Highly Efficient Transdithioacetalization of Acetals Catalyzed by Silica Chloride

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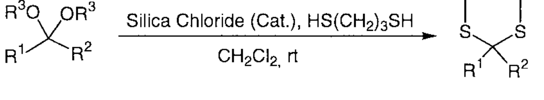
Abstract: A modified procedure for the preparation of a silica chloride with higher chloride capacity than that reported is described. Moreover, this silica chloride was found to be an effective catalyst for chemoselective and highly efficient transdithioacetalization of different classes of acetals.

Key words: silica chloride, thioacetals, protection, transdithioacetalization, acetals

Protection of carbonyl compounds as dithioacetals or acetals is an indispensable part of the synthesis of many polyfunctional molecules.[1] Moreover, dithioacetals often serve as precursors of acyl anion equivalent displaying a reactivity umpolung,[2] and masked methylene functions.[3] Several types of methods that are reported for the preparation of dithioacetals include the use of some silicon reagents,[1] protic acids,[1] Lewis acids,[1,4] solid inorganic acids and supported reagents.[5] Transdithioacetalization of acetals has been used as an alternative method for the preparation of dithioacetals.[6] Due to many useful properties of solid reagents such as ease of handling, low costs, and ease of work up of the reaction products, the use of heterogeneous reagents for functional group transformations is of value to synthetic organic chemists.[7] Nevertheless, a literature survey shows that less attention has been paid to the use of heterogeneous reagents in transdithioacetalization reactions. In this communication we first introduce a modified procedure for the preparation of a high surface and efficient silica chloride by refluxing silica gel (for plate chromatography) with thionyl chloride ($SOCl_2$) for 48 h.[8] In the subsequent studies we have found that this chloride can act as a highly efficient and reactive heterogeneous catalyst for transdithioacetalization of different types of acetals (Scheme1).



R^1, R^2 = aryl, alkyl, vinyl, or H

R^3 = Me, Et, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$

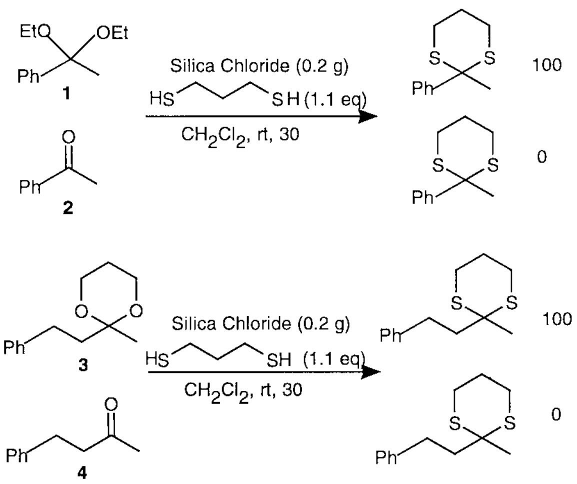
Silica Chloride = SiO_2 / $SOCl_2$

Scheme 1

The present method is applicable to both open-chain acetals (dimethyl and diethyl acetals) and cyclic acetals (1,3-dioxanes and 1,3-dioxolanes). As shown in the Table, open-chain acetals derived from aromatic and aliphatic carbonyl compounds on treatment with silica chloride (0.2g, 0.4 mmol) and thiols (2.2mmol) or dithiols (1.1mmol) were all cleanly and rapidly thioacetalized giving the corresponding *S*,*S*-acetal in good to excellent yields (Table, entries 1-6). Both 1,3-dioxanes and 1,3-dioxalanes on treatment with thiols and the silica chloride were also furnished the corresponding dithioacetals in good to excellent yields (Table, entries 7-13). By this method sterically hindered acetals such as 1,2-diphenyl-1,3-dioxalane were also successfully converted to 2,2-diphenyl-1,3-dithiane in excellent yield (Table, entry 13). Our studies show that this type of silica chloride is much more reactive[8] than that reported by Hojo et al[5g], in which a lesser number of silanol groups were replaced by chlorine.[9] We have used TMSCl as a catalyst for this purpose. Our observation was that when electron withdrawing groups are attached to the aromatic rings the rate of the reactions were much slower than that observed with the silica chloride. Another problem with using TMSCl is its low boiling point which puts some restriction on its use at high temperatures. Chemoselective catalytic activity of the catalyst is demonstrated by transthioacetalization of acetals in the presence of ketones. e.g. acetophenone diethylacetal (**1**) is preferentially protected in the presence of acetophenone (**2**) in a quantitative yield (Scheme 2). Similarly, 2-methyl-2-(2-phenylethyl)-1,3-dioxane (**3**) in the presence of benzylacetone (**4**) is converted to the corresponding 1,3-dithianes almost exclusively (Scheme 2).

