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A general and efficient reduction of acyl chlorides to aldehydes by Sm(0)/Bu_3P

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Abstract—A facile and efficient reduction of aromatic and aliphatic acyl chlorides to their corresponding aldehydes in the presence of Sm(0)/Bu_3P has been developed with broad scope. This method prevents over reduction of products, that is, the over-reduction of aldehydes to alcohols.
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The conversion of carboxylic acids and their derivatives to aldehydes is one of the most important transformations in organic synthesis. Among them, transformation of acyl chlorides to the corresponding aldehydes remains as a challenge.[1] Over the past decades, considerable efforts have been contributed to this area and a variety of methods have been developed.[2] Besides the classical Rosenmund reduction,[3] the complex metallic hydrides such as Li(*t*-BuO)$_3$AlH,[4] Na(*t*-BuO)$_3$AlH,[5] transition metal borohydrides and organosilicon hydrides have been extensively investigated.[6] Furthermore, trialkyltin hydrides reduction of acyl chlorides to aldehydes catalyzed by palladium complexes was also successfully applied to total organic synthesis.[7] However, organotin reagents are toxic and expensive.[8] Thus, a novel strategy of acyl chlorides reduction to their aldehydes with greater selectivity and efficiency is still desirable.

As a powerful, versatile and ether-soluble one-electron transfer agent, SmI_2 has played an ever-increasing role in organic synthesis.[9] Among these methods, the reduction of acyl chlorides has been studied extensively. For instance, samarium diiodide in THF can achieve the coupling of aroyl chlorides into α-diketones, whereas α-hydroxy ketones are usually obtained from aliphatic acyl chlorides under the same conditions.[10] Moreover, using Sm(II) species and an acyl chloride with a tertiary carbon at low temperature (−20 °C), followed by a sequential addition of deuterated water affords a deuterated aldehyde. Nevertheless, this reaction has limited scope and utility.[11] But the interesting experimental findings still prompted us to carry out the following investigation.

The direct use of samarium(0) as a reducing agent in organic synthesis has attracted much attention in the past several years.[12] This is due to the fact that metallic samarium is stable in air and has strong reducing power ($Sm^{3+}/Sm = -2.41$ V). It is also cheap and easy to handle. Recently, we have reported the reduction of Baylis–Hillman adducts as well as the acylation of alcohols with acyl chlorides promoted by samarium(0).[13] Herein we wish to report a first mild and general reduction of acyl chlorides to aldehydes by samarium(0) with Bu_3P.

First, we investigated the direct reduction of acyl chlorides with samarium(0) without any other additives or using the usual additives such as iodine, TMSCl and allylic bromide to activate metallic samarium. However, only the coupling products were obtained and no aldehydes were observed even under various temperatures, solvents and proton sources.[14] Subsequently, we turned our attention to the activation of carbonyl group. Tributylphosphine had proved to be a remarkable acylation catalyst via the in situ formation of phosphonium ion with acyl chloride.[15] Thus, we attempt to convert acyl chlorides to aldehydes with samarium(0) by using tributylphosphine as the auxiliary catalyst.[16]

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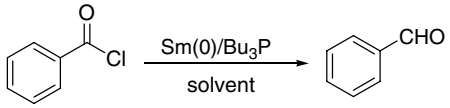
Our initial experiments were carried out by using benzoyl chloride **1a** as a model substrate (Scheme 1). At room temperature, when 1 mmol **1a** was added to a solution of 1.2 mmol Bu_3P in CH_3CN under nitrogen atmosphere, benzoyl tributylphosphonium chloride salt was immediately formed.[17] Then CH_3SO_3H was injected as a proton source followed by the addition of 2/3 mmol samarium powder to afford benzaldehyde in 49% yield (Table 1, entry 1). A better yield was obtained when the reaction proceeded at −20 °C (entry 10), while the same reaction became quite sluggish at lower temperature together with a decreased yield of **2a** (entry 2).

Significant solvent effect was observed in our experiments and CH_3CN was found to be the best choice. As shown in Table 1, when DMF was used as a solvent in this reaction, only trace amount of the desired product **2a** was isolated (entry 6). THF and CH_2Cl_2 also gave relatively lower yields compared with CH_3CN (entries 5 and 7). In addition, the proton source also affected the yield of the reaction. Experimental results showed that CH_3SO_3H and HCl were superior, while the use of HCl instead of CH_3SO_3H significantly shortened the reaction time.

