

Electronic Supplementary Information

A novel multifunctional coupler; Concept of coupling and proof of principle

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1 Experimental Part

1.1 Materials

D,L-homocysteine thiolactone hydrochloride (HCTL·HCl, 99%, ABCR), glycerol carbonate chloroformate, N,N-diisopropylethylamine (DIPEA, 99%, ABCR), hexyl amine (99%, Sigma Aldrich), methyl acrylate (MA, 99%, Sigma Aldrich), triethylamine ($\geq 99\%$, Sigma Aldrich), 3-(dimethylamino)-1-propylamine (99%, Acros Organics), α -bromoisobutyryl bromide (98%, Sigma Aldrich) were used without further purification. Unless otherwise indicated, all solvents were purchased from commercial sources and were used without further purification. All reactions were performed under an Argon atmosphere, unless otherwise noted. Argon (Linde) was passed over molecular sieves (4 Å) and finely dispersed potassium on aluminum oxide before use.

1.2 Measurements

^1H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 FT NMR spectrometer (400 MHz and 100 MHz, respectively) and are reported as follows: chemical shift δ (ppm) (multiplicity, coupling constant J (Hz), number of protons, assignment). Dimethylsulfoxide (DMSO, $\delta_{\text{H}} = 2.50$ ppm, $\delta_{\text{C}} = 39.5$ ppm) was used as an internal standard. Chemical shifts are reported in ppm to the nearest 0.01 ppm for ^1H and the nearest 0.1 ppm for ^{13}C .

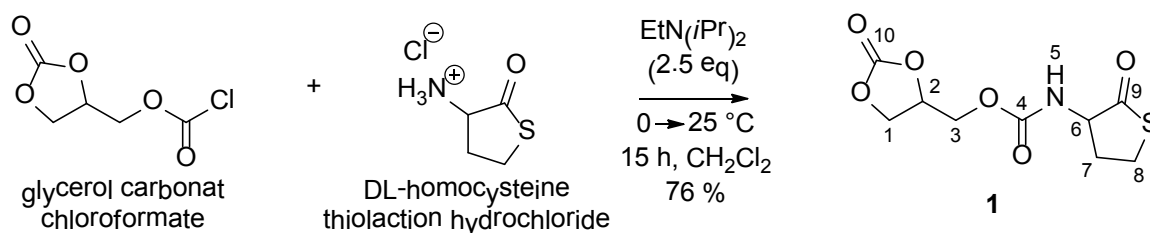
Infrared spectra were carried out on a ThermoNicolet FT-IR Nexus spectrometer and are recorded between KBr disks or using an ATR unit (ThermoNicolet, Smart SplitPEA). Transmission maxima are reported in wavenumbers (cm^{-1}) and only selected intensities are reported.

Mass spectra were recorded on a Finnigan SSQ 7000 spectrometer and HRMS spectra on a Thermo Scientific LTQ Orbitrap XL spectrometer.

Differential scanning calorimetry (DSC) analysis was performed on a Netzsch DSC 204 'Phoenix' (Netzsch, Selb, Germany) under nitrogen atmosphere using a scan rate of $10 \text{ K}\cdot\text{min}^{-1}$. For mp the inflexion point was selected.

1.3 Syntheses

1.3.1 Synthesis of the coupler (1)



To a stirred suspension of DL-homocysteine thiolactone hydrochloride (5 g, 32.5 mmol) and glycerol carbonate chloroformate (5.876 g, 32.5 mmol) in CH_2Cl_2 (40 mL) at $0 \text{ }^\circ\text{C}$ was added slowly (8 mL/h) ethyl-diisopropylamine (14 mL, 81.4 mmol). The reaction mixture was allowed to warm slowly to room temperature and stirred at room temperature for 15 h. The organic layer was washed with 1M $\text{HCl}_{(\text{aq})}$ (2 x 20 mL). Then, the aqueous layer was extracted with CH_2Cl_2 (5 x 15 mL). The combined organic layers were dried (MgSO_4), the solvent was evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica gel with EtOAc-DCM (3:1) as eluent, gave the urethane **1** (6.411, 76%) as a

colorless oil. Mp 162.8 °C; ^1H NMR (400 MHz, DMSO) δ = 7.80 (d, J = 8.6 Hz, 1H, H5), 5.14 – 4.90 (m, 1H, H2), 4.57 (td, J = 8.6, 2.6 Hz, 1H, H3), 4.43 – 4.32 (m, 1H, H6), 4.31 – 4.17 (m, 3H, H1 and H3), 3.45 – 3.36 (m, 1H, H8), 3.26 (dd, J = 10.6, 6.8 Hz, 1H, H8), 2.46 – 2.37 (m, 1H, H7), 2.18 – 2.03 (m, 1H, H7). ^{13}C NMR (101 MHz, DMSO) δ = 205.5 (C9), 155.5 (C4), 154.7 (C10), 74.7 (C2), 65.8 (C3), 63.6 (C1), 59.9 (C6), 29.7 (C7), 26.4 (C8). IR (KBr) 3297 (NH), 3077, 2926, 1777 ($\text{O}_2\text{C}=\text{O}$), 1732 (CONH), 1720, 1690 (COS), 1556, 1407, 1298, 1273, 1252, 1193, 1176, 1070, 920, 850, 773 cm^{-1} . HRMS (ESI) m/z for $\text{C}_9\text{H}_{11}\text{NO}_6\text{S}$ ($\text{M} + \text{H}$) $^+$ 262.0370, ($\text{M} + \text{Na}$) $^+$ 284.0188.

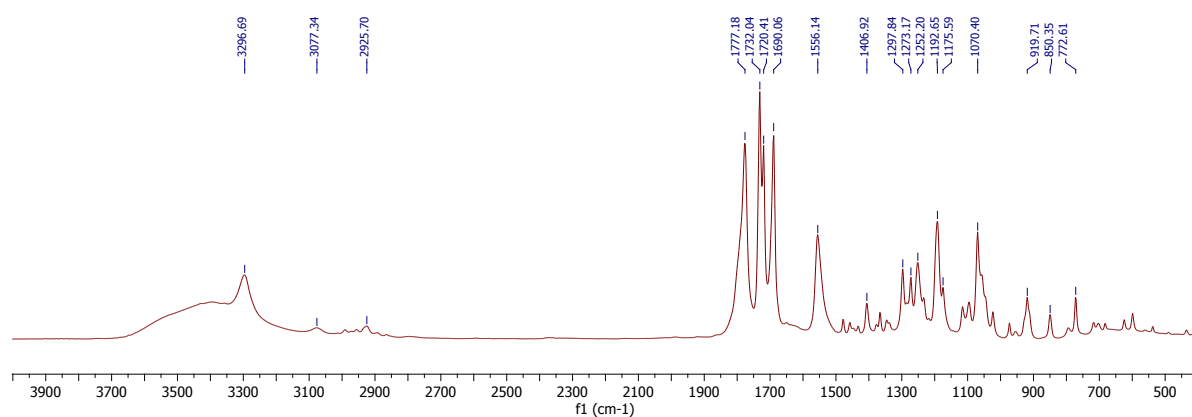


Fig. S1 FTIR spectrum of multifunctional coupler **1**.

The precipitate, which occurred after the reaction time, was assumed to be ethyl-diisopropylamine hydrochloride. Therefore, it was initially included into the workup. Later by filtration it was investigated separately and turned out to be a mixture of remaining ethyl-diisopropylamine hydrochloride and the RR/SS diastereomer. The partially precipitated but pure RR/SS diastereomer **1** was obtained washing this mixture with CH_2Cl_2 and 1M $\text{HCl}_{(\text{aq})}$. The RS/SR diastereomers could be accumulated via flash column chromatography.

^{13}C NMR spectra were recorded of both diastereomers (RR/SS and RS/SR) to trace subtle differences. Different chemical shifts could be observed for signal 4 and 1.

