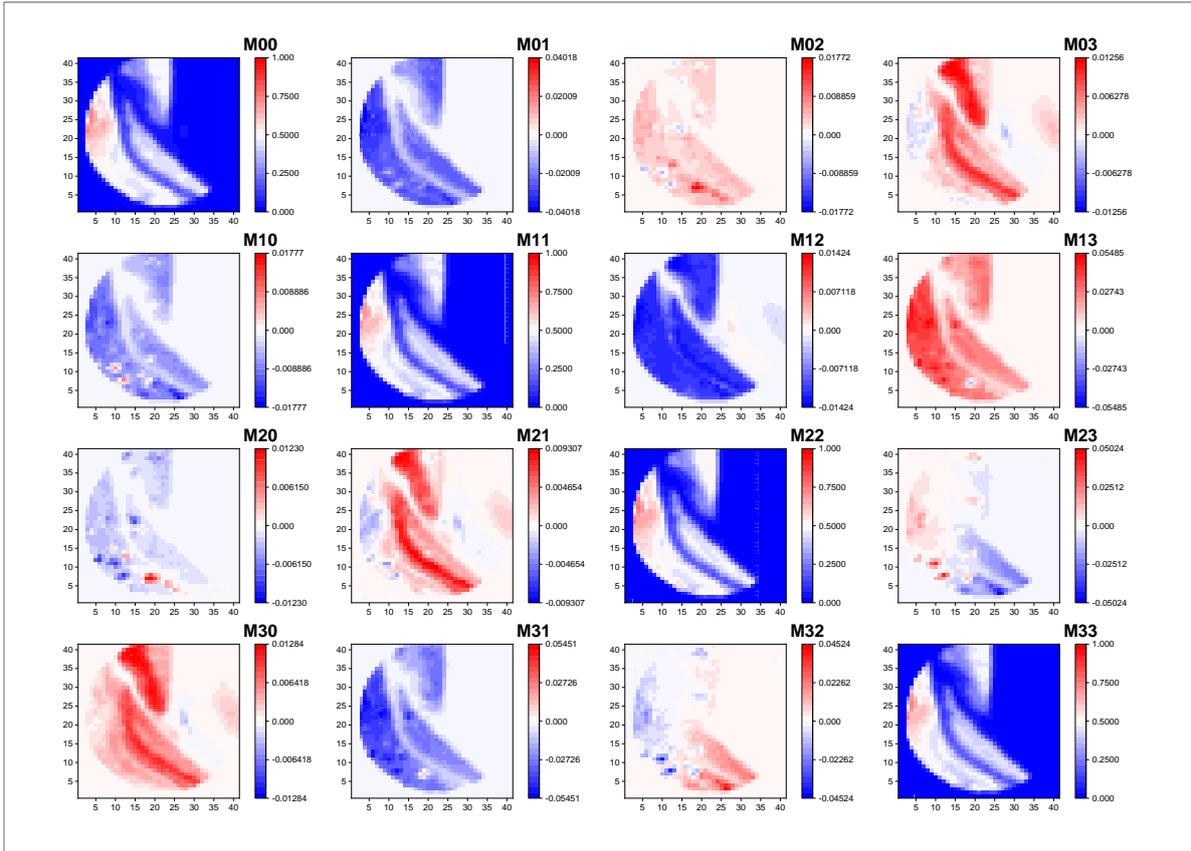


Figure S20: The differential 16 Mueller Matrix (MM) elements of the large area of the drop coated film in Figure 3 of the main text. Much of the film exceeds the optimal transmission range (it is too thick). Nevertheless, subsequent mapping of the smaller area that reveal a more transparent film was conducted as revealed in the Figure S18.