With the Sm(0)/Bu_3P/HCl reduction system optimized, we then turned our attention to the scope of the substrates (Scheme 2). Substituted aromatic acyl chlorides were firstly examined and the results are summarized in Table 2. In all cases, aromatic acyl chlorides bearing both electron-withdrawing and electron-donating groups underwent reduction smoothly to the corresponding aromatic aldehydes within 1 h with high yields (Table 2, entries 1–7). No over reduced by-product was



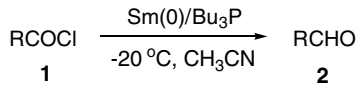
1a **2a**

Scheme 1.

Table 1. Effect of solvents and other factors on the reduction of benzoyl chlorides to benzaldehyde[a]

Entry	Solvent	T (°C)	Proton source[b]	Yield[d] (%)
1	CH_3CN	25	CH_3SO_3H[c]	49
2	CH_3CN	−40	CH_3SO_3H[c]	49
3	CH_3CN	0	CH_3SO_3H[c]	70
4	CH_3CN	−20	HCl	87
5	THF	−20	HCl	64
6	DMF	−20	HCl	5
7	CH_2Cl_2	−20	HCl	32
8	CH_3CN	−20	H_2O	20
9	CH_3CN	−20	CH_3OH	10
10	CH_3CN	−20	CH_3SO_3H[c]	85

[a] All attempts were carried out with 2/3 equiv samarium powder within 1 h.
[b] The concentration of HCl used was 6 M.
[c] In such cases, the reaction time was prolonged to 3 h.
[d] Isolated yields.



1 **2**

Scheme 2.

Table 2. Samarium-mediated novel routine to aldehydes from acyl chlorides in the presence of tributylphosphine[a,b]

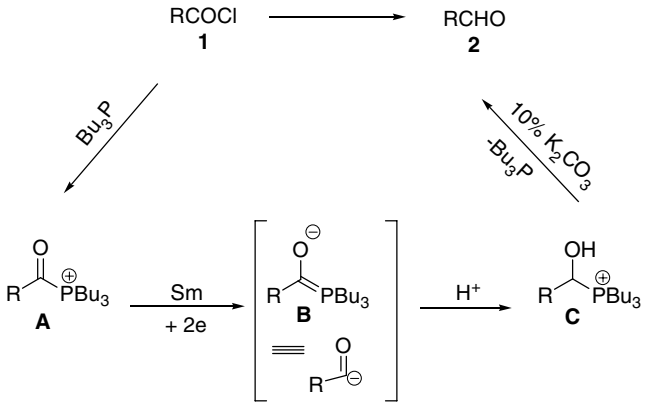
Entry	R	Time (h)	Yield (%)
1	C_6H_5	1	87 (100)[c,d]
2	4-CH_3–C_6H_4	1	92 (100)[c,d]
3	4-CH_3O–C_6H_4	1	90 (100)[c,d]
4	4-O_2N–C_6H_4	1	95 (100)[c,d]
5	2-Cl–C_6H_4	1	92 (100)[c,d]
6	4-Cl–C_6H_4	1	89 (100)[c,d]
7	C_6H_5CH=CH	1	94 (100)[c,d]
8	$CH_3(CH_2)_6$	3	93 (100)[d,e]
9	$C_6H_5(CH_2)_2$	3	95 (100)[d,e]
10	$EtOOC(CH_2)_2$	3	89 (100)[d,e]

[a] Unless otherwise noted, all reactions proceeded in 10 mL CH_3CN with 1 mmol **1** and 1.2 mmol Bu_3P in the presence of 2/3 mmol samarium powder.
[b] All products were characterized satisfactorily (IR, ^1H NMR, ^{13}C NMR and MS).
[c] Isolated yields.
[d] GC yield.
[e] In such cases, acid chlorides **1** were carried out with THF/CH_3SO_3H under the same conditions and isolated yields with 2,4-dinitrophenylhydrazine.

detected. Many functional groups such as nitro, carbonyl and carbon–carbon double bond remained intact during this process and the yields were not to be affected by the substitution of the aromatic ring.

