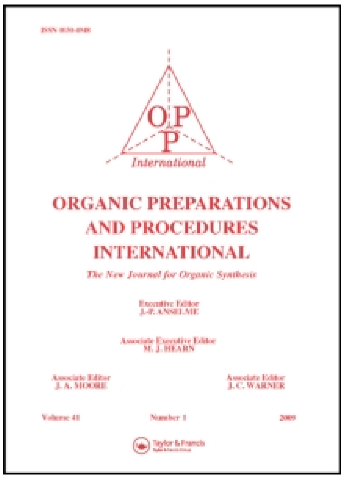

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CONVERSION OF ACID CHLORIDES TO ALDEHYDES BY OXIDATION OF ALKOXYALUMINUM INTERMEDIATES WITH PYRIDINIUM CHLOROCHROMATE OR PYRIDINIUM DICHROMATE

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CONVERSION OF ACID CHLORIDES TO ALDEHYDES BY OXIDATION OF ALKOXYALUMINUM INTERMEDIATES WITH PYRIDINIUM CHLOROCHROMATE OR PYRIDINIUM DICHROMATE

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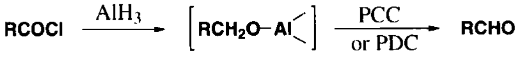
The reduction of acid chlorides to aldehydes is one of the most useful synthetic transformation in organic synthesis. Many useful reducing methods have been reported for such conversions.[1,2] Among these, sodium tri-*tert*-butoxyaluminohydride (STBA)[2] has appeared to be the most outstanding reducing agent, which can achieve a very general reduction of both aliphatic and aromatic acid chlorides to aldehydes in high yields at -78°.[2] Very recently, we reported that the oxidation of alkoxyaluminum intermediates with pyridinium chlorochromate (PCC) or pyridinium dichromate (PDC) affords aldehydes in high yields at room temperature. This procedure provides a convenient procedure for conversion of primary alcohols,[3] carboxylic acids[4] and esters[5] to aldehydes under mild conditions. The method involves the reduction of such compounds with aluminum hydride, followed by oxidation of the resultant alkoxyaluminum intermediates with PCC or PDC. From this mechanistic point of view, we decided to extend the procedure to the conversion of acid chlorides to aldehydes. Herein, we introduce a new method, which effects the transformation of acid chlorides to aldehydes in high yields at room temperature.



$$\mathrm{RCOCl} \xrightarrow{\mathrm{AlH_3}} \left[\mathrm{RCH_2O{-}Al}{<}\right] \xrightarrow[\text{or PDC}]{\text{PCC}} \mathrm{RCHO}$$

There is no difference in the yields of aldehydes with PCC or PDC. Alicyclic derivatives, such as cyclopropanecarbonyl chloride and cyclohexanecarbonyl chloride, work equally well. Derivatives are readily accommodated. Thus, trichloroacetyl chloride yields the corresponding aldehyde in yields of 94-95%. Similarly, α,β-unsaturated acid chlorides such as cinnamoyl chloride afford the olefinic aldehyde in 97-98% 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 97-98% yields. Methyl-substituted benzoyl chlorides such as *o*-toluoyl and *p*-toluoyl chloride afford the corresponding aldehydes in 95-97% yields. Finally, chloro, methoxy and nitro groups on the benzene ring are readily accommodated and gave aldehydes in better than 94% yield.

This reaction 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. Moreover, the oxidizing agents applied are reagents of choice: PCC is mildly acidic, whereas PDC is neutral. Consequently, this method provides another convenient procedure for conversion of acid chlorides to aldehydes under mild conditions.

TABLE 1. Conversion of Acid Chlorides to Aldehydes by Oxidation of Alkoxyaluminum Intermediates[a,b]

Acid chloride	Product	Time (hrs)	PCC Yield(%)[c]	PDC Yield(%)[c]
Butyryl	Butyraldehyde	6	95	94
Isobutyryl	Isobutyraldehyde	6	96	97
Hexanoyl	Hexanal	6	98(81)	96
Trimethylacetyl	Trimethylacetaldehyde	6	97	98
Trichloroacetyl	Trichloroacetaldehyde	6	95	94
Cyclopropanecarbonyl	Cyclopropanecarboxaldehyde	6	98	97
Cyclohexanecarbonyl	Cyclohexanecarboxaldehyde	6	98	96
Cinnamoyl	Cinnamaldehyde	3	97	98
Benzoyl	Benzaldehyde	3	98 (82)	97 (80)
1-Naphthoyl	1-Naphthaldehyde	3	98	97
2-Naphthoyl	2-Naphthaldehyde	3	97	98
o-Toluoyl	*o*-Tolualdehyde	3	96	97
p-Toluoyl	*p*-Tolualdehyde	3	97	95
2-Chlorobenzoyl	2-Chlorobenzaldehyde	3	97	96
4-Chlorobenzoyl	4-Chlorobenzaldehyde	3	98	96
o-Anisoyl	*o*-Anisaldehyde	3	96	95
m-Anisoyl	*m*-Anisaldehyde	3	97	97
p-Anisoyl	*p*-Anisaldehyde	3	96	94
4-Nitrobenzoyl	4-Nitrobenzaldehyde	3	94	95

a) Fifty% excess oxidizing agent used. b) In a THF-methylene chloride mixture solvent. c) GC yields. The values in parentheses are isolated yields.

