Supplementary Information

Templated polar order of a guest in a quasi-racemic organic crystal

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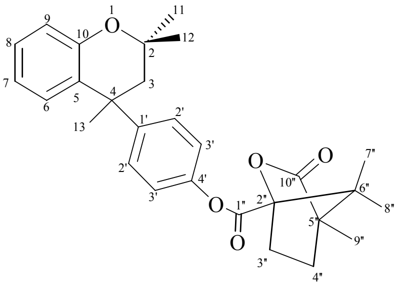
1. General Procedures and Instrumental Analyses

Dianin's compound **1** were prepared according to Baker *et al.*[1] Literature methods were adapted for the synthesis of compounds **2**-**12**.[2-4] N,N′-dimethylformamide (DMF) was distilled over anhydrous $MgSO_4$ and dimethylthiocarbamoyl chloride was crystallized twice from petroleum-ether. Flash chromatography was carried out using silica gel Art 9385 Kieselgel 60.

Melting points were determined on a TA Instruments Q100 differential scanning calorimeter or a Gallenkamp melting point apparatus, and are uncorrected. Mass spectra were recorded on an Agilent MSD 5975 GCMS instrument AMD 604 (EI+, 70 eV). NMR spectra were recorded on a Varian 300/400 FT or INOVA 600 MHz spectrometer (^{1}H NMR at 300/400/600 MHz, ^{13}C NMR at 75/100/150 MHz) with chemical shifts reported relative to an internal solvent resonance. The specific rotation for optically active substances was measured on a Bellingham and Stanley Ltd. ADP220 polarimeter in spectroscopic grade ethanol. Optical rotations could not be determined for **4a**, **6a** and **8** since these materials crystallize from ethanol even at high dilution before measurements can be carried out. Owing to limited sample availability, a measurement of optical rotation for **10** could also not be obtained. Attenuated total reflection infrared spectroscopy was carried out on a Thermo Nicolet instrument using a Smart Golden Gate ATR attachment.

2. Synthesis and Characterization

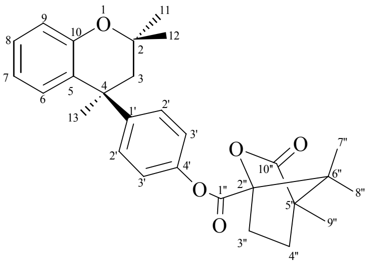
(*S*,*S*) and (*R*,*S*)-[*p*-(2,2,4-Trimethylchroman-4-yl)phenyl]camphanate (4)



Dianin's compound (19.09 mmol, 5.371 g), DMAP (2.1 mmol, 256 mg) and triethylamine (60.24 mmol, 6.096 g) were dissolved in *ca* 70 mL dichloromethane. (1*S*)-(-)-camphanic chloride was added (23.08 mmoL, 5.00 g). The mixture was stirred at room temperature for 27 hours to afford a clear orange solution, after which ice was added to quench the reaction. The aqueous phase was extracted with dichloromethane and the combined organic phases were washed with water, dried over $MgSO_4$ and the solvent removed under reduced pressure to afford an off-white solid material. Ethanol was added and the mixture refluxed. The flask was then cooled in an ice bath and the solution filtered to separate the white powder, which was washed with cold ethanol. The product was dried under vacuum for 3 hours.

Yield: 78.8%; M.p. 140.0-150.0 ºC (Ethanol); **δ_H ($CDCl_3$, 400 MHz)** 0.924 (3H, s, H-12), 1.084 (3H, s, H-7''), 1.133 (3H, s, H-8''), 1.158 (3H, s, H-9''), 1.353 (3H, s, H-11), 1.713 (3H, s, H-13), 1.755 (1H, ddd, ^2J = 13.1, ^3J = 9.4, ^4J = 4.2 Hz, H-4''en), 1.982 (1H, ddd, ^2J = 13.2, ^3J = 10.7, ^4J = 4.4 Hz, H-4''ex), 2.095 (1H, d, ^2J = 14.2 Hz, H-3α), 2.180 (1H, ddd, ^2J = 13.5, ^3J = 9.3, ^4J = 4.5 Hz, H-3''en), 2.374 (1H, d, ^2J = 14.2 Hz, H-3β), 2.547 (1H, ddd, ^2J = 13.4, ^3J = 11.0, ^4J = 4.2 Hz, H-3''ex), 6.883 (1H, d, ^3J = 8.3 Hz, H-9), 6.932 (1H, t, ^3J = 7.3 Hz, H-7), 7.001 (2H, d, ^3J = 8.6 Hz, H-3'), 7.173 (1H, t, ^3J = 6.9 Hz, H-8), 7.186 (1H, d, ^3J = 7.7 Hz, H-6), 7.230 (2H, d, ^3J = 8.5 Hz, H-2'); **δ_C ($CDCl_3$, 100 MHz)** 9.72 (C-9''), 16.85 (C-7'', C-8''), 27.44 (C-12), 27.46 (C-12), 28.97 (C-4''), 29.94 (C-11), 30.74 (C-3''), 32.41 (C-13), 32.43 (C-13), 39.19 (C-4), 50.30 (C-3), 54.65 (C-6''), 54.88 (C-5''), 74.51 (C-2), 90.83 (C-2''), 118.22 (C-9), 120.21 (C-7), 120.68 (C-3'), 127.46 (C-1'), 127.48 (C-1'), 127.95 (C-8), 128.14 (C-2'), 129.35 (C-6), 147.38 (C-4'), 148.33 (C-5), 148.36 (C-5), 153.58 (C-10), 166.10 (C-1''), 177.80 (C-10''); IR ν_{max} (ATR, cm^{-1}) 2973 (sp^3 C-H stretch), 1791 and 1763 (C=O (ester) stretch), 1502 (C=C (aromatic) stretch), 1204, 1174 and 1053 (C-O stretch), 810 (out-of-plane C-H (para) aromatic bend), 760 (out-of-plane C-H (ortho) aromatic bend).

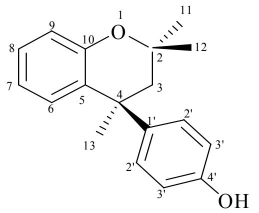
(*S*,*S*)-[*p*-(2,2,4-Trimethylchroman-4-yl)phenyl]camphanate (4a)



A diastereomeric mixture of Dianin-camphanoates (13.93 mmol, 6.25 g) was dissolved in a minimum of 2-methoxy-ethanol at 60 °C. Upon standing, white crystals formed, which were filtered and washed with methoxy-ethanol. The product was dried under high vacuum.

Yield: 28%; M.p. 180.7 ºC (Methoxy-ethanol); $[\alpha]_D^{25.5}$ = -134.4±2.6º (c = 0.99, Benzene); **δ_H** equivalent to diastereomeric mixture (**4**); **δ_C ($CDCl_3$, 75.5 MHz)** 9.72 (C-9''), 16.85 (C-7'', C-8''), 27.47 (C-12), 28.97 (C-4''), 29.94 (C-11), 30.74 (C-3''), 32.45 (C-13), 39.19 (C-4), 50.30 (C-3), 54.65 (C-6''), 54.88 (C-5''), 74.51 (C-2), 90.83 (C-2''), 118.22 (C-9), 120.21 (C-7), 120.68 (C-3'), 127.49 (C-1'), 127.95 (C-8), 128.14 (C-2'), 129.35 (C-6), 147.83 (C-4'), 148.36 (C-5), 153.58 (C-10), 166.10 (C-1''), 177.80 (C-10'').

