

## A Novel Debromination of *vic*-Dibromides to Alkenes with InCl<sub>3</sub>(cat.)/Sm System in Aqueous Media

WANG, Min<sup>a</sup>(王敏)    WANG, Lei<sup>\*a,b</sup>(王磊)    LI, Pin-Hua<sup>a</sup>(李品华)  
YAN, Jin-Can<sup>a</sup>(晏金灿)

<sup>a</sup> Department of Chemistry, Huaibei Coal Teachers College, Huaibei, Anhui 235000, China

<sup>b</sup> State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

A novel debromination of *vic*-dibromides to alkenes with InCl<sub>3</sub>(cat.)/Sm system in aqueous media has been developed. The reaction gives the *E*-isomers with excellent yields.

**Keywords**    debromination, *vic*-dibromide, alkene, indium trichloride, samarium metal, aqueous media

### Introduction

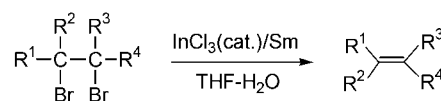
The debromination of *vic*-dibromides to alkenes is of some importance in organic synthesis. For example, bromination of alkenes is a standard method of protecting carbon-carbon double bond functional group, and bromination and debromination are widely used for the purification of steroids through their dibromides. Although bromination generally proceeds smoothly to give high yields of dibromide, debromination at a later procedure often proves more difficult in the synthesis.<sup>1</sup> However, a variety of debromination agents, such as sodium,<sup>2</sup> magnesium,<sup>3</sup> zinc,<sup>4</sup> sodium selenide,<sup>5</sup> lithium aluminum hydride,<sup>6</sup> sodium sulfide,<sup>7</sup> titanium(III),<sup>8</sup> cobalt(II),<sup>9</sup> copper(I),<sup>10</sup> chromium(II),<sup>11</sup> and tributyltin hydride<sup>12</sup> have been devised to accomplish this transformation.

In the last decade, metal-mediated organic reactions in aqueous media have received considerable attention because of economical and environmental concerns.<sup>13</sup> Such aqueous reactions offer a number of advantages over traditional organometallic reactions in organic solvent. The practical convenience is that to handle flammable and anhydrous organic solvents is not necessary.

Indium has emerged as one of the metals of growing interest because of its great potential in organic synthesis.<sup>14</sup> Although indium metal has been used extensively to mediate Barbier-type, Reformatsky-type, Michael-addition, and cross-aldol reactions,<sup>15</sup> its use in the reduction has been also received much more attention in recent years.<sup>16</sup> In addition, indium metal promoted organic reactions are generally carried out in water or in aqueous media, providing an optimal "green chemistry"

reaction. Unfortunately, expensive price of indium metal is the disadvantage and in some cases of these metallic indium powder mediated reactions, the indium powder and organic substrate clumps, making the mixture difficult to stir.

The first ionization potential of metallic samarium is 5.63 eV, similar to that of metallic lithium (5.39 eV), and metallic samarium is stable in air and has stronger reducing power ( $\text{Sm}^{3+}/\text{Sm} = -2.41 \text{ V}$ ). This property prompted us to use it as reducing agent to reduce indium(III) to its low valent species to promote the reaction. Here, we wish to report a novel debromination of *vic*-dibromides to alkenes with zero valent indium generated *in situ* from the reaction of InCl<sub>3</sub> with Sm(0) in aqueous solution at room temperature. The method affords the corresponding alkenes in good to excellent yields.



### Results and discussion

The effect of amount of indium(III) chloride and samarium metal on the debromination of *vic*-dibromides to the alkenes in aqueous media was investigated. Styrene dibromide was chosen as model compound for this study. The results are summarized in Table 1.

From Table 1, it is evident that indium(III) chloride and samarium metal both are essential in the debromination of styrene dibromide. The reaction does not oc-

\* E-mail: leiwang@hbcnc.edu.cn

Received November 19, 2003; revised April 5, 2004; accepted April 12, 2004.

