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Polymer Supported Nitrobenzaldehyde : Efficient, Highly Selective Catalytic, Deprotection of Oxathioacetals+

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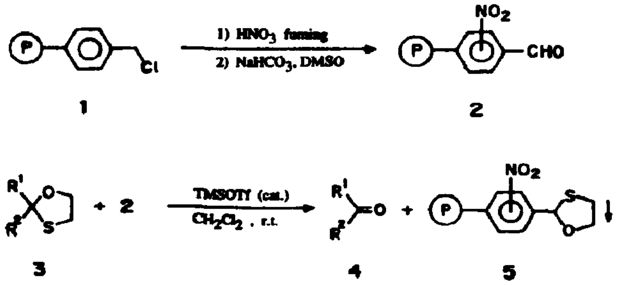
Abstract: *Oxathioacetals are smoothly deprotected to carbonyl compounds by polymer supported nitrobenzaldehyde at room temperature under* $CF_3SO_3Si(Me)_3$ *catalysed conditions.*

Pioneering work of Eliel[1] and others[2] has clearly established use of oxathioacetals as acyl anion equivalents for carbon-carbon bond formation and have used it elegantly for the syntheses of chiral alcohols. Similarly oxathioacetals have been used as protective groups for carbonyl compounds. Although quite a few efficient protocols are available for their preparation, no efficient selective general method exists for their removal to unmask carbonyl compounds. Conventional methods for their deprotection employ harsh conditions involving stoichiometric amounts of oxidants[1a,1b,3c,4a-d],refluxing with Raney Ni[3a,3b]which is often marred by side reactions thus limiting their usage in a synthetic sequence of reactions especially on a larger scale.

Search for efficient methods to effect functional group transformation under mild conditions continues to attract synthetic chemists[4e]. Development of a catalytic, mild and efficient protocol for deprotection of carbonyl compounds has been the focus of our interest. A recent publication[4e] prompts us to disclose our findings. In this connection, we have developed catalytic efficient mild protocol for unmasking of carbonyl compounds employing p-nitrobenzaldehyde.[5,6] Practically irreversible and one to one exchange of thioacetals and oxathioacetals was demonstrated to furnish carbonyl compounds in excellent yields. However, this method suffered from a drawback viz. the difficulty of removal of the by product oxathioacetal derived from p-nitrobenzaldehyde by column chromatography or distillation. Based on our success of use of p-nitrobenzaldehyde as efficient acceptor in deprotection of oxathioacetals[6], it occurred to us that if nitrobenzaldehyde were to be supported on polymer, it should still be possible to bring about the transfer of mercaptoethanol from oxathioacetals to furnish the carbonyl compounds. The polymer supported nitroaldehyde would be insoluble, thus would facilitate easy work up and recovery of the carbonyl compounds.



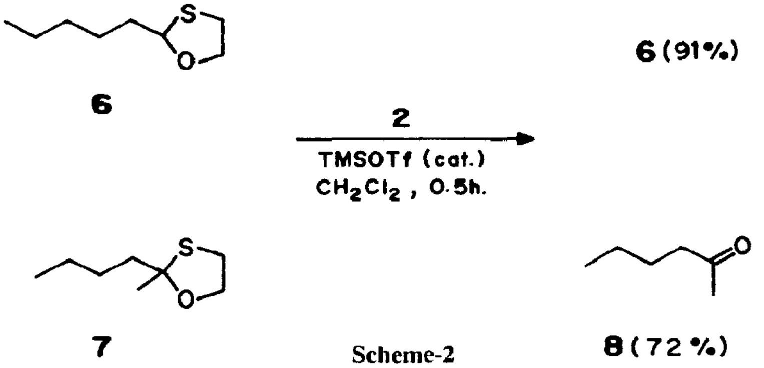
(Scheme-1)

This communication describes successful realisation of our premise for deprotection of oxathioacetal. The polymer supported nitroaldehyde 2 was prepared from 20% chloromethylated polystyrene (4% cross linked) 1 by nitration[7] followed by oxidation by treatment with DMSO according to adaptation of literature procedure[8] (Scheme-1)

The oxathioacetals[9], when subjected to treatment with polymer supported benzaldehyde 2 in the presence of $CF_3SO_3Si(Me)_3$ as the catalyst, furnished the corresponding carbonyl compounds 4 readily (Scheme-1). It is evident from the table-1, that a variety of oxathioacetals were deprotected to carbonyl compounds in excellent yields.

