Phosphine-Catalyzed Disulfide Metathesis

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General Methods
Reagents were purchased from Sigma-Aldrich, Merck and Lancaster and used as received. $^1$H-NMR and $^{13}$C-NMR spectra were recorded on a Bruker Avance 400 spectrometer at 400 (100) MHz and/or Bruker Avance DMX 500 at 500 (125) MHz respectively. Chemical shifts are reported as $\delta$ values (ppm) with CDCl$_3$ ($^1$H-NMR $\delta$ 7.26, $^{13}$C-NMR $\delta$ 77.16) or DMSO-d6 ($^1$H-NMR $\delta$ 2.50, $^{13}$C-NMR $\delta$ 39.52) as an internal standard. $J$ values are given in Hertz (Hz). $^{31}$P-NMR spectra were recorded on a Bruker Avance DMX 500 at 200 MHz. GC-MS analysis were performed on a DB-wax column (J&W Scientific, 30m, 0.25 mm id and 0.15 µm film thickness) connected to a Finnigan SSQ 7000 mass spectrometer (EI, 70 eV, ion source temperature: 150°C).

Tricyclohexylphosphine (PCy$_3$).
Air exposed PCy$_3$ was analyzed by quantitative $^{31}$P-NMR (200 MHz, CDCl$_3$) $\delta$ 9.16 (PCy$_3$, 55%), $\delta$ 48.25 (OPCy$_3$, 45%).

Preparation of tricyclohexylphosphine oxide (OPCy$_3$).
Tricyclohexylphosphine (PCy$_3$) (20 mg, 0.07 mmol) was dissolved in Toluene (5 ml). The mixture was then heated for 2h at 80°C with air bubbling. Solvent evaporation under reduced pressure led to a white powder. $^{31}$P-NMR (200 MHz, CDCl$_3$) $\delta$ 48.25 (OPCy$_3$).

Methyl disulfide 1. $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$ 2.40 (6H, s). $^{13}$C-NMR (500 MHz, CDCl$_3$) $\delta$ 22.14. MS (EI) m/z 94.1.

Ethyl disulfide 2a. $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$ 1.31 (6H, t, $J = 7.25$ Hz), 2.67 (4H, q, $J = 7.25$ Hz). $^{13}$C-NMR (500 MHz, CDCl$_3$) $\delta$ 14.48, 32.91. MS (EI) m/z 122.1.

Propyl disulfide 2b. $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 0.99 (6H, t, $J = 7.3$ Hz), 1.70 (4H, sixtet, $J = 7.3$ Hz), 2.66 (4H, t, $J = 7.3$ Hz). $^{13}$C-NMR (500 MHz, CDCl$_3$) $\delta$ 13.20, 22.58, 41.25.

Phenyl disulfide 2c. $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$ 7.20 (4H, t, $J = 7.25$ Hz), 7.28 (2H, t, $J = 7.56$ Hz), 7.48 (4H, d, $J = 7.25$ Hz). $^{13}$C-NMR (500 MHz, CDCl$_3$) $\delta$ 127.30, 127.66, 129.20, 137.17.
Allyl disulfide 2d. $^1$H-NMR (500 MHz, DMSO-d6) δ 3.38 (4H, d, $J = 7.35$ Hz), 5.15 (2H, m), 5.18 (2H, dq, $J = 1.35$ Hz, $J = 16.9$ Hz), 5.80 (2H, m). $^{13}$C-NMR (500 MHz, DMSO-d6) δ. 40.87, 118.61, 133.61.

Benzyl disulfide 2e. $^1$H-NMR (500 MHz, DMSO-d6) δ 3.74 (4H, s), 7.28 (6H, m), 7.33 (4H, m). $^{13}$C-NMR (500 MHz, DMSO-d6) δ. 41.61, 127.29, 128.39, 129.36, 137.29.

Ethyl methyl disulfide 3a. $^1$H-NMR (500 MHz, CDCl$_3$) δ 1.31 (3H, t, $J = 7.25$ Hz), 2.38 (3H, s), 2.70 (2H, q, $J = 7.25$ Hz). $^{13}$C-NMR (500 MHz, CDCl$_3$) δ 14.48, 23.49, 32.03. MS (EI) m/z 108.

Methyl propyl disulfide 3b. $^1$H-NMR (500 MHz, CDCl$_3$) δ 0.98 (3H, t, $J = 7.25$ Hz), 1.70 (2H, sixtet, $J = 7.25$ Hz), 2.38 (3H, s), 2.67 (2H, t, $J = 7.25$ Hz). $^{13}$C-NMR (500 MHz, CDCl$_3$) δ. 13.20, 22.58, 23.44, 40.42.

Methyl phenyl disulfide 3c. $^1$H-NMR (500 MHz, CDCl$_3$) δ 2.42 (3H, s), 7.21 (2H, t, $J = 7.25$ Hz), 7.32 (1H, t, $J = 7.25$ Hz), 7.52 (2H, d, $J = 7.25$ Hz). $^{13}$C-NMR (500 MHz, CDCl$_3$) δ 22.98, 126.95, 127.67, 129.10, 137.00.

Allyl methyl disulfide 3d. $^1$H-NMR (500 MHz, DMSO-d6) δ 2.39 (3H, s), 3.40 (2H, m), 5.15 (1H, m), 5.21 (1H, dq, $J = 1.30$ Hz, $J = 16.95$ Hz), 5.84 (1H, m). $^{13}$C-NMR (500 MHz, DMSO-d6) δ. 22.52, 40.21, 118.49, 133.74.

