

Reductive Oxidation of Acid Chlorides to Aldehydes with Lithium Aluminum Hydride and Pyridinium Chlorochromate or Pyridinium Dichromate

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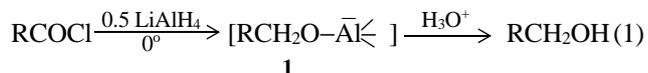
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The conversion of acid chlorides to aldehydes plays a very important role in organic synthesis. The most useful synthetic method for such conversion is reduction. Therefore, many useful reduction methods have been reported for such conversion.^{1,2} Among these, sodium tri-*tert*-butoxyaluminumhydride (STBA)² has appeared to be the most outstanding reducing agent, which can achieve a very general reduction of both aliphatic and aromatic acid chlorides to aldehydes in high yields at -78 °C. Very recently, we reported that the oxidation of alkoxyaluminum intermediates, which are formed by reaction of primary alcohols,³ carboxylic acids,⁴ esters⁵ and acid chlorides⁶ with aluminum hydride, by pyridinium chlorochromate (PCC) or pyridinium dichromate (PDC) affords aldehydes in high yields at room temperature. Furthermore, the procedure has been extended to involve the reduction of carboxylic acids⁷ and esters⁸ with lithium aluminum hydride (LAH), followed by oxidation of the resultant alkoxyaluminum intermediates with PCC or PDC. In this paper, we wish to add acid chlorides to the list, which can be applied successfully to such reductive oxidation procedure. Herein, we introduce a new method, which effects the transformation of acid chlorides to aldehydes in high yields at room temperature.

Results and Discussion

It is well known that LAH reduces acid chlorides to the alcohol stage to form an intermediate in the reaction mixture containing alkoxy moiety as in **1**, which then produces the corresponding alcohols upon hydrolysis⁹ (Eq. 1). Actually, acid chlorides were readily reduced to the corresponding alcohol stage by LAH (0.5 equiv) at 0 °C.



The present method involves the rapid reduction of acid chlorides with a half equivalent of LAH at 0 °C, followed by oxidation of the resultant alkoxyaluminum intermediate (**1**) (without isolation) with PCC or PDC at room temperature (Eq. 2).

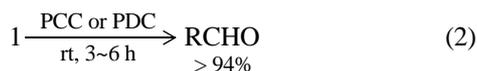


Table 1 shows that this procedure provides a clean and convenient conversion of acid chlorides to aldehydes. There is no difference in the yields of aldehydes with PCC or PDC.

Alicyclic derivative, such as cyclohexanecarbonyl chloride, works equally well. Derivatives are readily accommodated. Thus, trichloroacetyl chloride yields the corresponding aldehyde in yields of 96-97%. Similarly, α,β -unsaturated acid chlorides, such as crotonyl and cinnamoyl chlorides, afford the olefinic aldehydes in 93-95% yields. The conversion of aromatic acid chlorides by this procedure provides the corresponding aldehydes in yields of 94-98%. The unsubstituted aromatic acid chlorides such as benzoyl and naphthoyl chlorides are converted into the corresponding aldehydes in 96-98% yields. Methyl-substituted benzoyl chlorides such as *o*-toluoyl and *p*-toluoyl chlorides afford the corresponding aldehydes in 95-96% yields. Finally, chloro, methoxy and nitro groups on the benzene ring are readily accommodated and gave aldehydes in better than 94% yield.

This procedure is broadly applicable, tolerating many substituents, such as chloro, methoxy, nitro and olefinic groups. It appears to be equally applicable to both aliphatic and aromatic acid chlorides. This procedure using LAH as a reducing agent affords actually the same results as the procedure using aluminum hydride does. However, the most remarkable feature of this procedure is that we can use LAH, a simple reducing agent, without modification for such conversion. For example, it is not necessary to suffer preparing a solution of aluminum hydride from LAH, that procedure was adopted in the previous paper⁶ for the same conversion. Furthermore, the present procedure requires only a ten % excess of oxidizing agents used for oxidation of the alkoxy-intermediates to the corresponding aldehydes, whereas the previous procedure needed a fifty % excess of oxidizing agents. In addition, the oxidizing agents are reagents of choice: the problem caused by the acidic nature of PCC can be largely eliminated by using the more neutral reagent PDC.¹⁰ It is noteworthy that the use of sodium aluminum hydride (SAH) as a reducing agent provided actually the same results as LAH did: SAH is a reagent of choice in this procedure because of its ease of handling and lower cost.¹¹

