# Chemoselective (Trans)thioacetalization of Carbonyl Compounds with a Reusable Lewis Acid–Surfactant-Combined Copper Bis(dodecyl sulfate) Catalyst in Water

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**Abstract:** A Lewis acid–surfactant-combined copper bis(dodecyl sulfate) [$Cu(DS)_2$] catalyst served as an efficient and reusable catalyst for the thioacetalization and transthioacetalization of carbonyl compounds and *O*,*O*-acetals in water at room temperature. Some of the major advantages of this procedure are high chemoselectivity, ease of operation and purification without any organic solvent, and high yields.

**Key words:** thioacetalization, transthioacetalization, Lewis acid–surfactant-combined catalysts, copper bis(dodecyl sulfate), reusability

Thioacetalization is a well-documented process for the conversion of carbonyl compounds into their corresponding thioacetals because, compared to *O*,*O*-acetals, thioacetals are remarkably stable under acidic and nonbasic conditions.[1] Protected oxathiolanes, dithiolanes, and dithianes constitute an important class of compounds as acyl anion equivalents or masked methylene functions in carbon–carbon bond-forming reactions and in the total synthesis of both natural and synthetic multifunctional complex molecules.[2,3] These compounds are usually prepared by the condensation of carbonyl compounds with thiols or dithiols using protic or Lewis acids [such as $ZnCl_2$,[4] $LnCl_3$,[5] $FeCl_3/SiO_2$,[6] $HClO_4/SiO_2$ or $SOCl_2/SiO_2$,[7] $ZrCl_4/SiO_2$,[8] $Cu(OTf)_2/SiO_2$,[9] $AlCl_3$,[10] $TeCl_4$,[11] $SnCl_2$,[12] $SiCl_4$,[13] $TiCl_4$,[14] $InCl_3$,[15] $BF_3{\cdot}OEt_2$,[16] $Mg(OTf)_2$ or $Zn(OTf)_2$,[17] $I_2$,[18] Amberlyst® 15,[19] $LiClO_4$,[20] $Pr(OTf)_3$,[21] $CoCl_2$,[22] $WCl_6$,[23] $LiBF_4$,[24] NBS,[25] $Sc(OTf)_3$,[26] and $VO(OTf)_2$[27]]; however, many methods using these acids are associated with a number of drawbacks, such as the treatment with strong acids, drastic reaction conditions, the use of expensive, corrosive, or toxic reagents, the necessity of working under inert atmosphere, and long reaction times. Additionally, the use of hazardous organic solvents, difficulties in recovery of the catalyst, and the tedious purification processes further limit their synthetic utility, especially for large-scale preparations and industrial applications. Finally, the aforementioned disadvantages and limitations are unacceptable from an environmental point of view.

In recent years, the use of water as a reaction solvent has received remarkable attention in organic synthesis due to its environmentally friendly and economical nature.[28] Although numerous catalytic systems using water have been developed, rare earth metal trifluoromethanesulfonates and Lewis acid–surfactant-combined (LASC) catalysts used as water-compatible catalysts have attracted the most attention due to their stability in water and their reusable nature.[29] Engberts and co-workers have reported that a very low concentration ($5 \times 10^{-3}$ M) of copper bis(dodecyl sulfate) [$Cu(DS)_2$] micelles accelerates the Diels–Alder reaction in water by a factor of $1.8 \times 10^6$ compared to the corresponding uncatalyzed reaction in organic solvents.[30] Later, Kobayashi and co-workers reported that colloidal scandium-based LASC and chiral $Cu(DS)_2$–bis(oxazoline) catalyzed asymmetric aldol reactions in water led to the production of aldol adducts with excellent yields and enantiomeric excesses.[31] Other successful dehydration reactions, including esterification, etherification, thioetherification, and dithioacetalization, catalyzed by dodecylbenzenesulfonic acid (DBSA) as a Brønsted acid–surfactant-combined (BASC) catalyst in aqueous media have also been established by the same group.[29a,b] They have shown highly efficient dehydrative thioacetalization of aldehydes and ketones catalyzed by 10 mol% DBSA in water; however, compared to the use of DBSA, the reaction was slow and sluggish when LASC-type catalysts such as $Sc(DS)_3$ and $Yb(DS)_2$ were employed for dehydrative esterification and thioacetalization in water.[29b] Peppe and co-workers have also reported successful stoichiometric $InBr_3$-catalyzed thioacetalizations of carbonyl compounds in aqueous organic solvents and that the catalyst could be reused in at least 10 reactions; however, an appreciable decrease in the reaction yield (20–90%) was observed compared to a reaction performed in a chlorinated organic solvent with the same catalytic system. Moreover, since tedious purification processes and the use of chlorinated solvent was necessary, their protocol does not meet the standard of green chemistry.[32] Therefore, a new catalytic system for thioacetalization that is superior to existing methods with regards to toxicity, economic viability, atom efficiency, operational simplicity, and recyclability, and that could be used in water without any organic solvent, is still needed. Based on the recent advances in LASC-catalyzed organic transformations in water, we have devoted our attention to a new LASC-based

