Supporting information:

Highly Efficient Coupling of β -Substituted Aminoethane Sulfonyl Azides with Thio Acids, towards a New Chemical Ligation Reaction

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Instruments and methods: Analytical HPLC runs were performed on a Shimadzu HPLC workstation on an Adsorbosphere XL C8 reversed phase column (90 Å, 5 μ m, 250x4.6 mm) in a linear gradient of 100% buffer A (0.1% TFA in H₂O) to 100% buffer B (0.085% TFA in CH₃CN/H₂O 95/5 v/v) in 20 min at 1 mL/min. Liquid chromatography electrospray ionization mass spectrometry was measured on a Shimadzu LCMS-QP8000 single quadrupole bench-top mass spectrometer operating in a positive or negative ionization mode. ¹H NMR spectra were recorded on a Varian G-300 (300.1 MHz) or a Varian INOVA-500 (499.9 MHz) spectrometer and chemical shifts are given in ppm (δ) relative to TMS (0.00 ppm). ¹³C NMR spectra were recorded on a Varian G-300 (75.5 MHz) spectrometer and chemical shifts are given in ppm relative to CDCl₃ (77.0 ppm) or DMSO-d₆ (39.7 ppm). The ¹³C NMR spectra were recorded using the attached proton test (APT) sequence. *R_f* values were determined by thin layer chromatography (TLC) on Merck precoated silicagel 60F₂₅₄ plates. Spots were visualized by UV-quenching, ninhydrin or Cl₂/TDM.^[1] Melting

points were measured on a Büchi Schmelzpunktbestimmungsapparat (according to dr. Tottoli) and are uncorrected. Specific optical rotations were measured using a Jasco P1010 polarimeter. Elemental analyses were done by Kolbe Mikroanalytisches Labor (Mülheim an der Ruhr, Germany).

General Procedure for the synthesis of *N*^β-protected acyl sulfon amides

To a mixture of sulfonyl azide (1 equiv) and 2,6-lutidine (1.3 equiv) in CHCl₃ or DMF, the thio acid (1.3 equiv) is added dropwise. After completion of the addition, the reaction mixture is allowed to stir for 15 min at room temperature. Then, the reaction mixture is evaporated to dryness and the residue is either crystallized from EtOAc/hexane or purified by column chromatography.

Compound 1

The reaction was carried out following the general procedure, using 200 mg (0.54 mmol) of Fmoc-GlyΨ[CH₂SO₂]-N₃, 82 μL (0.70 mmol) of 2,6-lutidine and 50 μL (0.70 mmol) of thioacetic acid in 2.5 mL DMF (0.21 M conc. of sulfonyl azide). The product (188 mg, 90%), was isolated by column chromatography (EtOAc/hexane) as a white solid. *R_f* 0.14 (EtOAc/hexane, 4:1 v/v). *R_t* 16.01. Mp 161 °C. ¹H NMR (300 MHz, DMSO-d₆): δ 11.70 (s, 1H), 7.91 (d, *J*=7.4 Hz, 2H), 7.70 (d, *J*=7.1 Hz, 2H), 7.49-7.31 (m, 5H), 4.35 (d, *J*=6.6 Hz, 2H), 4.25 (t, *J*=6.6 Hz, 1H), 3.50 (m, 2H), 3.39 (m, 2H), 1.98 (s, 3H). ¹³C NMR (75 MHz, CDCl₃/CD₃OD): δ 170.6, 156.9, 143.9, 141.4, 127.9, 127.3, 125.2, 120.2, 67.1, 52.6, 47.2, 35.7, 29.9, 23.4. ESMS calcd. for C₁₉H₂₀N₂O₅S

388.11, found 389.35 $[M + H]^+$, 411.15 $[M + Na]^+$, 387.30 $[M - H]^-$. Anal. Calcd. for $C_{19}H_{20}N_2O_5S$, C, 58.75; H, 5.19; N, 7.21. Found C, 58.69; H, 5.08; N, 7.11.

