

SUPPLEMENTARY DATA FOR

Naphthoquinone amino acid derivatives, synthesis and biological activity as proteasome inhibitors

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Analytical data of R'-Xaa-NH-R-NH₂

NBz-Leu-NH-(CH₂)₂-NH₂: white solid, yield 62%; ¹H NMR (400 MHz, CDCl₃) δ 8.32 (d, *J* = 7.4 Hz, 2H), 8.12 (d, *J* = 7.4 Hz, 2H), 6.13 (s, 3H), 5.72 (t, *J* = 7.2 Hz, 1H), 5.45 (s, 1H), 5.28 (s, 1H), 3.96 (t, *J* = 4.6 Hz, 1H), 3.89 (t, *J* = 4.6 Hz, 1H), 3.07 (t, *J* = 4.6 Hz, 2H), 1.78 (t, *J* = 7.3 Hz, 1H), 1.65 (t, *J* = 7.3 Hz, 1H), 1.55 – 1.36 (m, 1H), 1.01 (d, *J* = 6.3 Hz, 6H); MS (M+H⁺) 323.30.

Bz-Leu-NH-(CH₂)₂-NH₂: white solid, yield 74%; ¹H NMR (400 MHz, CDCl₃) δ 7.94–7.73 (m, 2H), 7.55–7.26 (m, 3H), 6.13 (s, 3H), 5.45–5.51 (m, 2H), 5.22 (s, 1H), 3.94 (t, *J* = 4.7 Hz, 1H), 3.89 (t, *J* = 4.7 Hz, 1H), 3.06 (t, *J* = 4.7 Hz, 2H), 1.86 – 1.42 (m, 3H), 1.17 – 0.87 (m, 6H); MS (M+H⁺) 278.18.

1-NaftCO-Leu-NH-(CH₂)₂-NH₂: pale yellow solid, yield 54%; ¹H NMR (400 MHz, CDCl₃) δ 9.04–8.82 (m, 1H), 7.98–7.96 (m, 1H), 7.89–7.74 (m, 2H), 7.66–7.27 (m, 3H), 6.23 (s, 3H), 5.55 (t, *J* = 6.2 Hz, 1H), 5.45 (s, 1H), 5.26 (s, 1H), 3.94 (t, *J* = 4.7 Hz, 1H), 3.90 (t, *J* = 4.7 Hz, 1H), 3.07 (t, *J* = 4.7 Hz, 2H), 1.94–1.67 (m, 2H), 1.63–1.60 (m, 1H), 1.17–0.83 (m, 6H); MS (M+H⁺) 328.27.

NBz-Asn-NH-(CH₂)₂-NH₂: white solid, yield 62 %; ¹H NMR (400 MHz, CDCl₃) δ 8.33 (d, *J* = 7.4 Hz, 2H), 8.20 (d, *J* = 7.4 Hz, 2H), 7.28 (s, 1H), 5.71 (s, 2H), 5.11 (s, 3H), 4.68 (t, *J* = 3.2 Hz, 1H), 3.87 (t, *J* = 4.8 Hz, 1H), 3.79 (t, *J* = 4.8 Hz, 1H), 3.70 (s, 1H), 3.25–3.02 (m, 3H), 2.82–2.79 (m, 1H); MS(M+H⁺) 324.27.

Bz-Asn-NH-(CH₂)₂-NH₂: white solid, yield 59 %; ¹H NMR (400 MHz, CDCl₃) δ 7.96–7.76 (m, 2H), 7.65–7.28 (m, 3H), 5.99–5.90 (m, 4H), 5.59 (s, 1H), 5.38 (s, 2H), 5.33 (s, 1H), 3.99 (t, *J* = 4.4 Hz, 1H), 3.90 (t, *J* = 4.4 Hz, 1H), 3.09–3.05 (m, 3H), 2.85–2.83 (m, 1H); MS(M+H⁺) 279.17.

1-NaftCO-Asn-NH-(CH₂)₂-NH₂: white solid, yield 72 %; ¹H NMR (400 MHz, CDCl₃) δ 8.84–8.78 (m, 1H), 8.07 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.96–7.94 (m, 1H), 7.88–7.74 (m, 1H), 7.62–7.35 (m, 3H), 6.06–5.88 (m, 4H), 5.58 (s, 1H), 5.41 (s, 2H), 5.38 (s, 1H), 3.98–3.97 (m, 2H), 3.27–2.97 (m, 3H), 2.87–2.85 (m, 1H); MS(M+H⁺) 329.21.

NBz-Phe-NH-(CH₂)₂-NH₂: pale yellow solid, yield 46 %; ¹H NMR (400 MHz, CDCl₃) δ 8.35 (d, *J* = 7.4 Hz, 2H), 8.22 (d, *J* = 7.4 Hz, 2H), 7.39–7.21 (m, 4H), 7.22–7.09 (m, 1H), 6.49 (s, 1H), 4.90–4.87 (m, 1H), 4.09–3.94 (m, 4H), 3.91 (t, *J* = 5.4 Hz, 1H), 3.34–3.32 (m, 1H), 3.10–2.87 (m, 3H); MS(M+H⁺) 357.12.

Bz-Phe-NH-(CH₂)₂-NH₂: white solid, yield 67 %; ¹H NMR (400 MHz, CDCl₃) δ 7.97–7.79 (m, 2H), 7.46–7.42 (m, 3H), 7.34–7.10 (m, 6H), 5.21 (bs, 3H), 4.72–4.70 (m, 1H), 4.16 (s, 1H), 3.88–3.85 (m, 2H), 3.26–3.24 (m, 1H), 3.19–3.04 (m, 2H), 2.89 (m, 1H); MS (M+H⁺) 312.23.

1-NaftCO-Phe-NH-(CH₂)₂-NH₂: white solid, yield 57 %; ¹H NMR (400 MHz, CDCl₃) δ 8.89–8.85 (m, 1H), 8.03–8.01 (m, 1H), 7.92–7.90 (m, 1H), 7.81–7.79 (m, 1H), 7.69–7.65 (m, 3H), 7.24–7.22 (m, 2H), 7.19–6.95 (m, 3H), 5.00–4.98 (m, 1H), 4.61 (s, 3H), 3.98–3.97 (m, 1H), 3.91–3.88 (m, 2H), 3.01–2.99 (m, 2H), 2.47–2.46 (m, 1H); MS (M+H⁺) 362.12.