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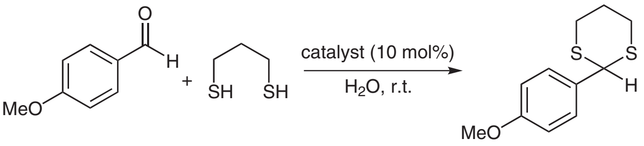
protocol for thioacetalization using water as the solvent. In this paper, we describe a new, reusable catalytic system for the thioacetalization of carbonyl compounds in water which employs reusable Cu(DS)$_2$ as the catalyst.

Initially, several LASC catalysts, including copper bis(dodecyl sulfate) [Cu(DS)$_2$],[33] scandium(III) dodecyl sulfate [Sc(DS)$_3$], oxovanadium(IV) dodecyl sulfate [VO(DS)$_2$], and zinc dodecyl sulfate [Zn(DS)$_2$],[34] and their corresponding trifluoromethanesulfonate (triflate) salts, were screened for the model reaction between 4-methoxybenzaldehyde and 1,3-propanedithiol at room temperature in water. The thioacetalization reaction was carried out in water in the presence of 10 mol% of the catalyst under vigorous stirring (>1200 rpm) and was monitored by TLC, GC, or $^1$H NMR spectroscopy. The results are shown in Table 1. The LASC-type catalysts gave promising yields (89–97%; entries 1, 2, 4, 6, and 8) compared to the corresponding triflate salts (7–18%, entries 3, 5, 7, and 9). The LASC-type catalyst plays the role of a Lewis acid in activating the substrates and also acts as a surfactant to produce emulsion droplets, bringing the lipophilic organic reactants into the droplets where the reaction occurs. As water is excluded from the hydrophobic interior of the emulsion droplet, the reaction equilibrium shifts toward the formation of the product.[29–31] On the other hand, even though Cu(OTf)$_2$,[9] Zn(OTf)$_2$,[17] Sc(OTf)$_3$,[26] and VO(OTf)$_2$[27] display excellent catalytic efficiencies for the thioacetalization of carbonyl compounds in organic solvents, low yields were obtained when the reaction was performed in water. Among the LASC-type catalysts, Cu(DS)$_2$ was found to catalyze the reaction most efficiently and generated the 2-phenyl-1,3-dithiane in 97% yield (>99% conversion) in 15 minutes in the presence of as little as 5 mol% Cu(DS)$_2$ (entry 1). It is noteworthy that the yield of the corresponding dithiolane dropped to 92% when 1,2-ethanedithiol was used instead of 1,3-propanedithiol (entry 2). Although the LASC-type scandium, vanadium, and zinc catalysts led to satisfactory yields, the catalytic rates were much lower than that of Cu(DS)$_2$ (cf. entry 1 with entries 4, 6, and 8). Additionally, no product was detected when sodium dodecyl sulfate (SDS) was employed as the catalyst (entry 10). Even though BASC-type catalysts such as DBSA were found to be efficient in this thioacetalization reaction upon heating to 40 °C (entry 11, parentheses),[29b] only a moderate yield was observed when the reaction was performed at room temperature (72%, entry 11). These results clearly indicate that Cu(DS)$_2$ is superior to the other LASC-type catalysts and to BASC-type catalysts.

