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Supporting Information

Self-Assembly of Tetraphenylalanine Peptides

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Peptide Synthesis

Characteristics of all intermediates obtained during the synthesis of the four FFFF-based peptides under study.

Boc-L-Phe-OBzl (x). White solid, mp 68°C. $[\alpha]_D^{20}$: –11.7 (c = 1.0, MeOH). IR (KBr) ν 3360, 1729, 1678 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.45 (s, 9H), 3,07–3,17 (m, 2H), 4.67 (dd, 1H, *J* = 13,3 Hz, *J* = 6,0 Hz), 5.03 (m, 1H), 5.17 (m, 2H), 7,07–7,43 (m, 10H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.40, 38.35, 54.54, 67.19, 79.99, 127.06, 128.55, 128.63, 128.67, 129.44, 135.29, 135.97, 155.17, 171.81. HRMS (ESI) $C_{21}H_{25}NO_4Na$ $[M+Na]^+$: calcd. 378.1676, found 378.1724.

Boc-L-Phe-L-Phe-OBzl (x). White solid, mp 181°C. $[\alpha]_D^{20}$: –17.7 (c = 0.33, MeOH). IR (KBr) ν 3332, 1741, 1696, 1664 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.41 (s, 9H), 3.02–3.11 (m, 4H), 4.30–4.41 (m, 1H), 4.84 (dd, 1H, J = 12.7 Hz, J = 5.9 Hz), 4.91–5.02 (m, 1H), 5.12 (m, 2H), 6.31 (d, 1H, J = 7.0 Hz), 6.91–6.94 (m, 2H), 7.17–7.41 (m, 13H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.36, 38.07, 38.43, 53.44, 55.82, 67.35, 80.32, 127.11, 127.19, 128.65, 128.67, 128.70, 128.74, 128.79, 129.41, 129.49, 135.14, 135.61, 136.62, 155.39, 170.85, 170.90. HRMS (ESI) $C_{30}H_{34}N_2O_5Na$ $[M+Na]^+$: calcd. 525.2360, found 525.2359.

Boc-L-Phe-L-Phe-L-Phe-OBzl (x). White solid, mp 179°C. $[\alpha]_D^{20}$: –25.3 (c = 0.35, MeOH). IR (KBr) ν 3280, 1734, 1692, 1643 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.40 (s, 9H), 2.90–3.09 (m, 6H), 4.26–4.38 (m, 1H), 4.58 (dd, 1H, J = 13.9 Hz, J = 7.2 Hz), 4.77 (dd, 1H, J = 13.7 Hz, J = 6.3 Hz), 4.83–4.92 (m, 1H), 5.11 (m, 2H), 6.26 (m, 1H), 6.47 (d, 1H, J = 7.0 Hz), 6.94–7.40 (m, 20H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.35, 37.98, 38.12, 53.65, 54.42, 55.81, 67.32, 80.49, 127.18, 127.22, 128.64, 128.68, 128.71, 128.78, 128.87, 129.35, 129.41, 135.18, 135.65, 136.28, 136.54, 155.48, 170.01, 170.76, 171.14. HRMS (ESI) $C_{39}H_{34}N_3O_6Na$ $[M+Na]^+$: calcd. 672.3044, found 672.3044.

Boc-L-Phe-L-Phe-L-Phe-L-Phe-OBzl (x). White solid, mp 210°C. $[\alpha]_D^{20}$: –31.2 (c = 0.37, MeOH). IR (KBr) ν 3278, 1739, 1691, 1641 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.26 (s, 9H), 2.73–3.07 (m, 8H), 4.11 (dd, 1H, J = 13.0 Hz, J = 6.4 Hz), 4.41 (dd, 1H, J = 13.2 Hz, J = 6.5 Hz), 4.50–4.59 (m, 1H), 4.68–4.76 (m, 2H), 5.04 (m, 2H), 6.25 (m, 1H), 6.46 (m, 1H), 6.50 (m, 1H), 6.84–7.31 (m, 25H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.33, 37.60, 37.99, 53.67, 54.42, 56.04, 67.25, 80.66, 126.96, 127.08, 127.20, 128.53, 128.58, 128.63, 128.67, 128.85, 129.20, 129.27, 129.34, 129.41, 135.27, 136.04, 136.14, 136.35, 136.68, 155.74, 170.28, 170.54, 171.01, 171.69. HRMS (ESI) $C_{48}H_{52}N_4O_7Na$ $[M+Na]^+$: calcd. 819.3728, found 819.3731.