NBz-Ser-NH-(CH₂)₂-NH₂: white solid, yield 84 %; ¹H NMR (400 MHz, CDCl₃) δ 8.32 (d, *J* = 7.4 Hz, 2H), 8.15 (d, *J* = 7.4 Hz, 2H), 7.05 (s, 1H), 6.25 (s, 3H), 5.09 (s, 1H), 4.44–4.42 (m, 1H), 4.29–4.27 (m, 1H), 3.94–3.92 (m, 2H), 3.86–3.84 (m, 1H), 3.02–3.00 (m, 2H); MS (M+H⁺) 297.12.

Bz-Ser-NH-(CH₂)₂-NH₂: white solid, yield 66 %; ¹H NMR (400 MHz, CDCl₃)δ 8.01–7.86 (m, 2H), 7.56–7.39 (m, 3H), 6.08 (s, 3H), 5.39–5.20 (m, 2H), 5.15 (s, 1H), 4.16–4.13 (m, 1H), 4.06–4.02 (m, 1H), 4.00–3.85 (m, 2H), 3.06–3.02 (m, 2H); MS (M+H⁺) 252.17.

1-NaftCO-Ser-NH-(CH₂)₂-NH₂: white solid, yield 49 %; ¹H NMR (400 MHz, CDCl₃)δ 9.13–9.10 (m, 1H), 7.96–7.94 (m, 1H), 7.87–7.74 (m, 2H), 7.69–7.64 (m, 1H), 7.62–2.26 (m, 2H), 5.93 (s, 3H), 5.38–5.36 (m, 2H), 4.70–4.67 (m, 1H), 4.27–4.24 (m, 1H), 4.08–4.05 (m, 1H), 3.99–3.79 (m, 2H), 2.98–2.96 (m, 2H); MS (M+H⁺) 302.18.

NBz-Leu-NH-(CH₂)₄-NH₂: white solid, yield 81 %; ¹H NMR (400 MHz, CDCl₃)δ 8.30 (d, *J* = 7.4 Hz, 2H), 7.99 (d, *J* = 7.6 Hz, 2H), 5.61 (s, 1H), 4.83 (s, 1H), 4.72–4.54 (m, 4H), 3.31–3.16 (m, 2H), 2.78–2.71 (m, 2H), 2.38–2.10 (m, 1H), 2.13–1.94 (m, 2H), 1.74–1.73 (m, 1H), 1.68–1.50 (m, 3H), 1.01 (d, *J* = 6.3 Hz, 6H); MS (M+H⁺) 351.31.

Bz-Leu-NH-(CH₂)₄-NH₂: white solid, yield 61 %; ¹H NMR (400 MHz, CDCl₃)δ 8.01–7.81 (m, 2H), 7.58–7.36 (m, 3H), 7.31 (s, 1H), 5.81 (s, 1H), 5.07 (s, 3H), 4.42–4.40 (m, 1H), 3.23–3.19 (m, 2H), 2.79–2.64 (m, 2H), 2.03–1.95 (m, 2H), 1.94–1.88 (m, 1H), 1.83–1.57 (m, 4H), 1.2–1.00 (m, 6H); MS (M+H⁺) 306.42.

1-NaftCO-Leu-NH-(CH₂)₄-NH₂: white solid, yield 89 %; ¹H NMR (400 MHz, CDCl₃)δ 8.92–8.72 (m, 1H), 8.02–7.98 (m, 1H), 7.97–7.81 (m, 2H), 7.70–7.45 (m, 3H), 4.83 (s, 1H), 4.70–4.52 (m, 4H), 3.28–3.19 (m, 2H), 2.77–2.67 (m, 2H), 2.00–1.75 (m, 4H), 1.65–1.48 (m, 3H), 1.12–0.95 (m, 6H); MS (M+H⁺) 356.32.

NBz-Asn-NH-(CH₂)₄-NH₂: pale yellow solid, yield 78 %; ¹H NMR (400 MHz, CDCl₃)δ 8.32 (d, *J* = 7.4 Hz, 2H), 8.10 (d, *J* = 7.4 Hz, 2H), 5.77–5.76 (m, 5H), 5.66 (s, 1H), 5.25–5.26 (m, 1H), 5.05 (s, 1H), 3.41–3.05 (m, 3H), 2.87–2.65 (m, 3H), 1.97–1.82 (m, 2H), 1.72–1.66 (m, 2H); MS (M+H⁺) 352.19.

Bz-Asn-NH-(CH₂)₄-NH₂: white solid, yield 69 %; ¹H NMR (400 MHz, CDCl₃)δ 7.87–7.70 (m, 2H), 7.50–7.32 (m, 3H), 5.85 (s, 2H), 5.66 (s, 1H), 5.55 (s, 3H), 5.41–5.38 (m, 1H), 4.98 (s, 1H), 3.41–3.06 (m, 3H), 2.79–2.54 (m, 3H), 2.01–1.95 (m, 2H), 1.77–1.72 (m, 2H); MS (M+H⁺) 307.12.

1-NaftCO-Asn-NH-(CH₂)₄-NH₂: white solid, yield 84 %; ¹H NMR (400 MHz, CDCl₃)δ 8.76–8.73 (m, 1H), 8.06–7.98 (m, 1H), 7.88–7.85 (m, 2H), 7.61–7.35 (m, 3H), 6.45 (s, 3H), 5.45 (s, 1H), 4.83 (s, 3H), 4.67–4.63 (m, 1H), 3.39–3.17 (m, 3H), 2.89–2.69 (m, 3H), 2.03–1.88 (m, 2H), 1.62–1.55 (m, 2H); MS (M+H⁺) 357.24.

NBz-Phe-NH-(CH₂)₄-NH₂: pale yellow solid, yield 76 %; ¹H NMR (400 MHz, CDCl₃)δ 8.33 (d, *J* = 7.4 Hz, 2H), 8.12 (d, *J* = 7.4 Hz, 2H), 7.34–7.03 (m, 5H), 5.72 (s, 1H), 5.43 (s, 3H), 4.80–4.72 (m, 1H), 3.41–3.25 (m, 3H), 2.97–2.95 (m, 1H), 2.79–2.74 (m, 2H), 1.94–1.85 (m, 2H), 1.64–1.47 (m, 2H); MS (M+H⁺) 385.27.