Compound 2

The reaction was carried out following the general procedure as described for **1**. The product was isolated by column chromatography (EtOAc/hexane) as a white solid in quantitative yield. R_f 0.52 (EtOAc/hexane, 4:1 v/v). R_t 17.56. Mp 176 °C. 1H NMR (300 MHz, DMSO- d_6): δ 12.08 (broad s, 1H), 7.95-7.92 (m, 4H), 7.89 (d, $J=7.4$ Hz, 2H), 7.48-7.29 (m, 8H), 4.27-4.17 (m, 3H), 3.37 (broad m, 4H). ^{13}C NMR (75 MHz, DMSO- d_6): δ 169.7, 156.2, 144.1, 141.0, 137.0, 131.4, 128.7, 128.1, 127.9, 127.4, 125.4, 120.4, 65.7, 51.6, 46.9, 36.1. ESMS calcd. for $C_{24}H_{22}N_2O_5S$ 450.12, found 449.35 $[M - H]^-$. Anal. Calcd. for $C_{24}H_{22}N_2O_5S$, C, 63.98; H, 4.92; N, 6.22. Found C, 64.11; H, 4.85; N, 6.12.

Compound 3

The reaction was carried out following the general procedure as described for **1**. The product was isolated by column chromatography (EtOAc/hexane) as a white solid in quantitative yield. R_f 0.30 (EtOAc/hexane, 4:1 v/v). R_t 12.96. Mp 149 °C. 1H NMR (300 MHz, DMSO- d_6): δ 11.71 (broad s, 1H), 7.46-7.30 (m, 6H), 5.03 (s, 2H), 3.43 (m, 2H), 3.16 (m, 2H), 1.99 (s, 3H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 170.1, 156.2,

137.2, 128.6, 128.1, 65.8, 51.5, 35.3, 23.5. ESMS calcd. for $C_{12}H_{16}N_2O_5S$ 300.08, found 323.15 $[M + Na]^+$, 299.15 $[M - H]^-$. Anal. Calcd. for $C_{12}H_{16}N_2O_5S$, C, 47.99; H, 5.37; N, 9.33. Found C, 48.12; H, 5.38; N, 9.22.

Compound 4

The reaction was carried out following the general procedure as described for **1**. The product was isolated by column chromatography (EtOAc/hexane) as a white solid in quantitative yield. R_f 0.41 (EtOAc/hexane, 4:1 v/v). R_t 17.55. Mp 108 °C. 1H NMR (300 MHz, DMSO- d_6): δ 12.12 (broad s, 1H), 7.94 (d, $J=7.1$ Hz, 2H), 7.66 (m, 1H), 7.53 (m, 2H), 7.42-7.27 (m, 6H), 4.96 (s, 2H), 3.65 (m, 2H), 3.44 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3/CD_3OD$): δ 167.5, 156.9, 136.2, 134.7, 133.7, 131.9, 129.3, 129.0, 128.7, 128.6, 128.4, 128.2, 67.2, 53.0, 35.9. ESMS calcd. for $C_{17}H_{18}N_2O_5S$ 362.09, found 363.15 $[M + H]^+$, 385.20 $[M + Na]^+$, 361.20 $[M - H]^-$. Anal. Calcd. for $C_{17}H_{18}N_2O_5S$, C, 56.34; H, 5.01; N, 7.73. Found C, 56.25; H, 4.93; N, 7.61.

Compound 5

The reaction was carried out following the general procedure as described for **1**. The product was isolated by column chromatography (EtOAc/hexane) as a white solid in 91% yield. R_f 0.52 (EtOAc/hexane, 4:1 v/v). R_t 17.53. Mp 181 °C. $[\alpha]_D^{23}$ -31.2 ($c = 0.1$ DMF). 1H NMR (300 MHz, DMSO- d_6): δ 11.71 (s, 1H), 7.90 (d, $J=7.4$ Hz, 2H),