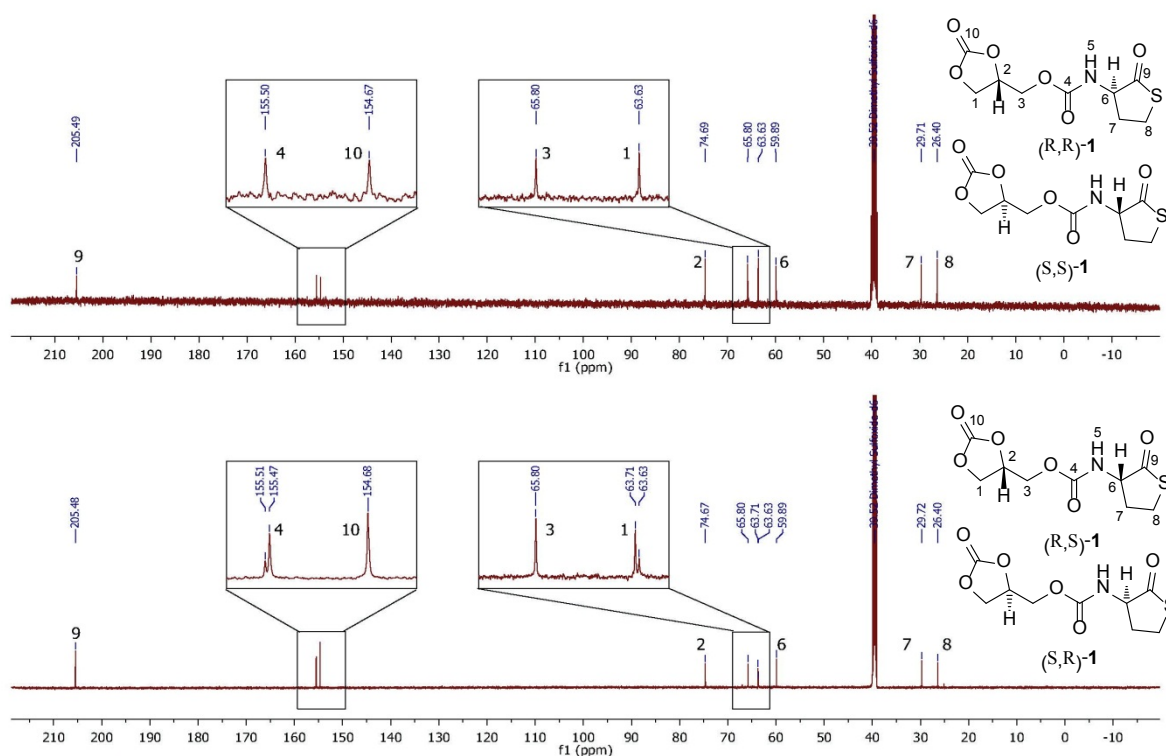
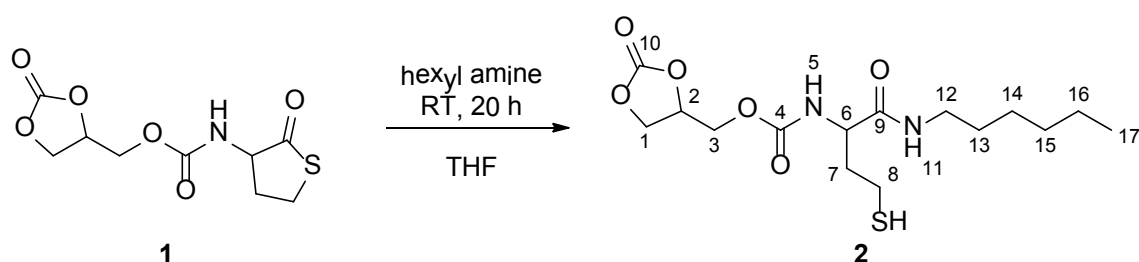


Fig. S2 Comparison of the ^{13}C NMR spectra of the RR/SS- (up) and the RS/SR diastereomers (down).

The RR/SS diastereomers shows the urethane carbon at $\delta = 155.51$ ppm, whereas the same signal for the RS/SR diastereomers appears at $\delta = 155.47$ ppm. The methylene carbon 1 of the RR/SS diastereomers can be found at $\delta = 63.63$ ppm. For the RS/SR diastereomers this signal is shifted to $\delta = 63.71$ ppm. Since the spectra of the RS/SR diastereomers is not entirely pure, a small peak of the RR/SS diastereomers can be observed, which allows the distinction of both mixtures of enantiomers.

1.3.2 Synthesis of the thiol (2)



Hexyl amine (630 μ L, 4.8 mmol) was added to a stirred solution of **1** (1.246 g, 4.8 mmol) in DMF (14 mL) at room temperature. The reaction mixture was stirred at room temperature for 20 h. Then, the solvent was evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on silica gel with EtOAc-CH₂Cl₂-MeOH (9:1:0.1) as eluent gave thiol **2** (1.095 g, 63 %) as a colorless oil. ¹H NMR (400 MHz, DMSO) δ = 7.92 (br. t, J = 5.4 Hz, 1H, H11), 7.61 (dd, J = 7.9, 5.3 Hz, 1H, H5), 5.11 – 5.02 (m, 1H, H2), 4.62 (t, J = 8.5 Hz, 1H, H3), 4.37 – 4.18 (m, 3H, H3 and H1), 4.14 – 4.03 (m, 1H, H6), 3.19 – 2.97 (m, 2H, H12), 2.55 – 2.43 (m, 2H, H8), 2.38 (td, J = 7.8, 3.6 Hz, 1H, SH), 1.99 – 1.78 (m, 2H, H7), 1.49 – 1.38 (m, 2H, H13), 1.38 – 1.26 (m, 6H, H14 and H15 and H16), 0.92 (t, J = 6.8 Hz, 3H, H17). ¹³C NMR (101 MHz, DMSO) δ = 170.9 (C9), 155.5 (C4), 154.7 (C10), 74.8 (C2), 65.8 (C3), 63.4 (C1), 53.7 (C6), 38.5 (C12), 36.3 (C7), 30.9 (C14), 29.0 (C13), 26.0 (C15), 22.1 (C16), 20.5 (C8), 13.9 (C17). IR (KBr) 3308, 3083 (NH), 2956, 2930, 2858, 2563 (SH), 1794 (O₂C=O), 1723 (OCONH), 1657 (CONH), 1536, 1443, 1393, 1244, 1173, 1100, 1057, 772, 716, 661 cm⁻¹. HRMS (ESI) m/z for C₁₅H₂₆N₂O₆S (M + H)⁺ 363.1575, (M + Na)⁺ 385.1395.

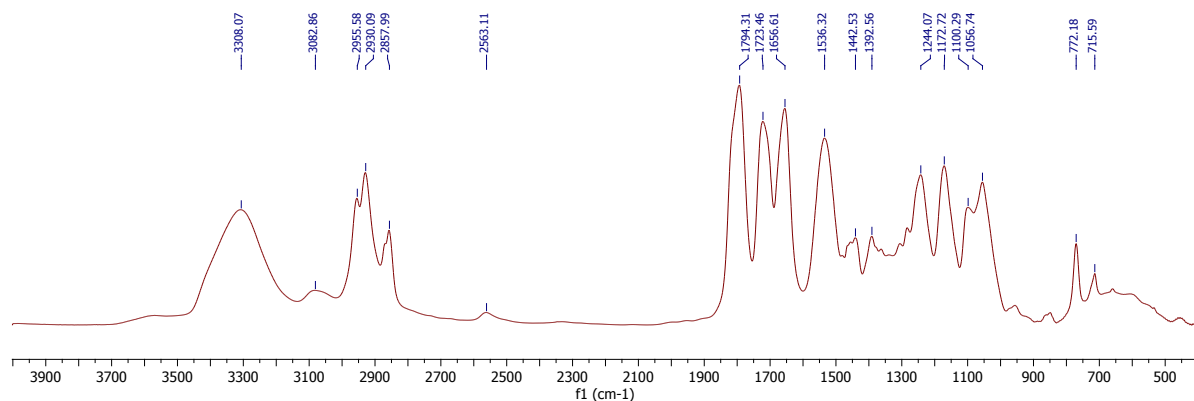


Fig. S3 FTIR spectrum of thiol **2**.