(*S*)-4-*p*-Hydroxyphenyl-2,2,4-trimethylchroman (5)



(*S,S*)-Dianin camphanoate (3.34 mmol, 1.5 g) and sodium hydroxide (30.06 mmol, 1.20 g) were suspended/dissolved in a methanol/water (4:1) mixture. The reaction mixture was initially milky but clarified after some stirring. After an additional 2 hours of stirring, the methanol was removed under reduced pressure and this afforded a milky residue. Water was added and the clear solution acidified (pH 2). The aqueous mixture was extracted with three portions of dichloromethane, the combined organic phases dried over $MgSO_4$ and the solvent removed under reduced pressure. A milky white oil was obtained. The crude product was dissolved in a minimum of methanol under reflux and left for 2 days to crystallize. Trace amounts of (*R*)-DC were still present and clathrates formed. The crystals of racemic clathrates were removed by filtration and a few drops of water were added to the methanol mother liquor which now only contained the product (*S*)-DC. Upon slow evaporation of the solvent, colorless resolved crystals of **1** formed. The product was dried under high vacuum. These results were confirmed by determining the melting points of the racemic clathrates and the (*S*)-**1**, respectively by differential scanning calorimetry.

Yield: 72.52%; M.p. 135.6-139.7 ºC (Methanol/H_2O); $[\alpha]_D^{18.2}$ = -24.10º (c=0.996, Ethanol); **δ_H ($CDCl_3$, 300 MHz)** 0.914 (3H, s, H-12), 1.344 (3H, s, H-11), 1.678 (3H, s, H-13), 2.059 (1H, d, ^2J = 14.08 Hz, H-3α), 2.347 (1H, d, ^2J = 14.11 Hz, H-3β), 4.940 (1H, s, OH), 6.701 (2H, td, ^3J = 8.93, ^4J = 2.19 Hz, H-3'), 6.871 (1H, dd, ^3J = 8.35, ^4J = 1.06 Hz, H-9), 6.925 (1H, td, ^3J = 7.47, ^4J = 1.29 Hz, H-7), 7.051 (2H, td, ^3J = 8.83, ^4J = 2.15 Hz, H-2'), 7.170 (1H, td, ^3J = 8.55, ^4J = 1.67 Hz, H-8), 7.198 (1H, dd, ^3J = 7.42, ^4J = 1.75 Hz, H-6); **δ_C ($CDCl_3$, 75.5 MHz)** 27.33 (C-12), 30.13 (C-11), 32.54 (C-13), 38.74 (C-4), 50.22 (C-3), 74.59 (C-2), 114.76 (C-3'), 118.04 (C-9), 120.03 (C-7), 127.69 (C-8), 128.07 (C-2'), 128.13 (C-1'), 129.37 (C-6), 142.37 (C-5), 153.33 (C-10), 153.58 (C-4'); MS (EI^+) m/z 268 ($M^{+\cdot}$), m/z 253 (100%, $M^{+\cdot}$- CH3$^{\cdot}$); IR ν_{max} (ATR, cm^{-1}) 3431 (O-H stretch (3257 broad band for rac-OH)), 3025 (sp^2 C-H stretch), 2977 and 2929 (sp^3 C-H stretch), 1608 and 1511 (C=C (aromatic) stretch), 1381 and 1373 (CH_3 bend), 1196, 1178 and 1148 (C-O stretch), 836 (out-of-plane C-H (para) aromatic bend), 766 (out-of-plane C-H (ortho) aromatic bend).

(*R,R*) and (*S,R*)-[*p*-2,2,4-Trimethylchroman-4-yl)phenyl]camphanate (6)

The same procedure was followed as for the synthesis of **4**, in this case (1*R*)-(+)-camphanic chloride was reacted with racemic **1**.

(*R,R*)-[*p*-2,2,4-Trimethylchroman-4-yl)phenyl]camphanate (6a)

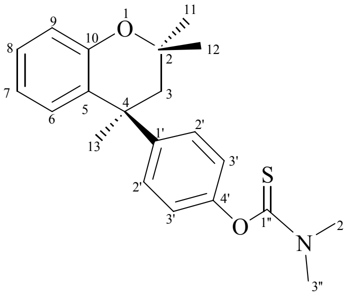
The same procedure was followed as for the fractional crystallization of **4a** from the diastereomeric mixture **4**.

(*R*)-4-*p*-Hydroxyphenyl-2,2,4-Trimethylchroman) (7)

The chirally pure **7** was obtained in the same way as compound **5**.

M.p. 136.5-139.4 ºC (Methanol); $[\alpha]_D^{19.1}$ = +25.15º (c = 0.994, Ethanol).

(*S*)-O-[*p*-(2,2,4-Trimethylchroman-4-yl)phenyl] Dimethylthiocarbamate (8)

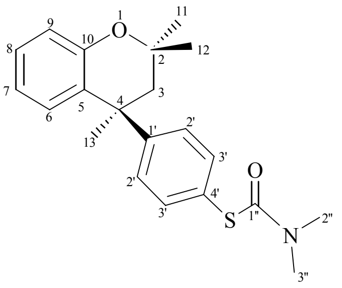


Sodium metal (2.74 mmol, 0.063 g) was dissolved in absolute ethanol and (*S*)-4-*p*-hydroxyphenyl-2,2,4-trimethylchroman (2.39 mmol, 0.6422 g) was added to the solution. The reaction was carried out in an argon atmosphere. The solvent was removed under vacuum to produce the sodium phenoxide salt as a light orange glass. Dimethylthiocarbamoyl chloride (4.12 mmol, 0.51 g) dissolved in N,N′-dimethylformamide was added drop-wise to a solution of the Dianin phenoxide in the same solvent at 10 °C under a positive argon pressure. The reaction mixture was stirred for 1.5 hours at 40-45 °C. Upon cooling, the reaction mixture was added to water and extracted with benzene/hexane (4:1). The combined organic extracts were washed with water, 5% NaOH- , NaCl-solution (3x) and dried over $MgSO_4$. The organic layer was then filtered and the solvent removed under reduced pressure to afford a yellow solid. The yellow solid was dissolved in a minimum volume of methanol and a few drops of benzene at 60 °C and recrystallised twice, washing each time with cold methanol, to yield white crystals. The product was dried under vacuum.