Boc-L-Phe-L-Phe-L-Phe-L-Phe-OH (x). White solid, mp 189°C. $[\alpha]_D^{20}$: –17.5 (c = 0.41, MeOH). IR (KBr) ν 3800-3000, 3290, 1740, 1693, 1644 cm^{-1}. ^{1}H NMR ($MeOD_4$, 400 MHz) δ 1.33 (s, 9H), 2.60–3.25 (m, 8H), 3.96–4.26 (m, 1H), 4.58–4.70 (m, 3H), 7.09–7.33 (m, 20H). ^{13}C NMR ($MeOD_4$, 60ºC, 100 MHz) δ 28.66, 38.68, 38.95, 55.65, 55.87, 56.31, 57.43, 80.91, 127.59, 127.68, 127.70, 129.36, 129.37, 129.41, 129.44, 130.31, 130.32, 130.36, 130.42, 130.47, 130.50, 138.12, 138.19, 138.41, 138.60, 157.38, 172.59, 172.71, 173.87. HRMS (ESI) $C_{41}H_{46}N_4O_7Na$ $[M+Na]^+$: calcd. 729.3259, found 729.3263.

Table S1. Conformational parameters experimentally determined (ref. 33) and calculated (without and with water molecules) for FF, and calculated for FFFF in nanotubes. All the averaged dihedrals and their corresponding standard deviations (in parenthesis) are in degrees.

	FF (ref. 33)	FF	FF+6H_2O	FF+12H_2O	FFFF
ψ_1 (N_1-C_1^{α}-$C_1^{'}$-N_2)	157.8	161.2 (0.9)	160.9 (1.9)	163.5 (6.3)	115.6 (40.4)
ω_1 (C_1^{α}-$C_1^{'}$-N_2- C_2^{α})	-179.1	179.1 (1.1)	-176.8 (5.1)	-178.7 (6.7)	164.4 (7.4)
φ_2 ($C_1^{'}$-N_2- C_2^{α}-C_2')	55.4	50.7 (1.1)	47.4 (3.2)	45.5 (4.2)	70.9 (22.6)
ψ_2 (N_2- C_2^{α}-C_2'-O_2')	43.8	49.6 (1.1)	48.7 (6.3)	49.1 (7.3)	-60.8 (44.0)
ω_2 (C_2^{α}-$C_2^{'}$-N_3- C_3^{α})	-	-	-	-	-12.1 (45.2)
φ_3 ($C_2^{'}$-N_3- C_3^{α}-C_3')	-	-	-	-	-179.7 (31.4)
ψ_3 (N_3- C_3^{α}-C_3'-N_4)	-	-	-	-	168.2 (7.6)
ω_3 (C_3^{α}-$C_3^{'}$-N_4- C_4^{α})	-	-	-	-	166.6 (1.7)
φ_4 ($C_3^{'}$-N_4- C_4^{α}-C_4')	-	-	-	-	55.5 (1.3)
ψ_4 (N_4- C_4^{α}-C_4'-O)	-	-	-	-	48.6 (7.7)
θ_1 (C_1^{β}-$C_1^{\alpha}\cdots C_2^{\alpha}$- C_2^{β})	40.2	36.7 (3.0)	37.7 (4.3)	37.7 (3.3)	14.5 (15.7)
θ_2 (C_2^{β}-$C_2^{\alpha}\cdots C_3^{\alpha}$- C_3^{β})	-	-	-	-	-55.3 (7.2)
θ_2 (C_3^{β}-$C_3^{\alpha}\cdots C_4^{\alpha}$- C_4^{β})	-	-	-	-	41.4 (5.1)