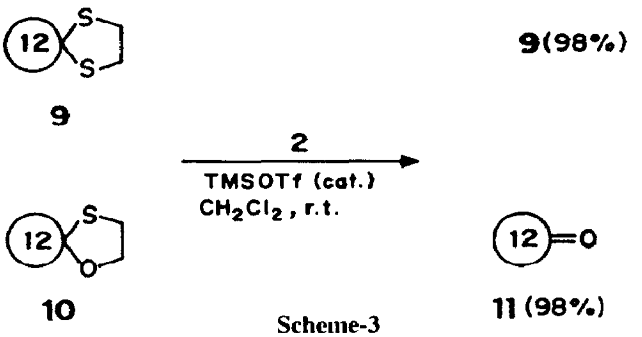
It is pertinent to mention that both 2 and 5 being insoluble in the solvent render the recovery of carbonyl compounds an easy affair, involving removal of the polymer by filtration. The carbonyl compounds thus obtained were devoid of contamination of the by-product oxathioacetal thus facilitating purification.

Another aspect worthy of comment is the dual selectivity exhibited by the polymer supported nitrobenzaldehyde 2. Ability of 2 to discriminate between oxathioacetals derived from a ketone and aldehyde became evident when an equimolar mixture of oxathioacetals 6 and 7 derived from hexanal and 2-hexanone (8) respectively were treated with 2 in the presence of $CF_3SO_3Si(Me)_3$ as the catalyst. Smooth and selective deprotection of 7 to ketone 8 was observed while the oxathioacetal 6 was recovered unchanged in 91% isolated yield. (Scheme-2).



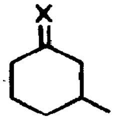
Scheme-2

The ease with which oxathioacetals can be deprotected can be used to advantage for their selective deprotection in the presence of thioacetals. An illustrative example is depicted in Scheme-3.

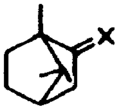


Scheme-3

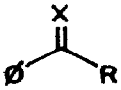
12. $X = -O-CH_2-CH_2-S-$
13 $X = O$



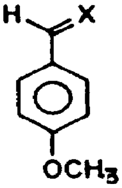
14. $X = -O-(CH_2)_2-S-$
15. $X = O$



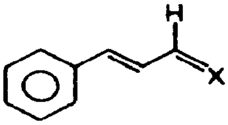
16. $X = -OCH_2-CH_2-S-$
17. $X = O$



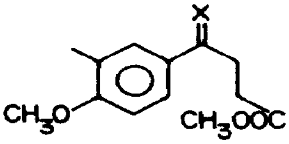
18. $R = CH_3$, $X = -O-CH_2-CH_2-S-$
19. $R = CH_3$, $X = O$
20. $R = C_2H_5$, $X = -O-CH_2-CH_2-S-$
21. $R = C_2H_5$, $X = O$



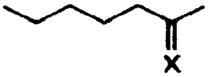
22. $X = -O-CH_2-CH_2-S-$
23. $X = O$



24. $X = -O-(CH_2)_2-S-$
25. $X = O$



26. $X = -O-(CH_2)_2-S-$
27. $X = O$



28. $X = -O-(CH_2)_2-S-$
29. $X = O$

Table

Entry	Substrate	Product	Time (h)	% Yield
1	7	8	6	88
2	10	11	0.5	86
3	12	13	3	92
4	14	15	3	96
5	16	17	2	98
6	18	19	3	89
7	20	21	2	96
8	22	23	3	83
9	24	25	2	95
10	26	27	1.25	95
11	28	29	3	89

When an equimolar proportion of dithiolane **9** and oxathiolane **10** were treated with **2** in the presence of catalyst, ketone **11** was obtained in 98% isolated yield. The thiolane **9** was recovered unchanged in 98% isolated yield. The difference in reactivity between **6** & **7** may be attributed to the stability of the resultant carbocations generated. Since the carbocation generated from **7** would be more stable, it is readily formed and hence selectively deprotected, whereas, the difference in reactivity between **9** & **10** may be ascribed to the preferential silylation of **10** at oxygen, and C-O bond rupture, O-Si bond being stronger than S-Si bond.

Thus, a highly convenient, catalytic and efficient protocol for oxathiol transfer using polymer supported nitroaldehyde **2** has been developed for deprotection of oxathioacetals to carbonyl compounds. The obvious advantages that polymers exhibit viz. ease of retrieval of the desired compound (carbonyls) just by mere filtration coupled with the dual selectivity and mildness of the conditions employed should make this protocol an attractive choice for functional group transformation.

General Procedure: To a stirred mixture of oxathioacetal (1 mmol) and nitrobenzaldehyde polymer (1g) in dichloromethane (5mL), under an atmosphere of nitrogen, at room temperature, was added $CF_3SO_3Si(Me)_3$ (0.02 mL). After completion of the reaction (TLC) aqueous sodium bicarbonate was added. The organic layer was separated after filtration and was washed with water, brine and dried (anhydrous Na_2SO_4). Removal of the organic layer under reduced pressure furnished a residue which was essentially pure, but was further chromatographed to furnish pure carbonyl compounds.

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