Yield: 51.4%; M.p. 175.0-175.8 ºC (Methanol); **δ_H ($CDCl_3$, 300 MHz)** 0.949 (3H, s, H-12), 1.360 (3H, s, H-11), 1.739 (3H, s, H-13), 2.100 (1H, d, ^2J = 14.31 Hz, H-3α), 2.406 (1H, d, ^2J = 14.10 Hz, H-3β), 3.327 (3H, s, H-3"), 3.455 (3H, s, H-2"), 6.886 (1H, dd, ^3J = 8.09, ^4J = 1.3 Hz, H-9), 6.938 (2H, d, ^3J = 8.92 Hz, H-3'), 6.938 (1H, td, ^3J = 8.08, ^4J = 1.35 Hz, H-7), 7.186 (1H, td, ^3J = 7.77, ^4J = 1.66 Hz, H-8), 7.216 (2H, d, ^3J = 8.71 Hz, H-2'), 7.213 (1H, dd, ^3J =

7.67, ^4J = 1.66 Hz, H-6); **δ_C (CDCl$_3$, 75.5 MHz)** 27.46 (C-12), 29.95 (C-11), 32.42 (C-13), 38.64 (C-3''), 39.15 (C-4), 43.22 (C-2''), 50.33 (C-3), 74.54 (C-2), 118.07 (C-9), 120.11 (C-7), 122.05 (C-3'), 127.69 (C-2'), 127.72 (C-1'), 127.79 (C-8), 129.49 (C-6), 147.53 (C-5), 151.84 (C-4'), 153.55 (C-10), 188.69 (C-1''); IR ν_{max} (ATR, cm^{-1}) 3025 (sp^2 C-H stretch), 2961 and 2926 (sp^3 C-H stretch), 1578 and 1498 (C=C (aromatic) stretch), 1348 (CH$_3$ bend), 1201 and 1128 (C-O stretch), 827 (out-of-plane C-H (para) aromatic bend), 766 (out-of-plane C-H (ortho) aromatic bend).

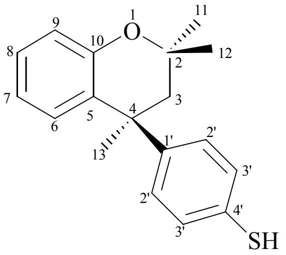
(*S*)-S-[*p*-(2,2,4-Trimethylchroman-4-yl)phenyl] Dimethylthiocarbamate (9)



(*S*)-O-[p-(2,2,4-Trimethylchroman-4-yl)phenyl] dimethylthiocarbamate (1.4 mmol ,0.5 g) was placed in a glass tube to which a glass stopcock was attached. The sample was then evacuated and the stopcock closed. Using a flame, the glass tube was then sealed under vacuum. The evacuated ampoule was heated at 270 °C for 9 hours in a Büchi oven and the white crystals converted to a yellow material. The ampoule was opened and the yellow compound was dissolved in CH$_2$Cl$_2$ and washed into a round bottomed flask. Flash chromatography was carried out with gradient elution, starting with a 1% ethyl-acetate mixture and ending with a 50/50 ethyl-acetate, petroleum-ether solution. The desired fractions were combined and the solvent was removed under reduced pressure to afford a clear oil. The product was then dissolved and crystallized from petroleum-ether (ethanol-benzene used in literature for racemic product).[1] It is also possible to selectively crystallize unconverted (*S*)-O-Dianin-thiocarbamate (**8**) from MeOH.

Yield: 71.2%; M.p. 84.7-84.4 ºC (Petroleum-ether); R$_f$(**9**) = 0.33 in 10% ethylacetate, petroleum-ether; $[\alpha]_D^{15.7}$ = +32.87º (c=0.998, Ethanol); **δ_H (CDCl$_3$, 300 MHz)** 0.949 (3H, s, H-12), 1.360 (3H, s, H-11), 1.722 (3H, s, H-13), 2.101 (1H, d, ^2J = 14.23 Hz, H-3α), 2.405 (1H, d, ^2J = 14.22 Hz, H-3β), 3.060 (6H, br s, H-2'' and H-3''), 6.889 (1H, dd, ^3J = 8.15, ^4J = 1.57 Hz, H-9), 6.932 (1H, td, ^3J = 7.630, ^4J = 1.38 Hz, H-7), 7.188 (1H, td, ^3J = 7.068, ^4J = 1.40 Hz, H-8), 7.194 (1H, dd, ^3J = 7.147, ^4J = 1.70 Hz, H-6), 7.238 (2H, d, ^3J = 8.80 Hz, H-3'), 7.370 (2H, d, ^3J = 8.53 Hz, H-2'); **δ_C (CDCl$_3$, 75.5 MHz)** 27.42 (C-12), 29.85 (C-11), 32.35 (C-13), 36.88 (C-2'' and C-3''), 39.37 (C-4), 50.19 (C-3), 74.49 (C-2), 118.11 (C-9), 120.14 (C-7), 125.75 (C-4'), 127.41 (C-5), 127.60 (C-2'), 127.85 (C-8), 129.55 (C-6), 135.32 (C-3'), 151.36 (C-1'), 153.54 (C-10), 167.05 (C-1''); IR ν_{max} (ATR, cm^{-1}) 3025 (sp^2 C-H stretch), 2967 and 2920 (sp^3 C-H stretch), 1665 (C=O (amide) stretch), 1577 and 1486 (C=C (aromatic) stretch), 1389 (CH_3 bend), 1204 and 1089 (C-O stretch), 825 (out-of-plane C-H (para) aromatic bend), 760 (out-of-plane C-H (ortho) aromatic bend).

(*S*)-4-*p*-Mercaptophenyl-2,2,4-trimethylchroman (10)



(*S*)-S-[*p*-(2,2,4-Trimethylchroman-4-yl)phenyl] dimethylthiocarbamate (1.97 mmoles, 0.7 g) was dissolved in methanol and upon the addition of 15 ml aq. 10% NaOH solution the reaction mixture turned light orange and then milky white. The reaction was continually stirred for 2 days at 70 ºC under nitrogen and gradually turned clear. The mixture was allowed to cool to room temperature and was acidified to pH 2 using HCl. Upon acidification, a white precipitate formed, and the mixture was transferred to a separating funnel. The product was extracted three times with chloroform, the combined organic extracts washed once with water and dried using $MgSO_4$. After filtration the excess solvent was removed under reduced pressure to afford a yellow oil, which solidified partially on standing. Flash chromatography was done using ethyl-acetate:petroleum-ether (1:7) as eluent. The fractions containing product were combined and the solvent removed under reduced pressure to afford a white powder. The white powder was then dissolved in a minimum of cyclohexane at 80 ºC. After seeding, colorless crystals started to form. Crystals were filtered and washed with cold cyclohexane and dried under vacuum. Colorless plates suitable for single-crystal diffraction could be isolated from dichloromethane-cyclohexane.

