Chemoselective Protection of Aldehydes as Dithioacetals in Lithium Perchlorate–Diethyl Ether Medium. Evidence for the Formation of Oxocarbenium Ion Intermediate from Acetals†

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Aldehydes and acetals were very efficiently converted to acyclic and cyclic dithioacetals in 5 M lithium perchlorate/diethyl ether (LPDE) medium at ambient temperature in high yields. Spectroscopic and other experimental evidences strongly suggest the formation of oxocarbenium ion intermediates from acetals in 5 M LPDE which subsequently reacted with thiols to give the dithioacetals. Under the same conditions ketones and their acetals also reacted, albeit very slowly compared to aldehydes and acetals, to yield dithioacetals. The difference in their reactivity was successfully employed in the chemoselective dithioacetalization of aldehydes and acetals in the presence of ketones and their acetals. The chemoselective dithioacetalization of keto aldehydes has been realized with the keto group remaining intact. The present method offers a convenient, efficient, and neutral medium for the deprotection of acetals to aldehydes and also the chemoselective protection of aldehydes to dithioacetals.

Introduction

Protection and deprotection of functional groups are indispensable ingredients of the synthesis of polyfunctional compounds.[1] The protection of carbonyl groups as acetals and dithioacetals is an important synthetic method.[2] Dithioacetals often serve as protecting groups as well as masked acyl anions in organic synthesis.[3] Though a number of methods using protic and Lewis acids have been developed for the protection of aldehydes and ketones as dithioacetals,[1,2] chemoselective thioacetalization methods capable of discerning aldehydes from ketones have been rare.[4] Moreover, dithioacetalization of aldehydes under neutral conditions has not been reported. In recent years the use of lithium perchlorate in diethyl ether (LPDE)[5] as a medium has attracted attention due to the enhanced rate and selectivity observed for Diels–Alder and other cycloadditions,[6] sigmatropic rearrangement,[7] Michael addition,[8] and aldol condensation.[9] We have focused our attention on the use of LPDE medium for carbonyl activation. In this paper we wish to report a mild, efficient, and very chemoselective conversion of aldehydes and acetals to dithioacetals in LPDE medium. The present method offers a convenient procedure for the preparation of dithioacetals under essentially neutral reaction and workup conditions compared to the acidic workup involved in conventional Lewis acid catalyzed thioacetalization.

Chart 1

aldehydes: RCHO

R		R	X	
C_6H_5	**4a**	C_6H_5	S	**4b**
p-$NO_2C_6H_4$	**5a**	p-$MeOC_6H_4$	S	**7b**
p-ClC_6H_4	**6a**	3,4-$(MeO)_2C_6H_3$	S	**8b**
p-$MeOC_6H_4$	**7a**	$C_6H_5CH{=}CH$	S	**9b**
3,4-$(MeO)_2C_6H_3$	**8a**	$(CH_3)_2CH$	S	**10b**
$C_6H_5CH{=}CH$	**9a**			
$(CH_3)_2CH$	**10a**	C_6H_5	O	**12a**

Acyclic acetals and dithioacetals: $RCH(XR')_2$

R	R′	X		R	R′	X	
C_6H_5	n-Bu	S	**4c**	C_6H_5	Ph	S	**4d**
p-$NO_2C_6H_4$	n-Bu	S	**5c**				
p-ClC_6H_4	n-Bu	S	**6c**				
p-$MeOC_6H_4$	n-Bu	S	**7c**	p-$MeOC_6H_4$	Ph	S	**7d**
				3,4-$(MeO)_2C_6H_3$	Ph	S	**8d**
$C_6H_5CH{=}CH$	n-Bu	S	**9c**	$C_6H_5CH{=}CH$	Ph	S	**9d**
$(CH_3)_2CH$	n-Bu	S	**10c**	$(CH_3)_2CH$	Ph	S	**10d**
C_6H_5	Me	O	**11a**	p-$MeOC_6H_4$	Et	O	**13a**
3,4-$(MeO)_2C_6H_3$	Et	O	**14a**	$C_6H_5CH{=}CH$	Et	O	**15a**
$(CH_3)_2CH$	Et	O	**16a**				

Results and Discussion

The reactions were carried out in 5 M LPDE solution. 1,2-Ethanedithiol (**1**), 1-butanethiol (**2**), and thiophenol (**3**) were used as reagents for thioacetalization. The structures of the carbonyl compounds and their derivatives are given in Charts 1–3..

† Dedicated to Prof. V. Ramakrishnan, Department of Chemistry, IIT, Madras, on the occasion of his 60th birthday.