The surfactant-type catalyst Cu(DS)$_2$ can be easily dissolved in water and the products of thioacetalization are hydrophobic, which make the catalyst recycling procedures convenient. In fact, the thioacetalization reaction of an equal amount of 4-methoxybenzaldehyde (10.0 mmol) with 1,3-propanedithiol (10.1 mmol) on a 1-gram scale in the presence of 5 mol% Cu(DS)$_2$ was exothermic and fast, and the product gradually solidified and precipitated out from the aqueous medium during the course of the reac-

**Table 1** Effect of the Catalyst on the Thioacetalization of 4-Methoxybenzaldehyde with 1,3-Propanedithiol in Water[a]



| Entry | Catalyst[b] | Time | Conversion[c] (%) | Yield[d] (%) |
|---|---|---|---|---|
| 1 | Cu(DS)$_2$ | 5 (15[e]) min | >99 (>99[e]) | 96 (97[e]) |
| 2 | Cu(DS)$_2$ | 15[e,f] min | 94[e,f] | 92[e,f] |
| 3 | Cu(OTf)$_2$ | 4 h | 12 | 9 |
| 4 | Sc(DS)$_3$ | 1 h | >99 | 95 |
| 5 | Sc(OTf)$_3$ | 4 h | 21 | 18 |
| 6 | VO(DS)$_2$ | 40 min | >99 | 96 |
| 7 | VO(OTf)$_2$ | 4 h | 7 | –[g] |
| 8 | Zn(DS)$_2$ | 4 h | 92 | 89 |
| 9 | Zn(OTf)$_2$ | 4 h | 8 | –[g] |
| 10 | SDS | 4 h | 0 | –[g] |
| 11 | DBSA | 4 h | 78 (>99[h]) | 72 (97[h]) |

[a] All reactions were performed in H$_2$O (at 0.5 M) at r.t. in the presence of 10 mol% catalyst, unless otherwise noted.
[b] DS = dodecyl sulfate; OTf = trifluoromethanesulfonate.
[c] Determined by GC or $^1$H NMR spectroscopy.
[d] Isolated yield after column chromatography.
[e] 5 mol% catalyst was used.
[f] 1,2-Ethanedithiol was used instead of 1,3-propanedithiol.
[g] Not determined.
[h] At 40 °C.

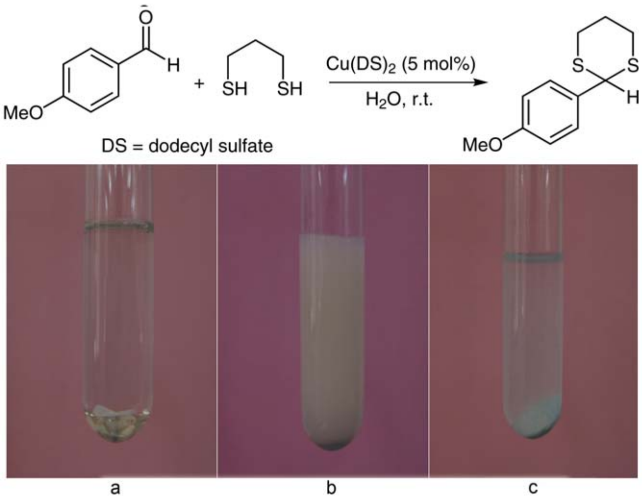


**Figure 1** (a) Top phase: Cu(DS)$_2$ (5 mol%) in water, lower phase: mixture of 4-methoxybenzaldehyde (10 mmol) and 1,3-propanedithol (10.1 mmol); (b) formation of a colloidal dispersion after vigorous stirring (>1200 rpm); (c) centrifugal deposit of the product (1500 rpm, 30 min); top phase: aqueous solution of Cu(DS)$_2$, lower phase: 2-(4-methoxyphenyl)-1,3-dithiane precipitate.

tion. The pure product can be collected by filtration on a glass filter after centrifugal deposit (1500 rpm, 30 min), followed by aqueous resuspension and washing without any organic solvent (Figure 1).

Nonsolid, syrup-like thioacetal products, such as 2-phenyl-1,3-dithiane and 2-phenyl-1,3-dithiolane, derived from benzaldehyde and either 1,3-propanedithiol or 1,2-ethanedithiol, could also be isolated by extraction with ethyl acetate after completion of the reaction. Furthermore, an easier workup procedure for the isolation of syrup-like products of the Cu(DS)$_2$-catalyzed thioacetalization without any organic solvent was achieved by high-speed centrifugal deposit (4500 rpm, 30 min); the syrup-like organic product aggregated on the bottom of the reaction tube after centrifugation. The product was separated from the supernatant aqueous solution, resuspended with water, and centrifuged twice, and the crude product was purified by distillation using a Kugelrohr apparatus under reduced pressure.

