Supporting Information

Homochiral Crystal Generation via Sequential Dehydration and Viedma Ripening

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Materials and Methods

Cytosine (**1**) ([CAS 71-30-7], 6 % *ee* [CD(−)290 nm]) and potassium bromide ([7758-02-3]) were purchased from Sigma-Aldrich. 1,2-bis(N-benzoyl-N-methylamino)benzene (**2**) and 1,2-bis-(*N*-benzenesulfonyl-*N*-methylamino)benzene (**3**) were synthesized in a two-step reaction *via* the formation of a secondary anilide with subsequent *N*-methylation as described below (Figure S1 & S2). TLC was carried out on silica gel 60 F_{254} with aluminum support. ^{1}H-NMR spectra were acquired on a Varian VNMR 500 MHz spectrometer. CD absorption spectra were recorded using a Jasco J-710 spectropolarimeter. X-ray powdered diffraction patterns were obtained using a Bruker D2 Phaser, Ni-filtered Cu Kα radiation was applied and a Lynxeye detector was used. Single crystal X-ray diffraction was run on a Bruker DUO system, which was either equipped with a Molybdenum Kα source (λ = 0.71073 Å), a graphite monochromator and an APEX II CCD detector or a system equipped with a Copper Kα microfocus source (λ = 1.54184 Å) and an APEX II CCD detector. Polarized light microscopy was performed on a Nikon SMZ1500 stereomicroscope. Mass spectroscopic analysis was completed using Quattro LC triple quadrupole mass spectrometer. DSC measurements were carried out using TA instruments, DSC Q2000 differential scanning calorimeter.

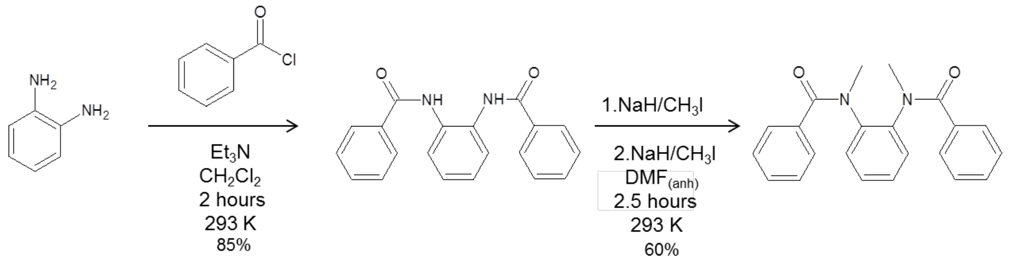

Figure S1: Reaction scheme for synthesis of **2**

1,2-bis(N-benzoyl-N-methylamino)benzene (2)

This compound was prepared using a similar protocol to that reported by Azumaya *et al.* (Figure S1).[1] A solution of *ortho*-phenylenediamine (1.1 g, 10 mmol) and triethylamine (3.5 mL, 25 mmol) in 50 mL of CH_2Cl_2 in a 250 mL round bottom flask was cooled in an ice bath. A solution of benzoyl chloride (2.32 mL, 20 mmol) in CH_2Cl_2 (50 mL) was subsequently added dropwise and the reaction mixture was stirred for an additional two hours at room temperature. The reaction mixture was washed with water (2 x 10 mL), dried with anhydrous $MgSO_4$ and evaporated to dryness. This intermediate product (2.689 g, 85%; $R_f = 0.54$ (50:50 ethyl acetate: hexanes) was used as obtained for the subsequent methylation step. A suspension of sodium hydride (0.1967 g, 8.20 mmol) in anhydrous DMF was prepared. A solution of the intermediate product (1.297 g; 4.10 mmol) in anhydrous DMF (25 mL) was added to the suspension and the mixture was stirred at room temperature for 30 minutes. Iodomethane (0.255 mL; 4.10 mmol) was subsequently added dropwise and the stirring continued for another hour. An additional aliquot of sodium hydride (0.198 g; 8.20 mmol) and iodomethane (0.255 mL; 4.10 mmol) was made. After one hour of stirring the solvent was removed under vacuum. The residue was diluted with CH_2Cl_2 and washed with 2 N HCl (10 mL), brine (10 mL) and water (10 mL). The organic layer was dried with anhydrous $MgSO_4$ and evaporated to dryness. Purification by silica chromatography (50:50 hexane: ethyl acetate) yielded the desired product (0.838 g, 60%): R_f = 0.20 (50:50 hexane: ethyl acetate); ^{1}H-NMR: A broadening of the *N*-methyl peaks between 2 and 4 ppm was observed when going from 25 to 50 °C. This conformational broadening is due to the increased *cis/trans* interconversion about the chiral axes (Ar-N bonds) as reported by Azumaya *et al.*,[1] MS (ESI): m/z 345.3 $[M+H]^+$ and m/z 367.3 $[M+Na]^+$