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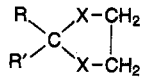
Chart 2

ketones

R-CO-R′

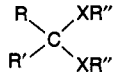
R	R′		
Ph	Me	**17a**	
$PhCH_2$	$PhCH_2$	**18a**	
R- - -R′ = $-(CH_2)_5-$		**19a**	

cyclic acetals and dithioacetals



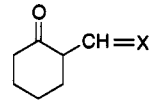
R	R′	X	
Ph	Me	O	**20a**
Ph	Me	S	**17b**
$PhCH_2$	$PhCH_2$	O	**21a**
$PhCH_2$	$PhCH_2$	S	**18b**
Me	Me	S	**22b**

Acyclic acetals and dithioacetals



R	R′	R″	X	
Ph	Me	n-Bu	S	**17c**
Ph	Me	Ph	S	**17d**
$PhCH_2$	$PhCH_2$	n-Bu	S	**18c**
$PhCH_2$	$PhCH_2$	Ph	S	**18d**
R- - -R′ = $-(CH_2)_5-$		n-Bu	S	**19c**
Me	Me	Me	O	**22a**
Me	Me	n-Bu	S	**22c**
Me	Me	Ph	S	**22d**

Chart 3. Ketoaldehydes and Their Dithioacetal Derivatives



p-$MeCOC_6H_4CH{=}X$

X = O **23a**

X = $-SCH_2-SCH_2$ **23b**

$RCO(CH_2)_4CH{=}X$

R = Me, X = O **24a**

R = Me, X = $-SCH_2-SCH_2$ **24b**

R = Ph, X = O **25a**

R = Ph, X = $-SCH_2-SCH_2$ **25b**

X = O **26a**

X = $-SCH_2-SCH_2$ **26b**

Thioacetalization of Aldehydes in LPDE. When equimolar amounts of benzaldehyde (**4a**) and dithiol **1** were mixed in 5 M LPDE at room temperature under nitrogen atmosphere, within 15 min the starting materials disappeared and TLC indicated the formation of a single product. After aqueous workup, the crude product was isolated (77%) and characterized as the cyclic dithioacetal **4b**. The crude product was essentially pure as indicated by TLC and the ^{1}H-NMR spectrum. Similarly, when the reaction was carried out with 2 equiv of **2** or **3** the corresponding acyclic dithioacetals **4c** and **4d** were obtained in 86 and 90% yield, respectively (eq 1). Table

$$RCHO + 2R'SH \xrightarrow[rt]{5\ M\ LPDE} RCH(SR')_2 + H_2O \quad (1)$$

1 summarizes the results obtained in the thioacetalization of various aldehydes. In Table 1 a few points are noteworthy. The thioacetalization reaction proceeded with the same facility in 2.5 M LPDE as in 5 M solution (Table 1, entry 2). While aldehydes **4a**, **5a**, and **6a** underwent the thioacetalization reaction smoothly within 15 min, **7a** and **8a** did not react under the same conditions. While **7a** reacted with thiol **3** to yield dithioacetal **7d** in 16% yield after 14 h, aldehyde **8a** did not react at all even after 2 days of stirring at room temperature. In order to activate these substrates for thioacetalization, we explored the possibility of using the corresponding acetals, since the Lewis acid mediated

Table 1. Thioacetalization of Aldehydes in 5 M LPDE at 28 °C

aldehyde	thiol	dithioacetal	yield[a]	duration[b]
4a	**1**	**4b**	77	15
4a	**1**	**4b**	75	15[c]
4a	**2**	**4c**	86	15
4a	**3**	**4d**	90	15
5a	**2**	**5c**	95	10
6a	**2**	**6c**	85	10
7a	**3**	**7d**	16[d]	14 h
8a	**3**	**8d**	0[d]	2 days
9a	**2**	**9c**	20[d]	25
9a	**2**	**9c**	80[d]	2 days
10a	**2**	**10c**	90	10

[a] Isolated yield (%) of the dithioacetal. [b] In minutes unless otherwise indicated. [c] in 2.5 M LPDE. [d] Remainder unreacted aldehyde.

Table 2. Thioacetalization of Acetals in 5 M LPDE at 28 °C

acetal	thiol	dithioacetal	yield[a]	duration (min)
11a	**1**	**4b**	86	10
11a	**2**	**4c**	83	10
11a	**3**	**4d**	82	10
12a	**1**	**4b**	75	40
12a	**2**	**4c**	87	15
12a	**3**	**4d**	87	30
13a	**1**	**7b**	81	15
13a	**2**	**7c**	91	10
13a	**3**	**7d**	80	10[b]
14a	**1**	**8b**	92	10[c]
15a	**1**	**9b**	87	20
15a	**2**	**9c**	70	15
15a	**3**	**9d**	70	15
16a	**1**	**10b**	95	20
16a	**2**	**10c**	83	10
16a	**3**	**10d**	82	10

[a] Isolated yield (%) of the dithioacetal. [b] 20% of **7a** was formed. [c] 5% of **8a** was formed.

activation of acetals is well known.[10] Using lithium ion as the Lewis acid and the thiols as nucleophiles, we systematically investigated the thioacetalization of acetals in LPDE medium.

Thioacetalization of Acetals in LPDE. When equimolar amounts of acetal **11a** and **1** were mixed in 5 M LPDE at room temperature the starting materials disappeared within 20 min, and TLC and the ^{1}H-NMR spectrum of the crude product obtained after aqueous workup indicated a single product (86%) identified as the cyclic dithioacetal **4b**. Similarly, the reaction proceeded smoothly with 2 equiv of the thiols **2** and **3** to furnish the corresponding dithioacetals **4c** and **4d** in 83 and 82%, respectively (eq 2). In all these cases the crude product

$$RCH(OR')_2 + 2R''SH \xrightarrow[rt]{5\ M\ LPDE} RCH(SR'')_2 + 2R'OH \quad (2)$$

was sufficiently pure (TLC and ^{1}H-NMR) and further purification was not necessary. Table 2 summarizes the results obtained in the thioacetalization of various acetals. It is noteworthy that the *p*-methoxybenzaldehyde diethyl acetal (**13a**) reacted with thiols **1**, **2**, and **3** to give **7b**, **7c**, and **7d**, respectively, in good yields, whereas the aldehyde (**7a**) itself did not undergo thioacetalization in 5 M LPDE. Similarly, acetal **14a** reacted with thiol **1** to

(10) Mori, I.; Ishihara, K.; Flippin, L. A.; Nozaki, K.; Yamamoto, H.; Bartlett, P. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 6107 and references cited therein. Sammakia, T.; Smith, R. S. *J. Org. Chem.* **1992**, *57*, 6107.