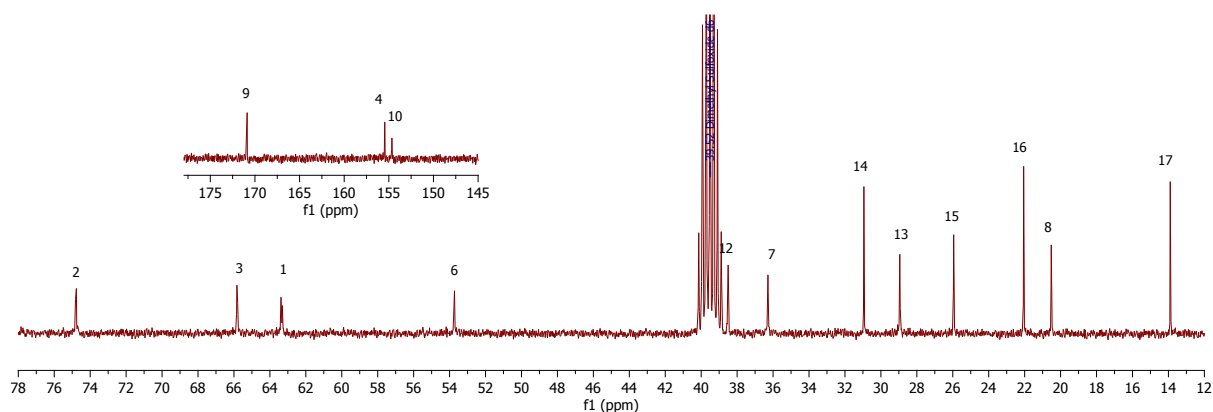
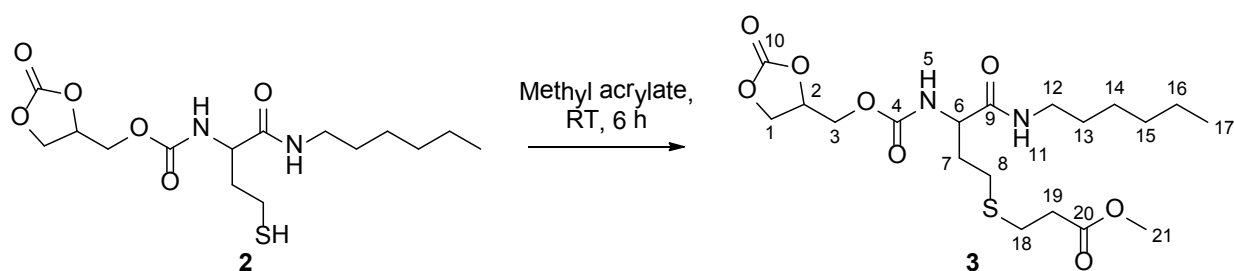


Fig. S4 ¹³C NMR spectrum of thiol **2**.

1.3.3 Synthesis of the thioether (**3**)



Methyl acrylate (2.9 mL, 32.0 mmol) and Et₃N (10 μL, 0.064 mmol) were added to a stirred solution of **2** (2.317 g, 6.4 mmol) in THF (12 mL) at room temperature. The reaction mixture was stirred at room temperature for 6 h. Then, the solvent was evaporated under reduced pressure to give the crude product. Purification by flash

column chromatography on silica gel with EtOAc-CH₂Cl₂-MeOH (9:1:0.1) as eluent gave thioether **3** (1.462 g, 51 %) as a colorless oil. ¹H NMR (400 MHz, DMSO) δ = 7.85 (br. t, *J* = 5.4 Hz, 1H, H11), 7.58 (dd, *J* = 7.8, 4.9 Hz, 1H, H5), 5.06 – 4.92 (m, 1H, H2), 4.56 (t, *J* = 8.5 Hz, 1H, H3), 4.30 – 4.12 (m, 3H, H3 and H1), 4.06 – 3.94 (m, 1H, H6), 3.61 (s, 3H, H21), 3.14 – 2.94 (m, 2H, H12), 2.75 – 2.63 (m, 2H, H19), 2.63 – 2.55 (m, 2H, H18), 2.51 – 2.39 (m, 2H, H8), 1.90 – 1.70 (m, 2H, H7), 1.46 – 1.31 (m, 2H, H13), 1.31 – 1.17 (m, 6H, H14 and H15 and H16), 0.86 (t, *J* = 6.8 Hz, 3H, H17). ¹³C NMR (101 MHz, DMSO) δ = 171.9 (C20), 170.9 (C9), 155.5 (C4), 154.7 (C10), 74.7 (C2), 65.8 (C3), 63.3 (C1), 54.0 (C6), 51.4 (C21), 38.4 (C12), 34.1 (C18), 32.1 (C7), 30.9 (C14), 28.9 (C13), 27.4 (C8), 26.0 (C19), 25.9 (C15), 22.0 (C16), 13.9 (C17). IR (KBr) 3319, 2955, 2930, 2858, 1797 (O₂C=O), 1731 (OCOO and OCONH), 1659 (CONH), 1535, 1439, 1362, 1246, 1172, 1096, 1056, 772, 716 cm⁻¹. HRMS (ESI) *m/z* for C₁₉H₃₂N₂O₈S (M + H)⁺ 449.1921, (M + Na)⁺ 471.1739.

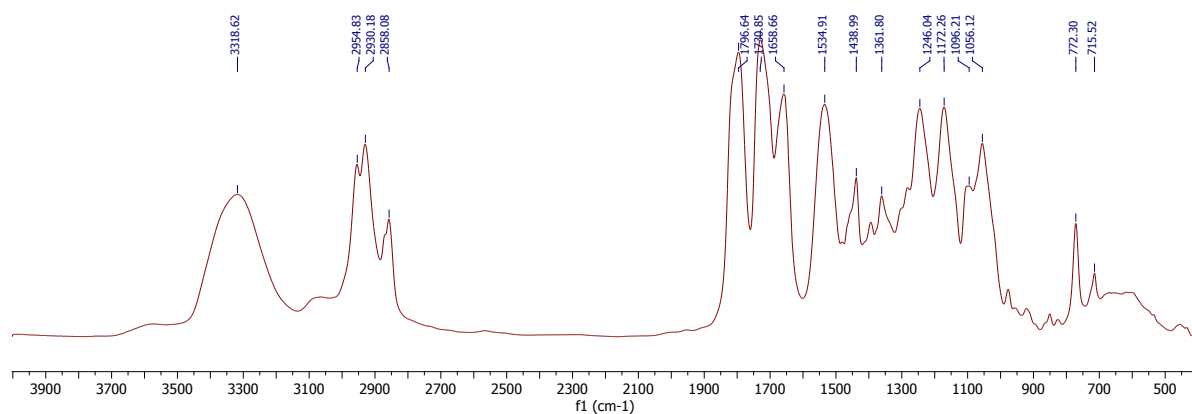


Fig. S5 FTIR spectrum of thioether **3**.

