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Bis(trimethylsilyl) sulfate-Silica Catalysed Thioacetalisation of Carbonyl Compounds

Harish K. Patney

Department of Chemistry, School of Physical Sciences
University of Technology, Sydney, P O Box 123, Broadway
Sydney NSW 2007, Australia

Abstract: Bis(trimethylsilyl) sulfate-silica has been shown to be an efficient reagent system for promoting thioacetalisation of carbonyl compounds at room temperature.

1,3-Dithiolanes have long been used as carbonyl protecting groups[1,2] and as masked methylene functions[3] in organic synthesis. They are generally obtained by protic acid or Lewis acid catalysed condensation of carbonyl compounds with thiols[1]. More recently, anhydrous lanthanum trichloride[4], tellurium tetrachloride[5], tetrachlorosilane[6], polyphosphoric acid trimethylsilyl ester[7] and supported reagents such as silica gel treated with thionyl chloride[8], anhydrous iron (III) chloride dispersed on silica gel[9], sulfonated charcoal[10] and zeolites[11] have also been developed for thioacetalisation. However, many of these methods suffer from harsh conditions, expensive reagents and poor yields when applied to hindered and aromatic ketones; consequently there is a continuing need to develop milder and more efficient reagents for this reaction.

We now report that bis(trimethylsilyl) sulfate[12,13,14] (BTS), in the presence of silica gel, is a very mild and efficient reagent for the conversion of a variety of carbonyl compounds into their respective thioacetals. Both reaction conditions and work-up procedure are very simple and convenient. When a mixture of a carbonyl compound and 1,2-ethanedithiol in dry dichloromethane is treated with BTS and silica, the reaction proceeds smoothly at room temperature and dithioacetals are obtained in excellent yields (see Table 1). The high reactivity of the BTS-silica reagent system is clearly demonstrated in that the less reactive aromatic ketones also reacted at room temperature and gave the corresponding dithioacetals in high yields (Table 1, entry 13-16). The efficiency of the BTS-promoted thioacetalisation is not surprising in view of its high Lewis acidity[13]. Presumably the presence of silica makes this system even more effective, as it acts as a water scavenger. It should be noted that in the absence of silica the reaction required forcing conditions, boiling benzene with azeotropic removal of water. In conclusion, BTS-silica has been demonstrated to be a highly efficient and mild reagent system for thioacetalisation of carbonyl compounds at room temperature. Further synthetic applications of this reagent system are currently under investigation and will be reported in due course.

General Procedure. To a stirred solution of carbonyl compound (10 mmol) and 1,2-ethanedithiol (10-20 mmol, see Table 1) in anhyd. dichloromethane (15 mL) was added bis(trimethylsilyl) sulfate[15] (1-2 mmol), followed by silica (4-8 g, 230-400 mesh, dried overnight 100°C). The progress of the reaction was followed by GLC, IR and NMR spectroscopy. Upon completion of the reaction, the mixture was filtered and silica washed with fresh dichloromethane (~ 60 mL). The combined dichloromethane layer was washed with a 10% aqueous NaOH solution (2 X 15 mL), water (15 mL), brine (15 mL) and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure gave the crude product which was purified by chromatography over neutral alumina.

Table 1. Thioacetalisation of Carbonyl Compounds using BTS/Silica Reagent

Entry	Substrate	BTS (mmol)	1,3-Dithiolanes^{a,b} Yield (%)	Reaction time
1	Octanal	1	95	15 min
2	Anisaldehyde	1	97	15 min
3	Benzaldehyde	1	97	15 min
4	p-Nitrobenzaldehyde	1	89	30 min
5	Cinnamaldehyde	1	90	15 min
6	Cyclohexanone	1	93	30 min
7	2-Methylcyclohexanone	1	96	1 h
8	2-Adamantanone	1	92	2 h
9	2-Hexanone	1	98	1 h^{c}
10	Cyclopentanone	2	99	1 h
11	3-Pentanone	2	95	3 h
12	2-Octanone	2	97	3 h
13	Acetophenone	2	96	8 h^{d}
14	9-Fluorenone	2	95	5 h^{c,d}
15	1,3-Diphenyl-2-propanone	2	94	8 h^{d}
16	Benzophenone	2	94	2 days^{c,d}
17	Camphor	2	75^{e}	2 days^{c,d}

a) Yield of isolated product characterised by physical and spectral data; b) Purity ≥ 98% by GLC; c) 20 mmol of 1,2-ethanedithiol used; d) 8 g of silica gel used; e) 75% conversion by GLC.

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