

Chemoselective Deprotection Of 1,3-Oxathiolanes Using Amberlyst 15 and Glyoxylic Acid under Solvent Free Conditions

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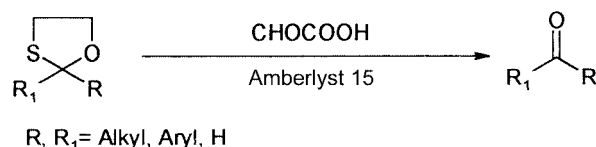
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Abstract: Carbonyl compounds were regenerated from corresponding 1,3-oxathiolanes via equilibrium exchange with glyoxylic acid and Amberlyst 15 as the heterogeneous catalyst, under solvent free conditions.

Key words: Amberlyst 15, 1,3-oxathiolane, microwave heating



Scheme 1

1,3-Oxathiolanes are frequently used to protect carbonyl compounds in the course of total syntheses and hence several systems¹ have been developed for their deprotection. Some of them include mercuric cyanide,² iodonium dicyclohexylidene perchlorate,³ Raney Ni,⁴ SeO₂/H₂O₂.⁵ However most of these methods involve use of toxic, corrosive oxidants at elevated temperatures. The identification of a mild and chemoselective glyoxylic acid and Amberlyst 15 system for the deprotection of 1,3-oxathiolanes forms the basis of this investigation. Glyoxylic acid is readily available at low cost and requires no special handling.

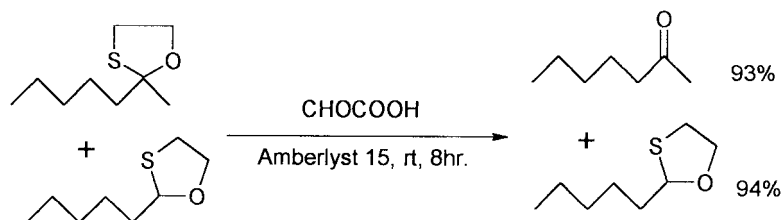
We describe in this communication conditions whereby 1,3-oxathiolanes are efficiently deprotected by an equilibrium driven exchange with glyoxylic acid in the presence of Amberlyst 15⁶ as the catalyst, both under microwave conditions as well as at room temperature (Scheme 1).

We have found a distinct rate enhancement under microwave conditions where reactions were completed in just 1 to 3 min as compared to few hours required at room temperature. The experimental procedure is very simple and involves stirring the 1,3-oxathiolanes (1 mmole) with glyoxylic acid (10 mmole) and Amberlyst 15 (125mg/mmole) in open vessel at room temperature for few hours or irradiating in a domestic microwave oven for few minutes. The reaction is fast and the product is isolated by a simple aqueous workup. A wide variety of 1,3-oxathiolanes derived from ketones and aldehydes was shown to undergo facile deprotection under these conditions (Table).

All the compounds were characterized by ¹H NMR, IR and mass spectral analysis. Microwave reactions were carried out in an Essentia made domestic microwave oven operating at 300 Watt.

Table Deprotection of 1,3-Oxathiolanes with Glyoxylic Acid and Amberlyst 15⁷

Entry	Oxathioacetals of	Thermal			Microwave	
		Temp	Time (h)	Yield (%)	Time (min)	Yield (%)
1	<i>p</i> -Methoxybenzaldehyde	rt	6	92	1	94
2	<i>p</i> -Nitro benzaldehyde	rt	7	93	2	95
3	Cinnamaldehyde	rt	7	92	1.5	93
4	Acetophenone	rt	7	93	1.5	94
5	Benzophenone	rt	7	93	1.5	93
6	α -Tetralone	rt	7	94	2	94
7	β -Tetralone	rt	9	93	3	94
8	Cyclohexanone	rt	10	92	3	93
9	Cyclopentanone	rt	10	93	3	94
10	Cyclododecanone	rt	10	94	3	94
11	Valeraldehyde	80°C	3	80	6	78
12	Decanal	80°C	3	81	6	80



Scheme 2

From the Table it is evident that thioacetals of aromatic ketones (entries 4,5 and 6) are deprotected faster than normal ketones (entries 8, 9 and 10). 1,3-Oxathiolanes of aromatic aldehydes are deprotected with equal ease (entries 1, 2 and 3). 1,3-Oxathiolanes of aliphatic aldehydes were more resistant to the reagent and reaction goes only at high temperature (entries 11 and 12). The difference in reactivity of 1,3-oxathiolanes of aldehydes and ketones can be used to advantage in effecting selective deprotection of 1,3-oxathiolanes derived from ketones in the presence of aldehydes.

The example in Scheme 2 illustrates the difference in the rate of reaction for selective deprotection of the 1,3-oxathiolanes derived from ketones (analyzed by GC).

In conclusion the present protocol is chemoselective, efficient, rapid, nonhazardous, solvent free and therefore should find widespread utility in organic synthesis. We are currently exploring the utility of the present protocol for other functional group transformations.

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- (7) **General Procedure:**
A mixture of 1,3-oxathiolane (1 mmol), glyoxylic acid (10 mmol) and Amberlyst 15 (0.125 gm) was stirred at room temperature or added in a glass test tube and mixed thoroughly followed by irradiation in a microwave oven. Progress of the reaction was monitored by TLC. After the completion of the reaction, this mixture was extracted with ether. The ether extract was washed with 10 mL NaHCO₃ (20%) solution and dried over anhydrous Na₂SO₄ and filtered. Evaporation of the solvent under reduced pressure gave pure carbonyl compound.

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