



## Iodine–alumina as an efficient and useful catalyst for the regeneration of carbonyl functionality from the corresponding 1,3-oxathiolanes and 1,3-dithiolanes in aqueous system

Md. Rumum Rohman, Mantu Rajbangshi, Badaker M. Laloo, Priti R. Sahu, Bekington Myrboh\*

Department of Chemistry, North-Eastern Hill University, Mawlai-Mawkynroh, Shillong 793022, India

### ARTICLE INFO

#### Article history:

Received 15 February 2010

Revised 17 March 2010

Accepted 19 March 2010

Available online 25 March 2010

#### Keywords:

Cleavage

1,3-Oxathiolanes

1,3-Dithiolanes

Iodine–alumina

Hydrolysis

### ABSTRACT

A simple and useful method has been demonstrated for the deprotection of 1,3-oxathiolanes and 1,3-dithiolanes to the corresponding carbonyl compounds in excellent yield by employing catalytic amount (30 mol %) of iodine supported on neutral alumina in ethanol–water or water. The major advantages of this protocol are mild reaction conditions, less reaction time, easy to handle, high yields, inexpensive reagent and environmentally benign.

© 2010 Elsevier Ltd. All rights reserved.

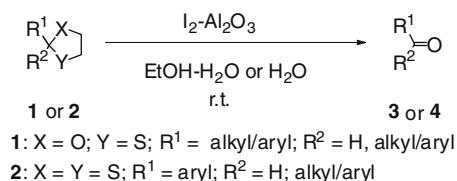
The protection and deprotection of various functional groups is a common practice in multistep organic synthesis. Among various protecting groups, thioacetals and thioketals play a vital role in the synthesis of natural products<sup>1,2</sup> and their deprotection to carbonyl groups, especially under mild reaction conditions has been the subject of interest in organic synthesis.

Though several methods have been employed for the regeneration of the carbonyl functionality, there is scope for the development of newer and simpler methodology. The common deprotection protocols involve the use of hazardous heavy metal salt, for example, mercury(II) chloride,<sup>3</sup> and toxic reagent such as  $\text{SeO}_2$ ,<sup>4a</sup>  $(\text{PhSeO})_2\text{O}$ ,<sup>4b</sup> which besides being costly reagents also adds to waste disposal problem. Similarly, a few methods are also reported in the literature for the cleavage of oxathioacetals using (i) isoamyl nitrate<sup>5a</sup> and chloroamine T,<sup>5b</sup> (ii) TMSOTf alone,<sup>5c</sup> or TMSOTf in the presence of *p*-nitro benzaldehyde,<sup>5d,e</sup> (iii) halonium ion sources in presence of silver salts,<sup>5f</sup> and (iv) reaction with NBS in acetone.<sup>5g</sup> However, these methods suffer from certain disadvantages such as removal of by-products, longer reaction times and use of expensive reagents.<sup>5d–f</sup>

In general, the deprotection of dithioacetals and oxothioacetals to the parent carbonyl compounds involves a suitable electrophile, which is captured by the soft nucleophilic sulfur atom followed by hydrolysis with water. Literature survey reveals that in situ gener-

ated iodonium ion from  $\text{HIO}_4$ -alumina have been used for the iodination of activated aromatic as well as 1,3-dicarbonyl compounds.<sup>6a</sup> Pagni et al. have also showed the iodination of unsaturated compounds using iodine absorbed on alumina ( $\text{I}_2\text{-Al}_2\text{O}_3$ ) as a iodinating reagent.<sup>6b</sup> Recently, the use of molecular iodine as catalyst in aqueous micellar system and aqueous  $\text{H}_2\text{O}_2$  for the deprotection of 1,3-dithiane has been reported.<sup>6c</sup> However, iodine supported on neutral alumina has not been studied for the catalytic deprotection of 1,3-oxathiolane and 1,3-dithiolane. Therefore, we decided to use activated iodonium ion produced from iodine absorbed on neutral alumina as an electrophilic species for the regeneration of carbonyl functionality and report herein an alternative protocol for the cleavage of 1,3-oxathiolanes and 1,3-dithiolanes using catalytic  $\text{I}_2\text{-Al}_2\text{O}_3$  as a source of electrophilic iodine in ethanol–water as well as in water (Scheme 1).

