Highly Efficient Transthioacetalization of *O,O*-Acetals Catalyzed by Indium(III) Chloride

Brindaban C. Ranu,* Arijit Das, Sampak Samanta

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta – 700 032, India
Fax +91(33)4732805; E-mail: ocbcr@mahendra.iacs.res.in

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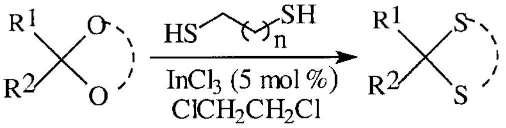
Abstract: A simple, efficient and general procedure has been developed for the transthioacetalization of *O,O*-acetals catalyzed by indium(III) chloride in 1,2-dichloroethane.

Key words: transthioacetalization, indium(III) chloride, *O,O*-acetals, *S,S*-thioacetals



Scheme

The protection and subsequent deprotection of a functional group is a usual practice in a multistep synthetic strategy and a switchover of one protective group to another is also often required as demanded by their stability under the reaction conditions in subsequent steps. Thus, a direct method for this transformation bypassing the intermediate step of going back to the parent functionality is becoming much more important in order to improve the overall synthetic efficiency.[1] *O,O*-Acetals and *S,S*-acetals are two useful protecting groups for carbonyl functionalities and are widely used in organic synthesis. However, *S,S*-acetals are quite stable toward a variety of reagents including acidic ones, while *O,O*-acetals are not suitable for being handled in acidic environment.[2] Moreover, *S,S*-acetals are used in organic synthesis as acyl carbanion equivalents[3] and intermediates for the conversion of carbonyl function to the parent hydrocarbons.[4] Thus, transthioacetalization of *O,O*-acetals to *S,S*-acetals is a synthetically useful transformation and is usually carried out under the catalysis of a variety of Lewis acids such as $MgBr_2$,[5a] $TeCl_4$,[5b] LPDE,[5c] WCl_6,[5d] $ZrCl_4$,[5e] $SiO_2/SOCl_2$,[5f] trichloroisocyanuric acid,[5g] and elements like I_2.[6] However, many of these reported methods require long reaction times, stoichiometric use of expensive and hazardous reagents and lack general applicability. Thus, an improved alternative procedure for this useful transformation is appreciated.

Recently, indium(III) chloride has emerged as a Lewis catalyst of high potential imparting remarkable regio- and chemoselectivity in various chemical transformations, as demonstrated by several groups[7] and us.[8] As a part of this continuing program we wish to disclose here an efficient transthioacetalization of *O,O*-acetals under catalysis of indium(III) chloride (Scheme).

In a typical general procedure, a solution of *O,O*-acetal (1 mmol) and thiol (1.2 mmol) in 1,2-dichloroethane (2 mL) was heated under reflux in presence of a catalytic amount (5 mol%) of indium(III) chloride for a certain period of time as required to complete the reaction (TLC). The reaction mixture was then quenched with an aqueous solution of NaOH (10%, 5 mL) and extracted with ether (3 × 10 mL). The ether extract was washed with brine, dried (Na_2SO_4) and evaporated to leave the crude product, which was reasonably pure (> 95% by ^{1}H NMR). However, further purification by column chromatography over silica gel provides analytically pure sample.

A wide range of structurally varied *O,O*-acetals derived from open-chain, cyclic, heterocyclic and aromatic aldehydes and ketones underwent clean transthioacetalizations with a variety of thiols and dithiols by this procedure to furnish the corresponding *S,S*-acetals in nearly quantitative yields. The results are presented in the Table. The present method is equally effective for the transformation of open-chain and cyclic acetals to the corresponding open-chain or cyclic dithioacetals depending on the use of thiol or dithiol. The presence of electron-donating and electron-withdrawing group on the aromatic ring of acetals (entries 5–11) does not make any difference in transthioacetalization. Acetals of conjugated carbonyl compounds (entries 15, 16, 20 and 21) are also converted to the corresponding thioacetals without any isomerization. A variety of functional groups such as NO_2, Cl, CO_2Et, OMe, O-allyl, OTBDMS, OTHP, methylenedioxy are found to be quite stable during the reaction. In general, the reactions are very fast and clean. A catalytic amount (5 mol%) of indium trichloride is sufficient to push the reaction efficiently.