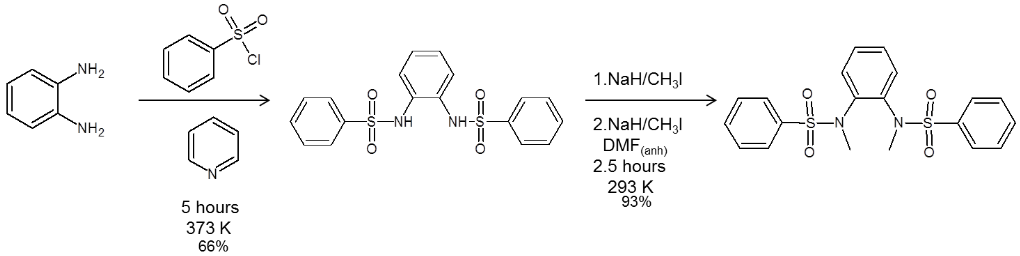

Figure S2: Reaction scheme for synthesis of **3**

1,2-bis-(phenylsulfonamido)benzene

The intermediate product was prepared using a similar protocol to that reported by Shang *et al.* whereas the final product was synthesized through a methylation step using a similar protocol to that reported by Azumaya *et al.* (Figure S2).[1,2] A solution of *ortho*-phenylenediamine (1.08 g, 0.01 mol) in pyridine (40 mL) was slowly added to a 100 mL round bottom flask containing a solution of benzenesulfonyl chloride (2.750 mL, 0.020 mol) in pyridine (0.808 mL, 0.010 mol). The reaction mixture was stirred under reflux at 100 °C for 5 hours. The reaction mixture was allowed to cool to room temperature and 150 mL of distilled water was added to precipitate the intermediate product. The crude product was filtered and washed with cold distilled water (10 mL) and dried under vacuum. Purification by silica chromatography (97.5:2.5 followed by 1:1 (toluene: ethyl acetate)) yielded the desired product (2.57 g, 66%): $R_f = 0.55$ (1:1

toluene: ethyl acetate); m.p. = 190 °C (lit.,[3] 190.3-190.8 °C); ^{1}H NMR (500 MHz, $CDCl_3$-d, Me_4Si) δ = 7.75 - 7.62 (2H, m, ph-H), 7.57 (1 H, d, *J* = 7.3 Hz, ph-H), 7.49 - 7.41 (2H, m, ph-H), 7.06 (1 H, dd, *J* = 3.4, 5.9 Hz, ph-H), 6.99 - 6.90 (1H, m, ph-H), 1.55 (3 H, s, N-H).

1,2-bis-(*N*-benzenesulfonyl-*N*-methylamino)benzene (3)

1,2-bis-(phenylsulfonamido)benzene (1.4418 g, 0.0037 moles) was dissolved in anhydrous DMF and added to a suspension of NaH (0.1775 g, 0.0074 moles) in anhydrous DMF. The mixture was stirred for 30 minutes prior to the addition of iodomethane (0.231 mL, 0.0037 moles). The mixture was stirred at room temperature for 1 hour before another addition of NaH (0.1775 g, 0.0074 moles) and iodomethane (0.231 mL, 0.0037 moles). After an additional hour, excess solvent was removed under vacuum. Purification by silica chromatography (50:50 hexane: ethyl acetate) yielded the desired product (1.442 g, 93%): R_f = 0.67; m.p. = 225 °C (lit.,[4] 223 °C); ^{1}H NMR (500 MHz ,$CDCl_3$-d, Me_4Si) δ = 7.89 - 7.83 (4H, m, ph-H), 7.68 - 7.62 (2H, m, ph-H), 7.60 - 7.54 (4H, m, ph-H), 7.29 - 7.24 (8H, m, ph-H + $CDCl_3$ interference), 6.89 (2H, dd, *J* = 3.4, 5.9 Hz, ph-H), 3.25 (6H, s, N-CH_3). Overlap of the chloroform peak with product signal at 7.29-7.24 ppm resulted in an increased integration (8 H), the actual integration for the peak is 2H. An additional peak at *ca.* 1.56 ppm is assigned to water within the sample.

Crystallization through Slow Evaporation

Crystals of **1**•H_2O were grown through slow evaporation from water in a 12.5 cm by 6 cm crystallizing dish at room temperature. 1.0 g of **1** was dissolved in 130 mL of water with heating and stirring and subsequently covered with aluminum foil containing small perforations. Crystallization of **1**•H_2O typically occurred within one week, resulting in crystals that were typically 2 x 0.5 x 0.25 cm in size.

Compound **2** was recrystallized with water-saturated ethyl acetate to obtain achiral crystals (*i.e.* **2**•xH_2O) and anhydrous ethyl acetate to obtain chiral crystals. The recrystallization was carried out in a 250 mL beaker covered with aluminum foil and placed on a bench top at room temperature. Depending on the desired speed of evaporation, the number of perforations on the aluminum foil covering the beaker varied. Crystal growth would normally occur within 1-2 weeks. A non-stochastic crystallization was observed, where there was a large preference for crystals with (-) CD signal ([CD(−)260 nm]). Achiral crystals of **2**•xH_2O were typically 0.5 x 0.5 x 0.25 cm in size whereas the chiral crystals (**2**) were slightly larger. The crystals were viewed under a microscope to isolate single crystals for subsequent measurements. **2**•xH_2O appeared to readily lose water as indicated by the emergence of white spots on the initially clear crystals. The dehydration of **2**•xH_2O was investigated by DSC and TGA measurements.

Compound **3** was recrystallized at room temperature from ethyl acetate in a 250 mL beaker. In the case of **3,** crystallization occurred rapidly and the evaporation of solvent was slowed down with aluminium foil. Typical crystals were 0.2 x 0.2 x 0.2 cm in size.

Differential Scanning Calorimetry

DSC thermograms were recorded using TA instruments, DSC Q2000 differential scanning calorimeter. Finely ground samples of **1**•H_2O (18.67 mg) and **2**•xH_2O (14.59 mg) were placed in an aluminum pan and subsequently crimped with an aluminum lid before sampling. An empty pan was used as a reference during the measurements. Different parameters were used for the heating cycle for each sample. The heating rate was 5 °C/min and 10 °C/min for **1**•H_2O and **2**•xH_2O, respectively. The heating ramp was carried out from 20 - 150 °C and 100 - 180 °C for **1**•H_2O and **2**•xH_2O, respectively (Figure S3).

