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A RAPID MILD AND EFFICIENT METHOD OF THIOACETALIZATION USING ANHYDROUS IRON(III) CHLORIDE DISPERSED ON SILICA GEL

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Summary: Carbonyl compounds are rapidly thioacetalized in near quantitative yields by using anhydrous iron(III) chloride dispersed on silica gel at room temperature.

The conversion of carbonyl compounds to the cyclic dithioacetals constitutes an important part of many organic synthetic transformations[1]. Dithioacetals are also useful in organic synthesis as acyl carbanion equivalents[2]. Numerous methods that are reported for this conversion include the use of protic acids, Lewis acids and some silicon reagents.[1]. More recently Nafion-H catalyst[3], silica gel treated with thionyl chloride[4] and anhydrous lanthanum trichloride[5] have also been employed for thioacetalization. However, many of these methods suffer from harsh conditions, expensive reagents, slow reaction rates and poor yields when applied to hindered and aromatic ketones; consequently, there is a need to develop new reagents for this reaction.

We now report that anhydrous iron(III) 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 into their respective thioacetal. 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 iron(III) chloride - silica gel reagent at room temperature, the reaction takes place instantly in most of the cases and excellent yields of dithioacetals are obtained[8] (Table, Entries 1-10). The reaction mixture turns from grey to pale yellow indicating the completion of the reaction. The high reactivity of this reagent is clearly manifested in that the less reactive aromatic ketones also reacted very fast at room temperature (Table, Entries 11-14) and gave excellent yields of corresponding dithioacetals. The efficiency of the anhydrous iron(III) chloride - silica reagent may presumably be attributed to its strong affinity for carbonyl oxygen thereby facilitating the substitution of the hemithioacetal intermediate and its remarkable ability to act as a water scavenger. Product isolation is very simple and merely involves quenching of the reaction mixture with dilute sodium hydroxide, decantation, followed by distillation or crystallization. In conclusion, this method provides a simple, yet rapid and convenient means of thioacetalization of carbonyl compounds under mild reaction conditions.

Table . Thioacetalization of Carbonyl Compounds Using Anhyd. $FeCl_3$ -SiO_2 Reagent[a]

Entry	Carbonyl Compound	Thioketal[b,c] yield (%)	Reaction Time
1	2-Adamantanone	97	< 1 min
2	Cyclohexanone	99	< 1 min
3	Cyclopentanone	98	< 1 min
4	2-Octanone	98	< 1 min
5	2-Methylcyclohexanone	97	< 1 min
6	4-Methylcyclohexanone	99	< 1 min
7	Benzaldehyde	96	< 1 min
8	4-Nitrobenzaldehyde	95	< 1 min
9	Anisaldehyde	98	< 1 min
10	Cinnamaldehyde	94	< 1 min
11	1,3-Diphenyl-2-propanone	98[d]	< 1 min
12	Acetophenone	98[d]	< 1 min
13	Benzophenone	98[d]	5 min
14	9-Fluorenone	95[d]	15 min
15	Camphor	91[d,e]	7 h

a) Reaction conditions: carbonyl compound (10 mmol), 1,2-ethanedithiol (12 mmol), dichloromethane (10 ml), anhyd. $FeCl_3$-SiO_2 reagent (2.0g, equiv. to 2 mmol of $FeCl_3$) unless stated otherwise, magnetic stirring at room temperature; b) yield of isolated product characterized by physical and spectral data; c) Purity $\geqslant$98% by G.L.C.; d) 4.0 g of anhyd. $FeCl_3$-SiO_2 reagent used; e) 94% conversion by G.L.C.

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References and Notes:

1. (a) T.W. Greene, "Protective Groups in Organic Synthesis", John Wiley, New York, (1981). (b) H.J.E. Loewanthal, "Protective Groups in Organic Chemistry", J.F.W. McOmie. Ed., Plenum, New York and London (1973).
2. (a) H. Haptmann and M.M. Campos, J. Amer. Chem. Soc., 72, 1405 (1950). (b) S. Patai, "The Chemistry of the thiol group", John Wiley, New York (1974).
3. G.A. Olah, S.C. Narang, D. Meider and G.F. Salem, Synthesis, 282 (1981).
4. Y. Kamitori, M. Hojo, R. Masuda, T. Kimura and T. Yoshida, J. Org. Chem. 51 1427 (1986).
5. L. Garlaschelli and G. Vidari, Tetrahedron, 40, 5815 (1990).
6. This reagent has been shown to be very effective for ring enlargement of tertiary cycloalkanols and deacetalization reaction. See: (a) A. Fadel and J. Salaiin, Tetrahedron, 41, 413 and 1267 (1985). (b) A. Fadel, R. Yefsah and J. Salaiin, Synthesis, 37 (1987).
7. The reagent used in the present work was prepared as described in ref. 6(a) except 10 gram of anhydrous iron(III) chloride was dispersed on 50 gram of silica gel.
8. Use of ferric chloride - silica as reported by Mazur and Keinan required forcing conditions (boiling benzene with azeotropic removal of water). See E. Keinan and Y. Mazur, J. Org. Chem. 43, 1020 (1978).

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