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Supporting Information

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Supporting Information

A fiber-like peptide material stabilized by single intermolecular hydrogen bonds

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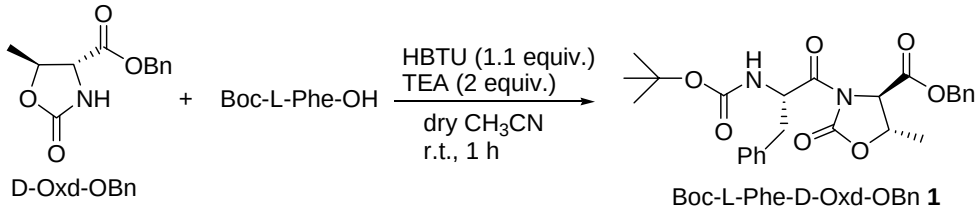
Synthesis

Preparation of Boc-L-Phe-D-Oxd-OBn 1



To a stirred solution of Boc-L-Phe-OH (0.66 g, 2.5 mmol) in acetonitrile (20 mL), HBTU (0.98 g, 2.6 mmol), then D-Oxd-OBn (0.59 g, 2.5 mmol) and lastly triethylamine (0.75 mL, 5 mmol) were added. The mixture was stirred over 1 hour, then acetonitrile was removed under reduced pressure and replaced by ethyl acetate. The mixture was washed with brine, 1 N aqueous HCl (1 x 30 mL), and 5% aqueous $NaHCO_3$ (1 x 30 mL), dried over sodium sulphate and concentrated in vacuo. Product **1** was obtained pure in 88% yield (0.89 g) as a solid after silica gel chromatography (cyclohexane/ethyl acetate 8:2 → 1:1 as eluant). Fibers were obtained after slow evaporation of the solvent mixture. Proton signals were assigned by *g*COSY spectra.

M.p. = 118-120 °C.

$[\alpha]_D$ +36.7 (c 1.0, CH_2Cl_2).

IR (CH_2Cl_2, 3 mM): ν = 3433, 1793, 1756, 1710 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ 1.20-1.60 (m, 12 H, Me + *t*-Bu), 2.80-3.18 (m, 2H, CHN-C*H*$_2$-Ph), 4.40 (d, 1H, *J* = 3.9 Hz, CHN), 4.51 (dq, 1H, *J* = 3.9, 6.3 Hz, CHO), 4.90 (bs, 1H, NH) 5.12-5.31 (m, 2H, OC*H*$_2$Ph), 5.85 (bs, 1H, C*H*N-CH_2Ph), 7.20-7.45 (m, 10H, 2 x Ph).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.0, 28.2, 39.1, 53.7, 61.8, 68.0, 73.5, 79.8, 127.0, 128.3, 128.4, 128.7, 129.5, 134.6, 135.7, 151.1, 154.6, 167.4, 172.6.

$C_{26}H_{30}N_2O_7$ (482.53): calcd. C 64.72, H 6.27, N 5.81. Found: C 64.81, H 6.34, N 5.72.

FT-IR Spectra - The infrared spectra (64 scans) were recorded at 2 cm^{-1} resolution using a Nicolet 210 FTIR spectrometer.