In order to analyze the reusability of Cu(DS)$_2$, the filtered aqueous solution from the above-stated reaction that contained water-soluble Cu(DS)$_2$ was recharged with 1.0 equivalent of 4-methoxybenzaldehyde and 1.05 equivalents of 1,3-propanedithol. The corresponding solid dithiane was obtained in 99% yield (based on GC conversion) after a reaction time of 15 minutes. Furthermore, the filtered aqueous solution could be reused five times with a slight decrease in activity under similar conditions at a prolonged reaction time (Table 2). It is noteworthy that the advantages of this efficient catalytic system are the existence of easy workup procedures, the fact that the purification does not require the use of any organic solvent, and the fact that the catalyst can be reused from the aqueous solution of the last completed reaction without loss of catalytic activity, even after five cycles. Thus, the protocol meets the standards of green chemistry for synthetic and industrial applications.

**Table 2** Reusability Study of Cu(DS)$_2$ for the Thioacetalization of 4-Methoxybenzaldehyde with 1,3-Propanedithiol in Water[a]

| Run | 1st | 2nd | 3rd | 4th | 5th | 6th |
|---|---|---|---|---|---|---|
| Conversion (%) | >99[b] | 95[b] | 96[b] | 87[b] (98[c]) | 94[c] | 87[c] |

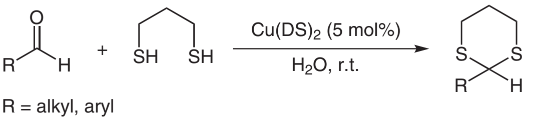
[a] All reactions were performed in $H_2O$ (at 0.5 M) at r.t. in the presence of 5 mol% catalyst, and the conversion was determined by GC or $^1H$ NMR spectroscopy.

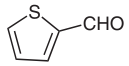
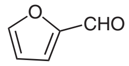
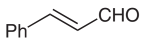
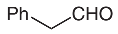
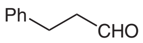
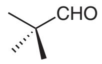
[b] Reaction time: 15 min.

[c] Reaction time: 40 min.

With the optimal thioacetalization protocol in hand [5 mol% Cu(DS)$_2$, at 0.5 M in $H_2O$], various aromatic, aliphatic, heterocyclic, α,β-unsaturated, and propargylic aldehydes were reacted with 1,3-propanedithiol (Table 3). In general, reactions with liquid aldehydes (entries 1, 6, and 8–13) proceeded faster than those with solid aldehydes (entries 2–5 and 7) due to faster formation of colloidal dispersions of the liquid aldehydes in aqueous solution. As solid aldehydes are dispersed more slowly in aqueous solution, vigorous stirring (>1200 rpm) is necessary.[29] Substituted aromatic aldehydes with electron-withdrawing groups were found to be more reactive than aldehydes bearing electron-donating groups (cf. entries 2–5 and 7). Unsaturated, propargylic, and acid-sensitive furfuryl aldehydes remain unaffected under the reaction conditions (entries 8–11). Aliphatic aldehydes, such as 2-phenylethanal, 3-phenylpropanal, and the sterically hindered *tert*-pivalaldehyde, reacted quickly to generate the corresponding dithianes in excellent yields (entries 12–14). It is noteworthy that the aldehyde bearing a basic dimethylamino group serving as an acid inhibitor was also applicable, even though a prolonged reaction time was needed (entry 7). Therefore, the involvement of acidic co-catalysis could be excluded in our catalytic system.