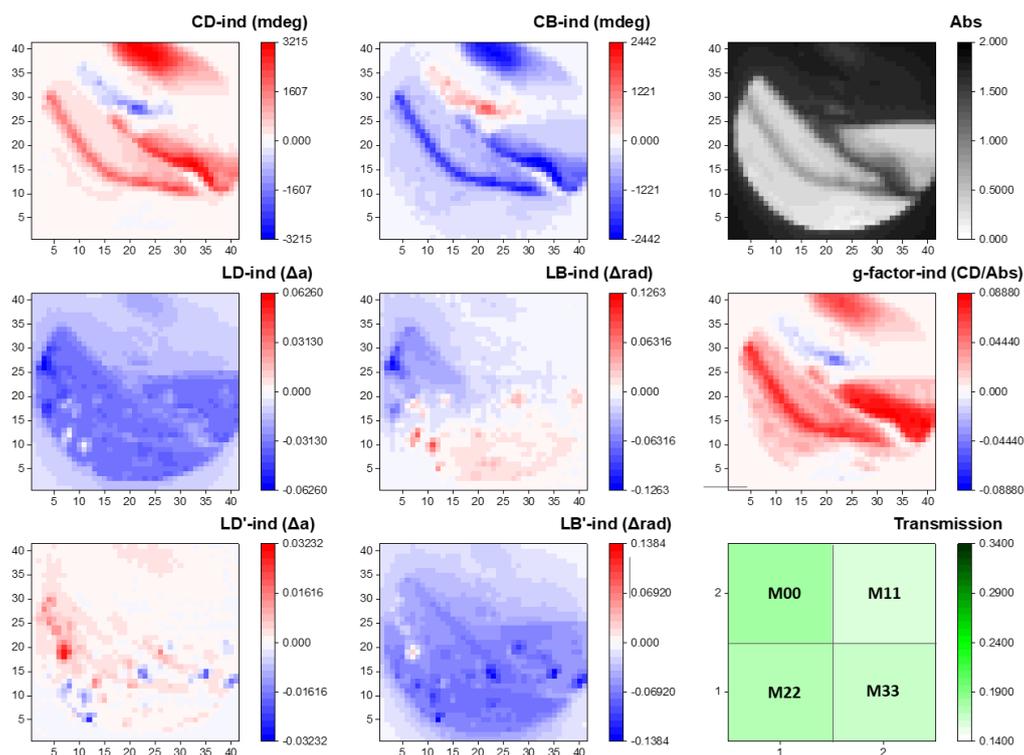


Figure S21: Optical and Chiroptical properties extracted from the 16MM plots using the Independent method. This figure illustrates the whelm of information that the MMP measurement can provide. For the purpose of this manuscript we focus mainly on the CD characterisation. The presence of some degree of diattenuation and the fact that the M02 has opposite sign to M20 and that a smaller areas of M30 and M03 that should have the same sign are in fact opposite, suggest the presence of some crystallinity making the analysis of this film much more complicated and complex..