Project supported by the National Natural Science Foundation of China (Nos. 20372024 and 20172018), the Excellent Scientist Foundation of Anhui Province (No. 2001040), the Natural Science Foundation of the Education Department of Anhui Province (No. 2002kj254zd), the Scientific Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry (No. 2002247) and the Excellent Young Teachers Program of Ministry of Education (No. 2024), China.

cur in the absence of indium(III) chloride or samarium metal. The amount of indium(III) chloride and samarium metal used in the reaction has also been examined. The results show that only a catalytic amount of indium(III) chloride (5%—10% mol) is needed for the reaction in the presence of stoichiometric amount of samarium metal. In the presence of  $\text{InCl}_3$  (5%—10% mol), less than the stoichiometric amount of samarium metal does not afford a high yield of styrene because of insufficient zero valent indium species generated *in situ* from the reaction of metallic samarium with indium(III) chloride.

**Table 1** Effect of amount of indium(III) chloride and samarium metal on the debromination of styrene dibromide to styrene<sup>a</sup>

Entry	Amount of $\text{InCl}_3$	Amount of samarium metal	Yield <sup>b</sup> /%
1	0 equiv.	1.00 equiv.	0
2	0.50 equiv.	0 equiv.	0
3	0.50 equiv.	1.00 equiv.	94
4	0.25 equiv.	1.00 equiv.	96
5	0.10 equiv.	1.00 equiv.	95
6	0.05 equiv.	1.00 equiv.	94
7	0.10 equiv.	2.00 equiv.	96
8	0.10 equiv.	0.50 equiv.	78
9	0.10 equiv.	0.25 equiv.	42
10	0.10 equiv.	0.10 equiv.	16



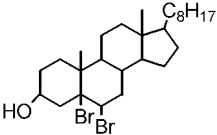
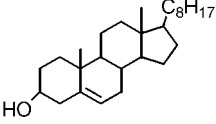
<sup>a</sup> Reaction condition: styrene dibromide (1 mmol), THF-H<sub>2</sub>O (V/V, 4/1, 5 mL), 45 °C, 3 h. <sup>b</sup> Isolated yields.

A variety of *vic*-dibromides were successfully reduced to alkenes with good to excellent yields in elimination of bromine manner by  $\text{InCl}_3$  (5%—10% mol) and Sm metal reductive system under reaction conditions.

Table 2 summarized the results concerning the debromination of *vic*-dibromide. *trans*-Stilbene was produced from *meso*-1,2-dibromo-1,2-diphenylethane in an excellent yield (Entry 1, Table 2), as well as from *dl*-1,2-dibromo-1,2-diphenylethane (Entry 2, Table 2) within 3 h at 45 °C. In the series of vicinal  $\alpha,\beta$ -dibromo cinnamic acid and its derivatives, such as 2,3-dibromo-3-phenylpropionic acid, ethyl 2,3-dibromo-3-phenylpropionate, methyl 2,3-dibromo-3-(4-chlorophenyl)propionate, and methyl 2,3-dibromo-3-(4-methoxyphenyl)propionate, they were debrominated smoothly to afford the corresponding cinnamic acid and its derivatives in excellent yields, and (*E*)-isomer products are in majority (Entries 5, 6, 7 and 8, Table 2). The other benzylic *vic*-dibromides, such as styrene dibromide, similarly gave the corresponding (*E*)-alkenes in a high yield (Entry 3, Table 2). In the case of aliphatic *vic*-dibromide, *trans*-1,2-dibromocyclohexane, 2,3-dibromopropyl benzoate, cholesterol dibromide, longer reaction time was needed to obtain high yields of the corresponding alkenes (Entries 4, 10 and 11, Table 2).

The reactivity of *vic*-dibromides decreases in the order: 1,2-dibromo-1,2-diphenylethane > 1,2-dibromo-1-phenylethane > 1,2-dibromo-1,2-dialkylethane, due to the radical or anion intermediate of aliphatic *vic*-dibromide being less stable than that of the aromatic analogues.