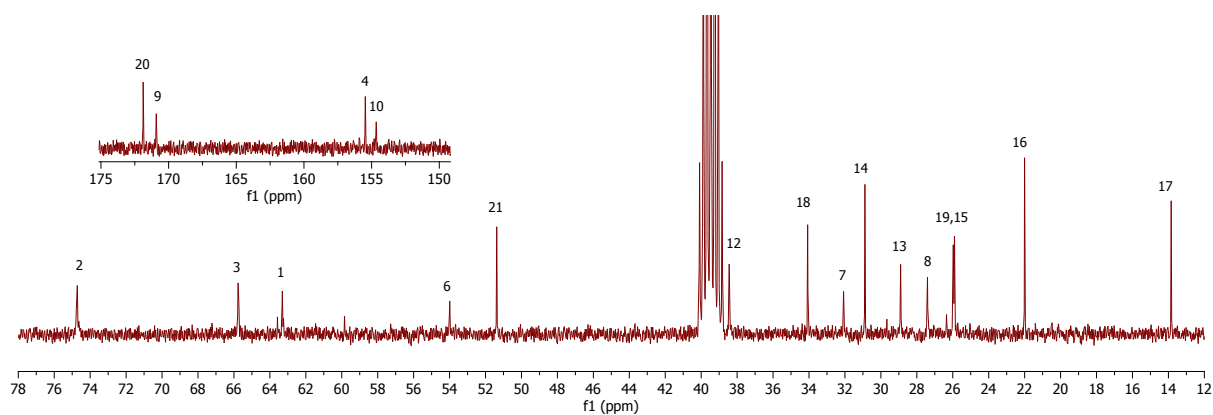
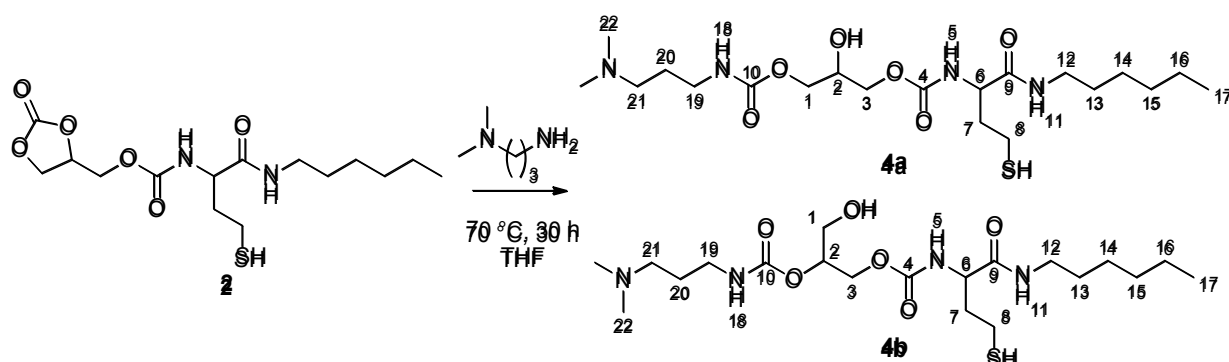


Fig. S6 ¹³C NMR spectrum of thioether 3.

1.3.4 Synthesis of the thiol-alcohol (4a/4b)



3-(Dimethylamino)-propylamine (450 μ L, 3.6 mmol) was added to a stirred solution of **2** (1.301 g, 3.6 mmol) in THF (11 mL) at 70 °C. The reaction mixture was stirred at 70 °C for 30 h. Then, the solvent was evaporated under reduced pressure to give the crude product, which contained an 82:18 mixture of isomeric alcohols **4a** and **4b** (by ¹H NMR spectroscopy). Purification by flash column chromatography on aluminum oxide with CH₂Cl₂-MeOH (9:1) as eluent gave a 82:18 mixture (by ¹H NMR spectroscopy) of alcohols **4a** and **4b** (1.016 g, 61 %) as a colorless oil. ¹H NMR (400 MHz, DMSO) δ = 7.85 (s, 1H, H11), 7.45 – 7.27 (m, 1H, H5), 7.14 (br. t, J = 4.8 Hz, 1H, H18), 5.12 (d, J = 4.9 Hz, 0.82H, OH^a), 4.89 (dd, J = 10.8, 5.0 Hz, 0.18H, OH^b), 4.76 (br. s, 0.18H, H2b), 4.26 – 4.07, 3.99 – 3.83 (m, 0.36H, H3b), 4.06 – 3.95 (m, 1H, H6), 3.99 – 3.83 (m, 3.28H, H1a and H3a), 3.86 – 3.71 (m, 0.82H, H2a), 3.53 –

3.44 (m, 0.32H, H1b), 3.13 – 2.90 (m, 4H, H12 and H19), 2.53 – 2.38 (m, 2H, H8), 2.33 (t, $J = 7.1$ Hz, 1H, SH), 2.18 (t, $J = 7.1$ Hz, 2H, H21), 2.10 (s, 6H, H22), 1.91 – 1.73 (m, 2H, H7), 1.59 – 1.45 (m, 2H, H20), 1.45 – 1.32 (m, 2H, H13), 1.32 – 1.14 (m, 6H, H14 and H15 and H16), 0.86 (t, $J = 6.2$ Hz, 3H, H17). ^{13}C NMR (101 MHz, DMSO) $\delta = 171.1$ (C9), 156.2 (C4), 156.0 (C10), 72.3 (C2b), 67.0 (C2a), 65.4 (C1a), 65.1 (C3a), 63.8 (C3b), 60.0 (C1b), 56.6 (C21), 53.7 (C6), 45.1 (C22), 38.6 (C19 and C12), 36.4 (C7), 31.0 (C14), 29.0 (C13), 27.4 (C20), 26.0 (C15), 22.1 (C16), 20.6 (C8), 13.96 (C17). IR (ATR) 3313 (NH), 3079, 2953, 2932, 2859, 2821, 2779, 2559 (SH), 1705 (CONH), 1660 (CONH), 1538, 1464, 1252, 1145, 1051, 776 cm^{-1} . HRMS (ESI) m/z for $\text{C}_{20}\text{H}_{40}\text{N}_4\text{O}_6\text{S}$ ($\text{M} + \text{H}$) $^+$ 465.2727.

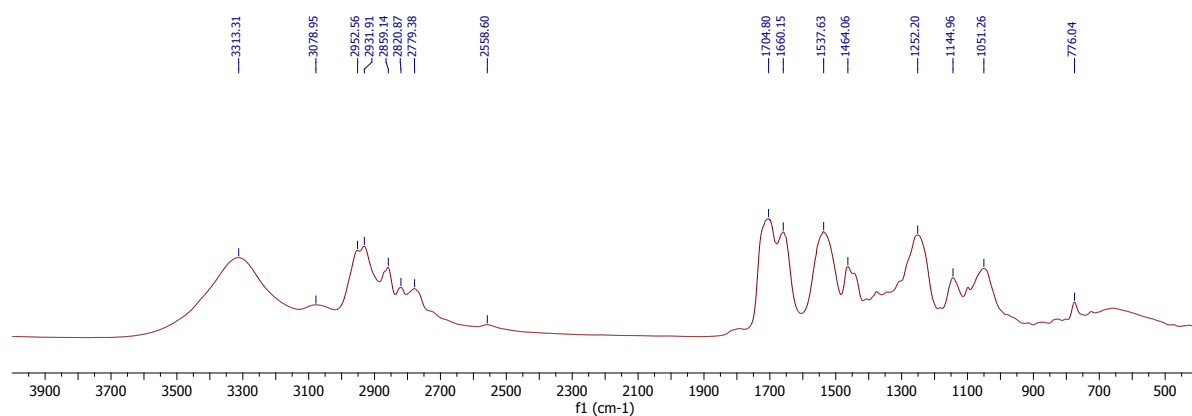


Fig. S7 FTIR spectrum of thiol-alcohol **4a/b**.

