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1. Syntheses and characterization of compounds

General information

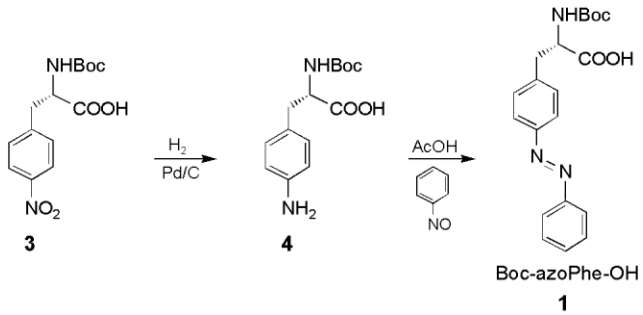
All reagents were used as received from commercial suppliers without further purification. Thin-layer chromatography (TLC) was performed on Macherey-Nagel Polygram® SIL G/UV precoated silica gel polyester plates. The products were visualized by exposure to UV light (254 nm) or submersion in ninhydrin or phosphomolybdic acid. Column chromatography was performed using Macherey-Nagel 60Å silica gel. Melting points were determined on a Gallenkamp apparatus. Optical rotations were measured in a JASCO P-1020 polarimeter. IR spectra were recorded on a Nicolet Avatar 360 FTIR spectrophotometer; *ν*max is given for the main absorption bands. 1H and 13C NMR spectra were registered on a Bruker AV-400 or ARX-300 instrument at room temperature (unless otherwise indicated) using the residual solvent signal as the internal standard; chemical shifts (δ) are expressed in ppm and coupling constants (J) in Hertz. High-resolution mass spectra were recorded on a Bruker Microtof-Q spectrometer.

General procedures for peptide synthesis

Cleavage of the *N*-Boc protecting group: Trifluoroacetic acid (10 mL) was added to an ice-cooled solution of the corresponding *N*-Boc-protected compound (ca. 2 g) in dichloromethane (15 mL). The solution was stirred at room temperature for 2 h (unless otherwise indicated) and evaporated. The residue obtained was repeatedly dissolved in dichloromethane and the solvent evaporated to yield the crude trifluoroacetate salt, which was used in the next step without further purification.

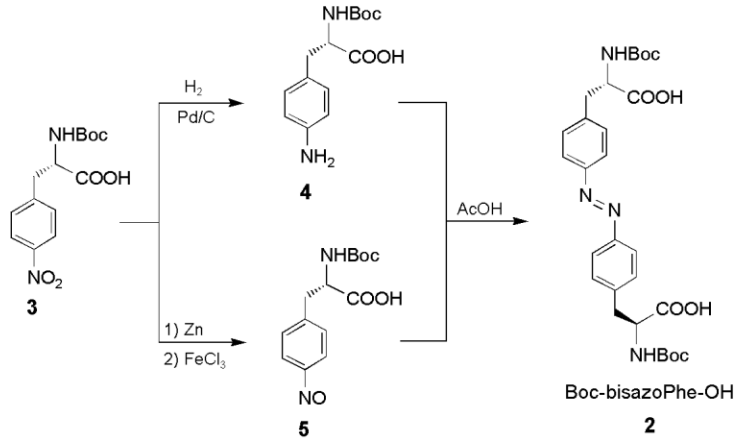
Peptide bond formation: The trifluoroacetate salt obtained in the previous step (1 equiv) was dissolved in dichloromethane (10 mL), the solution was cooled to 0 ºC and NMM (*N*-methylmorpholine) (1.5 equiv) was added to generate the free amino group. Separately, the *N*-Boc-protected amino acid (1.2 equiv, unless otherwise indicated) was dissolved in dichloromethane (10 mL), cooled to 0 ºC, and treated with EDC [*N*-(3- dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride] (1.2 equiv) and HOBt (1-hydroxybenzotriazole) (1.2 equiv). After stirring for 15–30 min, NMM (1.2 equiv) was added. The two solutions were then combined and the reaction mixture was stirred at room temperature for 2 d. The solvent was eliminated and the residue was taken up in ethyl acetate (100 mL). The solution was successively washed with 5% aqueous KHSO4 (3 x 30 mL), 5% aqueous NaHCO3 (3 x 30 mL) and brine (1 x 30 mL). After drying and filtering, the solvent was eliminated and the residue was purified by column chromatography with the eluent indicated in each case.

Synthesis of **Boc-azoPhe-OH (1)**



A mixture of **3** (7.50 g, 24.19 mmol) and 10% palladium-carbon (1.00 g) in methanol (50 mL) was stirred at room temperature under an atmospheric pressure of hydrogen gas for 24 h. After filtration of the catalyst, the solvent was evaporated and the compound obtained (**4**) was dissolved in glacial acetic acid (50 mL). A solution of nitrosobenzene (2.85 g, 26.60 mmol) in glacial acetic acid (80 mL) was added and the reaction was kept at room temperature for 3 d. The solvent was evaporated and the residue was dissolved in ethyl acetate (300 mL) and washed with 5% aqueous $KHSO_4$ (3 x 80 mL). The organic phase was dried over anhydrous $MgSO_4$ and filtered. Elimination of the solvent and purification by column chromatography (eluent: dichloromethane/isopropanol 95/5) afforded Boc-azoPhe-OH (**1**) as a yellow solid (7.05 g, 19.11 mmol, 79% yield); m.p. 137 ºC; IR (nujol) ν 3423–2208, 3355, 3307, 3245, 1715, 1694, 1652, 1646, 1457, 1155, 1056 cm^{-1}; $[\alpha]_D$ = +22.09 (*c* 0.44, MeOH); ^{1}H-NMR ($CDCl_3$, 300 MHz, 50 ºC) δ 7.94–7.84 (m, 4H), 7.54–7.42 (m, 3H), 7.38–7.32 (m, 2H), 4.97 (d, *J* = 8.3 Hz, 1H), 4.63 (m, 1H), 3.30 (dd, *J* = 14.0, 5.7 Hz, 1H), 3.16 (dd, *J* = 14.0, 6.7 Hz, 1H), 1.44 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz, 50 ºC) δ 173.71, 155.68, 153.29, 152.43, 139.40, 131.05, 130.30, 129.24, 123.33, 123.07, 80.97, 54.80, 38.21, 28.54 ppm; HRMS (ESI) $C_{20}H_{22}N_3O_4$ $[M–H]^-$: calcd. 368.1616, found 368.1614.

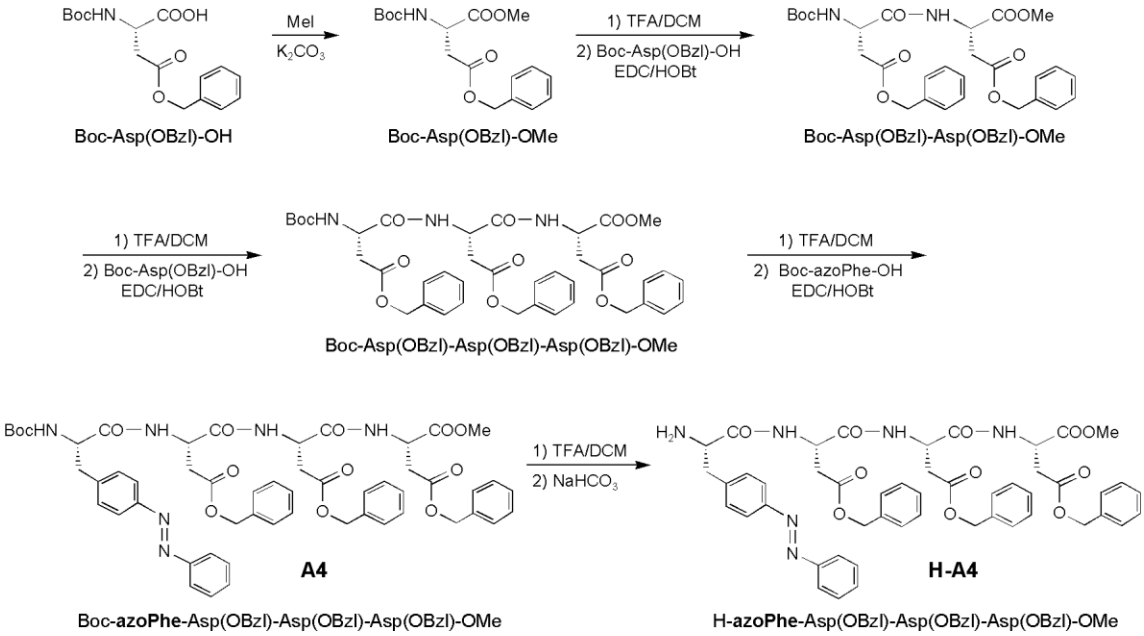
Synthesis of **Boc-bisazoPhe-OH** (**2**)



Compound **3** (620 mg, 2.00 mmol) and ammonium chloride (342 mg, 6.40 mmol) were dissolved in ethanol/water 5/1 (9 mL) and zinc dust (261 mg, 4.00 mmol) was added in small portions. The suspension obtained was stirred at room temperature for 90 min and then filtered through Celite®. The filtrate was cooled to 0 ºC and a solution of iron (III) chloride (1.62 g, 10.00 mmol) in ethanol/water 5/1 (21 mL) kept at 0 ºC was added. The mixture was stirred at this temperature for 45 min, concentrated to eliminate the ethanol, diluted with water (40 mL), and extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were washed with brine (3 x 40 mL), dried over anhydrous $MgSO_4$, and filtered. The solvent was evaporated and the residue was rapidly chromatographed (eluent: dichloromethane/methanol 8/2) to afford **5** as a greenish oil (498 mg, 1.69 mmol, 84% yield), which was used immediately for the next synthetic step.

Separately, a mixture of **3** (1.01 g, 3.25 mmol) and 10% palladium-carbon (120 mg) in methanol (10 mL) was stirred at room temperature under an atmospheric pressure of hydrogen gas for 24 h. The catalyst was eliminated by filtration through Celite® and the solvent was removed to afford **4**. This compound was dissolved in glacial acetic acid (10 mL) and freshly prepared **5** (498 mg, 1.69 mmol) dissolved in glacial acetic acid (10 mL) was added. The reaction was kept at room temperature overnight and then the solvent was evaporated. The resulting residue was dissolved in ethyl acetate (100 mL), washed with 5% aqueous $KHSO_4$ (3 x 40 mL) and brine (1 x 40 mL). After drying and filtering, elimination of the solvent and purification by column chromatography (eluent: dichloromethane/methanol 14/1 containing 1% acetic acid (v/v)) provided Boc-bisazoPhe-OH (**2**) as an orange solid (461 mg, 0.83 mmol, 49% yield); m.p. 320 ºC (dec.); IR (nujol) ν 3420–2364, 3364, 1714, 1689, 1520 cm^{-1}; $[\alpha]_D = +30.5$ (*c* 0.39, MeOH); ^{1}H-NMR (CD_3OD, 400 MHz) δ (major *trans* isomer) 7.81 (d, J = 8.2 Hz, 4H), 7.39 (d, J = 8.3 Hz, 4H), 4.39 (dd, J = 9.2, 5.0 Hz, 2H), 3.24 (dd, J = 13.8, 5.0 Hz, 2H), 2.98 (dd, J = 13.8, 9.2 Hz, 2H), 1.36 (s, 18H) ppm; ^{13}C-NMR (CD_3OD, 100 MHz) δ 175.26, 157.82, 152.86, 142.41, 131.24, 123.76, 80.57, 56.17, 38.60, 28.66 ppm; HRMS (ESI) $C_{28}H_{35}N_4O_8$ $[M–H]^-$: calcd. 555.2460, found 555.2459.

Synthesis of **A4** and **H-A4**



Boc-Asp(OBzl)-OMe:

Potassium carbonate (11.54 g, 83.53 mmol) was added to a solution of Boc-Asp(OBzl)-OH (9.00 g, 27.84 mmol) in DMF (100 mL). After 2 h at room temperature, iodomethane (5.20 mL, 83.53 mmol) was added and stirring was continued for additional 24 h. The solvent was evaporated to dryness and the residue was partitioned between ethyl acetate (100 mL) and water (120 mL). The phases were separated and the aqueous layer was further extracted with ethyl acetate (2 x 100 mL). The combined organic extracts were washed successively with water (1 x 90 mL), 5% aqueous $Na_2S_2O_3$ (3 x 90 mL), and brine (3 x 90 mL), dried over anhydrous $MgSO_4$ and filtered. Elimination of the solvent afforded Boc-Asp(OBzl)-OMe as a white solid (9.21 g, 27.28 mmol, 98% yield); m.p. 64 ºC; $[\alpha]_D$ = –8.7 (*c* 0.38, MeOH); IR (nujol) *v* 3399, 1735, 1704, 1506, 1456 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.39–7.30 (m, 5H), 5.49 (d, *J* = 8.2 Hz, 1H), 5.14 (d, *J* = 15.8 Hz, 1H), 5.11 (d, *J* = 15.8 Hz, 1H), 4.59 (m, 1H), 3.69 (s, 3H), 3.04 (dd, *J* = 17.0, 4.5 Hz, 1H), 2.87 (dd, *J* = 17.0, 4.8 Hz, 1H), 1.44 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.59, 170.88, 155.45, 135.47, 128.71, 128.53, 128.42, 80.27, 66.91, 52.78, 50.07, 37.01, 28.40 ppm; HRMS (ESI) $C_{17}H_{23}NNaO_6$ $[M+Na]^+$: calcd. 360.1418, found 360.1454.

Boc-Asp(OBzl)-Asp(OBzl)-OMe:

Boc-Asp(OBzl)-OH (2.33 g, 7.20 mmol) was coupled with TFA·H-Asp(OBzl)-OMe [obtained by treatment of Boc-Asp(OBzl)-OMe (2.02 g; 6.00 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 96% (3.12 g, 5.74 mmol); m.p. 68 ºC; IR (nujol) *v* 3455, 3436, 1753, 1735, 1701, 1653, 1458 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.40 (d, *J* = 9.1 Hz, 1H) overlapped with 7.38–7.29 (m, 10H), 5.58 (d, *J* = 8.3 Hz, 1H), 5.16–5.06 (m, 4H), 4.83 (m, 1H), 4.61–4.52 (m, 1H), 3.67 (s, 3H), 3.09–3.00 (m, 2H), 2.86 (dd, *J* = 17.1, 4.8 Hz, 1H), 2.74 (dd, *J* = 17.2, 6.0 Hz, 1H), 1.45 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.70, 170.81, 170.72, 170.62, 155.44, 135.51, 135.49, 128.72, 128.54, 128.51, 128.48, 128.39, 80.64, 66.96, 66.95, 52.87, 50.67, 48.85, 36.39, 36.25, 28.38 ppm; HRMS (ESI) $C_{28}H_{34}N_2NaO_9$ $[M+Na]^+$: calcd. 565.2157, found 565.2183.

Boc-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe:

Boc-Asp(OBzl)-OH (2.14 g, 6.63 mmol) was coupled with TFA·H-[Asp(OBzl)]$_2$-OMe [obtained by treatment of Boc-[Asp(OBzl)]$_2$-OMe (3.00 g, 5.53 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 95/5. Yield: 92% (3.82 g, 5.11 mmol); m.p. 94 ºC; IR (nujol) ν 3411, 3292, 1743, 1727, 1712, 1686, 1642, 1457 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.56 (d, J = 7.9 Hz, 1H), 7.49 (d, J = 8.3 Hz, 1H), 7.38–7.28 (m, 15H), 5.61 (d, J = 7.7 Hz, 1H), 5.20–5.07 (m, 6H), 4.90–4.82 (m, 2H), 4.53–4.46 (m, 1H), 3.63 (s, 3H), 3.09–2.69 (m, 6H), 1.45 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.59, 171.48, 170.79, 170.64, 170.33, 169.88, 155.39, 135.49, 135.42, 135.34, 128.59, 128.58, 128.56, 128.40, 128.35, 128.32, 128.26, 80.60, 66.94, 66.87, 66.82, 52.64, 50.87, 49.31, 48.86, 36.07, 36.06, 35.66, 28.25 ppm; HRMS (ESI) $C_{39}H_{45}N_3NaO_{12}$ $[M+Na]^+$: calcd. 770.2895, found 770.2888.

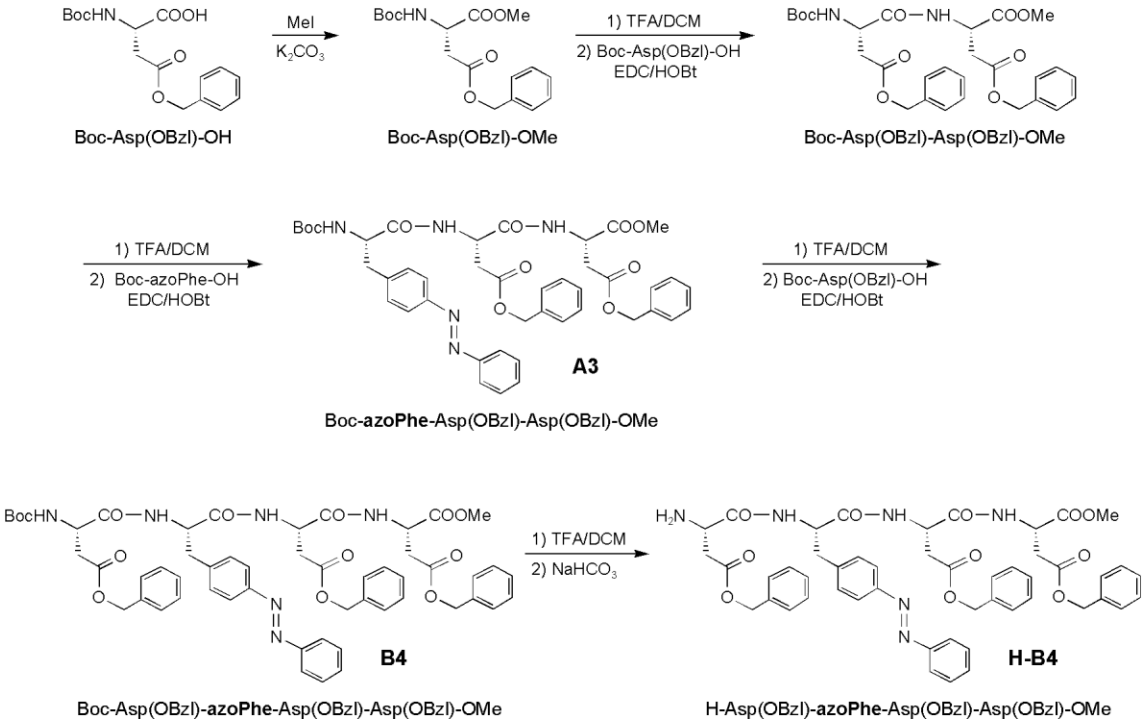
Boc-azoPhe-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe (A4):

Boc-azoPhe-OH (**1**) (2.13 g, 5.77 mmol) was coupled with TFA·H-[Asp(OBzl)]$_3$-OMe [obtained by treatment of Boc-[Asp(OBzl)]$_3$-OMe (3.60 g, 4.81 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 98% (4.71 g, 4.71 mmol); m.p. 126 ºC; IR (nujol) ν 3315, 3281, 1734, 1687, 1647 cm^{-1}; $[\alpha]_D$ = –4.4 (c 0.34, MeOH); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.92–7.82 (m, 4H), 7.57–7.45 (m, 4H), 7.43–7.20 (m, 19H), 5.18–5.04 (m, 6H), 4.98 (d, J = 6.1 Hz, 1H), 4.90–4.79 (m, 2H), 4.73 (m, 1H), 4.36 (m, 1H), 3.63 (s, 3H), 3.22 (dd, J = 13.8, 5.0 Hz, 1H), 3.10–2.70 (m, 7H), 1.39 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.59, 171.58, 171.36, 170.79, 170.51, 170.02, 169.77, 155.82, 152.66, 151.85, 139.64, 135.59, 135.57, 135.31, 131.17, 130.05, 129.19, 128.68, 128.63, 128.52, 128.40, 128.32, 123.31, 122.94, 81.00, 67.15, 66.92, 66.88, 56.05, 52.73, 49.84, 49.71, 48.97, 37.52, 36.22, 35.60, 35.48, 28.33 ppm; HRMS (ESI) $C_{54}H_{59}N_6O_{13}$ $[M+H]^+$: calcd. 999.4135, found 999.4147.

H-azoPhe-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe (H-A4):

Boc-azoPhe-[Asp(OBzl)]$_3$-OMe (**A4**) (1.50 g, 1.50 mmol) was treated with trifluoroacetic acid according to the general procedure. The trifluoroacetate salt obtained, TFA·H-azoPhe-[Asp(OBzl)]$_3$-OMe, was redissolved in dichloromethane (80 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 30 mL). After drying and filtering, evaporation of the solvent afforded pure **H-A4** (1.30 g, 1.45 mmol, 96% yield); m.p. 120 ºC; IR (nujol) ν 3373, 3304, 1729, 1701, 1684, 1670, 1653 cm^{-1}; $[\alpha]_D$ = –35.1 (c 0.36, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.30 (d, J = 8.4 Hz, 1H), 7.93–7.85 (m, 4H), 7.62 (d, J = 8.4 Hz, 1H), 7.55–7.43 (m, 4H), 7.38–7.27 (m, 17H), 5.15–5.08 (m, 6H), 4.88–4.75 (m, 3H), 3.74 (dd, J = 9.1, 3.9 Hz, 1H), 3.64 (s, 3H), 3.27 (dd, J = 13.7, 3.9 Hz, 1H), 3.09–2.68 (m, 7H), 1.82 (brs, 2H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 174.70, 171.87, 171.39, 170.76, 170.49, 170.44, 169.88, 152.69, 151.82, 140.82, 135.56, 135.46, 135.39, 131.15, 130.16, 129.20, 128.68, 128.50, 128.45, 128.41, 128.40, 128.29, 123.27, 122.95, 67.07, 67.00, 66.97, 56.20, 52.82, 49.52, 49.45, 49.00, 40.45, 36.22, 35.69, 35.52 ppm; HRMS (ESI) $C_{49}H_{51}N_6O_{11}$ $[M+H]^+$: calcd. 899.3610, found 899.3589.

Synthesis of **A3**, **B4** and **H-B4**



Boc-Asp(OBzl)-OMe:

See page S5.

Boc-Asp(OBzl)-Asp(OBzl)-OMe:

See page S5.

Boc-azoPhe-Asp(OBzl)-Asp(OBzl)-OMe (A3):

Boc-azoPhe-OH (**1**) (2.04 g, 5.52 mmol) was coupled with TFA·H-[Asp(OBzl)]$_2$-OMe [obtained by treatment of Boc-[Asp(OBzl)]$_2$-OMe (2.50 g, 4.61 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 94% (3.44 g, 4.33 mmol); m.p. 118 ºC; IR (nujol) ν 3317, 3291, 1739, 1734, 1718, 1696, 1685, 1652 cm^{-1}; $[\alpha]_D$ = +1.8 (*c* 0.46, MeOH); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.92–7.83 (m, 4H), 7.54–7.43 (m, 3H), 7.39 (d, *J* = 8.3 Hz, 1H), 7.36–7.27 (m, 12H), 7.14 (d, *J* = 8.1 Hz, 1H), 5.17–5.06 (m, 4H), 4.89 (d, *J* = 6.5 Hz, 1H), 4.85–4.74 (m, 2H), 4.36 (m, 1H), 3.63 (s, 3H), 3.20 (dd, *J* = 14.0, 6.0 Hz, 1H), 3.14–2.92 (m, 3H), 2.84 (dd, *J* = 17.1, 5.2 Hz, 1H), 2.67 (dd, *J* = 17.1, 6.7 Hz, 1H), 1.40 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.66, 171.19, 170.65, 170.56, 169.87, 152.73, 151.88, 139.76, 135.78, 135.57, 135.42, 131.17, 130.12, 129.23, 128.73, 128.72, 128.54, 128.52, 128.49, 128.47, 123.36, 122.98, 80.82, 67.11, 67.01, 55.68, 52.83, 49.27, 48.97, 37.81, 36.16, 35.97, 28.36 ppm; HRMS (ESI) $C_{43}H_{48}N_5O_{10}$ $[M+H]^+$: calcd. 794.3396, found 794.3403.

Boc-Asp(OBzl)-azoPhe-Asp(OBzl)-Asp(OBzl)-OMe (B4):

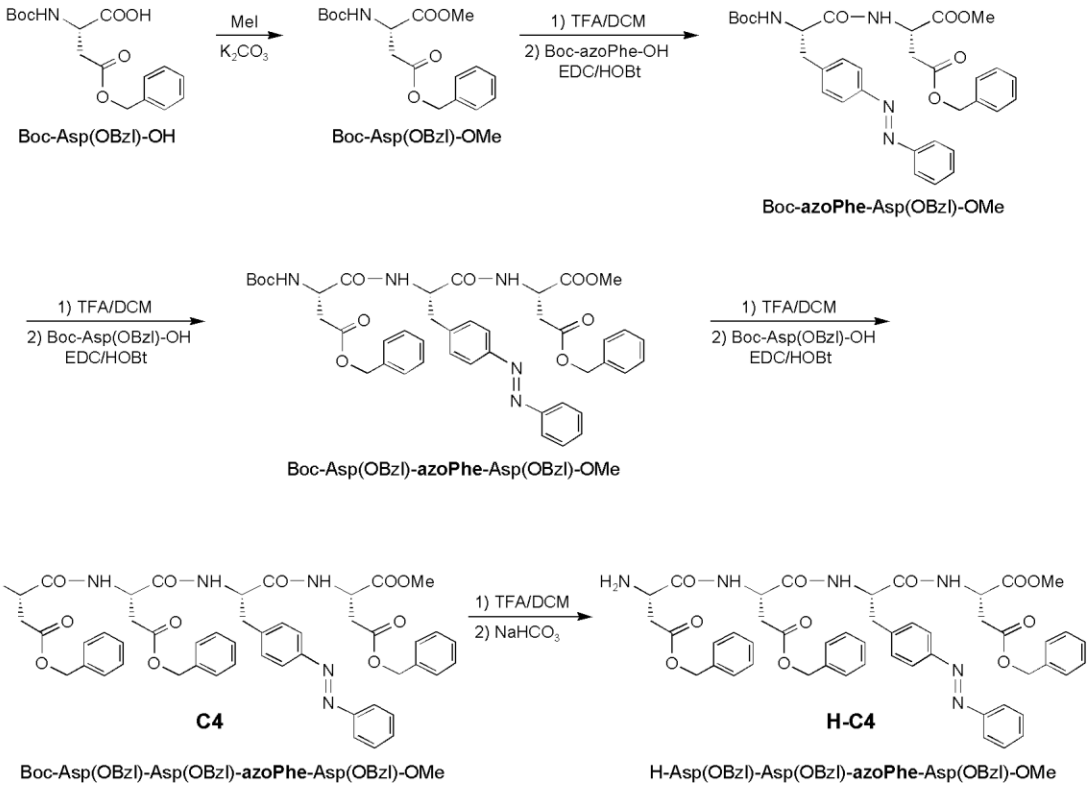
Boc-Asp(OBzl)-OH (1.71 g, 5.29 mmol) was coupled with TFA·H-azoPhe-[Asp(OBzl)]$_2$-OMe [obtained by treatment of Boc-azoPhe-[Asp(OBzl)]$_2$-OMe (**A3**) (3.50 g, 4.41 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent:

dichloromethane/methanol 95/5. Yield: 94% (4.14 g, 4.14 mmol); m.p. 133 ºC; IR (nujol) ν 3303, 3280, 1734, 1718, 1700, 1696, 1684, 1652 cm^{-1}; $[\alpha]_D = -31.1$ (c 0.51, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.90–7.85 (m, 4H), 7.53–7.45 (m, 3H), 7.37–7.27 (m, 18H), 7.11 (d, J = 6.7 Hz, 1H), 6.94 (d, J = 6.1Hz, 1H), 5.51 (d, J = 7.6 Hz, 1H), 5.15–5.03 (m, 6H), 4.86–4.78 (m, 2H), 4.58 (m, 1H), 4.45 (m, 1H), 3.63 (s, 3H), 3.18 (d, J = 6.5 Hz, 2H), 3.00–2.73 (m, 6H), 1.37 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.96, 171.51, 171.39, 170.72, 170.54, 170.28, 169.79, 155.59, 152.70, 151.83, 139.46, 135.61, 135.50, 135.31, 131.14, 130.14, 129.21, 128.73, 128.68, 128.67, 128.57, 128.45, 128.43, 128.38, 128.37, 123.45, 122.95, 80.98, 67.21, 66.96, 66.95, 54.94, 52.80, 50.89, 49.51, 48.99, 37.01, 36.20, 35.82, 35.72, 28.34 ppm; HRMS (ESI) $C_{54}H_{58}N_6NaO_{13}$ $[M+Na]^+$: calcd. 1021.3954, found 1021.4009.

H-Asp(OBzl)-azoPhe-Asp(OBzl)-Asp(OBzl)-OMe (H-B4):

Boc-Asp(OBzl)-azoPhe-[Asp(OBzl)]$_2$-OMe (**B4**) (1.50 g, 1.50 mmol) was treated with trifluoroacetic acid according to the general procedure. The trifluoroacetate salt obtained, TFA·H-Asp(OBzl)-azoPhe-[Asp(OBzl)]$_2$-OMe, was redissolved in dichloromethane (80 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 30 mL). After drying and filtering, evaporation of the solvent afforded pure **H-B4** (1.24 g, 1.38 mmol, 95% yield); m.p. 143 ºC; IR (nujol) ν 3366, 3303, 1733, 1719, 1669, 1653, 1646 cm^{-1}; $[\alpha]_D = -8.7$ (c 0.50, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.86 (d, J = 7.0 Hz, 1H), 7.84–7.76 (m, 4H), 7.47–7.37 (m, 3H), 7.33 (d, J = 8.3 Hz, 1H), 7.30–7.18 (m, 17H), 7.15 (d, 1H, J = 8.1 Hz), 5.08–4.96 (m, 6H), 4.80–4.69 (m, 2H), 4.48 (m, 1H), 3.61–3.55 (m, 1H) overlapped with 3.56 (s, 3H), 3.21–3.07 (m, 2H), 3.00 (dd, J = 17.2, 4.7 Hz, 1H), 2.92–2.71 (m, 3H), 2.69–2.58 (m, 2H), 1.71 (brs, 2H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 174.40, 171.95, 171.70, 170.72, 170.60, 170.49, 169.84, 152.63, 151.76, 142.76, 139.87, 135.55, 135.40, 131.14, 130.10, 129.19, 128.66, 128.42, 128.32, 128.30, 123.26, 122.94, 66.95, 66.94, 66.80, 54.81, 52.80, 51.78, 49.39, 48.98, 38.91, 36.94, 36.19, 35.65 ppm; HRMS (ESI) $C_{49}H_{51}N_6O_{11}$ $[M+H]^+$: calcd. 899.3610, found 899.3598.

Synthesis of **C4** and **H-C4**



Boc-Asp(OBzl)-OMe:

See page S5.

Boc-azoPhe-Asp(OBzl)-OMe:

Boc-azoPhe-OH (**1**) (2.63 g, 7.12 mmol) was coupled with TFA·H-Asp(OBzl)-OMe [obtained by treatment of Boc-Asp(OBzl)-OMe (2.00 g, 5.93 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 98% (3.40 g, 5.78 mmol); m.p. 133 ºC; IR (nujol) ν 3325, 3305, 1749, 1733, 1718, 1685, 1653, 1457 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.92–7.81 (m, 4H), 7.55–7.44 (m, 3H), 7.39–7.30 (m, 7H), 6.91 (d, J = 7.9 Hz, 1H), 5.10 (d, J = 16.0 Hz, 1H), 5.07 (d, J = 16.0 Hz, 1H), 5.00 (d, J = 7.0 Hz, 1H), 4.82 (m, 1H), 4.44 (m, 1H), 3.66 (s, 3H), 3.22–3.09 (m, 2H), 3.05 (dd, J = 17.2, 4.4 Hz, 1H), 2.89 (dd, J = 17.2, 4.7 Hz, 1H), 1.42 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 170.91, 170.69, 170.64, 155.28, 152.73, 151.78, 139.79, 135.40, 131.09, 130.21, 129.20, 128.72, 128.57, 128.46, 123.23, 122.92, 80.45, 67.00, 55.54, 52.92, 48.78, 38.22, 36.37, 28.37 ppm; HRMS (ESI) $C_{32}H_{36}N_4NaO_7$ $[M+Na]^+$: calcd. 611.2476, found 611.2465.

Boc-Asp(OBzl)-azoPhe-Asp(OBzl)-OMe:

Boc-Asp(OBzl)-OH (1.96 g, 6.06 mmol) was coupled with TFA·H-azoPhe-Asp(OBzl)-OMe [obtained by treatment of Boc-azoPhe-Asp(OBzl)-OMe (2.98 g, 5.05 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 96% (3.85 g, 4.85 mmol); m.p. 115 ºC; IR (nujol) ν 3287, 1733, 1719, 1699, 1684, 1646, 1457 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.91–7.86 (m, 4H), 7.53–7.44 (m, 3H), 7.40–7.27 (m, 12H), 7.04 (d, J = 7.9 Hz, 1H), 6.91 (d, J = 7.9 Hz, 1H), 5.58 (d, J = 8.3 Hz, 1H), 5.15–5.04 (m, 4H), 4.81 (m, 1H), 4.72 (m, 1H), 4.49 (m, 1H), 3.63 (s, 3H), 3.17 (d, J = 6.5 Hz, 2H), 3.08–2.96 (m, 2H), 2.85 (dd, J = 17.2, 4.9 Hz, 1H), 2.75 (dd, J =

17.3, 6.1 Hz, 1H), 1.40 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.85, 170.77, 170.63, 170.56, 170.01, 155.51, 152.73, 151.74, 139.56, 135.42, 131.04, 130.32, 129.18, 128.69, 128.51, 128.49, 128.45, 128.37, 123.27, 122.90, 80.82, 67.06, 67.00, 54.29, 52.88, 50.83, 48.82, 37.78, 36.26, 35.97, 28.34 ppm; HRMS (ESI) $C_{43}H_{47}N_5NaO_{10}$ $[M+Na]^+$: calcd. 816.3215, found 816.3249.