**Table 2** Debromination of *vic*-dibromides to alkenes with  $\text{InCl}_3$  (10% mol) and Sm<sup>a</sup>

Entry	<i>vic</i> -Dibromides	Alkenes	Yield <sup>b</sup> /%
1	$\text{C}_6\text{H}_5\text{CH}(\text{Br})\text{CH}(\text{Br})\text{C}_6\text{H}_5$ ( <i>meso</i> )	( <i>E</i> )- $\text{C}_6\text{H}_5\text{CH}=\text{CHC}_6\text{H}_5$	98
2	$\text{C}_6\text{H}_5\text{CH}(\text{Br})\text{CH}(\text{Br})\text{C}_6\text{H}_5$ ( <i>dl</i> )	( <i>E</i> )- $\text{C}_6\text{H}_5\text{CH}=\text{CHC}_6\text{H}_5$	94
3	$\text{C}_6\text{H}_5\text{CH}(\text{Br})\text{CH}_2\text{Br}$	$\text{C}_6\text{H}_5\text{CH}=\text{CH}_2$	95
4	$\text{C}_6\text{H}_5\text{CO}_2\text{CH}_2\text{CH}(\text{Br})\text{CH}_2\text{Br}$	$\text{C}_6\text{H}_5\text{CO}_2\text{CH}_2\text{CH}=\text{CH}_2$	91 <sup>c</sup>
5	$\text{C}_6\text{H}_5\text{CH}(\text{Br})\text{CH}(\text{Br})\text{CO}_2\text{C}_2\text{H}_5$	( <i>E</i> )- $\text{C}_6\text{H}_5\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$	95
6	$\text{C}_6\text{H}_5\text{CH}(\text{Br})\text{CH}(\text{Br})\text{CO}_2\text{H}$	( <i>E</i> )- $\text{C}_6\text{H}_5\text{CH}=\text{CHCO}_2\text{H}$	95
7	<i>p</i> - $\text{ClC}_6\text{H}_4\text{CH}(\text{Br})\text{CH}(\text{Br})\text{CO}_2\text{CH}_3$	( <i>E</i> )- <i>p</i> - $\text{ClC}_6\text{H}_4\text{CH}=\text{CHCO}_2\text{CH}_3$	98
8	<i>p</i> - $\text{CH}_3\text{OC}_6\text{H}_4\text{CH}(\text{Br})\text{CH}(\text{Br})\text{CO}_2\text{CH}_3$	( <i>E</i> )- <i>p</i> - $\text{CH}_3\text{OC}_6\text{H}_4\text{CH}=\text{CHCO}_2\text{CH}_3$	96
9	$\text{C}_2\text{H}_5\text{O}_2\text{CCH}(\text{Br})\text{CH}(\text{Br})\text{CO}_2\text{C}_2\text{H}_5$ ( <i>meso</i> )	( <i>E</i> )- $\text{C}_2\text{H}_5\text{O}_2\text{CCH}=\text{CHCO}_2\text{C}_2\text{H}_5$	90
10			84 (90) <sup>d</sup>
11			92 <sup>c</sup>

<sup>a</sup> Reaction conditions: *vic*-dibromide (1 mmol),  $\text{InCl}_3$  (0.1 mmol), Sm powder (1 mmol), THF-H<sub>2</sub>O (V/V, 4/1, 5 mL), 45 °C, 3 h. <sup>b</sup> Isolated yields. <sup>c</sup> Reaction time 5 h. <sup>d</sup> Yield given in parenthesis was determined by GC.