7.64 (m, 2H), 7.58 (d, $J=8.5$ Hz, 1H), 7.44-7.17 (m, 9H), 4.23 (m, 2H), 4.16 (m, 2H), 3.59 (m, 1H), 3.47 (m, 1H), 2.83 (m, 2H) 1.90 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.3, 156.2, 143.5, 141.1, 136.0, 129.3, 128.6, 127.7, 127.0, 124.9, 124.8, 119.9, 54.8, 48.6, 46.9, 40.7, 29.6, 23.2. ESMS calcd. for $\text{C}_{26}\text{H}_{26}\text{N}_2\text{O}_5\text{S}$ 478.16, found 479.35 $[\text{M} + \text{H}]^+$, 501.30 $[\text{M} + \text{Na}]^+$, 477.35 $[\text{M} - \text{H}]^-$. Anal. Calcd. for $\text{C}_{26}\text{H}_{26}\text{N}_2\text{O}_5\text{S}$, C, 65.25; H, 5.48; N, 5.85. Found C, 65.06; H, 5.42; N, 5.69.

Compound 6

The reaction was carried out following the general procedure as described for **1**. The product was obtained by crystallization from EtOAc/hexane as a white solid in 87% yield. R_f 0.61 (EtOAc/hexane, 4:1 v/v). R_t 18.75. Mp 234 °C (decomp.). $[\alpha]_D^{23}$ -21.8 ($c = 0.1$ DMF). ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 12.18 (broad s, 1H), 7.91 (m, 4H), 7.58-7.19 (broad m, 15H), 4.19-4.03 (m, 4H), 3.82 (m, 1H), 3.63 (m, 1H), 2.85 (m, 2H). ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$): δ 166.8, 155.6, 144.3, 141.1, 138.1, 133.6, 132.1, 129.7, 129.0, 128.7, 128.1, 127.5, 126.8, 125.6, 120.6, 65.7, 56.2, 48.9, 47.0. ESMS calcd. for $\text{C}_{31}\text{H}_{28}\text{N}_2\text{O}_5\text{S}$ 540.17, found 541.55 $[\text{M} + \text{H}]^+$, 563.30 $[\text{M} + \text{Na}]^+$, 539.45 $[\text{M} - \text{H}]^-$. Anal. Calcd. for $\text{C}_{31}\text{H}_{28}\text{N}_2\text{O}_5\text{S}$, C, 68.87; H, 5.22; N, 5.18. Found C, 68.97; H, 5.16; N, 5.06.

Compound 7

The reaction was carried out following the general procedure as described for **1**. The product was obtained by crystallization from EtOAc/hexane as a white solid in 95% yield. R_f 0.52 (EtOAc/hexane, 4:1 v/v). R_t 15.88. Mp 178 °C. $[\alpha]_D^{23}$ -37.1 (c = 0.1 DMF). ^1H NMR (300 MHz, DMSO- d_6): δ 11.73 (s, 1H), 7.54 (d, J =8.8 Hz, 1H), 7.34-7.18 (m, 10H), 4.96 (m, 2H), 4.15 (m, 1H), 3.61 (m, 1H), 3.48 (m, 1H), 2.85 (m, 2H), 1.92 (s, 3H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 170.4, 155.9, 138.3, 137.8, 129.9, 129.0, 128.4, 128.1, 127.6, 127.1. ESMS calcd. for $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_5\text{S}$ 390.12, found 391.35 $[\text{M} + \text{H}]^+$, 413.25 $[\text{M} + \text{Na}]^+$, 389.30 $[\text{M} - \text{H}]^-$. Anal. Calcd. for $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_5\text{S}$, C, 58.45; H, 5.68; N, 7.17. Found C, 58.37; H, 5.67; N, 7.12.