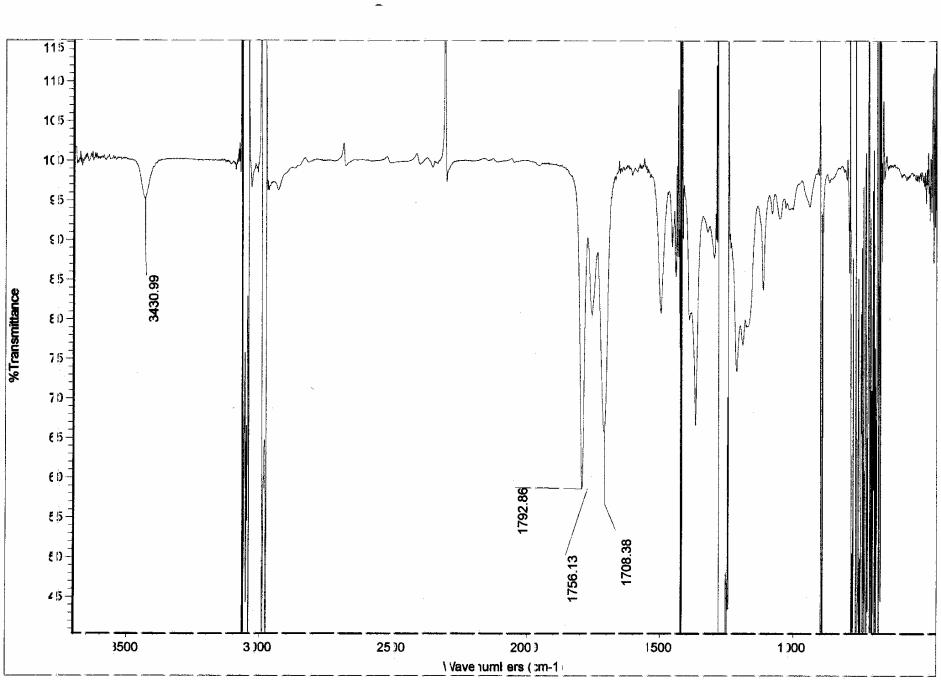


Figure S1. FT-IR absorption spectrum for a 3 mM concentration sample of **1** in pure CH_2Cl_2 at room temperature.

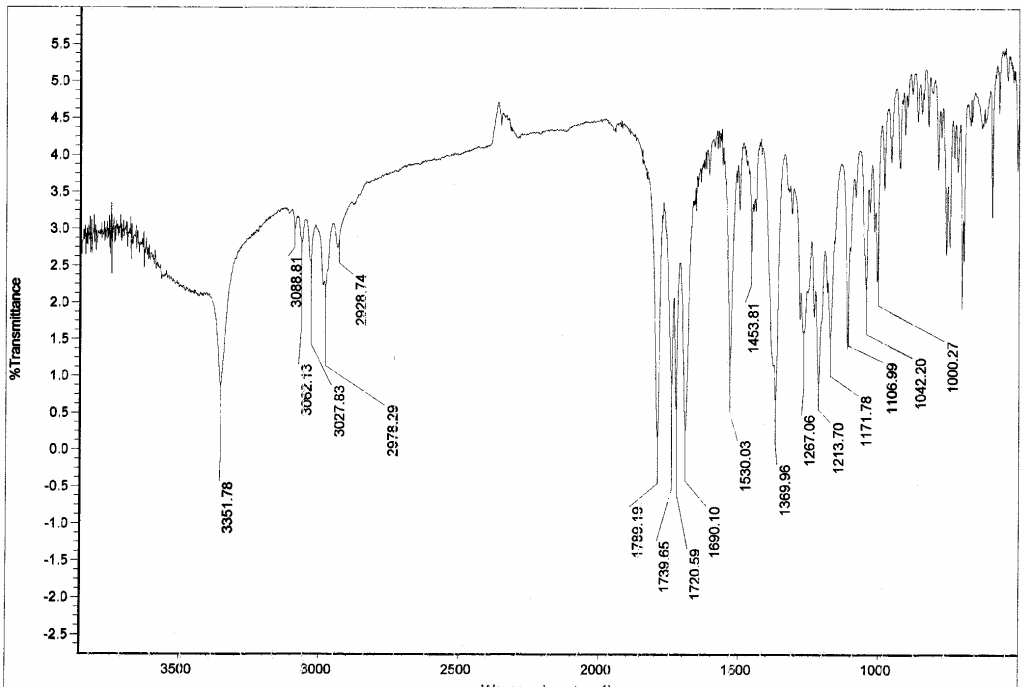


Figure S2. FT-IR absorption spectrum for **1** as an 1% solid mixture with KBr at room temperature.

