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Supporting Information

Dynamic disulfide metathesis induced by ultrasound

Urs Fabian Fritze and Max von Delius*

Department of Chemistry and Pharmacy, University of Erlangen-Nürnberg,

Henkestr. 42 91054 Erlangen, Germany.

* Fax: +49 9131 85 26864; Tel: +49 9131 85 22946; E-mail: max.vondelius@fau.de

Content

General Experimental Section

Reagents and instruments

All commercially purchased reagents were used without further purification. Chloroform was purchased from Sigma-Aldrich (anhydrous > 99%, 0.5% - 1% ethanol as stabilizer). NMR spectra were recorded on Bruker Avance 300 (^{1}H: 300 MHz), Bruker Avance 400 (^{1}H: 400 MHz), Jeol EX 400 (^{1}H: 400 MHz) and Jeol Alpha 500 (^{1}H: 500 MHz) spectrometers at 298 K and referenced to the residual solvent peak (^{1}H: $CDCl_3$, 7.24 ppm; ^{13}C: $CDCl_3$, 77.16 ppm). Coupling constants (*J*) are denoted in Hz and chemical shifts (δ) in ppm. Mass spectra were obtained on Bruker micro TOF II and Bruker Maxis 4G (ESI$^+$, Toluene/Acetonitrile) instruments. HPLC-MS analysis was performed on a Shimadzu LCMS 2020 instrument (column: ASC Amide, 2.6 µm, 150 x 4.6 mm; mobile phase: H_2O/MeCN 70% → 100 % MeCN; flow rate: 0.3 mL/min; Kinetex C18, 2.6 µm, 100 x 4.6 mm; mobile phase: H_2O/MeCN 80% → 100 % MeCN; flow rate: 0.3 mL/min). IR spectra were recorded on a Bruker Tensor 27- IR spectrometer as solids in ATR-mode. The microwave experiments were carried out on a Biotage initiator$^+$ system.

General Sonication Considerations:

The “**sonotorode**” experiments were performed under an atmosphere of argon using a Bandelin Sonopuls 3200 HD sonicator at 20 kHz equipped with a 13 mm replaceable tip titanium probe (Bandelin VS 70 T).

Calorimetry[1] was used to calibrate the ultrasonic intensity produced by the probe. Therefore a Dewar was filled with 250 g of deionized ice water and the probe was submerged 1 cm into the water. The amplitude was set to 15% and sonication was started. The water temperature was recorded every 15 seconds for 4 minutes. Δ temp / Δ time was obtained by the slope of the linear fit. This procedure was repeated for 25, 40, 60 and 80%.

The heat due to cavitation in W was determined from the following equation:

$q = \text{specific heat } [Jg^{-1\circ} C^{-1}] \times \text{mass } [g] \times \Delta \text{ temp} / \Delta \text{ time } [^\circ Cs^{-1}]$

The specific heat of the water is 4.179 $Jg^{-1\circ} C^{-1}$, the mass of the water is 250 g and Δ temp / Δ time is the slope of the linear fit of the plot.

The resulting value, q, was divided by the surface area of the horn tip (1.327 cm^2 for a 13 mm tip) to obtain W/cm^2. The Power produced was plotted against the percentage of the amplitude to generate the calibration curve. (24.3 W/cm^2 at 25% amplitude; no pulsing)

Custom Suslick cells were fabricated in house. Argon was bubbled through the solvent for 30 min prior to each experiment performed. An argon line was attached to a cell’s side arm and a steady argon flow was maintained during the reaction time. Pulsed ultrasound was applied (0.5 s on and 1.0 s off) at 25% amplitude for each experiment performed.

The following instruments were used for “**ultrasonic bath**” (US bath) conditions: VWR ultrasonic cleaner USC-THD, Bandelin sonorex digiplus and Bandelin sonorex.

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[1] K. L. Berkowski, S. L. Potisek, C. R. Hickenboth and J. S. Moore *Macromolecules*, 2005, **38**, 8975.

General procedure “sonotrode”:

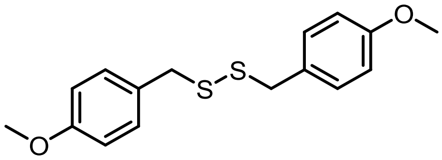
Anhydrous chloroform with 0.5% - 1% ethanol as stabilizer was degassed by bubbling through argon for 30 minutes. Compound **AA** (36.7 mg, 0.15 mmol) and compound **BB** (45.9 mg, 0.15 mmol) were placed in a three-neck Suslick cell and dissolved in 15 mL of the degassed solvent and kept under a slight argon flow during the reaction. The reaction mixture was placed in an ice bath during the whole time of the reaction to avoid heating of the solvent. Pulsed ultrasound was applied (0.5 s on and 1.0 s off) at 25% amplitude for the desired time.

General procedure “ultrasonic bath”:

For the reaction in an ultrasonic bath, anhydrous chloroform with 0.5% - 1% ethanol as stabilizer was degassed by bubbling through argon for 30 minutes. Compound **AA** (36.7 mg, 0.15 mmol) and compound **BB** (45.9 mg, 0.15 mmol) were placed in a sealed ACE pressure tube and dissolved in 15 mL of the degassed solvent. The sealed tube was placed in the ultrasonic bath and a cooling finger was immersed into the bath to keep the water temperature constant at 27 °C.

Synthesis and characterization data

Synthesis of bis(4-methoxybenzyl)disulfide(**BB**)



In a 250 mL round necked flask K_2CO_3 (4.48 g, 32 mmol) was dissolved in a mixture of MeOH (20 mL) and H_2O (20 mL). 4-methoxy-a-toluenethiol (2.50 g, 2.25 mL, 16 mmol) was added together with dichloromethane (20 mL) and the reaction mixture was stirred vigorously. A solution of iodine in dichloromethane (2 g in 50 mL) was added drop wise until the color of the iodine persisted and the reaction was stirred for further 15 minutes. The excess of iodine was quenched by the addition of sodium thiosulfate, the layers were separated and the aqueous layer was extracted with dichloromethane (50 mL). The combined organic layers were washed with a diluted solution of sodium thiosulfate and brine, dried over $MgSO_4$ and the solvents were removed under reduced pressure to give the desired product as a colorless solid.

Yield: 2.09 g 6.82 mmol, 84%

^{1}H NMR (300 MHz, 298 K, $CDCl_3$): δ = 7.15 (d, *J* = 8.7 Hz, 4H), 6.84 (d, *J* = 8.7 Hz, 4H), 3.78 (s, 6H), 3.57 (s, 4H).

The ^{1}H-NMR data matches those reported in the literature[2]

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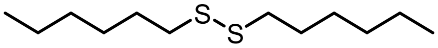
[2] Y. Yin, H. Zhou, X. Liu, H. Chen, F. Wu, H. Zhang, R.Tao, F. Cheng and Y. Feng, *Tetrahedron. Lett.*, 2015 , **56**, 1709.

Synthesis of 1,2-dihexyldisulfide (**DD**)



Hexane-1-thiol (2.50 g, 21.11 mmol) was dissolved in MeOH and then titrated with a solution of iodine in MeOH until the color of the iodine remained. The excess of iodine was quenched with a saturated aq. solution of $NaHSO_3$, the reaction mixture diluted with H_2O and extracted 3 times with CH_2Cl_2 (20 mL). The organic layers were combined, dried and the solvent was removed under reduced pressure to obtain a colorless oil.

Yield: 2.01 g, 8.65 mmol, 82%

^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ 2.66 (t, *J* = 7.2 Hz 4H), 1.65 (q, *J* = 7.4 Hz, 4H), 1.39 – 1.33 (m, 4H), 1.31 – 1.23 (m, 8H), 0.87 (t, *J* = 6.7 Hz 6H).

The ^{1}H-NMR data matches those reported in the literature **[3]**

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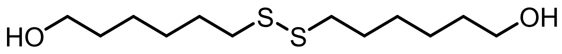
[3] J. Su, Y. Qui, K. Ma, Z. Wang, X. Li, D. Zhang, Z. Tu and S. Jiang, *Tetrahedron*, 2014, **42**, 7763.

Synthesis of 6,6´-disulfanediylbis(hexane-1-ol) (**EE**)



6-mercaptohexan-1-ol (1.96 g, 14.6 mmol) was dissolved in MeOH (20 mL) and then titrated with a solution of iodine in MeOH until the color of the iodine remained. The excess of iodine was quenched with a saturated solution of $NaHSO_3$, the reaction mixture diluted with H_2O and extracted three times with CH_2Cl_2 (20 mL). The organic layers were combined, dried and the solvent was removed under reduced pressure to obtain a colorless solid.

Yield: 1.71 g, 6.399 mmol, 88%

^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ 3.63 (t, *J* = 6.5 Hz, 2H), 2.66 (t, *J* = 7.2 Hz 2H), 1.74 – 1.61 (m, 2H), 1.62 – 1.48 (m, 2H), 1.42 – 1.33 (m, 4H).

The ^{1}H-NMR data matches those reported in the literature [4]

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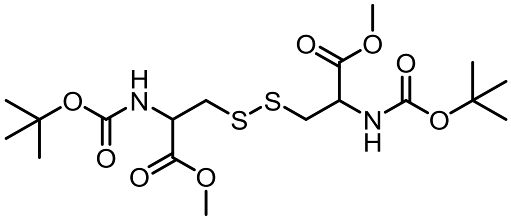
[4] E. Miyoshi, K. Naka, K. Tanaka, A. Narita and Y. Chujo, *Colloids Surf., A*, 2011, **390**, 126.

Synthesis of dimethyl 3,3´-disulfanediylbis(2-((tert-butoxycarbonyl)amino)propanoate (**FF**)



N-(tert-Butoxycarbonyl)-L-cysteine methyl ester (0.24 g, 2.0 mL, 1.0 mmol) was dissolved in dest. H_2O (3mL) under vigorous stirring. NaI was added together with H_2O_2 (11 mL). The reaction mixture was stirred over night. The precipitate was filtered off and dried under vacuum. Flash purification with a mixture of hexanes and ethyl acetate (100/0 → 80/20 gradient) gave the desired product as a colorless solid.

Yield: 115.2 mg, 0.245 mmol, 49%

^{1}H NMR (300 MHz, 298 K, $CDCl_3$) δ 5.36 (d, *J* = 8.1 Hz, 2H), 4.57 (m, 2H), 3.74 (s, 6H), 3.13 (d, *J* = 5.3 Hz, 4H), 1.42 (s, 18H).

The ^{1}H-NMR data matches those reported in the literature [5]

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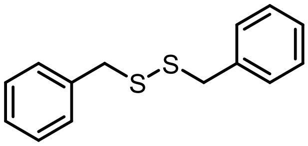
[5] Y. A. Lin, J. M. Chalker, N. Floyd, G. J. L. Bernardes and B. G. Davis*, J. Am. Chem. Soc.*, 2008, **130**, 9642.

