## Sm/I<sub>2</sub>-Mediated Selective Cleavage of the S–S or C–S Bonds of Sodium (*Z*)-Allyl Thiosulfates in Aqueous Media: Selective Formation of Di(*Z*-allyl) Disulfides or (2*E*)-Methyl Cinnamic Esters

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Abstract: Selective cleavage of the S–S or C–S bonds in sodium (*Z*)-allyl thiosulfates in the presence of a Sm/I<sub>2</sub>-system was achieved to form the corresponding di(*Z*-allyl) disulfides or (2*E*)-methyl cinnamic esters in moderate to good yields in aqueous media.

**Key words:** selective cleavage, sodium (*Z*)-allyl thiosulfates, di(*Z*-allyl) disulfides, (2*E*)-methyl cinnamic esters, samarium metal

Recently, there has been a growing interest in metalmediated organic reactions in media containing water.<sup>1</sup> Such aqueous reactions have a number of advantages over conventional non-aqueous reactions, such as, simple operation, environmentally benign process, and no requirements for anhydrous organic solvents, etc. To date, several metals, such as In, Zn, and Sn, have been widely applied in aqueous media to conduct various reactions.<sup>1b,1d,f</sup> Metallic samarium is stable in air and its reducing power (Sm<sup>3+</sup>/Sm = -2.41V) is similar to that of magnesium (Mg<sup>2+</sup>/Mg = -2.37V) and superior to that of zinc (Zn<sup>2+</sup>/Zn = -0.71V). However, the reactions promoted by samarium in aqueous media have been investigated less.<sup>2,3</sup>

The Baylis–Hillman reaction has drawn much attention as a useful carbon–carbon bond-forming reaction in the last decades.<sup>4</sup> The main attraction of this reaction lies in its atom economy, catalytic process, and the high degree of functionality present in the products for further transformations. Up to now, a number of novel reactions based on Baylis–Hillman adducts have been reported, especially those that provide good stereoselectivities.<sup>4,5</sup>

As part of our continued interest in the conversion of Baylis–Hillman adducts into trisubstituted alkenes,<sup>6</sup> we have recently described a convenient synthesis of sodium (*Z*)-allyl thiosulfates by treatment of Baylis–Hilman acetates with sodium thiosulfate and reported their further conversion to unsymmetrical diallylsulfides in a one-pot manner.<sup>7</sup> Following on from this we found that the S–S and C–S bonds in sodium (*Z*)-allyl thiosulfates could be selectively cleaved by samarium and a trace amount of I<sub>2</sub> in aqueous media depending on the different substituents (alkyl or aryl group) attached to them, thus affording di(*Z*-allyl) disulfides or (2*E*)-methyl cinnamic esters in moderate to good yields, respectively (Scheme 1).<sup>8</sup>

Sodium (*Z*)-allyl thiosulfates **2** were synthesized in almost quantitative yield via reaction of the Baylis–Hillman acetates **1** with Na<sub>2</sub>SSO<sub>3</sub>·5H<sub>2</sub>O in anhydrous methanol at room temperature.<sup>7,8</sup> Our initial attempt was to obtain diallyl disulfides from the in situ generated **2** in a one-pot strategy by treatment with Sm/I<sub>2</sub> in aqueous media<sup>3a</sup> because diallyl disulfides are a class of useful and important building blocks in organic synthesis as well as potential bioactive compounds.<sup>9,10</sup> Indeed, when **2** derived from alkyl-substituted **1**<sup>11</sup> were used as substrates, the reaction proceeded smoothly and gave di(*Z*-allyl) disulfides **3** in moderate to good yields (Table 1, entry 1–3). Upon formation of **3** the *Z* configuration of the allylic moiety in **2** was entirely conserved, which was confirmed by NOESY experiments.<sup>12</sup>



Scheme 1 Selective formation of the di(Z-allyl) disulfides or (2E)-methyl cinnamic esters.

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Table 1	Preparation of Di(Z-allyl) Disulfides or (2E)-Methyl
Cinnamic	Esters <sup>a</sup>