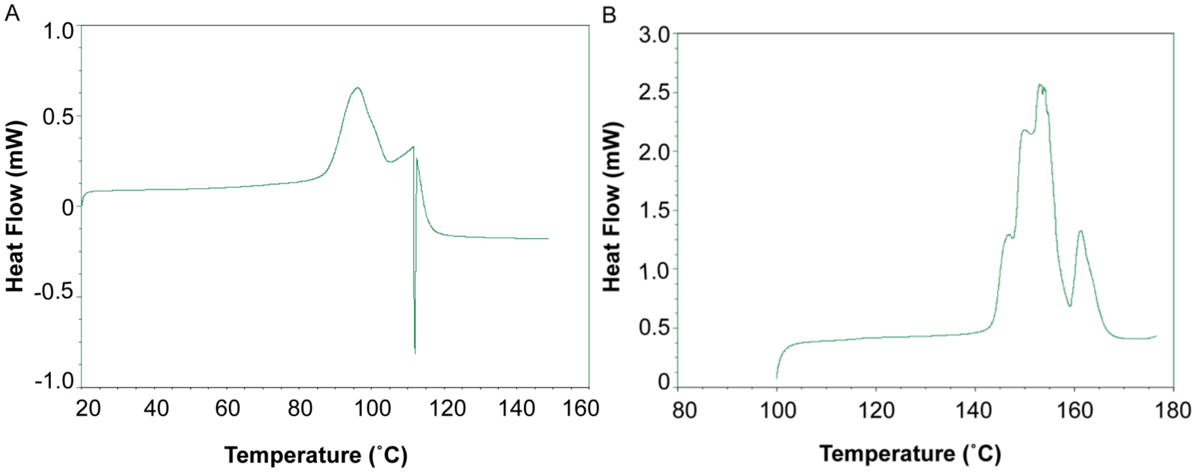

Figure S3: DSC thermogram of **1**• H_2O (A) and **2**•xH_2O (B)

Thermogravimetric Analysis

Thermal gravimetric analysis (TGA) analysis was performed on TGA 500 instrument. In a typical experiment, the crystal was carefully transferred to the furnace of the instrument where it was carefully weighed at 11.8820 mg. The sample was then heated under nitrogen through a range of 25 ˚C – 200 ˚C, at a rate of 5 ˚C/min in order to determine the weight loss as a function of temperature (Figure S4).

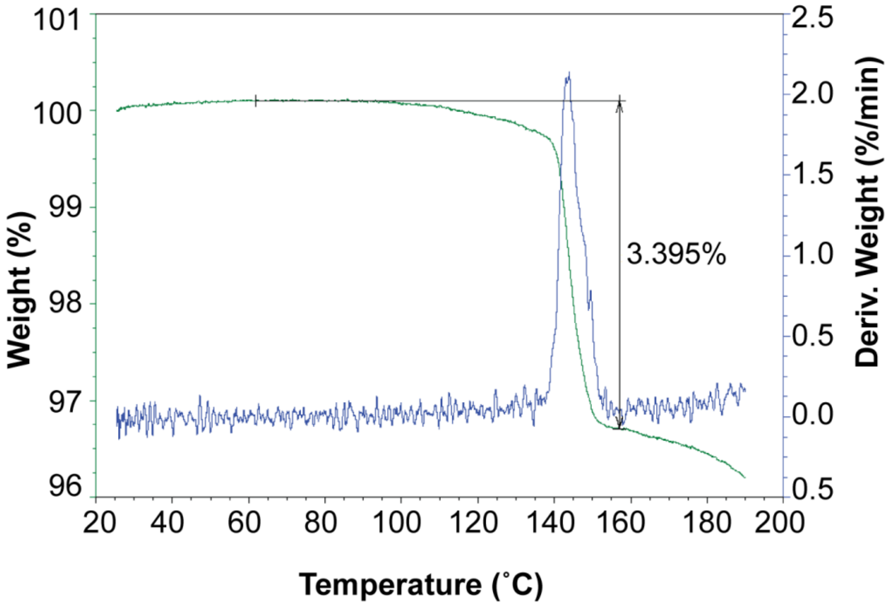

Figure S4: TGA thermogram of **2**•xH_2O. The total amount of water lost during the heating process was determined from the percentage of mass lost ((11.8820 mg of sample*0.03395 = 0.403394 mg; 22.3918 µmoles). This mass of water lost from **2**•xH_2O (0.403394 mg) was subtracted from total mass (11.8820 mg) to determine the mass of **2** (11.4786 mg; 33.3286 µmoles). The amount of water, x, in the hydrated crystal was calculated from the molar ratio of the water to 2 (22.3918 µmoles/33.3286 µm) to be 0.67.

Dehydration of Achiral Crystals

Dehydration of achiral crystals was carried out in a similar fashion for both **1**•H_2O and **2**•xH_2O. Achiral crystals were crushed with a mortar and pestle and placed in a 15 x 45 mm vial. The open vials were placed in a digitally controlled Chemglass aluminium heating block/stirrer (**2**•xH_2O was heated at 140 °C and **1**•H_2O was heated at 90 °C).[5] The hotplate was set at the desired temperature for 30 minutes to equilibrate and the sample was subsequently placed in the center wells of the heating block. The time required for the transformation from achiral crystals to chiral crystals was *ca.* 3 hours for **1**•H_2O and *ca.* 30 minutes for **2**•xH_2O. The transition between space groups was verified using X-ray powder diffraction. The presence of an amorphous phase in the sample of **2** was responsible for the halo effect observed in the XRPD pattern, but this did not influence the subsequent Viedma amplification process (Figure 3c).

Face-selective dehydration was attempted by directly placing crystals (*ca.* 0.5 x 0.5 x 0.25 cm) of **2**•$x$$H_2O$ on the center of the hotplate at 140 °C. The most prominent face was placed against the hotplate until a structural change was observed *via* XRPD pattern or until the crystal melted. If the crystal is too small, there would be less face-selectivity but if the crystal is too big, the dehydration would take more time and chirality was not observed. This can be attributed to the development of an amorphous phase or lack of selectivity during dehydration.