HPLC traces at 254 nm or ^{1}H-NMR spectra of starting materials for reaction monitoring:

AA



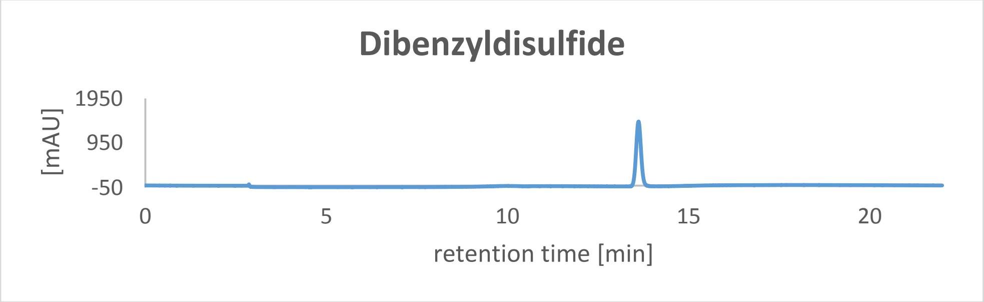
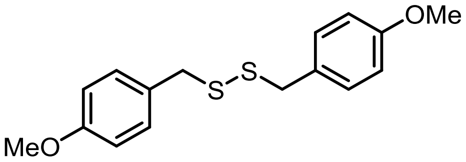


Figure S 1:HPLC trace of dibenzyldisulfide at 254 nm (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

BB



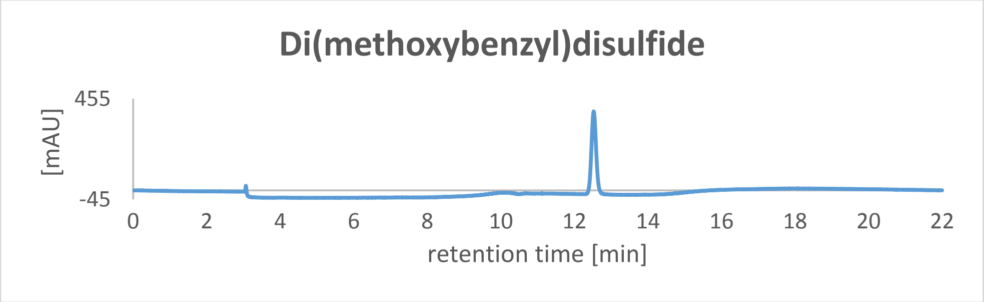
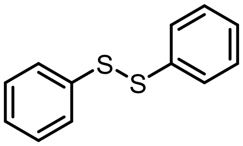


Figure S 2: HPLC trace of di(methoxybenzyl)disulfide at 254 nm (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

CC



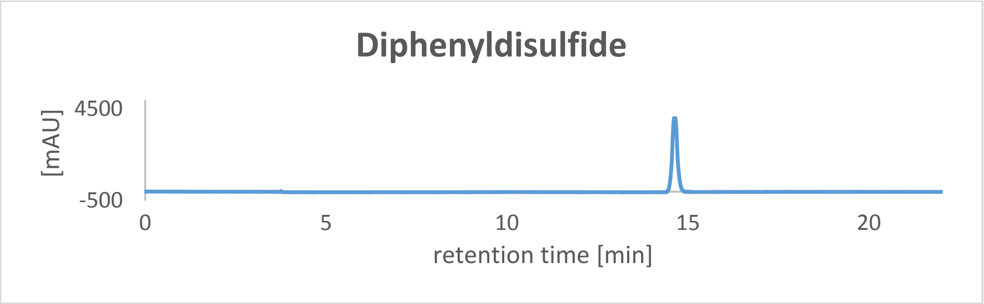
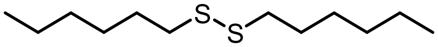


Figure S 3: HPLC trace of diphenyldisulfide at 254 nm (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

DD



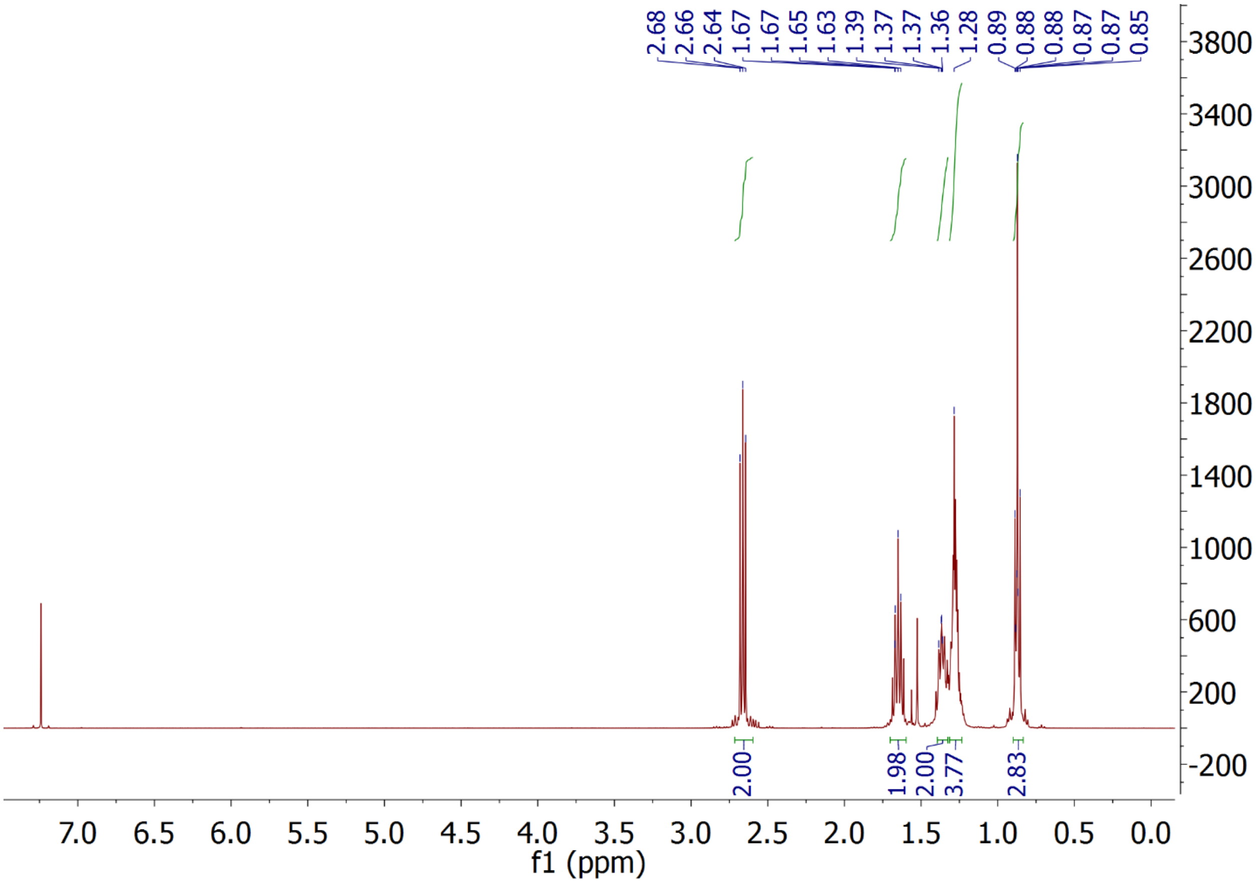
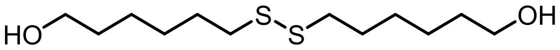


Figure S 4: ^{1}H-NMR of 1,2-Dihexylsulfane in $CDCl_3$, 400MHz.

EE



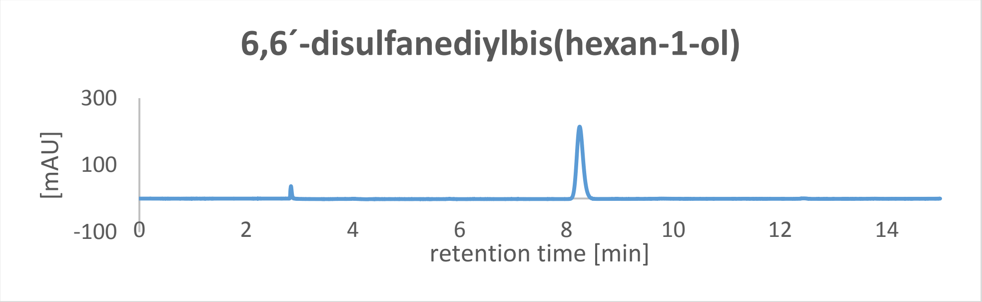


Figure S 5: HPLC trace of 6,6´-disulfanediylbis(hexan-1-ol) at 254 nm (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

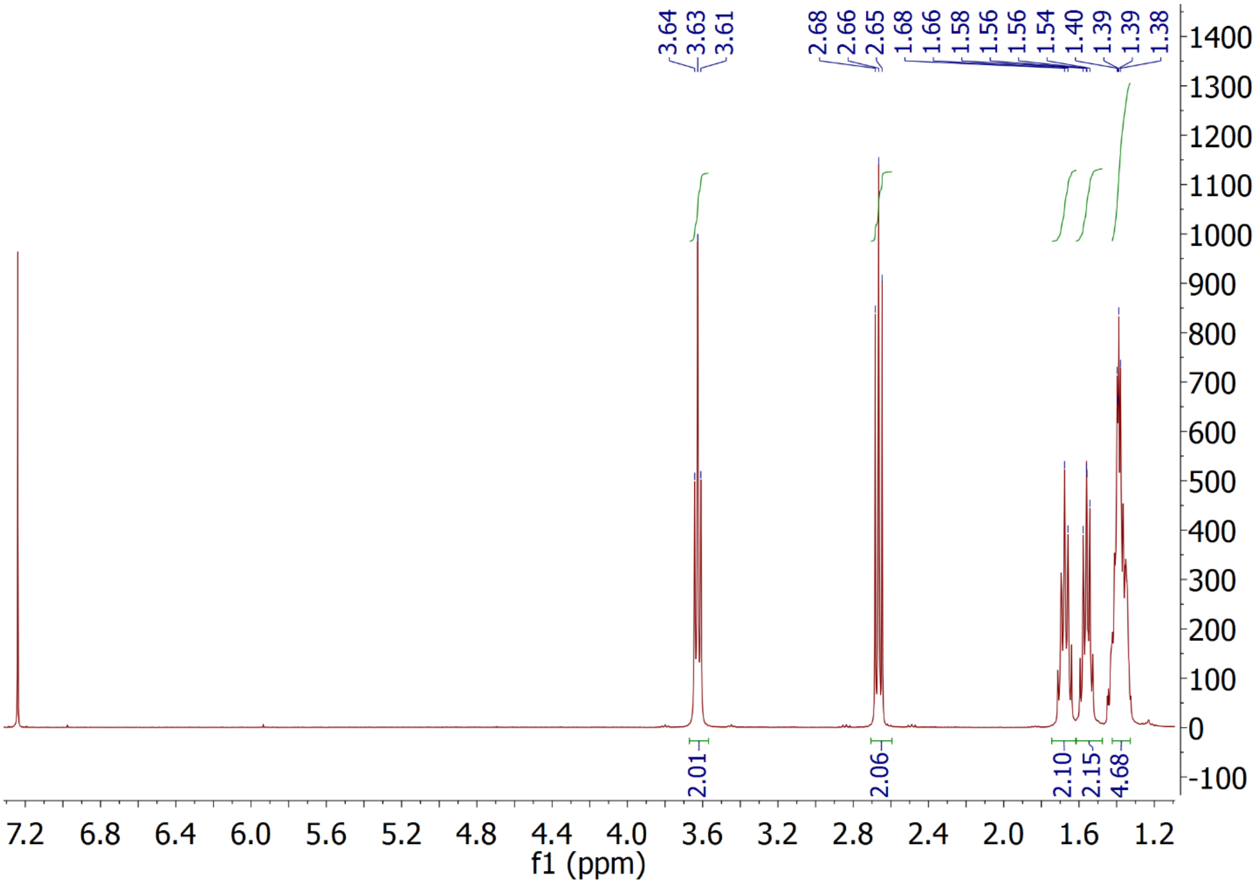
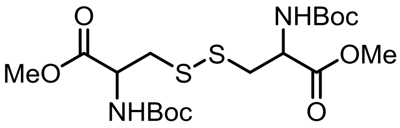


Figure S 6: ^{1}H-NMR of 6,6´-disulfanediylbis(hexan-1-ol) in CDCl$_3$, 400MHz.

