

Highly Efficient Dithioacetalization of Carbonyl Compounds Catalyzed with Iodine Supported on Neutral Alumina

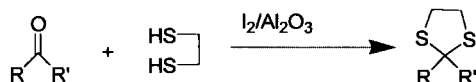
Nabajyoti Deka[#] and Jadab C. Sarma^{##*}

Organic Chemistry Division, Regional Research Laboratory, Jorhat 785006, Assam, India

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Aldehydes and ketones are protected as their corresponding dithioacetals with ethane-1,2-dithiol in the presence of a catalytic amount of iodine supported on neutral alumina surface. This is a high yielding method of carbonyl group protection under mild, neutral and solvent free conditions.

Protection of carbonyl functions as their dithioacetals is an important transformation in organic synthesis frequently used during the course of a multi-step synthesis of complex molecules.¹ Moreover dithioacetal is an important intermediate through which a carbonyl compound can be converted into its parent hydrocarbon by reductive desulfurization method.² Normally dithioacetals are prepared by the acid catalyzed condensation of carbonyl compounds with thiols or dithiols. WCl_6 ,³ TeCl_4 and several other Lewis acid catalysts like BF_3 -etherate, ZnCl_2 , AlCl_3 , TiCl_4 , LaCl_3 , SiCl_4 etc. have been reported for this transformation.⁴ Sato et al.⁵ and Das et al.⁶ had also reported two tin compounds as suitable catalysts. Among many of the recently developed catalysts, solid catalysts are gaining popularity due to easier handling, milder reaction conditions and simpler work-up procedure.⁷



Very recently Firouzabadi et al.⁸ and Anand et al.⁹ have reported two different methods using solid catalysts under solvent free conditions for thioacetalization reaction. Because of our interest in iodine-catalyzed reactions,¹⁰ we ventured to observe that iodine supported on neutral alumina under solvent free conditions as well as in solution acted as a highly efficient catalyst in the preparation of dithioacetals from carbonyl compounds giving a fast and clean reaction with high yield. When a carbonyl compound was treated with ethane-1,2-dithiol in the presence of a catalytic amount (10%) of iodine supported on neutral alumina surface, the corresponding dithioacetal was obtained in 89 to 95% yield.^{11,12} In a blank reaction, neutral alumina alone without iodine was found to give no product. The neutral alumina was the preferred choice as support to keep the reaction medium under mild and neutral condition. Because of the inherent acidity or basicity, other two forms of alumina were not used. The results are presented in Table 1.

In the present method it was observed that dithioacetalization of aldehydes proceeded more quickly than ketones. Yields of the corresponding thioacetals of aldehydes were also found to be a little higher than that of ketones. Hindered and unreactive ketones such as benzophenone gave better yield only under

reflux in dichloromethane. This may be due to homogeneity of the reaction medium in solution phase. The carbonyl function of a β -keto ester (methyl acetoacetate) could also be thioacetalized by this method in a short period with a high yield. When compared with the existing methods, the present method was found to be superior in many respects. It is suitable to aldehydes and ketones both aliphatic and aromatic as well as α,β -unsaturated carbonyl compounds, while the activity of lithium triflate^{8a} and lithium bromide^{8b} is limited to aromatic and α,β -unsaturated systems only. Moreover, in case of ketones the reaction is very slow with these reagents. Both these reagents are hygroscopic in nature and lithium triflate needs elevated temperature for completion of the reaction. Although copper triflate-silicagel⁹ reacts with both aliphatic and aromatic aldehydes and ketones yet the reaction is very slow (benzophenone, 24 h; camphor, 60 h) as compared to the present method (benzophenone, 4 h; camphor, 4.5 h). This method is free from the problem of Michael addition encountered in some cases of α,β -unsaturated systems with some reagents.¹³

Table 1. $\text{I}_2/\text{Al}_2\text{O}_3$ catalyzed dithioacetalization of carbonyl compounds^a