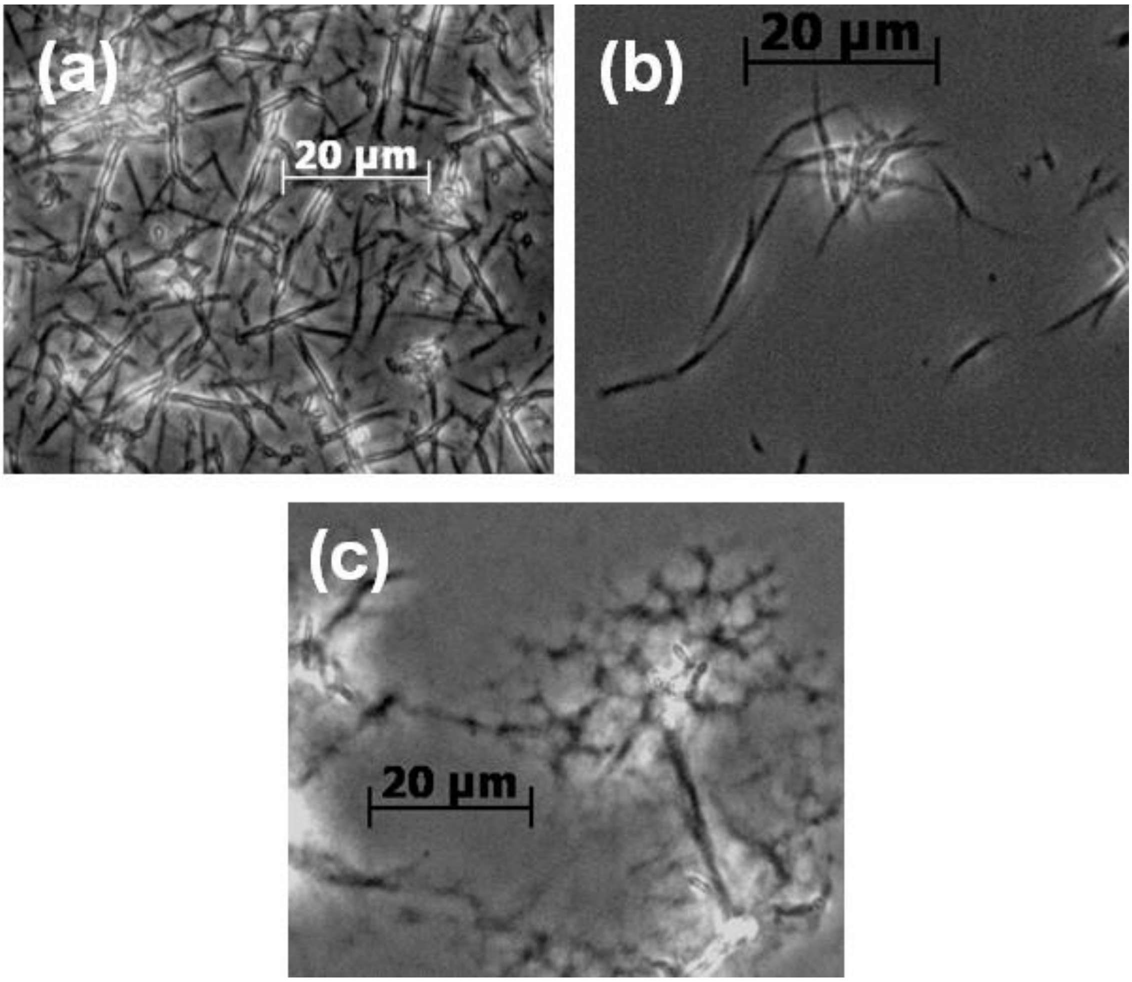

Figure S1. Optical micrographs of tubes obtained at 4 ºC for FFFF dissolved at a final concentration of 0.5, 0.1 and 0.05 mg/mL in DMF:water 1:9, 1:49 and 1:99, respectively.