Yield: 57.1%; M.p. 133.8-134.9 ºC (Cyclohexane); R_f = 0.44 in ethyl-acetate:petroleum-ether (1:7);**δ_H ($CDCl_3$, 300 MHz)** 0.916 (3H, s, H-12), 1.346 (3H, s, H-11), 1.675 (3H, s, H-13), 2.068 (1H, d, ^2J = 14.16 Hz, H-3α), 2.347 (1H, d, ^2J = 14.17 Hz, H-3β), 3.375 (1H, s, SH), 6.878 (1H, dd, ^3J = 7.93, ^4J = 1.10 Hz, H-9), 6.927 (1H, td, ^3J = 7.57, ^4J = 1.22 Hz, H-7), 7.071 (2H, d, ^3J = 8.55 Hz, H-2'), 7.154 (2H, d, ^3J = 8.30 Hz, H-3'), 7.166 (1H, dd, ^3J = 7.57, ^4J = 1.71 Hz, H-6), 7.179 (1H, td, ^3J = 7.32, ^4J = 1.71 Hz, H-8); **δ_H ($CDCl_3$, 75.5 MHz)** 27.41 (C-12), 30.01 (C-11), 32.37 (C-13), 39.06 (C-4), 50.09 (C-3), 74.52 (C-2), 118.15C-9), 120.12C-7), 127.48C5 or C4'), 127.51C5 or C4'), 127.75C-2'), 127.86C-8), 129.33C-6), 129.37C-3'), 147.91C-1'), 153.58C-10); MS (EI^+) m/z 284 ($M^{+\cdot}$), m/z 269 (100%, $M^{+\cdot}$- $CH3^{\cdot}$); IR ν_{max} (ATR, cm^{-1}) 3025 (sp^2 C-H stretch), 2974 and 2929 (sp^3 C-H stretch), 2501 (S-H stretch), 1577 and 1483 (C=C (aromatic) stretch), 1384 (CH_3 bend), 1204 (C-O stretch), 1101 (C-O stretch), 827 (out-of-plane C-H (para) aromatic bend), 760 (out-of-plane C-H (ortho) aromatic bend).

O-[*p*-(2,2,4-Trimethylchroman-4-yl)phenyl] Dimethylthiocarbamate (11)

The same procedure was followed as for the synthesis of **8**, using racemic **1** as starting material.

Yield: 57.57%; M.p. 141.9-144.7 ºC (Methanol); Characterization equivalent to **8**.

S-[*p*-(2,2,4-Trimethylchroman-4-yl)phenyl] Dimethylthiocarbamate (12)

The same procedure was followed as for the synthesis of **9**. The crude product (light yellow solid) was purified by flash chromatography by adsorbing the product onto silica gel and carrying out a gradient elution starting with a 7% ethyl-acetate, petroleum-ether mixture and increasing the polarity gradually to 20% ethyl-acetate content. The product was obtained as a white crystalline solid. The material was recrystallized from ethanol-benzene to afford light yellow crystals. Unconverted **11** was also recovered after chromatography (R_f = 0.48, 15% Ethyl-acetate:petroleum-ether). The product was dried under vacuum. A small amount of material was redissolved in methanol, and slow evaporation yielded crystals suitable for single crystal diffraction.

Yield: 96.43%, M.p. 124.4-126.5 ºC; $R_f = 0.36$ in 15% ethyl-acetate, petroleum-ether; Characterization equivalent to **9**.

4-*p*-Mercaptophenyl-2,2,4-trimethylchroman (2)

The same procedure was followed as for the synthesis of **10**. Crystals of the racemic clathrate suitable for single crystal diffraction were grown from carbon tetrachloride.

Yield: 75.23%; M.p. 105.8-109.6 ºC (Carbon tetrachloride); Characterization equivalent to **10**.

3. Crystallographic Information

Note: Structures of **1a** and **2a** have been reported before (CCDC Refcodes: SIHJEY and MPMCHR), but we repeated the structure determinations in order to compare all three structures at the same temperature (100 K).

Intensity data were collected on a Bruker SMART Apex CCD diffractometer[5] using graphite monochromated Mo-K_α radiation (λ = 0.71073 Å). The temperature of the crystals was controlled using an Oxford Cryostream Cooler. Data reduction was carried out by means of a standard procedure using the Bruker software package SAINT.[6] Where necessary, systematic errors in the intensity data were corrected for absorption using SADABS.[7,8] The structures were solved by direct methods and expanded using SHELXS-97.[9] All ordered non-hydrogen atoms were refined anisotropically by means of full-matrix least-squares calculations on F^2 using SHELXL-97[9] within the X-Seed[10] environment. Where appropriate, the hydrogen atoms were placed in calculated positions using riding models and assigned isotropic thermal parameters 1.2 times those of their parent atoms for CH_2, aromatic C and O-H groups, or 1.5 times those of their parent atoms for CH_3 groups. In special cases, hydrogen atoms were located in difference electron density maps and their isotropic thermal parameters were refined freely. Crystals were selected based on their appropriate size for data collection, and they were therefore not cut prior to analysis.

Modeling guest disorder: In all three structures, the host non-hydrogen atoms were located by direct methods and guest molecules were modeled during subsequent structure expansion by rationalizing difference electron density maps.

In **1a**, three unique guest atoms were located (⅓ of a carbon atom and ⅓ of a chlorine atom, each situated on a threefold axis, and one chlorine atom in a general position). The guest molecule is required by symmetry to be equally disordered over two positions (each with a site-occupancy of 0.5) about a site of 3-bar symmetry such that each guest-accessible cavity only contains one guest molecule. According to this model, the guest within any cavity can assume one of two possible orientations (Fig. S1) – i.e. with one of its C–Cl bonds aligned along either [001] or [00-1]. Owing to centrosymmetry of the guest-accessible cavity, both orientations are equally likely, thus accounting for the 1:1 disorder.

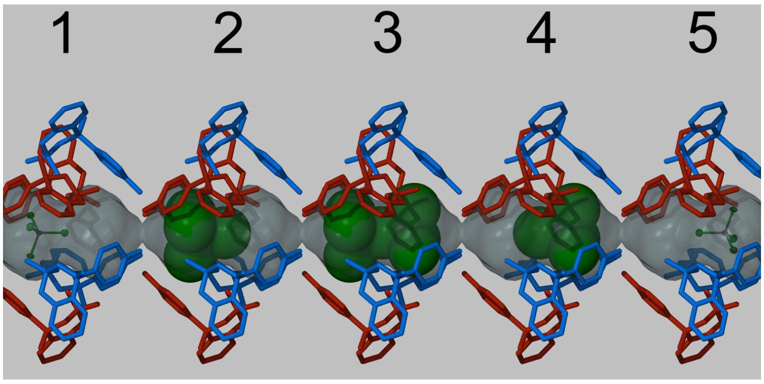


Fig. S1: Rationalization of the disorder of the guest molecules in **1a**. Positions 1 and 5 show thermal ellipsoid (50% probability) representations of the two equally likely orientations of the guest within a cavity. Positions 2 and 4 show the two possible guest molecule orientations as van der Waals surfaces and position 3 shows the disordered model of the guest molecules. It is apparent that the guest-accessible cavities are not sufficiently large to each accommodate two guest molecules. Host molecules are shown in capped-stick representation with the two enantiomers colored blue and red. Hydrogen atoms are omitted for clarity and guest-accessible space is shown as a semitransparent grey surface mapped with MSROLL[11] and using a probe radius of 1.5 Å.

In **2a**, two unique guest molecules were located, each consisting of one half of a CCl_4 molecule situated on a threefold axis (i.e. $^1/_6$ of a carbon atom and $^1/_6$ of a chlorine atom, each situated on a threefold axis, and ½ of a chlorine atom in a general position). This model is consistent with the presence of a total of two guest molecules per cavity. Each molecule is required by symmetry to be equally disordered over two possible positions and orientations (Fig. S2).