A wide variety of structurally different 1,3-oxathiolanes (entry **1a–o**) were synthesized by following the reported procedure.<sup>7a</sup> To optimize the reaction conditions, we studied the conversion of



Scheme 1.

\* Corresponding author. Tel.: +91 364 2722612; fax: +91 364 2228213.  
E-mail address: [bmyrboh@nehu.ac.in](mailto:bmyrboh@nehu.ac.in) (B. Myrboh).

2-(*p*-hydroxyphenyl)-1,3-oxathiolane (**1a**) to *p*-hydroxybenzaldehyde (**3a**) in the presence of  $I_2$ - $Al_2O_3$  (30 mol %) in ethanol and water in the ratio 9:1. The substrate 2-(*p*-hydroxyphenyl)-1,3-oxathiolane (**1a**) was cleanly converted to *p*-hydroxybenzaldehyde (**3a**) within 12 min in 96% yield. It was observed that, when the amount of  $I_2$ - $Al_2O_3$  was increased from 20 to 30 mol % there is a decrease in the reaction time. The compound **3a** was characterized by comparison of its IR and  $^1H$  NMR spectra with the authentic sample. Similarly, substrates (**1c–o**) were smoothly converted to the corresponding carbonyl compounds (**3c–o**) without any difficulty under identical reaction conditions in good to excellent yields. The control experiments revealed that the deprotection for **1a** and **1b** prolonged to 4 and 5.5 h, respectively, when  $I_2$ - $Al_2O_3$  was replaced with molecular iodine (30 mol %). The substrate 2-(*p*-nitrophenyl)-1,3-oxathiolane (**1b**) was easily converted to *p*-nitrobenzaldehyde (**3b**) by adding  $I_2$ - $Al_2O_3$  (30 mol %) to a stirring mixture of **1b** in ethanol for 10 min followed by addition of water. The reaction was completed after an additional 20 min of stirring giving **3b** in 98% yield. It is important to highlight that,

the same compound (**3b**) was obtained from (**1b**) on treatment with NBS,<sup>5g</sup> and  $V_2O_5$ - $H_2O_2$ - $NH_4Br$ ,<sup>5d</sup> after 6 and 2.5 h, respectively, which indicates that our protocol is much more effective in comparison to the earlier reported methods.

In another attempt, to establish the deprotection protocol in water, we have thoroughly mixed 2-(*p*-hydroxyphenyl)-1,3-oxathiolane (**1a**) and  $I_2$ - $Al_2O_3$  (40 mol %) for 20 min and water (1 mL) was added dropwise at room temperature. The reaction mixture was stirred at the same temperature for an extra 15 min. Interestingly, the reaction led to deprotected carbonyl compound **3a**. Though, the reaction in water needed slightly longer time and requires 40 mol % of the catalyst, we have extended our study and compared the results for the cleavage of the substrates (**1b–o**) to obtain their corresponding carbonyl compounds in water. The comparative results for the deprotection of 1,3-oxathiolanes in ethanol–water as well as in water in the presence of  $I_2$ - $Al_2O_3$  are summarised in Table 1.

Next, we turned our attention to the cleavage of various 1,3-dithiolanes, which were prepared by the known literature procedure.<sup>7a</sup> It was observed that compound **2a**, when treated with  $I_2$ - $Al_2O_3$  (30 mol %) in ethanol/water (9:1), converted efficiently to the parent carbonyl compound (**3a**) with satisfactory yield. Likewise, various aliphatic and aromatic 1,3-dithiolanes (**2b–m**) were cleaved to their corresponding aldehydes and ketones. The deprotection of the 1,3-dithiolanes (**2b–m**) were also car-