FF



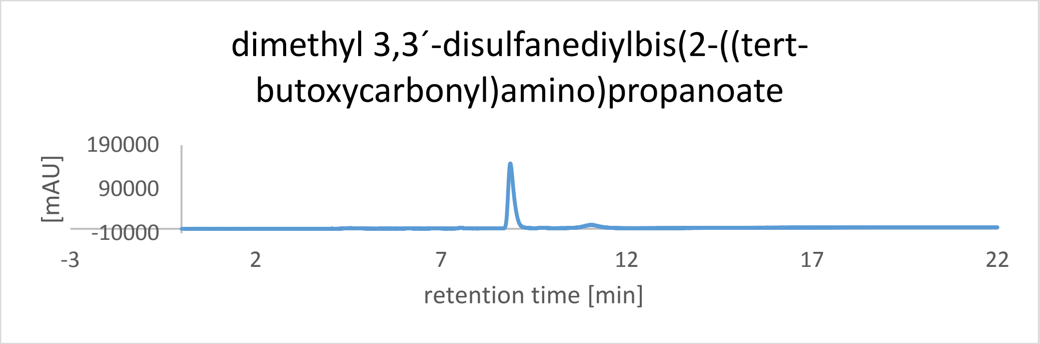
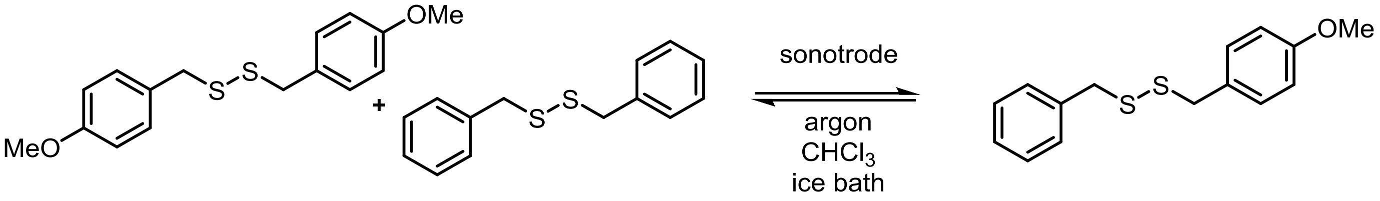


Figure S 7: HPLC trace of dimethyl 3,3´-disulfanediylbis(2-((tert-butoxycarbonyl)amino)propanoate at 254 nm (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

HPLC traces at 254 nm for reactions of Table 1:

Bandelin HD 3200 Sonotrode



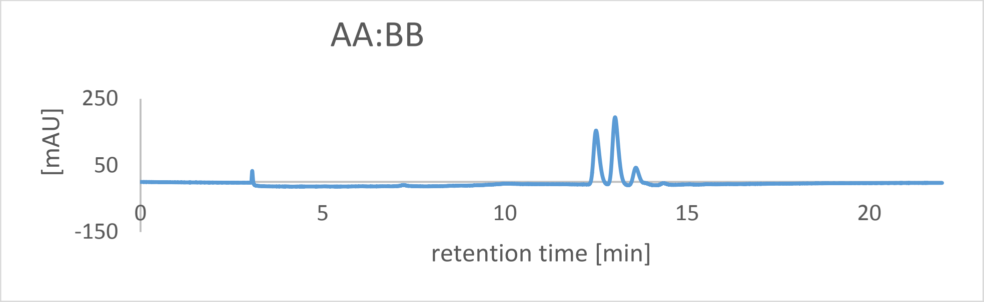
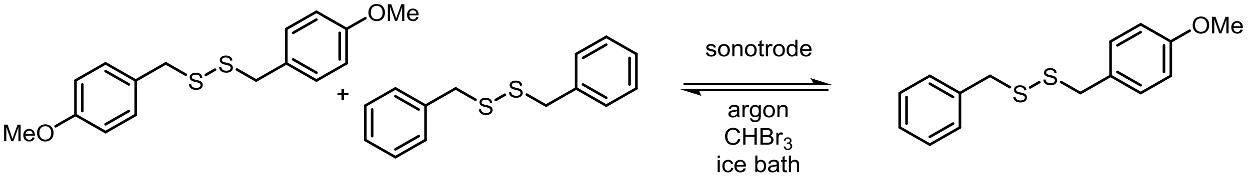


Figure S 8: HPLC trace of reaction Table 1, entry 1 at 254 nm after 1h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

Bandelin HD 3200 Sonotrode in bromoform



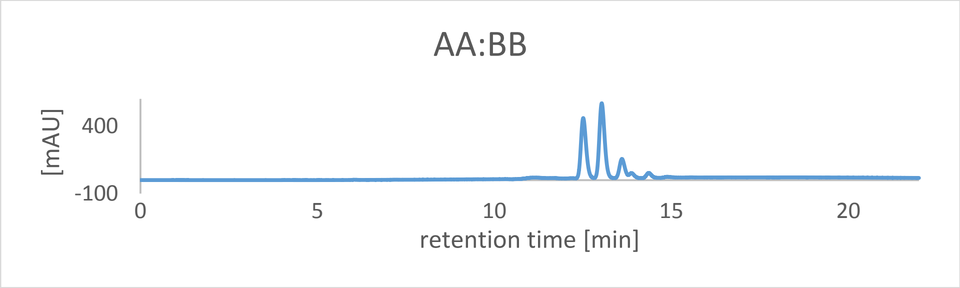


Figure S 9: HPLC trace of reaction Table 1, entry 2 at 254 nm after 45 s reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

Iodoform induced exchange in THF

For the iodoform-induced exchange, the inhibitor present in solvent tetrahydrofuran (BHT) was removed by filtering the solvent through a plug of activated basic alumina and the solvent consecutively was degassed by bubbling through argon for 15 minutes. Compound **AA** (18.45 mg, 0.075 mmol) and compound **BB** (22.95 mg, 0.075 mmol) were placed together with CHI_3 (0.15 mmol, 29.5 mg) in a three-neck Suslick cell and dissolved in 15 mL of the degassed solvent and kept under a slight argon flow during the reaction. The reaction mixture was placed in an ice bath during the whole time of the reaction to avoid heating of the solvent. Pulsed ultrasound was applied (0.5 s on and 1.0 s off) at 25% amplitude for the desired time.

Reference HPLC trace for iodoform:

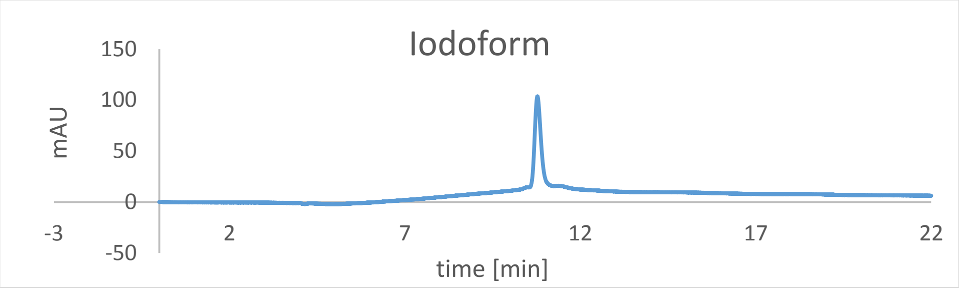


Figure S 10: HPLC trace of reaction Table 1, entry 4 at 254 nm after 24 h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

After 1h US: exchange 3%

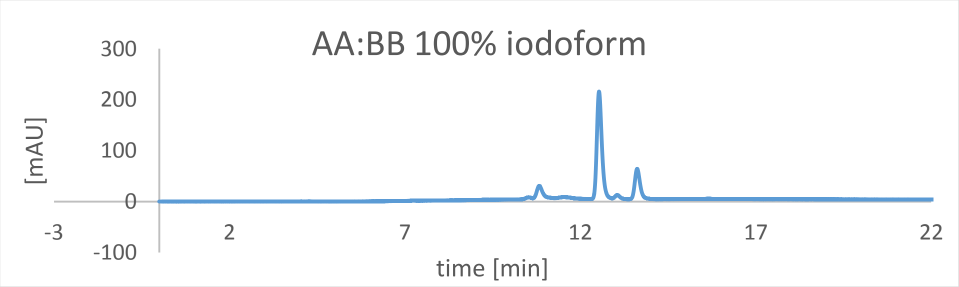


Figure S 11: HPLC trace of reaction Table 1, entry 4 at 254 nm after 24 h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

After 1h US and 44h rest: exchange 49%

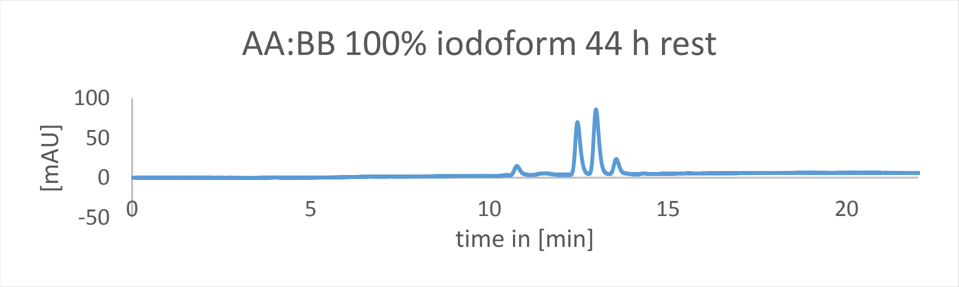
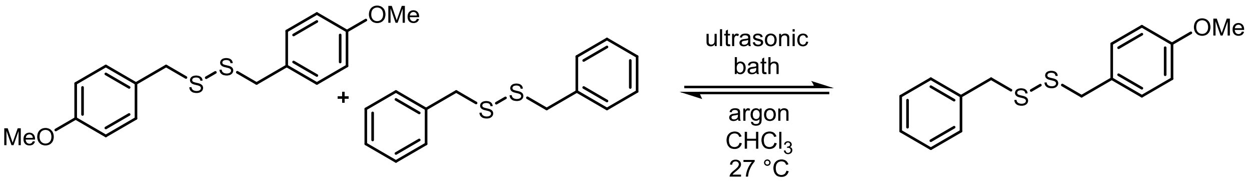


Figure S 12: HPLC trace of reaction Table 1, entry 4 at 254 nm after 24 h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

Disulfide metathesis induced via ultrasonic bath



Bandelin sonorex

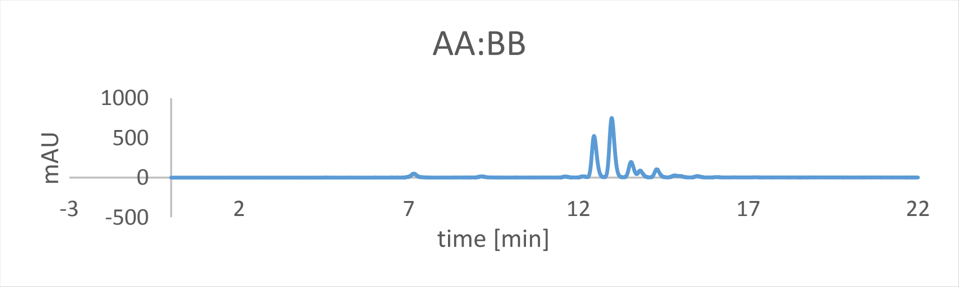


Figure S 13: HPLC trace of reaction Table 1, entry 5 at 254 nm after 24 h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water →100% acetonitrile over 10 minutes).

