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Chiral suprastructures of asymmetric oligothiophene-hybrids induced by a single proline

Supporting Information (SI)

Angela Digennaro, Helma Wennemers, Gururaj Joshi, Sylvia Schmid, Elena Mena-Osteritz, Peter Bäuerle*

General remarks: NMR spectra were recorded on a Bruker AMX 400 spectrometer at 25°C (¹H NMR: 400 MHz, 13 C NMR: 100 MHz). Chemical shifts values (δ) are expressed in parts per million [ppm] using the internal standard tetramethylsilane (¹H NMR, $\delta_{\rm H} = 0.00$) or the solvent as reference (¹H, NMR $\delta_{\rm H} = 7.26$; ¹³C, NMR $\delta_{\rm C} = 77.0$; ¹H, NMR $\delta_{\rm H} = 3.58$, $\delta_{\rm H} = 1.72$ for THF- d_8 , ¹³C NMR, $\delta_{\rm C} = 1.72$ 67.21, $\delta_{\rm C} = 25.31$ for THF- d_8). The following abbreviations reflect the multiplicity of the signals obtained: s = singlet, d = doublet, t = triplet, m = multiplet, combination of dd = doublet of doublets. Infrared (FT-IR) spectra were recorded on a Perkin-Elmer FTIR Spectrum 2000. Matrix-assisted laser desorption ionisation time-of-flight mass spectrometry (MALDI-TOF MS) measurements were carried out on a Bruker Daltonik Reflex III mass spectrometer using trans-2-[3-(4-tert-Butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) as matrix. Chemical ionization (CI) mass spectroscopy was performed on a Finnigan MAT SSQ-7000. High resolution mass spectra were carried out on a Bruker solariX. Dynamic light scattering (DLS) was performed on a Malvern Zetasizer Nano ZS (angle: 173°, λ: 633 nm) at 20 °C. Absorption spectra were recorded on a *Perkin Elmer* Lambda 19 spectrometer and fluorescence emission spectra on a Perkin Elmer LS 55 spectrometer in 1 cm cuvettes. For all spectroscopic measurements, pure Uvasol THF (Merk) and demineralized water were used. Absorption spectroscopy and circular dichroism (CD) measurements of molecular dissolved OT hybrids **10S** and **10R** were prepared with a concentration of 10⁻⁵ M in THF. Aggregated samples were prepared at the same concentration in a mixture 1:9 of THF/ H₂O. Fluorescence spectroscopy: excitation of a 10⁻⁶ M solution at 360 nm. The powder X-ray diffraction experiment on the grinded (2R,4R)-Hybrid **10R** were performed using as diffractometer a X'Pert Pro purchased from the PANalytical company. Electrochemistry was performed using a Metrohm Autolab PGSTAT 10 Potentiostat. In CV-measurements, all potentials were internally referenced to the ferrocene/ferricenium couple (Fc/Fc⁺). Melting points were uncorrected and were determined using Büchi B-545 apparatus. CD spectra were recorded on a JASCO J 600 spectropolarimeter. The transmission electron microscopy (TEM) images were carried out with a Jeol 1400 Transmissions-Elektronenmikroskop. TEM micrographs were obtained from drop-casting of a solution of compound 10S ($[c] = 10^{-5}$ M), using a mixture of THF:water = 1:9, on a copper grid using uranyl acetate as contrast agent.

Chemicals: Sodium bicarbonate, sodium hydride (NaH) (60% suspension in paraffin oil), potassium carbonate, copper powder, ethylene diamine tetraacetic acid (EDTA), tetrahydrofuran (THF), N,N-di-methylformamide (DMF), dichloroethane (DCE), dichloromethane (DCM) and methanol (MeOH) were purchased from *Merck*, phosphorylchloride, dimethyl(2-oxopropyl)-phosphonate, tetrakis(aceto-nitrile)copper(I) hexafluorophosphate and N-Boc–cis-4-azido-L-proline (dicyclohexylammonium) salt were purchased from *Sigma Aldrich*. All reactions were performed using flame-dried glassware under

argon and were monitored by thin layer chromatography (TLC) using aluminium plates, pre-coated with silica gel 60 F_{254} (Merck). Preparative flash column chromatography was performed using glass columns packed with silica gel 60 (particle size 0.040-0.063 mm *Merck*). Solvents were purchased from Merck and distilled prior to use. Water-free dichloromethane was obtained using calcium hydride as drying agent.