**Table 1**  
Cleavage of various 1,3-oxathiolanes using catalytic  $I_2$ - $Al_2O_3$

Entry	Substrate <b>1</b>	Product <b>3</b> <sup>a</sup>	Method <sup>c</sup>	Time (min)	Yield <sup>b</sup> (%)
<b>a</b>			A	12	96
			B	35	93
<b>b</b>			A	30	98
			B	43	90
<b>c</b>			A	10	97
			B	25	89
<b>d</b>			A	12	92
			B	23	86
<b>e</b>			A	25	94
			B	40	89
<b>f</b>			A	10	86
			B	32	89
<b>g</b>			A	15	97
			B	36	86
<b>h</b>			A	20	94
			B	38	87
<b>i</b>			A	25	86
			B	60	79
<b>j</b>			A	25	92
			B	38	89
<b>k</b>			A	15	93
			B	28	86
<b>l</b>			A	20	94
			B	50	87
<b>m</b>			A	10	98
			B	39	98
<b>n</b>			A	10	96
			B	15	81
<b>o</b>			A	22	93
			B	50	90

<sup>a</sup> Products have been characterized by comparison of IR with the authentic compounds,  $^1H$  NMR and elemental analysis.

<sup>b</sup> Isolated yields.

<sup>c</sup> Method A and B are described in Ref. 8.

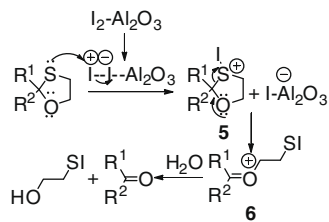
**Table 2**  
Cleavage of various 1,3-dithiolanes using catalytic  $I_2$ - $Al_2O_3$

Entry	Substrate <b>2</b>	Product <b>4</b> <sup>a</sup>	Method <sup>c</sup>	Time (min)	Yield <sup>b</sup> (%)
<b>a</b>		<b>3a</b>	A	20	95
			B	58	96
<b>b</b>		<b>3b</b>	A	35	96
			B	56	89
<b>c</b>		<b>3f</b>	A	20	84
			B	45	87
<b>d</b>		<b>3g</b>	A	22	93
			B	45	89
<b>e</b>		<b>3h</b>	A	30	92
			B	52	91
<b>f</b>		<b>3j</b>	A	36	89
			B	60	83
<b>g</b>			A	42	86
			B	70	79
<b>h</b>		<b>3k</b>	A	22	93
			B	36	91
<b>i</b>		<b>3l</b>	A	32	97
			B	60	94
<b>j</b>			A	25	91
			B	49	87
<b>k</b>			A	25	94
			B	41	79
<b>l</b>		<b>3m</b>	A	17	97
			B	45	91
<b>m</b>		<b>3n</b>	A	15	96
			B	20	95

<sup>a</sup> Products have been characterized by comparison of IR with the authentic compounds,  $^1H$  NMR and elemental analysis.

<sup>b</sup> Isolated yields.

<sup>c</sup> Method A and B are described in Ref. 8.



Scheme 2.

ried out in water using I<sub>2</sub>-Al<sub>2</sub>O<sub>3</sub> (30 mol %) as described for the deprotection of 1,3-oxathiolanes to their carbonyl functionalities with slight variation in time and yields (Table 2). In either case, it was noticed that the cleavage of 1,3-dithiolane to the parent carbonyl compounds require slightly longer reaction time as compared to the corresponding 1,3-oxathiolane derivatives. It is noteworthy to mention that no iodination (for entries 1h–j) takes place either at the double bond or allylic position. Significantly, the protecting groups such as benzyl and acetyl (entries 2c and 2d) remain unaffected under the experimental conditions. The work-up procedure includes the filtration of the reaction mixture through a Celite bed followed by extraction and evaporation under reduced pressure to obtain the corresponding carbonyl compounds in high yield. However, in some cases column purification was required to obtain the desired compound in pure form. All the deprotected carbonyl compounds were fully characterized by IR and <sup>1</sup>H NMR and by comparison with the spectra of the authentic samples.<sup>9</sup>

The deprotection of various 1,3-oxathiolanes and 1,3-dithiolanes into the corresponding carbonyl compounds can be explained as follows: alumina polarizes the iodine molecule and it acts as an activating agent to produce a strongly electrophilic I<sup>+</sup> species. The I<sup>+</sup> species react with the soft nucleophilic sulfur atom of the dithiolane as well as oxathiolane to form the corresponding iodosulfonium complex (5), which is finally hydrolyzed with water to give the corresponding carbonyl compounds, as depicted in Scheme 2.

