

# Indium(I) iodide promoted cleavage of dialkyl/diaryl disulfides and subsequent anti-Markovnikov addition to styrenes: a new route to linear thioethers

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Received 6 May 2006; revised 26 June 2006; accepted 6 July 2006

Available online 4 August 2006

**Abstract**—The reaction of thiolate anions, generated in situ by indium(I) iodide promoted cleavage of dialkyl/diaryl disulfides, with styrenes has been investigated. Thiolate anions add to a variety of styrenes in an anti-Markovnikov manner producing linear thioethers in high yields. This method provides a new route to the synthesis of thioethers.

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The synthesis of thioethers by the addition of thiolate anions to olefins is of much importance. The reaction is usually carried out using thiols and is catalyzed by protic<sup>1</sup> as well as Lewis acids.<sup>2</sup> Although the addition of thiols to carbon–carbon double bonds has been well studied, reactions with styrenes have not been adequately addressed, probably due to their facile polymerization under acidic conditions.<sup>2</sup> Thus, addition of thiols to styrenic substrates has been investigated with a variety of mild catalysts.<sup>3</sup> Although Markovnikov additions to styrenes are common,<sup>1,2,3a</sup> only a few reagents such as H-rho-zeolite<sup>3b</sup> and benzene-reflux<sup>3a</sup> lead to anti-Markovnikov products. Several of these procedures are associated with disadvantages such as unsatisfactory yields, long reaction times and they also lack systematic study. This prompted us to find a more convenient and general method for this transformation.

We have been actively engaged in exploring new derivatives of indium for organic reactions and as a part of this program we have already disclosed several applications<sup>4</sup> of indium(I) iodide, which include cleavage of diaryl diselenides and disulfides and subsequent reactions with alkyl halides,<sup>4a</sup> acyl halides,<sup>4b</sup> vinyl halides,<sup>4c</sup> conjugated carbonyl compounds<sup>4d</sup> and more recently, the use of InI as a radical initiator.<sup>4e</sup>

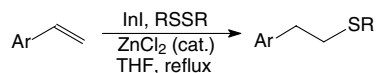
We report here a new strategy for the synthesis of thioethers via the anti-Markovnikov addition of thiolate anions, generated in situ by InI-promoted cleavage of dialkyl/diaryl disulfides to styrenes in the presence of zinc chloride (Scheme 1). We are not aware of any other method using the reaction of dialkyl/diaryl disulfides with styrenes for the synthesis of thioethers.

The experimental procedure is very simple.<sup>5</sup> Several substituted styrenes underwent reactions with a variety of dialkyl or diaryl disulfides to produce the corresponding linear thioethers via regioselective anti-Markovnikov addition. The results are summarized in Table 1. Several sensitive functional groups such as Cl, Br, OMe and methylenedioxy remained unaffected under the reaction conditions. Sensitive molecules such as dihydropyran and dihydrofuran (entries 14 and 15) also underwent addition at the more electrophilic C-2 centres giving good yields (60–70%) of products. All the additions were regioselective and anti-Markovnikov in nature. The other regioisomer (Markovnikov addition product) was not isolated from any of the reactions.

In general, the reactions were fast, clean and high yielding. Diaryl disulfides react faster than dialkyl disulfides. It was also observed that diselenides did not react at all

**Keywords:** Thioether; Anti-Markovnikov addition; Styrene; Dialkyl disulfide; Indium(I) iodide; Zinc chloride.

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Scheme 1.

**Table 1.** Synthesis of linear thioethers via anti-Markovnikov addition of dialkyl/diaryl disulfides to styrenes

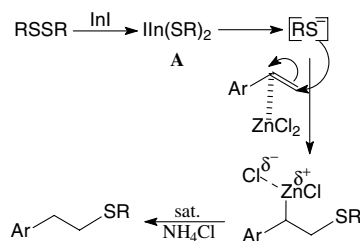
$$\text{Ar}-\text{CH}=\text{CH}_2 \xrightarrow[\text{THF, reflux}]{\text{InI, RSSR; ZnCl}_2 \text{ (cat.)}} \text{Ar}-\text{CH}_2-\text{CH}_2-\text{SR}$$