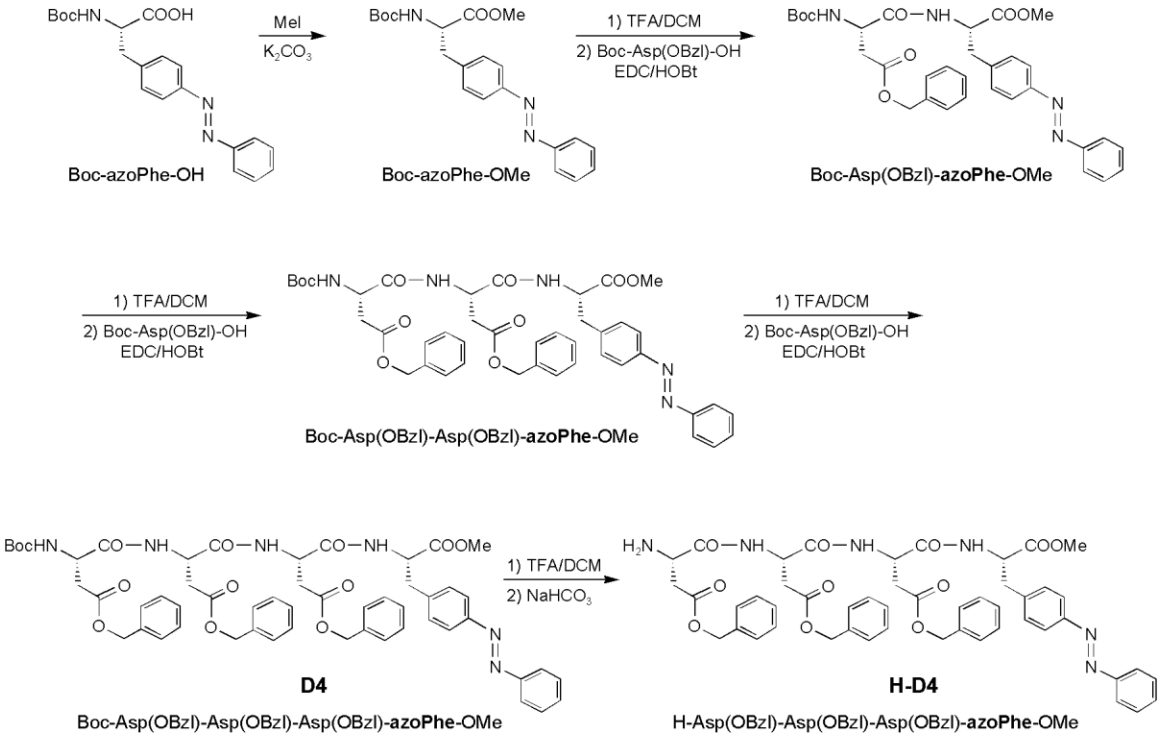
Boc-Asp(OBzl)-Asp(OBzl)-azoPhe-Asp(OBzl)-OMe (C4):

Boc-Asp(OBzl)-OH (1.59 g, 4.92 mmol) was coupled with TFA·H-Asp(OBzl)-azoPhe-Asp(OBzl)-OMe [obtained by treatment of Boc-Asp(OBzl)-azoPhe-Asp(OBzl)-OMe (3.26 g, 4.10 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 95/5. Yield: 91% (3.72 g, 3.73 mmol); m.p. 148 ºC; IR (nujol) ν 3276, 1733, 1716, 1696, 1685, 1668, 1638 cm^{-1}; $[\alpha]_D$ =–38.3 (*c* 0.42, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.89–7.84 (m, 4H), 7.53–7.42 (m, 4H), 7.39–7.26 (m, 18H), 7.02 (d, *J* = 8.1 Hz, 1H), 5.49 (d, *J* = 7.8, 1H), 5.13–5.00 (m, 6H), 4.83 (ddd, *J* = 8.2, 5.0, 5.0 Hz, 1H), 4.75–4.65 (m, 2H), 4.42 (m, 1H), 3.62 (s, 3H), 3.31 (dd, *J* = 14.2, 5.8 Hz, 1H), 3.12 (dd, *J* = 14.2, 8.1 Hz, 1H), 3.06–2.68 (m, 6H), 1.43 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.84, 171.61, 171.16, 170.75, 170.53, 170.15, 170.07, 155.51, 152.72, 151.65, 140.26, 135.51, 135.35, 135.27, 130.98, 130.18, 129.14, 128.72, 128.66, 128.56, 128.47, 128.45, 128.42, 128.39, 128.34, 123.19, 122.92, 80.93, 67.20, 67.09, 66.95, 54.65, 52.81, 51.08, 49.87, 48.89, 37.04, 36.31, 36.05, 35.13, 28.37 ppm; HRMS (ESI) $C_{54}H_{59}N_6O_{13}$ $[M+H]^+$: calcd. 999.4135, found 999.4142.

H-Asp(OBzl)-Asp(OBzl)-azoPhe-Asp(OBzl)-OMe (H-C4):

Boc-[Asp(OBzl)]$_2$-azoPhe-Asp(OBzl)-OMe (**C4**) (1.19 g, 1.19 mmol) was treated with trifluoroacetic acid according to the general procedure. The trifluoroacetate salt obtained, TFA·H-[Asp(OBzl)]$_2$-azoPhe-Asp(OBzl)-OMe, was redissolved in dichloromethane (80 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 30 mL). After drying and filtering, evaporation of the solvent afforded pure **H-C4** (1.01 g, 1.12 mmol, 94% yield); m.p. 109 ºC; IR (nujol) ν 3396, 3304, 3262, 1747, 1731, 1645 cm^{-1}; $[\alpha]_D$ = –24.3 (*c* 0.43, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.22 (d, *J* = 7.8 Hz, 1H), 7.84–7.71 (m, 4H), 7.47–7.36 (m, 3H), 7.32–7.11 (m, 18H), 6.97 (d, *J* = 8.1 Hz, 1H); 5.07–4.94 (m, 6H), 4.74 (m, 1H), 4.65–4.53 (m, 2H), 3.65–3.58 (m, 1H), 3.54 (s, 3H), 3.20 (dd, *J* = 14.0, 5.9 Hz, 1H), 3.05 (dd, *J* = 14.1, 8.0 Hz, 1H), 2.95–2.66 (m, 6H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.58, 171.51, 171.49, 170.87, 170.64, 170.31, 170.28, 152.72, 151.70, 140.16, 135.50, 135.47, 135.40, 131.10, 130.27, 129.21, 128.74, 128.71, 128.67, 128.56, 128.52, 128.46, 128.42, 128.38, 123.13, 122.95, 67.04, 67.03 (x2), 54.64, 52.88, 51.47, 49.88, 48.93, 38.22, 37.06, 36.30, 35.21 ppm; HRMS (ESI) $C_{49}H_{51}N_6O_{11}$ $[M+H]^+$: calcd. 899.3610, found 899.3579.

Synthesis of **D4** and **H-D4**



Boc-azoPhe-OMe:

Potassium carbonate (2.87 g, 20.76 mmol) was added to a solution of Boc-azoPhe-OH (**1**) (2.55 g, 6.92 mmol) in DMF (40 mL). After 2 h at room temperature, iodomethane (1.29 mL, 20.76 mmol) was added and stirring was continued for additional 24 h. The solvent was evaporated and the residue was partitioned between ethyl acetate (50 mL) and water (60 mL). The phases were separated and the aqueous layer was further extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were washed successively with water (1 x 40 mL), 5% aqueous $Na_2S_2O_3$ (3 x 40 mL) and brine (3 x 40 mL). After drying and filtering, evaporation of the solvent afforded Boc-azoPhe-OMe as an orange solid (2.21 g, 5.74 mmol, 83% yield); m.p. 73 ºC; IR (nujol) ν 3401, 1751, 1717, 1689, 1457 cm^{-1}; $[\alpha]_D$ = +37.9 (*c* 0.46, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.93–7.84 (m, 4H), 7.55–7.44 (m, 3H), 7.31–7.25 (m, 2H), 5.06 (d, *J* = 7.8 Hz, 1H), 4.65 (m, 1H), 3.73 (s, 3H), 3.22 (dd, *J* = 13.7, 5.8 Hz, 1H), 3.13 (dd, *J* = 13.7, 6.1 Hz, 1H), 1.43 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 172.21, 155.15, 152.73, 151.80, 139.49, 131.08, 130.17, 129.19, 123.11, 122.91, 80.16, 54.46, 52.43, 38.36, 28.41 ppm; HRMS (ESI) $C_{21}H_{25}N_3NaO_4$ $[M+Na]^+$: calcd. 406.1737, found 406.1721.

Boc-Asp(OBzl)-azoPhe-OMe:

Boc-Asp(OBzl)-OH (1.96 g, 6.06 mmol) was coupled with TFA·H-azoPhe-OMe [obtained by treatment of Boc-azoPhe-OMe (1.94 g, 5.05 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 93% (2.77 g, 4.70 mmol); m.p. 121 ºC; IR (nujol) ν 3336, 3301, 1745, 1733, 1685, 1667, 1653, 1457 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.92–7.85 (m, 4H), 7.55–7.44 (m, 3H), 7.38–7.27 (m, 7H), 7.02 (d, J = 7.3 Hz, 1H), 5.68 (d, J = 8.3 Hz, 1H), 5.15 (d, J = 19.1 Hz, 1H), 5.12 (d, J = 19.1 Hz, 1H), 4.87 (m, 1H), 4.58–4.52 (m, 1H), 3.71 (s, 3H), 3.25–3.05 (m, 3H), 2.71 (dd, J = 17.3, 5.9 Hz, 1H), 1.40 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.96, 171.31, 170.57, 155.58, 152.75, 151.79, 139.19, 135.47, 131.08, 130.27, 129.20, 128.71, 128.50, 128.37, 123.20, 122.92, 80.75, 67.01, 53.50, 52.54, 50.62, 37.82, 35.92, 28.33 ppm; HRMS (ESI) $C_{32}H_{37}N_4O_7$ $[M+H]^+$: calcd. 589.2657, found 589.2681.

Boc-Asp(OBzl)-Asp(OBzl)-azoPhe-OMe:

Boc-Asp(OBzl)-OH (1.66 g, 5.15 mmol) was coupled with TFA·H-Asp(OBzl)-azoPhe-OMe [obtained by treatment of Boc-Asp(OBzl)-azoPhe-OMe (2.53 g, 4.29 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 75% (2.55 g, 3.22 mmol); m.p. 146 ºC; IR (nujol) ν 3305, 1727, 1686, 1646 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.90–7.85 (m, 4H), 7.57 (d, J = 8.3 Hz, 1H), 7.53–7.45 (m, 3H), 7.36–7.27 (m, 12H), 7.16 (d, J = 7.8 Hz, 1H), 5.51 (d, J = 7.9 Hz, 1H), 5.13 (d, J = 20.3 Hz, 1H), 5.10 (d, J = 20.3 Hz, 1H), 5.02 (s, 2H), 4.87–4.79 (m, 2H), 4.49–4.42 (m, 1H), 3.68 (s, 3H), 3.24–3.12 (m, 2H), 3.08 (dd, J = 17.4, 4.1 Hz, 1H), 3.00 (dd, J = 17.2, 4.3 Hz, 1H), 2.78 (dd, J = 17.2, 6.5 Hz, 1H), 2.67 (dd, J = 17.4, 6.3 Hz, 1H), 1.44 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.81, 171.78, 171.35, 170.97, 169.90, 155.47, 152.74, 151.82, 139.42, 135.45, 135.36, 131.06, 130.23, 129.17, 128.71, 128.70, 128.52, 128.49, 128.42, 128.36, 123.23, 122.96, 80.83, 67.06, 67.06, 53.71, 52.49, 50.98, 49.36, 37.71, 36.11, 35.51, 28.39 ppm; HRMS (ESI) $C_{43}H_{47}N_5NaO_{10}$ $[M+Na]^+$: calcd. 816.3215, found 816.3220.

Boc-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-azoPhe-OMe (D4):

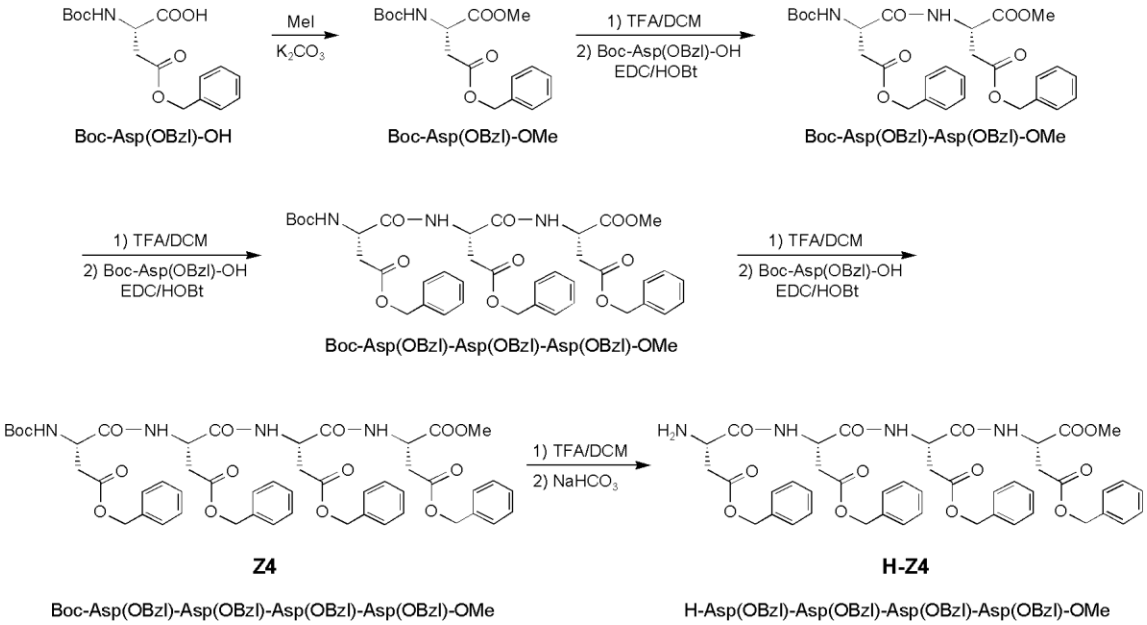
Boc-Asp(OBzl)-OH (1.09 g, 3.36 mmol) was coupled with TFA·H-[Asp(OBzl)]$_2$-azoPhe-OMe [obtained by treatment of Boc-[Asp(OBzl)]$_2$-azoPhe-OMe (2.22 g, 2.80 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 95/5. Yield: 91% (2.55 g, 2.55 mmol); m.p. 136 ºC; IR (nujol) ν 3282, 1734, 1718, 1699, 1696, 1639 cm^{-1}; $[\alpha]_D$ = –11.1 (c 0.46, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.90–7.85 (m, 4H), 7.60 (d, J = 8.4 Hz, 1H), 7.52–7.44 (m, 3H) overlapped with 7.42 (d, J = 7.6 Hz, 1H), 7.36–7.26 (m, 17H), 7.18 (d, J = 7.9 Hz, 1H), 5.52 (d, J = 7.7 Hz, 1H), 5.13–5.02 (m, 6H), 4.87–4.77 (m, 2H), 4.72 (m, 1H), 4.48–4.41 (m, 1H), 3.67 (s, 3H), 3.23–3.10 (m, 2H), 3.05–2.95 (m, 3H), 2.84–2.73 (m, 3H), 1.44 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.80, 171.65, 171.49, 171.38, 171.07, 170.14, 169.78, 155.55, 152.74, 151.74, 139.53, 135.56, 135.32, 135.27, 131.00, 130.23, 129.14, 128.72, 128.69, 128.64, 128.55, 128.51, 128.40, 128.38, 128.36, 123.17, 122.93, 80.96, 67.18, 67.10, 66.95, 53.66, 52.43, 51.05, 49.88, 49.71, 37.74, 36.03, 35.42, 35.31, 28.37 ppm; HRMS (ESI) $C_{54}H_{58}N_6NaO_{13}$ $[M+Na]^+$: calcd. 1021.3954, found 1021.3950.

H-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-azoPhe-OMe (**H-D4**):

Boc-[Asp(OBzl)]$_3$-azoPhe-OMe (**D4**) (1.10 g, 1.10 mmol) was treated with trifluoroacetic acid according to the general procedure. The trifluoroacetate salt obtained, TFA·H-[Asp(OBzl)]$_3$-azoPhe-OMe, was redissolved in dichloromethane (80 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 30 mL). After drying and filtering, evaporation of the solvent afforded pure **H-D4**

(0.99 g, 1.10 mmol, 100% yield); m.p. 110 ºC; IR (nujol) ν 3359, 3297, 1733, 1673, 1650 cm^{-1}; $[\alpha]_D = -5.2$ (*c* 0.43, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.32 (d, J = 7.5 Hz, 1H), 7.90–7.83 (m, 4H), 7.66 (d, J = 8.3 Hz, 1H), 7.52–7.42 (m, 3H), 7.35–7.27 (m, 17H), 7.22 (d, J = 7.9 Hz, 1H), 5.12–4.99 (m, 6H), 4.83 (m, 1H), 4.76 (m, 1H), 4.67 (m, 1H), 3.74 (brs, 1H), 3.65 (s, 3H), 3.23–2.70 (m, 8H), 2.42 (brs, 2H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.90, 171.59, 171.58, 171.56, 170.29, 170.27, 169.90, 152.75, 151.74, 151.72, 139.58, 135.51, 135.46, 135.44, 131.03, 130.24, 129.18, 128.74, 128.69, 128.67, 128.56, 128.49, 128.42, 128.40, 128.33, 123.17, 122.94, 67.03, 67.00, 66.94, 53.71, 52.48, 51.65, 49.99, 49.75, 38.60, 37.69, 35.46, 35.23 ppm; HRMS (ESI) $C_{49}H_{51}N_6O_{11}$ $[M+H]^+$: calcd. 899.3610, found 899.3587.

Synthesis of ***Z4*** and ***H-Z4***



Boc-Asp(OBzl)-OMe:

See page S5.

Boc-Asp(OBzl)-Asp(OBzl)-OMe:

See page S5.

Boc-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe:

See page S6.

Boc-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)$]_4$-OMe (*Z4*):

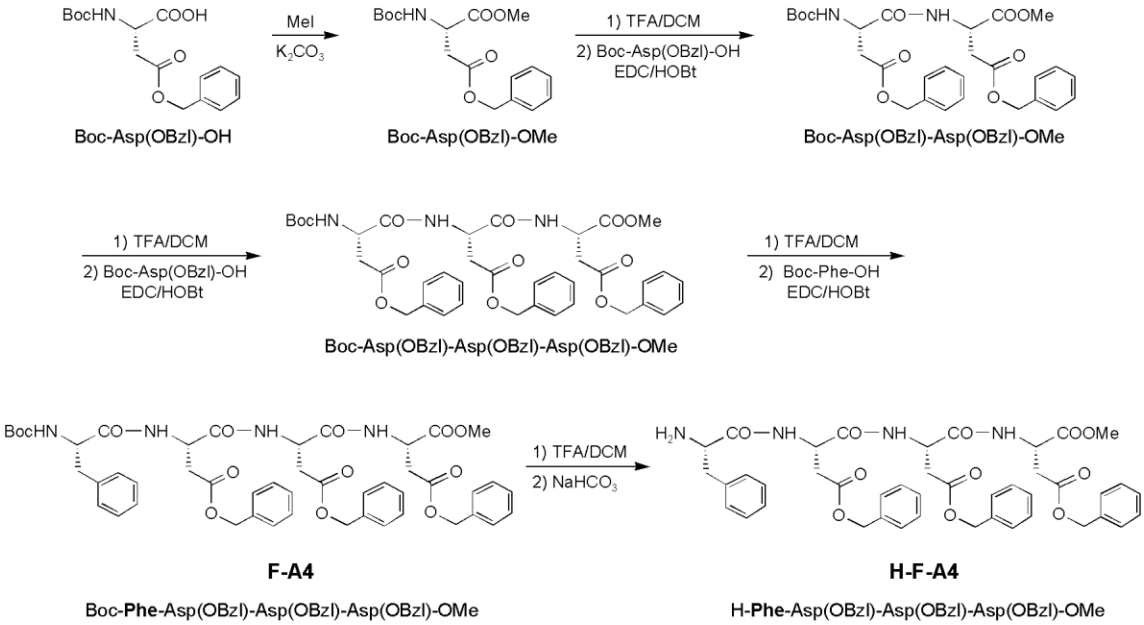
Boc-Asp(OBzl)-OH (1.06 g, 3.29 mmol) was coupled with TFA·H-[Asp(OBzl)$]_3$-OMe [obtained by treatment of Boc-[Asp(OBzl)$]_3$-OMe (2.05 g, 2.74 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 100% (2.61 g, 2.74 mmol); m.p. 82 ºC; IR (nujol) ν 3392, 3317, 3288, 1754, 1735, 1725, 1708, 1691, 1669 cm^{-1}; $[\alpha]_D$ = –28.3 (*c* 0.46, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.52 (d, *J* = 8.2 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.3, 1H), 7.36–7.29 (m, 20H), 5.50 (d, *J* = 7.8 Hz, 1H), 5.17–5.07 (m, 8H), 4.87–4.77 (m, 2H), 4.75–4.69 (m, 1H), 4.50–4.43 (m, 1H), 3.62 (s, 3H), 3.06–2.93 (m, 4H), 2.88–2.74 (m, 4H), 1.44 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.90, 171.65, 171.43, 171.15, 170.81, 170.51, 170.08, 169.84, 160.75, 135.64, 135.48, 135.41, 135.32, 128.75, 128.68, 128.59, 128.56, 128.47, 128.44, 128.41, 82.97, 67.23, 67.16, 66.96, 66.93, 52.76, 51.03, 49.91, 49.77, 48.98, 36.25, 36.10, 35.54, 35.40, 28.38 ppm; HRMS (ESI) $C_{50}H_{57}N_4O_{15}$ $[M+H]^+$: calcd. 953.3815, found 953.3824.

H-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)$]_4$-OMe (H-*Z4*):

Boc-[Asp(OBzl)$]_4$-OMe (***Z4***) (1.00 g, 1.05 mmol) was treated with trifluoroacetic acid according to the general procedure. The trifluoroacetate salt obtained, TFA·H-[Asp(OBzl)$]_4$-

OMe, was redissolved in dichloromethane (80 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 30 mL). After drying and filtering, evaporation of the solvent afforded pure **H-Z4** (0.86 g, 1.01 mmol, 96% yield); m.p. 69 ºC; IR (nujol) ν 3359, 3308, 1734, 1717, 1700, 1684, 1672, 1652 cm^{-1}; $[\alpha]_D = -23.6$ (*c* 0.45, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.31 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 8.2 Hz, 1H), 7.44 (d, J = 8.3, 1H), 7.37–7.26 (m, 20H), 5.16–5.07 (m, 8H), 4.85 (m, 1H), 4.77 (m, 1H), 4.68 (m, 1H), 3.74 (m, 1H), 3.62 (s, 3H), 3.05–2.77 (m, 8H), 2.35 (brs, 2H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 173.77, 173.60, 171.64, 171.47, 170.79, 170.43, 170.23, 169.88, 135.54, 135.50, 135.45, 135.43, 128.67, 128.64, 128.62, 128.61, 128.48, 128.45, 128.38, 128.33, 128.30, 66.98, 66.89 (x2), 66.87, 52.72, 51.64, 49.90, 49.69, 48.95, 38.79, 36.18, 35.45, 35.41 ppm; HRMS (ESI) $C_{45}H_{49}N_4O_{13}$ $[M+H]^+$: calcd. 853.3291, found 853.3307.

Synthesis of **F-A4** and **H-F-A4**



Boc-Asp(OBzl)-OMe:

See page S5.

Boc-Asp(OBzl)-Asp(OBzl)-OMe:

See page S5.

Boc-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe:

See page S6.

Boc-Phe-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe (F-A4):

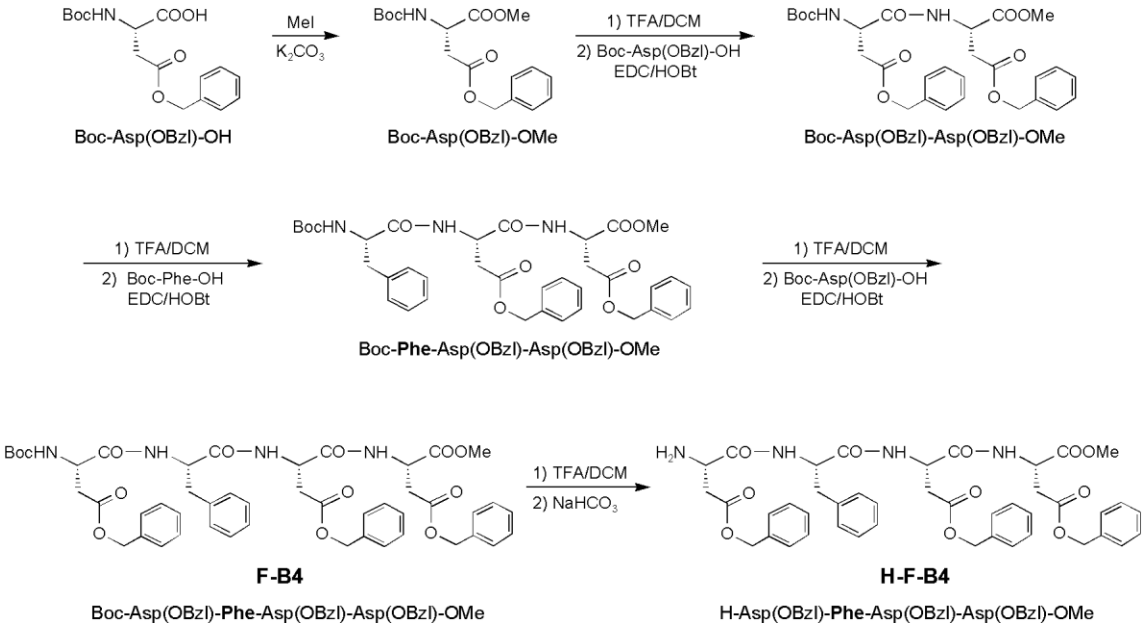
Boc-Phe-OH (934 mg, 3.47 mmol) was coupled with TFA·H-[Asp(OBzl)]$_3$-OMe [obtained by treatment of Boc-[Asp(OBzl)]$_3$-OMe (2.00 g, 2.67 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 87% (2.08 g, 2.32 mmol); m.p. 125 ºC; IR (nujol) ν 3315, 3284, 1736, 1728, 1691, 1648 cm^{-1}; $[\alpha]_D$ =–26.6 (*c* 0.51, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.39 (d, J = 8.3 Hz, 1H), 7.36 (m, 1H) overlapped with 7.35–7.20 (m, 20H), 7.10 (d, J = 7.2 Hz, 1H), 5.17–5.04 (m, 6H), 4.90–4.83 (m, 2H), 4.78 (m, 1H), 4.68 (m, 1H), 4.28 (m, 1H), 3.64 (s, 3H), 3.10 (dd, J = 14.1, 5.9 Hz, 1H), 3.04–2.82 (m, 6H), 2.68 (dd, J = 17.1, 6.2 Hz, 1H), 1.38 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.77, 171.70, 171.34, 170.86, 170.60, 170.07, 169.76, 163.17, 136.34, 135.68, 135.66, 135.37, 129.54, 129.31, 129.00, 128.75, 128.69, 128.59, 128.45, 128.42, 127.35, 80.83, 67.17, 66.98, 66.93, 56.31, 52.78, 49.82, 49.75, 48.98, 36.26, 35.68, 35.61, 35.41, 28.37 ppm; HRMS (ESI) $C_{48}H_{54}N_4NaO_{13}$ $[M+Na]^+$: calcd. 917.3580, found 917.3579.

H-Phe-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe (H-F-A4):

Boc-Phe-[Asp(OBzl)]$_3$-OMe (**F-A4**) (320 mg, 0.36 mmol) was treated with trifluoroacetic acid according to the general procedure. The trifluoroacetate salt obtained, TFA·H-Phe-[Asp(OBzl)]$_3$-OMe, was redissolved in dichloromethane (40 mL) and washed with saturated

aqueous $NaHCO_3$ (3 x 15 mL). After drying and filtering, evaporation of the solvent afforded pure **H-F-A4** (250 mg, 0.31 mmol, 87% yield); m.p. 47 ºC; IR (nujol) *v* 3455–3147, 1740, 1734, 1718, 1684, 1653 cm^{-1}; $[\alpha]_D = -42.3$ (*c* 0.73, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.19 (d, J = 8.4 Hz, 1H), 7.50 (d, J = 8.3 Hz, 1H), 7.37 (d, J = 8.3 Hz, 1H), 7.28–7.09 (m, 20H), 5.08–4.98 (m, 6H), 4.81–4.64 (m, 3H), 3.62 (m, 1H), 3.56 (s, 3H), 3.12 (dd, J = 13.7, 3.8 Hz, 1H), 3.00–2.76 (m, 4H), 2.71–2.55 (m, 3H), 1.66 (brs, 2H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 174.93, 171.88, 171.41, 170.78, 170.50, 170.48, 169.88, 137.46, 135.58, 135.47, 135.42, 129.41, 128.84, 128.71, 128.68, 128.54, 128.46, 128.43, 128.43, 128.32, 127.07, 67.06, 67.01, 66.98, 56.31, 52.82, 49.51, 49.38, 49.00, 40.57, 36.23, 35.67, 35.49 ppm; HRMS (ESI) $C_{43}H_{47}N_4O_{11}$ $[M+H]^+$: calcd. 795.3236, found 795.3218.

Synthesis of **F-B4** and **H-F-B4**



Boc-Asp(OBzl)-OMe:

See page S5.

Boc-Asp(OBzl)-Asp(OBzl)-OMe:

See page S5.

Boc-Phe-Asp(OBzl)-Asp(OBzl)-OMe:

Boc-Phe-OH (1.17 g, 4.42 mmol) was coupled with TFA·H-[Asp(OBzl)]$_2$-OMe [obtained by treatment of Boc-[Asp(OBzl)]$_2$-OMe (2.00 g, 3.69 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 68% (1.72 g, 2.50 mmol); m.p. 94 ºC; IR (nujol) ν 3318, 3293, 1730, 1692, 1647, 1462 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.44–7.13 (m, 17H), 5.18–5.10 (m, 4H), 4.92 (d, J = 6.4 Hz, 1H), 4.87–4.79 (m, 2H), 4.34 (m, 1H), 3.65 (s, 3H), 3.13 (dd, J = 14.0, 5.8 Hz, 1H), 3.09–2.95 (m, 3H), 2.88 (dd, J = 17.0, 5.4 Hz, 1H), 2.67 (dd, J = 17.2, 6.7 Hz, 1H), 1.41 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.62, 171.43, 170.65, 170.48, 169.94, 155.04, 136.43, 135.55, 135.44, 129.32, 128.87, 128.71, 128.68, 128.52, 128.48, 128.42, 127.19, 80.64, 67.03, 66.97, 56.03, 52.78, 49.18, 48.98, 37.93, 36.17, 35.88, 28.33 ppm; HRMS (ESI) $C_{37}H_{43}N_3NaO_{10}$ $[M+Na]^+$: calcd. 712.2841, found 712.2834.

Boc-Asp(OBzl)-Phe-[Asp(OBzl)]$_2$-OMe (F-B4):

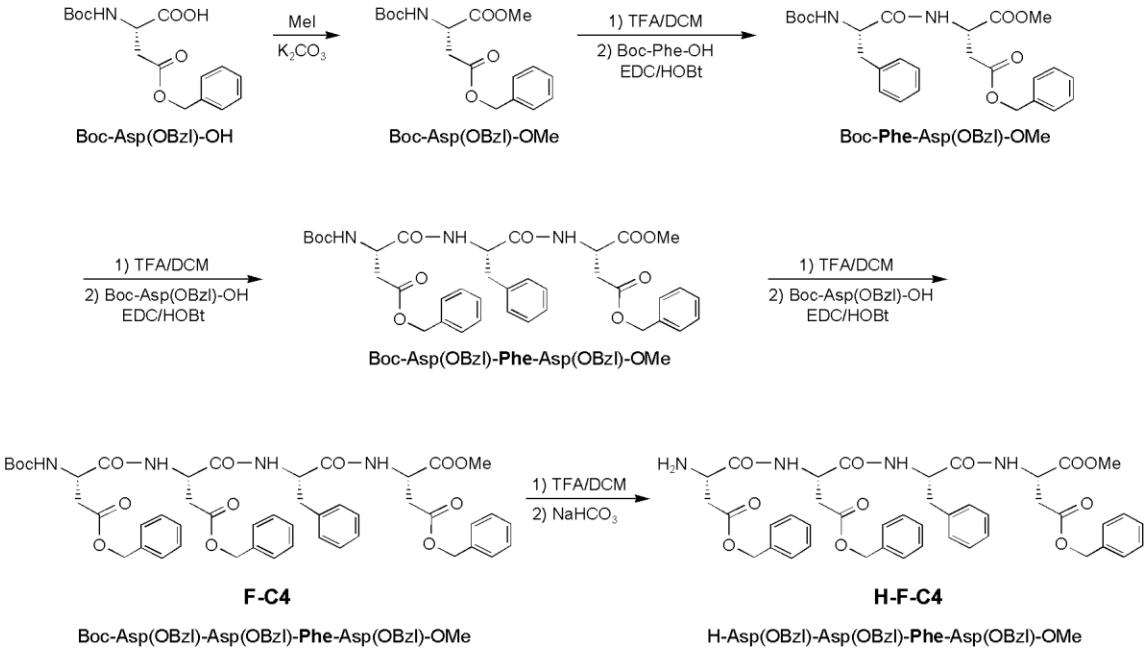
Boc-Asp(OBzl)-OH (847 mg, 2.62 mmol) was coupled with TFA·H-Phe-[Asp(OBzl)]$_2$-OMe [obtained by treatment of Boc-Phe-[Asp(OBzl)]$_2$-OMe (1.50 g, 2.17 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 95/5. Yield: 94% (1.83 g, 2.04 mmol); m.p. 147 ºC; IR (nujol) ν 3398, 3289, 1750, 1732, 1705, 1668, 1635 cm^{-1}; $[\alpha]_D$ = –33.3 (c 0.58, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.37–7.15 (m, 21H), 7.05 (d, J = 8.0 Hz, 1H), 6.86 (d, J = 6.5 Hz, 1H), 5.49 (d, J = 8.1 Hz, 1H), 5.15–5.03 (m, 6H), 4.84–4.77 (m, 2H), 4.50 (m, 1H), 4.42 (m, 1H), 3.63 (s, 3H), 3.08 (d, J = 6.5 Hz, 2H), 2.99–2.70 (m, 6H), 1.40 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ

177.85, 171.99, 171.52, 170.74, 170.50, 170.47, 169.86, 161.66, 136.15, 135.63, 135.55, 135.36, 129.33, 128.97, 128.76, 128.70, 128.70, 128.60, 128.48, 128.40, 128.38, 127.34, 81.83, 67.18, 66.97, 66.92, 55.22, 52.80, 50.85, 49.42, 49.03, 37.15, 36.25, 35.90, 35.70, 28.39 ppm; HRMS (ESI) $C_{48}H_{54}N_4NaO_{13}$ $[M+Na]^+$: calcd. 917.3580, found 917.3565.