X-ray Powder Diffraction

Achiral and chiral crystals were differentiated using XRPD, which also confirmed the transition between space groups upon dehydration. Samples were prepared and placed on a shallow well null sample holder. The sample was pressed flat with a glass plate to ensure an even layer and distribution of sample. The sample was run at room temperature using a 0.03° step and a count time of 0.5 s per step. A continuous scan mode was utilized. Patterns collected for samples without a literature reference are typically run from 0° to 90° in 2θ. **1**, **1**•H_2O, **2** and **2**•$x$$H_2O$ were run from 5° to 50° in 2θ. The sample time varied depending on the 2θ used for each sample.

Viedma Ripening

Samples were subjected to Viedma ripening using a modified Pine Industrial Company analytical rotator. Viedma ripening was carried out in a 5 mL sterile vial with a 20 mm Teflon-faced septum to prevent solvent evaporation. The vial contained 0.25 g of a racemic mixture of **1** or **2**, grinding media (3.0 g of 0.8 mm of YTZ Zirconia ceramic beads), a 10 mm by 5 mm stir bar and 3 mL saturated solution and was sealed with a vial crimper. The stirring speed for Viedma ripening experiments was either 1500 rpm or 2400 rpm. The time required to reach homochirality for **1**, **2** and **3** was *ca.* 65 hours (2400 rpm), *ca.* 6 hours (1500 rpm), and *ca.* 24 hours (2400 rpm), respectively. Slurry samples (*ca.* 100 μL) were taken from the vial to estimate the time required to reach homochirality for **2** and **3**. Viedma ripening of **1** has previously been reported by our group.[6]

Circular Dichroism

Circular dichroism was used to generate calibration curves and to quantify the crystal chirality achieved through Viedma ripening of **1**, **2** and **3**. A Jasco J-710 spectropolarimeter was used to record the circular dichroism spectra. The KBr pellet method was used to prepare solid state samples. Using a mortar and pestle, 100 mg samples were prepared with varying ratios of oven dried KBr. Sample concentrations were 1.2, 1.0 and 1.0% (*wt/wt*) for **1**, **2** and **3**, respectively. The sample was then divided into two portions, and each was vacuum pressed for 30 seconds at *ca.* 10 tons while placed in an evacuable 13 mm pellet press from Pike Technologies. Each pellet was placed into the instrument using a homemade cardstock pellet holder. Typically, three runs were acquired per pellet. The position of the KBr pellet in the pellet holder was varied to ensure homogeneity of the sample. The pellet was rotated so that the circularly polarized light made contact with another position within the pellet. The pellet holder was placed at a specified location as close to the detector as possible. The resolution, accumulations and scan rate were set to 5 points/nm, 4 accumulations and 50 nm/min, respectively. Spectra were recorded from 270 nm to 380 nm for **1**, 240 nm to 340 nm for **2** and 250 nm to 320 nm for **3**. Variability in CD spectra is attributed mainly to pellet preparation. Preparing completely homogenous samples in each preparation was difficult and therefore replicate CD spectra are often variable.

Enantiomeric Excess Calibration Curves

CD calibration curves were generated to determine the enantiomeric excess in single crystal as well as Viedma ripening samples. Samples varying in enantiomeric excess were prepared by mixing appropriate ratios of left-handed and right-handed crystalline powder while maintaining a constant total weight. A calibration curve was generated by plotting the CD signal at a specified wavelength versus the enantiomeric excess of the standards. For each standard, multiple pellets were prepared and measured to determine the average CD signal and standard deviation. The calibration curves were subsequently used to determine the enantiomeric excess of the samples from Viedma ripening experiments. Chiral crystallites used as standards for the construction of calibration curves were obtained either by crushing single crystals obtained from slow evaporation (**2** and **3**) or from the crystalline powders generated by Viedma ripening (**1**). The enantiomeric excess was calculated according to eq.1 where $m_{(+)}$ and $m_{(-)}$ are the weights of CD-positive and CD-negative crystals.

$$\%\boldsymbol{ee} = \frac{\boldsymbol{m}_{(+)} - \boldsymbol{m}_{(-)}}{\boldsymbol{m}_{(+)} + \boldsymbol{m}_{(-)}} \times \mathbf{100}\%$$

Equation S1: Determination of enantiomeric excess

The CD values for the calibration curve were taken from 290 nm, 260 nm and 275 nm for **1**, **2** and **3**, respectively. The average CD signals and standard deviations were calculated based on 3 replicate measurements.

Polarized Light Microscopy

Polarized light microscopy of **3** was carried out on a Nikon SMZ1500 stereomicroscope. The polarizer was rotated clockwise to visualize the optical rotatory dispersion along the optic axis.

Characterization of 1,2-bis-(*N*-benzenesulfonyl-*N*-methylamino)benzene (3)

Crystals of **3** obtained *via* slow evaporation from ethyl acetate resulted in crystals with prominent (001) and $(00\bar{1})$ faces. Chirality was determined through optical rotatory dispersion (ORD) using polarized light microscopy (Figure S5). This property is seen in various crystals found the tetragonal and hexagonal crystal systems.

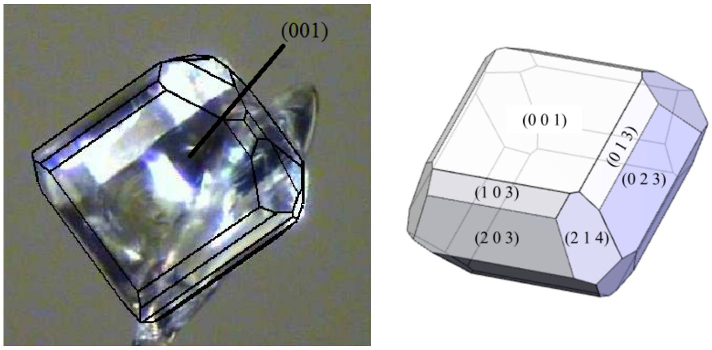

Figure S5: Indexed chiral crystal of **3** indicating face used for optical rotatory dispersion determined by single crystal X-ray diffraction (left) and indexed face simulated using WinXMorph™ software (right) [77]