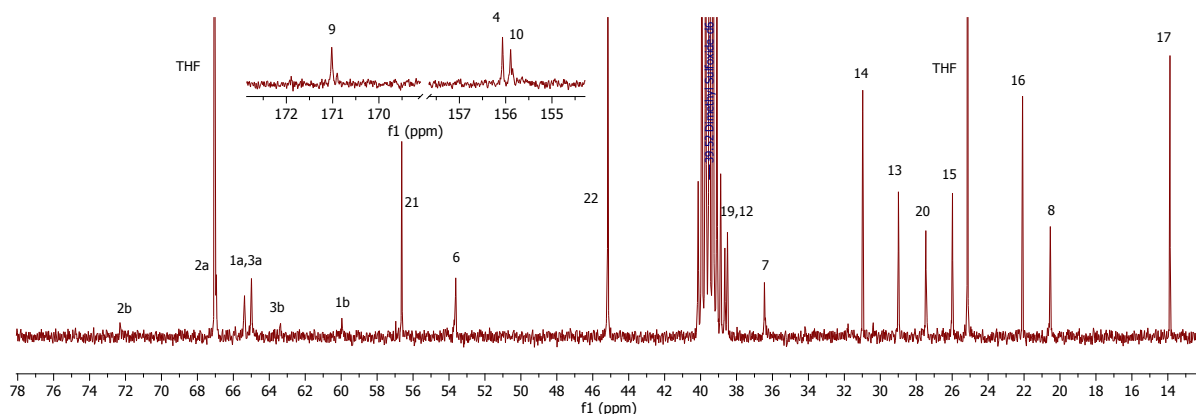
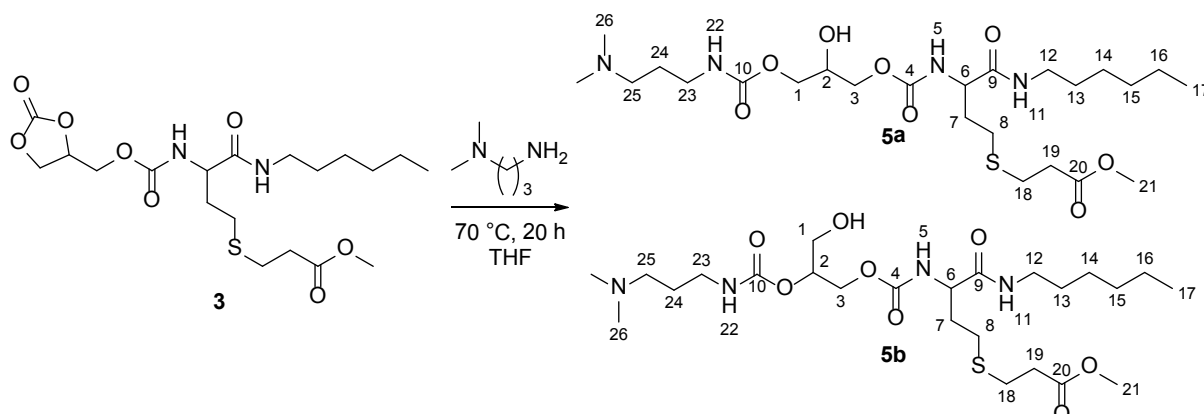


Fig. S8 ^{13}C NMR of thiol-alcohol **4a/b**.

1.3.5 Synthesis of the alcohol (**5a/5b**)



3-(Dimethylamino)-propylamine (535 μl , 4.2 mmol) was added to a stirred solution of **3** (1.902 g, 4.2 mmol) in THF (12 mL) at 70 $^{\circ}\text{C}$. The reaction mixture was stirred at 70 $^{\circ}\text{C}$ for 20 h. Then, the solvent was evaporated under reduced pressure to give the crude product, which contained an 80:20 mixture of isomeric alcohols **5a** and **5b** (by ^1H NMR spectroscopy). Purification by flash column chromatography on aluminum oxide with CH_2Cl_2 -MeOH (9:1) as eluent gave a 80:20 mixture (by ^1H NMR spectroscopy) of alcohols **5a** and **5b** (0.765 g, 37 %) as a colorless oil. ^1H NMR (400 MHz, DMSO) δ = 7.83 (br. t, J = 4.7 Hz, 1H, H11), 7.34 (d, J = 8.0 Hz, 1H, H5), 7.14 (t, J = 5.4 Hz, 1H, H22), 5.11 (d, J = 5.0 Hz, 0.80H, OH^{a}), 4.89 (dd, J = 11.2, 5.8 Hz, 0.20H, OH^{b}), 4.75 (br. s, 0.18H, H2b), 4.23 – 4.09, 3.98 – 3.84 (m, 0.40H, H3b), 4.03 – 3.84 (m, 1H, H6), 3.98 – 3.84 (m, 3.20H, H1a and H3a), 3.84 – 3.73 (m, 0.80H,

H2a), 3.60 (s, 3H, H21), 3.48 (br. s, 0.40H, H1b), 3.13 – 2.90 (m, 4H, H12 and H23), 2.75 – 2.64 (m, 2H, H19), 2.63 – 2.54 (m, 2H, H18), 2.51 – 2.38 (m, 2H, H8), 2.17 (t, $J = 7.1$ Hz, 2H, H25), 2.09 (s, 6H, H26), 1.90 – 1.66 (m, 2H, H7), 1.57 – 1.45 (m, 2H, H24), 1.44 – 1.32 (m, 2H, H13), 1.32 – 1.14 (m, 6H, H14 and H15 and H16), 0.86 (t, $J = 6.7$ Hz, 3H, H17). ^{13}C NMR (101 MHz, DMSO) $\delta = 171.9$ (C20), 171.1 (C9), 156.1 (C4), 155.9 (C10), 72.2 (C2b), 66.9 (C2a), 65.3 (C1a), 64.9 (C3a), 63.5 (C3b), 60.3 (C1b), 56.5 (C25), 53.9 (C6), 51.4 (C21), 45.1 (C26), 38.6 (C23), 38.4 (C12), 34.1 (C18), 32.2 (C8), 30.9 (C14), 28.9 (C13), 27.4 (C24 and C7), 26.0 (C19 and C15), 22.0 (C16), 13.9 (C17). IR (KBr) 3319 (NH), 3072, 2953, 2932, 2859, 2821, 2780, 1720 (CONH and OCOO), 1661 (CONH), 1537, 1462, 1439, 1359, 1249, 1145, 1050, 980, 829, 777, 661 cm^{-1} . HRMS (ESI) m/z for $\text{C}_{24}\text{H}_{46}\text{N}_4\text{O}_8\text{S}$ ($\text{M} + \text{H}^+$) 551.3095.

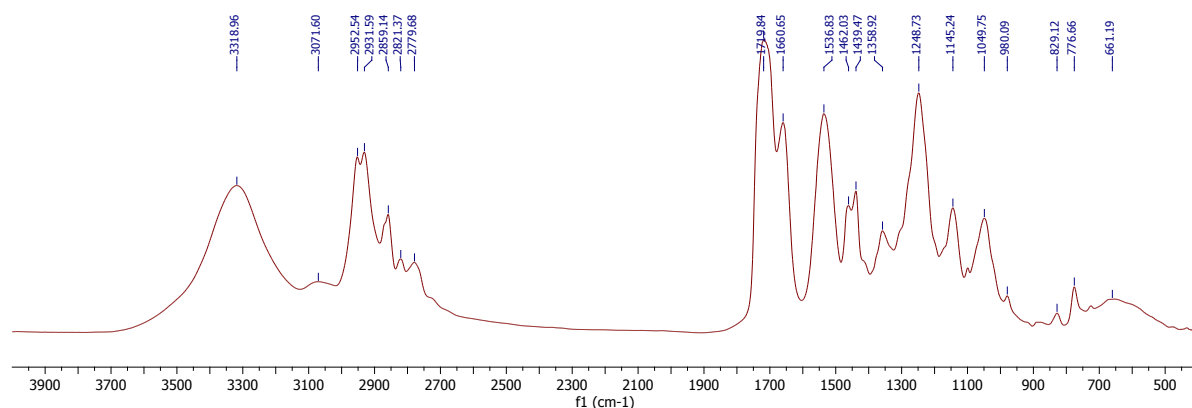


Fig. S9 FTIR spectrum of alcohol **5a/b**.