H-Asp(OBzl)-Phe-[Asp(OBzl)]$_2$-OMe (H-F-B4):

Boc-Asp(OBzl)-Phe-[Asp(OBzl)]$_2$-OMe (**F-B4**) (320 mg, 0.36 mmol) was treated with trifluoroacetic acid according to the general procedure. The trifluoroacetate salt obtained, TFA·H-Asp(OBzl)-Phe-[Asp(OBzl)]$_2$-OMe, was redissolved in dichloromethane (40 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 15 mL). After drying and filtering, evaporation of the solvent afforded pure **H-F-B4** (254 mg, 0.32 mmol, 89% yield); m.p. 114 ºC; IR (nujol) ν 3375, 3322, 1749, 1733, 1718, 1699, 1684, 1653 cm^{-1}; $[\alpha]_D = -15.9$ (*c* 0.36, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.79 (d, J = 6.8 Hz, 1H), 7.33–7.06 (m, 22H), 5.08–4.94 (m, 6H), 4.80–4.68 (m, 2H), 4.42 (m, 1H), 3.59 (m, 1H) overlapped with 3.56 (s, 3H), 3.12–2.93 (m, 3H), 2.92–2.70 (m, 3H), 2.65–2.50 (m, 2H), 1.82 (brs, 2H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 174.30, 171.76, 171.73, 170.77, 170.75, 170.50, 169.93, 136.50, 136.49, 135.59, 135.46, 129.34, 128.81, 128.74, 128.71, 128.70, 128.54, 128.49, 128.46, 128.45, 128.37, 128.33, 127.21, 66.97, 66.96, 66.82, 55.04, 52.82, 51.81, 49.27, 49.04, 38.89, 37.13, 36.24, 35.62 ppm; HRMS (ESI) $C_{43}H_{47}N_4O_{11}$ $[M+H]^+$: calcd. 795.3236, found 795.3243.

Synthesis of **F-C4** and **H-F-C4**



Boc-Asp(OBzl)-OMe:

See page S5.

Boc-Phe-Asp(OBzl)-OMe:

Boc-Phe-OH (2.28 g, 8.60 mmol) was coupled with TFA·H-Asp(OBzl)-OMe [obtained by treatment of Boc-Asp(OBzl)-OMe (2.42 g, 7.17 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 81% (2.82 g, 5.81 mmol); m.p. 99 ºC; IR (nujol) ν 3328, 3306, 1732, 1691, 1657 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.42–7.14 (m, 10H), 6.82 (d, J = 7.8 Hz, 1H), 5.09 (s, 2H), 4.94–4.86 (m, 1H), 4.80 (m, 1H), 4.41–4.31 (m, 1H), 3.66 (s, 3H), 3.12–2.99 (m, 3H), 2.87 (dd, J = 17.2, 4.7 Hz, 1H), 1.40 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.16, 170.75, 170.65, 152.19, 136.42, 135.44, 129.44, 128.79, 128.77, 128.62, 128.50, 127.09, 82.25, 66.99, 55.42, 52.89, 48.76, 38.39, 36.42, 28.38 ppm; HRMS (ESI) $C_{26}H_{32}N_2NaO_7$ $[M+Na]^+$: calcd. 507.2102, found 507.2108.

Boc-Asp(OBzl)-Phe-Asp(OBzl)-OMe:

Boc-Asp(OBzl)-OH (1.95 g, 6.02 mmol) was coupled with TFA·H-Phe-Asp(OBzl)-OMe [obtained by treatment of Boc-Phe-Asp(OBzl)-OMe (2.43 g, 5.02 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 97% (3.36 g, 4.87 mmol); m.p. 110 ºC; IR (nujol) ν 3342, 3296, 1734, 1693, 1651, 1537, 1497 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.39–7.19 (m, 15H), 6.95 (d, J = 7.8 Hz, 1H), 6.81 (d, J = 7.7 Hz, 1H), 5.53 (d, J = 8.1 Hz, 1H), 5.15–5.05 (m, 4H), 4.79 (ddd, J = 8.1, 4.9, 4.9 Hz, 1H), 4.63 (m, 1H), 4.51–4.43 (m, 1H), 3.64 (s, 3H), 3.11–2.93 (m, 4H), 2.84 (dd, J = 17.1, 5.0 Hz, 1H), 2.74 (dd, J = 17.2, 6.3 Hz, 1H), 1.42 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.85, 170.67, 170.66, 170.54, 170.22, 155.50, 136.23, 136.22, 135.46, 129.49, 128.77, 128.71, 128.53, 128.52, 128.47, 128.39, 127.13, 80.79, 67.05, 66.96, 54.49, 52.82, 50.79, 48.80, 37.84, 36.28, 36.09, 28.37 ppm; HRMS (ESI) $C_{37}H_{43}N_3NaO_{10}$ $[M+Na]^+$: calcd. 712.2841, found 712.2855.

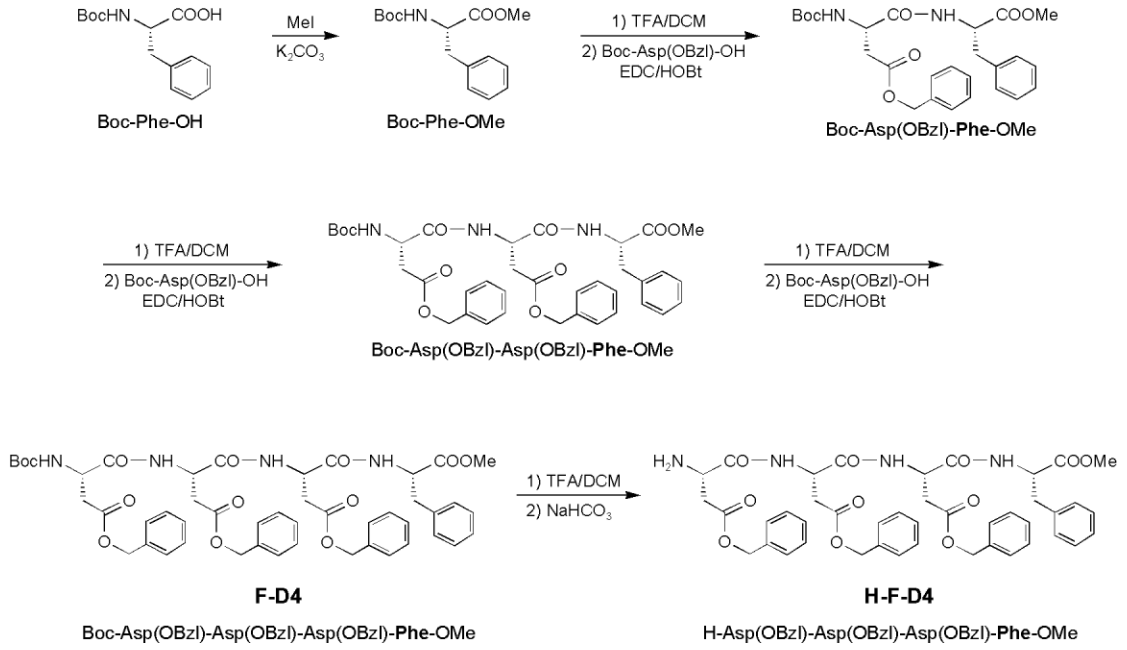
Boc-[Asp(OBzl)]$_2$-Phe-Asp(OBzl)-OMe (F-C4):

Boc-Asp(OBzl)-OH (1.63 g, 5.06 mmol) was coupled with TFA·H-Asp(OBzl)-Phe-Asp(OBzl)-OMe [obtained by treatment of Boc-Asp(OBzl)-Phe-Asp(OBzl)-OMe (3.78 g, 4.22 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 95/5. Yield: 87% (3.28 g, 3.67 mmol); m.p. 90 ºC; IR (nujol) ν 3274, 1734, 1717, 1698, 1685, 1673, 1637 cm^{-1}; $[\alpha]_D = -34.9$ (*c* 0.30, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.42 (d, *J* = 7.9 Hz, 1H), 7.38–7.17 (m, 20H) overlapped with 7.15 (d, *J* = 7.9 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 5.47 (d, *J* = 8.0 Hz, 1H), 5.14–5.05 (m, 6H), 4.80 (ddd, *J* = 8.1, 5.0, 5.0 Hz, 1H), 4.70 (m, 1H), 4.62 (m, 1H), 4.44–4.36 (m, 1H), 3.63 (3H, s), 3.20 (dd, *J* = 14.1, 6.0 Hz, 1H), 3.08–2.68 (m, 7H), 1.44 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.82, 171.59, 171.09, 170.79, 170.53, 170.35, 170.00, 155.48, 136.72, 135.53, 135.43, 135.32, 129.37, 128.74, 128.70, 128.68, 128.58, 128.52, 128.48, 128.44, 128.39, 126.95, 80.91, 67.18, 67.06, 66.91, 54.77, 52.76, 50.97, 49.80, 48.84, 37.17, 36.31, 36.03, 35.26, 28.37 ppm; HRMS (ESI) $C_{48}H_{54}N_4NaO_{13}$ $[M+Na]^+$: calcd. 917.3580, found 917.3561.

H-[Asp(OBzl)]$_2$-Phe-Asp(OBzl)-OMe (H-F-C4):

Boc-[Asp(OBzl)]$_2$-Phe-Asp(OBzl)-OMe (**F-C4**) (1.11 g, 1.24 mmol) was treated with trifluoroacetic acid according to the general procedure. The trifluoroacetate salt obtained, TFA·H-[Asp(OBzl)]$_2$-Phe-Asp(OBzl)-OMe, was redissolved in dichloromethane (80 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 30 mL). After drying and filtering, evaporation of the solvent afforded pure **H-F-C4** (830 mg, 1.04 mmol, 84% yield); m.p. 144 ºC; IR (nujol) ν 3282, 1733, 1718, 1699, 1651 cm^{-1}; $[\alpha]_D = -26.4$ (*c* 0.39, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.22 (d, *J* = 8.2 Hz, 1H), 7.40–7.16 (m, 20H), 7.10 (d, *J* = 7.7 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 5.15–5.07 (m, 6H), 4.81 (m, 1H), 4.69 (m, 1H), 4.61 (m, 1H), 3.64 (s, 3H), 3.59–3.53 (m, 1H), 3.17 (dd, *J* = 14.1, 5.8 Hz, 1H), 3.08–2.67 (m, 7H), 2.10 (brs, 2H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 173.76, 171.62, 171.54, 170.81, 170.54, 170.44, 170.28, 136.64, 135.53, 135.52, 135.49, 129.44, 128.73, 128.68, 128.66, 128.62, 128.54, 128.48, 128.46, 128.42, 128.37, 126.90, 66.96, 66.92, 66.85, 54.59, 52.78, 51.68, 49.57, 48.84, 38.91, 37.25, 36.28, 35.24 ppm; HRMS (ESI) $C_{43}H_{47}N_4O_{11}$ $[M+H]^+$: calcd. 795.3236, found 795.3197.

Synthesis of **F-D4** and **H-F-D4**



Boc-Phe-OMe:

Potassium carbonate (4.68 g, 33.96 mmol) was added to a solution of Boc-Phe-OH (3.00 g, 11.32 mmol) in DMF (40 mL). After 2 h at room temperature, iodomethane (2.11 mL, 33.96 mmol) was added and stirring was continued for additional 24 h. The solvent was evaporated to dryness and the residue was partitioned between ethyl acetate (50 mL) and water (80 mL). The phases were separated and the aqueous layer was further extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were washed successively with water (1 x 40 mL), 5% aqueous $Na_2S_2O_3$ (3 x 40 mL), and brine (3 x 40 mL), dried over anhydrous $MgSO_4$ and filtered. Elimination of the solvent afforded Boc-Phe-OMe as a white solid (3.13 g, 11.21 mmol, 99% yield); m.p. 39 ºC; IR (nujol) ν 3369, 1746, 1715, 1498 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.33–7.21 (m, 3H), 7.15–7.10 (m, 2H), 4.97 (d, J = 7.8 Hz, 1H), 4.59 (m, 1H), 3.71 (s, 3H), 3.12 (dd, J = 13.7, 5.8 Hz, 1H), 3.04 (dd, J = 13.7, 6.1 Hz, 1H), 1.41 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 172.47, 155.20, 136.12, 129.41, 128.66, 127.14, 80.03, 54.53, 52.32, 38.47, 28.41 ppm; HRMS (ESI) $C_{15}H_{21}NNaO_4$ $[M+Na]^+$: calcd. 302.1363, found 302.1374.

Boc-Asp(OBzl)-Phe-OMe:

Boc-Asp(OBzl)-OH (2.93 g, 9.06 mmol) was coupled with TFA·H-Phe-OMe [obtained by treatment of Boc-Phe-OMe (2.11 g, 7.55 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 87% (3.18 g, 6.57 mmol); m.p. 64 ºC; IR (nujol) ν 3356, 3332, 1738, 1699, 1683, 1670, 1653, 1458 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.39–7.22 (m, 8H), 7.16–7.12 (m, 2H), 6.92 (d, J = 7.0 Hz, 1H), 5.63 (d, J = 8.1 Hz, 1H), 5.14 (d, J = 18.2 Hz, 1H), 5.11 (d, J = 18.2 Hz, 1H), 5.06 (s, 2H), 4.81 (m, 1H), 4.57–4.50 (m, 1H), 3.69 (s, 3H), 3.15–3.02 (m, 3H), 2.71 (dd, J = 17.2, 6.1 Hz, 1H), 1.43 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.90, 171.51, 170.46, 155.48, 135.83, 135.50, 129.43, 128.72, 128.70, 128.50, 128.38, 127.24, 80.63, 66.98, 53.59, 52.40, 50.60, 37.96, 36.11, 28.36 ppm; HRMS (ESI) $C_{26}H_{32}N_2NaO_7$ $[M+Na]^+$: calcd. 507.2102, found 507.2089.

Boc-Asp(OBzl)-Asp(OBzl)-Phe-OMe:

Boc-Asp(OBzl)-OH (2.31 g, 7.14 mmol) was coupled with TFA·H-Asp(OBzl)-Phe-OMe [obtained by treatment of Boc-Asp(OBzl)-Phe-OMe (2.88 g, 5.95 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 98/2. Yield: 85% (3.49 g, 5.06 mmol); m.p. 111 ºC; IR (nujol) ν 3322, 3305, 1742, 1729, 1684, 1644 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.52 (d, 1H, J = 8.2 Hz), 7.39–7.11 (m, 15H), 7.05 (d, J = 7.8 Hz, 1H), 5.49 (d, J = 8.5 Hz, 1H), 5.14 (d, J = 20.4 Hz, 1H), 5.11 (d, J = 20.4 Hz, 1H), 5.06 (s, 2H), 4.82–4.73 (m, 2H), 4.47–4.41 (m, 1H), 3.66 (s, 3H), 3.14–2.96 (m, 4H), 2.74 (dd, J = 17.2, 6.2 Hz, 1H), 2.66 (dd, J = 17.3, 6.6 Hz, 1H), 1.45 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.77, 171.76, 171.54, 170.91, 169.82, 155.46, 135.98, 135.50, 135.40, 129.38, 128.74, 128.73, 128.72, 128.56, 128.51, 128.46, 128.40, 127.22, 80.85, 67.07, 67.02, 53.79, 52.38, 50.89, 49.34, 37.75, 36.09, 35.59, 28.39 ppm; HRMS (ESI) $C_{37}H_{43}N_3NaO_{10}$ $[M+Na]^+$: calcd. 712.2841, found 712.2845.

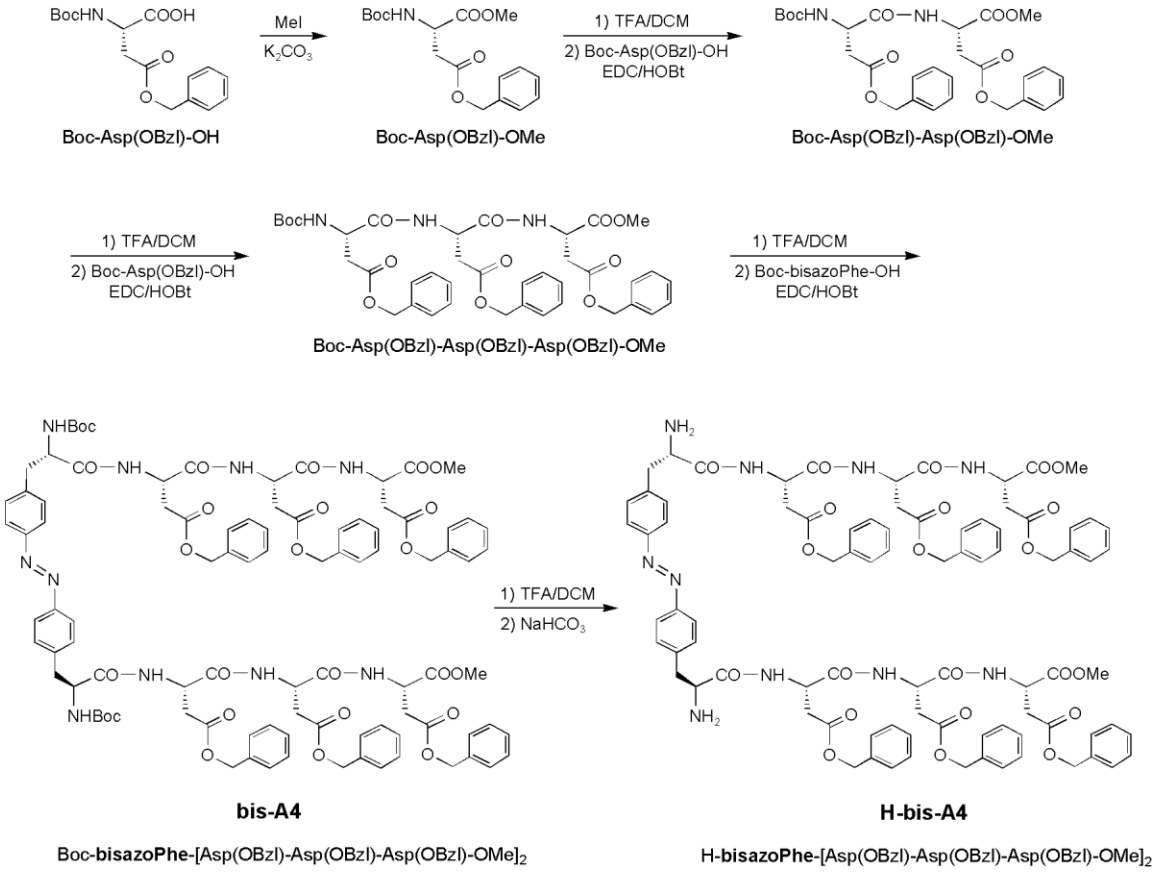
Boc-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-Phe-OMe (F-D4):

Boc-Asp(OBzl)-OH (1.52 g, 4.69 mmol) was coupled with TFA·H-[Asp(OBzl)]$_2$-Phe-OMe [obtained by treatment of Boc-[Asp(OBzl)]$_2$-Phe-OMe (2.69 g, 3.91 mmol) with trifluoroacetic acid] as indicated in the general procedures. Column chromatography eluent: dichloromethane/methanol 95/5. Yield: 95% (3.32 g, 3.71 mmol); m.p. 125 ºC; IR (nujol) ν 3310, 3280, 1739, 1734, 1694, 1669, 1640 cm^{-1}; $[\alpha]_D$ = –25.0 (c 0.41, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.52 (d, J = 8.3 Hz, 1H), 7.39 (d, J = 7.9 Hz, 1H) overlapped with 7.37–7.27 (m, 17H), 7.23–7.11 (m, 3H), 7.05 (d, J = 7.8 Hz, 1H), 5.49 (d, J = 7.7 Hz, 1H), 5.14–5.04 (m, 6H), 4.81–4.73 (m, 2H), 4.68 (m, 1H), 4.47–4.40 (m, 1H), 3.64 (s, 3H), 3.14–2.90 (m, 5H), 2.84–2.69 (m, 3H), 1.44 (s, 9H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.66, 171.61, 171.50, 171.24, 171.06, 170.13, 169.73, 160.57, 136.55, 135.63, 135.50, 135.32, 129.42, 128.77, 128.75, 128.69, 128.61, 128.58, 128.48, 128.43, 128.42, 127.15, 80.49, 67.24, 67.15, 66.96, 53.78, 52.37, 51.06, 49.79, 49.68, 37.80, 36.12, 35.43, 35.37, 28.41 ppm; HRMS (ESI) $C_{48}H_{55}N_4O_{13}$ $[M+H]^+$: calcd. 895.3760, found 895.3774.

H-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-Phe-OMe (H-F-D4):

Boc-[Asp(OBzl)]$_3$-Phe-OMe (**F-D4**) (1.20 g, 1.34 mmol) was treated with trifluoroacetic acid according to the general procedure. The trifluoroacetate salt obtained, TFA·H-[Asp(OBzl)]$_3$-Phe-OMe, was redissolved in dichloromethane (80 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 30 mL). After drying and filtering, evaporation of the solvent afforded pure **H-F-D4** (1.04 g, 1.31 mmol, 98% yield); m.p. 100 ºC; IR (nujol) ν 3364, 3300, 1734, 1717, 1700, 1670, 1684, 1653 cm^{-1}; $[\alpha]_D$ = –18.9 (c 0.44, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.34 (d, J = 7.1 Hz, 1H), 7.63 (d, J = 8.2 Hz, 1H), 7.38–7.09 (m, 21H), 5.13–5.03 (m, 6H), 4.80–4.69 (m, 2H), 4.65 (m, 1H), 3.88–3.78 (m, 1H), 3.62 (s, 3H), 3.14–2.69 (m, 8H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 172.02, 171.89, 171.80, 171.57, 170.94, 170.21, 169.88, 136.11, 136.10, 135.56, 135.50, 129.39, 128.76, 128.72, 128.70, 128.68, 128.59, 128.53, 128.45, 128.44, 128.38, 127.15, 67.07, 67.05, 66.99, 53.83, 52.39, 51.60, 49.97, 49.72, 37.74, 37.54, 35.43, 35.32 ppm; HRMS (ESI) $C_{43}H_{47}N_4O_{11}$ $[M+H]^+$: calcd. 795.3236, found 795.3242.

Synthesis of **bis-A4** and **H-bis-A4**



Boc-Asp(OBzl)-OMe:

See page S5.

Boc-Asp(OBzl)-Asp(OBzl)-OMe:

See page S5.

Boc-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe:

See page S6.

Boc-bisazoPhe-[Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe]$_2$ (bis-A4):

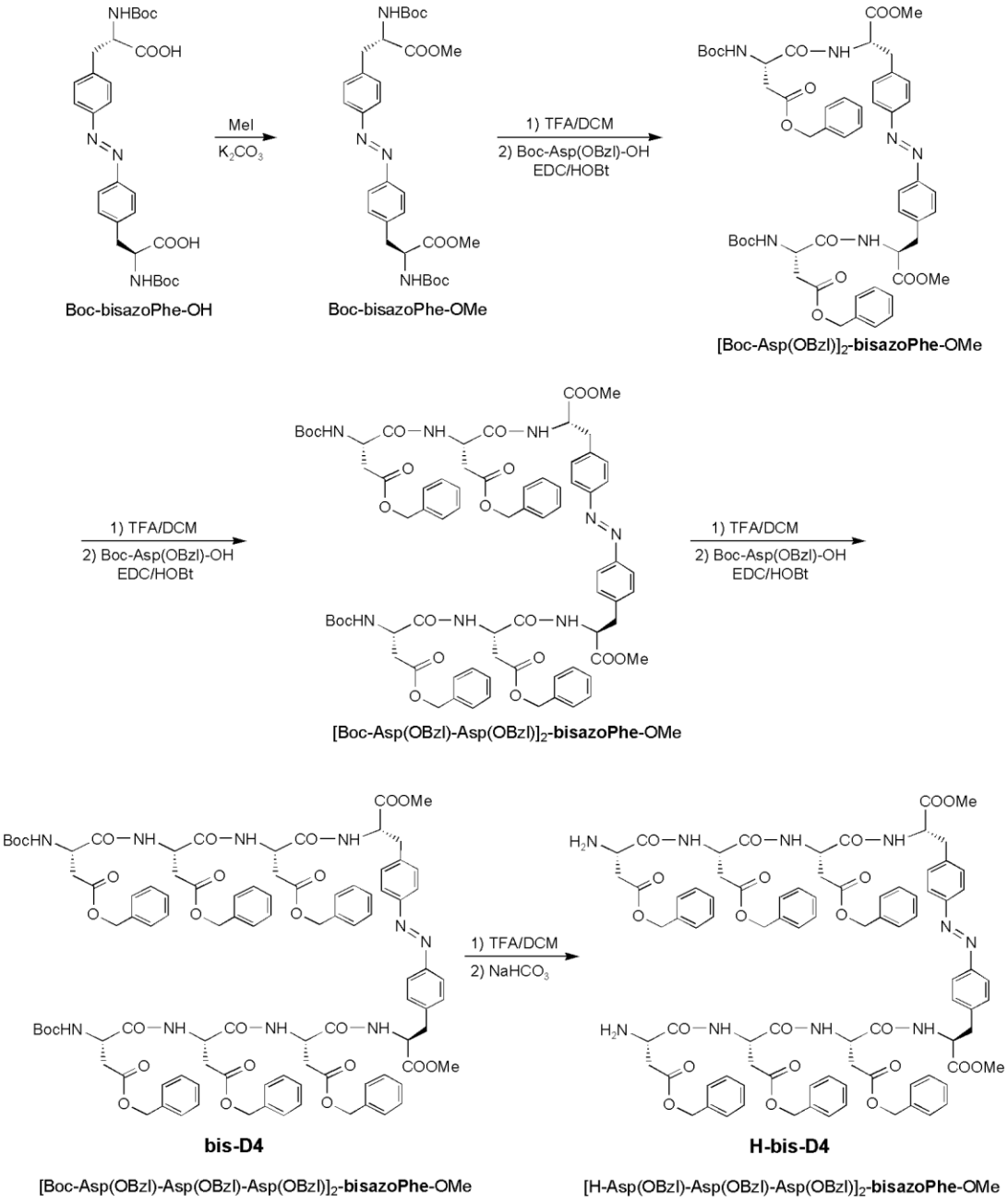
Boc-bisazoPhe-OH (**2**) (459 mg, 0.82 mmol, 0.90 equiv) was coupled with TFA·H-[Asp(OBzl)]$_3$-OMe [obtained by treatment of Boc-[Asp(OBzl)]$_3$-OMe (1.37 g, 1.83 mmol) with trifluoroacetic] using EDC·HCl (332 mg, 1.73 mmol, 0.95 equiv) and HOBt (234 mg, 1.73 mmol, 0.95 equiv) as indicated in the general procedures. Column chromatography eluent: dichloromethane/isopropanol 96/4 containing 1% acetic acid (v/v). Yield: 70% (1.05 g, 0.58 mmol); m.p. 139 ºC; IR (nujol) ν 3324, 3275, 1734, 1688, 1645, 1457 cm^{-1}; $[\alpha]_D$ = –20.7 (*c* 0.42, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.85–7.80 (m, 4H), 7.52 (d, J = 8.3 Hz, 2H), 7.39 (d, J = 8.3 Hz, 2H), 7.36–7.28 (m, 34H), 7.22 (d, J = 7.2 Hz, 2H), 5.16–5.05 (m, 12H), 4.89 (d, J = 5.8 Hz, 2H) overlapped with 4.88–4.78 (m, 4H), 4.71 (m, 2H), 4.34 (m, 2H), 3.63 (s, 6H), 3.21 (dd, J = 13.9, 5.4 Hz, 2H), 3.08–2.69 (m, 14H), 1.39 (s, 18H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.67, 171.56, 171.40, 170.84, 170.56, 170.01, 169.77, 155.25, 151.82, 139.78,

135.99, 135.63, 135.34, 131.48, 130.09, 128.74, 128.69, 128.59, 128.47, 128.44, 128.39, 123.39, 122.83, 81.08, 67.21, 66.97, 66.94, 56.07, 52.80, 49.85, 49.72, 48.99, 37.57, 36.28, 36.25, 35.70, 28.36 ppm; HRMS (ESI) $C_{96}H_{106}N_{10}Na_2O_{26}$ $[M+2Na]^{2+}$: calcd. 930.3532, found 930.3542.

H-bisazoPhe-[Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe]$_2$ (H-bis-A4):

Boc-bisazoPhe-[Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe]$_2$ (**bis-A4**) (162 mg, 0.089 mmol) was treated with trifluoroacetic acid for 4 h as described in the general procedure. The trifluoroacetate salt obtained, TFA·H-bisazoPhe-[Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe]$_2$, was redissolved in dichloromethane (40 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 15 mL). After drying and filtering, evaporation of the solvent afforded pure **H-bis-A4** (135 mg, 0.084 mmol, 94% yield); m.p. 133 ºC; IR (nujol) ν 3357, 3296, 1734, 1719, 1700, 1695, 1684, 1653, 1457 cm^{-1}; $[\alpha]_D = -40.4$ (*c* 0.39, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.29 (d, J = 7.9 Hz, 2H), 7.88–7.83 (m, 4H), 7.57 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 7.9 Hz, 2H), 7.38–7.27 (m, 34H), 5.17–5.06 (m, 12H), 4.88–4.74 (m, 6H), 3.75–3.68 (m, 2H), 3.64 (s, 6H), 3.32–3.25 (m, 2H), 3.09–2.65 (m, 14H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 174.78, 171.91, 171.42, 170.75, 170.52, 170.45, 169.87, 151.78, 141.00, 135.57, 135.46, 135.40, 130.17, 128.70, 128.54, 128.48, 128.43, 128.32, 123.30, 67.11, 67.03, 66.99, 56.24, 52.84, 49.49, 49.45, 49.01, 40.55, 36.23, 35.71, 35.54 ppm; HRMS (ESI) $C_{86}H_{92}N_{10}O_{22}$ $[M+2H]^{2+}$: calcd. 808.3188, found 808.3257.

Synthesis of **bis-D4** and **H-bis-D4**



Boc-bisazoPhe-OMe:

To a solution of Boc-bisazoPhe-OH (**2**) (603 mg, 1.08 mmol) in DMF (15 mL), potassium carbonate (896 mg, 6.48 mmol) was added. After 2 h at room temperature, iodomethane (0.40 mL, 6.48 mmol) was added and stirring was continued for additional 24 h. The solvent was evaporated to dryness and the residue was partitioned between ethyl acetate (30 mL) and water (40 mL). The phases were separated and the aqueous layer was further extracted with ethyl acetate (2 x 30 mL). The combined organic extracts were washed successively with water (1 x 30 mL), 5% aqueous $Na_2S_2O_3$ (3 x 30 mL) and brine (3 x 30 mL), dried over anhydrous $MgSO_4$ and filtered. Elimination of the solvent afforded Boc-bisazoPhe-OMe as an orange solid (608 mg, 1.04 mmol, 96% yield); m.p. 156 ºC; IR (nujol) ν 3376, 3358, 1760, 1740, 1690, 1679, 1520, 1462 cm^{-1}; $[\alpha]_D$ = +49.9 (*c* 0.44, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ (major *trans* isomer) 7.83 (d, *J* = 8.3 Hz, 4H), 7.27 (d, *J* = 8.7 Hz, 4H), 5.04 (d, *J* = 8.0 Hz, 2H), 4.64 (m, 2H), 3.73 (s, 6H), 3.21 (dd, *J* = 13.6, 5.8 Hz, 2H), 3.12 (dd, *J* = 13.6, 6.0 Hz, 2H),

1.42 (s, 18H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 172.24, 155.17, 151.83, 139.51, 130.21, 123.11, 80.20, 54.47, 52.46, 38.39, 28.42 ppm; HRMS (ESI) $C_{30}H_{40}N_4NaO_8$ $[M+Na]^+$: calcd. 607.2738, found 607.2774.