Materials: 5-hexyl-2,2':5',2":-quaterthiophene **7** was prepared according to the method described by ref. [1]. 5'''-Hexyl-2,2';5',2'';5'',2'''-quaterthiophene-5-carbaldehyde **8** was prepared according to a slightly modified protocol of ref. [2]. Synthesis of N-Boc–cis-4-azido-D-proline **4***R* was synthesized according to literature procedures. [3-5]

Syntheses:

5"'-**Hexyl-2**,**2**';**5**',**2**";**5**",**2**"'**:quaterthiophene**, **7**: A mixture of 0.335 g of 5-(trimethylstannyl)-5'hexyl-2,2'-bithiophene **5** (0.8 mmol, 1.2 eq), 0.160 g of 5-bromo-2,2'-bithiophene **6** (0.65 mmol, 1 eq), and 0.004 g of tetrakis(triphenylphosphine) palladium (0.003 mmol, 0.005 eq) in 10 ml dry DMF was degassed for 30 min and heated then up to 80° C. The reaction mixture was then kept stirring for one hour under argon. After cooling down to room temperature the solvent was removed in vacuo. Subsequently, the crude residue was redissolved in DCM and the organic phase was washed with water. The phases were separated, and the aqueous layer was further extracted with DCM (2 x 20 mL). The organic layers were combined and washed with 2% sodium hydroxide aqueous solution, brine, and water and dried over MgSO₄. After removal of the solvent the crude product was purified by column chromatography (silica, eluent: hexane) to yield 0.232 g (0.56 mmol, 86%) of the desired product **7** as a yellow solid. M.p.:185 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.22 (dd, *J* = 5.1, 1.1 Hz, 1H); 7.17 (dd, *J* = 3.6, 1.1 Hz, 1H); 7.07 (d, *J* = 3.8 Hz, 1H); 7.05 (d, *J* = 4.7 Hz, 2H); 7.02 (dd, *J* = 5.1, 3.6 Hz, 1H); 6.99 (dd, *J* = 5.8, 3.8 Hz, 2H); 6.68 (d, *J* = 3.6 Hz, 1H); 2.79 (t, *J* = 7.6 Hz, 2H); 1.68 (m, 2H); 1.32 (m, 6H); 0.89 (t, *J* = 6.8 Hz, 3H); MS (CI) *m/z* = 415.1 [M+ 2CH₃]⁺ (calc. for C₂₄H₂₂S₄: 414.67)

5'''-**Hexyl-2,2**';**5**',**2**'';**5**'',**2**'''-**quaterthiophene-5-carbaldehyde**, **8**: For the generation of the Vilsmeier reagent, 1.1 ml phosphoryl chloride was added dropwise to a mixture of 0.86 ml dry DMF (11.2 mmol, 1 eq) in 6 ml of dry DCE. The resulting mixture was stirred for two hours at room temperature. In a two-neck flask equipped with a reflux condenser, 0.232 g of 5-hexyl-2,2':5',2":5",2"'-quaterthiophene **7** (0.56 mmol, 1 eq) were dissolved in 15 ml of dry DCE. The solution was heated up to reflux and 2.53 g of Vilsmeier reagent (20 eqs) was added dropwise. After refluxing for 3 hours, the mixture was first allowed to cool to room temperature before being quenched with 25 ml of saturated NaHCO₃-solution and stirred overnight. The layers were separated; the aqueous layer was extracted three times with DCM. The combined organic layers were washed with water and dried over MgSO₄. The solvent was removed in vacuo. The crude product was purified by column chromatography (silica, eluent: DCM/hexane 1:1) to yield 0.170 mg (0.38 mmol, 70%) of the desired product **8** as an orange solid. M.p.: 170 °C; ¹H-NMR (400 MHz, CDCl₃): δ 9.86 (s, 1H); 7.67 (d, J = 4.0 Hz, 1H); 7.27 (d, J = 3.9 Hz, 1H); 7.23 (d, J = 4.0 Hz, 1H); 7.07 (dd, J = 3.8, 2.7 Hz, 2H); 7.01 (dd, J = 5.2, 3.8 Hz, 2H); 6.70 (d, J = 3.8 Hz, 1H); 2.79 (t, J = 7.5 Hz, 2H); 1.68 (m, 2H); 1.32 (m, 6H); 0.89 (t, J = 6.9 Hz, 3H); MS (CI) *m/z* = 442.1 [M+ 2CH₃]⁺ (calc. for C₂₄H₂₂S₄: 442.68)

