Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information for:

A more sustainable isothiocyanate synthesis by amine catalyzed sulfurization of isocyanides with elemental sulfur

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Instrumentation and Materials

Nuclear Magnetic Resonance (NMR) Spectroscopy:

^{1}H- and ^{13}C- and spectra were recorded on Bruker Avance DRX (500 MHz for ^{1}H- and 126 MHz for ^{13}C-NMR) or Bruker Ascend™ 400 (400 MHz for ^{1}H- and 101 MHz for ^{13}C-NMR). Unless otherwise stated, all spectra were measured at ambient temperature. The chemical shift for ^{1}H-NMR spectra was reported in parts per million (ppm) and referenced to characteristic solvent signals of partly deuterated solvents: $CDCl_3$ at 7.26 ppm and DMSO-d_6 at 2.50 ppm. ^{13}C-NMR spectra were reported in ppm relative to characteristic signals of partly deuterated solvents: the centroid peak of the $CDCl_3$ triplet at 77.16 ppm and DMSO-d_6 at 39.52 ppm. The spin multiplicity and corresponding signal patterns were abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, quint. = quintet, sext. = sextet, m = multiplet and br = broad signal. Coupling constants ^xJ were noted in Hz. Furthermore, 2D-NMR methods, e.g. heteronuclear multiple quantum coherence (HMQC), heteronuclear single quantum coherence (HSQC), heteronuclear multiple bond correlation (HMBC) and correlated spectroscopy (COSY) were carried out for signal assignment and structure conformation. If isomers (*e.g*. diastereomers, rotamers) of a substance were observed, all species which could be assigned were clearly labelled with additional appendices (a, b, c. etc.). Hereby, the main isomer was labelled with the appendix “a”, the second conformer with appendix “b” and so on.

Mass Spectrometry (MS):

Fast-atom-bombardment (FAB) and electron ionization (EI) spectra were recorded utilizing a Finnigan MAT 95 mass spectrometer. A Q Exactive (Orbitrap) mass spectrometer (Thermo Fisher Scientific, San Jose, CA, USA) equipped with a HESI II probe was employed to record high resolution electrospray ionization–MS (ESI-MS). Calibration was carried out in the m/z range 74–1,822 using premixed calibration solutions (Thermo Fisher Scientific). A constant spray voltage of 4.7 kV and a dimensionless sheath gas of 5 were employed. The S-lens RF level was set to 62.0, while the capillary temperature was set to 250 °C. All samples were dissolved at a concentration of 0.05 mg mL^{-1} in a mixture of THF and MeOH (3:2) doped with 100 µmol sodium trifluoroacetate and injected with a flow of 5 µl min^{-1}.

Column chromatography;

TLC silica gel F254 (Sigma Aldrich) and HPLC-grade solvents were used.

Infrared Spectroscopy (IR):

Infrared spectra (IR) were recorded on a BRUKER Alpha-p instrument applying ATR-technology (ATR = Attenuated Total Reflection) in a frequency range from 3998 to 374 cm^{-1}. The band intensities were characterized in relation to the most intense signal as follows: vs = very strong, s = strong, m = medium, w = weak, vw = very weak. In addition, broad signals were expressed by the term: br = broad

Gas Chromatography (GC):

Gas chromatography (GC) was performed on a Bruker 430 GC instrument equipped with capillary column FactorFour™ VF-5 ms (30.0 m × 0.25 mm × 0.25 µm), using flame ionization detection (FID). The oven temperature program was: initial temperature 95 °C, hold for 1 min, ramp at 15°C min^{-1} to 200 °C, hold for 4 min, ramp at 15°C min^{-1} to 300 °C, hold for 2 min. Measurements were performed in split-split mode using nitrogen as the carrier gas (flow rate 30 mL min^{-1}) and were recorded for 20 min in total.

Size exclusion chromatography (SEC):

SEC measurements were performed in HFIP containing 0.1 wt% potassium trifluoroacetate with Tosoh EcoSEC HLC-8320 SEC system. The solvent flow was 0.40 mL min^{-1} at 30 °C and the concentration of the samples was 1 mg min^{-1}. The analysis was performed on a three-column system: PSS PFG Micro precolumn (3.0 × 0.46 cm, 10000 Å), PSS PFG Micro (25.0 × 0.46 cm, 1000 Å) and PSS PFG Micro (25.0 × 0.46 cm, 100 Å). The system was calibrated with linear poly(methyl methacrylate) standards (Polymer Standard Service, Mp: 102-981 kDa).

Elemental analysis (EA)

EA was performed on an Elementar Vario Micro cube. O_2-Dosage time: 70 s, Auto zero delay N: 10 s, Auto zero delay S: 10 s, Peak expectation N: 50 s, peak expectation C: 100 s, peak expectation H: 80 s, peak expectation S: 70 s, desorpt. CO2: 60 °C, desorpt. H_2O: 140 °C, desorpt. SO_2: 240°C

Thin Layer Chromatography (TLC):

For TLC analysis, precoated aluminium foils with fluorescence indicator from MERCK (TLC Silica gel 60, F254, layer thickness: 0.25 mm) were employed as stationary phase. The spots were firstly visualized by fluorescence quenching under UV-light ($\lambda = 254$ nm), fluorescence ($\lambda = 365$ nm), and by staining with Seebach reagent: solution of 2.50 g cerium(IV) sulfate tetrahydrate ($Ce(SO_4)_2 \times 4\ H_2O$), 6.25 g ammonium heptamolybdate tetrahydrate ($(NH_4)_6Mo_7O_{24} \times 4\ H_2O$), 225 mL water and 25.0 mL concentrated sulfuric acid or by staining with vanillin solution: 15 g vanillin and 2.5 mL concentrated sulfuric acid dissolved in 250 mL ethanol.

Materials:

All chemicals were used as received, if not mentioned otherwise. All solvents used in HPLC grade or higher.

Adamantylisocyanide (95%, Aldrich Chemistry), benzylisocyanide (98%, Acros Organics), biphenyl (99%, Alfar Aesar), cyclohexyl isocyanide (99%, Acros Organics), Cyrene™ (Sigma-Aldrich), 1,5-diaminopentane (98%, Acros Organics), 1,4-diazabicyclo[2.2.2]octane (≥99%, Sigma-Aldrich), 1,8-diazabicyclo[5.4.0]undec-7-en (>98%, TCI), diisopropylamine (99%, abcr), 4-dimethylaminopyridin (99%, Acros Organics), 2,6-dimethylphenyl isocyanide (≥98%, Aldrich Chemistry), 1,1,1,3,3,3-hexafluro-2-propanol (HFIP) (fluorochem), 2-isocyanonaphthalene (95%, Aldrich Chemistry), isophorendiamine (99%, TCI, mixtures of isomers), 1-methylimidazole (NMI, ≥99%, Sigma-Aldrich), 4-methoxyphenyl isocyanide (97%, Aldrich Chemistry), 2-morpholinoethyl isocyanide (≥98%, Aldrich Chemistry), pentylisocyanide (97%, Aldrich Chemistry), phosphorus oxychloride (99%, Aldrich), potassium 2-isocyanoacetate (technical grade (85%, Aldrich Chemistry), sulphur (elemental, technical grade), *tert*-butyl isocyanide (98% Aldrich), tosylmethylisocyanide (Fluorochem), 3,5,7-triazabicylco[4.40]dec-5-en), triethylamine (99.5%, Fisher Chemical), 3,4,5-trimethoxyanilline (97%, Acros Organics).

Optimization of the reaction conditions *via* GC-screening

Every synthesis set up for subsequent GC screening was prepared with the same general procedure. In a 10 mL screw-cap vial, *n*-dodecyl isocyanide **1a** (195 mg, 1.00 mmol, 1.00 eq.) along with biphenyl (internal standard (IS) 38.6 mg, 250 µmol, 0.25 eq.) were dissolved in the respective amount of solvent. After complete dissolution of the isocyanide and biphenyl, a t_0 sample was taken for GC analysis. Subsequently, the appropriate amounts of catalyst and elemental sulphur were added along with a stirring bar and the mixture was stirred for the duration of the given reaction time and temperature. Unless there were no specific reaction conditions (runs 18, 39-41), a metal block with twelve slots was used to allow simultaneous stirring and heating of the reactions. After a certain reaction time, a GC-sample (1.5 mg/mL of substance dissolved in ethyl acetate and prefiltered) was taken immediately.

The isocyanide conversion was calculated by evaluating the ratio of integrals for the isocyanide and IS using the following equation:

$$Conversion(Isocyanide)\ [\%] = 100\% * (1 - \frac{A(IC, t_x) * A(IS, t_0)}{A(IC, t_0) * A(IS, t_x)})$$

$A(IC, t_0)$ = Integral of the isocyanide peak (t_0 = 0 min)
$A(IC, t_x)$ = Integral of the isocyanide peak (t_x = x min)
$A(IS, t_0)$ = Integral of IS peak (t_0 = 0 min)
$A(IS, t_x)$ = Integral of IS peak (t_x = x min)

Table 1: Complete screening of several reaction conditions for the conversion of isocyanides (IC) to isothiocyanates.

1	DMAP {1.00}	DMSO {1 mL}	2.00	r.t.	2 h	38
2	NMI {1.00}	DMSO {1 mL}	2.00	r.t.	2 h	38
3	DBU {1.00}	DMSO {1 mL}	2.00	r.t.	2 h	99
4	DABCO {1.00}	DMSO {1 mL}	2.00	r.t.	2 h	84
5	TEA {1.00}	DMSO {1 mL}	2.00	r.t.	2 h	76
6	TBD {1.00}	DMSO {1 mL}	2.00	r.t.	2 h	100
7a	TBD {0.50}	DMSO {1 mL}	2.00	r.t.	2 h	96
7b	TBD {0.50}	DMSO {1 mL}	2.00	r.t.	22 h	100
8a	TBD {0.20}	DMSO {1 mL}	2.00	r.t.	2 h	75
8b	TBD {0.20}	DMSO {1 mL}	2.00	r.t.	22 h	94
9a	TBD {0.10}	DMSO {1 mL}	2.00	r.t.	2 h	36
9b	TBD {0.10}	DMSO {1 mL}	2.00	r.t.	22 h	69
10a	DBU {0.10}	DMSO {1 mL}	2.00	r.t.	2 h	57
10b	DBU {0.10}	DMSO {1 mL}	2.00	r.t.	24 h	67
11	TBD {0.10}	DMSO {1 mL}	2.00	40	2 h	85
12	TBD {0.10}	DMSO {1 mL}	2.00	60	2 h	100
13	TBD {0.10}	DMSO {1 mL}	2.00	80	2 h	100
14	TBD {0.10}	ACN {1 mL}	2.00	40	2 h	22
15	TBD {0.10}	EA {1mL}	2.00	40	2 h	0.76
16[1]	TBD {0.10}	Acetone {1 mL}	2.00	40	2 h	69
17	TBD {0.10}	Me-THF {1 mL}	2.00	40	2 h	3.8
18	TBD {0.10}	DMC {1 mL}	2.00	40	2 h	4.2
19	TBD {0.10}	Cyclohexane {1 mL}	2.00	40	2 h	6.4
20	TBD {0.10}	GBL {1 mL}	2.00	40	2 h	92
21	TBD {0.10}	Cyrene™ {1 mL}	2.00	40	2 h	100
22	TBD {0.10}	MEK {1 mL}	2.00	40	2 h	8.2
23	TBD {0.10}	Cyrene™ {1 mL}	2.00	40	30 min	85
24	TBD {0.10}	Cyrene™ {500 µL}	2.00	40	30 min	99
25	TBD {0.10}	Cyrene™ {250 µL}	2.00	40	30 min	100
26	TBD {0.10}	Cyrene™ {167 µL}	2.00	40	30 min	100
27	TBD {0.10}	-	2.00	40	30 min	6.7
28	TBD {0.05}	Cyrene™ {167 µL}	2.00	40	30 min	98
29	TBD {0.02}	Cyrene™ {167 µL}	2.00	40	30 min	82
30	TBD {0.01}	Cyrene™ {167 µL}	2.00	40	30 min	40
31	TBD {0.10}	Cyrene™ {167 µL}	1.50	40	30 min	100
32	TBD {0.10}	Cyrene™ {167 µL}	1.12	40	30 min	98
33a	DBU{0.05}	Cyrene™ {500 µL}	1.12	40	30 min	59
33b	DBU{0.05}	Cyrene™ {500 µL}	1.12	40	4 h	100
34a	DBU{0.02}	Cyrene™ {500 µL}	1.12	40	30 min	29
34b	DBU{0.02}	Cyrene™ {500 µL}	1.12	40	20 h	99
35	DBU{0.02}	Cyrene™ {167 µL}	1.12	40	4 h	100
36a	DBU{0.01}	Cyrene™ {167 µL}	1.12	40	4 h	78
36b	DBU{0.01}	Cyrene™ {167 µL}	1.12	40	20 h	96
37[2]	TBD {0.10}	Cyrene™ {1 mL}	2.00	40	30 min	24
38[3]	TBD {0.10}	Cyrene™ {1 mL}	2.00	40	10 min	53
39a[4]	TBD {0.10}	Cyrene™ {1 mL}	2.00	40	10 min	63
39b[4]	TBD {0.10}	Cyrene™ {1 mL}	2.00	40	20 min	91
39c[4]	TBD {0.10}	Cyrene™ {1 mL}	2.00	40	30 min	98

[1] The experiment was performed in a pressure vial.

[2] The experiment was performed in a microwave.

[3] The experiment was performed in an ultrasonic bath at a frequency of 37 kHz.

[4] The experiment was performed in an ultrasonic bath at a frequency of 80 kHz.

Synthesis of Isothiocyanates

General synthesis of isothiocyanates (GP1-A)

The corresponding solid isocyanide (1.00 eq., mp. >40 °C) was dissolved in dihydrolevoglucosenone (Cyrene™; c(isocyanide) = 2 M) and elemental sulfur (1.12 eq. of sulfur atoms) was added. After addition of 5 mol% of 1,8-diazabicyclo[5.4.0] undec-7-ene (DBU) the reaction mixture was stirred for 4 hours at 40°C. After completion of the reaction the pure product was obtained by optimized flash column chromatography applying a dry loaded small column (typically height of silica loading around 5-8 cm, see Figure S1) and a mixture of cyclohexane and ethyl acetate. Deviations of this procedure are given in the section of the respective substrate.

General synthesis of isothiocyanates (GP1-B)

The corresponding liquid isocyanide (1.00 eq., mp. ≤40 °C) was dissolved in dihydrolevoglucosenone (Cyrene™; c(isocyanide) = 6 M) and elemental sulfur 1.12 eq. of sulfur atoms) was added. After addition of 2 mol% of 1,8-diazabicyclo[5.4.0] undec-7-ene (DBU) the reaction mixture was stirred for 4 hours at 40°C. After completion of the reaction pure product was obtained by optimized flash column chromatography applying a dry loaded small column (typically height of silica loading around 5-8 cm, see Figure S1) and a mixture of cyclohexane and ethyl acetate yielded the pure product. Deviations of this procedure are given in the section of the respective substrate.

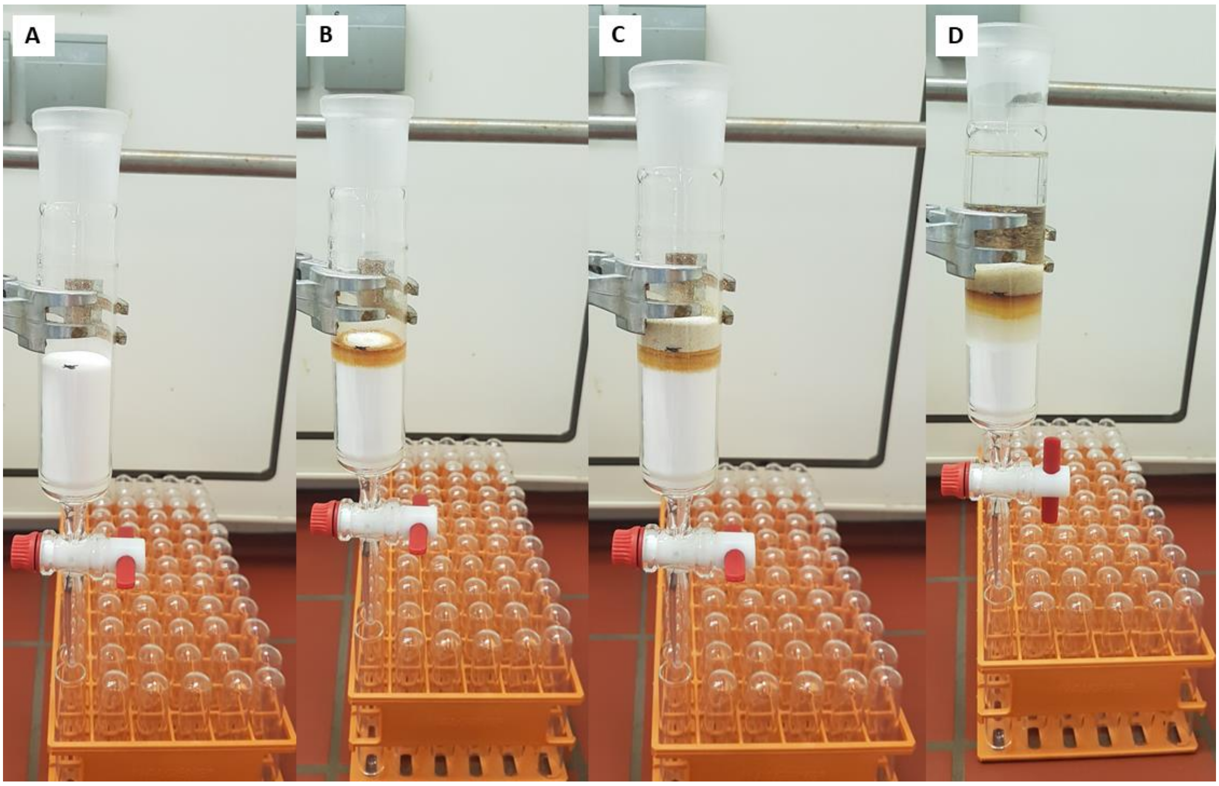


*Figure S1: Pictures of the purification of the obtained ITCs by a dry loaded column (height: 5 cm, width: 3 cm). The silica gel is put in the column (**A**) and then the crude product is applied directly after full conversion was observed via TLC (**B**). After adding sand, the eluent can be applied (**C**). The solvent frontier of the wetted silica gel can also be easily determined (compare **C** and **D**).*

n-Dodecyl isothiocyanate 3a

n-Dodecyl isocyanide (488 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (89.8 mg, 350 µmol, 1.120 eq.), DBU (7.46 µL, 7.61 mg, 50.0 µmol, 2 mol%) and 417 µL Cyrene™. Flash column chromatography was performed using a mixture of cyclohexane yielding the product (499 mg, 2.19 mmol) as colorless liquid in a yield of 88% (15.5 mmol scale, 87%).

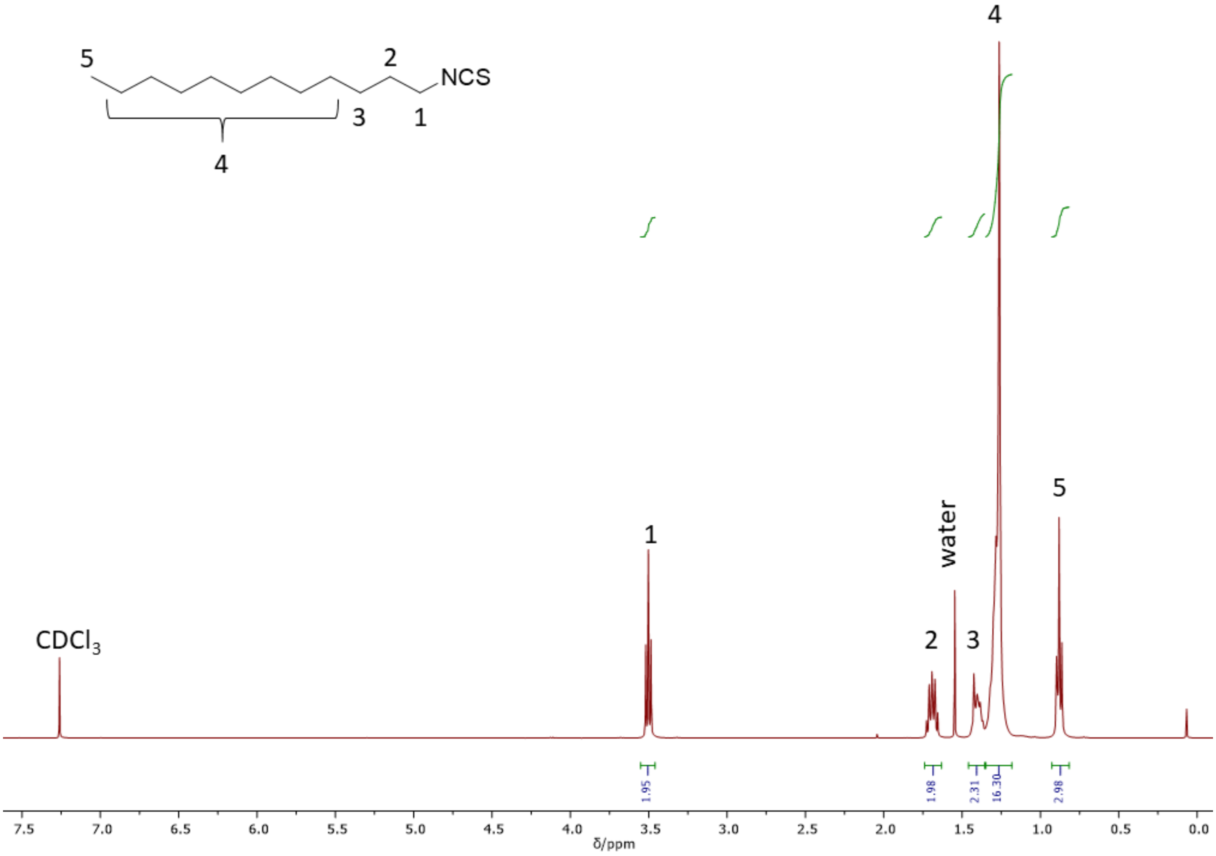
E-factor (2.5mmol): 1.26, E-factor (15.5mmol): 1.31

Purity was 97% according to GC-analysis.

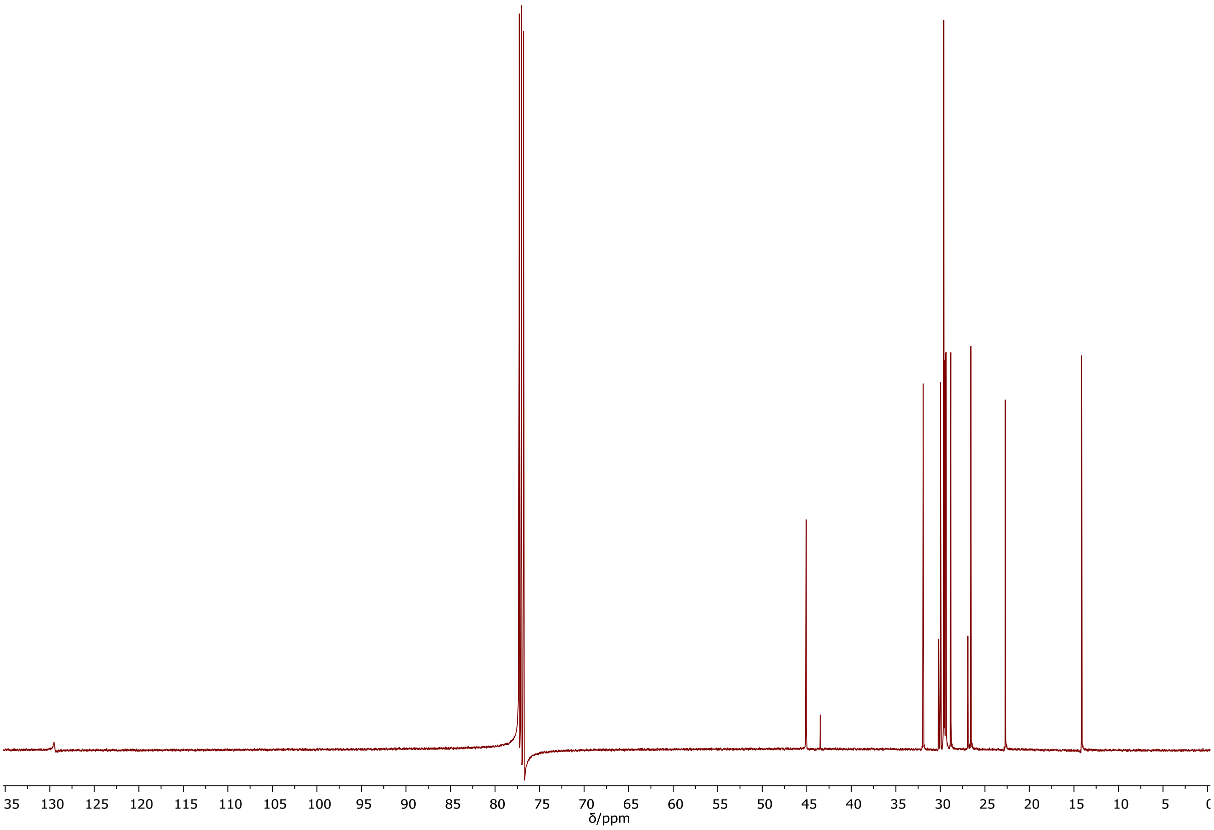
EA: Found: C, 68.85; H, 11.3; N, 6.3; S, 14.75%. Calc. for $C_{13}H_{25}NS$: C, 68.7; H, 11.1; N, 6.2; S, 14.1%

R_f = 0.56 in cyclohexane visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR (500 MHz, CDCl$_3$) δ / ppm = 3.50 (t, ^{3}J = 6.7 Hz, 2H,^{1}), 1.69 (m, 2H,^{2}), 1.40 (quint., ^{3}J = 6.7 Hz, 2H,^{3}), 1.28 (m, 16H,^{4}), 0.88 (t, ^{3}J = 6.9 Hz, 3H,^{5}).