It is worthwhile to point out that this reductive oxidation procedure is quite compatible to the reduction procedure using STBA² for such conversion: both are procedures of choice. In the case where a simple acid chloride function is applied, the reductive oxidation procedure using SAH or LAH and PCC or PDC is recommendable; in the case where an acid chloride function in a complex molecule is applied, the reduction procedure using STBA is amenable. Consequently, both procedures should find a wide application in organic synthesis.

Table 1. Conversion of Acid Chlorides to Aldehydes by Oxidation of Alkoxyaluminate Intermediate (1) with Pyridinium Chlorochromate (PCC) or Pyridinium Dichromate (PDC)^{a,b}

Acid chloride	Product	Reaction time (h)	PCC	PDC
			Yield (%) ^c	Yield (%) ^c
Butyryl	Butyraldehyde	6	94	93
Isobutyryl	Isobutyraldehyde	6	96	94
Hexanoyl	Hexanal	6	96(81)	97
Trimethylacetyl	Trimethylacetaldehyde	6	98	96
Trichloroacetyl	Trichloroacetaldehyde	6	96	97
Cyclohexanecarbonyl	Cyclohexanecarboxaldehyde	6	97	98
Crotonyl	Crotonaldehyde	6	93	94
Cinnamoyl	Cinnamaldehyde	6	95	95
Benzoyl	Benzaldehyde	3	98(82)	98(79)
1-Naphthoyl	1-Naphthaldehyde	3	97	96
<i>o</i> -Toluoyl	<i>o</i> -Tolualdehyde	3	96	95
<i>p</i> -Toluoyl	<i>p</i> -Tolualdehyde	3	95	95
4-Chlorobenzoyl	4-Chlorobenzaldehyde	3	97	97
<i>o</i> -Anisoyl	<i>o</i> -Anisaldehyde	3	96	94
<i>p</i> -Anisoyl	<i>p</i> -Anisaldehyde	3	96	95
4-Nitrobenzoyl	4-Nitrobenzaldehyde	3	94	94

^aAcid chloride : oxidant = 1 : 1.1. ^bIn a THF-methylene chloride mixture solvent. ^cGC yields. The values in parentheses are isolated yields.

Experimental Section

All reactions were performed under a dry N₂ atmosphere. All chemicals used were commercial products of the highest purity available; THF was dried over 4 Å molecular sieve and distilled from sodium-benzophenone ketyl prior to use. Methylene chloride was also dried over P₄O₁₀ and distilled. ¹H NMR spectra were recorded on a Bruker AMX 300 spectrometer. Gas chromatographic analyses were carried out with a Varian 3300 Chromatograph.

Reductive Oxidation of Acid Chlorides to Aldehydes.

The following reaction is typical of the procedure utilized in such conversion with PCC. A solution of lithium aluminum hydride (1.0 M, 31 mL, 31 mmol) in THF was placed in an oven-dried, 500-mL flask fitted with a side-arm and a reflux condenser leading to a mercury bubbler. To this solution 8.57 g (61 mmol) of benzoyl chloride was added dropwise with vigorous stirring at 0 °C and the mixture was stirred further for 3 h at room temperature. To a well-stirred suspension of PCC (14.5 g, 67 mmol) in methylene chloride (120 mL) taken in a 500-mL flask equipped as described above, was added dropwise the above reaction mixture in THF using a cannula. The mixture was stirred for 3 h at room temperature. GC analysis of an aliquot using tridecane as an internal standard indicated a yield of 98%.

Isolation of Aldehyde Products. The rest of reaction mixture (60 mmol) was diluted with ethyl ether (120 mL) and the supernatant liquid is then filtered through Florisil®

(120 g) contained in a 300-mL sintered glass funnel. The solid residue was triturated with ethyl ether (3 × 30 mL) and passed through the same Florisil column. The filtrate is concentrated and distilled under reduced pressure to give 5.2 g (82%) of pure benzaldehyde, bp. 62-63° (14 mm, n_D²² 1.5450).

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