Bandelin sonorex digiplus

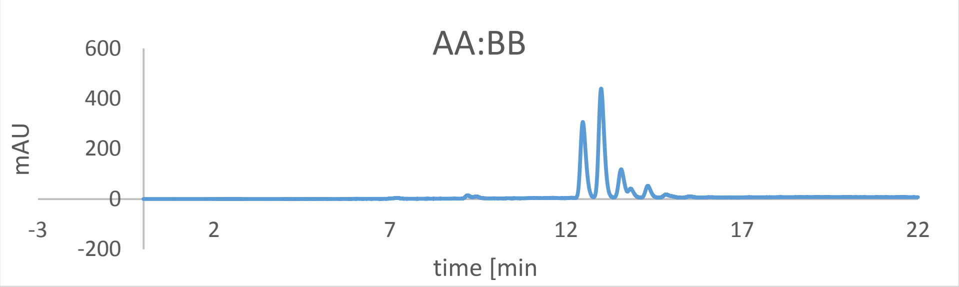


Figure S 14: HPLC trace of reaction Table 1, entry 5 at 254 nm after 24 h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water →100% acetonitrile over 10 minutes).

VWR ultrasonic cleaner USC-THD

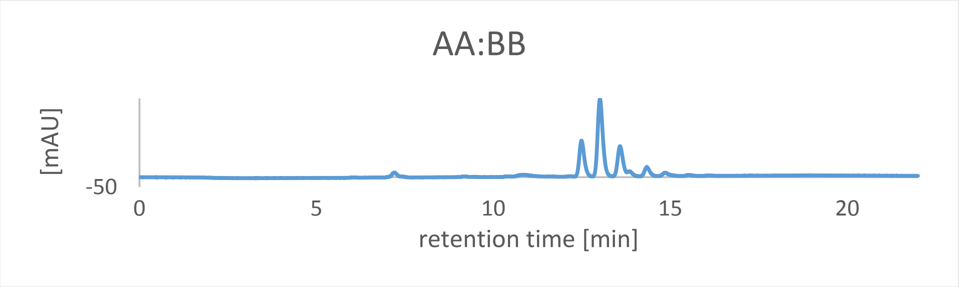
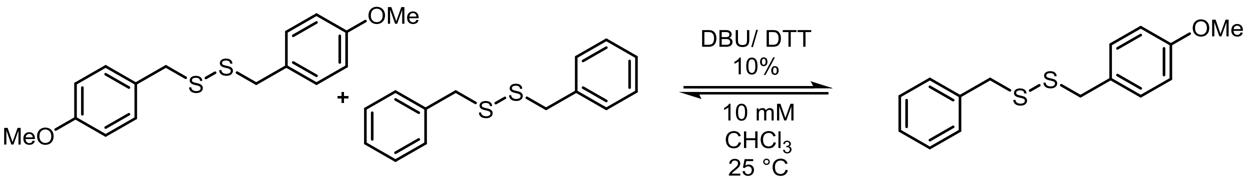


Figure S 15: HPLC trace of reaction Table 1, entry 5 at 254 nm after 24 h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

Base induced exchange (DBU/DTT 10 %)

For the base induced exchange compound **AA** (2,46 mg, 0.01 mmol) and compound **BB** (3.06 mg, 0.01 mmol) were placed in a screw capped vial and dissolved in 2 mL of the degassed $CHCl_3$. A stock solution(0.1 mmol/mL) of DBU and DTT in $CHCl_3$ was prepared. Then 10 µL of the stock solution were added to the reaction mixture and kept under stirring for 6 days at room temperature.



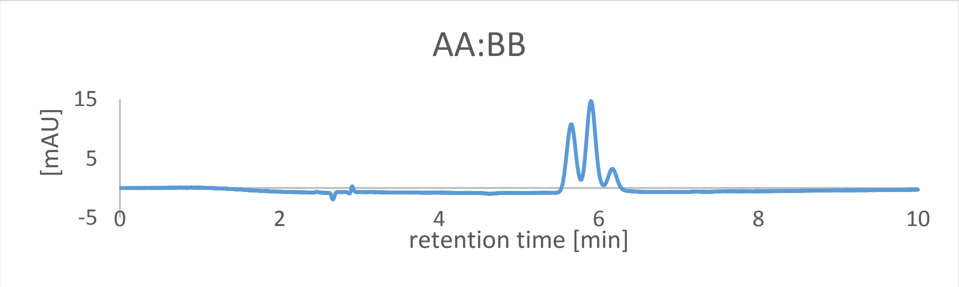
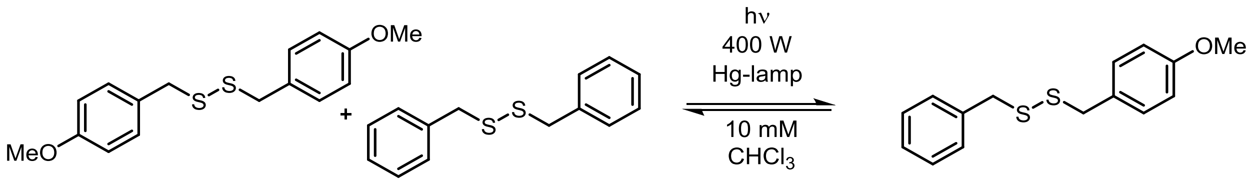


Figure S 16: HPLC trace of reaction Table 1, entry 6 at 254 nm after 6 day reaction time (Kinetex C18 cloumn, acetonitrile/water 80:20 → 100% aceonitrile).

UV induced exchange (400 W Hg lamp)

Anhydrous chloroform with 0.5% - 1% ethanol as stabilizer was degassed by bubbling through argon for 30 minutes. Compound **AA** (18.45 mg, 0.075 mmol) and compound **BB** (22.95 mg, 0.075 mmol) were placed in screw-capped glass vial, dissolved in 7.5 mL of the degassed solvent and placed in a UV-reactor, equipped with an 400 W Hg-Lamp, for 180 min.



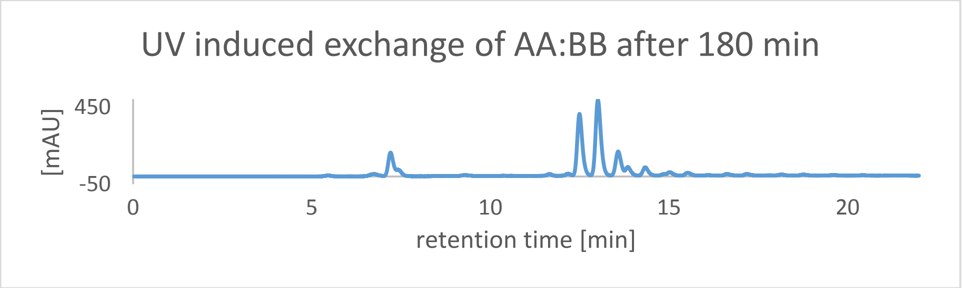
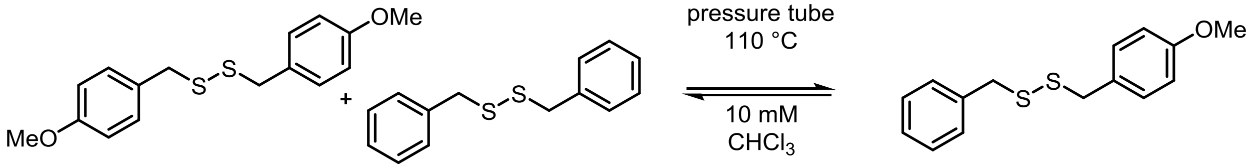


Figure S 17: HPLC trace of reaction Table 1, entry 7 at 254 nm after 180 min reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

Heat induced exchange

For this reaction, chloroform with 0.5% - 1% ethanol as stabilizer was degassed by bubbling through argon for 30 minutes. Compound **AA** (36.7 mg, 0.15 mmol) and compound **BB** (45.9 mg, 0.15 mmol) were placed in a sealed ACE pressure tube and dissolved in 15 mL of the degassed solvent. The sealed tube was placed in a preheated oil bath and kept at 110 °C for five hours.



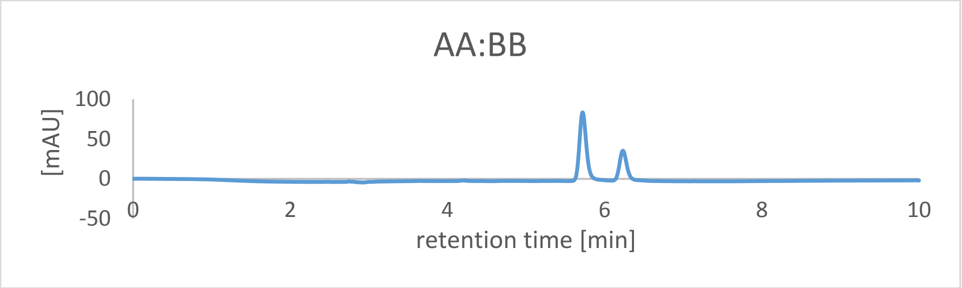
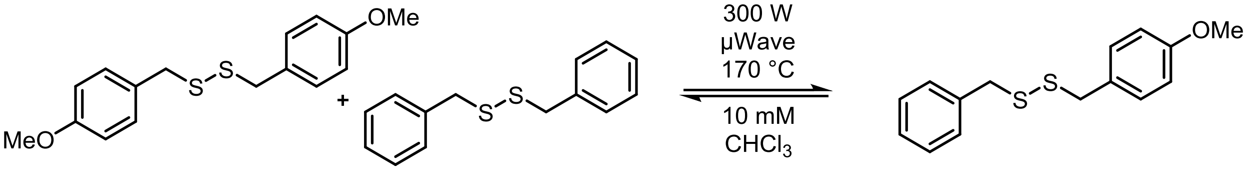


Figure S 18: HPLC trace of reaction Table 1, entry 8 at 254 nm after 5 h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

Microwave induced exchange (300 W, 170 °C, 11 bar)

For this reaction, chloroform with 0.5% - 1% ethanol as stabilizer was degassed by bubbling through argon for 30 minutes. Compound **AA** (12,3 mg, 0.05 mmol) and compound **BB** (15.3 mg, 0.05 mmol) were dissolved in 5 mL of the degassed solvent. 1 mL of the solution was transferred in a µW vial. The microwave was set to 300 W (11 bar, 170 °C) for 1 hour.