^{13}C NMR (126 MHz, $CDCl_3$) δ / ppm = 129.54 (NCS), 45.08 (**C**H_2-NCS), 30.19 (CH_2), 29.98 (CH_2), 29.62 (CH_2), 29.52 (CH_2), 29.41 (CH_2), 29.35 (CH_2), 28.83 (CH_2), 26.58 (CH_2), 22.70 (CH_2), 14.14 (CH_3).



HRMS (EI): calculated m/z for $C_{13}H_{25}N_1S_1$ [M^+] = 227.1708, found: 227.1706, Δ = - 0.1871 mmu.

IR: *v*/cm^{-1} = 2921.3 (vs), 2852.2 (s), 2082.2 (s), 1455.0 (m), 1345.4 (m), 721.5 (w), 446.1 (w).

n-Pentyl isothiocyanate 3b

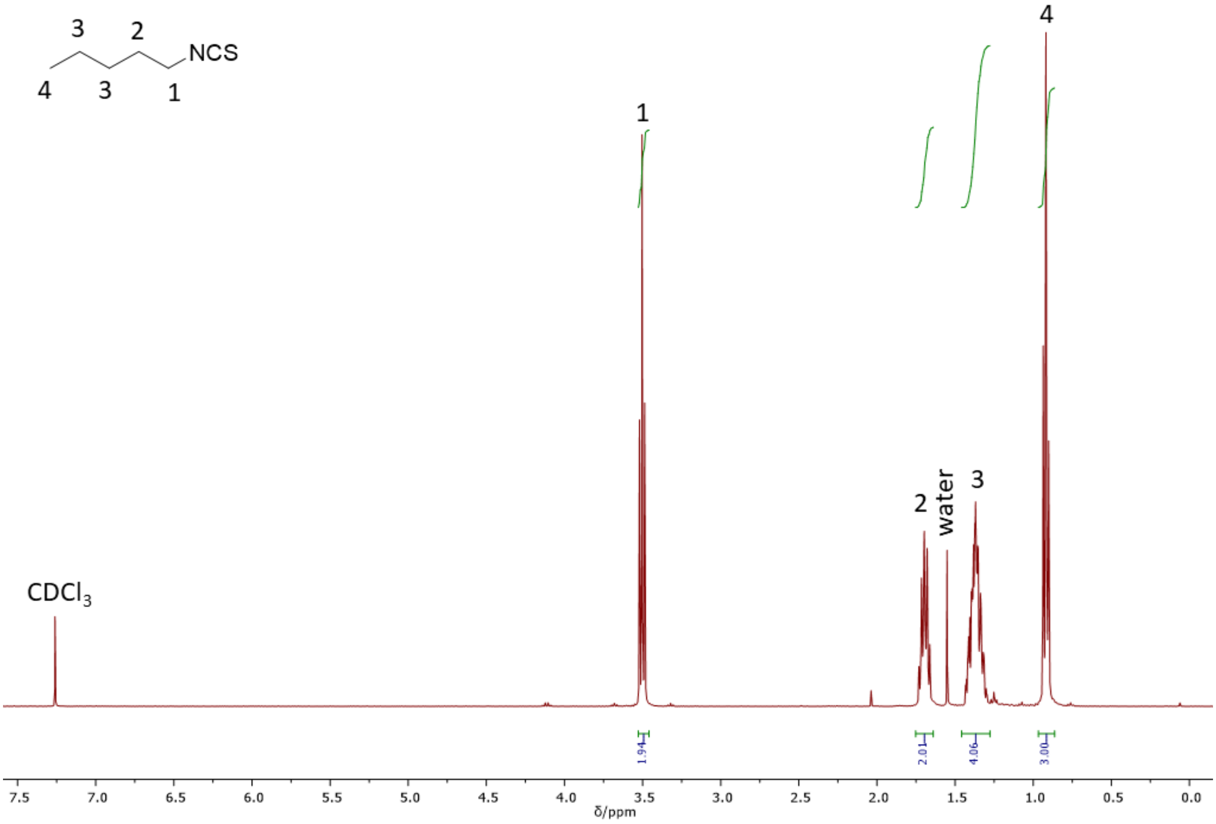
n-Pentyl isocyanide (243 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (89.2 mg, 350 µmol, 1.12 eq.), DBU (7.46 µL, 7.61 mg, 50.0 µmol, 2 mol%) and 417 µL Cyrene™. The reaction mixture was stirred for 5 hours. Flash column chromatography was performed using cyclohexane yielding the product (177 mg, 1.37 mmol) as a colorless liquid in a yield of 55%.

E-factor: 3.86

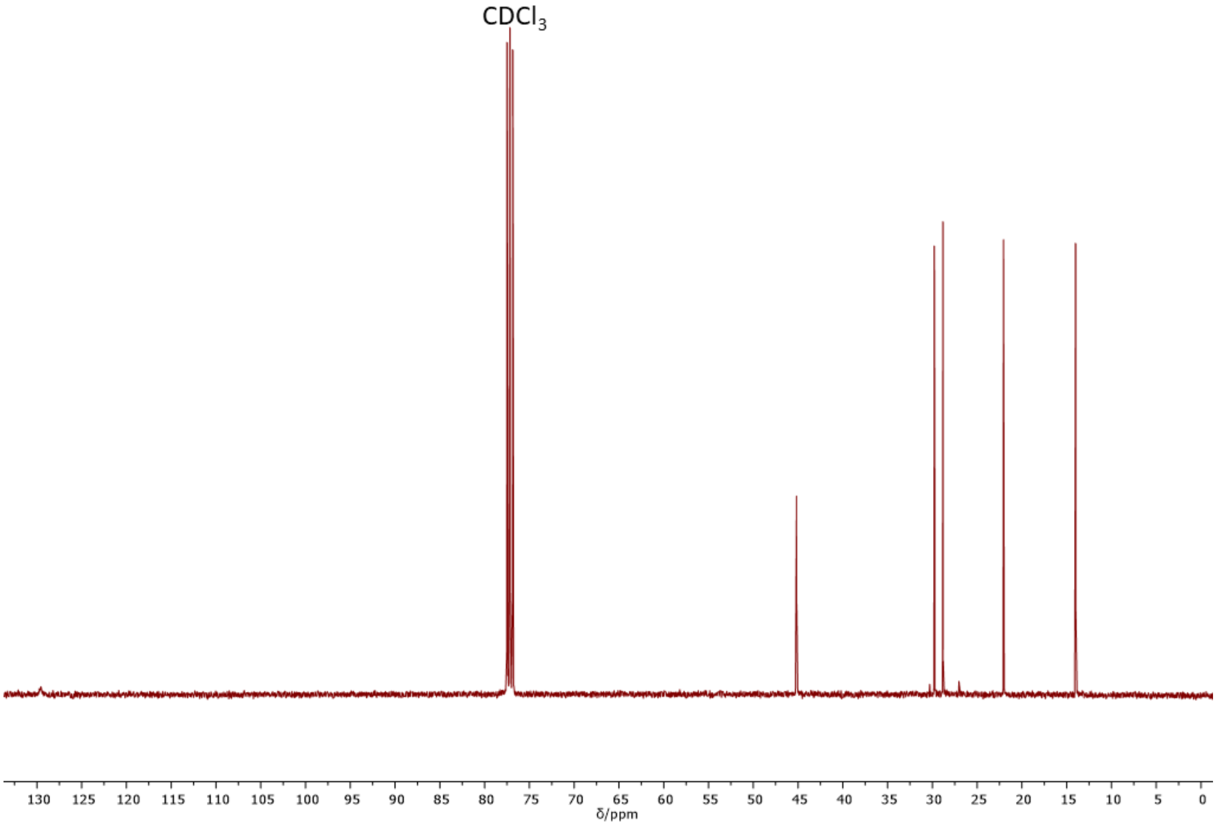
Purity was 98% according to GC-analysis.

R$_f$ = 0.77 in cyclohexane/ethyl acetate = 3:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 3.50 (t, ^3J = 6.6 Hz, 2H, CH_2, ^{1}), 1.70 (quint., ^3J = 7.0 Hz, 2H, CH_2, ^{2}), 1.47 – 1.25 (m, 4H, CH_2, ^{3}), 0.92 (t, ^3J = 7.1 Hz, 3H, CH_3, ^{4}).



^{13}C NMR (101 MHz, $CDCl_3$) δ / ppm = 129.56 (NCS), 45.16 (**C**H_2-NCS), 29.78 (CH_2), 28.81 (CH_2), 22.05 (CH_2), 13.99 (CH_3).



HRMS (ESI): calculated m/z for $C_6H_{12}N_1S_1$ [M+H$^+$] = 130.0685, found: 130.0685, Δ = 0.04 mmu.

IR: *v* / cm^{-1} = 2956 (m), 2929 (m), 2871 (w), 2860 (w), 2176 (s), 2149 (s), 2081 (vs), 1452 (w), 1344 (s), 921 (w), 731 (w), 684 (w), 640 (w), 524 (w), 450 (w).

1,10-Diisothiocyanato decane 3c

1,10-Diisocyanido decane (481 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (180 mg, 700 µmol, 2.24 eq.), DBU (7.46 µL, 7.61 mg, 50.0 µmol, 2 mol%) and 417 µL Cyrene™. Flash column chromatography was performed using cyclohexane yielding the product (531 mg, 2.07 mmol) as a yellowish liquid in a yield of 83%.

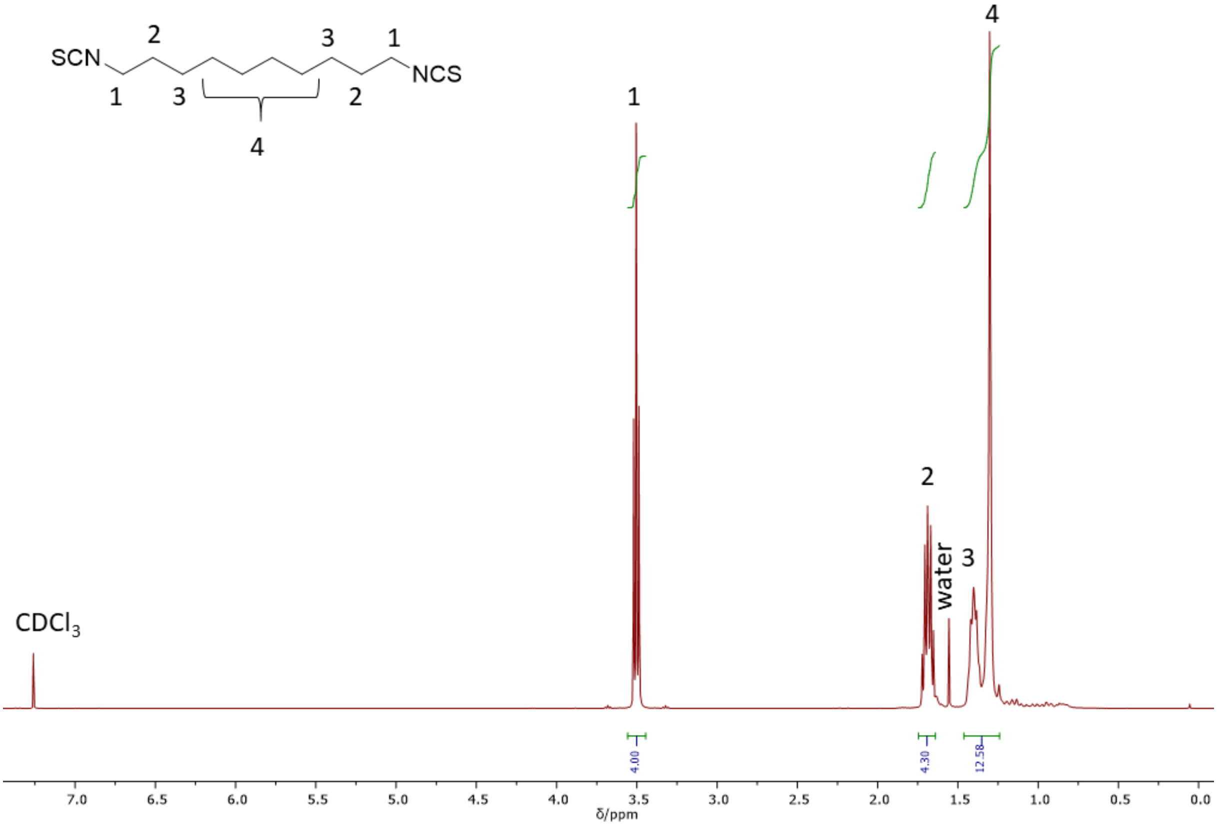
E-factor: 1.27

Purity was 97% according to GC-analysis.

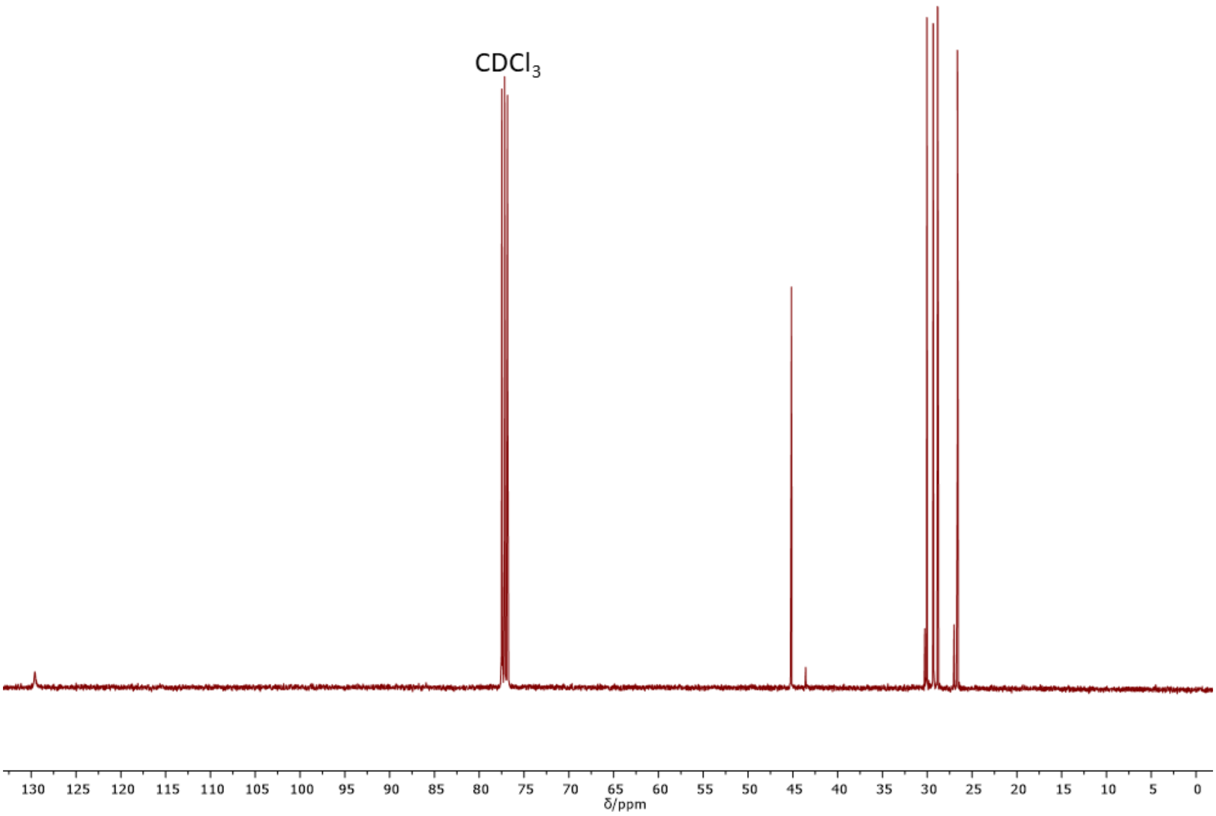
EA: Found: C, 56.95; H, 8.0; N, 10.8; S, 24.3 Calc. for $C_{12}H_{20}N_2S_2$: C, 56.2; H, 7.9; N, 10.9; S, 25.0%.

R$_f$ = 0.72 in cyclohexane/ethyl acetate = 3:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 3.50 (t, ^3J = 6.6 Hz, 4H, CH_2, ^{1}), 1.69 (quint., ^3J = 7.0 Hz, 4H, CH_2, ^{2}), 1.46-1.25 (m, 12H, CH_2, ^{3,4}).



^{13}C NMR (101 MHz, $CDCl_3$) δ / ppm = 129.59 (NCS), 45.16 (**C**H_2-NCS), 30.03 (CH_2), 29.31 (CH_2), 28.82 (CH_2), 26.62 (CH_2).



HRMS (EI): calculated m/z for $C_{12}H_{20}N_2S_2$ [M^+] = 256.1062, found: 256.1064, Δ = 0.1719 mmu.

IR: *v* / cm^{-1} = 2924 (s), 2853 (m), 2176 (s), 2075 (vs), 1449 (m), 1344 (s), 722 (w), 684 (w), 639 (w), 518 (w), 450 (w).

1,12-Diisothiocyanato dodecane 3d

1,12-Diisocyanido dodecane (551 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (180 mg, 700 µmol, 2.24 eq.), DBU (7.46 µL, 7.61 mg, 50.0 µmol, 2 mol%) and 417 µL Cyrene™. The reaction was stirred for 3 hours. Flash column chromatography was performed using a mixture of cyclohexane/ethyl acetate = 50:1 yielding the product (569 mg, 2.00 mmol) as a yellowish liquid in a yield of 80%.

E-factor: 1.21

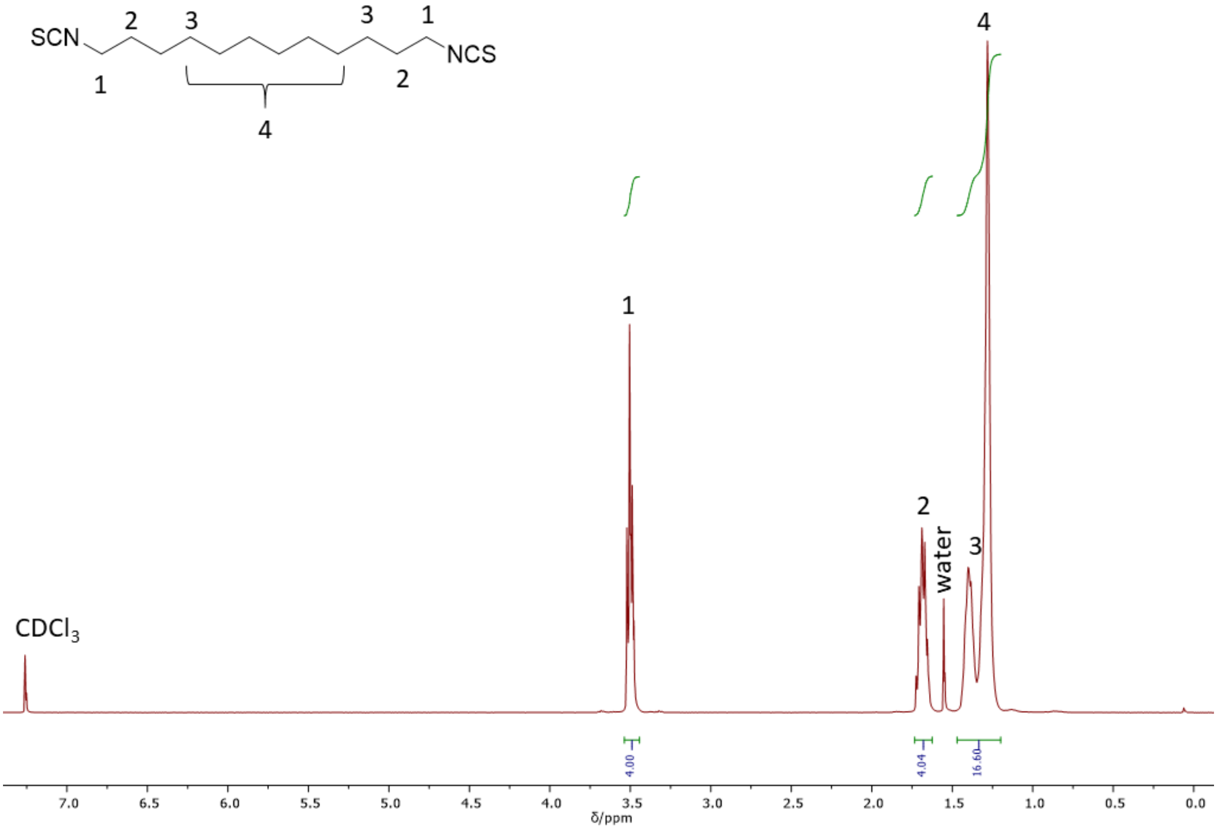
Purity was 98% according to GC-analysis.

EA: Found: C,59.55; H, 8.5; N, 10.1; S, 22.5 Calc. for $C_{14}H_{24}N_2S_2$: C, 59.1; H, 8.5; N, 9.85; S, 22.5%.

R$_f$ = 0.85 in cyclohexane/ethyl acetate = 3:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR was according to literature.[1]

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 3.50 (t, ^3J = 6.6 Hz, 4H, CH_2, ^{1}), 1.78-1.60 (m, 4H, CH_2, ^{2}), 1.49-1.15 (m, 16H, CH_2, ^{3,4}).



tert-Butyl isothiocyanate 3e

tert-Butyl isocyanide (1.75 mL, 1.29 mg, 15.5 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (557 mg, 2.17 µmol, 1.12 eq.), DBU (46.3 µL, 47.2 mg, 310 µmol, 2 mol%) and 2.6 mL Cyrene™. The reaction was stirred for 5 hours. The product (854 mg, 7.41 mmol) was obtained after distillation (50 °C, 10 mbar) as a colorless liquid in a yield of 48%.

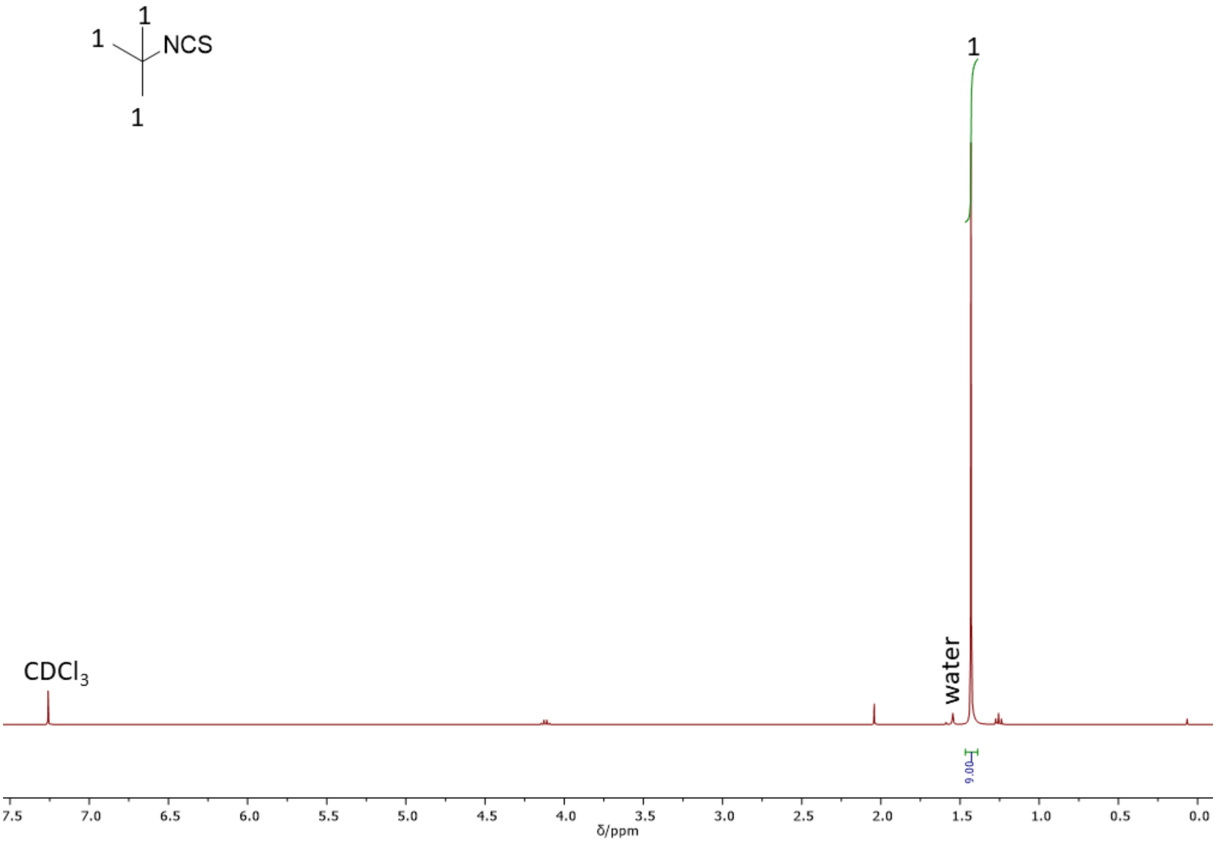
E-factor: 4.71

Purity was 97% according to GC-analysis.

R_f = 0.82 in cyclohexane/ethyl acetate = 9:1 visualized *via* UV quenching at 254 nm.

^{1}H-NMR was according to literature.[2]

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 1.43 (s, CH_3, ^{1}).



HRMS (ESI): calculated m/z for $C_5H_{10}N_1S_1$ [M+H$^+$] = 116.05306, found: 116.05285, Δ = - 0.15 mmu.