Compound 8

The reaction was carried out following the general procedure as described for **1**. The product was obtained by crystallization from EtOAc/hexane as a white solid in 96% yield. R_f 0.61 (EtOAc/hexane, 4:1 v/v). R_t 17.43. Mp 182 °C (decomp.). $[\alpha]_D^{23}$ -28.0 (c = 0.1 DMF). ^1H NMR (300 MHz, DMSO- d_6): δ 12.19 (broad s, 1H), 7.92 (d, J =7.1 Hz, 2H), 7.64 (m, 1H), 7.50 (m, 3H), 7.32-7.14 (m, 10H), 4.88 (dd, J =12.9 Hz, J =17.6 Hz, 2H), 4.21 (m, 1H), 3.85 (m, 1H), 3.62 (m, 1H), 2.92 (m, 1H), 2.82 (m, 1H). ^{13}C NMR (75 MHz, DMSO- d_6): δ 166.6, 155.5, 137.9, 137.2, 133.4, 132.0, 129.4, 128.7, 128.5,

127.9, 127.6, 127.1, 126.6. ESMS calcd. for $C_{24}H_{24}N_2O_5S$ 452.14, found 453.30 $[M + H]^+$, 475.30 $[M + Na]^+$, 451.35 $[M - H]^-$. Anal. Calcd. for $C_{24}H_{24}N_2O_5S$, C, 63.70; H, 5.35; N, 6.19. Found C, 63.66; H, 5.26; N, 6.08.

Compound 9

The reaction was carried out following the general procedure as described for **1**. The product was obtained by crystallization from EtOAc/hexane as a white solid in 95% yield. R_f 0.55 (EtOAc/hexane, 4:1 v/v). R_t 17.05. Mp 200 °C. $[\alpha]_D^{22} +36.7$ (c = 0.1 DMF). 1H NMR (300 MHz, DMSO- d_6): δ 11.73 (s, 1H), 7.91 (d, $J=7.7$ Hz, 2H), 7.4 (m, 2H), 7.53-7.30 (m, 5H), 4.32-4.22 (m, 3H), 3.87 (m, 1H), 3.49 (m, 2H), 1.94 (s, 3H), 1.78 (m, 1H), 0.82 (m, 6H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 170.0, 155.9, 144.2, 143.9, 140.9, 127.9, 127.3, 125.5, 120.4, 65.6, 53.7, 51.7, 47.0, 32.6, 23.4, 18.5, 17.8. ESMS calcd. for $C_{22}H_{26}N_2O_5S$ 430.16, found 431.25 $[M + H]^+$, 453.30 $[M + Na]^+$, 429.35 $[M - H]^-$. Anal. Calcd. for $C_{22}H_{26}N_2O_5S$, C, 61.38; H, 6.09; N, 6.51. Found C, 61.46; H, 5.98; N, 6.39.

Compound 10

The reaction was carried out following the general procedure as described for **1**. The product was obtained by crystallization from EtOAc/hexane as a white solid in 96% yield. R_f 0.66 (EtOAc/hexane, 4:1 v/v). R_t 18.42. Mp 231 °C. $[\alpha]_D^{22} +39.2$ (c = 0.1

DMF). ^1H NMR (300 MHz, DMSO- d_6): δ 12.20 (broad s, 1H), 7.91 (m, 4H), 7.67-7.28 (m, 10H), 4.23-3.94 (m, 4H), 3.68 (m, 2H), 1.79 (m, 1H), 0.82 (m, 6H). ^{13}C NMR (75 MHz, DMSO- d_6): δ 166.7, 155.8, 144.2, 143.8, 140.9, 133.3, 131.9, 128.7, 127.9, 127.31, 125.4, 120.3, 65.5, 54.2, 51.9, 46.9, 32.6, 18.6, 17.8. ESMS calcd. for $\text{C}_{27}\text{H}_{28}\text{N}_2\text{O}_5\text{S}$ 492.17, found 493.45 $[\text{M} + \text{H}]^+$, 515.40 $[\text{M} + \text{Na}]^+$, 491.25 $[\text{M} - \text{H}]^-$. Anal. Calcd. for $\text{C}_{27}\text{H}_{28}\text{N}_2\text{O}_5\text{S}$, C, 65.83; H, 5.73; N, 5.69. Found C, 65.72; H, 5.27; N, 5.58.