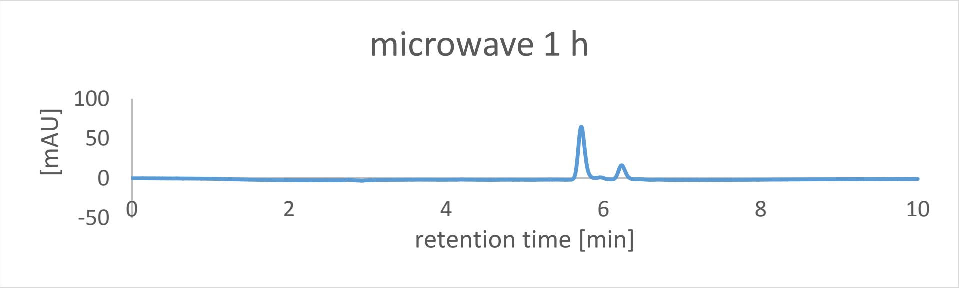
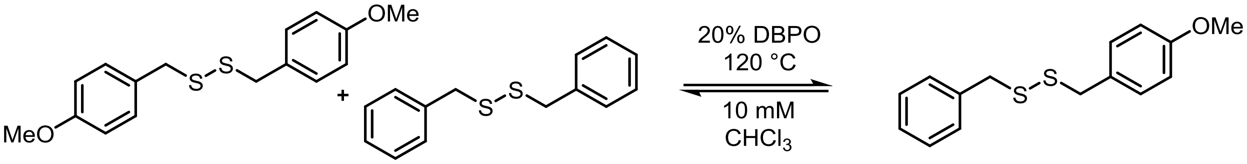


Figure S 19: HPLC trace of reaction Table 1, entry 9 at 254 nm after 1 h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water →100% acetonitrile over 10 minutes).

Radical initiator induced exchange (DBPO 20%)

For this reaction, anhydrous chloroform with 0.5% - 1% ethanol as stabilizer was degassed by bubbling through argon for 30 minutes. Compound **AA** (18.45 mg, 0.075 mmol) and compound **BB** (22.95 mg, 0.075 mmol) were placed in a sealed ACE pressure tube and dissolved in 15 mL of the degassed solvent. Then dibenzylperoxide (DBPO) with 25 wt% H_2O (5.0 mg, 15 µmol) was added and the sealed tube was placed in a preheated oil bath and kept at 120 °C for 5 h



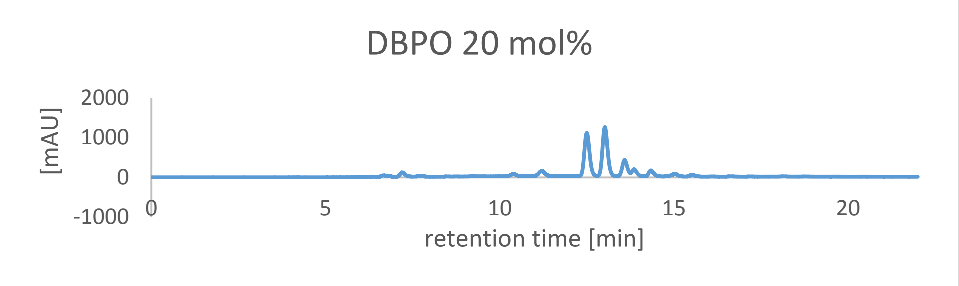
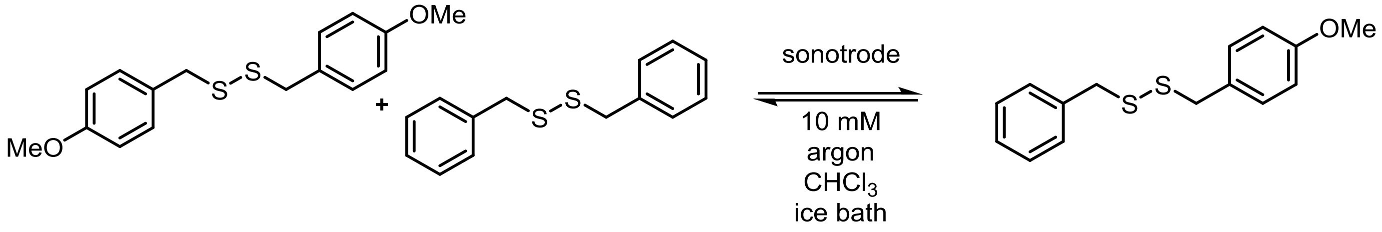


Figure S 20: HPLC trace of reaction Table 1, entry 10 at 254 nm after 5 h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

HPLC traces / ^{1}H-NMR spectra of Scope reactions with sonotrode Table 2

AA:BB



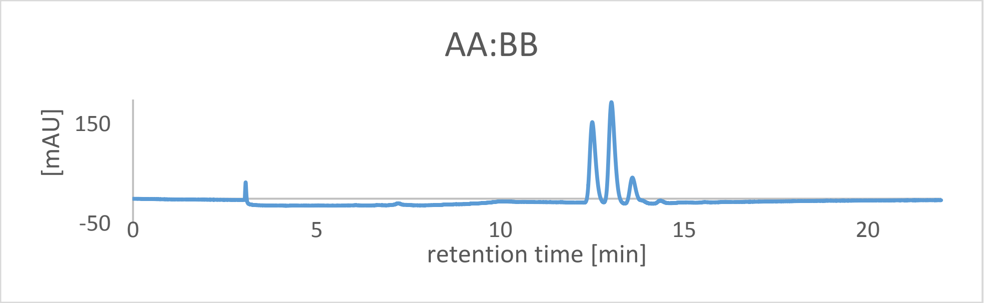
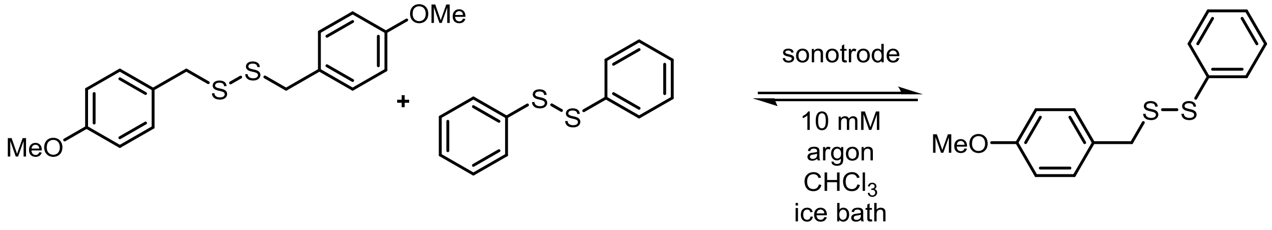


Figure S 21: HPLC trace of reaction Table 2, entry 1 at 254 nm after 1 h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

BB:CC



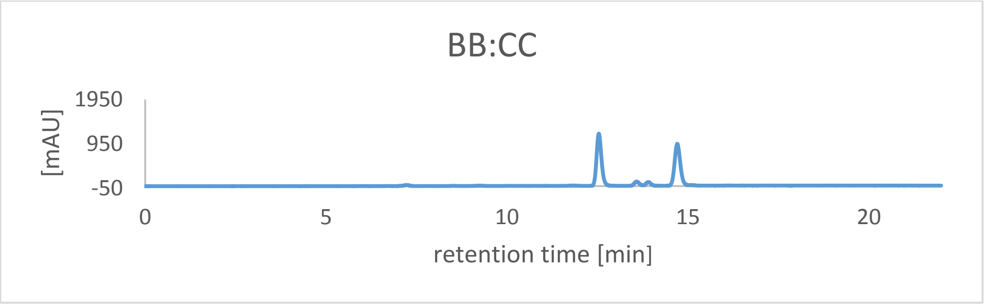
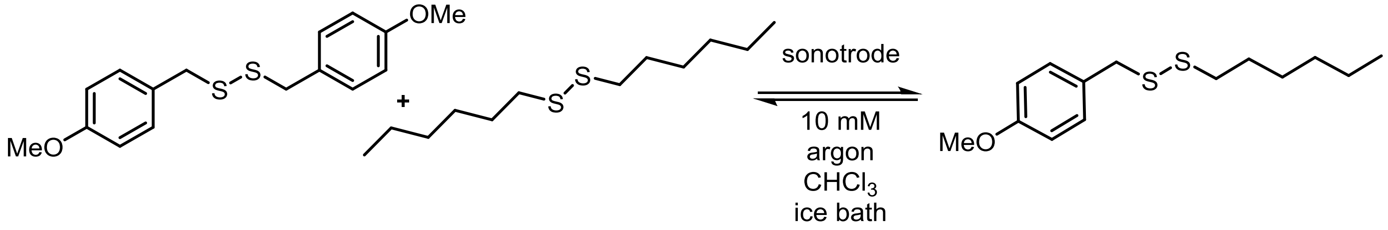


Figure S 22: HPLC trace of reaction Table 2, entry 2 at 254 nm after 1 h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

BB:DD



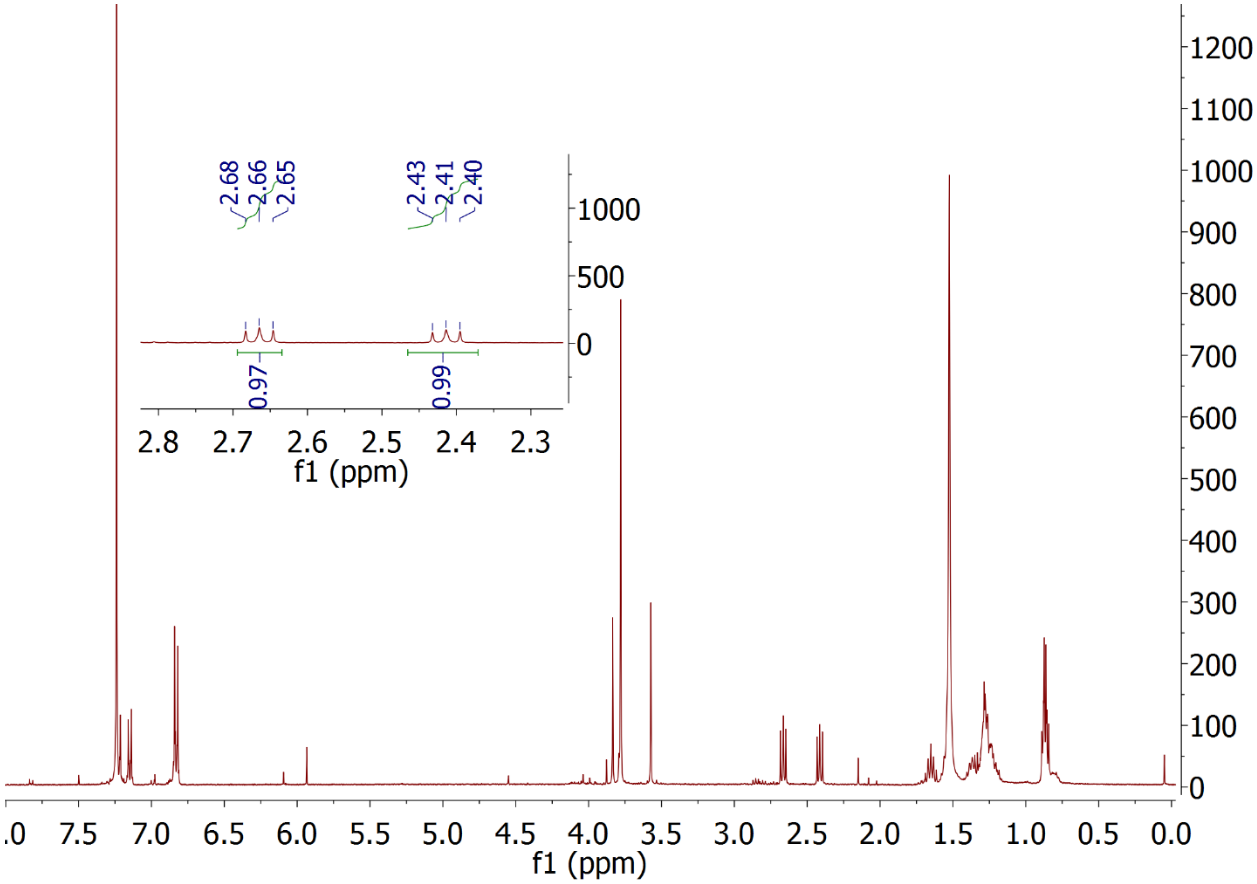
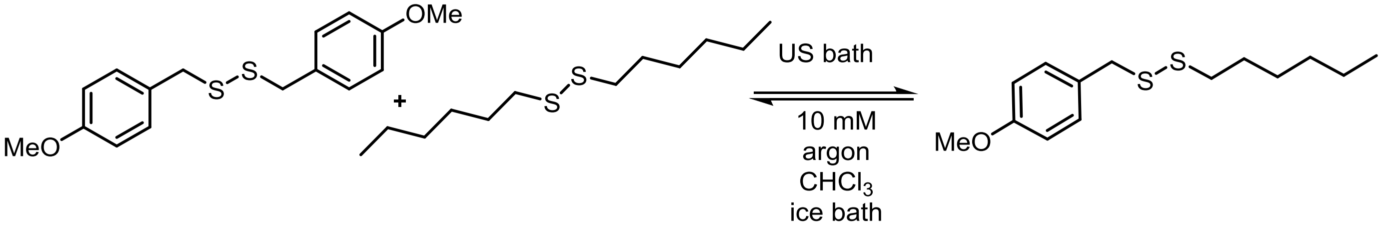