In summary, high rates and yields of the reactions, facile work up, low cost, easy availability of the catalyst and high chemoselectivity of the reaction are the strong practical points of the presented method. Further investigation for the use of this type of silica chloride, as a reagent or catalyst, is underway in our laboratory.

Preparation of Silica Chloride; To an oven-dried (120°C,vacuum) silica gel (10g) in a round bottomed flask (250mL) equipped with a condenser and a drying tube, was added thionyl chloride (40mL) and refluxed for 48h. The unreacted thionyl chloride was distilled off. The resulting white-grayish powder was flame-dried and stored in a tightly capped bottle. This silica chloride can be used for months without loosing its activity.



Scheme 2

General Procedure for Transdithioacetalization of Acetals; To a solution of diacetal **1** (5mmol), 1,3-propanedithiol (5.5-6mmol) in CH_2Cl_2 (25ml), silica chloride (1g) was added and the resulting mixture was stirred at room temperature. After completion of the reaction (TLC) the mixture was filtered through a silica gel pad and the pad was washed with CH_2Cl_2 (3×10ml). The resulting filtrate was washed with an aqueous solution of NaOH (10%, 25ml) and with H_2O (2×25ml). The organic layer was dried over anhydrous $MgSO_4$ and filtered. Evaporation of the solvent in vacuo gave the desired pure products in high yields (Table).

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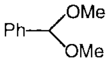
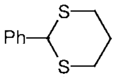
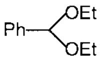
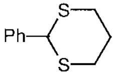
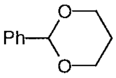
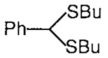
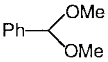
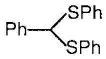
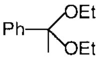
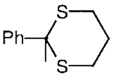
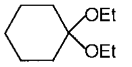
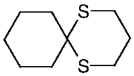
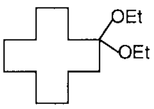
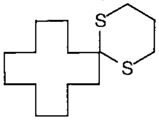
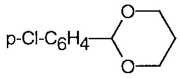
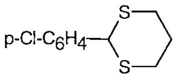
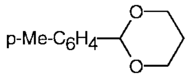
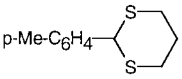
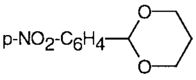
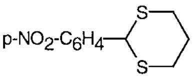
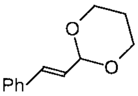
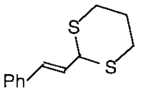
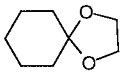
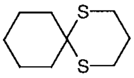
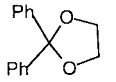
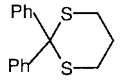
Table Transdithioacetalization of Acetals by Silica Chloride

Entry	Substrate	Product	Silica-Cl[c] (g/mmol)	time (min)	Yield%[a,b]
1			0.2	10	94
2			0.2	10	90
3			0.2	30	87
4			0.2	35	90
5			0.2	20	87
6			0.2	20	90
7			0.2	20	92
8			0.3	150	89
9			0.2	10	95
10			0.3	240	87
11			0.2	20	89
12			0.2	25	88
13			0.2	20	92

[a] Reactions were performed in CH_2Cl_2. [b] Products were identified by the comparison of their mp(bp) and ^{1}HNMR with those of the authentic samples. [c] Weight of silica chloride per mmol of the substrate.

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(8) We have repeated thioacetalization of benzaldehyde with Hojo's silica chloride and ours. The reactions were completed in 5 and 0.5h respectively,which shows that our catalyst is ten times more reactive than Hojo's catalyst.

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