Calorimetry

Calorimetric measurements were performed using a Perkin Elmer DSC-7 equipped with a model PH intracooler. Temperature and enthalphy calibrations were performed by using high purity standards (*n*-decane, benzene and indium). The material (1.4 mg of sample) was sealed in aluminium pans. Heating was carried out at 5 °C min^{-1} in the temperature range -40 to 200 °C. Denaturation temperature (TD) was determined as the peak value of the corresponding endothermic phenomena. The value of denaturation enthalpy was calculated with respect to the mass of the sample.

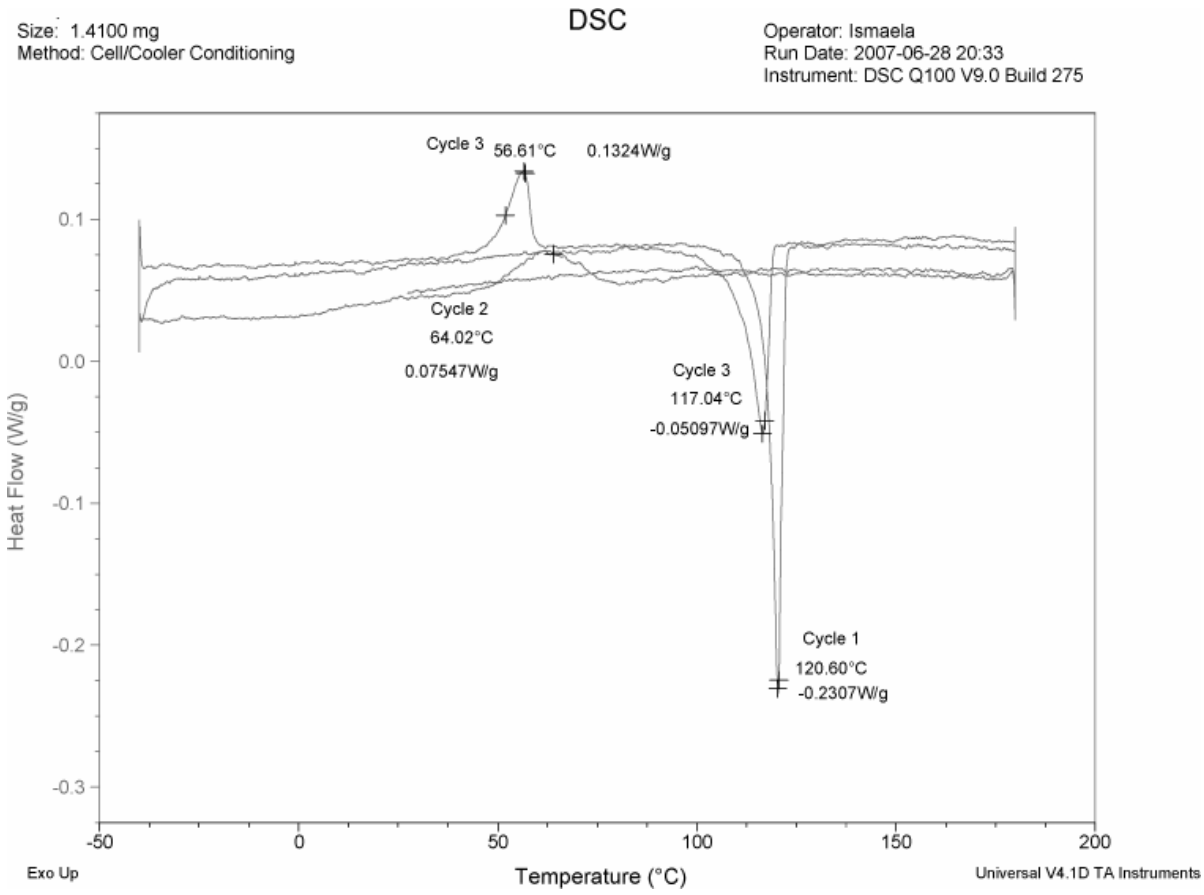


Figure S3. Differential Scanning Calorimetry (DSC) of **1**.