[Boc-Asp(OBzl)]$_2$-bisazoPhe-OMe:

Boc-Asp(OBzl)-OH (1.44 g, 4.45 mmol, 1.3 equiv) was coupled with TFA·H-bisazoPhe-OMe [obtained by treatment of Boc-bisazoPhe-OMe (1.00 g, 1.71 mmol) with trifluoroacetic acid for 6 h] using EDC·HCl (852 mg, 4.45 mmol, 1.3 equiv) and HOBt (601 mg, 4.45 mmol, 1.3 equiv), as described in the general procedures. Column chromatography eluent: dichloromethane/isopropanol 97/3. Yield: 86% (1.46 g, 1.47 mmol); m.p. 147 ºC; IR (nujol) ν 3319, 1738, 1696, 1684, 1666, 1652, 1458 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.87–7.82 (m, 4H), 7.36–7.26 (m, 14H), 7.02 (d, J = 6.5 Hz, 2H), 5.67 (d, J = 8.3 Hz, 2H), 5.14 (d, J = 18.9 Hz, 2H), 5.11 (d, J = 18.9 Hz, 2H), 4.86 (m, 2H), 4.58–4.50 (m, 2H), 3.70 (s, 6H), 3.26–2.96 (m, 6H), 2.71 (dd, J = 17.2, 5.9 Hz, 2H), 1.40 (s, 18H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.96, 171.32, 170.58, 155.59, 151.81, 139.18, 135.47, 130.27, 128.72, 128.52, 128.38, 123.15, 80.75, 67.03, 53.53, 52.53, 50.64, 37.85, 35.97, 28.34 ppm; HRMS (ESI) $C_{52}H_{62}N_6NaO_{14}$ $[M+Na]^+$: calcd. 1017.4216, found 1017.4193.

[Boc-Asp(OBzl)-Asp(OBzl)]$_2$-bisazoPhe-OMe:

Boc-Asp(OBzl)-OH (789 mg, 2.44 mmol, 1.3 equiv) was coupled with [TFA·H-Asp(OBzl)]$_2$-bisazoPhe-OMe [obtained by treatment of [Boc-Asp(OBzl)]$_2$-bisazoPhe-OMe (931 mg, 0.94 mmol) with trifluoroacetic acid for 6 h] using EDC·HCl (467 mg, 2.44 mmol, 1.3 equiv) and HOBt (329 mg, 2.44 mmol, 1.3 equiv) as described in the general procedures. Column chromatography eluent: dichloromethane/methanol 95/5. Yield: 94% (1.24 g, 0.88 mmol); m.p. 128 ºC; IR (nujol) ν 3301, 1735, 1690, 1671, 1645, 1457 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.84–7.80 (m, 4H), 7.58 (d, J = 8.3 Hz, 2H), 7.36–7.26 (m, 24H), 7.18 (d, J = 7.8 Hz, 2H), 5.51 (d, J = 8.0 Hz, 2H), 5.12 (d, J = 20.5 Hz, 2H), 5.09 (d, J = 20.5 Hz, 2H), 5.03 (s, 4H), 4.85–4.78 (m, 4H), 4.49–4.41 (m, 2H), 3.66 (s, 6H), 3.21–2.94 (m, 8H), 2.77 (dd, J = 17.2, 6.5 Hz, 2H), 2.67 (dd, J = 17.4, 6.4 Hz, 2H), 1.44 (s, 18H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.81, 171.79, 171.36, 170.97, 169.91, 155.47, 151.79, 139.36, 135.43, 135.34, 130.17, 128.72, 128.70, 128.54, 128.50, 128.43, 128.35, 123.21, 80.85, 67.08, 67.07, 53.77, 52.47, 50.96, 49.36, 37.77, 36.12, 35.57, 28.39 ppm; HRMS (ESI) $C_{74}H_{84}N_8NaO_{20}$ $[M+Na]^+$: calcd. 1427.5694, found 1427.5696.

[Boc-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)]$_2$-bisazoPhe-OMe (bis-D4):

Boc-Asp(OBzl)-OH (605 mg, 1.87 mmol, 1.3 equiv) was coupled with [TFA·H-Asp(OBzl)-Asp(OBzl)]$_2$-bisazoPhe-OMe [obtained by treatment of [Boc-Asp(OBzl)-Asp(OBzl)]$_2$-bisazoPhe-OMe (1.01 g, 0.72 mmol) with trifluoroacetic acid for 6 h] using EDC·HCl (358 mg, 1.87 mmol, 1.3 equiv) and HOBt (252 mg, 1.87 mmol, 1.3 equiv) as described in the general procedures. Column chromatography eluent: dichloromethane/methanol 95/5. Yield: 94% (1.23 g, 0.68 mmol); m.p. 148 ºC; IR (nujol) ν 3280, 1734, 1718, 1653, 1637, 1457 cm^{-1}; $[\alpha]_D$ = –14.35 (*c* 0.46, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.84–7.80 (m, 4H), 7.61 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 7.9 Hz, 2H), 7.36–7.27 (m, 34H), 7.20 (d, J = 7.9 Hz, 2H), 5.57 (d, J = 7.1 Hz, 2H), 5.12–5.02 (m, 12H), 4.86–4.78 (m, 4H), 4.73 (m, 2H), 4.44 (m, 2H), 3.64 (s, 6H), 3.14 (m, 4H), 3.05–2.92 (m, 6H), 2.87–2.73 (m, 6H), 1.43 (s, 18H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.76, 171.62, 171.43, 171.38, 171.09, 170.16, 169.76, 155.54, 151.68, 139.45, 135.54, 135.30, 135.24, 130.15, 128.68, 128.67, 128.62, 128.52, 128.50, 128.36, 128.34, 123.11, 80.92, 67.15, 67.08, 66.91, 53.70, 52.38, 51.05, 49.84, 49.69, 37.81, 36.01, 35.40, 35.31, 28.35 ppm; HRMS (ESI) $C_{96}H_{106}N_{10}Na_2O_{26}$ $[M+2Na]^{2+}$: calcd. 930.3532, found 930.3532.

[H-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)]$_2$-bisazoPhe-OMe (H-bis-D4):

[Boc-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)]$_2$-bisazoPhe-OMe (**bis-D4**) (161 mg, 0.089 mmol) was treated with trifluoroacetic acid for 4 h as described in the general procedure. The trifluoroacetate salt obtained, [TFA·H-Asp(OBzl)-Asp(OBzl)-Asp(OBzl)]$_2$-bisazoPhe-OMe, was redissolved in dichloromethane (30 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 10 mL). After drying and filtering, evaporation of the solvent afforded pure **H-bis-D4** (132 mg, 0.082 mmol, 92% yield); m.p. 126 ºC; IR (nujol) ν 3361, 3290, 1733, 1719, 1646, 1457 cm^{-1}; $[\alpha]_D = -10.3$ (c 0.22, THF); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.23 (d, J = 8.3 Hz, 2H), 7.84–7.79 (m, 4H), 7.60 (d, J = 8.4 Hz, 2H), 7.35–7.26 (m, 34H), 7.19 (d, J = 7.8 Hz, 2H), 5.14–5.01 (m, 12H), 4.81 (m, 2H), 4.75 (m, 2H), 4.66 (m, 2H), 3.65 (s, 6H) overlapped with 3.64–3.57 (m, 2H), 3.15 (m, 4H), 3.07–2.94 (m, 4H), 2.88–2.68 (m, 8H), 1.77 (brs, 4H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 174.16, 171.82, 171.74, 171.57, 171.45, 170.37, 169.85, 151.72, 139.51, 135.53, 135.50, 135.42, 130.17, 128.73, 128.68, 128.66, 128.53, 128.51, 128.43, 128.39, 128.37, 128.32, 123.13, 67.01, 66.98, 66.86, 53.71, 52.43, 51.78, 49.82, 49.65, 39.18, 37.70, 35.48, 35.25 ppm; HRMS (ESI) $C_{86}H_{92}N_{10}O_{22}$ $[M+2H]^{2+}$: calcd. 808.3188, found 808.3166.

2. General remarks on gel formation and gelation ability

Typically, a weighted amount of the corresponding peptide and 1 mL of the appropriate solvent were placed into a screw-capped glass vial (4 cm length and 1 cm diameter) and gently heated with a heatgun until the solid material was completely dissolved. The resulting isotropic solution was then cooled down (spontaneously) to RT. No cotrol over temperature rate during the heating-cooling process was applied. The material was preliminary classified as "gel" if it did not exhibit gravitational flow upon turning the vial upside-down at RT. The state was further confirmed by rheological measurements. Gelation of the total solvent volume was observed under the described conditions in Table S1: Approximately 34% of the matrix elements afforded organogels, 47% clear solutions, 2% gave precipitates and no isotropic solution was achieved in 17% of the cases.

Phase selective gelation (PSG): Typically, a weighted amount of the corresponding peptide was added to a biphasic mixture of water (1.0 mL) and an appropriate organic solvent (0.5 mL), which was treated in an ultrasound bath at RT for 1 min. The mixture was gently heated until all solid material was completely dissolved. After cooling to RT selective gelation of the organic phase was achieved and verified by inverting the vial. Only materials that were able to keep the weight of the aqueous phase without exhibiting gravitational flow were classified as "gels". Alternatively PSG can be induced by dissolving the compound using ultrasonication at RT and resulting *in situ* formation of gel-materials, or adding concentrated solutions (20-40 %w/v) of a suitable gelator in an organic solvent or oil to biphasic mixtures.

MGC values were estimated by continuosly adding solvent in several portions (50 μL each) into the vial where no gelation was achieved at the previous concentration and some material remained unsoluble. The initial concentration for gelation tests was 20 % w/v. The state of the new mixture was determined after the heating-cooling cycle as explained above. New experiments were made at lower concentration if stable clear solutions were obtained at 20 % w/v. No further experiments were made if gelation was not achieved at 50 % w/v. Non-gel containing vials (i.e. clear solution after 1 day) were frequivuently left at RT and visually monitored for possible gelation/crystallization over time. In general, the peptides were able to immobilize between hundred and thousands of solvent molecules (SM) per molecule of gelator (GM) (e.g. SM/GM = 2857 (gel made from **bis-A4** in toluene); 2374 (gel made from **bis-A4** in iPrOH); 1979 (gel made from **bis-A4** in 2-BuOH); 470 (gel made from **A4** in iPrOH)).

T_{gel} values were usually determined by the inverse flow method (the seal vial containing the organogel was hung horizontally into an oil bath, which was heated up at 2 ºC min^{-1}. Herein, the temperature at which the gel started to break was defined as T_{gel}. Each measurement was made by duplicate and the average values reported. These values were correlated with the first DSC endothermic transition of selected examples. Solvents used for gelation tests were purchased from commercial suppliers and were at least of p.a. quality. Xylene (mixed isomers) was double distilled prior to use. Concerning materials derived from PSG: The aqueous phase after PSG was removed from the vial using a syringe. The remaining gel-body was melted applying gentle heat and left for cooling at RT. After reformation of stable gel-materials T_{gel} values were determined using the IFM as reported above.

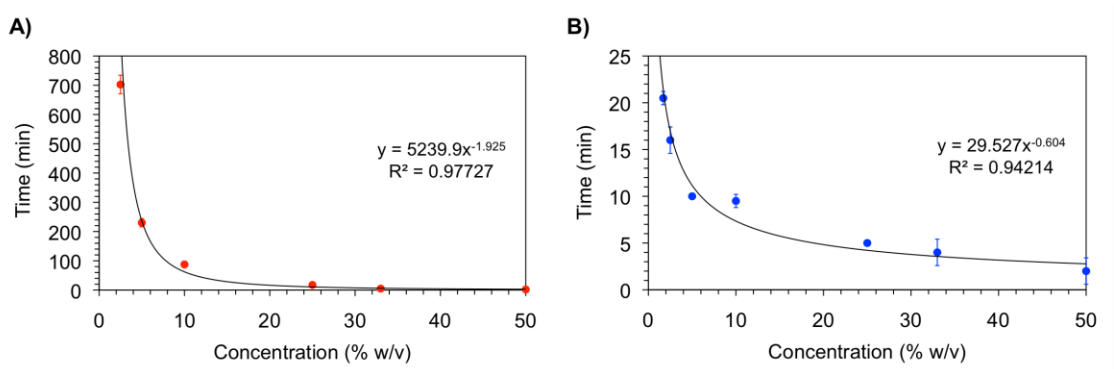


Figure S1. Evolution of gelation time in function of gelator concentration (potential curve fitting): A) Gel made of **A4** in iPrOH. B) Gel made of **A4** in toluene.

Table S1. Overview of solubility properties and gelation ability of LMW peptides[a]

Peptide \ Solvent	Water	DMSO	Glycerol	CH_3CN	MeOH	EtOH	Acetone	*i*-PrOH	2-Butanol	1-Hexanol	CH_2Cl_2	EtOAc	THF	$CHCl_3$	Et_2O	Toluene	Benzene	Xylene[b]	1,4-Dioxane	*n*-Hexane
A4	I	S	I	IG (10) 12 h; 33 ºC	P	OG (7) 1-2 h; 52 ºC	S	OG (2) 30 min; 56 ºC	OG (3) 10 min; 55 ºC	OG (11) 45 min; 58 ºC	S	S	S	S	S	TG (2) 1 h; 37 ºC	TG (11) 2 h; 43 ºC	TG (7) 12 h; 59 ºC	S	I
H-A4	I	S	I	S	P	OG (10) 12 h; 58 ºC	S	OG (10) 12 h; 54 ºC	OG (5) 12 h; 47 ºC	OG (10) 0.5-1 h; 61 ºC	S	S	S	S	S	TG (7) 1 h; 51 ºC	TG (5)[c] 30 min; 52 ºC	TG (10) 1 h; 53 ºC	S	I
B4	I	S	I	PG (10) 48 h	S	OG (5) 12 h; 56 ºC	S	OG (4) 10 min; 63 ºC	OG (2) 1 h; 54 ºC	OG (10) 12 h; 59 ºC	S	S	S	S	S	TG (1.5) 1 h; 45 ºC	TG (10) 2 h; 34 ºC	TG (2) 1 h; 56 ºC	S	I
H-B4	I	S	I	S	P	OG (10) 12 h; 63 ºC	S	OG (1.5) 1 h; 52 ºC	OG (1.5) 1 h; 55 ºC	OG (10) 12 h; 67 ºC	S	OG (10) 12 h; 36 ºC	S	S	S	TG (3) 1 h; 48 ºC	TG (10) 2-3 h; 40 ºC	TG (5) 1 h; 63 ºC	S	I
C4	I	S	I	S	IG (10)[c] 12 h; 48 ºC	OG (9) 12 h; 73 ºC	S	OG (6) 2 h; 66 ºC	OG (6) 2 h; 70 ºC	OG (3) 12 h; 69 ºC	S	S	S	S	S	TG (2) 20 min; 59 ºC	TG (10) 12 h; 59 ºC	TG (2) 1 h; 72 ºC	S	I
H-C4	I	S	I	S	P	OG (10) 12 h; 60 ºC	S	OG (3) 2 h; 58 ºC	OG (5) 2 h; 49 ºC	OG (10) 30 min; 68 ºC	S	PG (10) 12 h	S	S	S	TG (2.5) 5 h; 54 ºC	TG (3.5) 20 min; 52 ºC	TG (1) 1 h; 69 ºC	S	I
D4	I	S	I	IG (15)[c] 12 h; 56 ºC	S	S	S	OG (10) 5 min; 56 ºC	OG (10) 1 h; 58 ºC	OG (4) 1 h; 61 ºC	S	S	S	S	P	TG (4) 20 min; 54 ºC	TG (10) 2 h; 49 ºC	TG (1) 10 min; 49 ºC	S	I
H-D4	I	S	I	S	S	S	S	OG (5) 10 min; 56 ºC	OG (2.5) 1 h; 57 ºC	OG (10) 1 h; 64 ºC	S	S	S	S	IG (2) 5 s; 46 ºC	TG (2.5) 5 min; 50 ºC	TG (5) 2-3 h; 47 ºC	TG (2) 5 min; 58 ºC	S	I
F-A4	I	S	I	S	S	S	S	OG (4) 1 h; 37 ºC	OG (10) 12 h; 57 ºC	OG (5) 12 h; 39 ºC	S	S	S	S	P	TpG (2.5) 20 min; 35 ºC	S	TpG (2) 10 min; 37 ºC	S	I
H-F-A4	I	S	I	S	S	S	S	OG (10) 12 h; 38 ºC	OG (7) 2 h; 37 ºC	OG (15) 24 h; 43 ºC	S	S	S	S	S	S	S	S	S	I
F-B4	I	S	I	P	OG (5)[c] 12 h; 41 ºC	OG (10) 12 h; 36 ºC	P	OG (1) 1 h; 43 ºC	S	OG (2) 2-4 h; 47 ºC	S	S	S	S	P	TpG (0.5) 5 min; 51 ºC	TpG (1.5) 1 h; 36 ºC	TpG (5) 30 min; 47 ºC	S	I
H-F-B4	I	S	I	S	S	S	S	OG (2.5) 0.5-1 h; 36 ºC	S	PG (10) 12 h	S	S	S	S	S	TG (5) 20 min; 53 ºC	S	TG (10)[c] 12 h; 48 ºC	S	I
F-C4	I	S	I	IG (15) 12 h; 34 ºC	S	OG (15)[c] 12 h; 36 ºC	S	OG (13.5) 1 h; 39 ºC	OG (10) 1 h; 49 ºC	OG (10) 2-4 h; 49 ºC	S	S	S	S	IG (10)[c] 5 s; 48 ºC	TpG (7) 10 min; 41 ºC	S	S	S	I
H-F-C4	I	S	I	S	S	S	S	S	S	OG (15)[c] 12 h; 47 ºC	S	S	S	S	I	TG (5) 1 h; 36 ºC	TG (15) 2-3 h; 50 ºC	TG (2) 30 min; 41 ºC	S	I
F-D4	I	S	I	S	S	S	S	OG (5) 12 h; 48 ºC	S	OG (6)[c] 2 h; 42 ºC	S	S	S	S	I	TpG (9.5) 30 min; 39 ºC	TpG (3) 20 min; 36 ºC	TpG (7) 45 min; 50 ºC	S	I
H-F-D4	I	S	I	S	S	S	S	S	S	S	S	S	S	S	I	TG (2.5) 10 min; 49 ºC	TG (10) 30 min; 50 ºC	TG (1) 20 min; 52 ºC	S	I
bis-A4	I	S	I	OG (3.5) 1 min; 38 ºC	S	OG (6) 1 h; 66 ºC	S	OG (1) 5 min; 69 ºC	OG (1) 30 min; 62 ºC	OG (1.5) 10 min; 75 ºC	S	OG (5.5) 5 min; 63 ºC	S	S	I	TG (0.6) 1 min; 70 ºC	TG (10) 15 min; 55 ºC	TG (3.5) 5 min; 76 ºC	S	I
H-bis-A4	I	S	I	S	S	P	S	OG (2) 10 min; 62 ºC	OG (1.5) 5 min; 67 ºC	OG (2) 10 min; 71 ºC	S	OG (2.5) 10 min; 53 ºC	S	S	I	TG (1) 2 min; 69 ºC	TG (5)[c] 30 min; 58 ºC	TG (1) 2 min; 78 ºC	S	I
bis-D4	I	S	I	S	OG (4) 1 h; 64 ºC	OG (2) 10 min; 70 ºC	S	OG (2) 5 min; 53 ºC	OG (1.5) 5 min; 76 ºC	OG (2) 10 min; 73 ºC	S	S	S	S	I	TG (1) 1 min; 80 ºC	TG (1) 1 min; 60 ºC	TG (1) 1 min; 74 ºC	S	I
H-bis-D4	I	S	I	PG (10)	S	PG (10)	S	OG (5)[c] 30 min; 63 ºC	OG (1) 30 min; 53 ºC	OG (3) 10 min; 75 ºC	S	OG (2.5) 30 min; 46 ºC	S	S	I	TG (1) 20 min; 72 ºC	TG (2) 10 min; 68 ºC	TG (10)[c] 12 h; 61 ºC	S	I
***Z*4**	I	S	I	S	S	S	S	S	S	OG (10) 12 h; 41 ºC	S	S	S	S	I	S	S	S	S	I
H-*Z*4	I	S	I	S	S	S	S	S	S	S	S	S	S	S	I	TG (5) 12 h; 49 ºC	S	S	S	I
A3	I	S	I	S	S	S	S	S	S	S	S	S	S	S	I	TG (10) 5 min; 42 ºC	S	TG (3.5) 30 min; 48 ºC	S	I

[a] The gelation ability was determined upon heating-cooling process. MGC (value in parenthesis, % w/v), gelation time (h, min or s) and T_{gel} (ºC) are given for each gel. Unless otherwise indicated, the estimated random errors for MGC and T_{gel} were ± 0.2–0.3% w/v and ± 1–2 ºC respectively. All given values represent the average of at least two random measurements. For practical reasons, if gelation was not observed at 20% w/v no further studies at higher concentrations were made. Abbreviations: I = insoluble (in the range 0.1–20% w/v), S = solution (in the range 0.1–20% w/v), P = precipitates at 5–10% w/v, OG = opaque gel (homogeneous), TG = translucent gel (homogeneous), TpG = transparent gel (homogeneous), PG = partial gel (ca. 50% of the initial liquid volume), IG = inhomogeneous opaque gel in which all initial volume was immobilized. [b] A mixture of the three possible isomers was used for the gelation experiments. [c] Estimated error = ± 1% w/v.

3. Comparison between thermal and ultrasound treatment

Table S2. Gel formation via thermal (heating-cooling) or ultrasound treatment[a]

Entry	Method	Compound	Solvent	Gelation time (min)	Concentration (% w/v)	T_{gel} (ºC)[b]	Sonication[c] time (min)	Appearance
1	Thermal	**A4**	Toluene	60	2.0	37	-	TG
2	Ultrasound	**A4**	Toluene	30	2.0	41	30–40	TG
3	Thermal	**A4**	iPrOH	30	3.0	57	-	OG
4	Ultrasound	**A4**	iPrOH	30	3.0	56	30	OG
5	Thermal	**B4**	Toluene	60	1.5	45	-	TG
6	Ultrasound	**B4**	Toluene	60	1.5	47	10	TG
7	Thermal	**H-B4**	iPrOH	60	1.5	52	-	OG
8	Ultrasound	**H-B4**	iPrOH	20	1.5	48	30	OG
9	Thermal	**BisA4**	EtOAc	5	5.5	63	-	OG
10	Ultrasound	**BisA4**	EtOAc	instant.	5.5	59	5	OG
11	Thermal	**BisA4**	iPrOH	5	1.0	69	-	OG
12	Ultrasound	**BisA4**	iPrOH	2	1.0	69	5–10	OG
13	Thermal	**D4**	1-Hexanol	60	4.0	61	-	OG
14	Ultrasound	**D4**	1-Hexanol	30	4.0	64	5–10	OG
15	Thermal	**D4**	Xylenes	10	1.0	49	-	TG
16	Ultrasound	**D4**	Xylenes	instant.	1.0	47	10	OG
17	Thermal	**BisD4**	Benzene	1	1.0	63	-	TG
18	Ultrasound	**BisD4**	Benzene	instant.	1.0	65	10	TG
19	Thermal	**BisD4**	iPrOH	10	2.5	57	-	OG
20	Ultrasound	**BisD4**	iPrOH	60	2.5	61	30	OG
21	Thermal	**C4**	Toluene	20	2.0	59	-	TG
22	Ultrasound	**C4**	Toluene	60	2.0	56	10–20	TG
23	Thermal	**C4**	2-Butanol	120	6.0	66	-	OG
24	Ultrasound	**C4**	2-Butanol	30	6.0	70	40–60	OG
25	Thermal	**F-A4**	Toluene	20	3.0	37	-	TpG
26	Ultrasound	**F-A4**	Toluene	5	3.0	39	5–10	TpG

[a] Abbreviations: TG = translucent gel (homogeneous); OG = opaque gel (homogeneous); TpG = transparent gel; instant. = instantaneous (gelation occurs during sonication). [b] Estimated error = ± 2 ºC. [c] The temperature of the ultrasound bath was kept constant at 23 ± 2 ºC.

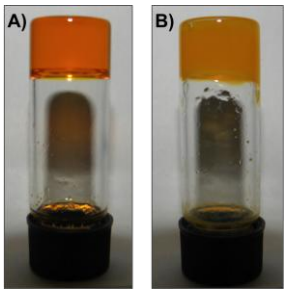


Figure S2. Digital photographs of the gels made of **D4** (1.5 % w/v) in xylenes via A) heating-cooling and B) ultrasound treatment. Note that this is the example in which the difference in opacity of the gels prepared by the two methods was more evident. In other cases, such difference was less marked.

4. Additional photographs: Gels prepared in different solvents

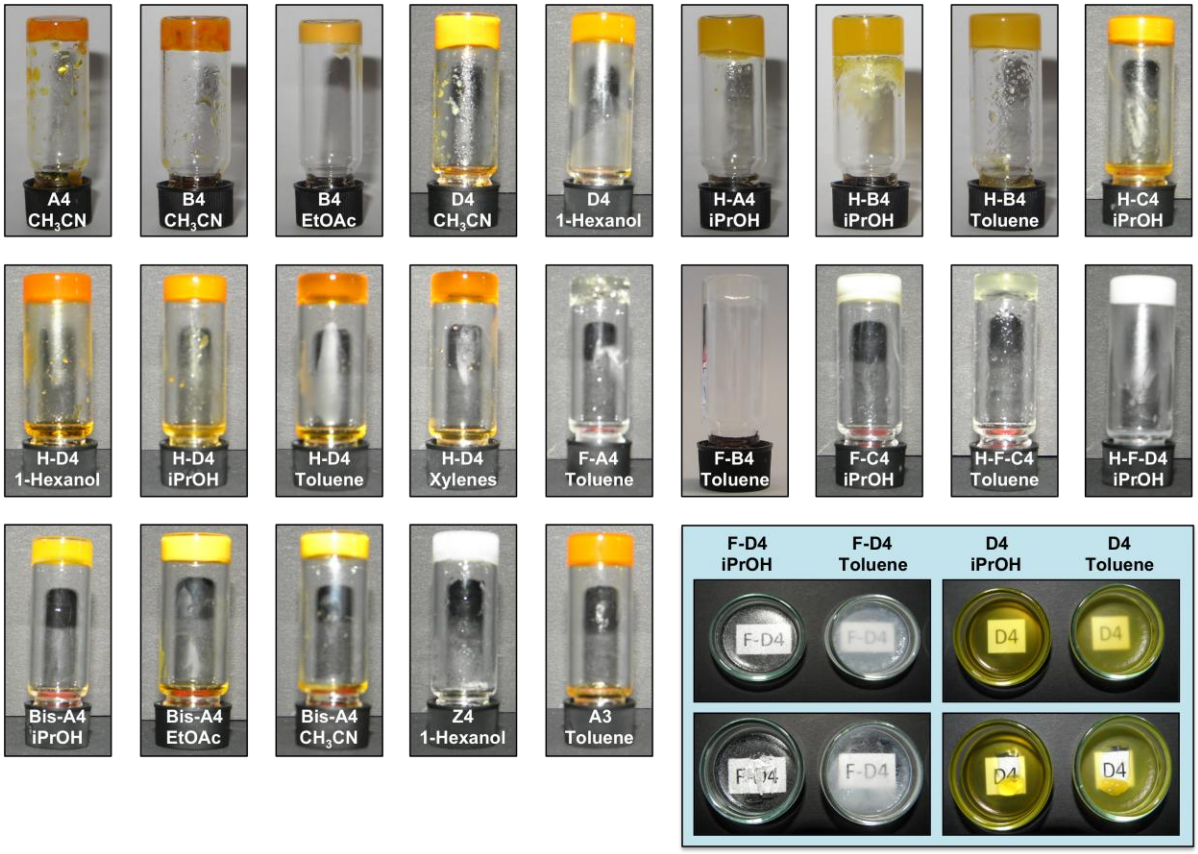


Figure S3. Additional digital photographs of upside-down vials containing organogels prepared with different peptides and solvents. The gels were prepared under the conditions reported in Table S1. At the bottom right: Thin films of organogels made in Petri dishes (∅ = 3 cm) to highlight the difference in translucence of the materials prepared in iPrOH and toluene. The pictures at the bottom line were taken after destroying the gel film with a spatula. In general, the gels in CH_3CN were more orangish than in other solvents. Moreover, gels prepared from bisazoPhe series were more yellowish than the azoPhe-based tetrapeptides.

5. Additional photographs: Gels treated under different conditions

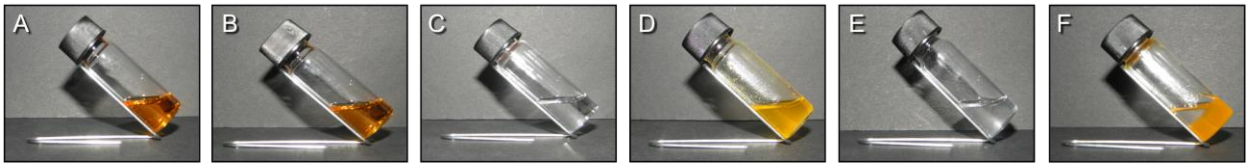


Figure S4. Additional digital photographs of selected organogels that were exposed to different chemical additives: A) spontaneous clear solution obtained from the organogel made of **A3** in xylenes after treatment with THF; B) clear solution obtained from the organogel made of **C4** in toluene after treatment with 1,4-dioxane; C) clear solution obtained from the organogel made of **F-A4** in iPrOH after treatment with CH_2Cl_2; D) turbid solution obtained from the organogel made of **bis-D4** in iPrOH after treatment with NaOH (0.1 M aqueous solution) and gentle shaking; E) D) turbid solution obtained from the organogel made of **F-A4** in iPrOH after treatment with NaOH (0.1 M aqueous solution) and gentle shaking; F) stable gel made of **A4** in toluene in the presence of TBAF solution after 3 days. In all cases the ratio (gel volume):(second solvent volume) = 1:1.

No significant response of the gels prepared either in iPrOH or toluene was found to external anions such as fluoride or bromide –added as their TBA salts–. The gels could be only fragmented by vigorous shaking after 3 days in contact with TBA salts. Some of these fragmented gels could be even reformed upon resting due to their thixotropic nature. Similar stability was found when the gels were overlayered with either HCl (0.1 M aqueous solution) or some metal salt solutions (i.e. 5 equivuiv $CuSO_4$ or $FeSO_4$ in 0.5 mL of H_2O).

6. Correlation with KamLet-Taft parameters

Table S3. Selection of solvent properties and parameters

Entry	Solvent	Solvent group[a]	ε_r[b]	μ (D)[c]	α[d]	β[e]	π^*[f]	bp[g] (ºC)
1	H_2O	PP	80.1	1.82	1.17	0.47	1.09	100
2	DMSO	PA	46.7	3.96	0.00	0.76	1.00	189
3	Glycerol	PP	43.0	2.70	1.21	0.51	0.62	290
4	CH_3CN	PA	36.6	3.92	0.19	0.40	0.75	82
5	MeOH	PP	33.0	1.70	0.98	0.66	0.60	65
6	EtOH	PP	24.5	1.69	0.86	0.75	0.54	78
7	Acetone	PA	21.0	2.88	0.08	0.43	0.71	56–57
9	iPrOH	PP	18.0	1.56	0.76	0.84	0.48	83
9	2-Butanol	PP	16.6	1.63	0.69	0.80	0.40	98–100
10	1-Hexanol	NP to WPA[h]	13.3	1.42	0.80	0.84	0.40	155–159
11	CH_2Cl_2	NP to WPA (halog.)	9.1	1.60	0.13	0.10	0.82	40
12	EtOAc	NP to WPA	6.1	1.78	0.00	0.45	0.55	77
13	THF	NP	5.7	1.75	0.00	0.55	0.58	66
14	$CHCl_3$	NP (halog.)	4.8	1.04	0.20	0.10	0.58	61
15	Et_2O	NP	4.3	1.15	0.00	0.47	0.27	35
16	Toluene	NP (arom.)	2.4	0.38	0.00	0.11	0.54	111
17	Benzene	NP (arom.)	2.3	0.00	0.00	0.10	0.59	80
18	*p*-Xylene	NP (arom.)	2.3	0.07	0.00	0.12	0.43	139
19	1,4-Dioxane	NP	2.2	0.45	0.00	0.37	0.55	101
20	*n*-Hexane	NP	1.9	0.00	0.00	0.00	–0.04	69

[a] Abbreviations: PP = polar protic; PA = polar aprotic; NP = non-polar; WPA = weak polar aprotic; arom. = aromatic; halog. = halogenated. [b] Relative permitivity (dielectric constant)[1] measured in the range 20–25 ºC. The values were rounded off to one decimal place and those highlighted in red color correspond to solvents that were not gelled with the MGS. [c] Dipole moment of solvents measured at 20 or 25 ºC and provided by commercial suppliers. [d] KamLet-Taft parameter[2] defining the hydrogen bond donor ability. [e] KamLet-Taft parameter defining the hydrogen bond aceptor ability. [f] KamLet-Taft parameter defining the polarisability of the solvent. [g] Boiling point (values rounded off wihout decimals are presented). [h] In general, a solvent is treated as non-polar if its the dielectric constant is below 15.[3]

A Gaussian function was applied when appropriated for correlations studies between gelation ability, gel properties and solvent-parameters (equivuation (1)):

$$\mathcal{F}(x) = A \times e^{\frac{-(x-SD)^2}{2c^2}} \qquad (1)$$

where A and c are real constants (> 0), SD is the standard deviation and $e \approx 2.718281828$ (Euler's number). The fitting values for Figure 2 in main text were established upon minimisation of the sum of square errors of experimental data with expected data: α-parameter: Mean value = 0.78; standard deviation = 0.1077; A parameter = 21.5874; number of calculated data points = 130; β-parameter: Mean value = 0.84; standard deviation = 0.0955; A parameter = 18.3375; number of calculated data points = 80; π^*-parameter: Mean value = 0.45; standard deviation = 0.1710; A parameter = 33.9851; number of calculated data points = 110. The margin of error provided by theoretical data was considered negligible in this context. Due to the similarity of gelation ability for the same solvent and different peptides, tested solvents were categorized according to their KamLet-Taft parameters in steps of 0.1 units for each parameter. The standard error of the mean for the quantification of gel properties (i.e. T_{gel}, MGC) was calculated by the ratio between standard deviation of the range of values and the square root of the population size of all the possible random samples.