Figure S 23: ^{1}H-NMR of reaction Table 2, entry 3 in $CDCl_3$, 400MHz, after 3.5 h of reaction time.



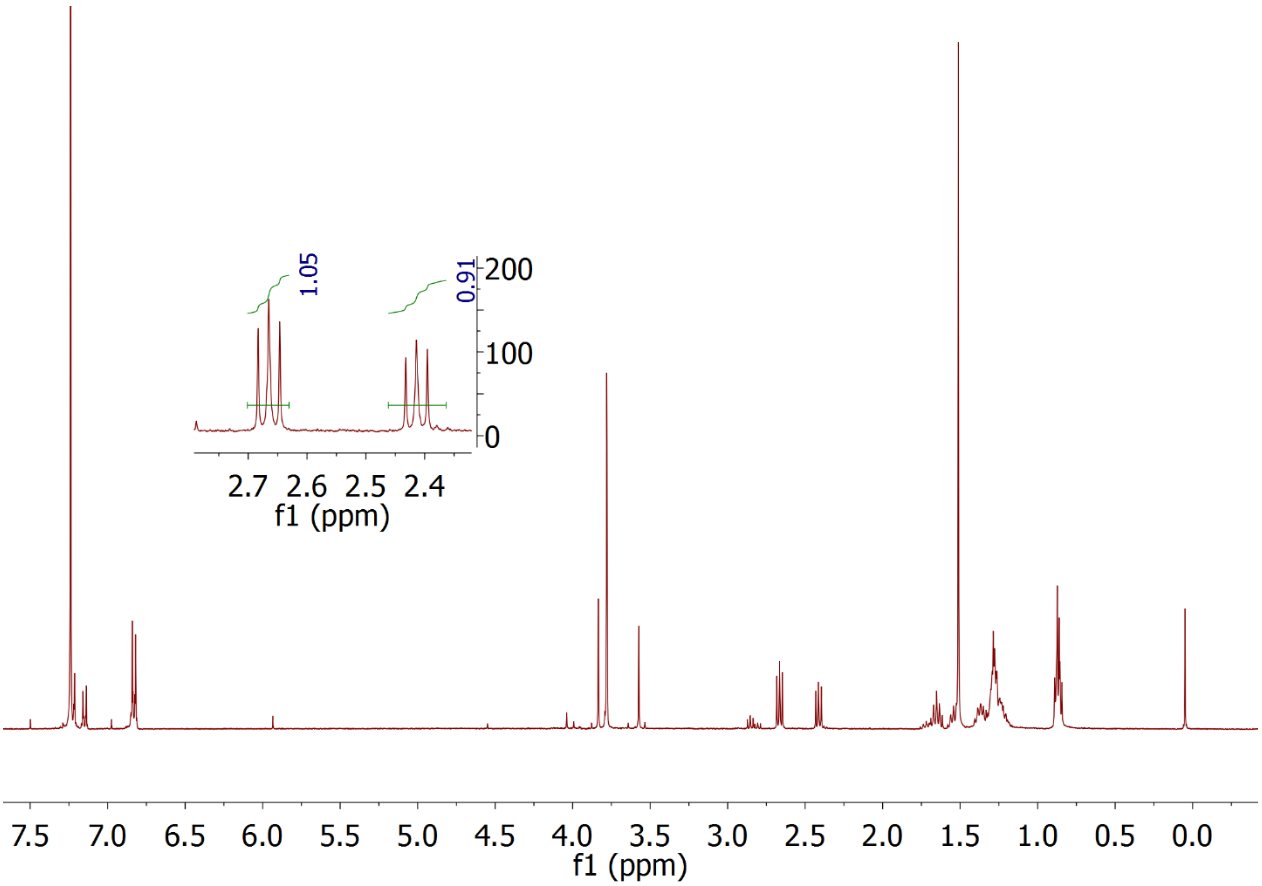
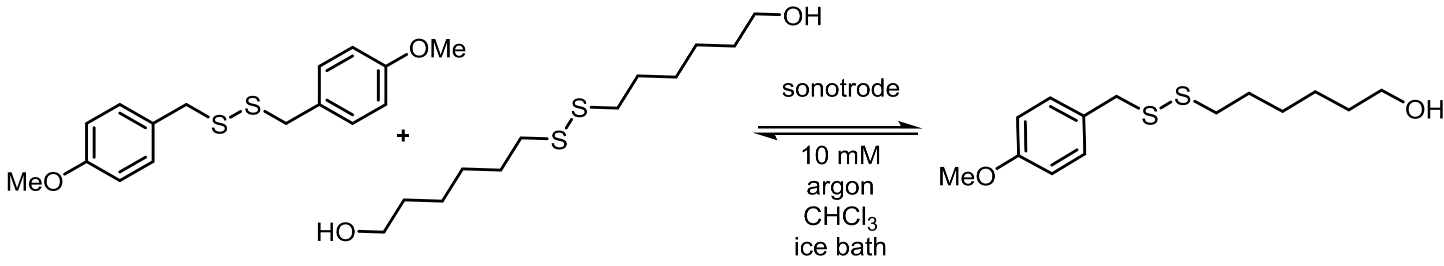


Figure S 24: ^{1}H-NMR of reaction Table 2, entry 3 in $CDCl_3$, 400MHz, after 22 h of reaction time.

BB:EE



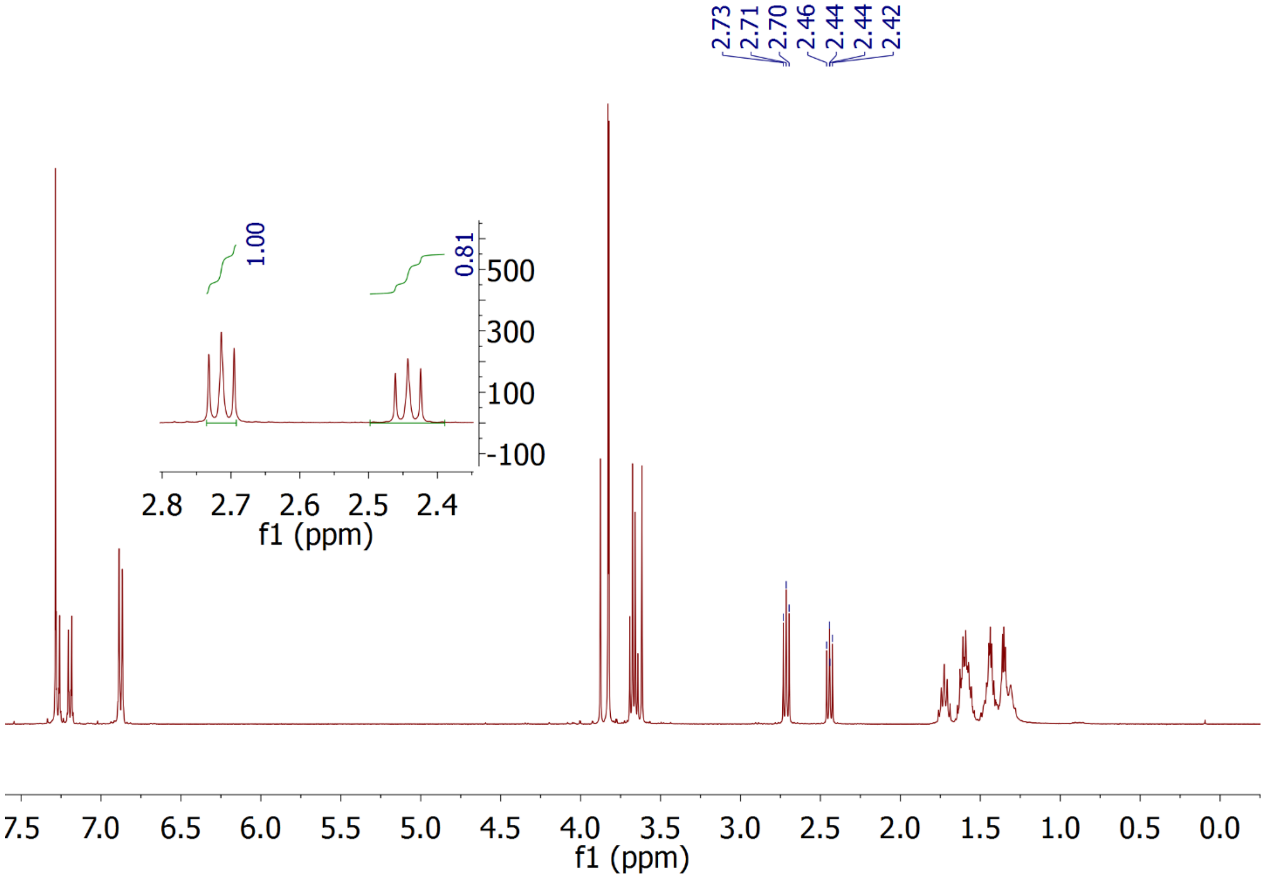
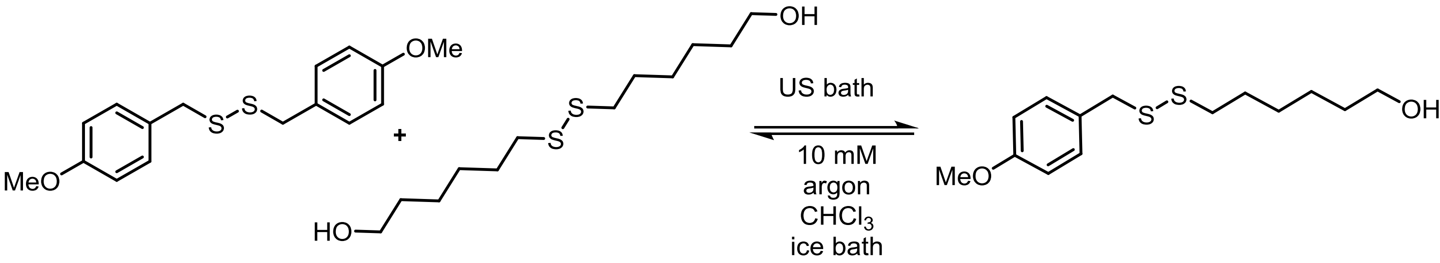


Figure S 25: ^{1}H-NMR of reaction Table 2, entry 4 in $CDCl_3$, 400MHz, after 1 h of reaction time.