Entry	Styrene	R	Product	Time (h)	Yield <sup>a</sup> (%)	Ref.
1		C <sub>6</sub> H <sub>5</sub>		4.5	90	3a
2		C <sub>6</sub> H <sub>5</sub>		4.5	80	3b
3		<i>n</i> -C <sub>4</sub> H <sub>9</sub>		6.0	65	
4		C <sub>6</sub> H <sub>5</sub>		5.0	70	7
5		( <i>p</i> -Cl)C <sub>6</sub> H <sub>4</sub>		5.0	69	
6		C <sub>6</sub> H <sub>5</sub>		6.0	65	
7		C <sub>6</sub> H <sub>5</sub>		5.5	71	
8		( <i>p</i> -Cl)C <sub>6</sub> H <sub>4</sub>		5.5	72	
9		C <sub>6</sub> H <sub>5</sub>		5.5	70	
10		<i>n</i> -C <sub>4</sub> H <sub>9</sub>		6.0	69	
11		C <sub>6</sub> H <sub>5</sub>		5.75	71	8
12		C <sub>6</sub> H <sub>5</sub>		5.5	70	
13		( <i>p</i> -Cl)C <sub>6</sub> H <sub>4</sub>		6.0	73	
14		C <sub>6</sub> H <sub>5</sub>		5.0	70	3d
15		C <sub>6</sub> H <sub>5</sub>		5.5	60	3d

<sup>a</sup> Yields refer to those of pure isolated products characterized by IR and <sup>1</sup>H and <sup>13</sup>C NMR spectroscopic data.

using this procedure. The products were obtained in high purity after simple column chromatography. All the compounds were characterized from spectroscopic

data and elemental analysis. THF was found to be the solvent of choice as other solvents including CH<sub>3</sub>CN and CH<sub>2</sub>Cl<sub>2</sub> did not give the desired products. It was



Scheme 2.

observed that the reaction did not proceed at all in the absence of either InI or ZnCl<sub>2</sub>. It is speculated<sup>6</sup> that the reaction proceeds through the intermediacy of bis(thioalkyl)-iodo-indium(III) species (A) formed readily by the reaction of equimolar quantities of InI and the dialkyl/diaryl disulfide, which then releases a thiolate anion, which adds to the styrene (Scheme 2). The presence of ZnCl<sub>2</sub> facilitates the addition through polarization of the double bond. Zinc chloride was used in a catalytic amount and is probably regenerated by transmetalation to indium during the reaction.

In conclusion, the present procedure using the indium(I) iodide–ZnCl<sub>2</sub> system provides a new route to linear thioethers via a highly regioselective anti-Markovnikov addition of dialkyl/diaryl disulfides to styrenes. The significant features of this methodology are the use of more stable disulfides in place of thiols, good isolated yields of products (60–90%), fast reactions and atom economy.

### Acknowledgements

We are pleased to acknowledge the financial support from CSIR, New Delhi [Grant No. 01(1936)/04], for this investigation. T.M. is also thankful to CSIR for his fellowship.

### References and notes

1. Screttas, C. G.; Micha-Screttas, M. *J. Org. Chem.* **1979**, *44*, 713–719, and references cited therein.
2. (a) Mukaiyama, T.; Izawa, T.; Saigo, K.; Takai, H. *Chem. Lett.* **1973**, 355–356; (b) Belley, M.; Zamboni, R. *J. Org. Chem.* **1989**, *54*, 1230–1232.
3. (a) Kanagasabapathy, S.; Sudalai, A.; Benicewicz, B. C. *Tetrahedron Lett.* **2001**, *42*, 3791–3794, and references cited therein; (b) Kumar, P.; Pandey, R. K.; Hegde, V. R. *Synlett* **1999**, 1921–1922; (c) Converso, A.; Saaidi, P.-L.; Sharpless, K. B.; Finn, M. G. *J. Org. Chem.* **2004**, *69*, 7336–7339; (d) Braga, A. L.; Silveira, C. C.; Dornelles, L.; Zeni, G.; Galarza, F. A. D.; Wessjohann, L. A. *Synth. Commun.* **1995**, *25*, 3155–3162.
4. (a) Ranu, B. C.; Mandal, T.; Samanta, S. *Org. Lett.* **2003**, *5*, 1439–1441; (b) Ranu, B. C.; Mandal, T. *J. Org. Chem.* **2004**, *69*, 5793–5795; (c) Ranu, B. C.; Mandal, T. *Synlett* **2004**, 1239–1242; (d) Ranu, B. C.; Chattopadhyay, K.; Banerjee, S. *J. Org. Chem.* **2006**, *71*, 423–425; (e) Ranu, B. C.; Mandal, T. *Tetrahedron Lett.* **2006**, *47*, 2859–2861.
5. Representative experimental procedure for the cleavage of diphenyl disulfide and subsequent anti-Markovnikov addition to  $\alpha$ -methyl styrene (Table 1, entry 2). Indium(I) iodide

