

# A novel method for the synthesis of unsymmetrical sulfides, thioesters and $\beta$ -thioesters<sup>†</sup>

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The S–S bond in disulfides was reduced by the Zn/ZrCl<sub>4</sub> system in THF to produce sulfur anions, which react with alkyl halides,  $\alpha,\beta$ -unsaturated esters and acyl chlorides or anhydrides to afford unsymmetrical sulfides, thioesters and  $\beta$ -thioesters, respectively.

**Keywords:** unsymmetrical sulfides, thioesters and  $\beta$ -thioesters

Recently, organic sulfur compounds have become of increasing importance in organic synthesis. As an attractive synthetic intermediate in organic synthesis, thioesters have received considerable attention.<sup>1–4</sup> A number of new methods have been developed for the preparation of thioesters in recent years, for example, the reaction between sodium thiobenzoate and arenediazonium tetrafluoroborates,<sup>5</sup> treatment of nitrosoamides or nitroamides with mercaptans in the presence of sodium hydride,<sup>6</sup> the cobalt carbonyl catalysed carbonylation of mercaptans and the cobalt chloride catalysed coupling of thiols and anhydrides.<sup>7</sup> Use of samarium diiodide in THF/HMPA for cleavage of S–S bonds in disulfides has been reported to give thioesters<sup>8</sup>. There also appeared some similar methods such as using Sm/CoCl<sub>2</sub><sup>9</sup> or Zn/TiCl<sub>4</sub><sup>10</sup> to reductively cleave S–S bond in disulfides to give thioesters. Unfortunately most of these methods suffer from significant drawbacks, which include strongly basic conditions, expensive starting materials, and long reaction times. Therefore, we strive to look for other reagents to overcome them.

Metals are versatile reagents in organic synthesis, for example zinc has been employed in Barbier type reactions, reductive coupling reactions and Reformatsky reactions. But to the best of our knowledge, there have been few reports on the application of zinc in the preparation of thioesters; our previous work on the reductive cleavage of the Se–Se bond with Zn/ZrCl<sub>4</sub> has been reported.<sup>11</sup> Herein we wish to report that

reductive cleavage of S–S bonds in disulfides by Zn/ZrCl<sub>4</sub> system led to sulfur anions, which react with  $\alpha,\beta$ -unsaturated esters and acyl chlorides or anhydrides to afford thioesters in THF in mild and neutral conditions.

## Experimental

Melting points were uncorrected. IR spectra were obtained on a PE-683 infrared spectrophotometer. <sup>1</sup>H NMR spectra were recorded on a PMX-60 MHz instrument. All NMR samples were measured in CCl<sub>4</sub> using TMS as internal standard. Metallic zinc was activated before use. The solvent THF was freshly distilled from sodium/benzophenone ketyl prior to use.

**General procedure:** Under an inert atmosphere of nitrogen gas, zinc powder (1.5 mmol), zirconium(IV) chloride (0.3 mmol) and disulfide (0.5 mmol) were placed in a well-dried, two neck, round bottom flask containing a magnetic stirrer bar. Freshly distilled dry THF (10 ml) was added by a syringe. The resulting mixture was stirred in THF at 40°C for about 5 h, when the zinc powder had almost completely appeared, which indicated the cleavage of the S–S bond and the generation of sulfur anions. Then acyl chloride (1.5 mmol) or anhydride (1.5 mmol) in THF (2 ml) was added to the mixture and stirred for 1–3 h, then the whole solution was poured into dilute HCl (1.2 mol/l, 20 ml) and the mixture was extracted with ether (15 ml  $\times$  3). The organic layer was washed with saturated NaCl and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure, the residue was then purified by preparative TLC on silica gel (light petroleum/acetone anhydride and light petroleum/ether as eluent) to give pure product.

In conclusion, we have demonstrated a novel method for the synthesis of thioesters from disulfides by the Zn/ZrCl<sub>4</sub> system. The advantages of the present method are easy availability of cheap starting materials, single product, simple manipulation, mild and neutral conditions.

**Data of products:** PhSCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>CH<sub>3</sub><sup>10</sup>: Oil,  $\nu_{\max}$ (cm<sup>-1</sup>), 3060, 3020, 2951, 2848, 1739, 1584, 1481, 1438, 1358, 1246, 1174, 1091, 979, 741, 692. <sup>1</sup>H NMR 7.38–7.12 (5H, m), 3.61(3H, s), 3.10 (2H, t), 2.52 (2H, t).

