

Conversion of Carboxylic Acids to Aldehydes with Cyclic Dialkyldiaminoaluminum Hydrides[†]

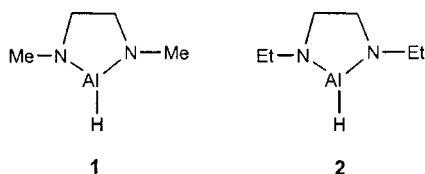
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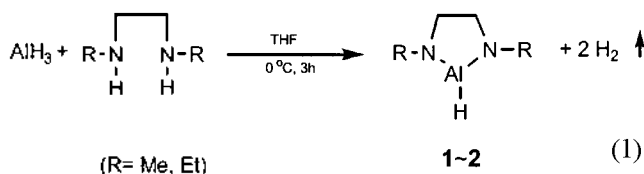
Key Words : Reduction, Carboxylic acids, Aldehydes synthesis, Cyclic dialkyldiaminoaluminum hydrides

A series of bis(dialkylamino)aluminum hydride reagents, which possesses various dialkylamines of different steric environments, has been reported as good reducing agents for the direct conversion of free carboxylic acids to the corresponding aldehydes.¹⁻³ In continuation of our efforts to explore new reducing agents for such transformation, we prepared cyclic dialkyldiaminoaluminum hydrides (**1** and **2**) and examined their general reducing action toward various organic functional groups. In the course of a systematic study, we found that these cyclic diaminoaluminum hydrides appear to be the reagents of choice for converting aromatic carboxylic acids to the corresponding aldehydes. Herein, we report such a transformation using newly-devised reducing agents.



Results and Discussion

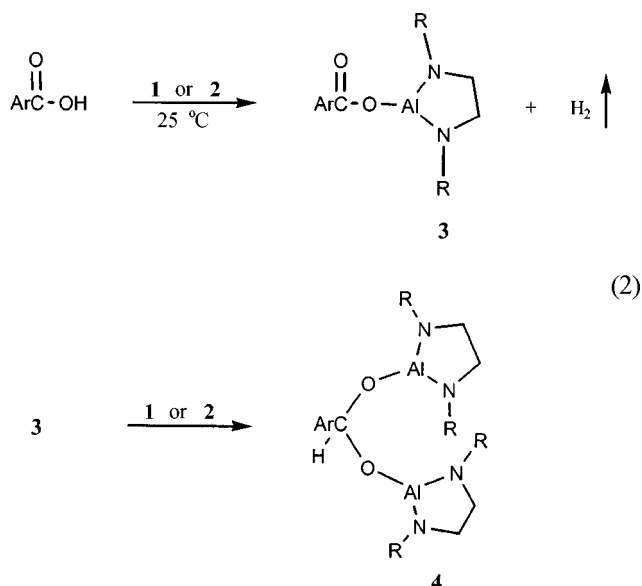
The reagents **1** and **2** are readily prepared by a simple reaction of aluminum hydride (AlH₃) with *N,N'*-dialkyl-ethylenediamine (**1**, R = Me; **2**, R = Et) in THF (Eq. 1). A solution of aluminum hydride in THF reacts with diamines readily to evolve 2 equiv of hydrogen.



²⁷Al NMR showed a doublet (*J*_{Al-H} = 265 Hz for **1** and 360 Hz for **2**) centered at δ 108 for **1** and δ 106 for **2** relative to [Al(H₂O)₆]³⁺ as a reference. A solution of the cyclic diaminoaluminum hydride in THF displayed typical absorption in the IR: a strong absorption around 1820 cm⁻¹, attributed to the Al-H stretching vibration. The reagents

were stable for at least a month when the THF solution of reagents was maintained under a positive pressure of nitrogen at 0 °C.

The general reducing power of these reagents toward organic functionalities appeared to be much weaker than that of parent aluminum hydride⁴: an extended period of reaction time at room temperature was needed to reduce even aldehydes and ketones. However, rather surprisingly, the reduction of aromatic carboxylic acids proceeded relatively faster after the evolution of 1 equiv hydrogen and stopped at the aldehyde stage. This phenomenon indicates that the acyloxyalane intermediate **3** is favorable to the reduction by the reagent but the resultant aldehyde intermediate **4** is relatively stable toward the further reduction (Eq. 2). However, the reaction of aliphatic carboxylic acids provided unsatisfactory results: over reduction to the alcohol stage is favorable under these reaction conditions.