Bz-Phe-NH-(CH₂)₄-NH₂: white solid, yield 83 %; ¹H NMR (400 MHz, CDCl₃)δ 7.98–7.81 (m, 2H), 7.56–7.40 (m, 3H), 7.35 (s, 1H), 7.32–7.11 (m, 5H), 6.30–6.14 (s, 3H), 4.71 (s, 1H), 4.38 (s, 1H), 3.31–3.20 (m, 2H), 3.18–3.16 (m, 1H), 2.92–2.89 (m, 1H), 2.83–2.65 (m, 2H), 2.10–1.91 (m, 2H), 1.66–1.45 (m, 2H); MS (M+H⁺) 340.42.

1-NaftCO-Phe-NH-(CH₂)₄-NH₂: white solid, yield 71 %; ¹H NMR (400 MHz, CDCl₃)δ 8.83–8.68 (m, 1H), 8.01–7.98 (m, 1H), 7.95–7.82 (m, 1H), 7.84–7.71 (m, 1H), 7.67–7.41 (m, 3H), 7.28–7.11 (m, 4H), 7.08–6.89 (m, 1H), 5.46 (s, 1H), 4.82–4.67 (m, 1H), 4.01 (s, 3H), 3.41–3.35 (m, 1H), 3.23–3.19 (m, 2H), 2.96–2.95 (m, 1H), 2.80–2.74 (m, 2H), 1.94–1.91 (m, 2H), 1.76–1.59 (m, 2H); MS (M+H⁺) 390.28.

NBz-Ser-NH-(CH₂)₄-NH₂: white solid, yield 54 %; ¹H NMR (400 MHz, CDCl₃)δ 8.31 (d, *J* = 7.4 Hz, 2H), 8.14 (d, *J* = 7.4 Hz, 2H), 5.82 (s, 3H), 5.32 (s, 1H), 4.74 (s, 1H), 4.62–4.58 (m, 1H), 4.23–4.17 (m, 1H), 3.92–3.89 (m, 1H), 3.50–3.21 (m, 2H), 2.80–2.76 (m, 2H), 2.05–1.77 (m, 2H), 1.64–1.58 (m, 2H); MS (M+H⁺) 325.33.

Bz-Ser-NH-(CH₂)₄-NH₂: white solid, yield 63 %; ¹H NMR (400 MHz, CDCl₃)δ 7.90–7.75 (m, 2H), 7.56–7.24 (m, 3H), 5.30–5.25 (m, 2H), 5.11 (s, 3H), 4.84–4.82 (m, 1H), 4.19–4.16 (m, 1H), 3.91–3.87 (m, 1H), 3.40–3.33 (m, 2H), 2.77–2.73 (m, 2H), 1.97–1.94 (m, 2H), 1.71–1.65 (m, 2H); MS (M+H⁺) 280.34.

1-NaftCO-Ser-NH-(CH₂)₄-NH₂: white solid, yield 59 %; ¹H NMR (400 MHz, CDCl₃)δ 8.80–8.72 (m, 1H), 8.03–7.97 (m, 1H), 7.84–7.82 (m, 1H), 7.77–7.74 (m, 1H), 7.52–7.44 (m, 3H), 5.34 (s, 1H), 5.21 (s, 1H), 5.12 (s, 3H), 4.88–4.82 (m, 1H), 4.19–4.17 (m, 1H), 3.92–3.89 (m, 1H), 3.41–3.33 (m, 2H), 2.78–2.74 (m, 2H), 1.98–1.87 (m, 2H), 1.71–1.65 (m, 2H); MS (M+H⁺) 330.14.

NBz-Leu-NH-cHx-NH₂: pale yellow solid, yield 89 %; ¹H NMR (400 MHz, CDCl₃)δ 8.32 (d, *J* = 7.4 Hz, 2H), 8.21 (d, *J* = 7.4 Hz, 2H), 6.69 (s, 1H), 5.87 (s, 1H), 4.69 (s, 3H), 4.47–4.43 (m, 1H), 3.67–3.62 (m, 1H), 3.56–3.41 (m, 1H), 2.46–2.26 (m, 2H), 2.17–1.97 (m, 2H), 1.92–1.75 (m, 2H), 1.72–1.40 (m, 5H), 1.07–0.93 (m, 6H); MS (M+H⁺) 377.18.

Bz-Leu-NH-cHx-NH₂: white solid, yield 75 %; ¹H NMR (400 MHz, CDCl₃)δ 7.88–7.73 (m, 2H), 7.56–7.29 (m, 3H), 6.67 (s, 1H), 5.21 (s, 1H), 5.06 (s, 3H), 4.42–4.39 (m, 1H), 3.31–3.28 (m, 1H), 3.08–3.02 (m, 1H), 2.24–2.16 (m, 2H), 2.12–2.04 (m, 2H), 1.87–1.80 (m, 1H), 1.72–1.50 (m, 4H), 1.41–1.28 (m, 2H), 1.03–0.99 (m, 6H); MS (M+H⁺) 332.15.

1-NaftCO-Leu-NH-cHx-NH₂: white solid, yield 74 %; ¹H NMR (400 MHz, CDCl₃)δ 8.78–8.69 (m, 1H), 7.99–7.91 (m, 1H), 7.89–7.86 (m, 1H), 7.72–7.65 (m, 1H), 7.62–7.44 (m, 3H), 5.84 (s, 1H), 5.17 (s, 3H), 5.03 (t, *J* = 7.0 Hz, 1H), 4.92 (s, 1H), 3.97–3.93 (m, 1H), 3.52–3.45 (m, 1H), 2.42–2.36 (m, 2H), 2.24–2.14 (m, 2H), 2.08–2.01 (m, 2H), 1.82–1.67 (m, 1H), 1.65–1.47 (m, 4H), 1.07–1.01 (m, 6H); MS (M+H⁺) 382.28.

NBz-Asn-NH-cHx-NH₂: white solid, yield 57 %; ¹H NMR (400 MHz, CDCl₃)δ 8.38 (s, 1H), 8.33 (d, *J* = 7.4 Hz, 2H), 8.18 (d, *J* = 7.6 Hz, 2H), 7.04 (s, 1H), 5.32 (s, 2H), 5.03 (s, 3H), 4.66–4.42 (m, 2H), 3.60–3.44 (m, 1H), 3.02–2.97 (m, 1H), 2.77–2.71 (m, 1H), 2.13–2.10 (m, 2H), 2.03–1.89 (m, 2H), 1.71–1.65 (m, 2H), 1.39–1.36 (m, 2H); MS (M+H⁺) 378.32.