Scanning Electron Microscopy

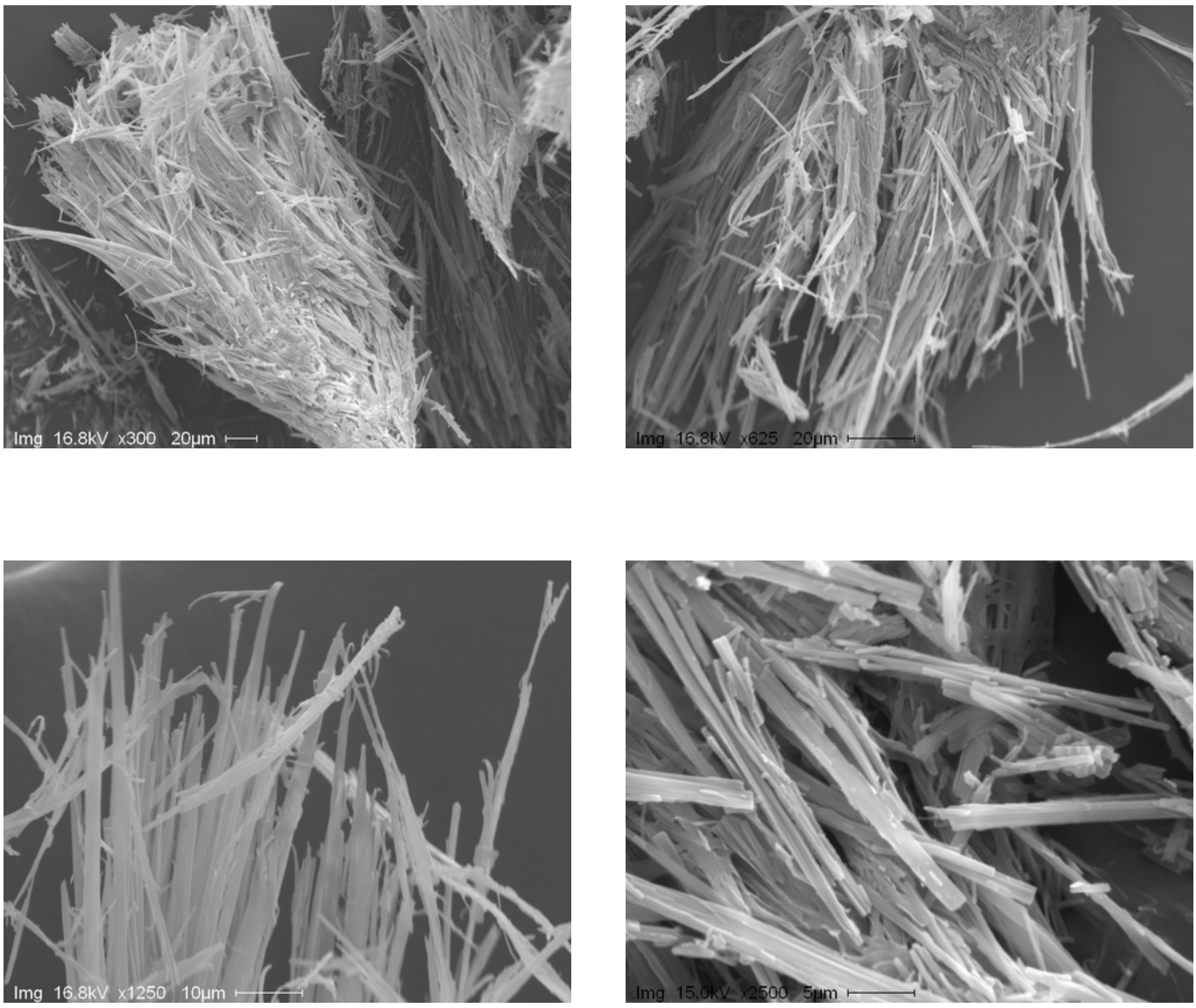


Figure S4. SEM images of **1** at different magnifications.

