Supplementary Material (ESI) for Chemical Communications

Electronic Supplementary Information

Tailbiter: a new amide foldamer

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Synthesis of 1a.

0.942 g of acid chloride **3** (4.85 mmol) were dissolved in 90 mL of dry CH_2Cl_2 and added drop wise over a solution of 2.029 g **2** (1.94 mmol) and 0.384 g of pyridine (4.85 mmol) in 40 mL of dry CH_2Cl_2. The reaction was stirred under nitrogen for 16 h. Then the solvent was removed under reduced pressure and the crude was purified by flash chromatography on silica, eluting with a gradient mixture from CH_2Cl_2:THF 90:10 v/v to CH_2CL_2:THF:Methanol 90:8:2. Obtained 1.922 g of **1a** as a white solid (75% yield).

1H-NMR ($CDCl_3$/DMSO-*d6* 5:1 v/v): 12.36 (s, 2 H), 9.32 (s, 2H), 9.29 (s, 2H) 8.57 (s, 1H), 8.07 (d, J = 7.2 Hz, 2H), 7.61 (s, 2H), 7.54 (s, 2H), 7.50 (t, J= 7.6, 1H), 7.25 (m, 10H) 6.95 (s, 4H), 6.92 (s, 4H), 5.02 (s, 4H), 3.48 (broad, 8H), 2.31 (broad, 8H), 2.16 (s, 12H), 2.13 (s, 12H) ppm.

HR-MS: Calculated for $C_{76}H_{76}N_{10}O_{12}$: 1321.572244. Found: 1321.574510.

Synthesis of 1b

0.500 g of **1a** (0.38 mmol) were dissolved in 30 mL of dry acetonitrile; over this, 400 μL of trimethylsilyl iodine (TMSI, 1.52 mmol) were added and the solution was stirred under nitrogen for 16 hours. Then, the solvent was removed under reduced pressure, and was re-dissolved in methanol. The methanol was removed under reduced pressure and the solid was triturated in 30 mL of CH_2Cl_2. Suspension was filtered of and the solid remnant was dried under vacuum and carried out in the next step without further purification.). 0.328 g of the intermediate (0.31 mmol) were then dissolved in 10 mL of dry acetonitrile, and added drop wise over 30 mL of dry CH_2CL_2 containing 0.71 g of soubilising acid (0.93 mmol), 0.127g of 1-hydroxybenzotriazole hidrate (HOBT, 0.97 mmol), 0.181 g of 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hidrochloride (EDC, 0.97 mmol) and 130 mL of Triethylamine (0.97 mmol). The mixture was stirred for 16 hours. Then the solvent was removed under reduced pressure and the crude was purified by flash chromatography on silica, using as eluent a mixture CH_2CL_2:Methanol 98:2 v/v. Obtained 0.200 g of **1b** as a white solid. (25 % yield).

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1H NMR ($CDCl_3$/DMSO-*d6* 5:1 v/v): 12.00 (s, 2 H), 8.97 (s, 4H), 8.32 (s, 1H), 7.83 (d, J = 7.9 Hz, 2H), 7.36 (dd, J= 3.6 and 1,5 Hz, 2H), 7.29 (t, J = 2.03 Hz, 2H), 7.25 (t, J= 7.9, Hz 1H), 6.69 (s, 4H), 6.66 (s, 4H), 6.22 (s, 4H); 3.61 (m, 12H); 3.45 (broad, 4H), 3.21 (broad, 4H), 2.14 (br, 4H), 2.01 (br, 4H), 1.92 (s, 12H), 1.88 (s, 12H),1.42 (m, 12H), 1.13 (m, 12H), 0.90 (s, 120H), 0.53 (t, J = 6.6 Hz, 18H) ppm.

MS-MALDI Calculated for $C_{160}H_{244}N_{10}O_{16}$: 2561.9. Found 2562

Table 1 ESI. Folding induced changes in chemical shift (Δδ ppm).

Proton	$\Delta\delta_{exp}$	$\Delta\delta_{calc}$	error ($\Delta\delta_{exp}$- $\Delta\delta_{calc}$)
A	-1.29	-1.25	-0.04
B	-2.52	-2.58	0.06
C	2.92	2.85	0.06
D	-0.12	-0.06	-0.06
E	-0.09	0.00	-0.09
H	-0.05	-0.01	-0.04
I	0.63	0.42	0.21
J	0.25	0.10	0.16
K	0.07	-0.03	0.10
L	-0.16	-0.10	-0.06
J'	0.31	0.09	0.22
I'	0.94	0.92	0.02
H'	-0.05	-0.04	-0.01
F'	0.01	0.02	-0.01
E'	-0.07	-0.04	-0.03
D'	0.39	0.13	0.26
C'	2.51	2.50	0.01
B'	0.05	0.09	-0.04
A'	0.06	0.06	0.00