The possible mechanism for the formation of alkenes from the reductive elimination of *vic*-dibromide with indium(III) chloride (cat.) and metallic samarium system is probably similar to that proposed by Kornblum<sup>17</sup> for the reductive elimination of *vic*-dinitro compounds [single-electron-transfer (SET) mechanism]. It is well known that one-electron reductants, such as Cu(I), Ti(III), Cr(II), Sn(II), convert the *dl*-1,2-dibromo-1,2-diphenylethane mainly into *trans*-stilbene.<sup>18</sup> In addition, metallic indium promoted organic reaction is also through SET mechanism.<sup>14,15</sup> The possible mechanism for the formation of alkenes from the corresponding *vic*-dibromides by indium(III) chloride (cat.) and metallic samarium system involves a common, relatively stable radical intermediate, which directly collapses to the (*E*)-alkene. Zero valent indium is generated *in situ* through the reaction of metallic samarium with indium(III) chloride in aqueous media in the first step, and then *vic*-dibromide forms a free radical with zero valent indium under the reaction conditions, along with the cleavage of carbon-bromine bond in substrate. The generated radical occurs an elimination process to afford alkene, making *trans*-alkene as major product. The study on more detailed reaction mechanism is in progress in our laboratory.

## Conclusion

In summary, we have found that InCl<sub>3</sub>(cat.)/Sm system is a useful reductive agent for the debromination of *vic*-dibromides to the corresponding alkenes in aqueous media. The remarkable advantages of this reaction are mild, neutral and environmentally friendly reaction condition, simple operation, and good to excellent yields.

## Experimental

Melting points were recorded on a WRS-1B melting point apparatus and are uncorrected. All <sup>1</sup>H NMR spectra were recorded on a 60 MHz JEOL MY 60 FT-NMR or a 300 MHz Bruker AZ 300 spectrometer. Chemical shifts are given as  $\delta$  value with reference to tetramethylsilane (TMS) as internal standard. IR spectra were obtained by using a Nicolet NEXUS 470 spectrophotometer. The reagents were received from commercial supply without purification prior to use. Products were purified by flash column chromatography.

### General procedure for the preparation of alkenes via the debromination of *vic*-dibromides

The synthesis of styrene is representative. Under an inert atmosphere of nitrogen, indium(III) chloride (0.1 mmol), metallic samarium powder (1 mmol) and styrene dibromide (1 mmol) were placed in a round-bottomed flask, and THF-H<sub>2</sub>O (V/V, 4/1, 5 mL) was added in one portion. The mixture was stirred at room temperature for 3 h. After having quenched with dilute hydrochloric acid (0.2 mol/L, 3 mL), the product was extracted with

ether (2×20 mL). After the organic layer was dried over anhydrous sodium sulfate, the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel using hexane-ethyl acetate as the eluant to give styrene (100 mg, 96% yield).

***trans*-Stilbene** White solid, m.p. 123—124 °C (lit.<sup>19</sup> 123—124 °C); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 7.10 (s, 2H), 7.15—7.60 (m, 10H); IR (KBr)  $\nu$ : 3080, 3060, 3040, 1610, 1500, 1460 cm<sup>-1</sup>.

**Cyclohexene** Oil, b.p. 81—83 °C (lit.<sup>20</sup> 81—83 °C); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 1.47—2.48 (m, 8H), 5.30—5.52 (m, 2H); IR (film)  $\nu$ : 3030, 2980, 2840, 1650, 1440, 720 cm<sup>-1</sup>.

**(*E*)-Ethyl cinnamate** Oil, b.p. 130—132 °C (lit.<sup>21</sup> 128—130 °C); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 1.30 (t, *J*=7.3 Hz, 3H), 4.18 (q, *J*=6.8 Hz, 2H), 6.33 (d, *J*=15.8 Hz, 1H), 7.20—7.33 (m, 6H); IR (film)  $\nu$ : 3040, 2980, 1710, 1640, 1580, 1500, 1460 cm<sup>-1</sup>.

**Styrene** Oil, b.p. 145—146 °C/1.01×10<sup>5</sup> Pa (lit.<sup>7</sup> 47—48 °C/2.67×10<sup>3</sup> Pa); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 5.10 (d, *J*=10.4 Hz, 1H), 5.75 (d, *J*=17.5 Hz, 1H), 6.43—6.76 (m, 1H), 7.20—7.58 (m, 5H); IR (film)  $\nu$ : 3035, 2985, 1590, 1450 cm<sup>-1</sup>.