(121 mg, 0.5 mmol) was added to a solution of diphenyl disulfide (109 mg, 0.5 mmol) in freshly distilled THF (2.5 mL) under argon followed by the addition of  $\alpha$ -methyl styrene (118 mg, 1 mmol) and ZnCl<sub>2</sub> (20.7 mg, 15 mol %). The reaction mixture was heated under reflux for 4.5 h (TLC). THF was then evaporated and the residue was quenched with saturated ammonium chloride solution and extracted with Et<sub>2</sub>O (3 × 20 mL). The Et<sub>2</sub>O extract was successively washed with water, 2% NaOH solution and brine and then dried (Na<sub>2</sub>SO<sub>4</sub>). Evaporation of the solvent gave a crude product, which was purified by column chromatography over silica gel (hexane–Et<sub>2</sub>O, 95:5) to provide 1-(1-methyl-2-phenylsulfanyl-ethyl)-benzene (182.4 mg, 80%) as a colourless liquid, IR (neat): 1438, 1479, 1581 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  1.55 (d, *J* = 6.5 Hz, 3H), 3.10–3.24 (m, 2H), 3.35–3.40 (m, 1H), 7.27–7.48 (m, 10H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  21.2, 39.6, 42.1, 125.9, 126.7, 127.1 (2C), 128.6 (2C), 129.0 (2C), 129.1 (2C), 137.0, 145.6. These data are in good agreement with those reported.<sup>3b</sup> This procedure was followed for the reactions of all the substrates listed in Table 1.

The products from entries 1, 2, 4, 11, 14 and 15, which are known, were identified by comparison of their spectroscopic data (IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR) with those reported. New compounds (entries 3, 5, 6, 7, 8, 9, 10, 12 and 13) were characterized from their spectroscopic data and elemental analysis. These data are presented below:

*1-(2-Butylsulfanylethyl)-4-chlorobenzene* (entry 3): Colourless liquid; IR (neat): 1438, 1478, 1583 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  0.87–0.94 (m, 3H), 1.36–1.45 (m, 2H), 1.51–1.59 (m, 2H), 2.48–2.54 (m, 2H), 2.71–2.76 (m, 2H), 2.82–2.88 (m, 2H), 7.11–7.14 (m, 2H), 7.23–7.27 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  13.6, 21.9, 31.7, 31.9, 33.5, 35.6, 128.5 (2C), 129.8 (2C), 132.0, 139.0. Anal. Calcd for C<sub>12</sub>H<sub>17</sub>ClS: C, 63.00; H, 7.49. Found: C, 62.78; H, 7.32.

*1-[2-(4-Chlorophenyl)sulfanylethyl]-4-chlorobenzene* (entry 5): Colourless liquid; IR (neat): 1438, 1478, 1581 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  2.78–2.85 (m, 2H), 3.03–3.09 (m, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 7.20–7.23 (m, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  34.8, 35.4, 128.7 (2C), 129.1 (2C), 129.9 (2C), 130.7 (2C), 132.2, 132.3, 134.7, 138.3. Anal. Calcd for C<sub>14</sub>H<sub>12</sub>Cl<sub>2</sub>S: C, 59.37; H, 4.27. Found: C, 59.20; H, 4.13.

*1-(2-Phenylsulfanylethyl)-3-bromobenzene* (entry 6): Colourless viscous oil; IR (neat): 1438, 1478, 1582 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  2.84–2.90 (m, 2H), 3.11–3.16 (m, 2H), 7.11–7.37 (m, 9H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  34.9, 35.3, 126.2, 127.2, 129.0 (2C), 129.5 (2C), 129.6, 130.0, 131.1, 131.6, 135.9, 142.4. Anal. Calcd for C<sub>14</sub>H<sub>13</sub>BrS: C, 57.35; H, 4.47. Found: C, 57.13; H, 4.33.

*1-(2-Phenylsulfanylethyl)-2-methoxybenzene* (entry 7): Colourless liquid; IR (neat): 1438, 1475, 1580 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  3.05–3.10 (m, 2H), 3.25–3.30 (m, 2H), 3.88 (s, 3H), 6.92–7.02 (m, 2H), 7.22–7.50 (m, 7H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  31.5, 33.5, 55.7, 110.9, 121.0, 126.0, 128.4, 129.1 (2C), 129.3 (2C), 129.6, 130.8, 137.5, 158.0. Anal. Calcd for C<sub>15</sub>H<sub>16</sub>OS: C, 73.73; H, 6.60. Found: C, 73.51; H, 6.45.