In this study, we have devised a simple and environmentally benign protocol for the regeneration of the parent carbonyl compounds from their corresponding 1,3-oxathiolanes and 1,3-dithiolanes by using I<sub>2</sub>-Al<sub>2</sub>O<sub>3</sub>. In addition, these methodologies are compatible in the presence of other protecting groups such as acetyl, benzyl, allyl and also provide good yield for enolizable ketones. Due to its operational simplicity, this environment friendly procedure is expected to have wider applicability for conversion of various 1,3-oxathiolanes and 1,3-dithiolanes to the corresponding carbonyl functionalities.

## Acknowledgements

M.R.R. thanks the UGC for support under the Special Assistance Program and SAIF, NEHU for providing analytical supports.

## References and notes

- (a) Kocienski, P. J. *Protecting Groups*; Thieme: New York, 1994; (b) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley: New York, 1991; (c) Pearson, A. J.; Roush, W. J. In *Hand Book of Reagents for Organic Synthesis*, 1st ed.. In *Activating Agents and Protecting Groups*; John Wiley: New York, 1999.
- (a) Page, P. C. B.; van Niel, M. B.; Prodger, J. C. *Tetrahedron* **1989**, *45*, 7643; (b) Guanti, G.; Banfi, L.; Brusco, S.; Riva, R. *Tetrahedron Lett.* **1993**, *34*, 8549.
- (a) Corey, E. J.; Ericson, B. W. *J. Org. Chem.* **1971**, *36*, 3553; (b) Corey, E. J.; Bock, M. G. *Tetrahedron Lett.* **1975**, 2643.
- (a) Haroutounian, S. A. *Synthesis* **1995**, 39; (b) Barton, D. H.; Cussons, R. N. J.; Ley, S. V. *J. Chem. Soc., Chem. Commun.* **1977**, 751.
- (a) Fuji, K.; Ichikawa, K.; Fujita, E. *Tetrahedron Lett.* **1978**, 3561; (b) Emerson, D. W.; Wynberg, H. *Tetrahedron Lett.* **1971**, 3445; (c) Rabindranathan, T.; Chavan, S. P.; Dantale, S. W. *Tetrahedron Lett.* **1995**, *36*, 2285; (d) Rabindranathan, T.; Chavan, S. P.; Tejwani, R. B.; Vargese, J. P. *J. Chem. Soc., Chem. Commun.* **1991**, 1750; (e) Rabindranathan, T.; Chavan, S. P.; Tejwani, R. B.; Vargese, J. P. *J. Chem. Soc., Chem. Commun.* **1994**, 1937; (f) Nishide, K.; Yokata, K.; Nakamura, D.; Sumiya, T.; Node, M.; Ueda, M.; Fuji, K. *Tetrahedron Lett.* **1993**, *34*, 3425; (g) Karimi, B.; Seradj, H.; Tabaei, M. H. *Synlett* **2000**, 1798.
- (a) Khalizadeh, M. A.; Hosseini, A.; Shokrollahzadeh, M.; Halvagar, M. R.; Ahmadi, D.; Mohannazadeh, F.; Tajbkhsh, M. *Tetrahedron Lett.* **2006**, *47*, 3525; (b) Pagni, R. M.; Kabalka, G. W.; Boothe, R.; Gaetano, K.; Stewart, L. J.; Conaway, R.; Dial, C.; Gray, D.; Larson, S.; Luidhardt, T. *J. Org. Chem.* **1988**, *53*, 4477; (c) Ganguly, N. C.; Barik, S. K. *Synthesis* **2009**, 1393; (d) Mondal, E.; Sahu, P. R.; Bose, G.; Khan, A. T. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1026.
- (a) Firouzabadi, H.; Iranpoor, N.; Hazarkhani, H. *J. Org. Chem.* **2001**, *66*, 7527; (b) In *A Hand Book of Fine Chemicals and Laboratory Equipments*; 2000–2001; p. 917
