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Anhydrous Cobalt(II) Bromide Dispersed on Silica Gel: A Mild and Efficient Reagent for 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: Anhydrous cobalt(II) bromide dispersed on silica gel has been shown to be a very efficient reagent system for thioacetalisation of a variety of aldehydes and ketones at room temperature.

In view of the tremendous versatility of thioacetals in organic synthesis as carbonyl protecting groups[1], a wide variety of methods have been developed for their preparation. These thioacetals have also been used as an acyl carbanion equivalents[2] and as intermediate for the conversion of carbonyl function to parent hydrocarbon[3]. They are generally obtained by protic acid or Lewis acid catalysed condensation of carbonyl compounds with thiols[1]. However, many of the recently[4] developed reagents for thioacetalisation even suffer from harsh conditions, expensive reagents and poor yields when applied to less reactive aromatic ketones. Thus, the development of more efficient reagents is still actively pursued by synthetic chemists.

Supported reagents are playing an increasingly important role in organic synthesis[5,6]. We report here that anhydrous cobalt(II) bromide dispersed on silica gel[7,8] is a very efficient reagent for thioacetalisation of a variety of aldehydes and ketones under mild conditions. Both reaction conditions and work-up procedure are very simple and convenient. When a mixture of carbonyl compound, 1,2-ethanedithiol in dry dichloromethane is treated with anhydrous cobalt(II) bromide-silica reagent at room temperature, the reaction proceeds smoothly and excellent yields of dithioacetals are obtained (see Table 1). The superiority of cobalt bromide-silica reagent 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, Entries 14-17). The efficiency of the anhydrous cobalt(II) bromide-silica 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 in the absence of silica gel thioacetalisation of 2-heptanone proceeded to the extent of ca. 80% even after 7h period (vs 100% conversion in 30 min, Table 1: Entry 11). In conclusion, the present method[9] provides an excellent alternative to the existing methods for thioacetalisation of carbonyl compounds rapidly, with the added advantage that the reaction conditions are mild (rt) and simple, last but not least, the reaction is efficient for less reactive aromatic ketones.

General Procedure: To a stirred solution of carbonyl compound (10 mmol) and 1,2-ethanedithiol (12 mmol, unless stated otherwise) in anhydrous dichloromethane (25 mL) was added anhydrous cobalt(II) bromide-silica reagent (2.0-6.0 g, equiv. to 2-6 mmol of $CoBr_2$, see Table 1) at room temperature. The reaction mixture turns from bluish-green to dark in colour as the reaction proceeds further. 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 2M NaOH (2 x 15 mL), water (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. Anhydrous $CoBr_2$-Silica Promoted Thioacetalisation of Carbonyl Compounds

Entry	Substrate	$CoBr_2$-SiO_2 (g)	1,3-Dithiolanes[a,b] yield (%)	Reaction time
1	Cyclohexanealdehyde	2	99	3 min
2	Octanal	2	87	3 min
3	p-Methoxybenzaldehyde	2	98	15 min
4	Benzaldehyde	2	99	10 min
5	p-Chlorobenzaldehyde	2	99	12 min
6	Cinnamaldehyde	2	89	10 min
7	Cyclohexanone	2	99	17 min
8	Cyclopentanone	2	99	45 min
9	2-Octanone	3	97	40 min
10	2-Hexanone	4	99	20 min
11	2-Heptanone	4	98	30 min
12	2-Adamantanone	4	92	10 min
13	3-Pentanone	4	99	30 min
14	Acetophenone	6	99	75 min
15	1,3-Diphenyl-2-propanone	6	98	3 h
16	9-Fluorenone	6	99	3.5 h
17	Benzophenone	6	99	4 h[c]
18	Camphor	6	92[e]	24 h[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) 30 mmole of 1,2-ethanedithiol used; e) % conversion by GLC.

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. Pettit, G.R.; van Tamelen, E.E. *Org. Reactions* **1962**, 12, 356-529.
4. See references cited in: Patney, H.K. *Tetrahedron Lett.* **1993**, 44, 7127-7128.
5. 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
6. 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.
7. 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.* **1991**, 32, 2259-2260. c) Ref. 4.
8. The cobalt(II) bromide-silica reagent was prepared by mechanically shaking chromatographic grade silica gel (50g) (230-400 mesh, dried overnight 100°C) and powdered anhydrous cobalt(II) bromide (14g) for 24 hr. The bluish-green powder obtained was stable for months without losing its activity significantly.
9. A preliminary investigation into the thioacetalisation of α,β-unsaturated ketones using this reagent, however, gave only complex mixtures and no significant amount of dithioacetal was detected.

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