5-Ethynyl-5^{**}**-hexyl-2,2**^{*}**;5**^{*}**,2**^{**}**;7**^{**}**-quaterthiophene**, **9**:^[6] A suspension of 0.060 g of NaH (2.5 mmol; 10 eqs) in 15 ml of dry THF was cooled to 0 °C. 0.345 ml of dimethyl(2-oxopropyl) phosphonate (2.5 mmol; 10 eqs) were added dropwise to the solution. The resulting mixture was stirred at 0°C for one hour. Then 0.493 g tosylazide (2.5 mmol; 10 eqs) were added and the mixture was stirred for

another 10 min at 0 °C. The reaction mixture was quickly passed through a short filtration column (silica, eluent: ethyl acetate) and the solvent was removed in vacuo. The resulting colorless oil was dissolved in 16 ml of dry THF and was added to a previously prepared suspension of 0.585 g of K_2CO_3 (4.2 mmol, 18 eqs) and 0.104 g of 5'''-hexyl-2,2';5',2'';5'',2'''-quaterthiophene-5-carbaldehyde 8 (0.24 mmol; 1 eq) in 4 ml of dry MeOH. The resulting intensely yellow/orange mixture was allowed to stir at room temperature overnight (argon atmosphere). The solvent was removed and the residue was re-dissolved in DCM. After washing of the organic phase with a saturated solution of ammonium chloride the layers were separated and the aqueous phase was repeatedly extracted with DCM. The combined organic layers were dried over Na₂SO₄ and the solvent was removed in vacuo at room temperature due to the high sensitivity of the compound. The crude product was put onto silica and was purified by column chromatography (silica, eluent: hexane) to yield 0.072 g (0.16 mmol, 70%) of the desired product **9** as a brown solid. Decomposition at 165 °C; ¹H-NMR (400 MHz, THF- d_8): δ 7.19 (d, J = 1.7 Hz, 1H); 7.18 (d, J = 1.7 Hz, 1H); 7.15 (d, J = 2.0 Hz, 1H); 7.14 (d, J = 2.8 Hz, 1H); 7.11 (d, J = 3.8 Hz, 1H); 7.06 (d, J = 3.8 Hz, 1H); 7.03 (d, J = 3.6 Hz, 1H); 6.71 (d, J = 3.6 Hz, 1H); 4.00 (s, 1H-alkyn); 2.79 (t, J = 7.5 Hz, 2H); 1.67 (m, 2H); 1.34 (m, 6H); 0.89 (m, 3H); ¹³C-NMR (101 MHz, THF-*d*₈): δ 14.21, 23.28, 29.47, 30.46, 30.56, 32.41, 77.01(C-alkyne), 84.33 (C-alkyne), 121.84, 124.07, 124.26, 124.34, 124.99, 125.38, 125.80, 124.99, 134.58, 135.02, 135.41, 135.63, 137.52, 137.99, 139.13, 146.30; MS (CI) $m/z = 438.1 \left[M + 2CH_3\right]^+$ (calc. for C₂₄H₂₂S₄: 438.65)