7. DSC measurements

For DSC measurements, an appropriate amount of gel was placed into a preweighted Al pan, which was sealed and weight on a six-decimal plate balance. Heating and cooling scans were measured on a DSC7 (Perkin Elmer) instrument at a scan rate of 10 ºC min^{-1} under nitrogen atmosphere. In order to ensure reproducibility, two heating-cooling cycles were recorded and the second curves used for comparative studies. The pans were weighted again after each measurements to check for possible leakage.

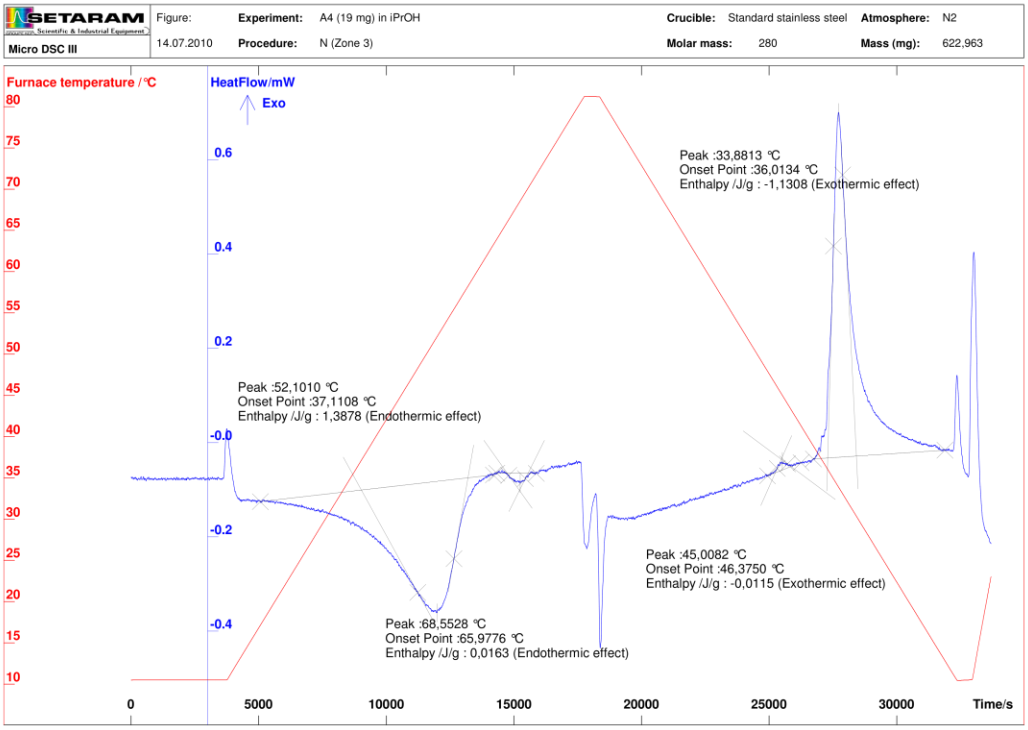


Figure S5. Representative DSC spectrum of the gel made of **A4** in iPrOH (1.9 % w/v). *Gel*-to-*sol* transition temperature (endothermic effect) was estimated in ca. 52 °C in two different cycles (first-order transition), which was in good agreement with the value obtained using IFM (T_{gel} = 56 ± 1 ºC). In the other hand, *sol*-to-*gel* transition temperature (exothermic effect) was estimated in ca. 45 °C due to thermal cycling hysteresis. In general, gelator molecules assemble into fibers by a first-order process. Such assembles link together to form clusters and finally the 3D network. The evolution of the cluster size is usually dominated by second-order thermal transitions.

8. Temperature-dependent FT-IR

FT-IR spectra of solid samples were obtained using a high pressure diamond ATR accessory (Bio-Rad) at room temperature over the wavenumber range 7000−550 cm^{-1}. Spectra of the gels at different temperatures were obtained on a Varian 3100 FT-IR spectrophotometer equivuipped with a variable temperature cell controller (SPECAC, PIN 21525) with the samples sandwiched (0.5 mm layer thickness) between BaF_2 or CaF_2 cells (4 cm^{-1} resolution, 250 scans, 1 mm aperture). Typically, the gel was first heated with a heat gun until it melted and placed into the cuvette, which was then kept at 10 °C for 2 hours. After this time, the cuvette was allowed to warm to RT before measurement. The temperature was raised at 10 °C min^{-1} during the heating cycle. The cooling was performed after 20 min for sample equivuilibration.

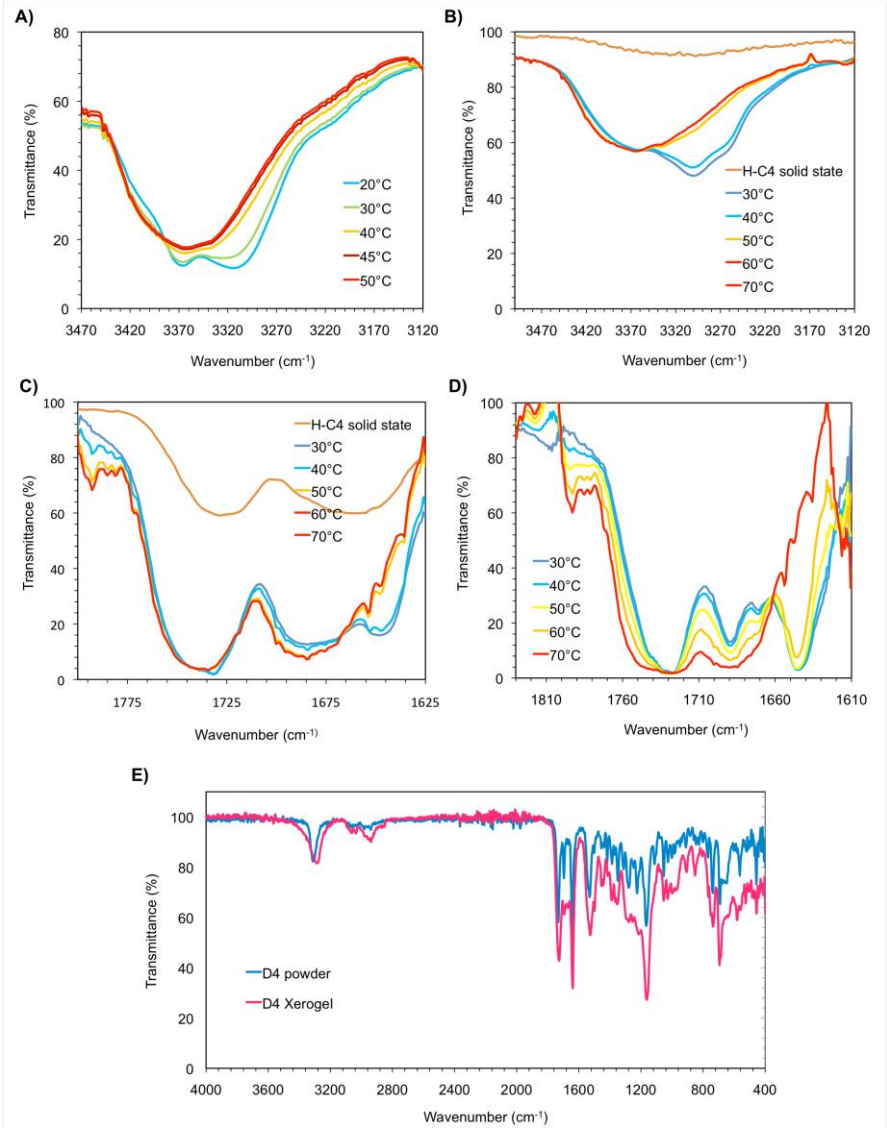


Figure S6. A-D) Selected regions of temperature controlled FT-IR measurements: A = **H-D4** in benzene at MGC (–NH amide stretching region; T_{gel} = 47 ± 2 ºC), B = **H-C4** in toluene at MGC (–NH amide stretching region; T_{gel} = 54 ± 2 ºC), C = **H-C4** in toluene at MGC (amide I region; T_{gel} = 54 ± 2 ºC), D = **C4** in toluene at MGC (amide I region; T_{gel} = 59 ± 2 ºC). E) FT-IR spectra of azopeptide **D4** as solid and as xerogel preprared from the corresponding organogel. As expected, developed hydrogen-bonding shifted both carbonyl and –NH resonances to lower energy.

9. Temperature-dependent NMR

Temperature-dependent ^{1}H-NMR studies were on a 400 MHz Bruker Avance instrument equivuipped with a BVT 2000 heating system (Bruker BioSpin GmbH).

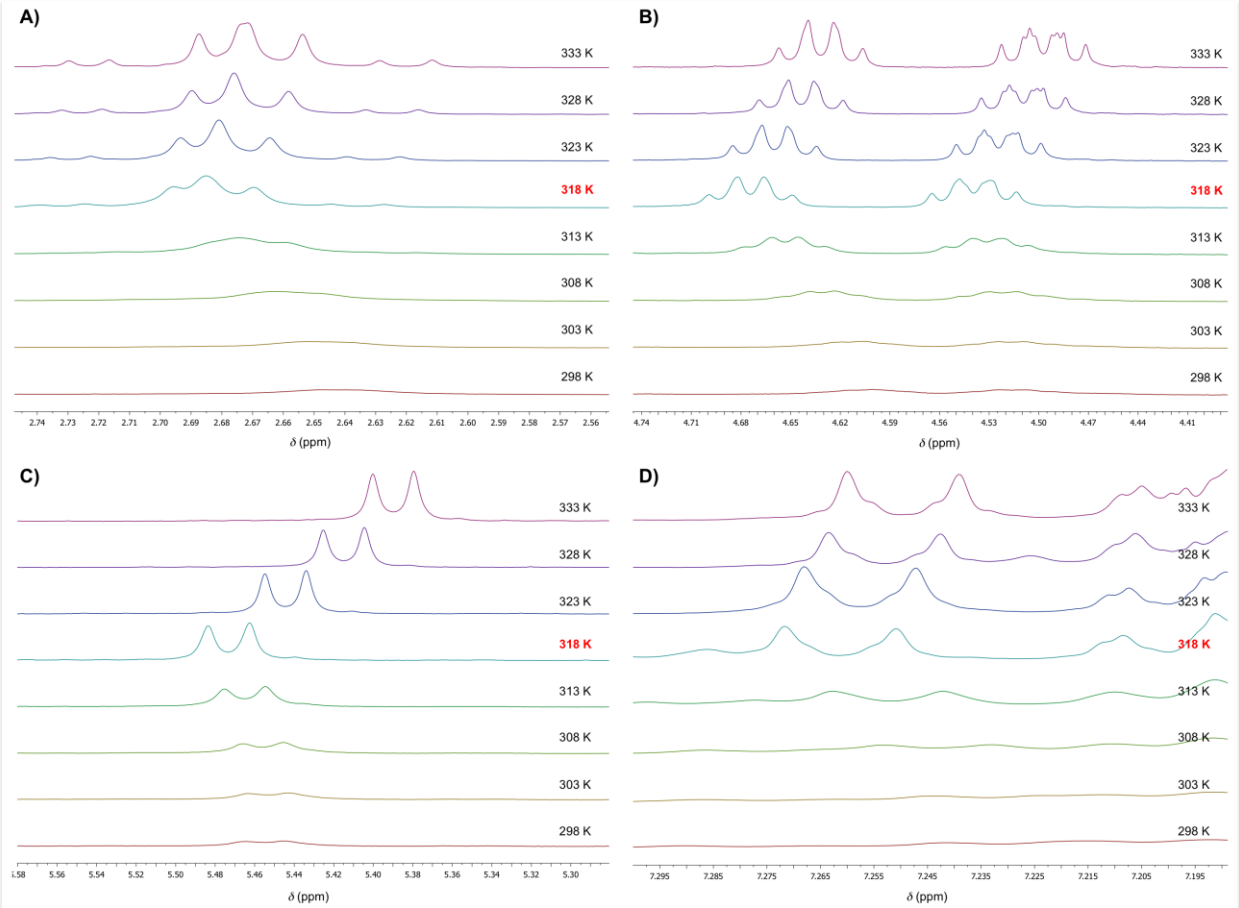


Figure S7. Selected regions of temperature-dependent ^{1}H-NMR spectra corresponding to the organogel made of **B4** in d_8-toluene (1.5 % w/v). A) BzlOCO-C***H*****$_2$**- proton, B) Boc-CO-NH-C***H***-CO-NH-C***H***- protons, C) Boc-CO-N***H***- proton, D) Boc-CO-NH-CH-CO-NH-CH-CO-N***H***- proton. T_{gel} calculated by IFM = 45 °C = 318 K.

10. UV-vis experiments

UV-vis spectra were recorded in a Varian Cary 50 UV-vis scanning spectrophotometer. The gels were prepared in a 0.1 mm quartz cell (Suprasil ®, Hellma) and the UV-vis spectra recorded at different times upon appropriate irradiation as indicated in the main text. Photoresponsive tests were carried out using UV-lamp from Original Hanau Quarzlampen GmbH (20 Watt, 366 nm). The use of lower intensity lamps (i.e. NU-4 UV-handlamp from Herolab GmbH (4 Watt, 366 nm)) was also successful. A constant distance of 10 cm was mantained between the UV-lamp and the samples.

Table S4. Response of organogels to UV-irradiation[a]

Entry	Peptide gelator	Solvent	Time of irradiation	Photoresponse	Time to reform the gel under room light[c]
1	C4	Toluene	2 days	no response	-
2	C4	iPrOH	2 days	no response	-
3	D4	Toluene	2 days	no response	-
4	H-A4	Toluene	30 min	solution	7 h
5	H-B4	Toluene	50 min	solution	3.5 h
6	H-C4	Toluene	60 min	solution	nd[b]
7	H-C4	iPrOH	12 h	partial solution	nd[b]
8	H-D4	Toluene	45 min	solution	4 h
9	H-D4	Benzene	70 min	solution	8 h
10	H-D4	Xylenes	30 min	solution	3 h
11	Bis-A4	Benzene	2 days	no response	-
12	Bis-D4	Toluene	2 days	no response	-
13	H-Bis-A4	Toluene	45 min	solution	8 h
14	H-Bis-A4	iPrOH	90 min	solution	20 h
15	H-Bis-D4	Toluene	30 min	solution	4 h
16	H-Bis-D4	iPrOH	115 min	solution	24 h

[a] Gels prepared at MGC into 0.1 mm UV-cuvettes. Light source: 4 W-black light lamp (λ_{max} = 366 nm). [b] nd = no determined. [c] Gel completely recovered by visual inspection.

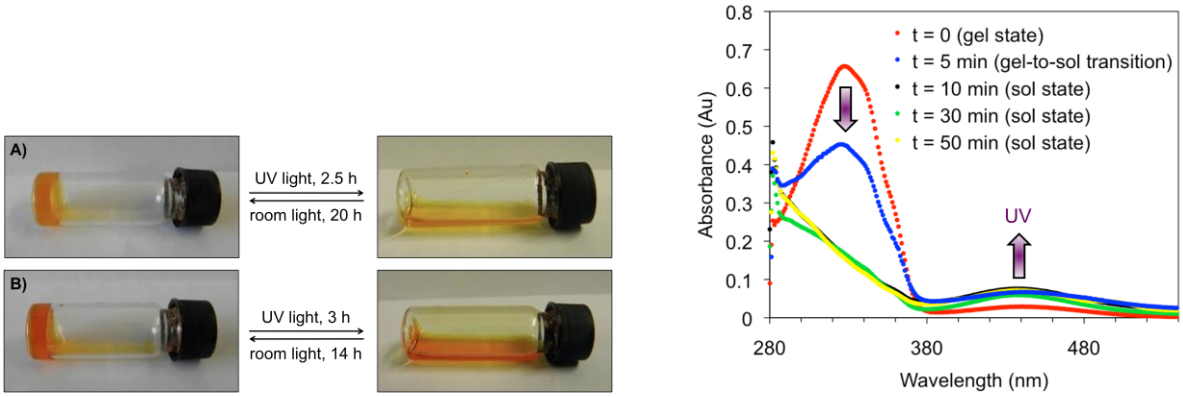


Figure S8. *Left:* Light-induced macroscopic *gel*-to-*sol* transition of organogels made of A) **H-B4** in toluene (3 % w/v) and B) **H-D4** in benzene (5% w/v). Volume of gel = 0.5 mL. *Right:* UV-vis absorption spectra of the gel made from **H-C4** in toluene (2.5% w/v; 5 mm path length) showing the *gel*-to-*sol* transition upon UV irradiation at 366 nm. The figure shows the complementary profile to that in Figure 12 of the main paper (*sol*-to-*gel* transition).

A precise control of the temperature of all samples was maintained during irradiation. Herein, different types of UV-lamps were tested to rule out a critical thermal effect and we used an external beaker filled with water, which was kept to a constant temperature during irradiation. The results showed that a constant temperature could be easily achieved in this way and by using a UV-lamp of 20 Watt as maximum intensity.

11. Rheological studies

Oscillatory rheology was performed with an AR 2000 Advanced rheometer (TA Instruments) equipped with a Julabo C cooling system. A 1000 µm gap setting and a torque setting of 40,000 dynes/cm^2 at 25 ºC were used for the measurements in a plain-plate (20 mm, stainless steel). The data were found to be highly reproducible for independent batches. The following experiments were carried out for each sample, using ca. 1 mL total gel volume: a) Dynamic Strain Sweep (DSS): variation of *G'* and *G''* with strain (from 0.01 to 100%); b) Dynamic Frequivuency Sweep (DFS): variation of *G'* and *G''* with frequivuency (from 0.1 to 10 Hz at 0.1% strain); c) Dynamic Time Sweep (DTS): variation of *G'* and *G''* with time keeping the strain and frequivuency values constant and within the linear viscoelastic regime (strain = 0.1% strain; frequivuency = 1 Hz).

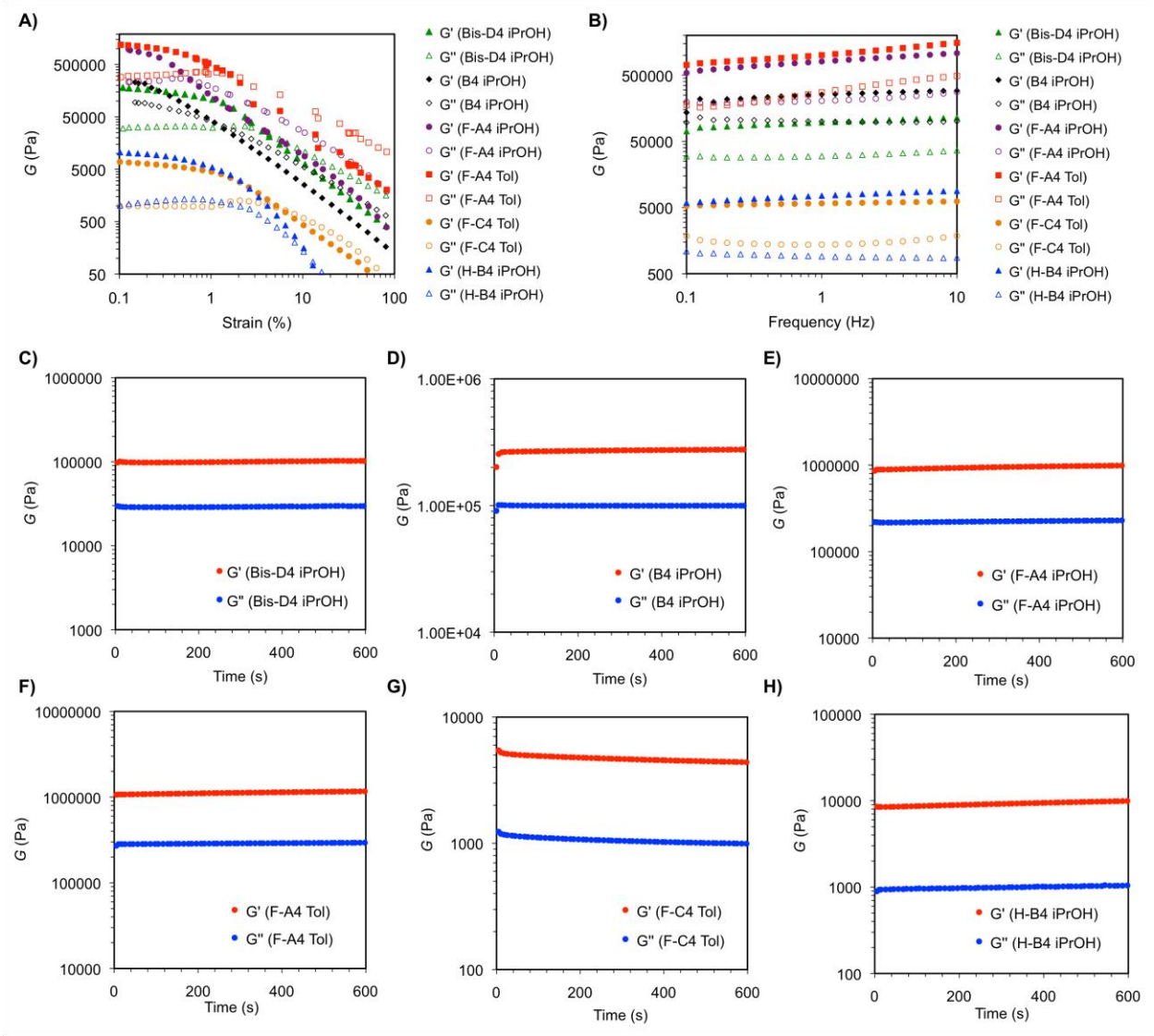


Figure S9. Additional oscillatory rheological measurements of gels prepared from different peptides in toluene or iPrOH: A) DSS experiments. B) DFS experiments. C-H) DTS experiments. Tan δ = 0.293 ± 0.001 (C), 0.369 ± 0.002 (D), 0.237 ± 0.001 (E), 0.490 ± 0.01 (F), 0.226 ± 0.001 (G), 0.108 ± 0.001 (H). The gels were prepared at their MGC. Tol = toluene.

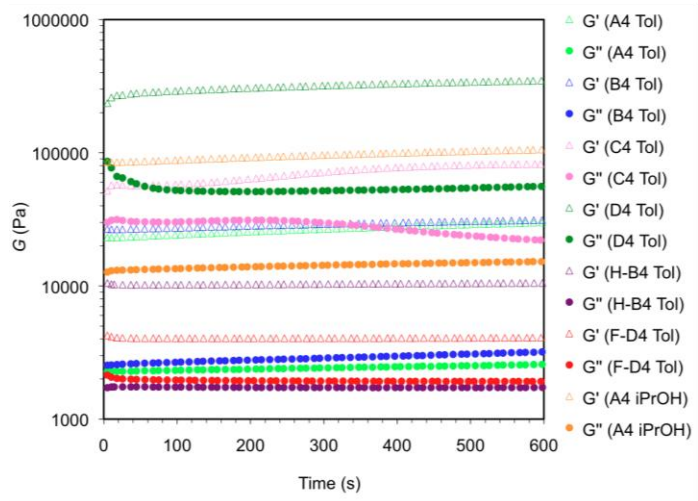


Figure S10. Additional DTS experiments of gels prepared from different peptides in toluene or isopropanol. All gels were prepared at their MGC as indicated in Table S1. Tol = toluene.

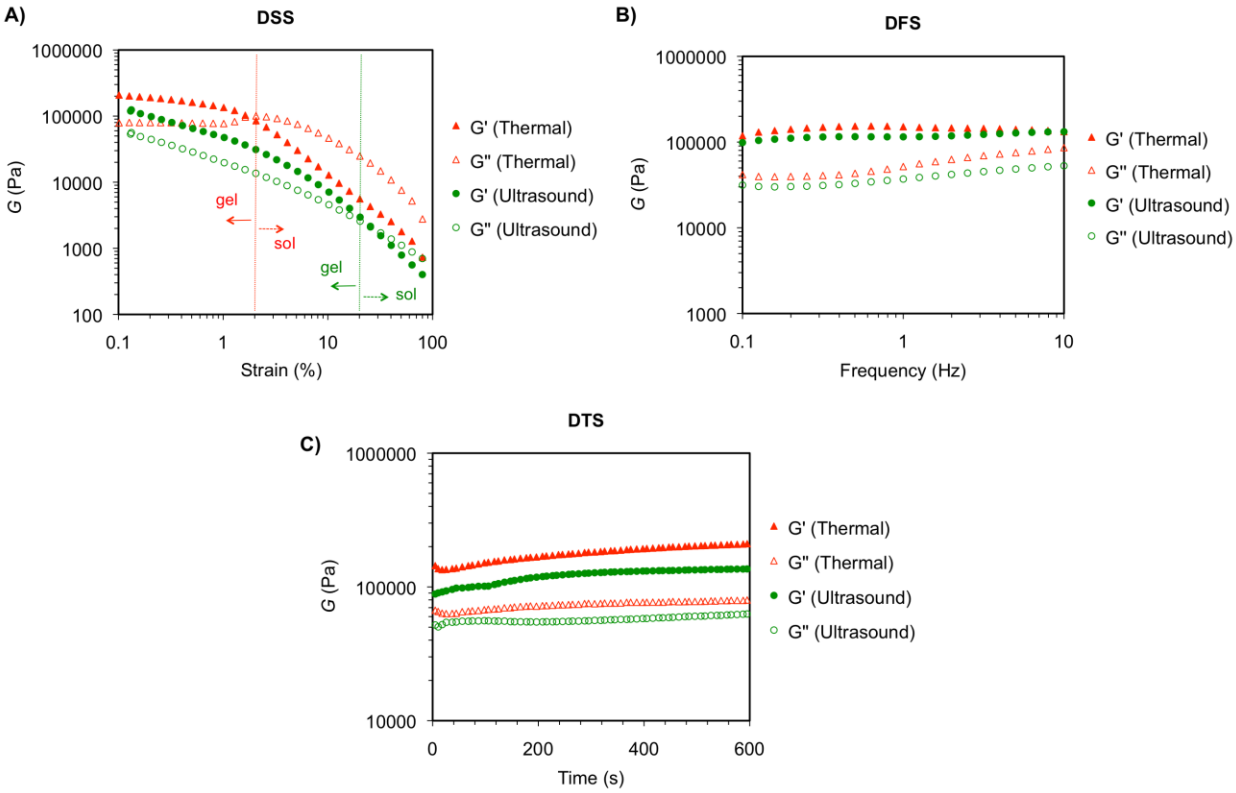


Figure S11. Comparison of the flow properties corresponding to the gels made from azopeptide **H-D4** (2.5 % w/v) in toluene via heating-cooling or ultrasound treatment: A) DSS experiment. B) DFS experiment at 0.1 % strain. C) DTS experiment at 0.1 % strain and 1 Hz frequency.

Mechanical inertial effects of the measuring head was accounted by the software package to accurate evaluate the thixotropic nature of the materials. For this, fixed rest time after sample loading and pre-shearing to equivuilibrium at different shear rates were rutinately made in order to minimize prehistory effects.

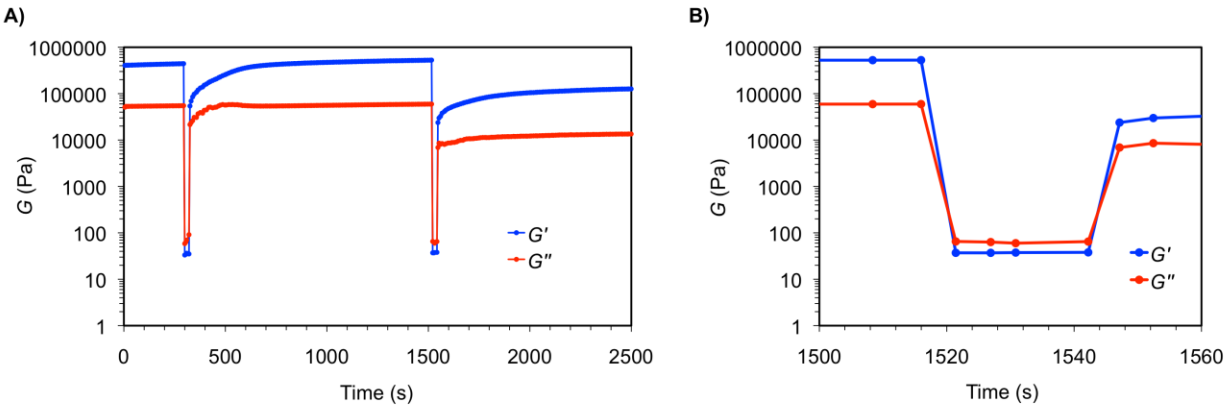


Figure S12. A) Thixotropy loop test of the gel made from azopeptide **H-D4** (2.5 % w/v) in toluene. B) Individual step of the thixotropy loop test. Different shear rates and resting times provided similar behavior.

12. Electron microscopy

Samples were observed with the following instrument: (1) JEOL-2000 FXII transmission electron microscope (TEM, resolution = 0.28 nm) equivuipped with a CCD Gatan 694 digital camaera and operating at 10 kV (accelerating voltage). (2) JEOL JSM 6400 scanning electron microscope (SEM, resolution 3.5 nm) equivuipped with a digital camera and operating at 15 kV (accelerating voltage). (3) Carl Zeiss Merlin field emission scanning electron microscope (FESEM, resolution 0.8 nm) equivuipped with a digital camera and operating at 5 kV (accelerating voltage) and 10 μA (emission current). The aspect ratio of a fibre is defined as the ratio of its length to its width.

Preparation of the samples for TEM: 10 μL of the gel suspension was allowed to adsorb for 30 s onto carbon-coated grids (300 mesh, from TED PELLA, Inc.). After the adsorption, the excess solvent was removed by touching the edges with a small piece of filter paper (Whatman). The specimens were then dried overnight in a desecator at low pressure and RT. Patches of the gel were first searched to be sure that the observed structures originate from the gel. Micrographs were taken from structures at the periphery of the patches where the fibers were deposited in a layer thin enough to be observed by TEM.

Preparation of the samples for SEM/FE-SEM: Samples of the cryogels were prepared by the freeze-drying (FD) method:[4] An eppendorf tube containing the corresponding organogel (100–200 μΛ) was frozen in liquid nitrogen or dry ice/acetone and the sample was immediately evaporated under reduced pressure (0.6 mmHg) for 2 days at room temperature. A fibrous solid was obtained, which was placed on top of a tin plate and shielded by Pt (40 mA during 60 s for SEM and 30 s for FE-SEM (film thickness ≈ 10 nm and 5 nm respectively).

Note: It should be indicated that samples for electron microscopy were prepared without quantitative control of their thickness. However, for relative comparison, all samples were always prepared following the same procedure as described above.

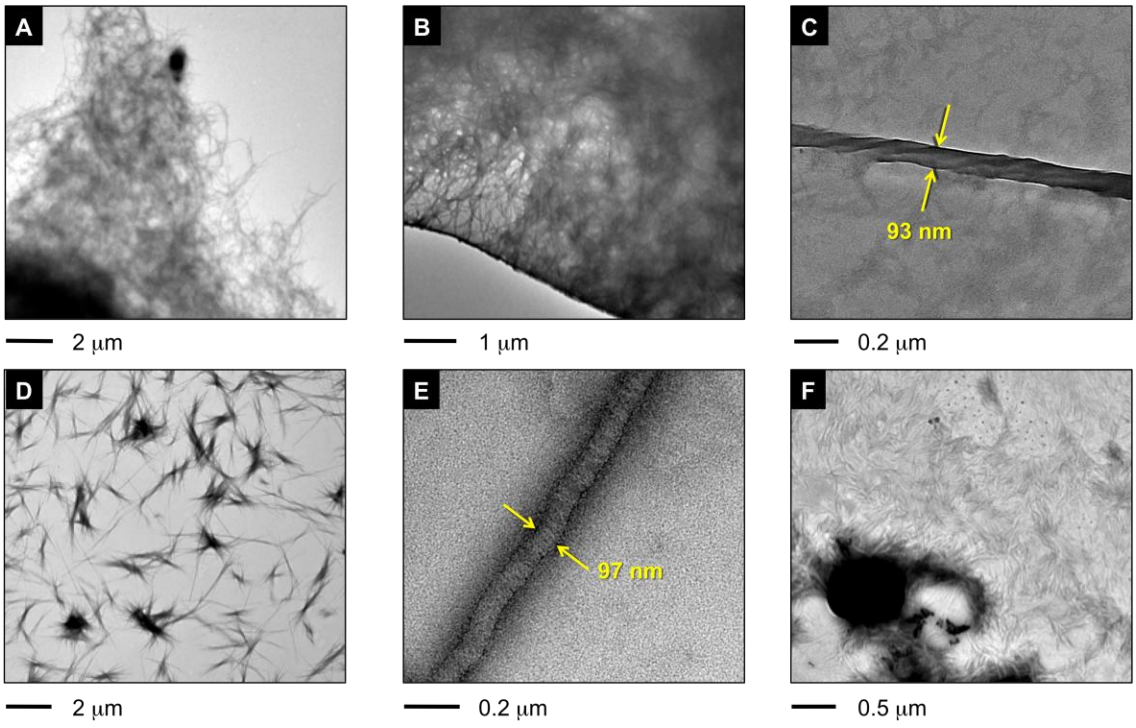


Figure S13. Additional TEM images of the fibrilar xerogels obtained from the corresponding organogels prepared as shown in Table S1. A) **Bis-A4** in iPrOH; B) **C4** in iPrOH; C) **D4** in toluene; D) **A4** in toluene; E) **A4** in iPrOH; F) **F-A4** in toluene. In both solvents (toluene, iPrOH) apparently twisted morphology of individual fibrils (ca. 90-100 nm in diameter) could be observed (C, E).