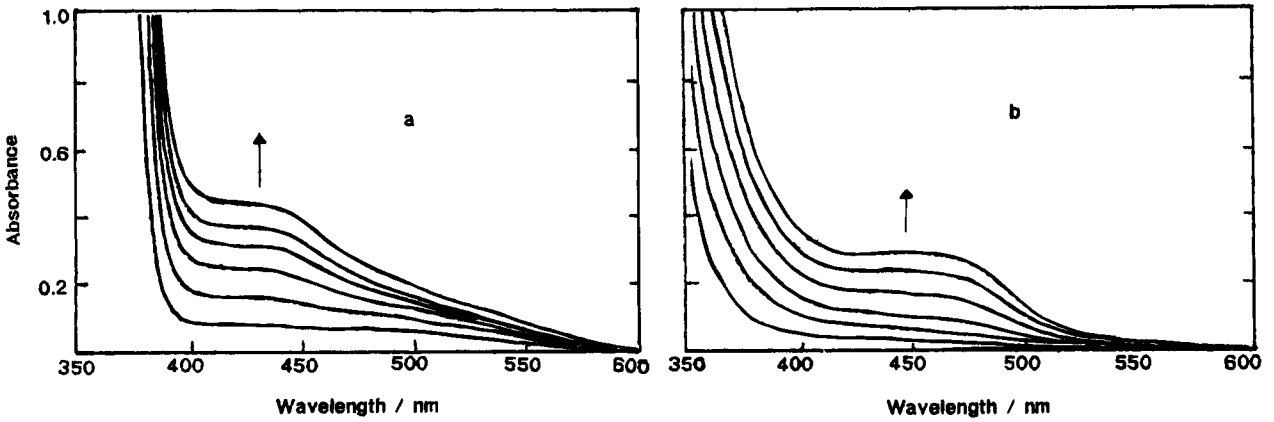


Figure 1. Spectral changes observed upon addition of (a) **13a** (0.47, 0.95, 1.43, 1.90, 2.38, 2.85 M) and (b) **11a** (0.65, 1.30, 1.97, 2.63, 3.29, 3.95 M) to 5 M LPDE under nitrogen atmosphere at ambient temperature.

Table 3. Thioacetalization of Ketones and Acetals in 5 M LPDE at 28 °C

ketone/acetal	thiol	dithioacetal	yield (%)	duration (h)
17a	**2**	**17c**	0	17
18a	**2**	**18c**	0	20
19a	**2**	**19c**	0	1
19a	**2**	**19c**	95	24
20a	**1**	**17b**	87	24
20a	**2**	**17c**	92	14
20a	**3**	**17d**	85	16
21a	**1**	**18b**	0	36
21a	**2**	**18c**	0	20
21a	**3**	**18d**	0	20
22a	**1**	**22b**	71[a]	15 min
22a	**2**	**22c**	90[a]	15 min
22a	**3**	**22d**	90[a]	15 min

[a] Yields based on thiol as the limiting reagent, as **22a** is volatile.

give the cyclic dithioacetal **8b** in 92% yield within 10 min, whereas the aldehyde **8a** failed to react under identical conditions. Furthermore, addition of colorless **13a** to 5 M LPDE resulted in the immediate development of a pinkish red color. Similarly, addition of colorless benzaldehyde dimethyl acetal (**11a**) resulted in the immediate development of bright yellow color. These color changes are exemplified in Figure 1 which illustrates the changes in the absorbance with increasing concentration of the acetals. Addition of thiols to these colored solutions led to the bleaching of the color with the concomitant formation of the dithioacetals.

Encouraged by these results on the thioacetalization of aldehydes and acetals we proceeded to investigate the thioacetalization of ketones and their acetals in LPDE medium.

Thioacetalization of Ketones and Their Acetals in LPDE. When a mixture of acetophenone (**17a**) and 2 equiv of **2** was stirred at room temperature in 5 M LPDE, no reaction was observed up to 17 h, and the starting materials were recovered intact after workup. On the other hand, the cyclic acetal **20a** reacted very slowly with the thiols and gave the dithioacetals in excellent yields. Cyclohexanone (**19a**) reacted slowly with **2** and yielded **19c** in 95% yield after 24 h. Table 3 summarizes the results of the thioacetalization of ketones and their acetals. 2,2-Dimethoxypropane (**22a**) is an exception among the acetals that were studied, because it reacted with the thiols within 15 min and furnished the dithioacetals (**22b–d**) in very good yields.