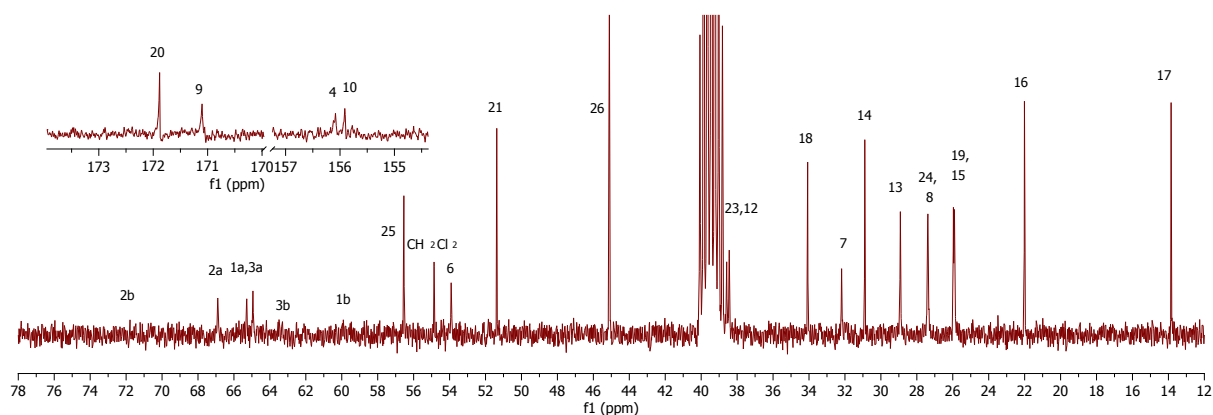
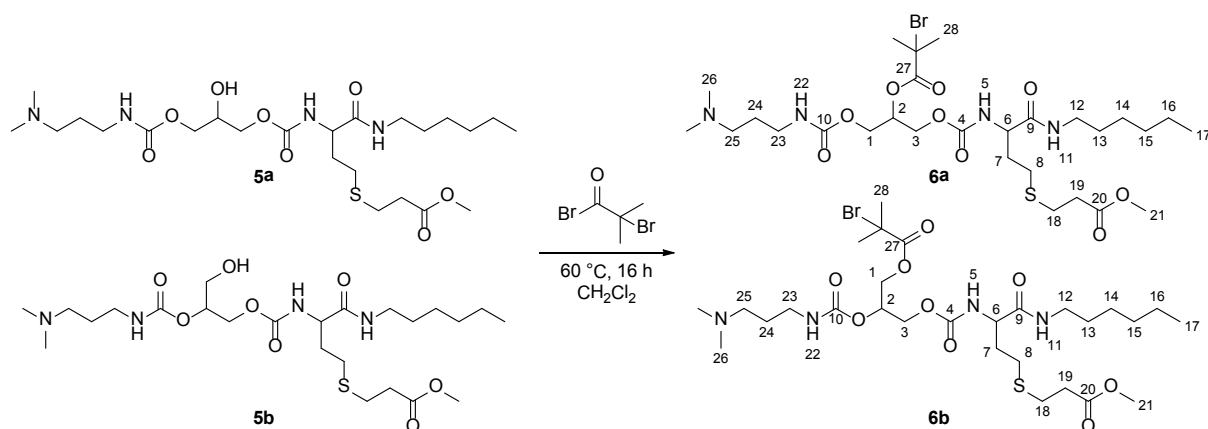


Fig. S10 ^{13}C NMR spectrum of alcohol **5a/b**.

1.3.6 Synthesis of the fully functionalized coupler (**6a/6b**)



α -Bromoisobutyryl bromide (140 μL , 1.1 mmol) was added to a stirred solution of **5a/b** (0.511 g, 0.9 mmol) in CH_2Cl_2 (5 mL) at room temperature. The reaction mixture was stirred at 60 $^\circ\text{C}$ for 20 h. Then, saturated $\text{NaCl}_{(\text{aq})}$ (5 mL) was added. The layers were separated, and the organic layer was washed with saturated $\text{NaCl}_{(\text{aq})}$ (5 mL). The aqueous layers were extracted with CH_2Cl_2 (5 x 5 mL). The combined organic layers were dried (MgSO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on aluminum oxide with CH_2Cl_2 -MeOH (9.8:0.2) as eluent gave the fully functionalized coupler **6** (0.294 g, 17%) as a light brown oil. ^1H NMR (400 MHz, DMSO) δ = 7.94 – 7.81 (m, 1H, H11),

7.57 – 7.45 (m, 1H, H5), 7.28 (br. t, $J = 5.1$ Hz, 1H, H22), 5.30 – 5.08 (m, 1H, H2), 4.45 – 4.09 (m, 4H, H1 and H3), 4.09 – 3.94 (m, 1H, H6), 3.66 (s, 3H, H21), 3.19 – 2.96 (m, 4H, H12 and H23), 2.82 – 2.70 (m, 2H, H19), 2.70 – 2.60 (m, 2H, H18), 2.56 – 2.43 (m, 2H, H8), 2.23 (t, $J = 7.1$ Hz, 2H, H25), 2.15 (s, 6H, H26), 1.93 (s, $J = 5.5$ Hz, 6H, H28), 1.90 – 1.74 (m, 2H, H7), 1.66 – 1.50 (m, 2H, H24), 1.43 (s, 2H, H13), 1.38 – 1.22 (m, 6H, H14 and H15 and H16), 0.92 (t, $J = 6.7$ Hz, 3H, H17). ^{13}C NMR (101 MHz, DMSO) $\delta = 171.9$ (C20), 171.0 (C9), 170.4 (C27), 155.7 (C4), 155.5 (C10), 71.9 (C2a), 69.2 (C2b), 62.2 (C1), 61.8 (C3), 56.9 (C28), 56.4 (C25), 54.0 (C6), 51.4 (C21), 44.9 (C26), 39.5 (C23 and C12), 34.1 (C18), 32.1 (C7), 31.0 (C14), 30.2 (C29), 29.0 (C13), 27.5 (C8), 27.1 (C24), 26.0 (C19 and C15), 22.1 (C16), 13.9 (C17). IR (KBr) 3292 (NH), 2955, 2858, 2678, 2511, 2471, 1725 (OCONH), 1662 (CONH), 1530, 1462, 1439, 1359, 1245, 1166, 1058, 980, 949, 814, 775, 726, 651 cm^{-1} . HRMS (ESI) m/z for $\text{C}_{28}\text{H}_{51}\text{BrN}_4\text{O}_9\text{S}$ ($\text{M} + \text{H}$) $^+$ 701.2602, ($\text{M} + \text{H} - \text{HBr}$) $^+$ 619.3359.

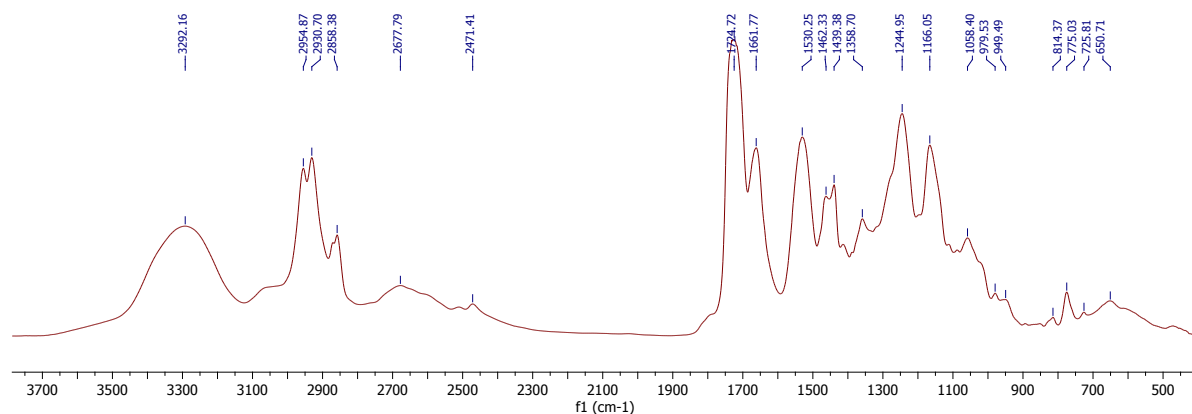


Fig. S11 FTIR spectrum of alcohol **6a/b**.