Adamantyl isothiocyanate 3f

Adamantyl isocyanide (403 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-A using elemental sulfur (89.8 mg, 350 µmol, 1.12 eq.), DBU (18.7 mL, 19.0 mg, 125 µmol, 5 mol%) and 1.25 mL Cyrene™. The reaction was stirred for 5 hours. Flash column chromatography was performed using cyclohexane yielding the product (407 mg, 2.10 mmol) as colorless crystals in a yield of 84%.

E-factor: 4.10

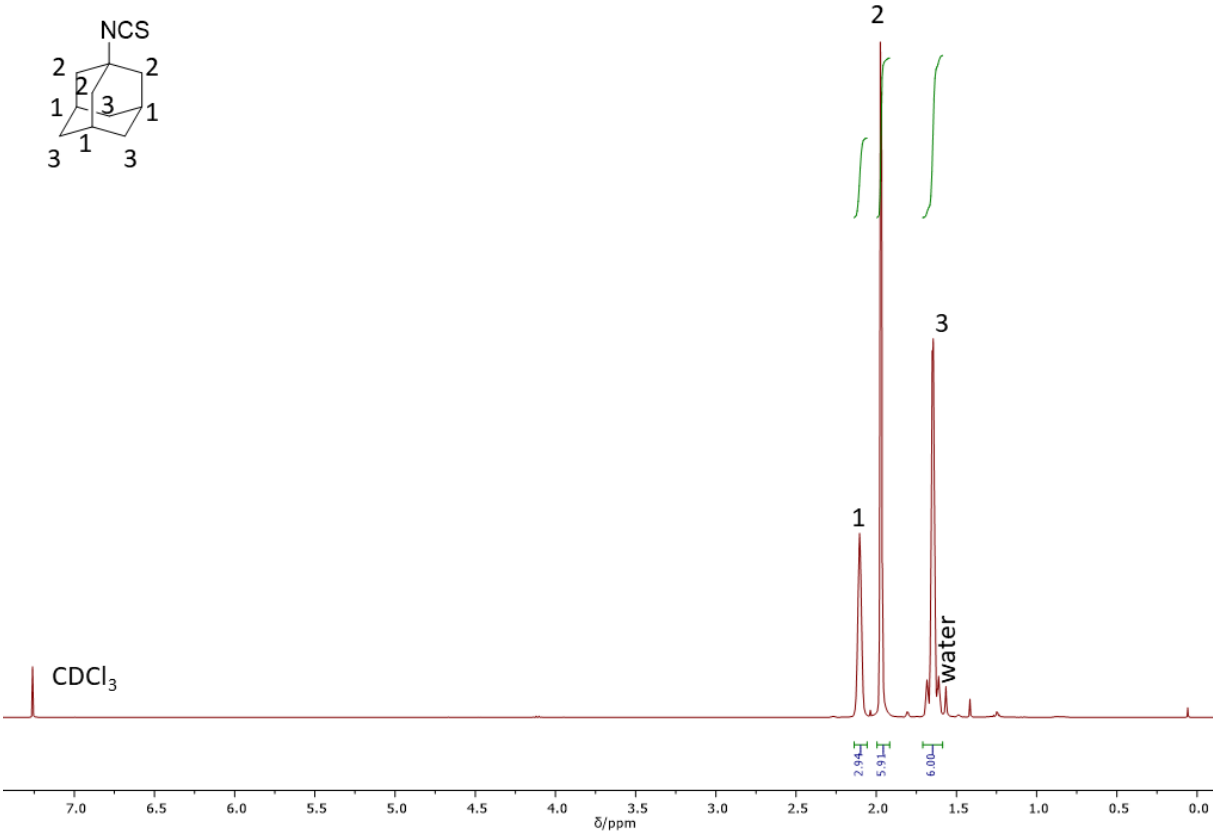
Purity was 99% according to GC-analysis.

EA: Found: C, 68.3; H, 7.8; N, 7.3; S, 16.4 Calc. for $C_{11}H_{15}NS$: C, 68.35; H, 7.8; N, 7.25; S, 16.6 %.

R_f = 0.79 in cyclohexane/ethyl acetate = 9:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR was according to literature.[3]

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 2.10 (s, br, 3H, CH, ^{1}), 1.97 (d, ^3J = 2.9 Hz, 6H, CH_2, ^{2}), 1.69-1.60 (m, 6H, CH_2, ^{3}).



Cyclohexyl isothiocyanate 3g

Cyclohexyl isocyanide (273 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (89.8 mg, 350 µmol, 1.12 eq.), DBU (7.46 µL, 7.61 mg, 50.0 µmol, 2 mol%) and 417 µL Cyrene™ or GBL. The reaction mixture was stirred for 4 hours in Cyrene™ and 23 hours in GBL. Flash column chromatography was performed using cyclohexane yielding the product (290 mg, 2.06 mmol in Cyrene™ or 238 mg, 1.68 mmol in GBL)) as a colorless liquid in a yield of 82% (Cyrene™) or 67% (GBL), (15.5 mmol scale in Cyrene™, 5h, 85%).

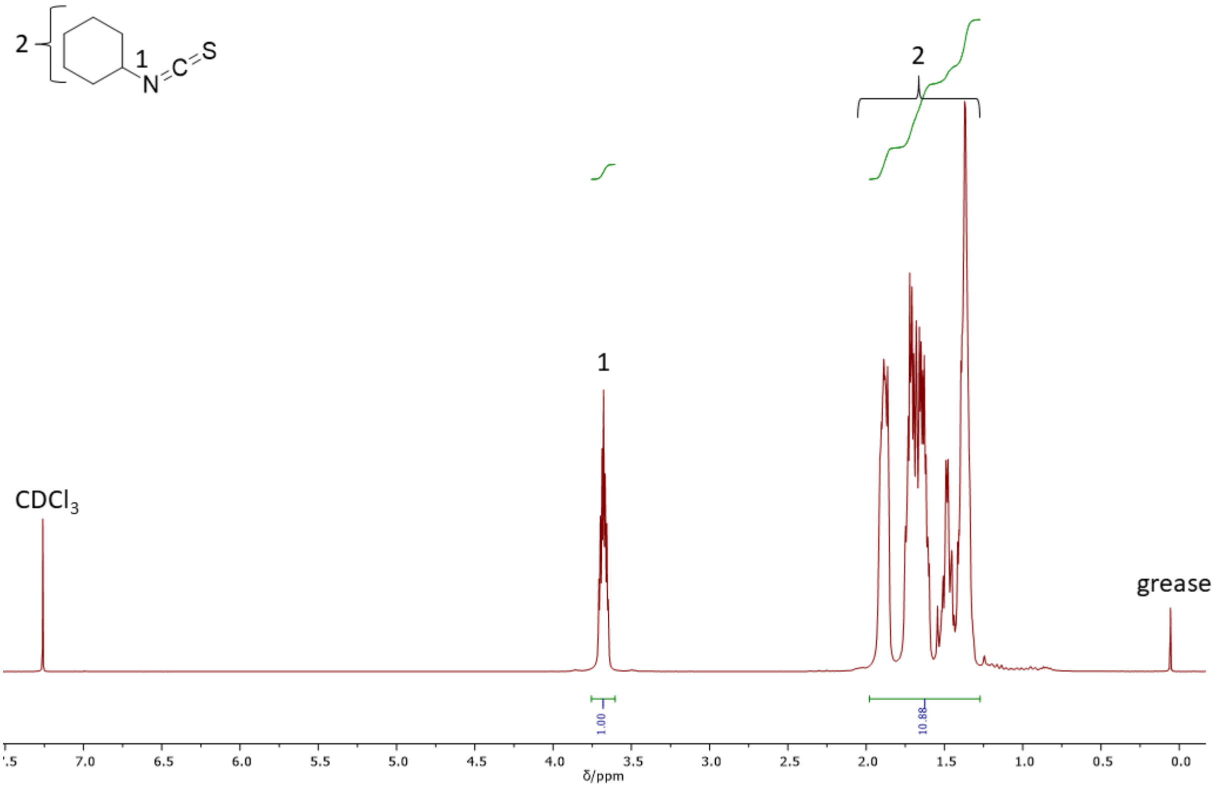
E-factor (2.50 mmol, Cyrene™): 2.08, E-factor (2.50 mmol, GBL): 2.81, E-factor (15.5 mmol): 1.99

Purity was 97% (Cyrene™), 98% (GBL), 99% (15.5 mmol scale) according to GC-analysis.

R_f = 0.77 in cyclohexane/ethyl acetate = 9:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR was according to literature.[4]

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 3.68 (tt, ^3J = 7.8, 3.7 Hz, 1H, CH, ^{1}), 1.98-1.29 (m, 10H, CH_2, ^{2}).



IR: *ν* / cm^{-1} = 2932 (vs), 2857 (m), 2174 (m), 2091 (vs), 2054 (vs), 1448 (m), 1361 (s), 1347 (w), 1319 (m), 1310 (m), 1262 (w), 1244 (w), 1145 (vw), 1133 (vw), 1088 (vw), 1010 (w), 986 (w), 891 (w), 861 (w), 854 (w), 800 (w), 720 (m), 701 (m), 537 (w), 497 (m), 473 (w), 441 (w).

5-Isothiocyanato-1-(isothiocyanatomethyl)-1,3,3-trimethyl cyclohexane 3h

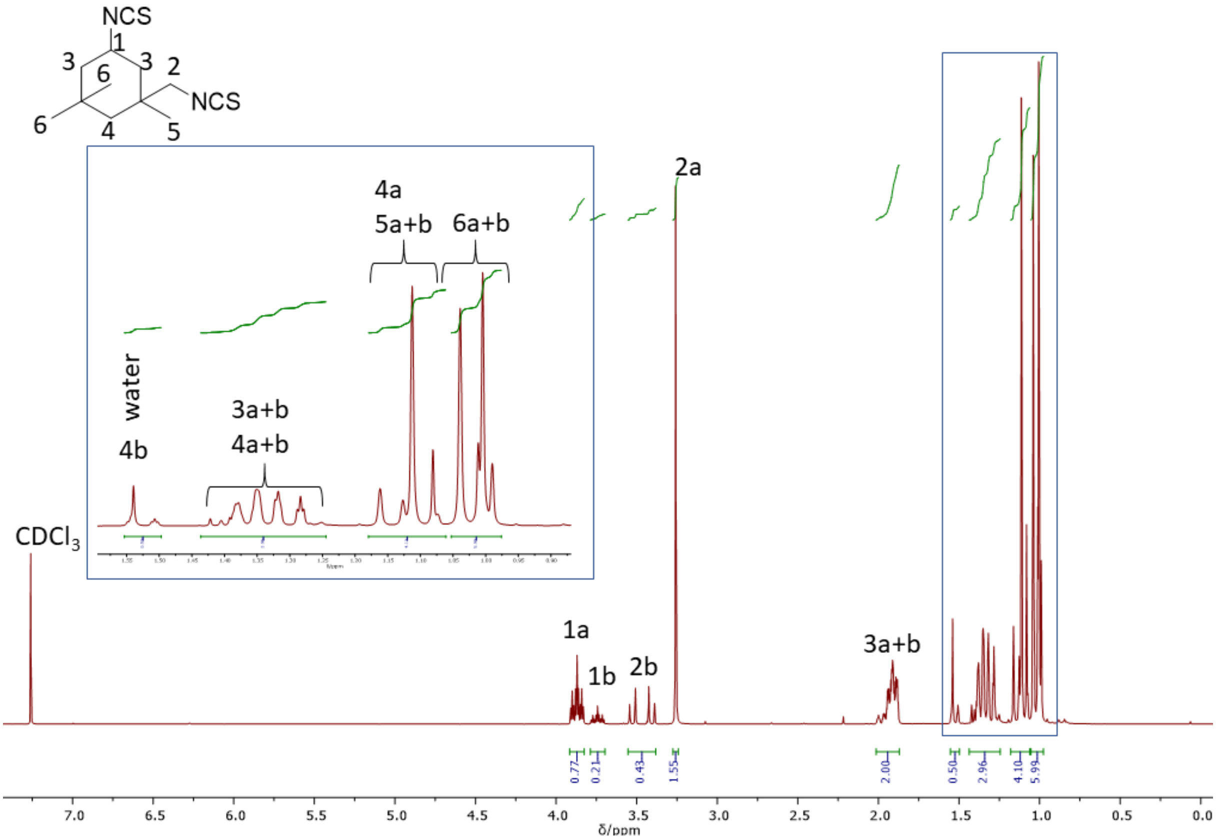
5-Isocyanido-1-(isocyanidomethyl)-1,3,3-trimethyl cyclohexane (421 mg, 2.21 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (159 mg, 619 µmol, 2.24 eq.), DBU (6.60 µL, 6.73 mg, 44.2 µmol, 2 mol%) and 368 µL Cyrene™. Flash column chromatography was performed using cyclohexane yielding the product (511 mg, 2.01 mmol) as a colorless solid in a yield of 91% (d.r. = 3.95:0 determined *via* GC).

E-factor: 1.06

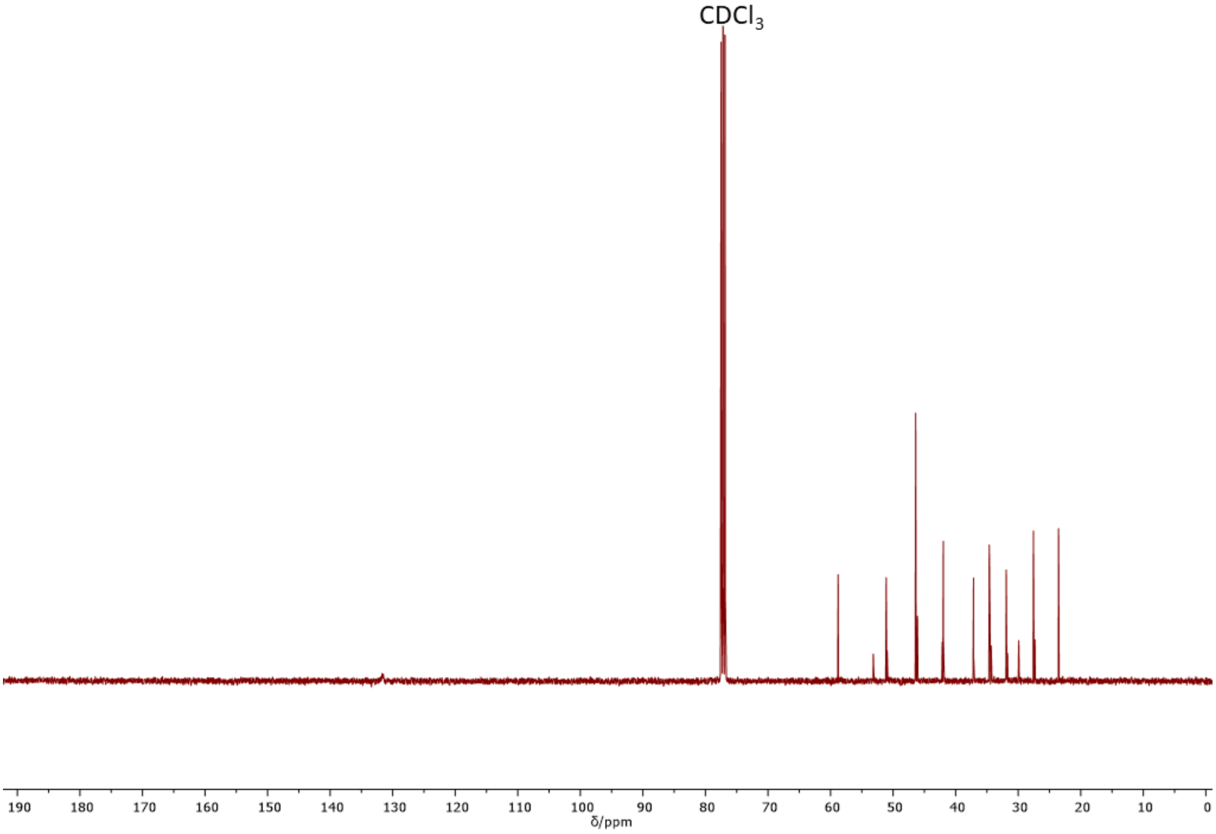
Purity was 99% according to GC-analysis.

R_f = 0.82 and 0.89 in cyclohexane/ethyl acetate = 3:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 3.87 (tt, ^3J = 11.9 Hz, 3.7 Hz, 0.77H, CH, ^{1a}), 3.74 (tt, ^3J = 11.8 Hz, 3.8 Hz, 0.21H, CH, ^{1b}), 3.52 (d, ^2J = 14.3 Hz, 0.22H, SCN-CH_2, ^{2b}), 3.41 (d, ^2J = 14.3 Hz, 0.22H, SCN-CH_2, ^{2b}), 3.26 (s, 1.55H, SCN-CH_2, ^{2a}), 2.02-1.86 (m, 2H, CH_2, $^{3a+b}$), 1.52 (m, 0.21H CH_2, ^{4b}), 1.44-1.23 (m, 3H, CH_2, $^{3a+b,\ 4a+b}$), 1.18-1.06 (m, 4H, CH_2, CH_3, $^{4a,\ 5a+b}$), 1.06-0.96 (m, 6H, CH_3, $^{6a+b}$).



^{13}C-NMR (101 MHz, $CDCl_3$) δ / ppm = 131.65 (NCS), 58.78 (NCS-**C**H_2, a), 53.16 (NCS-**C**H_2, b), 51.08 (CH, a), 50.93 (CH, b), 46.38 (CH_2, a), 46.10 (CH_2, b), 42.14 (CH_2, b), 41.97 (CH_2, a), 37.16 ($C_{quart.}$, b), 37.13 ($C_{quart.}$, a), 34.61 (CH_3, a), 34.32 (CH_3, b), 31.91 ($C_{quart.}$, a), 31.70 ($C_{quart.}$, b), 29.90 (CH_3, b), 27.56 (CH_3, a), 27.30(CH_3, b), 23.53 (CH_3, a).



HRMS (EI): calculated m/z for $C_{12}H_{18}N_2S_2$ [M^+] = 254.0906, found: 254.0905, Δ = - 0.1426 mmu.

IR: *v*/cm^{-1} = 2953 (w), 2932 (w), 2870 (w), 2174 (vs), 2067 (vs), 1460 (m), 1446 (w), 1388 (w), 1368 (m), 1360 (s), 1333 (m), 1300 (w), 1249 (w), 1213 (w), 1198 (w), 1142 (w), 1078 (vw), 1064 (vw), 1033 (vw), 1000 (vw), 959 (w), 922 (w), 904 (w), 892 (w), 870 (w), 793 (m), 713 (m), 694 (s), 594 (w), 518 (w), 492 (w), 466 (m), 445 (m), 402 (w).

Oleyl isothiocyanate 3i

Oleyl isoycanide (694 mg, 81 w%, 2.02 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (89.8 mg, 350 µmol, 1.38 eq.), DBU (7.46 µL, 7.61 mg, 50.0 µmol, 3 mol%) and 417 µL Cyrene™. Flash column chromatography was performed using cyclohexane yielding the product (704 mg, 1.90 mmol) as a colorless liquid in a yield of 94%.

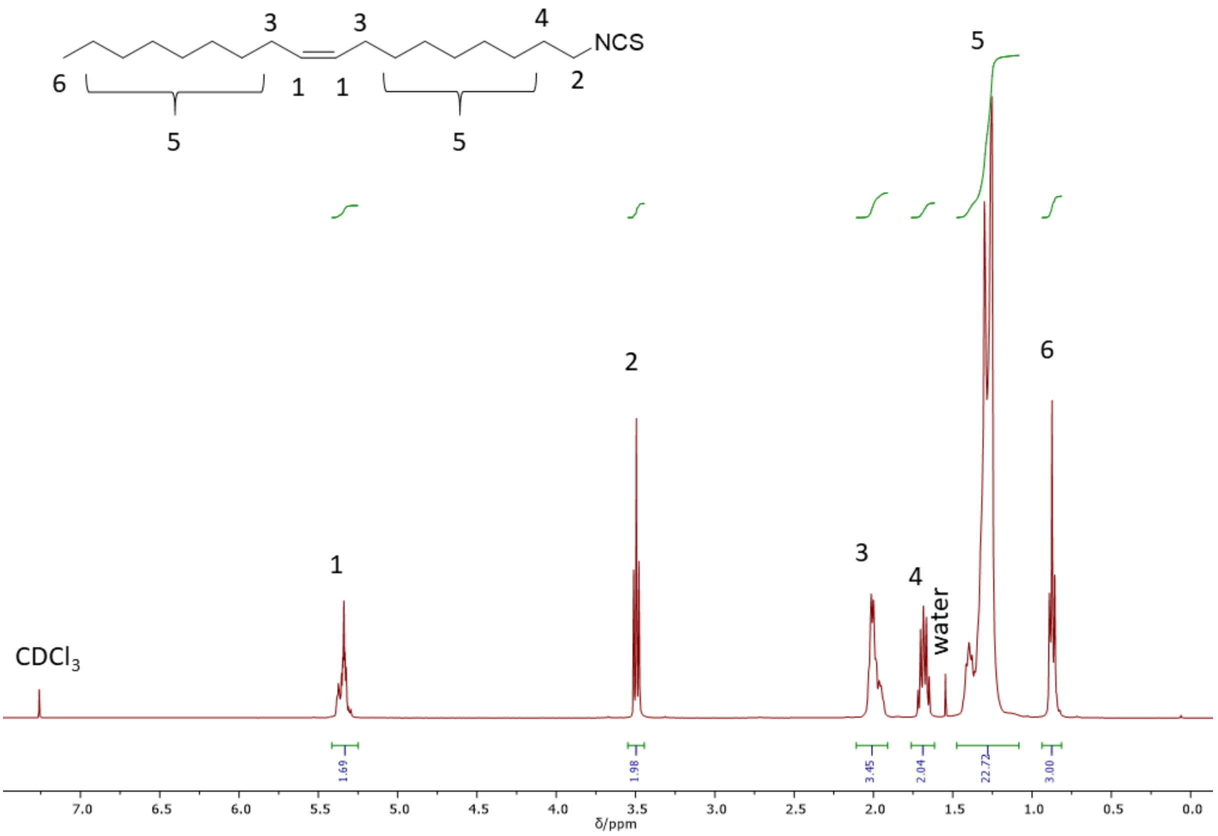
E-factor (2.50 mmol, Cyrene™): 1.22

Purity was 83% according to GC-analysis.

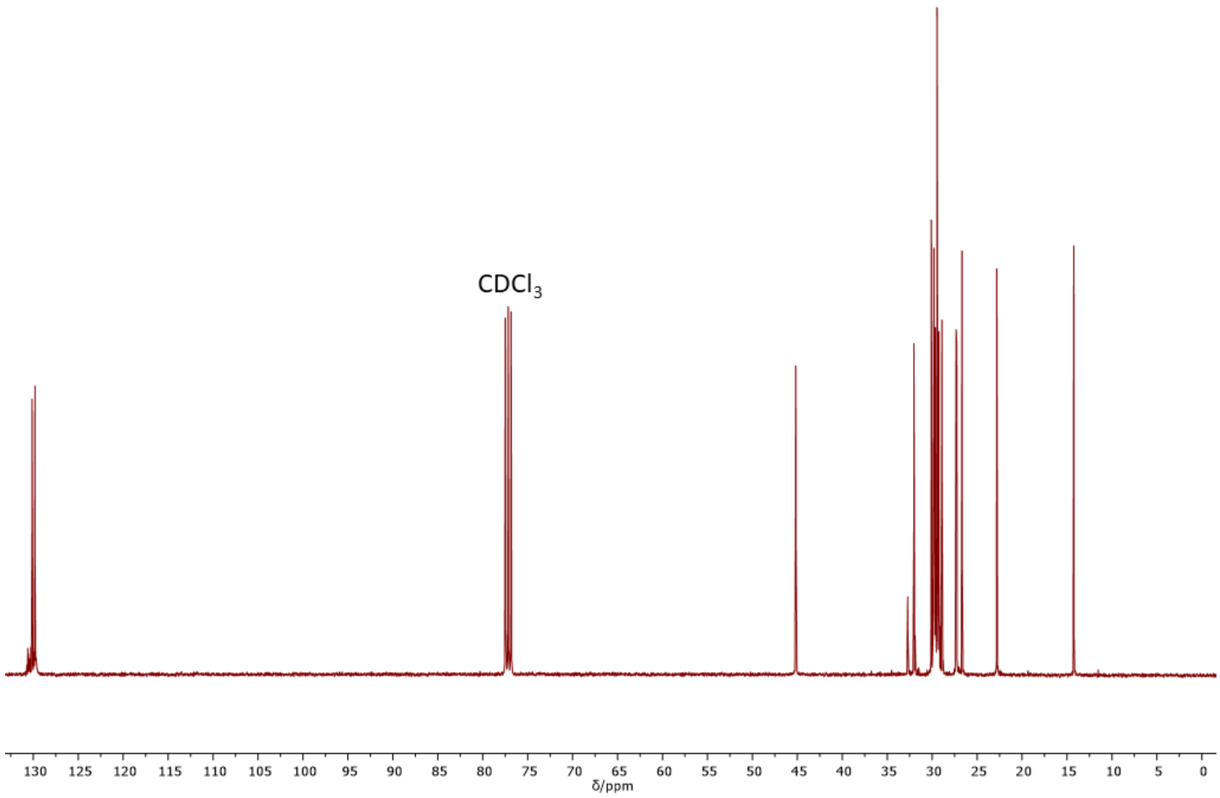
EA: Found: C, 73.3; H, 11.6; N, 5.1; S, 10.5 Calc. for $C_{19}H_{35}NS$: C, 73.7; H, 11.4; N, 4.5; S, 10.4%.