The fact that *ortho*-chloride benzoyl chloride was converted to the corresponding aldehyde in 92% yields may indicate that this reaction is not sensitive to steric hindrance (Table 2, entry 5). Since few methods could achieve complete efficiency both to aromatic and aliphatic acyl chlorides, it became essential to test the conversion of aliphatic analogues.[18] Several aliphatic acyl chlorides were conducted under the optimized Sm(0)/Bu_3P/HCl condition to afford the corresponding aldehydes in moderate to good yields (37–70% yield). However, this problem was solved by the replacement of HCl with CH_3SO_3H as a proton source in THF solution.

As shown in Table 2, the Sm(0)/Bu_3P/CH_3SO_3H was optimal for the conversion of aliphatic acyl chlorides to aldehydes except for the longer reaction time (Table 2, entries 8–10). For example, the yield of octanal from the conversion of octanoyl chloride under this new THF/CH_3SO_3H protocol was increased significantly up to 93% from 37% compared with the CH_3CN/HCl condition (entry 8). The yield of the reduction of hydrocinnamonyl chloride (3-phenylpropionyl chloride) was also greatly improved from 42% under the CH_3CN/HCl condition (entry 9). In addition, this improvement also demonstrated its superiority in the selective chemi-



Scheme 3.

cal reduction of acyl chloride in the presence of ester functionality (entry 10).

The mechanism of the above conversion could be depicted as follows (Scheme 3): acyl chloride may react with Bu_3P to form an acyltributylphosphonium ion **A**,[15] which could accept two electrons from samarium(0) to form the corresponding intermediate α-oxyylide **B**, an equivalent of acyl anion. Further protonation of **B** would afford the α-hydroxyalkalphosphonium ion **C**, which could be converted to the corresponding aldehyde under weak basic conditions. As shown in this catalytic cycle, the formation of phosphonium salt **A** was considered to be the key step.

In summary, we have developed a facile and novel method for the synthesis of aldehydes from acyl chlorides.[19,20] This new protocol allows for the efficient conversion of both aromatic and aliphatic acyl chlorides to their corresponding aldehydes without the occurrence of over-reduction to alcohols. The mild conditions, high yields and broad scope of this reaction make it an excellent alternative to the existing methods.

Acknowledgement

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19. A typical procedure for the preparation of aromatic aldehydes **2** is as follows: To a stirred solution of 1 mmol acyl chloride **1** dissolved in 10 mL CH_3CN was added 1.2 mmol Bu_3P at −20 °C under a nitrogen atmosphere. About 15 min later, 0.33 mL HCl (6 M) and 2/3 mmol samarium powder (0.1 g) were added successively. After being stirred for 1 h, the reaction mixture was allowed to warm to room temperature gradually. Upon completion of the reaction, the resulting mixture was poured into aqueous 10% HCl (30 mL) and extracted with CH_2Cl_2 (50 mL × 2). The organic phase was washed with aqueous 10% K_2CO_3 (80 mL), dried over anhydrous Na_2SO_4, filtered, concentrated and the residue was purified by column chromatography on silica gel eluting with hexane/ethyl acetate (10:1) to afford the products. All of the products are known and were characterized by comparison of their spectral data with those of authentic samples.

20. A typical procedure for the preparation of aliphatic aldehydes **2** is as follows: To a stirred solution of 1 mmol acyl chloride **1** dissolved in 10 mL THF was added 1.2 mmol Bu_3P at −20 °C under a nitrogen atmosphere. About 15 min later, 0.13 mL CH_3SO_3H and 2/3 mmol samarium powder (0.1 g) were added successively. After being stirred for 3 h, the reaction mixture was allowed to warm to room temperature gradually. Upon completion of the reaction, the resulting mixture was poured into aqueous 10% HCl (30 mL) and extracted with CH_2Cl_2 (50 mL × 2). The organic phase was washed with aqueous 10% K_2CO_3 (80 mL), dried over anhydrous Na_2SO_4, filtered, concentrated and treated with 2,4-dinitrophenylhydrazine. All of the products are known and were characterized by comparison of their spectral data with those of authentic samples.