**(*E*)-Cinnamic acid** White solid, m.p. 133—134 °C (lit.<sup>22</sup> 133—134 °C); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 6.42 (d, *J*=15.4 Hz, 1H), 7.38—7.52 (m, 5H), 7.78 (d, *J*=15.8 Hz, 1H), 12.7 (s, br, 1H); IR (KBr)  $\nu$ : 3200, 3060, 1685, 1586, 1400 cm<sup>-1</sup>.

**Diethyl fumarate** Oil, b.p. 103—104 °C/1.20×10<sup>3</sup> Pa (lit.<sup>7</sup> 100—102 °C/1.33×10<sup>3</sup> Pa); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 1.28 (t, *J*=7.1 Hz, 6H), 4.25 (q, *J*=6.5 Hz, 4H), 6.84 (s, 2H); IR (film)  $\nu$ : 3028, 2985, 1725, 1650, 1470, 1382, 1300 cm<sup>-1</sup>.

**Cholesterol** White solid, m.p. 148—150 °C (lit.<sup>7</sup> 148—149 °C); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 0.98—2.24 (m, 44H), 3.46 (m, 1H), 5.26 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$ : 11.81(2C), 18.67, 19.36, 21.02, 22.53, 22.80, 23.77, 24.24, 27.97, 28.20, 31.51, 31.82, 35.74, 36.13, 36.42, 37.19, 39.46, 39.70, 42.15, 42.25, 50.03, 56.06, 56.70, 71.73, 121.68, 140.67; IR (KBr)  $\nu$ : 3612, 3018, 1636, 1500, 1460, 1380, 725 cm<sup>-1</sup>.

**Allyl benzoate** Oil, b.p. 122—123 °C/1.33×10<sup>3</sup> Pa (lit.<sup>23</sup> 128—129 °C/1.47×10<sup>3</sup> Pa); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 4.82 (d, *J*=6.5 Hz, 2H), 5.25—5.84 (m, 3H), 7.25—8.03 (m, 5H); IR (film)  $\nu$ : 3038, 2983, 1720, 1600, 1470, 1300 cm<sup>-1</sup>.

**(*E*)-Methyl 3-(4-chlorophenyl)acrylate** White solid, m.p. 75—76 °C (lit.<sup>24</sup> 74—75 °C); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 3.68 (s, 3H), 6.38 (d, *J*=16.2 Hz, 1H), 7.32—7.56 (m, 5H); IR (KBr)  $\nu$ : 3030, 2975, 1700, 1650, 1600, 1500, 1460 cm<sup>-1</sup>.

**(*E*)-Methyl 3-(4-methoxyphenyl)acrylate** White solid, m.p. 86—88 °C (lit.<sup>25</sup> 88—89 °C); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 3.68 (s, 3H), 3.72(s, 3H), 6.35 (d, *J*=16.0 Hz, 1H), 6.75 (d, *J*=7.2 Hz, 2H), 7.20 (d, *J*=7.0 Hz, 2H), 7.65 (d, *J*=16.4 Hz, 1H); IR (KBr)  $\nu$ : 3028, 2970, 1705, 1640, 1610, 1490, 1450 cm<sup>-1</sup>.

