A helical, aromatic, peptide nanotube

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Supporting Information

General remarks:

NMR spectra of peptide **1** were recorded on a Bruker Avance DRX 400 spectrometer at room temperature, using the residual non-deuterated solvent signal as the internal standard; chemical shifts (δ) are expressed in ppm and coupling constants (J) in Hertz. Peak assignment was made according to the information provided by COSY, HSQC and HMBC experiments. The IR spectrum was registered on a Mattson Genesis FTIR spectrophotometer; ν_{max} is given for the main absorption bands. The optical rotation was measured at room temperature using a JASCO P-1020 polarimeter. The high-resolution mass spectrum was obtained on a Bruker Microtof-Q spectrometer. The melting point was determined on a Gallenkamp apparatus. The preparation and characterization of compounds Boc-(*S*,*S*)$c_3$diPhe-OH[S1] and Boc-(*R*,*R*)$c_3$diPhe-NH^{i}Pr[S2] were already reported.

Synthesis of Boc-(*S*,*S*)$c_3$diPhe-(*R*,*R*)$c_3$diPhe-NH^{i}Pr (1). To a solution of Boc-(*S*,*S*)$c_3$diPhe-OH (304 mg, 0.86 mmol) in dry CH_2Cl_2 (4 mL) at 0ºC, HOAt (59 mg, 0.43 mmol), HATU[S3] (327 mg, 0.86 mmol) and DIEA (0.57 mL, 3.44 mmol) were added. After 10 min, HCl·H-(*R*,*R*)$c_3$diPhe-NH^{i}Pr [obtained by treatment of the corresponding Boc-protected amino acyl isopropylamide (355 mg, 0.90 mmol) with a 3N solution of HCl in dry EtOAc] was added. The reaction mixture was stirred at room temperature for 4 days and then evaporated *in vacuo*. The residue was dissolved in EtOAc (300 mL) and the solution was washed with 10% $KHSO_4$ (3×100 mL), water (2×100 mL), 5% $NaHCO_3$ (2×100 mL), water (2×100 mL), dried over anhydrous Na_2SO_4, filtered and evaporated to dryness. Recrystallization of the crude product from Et_2O/PE afforded the title compound (489 mg, 0.78 mmol, 90% yield) as a white solid.

mp: 122–123ºC (Et_2O/PE)

$[\alpha]^{26}_D$: –65.6 (*c* 0.50, MeOH)

R_f: 0.69 (CH_2Cl_2/EtOAc 8/2)

IR (nujol): ν 3420, 3368, 1700, 1643 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (d, J = 6.4 Hz, 3H, ^{i}Pr CH_3), 1.02 (d, J = 6.4 Hz, 3H, ^{i}Pr CH_3), 1.26 (s, 9H, Boc CH_3), 2.44 (d, J = 8.6 Hz, 1H, $c_3$diPhe H^β), 3.03 (d, J = 8.4 Hz, 1H, $c_3$diPhe H^β), 3.72 (d, J = 8.6 Hz, 1H, $c_3$diPhe H^β), 3.79 (m, 1H, ^{i}Pr CH), 3.99 (br d, J = 8.4 Hz, 1H, $c_3$diPhe H^β), 4.64 (br s, 1H, $c_3$diPhe NH), 6.49 (br s, 1H, $c_3$diPhe NH), 6.85 (m, 1H, NH^{i}Pr), 7.10–7.50 (m, 20H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ 22.29 (^{i}Pr CH_3), 22.37 (^{i}Pr CH_3), 28.07 (Boc CH_3), 32.70 ($c_3$diPhe C^β), 33.34 ($c_3$diPhe C^β), 37.35 ($c_3$diPhe C^β), 38.53 ($c_3$diPhe C^β), 41.65 (^{i}Pr CH), 46.63 ($c_3$diPhe C^α), 48.54 ($c_3$diPhe C^α), 80.91 (Boc C), 126.70, 127.23, 127.27, 127.64, 127.86, 128.23, 128.48, 128.57, 128.98, 129.00, 129.09, 129.15, 134.11, 134.35, 134.88, 135.60 (Ar), 156.07 (Boc CO), 166.46 ($c_3$diPhe CO), 169.65 ($c_3$diPhe CO).

HRMS (ESI) $C_{40}H_{44}N_3O_4$ $[M+H]^+$: calcd 630.332633, found 630.333899.

Abbreviations

Boc, *tert*-butyloxycarbonyl; DIEA, *N*,*N*-diisopropylethylamine; HATU, {*N*-[(dimethylamino)-1*H*-1,2,3-triazolo[4,5-*b*]pyridin-1-yl-methylene]-*N*-methylmethanaminium hexafluorophosphate *N*-oxide}; HOAt, 1-hydroxy-7-azabenzotriazole; PE, petroleum ether; ^{i}Pr, isopropyl.