Substrate	Reaction Time /min	Yield /%	Ref
Benzaldehyde	10	95	4
4-Methoxybenzaldehyde	10	94	9
4-Chlorobenzaldehyde	10	93	9
4-Nitrobenzaldehyde	10	93	14
Cinnamaldehyde	9	93	9
Crotonaldehyde	9	92	15
Furfural	10	94	9
2-Hydroxybenzaldehyde	10	92	9
Hexadecanal	20	94	17a
Methyl acetoacetate	35	85	9
Acetophenone	35	87	9
Cyclohexanone	40	86	4
Menthone	40	86	9
α -Ionone	15	88	17b
6-Methoxy-1-tetralone	40	90	17c
Camphor	270 ^b	89	9
Benzophenone	240 ^b	89	9
Cholest-4-en-3-one	20	95	16

^aProducts were characterized by spectroscopic (NMR, IR, MS) and elemental analysis and also by comparing with the authentic samples prepared by reported method. ^bReactions were done in refluxing CH_2Cl_2 .

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References and Notes

- # Present address: Department de Phamacochimie Moleculaire, Universite Joseph Fourier, UMR CNRS 5063, France.
- ## Present address: JSPS Fellow, Department of Environmental Chemistry & Materials, Okayama University, 1-1 Naka 2-Chome, Tsushima, Okayama 700-8530, Japan.
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 - Procedure for preparation of the catalyst: The catalyst was prepared by making a slurry of activated neutral alumina (1 g, Aldrich, standard grade, 150 mesh) with a solution of 51 mg (0.20 mmol) of iodine in 2 mL of dichloromethane. The slurry was stirred magnetically at room temperature for 30 minutes and the excess solvent was removed by evaporation under reduced pressure and at low temperature. When the slurry became dry and free falling it was ready for use.
 - Typical procedure for dithioacetalization: To a freshly prepared catalyst (1 g, 0.2 mmol of iodine) under stirring, a mixture of benzaldehyde (2 mmol) and ethane-1,2-dithiol (2.2 mmol) was added and stirring continued for 10 min or till the reaction was complete. For TLC monitoring, a small amount of the solid reaction mixture was taken out with a spatula and washed with a little amount of ethyl acetate to get a solution. On completion the reaction mixture was loaded on a short column of silica gel (60 to 120 mesh) and eluted with ethyl acetate. The organic layer was washed with a dilute solution of sodium thiosulfate followed by water and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure and purification of the residue by column chromatography yielded the pure product.
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 - a) ^1H NMR (CDCl_3 , 60 MHz) δ 4.15 (t, $J = 6\text{ Hz}$, 1H), 2.95 (s, 4H), 1.75 to 1.05 (m, 28H), 0.75 (t, $J = 6.5\text{ Hz}$, 3H); IR 2950, 2900, 1480, 1220 cm^{-1} . Anal. Calcd for $\text{C}_{18}\text{H}_{36}\text{S}_2$: C, 68.28; H, 11.46; S, 20.25%. Found: C, 68.27; H, 11.73; S, 20.08%. b) ^1H NMR (CDCl_3 , 60 MHz) δ 5.65 to 5.05 (m, 3H), 3.25 (s, 4H), 2.15 to 1.05 (overlapping multiplet, 11H), 0.90 (s, 3H), 0.80 (s, 3H); IR 2975, 2900, 1480, 1380, 1250, 1050, 980 cm^{-1} . Anal. Calcd for $\text{C}_{15}\text{H}_{24}\text{S}_2$: C, 67.11; H, 9.01; S, 23.89%. Found: C, 67.57; H, 9.08; S, 23.24%. c) ^1H NMR (CDCl_3 , 60 MHz) δ 7.40 (d, $J = 8\text{ Hz}$, 1H), 6.45 to 6.05 (m, 2H), 3.53 (s, 3H), 3.20 (s, 4H), 2.55 (overlapping triplet, 4H), 2.45 to 2.00 (m, 2H); IR 2950, 2900, 1610, 1590, 1500, 1450, 1320, 1300, 1250, 1050 cm^{-1} . Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{OS}_2$: C, 61.86; H, 6.39; O, 6.34; S, 25.41%. Found: C, 61.32; H, 6.44; S, 25.86%.