Exceptionally Facile Conversion of Carboxylic Acid Salts to Aldehydes by Reductive Oxidation with Borane and Pyridinium Chlorochromate

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Some ten years ago, we reported that carboxylic acid metal salts are converted to the corresponding aldehydes in moderate to high yields by two equivalents of thexylbromoborane-methyl sulfide[1] or 9-borabicyclo[3.3.1]nonane (9-BBN).[2] Although these procedures provided promising routes to convert carboxylic acid salts to the corresponding aldehydes, a really clean conversion has escaped us. Thus, the yields of aromatic aldehydes are significantly lower than those in the aliphatic series and appear to be influenced by substituents on the aromatic ring. Recently, we have found that the reductive oxidation method provides an apparently ideal procedure for conversion of carboxylic acid derivatives, such as free carboxylic acids,[3] esters[4] and acid chlorides[5] to the corresponding aldehydes. This procedure involves the complete reduction of such derivatives to an alcohol stage with a suitable reducing agent, followed by oxidation of the resultant intermediate with pyridinium chlorochromate (PCC) or pyridinium dichromate (PDC). This method intrigued us, because we have already been ready to get aldehydes if carboxylic acid salts could be reduced to alcohol stage. This paper describes such an equally facile conversion of carboxylic acid salts to aldehydes.

Results and Discussion

Carboxylic acids are readily reduced to alcohols by stepwise treatment with sodium borohydride and dimethyl sulfate (eq 1). This method involves the reaction of carboxylic acid with sodium borohydride to form acyloxyborohydride **1**, followed by the treatment of **1** with dimethyl sulfate to yield acyloxyborane **2**, a reactive intermediate. The initial reaction product in such reduction has been identified as the corresponding trialkoxyboroxine **3**.[6]
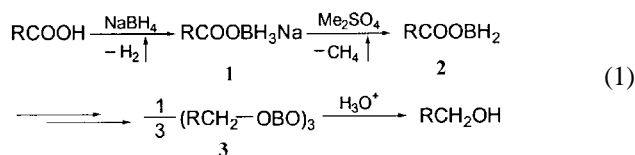
On the basis of this mechanistic point of view, if a carboxylate reacts with borane in THF to form an ate complex, which is the same species **1** as depicted in eq 1, we should expect that in the presence of dimethyl sulfate the system follows the exactly same reduction pathway until the boroxine **3**

form.

Actually carboxylate readily reacts with borane in THF to form ate complex (acyloxyborohydride **1**), the equilibrium being driven over to the right by the reaction with dimethyl sulfate and hence evolution of methane gas to yield acyloxyborane **2**. Finally, the oxidation of the resultant boroxine **3** with PCC yields aldehydes (eq 2).
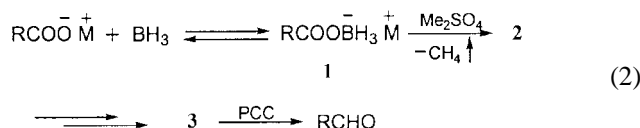
This procedure converts both sodium and lithium salts of most aliphatic carboxylic acids to aldehydes in essentially quantitative yields, as shown in Table 1, except α,β-unsaturated acids such as cinnamic and crotonic acids. In all cases there is no bias in yields between sodium and lithium salts. The reduction proceeds readily as the mixture of a carboxylate and 1.1 equiv of borane in the presence of dimethyl sulfate in THF; the oxidation also proceeds readily *in situ* in the reaction mixture with 10% excess PCC.

Just as in the reaction of aliphatic carboxylic acid salts by this procedure, the reaction of both sodium and lithium salts of aromatic series gives the corresponding aldehydes in essentially quantitative yields. Moreover, there is no variance in yields with the substituents on the benzene ring. However, the derivatives bearing a readily reducible cyano group by borane, such as *p*-cyanobenzoic acid salts, afford very low yields of aldehydes. Dicarboxylic acid salts such as disalts of terephthalic acid also fail to provide satisfactory yields of dialdehyde (35-40%).

This procces is broadly applicable so far as the borane-sensitive groups,[6] such as cyano and alkenyl functions, are absent. The mild nature of both borane and PCC makes this method simple, general and practical. Consequently, this new process, based on the reductive oxidation method, provides an apparently ideal procedure for conversion of carboxylic acid salts to the corresponding aldehydes.