(4*R*)-4-Azido-1-(*tert*-butoxycarbonyl)-D-proline, 4*R*: To a solution of 9.60 g of BOC-(4*S*)Azp-OMe (35.5 mmol, 1.0 eq) in a mixture of 18 ml of THF and 18 ml of MeOH, a solution of 2.84 g of NaOH (71.0 mmol, 2.0 eqs) in 6 ml of water was added. The mixture was stirred for 4 h at room temperature and then dissolved in 100 ml of ethyl acetate. The solution was acidified with 150 ml of 1 M HCl and the aqueous phase extracted with ethyl acetate (3 x 100 ml). The organic layers were dried over Na₂SO₄ and the solvent was removed in vacuo to yield 8.89 g (34.8 mmol, 98 %) of 4*R* as colorless liquid. ¹H-NMR (400 MHz, DMSO): δ 12.42 (s, 1H; OH); 4.41-4.31(m, 1H; Ha); 4.24-4.15 (m, 1H; H γ); 3.65-3.58 (m, 1H; H δ); 3.32 (dd, JHH = 3.3 Hz, 11.5 Hz, 1H; H δ); 2.49-2.45 (m, 1H; H β); 2.01-1.96 (m, 1H; H β); 1.36 (s, 9H; tBu); ¹³C-NMR (101 MHz, DMSO): δ 173.0 (Carbonyl), 152.9 (Carbamate), 79.0 (Boc), 57.8, 57.3, 50.6 (C α , C γ , C δ), 35.2 (C β), 27.8 (Boc); ESI-MS m/z = 279.1 [M+Na]⁺, 535.3 [2M+Na]⁺ (calc. for C₁₀H₁₆N₄O₄: 256)

(4*S*)-1-*Tert*-butoxycarbonyl-[(5'''-hexyl-2,2';5',2'';5'',2'''-quaterthien-5-yl)-1*H*-1,2,3-triazol-1yl] -L-proline, 10*S*, and (4*R*)-1-*Tert*-butoxycarbonyl-[(5'''-hexyl-2,2';5',2'';5'',2'''-quaterthiene-5yl)-1*H*-1,2,3-triazol-1yl]-D-proline, 10*R*: A representative synthetic procedure is given for both enantiomers: To a solution of 0.050 g (0.11 mmol, 1 eq) of 5-ethynyl-5'''-hexyl-2,2';5',2'';5'',2'''quaterthiophene 7 in a mixture of 2 ml THF and 2 ml of DCM 0.060 g of the N-BOC-cis-4-azido-Lproline (dicyclohexylammonium) salt 4*S* (0.13 mmol, 1.2 eqs) or 0.035 g of 4*R* (0.13 mmol, 1.2 eqs), 0.002 g of copper powder (0.023 mmol, 0.2 eqs) and 0.051 g of tetrakis(acetonitrile) copper(I) hexafluorophosphate (0.13 mmol, 1.2 eqs) were added, under argon.* The reaction was stirred at room temperature overnight. The reaction mixture was washed several times with a saturated EDTA solution. The aqueous layers were repeatedly extracted with DCM. The organic layers were combined and the solvent was removed. The crude product was suspended in dry *n*-hexane and filtered off to give a dark brown solid.

*Note: The Cu(I) complex is not used as a catalyst here, but in stoichiometric amounts due to the possible complex-formation of Cu(I) by the carboxylic acid group. (4S)-1-*Tert*-butoxycarbonyl-[(5'''-hexyl-2,2';5',2'';5'',2'''-quaterthien-5-yl)-1*H*-1,2,3-triazol-1yl] -L-proline, 10S: Yield: 0.071 g (0.1 mmol, 89%); decomposition at 282 °C; ¹H-NMR (400 MHz, THF- d_8): δ 8.31 (s, 1H-triazole); 7.28 (d, J = 3.6 Hz, 1H); 7.18 (dd, J = 3.6, 2.4 Hz, 2H); 7.14 (t, J = 4.0 Hz, 2H); 7.05 (d, J = 3.8 Hz, 1H); 7.03 (d, J = 3.6 Hz, 1H); 6.72 (d, J = 3.6 Hz, 1H); 5.22 (bs, 1H); 4.32 (bs, 1H); 4.12 (bs, 1H); 3.80 (bs, 1H); 2.93 (bs, 1H); 2.80 (t, *J* = 7.5 Hz, 2H); 2.52 (bs, Hcarboxylic acid); 1.67 (m, 2H); 1.34 (m, 15H); 0.89 (m, 3H); HRMS(MALDI-TOF, (DCTB)): *m*/*z* [M+H]⁺ = 694.1762 (calc. for C₃₄H₃₈N₄O₄S₄: 694.17, deviation from the calculated mass = -1.9 ppm).