Analysis of **3** crystals displayed an optical rotatory dispersion of blue-amber-clear which is indicative of a crystal with (+) CD signal ([CD(+)275 nm]) whereas an optical rotatory dispersion of amber-blue-clear is indicative of a crystal with (-) CD signal ([CD(−)275 nm]) (Figure S6). Crystals were harvested according to their respective color transitions and subsequently subjected to CD measurements to correlate CD transitions with ORD. Compound **3** crystallizes in enantiomorphic space groups, the resulting CD signal can be correlated to the space group in which the crystal is found. Single crystal X-ray diffraction was carried out to assign the absolute configuration to the CD signal. Crystals with (+) CD signal are representative of crystals that reside in space group $P4_12_12$ whereas crystals with (-) CD signal are representative of crystals that reside in space group $P4_32_12$, which agreed with previously reported results.[4]

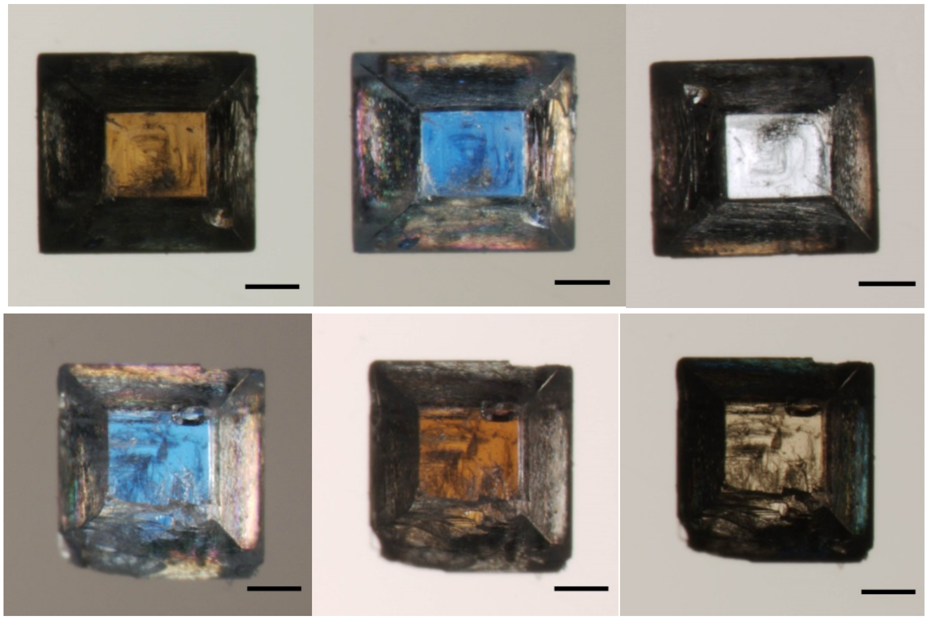

Figure S6: Transition observed upon analysis of chiral crystals of 1,2-bis-(*N*-benzenesulfonyl-*N*-methylamino)benzene using polarized light microscopy (rotating the analyzer clockwise). 1,2-bis-(*N*-benzenesulfonyl-*N*-methylamino)benzene crystals observed: (-) crystals (*top row)*, (+) crystals (*bottom-row*). Scale bar = 0.02 cm.

After manual separation of enantiomorphous crystals of **3,** attrition-enhanced deracemization was carried out. In an attempt to attain an initial enantiomeric excess of 0, equal amounts of chiral crystallites were mixed and finely ground to prepare the starting material for Viedma ripening. Compound **3** has been shown to reach homochirality within 24 hours. CD measurements using chiral crystallites were used to generate a calibration curve to quantify enantiomeric excess of samples at various intervals during Viedma ripening experiments. Of 3 experiments, 1 experiment produced homochiral crystals with (-) CD signal ([CD(−)275 nm]) and 2 experiments produced homochiral crystals with (+) CD signal ([CD(−)275 nm]) (Figure S7).

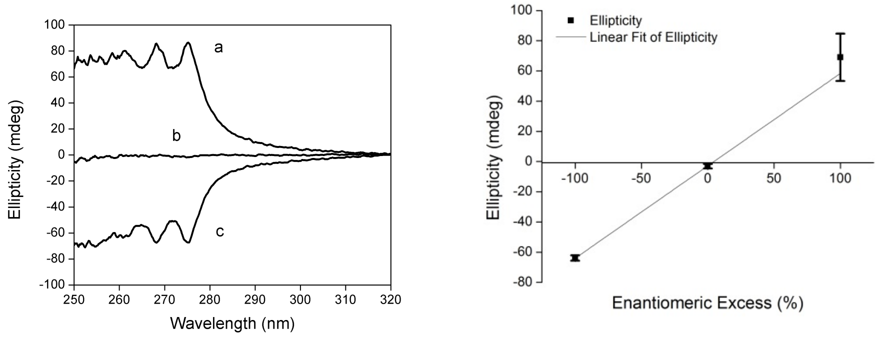

Figure S7: Left: Solid-state CD spectra of the chiral crystals of **3** in KBr: (b) After dehydration, (a) and (c) following Viedma ripening. Viedma ripening was carried out using 0.25 g of sample suspended in 3 mL of saturated solution in anhydrous ethyl acetate with 3 g of ceramic grinding media (0.8 mm) stirring at 2400 rpm for *ca.* 24 hours. Right: CD calibration of **3** in KBr prepared from mixtures of homochiral crystals ([CD(±)275 nm])

Crystallographic Data

Analysis of Cambridge Structural Database (CSD)

The percentage of achiral molecules that crystallize as chiral crystals was determined through the use of Mercury 3.6, ConQuest 1.17, ChiralFinder and CSD 5.36 database (Updated 3 May 2015).[8–11] The entire database of crystal structures was probed for crystals that reside in Sohncke space groups using ConQuest. Upon opening ConQuest the following steps were taken to carry out the determination of crystal structures that crystallize in Sohncke space groups.