Compound 11

The reaction was carried out following the general procedure as described for **1**. The product was obtained by crystallization from EtOAc/hexane as a white solid in 93% yield. R_f 0.59 (EtOAc/hexane, 4:1 v/v). R_t 17.62. Mp 96 °C. $[\alpha]_D^{22}$ +33.9 ($c = 0.1$ DMF). ^1H NMR (300 MHz, DMSO- d_6): δ 11.74 (s, 1H), 7.91 (d, $J=7.4$ Hz, 2H), 7.71 (d, $J=7.4$ Hz, 2H), 7.69-7.33(m, 5H), 4.38-4.20 (m, 3H), 3.97, (m, 1H), 3.61-3.28 (m, 4H), 1.98 (s, 3H), 1.10 (s, 9H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 169.9, 155.7, 144.1, 144.0, 141.0, 127.9, 127.3, 125.4, 120.4, 73.1, 65.7, 62.7, 52.9, 47.6, 46.9, 27.4, 23.5. ESMS calcd. for $\text{C}_{24}\text{H}_{30}\text{N}_2\text{O}_6\text{S}$ 474.18, found 475.18 $[\text{M} + \text{H}]^+$, 497.35 $[\text{M} + \text{Na}]^+$, 473.45 $[\text{M} - \text{H}]^-$. Anal. Calcd. for $\text{C}_{24}\text{H}_{30}\text{N}_2\text{O}_6\text{S}$, C, 60.74; H, 6.37; N, 5.90. Found C, 60.58; H, 6.33; N, 5.82.

Compound 12

The reaction was carried out following the general procedure as described for **1**. The product was obtained by crystallization from EtOAc/hexane as a white solid in 94% yield. R_f 0.66 (EtOAc/hexane, 4:1 v/v). R_t 18.82. Mp 157 °C. $[\alpha]_D^{22} +32.7$ ($c = 0.1$ DMF). ^1H NMR (300 MHz, DMSO- d_6): δ 12.21 (s, 1H), 7.93 (m, 4H), 7.64-7.32 (m, 10H), 4.13 (m, 4H), 3.77 (m, 2H), 3.39-3.19 (m, 2H) 1.07 (s, 9H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 167.0, 156.1, 144.6, 144.3, 141.4, 133.8, 132.4, 129.2, 128.3, 127.8, 125.9, 120.8, 73.6, 66.1, 63.1, 53.8, 48.2, 47.3, 27.9. ESMS calcd. for $\text{C}_{29}\text{H}_{32}\text{N}_2\text{O}_6\text{S}$ 536.20, found 537.35 $[\text{M} + \text{H}]^+$, 559.40 $[\text{M} + \text{Na}]^+$, 535.45 $[\text{M} - \text{H}]^-$.

Compound 13

Boc-Leu-SH was synthesized according to method B as described by Goldstein *et al.*^[2]

Compound 14

The reaction was carried out following the general procedure as described for **1**, Boc-Leu-SH (**13**) was added as a solution in DMF. The product was obtained by

crystallization from EtOAc/hexane as a white solid in 98% yield. R_f 0.31 (EtOAc/hexane/HOAc, 50:50:1 v/v/v). R_t 20.15. ^1H NMR (300 MHz, DMSO- d_6): δ 11.94 (s, 1H), 7.91 (d, $J=7.4$ Hz, 2H), 7.69 (d, $J=7.4$ Hz, 2H), 7.49-7.30 (m, 5H), 7.21 (d, $J=7.1$ Hz, 1H), 4.34 (d, $J=7.1$ Hz, 2H), 4.24 (m, 1H), 4.02 (m, 1H), 3.48-3.36 (m, 4H), 1.63-1.24 (m, 3H), 1.38 (s, 9H), 0.86 (m, 6H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 173.7, 156.1, 155.8, 144.0, 141.0, 127.9, 127.3, 125.4, 120.4, 53.4, 51.6, 46.9, 35.1, 31.2, 31.2, 28.4, 24.5, 23.2, 21.3. ESMS calcd. for $\text{C}_{28}\text{H}_{37}\text{N}_3\text{O}_7\text{S}$ 559.24, found 560.55 $[\text{M} + \text{H}]^+$, 582.40 $[\text{M} + \text{Na}]^+$, 558.50 $[\text{M} - \text{H}]^-$.

