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Zirconium(IV) Chloride-Silica Catalysed Thioacetalisation of Carbonyl Compounds

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Abstract: Anhydrous anhydrous zirconium(IV) chloride dispersed on silica gel efficiently thioacetalised a variety of carbonyl compounds in near quantitative yields Copyright © 1996 Elsevier Science Ltd

Thioacetalisation of carbonyl compounds plays an important role in organic synthesis; either the thioacetal group acting as a protecting group or as an acyl anion equivalent[1,2]. The reaction is generally catalysed by protic acids or Lewis acids[1]. However, many of the recently developed reagents[3] for thioacetalisation require harsh conditions and expensive reagents and give poor yields when applied to less reactive aromatic ketones. Thus, there is continuing need to develop milder and more efficient reagents for this reaction.

Supported reagents have recently found favour in organic synthesis[4,5] in view of their higher selectivity, milder reaction conditions, and easier work-up. We now report that anhydrous zirconium(IV) chloride dispersed on silica gel[6,7] is a remarkably effective reagent for the rapid, high yield, room temperature conversion of a variety of carbonyl compounds to their respective thioacetal. The reaction proceeds in a clean manner and the conditions employed are both simple and convenient. When a mixture of carbonyl compound and 1,2-ethanedithiol in dry dichloromethane is treated with anhydrous zirconium(IV) chloride-silica gel at room temperature, the reaction takes place rapidly and excellent yields of dithioacetals are obtained (see Table 1). The high reactivity of this reagent is clearly demonstrated in that the less reactive aromatic ketones also react at room temperature to give the corresponding dithioacetals in high yields (Table1, entries 13-16). Under these conditions, an α,β-unsaturated aldehyde (Table 1, entry 5) is also converted to its dithioacetal in excellent yield but we have found that α,β-unsaturated ketones fail to give the corresponding product in appreciable yield. The efficiency of zirconium(IV) chloride -silica gel reagent may presumably be attributed to its strong affinity for carbonyl oxygen, large surface area and its ability to act as a water scavenger. It is worth noting that with zirconium(IV) chloride in the absence of silica gel, thioacetalisation of acetophenone proceeded to the extent of only 65% (vs 100% conversion in 30 min, Table1: entry 13).

In conclusion, the present method provides a very simple and convenient procedure for thioacetilisation of carbonyl compounds. The notable advantages of this method to that currently in the literature are that the reaction conditions are mild (rt) and require small amounts of catalyst. The reaction is rapid, and is applicable to less reactive aromatic ketones. Further synthetic investigations of this reagent system are currently in progress and will be reported in due course.

Standard Procedure: To a stirred solution of carbonyl compound (10 mmol) and 1,2-ethanedithiol (12-30 mmol, see Table 1) in anhydrous dichloromethane (25 mL) was added zirconium(IV) chloride-silica reagent (1.0-6.0 g, equiv. to 1-6 mmmol of $ZrCl_4$, see Table 1) at room temperature. When the reaction was

complete, as followed by GLC, IR and NMR spectroscopy, it was quenched with 2M NaOH (2mL), solid Na_2SO_4 (5g). After removal of silica by filtration the 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 Anhyd. $ZrCl_4$-SiO_2 Reagent

Entry	Substrate	$ZrCl_4$-SiO_2 (g)	1,2-Ethanedithiol (mmmol)	Thioketal [a,b] Yield (%)	Reaction Time
1	Octanal	1	12	99	<1 min
2	p-Methoxybenzaldehyde	1	12	96	<5 min
3	Benzaldehyde	1	12	98	1 min
4	p-Chlorobenzaldehyde	1	12	98	<2 min
5	Cinnamaldehyde	1	12	97	<1 min
6	Cyclohexanone	1	12	98	<5 min
7	Cyclopentanone	1	12	97	15 min
8	2-Hexanone	2	15	98	<5 min
9	2-Heptanone	2	15	99	<5 min
10	2-Octanone	1.5	15	97	10 min
11	2-Adamantanone	2	15	97	<4 min
12	3-Pentanone	2	15	96	<5 min
13	Acetophenone	2	15	99	30 min
14	1,3-Diphenyl-2-propanone	2	15	99	30 min
15	9-Fluorenone	2	15	98	30 min
16	Benzophenone	3	20	98	3 h
17	Camphor	6	30	96[c]	72 h

a) Yield of isolated product characterised by physical and spectral data; b) Purity ≥98% by GLC; c) % conversion by GLC.

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References and Notes

1. a) Greene, T.W.; Wutts, P.G.M. *Protective Groups in Organic Synthesis*; John Wiley and Sons, Inc.: New York, 2nd Ed. 1991; pp. 201-207.
   b) Loewanthal, H.J.E. *Protective Groups in Organic Chemistry*; McOmie, J.F.W., Ed., Plenum: New York, 1973; pp. 323-402.
2. a) Seebach, D.; Corey, E.J. *J. Org. Chem.* **1975**, 40, 231-237.
   b) Hauptmann, H.; Campos, M.M. *J. Amer. Chem. Soc.* **1950**, 72, 1405-1406.
3. See references cited in: Patney, H.K. *Tetrahedron Lett.* **1993**. 44, 7127-7128.
4. a) McKillop, A. and Young, D.W. *Synthesis* **1979**, 401-422 and 481-500.
   b) Posner, G.H. *Angew. Chem. Int. Ed. Engl.* **1978**, 17, 487-496.
5. a) Clark, H.J.; Kybett, A.P.; Macquarie, D.J. *Supported Reagents: Preparation, Analysis and Applications*; VCH: New York. 1992.
   b) Laszlo, P. Ed., *Preparative Chemistry Using Supported Reagents*; Academic: San Diego, 1987.
6. For thioacetalisation procedures involving silica gel see: a) Kamitori, Y.; Hojo, M,; Masuda, R.; Kimura, T.; and Yoshida, T. *J. Org. Chem.* **1986**, 51, 1427-1431. b) Patney, H.K. *Tetrahedron Lett.* **1994**, 35, 5717-5718.
7. The zirconium(IV) chloride-silica reagent was prepared by mechanically shaking chromat. grade silica gel (50g) (70-230 mesh, dried overnight 100° C) and powdered zirconium(IV) chloride (15.2g) for 24 hr.

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