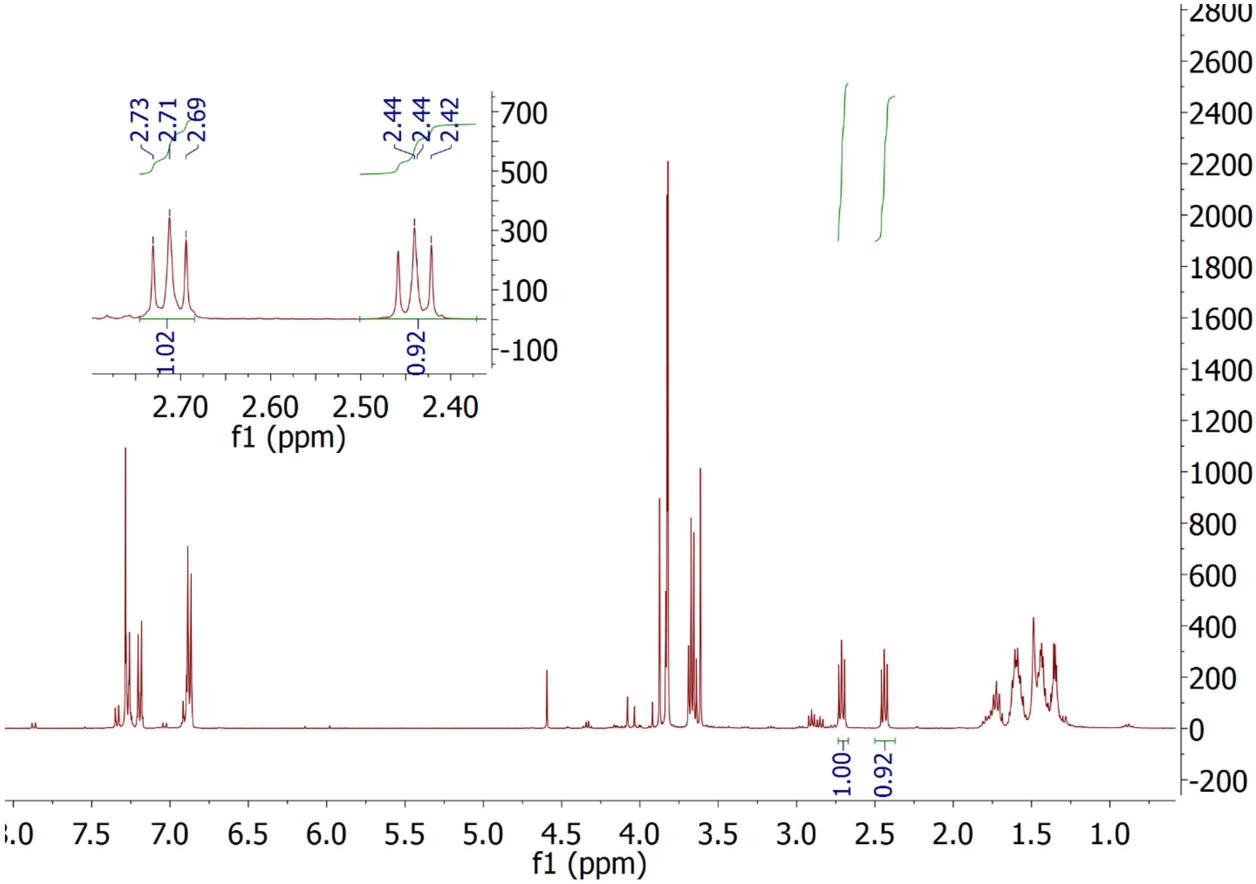
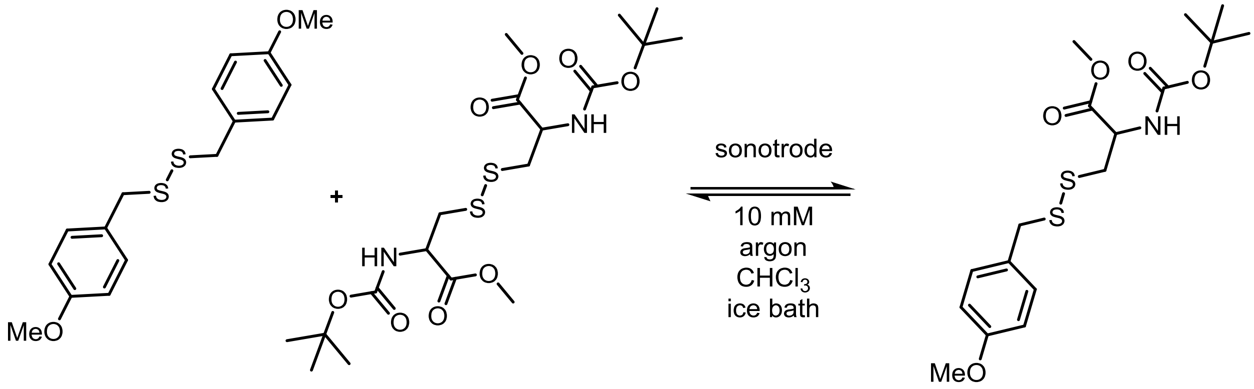


Figure S 26: : ^{1}H-NMR of reaction Table 2, entry 4 in CDCl$_3$, 400MHz, after 17 h of reaction time.

BB:FF



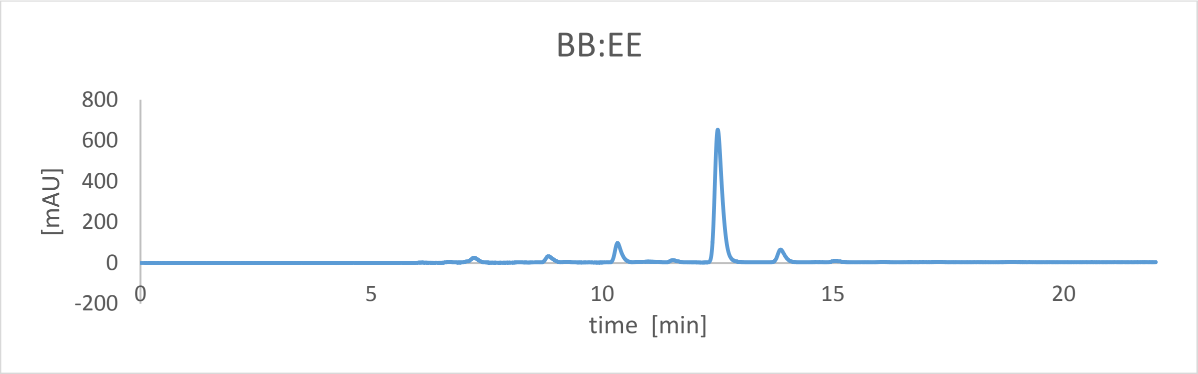
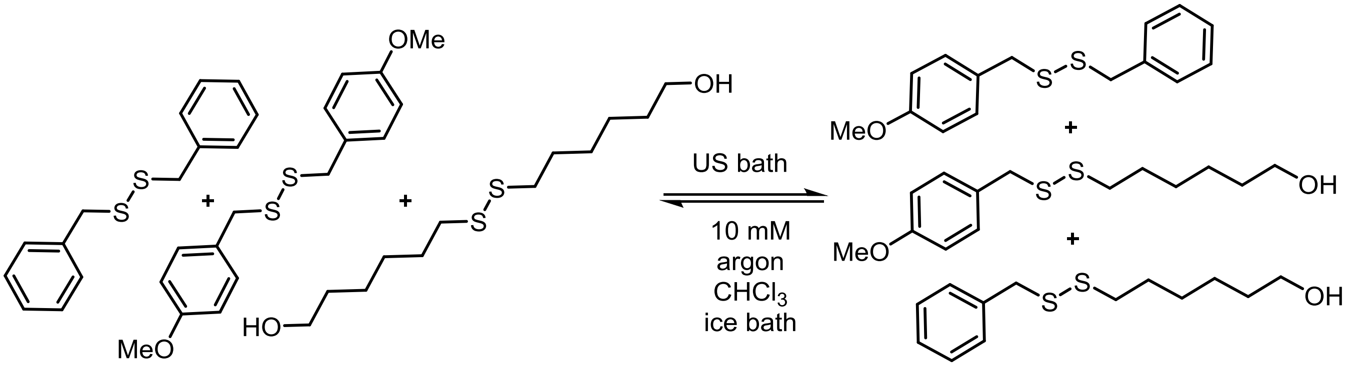


Figure S 27: HPLC trace of reaction Table 2, entry 5 at 254 nm after 3h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

AA:BB:EE



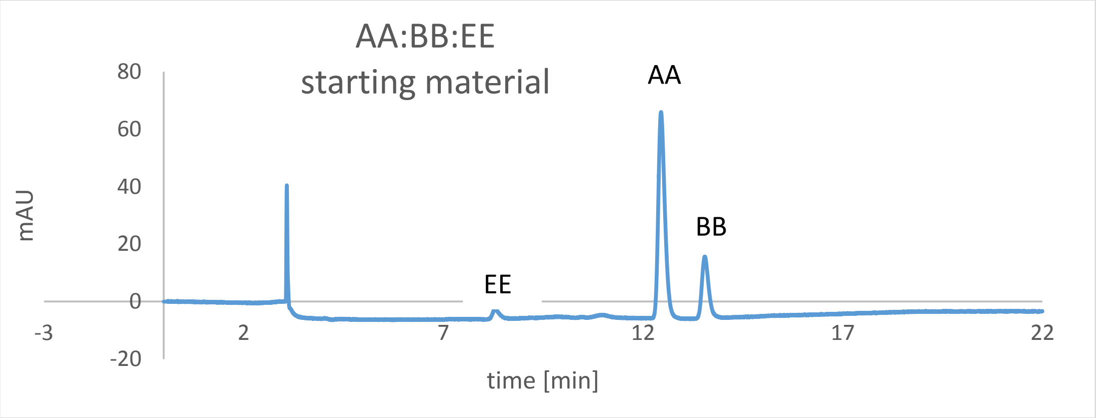


Figure S 28: HPLC trace of reaction Table 2, entry 6 at 254 nm at start of the reaction (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

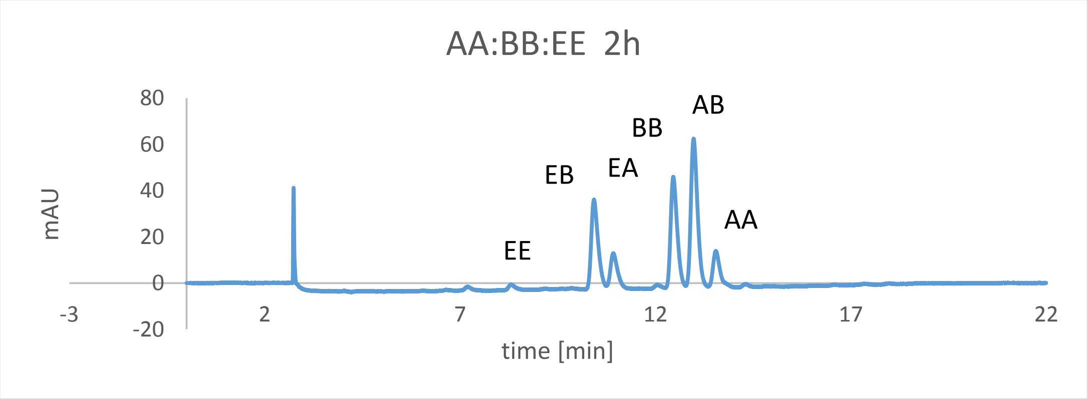


Figure S 29: HPLC trace of reaction Table 2, entry 6 at 254 nm after 1.5 h reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).