Bz-Asn-NH-cHx-NH₂: pale yellow, yield 51 %; ¹H NMR (400 MHz, CDCl₃)δ 8.45 (s, 1H), 7.98–7.82 (m, 2H), 7.68 (s, 1H), 7.58–7.22 (m, 3H), 5.14 (s, 2H), 5.09 (s, 3H), 4.45–4.39 (m, 1H), 3.35–3.37 (m, 1H), 3.07–3.01 (m, 1H), 2.95–2.89 (m, 1H), 2.58–2.54 (m, 1H), 2.38–2.34 (m, 2H), 2.20–2.16 (m, 2H), 1.75–1.71 (m, 4H); MS (M+H⁺) 333.12.

NaftCO-Asn-NH-cHx-NH₂: white solid, yield 48 %; ¹H NMR (400 MHz, CDCl₃)δ 9.18–9.03 (m, 1H), 8.06–8.03 (m, 1H), 7.96–7.93 (m, 1H), 7.83–7.77 (m, 1H), 7.66–7.51 (m, 2H), 7.47–7.42 (m, 1H),

6.95 (s, 1H), 6.47 (s, 1H), 5.16 (s, 2H), 4.60–4.35 (m, 4H), 3.67–3.58 (m, 1H), 3.57–3.41 (m, 1H), 3.09–3.06 (m, 1H), 2.78–2.74 (m, 1H), 2.51–2.22 (m, 4H), 2.00–1.80 (m, 2H), 1.73–1.45 (m, 2H); MS ($M+H^+$) 383.71.

NBz-Phe-NH-cHx-NH₂: white solid, yield 82 %; ¹H NMR (400 MHz, CDCl₃) δ 8.34 (d, $J = 7.6$ Hz, 2H), 8.13 (d, $J = 7.5$ Hz, 2H), 7.32–6.97 (m, 5H), 6.71 (s, 1H), 5.21 (s, 1H), 5.03 (s, 3H), 4.75–4.67 (m, 1H), 3.76–3.68 (m, 1H), 3.54–3.47 (m, 1H), 3.44–3.37 (m, 1H), 3.01–2.89 (m, 1H), 2.86–2.81 (m, 2H), 1.88–1.76 (m, 4H), 1.23–1.16 (m, 2H); MS ($M+H^+$) 411.16.

Bz-Phe-NH-cHx-NH₂: pale yellow, yield 63 %; ¹H NMR (400 MHz, CDCl₃) δ 7.96–7.64 (m, 2H), 7.60–7.36 (m, 3H), 7.30–6.98 (m, 5H), 5.61 (s, 1H), 5.09 (s, 3H), 4.82–4.75 (m, 2H), 3.93–3.87 (m, 1H), 3.47–3.44 (m, 1H), 3.02–2.75 (m, 2H), 2.11–1.98 (m, 2H), 1.75–1.68 (m, 2H), 1.59–1.46 (m, 2H), 1.24–1.18 (m, 2H); MS ($M+H^+$) 366.18.

1-NaftCO-Phe-NH-cHx-NH₂: white solid, yield 65 %; ¹H NMR (400 MHz, CDCl₃) δ 8.62–8.50 (m, 1H), 7.99–7.96 (m, 1H), 7.91–7.84 (m, 1H), 7.73–7.65 (m, 1H), 7.60–7.45 (m, 3H), 7.35–7.07 (m, 5H), 5.72 (s, 1H), 5.27–5.14 (m, 4H), 5.09 (s, 1H), 4.34–4.26 (m, 1H), 3.48–3.45 (m, 1H), 3.23–3.18 (m, 1H), 2.94–2.88 (m, 1H), 2.64–2.55 (m, 2H), 2.38–2.30 (m, 2H), 1.95–1.67 (m, 4H); MS ($M+H^+$) 416.23.

NBz-Ser-NH-cHx-NH₂: white solid, yield 49 %; ¹H NMR (400 MHz, CDCl₃) δ 8.32 (d, $J = 7.4$ Hz, 2H), 8.15 (d, $J = 7.4$ Hz, 2H), 7.62 (s, 1H), 5.13 (s, 3H), 4.64 (s, 1H), 4.22–3.99 (m, 3H), 3.87–3.72 (m, 1H), 3.58–3.35 (m, 1H), 2.41–2.21 (m, 2H), 2.17–2.01 (m, 2H), 2.04–1.92 (m, 2H), 1.58–1.56 (m, 2H); MS ($M+H^+$) 351.37.

Bz-Ser-NH-cHx-NH₂: white solid, yield 50 %; ¹H NMR (400 MHz, CDCl₃) δ 7.89–7.70 (m, 2H), 7.57–7.32 (m, 3H), 6.23 (s, 1H), 5.20 (s, 1H), 5.05 (s, 3H), 4.38–4.15 (m, 2H), 3.91–3.88 (m, 1H), 3.32–2.28 (m, 1H), 3.07–3.02 (m, 1H), 2.22–2.12 (m, 2H), 2.11–2.08 (m, 2H), 1.67–1.65 (m, 2H), 1.45–1.40 (m, 2H); MS ($M+H^+$) 306.22.

1-NaftCO-Ser-NH-cHx-NH₂: pale yellow, yield 55 %; ¹H NMR (400 MHz, CDCl₃) δ 8.84–8.61 (m, 1H), 8.00–7.97 (m, 1H), 7.93–7.78 (m, 2H), 7.68–7.44 (m, 4H), 4.65–4.58 (m, 2H), 4.41–4.23 (m, 4H), 3.92–3.86 (m, 1H), 3.72–3.67 (m, 1H), 3.64 (s, 1H), 3.52–3.42 (m, 1H), 2.38–2.20 (m, 2H), 2.20–2.01 (m, 2H), 1.69–1.42 (m, 4H); MS ($M+H^+$) 356.38.

Analytical data of R'-Xaa-NH-R-NH-CINafQ

HMB-Leu-NH-(CH₂)₄-NH-CINafQ (17): white solid; yield 57%; mp = 121–124 °C; $[\alpha]_D^{20}$ -11.5 (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.26 (dd, $J = 7.4, 1.4$ Hz, 1H), 8.13 (dd, $J = 7.5, 1.6$ Hz, 1H), 7.80–7.76 (m, 1H), 7.70–7.66 (m, 1H), 7.30 (dd, $J = 7.5, 1.4$ Hz, 1H), 7.20 (s, 1H), 7.12 (t, $J = 7.5$ Hz, 1H), 6.89 (dd, $J = 7.5, 1.4$ Hz, 1H), 4.66 (s, 1H), 4.33–4.29 (m, 1H), 4.24 (s, 1H), 3.24–3.18 (m, 4H), 2.34 (s, 3H), 1.81–1.31 (m, 6H), 1.13–0.86 (m, 7H); MS (ESI): $[MH]^+ = 526.21$; HPLC (T_r) 15.40 min.