**Table 3** Thioacetalization of Aldehydes Catalyzed by Cu(DS)$_2$ in Water[a]



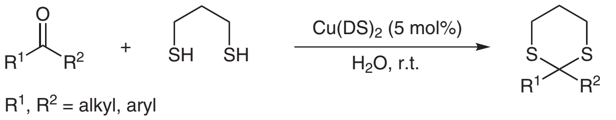
| Entry | Substrate | Time (min) | Yield[b] (%) |
|---|---|---|---|
| 1 | PhCHO | 15 | 95 |
| 2 | 4-$HOC_6H_4CHO$ | 30 | 92 |
| 3 | 4-$BrC_6H_4CHO$ | 40 | 93 |
| 4 | 4-$O_2NC_6H_4CHO$ | 40 | 95 |
| 5 | 4-$HOOCC_6H_4CHO$ | 40 | 93 |
| 6 | 4-$MeC_6H_4CHO$ | 20 | 94 |
| 7 | 4-$Me_2NC_6H_4CHO$ | 240 | 87 |
| 8 |  | 15 | 92 |
| 9 |  | 20 | 93 |
| 10 |  | 15 | 95 |
| 11 |  | 15 | 91 |
| 12 |  | 20 | 97 |
| 13 |  | 20 | 95 |
| 14 |  | 40 | 92 |

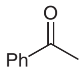
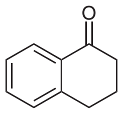
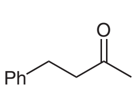
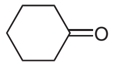
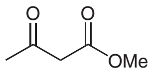
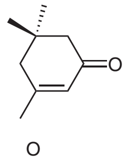
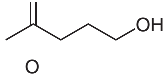
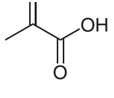
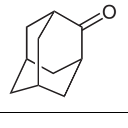
[a] All reactions were performed in $H_2O$ (at 0.5 M) at r.t. in the presence of 5 mol% catalyst.

[b] The yield refers to the isolated product.

Similarly, the Cu(DS)$_2$-catalyzed protection of different types of aromatic, aliphatic, cyclic, and α,β-unsaturated ketones to generate the corresponding 1,3-dithianes was performed with good yields (Table 4); however, longer reaction times were required compared to reactions involving aldehydes. For aromatic ketones such as acetophenone, α-tetralone, and benzophenone, the reactions were sluggish at room temperature (12–34%, entries 1–3); nevertheless, the yields could be improved by heating the reaction to 50 °C for 12 hours (entries 1 and 2, parentheses), although benzophenone did not react satisfactorily even after increasing the reaction time to 48 hours at 50 °C (entry 3, parentheses). For cyclic and acyclic aliphatic ketones bearing hydroxy, carboxylic acid, or ester groups, protection occurred without problem at room temperature, generating the corresponding thioketals in good or excellent yields (83–96%, entries 4–9). It is noteworthy that the double bond of isophorone remained intact under the reaction conditions (entry 7). In addition, the sterically hindered 2-adamantanone reacted but led to a moderate yield after 20 hours (71%, entry 10).

**Table 4** Thioacetalization of Ketones Catalyzed by $Cu(DS)_2$ in Water[a]



| Entry | Substrate | Time (h) | Yield[b] (%) |
|---|---|---|---|
| 1 |  | 20 (12[c]) | 34 (83[c]) |
| 2 |  | 20 (12[c]) | 26 (71[c]) |
| 3 | $Ph_2C{=}O$ | 20 (48[c]) | 12 (26[c]) |
| 4 |  | 8 | 87 |
| 5 |  | 8 | 86 |
| 6 |  | 6 | 92 |
| 7 |  | 12 | 83 |
| 8 |  | 6 | 96 |
| 9 |  | 8 | 90 |
| 10 |  | 20 | 71 |

[a] All reactions were performed in $H_2O$ (at 0.5 M) at r.t. in the presence of 5 mol% catalyst.

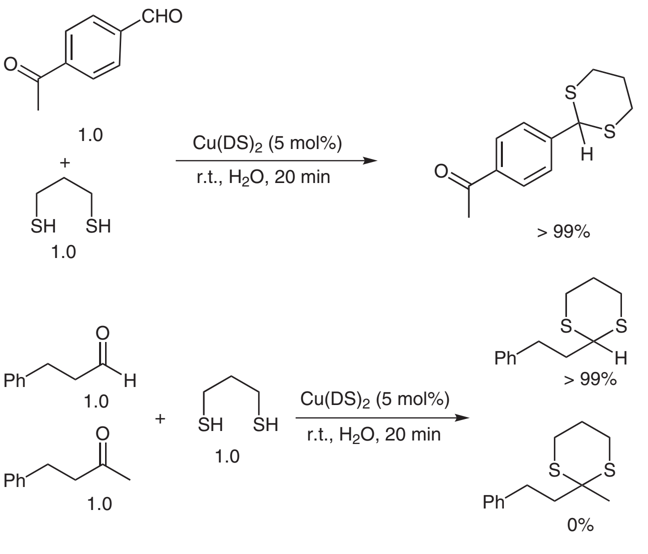
[b] The yield refers to the isolated product.