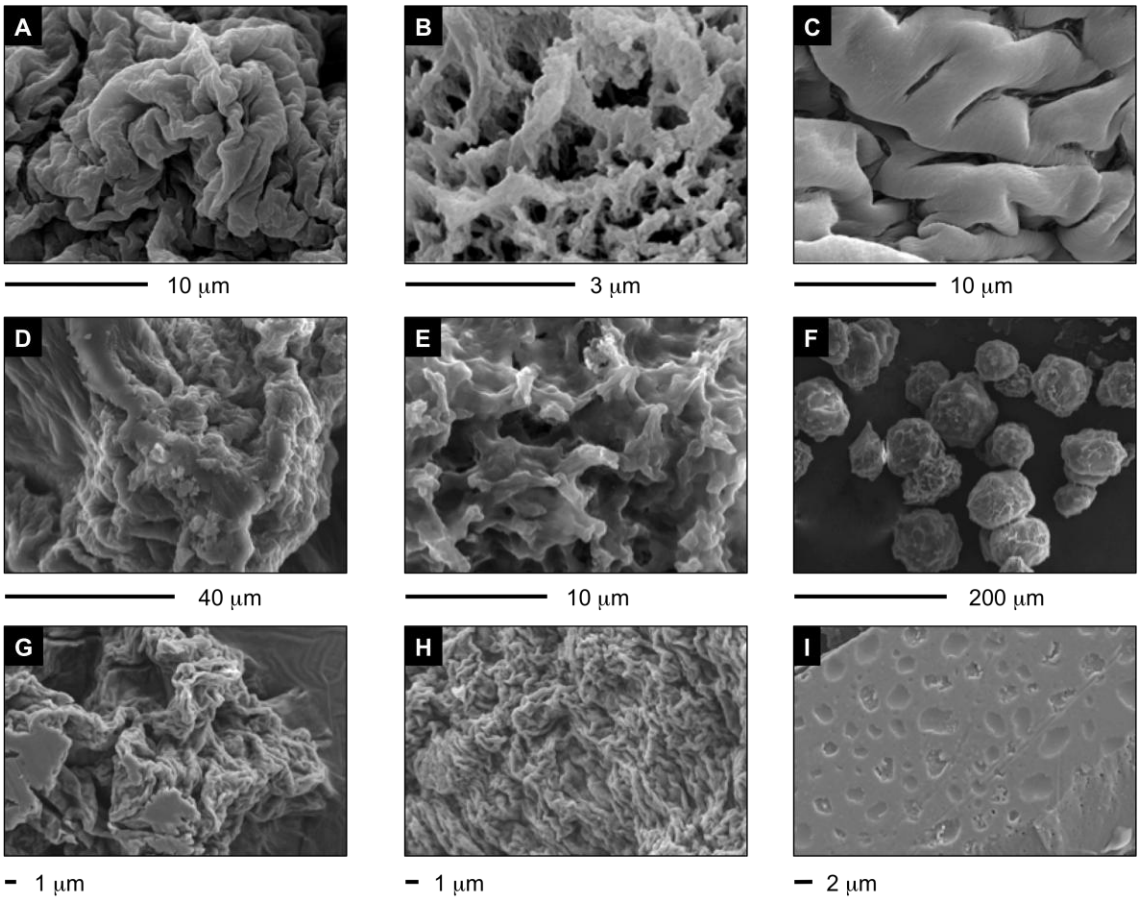


Figure S14. Additional SEM and FE-SEM images of cryogels obtained from the corresponding organogels prepared as shown in Table S1. A) **A4** in toluene (SEM); B) **A4** in iPrOH (SEM); C) **F-A4** in toluene (SEM); D) **C4** in iPrOH (SEM), E) **C4** in toluene (SEM); F) **D4** in iPrOH (SEM); G) **A4** in toluene (FE-SEM); H) **A4** in iPrOH (FE-SEM), I) **F-A4** in toluene (FE-SEM).

13. AFM imaging

AFM experiments were performed on a Ntegra Aura (NT-MDT) instrument in tapping mode at 1 Hz scanning rate using directly polycrystalline sapphire (24 × 19.3 × 0.5 mm) as substrate and a single crystal silicon tip coated with TiN (NSG01/TiN, 0.01–0.025 Ω-cm, Antimony doped) at 200–400 kHz drive frequivuency. Drive applitude ranged from 60 to 100 mV. The resolution limit is dictated by the size of the AFM tip. Preparation of the sample: 5–10 µL of a gel suspension (~ 10-fold dilution in the corresponding solvent) was placed on the substrate and homogeneously dispersed with a spatula to form a thin layer that was allowed to dry in air for at least 30–60 min before measurement.

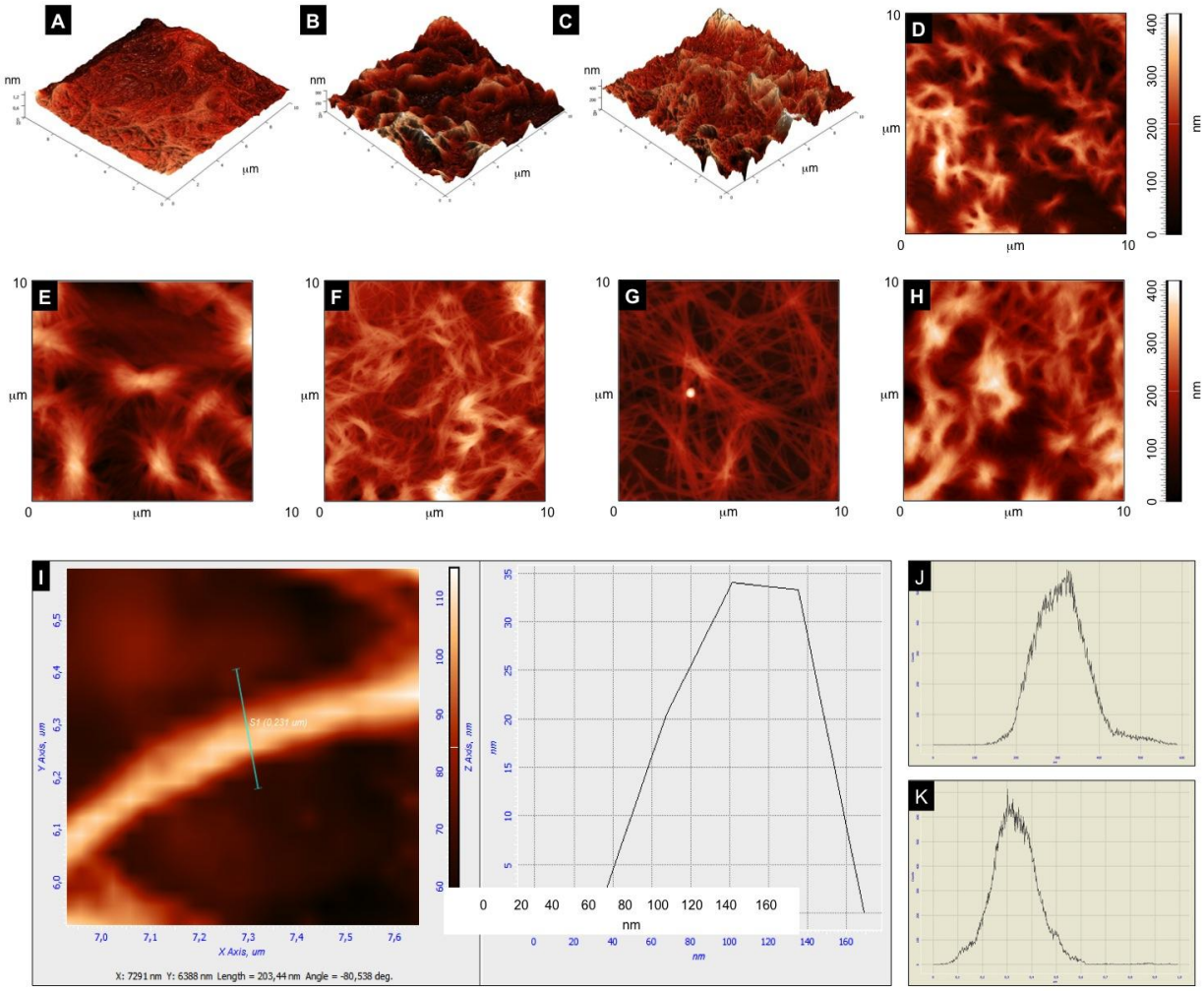


Figure S15. A-F) Additional AFM images (10 × 10 µm) of the xerogels prepared from the corresponding organogels at MGC: A) **A4** in iPrOH (3D surface topographic image, *Z*-axis = 1.2 nm). B) **F-A4** in toluene (3D surface topographic image, *Z*-axis = 300 nm). C) **A4** in toluene (3D surface topographic image, *Z*-axis = 400 nm). D) **F-A4** in toluene. E) **A4** in iPrOH. F) **A4** in toluene. G) **F-A4** in toluene. H) **B4** in toluene. I) Single fiber (ca. 35 × 100 nm) corresponding to the gel made of **B4** in toluene at MGC. J) Histogram centered at ca. 300 nm corresponding to the gel made of **A4** in toluene at MGC. K) Histogram centered at ca. 300 nm corresponding to the gel made of **A4** in iPrOH at MGC.

14. Polarized light microscopy

Polarized light microscopic images were obtained with a Wild Makroskop M420 1.25× equivuipped with a digital camera Canon Power shot A640. A piece of gel or a drop of solution was placed between two glass slides for observation.

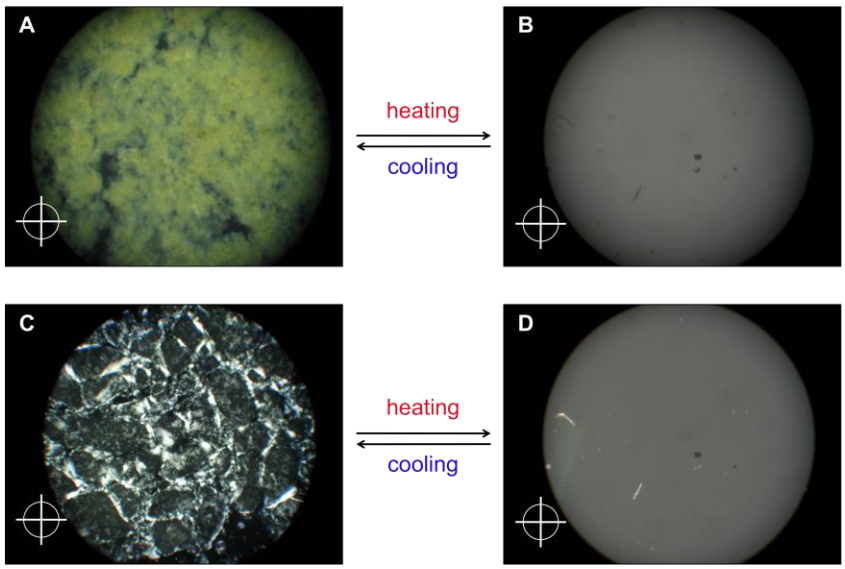
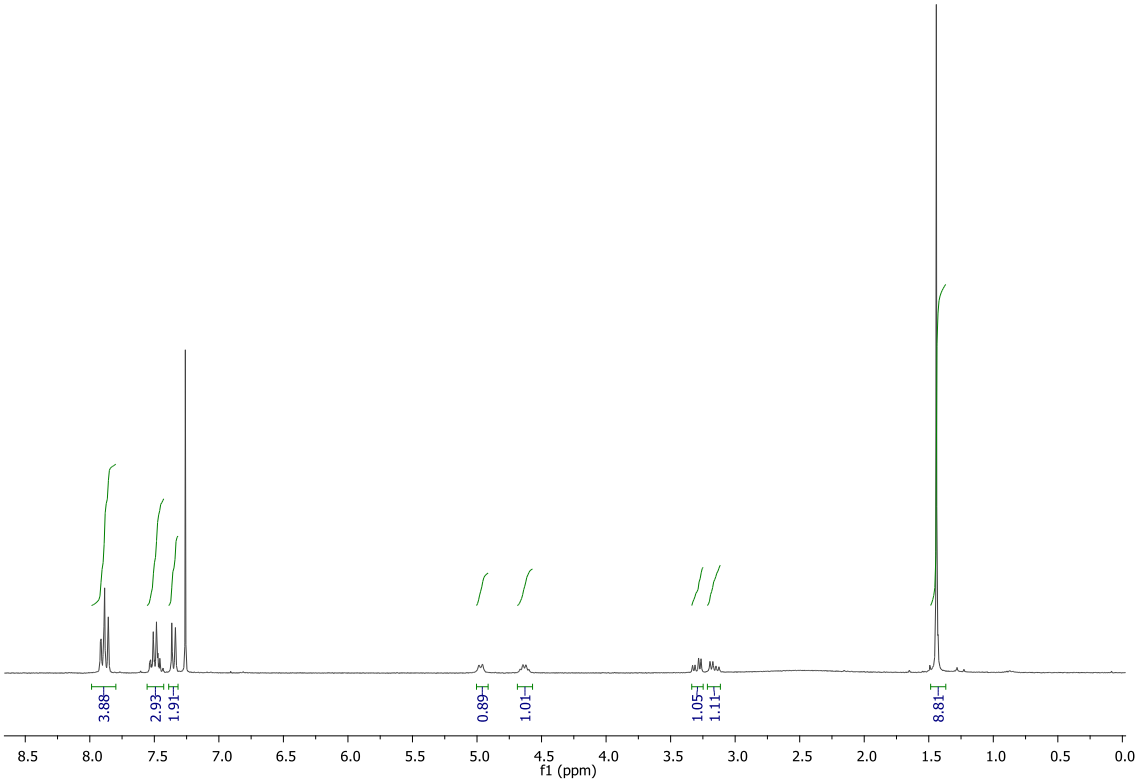
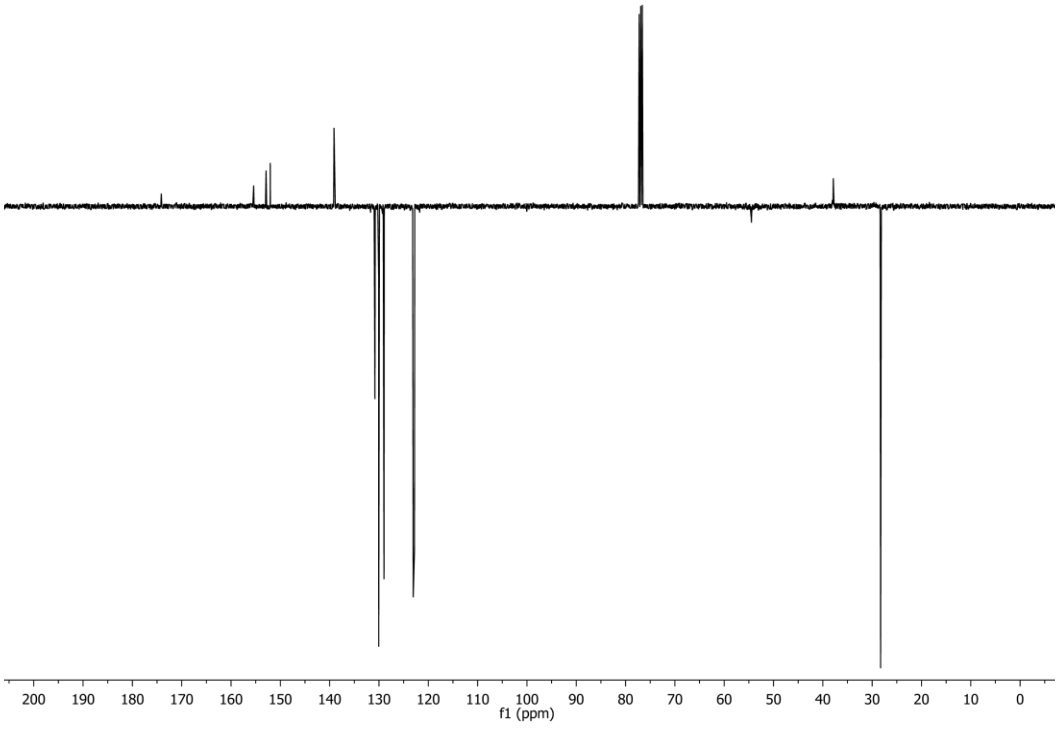


Figure S16. Polarized light microscope images: A) Organogel made of **A4** in iPrOH (2 % w/v). B) Solution obtained upon melting the gel A). C) Organogel made of **A4** in toluene (2 % w/v). D) Solution obtained upon melting the gel C). Polarizing filter is oriented 90 º to the plane of the polarized light. Magnification: A–B = 15×, C–D = 45×.

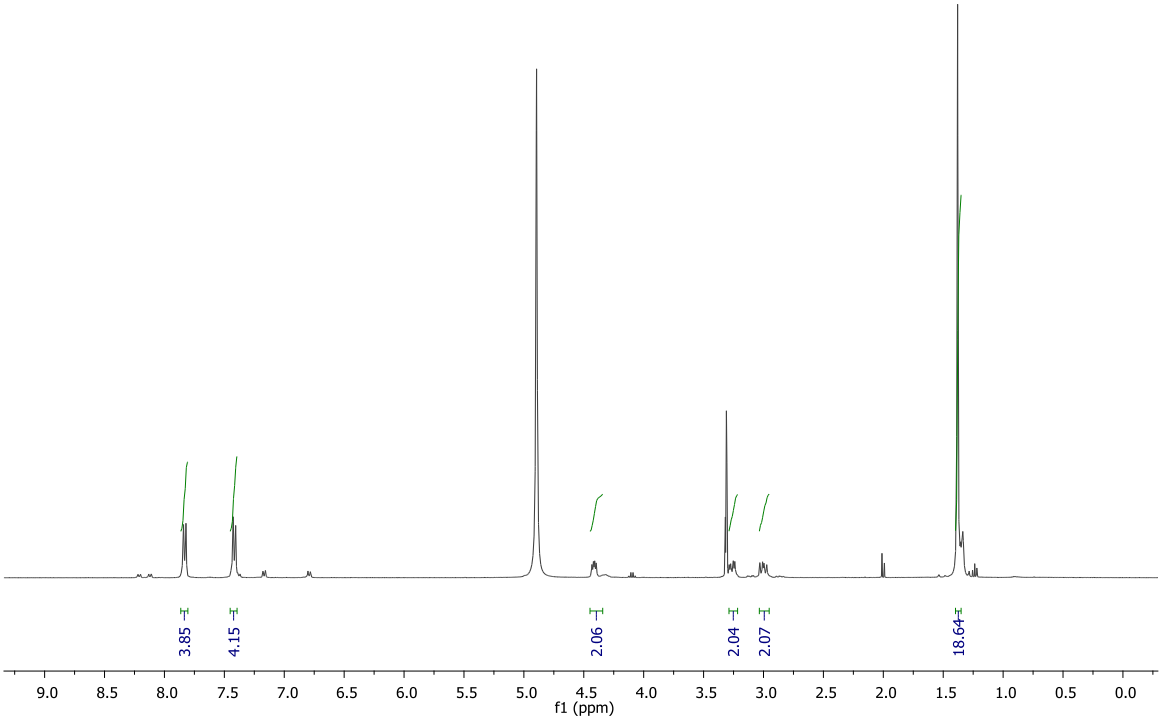
15. Collection of ^{1}H-NMR and ^{13}C-NMR of synthesized compounds

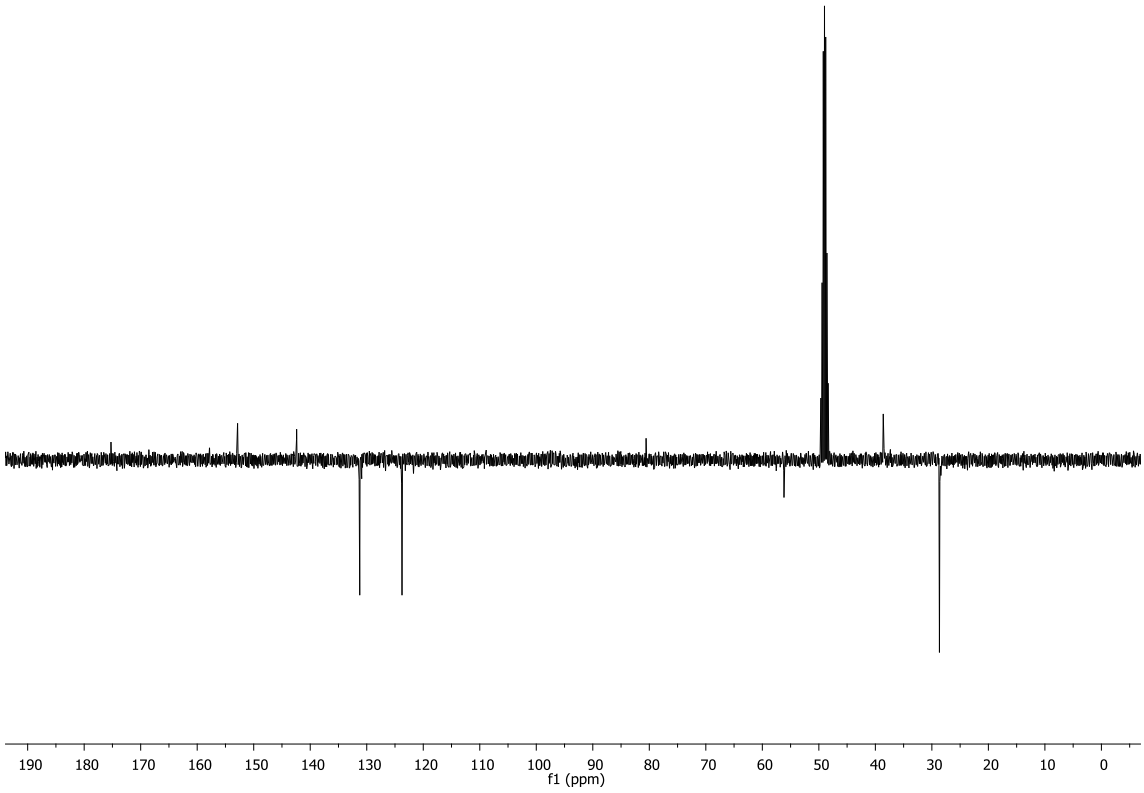
^{1}H-NMR and ^{13}C-NMR spectra of **Boc-azoPhe-OH (1)**



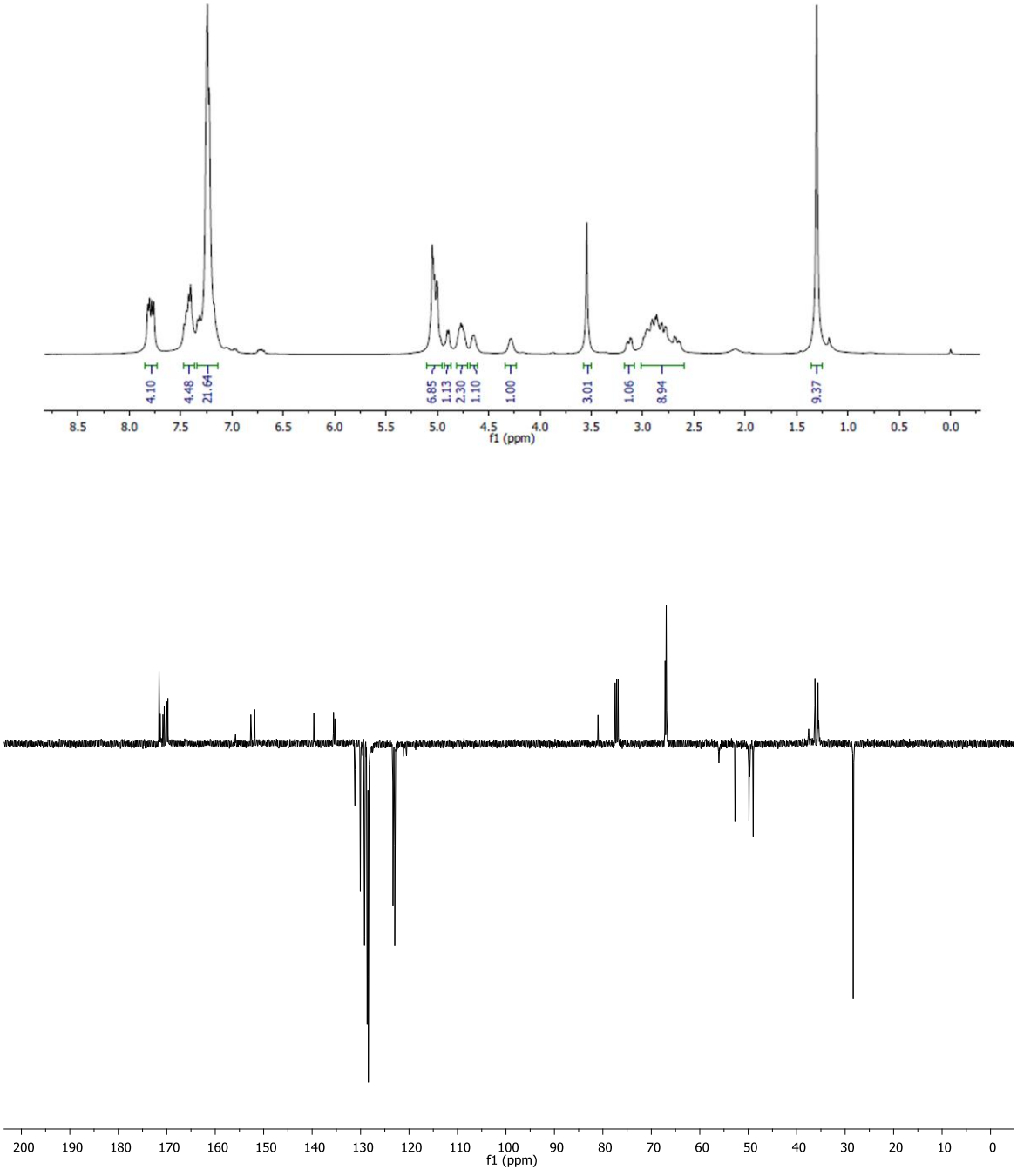


^{1}H-NMR and ^{13}C-NMR spectra of **Boc-bisazoPhe-OH** (**2**)

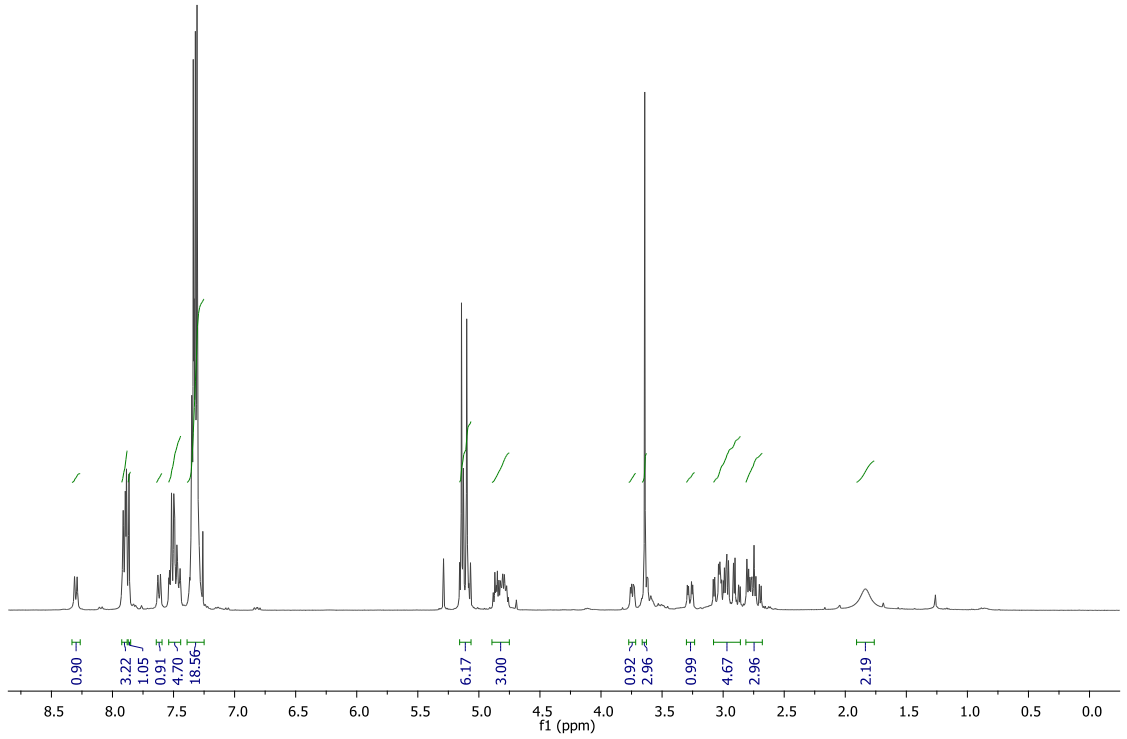


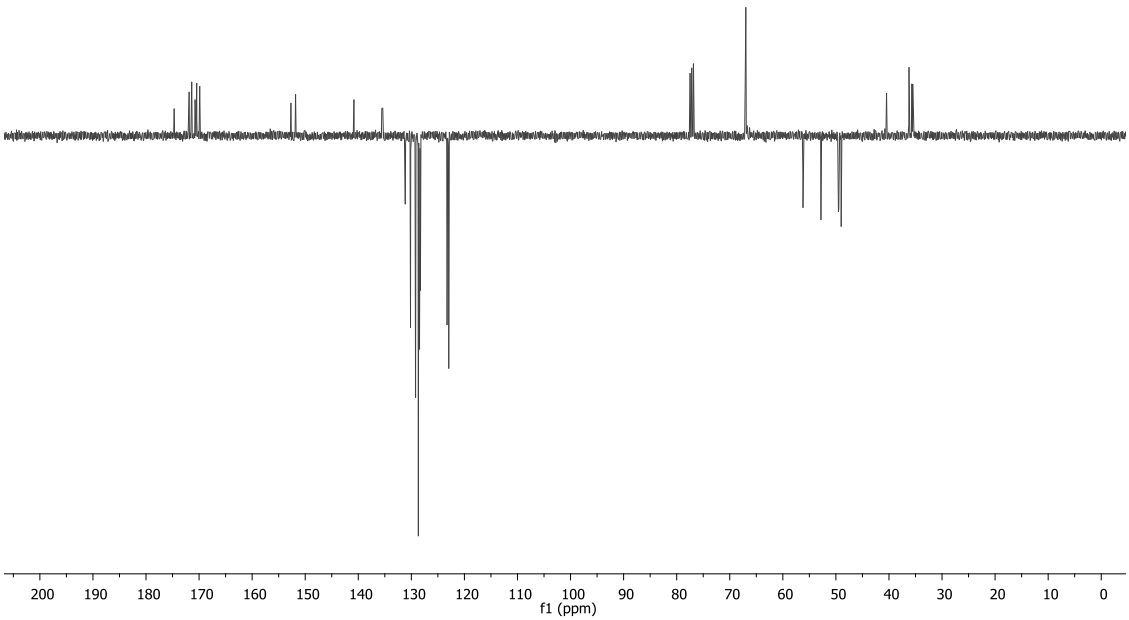


^{1}H-NMR and ^{13}C-NMR spectra of **Boc-azoPhe-[Asp(OBzl)]$_3$-OMe** (**A4**)

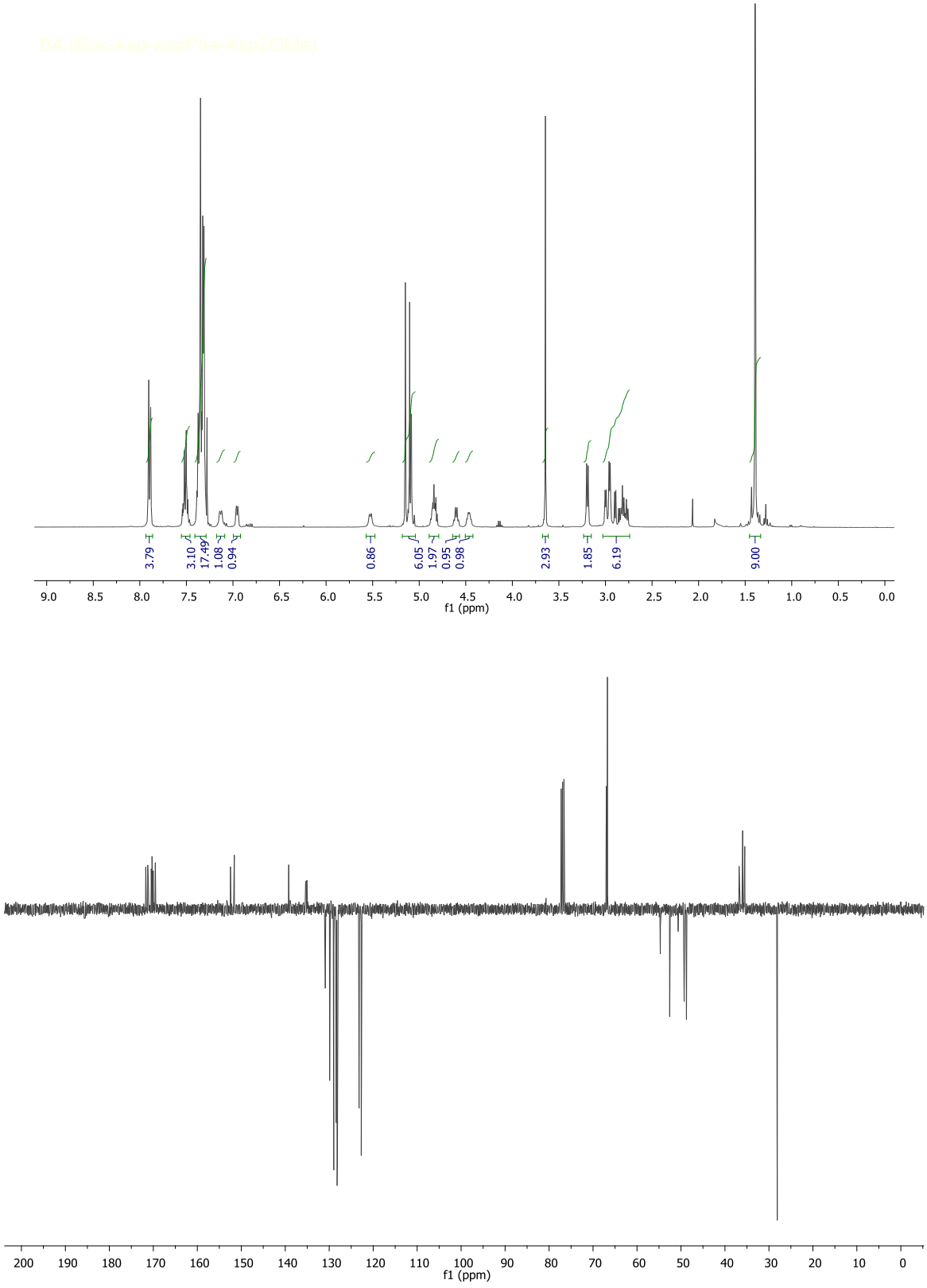


^{1}H-NMR and ^{13}C-NMR spectra of **H-azoPhe-[Asp(OBzl)]$_3$-OMe** (**H-A4**)