R$_f$ = 0.54 in cyclohexane visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 5.43 – 5.26 (m, 2H, CH, ^{1}), 3.50 (t, ^3J = 6.6 Hz, 2H, CH_2, ^{2}), 1.99 (m, 4H, CH_2, ^{3}), 1.68 (p, ^3J = 6.8 Hz, 2H, CH_2, ^{4}), 1.46 – 1.17 (m, 22H, CH_2, ^{5}), 0.87 (t, ^3J = 6.7 Hz, 3H, CH_3, ^{6}).



^{13}C-NMR (101 MHz, $CDCl_3$) δ / ppm = 130.13 (C=C), 129.81 (C=C), 129.69 (NCS), 45.17 (**C**H_2-NCS), 32.03 (CH_2), 30.09 (CH_2), 29.88 (CH_2), 29.80 (CH_2), 29.65 (CH_2), 29.44 (CH_2), 29.40 (CH_2), 29.25 (CH_2), 28.90 (CH_2), 27.33 (CH_2), 27.27 (CH_2), 26.66 (CH_2), 22.81 (CH_2), 14.23 (CH_3).



HRMS (EI): calculated m/z for $C_{19}H_{35}N_1S_1$ [M^+] = 309.2485, found: 309.2486, Δ = 0.1316 mmu.

IR: *v*/cm^{-1} = 3006 (vw), 2921 (vs), 2853 (vs), 2184 (w), 2082 (vs), 1456 (m), 1346 (m), 967 (w), 722 (w), 690 (w), 465 (w), 455 (w).

2-Morpholinoethyl isothiocyanate 3j

2-Morpholinoethyl isocyanide (351 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (89.8 mg, 350 µmol, 1.12 eq.), DBU (7.46 µL, 7.61 mg, 50.0 µmol, 2 mol%) and 417 µL Cyrene™. Flash column chromatography was performed using cyclohexane → cyclohexane/ethyl acetate = 2:1 yielding the product (307 g, 1.78 mmol) as a yellow liquid in a yield of 71%.

E-factor: 2.16

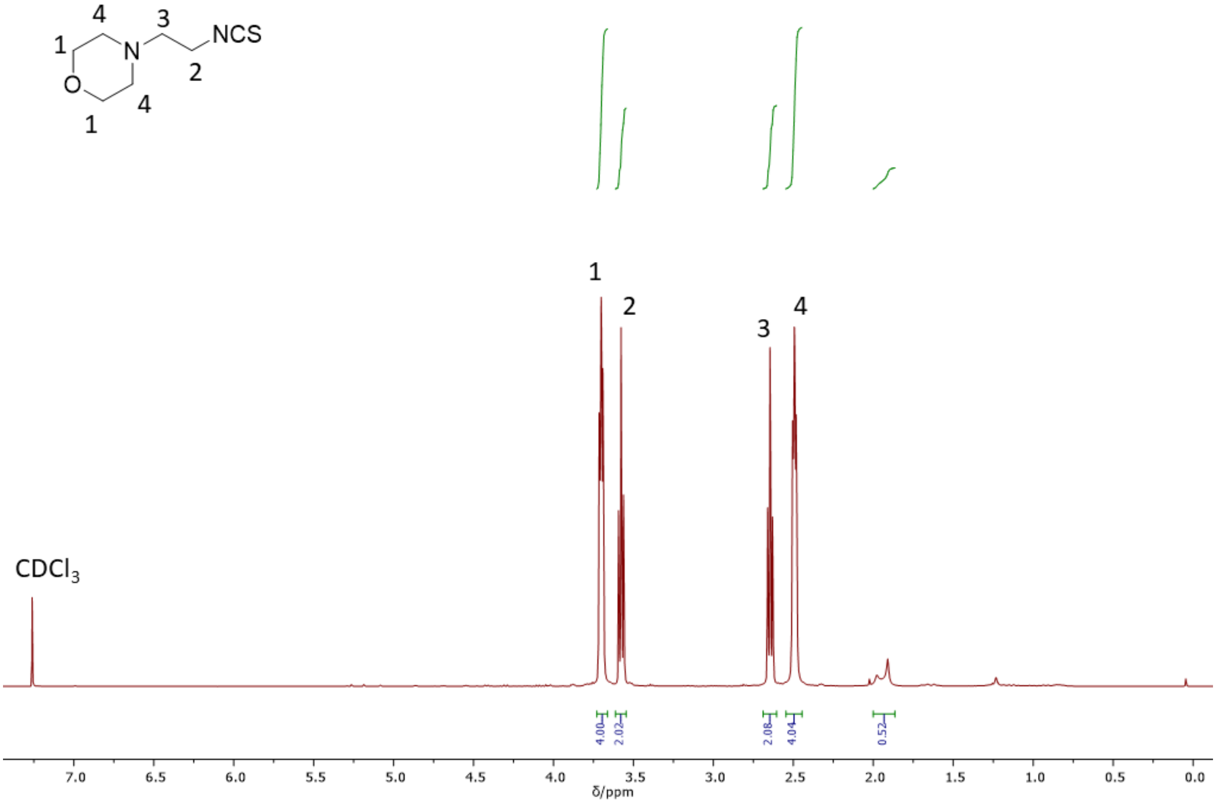
Purity was 97% according to GC-analysis.

EA: Found: C, 48.4; H, 7.0; N, 15.65; S, 17.5 Calc. for $C_7H_{12}N_2O_1S_1$: C, 48.8; H, 7.0; N, 16.3; S, 18.6%.

R$_f$ = 0.28 in cyclohexane/ethyl acetate = 1:3 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR was according to literature. [5]

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 3.72-3.68 (m, 4H, CH_2, [1]), 3.60-3.55 (m, 2H, CH_2, [2]), 2.67-2.62 (m, 2H, CH_2, [3]), 2.52-2.48 (m, 4H, CH_2, [4]).



Methyl-2-isothiocyanato-3-phenyl propionate 3k

Methyl-2-isocyanido-3-phenyl propionate (438 mg, 2.31 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (89.8 mg, 350 µmol, 1.21 eq.), DBU (7.46 µL, 7.61 mg, 50.0 µmol, 2 mol%) and 417 µL Cyrene™. The reaction was stirred for 23 hours. Flash column chromatography was performed using cyclohexane/ethyl acetate = 50:1 yielding the product (267 mg, 1.21 mmol) as a yellow liquid in a yield of 52%.

E-factor: 2.97

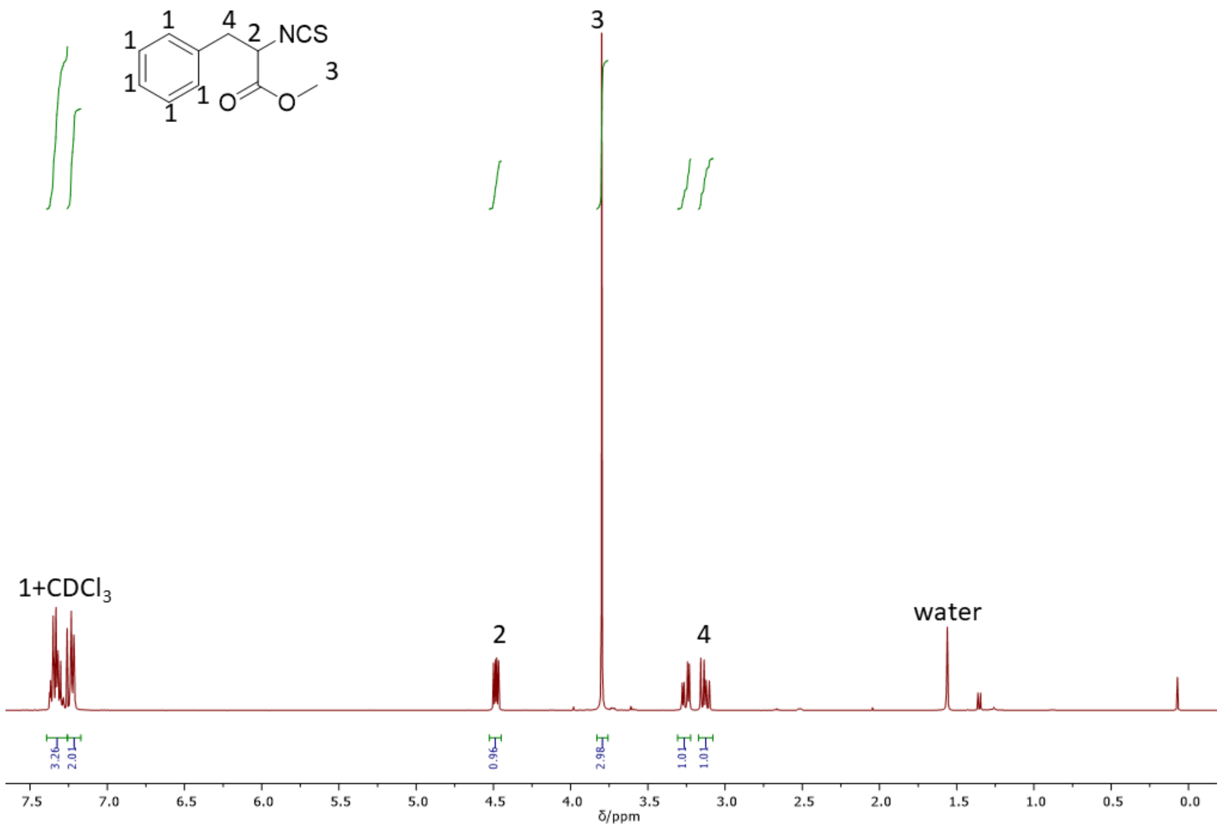
Purity was 98% according to GC-analysis.

R_f = 0.52 in cyclohexane/ethyl acetate = 3:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

EA: Found: C,59.15; H, 4.95; N, 7.2; S, 14.1 Calc. for $C_{11}H_{11}N_1O_2S_1$: C, 59.7; H, 5.0; N, 6.3; S, 14.5%.

^{1}H-NMR was according to literature.[3]

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 7.40-7.19 (m, 5H, aromatic, ^{1}), 4.48 (dd, ^3J = 8.4, 4.8 Hz, 1H, CH, ^{2}), 3.80 (s, 3H, CH_3, ^{3}), 3.25 (dd, ^2J = 13.8, ^3J = 4.7 Hz, 1H, CH_2, ^{4}), 3.13 (dd, ^2J = 13.8, ^3J = 8.4 Hz, 1H, CH_2, ^{4}).



Methyl-2-isothiocyanato-4-(methylthio) butanoate 3l

Methyl-2-isocyanido-4-(methylthio) butanoate (433 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (89.8 mg, 350 µmol, 1.12 eq.), DBU (7.46 µL, 7.61 mg, 50.0 µmol, 2 mol%) and 417 µL Cyrene™. The reaction was stirred for 6 hours. Flash column chromatography was performed using cyclohexane/ethyl acetate = 20:1 yielding the product (296 mg, 1.44 mmol) as a yellow liquid in a yield of 58%.

Purity was >99% according to GC-analysis.

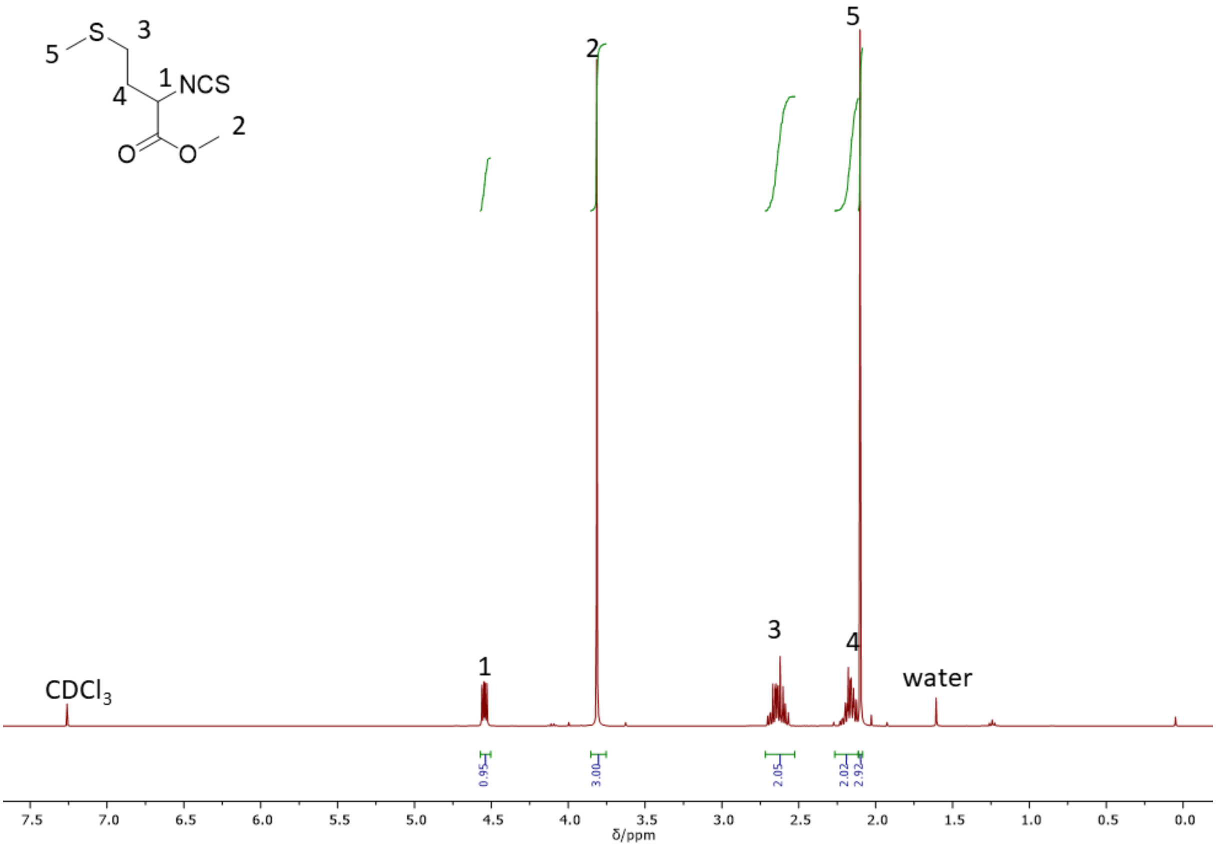
E-factor: 2.55

R$_f$ = 0.51 in cyclohexane/ethyl acetate = 5:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

EA: Found: C,40.9; H, 5.3; N, 7.0; S, 31.4 Calc. for $C_7H_{11}N_1O_2S_2$: C, 41.0; H, 5.4; N, 6.8; S, 31.2%.

^{1}H-NMR was according to literature.[3]

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 4.55 (dd, ^3J = 8.3 Hz, 4.8 Hz, 1H, CH, ^{1}), 3.81 (s, 3H, CH_3, ^{2}), 2.71-2.55 (m, 2H, CH_2, ^{3}), 2.23-2.11 (m, 2H, CH_2, ^{4}), 2.10 (s, 3H, CH_3, ^{5}).



Benzyl-11-isothiocyanato undecanoate 3m

Benzyl-11-isocyanido undecanoate (754 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (89.8 mg, 350 µmol, 1.12 eq.), DBU (7.46 µL, 7.61 mg, 50.0 µmol, 5 mol%) and 417 µL Cyrene™. Please note that for the 15.5 mmol scale, 2 mol% of DBU were used. The reaction was stirred for 22 hours. Flash column chromatography was performed using cyclohexane/ethyl acetate = 50:1 yielding the product (267 g, 1.21 mmol) as a colorless liquid in a yield of 77% (15.5 mmol scale, 24 h, 83%).

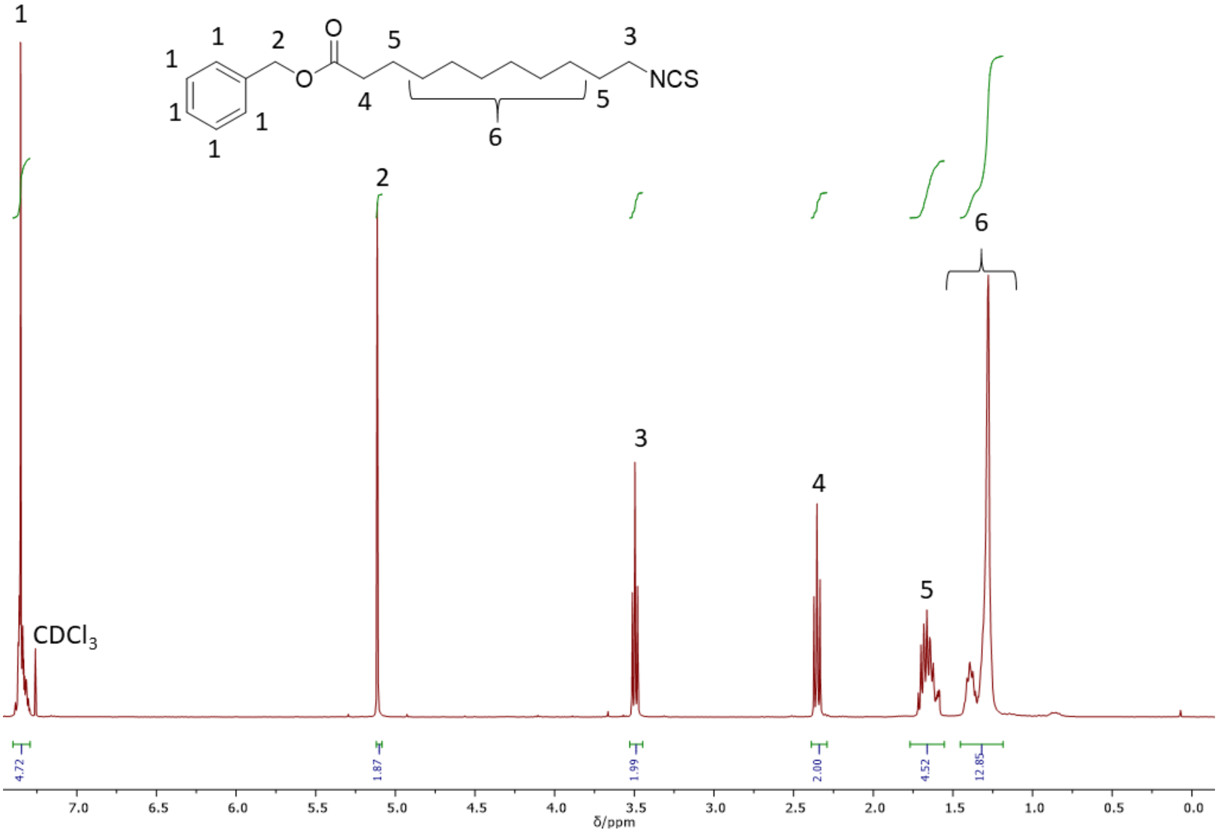
E-factor (2.50 mmol): 1.18, E-factor (15.5 mmol): 0.989

Purity was >99% according to GC-analysis.

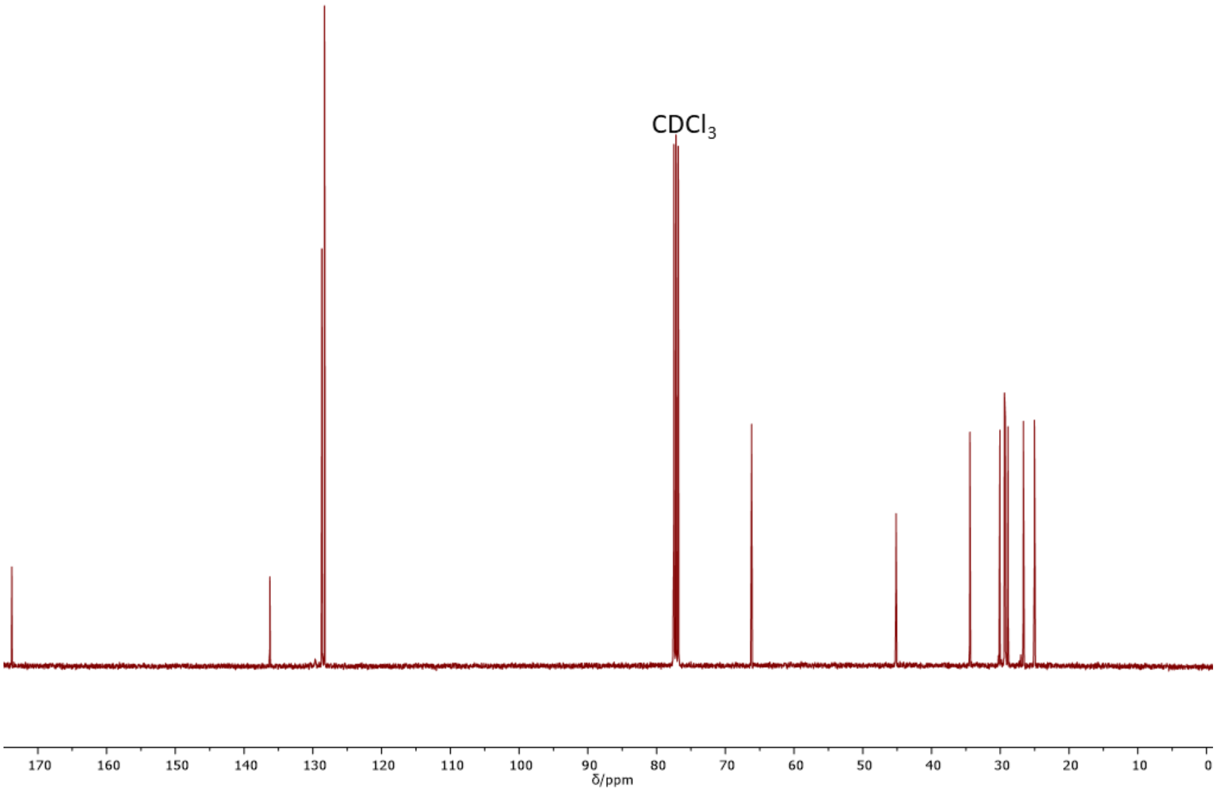
EA: Found: C, 68.6; H, 8.5, N, 4.6; S, 9.4 Calc. for $C_{19}H_{27}N_1O_2S_1$: C, 68.4; H, 8.2; N, 4.2; S, 9.6 %.

R$_f$ = 0.50 in cyclohexane/ethyl acetate = 9:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 7.40-7.29 (m, 5H, aromatic, ^{1}), 5.11 (s, 2H, CH_2, ^{2}), 3.50 (t, ^3J = 6.6 Hz, 2H, CH_2, ^{3}), 2.35 (t, ^3J = 7.5 Hz, 2H, ^{4}), 1.74-1.58 (m, 4H, CH_2, ^{5}), 1.45-1.21 (m, 12H, CH_2, ^{6}).



^{13}C-NMR (101 MHz, $CDCl_3$) δ / ppm = 173.79 (C=O), 136.26 (aromatic), 129.58 (NCS), 128.66 (aromatic), 128.28 (aromatic), 66.19 (**C**H_2-Ph), 45.17 (**C**H_2-NCS), 34.43 (**C**H_2-COOBn), 30.06 (CH_2), 29.40 (CH_2), 29.38 (CH_2), 29.27 (CH_2), 29.19 (CH_2), 28.88 (CH_2), 26.65 (CH_2), 25.04 (CH_2).



HRMS (EI): calculated m/z for $C_{19}H_{27}O_2N_1S_1$ [M^+] = 333.1757, found: 333.1758, Δ = 0.0781 mmu.

IR: *v*/cm^{-1} = 2925 (s), 2853 (m), 2179 (m), 2092 (vs), 1732 (vs), 1455 (m), 1346 (m), 1256 (m), 1228 (m), 1213 (m), 1160 (vs), 1102 (m), 1027 (w), 1001 (w), 980 (w), 735 (s), 696 (vs), 500 (w), 455 (w).

Benzyl isothiocyanate 3n

Benzyl isocyanide (304 µL, 298 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (89.8 mg, 350 µmol, 1.12 eq.), DBU (7.46 µL, 7.61 mg, 50.0 µmol, 2 mol%) and 417 µL Cyrene™. The reaction was stirred for 5 hours. Flash column chromatography was performed using cyclohexane yielding the product (281 g, 1.88 mmol) as a colorless liquid in a yield of 75%.

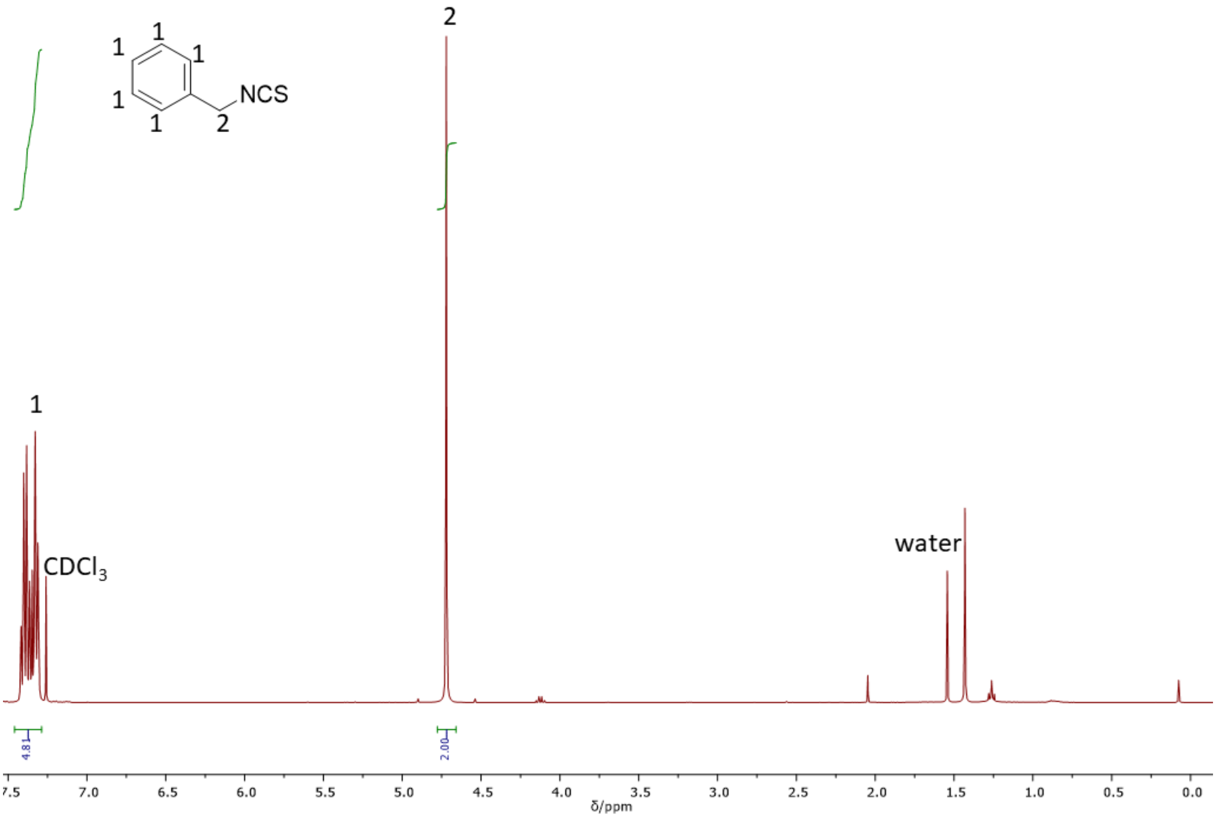
E-factor: 2.25

Purity was 97% according to GC-analysis.