Compound 15

Boc-Val-Gly-SH was synthesized according to method B as described by Goldstein *et al.*^[2] The product was obtained as a white solid in quantitative yield. R_f 0.19 (EtOAc/hexane/HOAc, 50:50:1 v/v/v). R_t 15.37. Mp 87 °C. $[\alpha]_D^{23} -12.7$ ($c = 0.1$ DMF). ^1H NMR (300 MHz, CDCl_3): δ 6.97 (broad s, 1H), 5.13, (d, $J=8.5$ Hz, 1H), 4.23 (d, $J=5.6$ Hz, 2H) 4.02, (m, 1H), 2.21 (m, 1H), 1.45 (s, 9H), 0.99 (m, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 196.0, 172.8, 156.1, 80.0, 59.7, 50.3, 30.7, 28.2, 19.2, 17.9. Anal. Calcd. for $\text{C}_{12}\text{H}_{22}\text{N}_2\text{O}_4\text{S}$, C, 49.63; H, 7.64; N, 9.65. Found C, 49.78; H, 7.57; N, 9.53.

Compound 16

The reaction was carried out following the general procedure as described for **1**, Boc-Val-Gly-SH (**15**) was added as a solid. The product was obtained by crystallization from EtOAc/hexane as a white solid in 98% yield. R_f 0.48 (EtOAc/hexane/HOAc, 50:50:1 v/v/v). R_t 17.08. Mp 191 °C. $[\alpha]_D^{23}$ -29.9 (c = 0.1 DMF). ^1H NMR (300 MHz, DMSO- d_6): δ 11.89 (s, 1H), 8.16 (m, 1H), 7.53 (d, $J=9.1$ Hz, 1H), 7.34-7.17 (m, 10H) 6.75 (d, $J=9.1$ Hz, 1H), 4.98 (m, 2H), 4.18 (m, 1H), 3.84 (m, 3H), 3.59 (m, 2H), 2.90 (m, 1H), 2.78 (m, 1H), 1.99 (m, 1H), 1.38, (s, 9H), 0.86 (m, 6H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 172.1, 169.2, 155.7, 155.4, 137.9, 137.3, 129.4, 128.5, 127.9, 127.6, 127.2, 126.6, 78.2, 65.3, 60.0, 59.7, 56.1, 48.4, 42.3, 30.6, 28.4, 19.4, 18.3. ESMS calcd. for $\text{C}_{29}\text{H}_{40}\text{N}_4\text{O}_8\text{S}$ 604.26, found 605.55 $[\text{M} + \text{H}]^+$, 627.50 $[\text{M} + \text{Na}]^+$. Anal. Calcd. for $\text{C}_{29}\text{H}_{40}\text{N}_4\text{O}_8\text{S}$, C, 57.60; H, 6.67; N, 9.27. Found C, 57.52; H, 6.65; N, 9.21.

Compound **17**

To a mixture of **3** (90 mg, 0.30 mmol) and DiPEA (99 μL , 0.60 mmol, 2 equiv) in DMF (5 mL) allyl bromide (26 μL , 0.30 mmol, 1equiv) was added. The reaction mixture was allowed to stir for 16 h at room temperature and subsequently concentrated to dryness. The residue was redissolved in EtOAc (100 mL) and washed with KHSO_4 (1 N, 50 mL, twice) and Brine (50 mL, twice) and dried (Na_2SO_4). After removal of the solvent the product was isolated by column chromatography (EtOAc/hexane) as a clear oil in 75% yield. R_f 0.27 (EtOAc/hexane, 1:1 v/v). R_t 16.95. ^1H NMR (300 MHz, CDCl_3): δ 7.35 (m, 5H), 5.83 (m, 1H), 5.46 (m, 1H), 5.29 (m, 2H) 5.10 (s, 2H), 4.32 (d, $J=5.2$ Hz, 2H), 3.65 (m, 4H), 2.28 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 171.5, 156.4,

136.4, 132.6, 132.6, 128.8, 128.5, 128.4, 118.7, 67.3, 54.9, 49.0, 35.8, 24.4. ESMS calcd. for $C_{15}H_{20}N_2O_5S$ 340.11, found 363.40 $[M + Na]^+$.