Experimental Section[7]

Reduction of Carboxylic Acid Salts. The following procedure for the reduction of lithium hexanoate is illustrative for both GC analysis and the larger scale reaction. An oven-

Table 1. Conversion of Sodium and Lithium Salts of Carboxylic Acids to Aldehydes by Reductive Oxidation with Borane and Pyridinium Chlorochromate (PCC) in Tetrahydrofuran[a]

Acid salt	Yield of aldehyde[b], %	
	Na salt	Li salt
butyric	98	100
hexanoic	98(81)[c]	100(82)[c]
decanoic	99	100
stearic	98	99
isobutyric	98	99
pivalic	100	100
cyclohexanecarboxylic	98	99
diphenylacetic	98	99
6-bromohexanoic	99	100
α-camphoric	98	99
cinnamic	8	9
crotonic	5	–
benzoic	100(80)[c]	100(81)[c]
o-chlorobenzoic	98	100
p-chlorobenzoic	99	100
p-methoxybenzoic	99	100
p-nitrobenzoic	100	99
m-toluic	99	100
p-toluic	99	100
p-cyanobenzoic	10	15
terephthalic	35	40

[a]Reacted with 10% excess BH_3-THF and dimethyl sulfate at 25 ℃, except that Na salts of aliphatic acids run at 15 ℃, followed by treatment with 10% excess PCC for 6 h at 25 ℃ for aromatic and for 3 h under reflux for aliphatic acid salts. [b]GC yields. [c]An isolated yield of distilled product.

dried, 250-mL flask, fitted with a side arm capped by a rubber septum and attached to a gas meter, was charged with 7.57 g (62 mmol) of lithium hexanoate and 62 mL of THF. The flask was maintained at 25 ℃ with a circular water bath. A 1.2 M solution of BH_3 in THF (56.9 mL, 68.2 mmol) was added slowly with stirring, and the slurry was stirred for 1 h at 25 ℃.[8] To this mixture, 6.4 mL (68.2 mmol) of dimethyl sulfate was added slowly at 25 ℃.[9] Methane gas was liberated in approximately 3 h.[10] A small portion of the reaction mixture was withdrawn and hydrolyzed with 2 N HCl. GC analysis of the dried organic layer using an internal standard (dodecane) indicated the presence of hexanol in a yield of 100%.

Oxidation of Intermediate 3. To a well-stirred suspension of PCC (14.4 g, 67 mmol) in CH_2Cl_2 (100 mL) taken in a 500-mL flask was added dropwise the above reaction mixture (61 mmol) using a cannula, the mixture was stirred for 3 h under gentle reflux.[11] A small portion of this mixture was withdrawn and tridecane was added as an internal standard. The mixture was then filtered through Florisil®. GC analysis indicated the presence of hexanal in a yield of 100%.

Isolation of product Aldehydes. After the GC analysis, the rest of the reaction mixture (60 mmol) was diluted with ethyl ether (200 mL). The supernatant liquid was filtered through Florisil® (200 g) contained on a 300-mL sintered glass funnel. The insoluble solid residue was triturated with ethyl ether (3×50 mL) and passed through the same Florisil® column. The combined filtrate was concentrated and distilled to give pure hexanal (4.93 g, 82%): bp 129-130 ℃ (755 mmHg); n_D^{20} 1.4037.

References and Notes

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7. All reactions were performed under a dry N_2 atmosphere. All chemicals used were commercial products of the highest purity available; CH_2Cl_2 was stirred under a N_2 atmosphere for 1 day over P_4O_{10} and distilled; THF was dried over 4-Å molecular sieves and distilled from sodium-benzophenone ketyl prior to use. The Na and Li salts of carboxylic acid were prepared by standard methods using NaOH and LiH. A solution of BH_3 in THF was prepared by the reaction $NaBH_4$ and Me_2SO_4 in THF.
8. The solid salt disappeared and the slurry became clearer.
9. In the case of Na salts of aliphatic carboxylic acid, the temperature should be maintained below 15 ℃; the yields of aldehydes drops significantly above that temperature.
10. The Na salts requires 6 hrs for the complete evolution of methane.
11. The oxidation requires 3 hrs under reflux or 12 hrs at room temperature for the aliphatic series; 6 hrs at room temperature for the aromatic series.