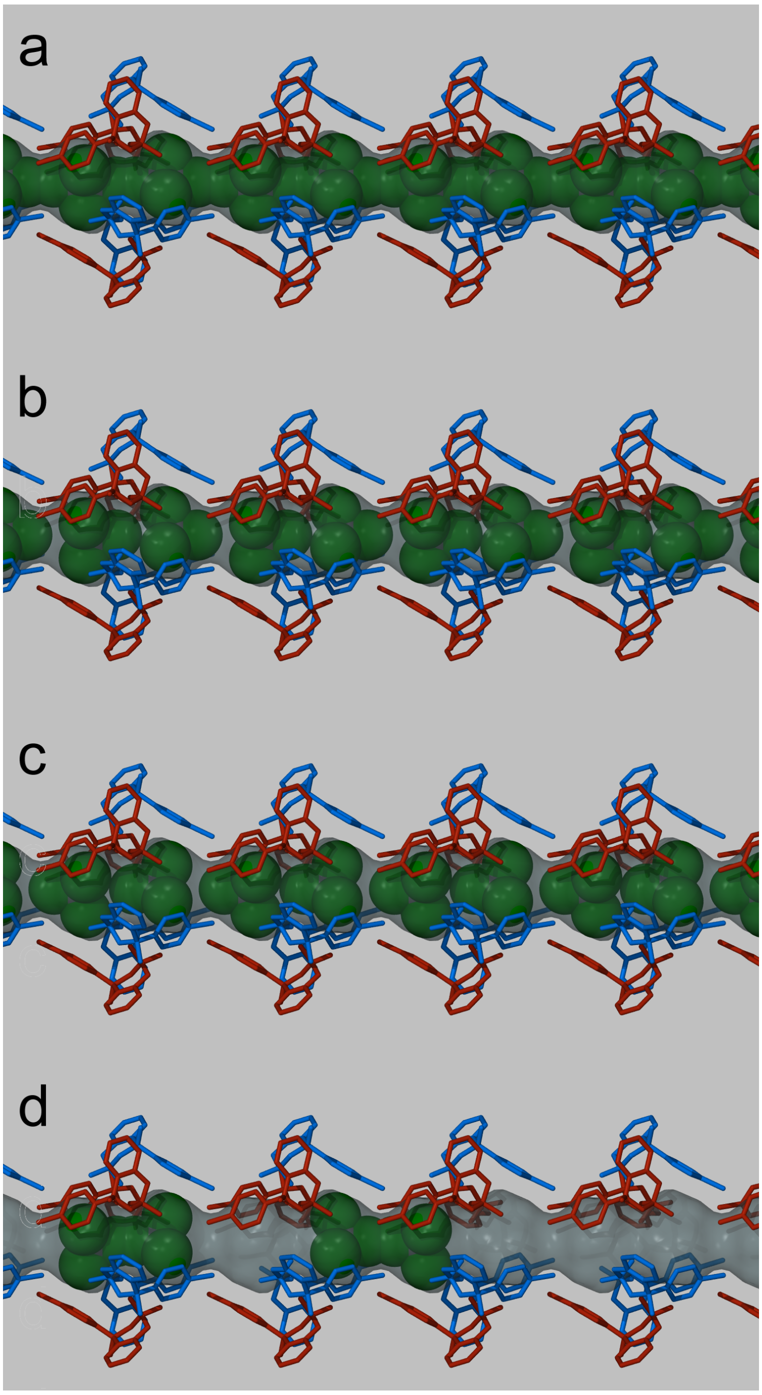


Fig. S2: Rationalization of the disorder of the guest molecules in **2a**. (a) The overall disordered model with guest molecules shown in space filling representation. (b) All the guests within one column of host molecules stacked along [001] oriented with a C–Cl directed towards the right. (c) All the guests within one column of host molecules stacked along [001] oriented with a C–Cl directed towards the left. (d) Space filling representation of guest molecules showing that two guests within one cavity (left) or adjacent guests of adjacent cavities (center) cannot be aligned antiparallel to each other without significant van der Waals overlap of Cl atoms. Therefore, assuming that each column is continuous and that each cavity is occupied by two guest molecules, the placement of any guest molecule requires parallel alignment of its partner within the same cavity. Furthermore, the placement of two guests within any cavity requires that the two guests within the two adjacent cavities be aligned in the same direction. The overall 50/50 orientational disorder of the guests required by the space group symmetry of the structure requires that, while each column might contain polar ordered guest molecules, neighboring columns need not be aligned in the same direction. Host molecules are shown in capped-stick representation with the two enantiomers colored blue and red. Hydrogen atoms are omitted for clarity and guest-accessible space is shown as a semitransparent grey surface mapped with MSROLL and using a probe radius of 1.5 Å.

In **3a**, four unique guest molecules were located in each cavity and the final model was consistent with guest disorder over two possible positions (Fig. S3). Electron density summation (using the program SQUEEZE[12]) indicated that each cavity is occupied by a total of two guest molecules. Two guest molecules are oriented such that each has a C–Cl bond situated on a crystallographic threefold axis and directed along [001]. Another pair of molecules are oriented in the opposite direction. Based on space filling considerations, it can be rationalized that positioning one CCl_4 molecule within the cavity requires the second guest to have the same orientation with respect to the *c* axis. Therefore, even though they are not related by symmetry, it follows that each pair of guest molecules with the same orientation should have the same site occupancy factor. In order to determine the final model, the site occupancies of the two orientations were allowed to refine, but with their sum constrained to unity. The final site occupancy of the orientation shown in light green (Fig. S3) converged to 15% while that of the dark green orientation was 85% (i.e. the balance of full occupancy).