(4*R*)-1-*Tert*-butoxycarbonyl-[(5'''-hexyl-2,2';5',2'';5'',2'''-quaterthien-5-yl)-1*H*-1,2,3-triazol-1yl]-D-proline 10*R*: Yield: 0.072 g (0.1 mmol, 90%); decomposition at 295 °C; ¹H-NMR (400 MHz, THF- d_8): δ 8.28 (s, 1H-triazole); 7.28 (d, J = 3.6 Hz, 1H); 7.18 (dd, J = 3.6, 2.7 Hz, 2H); 7.14 (t, J = 4.0 Hz, 2H); 7.05 (d, J = 3.7 Hz, 1H); 7.03 (d, J = 3.5 Hz, 1H); 6.72 (d, J = 3.5 Hz, 1H); 5.22 (bs, 1H); 4.37 (bs, 1H); 4.13 (bs, 1H); 3.81 (bs, 1H); 2.96 (bs, 1H); 2.80 (t, J = 7.5 Hz, 2H); 2.63 (bs, 1H); 2.50 (bs, H-carboxylic acid); 1.68 (m, 2H); 1.37 (m, 15H); 0.89 (m, 3H); MS (MALDI-TOF, DCTB): *m*/*z* [M+H]⁺ = 694.5 (calc. for C₃₄H₃₈N₄O₄S₄: 694.95)

Electrochemistry. Solvent: dichloroethane, supporting electrolyte: TBAPF₆ (0.1 M), $[c] = 10^{-3}$ mol/L, scan rate v = 100 mV/s, room temperature,



Figure S1: CV measurements of (2R,4R)-compound 10R. $E^{\circ}_{ox1} = 0.39 \text{ V}, E^{\circ}_{ox2} = 0.69 \text{ V} \text{ vs. Fc/Fc}^+$.



Figure S2: Normalized UV/Vis and fluorescence spectra of (2S,4S)-hybrid 10S and the (2R,4R)-hybrid 10R in THF, left and THF/water (10/90), right.

	Absorption ^a	Emission ^a	Absorption ^b
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	Table 1.	UV/Vis a	nd fluoresce	ence data for	hybrids	10S and	10 <i>R</i>
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	I.	$\lambda_{\max} [nm] \in [I \mod cm^{2}]$		λ_{\max} [nm]	λ_{\max} [nm]	λ_{\max} [nm]
	105	416	29702	<u>474</u> , 504	361	<u>504</u> , 533s
	10 <i>R</i>	413	31038	<u>473</u> , 505	363	<u>504</u> , 534s
¹ In THE ^b in 10% THE/90% water, underlined values are the maxima and s means shoulder						

water, underlined values are the maxima and s mea





Figure S3: Quenching of the fluorescence emission at different THF/water ratios, left and quantification of the quenching calculated from the integral of the fluorescence spectra (@ λ_{exc} =370 nm)

Emission^b

Powder X-ray diffraction^[7]



Figure S4: Wide-angle X-ray scattering pattern of (2R,4R)-compound **10R** as powder sample. The corresponding *d* spacing values are given next to the peaks for clarity.

Temperature dependent UV-vis and CD spectra



Figure S5: Temperature-dependent absorption spectra, left and temperature-dependent CD spectra, right, of (2*S*,4*S*)-compound **10***S* ranging from 20 °C to 60 °C, in 10% THF/water.

DLS measurements



Figure S6: DLS measurement of a solution of 10S in 10% THF/90% water, $[c] = 10^{-5}$ M, at room temperature

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¹H-NMR 7 in CDCl₃



¹H-NMR 8 in CDCl₃



¹H-NMR **9** in THF-*d*₈



¹³C-NMR **9** in THF-*d*₈



¹H-NMR **4***R* in CDCl₃



¹³C-NMR **4***R* in CDCl₃



¹H-NMR **10S** in THF- d_8



¹H-NMR **10***R* in THF- d_8