NBz-Leu-NH-(CH₂)₄-NH-CINafQ (18): white solid; yield 61%; mp = 115–117 °C; $[\alpha]_D^{20}$ -10.2 (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.21–8.15 (m, 1H), 8.12–8.06 (m, 6H), 7.78–7.74 (m, 1H), 7.70–7.66 (m, 1H), 7.57 (s, 1H), 5.72 (s, 1H), 4.40–4.37 (m, 1H), 3.29 (m, 4H), 1.94–1.88 (m, 1H),

1.72–1.61 (m, 3H), 1.58–1.48 (m, 3H), 1.00–0.92 (m, 6H); MS (ESI): $[MH]^+ = 541.18$; HPLC (T_r) 16.43 min.

Bz-Leu-NH-(CH₂)₄-NH-CINafQ (**19**): white solid; yield 64%; mp = 120–123 °C; $[\alpha]_D^{20} -9.4$ (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.34–8.15 (m, 1H), 7.94–7.81 (m, 2H), 7.81–7.72 (m, 2H), 7.69–7.62 (m, 1H), 7.53–7.41 (m, 3H), 7.12 (s, 1H), 4.81 (s, 1H), 4.65 (s, 1H), 4.50–4.95 (m, 1H), 3.41–3.23 (m, 2H), 3.23–3.04 (m, 2H), 1.79–1.76 (m, 1H), 1.59–1.45 (m, 5H), 1.41–1.37 (m, 1H), 1.05–0.99 (m, 6H); MS (ESI): $[MH]^+ = 496.20$; HPLC (T_r) 16.10 min.

1-NaftCO-Leu-NH-(CH₂)₄-NH-CINafQ (**20**): white solid; yield 51%; mp = 123–124 °C; $[\alpha]_D^{20} -13.5$ (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 9.34 (dd, $J = 7.5, 1.6$ Hz, 1H), 8.22 (dd, $J = 7.4, 1.6$ Hz, 1H), 8.14–8.04 (m, 2H), 7.97–7.94 (m, 1H), 7.81–7.79 (m, 1H), 7.73–7.41 (m, 6H), 5.41 (s, 1H), 4.24–4.16 (m, 2H), 3.34–3.27 (m, 1H), 3.28–3.11 (m, 3H), 1.78–1.65 (m, 3H), 1.63–1.54 (m, 2H), 1.49–1.45 (m, 1H), 1.26–1.01 (m, 1H), 0.83–0.76 (m, 6H); MS (ESI): $[MH]^+ = 546.24$; HPLC (T_r) 16.82 min.

HMB-Asn-NH-(CH₂)₄-NH-CINafQ (**21**): white solid; yield 81%; mp = 145–148 °C; $[\alpha]_D^{20} -25.6$ (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.48 (s, 1H), 8.24–8.21 (m, 1H), 8.14–8.12 (m, 1H), 7.71–7.65 (m, 2H), 7.34 (s, 1H), 7.31–7.16 (m, 2H), 7.02–6.85 (m, 1H), 5.26 (s, 2H), 5.03 (s, 1H), 4.85–4.77 (m, 1H), 3.25–3.22 (m, 2H), 3.17–3.14 (m, 2H), 3.10–3.06 (m, 1H), 2.66–2.60 (m, 1H), 2.31 (s, 3H), 1.69–1.59 (m, 2H), 1.58–1.50 (m, 2H); MS (ESI): $[MH]^+ = 527.11$; HPLC (T_r) 12.36 min.

NBz-Asn-NH-(CH₂)₄-NH-CINafQ (**22**): white solid; yield 59%; mp = 151–153 °C; $[\alpha]_D^{20} -18.1$ (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.37–8.30 (m, 1H), 8.26–8.08 (m, 3H), 8.00–7.89 (m, 2H), 7.81–7.71 (m, 2H), 7.65 (s, 1H), 7.13 (s, 1H), 5.45 (s, 2H), 5.38 (s, 1H), 4.66–4.61 (m, 1H), 3.30–3.20 (m, 4H), 2.81–2.76 (m, 1H), 1.66–1.61 (m, 2H), 1.44–1.38 (m, 2H); MS (ESI): $[MH]^+ = 542.14$; HPLC (T_r) 13.56 min.

Bz-Asn-NH-(CH₂)₄-NH-CINafQ (**23**): white solid; yield 74%; mp = 142–145 °C; $[\alpha]_D^{20} -15.4$ (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.37–8.21 (m, 1H), 8.21–8.01 (m, 1H), 7.75–7.62 (m, 5H), 7.51–7.30 (m, 3H), 6.10 (s, 1H), 5.35 (s, 1H), 5.21 (s, 2H), 4.76–4.68 (m, 1H), 3.23–3.20 (m, 4H), 3.07–2.96 (m, 1H), 2.81–2.76 (m, 1H), 1.68–1.51 (m, 4H); MS (ESI): $[MH]^+ = 498.24$; HPLC (T_r) 13.31 min.

1-NaftCO-Asn-NH-(CH₂)₄-NH-CINafQ (**24**): white solid; yield 62%; mp = 148–151 °C; $[\alpha]_D^{20} -22.6$ (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.41–4.38 (m, 1H), 8.25–8.07 (m, 3H), 7.99–7.95 (m, 1H), 7.86–7.76 (m, 2H), 7.75–7.62 (m, 3H), 7.58–7.53 (m, 1H), 7.49–7.45 (m, 1H), 6.62 (s, 1H), 5.18 (s, 1H), 5.10 (s, 2H), 4.97–4.88 (m, 1H), 3.35–3.16 (m, 4H), 3.16–3.02 (m, 1H), 2.64–2.62 (m, 1H), 1.64–1.46 (m, 4H); MS (ESI): $[MH]^+ = 547.28$; HPLC (T_r) 14.03 min.

HMB-Phe-NH-(CH₂)₄-NH-CINafQ (**25**): white solid; yield 81%; mp = 118–120 °C; $[\alpha]_D^{20} -21.5$ (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.75 (s, 1H), 8.08–8.02 (m, 1H), 7.95–7.92 (m, 1H), 7.70–7.65 (m, 2H), 7.33–7.17 (m, 6H), 7.09–7.05 (m, 1H), 6.88–6.86 (m, 2H), 5.91 (s, 1H), 4.73–4.68 (m, 1H), 3.42–3.40 (m, 1H), 3.27–3.13 (m, 5H), 2.29 (s, 3H), 1.70–1.48 (m, 4H); MS (ESI): $[MH]^+ = 560.17$; HPLC (T_r) 14.70 min.