X-ray Crystallography

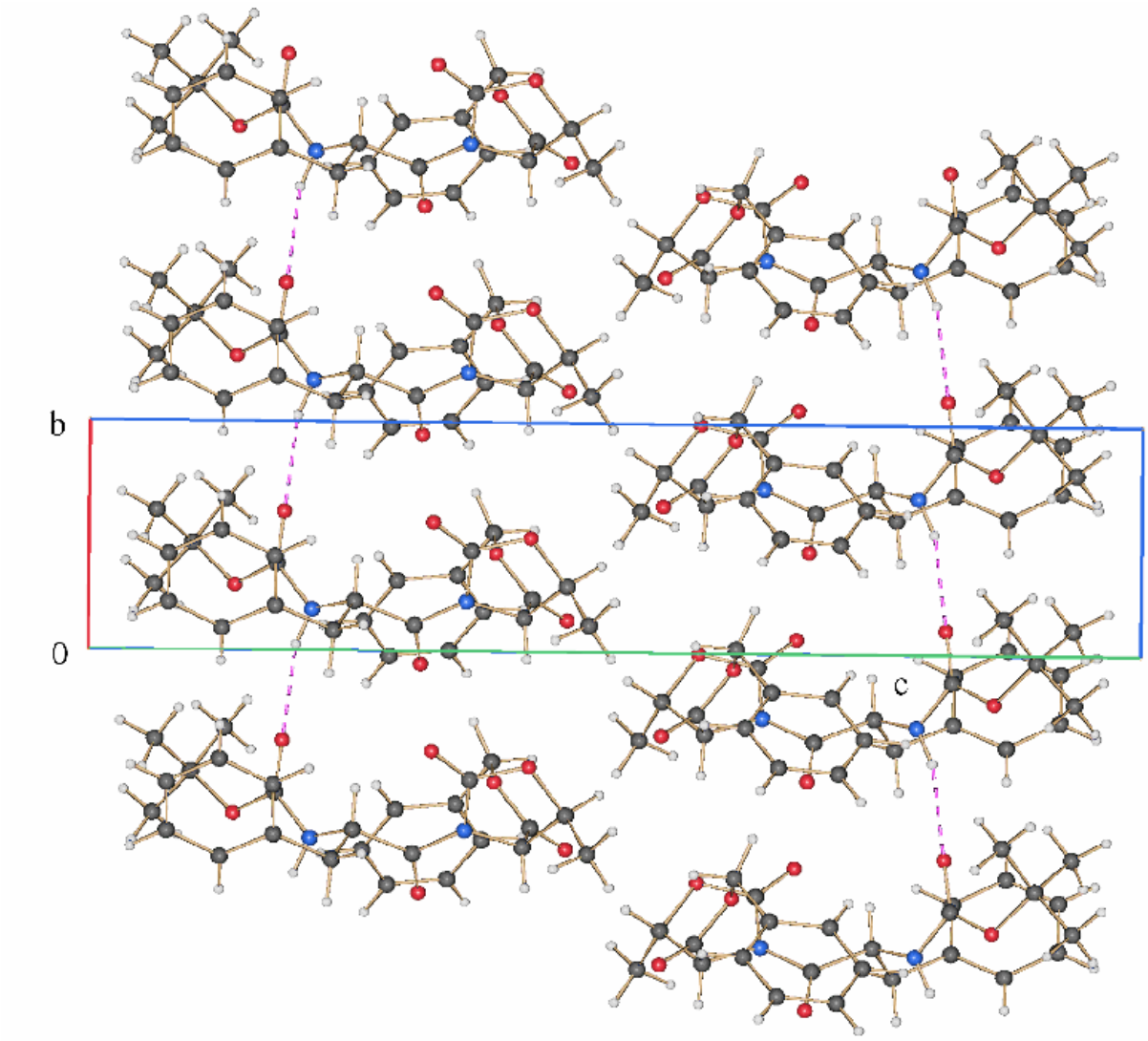


Figure S5. View down the *a* axis of the crystal packing of **1** showing the N-H…O=C hydrogen bonding.