In conclusion, the present indium(III) chloride catalyzed procedure provides a highly efficient methodology for the transthioacetalization of *O,O*-acetals. The significant advantages of this procedure are : (a) high yields (85–93%); (b) fast reaction (7–20 min); (c) general applicability to a varied acetals and thiols and (d) operational simplicity. Thus, it offers a better and more practical alternative to the existing methodologies.[5,6]

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Table Transthioacetalization of *O,O*-Acetals Catalyzed by $InCl_3$

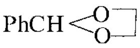
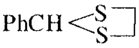
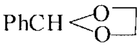
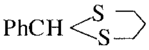
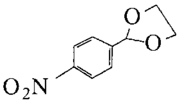
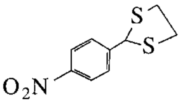
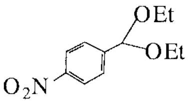
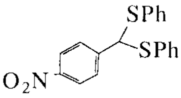
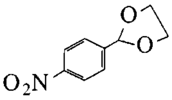
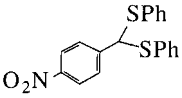
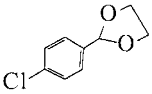
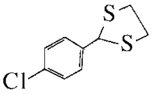
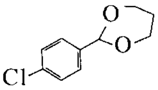
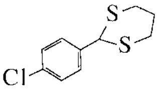
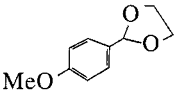
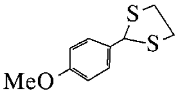
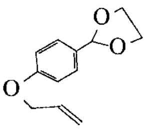
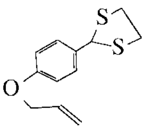
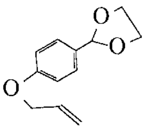
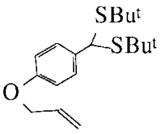
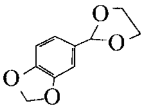
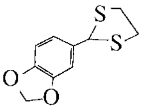
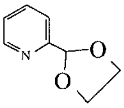
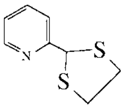
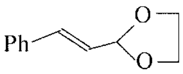
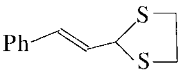
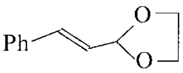
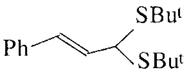
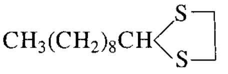
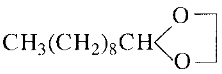
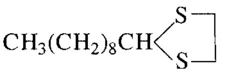
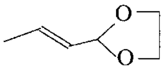
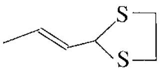
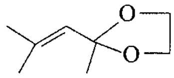
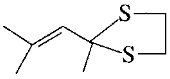
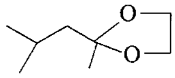
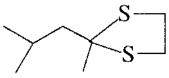
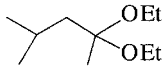
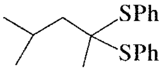
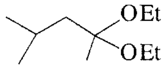
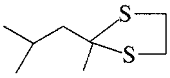
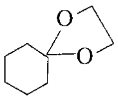
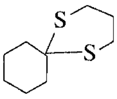
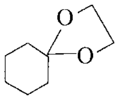
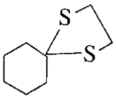
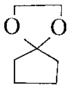
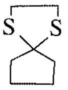
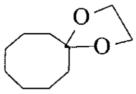
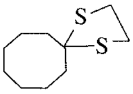
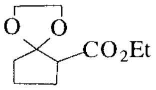
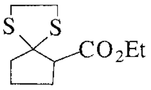
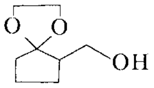
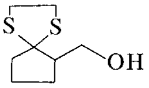
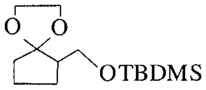
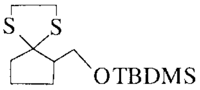
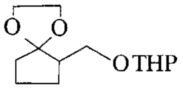
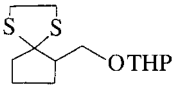
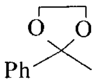
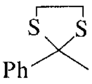
Entry	Acetal	Thiol	Time (min)	Product	Yield[a] (%)
1	$PhCH(OMe)_2$	EtSH	12	$PhCH(SEt)_2$	91
2	$PhCH(OEt)_2$	PhSH	8	$PhCH(SPh)_2$	92
3		$HS(CH_2)_2SH$	10		92
4		$HS(CH_2)_3H$	8		93
5		$HS(CH_2)_2SH$	7		92
6		PhSH	10		93
7		PhSH	12		90
8		$HS(CH_2)_2SH$	10		91
9		$HS(CH_2)_3H$	14		90
10		$HS(CH_2)_2SH$	12		92
11		$HS(CH_2)_2SH$	9		90
12		*t*-BuSH	12		91
13		$HS(CH_2)_2SH$	10		88
14		$HS(CH_2)_2SH$	20		85
15		$HS(CH_2)_2SH$	10		88
16		*t*-BuSH	12		85
17	$CH_3(CH_2)_8CH(OEt)_2$	*t*-BuSH	15	$CH_3(CH_2)_8CH(SBu^t)_2$	86
18	$CH_3(CH_2)_8CH(OEt)_2$	$HS(CH_2)_2SH$	13		85
19		$HS(CH_2)_2SH$	15		85