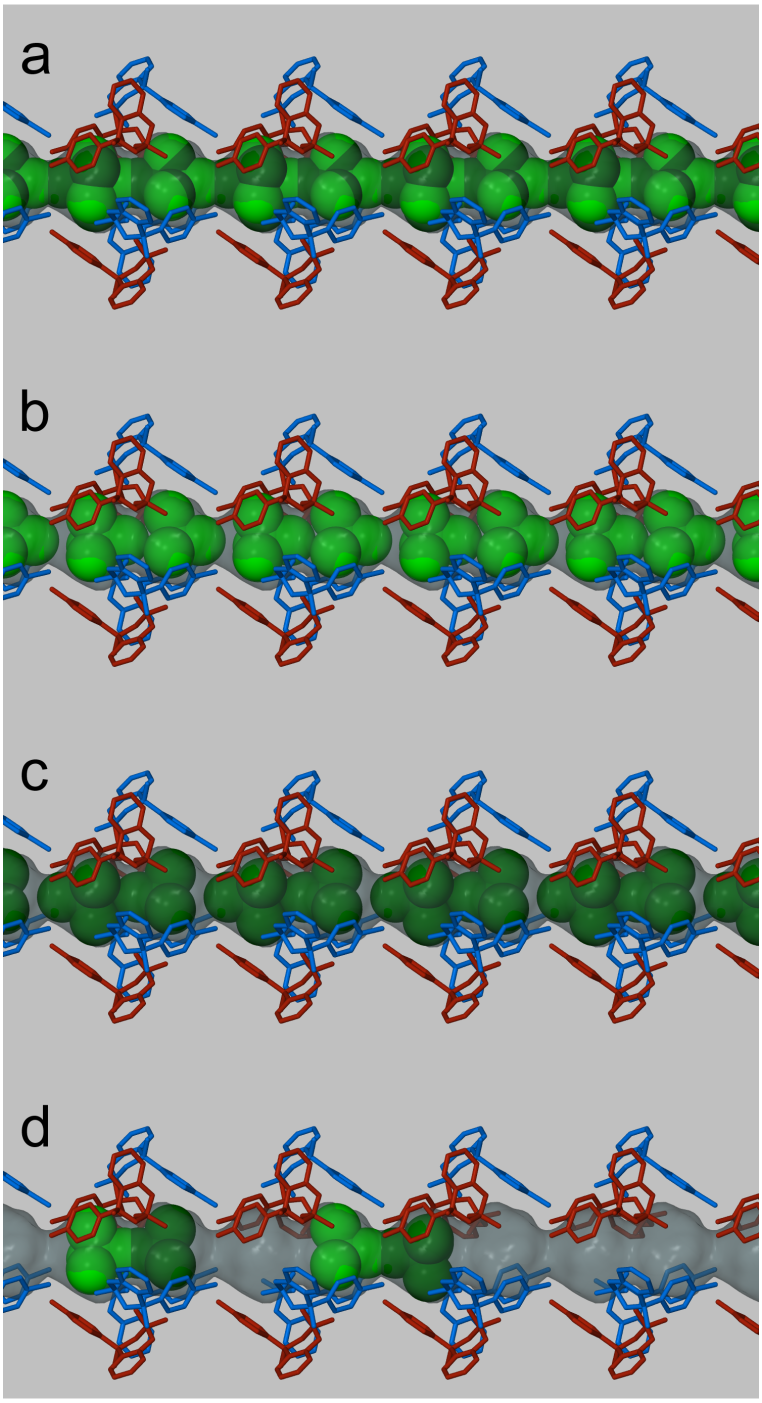


Fig. S3: Rationalization of the disorder of the guest molecules in **3a**. (a) The overall disordered model with guest molecules shown in space filling representation. (b) All the guests within one column of host molecules stacked along [001] oriented with a C–Cl directed towards the right. (c) All the guests within one column of host molecules stacked along [001] oriented with a C–Cl directed towards the left. (d) Space filling representation of guest molecules showing that two guests within one cavity (left) or adjacent guests of adjacent cavities (center) cannot be aligned antiparallel to each other without significant van der Waals overlap of Cl atoms. Therefore, assuming that each column is continuous and that each cavity is occupied by two guest molecules, the placement of any guest molecule requires parallel alignment of its partner within the same cavity. Furthermore, the placement of two guests within any cavity requires that the two guests within the two adjacent cavities be aligned in the same direction. Unlike the structure of **2a**, the two orientations are not required by space group symmetry to have equal site occupancies – indeed, the guest molecules shown as light green have a site occupancy factor of 15% while those shown in dark green have a site occupancy of 85%. Since the host columns all have the same orientation with respect to the crystallographic *c* axis, it follows that there is an overall polar arrangement of guest molecules in the ratio 85:15 in favor of one direction along *c* over the other. Host molecules are shown in capped-stick representation with the two enantiomers colored blue and red (representing the thiol and hydroxyl derivatives, respectively). Hydrogen atoms are omitted for clarity and guest-accessible space is shown as a semitransparent grey surface mapped with MSROLL and using a probe radius of 1.5 Å.

Crystal data for 1a: $C_{109}H_{120}Cl_4O_{12}$, *M* = 1763.96, colorless block, 0.38 × 0.23 × 0.11 mm^3, trigonal, space group *R*-3 (No. 148), *a* = *b* = 26.8078(12), *c* = 10.8706(10) Å, *V* = 6765.6(8) Å^3, *Z* = 18, D_c = 1.299 g/cm^3, F_{000} = 2814, Bruker APEX CCD area-detector, MoKα radiation, λ = 0.71073 Å, *T* = 100(2)K, $2\theta_{max}$ = 56.5°, 14393 reflections collected, 3588 unique (R_{int} = 0.0569). Final *GooF* = 1.037, *R1* = 0.0515, *wR2* = 0.1288, *R* indices based on 2853 reflections with I >2sigma(I) (refinement on F^2), 200 parameters, 2 restraints. Lp and absorption corrections applied, μ = 0.196 mm^{-1}.

Crystal data for 2a: $C_{110}H_{120}Cl_8O_6S_6$, *M* = 2014.08, light yellow block, 0.30 × 0.27 × 0.21 mm^3, trigonal, space group *R*-3 (No. 148), *a* = *b* = 26.6320(19), *c* = 12.0349(17) Å, *V* = 7392.3(13) Å^3, *Z* = 3, D_c = 1.357 g/cm^3, F_{000} = 3180, Bruker APEX CCD area-detector, MoKα radiation, λ = 0.71073 Å, *T* = 100(2)K, $2\theta_{max}$ = 56.6°, 15611 reflections collected, 3863 unique (R_{int} = 0.0602). Final *GooF* = 1.063, *R1* = 0.0651, *wR2* = 0.1855, *R* indices based on 3220 reflections with I >2sigma(I) (refinement on F^2), 215 parameters, 6 restraints. Lp and absorption corrections applied, μ = 0.412 mm^{-1}.

Crystal data for 3a: $C_{110}H_{120}Cl_8O_9S_3$, *M* = 1965.87, colorless block, 0.25 × 0.21 × 0.18 mm^3, trigonal, space group *R*3 (No. 146), *a* = *b* = 26.6670(16), *c* = 11.7710(14) Å, *V* = 7249.2(11) Å^3, *Z* = 3, D_c = 1.351 g/cm^3, F_{000} = 3108, Bruker APEX CCD area-detector, MoKα radiation, λ = 0.71073 Å, *T* = 100(2)K, $2\theta_{max}$ = 56.5°, 15661 reflections collected, 7407 unique (R_{int} = 0.0346). Final *GooF* = 0.976, *R1* = 0.0593, *wR2* = 0.1375, *R* indices based on 5469 reflections with I >2sigma(I) (refinement on F^2), 410 parameters, 35 restraints. Lp and absorption corrections applied, μ = 0.358 mm^{-1}. Absolute structure parameter = 0.06(7) (Flack, H. D. *Acta Cryst.* **1983**, *A39*, 876-881).

