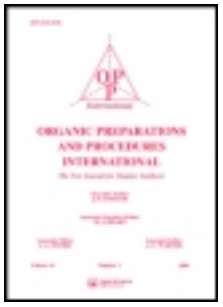

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REDUCTIVE OXIDATION OF CARBOXYLIC ACIDS TO ALDEHYDES WITH SODIUM BOROHYDRIDE AND PYRIDINIUM CHLOROCHROMATE

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saturated NaCl (50 mL), dried ($MgSO_4$) and evaporated. The orange residue (thioformamide, 1.2 g, 20%) solidified upon cooling, mp 26°.

To a solution of the crude thioformamide (1.9 g, 0.031 mol) obtained above in monoglyme (15 mL), was added with stirring a solution of bromopyruvic acid (2.7 g, 0.016 mol) in monoglyme (5.5 mL) at such a rate that the temperature remained under 28° (15-20 min.). The mixture was further stirred for 3 hrs, the yellow precipitate was collected and dried to give thiazole-4-carboxylic acid HBr (1.8 g, 53%), m.p. 244-246°. The salt was treated with ammonium hydroxide (1.5 mL) to afford 0.72 g (74%) of thiazole-4-carboxylic acid, mp. 196-197°, lit.[6] mp. 195-197°, identical in all respects with an authentic sample.[6]

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REDUCTIVE OXIDATION OF CARBOXYLIC ACIDS TO ALDEHYDES WITH SODIUM BOROHYDRIDE AND PYRIDINIUM CHLOROCHROMATE

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Carboxylic acids are readily reduced to aldehydes by stepwise treatment with sodium borohydride and dimethyl sulfate.[1] This method involves the reaction of carboxylic acids with sodium borohydride to form acyloxyborohydride (**1**), followed by the treatment of **1** with dimethyl sulfate to

form acyloxyborane (**2**), a reactive intermediate. The initial reaction product[2] in such reduction has been identified as the corresponding trialkoxyboroxine (**3**). This procedure intrigued us because the ready oxidation of the trialkoxyboroxine (**3**) by pyridinium chlorochromate (PCC) to the corresponding aldehyde has been demonstrated.[3] This communication reports a new, combined convenient procedure for transformation of carboxylic acids to aldehydes in high yields.

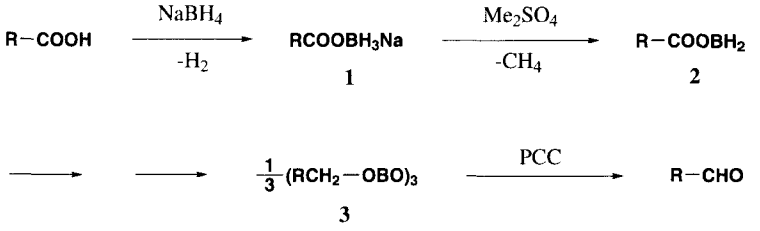

Table 1 shows that this procedure provides a clean and convenient conversion of acids to aldehydes. Both aromatic and aliphatic acids are readily converted to the corresponding aldehydes in essentially quantitative yields. The oxidation of aromatic boroxine proceeds at room temperature in 6 h, while the oxidation of aliphatic boroxine requires reflux in THF-methylene chloride for 3 h.

TABLE 1. Conversion of Carboxylic Acids to Aldehydes by Oxidation of Trialkoxyboroxine (**3**) with Pyridinium Chlorochromate (PCC)[a,b]

Acid	Product	Oxidation		Yield
		Temp.(°C)	Time (h)	(%)[c]
Benzoic	Benzaldehyde	25	6	96(82)
o-Toluic	*o*-Tolualdehyde	25	6	98
p-Toluic	*p*-Tolualdehyde	25	6	97
p-Anisic	*p*-Anisaldehyde	25	6	94
4-Chlorobenzoic	4-Chlorobenzaldehyde	25	6	98
p-Cyanobenzoic	*p*-Cyanobenzaldehyde	25	6	97
p-Nitrobenzoic	*p*-Nitrobenzaldehyde	25	6	96
Butyric	Butyraldehyde	reflux	3	94
Hexanoic	Hexanal	reflux	3	93(80)
Decanoic	Decylaldehyde	reflux	3	94
Isobutyric	Isobutyraldehyde	reflux	3	93
Trimethylacetic	Trimethylacetaldehyde	reflux	6	95
Cyclohexanecarboxylic	Cyclohexanecarboxaldehyde	reflux	3	92
Cinnamic	Cinnamaldehyde	reflux	3	94

a) Treated with 10% excess PCC. b) In a THF-methylene chloride mixture solvent.

c) GC yields ; the numbers in parentheses are isolated yields.

This reaction is broadly applicable as many substituents, such as chloro, methoxy, nitro,

cyano and alkenyl groups are tolerated. The tolerance of sodium borohydride toward a wide variety of functional groups as well as its ease of handling and low cost, combined with the mild nature of PCC as an oxidizing agent, makes this method simple, general and practical. It is noteworthy that the use of sodium borohydride can provide more selective reactions than the use of borane-methyl sulfide (BMS)[3], because sodium borohydride is milder and hence more selective than BMS.[4] Consequently, this method provides another useful procedure for direct conversion of carboxylic acids to the corresponding aldehydes.[5]

EXPERIMENTAL SECTION

All glassware used was dried thoroughly in a drying oven at 130°, assembled hot, and cooled under a stream of dry nitrogen prior to use. All reactions and manipulations of air and moisture-sensitive materials were carried out under a dry nitrogen atmosphere. All chemicals were commercial products of the highest purity which were carefully purified by standard methods before use. The carboxylic acids were commercial products and purified either by distillation or recrystallization. Tetrahedrofuran (THF) was distilled from benzophenone-sodium ketyl. Sodium borohydride ($NaBH_4$) and pyridinium chlorochromate (PCC) were used as received from Aldrich Chemical Co. Yields reported in all cases are of analytically pure compounds. GC analyses were carried out on a Varian 3300 FID chromatograph equipped with a Varian 4400 integrator.

Reduction of Carboxylic Acids.- The following procedure for the reaction of benzoic acid is representative. Into an oven-dried, 250-mL, round-bottomed flask with a side-arm, fitted with a silicon rubber cap, a magnetic stirring bar, and a reflux condenser connected to a mercury bubbler was introduced 2.35 g (62 mmol) of sodium borohydride, followed by 30 mL of THF. Finally, 31 mL (62 mmol) of a 2.0 M solution of benzoic acid in THF was added slowly with vigorous stirring at room temperature. Hydrogen gas was evolved immediately. To this mixture, 6.2 mL (66 mmol) of dimethyl sulfate was added slowly at room temperature. Methane gas was liberated in approximately 12 h.

To a well-stirred suspension of PCC (14.7 g, 68 mmol) in methylene chloride (100 mL) taken in a 500-mL flask equipped as described above, was added dropwise the solution of trialkoxyboroxine intermediate in THF prepared above using a cannula. The mixture was stirred for 6 h at room temperature. A small portion of this mixture was transferred to a vial and dodecane was added as an internal standard. GC analysis using a capillary column of Carbowax 20 M indicated the presence of benzaldehyde in a yield of 96%.

Isolation of Product Aldehydes.- The procedure for the isolation of benzaldehyde in the reaction mixture is illustrative. After 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 x 50 mL) and passed through the same Florisil column. The combined filtrate was concentrated and distilled under reduced pressure to give pure benzaldehyde (5.22 g, 82%), bp 62-63° (15 mm). The ^1H NMR spectrum agreed with that of an authentic sample.

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