Table Transthioacetalization of *O*,*O*-Acetals Catalyzed by $InCl_3$ (continued)

Entry	Acetal	Thiol	Time (min)	Product	Yield[a] (%)
20		$HS(CH_2)_2SH$	15		85
21		$HS(CH_2)_2SH$	15		86
22		$HS(CH_2)_2SH$	18		86
23		PhSH	18		90
24		$HS(CH_2)_2SH$	15		85
25		$HS(CH_2)_3H$	15		90
26		$HS(CH_2)_2SH$	13		90
27		$HS(CH_2)SH$	12		89
28		$HS(CH_2)SH$	15		90
29		$HS(CH_2)SH$	20		86
30		$HS(CH_2)SH$	15		87
31		$HS(CH_2)SH$	18		85
32		$HS(CH_2)SH$	15		86
33		$HS(CH_2)SH$	10		90

[a] Yields refer to those of pure isolated products characterized by spectral data (^1H and ^{13}C NMR).

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References

(1) (a) Oriyama, T.; Oda, M.; Gono, J.; Koga, G. *Tetrahedron Lett.* **1994**, *35*, 2027. (b) Yang, G.; Ding, X.; Kong, F. *Tetrahedron Lett.* **1997**, *38*, 6725. (c) Oriyama, T.; Kimura, M.; Koga, G. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 885.
(d) Oriyama, T.; Yatabe, K.; Sugauttra, S.; Machiguchi, Y.; Koga, G. *Synlett* **1996**, 523. (e) Ranu, B. C.; Hajra, A. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2262.

(2) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, **1999**.

(3) (a) Corey, E. J.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1075. (b) Corey, E. J.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1077. (c) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 639. (d) Grobal, B. T.; Seebach, D. *Synthesis* **1977**, 357.

(4) Pettit, G. R.; Van Tamelen, E. E. *Org. React.* **1962**, *12*, 356.

(5) (a) Park, J. H.; Kim, S. *Chem. Lett.* **1989**, 629. (b) Tani, H.; Masumoto, K.; Inamasu, T. *Tetrahedron Lett.* **1991**, *32*, 2039. (c) Saraswathy, V. G.; Sankaraman, S. *J. Org. Chem.* **1994**, *59*, 4665. (d) Firouzabadi, H.; Iranpoor, N.; Karimi, B. *Synlett* **1998**, 739. (e) Firouzabadi, H.; Iranpoor, N.; Karimi, B. *Synlett* **1999**, 319. (f) Firouzabadi, H.; Iranpoor, N.; Karimi, B.; Hazarkhani, H. *Synlett* **2000**, 263. (g) Firouzabadi, H.; Iranpoor, N.; Hazarkhani, H. *Synlett* **2001**, 1641.

(6) Firouzabadi, H.; Iranpoor, N.; Hazarkhani, H. *J. Org. Chem.* **2001**, *66*, 7527.

(7) (a) Li, C.-J.; Chan, T.-H. *Tetrahedron* **1999**, *55*, 11149. (b) Chauhan, K. K.; Frost, C. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3015. (c) Ghosh, R. *Indian J. Chem. Sect. B* **2001**, *40B*, 550. (d) Yadav, J. S.; Abraham, S.; Reddy, B. V. S.; Sabitha, G. *Tetrahedron Lett.* **2001**, *42*, 8063. (e) Loh, T.-P.; Feng, L.-C.; Wei, L.-L. *Tetrahedron* **2001**, *57*, 4231. (f) Yang, X.-F.; Mague, J. T.; Li, C.-J. *J. Org. Chem.* **2001**, *66*, 739.

(8) (a) Ranu, B. C.; Jana, U. *J. Org. Chem.* **1998**, *63*, 8212. (b) Ranu, B. C.; Hajra, A.; Jana, U. *Org. Lett.* **1999**, *1*, 1141. (c) Ranu, B. C.; Hajra, A.; Jana, U. *Tetrahedron Lett.* **2000**, *41*, 531. (d) Ranu, B. C.; Hajra, A.; Jana, U. *J. Org. Chem.* **2000**, *65*, 6270.