Solvent Free Thioacetalization of Carbonyl Compounds Catalyzed by $Cu(OTf)_2$ -SiO₂

R. Vijaya Anand, P. Saravanan, and Vinod K. Singh*

Department of Chemistry, Indian Institute of Technology Kanpur-208016, India Fax +91 512590007; E-mail vinodks@iitk.ac.in Received 1 February 1999

Abstract: Aldehydes and ketones were thioacetalyzed using 1,2ethanedithiol in the presence of a catalytic amount of $Cu(OTf)_2$ -SiO₂ under solvent free conditions in excellent yields.

Key words: thioacetalization, $Cu(OTf)_2$ -SiO₂, aldehydes, and ketones

Thioacetalization of carbonyl compounds is an important transformation in organic synthesis. The reaction is usually catalyzed by Lewis acids.¹ Among many of the recently developed reagents, solid supported reagents are of the choice for this purpose due to easier handling, milder reaction conditions, and simpler work-up procedure. Recently, zirconium (IV) chloride^{2a} and tantalum chloride^{2b}



$$\underset{R_2}{\overset{R_1}{\rightarrowtail}} \circ + HSCH_2CH_2SH \xrightarrow{Cu(OTf)_2-SiO_2} \underset{R_2}{\overset{R_1}{\longrightarrow}} \overset{S}{\underset{R_2}{\overset{S}{\longrightarrow}}}$$

Entry	Substrates	Time Is	olated yield	Entry	Substrates	Time Is	solated yield
1. 丶	СНО	2 h	93 %	11.	Me	5 h	94 %
2.		1.5 h	92 %		HO HO	0 11	21.10
3.	СНО	1.5 h	91 %	12.		4 h	96 %
4.	OMe	1.5 h	98 %	13.		6 h	75 %
М 5.	еО СНО	1 h	89 %	14. C		24 h	93 %
6. Cl	СНО	30 min	98 %	15.	t-Bu	4 h	94 %
7.		30 min	93 %	16.	O Me	5 h	92 %
8. M	СНО	30 min	99 %	17. 18		15 h OOMe	90 % 82 %
9. Me	СНО	30 min	99 %	19.		но 1 h	54 % (mono)
10.	СНО	1.5 h	96 %	20.	PhCOPh	24 h	21 % (018) 98 %
10.	СНО	1.5 h	96 %	20. 21.	PhCOPh Camphor	24 h 60 h	21 % (bis) 98 % 91 %

Table: Cu(OTf)2-SiO2 catalyzed thioacetalization of Carbonyl Compounds^a

^aAll the reactions were done in solvent free condition at rt except entries 20 & 21 which were done in toluene at 80 $^{\circ}$ C.

It was observed that thioacetalization reaction proceeded without solvent in an efficient manner (Table). Aldehydes reacted faster than ketones as expected. Ketone group of a β-keto ester could also be thioacetalized in a clean manner. Some chemoselectivity (2.6 : 1) was also obtained with aldehyde vs ketone (entry 19). Although the reaction was very clean in most of the cases, hindered and unreactive ketones such as benzophenone and camphor did not react in the solvent free condition at rt. But, it could be affected by doing the reaction in toluene at 80 °C (entries 20 & 21). It was also observed that the thioacetalization reaction could also be catalyzed using CuCl₂-SiO₂ in a solvent free condition, but the reaction was slow and the yield was a bit inferior (for example, 4-*t*-butyl cyclohexanone: 10 h, 88% yield). The present methodology for solvent free thioacetalization of carbonyl compounds will find a lot of application in organic synthesis, and to the best of our knowledge, is unprecedented in the literature.⁴

General Procedure for Thioacetalization reactions: The catalyst was prepared by mixing $Cu(OTf)_2$ (2 mmol) with 20 g of activated silica gel (activated at 120 °C at 1 mm Hg for 6 h) and mechanically rotated for 12 h. The procedure for thioacetalization reaction was as follows: A mixture of a carbonyl compound (1 mmol), 1,2-ethanedithiol (2 - 5 mmol), and the above catalyst (500 mg, 0.05 mmol) was taken in a 5 mL R.B. flask. The flask was stoppered with a septum and tied with the rod of a Bü-chi rotary evaporator. It was rotated till the reaction was complete (Table). The whole mixture was loaded over a silica gel column (2 x 8 cm) and eluted with EtOAc in petroleum ether to obtain a pure thioacetal in an excellent yield (Table).⁵

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References and Notes

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