Upon comparison of the data in Tables 1–3 it is clear that the aldehydes and acetals differ vastly in their

Table 4. Thioacetalization of Keto Aldehydes with 1,2-Ethanedithiol in 5 M LPDE at 28 °C

keto aldehyde	product	yield (%)	duration (min)
23a	**23b**	75	20
24a	**24b**	90	60
25a	**25b**	85	30
26a	**26b**	80	30

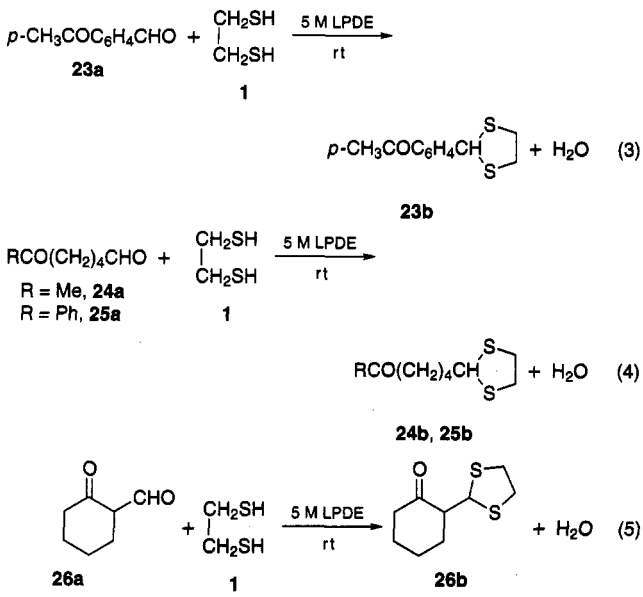
reactivity toward thiols compared to the ketones and their acetals. This prompted us to investigate the possible chemoselective thioacetalization of aldehydes in the presence of ketones.

Competitive Thioacetalization of Aldehydes and Acetals. When an equimolar mixture of the acetals **12a** and **20a** (1 mmol each) was allowed to react with **2** (2 mmol) in 5 M LPDE and the reaction mixture was worked up after stirring at room temperature for 30 min, analysis of the crude product by TLC and ^{1}H-NMR spectroscopy indicated the complete disappearance of acetal **12a** and **2**. The crude product consisted of a 1:1 mixture of the dithioacetal **4c** and the unreacted acetal **20a**. Similar experiments with a 1:1 mixture of benzaldehyde (**4a**) and acetophenone (**17a**) (2 mmol each) with **2** (4 mmol) resulted in the complete conversion of **4a** to **4c** while **17a** remained intact. These experiments clearly indicated the possibility of chemoselective protection of aldehydes as dithioacetals in keto aldehydes in LPDE.

Selective Thioacetalization of Aldehydes in Keto Aldehydes. In order to check the chemoselectivity of thioacetalization, keto aldehydes **23a–26a** were allowed to react with **1** in 5 M LPDE. For example, when a mixture of **23a** and **1** (2 mmol each) was stirred at room temperature, the starting materials disappeared after 20 min and the cyclic dithioacetal **23b** was obtained as the sole product in 75% yield. TLC and ^{1}H-NMR spectrum of the crude product showed the absence of any other side products. Table 4 shows the results obtained with the keto aldehydes, and from the data it is apparent that in all the cases the aldehyde carbonyl is very selectively protected as dithioacetal leaving the keto carbonyl intact (eqs 3–5).

Mechanism of Thioacetalization of Aldehydes in LPDE. The activation of the carbonyl group for nucleophilic addition by Bronsted and Lewis acids is well known.[11] Nucleophilic substitution of acetals is also known to be catalyzed by acids.[10,12] Lithium ion can act

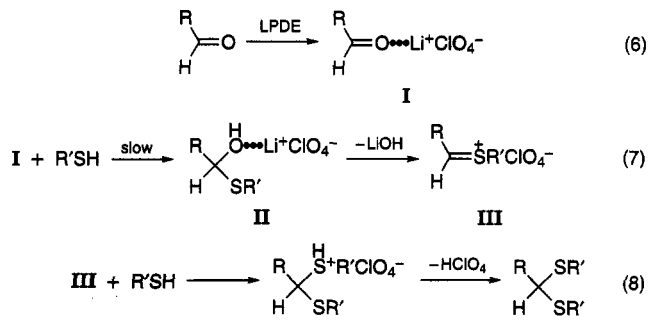
(11) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper and Row: New York, 1981; p 595.