1) In the Build Queries tab, select Space Group
2) Adjust space group symmetry to “allows enantiopure substances (Sohncke)”
3) Click search, a new window appears with further search options
4) Leave filters as is and begin search
5) Total number of structures is eventually generated (127 397 structures), the entries were subsequently exported
6) To export entries go to File, Export entries as
7) A new window appears in which the following options were selected
    a. File type – CSD coordinate file
    b. All selected entries checkbox was selected
    c. Fractional and all coordinates checkbox was selected
8) Finally the entries were saved via file pop-up and a .cor file was generated

The next step was to run the results through ChiralFinder. ChiralFinder is a program which separates the entries into different categories: achiral structures, chiral structures, racemic structures, meso structures and error structures.[11]

1) Upon program start-up, a dialog box opens in which an input file name and output files directory is required.
2) The input file name must include the files location i.e C:\Desktop\File A\A.cor
3) The output file directory must end in a similar fashion *i.e.* C:\Desktop\File A\

The coordinate file generated through ConQuest was run through ChiralFinder and the total number of achiral molecules that crystallize as chiral crystals was generated. The value was subsequently divided by the total number of entries in the CSD 5.36 database (776 408). The value obtained was 5%.ChiralFinder also reports error structures which were not included in the calculations; these error structures were also included in the calculation to determine the error. To generate the possible error, two assumptions were made. The error structures can be all achiral structures or they can all be other structures, using that parameter an error of ± 2% was determined. Error structures are a result of files with atoms with too many bonds (atoms with more than 4 bonds or hydrogens with 2 bonds) or atoms with metal elements which cannot be run by ChiralFinder. Incomplete molecular structures due to missing hydrogen atoms also result in error structures.[11] ChiralFinder was not able to process the following entries: DOGMAP, BEQXEB, NUDVIS, BOBDEC, JEJWEB, JUBXIP, XUKNOH, YAWHAG. RANCEQ, PUXGOE and JUBXAH. To generate the total number of Sohncke structures that crystallized in the $P2_1$ or $P2_12_12_1$ space group. The initial search in ConQuest was adjusted to restrict the desired space group to either $P2_1$ or $P2_12_12_1$ while only allowing for enantiopure substance (Sohncke). Furthermore, the generated coordinate files can be processed through ChiralFinder to determine the amount of structures in the $P2_1$ and $P2_12_12_1$ space groups that crystallize from achiral molecules.

WinXMorph™

Crystal structure of **3** was generated using WinXMorph™ software.[7] Recreation of experimental crystal structure required the point symmetry as well as the corresponding faces. The refinement of the structure was carried out through manipulation of the face sizes as well as minor details (crystal fill color, edge color, *etc.*).

Simulated Single Crystal X-ray Diffraction

Single crystal data for **1**•H_2O (CYTOSM), **1** (CYTSIN) and **3** (tka17112 & tka171101), which was used to simulate XRPD patterns, were obtained from the Cambridge Structural Database. Supplementary crystallographic data can be accessed free of charge from Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Experimental Single Crystal X-ray Diffraction

Achiral 1,2-bis(*N*-benzoyl-*N*-methylamino)benzene hydrate (2•0.59 H_2O**):** A clear colourless rhomb-like specimen of $C_{22}H_{21.18}N_2O_{2.59}$, approximate dimensions 0.62 mm x 0.58 mm x 0.25 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker DUO system equipped with a Molybdenum Kα source ($\lambda = 0.71073$ Å), a graphite monochromator and an APEX II CCD detector. A total of 1464 frames were collected. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 21466 reflections to a maximum θ angle of 27.64° (0.77 Å resolution), of which 4267 were independent (average redundancy 5.031, completeness = 99.6%, $R_{int} = 3.36\%$, $R_{sig} = 2.30\%$) and 3714 (87.04%) were greater than $2\sigma(F^2)$. The final cell constants of $\underline{a} = 9.1639(9)$ Å, $\underline{b} = 21.320(2)$ Å, $\underline{c} = 10.0007(10)$ Å, $\beta = 109.6520(10)°$, volume = 1840.1(3) Å^3, are based upon the refinement of the XYZ-centroids of 9480 reflections above 20 σ(I) with $4.728° < 2\theta < 55.28°$. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.937. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6985 and 0.7456. The structure was solved and refined using the Bruker SHELXTL software package, using the space group P 1 21/n 1, with Z = 4 for the formula unit, $C_{22}H_{21.18}N_2O_{2.59}$. The final anisotropic full-matrix least-squares refinement on F^2 with 247 variables converged at $R_1 = 4.44\%$, for the observed data and $wR_2 = 10.72\%$ for all data. The goodness-of-fit was 1.083. The largest peak in the final difference electron density synthesis was 0.305 e^-/Å^3 and the largest hole was -0.222 e^-/Å^3 with an RMS deviation of 0.040 e^-/Å^3. On the basis of the final model, the calculated density was 1.281 g/cm^3 and F(000), 752 e^-.

Another crystal, which was freshly picked out of wet solution, refined to 0.78 water occupancy (**2•**0.78 H_2O, data not shown).