Benzy1 methyl disulfide 3e. $^1$H-NMR (500 MHz, DMSO-d6) δ 2.17 (3H, s), 3.98 (2H, s), 7.28 (3H, m), 7.32 (2H, m). $^{13}$C-NMR (500 MHz, DMSO-d6) δ. 22.13, 41.31, 127.21, 128.36, 129.30, 137.55.

Ethyl propyl disulfide 4a. $^1$H-NMR (500 MHz, DMSO-d6) δ 0.94 (3H, t, $J = 7.25$ Hz), 1.25 (3H, t, $J = 7.25$ Hz), 1.64 (2H, sixtet, $J = 7.25$ Hz), 2.68 (2H, t, $J = 7.25$ Hz), 2.70 (2H, q, $J = 7.25$ Hz). $^{13}$C-NMR (500 MHz, DMSO-d6) δ. 12.70, 14.22, 21.86, 31.74, 39.99.

Allyl ethyl disulfide 4b. $^1$H-NMR (500 MHz, DMSO-d6) δ 1.24 (3H, t, $J = 7.30$ Hz), 2.70 (2H, q, $J = 7.30$ Hz), 3.37 (2H, m), 5.13 (1H, m), 5.20 (1H, dq, $J = 1.35$ Hz, $J = 16.95$ Hz), 5.80 (1H, m). $^{13}$C-NMR (500 MHz, DMSO-d6) δ. 14.26, 31.56, 41.10, 118.44, 133.68.
**Benzyl ethyl disulfide 4c.** $^1$H-NMR (500 MHz, DMSO-d6) δ 1.16 (3H, t, J = 7.25 Hz), 2.49 (2H, q, J = 7.25 Hz), 3.95 (2H, s), 7.28 (3H, m), 7.33 (2H, m). $^{13}$C-NMR (500 MHz, DMSO-d6) δ. 14.10, 31.21, 42.19, 127.20, 128.33, 129.25, 137.56.

**Allyl propyl disulfide 5a.** $^1$H-NMR (500 MHz, DMSO-d6) δ 0.94 (3H, t, J = 7.30 Hz), 1.63 (2H, sixtet, J = 7.15 Hz), 2.68 (2H, q, J = 7.15 Hz), 3.36 (2H, dt, J = 1 Hz, J = 4.85 Hz), 5.14 (1H, m), 5.21 (1H, dq, J = 1.30 Hz, J = 16.95 Hz), 5.80 (1H, m). $^{13}$C-NMR (500 MHz, DMSO-d6) δ. 12.75, 21.84, 39.79, 41.02, 118.43, 133.68.

**Benzyl propyl disulfide 5b.** $^1$H-NMR (500 MHz, DMSO-d6) δ 0.86 (3H, t, J = 7.30 Hz), 1.54 (2H, sixtet, J = 7.30 Hz), 2.44 (2H, t, J = 7.1 Hz), 3.95 (2H, s), 7.28 (3H, m), 7.33 (2H, m). $^{13}$C-NMR (500 MHz, DMSO-d6) δ. 12.75, 21.66, 39.28, 42.13, 127.18, 128.32, 129.25, 137.57.

**Allyl benzyl disulfide 6a.** $^1$H-NMR (500 MHz, DMSO-d6) δ 3.14 (4H, d, J = 7.35 Hz), 3.96 (2H, s), 5.10 (4H, m), 5.75 (2H, m), 7.28 (3H, m), 7.34 (2H, m). $^{13}$C-NMR (500 MHz, DMSO-d6) δ. 40.44, 41.97, 118.57, 127.24, 128.36, 133.34, 137.40.
Reversibility control experiment

1 and 2a (350 mM of each) were mixed together in CDCl₃ and in presence of 5 mol% of PCy₃. After equilibration of the reaction (1, 2a and 3a were present in solution with a ratio 1:1:2.2 respectively, Figure S1a-b), 2b (350 mM) was added. A new equilibration was formed, indicating reversibility of the reaction (Figure S1c-d).

Figure S1: ¹H-NMR spectra of the reaction mixture: a) after equilibration between 1 and 2a; b) enlarged area of the methyl region of a); c) after equilibration between 1, 2a and 2b (50 min); d) enlarged area of the methyl region. Compound numbering as in Table 1.
GC-MS analysis of 1 and 2a after reaction.

A GC-MS analysis was performed in order to confirm the $^1$H-NMR results and monitor the presence of the two symmetrical disulfides and the unsymmetrical disulfide resulting from the exchange reaction. A mixture of methyl disulfide 1 (0.23 mmol) and ethyl disulfide 2a (0.23 mmol) in benzene and in presence of 5 mol% of PCy$_3$ was injected after 11 days of reaction (around 150 ng) for separation on a DB-wax column. The following temperature program was used: 40 $^\circ$C (1 min), 5 $^\circ$C/min, 225 $^\circ$C (15 min). Injection was 220 $^\circ$C (split closed 30 s), and the transfer was held at 230 $^\circ$C. The GC chromatogram confirmed the $^1$H-NMR results. The retention time of 5.41 min, 6.95 min and 8.60 min (see Figure S1) correspond to 1, ethyl methyl disulfide 3a and 2a respectively. The reaction products were clearly identified by Mass Spectrometry (see Figure S2, Figure S3 and Figure S4).

Figure S2: GC chromatogram of a mixture of 1 (0.23 mmol), 2a (0.23 mmol) and PCy$_3$ (5 mol%) in benzene after 11 days. The three picks with a retention time (RT) of 5.41 min, 6.95 min and 8.60 min correspond to 1, 3a and 2a respectively.
Figure S3: MS spectrum of methyl disulfide 1 (retention time: 5.41 min)

Figure S4: MS spectrum of ethyl methyl disulfide 3a (retention time: 6.95 min)
**Figure S5:** MS spectrum of ethyl disulfide 2a (retention time: 8.60 min)