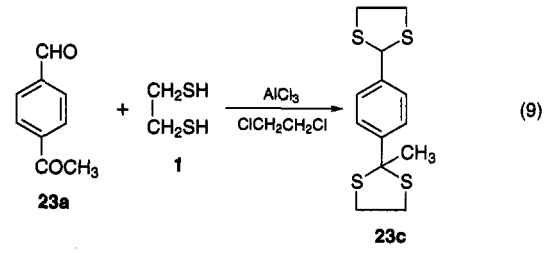
as a Lewis acid (hard acid), and by coordination to the carbonyl oxygen (hard base) it can activate the carbonyl functionality. In fact, metal hydride reduction of the carbonyl group is known to be catalyzed by the addition of lithium salts in aprotic solvents due to the increased electrophilicity of the carbonyl carbon upon lithium coordination.[13] In the present study, evidence for the Lewis acidity of lithium ion comes from the IR spectroscopic studies in 5 M LPDE. The carbonyl stretching frequency for benzaldehyde is 1708 cm^{-1} in ether compared to 1699 cm^{-1} in 5 M LPDE and that for isobutyraldehyde is 1734 cm^{-1} in ether compared to 1718 cm^{-1} in 5 M LPDE. Such a decrease in the carbonyl stretching frequency is consistent with the lithium coordination to the carbonyl oxygen. A similar conclusion has been reported based on IR and NMR spectroscopic studies of carbonyl compounds in solutions of lithium perchlorate.[14] The experimental observations are also consistent with the results from the theoretical calculations on the Lewis acidity of lithium ion.[14,15] On the basis of these evidences we propose the following mechanism for the dithioacetal formation from aldehydes in LPDE (Scheme 1). Though lithium perchlorate is solvated and likely to form ionic aggregates in 5 M LPDE,[16] for the sake of simplicity such details are not included in Scheme 1. The addition of the second molecule of thiol to **III** is likely to be a fast step because the hemithioacetal could not be isolated when only 1 equiv of the thiol was used. Thus, the reaction of **4a** with 1 equiv of **2** gave a 1:1 mixture of the dithioacetal **4c** and unreacted **4a**.

The gas-phase Lewis acidity of lithium ion is higher compared to that of the conventional Lewis acids such as $AlCl_3$ and BF_3. However, in a coordinating solvent such as ether its Lewis acidity is moderated and it is lower than that of $AlCl_3$ and BF_3. Lewis acids such as

Scheme 1



$AlCl_3$ and BF_3 do not show any selectivity between an aldehyde and a ketone. The dithioacetals of several ketones have been synthesized using $AlCl_3$ or $BF_3{\cdot}Et_2O$ as the catalyst at ambient temperature.[17] The reaction of ketoaldehyde **23a** with dithiol **1** in the presence of $AlCl_3$ yielded the bis-dithioacetal **23c** (eq 9).



However, in 5 M LPDE the reaction of **23a** with excess of **1** yielded only **23b**. The selectivity observed in the present study between aldehyde and ketone could be attributed to the moderate Lewis acidity of lithium ion combined with the steric effects associated with the addition of nucleophiles to the ketonic carbonyl group. Evidence for lithium ion coordination to oxygen of the ketonic carbonyl comes from the observed shift in the carbonyl stretching frequency in the IR spectrum from 1721 cm^{-1} in ether to 1712 cm^{-1} in 5 M LPDE for **18a**. The coordination of the solvated lithium ion would tend to increase the steric crowding around the carbonyl carbon, thus decreasing the reactivity of the ketonic carbonyl compared to an aldehydic carbonyl group. The reduced reactivity of **7a** and **8a** compared to **4a** is due to the electronic effects of the methoxy substituents which deactivate the carbonyl group toward nucleophilic addition.[11]

Mechanism of Thioacetalization of Acetals in LPDE. The Lewis acid mediated cleavage of acetals is a synthetically useful C—C bond-forming reaction.[10,12] The dithioacetalization of acetal could proceed either by the direct substitution of acetal coordinated to lithium ion (S_N2 type) by thiol or through the initial formation of an oxocarbenium ion intermediate (S_N1 type). These two extreme mechanistic possibilities are depicted in Scheme 2. Winstein and co-workers[18] have reported that the LPDE medium accelerated the ionization of *p*-methoxyneophyl *p*-toluenesulfonate. Similarly, Pocker and co-workers[19] have reported a 10^9-fold increase in the ionization of trityl chloride in LPDE medium compared to pure ether. In a recent report on the asymmetric

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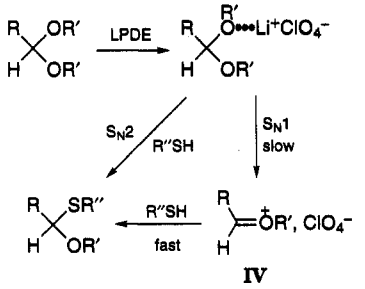
Scheme 2



IV

cleavage of chiral acetals, direct evidence for an oxocarbenium ion intermediate has been reported.[20] The Lewis acidity of lithium ion combined with the high ionic strength of LPDE medium would favor the formation of ionic intermediates such as **III** (Scheme 1) and **IV** (Scheme 2). Evidence for the formation of an oxocarbenium ion intermediate comes from the spectrophotometric studies on acetals **11a** and **13a**. Figure 1 illustrates the color changes associated with the addition of colorless acetals **11a** and **13a** to 5 M LPDE. We attribute these color changes to the formation of the corresponding oxocarbenium ion from **11a** and **13a** in LPDE medium. Exposure of these colored solutions to moisture led to bleaching with the formation of **4a** and **7a** from **11a** and **13a**, respectively. Similarly, addition of thiols led to bleaching of the color with the concomitant formation of the corresponding dithioacetal. These observations are best explained by invoking the formation of an intermediate oxocarbenium ion from acetals in 5 M LPDE.