4. Desolvation Experiments

The carbon tetrachloride clathrates **1a**-**3a** were studied by thermogravimetric analysis (TGA) to confirm the host:guest ratios and to determine the temperature range of guest removal. Thermograms were recorded using a heating rate of 2.5 °C min^{-1} and guest losses were observed at onset temperatures (T_{on}) of 154.2, 74.1 and 66.8 ºC for compounds **1a**-**3a**, respectively, corresponding to host:guest ratios of 3:1 and 3.53:1 for **2a** and **3a** (Fig. S4). The higher than expected host:guest ratio for **3a** was attributed to the presence of enantiomerically pure crystals (of (*R*)-**1** and (*S*)-**2**), which contain no solvent and would thus lower the overall guest:host ratio. Analysis of the single-crystal structure of **3a** using SQUEEZE[12] indicated the number of electrons within each guest-accessible cavity to be 148.8. This result is in excellent agreement with the presumed presence of two molecules of carbon tetrachloride per cavity (*i.e.* 74 electrons per molecule). In the case of **1a**, it was not possible to accurately determine the host:guest ratio from thermogravimetry because both desolvation and sublimation of the host occur within a very narrow temperature range. However, using single-crystal diffraction data and SQUEEZE[12] (74.4 electrons/cavity), it appears that there is only one guest molecule per cavity.

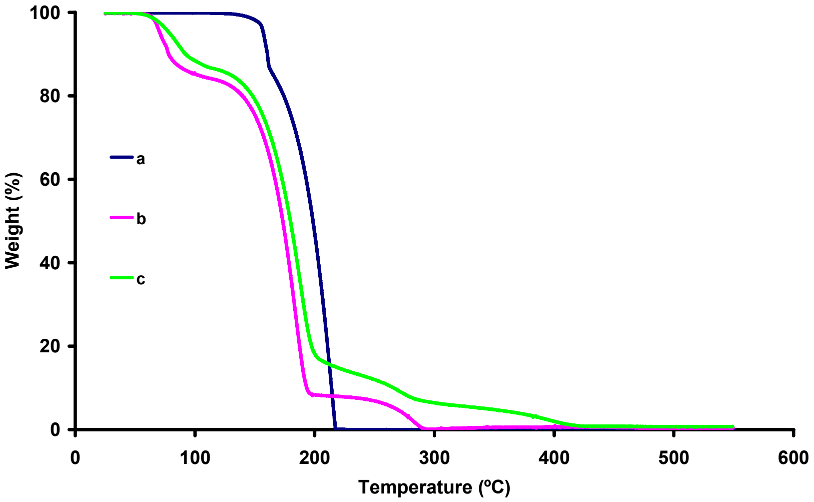


Fig. S4: TGA traces showing onset temperatures of (a) 154.2 ºC for **1a**, (b) 74.1 ºC for **2a** and (c) 66.8 ºC for **3a**.

The guest molecules were removed from crystals of **2a** and **3a** by heating samples of each phase at 75 ºC for 24 hours under vacuum. X-ray powder diffraction analysis (XRPD) analysis indicates that, upon guest desorption of **2a**, the host molecules resolve into their enantiomerically pure (*R*)-**2** and (*S*)-**2** phases, albeit as a polycrystalline mixture of these two phases (Fig. S5). Similarly, guest removal from **3a** results in resolution of the host molecules into (*R*)-**1** and (*S*)-**2** (Fig. S6).

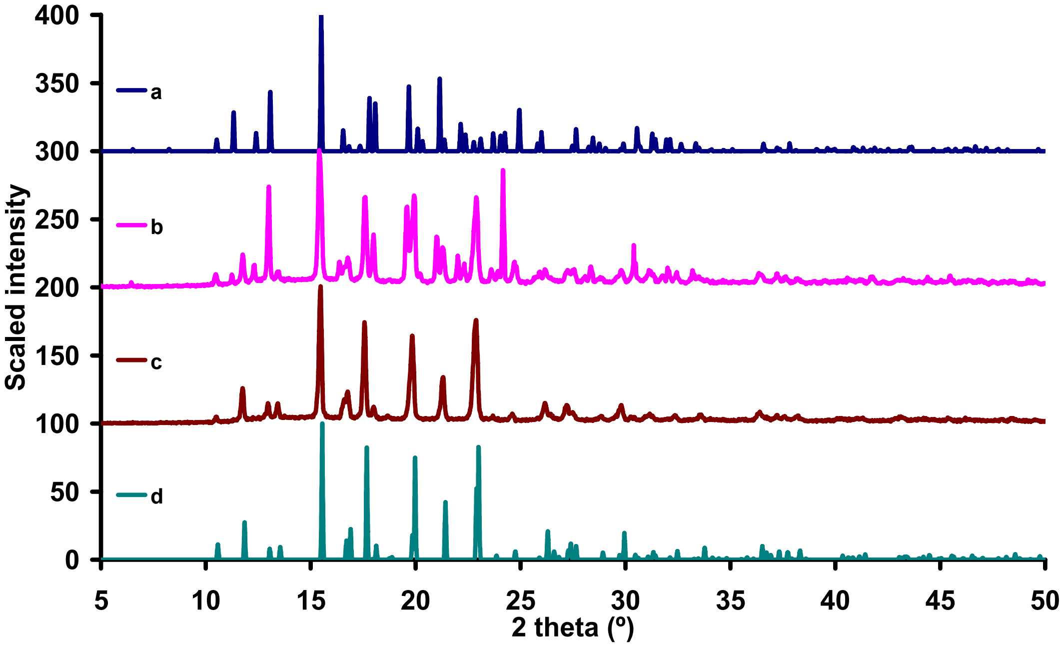


Fig. S5: (a) XRPD pattern simulated from the single-crystal structure of **2a** and experimentally determined XRPD patterns for **2a** (b) before desorption, (c) after desorption and (d) powder pattern calculated from the single-crystal structure of sublimed **2**.

