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One-pot two-step conversion of aromatic carboxylic acids and esters to aromatic aldehydes via indium-catalyzed reductive thioacetalization and desulfurization

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ABSTRACT

Described herein is that a new approach to a one-pot two-step conversion of aromatic carboxylic acids/esters to aromatic aldehydes, in which indium(III) iodide effectively catalyzes both the first reductive thioacetalization of carboxylic acids and a subsequent desulfurization of the in-situ formed thioacetal intermediates leading to aldehydes.

Introduction

Aldehydes have constituted a central and an important position in a variety of organic compounds, because they possess high electrophilicity and are easily converted to other highly valuable compounds, such as carboxylic acids and primary alcohols, via typical oxidation and reduction. There are numerous synthetic routes to prepare aldehydes.[1] The synthesis of aldehydes via directly reductive conversion of carboxylic acids, however, has yet to gain wide acceptance because the formed aldehydes are readily reduced to primary alcohols by the remaining reducing reagents in a series of transformations and because carboxylic acids generally show a relatively high tolerance to a mild reducing agent.

Thus, to solve these problematic issues, various transformations from carboxylic acids to aldehydes have been developed.[2] As a typical approach involves the reduction of carboxylic acids with lithium aluminum hydride to once produce alcohols, which is followed by re-oxidation to produce aldehydes.[3] A simple approach involves the hydrogenation of carboxylic acids in the presence of a metal catalyst.[4] Also, several groups have treated carboxylic acids with reducing reagents involving a methylamine solution with lithium,[5] thexylborane,[6] aminoaluminium hydride,[7] and a mixture of isobutylmagnesium bromide and titanocene dichloride,[8] and then directly isolated the corresponding aldehydes using only a common work-up (Eq. 1 in Scheme 1). Moreover, a two-step preparation involves converting carboxylic acids to activated intermediates, such as activated esters,[9] acid anhydrides,[10] thioesters,[11] and amides,[12] which is then followed by the reduction of those intermediates to obtain aldehydes (Eq. 2 in Scheme 1). After the initial work on a reductive conversion of carboxylic acids using a diarylhydrosilane tethered with an amino group by Corriu and co-workers,[13] Nagashima,[14] Darcel,[15] and Brookhart[16] groups independently found that a combination of a metal or metalloid catalyst, such as ruthenium, iron, and boron, and a hydrosilane effectively reduced carboxylic acids to aldehydes, respectively. Also, several reductive conversions of carboxylic acid derivatives, such as esters,[3,17] acid chlorides,[18] and amides,[19] to aldehydes in the presence of reducing reagents involving an aluminum hydride, tributyltin hydride and a hydrosilane, have been also developed.

We previously found that InI_3 effectively catalyzed the reductive thioacetalization of a variety of carboxylic acids in the presence of a mild reducing agent, such as a hydrosilane.[20,21] On the basis of the results, we expected an indium catalyst to catalyze the subsequent desulfurization step, and that it would be a novel approach to the one-pot preparation of aromatic aldehydes from aromatic carboxylic acids (Eq. 3 in Scheme 1). Practically, when *p*-toluic acid was treated with the combination of a reducing system composed of InI_3 and tetramethyldisiloxane (TMDS) and a subsequent desulfurization step using H_2O_2 aqueous solution, *p*-

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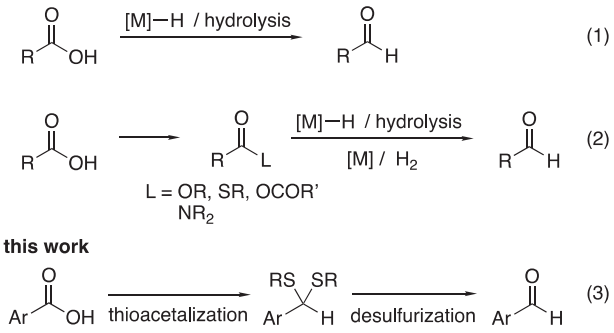


Scheme 1. Divergent approaches to aldehydes from carboxylic acids.