- Typical deprotection protocol; Method A:** A mixture of freshly prepared catalyst [iodine (0.30 mmol) adsorbed on neutral alumina (750 mg)] and 2-(*p*-hydroxyphenyl)-1,3-oxathiolane (**1a**) (198.31 mg, 1.00 mmol) in ethanol (900 μL) was stirred for 10 min at room temperature. Then water (100 μL) was added and the reaction mixture was allowed to stir for additional 2 min. The completion of the reaction was monitored by TLC. The reaction mixture was filtered through a Celite bed and washed thoroughly with ethyl acetate (10 mL × 3). The organic layer was separated and washed with sodium bisulfite (5% aqueous solution), water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated in vacuo to obtain a crude solid mass, which was triturated with hexane to give the desired compound (**3a**) as a light yellow solid (117.23 mg, 96%) in pure form.  
**Method B:** A mixture of freshly prepared catalyst [iodine (0.40 mmol) adsorbed on neutral alumina (**1g**)] and 2-(*p*-hydroxyphenyl)-1,3-oxathiolane (**1a**) (198.31 mg, 1.00 mmol) was stirred for 20 min at room temperature. Then water (1 mL) was added and the reaction mixture was allowed to stir for additional 15 min. The completion of the reaction was monitored by TLC. The reaction mixture was diluted with ethyl acetate (10 mL) and filtered through a Celite bed. The organic layer was separated and washed with sodium bisulfite (5% aqueous solution), water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated in vacuo to obtain a crude solid mass, which was triturated with hexane to give the desired compound (**3a**) as a light yellow solid (113.57 mg, 93%) in pure form.  
**Compound (3a)** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 6.94 (d, 2H, *J* = 8.4 Hz, ArH), 7.77 (d, 2H, *J* = 8.8 Hz, ArH), 9.79 (s, 1H, CHO). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 116.02, 128.92, 132.61, 163.31, 191.71. IR (KBr): 2925, 2854, 1669, 1601, 1456, 1288, 1217, 1161, 834 cm<sup>-1</sup>. Light yellow solid. Mp 114–116 °C (lit. mp 117–119 °C).<sup>7b</sup>
- Spectroscopic data for compound (3h):** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 4.64 (d, 2H, *J* = 5.2 Hz, -OCH<sub>2</sub>-CH=CH<sub>2</sub>), 5.46–5.33 (m, 1H, -OCH<sub>2</sub>-CH=CH<sub>2</sub>), 6.11–6.01 (m, 1H, -OCH<sub>2</sub>-CH=CH<sub>2</sub>), 7.02 (d, 2H, *J* = 8.8 Hz, ArH), 7.84 (d, 2H, *J* = 8.7 Hz, ArH), 9.89 (s, 1H, CHO). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 69.00, 114.99, 118.39, 130.01, 131.98, 132.26, 163.59, 190.85. IR (Neat): 1695, 1603, 1506, 1265, 1168, 1004, 840 cm<sup>-1</sup>. Light yellow liquid.  
**Compound (3j)** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 2.02–1.99 (m, 3H, -CH=CH-CH<sub>3</sub>), 6.15–6.09 (m, 1H, -CH=CH-CH<sub>3</sub>), 6.89–6.80 (m, 1H, -CH=CH-CH<sub>3</sub>), 9.47 (d, 1H, *J* = 8 Hz, CHO). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 18.70, 134.59, 154.24, 194.13. IR (Neat): 2975, 2934, 1705, 1655, 1444, 1380, 1292, 1219, 1142, 1101, 969, 899 cm<sup>-1</sup>. Viscous liquid.