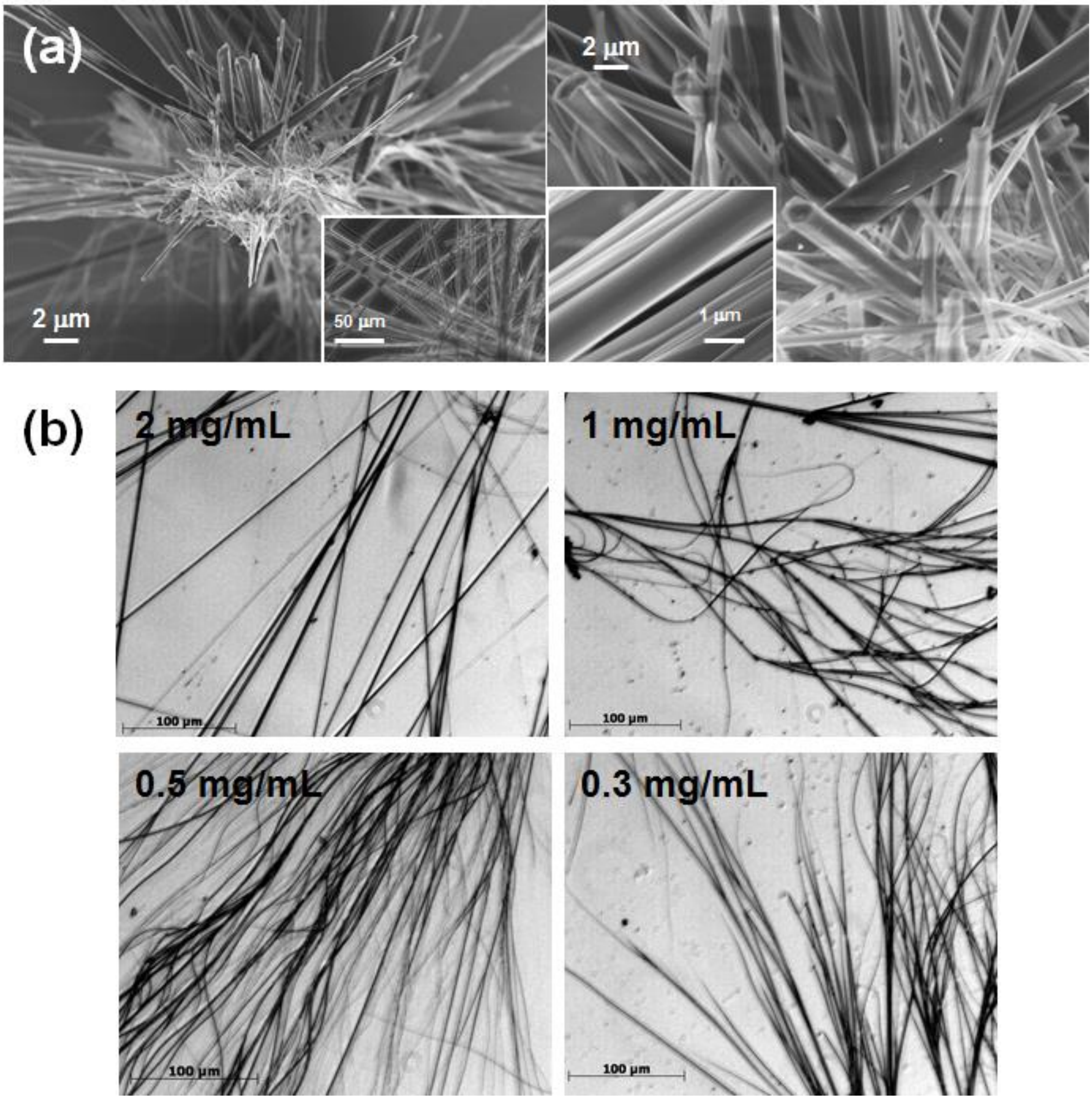

Figure S2. (a) Low and high magnification SEM micrographs of tubes obtained at 25 ºC for FF dissolved at a final concentration of 1 mg/mL in HFIP:water 1:4. (b) Optical micrographs of tubes obtained at 4 ºC for FF dissolved at a final concentration of 2, 1, 0.5 and 0.3 mg/mL in HFIP:water 4:6, 1:4, 1:9 and 3:47, respectively.

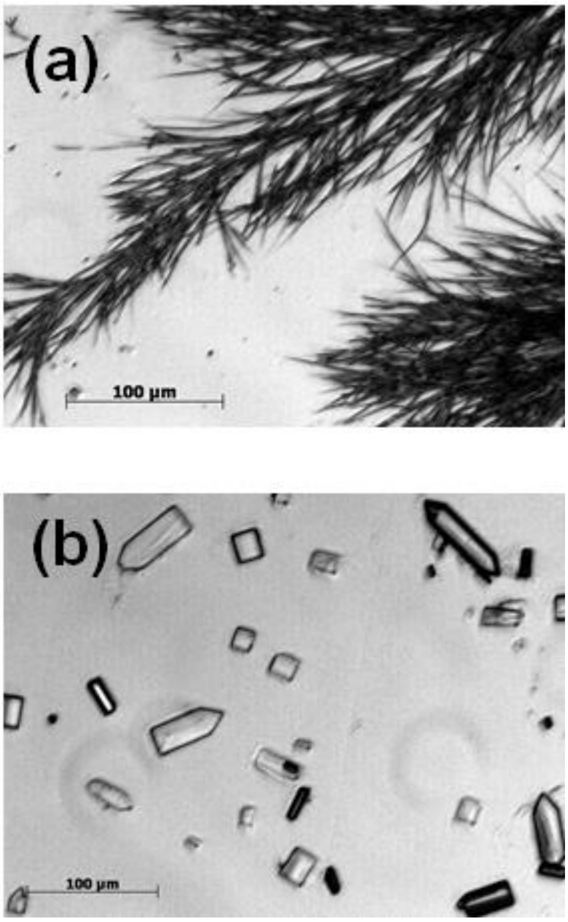

Figure S3. Optical micrographs of (a) tubes organized in dendritic branches and (b) FF monocrystals obtained at 4 ºC for FF dissolved at a final concentration of 1 mg/mL in DMF:water 1:4 and DMSO:water 1:4, respectively.