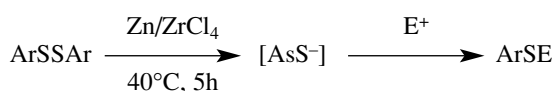
PhSCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Et<sup>10</sup>: Oil,  $\nu_{\max}$ (cm<sup>-1</sup>), 3080, 3061, 2982, 2936, 2870, 1735, 1585, 1481, 1440, 1372, 1345, 1244, 1180, 1094, 1025, 741, 692. <sup>1</sup>H NMR 7.41–7.05 (5H, m), 4.00–4.22 (2H, q), 3.06 (2H, t), 2.52 (2H, t), 1.18 (3H, t).

PhSCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Bu-n<sup>10</sup>: Oil,  $\nu_{\max}$ (cm<sup>-1</sup>), 3062, 2962, 2935, 2875, 1735, 1584, 1409, 1379, 1350, 1244, 1191, 1127, 1069, 742, 692. <sup>1</sup>H NMR 7.40–7.09(5H,m), 4.10(2H,t), 3.11(2H, t), 2.55 (2H, t), 1.17–1.58 (4H, m), 0.92 (3H, t).

PhSCH<sub>2</sub>CH(CH<sub>3</sub>)CO<sub>2</sub>CH<sub>3</sub><sup>10</sup>: Oil,  $\nu_{\max}$ (cm<sup>-1</sup>), 3060, 2960, 2926, 2854, 1739, 1584, 1481, 1459, 1211, 1166, 1025, 741, 692. <sup>1</sup>H NMR 7.39–7.14 (5H,m), 3.58(3H,s), 3.11–3.23(2H,d), 2.40–2.67 (1H, m), 1.42 (3H, d).

PhSCOCH<sub>3</sub><sup>12</sup>: Oil,  $\nu_{\max}$ (cm<sup>-1</sup>), 3063, 2926, 2855, 1712, 1584, 1478, 1442, 1378, 1240, 1115, 950, 747, 690. <sup>1</sup>H NMR 7.40 (5H, s), 2.38 (3H, s)

PhSCOPh<sup>13</sup>: M.p. 55–56°C (lit<sup>13</sup> 56°C)  $\nu_{\max}$ (cm<sup>-1</sup>), 3062, 2926, 1710, 1478, 1459, 1442, 1180, 1112, 996, 747, 690. <sup>1</sup>H NMR 7.55–7.28 (8H,m), 8.03–7.84 (2H,m),



**Table 1**

Entry	Ar	E	Yield/%
1	Ph	CH <sub>2</sub> CHCO <sub>2</sub> CH <sub>3</sub>	78
2	Ph	CH <sub>2</sub> CHCO <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>	75
3	Ph	CH <sub>2</sub> CHCO <sub>2</sub> Bu-n	73
4	Ph	CH <sub>2</sub> C(CH <sub>3</sub> )CO <sub>2</sub> CH <sub>3</sub>	55
5	Ph	CH <sub>3</sub> COCl	70
6	Ph	(CH <sub>3</sub> CO) <sub>2</sub> O	67
7	Ph	PhCOCl	62
8	PhCH <sub>2</sub>	CH <sub>3</sub> COCl	65
9	PhCH <sub>2</sub>	(CH <sub>3</sub> CO) <sub>2</sub> O	62
10	PhCH <sub>2</sub>	PhCOCl	66
11	PhCH <sub>2</sub>	PhCH <sub>2</sub> Cl	77
12	Ph	PhCH <sub>2</sub> Cl	80

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<sup>†</sup> This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.

$PhCH_2SCOH_3^{14}$ : Oil,  $\nu_{max}(cm^{-1})$ , 3065, 3031, 2979, 2928, 1693, 1496, 1454, 1412, 1352, 1134, 958, 703, 628.  $^1H$  NMR, 7.18 (5H, s), 4.02 (2H, s), 2.28 (3H, s).

$PhCH_2SCOPh^{15}$ : Oil,  $\nu_{max}(cm^{-1})$ , 3065, 3035, 2960, 2925, 2873, 1720, 1602, 1585, 1452, 1315, 1276, 1117, 1071, 1027, 713, 688.  $^1H$  NMR 7.50–7.20 (8H, m), 8.00–7.80 (2H, m), 4.02(2H,s)

$PhCH_2SCH_2Ph^{16}$ : M.p. 47–49°C (lit. 48–49°C),  $\nu_{max}(cm^{-1})$ , 3063, 3031, 2958, 2925, 1603, 1494, 1455, 1413, 1075, 1033, 776, 700.  $^1H$  NMR, 3.44 (4H, s), 7.15 (10H, s).

$PhSCH_2Ph^{16}$ : m.p. 38–39°C (lit. 39–40°C),  $\nu_{max}(cm^{-1})$ , 3061, 3031, 2961, 2911, 1495, 1454, 1443, 1087, 1037, 745, 694.  $^1H$  NMR 3.97 (2H, s), 7.00–7.28 (10H, m).

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