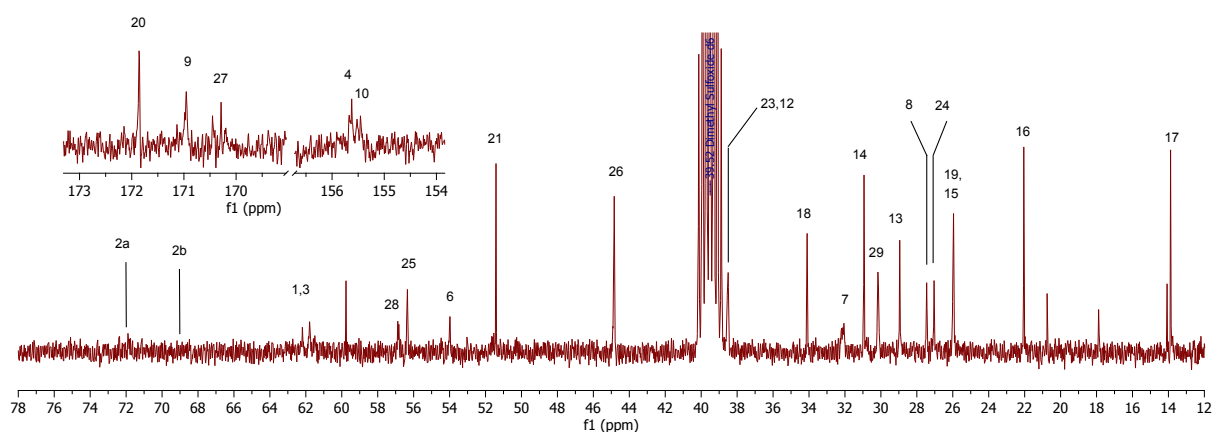
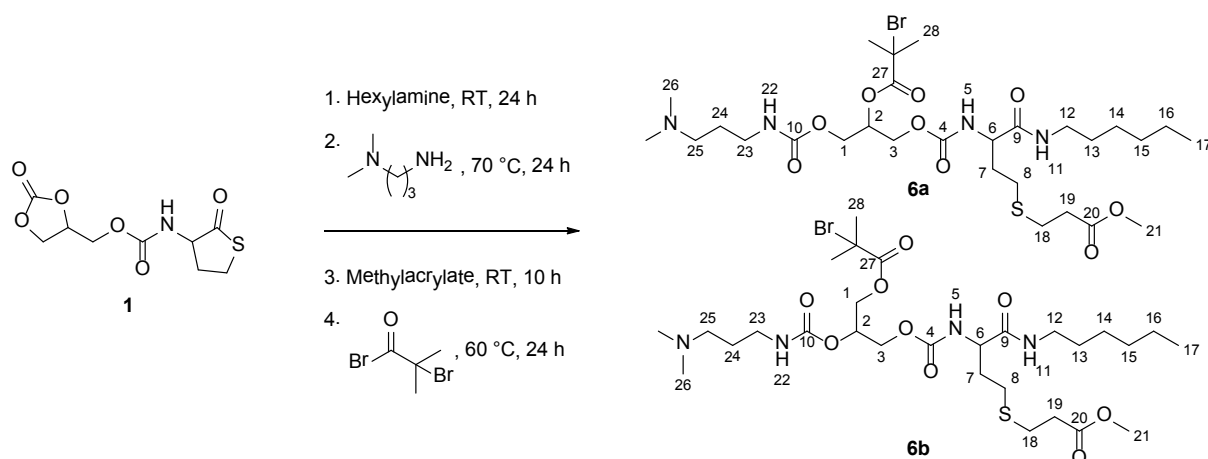


Fig. S12 ^{13}C NMR spectrum of the fully functionalized coupler **6a/b**.



Hexyl amine (379 μL , 2.9 mmol) was added to a stirred solution of the coupler **1** (0.801 mg, 2.9 mmol) in DMF (10 mL) at room temperature. The reaction mixture was stirred at room temperature for 24 h. Then, 3-(Dimethylamino)-propylamine (362 μL , 2.9 mmol) was added and the reaction mixture was stirred at 70 $^{\circ}\text{C}$ for 24 h. Next, methyl acrylate (1.3 mL, 14.4 mmol) and Et_3N (4 μL , 0.029 mmol) were added and the reaction mixture was stirred at room temperature for 24 h. The solvent and excess of methyl acrylate were evaporated under reduced pressure to give the crude alcohol (**5a/b**), which contained an 82:18 mixture of isomeric alcohols **5a** and **5b** (by ^1H NMR spectroscopy). Finally, α -bromoisobutyryl bromide (0.76 mL, 3.7 mmol) was

added to a stirred solution of **5a/b** in CH₂Cl₂ (10 mL) at 60 °C. The reaction mixture was stirred for 24 h at 60 °C. Then, 1 M NaOH_(aq) (20 mL) was added and the solution stirred for 10 minutes. The layers were separated. The organic layer was washed with 1 M NaOH_(aq) (2 x 20 mL). The aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL). All combined organic layers were dried (MgSO₄) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography on aluminum oxide with CH₂Cl₂-MeOH (10:0 → 9.8:0.2) as eluent gave the fully functionalized coupler (772 mg, 38%) as a light brown oil.

2 Crystallographic information for the RR/SS diastereomer of 1

Suitable crystals for single crystal X-ray diffraction were obtained by recrystallization from 2-butanone as colorless prisms. Intensity data were collected at 100 K on a Bruker D8 goniometer with a Bruker SMART APEX CCD detector in ω -scan mode using Mo-K α radiation ($\lambda = 0.71073 \text{ \AA}$) from an Incoatec microsource with multi layer optics. Temperature was controlled with an Oxford Cryostream 700. Data were processed with *SAINT*¹ and multi scan absorption corrections were applied with *SADABS*².

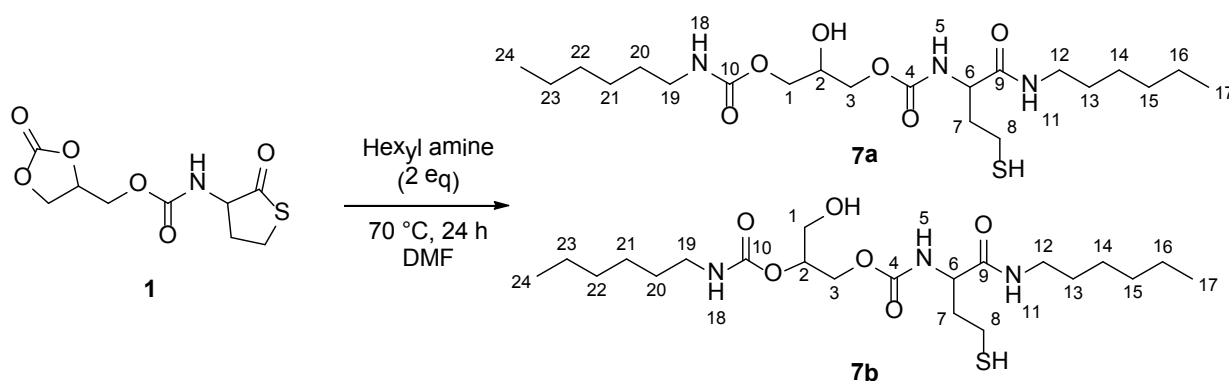
The structure was solved by direct methods using *SHELXS97*³ and refined on F^2 with *SHELXL97*³. Non-H atoms were refined with anisotropic displacement parameters. The amino-H was found in difference fourier map and refined freely with $U_{iso}(\text{H}) = 1.2 U_{eq}(\text{N})$; all other hydrogen atoms were placed in idealized positions with $U_{iso}(\text{H}) = 1.2 U_{eq}(\text{C})$. Supplementary crystallographic data can be obtained free of charge from the Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif (CCDC 919540).