Entry	R	Time (h) <sup>b</sup>	Yield (%) <sup>c</sup>	
			<b>3</b> <sup>d,15</sup>	<b>4</b> <sup>d</sup>
1	Et ( <b>1a</b> )	3	74 ( <b>3a</b> )	_e
2	$n-C_{7}H_{15}(1\mathbf{b})$	3	82 ( <b>3b</b> )	_e
3	$C_6H_5CH_2CH_2$ (1c)	3	84 ( <b>3c</b> )	_e
4	$C_{6}H_{5}(\mathbf{1d})$	4	<5	83 ( <b>4d</b> )
5	$4-CH_{3}C_{6}H_{4}(1e)$	4	<5	85 ( <b>4e</b> )
6	$4\text{-}\mathrm{ClC}_{6}\mathrm{H}_{4}\left(\mathbf{1f}\right)$	4	trace	84 ( <b>4f</b> )
7	$2\text{-}\mathrm{ClC}_{6}\mathrm{H}_{4}\left(\mathbf{1g}\right)$	4	trace	80 ( <b>4g</b> )
8	$2-CH_{3}OC_{6}H_{4}$ (1h)	4	<7	78 ( <b>4h</b> )
9	$3,4-OCH_2OC_6H_3(1j)$	4	<5	77 ( <b>4i</b> )

<sup>a</sup> Reagents and conditions: **1** (1 mmol),  $Na_2SSO_3 \cdot 5H_2O$  (1 mmol), MeOH (15 mL), r.t., 4–8 h, then Sm (1 mmol),  $I_2$  (trace), THF (20 mL), sat. aq solution of NH<sub>4</sub>Cl (4 mL), r.t., 3–4 h.

<sup>b</sup> Time needed for  $Sm/I_2$ -mediated reduction.

<sup>d</sup> All new products were characterized by <sup>1</sup>H NMR, MS, IR, and elemental analysis.

<sup>e</sup> Not detected.

Interestingly, when substrates 2, derived from aryl-substituted 1, were allowed to react in the same conditions, selective cleavage of the C–S bonds predominated to give (2E)-methyl cinnamic esters  $4^{13,14}$  in moderate to good yields, while diallyl disulfides 3 from the cleavage of the S–S bonds were only obtained in very small amounts (Table 1, entries 4–9).

On the basis of previous reports,<sup>3c</sup> a possible mechanism for the selective cleavage of the S–S or C–S bonds in **2** is depicted in Scheme 2. Perhaps the Sm powder was activated by  $I_2$  and aqueous NH<sub>4</sub>Cl, thus an electron was transferred to the substrate 2 to form the radical anion 5; when R was an alkyl group, cleavage of the S–S bond was preferred to form S-radical intermediate 6, which then dimerized to afford the di(Z-allyl) disulfide 3; but when R was an aryl group, cleavage of the C–S bond predominated to give allyl radical species 7 or 8. Radical 7 was favored over 8 due to the conjugated effect of the  $\alpha$ , $\beta$ double bond with the aromatic ring. Then 7 received another electron from Sm to produce allyl anion intermediate 9. Here the attached aryl group on the allyl moiety may be capable of stabilizing the allyl anion, so that the (2*E*)methyl cinnamic ester 4 could be formed by protonation of the intermediate 9.

In summary, it was found that the Sm and a trace amount of  $I_2$  could be used for the selective cleavage of the S–S or C–S bonds in sodium (Z)-allyl thiosulfates depending on the substituents to give the corresponding di(Z-allyl) disulfides or (2*E*)-methyl cinnamic esters in moderate to good yields in aqueous media. The notable advantages of the reaction were its high regioselectivity, simple one-pot operation, environmentally benign process, and mild reaction conditions.

## **References and Notes**

- (a) Lubineau, A.; Auge, J.; Queneau, Y. Synthesis 1994, 741. (b) Li, C. J. Chem. Rev. 1993, 93, 2023.
   (c) Yamamoto, Y.; Asao, N. Chem. Rev. 1993, 93, 2207.
   (d) Li, C. J. Tetrahedron 1996, 52, 5643. (e) Chan, T. H.; Isaac, M. B. Pure Appl. Chem. 1996, 68, 919. (f) Li, C. J. Chem. Rev. 2005, 105, 3095.
- (2) For recent examples, see: (a) Yu, C. Z.; Liu, B.; Hu, L. Q. J. Org. Chem. 2001, 66, 919. (b) Talukdar, S.; Fang, J. M. J. Org. Chem. 2001, 66, 330. (c) Laskar, D. D.; Prajapati, D.; Sandhu, J. S. Tetrahedron Lett. 2001, 42, 7883. (d) Wang, L.; Li, P. H.; Zhou, L. Tetrahedron Lett. 2002, 43, 8141. (e) Matsukawa, S.; Hinakubo, Y. Org. Lett. 2003, 5, 1221.
- (3) (a) Wang, L.; Zhou, L. H.; Zhang, Y. M. Synlett 1999, 1065.
  (b) Wang, L.; Zhang, Y. M. Tetrahedron 1999, 55, 10695.
  (c) Liu, X.; Liu, Y. K.; Zhang, Y. M. Tetrahedron Lett. 2002, 43, 6787.