NBz-Phe-NH-(CH₂)₄-NH-CINafQ (**26**): white solid; yield 71%; mp = 108–111 °C; $[\alpha]_D^{20} -18.2$ (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.31 (d, $J = 7.4$ Hz, 2H), 8.21–7.92 (m, 4H), 7.74–7.64 (m, 2H), 7.53 (s, 1H), 7.27–7.11 (m, 6H), 4.72–4.68 (m, 1H), 4.57 (s, 1H), 3.31–3.13 (m, 5H), 2.89–2.85 (m, 1H), 1.72–1.49 (m, 4H); MS (ESI): $[MH]^+ = 575.12$; HPLC (T_r) 15.88 min.

Bz-Phe-NH-(CH₂)₄-NH-CINafQ (**27**): white solid; yield 61%; mp = 110-113 °C; [α]_D²⁰ -13.4 (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.18–8.03 (m, 2H), 7.92–7.86 (m, 2H), 7.73–7.66 (m, 2H), 7.49–7.37 (m, 3H), 7.35 (s, 1H), 7.31–7.22 (m, 3H), 7.22–7.16 (m, 2H), 7.05 (s, 1H), 4.78-4.70 (m, 1H), 4.67 (s, 1H), 3.33-3.27 (m, 1H), 3.24-3.18 (m, 4H), 2.93-2.89 (m, 1H), 1.62-1.55 (m, 2H), 1.50–1.42 (m, 2H); MS (ESI): [MH]⁺ = 530.02; HPLC (T_r) 16.02 min.

1-NaftCO-Phe-NH-(CH₂)₄-NH-CINafQ (**28**): white solid; yield 66%; mp = 115-117 °C; [α]_D²⁰ -23.5 (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 9.19 (s, 1H), 8.79–8.65 (m, 1H), 8.42 (s, 1H), 8.17–8.00 (m, 2H), 7.98–7.74 (m, 3H), 7.73–7.59 (m, 2H), 7.56–7.34 (m, 3H), 7.20–7.00 (m, 5H), 6.31 (s, 1H), 4.96-4.91 (m, 1H), 3.36–3.10 (m, 4H), 3.02-3.05 (m, 1H), 2.86-2.84 (m, 1H), 1.79–1.45 (m, 4H); MS (ESI): [MH]⁺ = 580.19; HPLC (T_r) 16.39 min.

HMB-Ser-NH-(CH₂)₄-NH-CINafQ (**29**): white solid; yield 44%; mp = 135-138 °C; [α]_D²⁰ -35.6 (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.28–8.02 (m, 2H), 7.81–7.61 (m, 2H), 7.47 (s, 1H), 7.30-7.27 (m, 1H), 7.14-7.11 (m, 1H), 6.89-6.81 (m, 1H), 5.62 (s, 1H), 5.58 (s, 1H), 4.52-4.44 (m, 1H), 4.29-4.25 (m, 1H), 4.09-4.01 (m, 1H), 3.40–3.12 (m, 4H), 1.70–1.51 (m, 4H); MS (ESI): [MH]⁺ = 500.15; HPLC (T_r) 12.88 min.

NBz-Ser-NH-(CH₂)₄-NH-CINafQ (**30**): white solid; yield 82%; mp = 130-133 °C; [α]_D²⁰ -29.1 (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.23–7.94 (m, 6H), 7.80-7.70 (m, 2H), 6.34 (s, 1H), 5.46 (s, 1H), 4.47 (s, 1H), 4.32-4.20 (m, 2H), 3.95-3.91 (m, 1H), 3.29-3.16 (m, 4H), 1.78–1.49 (m, 4H); MS (ESI): [MH]⁺ = 515.17, HPLC (T_r) 13.99 min.

Bz-Ser-NH-(CH₂)₄-NH-CINafQ (**31**): white solid; yield 58%; mp = 132-135 °C; [α]_D²⁰ -20.4 (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.24–8.10 (m, 2H), 7.88–7.71 (m, 5H), 7.49–7.34 (m, 3H), 5.25 (s, 1H), 5.15 (s, 1H), 4.48-4.46 (m, 1H), 4.18-4.14 (m, 1H), 3.90-3.85 (m, 1H), 3.28-3.17 (m, 4H), 1.72–1.55 (m, 2H), 1.48-1.42 (m, 2H); MS (ESI): [MH]⁺ = 470.11; HPLC (T_r) 14.07 min.

1-NaftCO-Ser-NH-(CH₂)₄-NH-CINafQ (**32**): white solid; yield 61%; mp = 139-141 °C; [α]_D²⁰ -31.8 (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.62 (dd, J = 7.5, 1.6 Hz, 1H), 8.19–8.10 (m, 3H), 7.96–7.85 (m, 2H), 7.82-7.79 (m, 1H), 7.68-7.65 (m, 2H), 7.53-7.43 (m, 3H), 5.90 (s, 1H), 5.03-4.99 (m, 2H), 4.24-4.21 (m, 1H), 4.04-4.01 (m, 1H), 3.45–3.35 (m, 1H), 3.30–3.11 (m, 3H), 1.70–1.55 (m, 4H); MS (ESI): [MH]⁺ = 520.08; HPLC (T_r) 14.58 min.

HMB-Leu-NH-cHx-NH-CINafQ (**33**): white solid; yield 69%; mp = 118-120 °C; [α]_D²⁰ -9.7 (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.27 – 8.00 (m, 2H), 7.71-7.67 (m, 2H), 7.35-7.29 (m, 2H), 7.13-7.07 (m, 1H), 6.96–6.75 (m, 2H), 4.91 (s, 1H), 4.59-4.51 (m, 1H), 3.77–3.45 (m, 2H), 2.36–2.08 (m, 5H), 1.97-1.92 (m, 1H), 1.89–1.75 (m, 1H), 1.76–1.55 (m, 5H), 1.39–1.15 (m, 2H), 0.96-0.94 (m, 6H); MS (ESI): [MH]⁺ = 552.18; HPLC (T_r) 14.12 min.