The observed enhanced reactivity of the acetals **13a** and **14a** (Table 2) compared to the corresponding aldehydes **7a** and **8a** (Table 1) is best interpreted by involving the formation of an oxocarbenium ion intermediate in the rate-determining step followed by the addition of the thiol (Scheme 2). The methoxy substituents on the aromatic ring of **13a** and **14a** would tend to facilitate the formation of the oxocarbenium ion intermediate as the incipient positive charge can be stabilized by resonance. Compared to a lithium-coordinated carbonyl group, the oxocarbenium ion is likely to be a more reactive electrophile toward thiols.[21] Furthermore, the enhanced reactivity of acetal **20a** compared to ketone **17a** (Table 3) can be attributed to the formation of the corresponding oxocarbenium ion intermediate, which unlike the ketone **17a**, does not require any activation through lithium ion coordination for the addition of thiol. The inability of acetal **21a** to undergo reaction in 5 M LPDE might be purely due to steric hindrance.

Conclusions

The lithium perchlorate/diethyl ether medium has been found to be very effective for the dithioacetalization of aldehydes and acetals. Formation of oxocarbenium ion intermediates from acetals in 5 M LPDE has been suggested based on the spectroscopic and experimental evidences. Chemoselective conversion of aldehydes and acetals to dithioacetals in the presence of ketones and their acetals has been demonstrated. The striking chemoselectivity of the present reaction is utilized in the selective conversion of keto aldehydes to dithioacetals with the keto group remaining intact.

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Experimental Section

Materials. $LiClO_4 \cdot 3H_2O$ was prepared by the neutralization of an aqueous solution of LiOH with 70% aqueous $HClO_4$ and concentrating the resulting solution in the rotary evaporator. Anhydrous $LiClO_4$ was obtained by drying the trihydrate under vacuum in a drying pistol over refluxing xylene for 12 h. Anhydrous ether was prepared by refluxing and distilling reagent-grade ether over sodium wire and storing it under nitrogen over sodium wire. Carbonyl compounds **4a**–**10a**, **17a**, and **19a**, acetal **22a**, and thiols **1**–**3** were commercial samples and were purified by distillation (or recrystallization in case of solids) prior to use. Ketones **18a**,[22] **23a**,[23] **24a**–**25a**,[24] and **26a**[25] and acetals **11a**–**12a**,[10,26] **13a**–**16a**,[27] and **20a**–**21a**[26,28] were prepared according to literature reported methods and were characterized by IR, ^{1}H-NMR, and mass spectral data. Authentic samples of **4c**, **4d**, **9d**, **10c**, and **18d** were available from our previous study.[29]

Preparation of 5 M LPDE. Anhydrous $LiClO_4$ (27 g) and diethyl ether (50 mL) were cooled in an ice bath separately under nitrogen atmosphere, and then the ice-cold ether was added very slowly to $LiClO_4$ from a syringe. The dissolution was highly exothermic. The clear, viscous solution was stored in a desiccator. The density of the solution thus prepared was 1.0 g/mL.

General Procedure for the Reaction of Carbonyl Compounds with Thiols in 5 M LPDE. To a stirred solution of the thiol (2 mmol in case of **2** and **3** and 1mmol in case of **1**) in 2 mL of 5 M LPDE under nitrogen atmosphere was added the carbonyl compound (1 mmol) from a syringe. The reaction mixture was stirred at ambient temperature for the duration indicated in Tables 1–4, during which time the reaction was followed by TLC for the disappearance of starting materials. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and cooled in an ice bath, and then water was added slowly. The organic layer was separated, and the aqueous layer was extracted three times with CH_2Cl_2 (10 mL each). The combined organic extract was washed with 10% aqueous NaOH, followed by water. The organic layer was dried over anhydrous Na_2SO_4, and solvent was removed at the rotary evaporator to yield the crude product. In most cases the reaction yielded the dithioacetal in pure form as indicated by TLC and IR and ^{1}H-NMR spectral data. The crude product was further purified by column chromatography. The same procedure was followed for the reaction of the acetals and keto aldehydes with thiols.

Competitive Thioacetalization Reactions. To a mixture of **12a** and **20a** (1 mmol each) in 4 mL of 5 M LPDE was added thiol **2** (2 mmol), and the mixture was stirred at ambient temperature for 30 min and worked up as described above. TLC of the crude product indi-

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cated the absence of **12a** and **2** and the presence of **20a** and **4c**. From the ^{1}H-NMR spectral integration the ratio of **20a** to **4c** was found to be 1:1. The ^{1}H-NMR spectrum of the crude product matched with that of a 1:1 mixture of authentic **20a** and **4c**. The same result was obtained when the reaction was repeated with thiol **2** taken in excess (5 mmol). Similarly, when the reaction was repeated with a 1:1 mixture of **4a** and **17a** with thiol **2**, the crude product consisted of a 1:1 mixture of dithioacetal **4c** and ketone **17a**.