Scheme 2 Possible mechanism for the selective cleavage of the S–S or C–S bonds in 2 mediated by  $Sm/I_2$ (trace) system.

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<sup>&</sup>lt;sup>c</sup> Isolated yields.

- (4) For reviews, see: (a) Ciganek, E. Org. React. (N.Y.) 1997, 51, 201. (b) Basavaiah, D.; Rao, P. D.; Hyma, R. S. Tetrahedron 1996, 52, 8001. (c) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. Chem. Rev. 2003, 103, 811.
- (5) For recent examples, see: (a) Chandrasekhar, S.; Basu, D.; Rambabu, C. *Tetrahedron Lett.* 2006, 47, 3059.
  (b) Shanmugarn, P.; Rajasingh, P. *Synlett* 2005, 939.
  (c) Das, B.; Majhi, A.; Banerjee, J.; Chowdhury, N.; Venkateswarlu, K. *Tetrahedron Lett.* 2005, 46, 7913.
  (d) Das, B.; Mahender, G.; Chowdhury, N.; Banerjee, J. *Synlett* 2005, 1000. (e) Kabalka, G. W.; Venkataiah, B.; Dong, G. *Org. Lett.* 2003, *5*, 3803. (f) Kabalka, G. W.; Venkataiah, B.; Dong, G. *Tetrahedron Lett.* 2003, 44, 4673.
- (6) (a) Liu, Y. K.; Li, J.; Zheng, H.; Xu, D. Q.; Xu, Z. Y.; Zhang, Y. M. Synlett 2005, 2999. (b) Liu, Y. K.; Xu, D. Q.; Xu, Z. Y.; Zhang, Y. M. J. Zhejiang Univ. Science, B 2006, 7, 393. (c) Li, J.; Wang, X. X.; Zhang, Y. M. Synlett 2005, 1039. (d) Li, J.; Wang, X. X.; Zhang, Y. M. Tetrahedron Lett. 2005, 46, 5233.
- (7) Liu, Y. K.; Xu, X. S.; Zheng, H.; Xu, D. Q.; Xu, Z. Y.; Zhang, Y. M. Synlett 2006, 571.
- (8) One-Pot Synthesis of Di(Z-allyl) Disulfides or (2E)-Methyl Cinnamic Esters; General Procedure: In a 25-mL flask were added Na<sub>2</sub>SSO<sub>3</sub>·5H<sub>2</sub>O (0.25 g, 1.0 mmol), Baylis-Hillman acetate 1 (1.0 mmol), and anhyd MeOH (15 mL). The mixture was stirred at r.t. for 4-8 h until the sodium (Z)-allyl thiosulfates were formed.<sup>7</sup> MeOH was removed and THF (20 mL) was added under an inert atmosphere. Then Sm (0.15 g, 1 mmol) and a trace amount of I<sub>2</sub> were added to the resulting mixture followed by the addition of a sat. aq solution of  $NH_4Cl$  (4 mL) dropwise. The mixture was stirred at r.t. for the time given in Table 1. Upon completion, the reaction mixture was quenched with dil. HCl (5%, 15 mL), extracted with  $Et_2O$  (2 × 30 mL), washed with brine (15 mL), and dried over MgSO<sub>4</sub>. After evaporation of the solvent, the residue was purified by chromatography [cyclohexane–EtOAc (9:1) (R = alkyl groups) or cyclohexane–EtOAc (6:1) (R = aryl groups)].
- (9) (a) Karchner, J. H. *The Analytical Chemistry of Sulfur and its Compounds*; Wiley: New York, **1972**. (b) Ogawa, A. *Tetrahedron Lett.* **1987**, 28, 3271. (c) Antebi, S. *Tetrahedron Lett.* **1985**, 26, 2609.
- (10) (a) Parry, R. J. *Tetrahedron* 1983, *39*, 1215. (b) Arora, A.; Tripathi, C.; Shukla, Y. *Curr. Cancer Ther. Rev.* 2005, *1*, 199. (c) Arora, A.; Seth, K.; Shukla, Y. *Carcinogenesis* 2004, *25*, 941. (d) Thomas, R. D.; Green, M.; Wilson, C.; Sadrud-Din, S. *Carcinogenesis* 2004, *25*, 787. (e) Green, M.; Wilson, C.; Newell, O.; Sadrud-Din, S.; Thomas, R. *Food Chem. Toxicol.* 2005, *43*, 1323.