Compound 18

To a mixture of **3** (90 mg, 0.30 mmol) and DiPEA (99 μ L, 0.60 mmol, 2 equiv) in DMF (5 mL) tert-butyl bromoacetate (44 μ L, 0.30 mmol, 1 equiv) was added. The reaction mixture was allowed to stir for 16 h at room temperature and subsequently concentrated to dryness. The residue was redissolved in EtOAc (100 mL) and washed with $KHSO_4$ (1 N, 50 mL, twice) and Brine (50 mL, twice) and dried (Na_2SO_4). After removal of the solvent the product was isolated by column chromatography (EtOAc/hexane) as a clear oil in 94% yield. R_f 0.40 (EtOAc/hexane, 1:1 v/v). R_t 18.58. 1H NMR (300 MHz, $CDCl_3$): δ 7.34 (m, 5H), 5.77 (m, 1H), 5.10 (s, 2H), 4.38 (s, 2H), 3.75 (m, 4H), 2.30 (m, 3H), 1.47 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 168.1, 156.5, 136.5, 128.8, 128.4, 128.3, 83.7, 67.2, 55.1, 47.9, 35.8, 28.2, 24.3. ESMS calcd. for $C_{18}H_{26}N_2O_7S$ 414.15, found 437.25 $[M + Na]^+$.

Compound 19

To a mixture of **16** (90 mg, 0.15 mmol) and DiPEA (50 μ L, 0.30 mmol, 2 equiv) in DMF (2.5 mL) allyl chloroacetate (18 μ L, 0.30 mmol, 1 equiv) was added. The reaction mixture was allowed to stir for 16 h at room temperature. Since the reaction was not complete KI (25 mg, 0.15 mmol, 1 equiv) was added followed by the addition of allyl chloroacetate (18 μ L, 0.30 mmol, 1 equiv) and DiPEA (50 μ L, 0.30 mmol, 2 equiv) and the mixture was allowed to react at an elevated temperature of 40°C for 16 h. Then, the reaction mixture was concentrated to dryness and, the residue was redissolved in EtOAc (100 mL) and subsequently washed with KHSO₄ (1 N, 50 mL, twice) and brine (50mL, twice) and dried (Na₂SO₄). After removal of the solvent the product was isolated by column chromatography (EtOAc/hexane) as an off white solid in 35% yield. *R*_f 0.55 (EtOAc/hexane, 1:1 v/v). *R*_t 20.80. Mp 173 °C. $[\alpha]_D^{23}$ -14.1 (c = 0.1 DMF). ¹H NMR (500 MHz, DMSO-d₆): δ 8.20 (m, 1H), 7.54 (d, *J*=8.5 Hz, 1H), 7.33-6.70 (m, 10H), 6.68 (d, *J*=8.9 Hz, 1H), 5.90 (m, 1H), 5.36-5.24 (m, 2H), 4.96 (s, 2H), 4.62 (m, 2H), 4.51 (s, 2H), 4.34-4.16 (m, 4H), 3.85 (m, 2H), 2.87 (m, 1H) 2.80 (m, 1H), 1.96 (m, 1H) 1.38, (s, 9H), 0.87 (m, 6H). ¹³C NMR (75 MHz, DMSO-d₆) δ 172.2, 170.0, 168.1, 155.7, 155.5, 137.6, 137.3, 132.2, 129.5, 128.5, 127.9, 127.6, 127.3, 126.7, 118.4, 78.2, 65.7, 65.3, 59.7, 57.3, 48.3, 46.9, 42.7, 30.6, 28.4, 19.4, 18.3. ESMS calcd. for C₃₄H₄₆N₄O₁₀S 702.29, found 703.55 [M + H]⁺ 725.55 [M + Na]⁺. Anal. Calcd. for C₃₄H₄₆N₄O₁₀S, C, 58.10; H, 6.60; N, 7.97. Found C, 57.94; H, 6.57; N, 7.88.

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