Mild and efficient iodine catalyzed protection of carbonyl compounds as oxathiolane derivatives[†]

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A number of aldehydes and ketones have been protected as their corresponding 1,3-oxathiolane derivatives with 2-mercaptoethanol using catalytic amount of molecular iodine.

The electrophilic nature of the carbonyl functionality is a dominant feature of its extensive chemistry. During synthesis of natural and nonnatural products, a carbonyl functionality may have to be protected against an attack by various types of reagents such as nucleophiles, oxidants, reducing agents including organometallic substrates¹ until its electrophilic properties can be exploited. For this reason, the protection and deprotection of the carbonyl functional group remain a crucial challenge to organic chemists¹. Among the carbonyl protecting groups, 1,3-oxathiolanes are versatile² due to their ease of installation and also to their stability under basic or mildly acidic conditions. In addition to the carbonyl protection, oxathiolanes are very useful as masked acyl anions³ or masked methylene functions in carbon-carbon bond forming reactions⁴. Although there are a large number of reports regarding protection and deprotection of carbonyl compounds as 1,3-dithiolanes⁵, very few methodologies are available for 1,3-oxathiolanes⁶. The usual protocols for conversion of carbonyl compounds to their corresponding oxathiolanes involves HCl^{7a}, PTSA^{7b}, BF₃-OEt₂^{7c}, SO₂^{7d}, ZnCl₂^{7e}, TMSCl-NaI^{7e}. Eventually all these methods are associated with certain limitations such as low yield, harsh reaction condition, longer reaction time and expensive reagents (TMSOTf) as well as inconvenience of reagent handling. Therefore development of a newer methodology that is mild, clean, environmentally benign and cost effective is still desirable.

In an endeavour to gradually change the current working principles to greener alternatives and environmental demands⁸, we have developed an environmentally favorable methodology for conversion of aldehydes and ketones to their respective 1,3-oxathiolanes using catalytic quantity of

molecular iodine. In recent years some reports⁹ have disclosed the use of iodine in some organic transformations. In this paper we wish to report the protection of a number of carbonyl compounds as their 1,3-oxathiolane derivatives using 2-mercaptoethanol in the presence of a catalytic amount (1 mol%) of iodine at room temperature (Scheme 1). The rate of reaction was found to be extremely fast and the desired products were obtained in excellent yields (Table 1).

Scheme 1

In spite of the theoretical support for the contrast in reactivity of aldehydes and ketones, the rate of conversion of ketones have been found to be slightly slower than that of the aldehydes. Thus a series of carbonyl compounds were subjected to the protection reaction and the results are summarized in Table 1. It is noteworthy that no side products were formed in the reactions and α,β -unsaturated aldehydes and ketones afforded no addition products at all. Surprisingly, no significant electronic effect was found to be operative strictly during the course of the reaction.

In conclusion, we have developed a mild and efficient method for protection of carbonyl compounds to the corresponding 1,3-oxathiolanes in excellent yields using molecular iodine as the catalyst. It compares favorably and represents a valid alternative to the existing methods.

[†]Dedicated to Professor S. M. Mukherji.

Table 1. Iodine catalyzed protection of carbonyl compounds as 1,3-oxathiolanes^a

Entry	Substrate	Reaction time (min)	Yield (%) ^b
1	Cyclopentanone	5	94
2	Cyclohexanone	5	92
3	Benzaldehyde	25	88
4	<i>p</i> -Anisaldehyde	15	94
5	<i>m</i> -Anisaldehyde	20	92
6	<i>p</i> -Chlorobenzaldehyde	20	88
7	<i>p</i> -Nitrobenzaldehyde	10	90
8	Piperonal	15	88
9	2-Naphthaldehyde	20	90
10	Furfural	5	82
11	Acetophenone	25	85
12	Benzophenone	60	78
13	Acraldehyde	20	86
14	Crotonaldehyde	20	84
15	Cinnamaldehyde	20	88
16	<i>trans</i> -4-Phenyl-3-buten-2-one	30	80
17	Mesityl oxide	15	88

^aAll products showed satisfactory spectral (NMR and IR) data. ^bYields refer to pure isolated products.

Experimental

Representative procedure: Benzaldehyde 1,3-oxathiol : 2-mercaptoethanol (88.3 mg, 1.13 mmol) was added to a stirred solution of benzaldehyde (100 mg, 0.94 mmol) in dry dichloromethane (0.5 ml) under nitrogen atmosphere at ambient temperature. Then iodine (2.3 mg, 0.0094 mmol) was added to the reaction mixture. It was allowed to stir and the progress of the reaction was monitored by preparative TLC. After completion of the reaction (approx. 25 min), the mixture was quenched with water (2 ml) and diluted with ether (20 ml). The organic layer was washed successively with aqueous saturated sodium thiosulphate (3 × 5 ml), brine (2 × 5 ml) and then dried (Na₂SO₄). The solvent was removed under reduced pressure to afford a light yellow mass which was purified by column chromatography

over silica gel (10% ethyl acetate in petroleum ether) to furnish pure benzaldehyde 1,3-oxathiol as a viscous oil (117 mg, 88%).

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