[c] Reaction conducted at 50 °C.

The transthioacetalization of *O*,*O*-acetals with 1,3-propanedithiol in water was also examined. Various *O*,*O*-acetals derived from aromatic or aliphatic carbonyl compounds underwent clean transthioacetalization with 1,3-propanedithiol in the presence of 5 mol% $Cu(DS)_2$ in water to provide the corresponding *S*,*S*-acetals and *S*,*S*-ketals in very high yields (90–97%, Table 5, entries 1–10).[35] The results indicate that acetals are more reactive than ketals (cf. entries 1–5 with 6, 7, and 10) and that acyclic acetals react faster than cyclic acetals (cf. entry 1 with 2). Whereas it is known that acetals tend to hydrolyze to the parent carbonyl compounds in the presence of excess water under acidic conditions,[1] in our system predominant fast transthioacetalization occurred without hydrolysis of the starting acetals, which suggests that the transthioacetalization does not proceed through a deacetalization–thioacetalization process even in the presence of excess water. This is due to the exclusion of water by the hydrophobic interior of the emulsion droplet of the $Cu(DS)_2$, preventing hydrolysis of the acetals. Thus, the lipophilic thiols would react with activated acetals inside the emulsion droplet and lead to efficient transthioacetalization.

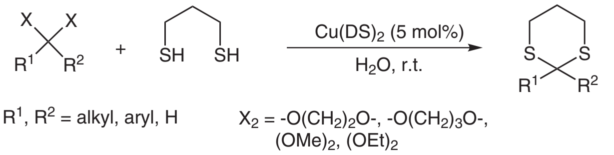
In order to examine the chemoselectivity of the present protocol, equimolar amounts of 4-acetylbenzaldehyde and 1,3-propanedithiol were reacted in water in the presence of 5 mol% $Cu(DS)_2$ for 20 minutes at room temperature. After workup, the crude reaction mixture was analyzed by $^1H$ NMR spectroscopy. It was observed that the formyl group was completely converted into the corresponding 1,3-dithiane and that the acetyl functionality remained unaffected. A similar chemoselectivity was also obtained when the experiment was performed on a mixture of 3-phenylpropanal and 4-phenyl-2-butanone as representative aliphatic substrates (Scheme 1).

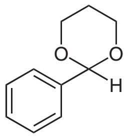
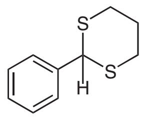
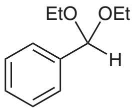
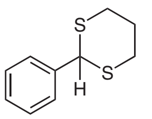
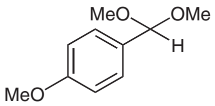
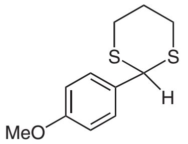
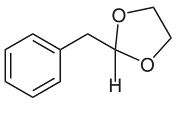
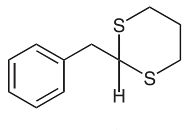
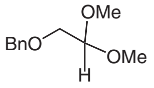
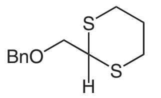
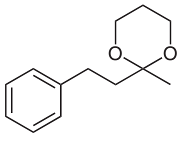
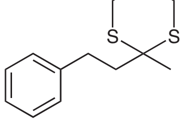
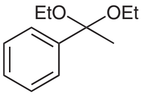
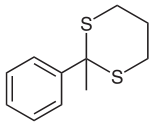
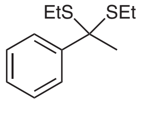
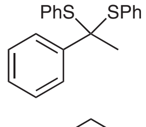
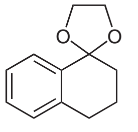
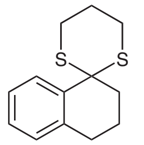
In the selective monothioacetalization of complex molecules, such as the steroid 4-androstene-3,17-dione with 1,2-propanedithiol, the predominant formation of the 3-dithiolane ketal has been reported.[36] In contrast, moderate