References

(S1) Jiménez, A. I.; López, P.; Oliveros, L.; Cativiela, C. *Tetrahedron* **2001**, *57*, 6019–6026.
(S2) Royo, S.; De Borggraeve, W. M.; Peggion, C.; Formaggio, F.; Crisma, M.; Jiménez, A. I.; Cativiela, C.; Toniolo, C. *J. Am. Chem. Soc.* **2005**, *127*, 2036–2037.
(S3) Carpino, L. A. *J. Am. Chem. Soc.* **1993**, *115*, 4397–4398.

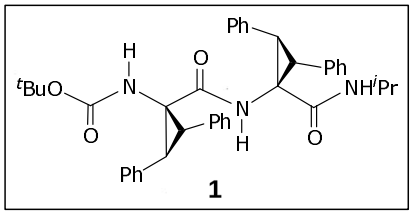

Figure S1. ^{1}H NMR (400 MHz) spectrum of peptide **1** in $CDCl_3$.

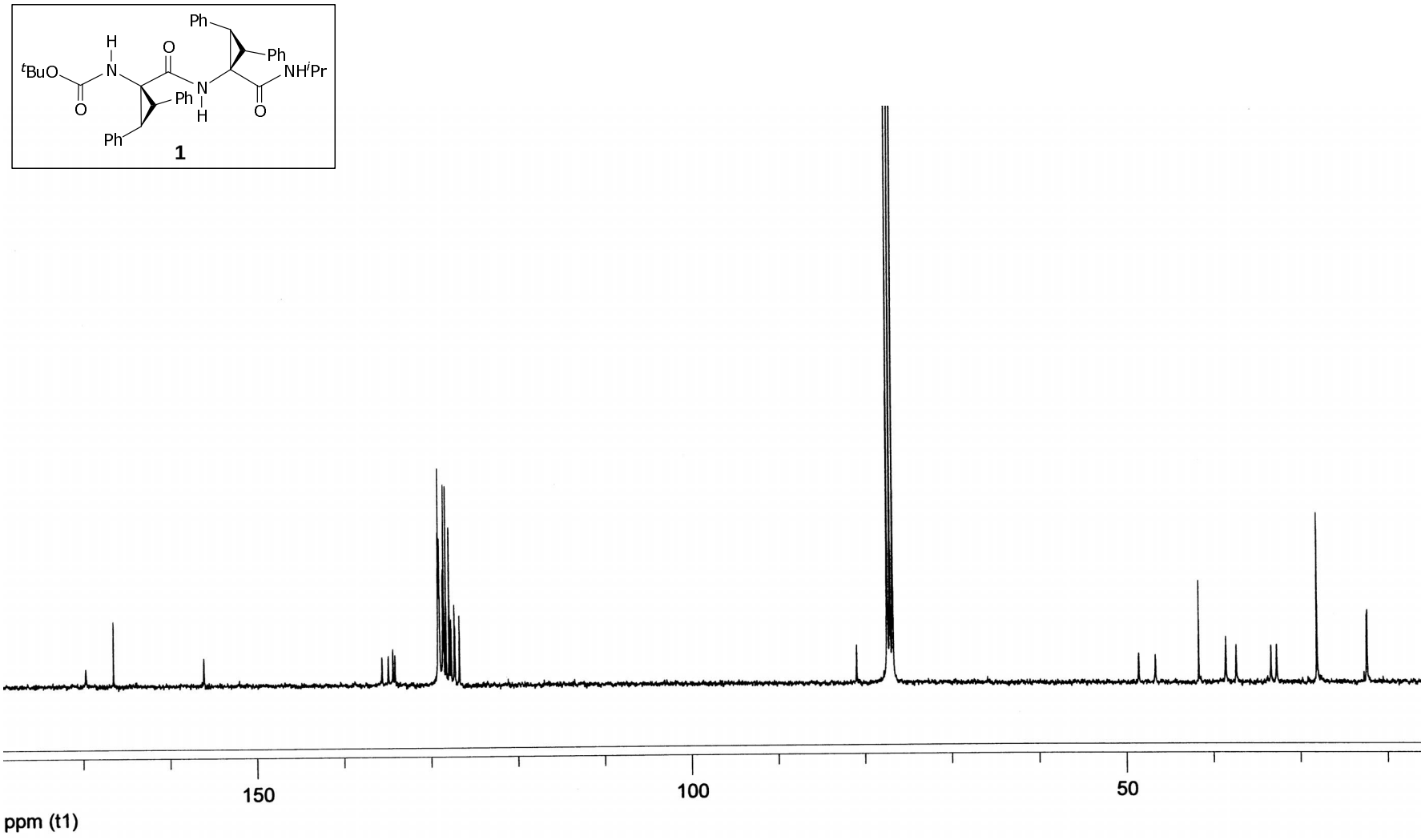

Figure S2. ^{13}C NMR (100 MHz) spectrum of peptide **1** in $CDCl_3$.