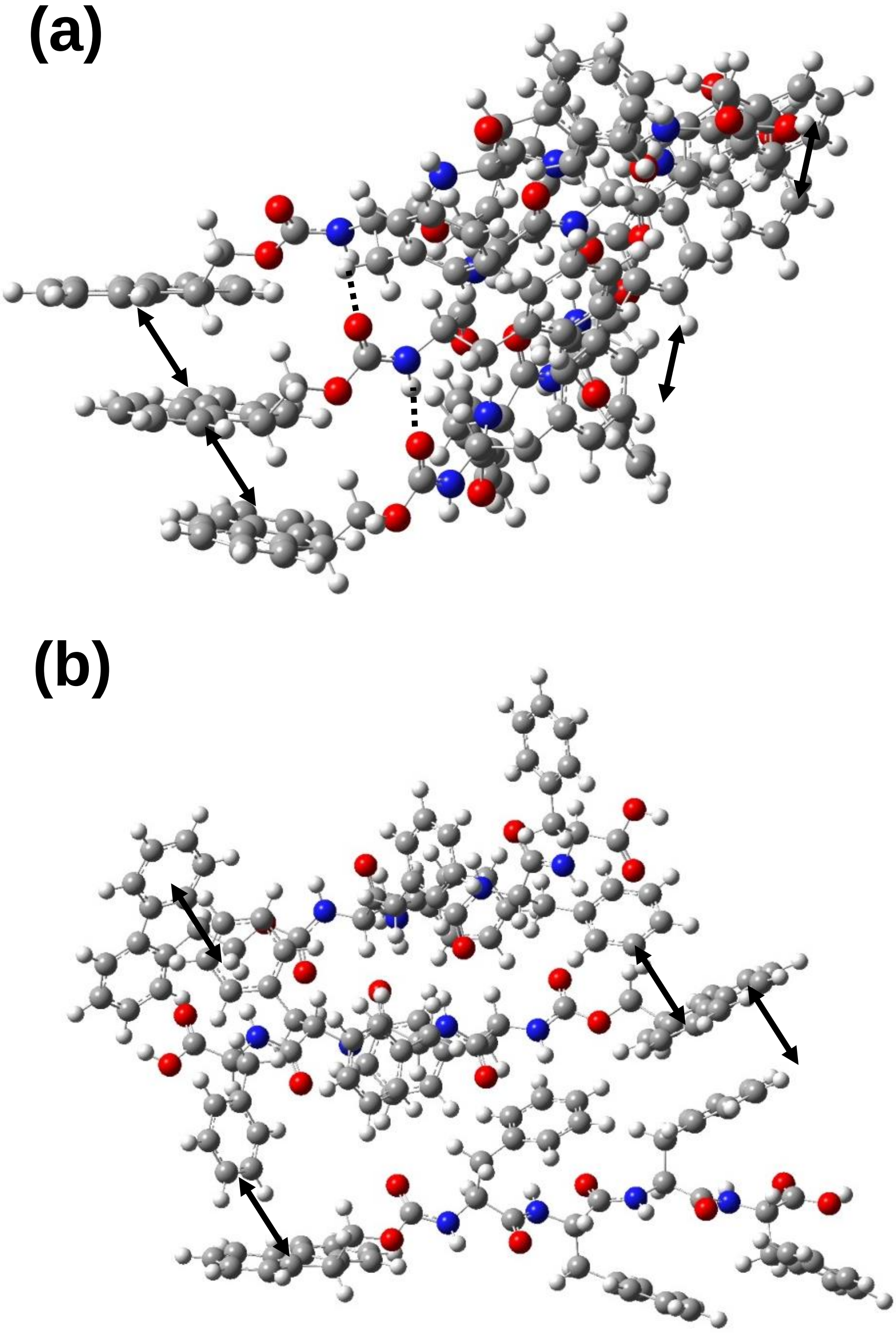

Figure S4. Parallel (a) and antiparallel (b) Fmoc-FFFF β-sheet configurations obtained from M06L/6-31G(d) calculations considering three explicit Fmoc-FFFF molecules.