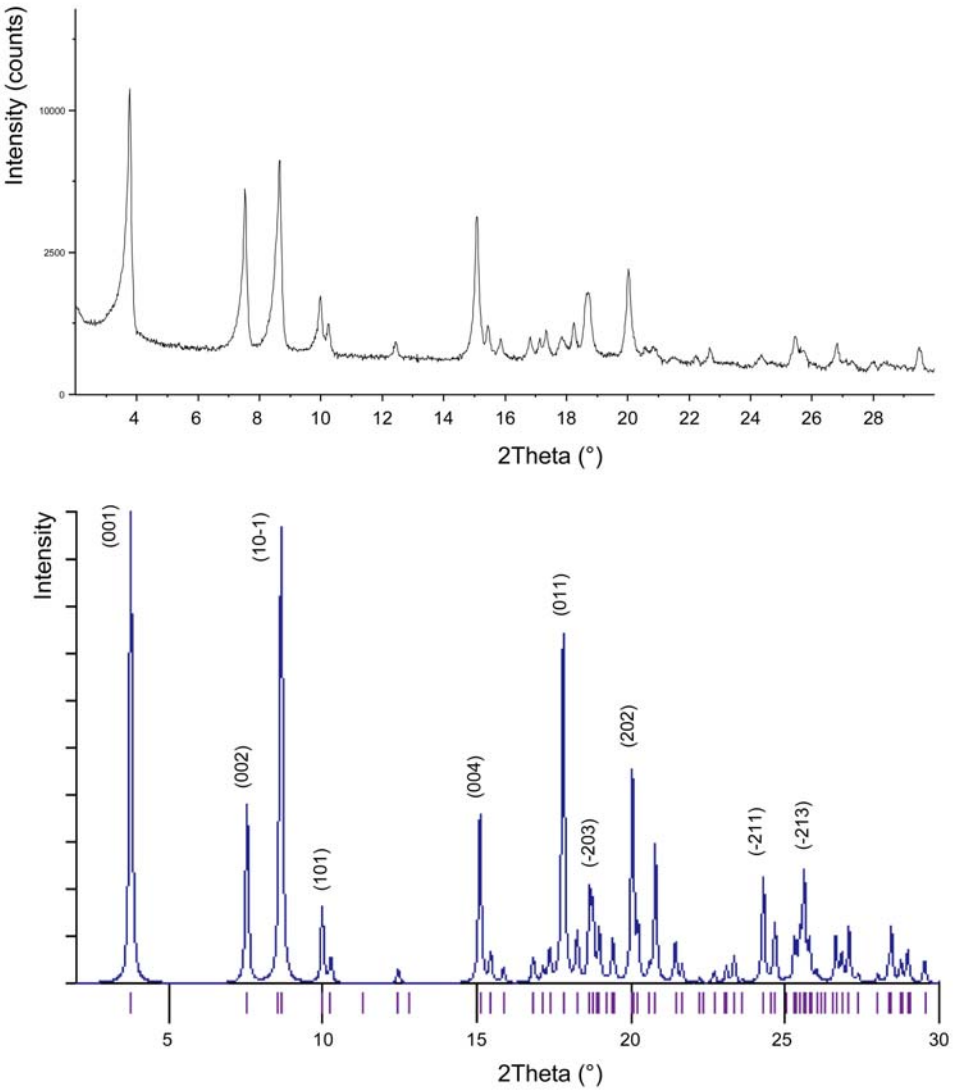


Figure S6. Experimental (top) and calculated (bottom) powder X-ray diffraction patterns of **1.**

Table S1. Lattice distances d in Å and relative intensities (rel. int.) of prominent observed oriented reflections in fiber X-ray diffraction pattern of **1** bundle.

equatorial			meridional		
d /Å	rel. int.	*hkl*	d / Å	rel. int.	*hkl*
23.5	s	001	4.97	s	011
11.7	s	002	4.67	w	012
10.2	s	10-1	4.42	w	111
8.78	m	101	4.27	m	013
7.08	m	102			
5.85	m	004			
4.85	w	201			
4.70	m	104			
4.28	m	-204			

Relative intensities were estimated as strong (s), medium (m) and very weak (w). They are listed as meridional (parallel to the bundle axis) and equatorial (normal to the bundle axis). The reflections were indexed according to the monoclinic unit cell with a = 10.53 Å, b = 5.10 Å, c = 23.90 Å, β = 101.1.