R_f = 0.69 in cyclohexane/ethyl acetate = 9:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR was according to literature.[4]

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 7.42-7.30 (m, 5 H, aromatic, ^{1}), 4.72 (s, 2H, CH_2, ^{2}).



IR: *v* / cm^{-1} = 3061 (vw), 3030 (vw), 2925 (vw), 2849 (vw), 2166 (m), 2073 (vs), 1495 (w), 1454 (m), 1438 (m), 1345 (s), 1302 (w), 1199 (w), 1072 (w), 1028 (w), 812 (w), 730 (m), 695 (vs), 574 (m), 453 (m).

Tosylmethyl isothiocyanate 3o

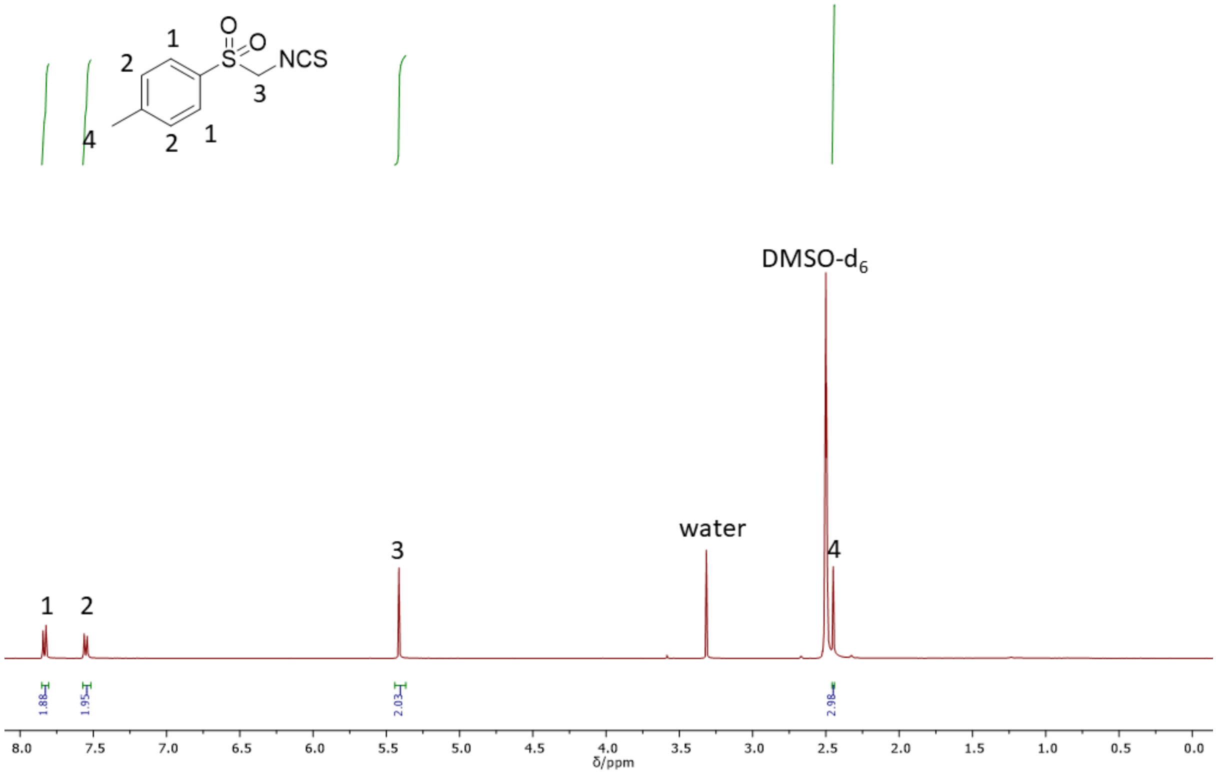
Tosylmethyl isocyanide (488 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-A using elemental sulfur (89.8 mg, 350 µmol, 1.12 eq.), DBU (18.7 µL, 19.0 mg, 125 µmol, 5 mol%) and 1.25 mL GBL. The reaction was stirred for 24 hours. Flash column chromatography was performed using cyclohexane/ethyl acetate (10:1→8:1) yielding the product (193 mg, 850 µmol) as an orange solid in a yield of 34%.

E-factor: 11.1

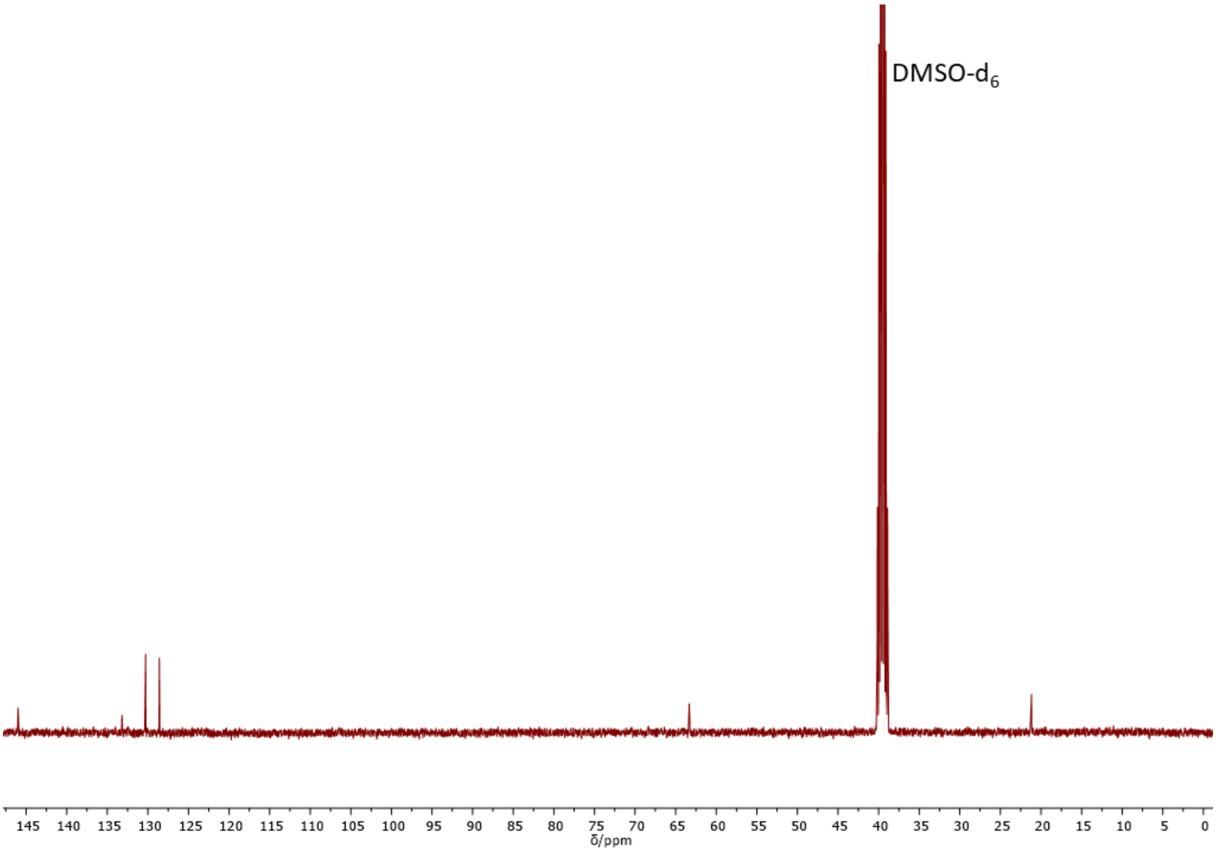
Purity was >99% according to GC-analysis.

R_f = 0.45 in cyclohexane/ethyl acetate = 3:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 7.86-7.79 (m, 2H, aromatic, ^{1}), 7.55 (d, ^3J = 8.0 Hz, 2H, aromatic, ^{2}), 5.41 (s, 2H, CH_2, ^{3}), 2.45 (s, 3H, CH_3, ^{4}).



^{13}C-NMR (101 MHz, $CDCl_3$) δ / ppm = 145.98 (aromatic), 133.20 (aromatic), 130.28 (aromatic), 128.59 (aromatic), 63.32 (CH_2), 21.17 (CH_3). Signal of the SCN-carbon was not observed.



HRMS (EI): calculated m/z for $C_9H_9O_2N_1S_2$ [M^+] = 227.0069, found: 227.0069, Δ = -0.0411 mmu.

IR: *v* / cm^{-1} = 2985 (w), 2927 (w), 2853 (vw), 2289 (w), 2057 (vs), 2045 (vs), 1594 (w), 1491 (w), 1417 (w), 1378 (w), 1323 (vs), 1302 (w), 1269 (vs), 1218 (w), 1142 (vs), 1082 (vs), 1041 (w), 1016 (w), 901 (s), 815 (s), 738 (vs), 703 (s), 625 (s), 553 (vs), 508 (vs), 457 (vs), 426 (s).

2,6-Dimethyl phenyl isothiocyanate 3p

2,6-Dimethylphenyl isocyanide (328 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-A using elemental sulfur (89.8 mg, 350 µmol, 1.12 eq.), DBU (18.7 µL, 19.0 mg, 125 µmol, 5 mol%) and 1.25 mL Cyrene™ or GBL, respectively. The reaction was stirred for 5 (Cyrene™) or 4 (GBL) hours. Flash column chromatography was performed using cyclohexane yielding the product (322 g, 1.98 mmol Cyrene™ or 388 mg, 2.37 mmol in GBL) as a colorless liquid in a yield of 80% (Cyrene™) or 95% (GBL, 15.5 mmol scale, 90% in Cyrene™).

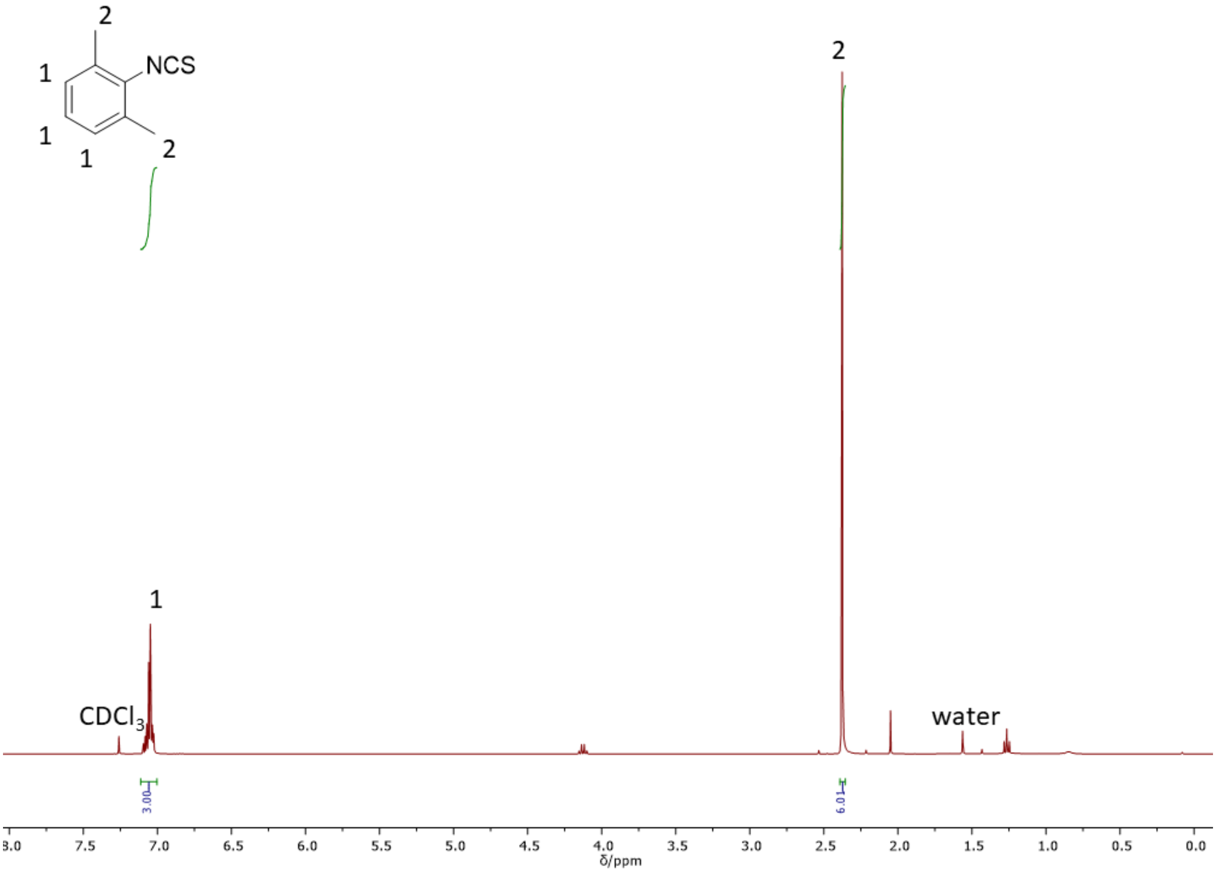
E-factor (2.50 mmol in Cyrene™): 5.30, E-factor (2.50 mmol in GBL): 3.84, E-factor (15.5 mmol in Cyrene™): 4.53

Purity was 98% (Cyrene™ and GBL), >99% (15.5 mmol in Cyrene™) according to GC-analysis.

R$_f$ = 0.73 in cyclohexane/ethyl acetate = 9:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR was according to literature.[6]

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 7.09-7.02 (m, 3H, aromatic, ^{1}), 2.38 (s, 6H, CH_3, ^{2}).



2-Isothiocyanato naphthalene 3q

2-Isocyanido naphthalene (383 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-A using elemental sulfur (89.8 mg, 350 µmol, 1.12 eq.), DBU (18.7 µL, 19.0 mg, 125 µmol, 5 mol%) and 1.25 mL Cyrene™. Flash column chromatography was performed using cyclohexane yielding the product (322 g, 1.39 mmol) as a colorless solid in a yield of 56%.

E-factor (2.50 mmol): 8.45

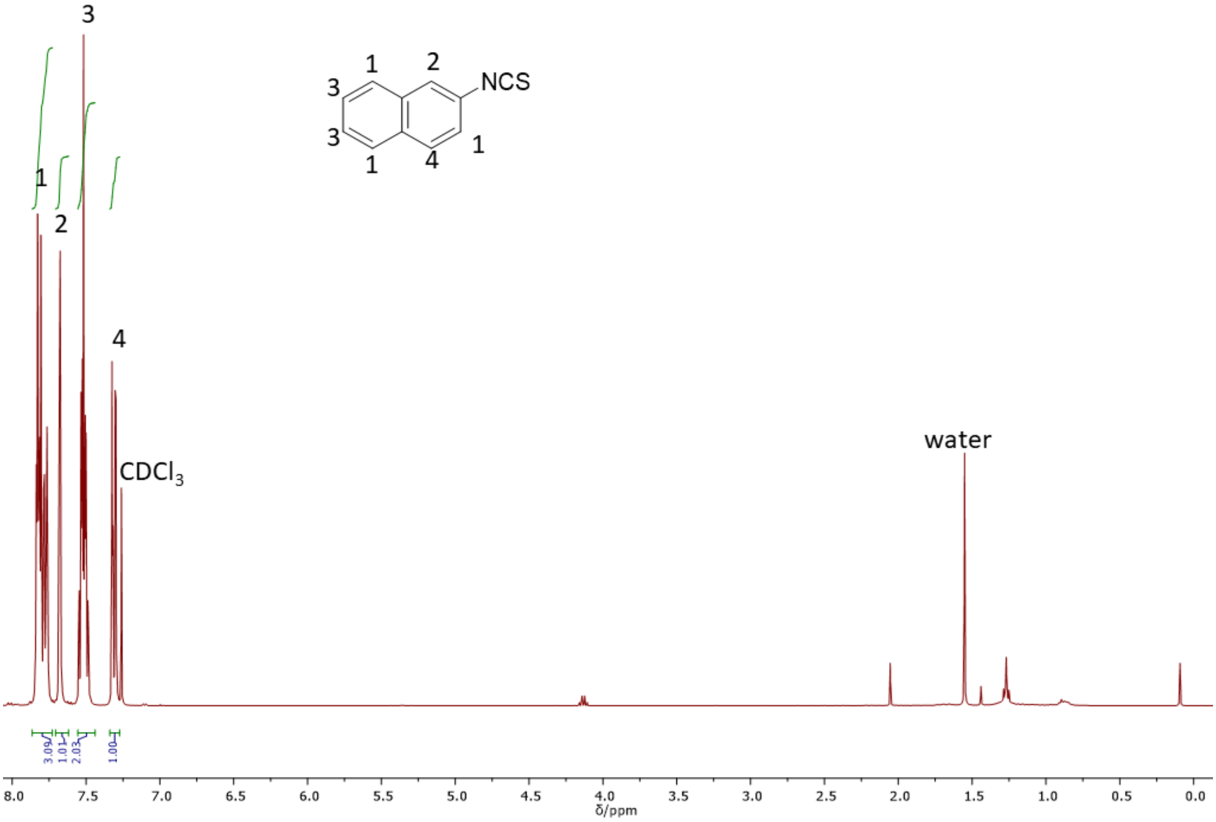
Purity was >99% according to GC-analysis.

EA: Found: C, 71.35; H, 3.7; N, 7.6; S, 17.1 Calc. for $C_{11}H_7N_1S_1$: C, 71.3; H, 3.8; N, 7.5; S, 17.3 %.

R$_f$ = 0.60 in cyclohexane visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

^{1}H-NMR was according to literature. [4]

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 7.86-7.75 (m, 3H, aromatic, ^{1}), 7.68 (d, ^4J = 2.1 Hz, 1H, aromatic, ^{2}), 7.56-7.47 (m, 2H, aromatic, ^{3}), 7.31 (dd, ^3J = 8.7 Hz, ^4J = 2.1 Hz, 1H, aromatic, ^{4}).



4-Methoxyphenyl isothiocyanate 3r

4-Methoxyphenyl isocyanide (333 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (89.8 mg, 350 µmol, 1.12 eq.), DBU (7.46 µL, 7.61 mg, 50 µmol, 2 mol%) and 417 µL Cyrene™ or GBL. The reaction was stirred for 5 hours for Cyrene™ and GBL. Flash column chromatography was performed using cyclohexane yielding the product (346 mg, 2.09 mmol in Cyrene™, 388, 2.35 mmol GBL) as a colorless liquid in a yield of 85% (Cyrene™) or 94% (GBL).

E-factor (2.50 mmol in Cyrene™): 1.74, E-factor (2.50 mmol in GBL): 1.32

Purity was 99 (Cyrene™) and 95% (GBL)% according to GC-analysis.

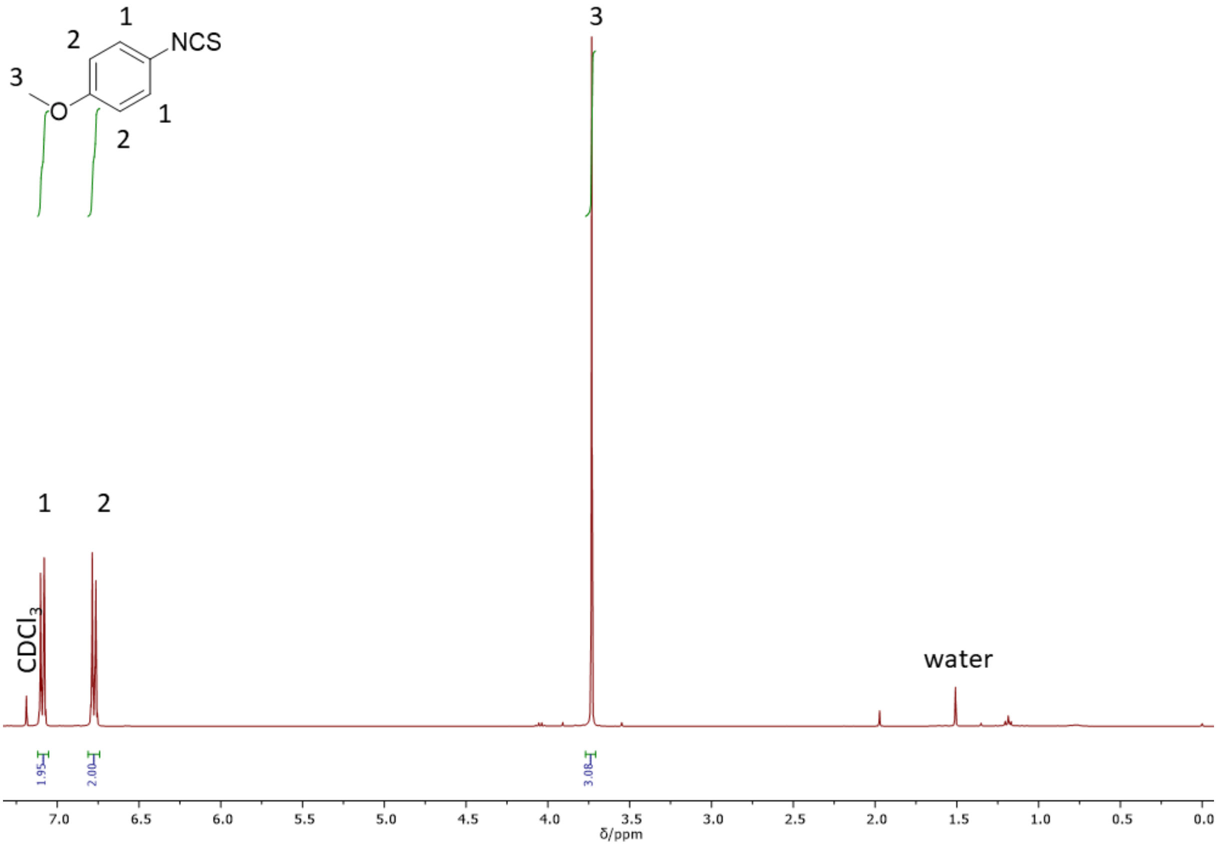
R$_f$ = 0.67 in cyclohexane/ethyl acetate = 3:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

EA (Cyrene™): Found: C, 57.2; H, 4.3; N, 8.5; S, 18.9 Calc. for C_8H_7NS: C, 58.2; H, 4.3; N, 8.5; S, 19.4%.

EA (GBL): Found: C, 57.9; H, 4.5; N, 8.2; S, 18.1 Calc. for C_8H_7NS: C, 58.2; H, 4.3; N, 8.5; S, 19.4%.

^{1}H-NMR was according to literature.[4]

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 7.16 (d, ^3J = 8.9 Hz, 2H, aromatic, ^{1}), 6.85 (d, ^3J = 9.0 Hz, 2H, aromatic, ^{2}), 3.80 (s, 3H, CH_3, ^{3}).



3,4,5-Trimethoxyphenyl isothiocyanate 3s

3,4,5-Trimethoxyphenyl isocyanide (483 mg, 2.50 mmol, 1.00 eq.) was converted as described in GP1-B using elemental sulfur (89.8 mg, 350 µmol, 1.12 eq.), DBU (7.46 µL, 7.61 mg, 50.0 µmol, 2 mol%) and 417 µL Cyrene™. Flash column chromatography was performed using cyclohexane yielding the product (390 mg, 1.73 mmol) as a colorless solid in a yield of 69%.

