# Unusually Facile Oxathioacetal Transfer Reaction: an Efficient, Highly Selective Catalytic Deprotection Protocol†

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$CF_3SO_3SiMe_3$-catalysed one-to-one exchange of oxathioacetals to carbonyl compounds in the presence of 4-nitrobenzaldehyde is performed efficiently at room temperature, the protocol developed provides selective and effective deprotection of oxathiolanes in the presence of thioacetals.

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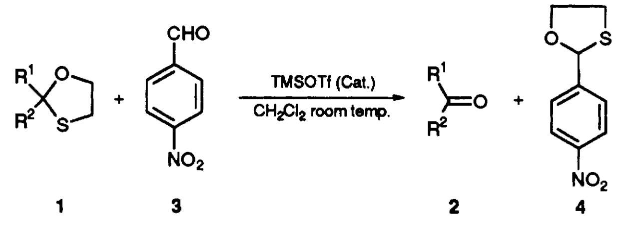
Oxathioacetals are useful protecting groups[1a–d] in functional group transformations and carbon–carbon bond formations by virtue of their stability and ability to act as an acyl anion equivalent. Although they can be formed readily from the carbonyl compounds, no efficient methods are available for their deprotection. This is often a critical bottleneck in the successful implementation of a synthetic sequence. Usual methods of deprotection involve stoichiometric amounts of oxidants[1c,1d,2,3], refluxing with Raney Ni[1a] or tedious multistep operations, a highly undesirable protocol, limiting their usage in synthetic sequences of reactions on a larger scale.

The search for an effective and mild protocol for deprotection of oxathioacetals is the focus of current interest.[4] A recent publication[4] describing a mild and efficient method for deprotection of oxathioacetals prompted us to disclose our findings in this area.

In connection with our interest in the synthesis of vitamin H [D(+) biotin], we have developed a mild and efficient deprotection protocol for thioacetal.[5]

Here we describe a highly convenient transoxathioacetalization method. It was observed that oxathioacetals could be smoothly and efficiently transformed to carbonyl compounds in excellent yields under anhydrous conditions. Thus, when oxathioacetals **1** were treated with an equivalent amount of 4-nitrobenzaldehyde **3** in the presence of TMSOTf in $CH_2Cl_2$ the corresponding carbonyl compounds **2** were obtained readily with the corresponding oxathioacetal of 4-nitrobenzaldehyde **4** in excellent yields. A variety of oxathioacetals were smoothly deprotected, see Table 1.



Scheme 1

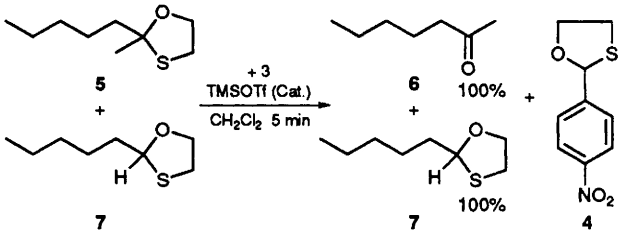
Table 1

| Substrate[a] | Product | Yield (%) | 4 (%) | t/min |
|---|---|---|---|---|
| 5 | 6 | 88 | 93 | 5[d] |
| 7 | 8 | 75 | 85 | 120[b,d] |
| 9 | 10 | 97 | 97 | 5[e] |
| 12 | 13 | 83 | 90 | 5[d] |
| 14 | 15 | 90 | 93 | 5[c,d] |
| 16 | 17 | 78 | 87 | 5[d] |
| 18 | 19 | 90 | 95 | 5[e] |
| 20 | 21 | 86 | 93 | 5[e] |
| 22 | 23 | 94 | 97 | 5[e] |
| 24 | 25 | 89 | 95 | 5[e] |
| 26 | 27 | 93 | 95 | 5[e] |
| 28 | 29 | 75 | 75 | 5[e] |

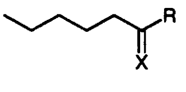
[a] Oxathiolanes were prepared according to the literature procedure.[6] [b] 2 equiv. of **3** were used. [c] Two isomeric oxathiolanes were formed. [d] The carbonyl compounds were isolated by bulb to bulb distillation. [e] The carbonyl compounds were isolated by column chromatography ($SiO_2$) using ethylacetate–petroleum ether as the eluent.