Chiral 1,2-bis(*N*-benzoyl-*N*-methylamino)benzene (2): A clear colourless rhomb-like specimen of $C_{22}H_{20}N_2O_2$, approximate dimensions 0.26 mm x 0.34 mm x 0.62 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker DUO system equipped with a Copper Kα microfocus source ($\lambda = 1.54184$ Å) and an APEX II CCD detector. A total of 3431 frames were collected. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 13866 reflections to a maximum θ angle of 68.25° (0.83 Å resolution), of which 3414 were independent (average redundancy 4.062, completeness = 99.9%, $R_{int} = 4.55\%$, $R_{sig} = 3.68\%$) and 3312 (97.01%) were greater than $2\sigma(F^2)$. The final cell constants of $\underline{a} = 8.2418(7)$ Å, $\underline{b} = 14.0963(12)$ Å, $\underline{c} = 16.1962(13)$ Å, volume = 1881.7(2) Å^3, are based upon the refinement of the XYZ-centroids of 736 reflections above 20 σ(I) with $5.554° < 2\theta < 137.6°$. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.901. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6789 and 0.7531. The structure was solved and refined using the Bruker SHELXTL software package, using the space group P 21 21 21, with Z = 4 for the formula unit, $C_{22}H_{20}N_2O_2$. The final anisotropic full-matrix least-squares refinement on F^2 with 238 variables converged at R_1 = 2.91%, for the observed data and wR_2 = 7.18% for all data. The goodness-of-fit was 1.060. The largest peak in the final difference electron density synthesis was 0.158 $e^-/Å^3$ and the largest hole was -0.127 $e^-/Å^3$ with an RMS deviation of 0.035 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.216 g/cm^3 and F(000), 728 e^-.

Chiral 1,2-bis-(*N*-benzenesulfonyl-*N*-methylamino)benzene (3): A colorless block-like specimen of $C_{10}H_{10}NO_2S$, approximate dimensions 0.38 mm x 0.53 mm x 0.54 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker DUO system equipped with a Molybdenum Kα source (λ = 0.71073 Å), a graphite monochromator and an APEX II CCD detector. A total of 1464 frames were collected. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a tetragonal unit cell yielded a total of 22948 reflections to a maximum θ angle of 27.71° (0.76 Å resolution), of which 2250 were independent (average redundancy 10.199, completeness = 100.0%, R_{int} = 4.05%, R_{sig} = 2.01%) and 2155 (95.78%) were greater than $2\sigma(F^2)$. The final cell constants of a = 8.3899(7) Å, b = 8.3899(7) Å, c = 27.226(2) Å, volume = 1916.4(4) Å^3, are based upon the refinement of the XYZ-centroids of 598 reflections above 20 σ(I) with 7.486° < 2θ < 58.27°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.964. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.7184 and 0.7456. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 43 21 2, with Z = 8 for the formula unit, $C_{10}H_{10}NO_2S$. The final anisotropic full-matrix least-squares refinement on F^2 with 128 variables converged at R_1 = 2.71%, for the observed data and wR_2 = 7.29% for all data. The goodness-of-fit was 1.101. The largest peak in the final difference electron density synthesis was 0.195 $e^-/Å^3$ and the largest hole was -0.412 $e^-/Å^3$ with an RMS deviation of 0.067 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.444 g/cm^3 and F(000), 872 e^-.

	Achiral (**2•**0.59 H_2O**)**	Chiral **(2)**	Chiral **(3)**
CCDC deposition number	1443506	1443507	1443508
Empirical formula	$C_{22}H_{22}N_2O_3$	$C_{22}H_{20}N_2O_2$	$C_{10}H_{10}NO_2S$
Formula weight	354.99	344.40	208.25
T (K)	110(2)	150(2)	150(2)
Wavelength (Å)	0.71073	1.54184	0.71073
Crystal system	Monoclinic	Orthorhombic	Tetragonal
Space group	$P2_1/n$	$P2_12_12_1$	$P4_32_12$

Unit cell dimensions			
a (Å)	9.1639(9)	8.2418(7)	8.3899(7)
b (Å)	21.320(2)	14.0963(12)	8.3899(7)
c (Å)	10.0007(10)	16.1962(13)	27.226(2)
α (°)	90	90	90
β (°)	109.6520(10)	90	90
γ (°)	90	90	90
V (Å^3)	1840.1(3)	1881.7(2)	1916.4(4)
Z	4	4	8
D_{calc}	1.281	1.216	1.444
Absorption coefficient (mm^{-1})	0.085	0.626	0.308
F(000)	752	728	872
Crystal size (mm)	0.62 x 0.58 x 0.25	0.26 x 0.34 x 0.62	0.38 x 0.53 x 0.54
θ (°)	1.91 – 27.64	4.16 – 68.25	2.54 – 27.71
Index ranges	$h = -11 \rightarrow 11$	$h = -9 \rightarrow 9$	$h = -10 \rightarrow 10$
	$k = -27 \rightarrow 27$	$k = -16 \rightarrow 16$	$k = -10 \rightarrow 10$
	$l = -12 \rightarrow 13$	$l = -19 \rightarrow 19$	$l = -35 \rightarrow 35$
Reflections collected	21466	13866	22948
Independent reflections	4267	3414	2250
Completeness (θ)	99.6%	99.9%	100%
Data/restraints/parameters	4267/0/247	3414 / 0 / 238	2250 / 0 / 128
Goodness of fit (GOF) on F^2	1.083	1.060	1.101
Final R indices [$I > 2\sigma(I)$] (%)	$R_1 = 4.44$ $wR_2 = 10.25$	$R_1 = 2.91$ $wR_2 = 7.10$	$R_1 = 2.71$ $wR_2 = 7.19$
R indices (all data) (%)	$R_1 = 5.22$ $wR_2 = 10.72$	$R_1 = 3.00$ $wR_2 = 7.18$	$R_1 = 2.86$ $wR_2 = 7.29$
Flack parameter	n/a	-0.03(10)	-0.05(3)
Largest difference in peak and hole (e Å^{-3})	0.305 and -0.222	0.158 and -0.127	0.195 and -0.412