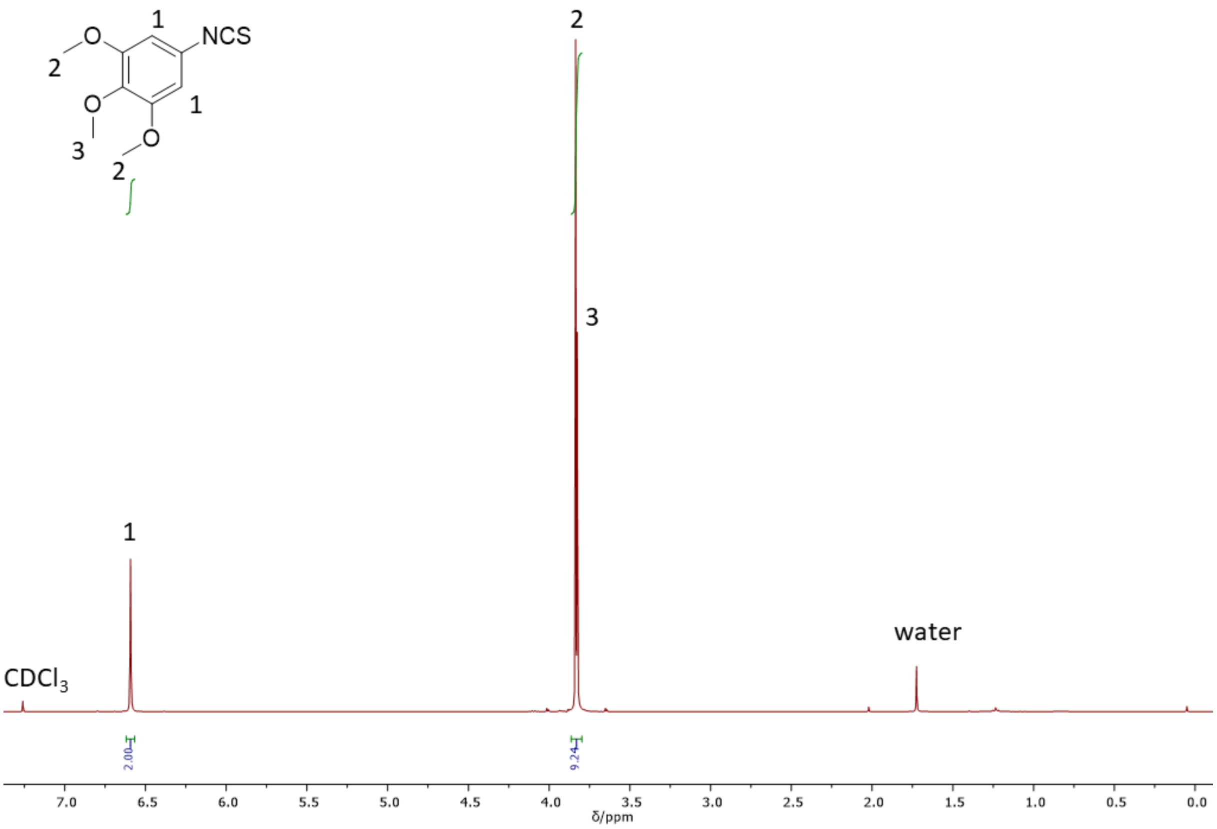
E-factor (2.50 mmol): 1.85

Purity was >99% according to GC-analysis.

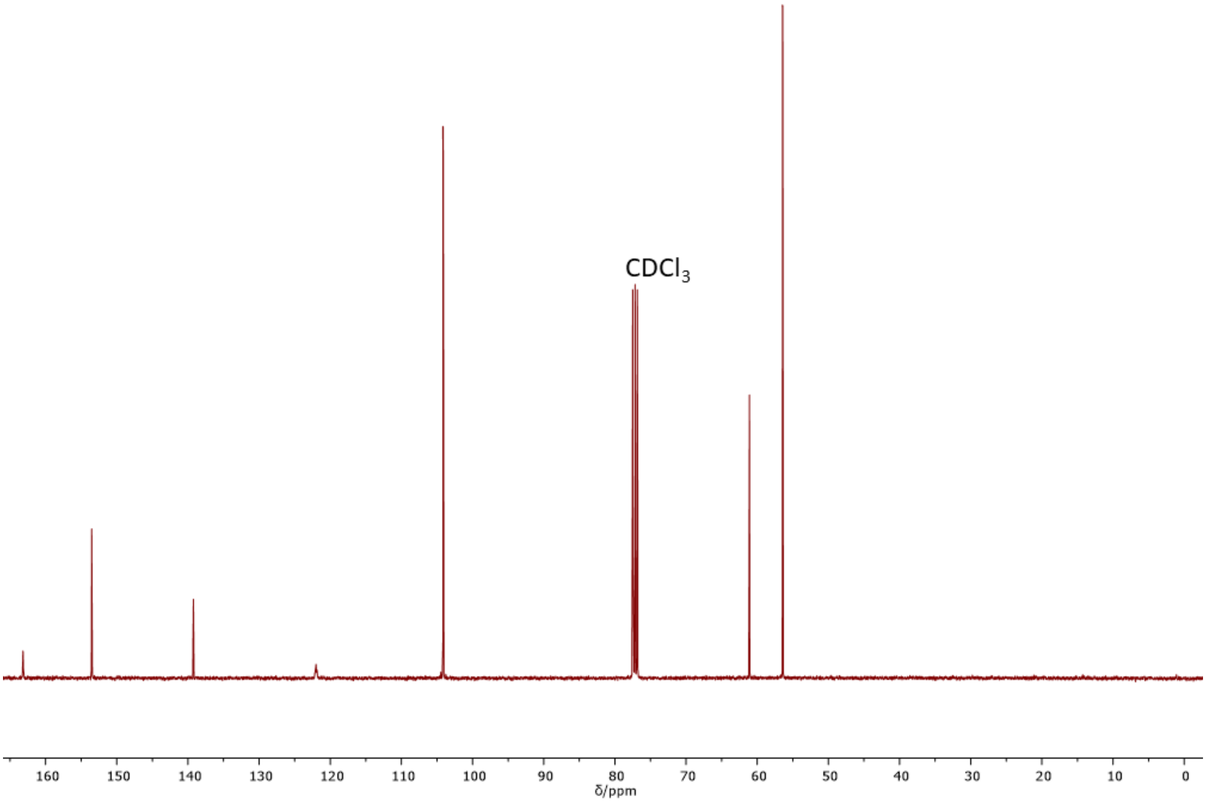
R$_f$ = 0.62 in cyclohexane/ethyl acetate = 3:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (deep blue).

EA: Found: C, 53.5; H, 5.0; N, 6.1; S, 13.6 Calc. for $C_{10}H_{11}N_1O_3S_1$: C, 53.3; H, 4.9; N, 6.2, S, 14.2%.

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 6.59 (s, 2H, aromatic, ^{1}), 3.84 (s, 6H, CH_3, ^{2}), 3.83 (s, 3H, CH_3, ^{3}).



^{13}C-NMR (101 MHz, $CDCl_3$) δ / ppm = 163.18 (aromatic), 153.52 (aromatic), 139.24 (aromatic), 122.00 (NCS), 104.13 (aromatic), 61.09 (CH_3), 56.41 (CH_3).



HRMS (EI): calculated m/z for $C_{10}H_{11}O_3N_1S_1$ [M^+] = 225.0454, found: 225.0453, Δ = -0.1382 mmu.

IR: *ν* / cm^{-1} = 2972 (w), 2943 (w), 2921 (w), 2836 (w), 2114 (vs), 2096 (s), 1582 (vs), 1499 (s), 1465 (s), 1456 (s), 1430 (s), 1415 (vs), 1339 (s), 1304 (w), 1230 (vs), 1185 (m), 1164 (m), 1119 (vs), 1014 (m), 991 (vs), 870 (w), 827 (vs), 808 (vs), 761 (s), 728 (vs), 671 (m), 605 (m), 525 (s), 483 (m), 430 (m).

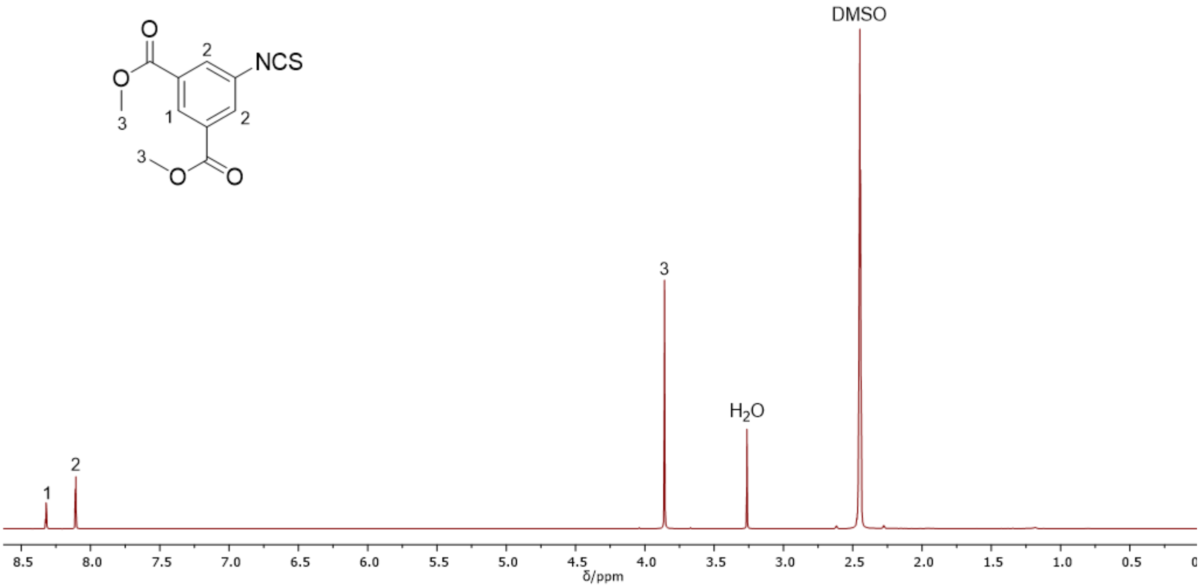
5-Isothiocyanatodimethyl isophthalate 3t

5-isocyanidodimethyl isophtlate (438 mg, 2.00 mmol, 1.00 eq.) was converted as described in GP1-A using elemental sulfur (71.8 mg, 280 µmol, 1.12 eq.), DBU (14.9 µL, 15.2 mg, 100 µmol, 5 mol%) and 1.0 mL GBL. Conventional flash column chromatography was performed using cyclohexane/ethyl acetate = 10:1 yielding the product (224 mg, 89.2 mmol) as a colorless solid in a yield of 45%.

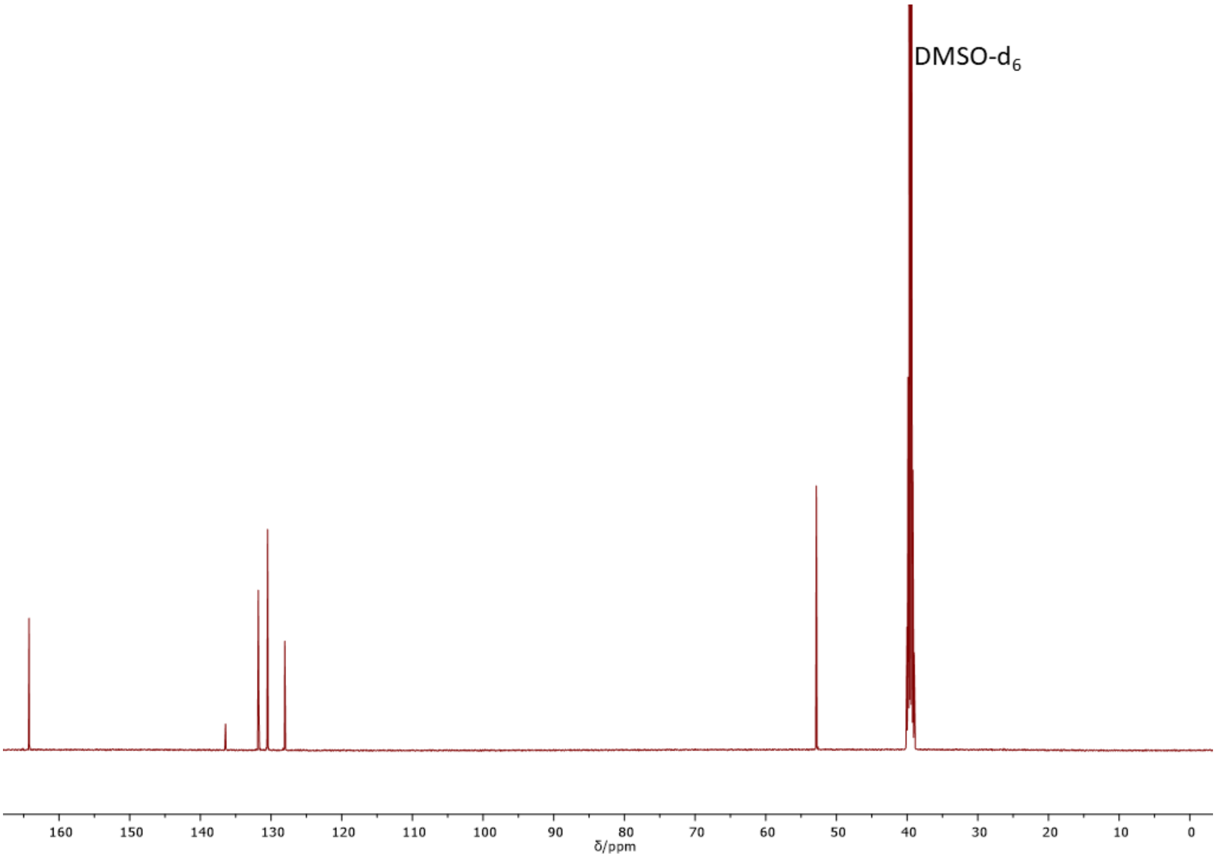
E-factor: 7.37

R_f = 0.37 in cyclohexane/ethyl acetate = 10:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (blue to greenish).

^{1}H-NMR (400 MHz, DMSO-d$_6$) δ / ppm = 8.32 (t, ^4J = 1.6 Hz, 1H, aromatic, ^{1}), 8.11 (d, ^4J = 1.5 Hz, 2H, aromatic, ^{2}), 3.86 (s, 6H, CH$_3$, ^{3}). Please note that, the compound is decomposing in DMSO-d$_6$ over time probably depending on the amount of water.



^{13}C-NMR (126 MHz, $CDCl_3$) δ / ppm = 164.23 (**C**OOMe), 136.44 (SCN), 131.81 (aromatic), 131.75 (aromatic), 130.49 (aromatic), 128.05(aromatic), 52.84 (CH_3).



HRMS (EI): calculated m/z for $C_{11}H_{10}O_4N_1S_1$ $[M+H]^+$ = 252.0331, found: 252.0331, Δ = - 0.1892 mmu

IR: *v* / cm^{-1} = 3085.1 (w), 2953.1 (w), 2129.0 (s,), 1722.9 (vs), 1600.1 (m), 1431.5 (s), 1336.5 (s), 1228.5 (vs), 1120.9 (s), 1102.3 (m), 994.3 (s), 945.8 (m), 911.1 (m), 872.7 (m), 814.0 (w), 751.3 (s), 721.0 (s), 664.7 (m), 480.1 (m), 439.7 (w), 412.3 (m).

Synthesis of Isocyanides

Dodecyl isocyanide 1a

Dodecyl isocyanide **1a** as synthesized according to the synthesis protocol of Waibel *et al.*.[7]

1,10-Diisocyano decane 1c

1,10-Diisocyano decane 1c was synthesized according to the synthesis protocol of Waibel *et al.*.[7]

1,10-Diisocyano dodecane 1d

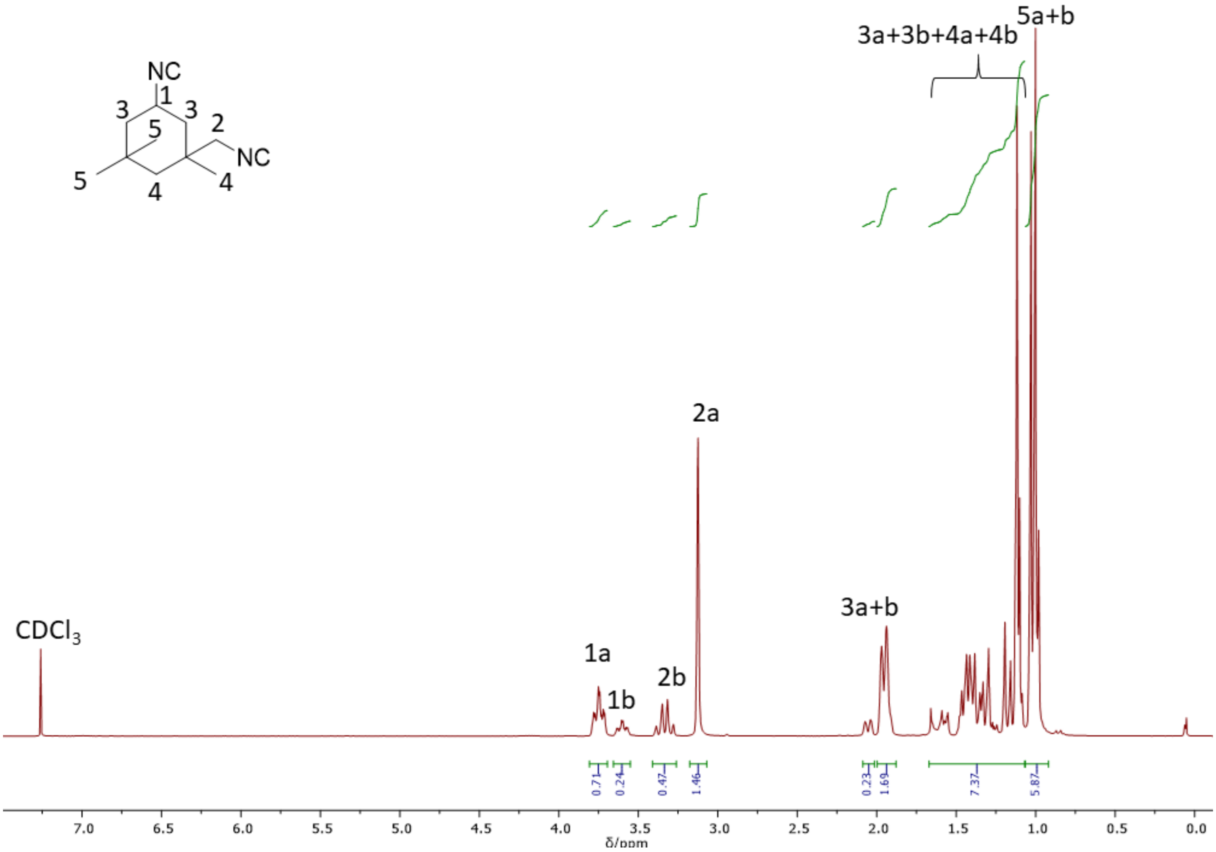
1,10-Diisocyano dodecane 1d was synthesized according to the synthesis protocol of Waibel *et al.*.[7]

5-Isocyanido-1-(isocyanidomethyl)-1,3,3-trimethyl cyclohexane 1h

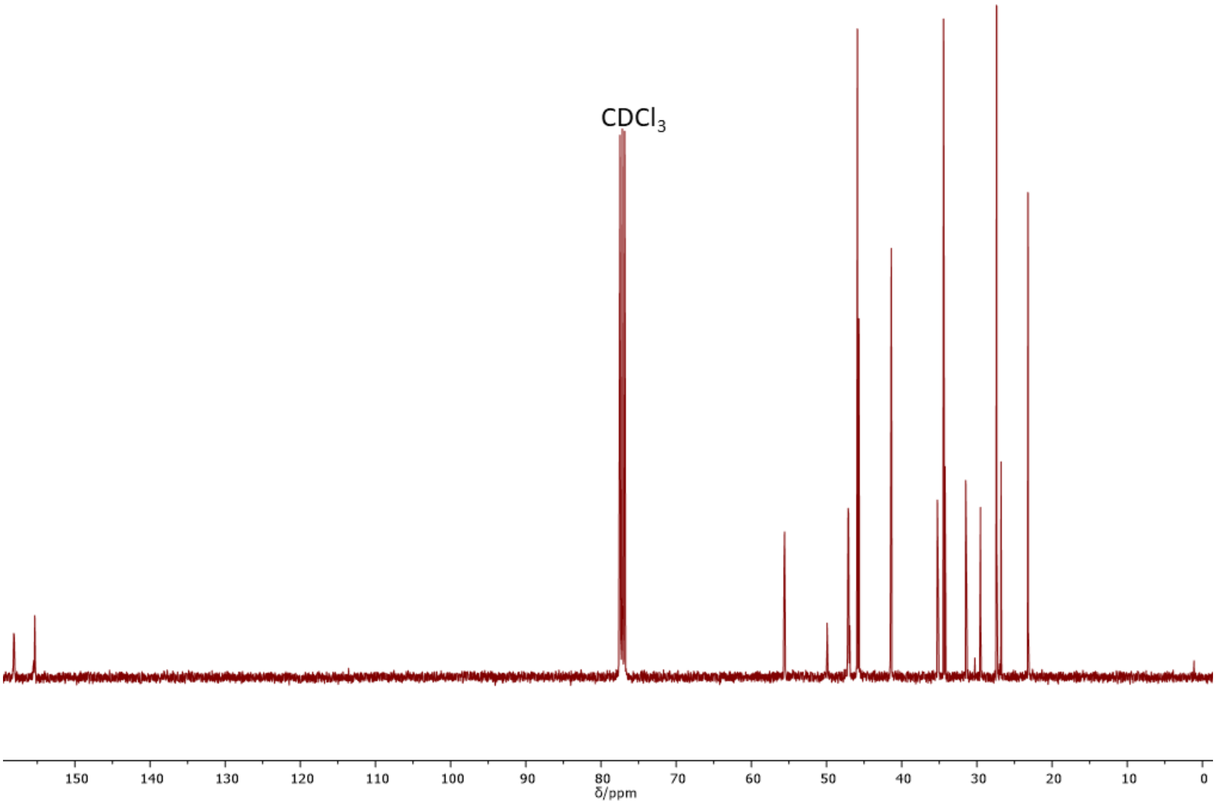
5-Formamido-1-(formamidomethyl)-1,3,3-trimethyl cyclohexane (5.30 g, 23.4 mmol, 1.00 eq.) and diisopropylamine (20.4 mL, 14.7 g, 145 mmol, 6.20 eq.) was dissolved in DCM (71 mL) and cooled to 0 °C with an ice-water bath. Then, phosphoryl chloride (5.7 mL, 9.34 g, 60.9 mmol, 2.60 eq.) were added dropwise keeping the tempearute at 0 °C. Afterwards, the ice-water bath was removed and the colorless reaction solution was stirred at room temperature for 4 hours. The yellow reaction mixture was quenched by adding 71 mL saturated, aqueous sodium hydrogen carbonate solution and stirred for further 15 minutes until CO_2 formation had ceased. The organic layer was separated and the aqueous phase was extracted with DCM (1 × 30 mL). The combined organic layers were removed from solvent under reduced pressure and purification by flash column chromatography using cyclohexane/ethyl acetate (10:1) yielded the product (2.88 mg, 15.1 mmol, mixture of isomers) as a yellow viscous liquid in a yield of 65% (d.r. = 2.96:1 determined *via* NMR).

R_f = 0.68 in cyclohexane/ethyl acetate = 3:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (orange).

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 3.80 – 3.71 (m, 0.73H, CN-CH, ^{1a}), 3.66 – 3.54 (m, 0.24H, CN-CH, ^{1b}), 3.44 – 3.23 (q, ^2J = 14.3 Hz, 0.48H, CN-CH_2, ^{2b}), 3.12 (s, 1.42H, CN-CH_2, ^{2a}), 2.09 – 1.89 (m, 2H, CH_2, $^{3a+b}$), 1.68 – 1.07 (m, 7H, CH_2, CH_3, $^{3a+3b+4a+4b}$), 1.05 – 0.96 (m, 6H, CH_3, $^{5a+b}$).



^{13}C-NMR (101 MHz, $CDCl_3$) δ / ppm = 158.24-158.01 (m, **C**N-CH_2, a+b), 155.51 (t, **C**N-CH, b), 155.33 (t, **C**N-CH, a), 55.58 (t, CN-**C**H_2, a), 49.92 (t, CN-**C**H_2, b),47.20-46.89 (m, CN-**C**H, a+b), 45.92 (CH_2), 45.88 (CH_2, a), 45.69 (CH_2, b), 41.49 (CH_2, b), 41.38 (CH_2, a), 35.25 ($C_{quart.}$, a), 35.11 ($C_{quart.}$, b), 34.42 (CH_3, a), 34.23 (CH_3, b), 31.48 ($C_{quart.}$, a), 31.34 ($C_{quart.}$, b), 29.52 (CH_3, b), 27.36 (CH_3, a), 26.79 (CH_3, b), 23.18 (CH_3, a).



HRMS (ESI): calculated m/z for $C_{12}H_{19}N_2$ [M+H$^+$] = 191.1543, found: 191.1541, Δ = - 0.18 mmu.

IR: *v* / cm^{-1} = 2956 (w), 2936 (w), 2874 (w), 2142 (vs), 1463 (m), 1391 (w), 1368 (w), 1251 (vw), 1201 (vw), 1145 (vw), 1017 (vw), 967 (w), 943 (m), 921 (w), 897 (vw), 864 (w), 769 (vw), 620 (vw), 503 (w), 442 (vw), 390 (vw).