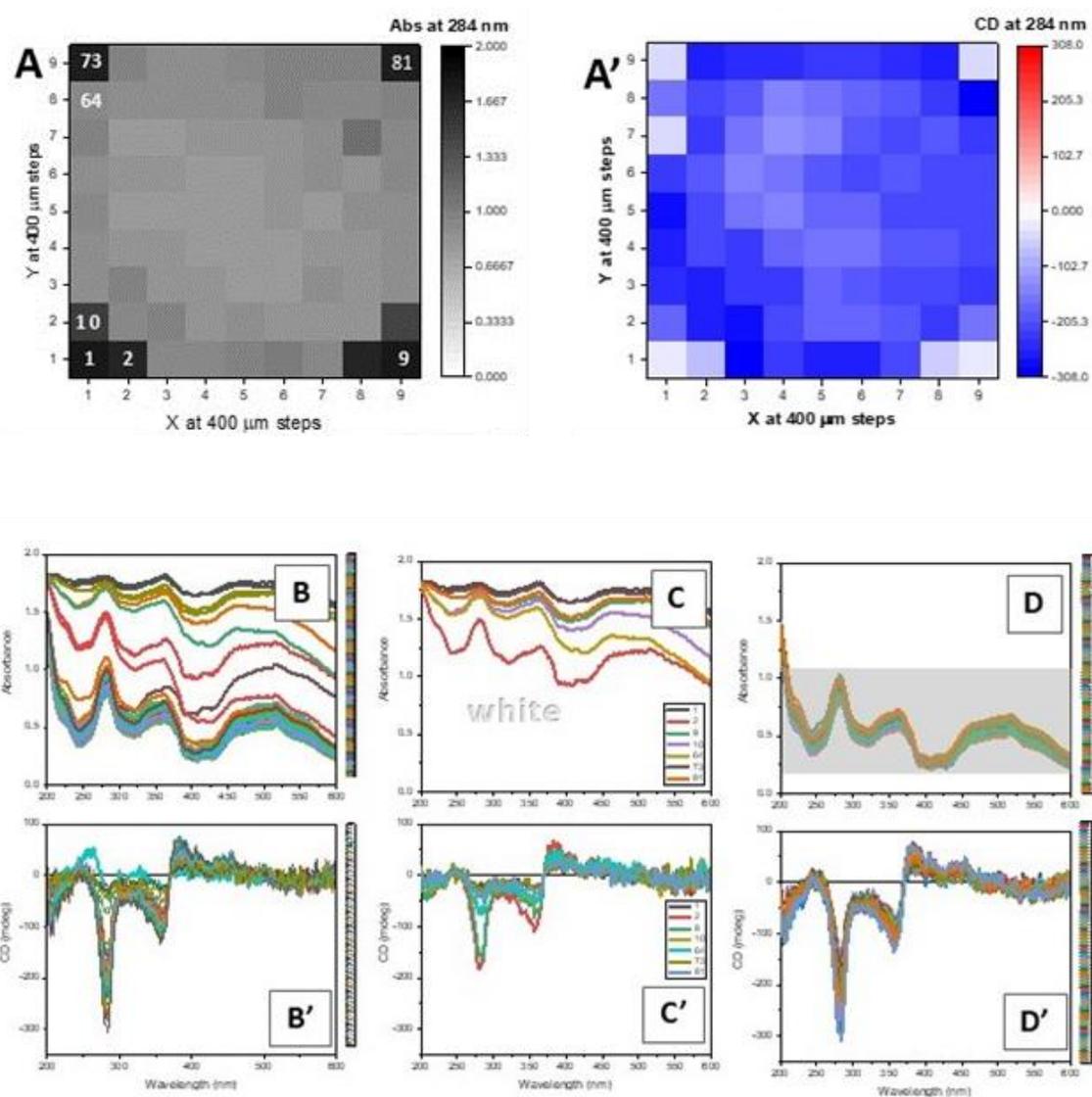


Figure S22. Absorption, Abs (A) and CD (A') spectra of the spin coated thin film of **1** from chloroform of 9 x 9 grid at 100 mm steps of which 2D maps at 284 nm is generated from the B and B' spectra The figures C-C' and D-D' are the spectra grouped in terms of Abs and CD similarities with the white colour labels used to identify the spots coordinates of the maps A and A'.

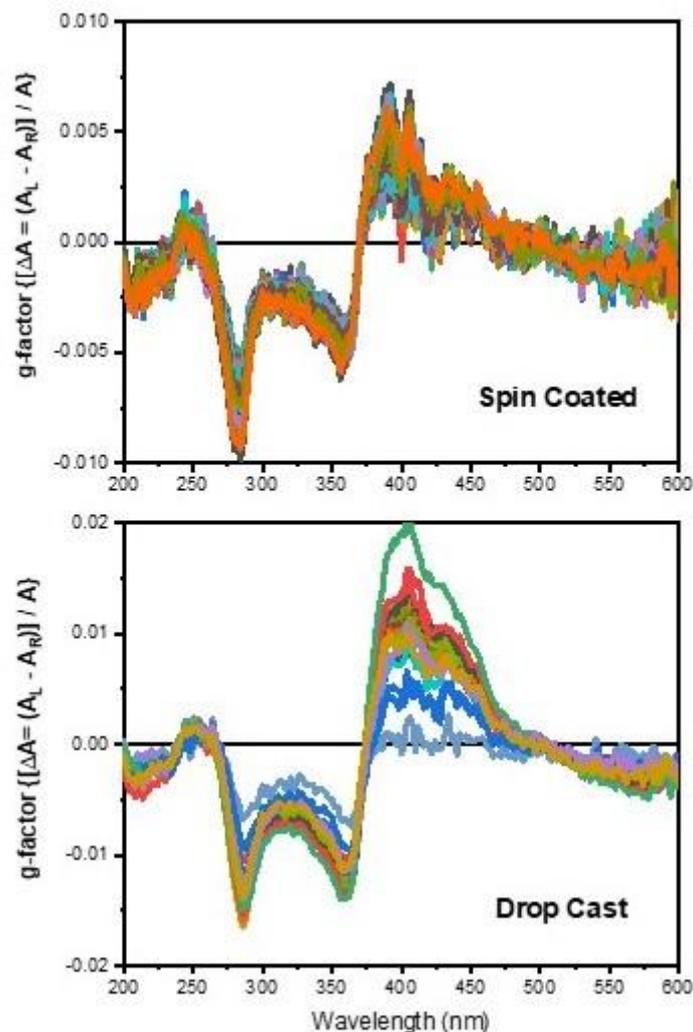


Figure S23 A) g-factor spectra of **1** from a drop-coated film generated from the ratio between the spectra converted from mdeg to ΔA for the spectra of Figure S17 (G' and G , respectively). B) g-factor spectra of **1** from a spin-coated film generated from the ratio between the spectra converted from mdeg to ΔA over the corresponding spectra of Figure S21 (D' and D , respectively).

References

1. S. Stas, J.Y. Balandier, V. Lemaury, O. Fenwick, G. Tregnago, F. Quist, F. Cacialli, J. Cornil and Y. H. Geerts, *Dyes and Pigments*, 2013, **97**, 198.
2. P. C. Ruentz, J. R. Bagley, C. K. W. Watts, R. E. Hall and R. L. Sutherland, *J. Med. Chem.*, 1986, **29**, 2513.