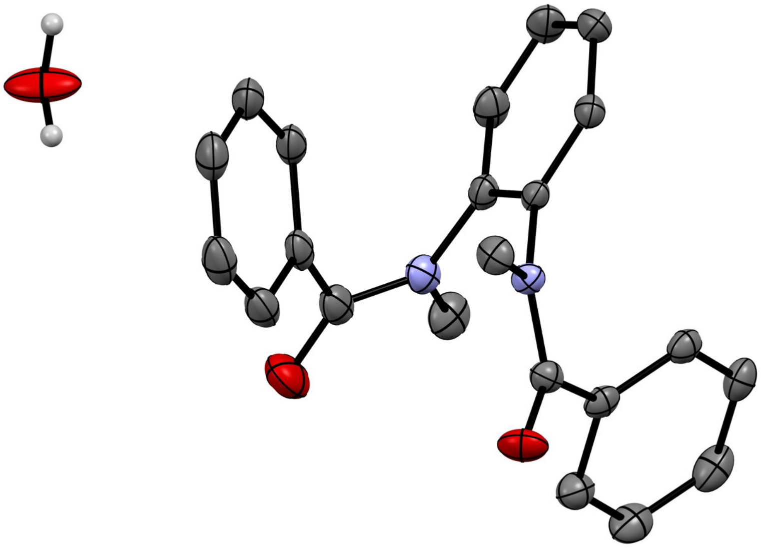

Figure S8: ORTEP representation of achiral **2**•0.59 H_2O at 50% ellipsoid probability. H atoms except on water were omitted for clarity.

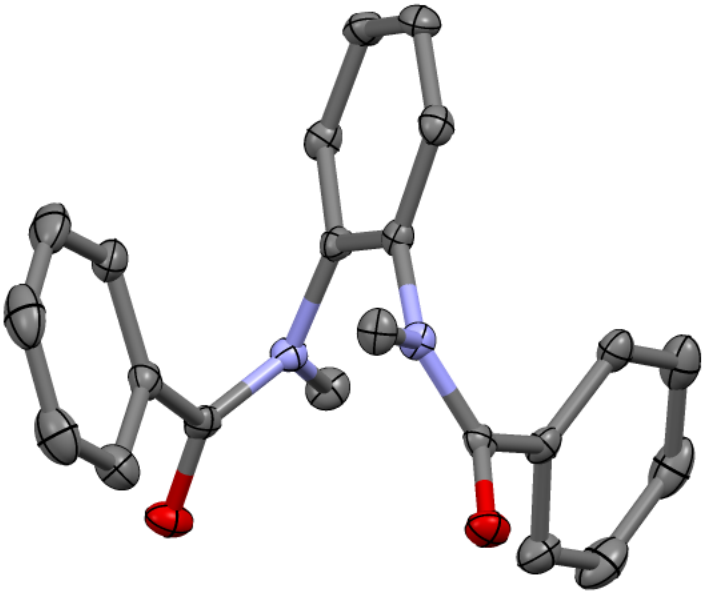

Figure S9: ORTEP representation of chiral **2** at 50% ellipsoid probability. H atoms were omitted for clarity.

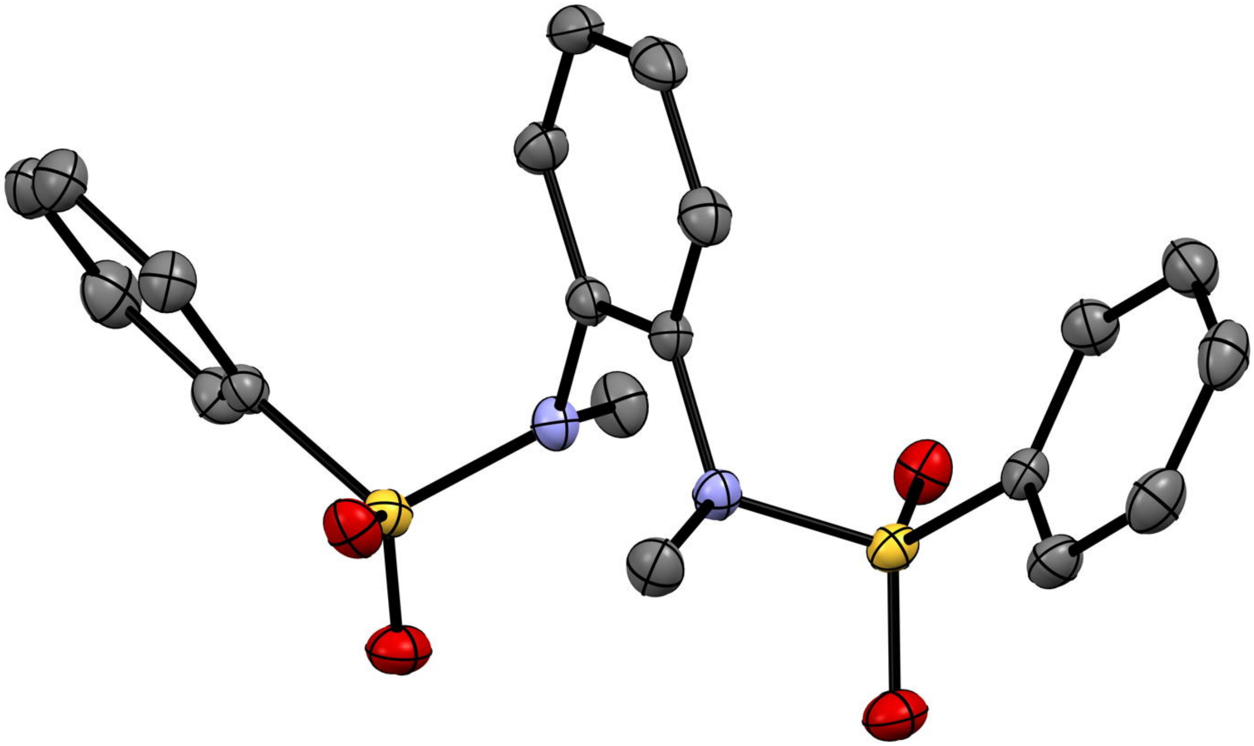

Figure S10: ORTEP representation of chiral **3** at 50% ellipsoid probability. H atoms were omitted for clarity.

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