Oleyl isocyanide 1i

Isocyanide **1i** was synthesized according to the synthesis protocol of Waibel *et al.*.[7]

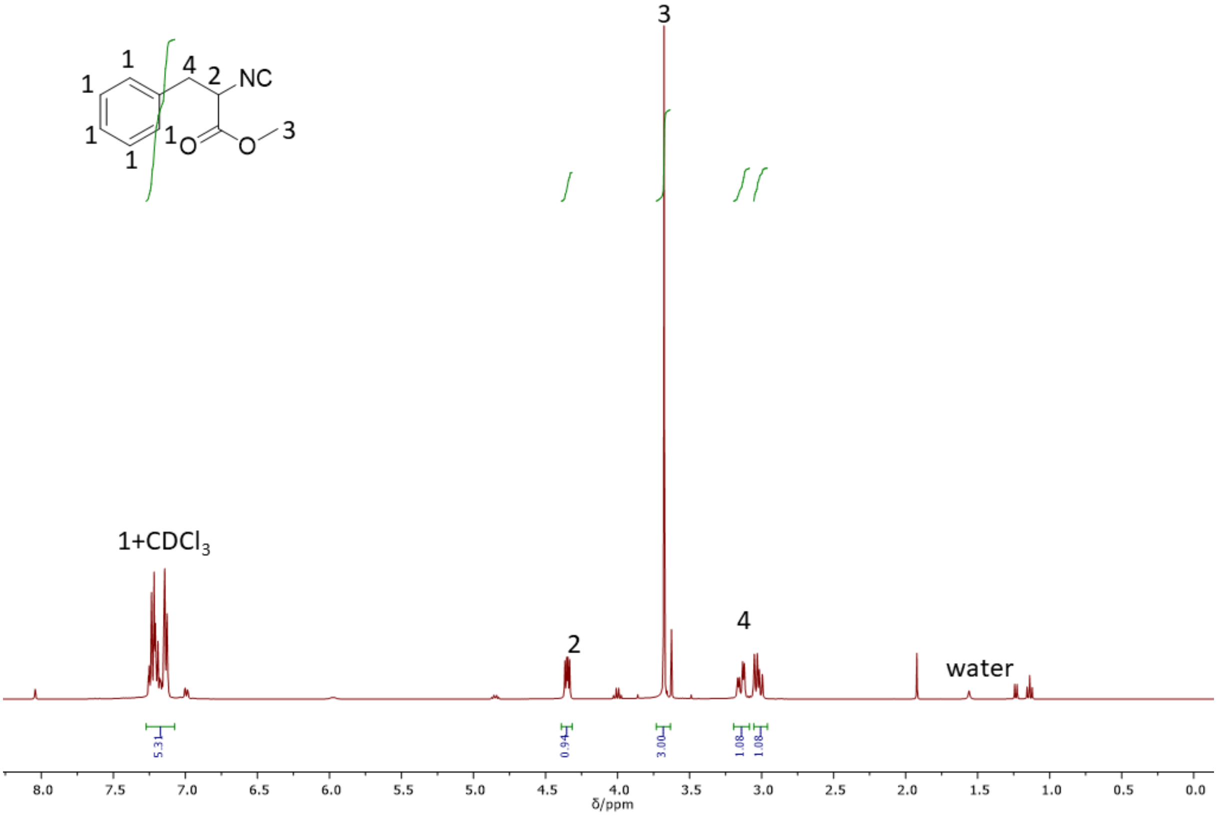
Methyl-2-isocyano-3-phenyl propionate 1k

Methyl-2-formamido-3-phenyl propionate (21.5 g, 104 mmol, 1.00 eq.) was dissolved in 343 mL dichloromethane and diisopropylamine (347.5 mL, 4.10 g, 321 mmol, 3.10 eq.) were added and the reaction mixture was cooled to 0 °C using an ice-water bath. Subsequently, phosphorous oxy chloride (12.6 mL, 20.6 g, 134 mmol, 1.30 eq.) was added dropwise keeping the temperature at 0 °C. Afterwards, the ice-water bath was removed and the reaction solution was stirred at room temperature for two hours. Subsequently, the reaction was quenched by addition of sodium carbonate solution (20 %, 126 mL) at 0 °C using an ice-water bath. After stirring this mixture for 30 minutes, 60 mL water and 60 mL dichloromethane were added. The aqueous phase was separated and the organic layer was washed with water (3 x 50 mL) and brine (50 mL). The combined organic layers were dried over sodium sulfate and the solvent was evaporated under reduced pressure. The crude product was then purified by column chromatography (cyclohexane / ethyl acetate 6:1). The product was obtained as slightly yellow oil (16.4 g, 86.7 mmol) in a yield of 84%.

R_f = 0.42 in cyclohexane/ethyl acetate = 4:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (orange).

^{1}H-NMR was according to literature.[8]

^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 7.26-7.11 (m, 5H, aromatic, ^{1}), 4.35 (dd, ^3J = 8.3, 4.9 Hz, 1H, CH, ^{2}), 3.68 (s, 3H, CH_3, ^{3}), 3.14 (dd, ^2J = 13.8 Hz, ^3J = 4.9 Hz, 1H, CH_2, ^{4}), 3.03 (dd, ^2J = 13.8 Hz, ^3J = 8.3 Hz, 1H, CH_2, ^{4}).



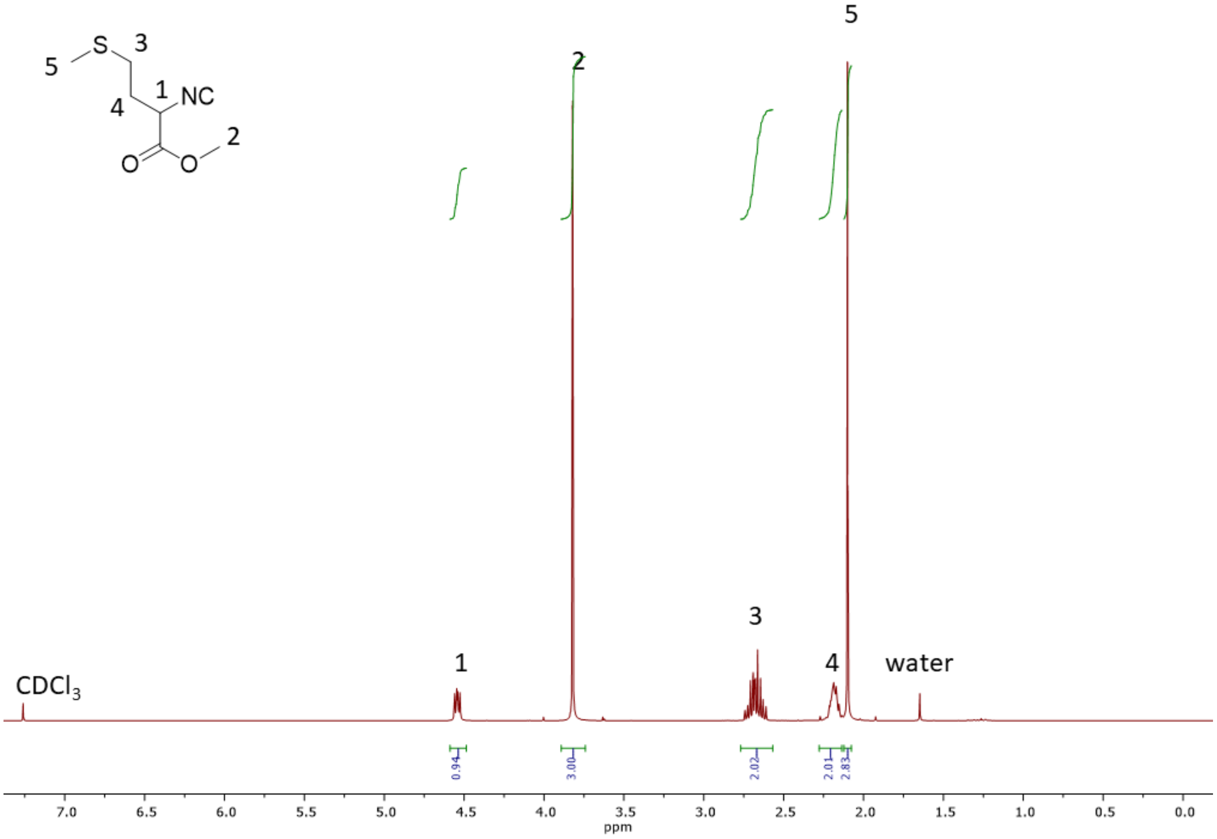
Methyl-2-isothiocyanato-4-(methylthio) butanoate 1l

Methyl-2-formamido-4-(methylthio) butanoate (4.00 g, 20.9 mmol, 1.00 eq.) was dissolved in 69 mL dichloromethane and diisopropylamine (9.15 mL, 6.56 g, 64.8 mmol, 3.10 eq.) was added and the reaction mixture was cooled to 0 °C using an ice-water bath. Subsequently, phosphorous oxy chloride (2.54 mL, 4.17 g, 27.2 mmol, 1.30 eq.) was added dropwise keeping the temperature at 0 °C. Afterwards, the ice-water bath was removed and the reaction solution was stirred at room temperature for two hours. The reaction was quenched by addition of sodium carbonate solution (20 %, 20 mL) at 0 °C using an ice-water bath. After stirring this mixture for 30 minutes, 15 mL water and 15 mL dichloromethane were added. The aqueous phase was separated and the organic layer was washed with water (3 x 25 mL) and brine (25 mL). The combined organic layers were dried over sodium sulfate and the solvent was evaporated under reduced pressure. The crude product was then purified by column chromatography (cyclohexane/ethyl acetate 9:1→8:1). The product was obtained as slightly yellow oil (2.86 g, 16.5mmol) in a yield of 79%.

R$_f$ = 0.32 in cyclohexane/ethyl acetate = 5:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (orange).

^{1}H-NMR was according to literature.[8]

^{1}H-NMR (400 MHz, CDCl$_3$) δ / ppm = 4.54 (dd, ^3J = 8.0 Hz, 5.3 Hz, 1H, CH, ^{1}), 3.82 (s, 3H, CH$_3$, ^{2}), 2.75-2.60 (m, 2H, CH$_2$, ^{3}), 2.24-2.13 (m, 2H, CH$_2$, ^{4}), 2.10 (s, 3H, CH$_3$, ^{5}).



11-isocyanobenzyl undecanoate 1k

11-isocyanobenzyl undecanoate 1k was synthesized according to the synthesis protocol of Waibel *et al.*.[7]

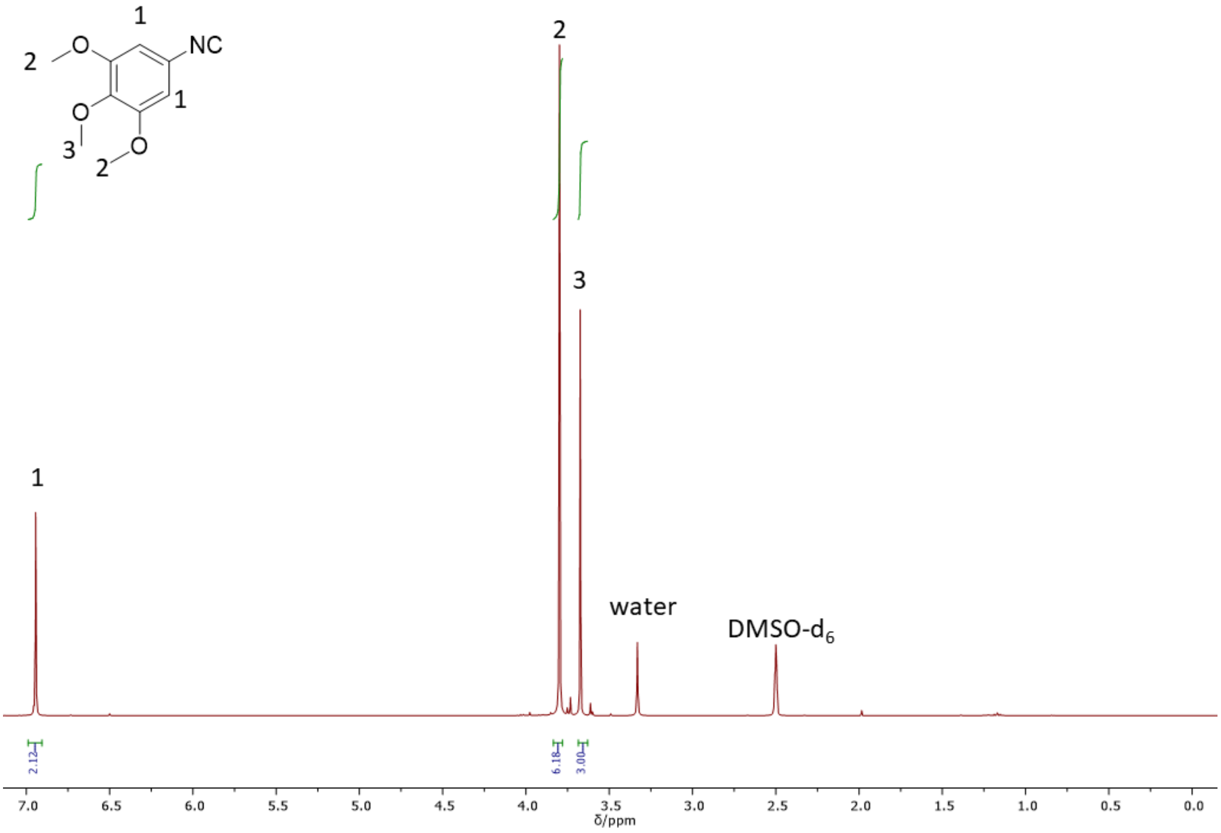
3,4,5-trimethoxypehnyl isocyanide 3s

3,4,5-Trimethoxyphenyl formamide (1.04 g, 4.95 mmol, 1.00 eq.) was dissolved in 15 mL dichloromethane and diisopropylamine (2.16 mL, 1.55 g, 15.34 mmol, 3.10 eq.) was added and the reaction mixture was cooled to 0 °C using an ice-water bath. Subsequently, phosphorous oxy chloride (587 µL, 986 mg, 6.43 mmol, 1.30 eq.) was added dropwise keeping the temperature at 0 °C. Afterwards, the ice-water bath was removed and the colorless reaction solution was stirred at room temperature for two hours. The reaction mixture was quenched by adding 15 mL saturated, aqueous sodium hydrogen carbonate solution and stirred for further 15 minutes until CO_2 formation had ceased. The organic layer was separated and the aqueous phase was extracted with DCM (1 × 10 mL). The combined organic layers were removed from solvent under reduced pressure and purification by flash column chromatography using cyclohexane/ethyl acetate (14:1→10:1) yielded the product (819 mg, 4.24 mmol) as a yellowish liquid in a yield of 86%.

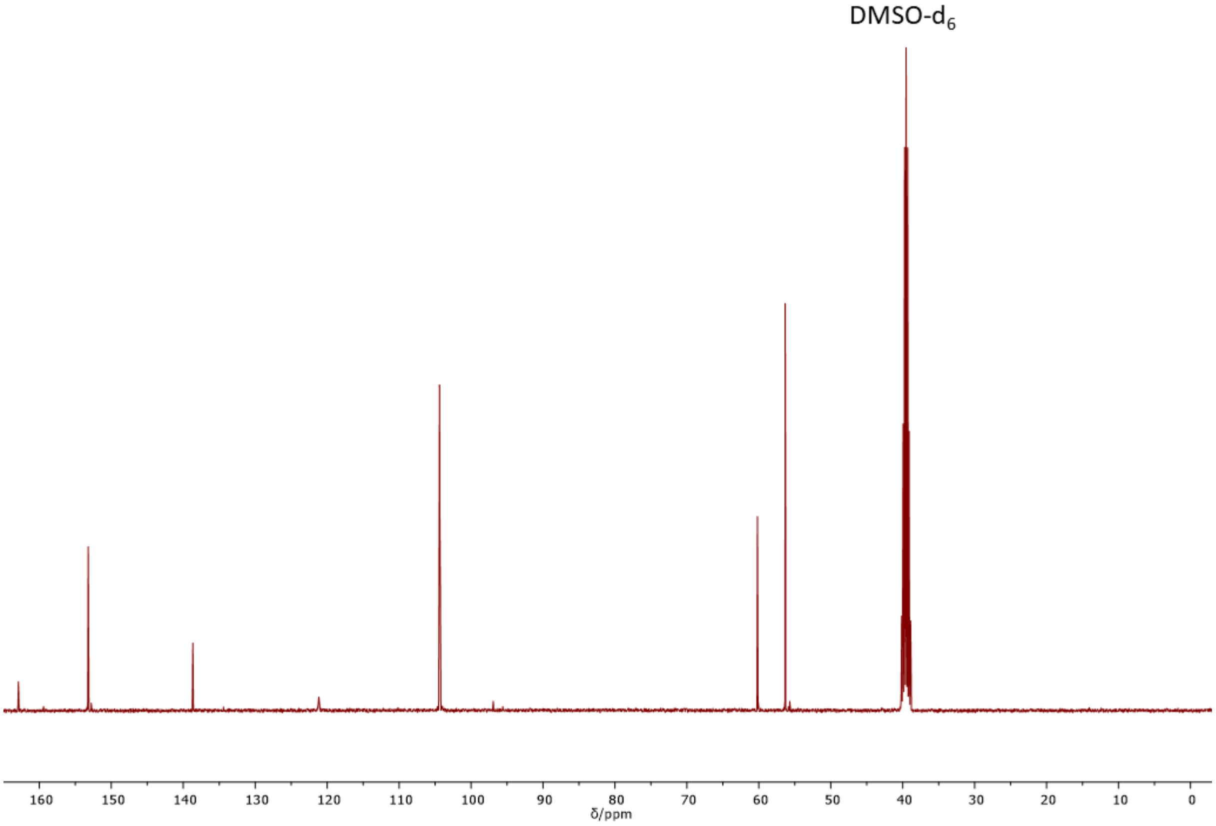
R_f = 0.46 in cyclohexane/ethyl acetate = 3:1 visualized *via* UV quenching at 254 nm and vanillin staining solution (orange).

^{1}H-NMR was according to literature.

^{1}H-NMR (400 MHz, DMSO-d_6) δ / ppm = 6.94 (s, 2H, aromatic, ^{1}), 3.80 (s, 6H, CH_3, ^{2}), 3.67 (s, 3H, CH_3, ^{3}).



^{13}C-NMR (101 MHz, DMSO-d_6) δ / ppm = 162.92 (aromatic-quaternary), 153.21 (aromatic-quaternary), 138.67 (aromatic-quaternary), 121.16 (CN), 104.35 (aromatic), 60.18 (CH_3), 56.33. (CH_3).



HRMS (EI): calculated m/z for $C_{10}H_{11}N_1O_3$ [M^+] = 193.0733, found: 193.0734, Δ = 0.0446 mmu.

IR: *v* / cm^{-1} = 3009 (vw), 2972 (w), 2939 (w), 2832 (w), 2131 (m), 1590 (s), 1502 (s), 1456 (s), 1444 (s), 1430 (m), 1417 (s), 1331 (m), 1230 (vs), 1177 (w), 1125 (vs), 1000 (vs), 961 (s), 839 (vs), 817 (m), 810 (m), 778 (s), 747 (w), 679 (w), 617 (m), 522 (w), 500 (w).

5-isocyanodimethyl isophtalate 1t

5-isocyanodimethyl isophtalate 1t was synthesized according to the synthesis protocol of Nickisch *et al.*.[9]

Synthesis of *N*-formamides

5-Formamido-1-(formamidomethyl)-1,3,3-trimethyl cyclohexane

Isophorendiamine (5.43 mL, 5.00 g, 29.4 mmol, 1.00 eq.) was dissolved in ethyl formiate (23.6 mL, 21.7 g, 294 mmol, 10.0 eq.) and was stirred under reflux for 24 hours. Afterwards, the remaining ethylformiate as well as the ethanol were removed under reduced pressure and the crude formamide (5.30 g) was used without further purification.

3,4,5-Trimethoxyphenyl formamide

3,4,5-trimethoxyphenyl amine (1.50 g, 8.19 mmol, 1.00 eq.) was dissolved in formic acid (1.24 mL, 1.51 g, 32.8 mmol, 4.00 eq.) and was stirred under reflux for 18 hours. Afterwards, the remaining formic acid as well as water were removed under reduced pressure and the crude formamide (1.83 g) was used without further purification.

Synthesis of Polythioureas

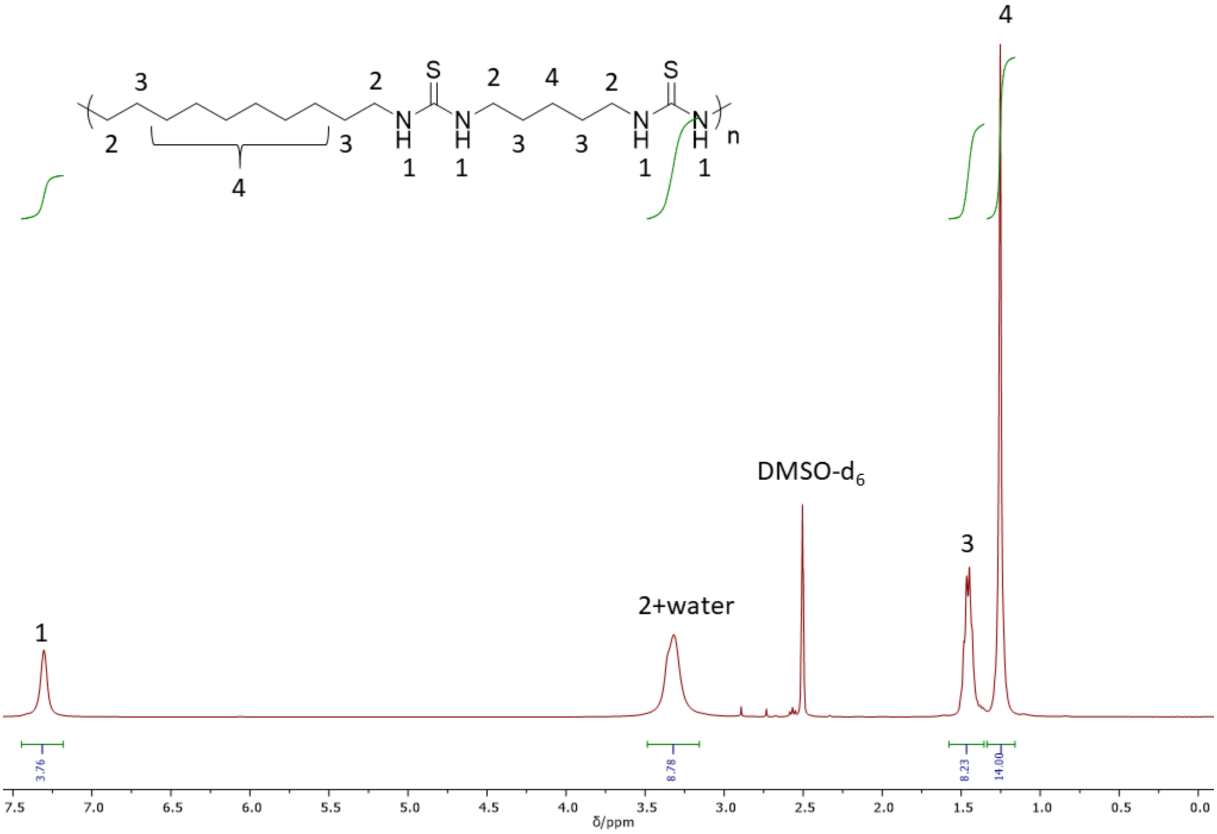
General synthesis of polythioureas (GP2)

The diisothiocyanate (1.00 eq.) was dissolved in DMF (c(diisothiocyaante) = 1.0 M) and diamino pentane (1.00 eq.) was added. The reaction was stirred at room temperature until full conversion of the diisothiocyanate was indicated by TLC. Subsequently, methanol (5 times the amount of used DMF) was added to precipitate the polythiourea. After filtration, the product was washed with minimal amounts of methanol and dried under reduced pressure to remove the remaining solvent. Deviations of this procedure are given in the section of the respective substrate.

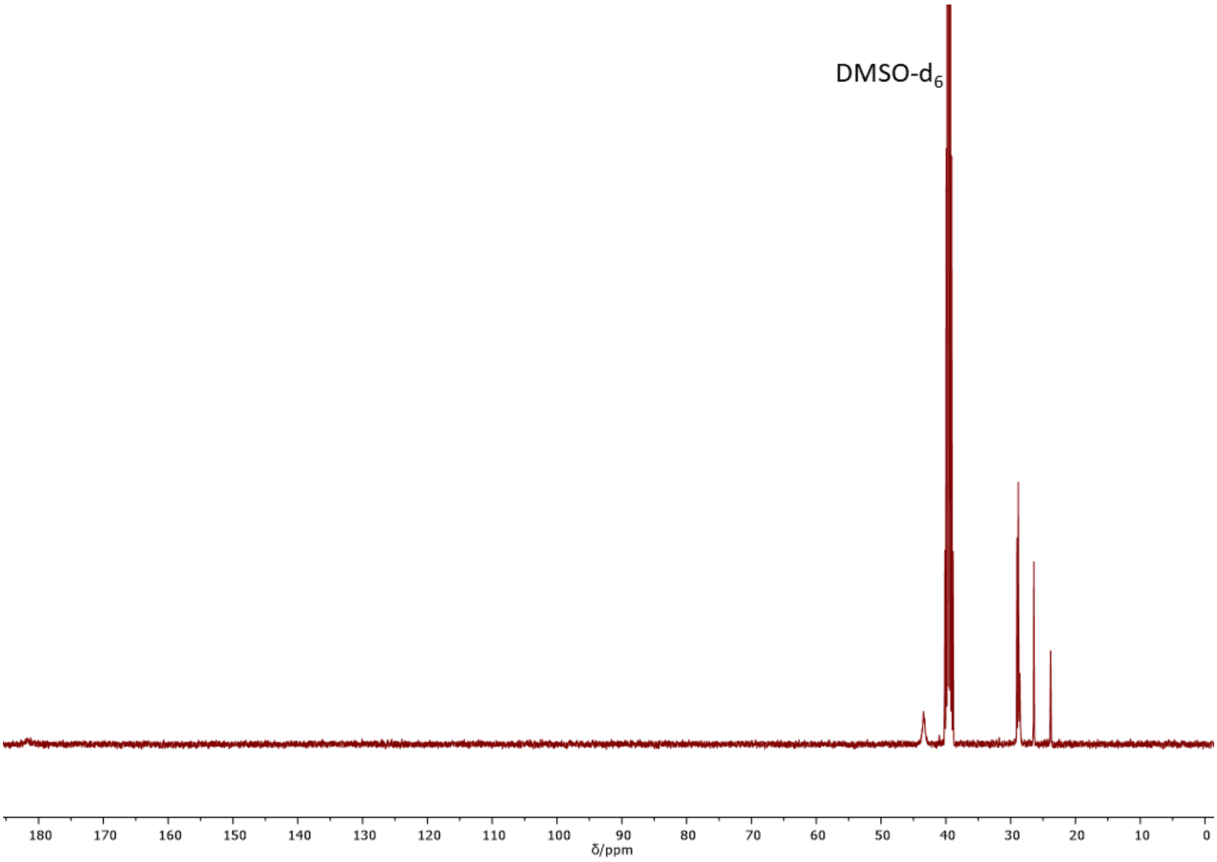
Polythiourea P1

The polymer was synthesized according to procedure GP2. Diisothiocyante **3c** (256 mg, 1.00 mmol, 1.00 eq.) and diamino pentane (117µL, 102 mg, 1.00 mmol, 1.00 eq.) were dissolved in 1 mL DMF and the reaction mixture was stirred for 2 h. The product was obtained as a colourless solid (314 mg) in a yield of 88%.