NMR spectroscopy

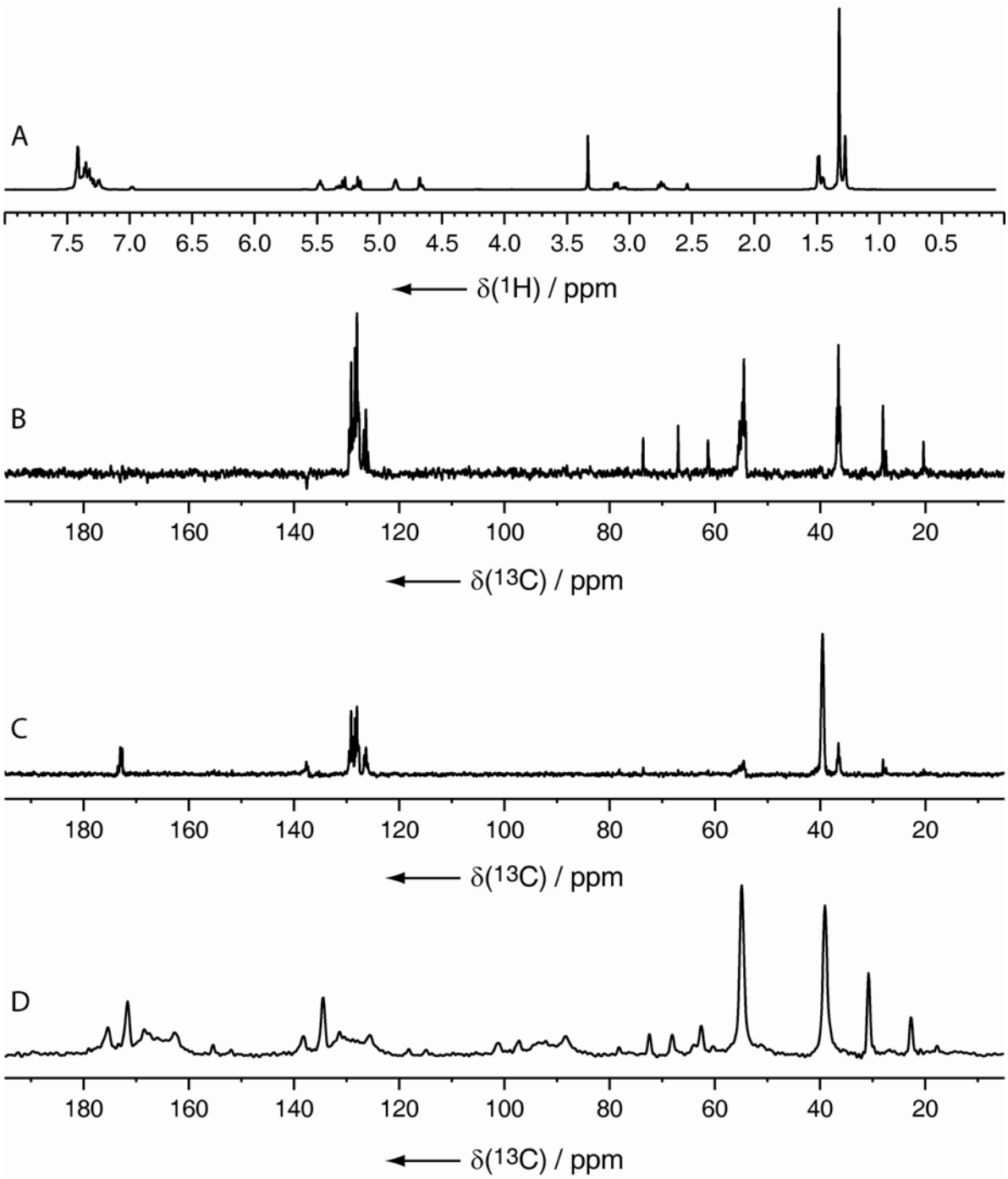


Figure S7. Solution and solid-state NMR spectra of **1** (containing 10% U-^{13}C enriched Phe) recorded at a magnetic field strengths of 14.1 T (A-C) and 17.6 T (D).

A) ^{1}H NMR spectrum of **1** in DMSO.

B) ^{13}C INEPT NMR spectrum of **1** in DMSO.

C) ^{13}C directly polarized NMR spectrum in DMSO.

D) ^{13}C CP MAS NMR spectrum of **1** in fibrillar form at a MAS frequency of 7 kHz.

All NMR spectra were recorded on a Bruker Avance 750 NMR spectrometer. The length of a ^{13}C 90° pulse was 5 µs and 4 µs for the ^{1}H 90° pulse. ^{13}C CP MAS spectra were acquired with CP contact time of 700 µs. For heteronuclear decoupling a ^{1}H radio-frequency field strength of 65 kHz was applied using the TPPM decoupling sequence. ^{13}C chemical shifts were referenced externally relative to TMS. NMR experiments were carried out at a temperature of 303 K and a MAS frequency of 7 kHz.

Quantum Chemical calculations

All quantum chemical calculations were performed employing the Gaussian 03 software package.[1]

A systematic conformational analysis of **1** was performed at the HF/6-31G* level of ab initio MO theory by variation of the backbone torsion angles of the L-Phe and D-Oxd residues. The most important conformers were reoptimized at the B3LYP/6-311+G(2d,p) level. The backbone torsion angles of the most important conformers are compared in Table S2.