- (11) All Baylis–Hillman acetates were prepared according to the literature: (a) Hoffman, H. M. R.; Rabe, J. Angew. Chem., *Int. Ed. Engl.* **1983**, 22, 795. (b) David, H. O.; Kenneth, M. N. J. Org. Chem. **2003**, 68, 6427.
- (12) According to NOESY experiments, there is no NOE correlation between the signal of the internal olefin proton and the allylic methylene protons.
- (13) The trisubstituted cinnamic ester moiety manifests a significant role in several biologically active compounds, see: (a) Senokuchi, K.; Nakai, H.; Nakayama, Y.; Odagaki, Y.; Sakaki, K.; Kato, M.; Maruyama, T.; Miyazaki, T.; Ito, H.; Kamiyasu, K.; Kim, S.; Kawamura, M.; Hamanaka, N. J. Med. Chem. 1995, 38, 4508. (b) Senokuchi, K.; Nakai, H.; Nakayama, Y.; Odagaki, Y.; Sakaki, K.; Kato, M.; Maruyama, T.; Miyazaki, T.; Ito, H.; Kamiyasu, K.; Kim, S.; Kawamura, M.; Hamanaka, N. J. Med. Chem. 1995, 38, 2521. (c) Watanabe, T.; Hayashi, K.; Yoshimatsu, S.; Sakai, K.; Takeyama, S.; Takashima, K. J. Med. Chem. 1980, 23, 50.
- (14) (2E)-Methyl cinnamic eaters prepared from Baylis–Hillman adducts or derivatives by other approaches, see:
  (a) Shadakshari, U.; Nayak, S. K. *Tetrahedron* 2001, *57*, 4599. (b) Ravichandran, S. *Synth. Commun.* 2001, *31*, 2055. (c) Das, B.; Banerjee, J.; Majhi, A.; Mahender, G. *Tetrahedron Lett.* 2004, *45*, 9225. (d) Li, J.; Qian, W. X.; Zhang, Y. M. *Tetrahedron* 2004, *60*, 5793. (e) Li, J.; Xu, H.; Zhang, Y. M. *Tetrahedron Lett.* 2005, *46*, 1931. (f) Chandrasekhar, S.; Chandrashekar, G.; Vijeender, K.; Reddy, M. S. *Tetrahedron Lett.* 2006, *47*, 3475.
- (15) Compound **3a**: IR (film): 1719, 1642 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta = 1.10$  (t, 6 H, J = 7.2 Hz), 2.30–2.37 (m, 4 H), 3.69 (s, 4 H), 3.77 (s, 6 H), 6.93 (t, 2 H, J = 7.2 Hz). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta = 13.34$ , 22.47, 35.00, 51.85, 127.44, 147.90, 166.97. MS (70 eV): m/z (%) = 318 (M<sup>+</sup>). Anal. Calcd for C<sub>14</sub>H<sub>22</sub>O<sub>4</sub>S<sub>2</sub>: C, 52.80; H, 6.96. Found: C, 53.23; H, 6.90.

Compound **3b**: IR (film): 1721, 1642 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta = 0.88$  (t, 6 H, J = 7.2 Hz), 1.25–1.47 (m, 20 H), 2.32 (q, 4 H, J = 7.2 Hz), 3.70 (s, 4 H), 3.77 (s, 6 H), 6.95 (t, 2 H, J = 7.2 Hz). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta = 22.59$ , 28.84, 29.09, 29.19, 29.24, 29.32, 31.71, 35.29, 51.89, 127.92, 146.78, 166.99. MS (70 eV): m/z (%) = 458 (M<sup>+</sup>). Anal. Calcd for C<sub>24</sub>H<sub>42</sub>O<sub>4</sub>S<sub>2</sub>: C, 62.84; H, 9.23. Found: C, 62.51; H, 9.28. Compound **3c**: IR (film): 1716, 1643 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>,

Composind 3c. IR (IIII): 1716; 1043 CHI 1: 111(MR (CDC)<sub>3</sub>, 400 MHz):  $\delta = 2.62$  (q, 4 H, J = 8.0 Hz), 2.78 (t, 4 H, J = 8.0Hz), 3.62 (s, 4 H), 3.72 (s, 6 H), 6.98 (t, 2 H, J = 8.0 Hz), 7.19–7.32 (m, 10 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta = 31.32$ , 35.23, 35.38, 52.29, 126.49, 128.66, 128.77, 128.86, 141.01, 145.43, 167.13. MS (70 eV): m/z (%) = 470 (M<sup>+</sup>). Anal. Calcd for C<sub>26</sub>H<sub>30</sub>O<sub>4</sub>S<sub>2</sub>: C, 66.35; H, 6.42. Found: C, 66.72; H, 6.48.