Physical and Spectroscopic Characterization of Products. **4b**:[4,30] ^{1}H-NMR (CCl_4) δ 7.35 (m, 5H), 5.55 (s, 1H), 3.39 (m, 4H); MS (70 eV) m/z 182 (M^+, 13), 121 (56), 119 (100), 117 (98). **4c**:[31] ^{1}H-NMR (CCl_4) δ 7.28 (m, 5H), 4.77 (s, 1H), 2.48 (m, 4H), 1.49 (m, 8H), 0.9 (m, 6H); MS (70 eV) m/z 268 (M^+, 13), 224 (53), 180 (99), 131 (100). **4d**:[29] mp 51–52 °C (lit.[29] mp 51–52 °C); ^{1}H-NMR (CCl_4) δ 7.22 (s, 15H), 5.31 (s, 1H); MS (70 eV) m/z 199 (M^+ – SPh, 100), 166 (15), 165 (18), 121 (16), 77 (14). **5c**:[31] IR (neat) 1523 and 1347 (NO_2) cm^{-1}; ^{1}H-NMR (CCl_4) δ 8.13 (d, 2H, J = 8.4 Hz), 7.51 (d, 2H, J = 8.4 Hz), 4.79 (s, 1H), 2.48 (m, 4H), 1.43 (m, 8H), 0.86 (m, 6H); MS (70 eV) m/z 313 (M^+, 23), 224 (M^+ – SBu, 100), 182 (65), 178 (75). **6c**:[32] ^{1}H-NMR (CCl_4) δ 7.26 (s, 4H), 4.74 (s, 1H), 2.48 (m, 4H), 1.43 (m, 8H), 0.86 (m, 6H); MS (70 eV) m/z 304 (9), 302 (M^+, 24), 216 (50), 215 (94), 214 (78), 213 (100), 177 (71), 158 (56), 156 (80), 138 (60), 121 (58). **7b**:[4,33] mp: 59–60 °C (lit.[33] mp 60–61 °C); ^{1}H-NMR (CCl_4) δ 7.41 (d, 2H, J = 8.4 Hz), 6.69 (d, 2H, J = 8.4 Hz), 5.56 (s, 1H), 3.79 (s, 3H), 3.40 (m, 4H); MS (70 eV) m/z 214 (80), 213 (83), 212 (M^+, 100), 211 (78), 186 (50), 185 (60), 184 (88), 181 (55), 152 (84), 150 (82), 108 (46). **7c**:[31] ^{1}H-NMR (CCl_4) δ 7.28 (d, 2H, J = 9 Hz), 6.75 (d, 2H, J = 9 Hz), 4.74 (s, 1H), 3.76 (s, 3H), 2.47 (m, 4H), 1.47 (m, 8H), 0.88 (m, 6H); MS (70 eV) m/z 182 (100), 179 (44), 154 (81), 153 (91), 120 (75). **7d**: mp 79–80 °C; ^{1}H-NMR (CCl_4) δ 7.18 (m, 12H), 6.68 (d, 2H, J = 9.6 Hz), 5.29 (s, 1H), 3.68 (s, 3H); MS (70 eV) m/z 231 (14), 230 (30), 229 (M^+ – SPh, 100); HRMS calcd for $C_{20}H_{18}OS_2$ 338.0800, found 338.0766. **8b**:[30] mp 58–59 °C (lit.[30] mp 62–65 °C); ^{1}H-NMR (CCl_4) δ 6.85 (m, 3H), 5.50 (s, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 3.38 (m, 4H); MS (70 eV) m/z 242 (M^+, 100), 211 (64), 199 (25), 183 (77), 182 (50), 181 (54). **9b**:[4,33] mp 58–59 °C (lit.[33] mp 59–59.5 °C); ^{1}H-NMR (CCl_4) δ 7.26 (m, 5H), 6.52 (d, 1H, J = 13.8 Hz), 6.00 (dd, 1H, J = 13.8, 6.6 Hz), 5.12 (d, 1H, J = 6.6 Hz), 3.27 (m, 4H); MS (70 eV) m/z 208 (M^+, 100), 147 (86), 116 (87). **9c**: ^{1}H-NMR (CCl_4) δ 7.26 (m, 5H), 6.48 (d, 1H, J = 14.4 Hz), 6.0 (dd, 1H, J = 14.4, 8.4 Hz), 4.35 (d, 1H, J = 8.4 Hz), 2.58 (m, 4H), 1.55 (m, 8H), 0.92 (m, 6H); MS (70 eV) m/z 178 (66), 122 (48), 119 (50), 117 (100), 82 (25), 57 (58); HRMS calcd for $C_{17}H_{26}S_2$ 294.1478, found 294.1464. **9d**: [29] mp 64 °C; ^{1}H-NMR (CCl_4) δ 7.26 (m, 15H), 6.11 (m, 2H), 4.88 (m, 1H); MS (70 eV) m/z 225 (M^+ – SPh, 100), 146 (75), 134 (62), 115 (75), 114 (80), 108 (60), 90 (64). **10b**: ^{1}H-NMR (CCl_4) δ 4.32 (d, 1H, J = 6.6 Hz), 3.13 (s, 4H), 1.80 (m, 1H), 1.03 (d, 6H, J = 6.0 Hz); MS (70 eV) m/z 148 (M^+, 52), 107 (16), 105 (100); HRMS calcd for $C_6H_{12}S_2$ 148.0382, found 148.0371. **10c**:[29] ^{1}H-NMR (CCl_4) δ 3.48 (d, 1H, J = 4.2 Hz), 2.53 (m, 4H), 2.05 (m, 1H), 1.49 (m, 8H), 0.96 (m, 12H); MS (70 eV) m/z 234 (M^+, 36), 145 (M^+ – SBu, 100), 89 (44). **10d**:[34] ^{1}H-NMR ($CDCl_3$) δ 7.25 (m, 10H), 4.27 (d, 1H, J = 3 Hz), 2.20 (m, 1H), 1.13 (d, 6H, J = 6.6 Hz). **17b**:[4] ^{1}H-NMR (CCl_4) δ 7.69 (m, 2H), 7.20 (m, 3H), 3.32 (m, 4H), 2.09 (s, 3H); MS (70 eV) m/z 196 (M^+, 88), 181 (91), 168 (60), 167 (79), 136 (45), 121 (100), 119 (70), 117 (68), 103 (50), 77 (40). **17c**: ^{1}H-NMR (CCl_4) δ 7.45 (m, 5H), 2.55 (m, 4H), 1.92 (s, 3H), 1.45 (m, 8H), 0.88 (m, 6H); MS (70 eV) m/z 213 (25), 193 (48), 192 (50), 178 (96), 177 (40), 136 (98), 122 (44), 121 (96), 119 (98), 117 (100), 57 (58); HRMS calcd for $C_{16}H_{26}S_2$ 282.1478, found 282.1481. **17d**:[35] ^{1}H-NMR (CCl_4) δ 7.44–7.22 (m, 15H), 1.76 (s, 3H); MS (70 eV) m/z 322 (M^+, 4), 314 (16), 299 (30), 215 (67), 214 (91), 213 (100), 212 (40), 205 (30), 177 (17), 178 (17), 165 (16), 136 (47), 121 (20), 105 (55). **19c**: ^{1}H-NMR (CCl_4) δ 2.48 (m, 4H), 1.57 (m, 18H), 0.90 (m, 6H); MS (70 eV) m/z 260 (M^+, 42), 178 (27), 171 (100), 170 (98), 135 (5), 121 (98), 95 (67), 86 (98); HRMS calcd for $C_{14}H_{28}S_2$ 260.1634, found 260.1612. **22b**:[33] ^{1}H-NMR (CCl_4) δ 3.34 (s, 4H), 1.78 (s, 6H); MS (70 eV) m/z 135 (13), 134 (M^+, 83), 121 (21), 119 (100), 106 (44), 78 (27), 65 (60). **22c**:[36] ^{1}H-NMR (CCl_4) δ 2.54 (m, 4H), 1.50 (m, 14H), 0.92 (m, 6H); MS (70 eV) m/z 220 (M^+, 6), 132 (10), 131 (M^+ – SBu, 100), 75 (48). **22d**:[35] ^{1}H-NMR (CCl_4) δ 7.61 (m, 4H), 7.36 (m, 6H), 1.47 (s, 6H); MS (70 eV) m/z 260 (M^+, 4), 218 (16), 151 (100), 135 (42), 110 (35), 109 (28), 59 (44). **23b**:[4] mp 92–93 °C (lit.[4] mp 95 °C); IR (neat) 1683 (C=O) cm^{-1}; ^{1}H-NMR (CCl_4) δ 7.88 (d, 2H, J = 9.6 Hz), 7.56 (d, 2H, J = 9.6 Hz), 5.62 (s, 1H), 3.38 (m, 4H), 2.55 (s, 3H); MS (70 eV) m/z 224 (M^+, 72), 196 (52), 153 (100), 149 (95), 135 (45), 119 (97), 106 (60), 93 (51), 77 (40). **23c**: colorless solid, mp 92 °C; ^{1}H-NMR ($CDCl_3$) δ 7.66 and 7.37 (AB quartet, 4H, J = 8.7 Hz), 5.58 (s, 1H), 3.35 (br s, 8H), 2.07 (s, 3H); MS (70 eV) 300 (M^+, 100), 285 (77), 239 (20), 211 (50), 195 (23), 179 (53); deprotection of the bis-dithioacetal **23c** using DDQ by the established procedure[29] gave the starting keto aldehyde **23a** in nearly quantitative yield which was identified by TLC, IR, and ^{1}H-NMR spectroscopic data by comparison with the authentic sample. **24b**: IR (neat) 1718 (C=O) cm^{-1}; ^{1}H-NMR (CCl_4) δ 4.3 (m, 1H), 3.11 (m, 4H), 2.33 (m, 2H), 1.98 (s, 3H), 0.84–1.45 (m, 6H); MS (70 eV) m/z 206 (30), 205 (33), 204 (M^+, 100), 132 (47), 105 (98); HRMS calcd for $C_9H_{16}OS_2$ 204.0644, found 204.0634. **25b**: IR (neat) 1686 (C=O) cm^{-1}; ^{1}H-NMR (CCl_4) δ 7.68 (m, 2H), 7.34 (m, 3H), 4.35 (m, 1H), 3.11 (s, 4H), 2.86 (m, 2H), 1.70 (m, 6H); MS (70 eV) 155 (100), 154 (66), 153 (56), 146 (30), 140 (46), 122 (40), 120 (86), 118 (90), 107 (45), 106 (69), 105 (40), 92 (74). **26b**: IR (neat) 1705 (C=O) cm^{-1}; ^{1}H-NMR (CCl_4) δ 4.60 (d, 1H, J = 7.2 Hz), 3.04 (s, 4H), 2.39 (m, 3H), 1.76 (m, 6H); MS (70 eV) m/z 202 (M^+, 29), 121 (32), 119 (98), 117 (100), 105 (53); HRMS calcd for $C_9H_{14}OS_2$ 202.0487, found 202.0468.

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