NBz-Leu-NH-cHx-NH-CINafQ (**34**): white solid; yield 54%; mp = 112-115 °C; [α]_D²⁰ -8.2 (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.27–8.18 (m, 3H), 8.18–8.11 (m, 1H), 8.08-8.01 (m, 2H), 7.95–7.59 (m, 2H), 7.21 (s, 1H), 5.75 (s, 1H), 5.23 (s, 1H), 4.86-4.82 (m, 1H), 3.87–3.59 (m, 1H), 3.56–3.36 (m, 1H), 2.22–1.91 (m, 4H), 1.8–1.59 (m, 6H), 1.61–1.45 (m, 1H), 1.04-1.00 (m, 6H); MS (ESI): [MH]⁺ = 567.18; HPLC (T_r) 16.04 min.

Bz-Leu-NH-cHx-NH-CINafQ (**35**): white solid; yield 56%; mp = 117-119 °C; [α]_D²⁰ -7.6 (c=1, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 8.14–8.01 (m, 2H), 7.90–7.80 (m, 2H), 7.77–7.59 (m, 3H), 7.53–7.30 (m, 3H), 6.20 (s, 1H), 4.82 (s, 1H), 4.57-4.51 (m, 1H), 3.76–3.49 (m, 2H), 2.24-2.17 (m, 2H), 2.04-1.88 (m, 2H), 1.91–1.74 (m, 2H), 1.75–1.49 (m, 5H), 1.08-0.98 (m, 6H); MS (ESI): [MH]⁺ = 522.14; HPLC (T_r) 15.74 min.

1-NaftCO-Leu-NH-cHx-NH-CINafQ (**36**): white solid; yield 81%; mp = 121-124 °C; $[\alpha]_{\text{D}}^{20}$ -11.8 (c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.90–8.64 (m, 1H), 8.20–8.04 (m, 2H), 8.04–7.93 (m, 1H), 7.92–7.87 (m, 1H), 7.76–7.59 (m, 3H), 7.53–7.48 (m, 2H), 7.43–7.37 (m, 1H), 6.05 (s, 1H), 5.60 (s, 1H), 5.30 (s, 1H), 4.53–4.44 (m, 1H), 4.09–4.01 (m, 1H), 3.89–3.66 (m, 1H), 2.11–1.95 (m, 1H), 1.97–1.66 (m, 7H), 1.62–1.40 (m, 3H), 1.06 (d, J = 6.3 Hz, 6H); MS (ESI): $[\text{MH}]^+$ = 572.10; HPLC (T_{r}) 16.40 min.

HMB-Asn-NH-cHx-NH-CINafQ (**37**): white solid; yield 57%; mp = 144-145 °C; $[\alpha]_{\text{D}}^{20}$ -21.2 (c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.29–8.08 (m, 2H), 7.83–7.57 (m, 2H), 7.25–7.03 (m, 3H), 6.97 (s, 1H), 6.86–6.77 (m, 1H), 5.24 (s, 1H), 5.17 (s, 2H), 4.70–4.65 (m, 1H), 4.22–4.05 (m, 1H), 4.01–3.81 (m, 1H), 3.08–3.00 (m, 1H), 2.74–2.65 (m, 1H), 2.25–2.21 (m, 3H), 2.22–2.01 (m, 4H), 1.91–1.69 (m, 4H); MS (ESI): $[\text{MH}]^+$ = 553.19; HPLC (T_{r}) 13.34 min.

NBz-Asn-NH-cHx-NH-CINafQ (**38**): white solid; yield 55%; mp = 148-151 °C; $[\alpha]_{\text{D}}^{20}$ -13.7 (c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.73 (s, 1H), 8.29–8.02 (m, 7H), 7.73–7.67 (m, 2H), 6.03 (s, 1H), 5.10 (s, 2H), 4.60–4.53 (m, 1H), 3.78–3.71 (m, 2H), 3.18–3.16 (m, 1H), 2.76–2.71 (m, 1H), 2.03–1.96 (m, 2H), 1.96–1.91 (m, 2H), 1.88–1.81 (m, 2H), 1.56–1.49 (m, 2H); MS (ESI): $[\text{MH}]^+$ = 568.16; HPLC (T_{r}) 14.66 min.

Bz-Asn-NH-cHx-NH-CINafQ (**39**): white solid; yield 62%; mp = 134-135 °C; $[\alpha]_{\text{D}}^{20}$ -12.2 (c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.29–8.14 (m, 2H), 8.07 (s, 1H), 7.87–7.81 (m, 3H), 7.80–7.59 (m, 2H), 7.56–7.34 (m, 3H), 7.24 (s, 1H), 4.34 (s, 2H), 4.27–4.08 (m, 2H), 4.10–3.85 (m, 1H), 2.96–2.93 (m, 1H), 2.74–2.69 (m, 1H), 2.20–2.04 (m, 2H), 2.03–1.86 (m, 4H), 1.74–1.56 (m, 2H); MS (ESI): $[\text{MH}]^+$ = 523.27; HPLC (T_{r}) 14.44 min.

1-NaftCO-Asn-NH-cHx-NH-CINafQ (**40**): white solid; yield 68%; mp = 151-152 °C; $[\alpha]_{\text{D}}^{20}$ -18.8 (c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 9.04–8.47 (m, 1H), 8.20–8.07 (m, 2H), 8.08–7.93 (m, 2H), 7.70–7.66 (m, 4H), 7.57–7.51 (m, 1H), 7.44–7.41 (m, 1H), 7.30 (s, 1H), 6.43 (s, 1H), 5.50 (s, 2H), 4.61–4.56 (m, 1H), 4.08–3.86 (m, 1H), 3.72 (s, 1H), 3.13–3.09 (m, 1H), 2.95–2.69 (m, 2H), 2.06–1.83 (m, 2H), 1.72–1.67 (m, 2H), 1.64–1.43 (m, 2H), 1.18–1.11 (m, 2H); MS (ESI): $[\text{MH}]^+$ = 573.21; HPLC (T_{r}) 15.70 min.

HMB-Phe-NH-cHx-NH-CINafQ (**41**): white solid; yield 77%; mp = 120-121 °C; $[\alpha]_{\text{D}}^{20}$ -11.4 (c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.20–7.98 (m, 2H), 7.77–7.56 (m, 3H), 7.31–2.25 (m, 1H), 7.25–7.02 (m, 6H), 6.89–6.83 (m, 1H), 5.40 (s, 1H), 5.24–5.17 (m, 1H), 5.14 (s, 1H), 3.89–3.67 (m, 2H), 3.34–3.29 (m, 1H), 3.00–2.93 (m, 1H), 2.31 (s, 3H), 2.07–1.80 (m, 6H), 1.76–1.62 (m, 2H); MS (ESI): $[\text{MH}]^+$ = 586.15; HPLC (T_{r}) 14.76 min.