*1-[2-(4-Chlorophenyl)sulfanylethyl]-4-methoxybenzene* (entry 8): Colourless oil; IR (neat): 1439, 1478, 1582 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  2.81–2.86 (m, 2H), 3.06–3.12 (m, 2H), 3.76 (s, 3H), 6.81–6.84 (m, 2H), 7.07–7.24 (m, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  34.6, 35.6, 55.2, 113.9 (2C), 127.8, 128.9 (2C), 129.4 (2C), 130.6 (2C), 132.0, 133.9, 158.2. Anal. Calcd for C<sub>15</sub>H<sub>15</sub>ClOS: C, 64.62; H, 5.42. Found: C, 64.40; H, 5.25.

*1-(2-Phenylsulfanylethyl)-3,4-methylenedioxybenzene* (entry 9): Colourless liquid; IR (neat): 1246, 1439, 1488, 1583 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  2.86–2.91 (m,

2H), 3.14–3.19 (m, 2H), 5.96 (m, 2H), 6.67–6.80 (m, 3H), 7.20–7.42 (m, 5H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  35.2 (2C), 100.7, 108.1, 108.8, 121.3, 125.8, 128.8 (2C), 129.1 (2C), 133.9, 136.2, 146.0, 147.5. Anal. Calcd for  $\text{C}_{15}\text{H}_{14}\text{O}_2\text{S}$ : C, 69.74; H, 5.46. Found: C, 69.51; H, 5.33.

*1-(2-Butylsulfanylethyl)-3,4-dimethoxybenzene (entry 10)*: Colourless liquid; IR (neat): 1437, 1477, 1583  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  0.92 (t,  $J = 7.20$  Hz, 3H), 1.35–1.45 (m, 2H), 1.51–1.63 (m, 2H), 2.54 (t,  $J = 7.20$  Hz, 2H), 2.72–2.86 (m, 4H), 3.86 (s, 3H), 3.88 (s, 3H), 6.70–6.82 (m, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  13.5, 21.8, 31.6, 31.9, 33.7, 35.8, 55.6, 55.7, 111.1, 111.7, 120.2, 133.2, 147.4, 148.7. Anal. Calcd for  $\text{C}_{14}\text{H}_{22}\text{O}_2\text{S}$ : C, 66.10; H, 8.72. Found: C, 65.90; H, 8.59.

*1-(2-Phenylsulfanylethyl)-naphthalene (entry 12)*: Colourless liquid; IR (neat): 1439, 1477, 1579  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  3.20–3.28 (m, 2H), 3.33–3.39 (m, 2H), 7.18–7.49 (m, 9H), 7.70–7.90 (m, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ,

75 MHz):  $\delta$  32.9, 34.5, 123.2, 125.4, 125.5, 126.0, 126.1, 126.3, 127.2, 128.8, 128.9 (2C), 129.0, 129.5 (2C), 131.5, 133.8, 136.1. Anal. Calcd for  $\text{C}_{18}\text{H}_{16}\text{S}$ : C, 81.77; H, 6.10. Found: C, 81.57; H, 5.95.

*1-[2-(4-Chloro-phenylsulfanyl)ethyl]-naphthalene (entry 13)*: Colourless liquid; IR (neat): 1437, 1475, 1596  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  3.07–3.13 (m, 2H), 3.16–3.22 (m, 2H), 7.15–7.42 (m, 8H), 7.68–7.88 (m, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  31.9, 33.8, 122.2, 124.5, 124.6, 125.2, 125.5, 126.4, 127.0, 127.7, 127.9, 128.2 (2C), 129.8 (2C), 129.9, 132.7, 134.9. Anal. Calcd for  $\text{C}_{18}\text{H}_{15}\text{ClS}$ : C, 72.35; H, 5.06. Found: C, 72.11; H, 4.94.

- Nobrega, J. A.; Goncalves, S. M. C.; Peppe, C. *Tetrahedron Lett.* **2000**, *41*, 5779–5782.
- Lewis, E. S.; Butler, M. M. *J. Am. Chem. Soc.* **1976**, *98*, 2257–2260.
- Baciocchi, E.; Lanzalunga, O.; Pirozzi, B. *Tetrahedron* **1997**, *53*, 12287–12298.