## References

- Schlosser, M. *Methoden der Organischen Chemie*, 4th ed., Ed.: Muller, E., Vol. V/1b, Georg Thieme Verlag, Stuttgart, **1972**, p. 202.
- Adam, W.; Arce, J. *J. Org. Chem.* **1972**, 37, 507.
- Schubert, W. M.; Rabinovitch, B. S.; Larson, N. R.; Sims, V. A. *J. Am. Chem. Soc.* **1952**, 74, 4590.
- Buckles, R. E.; Bader, J. M.; Thurmaier, R. J. *J. Org. Chem.* **1962**, 27, 4532.
- Prince, M.; Bremer, B. W.; Brenner, W. *J. Org. Chem.* **1966**, 31, 4292.
- King, J. F.; Pews, R. C. *Can. J. Chem.* **1964**, 42, 1294.
- Fukunaga, K.; Yamaguchi, H. *Synthesis* **1981**, 879.
- Olah, G. A.; Prakash, G. K. S. *Synthesis* **1976**, 607.
- Halpern, J.; Maher, J. P. *J. Am. Chem. Soc.* **1965**, 87, 5361.
- Nozaki, H.; Shirafuji, T.; Yamamoto, Y. *Tetrahedron* **1969**, 25, 3461.
- Kray, W. C.; Castro, C. E. *J. Am. Chem. Soc.* **1964**, 86, 4603.
- Strunk, R. J.; DiGiacomo, P. M.; Aso, K.; Kuivila, H. G. *J. Am. Chem. Soc.* **1970**, 92, 2849.
- (a) Lubineau, A.; Auge, J.; Queneau, Y. *Synthesis* **1994**, 741.  
(b) Li, C. J.; Chan, T. H. *Organic Reactions in Aqueous Media*, Wiley, New York, **1997**.  
(c) Lindstrom, U. M. *Chem. Rev.* **2002**, 102, 2751.
- (a) Li, C. J. *Chem. Rev.* **1993**, 93, 2023.  
(b) Li, C. J. *Tetrahedron* **1996**, 52, 5643.  
(c) Li, C. J.; Chan, T. H. *Tetrahedron* **1999**, 55, 11149.  
(d) Chauhan, K. K.; Frost, C. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3015.  
(e) Cintas, P. *Synlett* **1995**, 1087.
- (a) Li, C. J.; Chan, T. H. *Tetrahedron Lett.* **1991**, 32, 7017.  
(b) Chan, T. H.; Li, C. J. *J. Chem. Soc., Chem. Commun.* **1992**, 747.  
(c) Chan, T. H.; Li, C. J.; Lee, M. C.; Wei, Z. Y. *Can. J. Chem.* **1994**, 72, 1181.  
(d) Wang, L.; Sun, X.; Zhang, Y. *Synth. Commun.* **1998**, 32, 3263.
- (a) Ranu, B. C.; Guchhait, S. K.; Sarkar, A. *J. Chem. Soc., Chem. Commun.* **1998**, 2113.  
(b) Moody, C. J.; Pitts, M. R. *Synlett* **1998**, 1028.  
(c) Moody, C. J.; Pitts, M. R. *Synlett* **1998**, 1029.  
(d) Ranu, B. C.; Dutta, P.; Sarkar, A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1139.  
(e) Reddy, G. V.; Rao, G. V.; Iyenger, D. S. *Tetrahedron Lett.* **1999**, 40, 3937.  
(f) Chae, H.; Cho, S.; Keum, G.; Kang, S. B.; Pae, A. N.; Kim, Y. *Tetrahedron Lett.* **2000**, 41, 3899.  
(g) Ranu, B. C.; Samanta, S.; Guchhait, S. K. *J. Org. Chem.* **2001**, 66, 4102.
- Kornblum, N.; Boyd, S. D.; Pinnick, H. W.; Smith, R. G. *J. Am. Chem. Soc.* **1971**, 93, 4316.
- Mathai, I. M.; Schung, K.; Miller, S. I. *J. Org. Chem.* **1970**, 35, 1733.
- Kray, W. C.; Castro, C. E. *J. Am. Chem. Soc.* **1964**, 86, 4603.
- Corson, B. B.; Ipatieff, V. N. *Org. Synth. Collect. Vol. II* **1950**, 152.
- Marvel, C. S.; King, W. B. *Org. Synth. Collect. Vol. I* **1956**, 252.
- Buckingham, J. *Dictionary of Organic Compounds*, Chapman and Hall, New York, 5th ed., **1982**.
- Effenberger, F.; Bessey, E. *Chem. Ber.* **1980**, 113, 2100.
- Chenevert, R.; Desjardins, M. *Can. J. Chem.* **1994**, 72, 2312.
- Arvidsson, L. E.; Johansson, A. M.; Hacksell, U.; Nilsson, J. L.; Svensson, K.; Hjorth, S.; Magnusson, T.; Carlsson, A.; Lindberg, P.; Andersson, B. *J. Med. Chem.* **1988**, 31, 92.

(E0311191 CHENG, B.)