NBz-Phe-NH-cHx-NH-CINafQ (**42**): white solid; yield 59%; mp = 115-117 °C; $[\alpha]_{\text{D}}^{20}$ -9.4 (c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.29 (d, J = 7.4 Hz, 2H), 8.18–8.00 (m, 4H), 7.83–7.45 (m, 3H), 7.32–6.92 (m, 5H), 5.83 (s, 1H), 5.21–5.17 (m, 1H), 5.09 (s, 1H), 4.74–4.65 (m, 1H), 3.99–3.87 (m, 1H), 3.18–3.15 (m, 1H), 2.96–2.94 (m, 1H), 2.36–2.31 (m, 4H), 2.11–2.02 (m, 2H), 1.59–1.51 (m, 2H); MS (ESI): $[\text{MH}]^+$ = 601.17; HPLC (T_{r}) 16.88 min.

Bz-Phe-NH-cHx-NH-CINafQ (**43**): white solid; yield 71%; mp = 128-129 °C; $[\alpha]_{\text{D}}^{20}$ -10.6 (c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.09–7.98 (m, 2H), 7.88–7.79 (m, 2H), 7.74–7.63 (m, 3H), 7.50–7.31 (m, 3H), 7.29–7.02 (m, 5H), 6.24 (s, 1H), 5.30–5.25 (m, 1H), 5.13 (s, 1H), 4.58–4.51 (m, 1H), 4.43–4.37 (m, 1H), 3.19–3.15 (m, 1H), 2.96–2.89 (m, 1H), 2.33–2.27 (m, 2H), 2.24–2.16 (m, 2H), 1.91–1.83 (m, 2H), 1.70–1.65 (m, 2H); MS (ESI): $[\text{MH}]^+$ = 556.20; HPLC (T_{r}) 16.70 min.

1-NaftCO-Phe-NH-cHx-NH-ClNafQ (**44**): white solid; yield 78%;mp = 133-134 °C; $[\alpha]_D^{20}$ -15.4(c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.60–8.40 (m, 1H), 8.07–7.97 (m, 2H), 7.92-7.88 (m, 1H), 7.85–7.71 (m, 2H), 7.74–7.56 (m, 3H), 7.60–7.39 (m, 3H), 7.32–7.05 (m, 5H), 5.68 (s, 1H), 5.26-5.15 (m, 1H), 5.19 (s, 1H), 4.92-4.89 (m, 1H), 4.46-4.39 (m, 1H), 3.22-3.19 (m, 1H), 2.96-2.91 (m, 1H), 2.39-2.31 (m, 2H), 2.29-2.13 (m, 2H), 2.02-1.98 (m, 2H), 1.76-1.70 (m, 2H); MS (ESI): $[\text{MH}]^+ = 606.11$; HPLC (T_r) 17.10 min.

HMB-Ser-NH-cHx-NH-ClNafQ (**45**): white solid; yield 71%;mp = 142-146 °C; $[\alpha]_D^{20}$ -23.4 (c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.32–8.12 (m, 2H), 7.80–7.60 (m, 2H), 7.32-7.27 (m, 1H), 7.14-7.08 (m, 1H), 6.94–6.68 (m, 2H), 5.73 (s, 1H), 5.31 (s, 1H), 4.62-4.54 (m, 1H), 4.19-4.13 (m, 1H), 3.87-3.81 (m, 3H), 2.36 (s, 3H), 2.21–1.96 (m, 4H), 1.94–1.73 (m, 4H); MS (ESI): $[\text{MH}]^+ = 526.16$; HPLC (T_r) 11.6 min.

NBz-Ser-NH-cHx-NH-ClNafQ (**46**): white solid; yield 54%;mp = 147-150 °C; $[\alpha]_D^{20}$ -16.5 (c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.17–8.03 (m, 4H), 7.98–7.80 (m, 3H), 7.70-7.65 (m, 2H), 5.17 (s, 1H), 5.09 (s, 1H), 4.55-4.49 (m, 1H), 4.18-4.12 (m, 1H), 4.10–4.01 (m, 1H), 3.94-3.91 (m, 1H), 3.90–3.71 (m, 1H), 2.14–1.80 (m, 6H), 1.72–1.52 (m, 2H); MS (ESI): $[\text{MH}]^+ = 541.22$; HPLC (T_r) 13.74 min.

Bz-Ser-NH-cHx-NH-ClNafQ (**47**): white solid; yield 83%;mp = 138-141 °C; $[\alpha]_D^{20}$ -13.8 (c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.27–8.10 (m, 2H), 7.95–7.82 (m, 2H), 7.78–7.63 (m, 2H), 7.56–7.30 (m, 4H), 6.56 (s, 1H), 5.04 (s, 1H), 4.54-4.49 (m, 1H), 4.24-4.17 (m, 1H), 3.87-3.81 (m, 1H), 3.71–3.55 (m, 1H), 3.43-3.33 (m, 1H), 2.37-2.31 (m, 2H), 2.16-2.11 (m, 2H), 1.93-1.84 (m, 2H), 1.75-1.70 (m, 2H);MS (ESI): $[\text{MH}]^+ = 496.16$; HPLC (T_r) 13.41 min.

1-NaftCO-Ser-NH-cHx-NH-ClNafQ (**48**): white solid; yield 66%;mp = 145-148 °C; $[\alpha]_D^{20}$ -20.7 (c=1, MeOH); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.97 (s, 1H), 8.75 (dd, $J = 7.5, 1.6$ Hz, 1H), 8.21–8.05 (m, 3H), 7.87–7.77 (m, 2H), 7.76–7.62 (m, 3H), 7.58-7.51 (m, 1H), 7.48-7.40 (m, 1H), 5.29 (s, 1H), 4.25-4.21 (m, 1H), 4.14-4.07 (m, 1H), 4.01–3.92 (m, 1H), 3.92–3.83 (m, 1H), 3.38–3.22 (m, 1H), 3.17 (s, 1H), 2.17-2.11 (m, 2H), 1.88-1.76 (m, 2H), 1.53-1.46 (m, 2H), 1.30-1.24 (m, 2H); MS (ESI): $[\text{MH}]^+ = 546.13$; HPLC (T_r) 14.30 min.