Table S1: Crystal data and refinement results of the RR/SS diastereomer of **1**.

Chemical formula	C ₉ H ₁₁ N O ₆ S
M_r	261.25
Crystal system, space group	Monoclinic, $P 2_1/c$
a, b, c (Å)	8.6927(9), 15.1581(15), 8.4584(8)
β (°)	95.606(2)
V (Å ³)	1109.19(19)
Z	4
μ (mm ⁻¹)	0.309
Crystal size (mm)	0.27 x 0.21 x 0.18
Index ranges	$-11 \leq h \leq 11, -20 \leq k \leq 20, -11 \leq l \leq 11$
Reflections collected	15268
Independent reflections	2810 [$R_{int} = 0.0426$]
T_{min}, T_{max}	0.9212, 0.9465
Data / restraints / parameters	2810 / 0 / 157
Goodness-of-fit on F^2	1.038
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0347, wR_2 = 0.0879$
R indices (all data)	$R_1 = 0.0441, wR_2 = 0.0944$
Largest diff. peak and hole	0.410 and -0.192 e Å ⁻³

3 NMR Analysis of the isomers

To analyze the coupling patterns of the isomers formed by the reaction of the second amine and the ethylene carbonate ring, the coupler was converted with 2.0 equivalents of hexyl amine at 70 °C (Scheme 1):



Scheme 1. Reaction of the coupler with 2.0 equivalents of hexyl amine.

The ^1H NMR data show that both isomers bear different chemical shifts for the protons 1, 2 and 3. To start with the alkyl chains, protons 17 and 24 can be found as a triplet at $\delta = 0.85$ ppm. Methylene groups 14 to 16 and 21 to 23 appear at $\delta = 1.23$ ppm. Protons 13 and 20 show a broad singlet at $\delta = 1.38$ ppm. The multiplet at $\delta = 1.94 - 1.67$ ppm shows methylene group 7, whereas the methylene group adjacent to the thiol (8) overlaps with the DMSO signal at $\delta = 2.54 - 2.37$ ppm. Both CH_2 groups next to the NH groups can be observed as a multiplet at $\delta = 3.12 - 2.90$ ppm. The amide and urethane protons 11 and 18 can each be assigned to a broad triplet at $\delta = 7.84$ and 7.13 ppm, respectively. Urethane proton 5 appears as a doublet at $\delta = 7.30$ ppm with a 3J coupling value of 7.1 Hz. The adjacent proton at the stereocentre (6) is shifted to $\delta = 4.07 - 3.96$ ppm. The alcohol group of isomer **7a** can be found at $\delta = 5.11$ ppm, whereas OH^b is shifted to higher field ($\delta = 4.88$ ppm).

Methine protons 2a and 2b can be observed at $\delta = 3.79$ and 4.74 ppm, respectively. 1b shows a broad triplet at $\delta = 3.48$ ppm. Methylene group 1a is overlapping with methylene group 3a at $\delta = 3.99 - 3.83$ ppm. The signal of 3b is splitting up and shows two multiplets. The first is located at $\delta = 4.25 - 4.07$ ppm, the second overlaps with protons 3a and 1a at $\delta = 3.99 - 3.83$ ppm. The complex coupling interactions between the nuclei of each isomer could be resolved by $^1\text{H}, ^1\text{H}$ -COSY measurements (Figure S7).

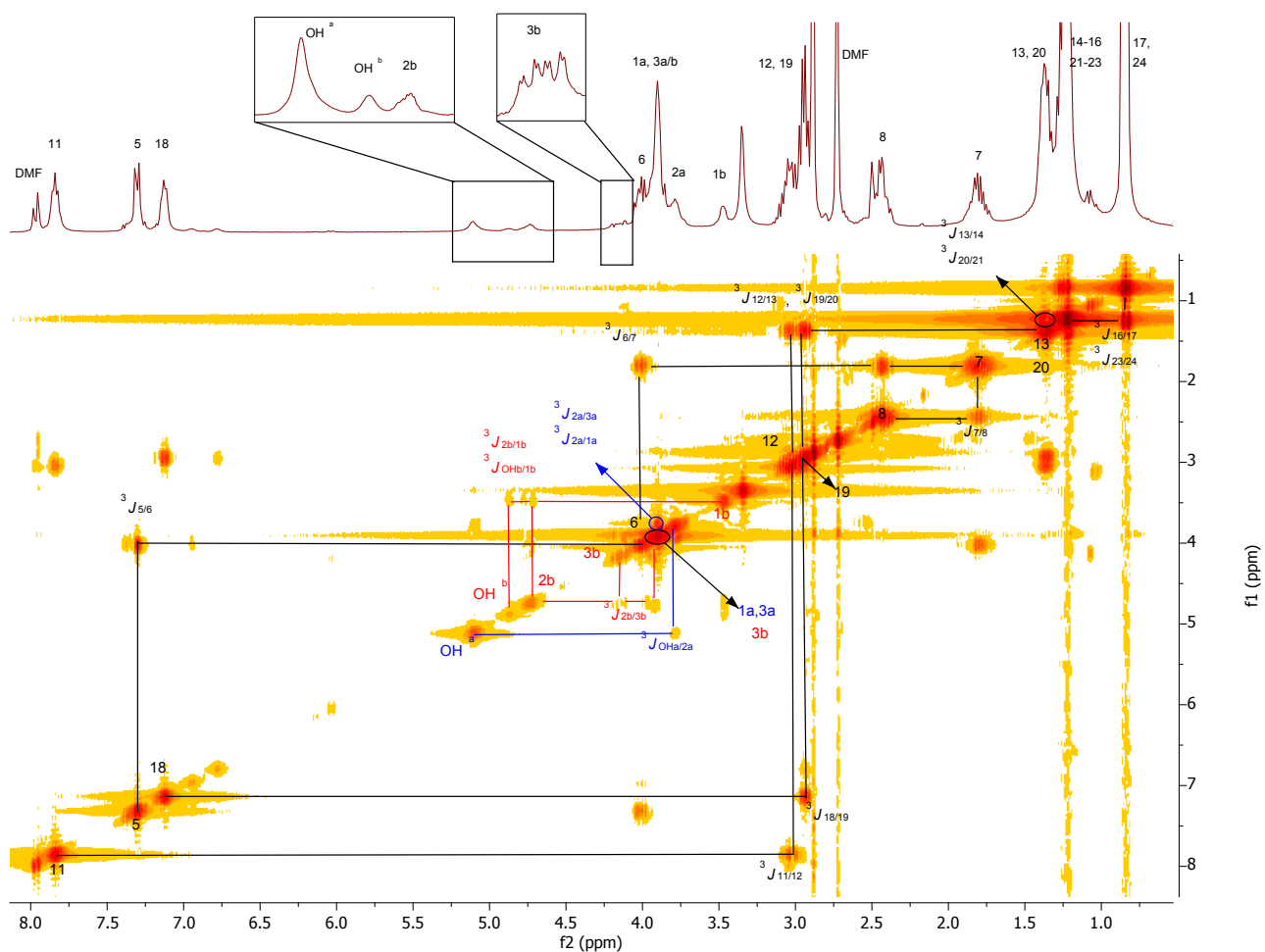


Fig. S13 $^1\text{H}, ^1\text{H}$ -COSY measurement of compound 7.

4 References

1. Bruker, SAINT+, Version 6.02. Bruker AXS Inc., **1999**, Madison, Wisconsin, USA.
2. Sheldrick, G. M, SADABS, Version 2.03., **1996**, University of Göttingen, Germany.
3. G. M. Sheldrick, *Acta Crystallogr. A64*, **2008**, 112–122.