**Scheme 1** Chemoselective thioacetalization between aldehydes and ketones

**Table 5** Transthioacetalization of *O*,*O*-Acetals Catalyzed by $Cu(DS)_2$ in Water[a]



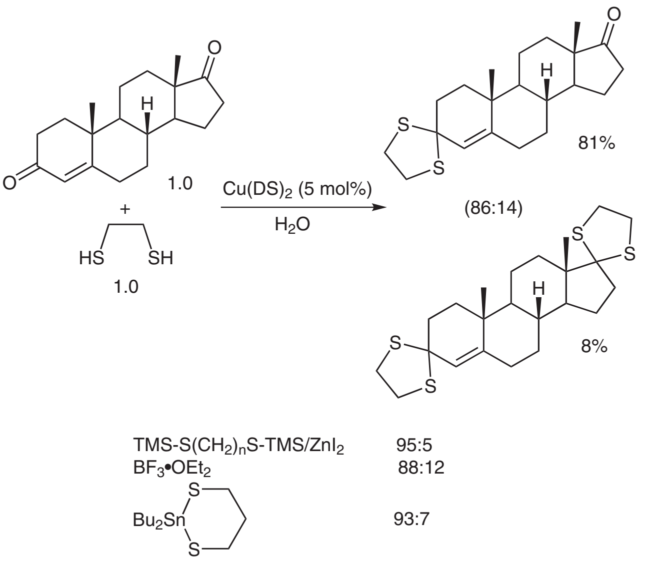
| Entry | Substrate | Time (min) | Product | Yield (%) |
|---|---|---|---|---|
| 1 |  | 10 |  | 95 |
| 2 |  | <5 |  | 97 |
| 3 |  | <5 |  | 96 |
| 4 |  | 15 |  | 94 |
| 5 |  | 15 |  | 96 |
| 6 |  | 35 |  | 97 |
| 7 |  | 20 |  | 92 |
| 8 |  | 15 |  | 94[b] |
| 9 |  | 15 |  | 95[c] |
| 10 |  | 50 |  | 90 |

[a] All reactions were performed in $H_2O$ (at 0.5 M) at r.t. in the presence of 5 mol% catalyst.

[b] EtSH (2.05 equiv) was used instead of 1,3-propanedithiol.

[c] PhSH (2.05 equiv) was used instead of 1,3-propanedithiol.

selectivity was found with our system, compared to reported results. Indeed, an 81% yield of the 3-monoketal, with only 8% of the bisketal was observed (Scheme 2).



**Scheme 2** Comparison of the selective monothioacetalization of 4-androstene-3,17-dione

In conclusion, we have demonstrated the use of the LASC-type $Cu(DS)_2$ catalyst for the synthesis of 1,3-dithianes of a variety of carbonyl compounds under mild conditions in water. The catalyst could be readily recovered and reused for five runs without loss of catalytic efficiency. In addition, the relatively low reaction rate of ketones allows the chemoselective protection of aldehydes in the presence of the ketone functionality. The present protocol offers an alternative for thioacetalization and transthioacetalization in water in terms of efficiency, operational simplicity, reusability of the catalyst, and environmental friendliness. These characteristics are valuable for potential applications in protection and industrial chemistry.

$^1H$ and $^{13}C$ NMR spectra were recorded in $CDCl_3$ on a Jeol JVM-EX400 spectrometer (400 MHz, $^1H$; 100 MHz, $^{13}C$) with $CHCl_3$ as an internal reference. Electron-impact (EI) mass spectra were recorded on a Thermo Finnigan spectrometer equipped with LCQ Advantage ionization and Spectra System detector systems. Analytical GC was carried out with an Agilent 6890C GC equipped with an Agilent DB-WAX column (30 m × 0.25 mm). Analytical GC-MS was carried out on a Varian CP-3800 GC/Saturn 2000 GC/MS spectrometer equipped with a CP-5860 column (30 m × 0.25 mm × 0.25 μm) using helium gas. Analytical TLC was visualized with UV light or with phosphomolybdic acid (PMA) and $KMnO_4$ staining agents. All reactions were run under nitrogen or argon atmosphere and the end products were isolated as pure materials.