Note: we also carried out a ternary exchange experiment with compounds **DD**, **EE** and **FF**. In this experiment, we observed appearance of product **DE** after 40 min, but could not observe any exchange products featuring residue **F** (hence **FF** seems to be rather unreactive but does not inhibit the reaction).

Kinetic Measurements

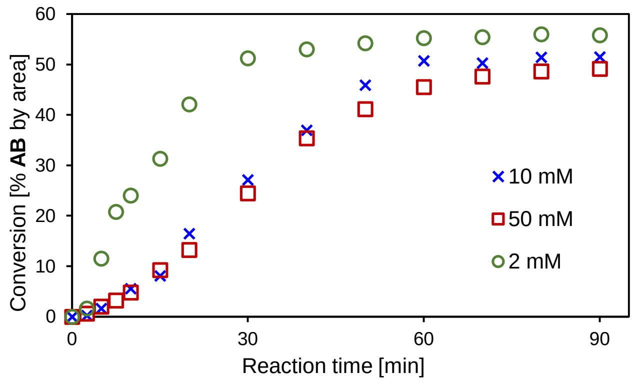


*Figure S 30: HPLC monitoring of the metathesis of disulfides **AA** and **BB** under sonotrode conditions in chloroform. Influence of starting material concentration (2 mM, 10 mM, 50 mM).*

Time [min]	10 mM [%**AB** by area]	50 mM [%**AB** by area]	2 mM [%**AB** by area]
2.5	0.255	0.612	1.605
5	1.639	1.972	11.538
7.5		3.212	20.771
10	5.554	4.779	24.006
15	8.124	9.227	31.336
20	16.489	13.206	42.115
30	27.108	24.499	51.235
40	36.95	35.379	53.011
50	45.907	41.154	54.199
60	50.742	45.559	55.217
70	50.285	47.615	55.441
80	51.434	48.673	56.018
90	51.493	49.135	55.792
100	51.785	50.831	56.646
110	51.574	51.051	56.64
120	51.838	50.932	56.405

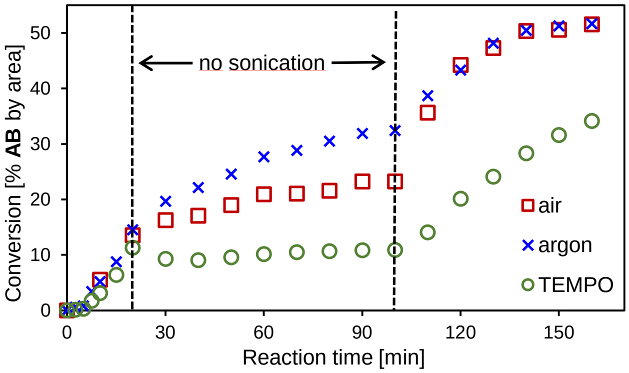


*Figure S 31: HPLC monitoring of the metathesis of disulfides **AA** and **BB** under sonotrode conditions in chloroform. Influence of switching off the ultrasound source (period: 20-100 min) under Argon, air or under Argon with addition of 40 mM radical scavenger TEMPO ((2,2,6,6-Tetramethylpiperidin-1-yl)oxyl) after 20 min.*

Time [min]	Air [%**AB** by area]	Argon [%**AB** by area]	TEMPO [%**AB** by area]
2.5		0.571	0.096
5		0.801	0.297
7.5		3.4	1.698
10	5.553	5.204	3.097
15		8.757	6.373
20	13.569	14.534	11.268
30	16.276	19.684	9.294
40	17.042	22.148	9.063
50	18.959	24.543	9.591
60	20.921	27.695	10.119
70	21.041	28.823	10.517
80	21.583	30.507	10.646
90	23.259	31.872	10.822
100	23.232	32.433	10.889
110	35.667	38.689	14.047
120	44.245	43.298	20.132
130	47.3	48.133	24.122
140	50.367	50.476	28.324
150	50.592	51.257	31.608
160	51.549	51.676	34.138

AA:**BB** in $H_2O/CHCl_3$ emulsion

Compound **AA** (36.7 mg, 0.15 mmol) and compound **BB** (45.9 mg, 0.15 mmol) were placed in a three-neck Suslick cell and dissolved in 7.5 mL $CHCl_3$, then 7.5 mL H_2O were. The reaction mixture was placed in an ice bath during the whole time of the reaction to avoid heating of the solvent. Pulsed ultrasound was applied (0.5 s on and 1.0 s off) at 25% amplitude for 1.5 h.

AA:**BB** in $H_2O/CHCl_3$ emulsion after 1.5 h of sonication (4% exchange):

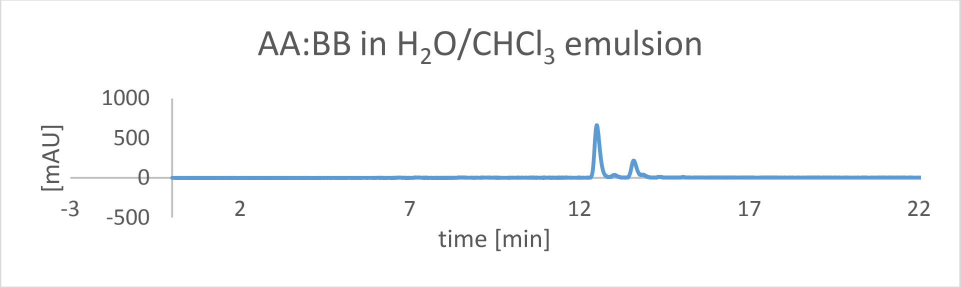


Figure S 32: HPLC trace of reaction ***AA:BB*** *in a $H_2O/CHCl_3$ emulsion at 254 nm after 90 min reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).*

AA:**BB** in $H_2O/CHCl_3$ emulsion after 1.5 h of sonication <u>and 24 h rest</u> (4% exchange):

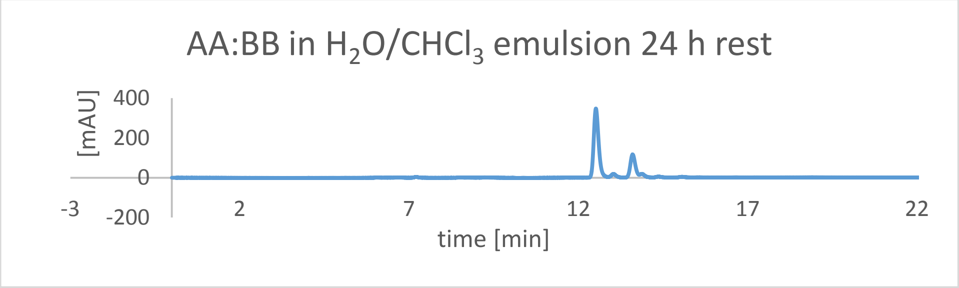


Figure S 33: HPLC trace of reaction ***AA:BB*** *in a $H_2O/CHCl_3$ emulsion at 254 nm after 90 min reaction time and 24 h rest (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).*

AA:BB in THF with $CHBr_3$ as additive

For the bromoform induced exchange the inhibitor of the tetrahydrofuran (BHT) was removed by filtering the solvent through a plug of activated basic alumina and then the solvents consecutively was degassed by bubbling through argon for 15 minutes. Compound **AA** (24.6 mg, 0.1 mmol) and compound **BB** (30.6 mg, 0.1 mmol) were placed together with $CHBr_3$ (100 eq., 2.5 g, 0.9 mL) in a three-neck Suslick cell and dissolved in 10 mL of the degassed solvent and kept under a slight argon flow during the reaction. The reaction mixture was placed in an ice bath during the whole time of the reaction to avoid heating of the solvent. Pulsed ultrasound was applied (0.5 s on and 1.0 s off) at 25% amplitude for the desired time.

AA:**BB** in THF with $CHBr_3$ as additive (100 eq.) after 1.5 h sonication (2% exchange):

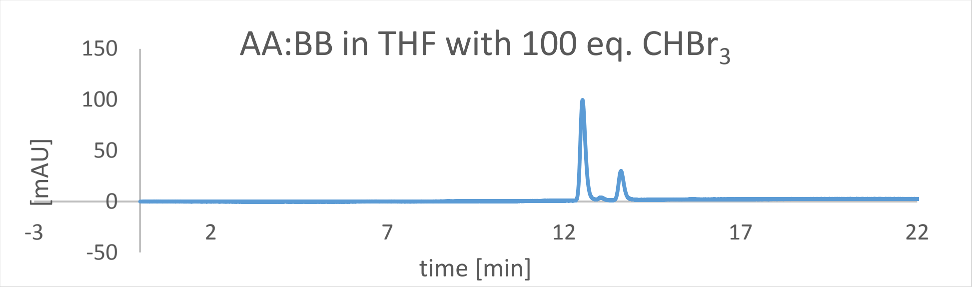


Figure S 34: HPLC trace of reaction ***AA:BB*** *in THF with 100 eq.* $CHBr_3$ *as additiv at 254 nm after 90 min reaction time (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).*

AA:**BB** in THF with $CHBr_3$ as additive (100 eq.) after 1.5 h sonication <u>and 18h rest</u>:

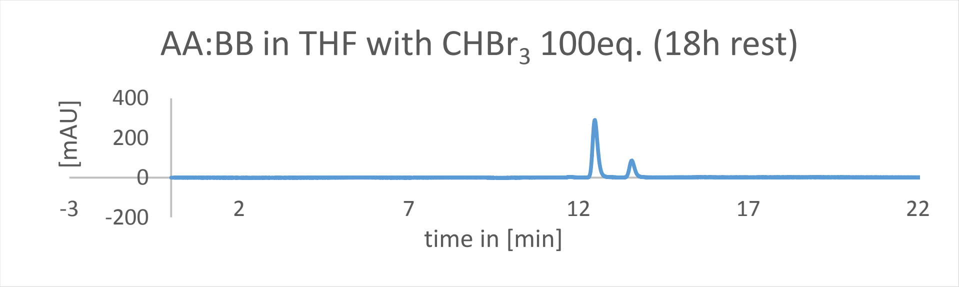


Figure S 35: HPLC trace of reaction ***AA:BB*** *in THF with 100 eq.* $CHBr_3$ *as additiv at 254 nm after 90 min reaction time and 18 h rest (Ascentis Amide cloumn, 70/30 acetonitrile/water → 100% acetonitrile over 10 minutes).*