EXPERIMENTAL SECTION

All glassware used was pre-dried at 140° for several hours, assembled hot, dried further with a flame and cooled under a stream of dry nitrogen. All reactions and manipulations were carried out under a dry nitrogen atmosphere. All chemicals were commercial products of the highest available purity, which were further purified by standard methods before use. Tetrahydrofuran (THF) was distilled from benzophenone-sodium ketyl prior to use. Methylene chloride was dried over phosphorus pentoxide and distilled. Lithium aluminum hydride, purchased from Aldrich Chemical Co., was used as a clear solution in THF after removing undissolved material. ^{1}H and ^{27}Al spectra were recorded on a Bruker AMX 300 spectrometer. GC analyses were performed on Donam DS 6200 and Varian 3300 FID chromatographs using Carbowax 20 M capillary column.

Preparation of a Solution of Aluminum Hydride in THF.- To an oven-dried, 500-mL flask fitted with a side arm and a reflux condenser leading to a mercury bubbler was added 200 mL of 2 M solution of $LiAlH_4$ (400 mmol) in THF and the solution was cooled to 0°. To this solution was added 38.5 g (400 mmol) of methanesulfonic acid slowly with vigorous stirring. The solution was stirred for 1h at 0° and then allowed to stand at that temperature to permit the lithium methanesulfonate precipitate to settle. The clear supernatant solution was removed by syringe and the ^{27}Al NMR spectrum of the solution showed a broad singlet centered at δ 125 (relative to $Al(H_2O)_6^{3+}$). The concentration of aluminum hydride in THF was measured gasometrically to be 1.8 M, which was then diluted with THF to be 1.0 M. This solution was used for further reactions.

Reduction of Carboxylic Acid Chlorides (Formation of Alkoxyaluminum Intermediates).- The following reaction is typical of the procedure utilized in the formation of alkoxyaluminum intermediate. The above THF solution of aluminum hydride (42 mL, 42 mmol) was placed in an oven-dried, 500-mL flask fitted with a side-arm and a reflux condenser leading to mercury bubbler. To this solution 8.57 g (61 mmol) of benzoyl chloride was added dropwise with vigorous stirring at room temperature and the solution was stirred for 1 h. The whole reaction mixture was then subjected to oxidation (*vide infra*).

Oxidation of Alkoxyaluminum Intermediate.- To a well-stirred suspension of pyridinium chlorochromate (19.4 g, 90 mmol) in methylene chloride (150 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 Product Aldehydes.- The rest of reaction mixture (60 mmol) was diluted with ethyl ether (200 mL) and the supernatant liquid is then filtered through Florisil· (150 g) contained in a 300-mL sintered glass funnel. The solid residue was triturated with ethyl ether (3x50 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. 62-64°/15 mm; n_D^{21} 1.5449.

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EXPEDIENT SYNTHESIS OF (1R,3S)-(+)-3-(TRIFLUOROMETHYL)CAMPHONANIC ACID AND DERIVATIVES

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Monoterpenes, particularly camphor and its derivatives such as cyclopentanoids, are versatile, chiral and enantiopure starting materials in natural product synthesis.[1] Recently, there is a growing interest in fluorinated derivatives of terpenic compounds which could serve as synthetic intermediates, mechanistic and ^{19}F NMR probes.[2-5] A preceeding paper[6] described a sulfur tetrafluoride fluorination of (1R,3S)-(+)-camphoric acid (**1**). This reaction resulted in a mixture of (1R,3S)-(+)-3-(trifluoromethyl)camphonanoyl fluoride (**2**), bicyclic tetrafluoroether (**3**) and camphoroyl difluoride (**4**) in ratios depending on the conditions used. The major and most interesting compound **2** was isolated by column chromatography and subsequently hydrolyzed to (1R,3S)-(+)-3-(trifluoromethyl)-camphonanic acid (**5**). This procedure is, however, inconvenient for a larger scale preparation of **5**. We now describe a simple and expedient method for the separation of the crude mixture of products resulting from the reaction of camphoric acid (**1**) with SF_4. This procedure affords pure **5** in good yield as the only product. The preparation of simple derivatives of **5** is also reported.

In the present procedure, a mixture of **2**, **3** and **4** is hydrolyzed with aqueous KOH and then the non-hydrolyzable compound (**3**) and other minor base insoluble impurities are removed by extraction with an organic solvent. Acidification of the basic solution gives a mixture of free acids **1** and **5** which are easily separated owing to the drastic difference in their solubility in aqueous media. Acid **5** is practically insoluble in water and could be isolated from **1** by washing with warm water.

The attempted acid-catalyzed esterification of **5** with methanol or ethanol failed presumably due to steric hindrance. However, treatment of **5** with $SOCl_2$ afforded the respective acid chloride **6** nearly quantitatively. Acid chloride **6** reacts in a conventional way with alcohols. Reaction with ethanol gave ester **7**. Reduction of **6** with $LiAlH_4$ yielded alcohol **8** which upon treatment with acetyl chloride gave acetate **9**. Compounds **5-9** exhibit high optical activity. With the exception of **5** and **6**,