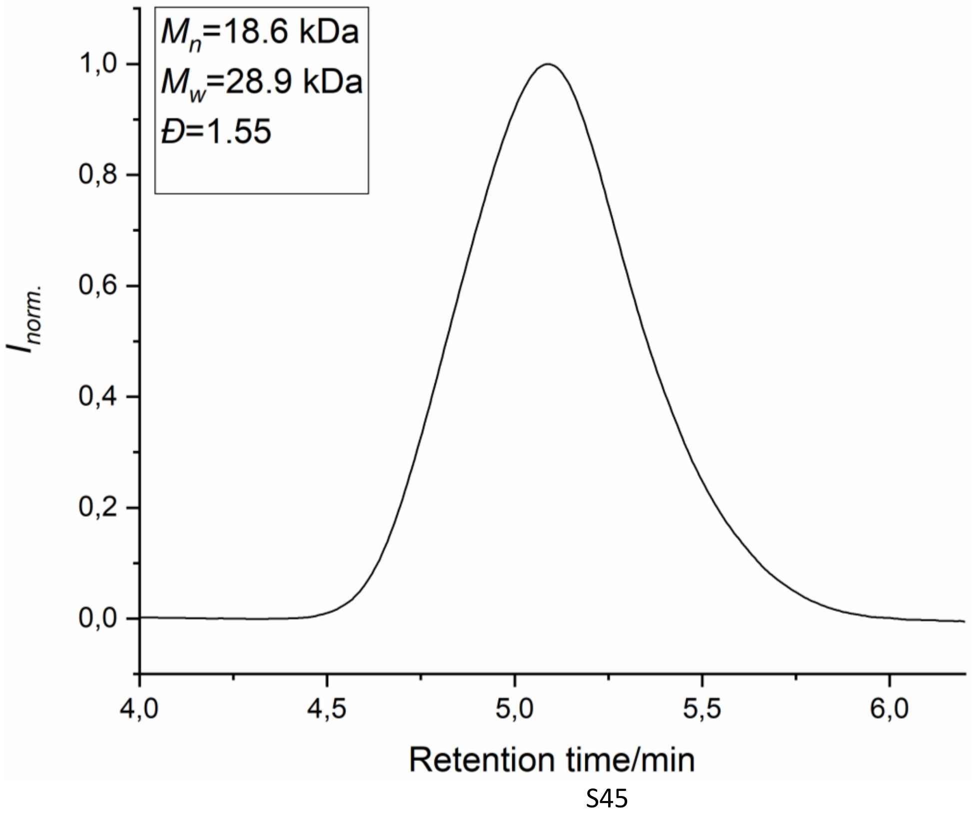
^{1}H-NMR (400 MHz, CDCl$_3$) δ / ppm = 7.30 (br, 4H, NH, ^{1}), 3.34 (br, 8H, CH$_2$, ^{2}), 1.47 (p, ^3J = 7.2 Hz, 8H, CH$_2$, ^{3}), 1.25 (br, 14H, CH$_2$, ^{4}).



^{13}C-NMR (101 MHz, $CDCl_3$) δ / ppm = 181.55 (br, HNC=SNH), 43.41 (NHC=SNH-**C**H_2), 29.01 (CH_2), 28.82 (CH_2), 28.59 (CH_2), 26.43 (CH_2), 23.82 (CH_2).



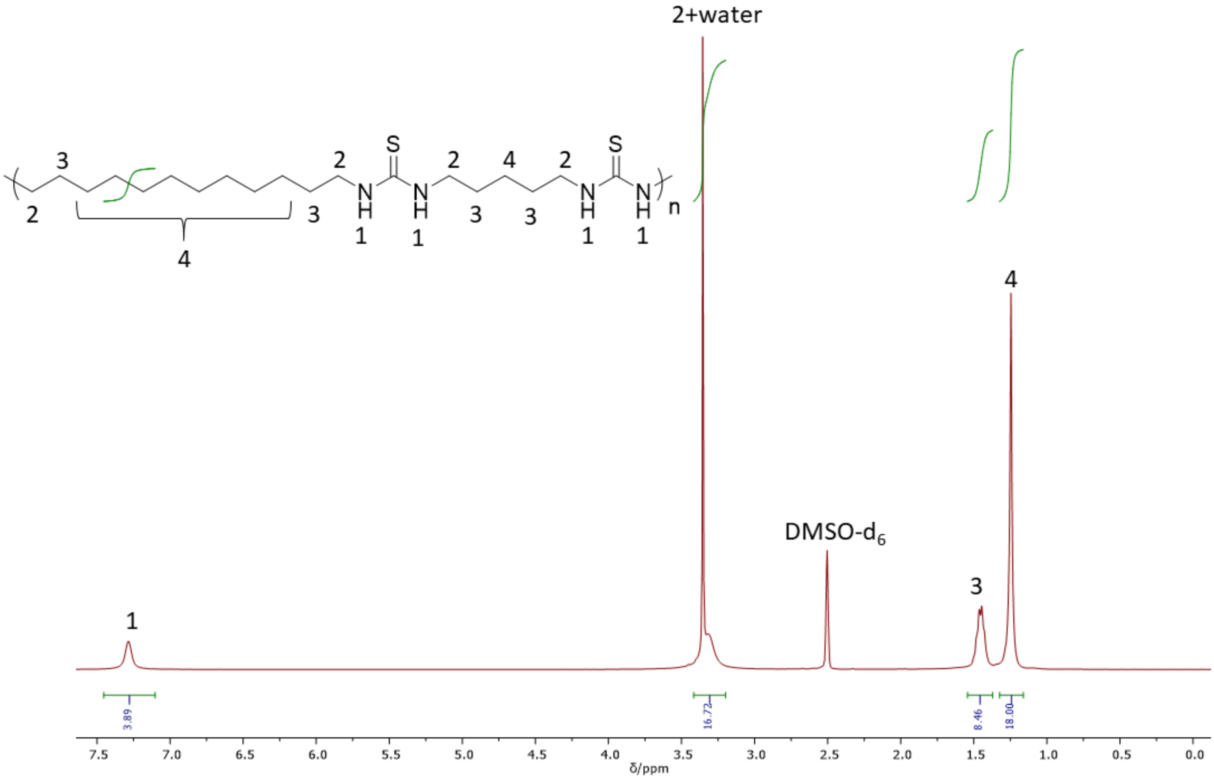
IR: ν / cm^{-1} = 3237 (br, m), 3065 (br, w), 2917 (s), 2849 (s), 1544 (vs), 1460 (m), 1349 (vs), 1290 (vs), 1237 (s), 1054 (m), 728 (s), 674 (vs), 579 (s), 540 (vs)



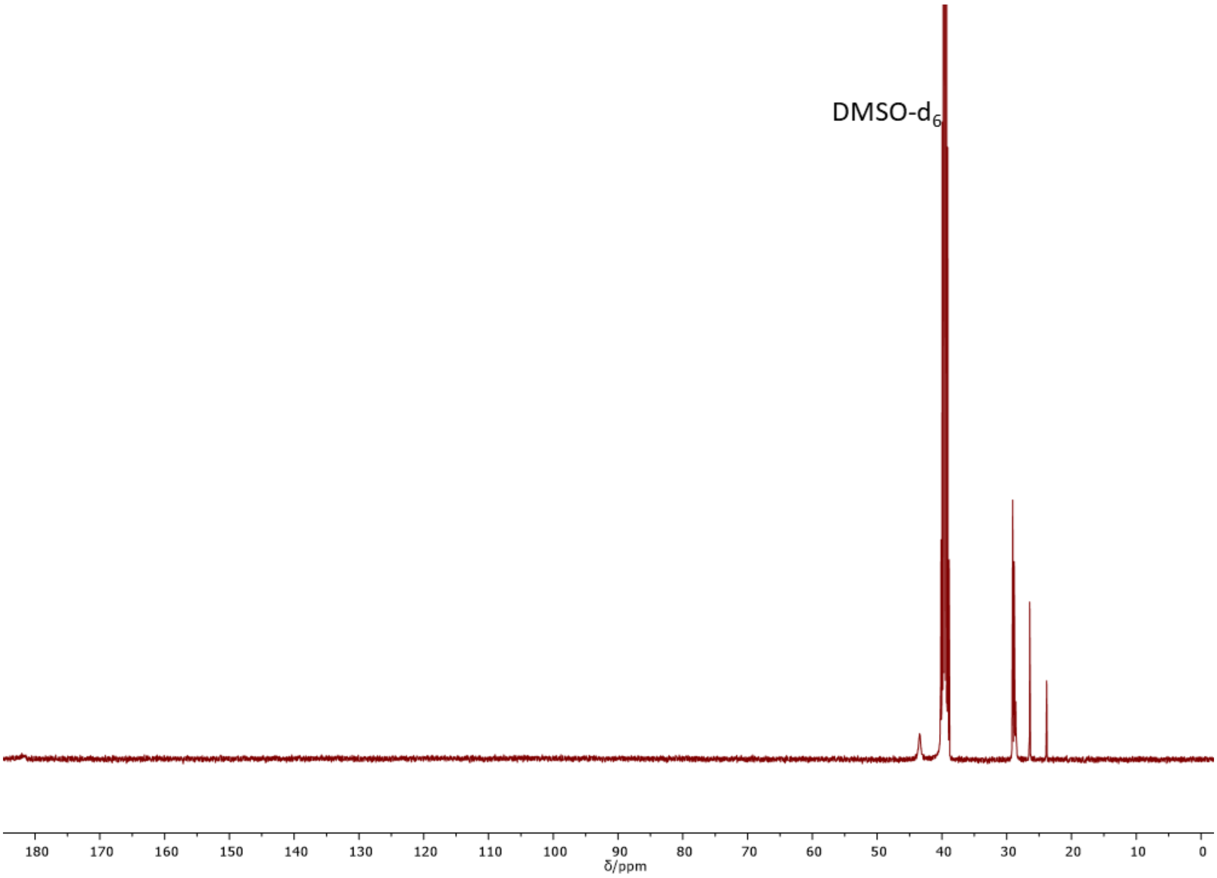
Polythiourea P2

The polymer was synthesized according to the procedure GP2. Diisothiocyante **3d** (284 mg, 1.00 mmol, 1.00 eq.) and diamino pentane (117µL, 102 mg, 1.00 mmol, 1.00 eq.) were dissolved in 1 mL DMF and the reaction mixture was stirred for 2 h. Remaining solvent was removed in a vacuum oven (80 °C, 10 mbar, 16 hours). The product was obtained as a colourless solid (387 mg) in a quantitative yield.

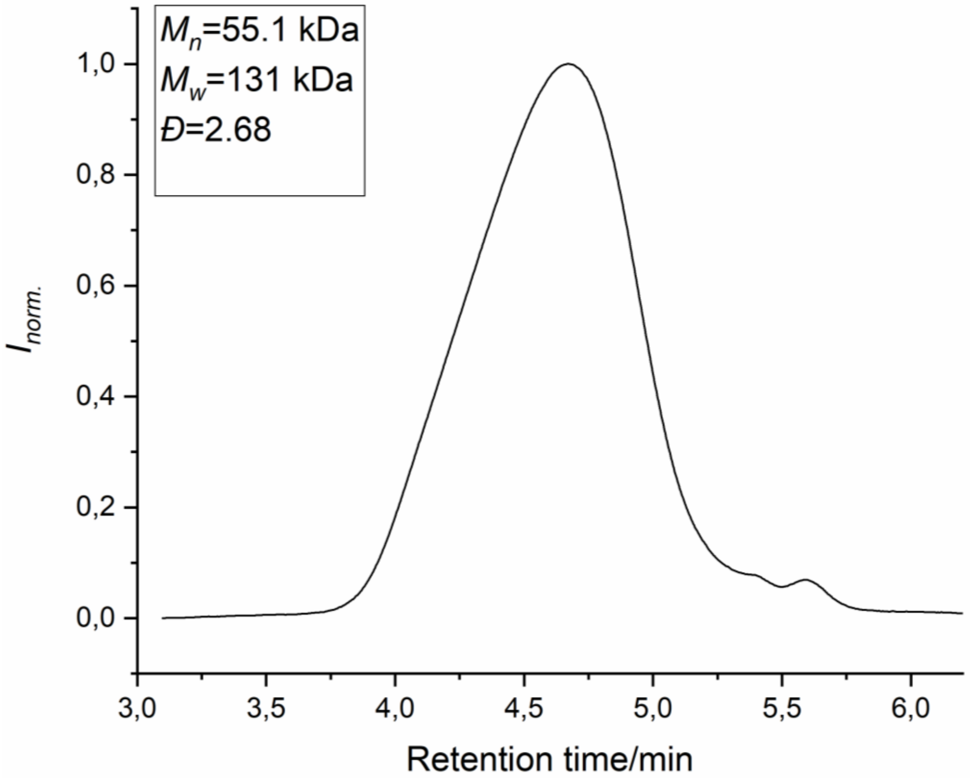
^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 7.29 (br, 4H, NH, ^{1}), 3.35 (br, 8H, CH_2, ^{2}), 1.46 (p, ^3J = 7.2 Hz, 8H, CH_2, ^{3}), 1.25 (br, 18H, CH_2, ^{4}).



^{13}C-NMR (101 MHz, $CDCl_3$) δ / ppm = 181.89 (br, HNC=SNH), 43.45 (HNC=SNH-**C**H_2), 29.08 (CH_2), 28.85 (CH_2), 28.61 (CH_2), 26.45 (CH_2), 23.84 (CH_2).



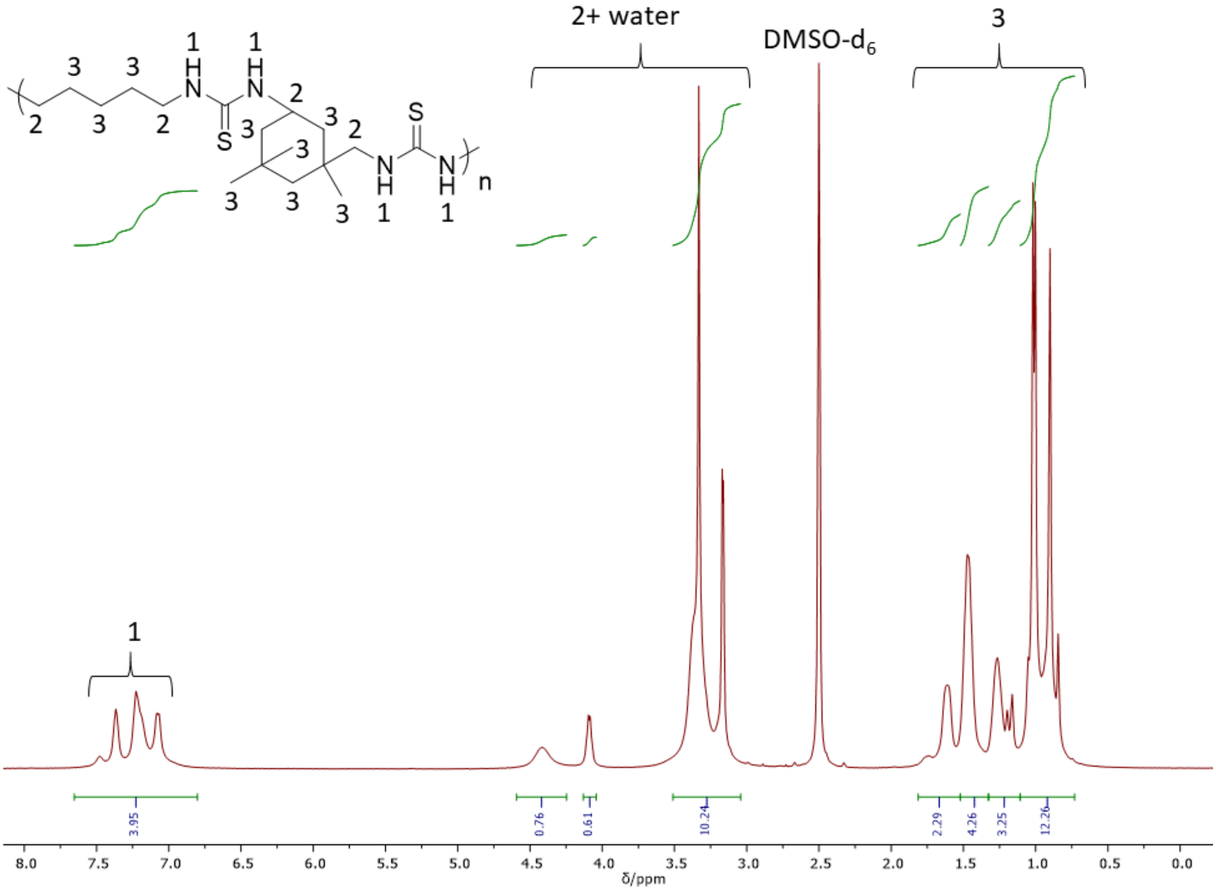
IR: *v* / cm^{-1} = 3237 (br, w), 3071 (br, w), 2919 (vs), 2850 (s), 1551 (vs), 1466 (w), 1353 (s), 1319 (m), 1285 (s), 1242 (m), 1064 (w), 728 (w), 669 (m), 577 (m), 544 (m), 509 (w), 475 (w).



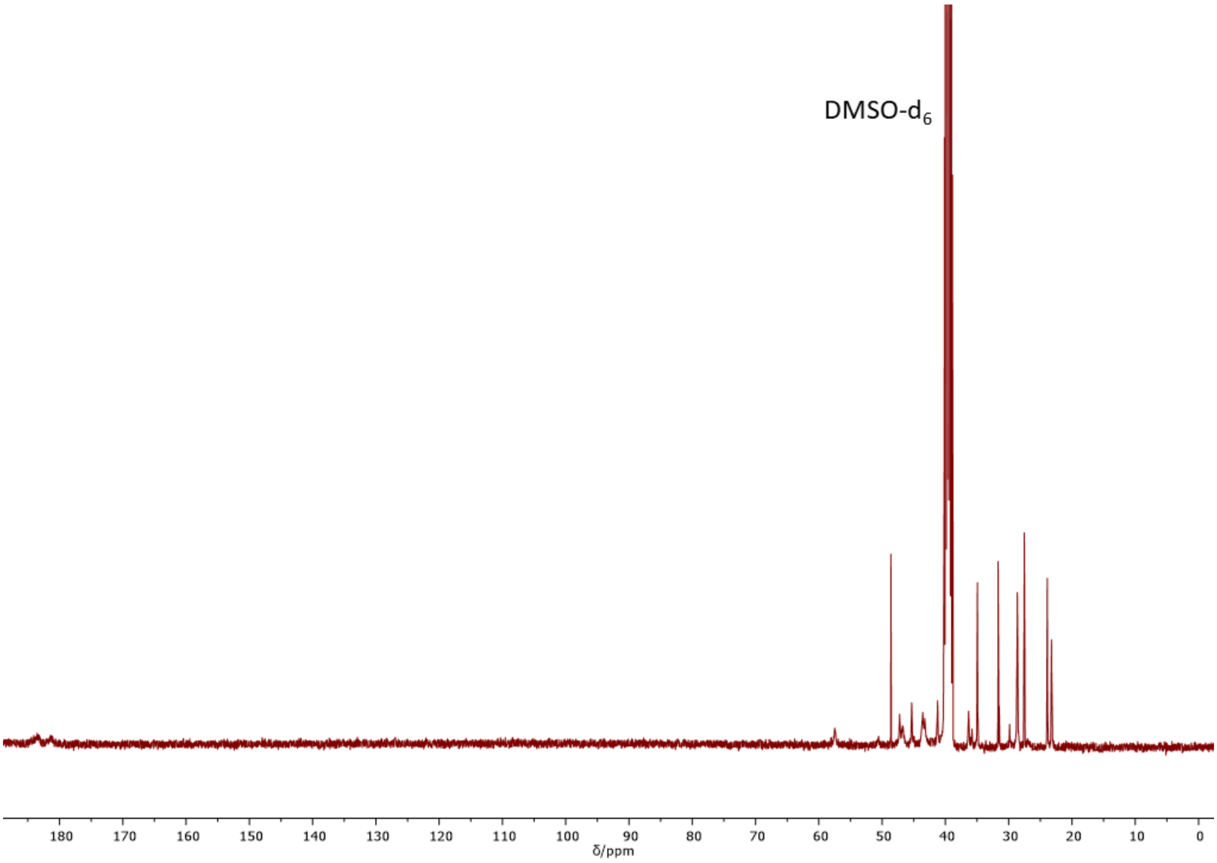
Polythiourea P3

The polymer was synthesized according to the procedure GP2. Diisothiocyante **3h** (254 mg, 1.00 mmol, 1.00 eq.) and diamino pentane (117µL, 102 mg, 1.00 mmol, 1.00 eq.) were dissolved in 1 mL DMF and the reaction mixture was stirred for 2 h. The crude product was obtained as a hollow polymer orb and thus, was crushed with a mortar. Remaining DMF was removed by vacuum oven (80 °C, 10 mbar, overnight) followed by washing in minimal amount of methanol under reflux to remove remaining DMF. The product was obtained as a colourless solid (376 mg) in a quantitative yield.

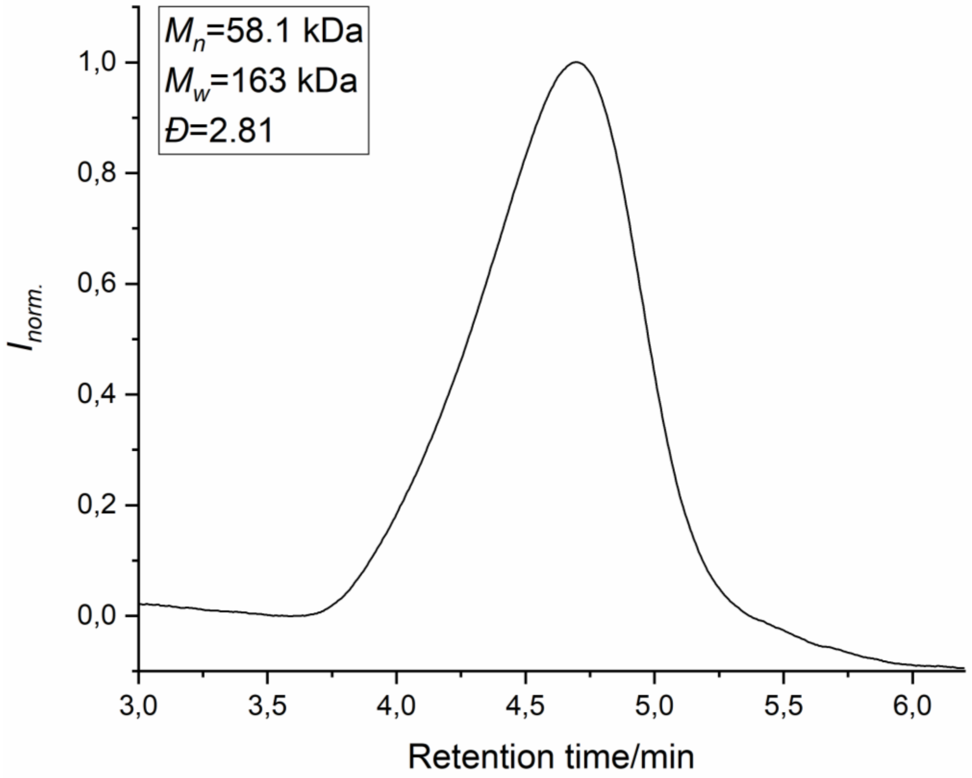
^{1}H-NMR (400 MHz, $CDCl_3$) δ / ppm = 7.58-6.89 (m, 4H, NH, ^{1}), 4.41 (br, 0.76H, CH, ^{2}), 4.09 (br, 0.61H, CH_2, ^{2}), 3.57-3.07 (m, 5.63H, CH_2, CH, ^{2}), 1.81-0.76 (m, 21H, CH_3, CH_2, ^{3}).



^{13}C-NMR (101 MHz, $CDCl_3$) δ / ppm = 183.53 (br, HNC=SNH), 181.34 (br, HNC=SNH), 57.48, 48.60, 47.24, 46.78, 45.32, 43.59, 43.35, 41.24, 36.33, 35.81, 34.93, 31.66, 31.50, 29.86, 28.62, 27.52, 23.89, 23.22.



IR: *v* / cm^{-1} = 3248 (br, s), 3060 (br, w), 2924 (br, s), 2850 (br, m), 1734 (w), 1534 (vs), 1460 (m), 1305 (s), 1235 (vs), 1210 (vs), 1196 (vs), 1068 (s), 1014 (vs), 696 (w), 660 (w), 507 (m), 456 (s)



E-factor calculation

E-factors were calculated with the following equation:

$$E = \frac{m_{waste}}{m_{product}} = \frac{\sum_{i=1}^{n}((n_i - \nu_i * n_{product}) * M_i) + m_{cat} + m_{solvent}}{m_{product}}$$

$m_{product}$ = isolated mass of product considering the GC-purity
$n_{product}$ = isolated molar amount of product
n_i = originally used molar amount of reactant i
ν_i = stoichiometric coefficient of reactant i (1 for IC, 0.125 for S_8)
m_{cat} = mass of used DBU
$m_{solvent}$ = mass of reaction solvent

m(product): was calculated considering the purity obtained by GC.

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