The NMR spectra were calculated on the basis of the GIAO method at the B3LYP/6-311+G(2d,p) level. The differences of the ^{13}C chemical shifts of the Cα and Cβ atoms of L-Phe are given in Table S2. To compare the X-ray packages of peptide **1** and the Aib peptide with Aib instead of L-Phe, dimers from the corresponding X-ray structures were taken as starting points for geometry optimization. In both packages, L-Phe and Aib were mutually exchanged and the structures reoptimized. The basic structures of both packages are kept after geometry optimization with both peptides.

Table S2. Backbone torsion angles,[a] total energy differences[b] and ^{13}C chemical shift differences[c] beween the Cα and Cβ atoms of L-Phe for important conformers of **1** obtained by ab initio MO theory at the HF/6-31G* and B3LYP/6-311+G(2d,p) levels.

Conformer	L-Phe		D-Oxd		ΔE	Δ(δ(Cα)-δ(Cβ))[d]
	φ	ψ	φ	ψ		
1a[e]	-114.7	159.9	73.9	14.8	**0.0**[f]	14.4
	-121.3	158.7	68.2	15.6	**0.0**	
1b	70.1	162.1	67.5	-158.2	1.9	27.8
	68.8	166.1	68.4	-161.3	0.8	
1c	69.6	59.7	76.9	-1.4	1.7	26.4
	72.9	60.3	72.8	0.3	0.7	
1d	-98.3	154.2	75.0	4.3	0.4	16.5
	-84.1	155.4	73.3	-7.4	0.0	

[a] In degrees; first line B3LYP/6-311+G(2d,p) level, second line HF/6-31G* level. [b] In kcal/mol. [c] In ppm. [d] B3LYP/6 311+G(2d,p) level. [e] Corresponding to the X-ray structure. [f] E_T(B3LYP/6-311+G(2d,p) = -1645.489706a.u.; E_T(HF/6-31G*) = -1635.099713 a.u.

Reference

1. Gaussian 03, Revision D.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Wallingford CT, 2004.