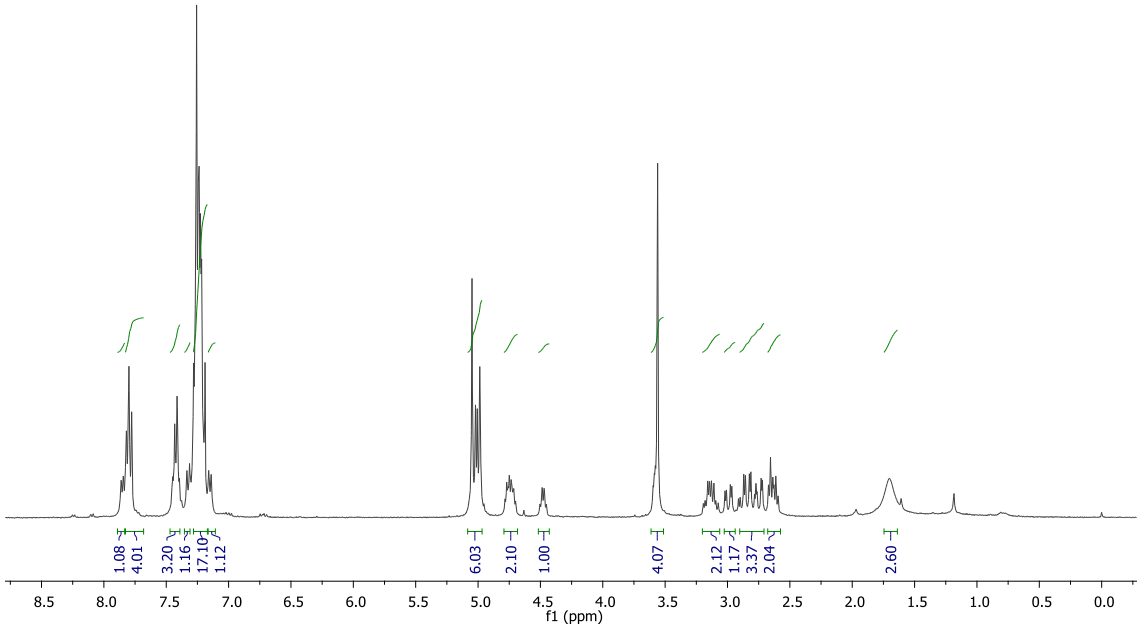


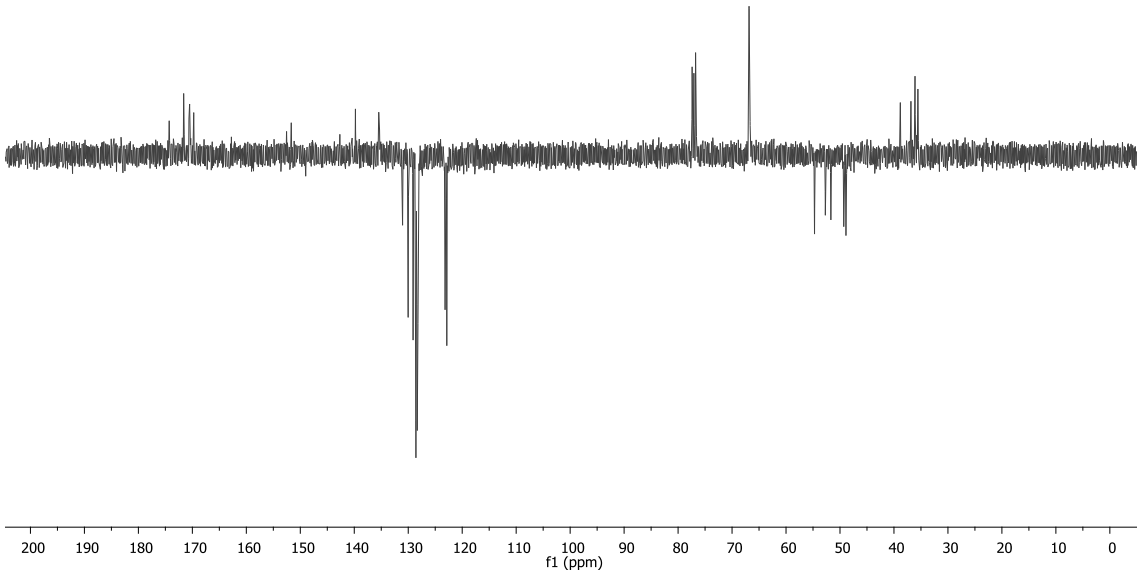


^{1}H-NMR and ^{13}C-NMR spectra of **Boc-Asp(OBzl)-azoPhe-[Asp(OBzl)]$_2$-OMe** (**B4**)

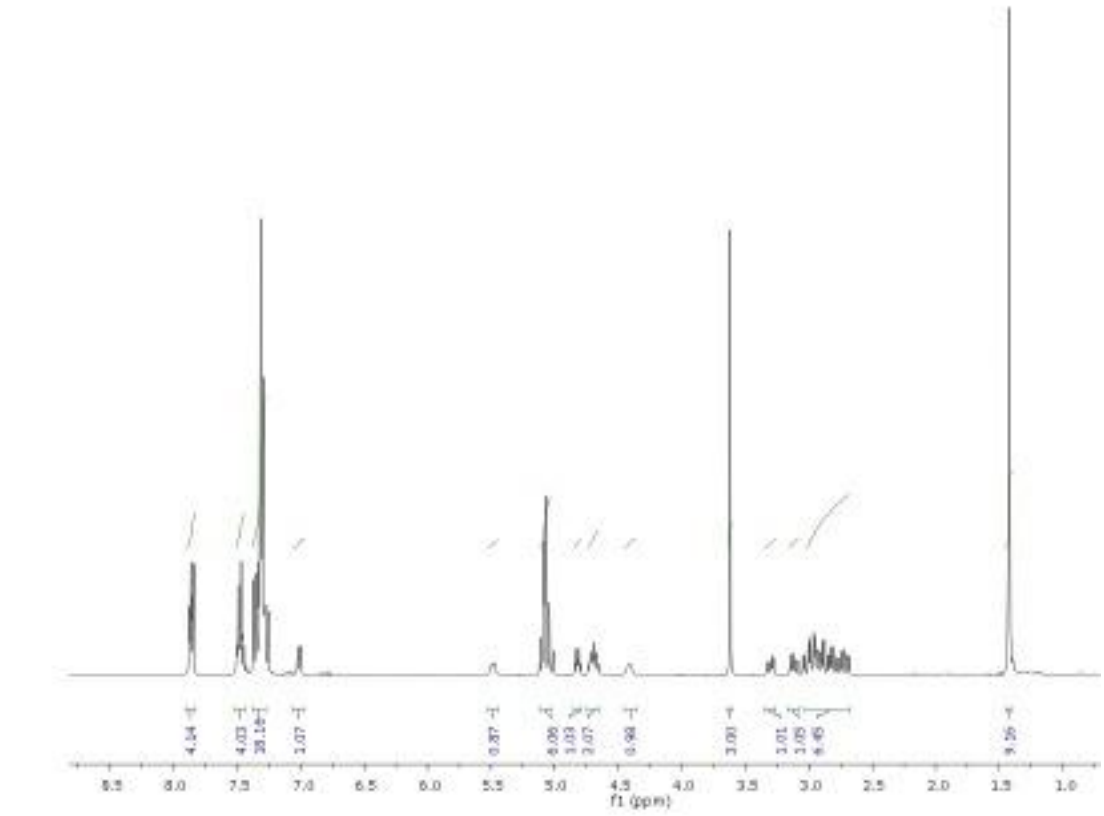


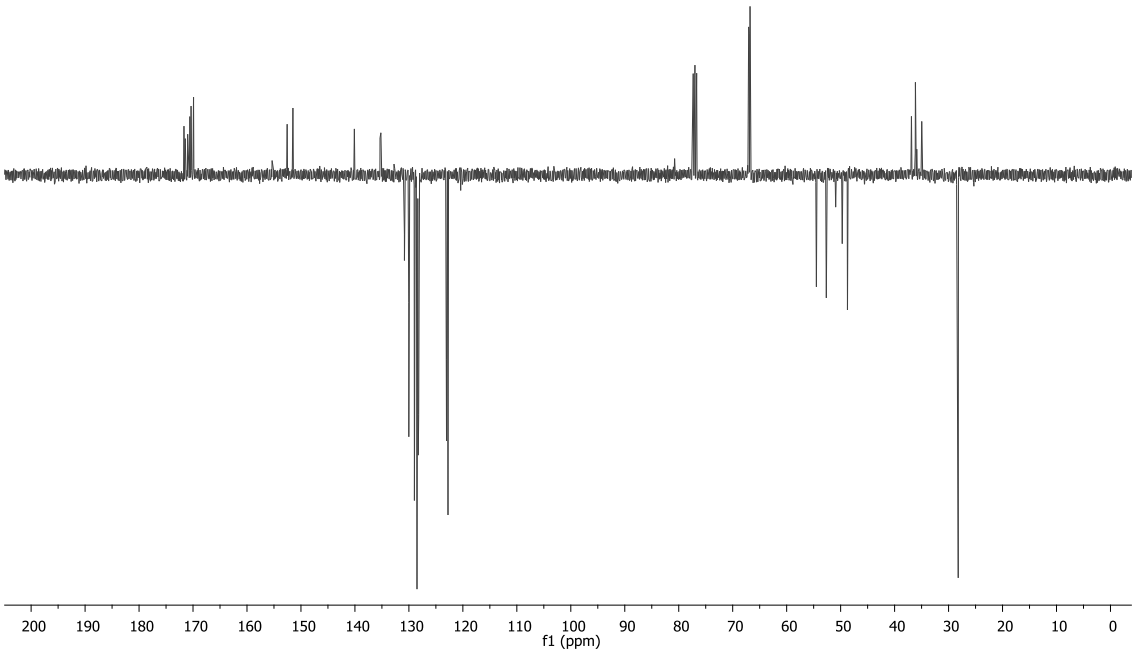
^{1}H-NMR and ^{13}C-NMR spectra of **H-Asp(OBzl)-azoPhe-[Asp(OBzl)]$_2$-OMe (H-B4)**



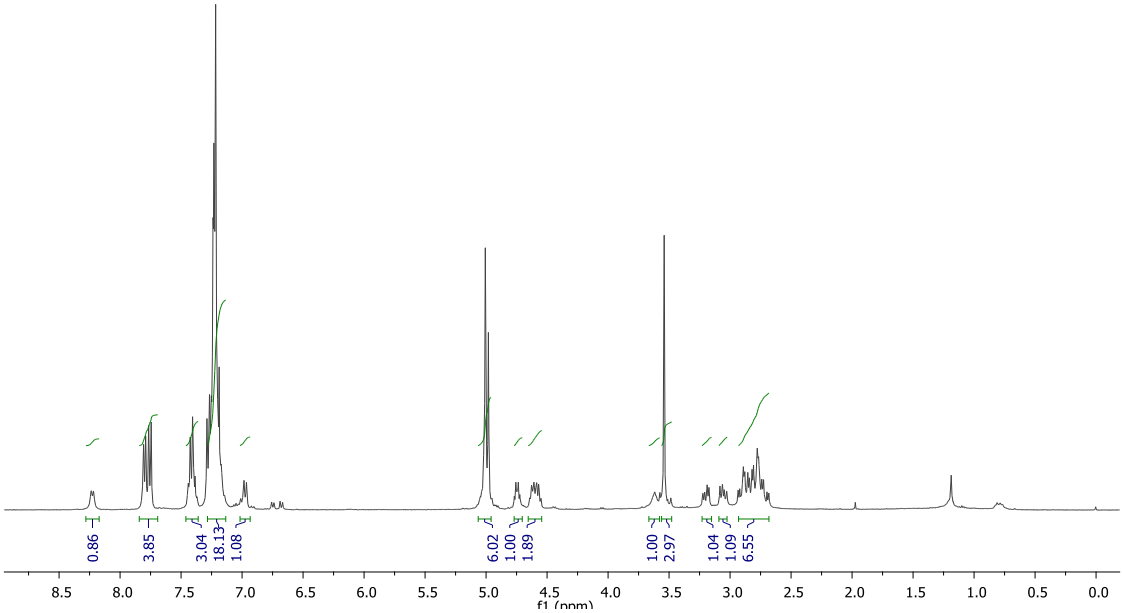


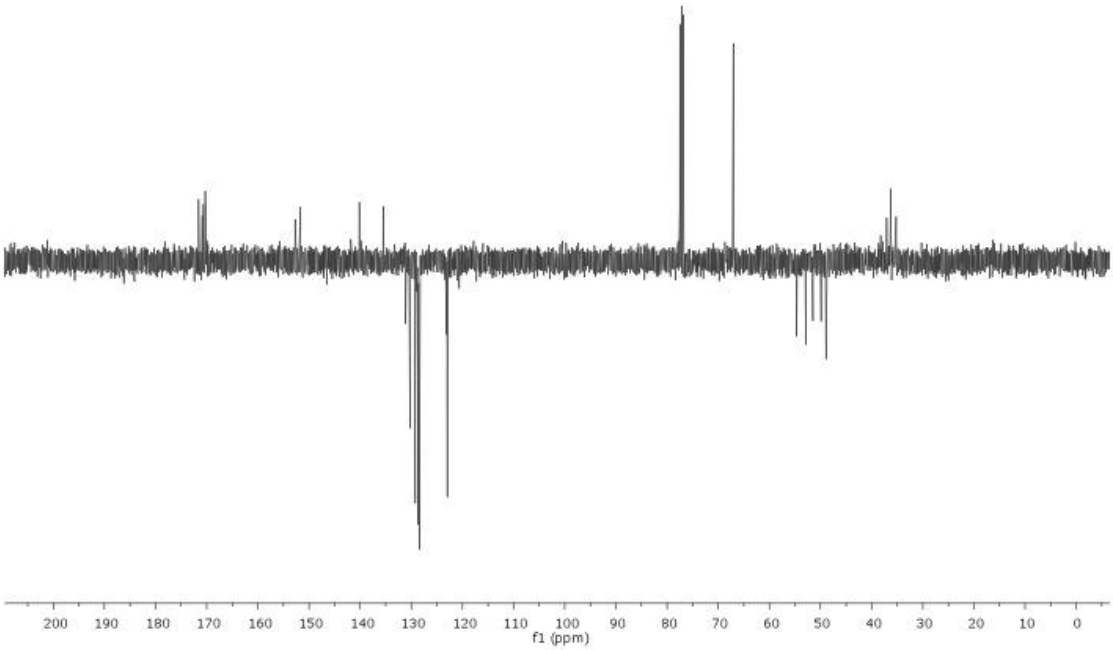
^{1}H-NMR and ^{13}C-NMR spectra of **Boc-[Asp(OBzl)]$_2$-azoPhe-Asp(OBzl)-OMe** (**C4**)



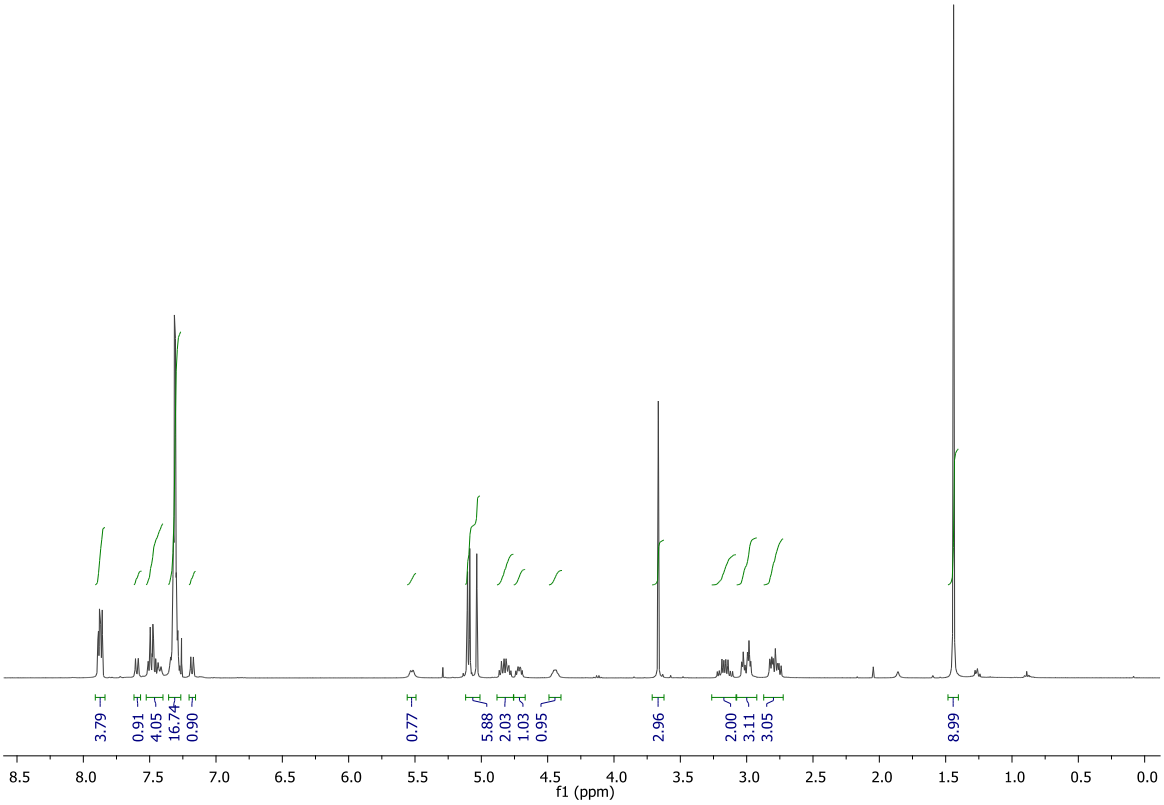


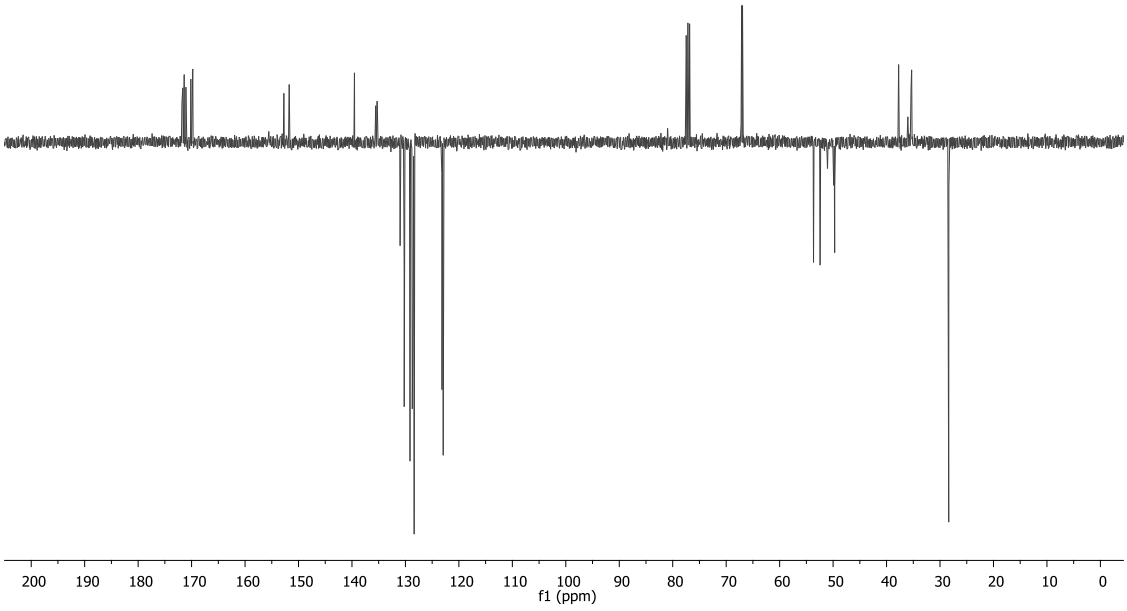
^{1}H-NMR and ^{13}C-NMR spectra of **H-[Asp(OBzl)]$_2$-azoPhe-Asp(OBzl)-OMe** (**H-C4**)



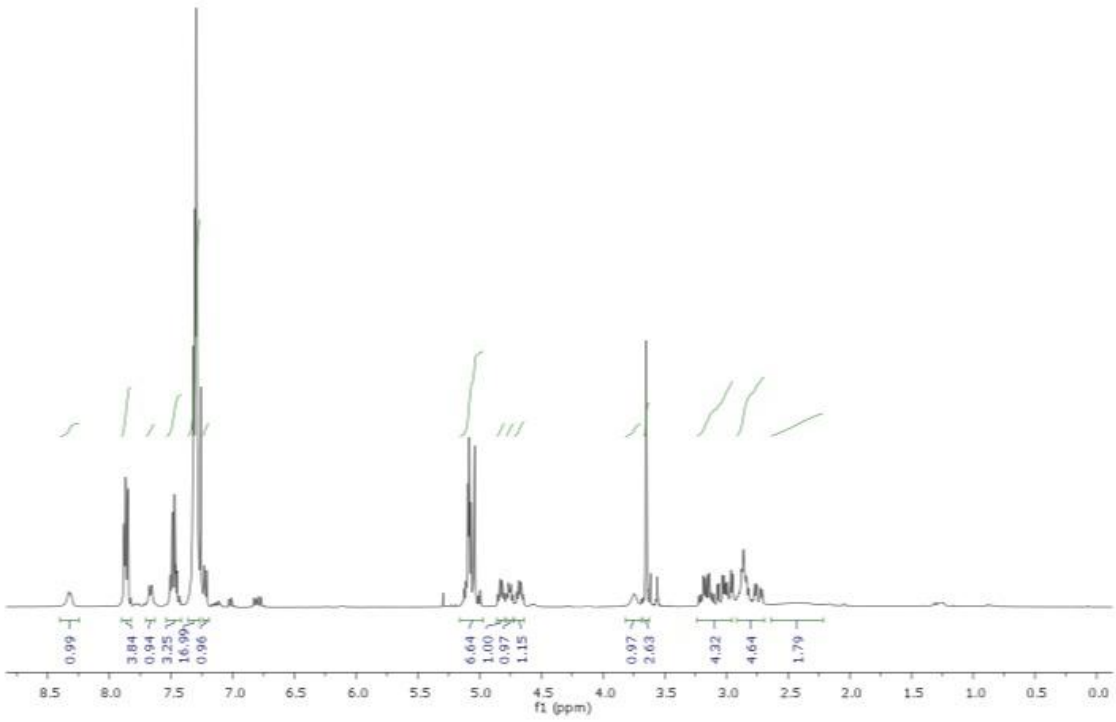


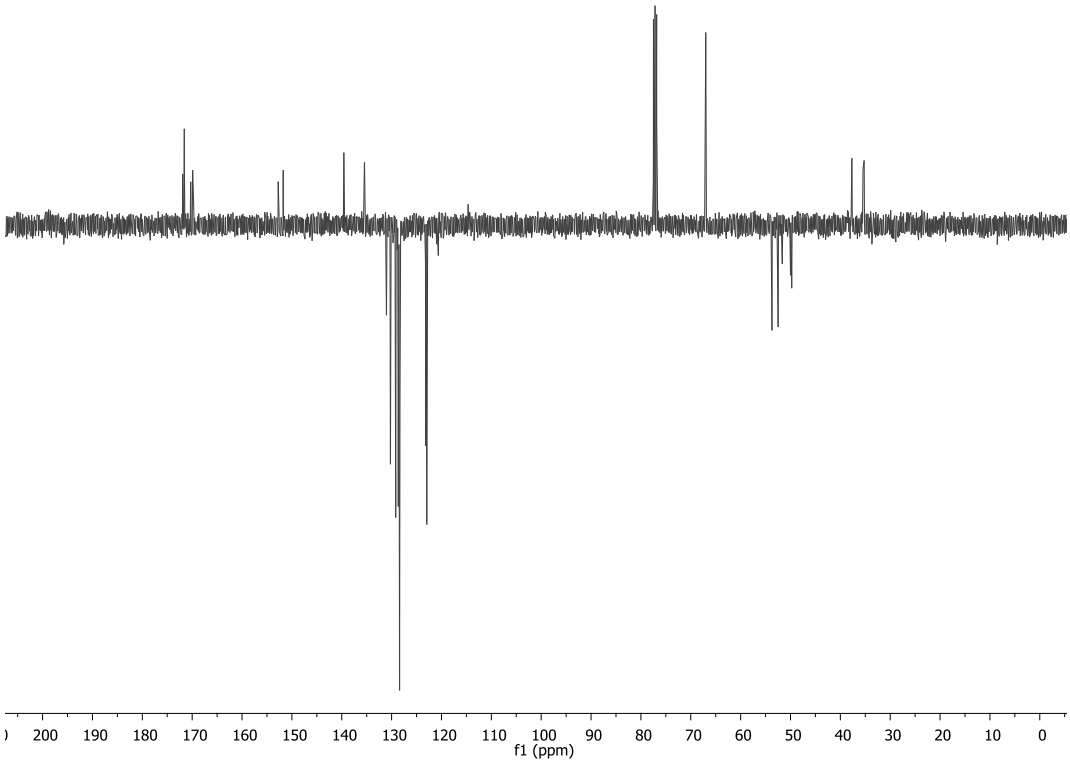
^{1}H-NMR and ^{13}C-NMR spectra of **Boc-[Asp(OBzl)]$_3$-azoPhe-OMe** (**D4**)





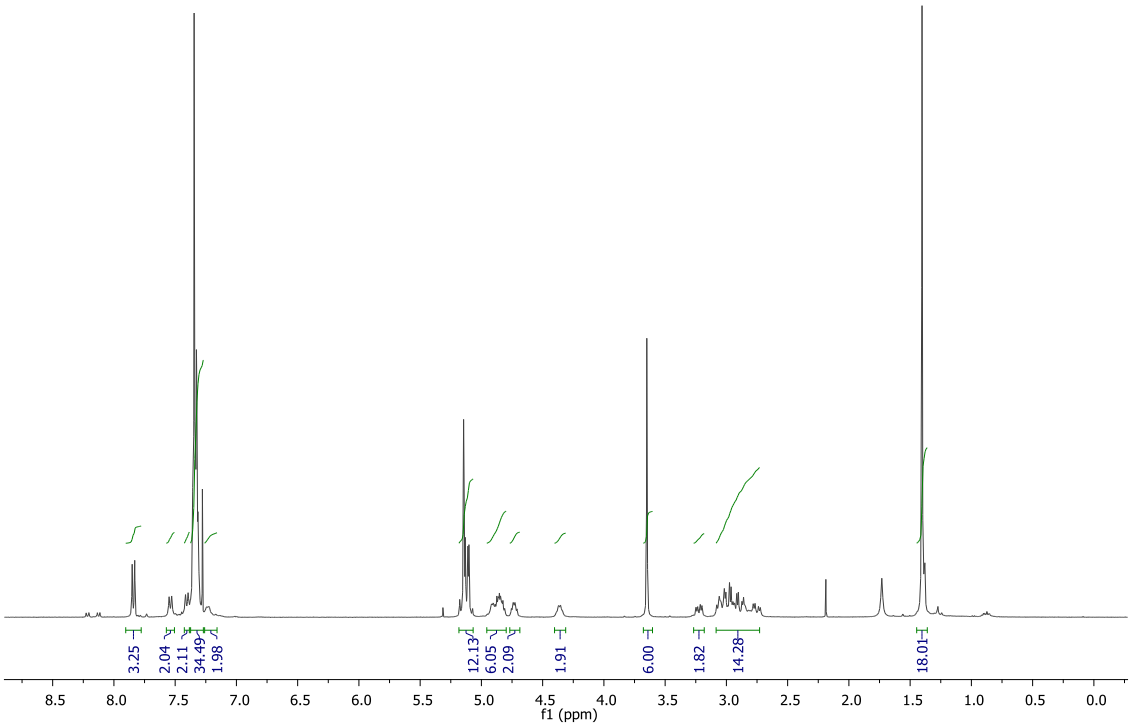
^{1}H-NMR and ^{13}C-NMR spectra of **H-[Asp(OBzl)]$_3$-azoPhe-OMe** (**H-D4**)

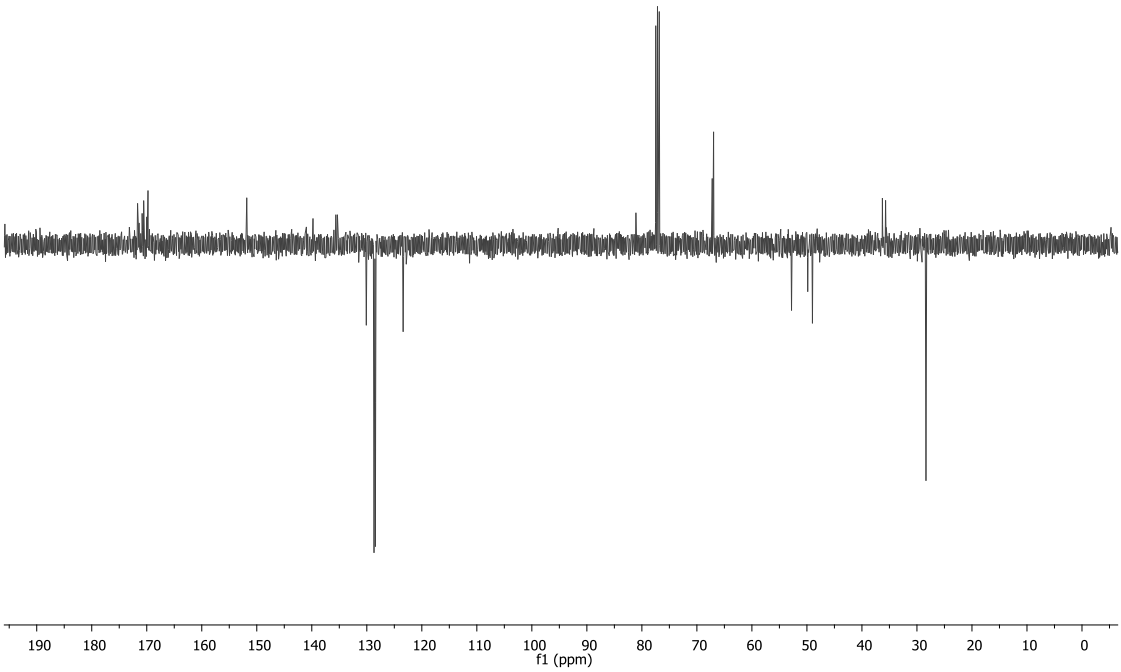




^{1}H-NMR and ^{13}C-NMR spectra of

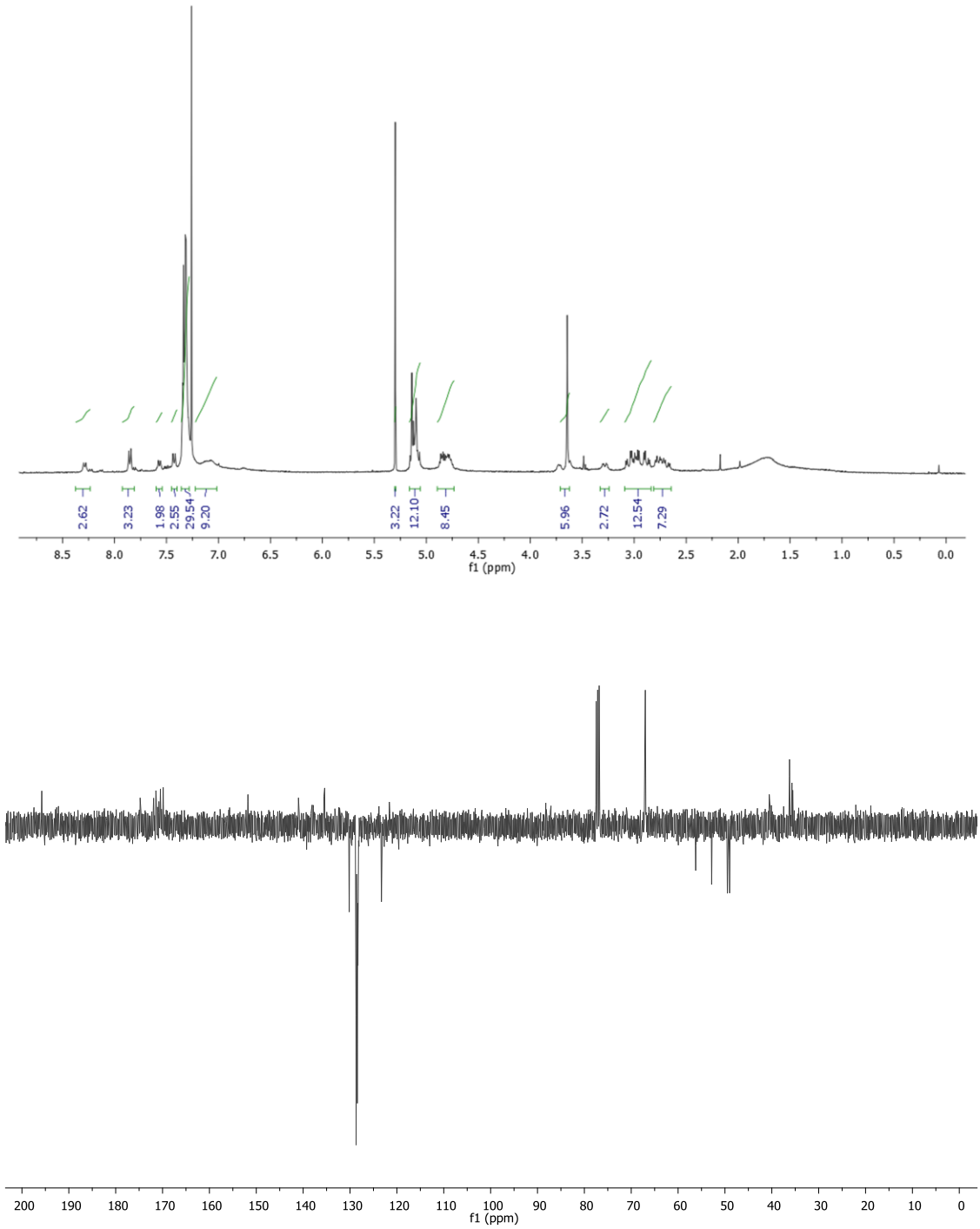
Boc-bisazoPhe-[Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe]$_2$ (bis-A4)