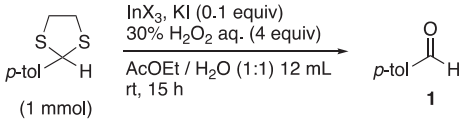
tolualdehyde was successfully obtained in one-pot. In this case, however, the conversion examined was limited to only one example. Based on that situation, we intended to re-examine the optimal conditions for the transformation, and to extend its scope. Herein, we report the results. We also disclose how the present method could be applied to the one-pot conversion of aromatic esters to aromatic aldehydes.

Results and discussion

Initially, on the basis of our previous work[20] and similar works found in the literature[22,23] the optimization of an indium(III) compound to promote a more effective desulfurization of a thioacetal to *p*-tolualdehyde (**1**) was investigated (Table 1). As a model reaction, prepared thioacetal was treated with several indium compounds (10 mol%) in the presence of KI (10 mol%) and H_2O_2 (4 equiv) as an oxidizing agent in a mixture of ethyl acetate and H_2O.[24] Consequently, regardless of a sort of a counter anion, all indium compounds examined led to a clean desulfurization (entries 1–3). Also, with decreases in the amount of InI_3 to 5 mol %, the desired desulfurization took place quantitatively (entry 4), but the use of only 1 mol% of the catalyst slightly reduced the product yield (entry 5). On the other hand, even though the desulfurization cleanly proceeded without the indium catalyst (entry 6), the monitoring of a series of desulfurization reactions showed that an additive effect of the indium compound remarkably accelerated the conversion (see Scheme S1 in SI). In particular, with the addition of 10 mol% of InI_3, the desired desulfurization was completed within 2 h. Moreover, it was noteworthy that the desulfurization proceeded smoothly and effectively without potassium iodide to produce the corresponding aldehyde **1** (entries 7 and 8).

Next, in order to effectively undertake a series of thioacetalization and desulfurization reactions in one-pot, we sought a mutual solvent by monitoring the model reaction via GC (Table 2). As expected, ethyl acetate examined in Table 1 hardly occurred in the first thioacetalization (entry 1). After several trials, with the exception of acetonitrile,[25] typical solvent, such as a halogenated solvent, benzene and toluene, successfully undertook the second desulfurization process in a relatively good yield. Therefore, it seemed that a successful key to the entire conversion was the proportion of the yield of the first thioacetalization step. Although the use of chloroform and benzene showed good results, from the viewpoint of an environmentally friendly solvent, we decided that

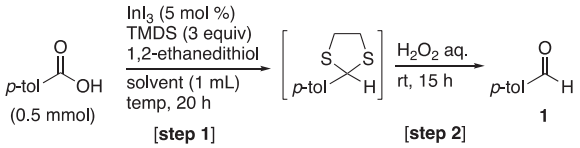
Table 1
Optimization of desulfurization with an indium(III) compound [a].



Entry	InX_3	(mol%)	GC yield (%)
1	$InCl_3$	10	93
2	$InBr_3$	10	95
3	InI_3	10	98
4	InI_3	5	99
5	InI_3	1	76
6	–	–	85
7[a]	InI_3	10	81
8[a]	InI_3	5	89

[a] Without KI.

Table 2
Solvent effects of a series of thioacetalization and desulfurization.



Entry	Solv	Temp (°C)	GC yield (%)		
			Step 1	Step 2[a]	Overall
1	AcOEt	60	5	ND	ND
2	1,2-DCE	60	25	91	23
3	$CHCl_3$	60	89	94	83
4	CH_3CN	60	ND	–	–
5	Benzene	60	88	81	71
6	Toluene	60	92	85	79 (69)[b]
7	Toluene	80	67	87[c]	58

[a] Conversion yield based on formed **1a** in the first step.
[b] Isolated yield.
[c] Reaction time at step 2 = 24 h.