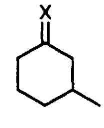
The usefulness of this method is evident by the ease of separation of the carbonyl compounds from **4** either by column chromatography or by distillation. In principle all the carbonyl compounds listed in Table 1 can be easily separated by distillation while **4**, having a high boiling point, remains as a residue. Compounds **6, 8, 13, 15, 17** and **29** (entries **1, 2, 4, 5, 6** and **12** in Table 1) were purified by bulb-to-bulb distillation while the remaining carbonyl compounds were separated by column chromatography over $SiO_2$. The carbonyl compounds, being less polar, are eluted first followed by oxathioacetal **4** using petroleum ether–ethylacetate as the eluent. (1% ethyl acetate–petroleum ether was used to elute the carbonyl compounds while oxathioacetal **4** was eluted with 5% ethyl-acetate-petroleum ether as the eluent).

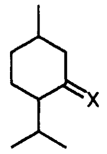
This deprotection protocol manifests itself in dual selectivity, *e.g.* differences in reactivity of oxathioacetals derived from ketones and aldehydes can be used to advantage in selective deprotection of oxathioacetals of ketones in presence



Scheme 2



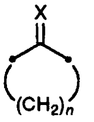


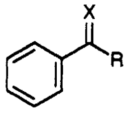


**5** R = Me, X = $SCH_2CH_2O$–
**6** R = Me, X = O
**7** R = H, X = $SCH_2CH_2O$–
**8** R = H, X = O

**12** X = $SCH_2CH_2O$–
**13** X = O

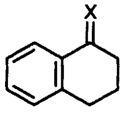
**14** X = $SCH_2CH_2O$–
**15** X = O

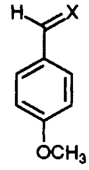


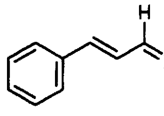


**16** *n* = 4, X = $SCH_2CH_2O$–
**17** *n* = 4, X = O
**18** *n* = 9, X = $SCH_2CH_2O$–
**19** *n* = 9, X = o

**20** R = Me, X = $SCH_2CH_2O$–
**21** R = Me, X = O
**22** R = Ph, X = $SCH_2CH_2O$–
**23** R = Ph, X = O



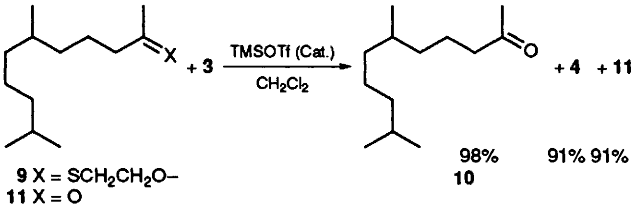




**24** X = $SCH_2CH_2O$–
**25** X = O

**26** X = $SCH_2CH_2O$–
**27** X = O

**28** X = $SCH_2CH_2O$–
**29** X = O



**Scheme 3**

of aldehydes. Thus, when a mixture of oxathioacetals **5** and **7** (1 : 1 equiv.) was treated with 4-nitrobenzaldehyde (1 equiv.) in the presence of catalytic amount of TMSOTf and quenched with saturated $NaHCO_3$ solution after 5 min, the $^1H$ NMR (200 MHz) analysis of the crude reaction mixture revealed clean transformation of oxathioacetal **5** to ketone **6**, 4-nitrobenzaldehyde **3** was converted to its oxathioacetal **4**. The oxathioacetal **7** derived from hexanal was recovered unchanged. This was further substantiated by isolation and characterization of the ketone **6** and oxathioacetals **7** and **4** in high yields (Scheme 2).

Another salient feature demonstrating the strength and efficiency of our methodology is the selective and effective deprotection of oxathiolanes in the presence of thioacetals. The difference in reactivity of oxathiolanes and dithiolanes also revealed that oxathiolanes could be effectively deprotected in the presence of dithiolanes. The following example illustrates the above point. Thus, when oxathiolane **9** and dithiolane **11** (1 : 1 equiv.) was treated with 4-nitrobenzaldehyde **3** (1 equiv.) in the presence of $CF_3SO_3SiMe_3$, ketone **10** was obtained in 98% yields on isolation. Unreacted dithiolane **11** was obtained in 91% yields. Correspondingly, **4** was obtained in 91% yields. The discrepancy in the conversion of oxathioacetal to ketone and corresponding formation of **4** could be accounted by small conversion of dithiolane **11** to the ketone **10** (Scheme 3).‡

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## Footnotes

† NCL Communication No. 5369.

‡ All the compounds were characterized by $^1H$ NMR, IR, and mass spectral analysis. The carbonyl compounds obtained by trans-thioacetalization were characterized by direct comparison of their spectra with those of starting carbonyl compounds.

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