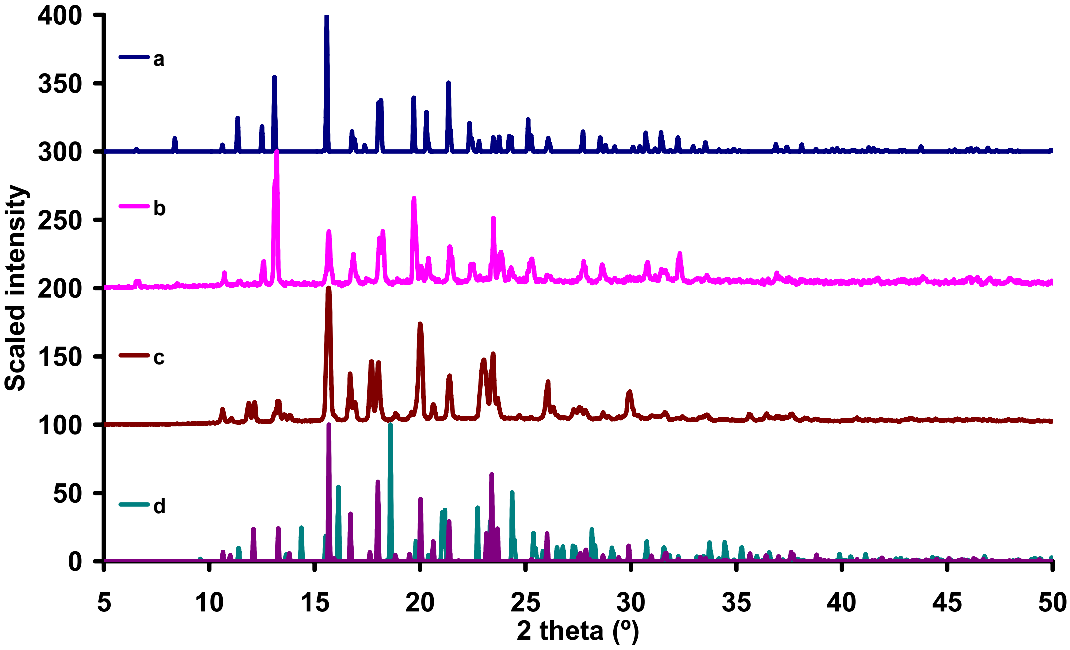


Fig. S6: (a) XRPD diffractogram for **3a** simulated from single-crystal X-ray diffraction and experimental powder patterns of **3a** (b) before and (c) after desorption. (d) Calculated powder pattern for resolved **1** and resolved **2** are shown in purple and green, respectively. The diffractogram of **3a** after desorption (c) appears to be far more consistent with the calculated pattern for **2** than for **1**. This is because resolved **1** is less crystalline than resolved **2** after desorption (as confirmed by electron microscopy, which shows that the particles of **1** are significantly finer than those of **2**).

X-ray powder diffraction experiments were carried out on a Bruker D8 Advance instrument using Cu-K_α radiation (λ = 1.5418 Å) and a point detector. Intensity data were collected using multiple θ-θ scans. Sample preparation included grinding of the material with a mortar and pestle and the sample was rotated (at 15 rpm) during data collection to minimize effects due to preferred orientation. Care was also taken when packing powders into sample holders to minimize peak displacement errors due to sample height inconsistencies. Where necessary, XRPD patterns were calculated from single-crystal X-ray structures using Lazy Pulverix[13] within the X-Seed[14] graphical interface.

Thermogravimetric analysis was carried out using a TA Instruments Q500 thermogravimetric analyser. The balance and sample were purged with dry N_2 gas flowing at a rate of 50 cm^3 min^{-1}. Samples were heated at a rate of either 5 ºC min^{-1}. All post-experimental analyses were carried out using the TA Instruments Universal Analysis program.

5. Second Harmonic Generation Experiments

The second harmonic generation (SHG) measurements (Fig. S7) were carried out using a femtosecond Ti:sapphire laser (Spectra-Physics, Tsunami) producing 80 fs pulses at a repetition rate of 80 MHz, with a center wavelength of 800 nm. The pulse energy of the input beam was attenuated using a polarizer and half-wave plate combination before being tightly focused onto the sample using a 35 mm achromatic lens. The beam diameter at the sample was determined to be 16 μm using the Z-scan technique. The SHG signal was measured in transmission using a photomultiplier tube and a lock-in-amplifier, after being separated from the fundamental by means of a suitable set of filters. The logarithmic plot (Fig. S8) of the SHG response for **3a** has a slope of approximately 2, as expected.

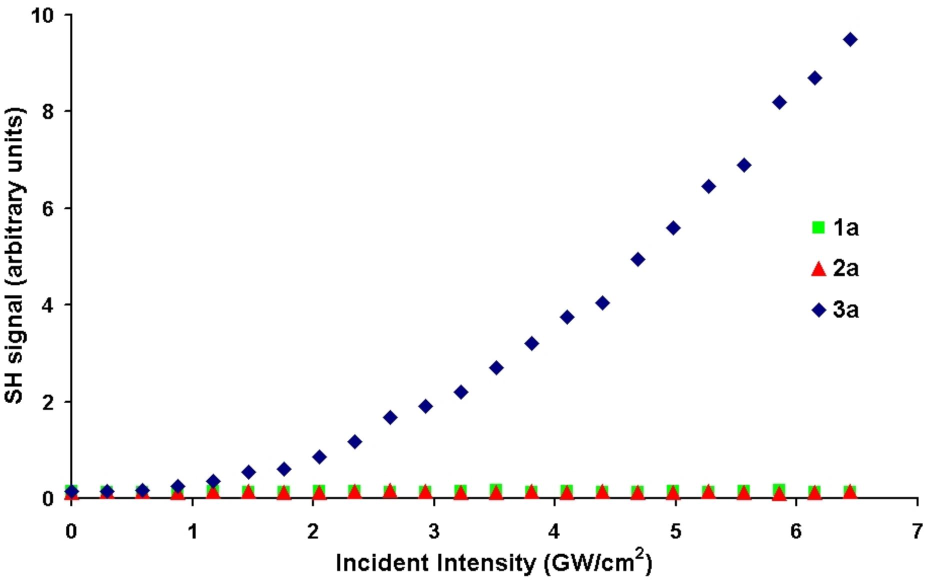


Fig. S7: Plot of the relationship between the input power of the fundamental wave (800 nm) and the measured intensity of the second harmonic wave (400 nm) for **1a** to **3a**.

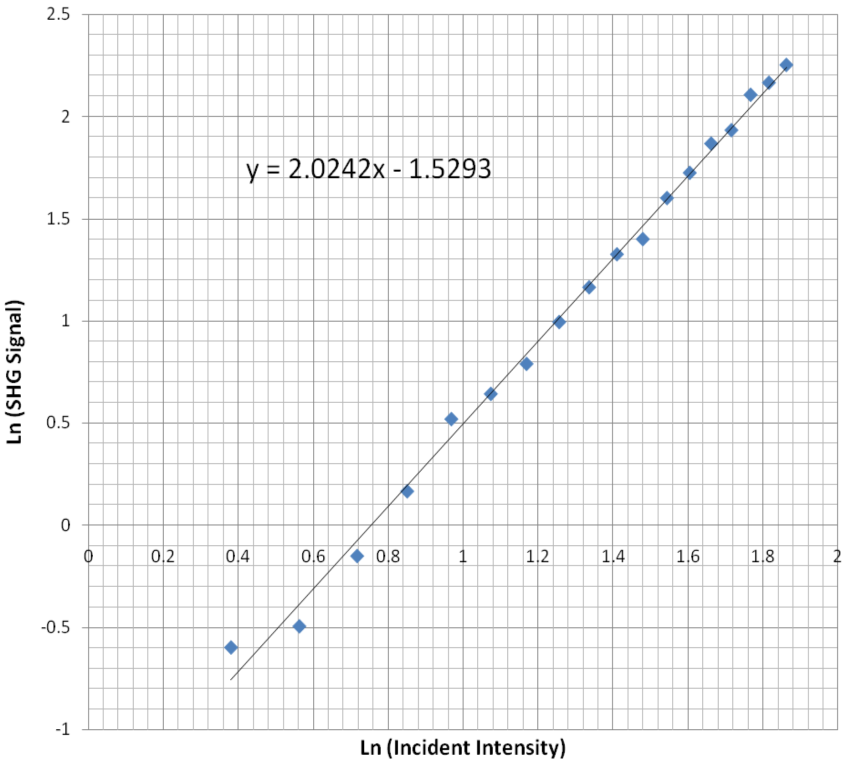


Fig. S8: Logarithmic plot of input power of the fundamental wave (800 nm) and the measured intensity of the second harmonic wave (400 nm) for **3a**. The first five points from Fig. S7 have been omitted owing to inaccuracies associated with measuring very low power levels.

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