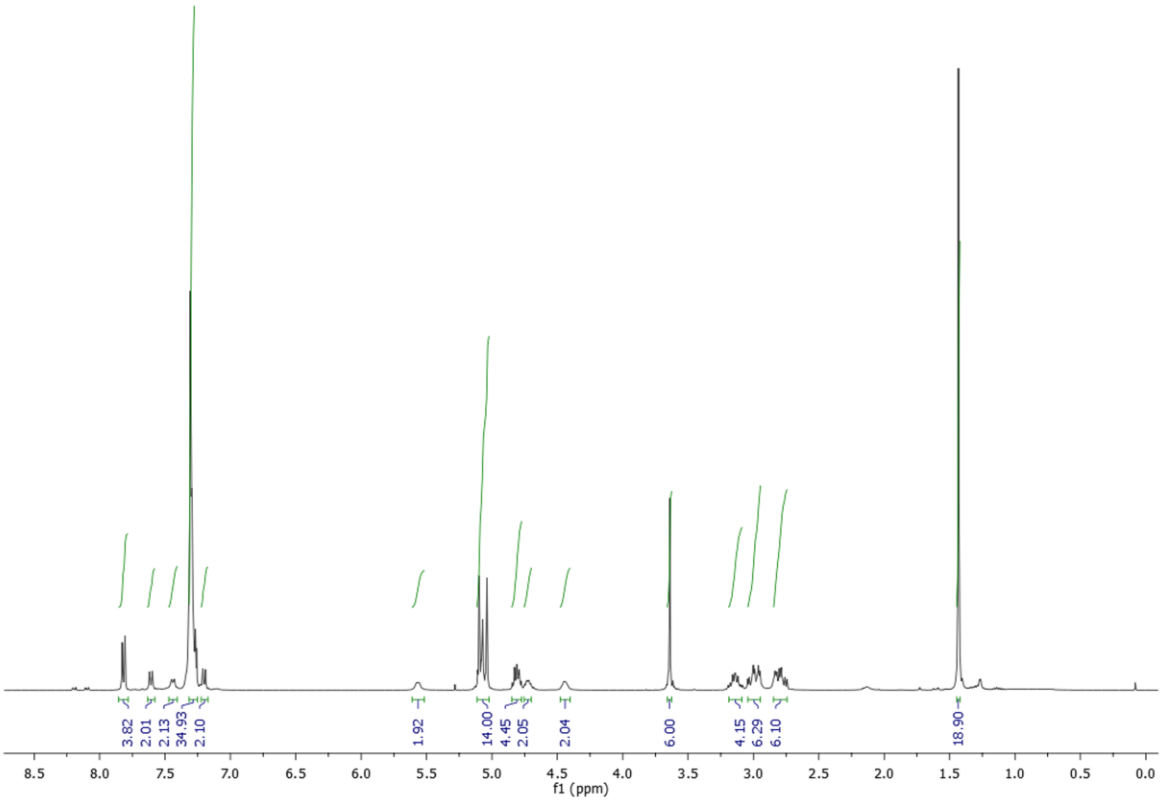
^{1}H-NMR and ^{13}C-NMR spectra of

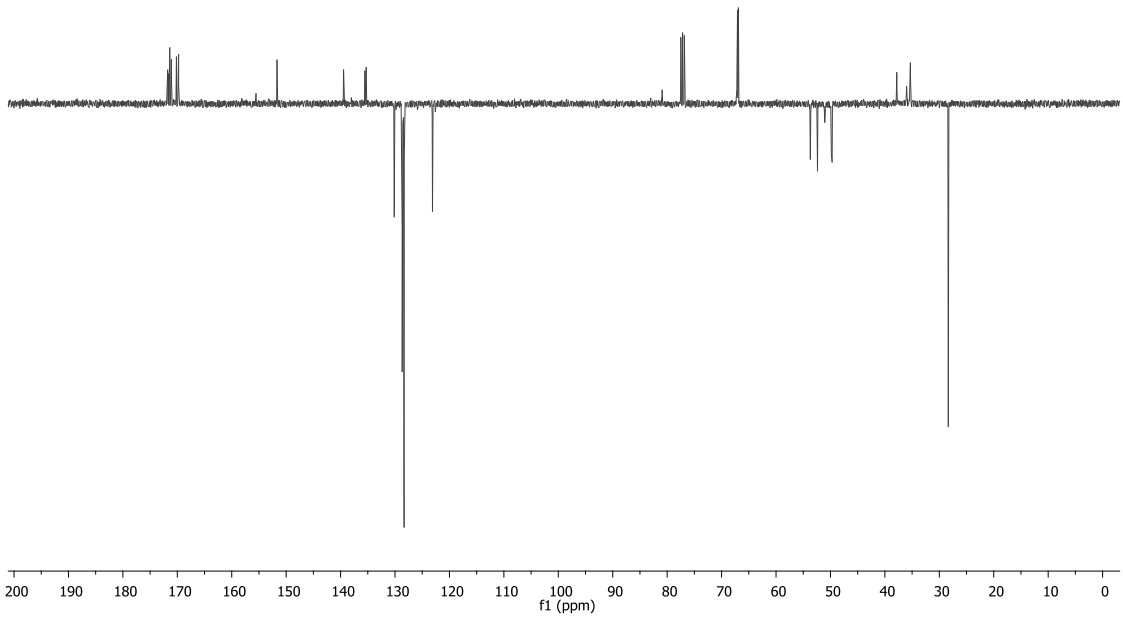
H-bisazoPhe-[Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe]$_2$ (H-bis-A4)



^{1}H-NMR and ^{13}C-NMR spectra of

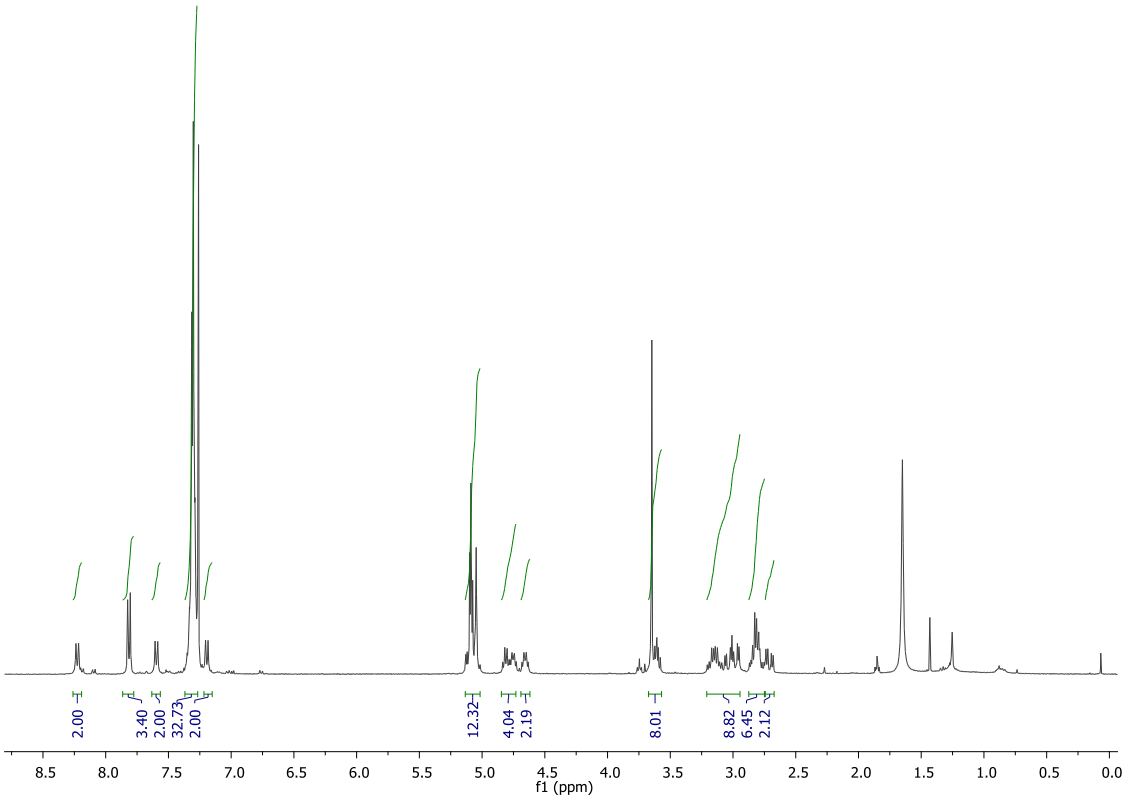
Boc-[Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe]$_2$-bisazoPhe (bis-D4)

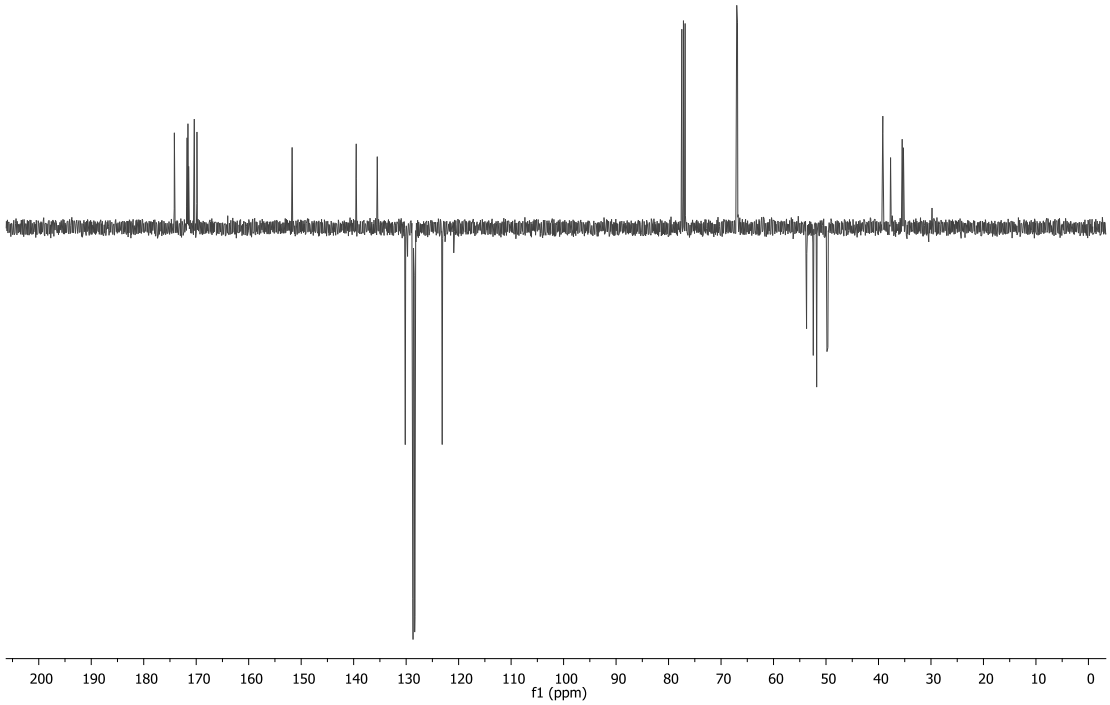




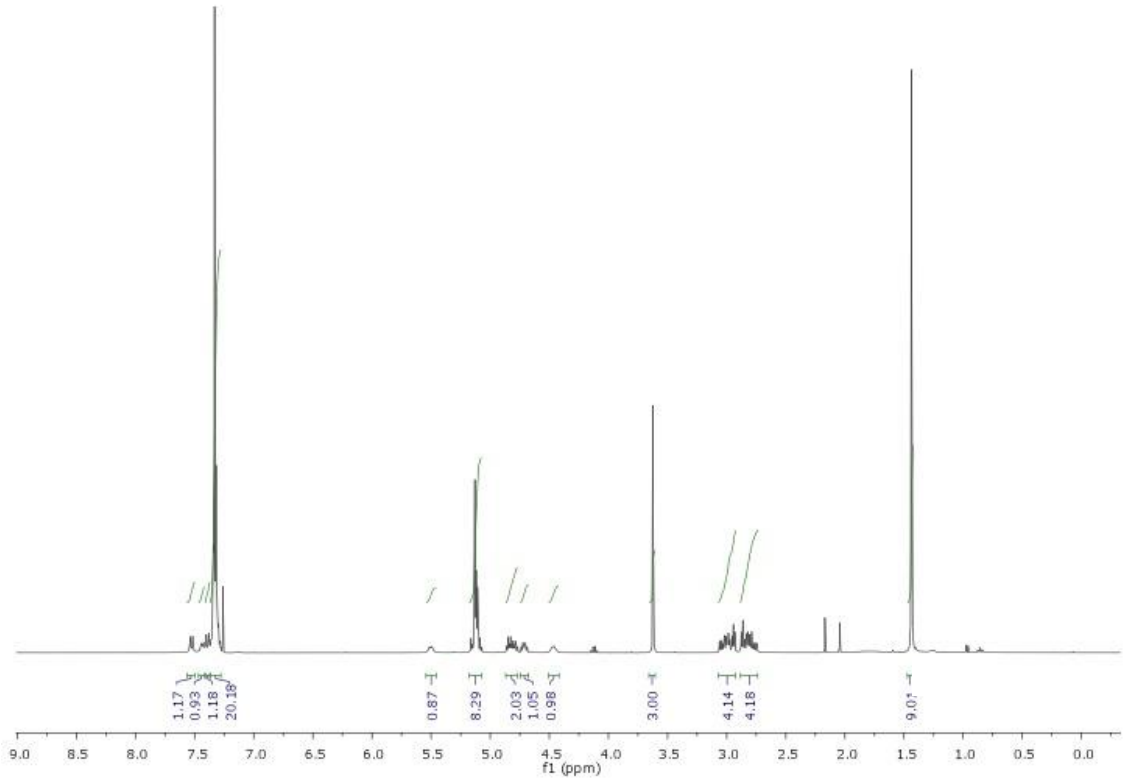
^{1}H-NMR and ^{13}C-NMR spectra of

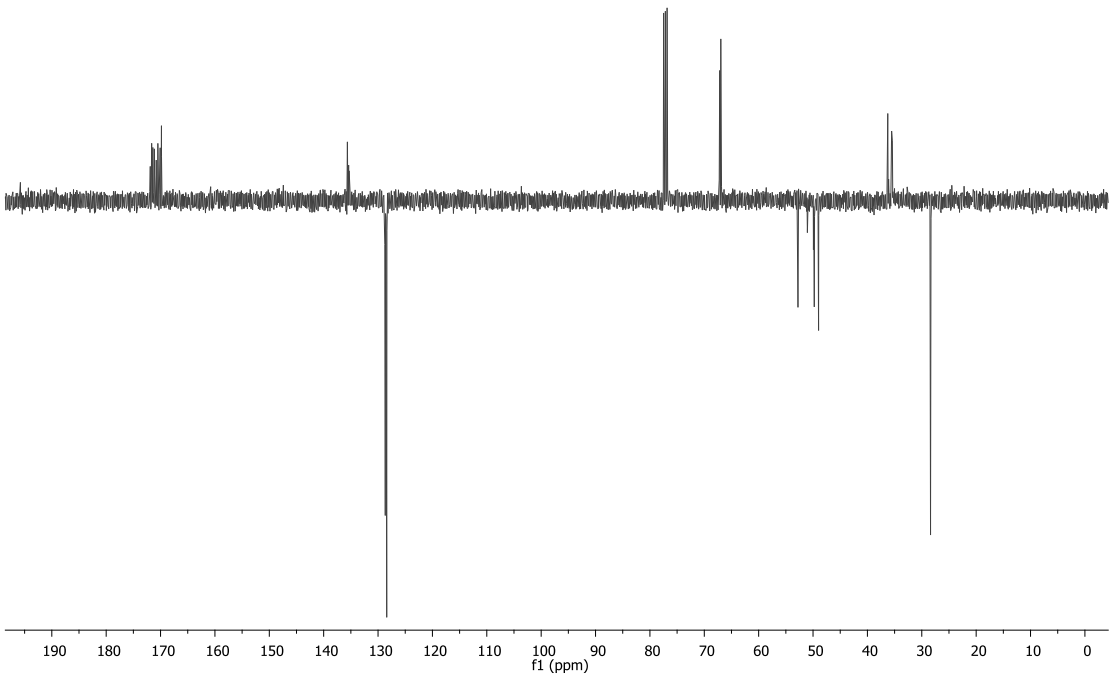
H-[Asp(OBzl)-Asp(OBzl)-Asp(OBzl)-OMe]$_2$-bisazoPhe (H-bis-D4)



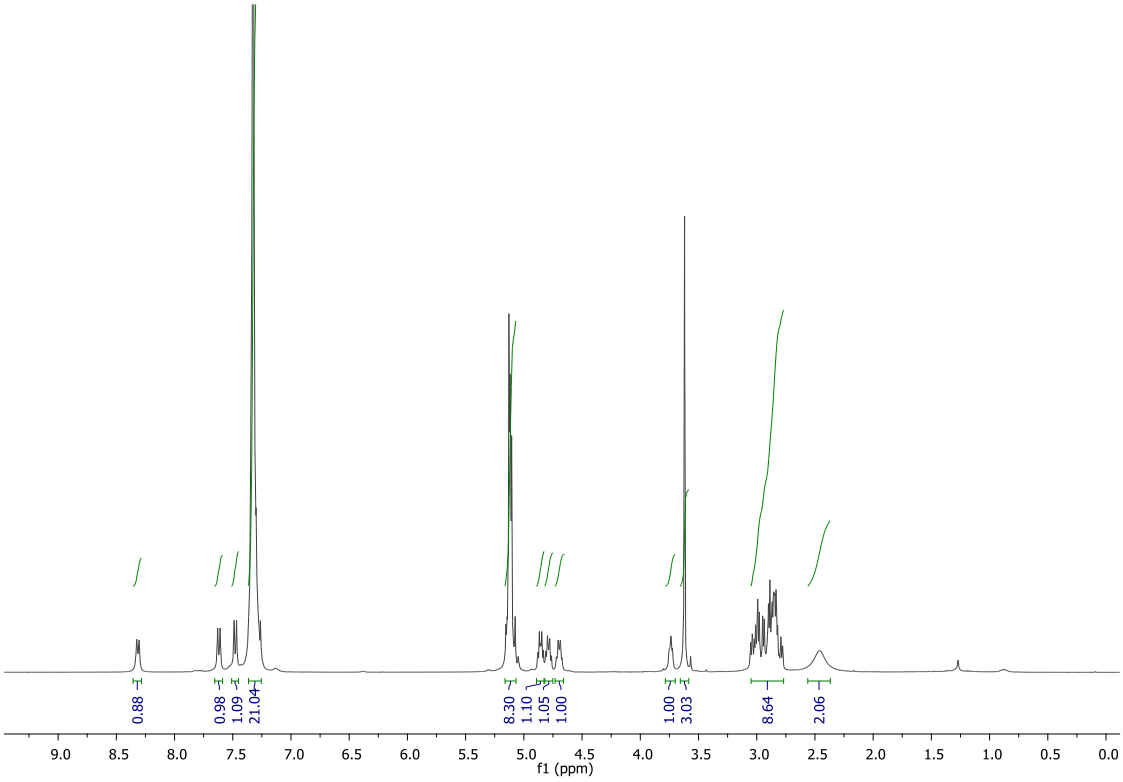


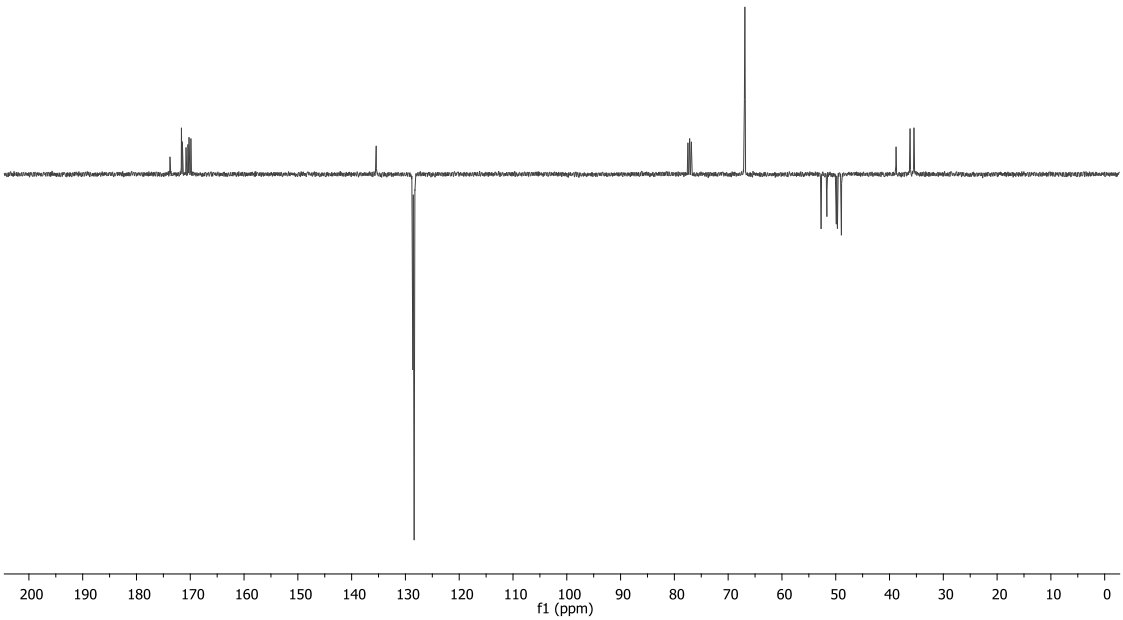
^{1}H-NMR and ^{13}C-NMR spectra of **Boc-[Asp(OBzl)]$_4$-OMe** (**Z4**)



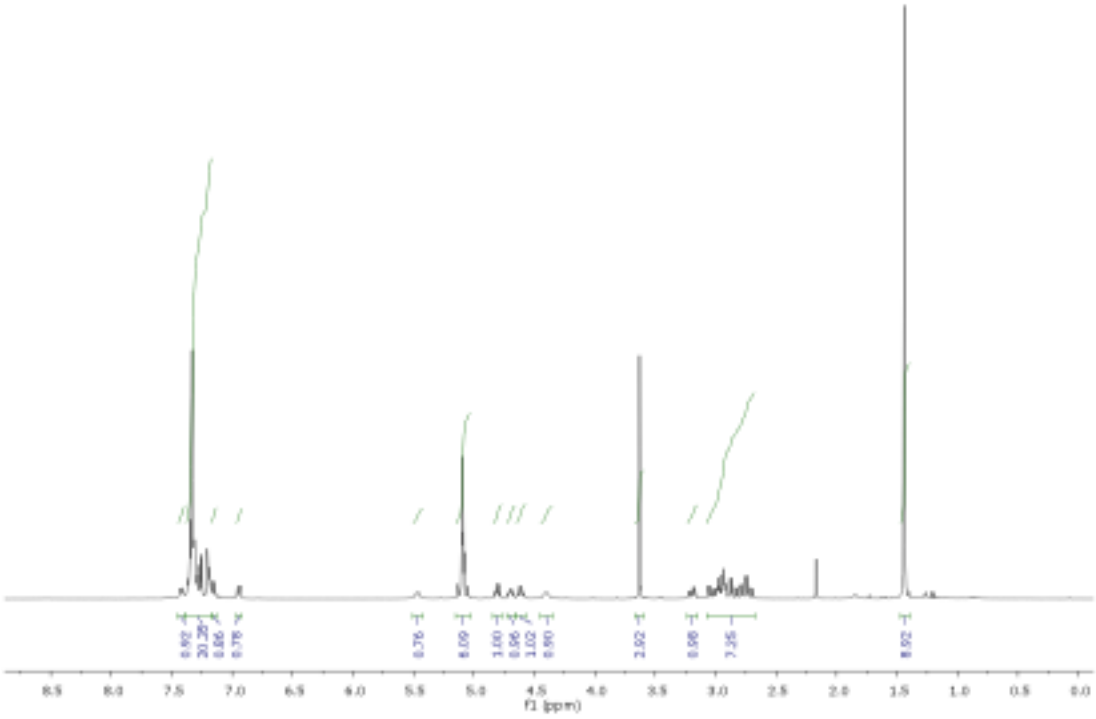


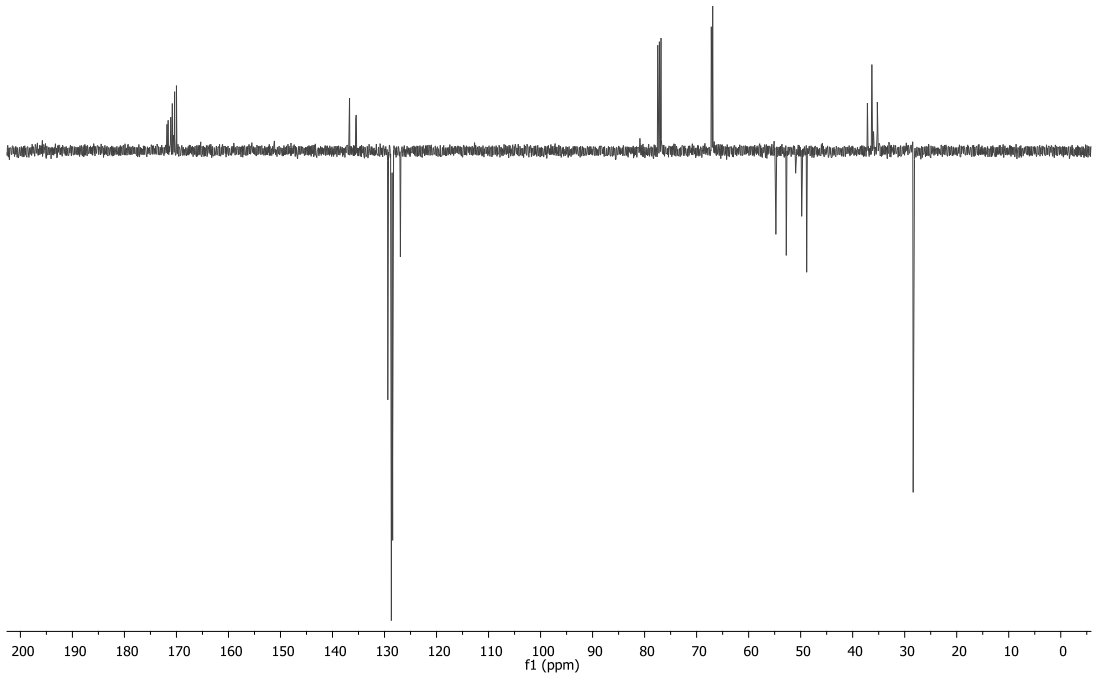
^{1}H-NMR and ^{13}C-NMR spectra of **H-[Asp(OBzl)]$_4$-OMe** (**H-Z4**)



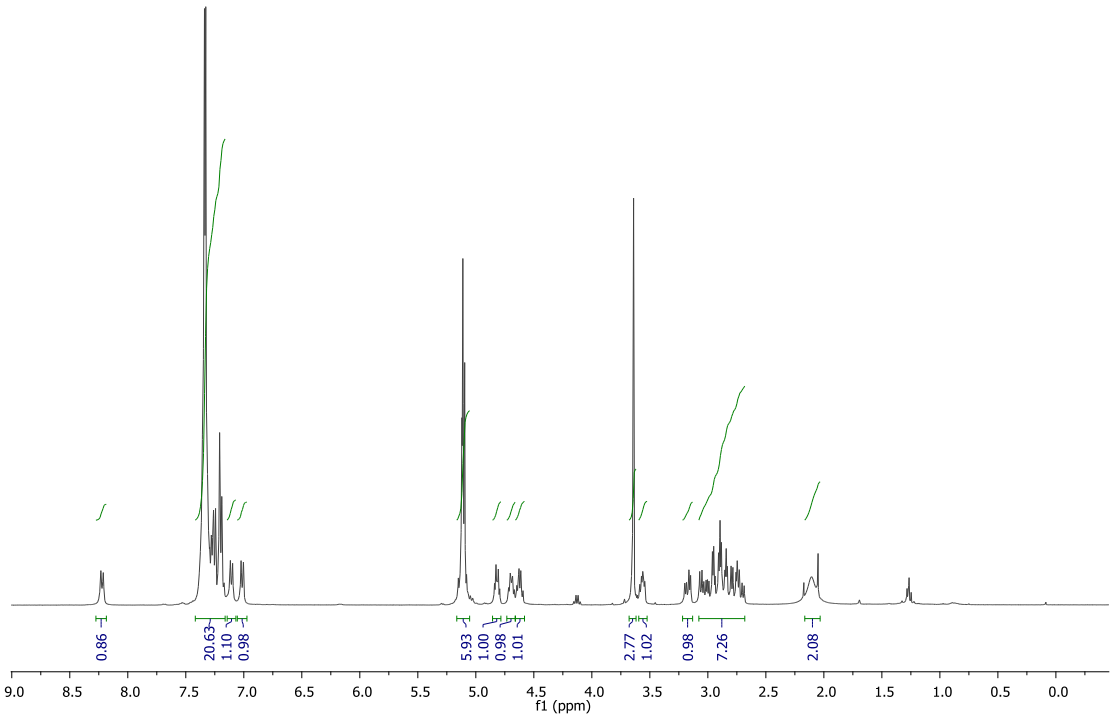


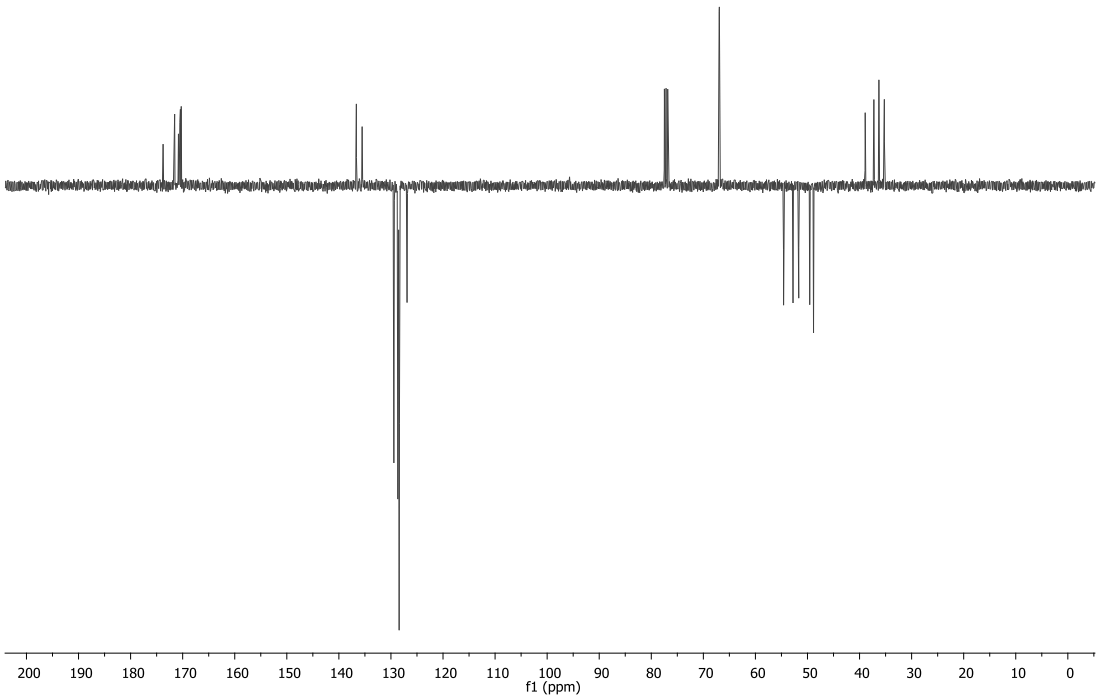
^{1}H-NMR and ^{13}C-NMR spectra of **Boc-[Asp(OBzl)]$_2$-Phe-Asp(OBzl)-OMe** (**F-C4**)





^{1}H-NMR and ^{13}C-NMR spectra of **H-[Asp(OBzl)]$_2$-Phe-Asp(OBzl)-OMe (H-F-C4)**





7. References

1. http://www.asiinstr.com/technical/Dielectric%20Constants.htm ("Dielectric Constants Chart". ChemicalLand21. Retrieved 9 June 2007).
2. http://www.stenutz.eu/chem/solv26.php (IUPAX Goldbook).
3. Lowery, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, Harper Collins Publishers 3rd. ed. 1987.
4. For the preparation of dry samples for SEM observations, see: Jeong, S. W.; Shinkai, S. *Nanotechnology* **1997**, *8*, 179-183.