### Copper Bis(dodecyl sulfate) [$Cu(DS)_2$][33]

To a soln of $CuCl_2$ (2.689 g, 20 mmol) in distilled $H_2O$ (20 mL) was added sodium dodecyl sulfate (SDS; 11.535 g, 40 mmol) at r.t. and the reaction mixture was stirred for 12 h. The aqueous solution was concentrated under reduced pressure at 60 °C. The resulting crude mixture was dissolved in EtOH (50 mL) and the NaCl precipitate was removed by filtration though a short pad of Celite®. The green filtrate was concentrated and dried under reduced pressure at 100 °C to give $Cu(DS)_2$ ($C_{24}H_{50}CuO_8S_2$, MW = 593) as a fine solid powder, which was used directly for the thioacetalization reactions.

ESI-MS: *m/z* = 616 $[M + Na]^+$.

### General Procedure for the Thioacetalization of Aldehydes

To a suspension of an aldehyde (10 mmol) and 1,3-propanedithiol (1136 mg, 10.5 mmol) in $H_2O$ (20 mL) was added $Cu(DS)_2$ (5 mol%; 296 mg, 0.5 mmol) at r.t. under $N_2$ atmosphere and vigorous stirring (>1200 rpm). The resulting colloidal dispersion was stirred at r.t. for an appropriate time (see Table 3) and the reaction was monitored by TLC, $^1H$ NMR spectroscopy, or GC-MS. After completion of the reaction, additional $H_2O$ (30 mL) was added to dilute the reaction mixture. The diluted reaction mixture was centrifuged for 30 min (4500 rpm) at r.t. and allowed to stand for a further 20 min. The supernatant aqueous solution was separated from the solid (or syrup-like) product by filtration on a glass filter. The crude product was washed, resuspended, and centrifuged with $H_2O$ (50 mL) twice. The analytically pure product was obtained by high-vacuum drying or by a Kugelrohr apparatus distillation (or sublimation) under reduced pressure. The products were characterized by $^1H$ and $^{13}C$ NMR spectroscopy, and MS analysis, and the data were identical with those of authentic samples.[15,26] The filtrated aqueous layer contains the $Cu(DS)_2$ which can be reused in subsequent thioacetalization reactions.

### General Procedure for the Thioacetalization of Ketones or the Transthioacetalization of *O*,*O*-Acetals

To a suspension of a ketone or an *O*,*O*-acetal (1 mmol) and 1,3-propanedithiol (114 mg, 1.05 mmol) in $H_2O$ (2 mL) was added $Cu(DS)_2$ (5 mol%; 29.6 mg, 0.05 mmol) at r.t. (or 50 °C) under $N_2$ atmosphere and vigorous stirring (>1200 rpm). The resulting colloidal dispersion was stirred for an appropriate time (see Tables 4 and 5) and the reaction was monitored by TLC or $^1H$ NMR spectroscopy. After completion of the reaction, additional $H_2O$ (5 mL) was added to dilute the reaction mixture. The diluted reaction mixture was centrifuged for 30 min (4500 rpm) at r.t. and allowed to stand for a further 20 min. The supernatant aqueous solution was separated from the solid (or syrup-like) product by filtration on a glass filter. The crude product was washed, resuspended, and centrifuged with $H_2O$ (20 mL) twice. The analytically pure product was obtained by high-vacuum drying or by a Kugelrohr apparatus distillation (or sublimation) under reduced pressure.

### Typical Procedure for the Competitive Thioacetalization of Aldehyde and Ketone

To a suspension of 4-acetylbenzaldehyde (148 mg, 1.0 mmol) and $Cu(DS)_2$ (5 mol%; 29.6 mg, 0.05 mmol) in $H_2O$ (2 mL) was added 1,3-propanedithiol (108 mg, 1.0 mmol) at r.t. under $N_2$ atmosphere and vigorous stirring (>1200 rpm), and the reaction was monitored by $^1H$ NMR spectroscopy. The resulting mixture was stirred for 20 min until the formyl group of the 4-acetylbenzaldehyde was totally consumed (determined by $^1H$ NMR spectroscopy). The reaction mixture was diluted with $H_2O$ (30 mL) and centrifuged for 30 min (4500 rpm) at r.t. The crude product was collected by filtration, then washed with $H_2O$, resuspended, and vacuum dried under reduced pressure. The formyl-protected dithiane was obtained in 99% yield and was identified by a comparison of its spectroscopic data with those of an authentic sample.[15]

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