We performed all the reductions under the standardized reaction conditions at 25 °C; we have not tried to get a maximum yield in each reaction of carboxylic acids. The general trend of aldehyde synthesis from carboxylic acids with these reagents has been examined and the results are summarized in Table 1.

Both the reagents reduce aromatic carboxylic acids to

[†]This paper is dedicated to Professor Sang Chul Shim for his distinguished achievements in chemistry.

Table 1. Reaction of Carboxylic Acids with Cyclic Dialkyl-diaminoaluminum Hydrides at 25 °C in Tetrahydrofuran^a

Carboxylic acids	Time (h)	Yield of aldehyde (%) ^b	
		Reagent 1	Reagent 2
benzoic	72	85	84
α -naphthoic	72	87	85
<i>o</i> -toluic	72	68	64
<i>m</i> -toluic	72	75	76
<i>p</i> -toluic	72	70	66
<i>o</i> -anisic	48	78	72
<i>p</i> -anisic	24	79	75
<i>o</i> -chlorobenzoic	24	63	61
<i>p</i> -chlorobenzoic	72	88	75
terephthalic ^c	72	75	71
cinnamic	24	78	70
hexanoic	72	31	32
trimethylacetic	72	30	27
cyclohexanecarboxylic	72	42	54
isobutyric	72	52	46
crotonic	24	52	44

^aRatio of reagent to compound is 2.1:1. ^bAnalyzed by GC using a suitable internal standard. The product other than aldehyde is alcohol along with unreacted starting carboxylic acid. ^cReagent to compound is 4.2:1.

aldehydes in 2-3 days at room temperature in yields of 70-90%, showing no significant bias in yields in the substituents on the benzene ring. Dicarboxylic acid, such as terephthalic acid, provides the corresponding dialdehyde in yields of 70-75%. α,β -Unsaturated carboxylic acid, such as cinnamic acid, works equally well. However, the yields from aliphatic carboxylic acids with both the reagents are not satisfactory under the reaction conditions. The yields are only in the range of 30-50%, along with the reduction products of the corresponding alcohols.

Generally, in aspect of the efficiency for aldehydes synthesis from carboxylic acids, the reagent 1 is better than 2: the reagent 1 favors in a yield of aldehyde and cost. The yields of aldehydes obtained by these reagents and dialkyl-aminoaluminum hydrides 1-3 are quite similar. However, the reductions by the former proceed under the much milder reaction conditions than the reductions by the latter: the latter reagents require drastic reaction conditions of a refluxing-THF temperature and a large excess amount of reagent up to four equivalents to get satisfactory results.

There have appeared various useful methods for transformation of carboxylic acids to aldehydes.^{1-3,5} Among them, thexylhaloboranes,^{5,6} the 9-BBN system with metal hydrides⁷ and the reduction-oxidation procedure⁸ seem to afford the most satisfactory results. However, every reducing system possesses its own limitation in use. For examples, the yields of aromatic aldehydes by thexylhaloboranes^{5,6} are relatively low and variable upon the substituents on benzene ring; the 9-BBN system with metal hydrides⁷ and the reduction-oxidation procedure⁸ can not be compatible with readily reducible functions other than carboxylic acid group. Therefore, chemists should find which procedure is suitable for their compounds to be transformed. Consequently, this

method should provide another procedure of choice to effect such conversion.

Experimental Section

All glassware utilized in this experiment was dried in oven, assembled hot, and cooled with a stream of dry nitrogen. All reactions were carried out under a static pressure of nitrogen atmosphere. Experimental techniques used in handling air- and moisture-sensitive materials are described elsewhere.⁹ THF was dried over a 4 Å molecular sieve and distilled from sodium benzophenone ketyl just prior to use. Lithium aluminum hydride (LAH) was obtained from the Aldrich Chemical Co. and used directly without further purification. *N,N'*-dialkylethylenediamine from the Aldrich Chemical Co. was purified by distillation after drying over KOH. ²⁷Al NMR spectra were recorded on a Bruker AMX 300 spectrometer and all chemical shifts were reported in δ (ppm) relative to [Al(H₂O)₆]³⁺. IR spectra were recorded on a Perkin-Elmer 1330 spectrometer. GC analyses were performed with a Varian 3300 chromatograph using a 30-m DB-WAX capillary column.

Preparation of Aluminum Hydride Solution in THF

By means of a double-ended needle, 250 mL of 1.2 M lithium aluminum hydride solution in THF (300 mmol) was introduced into a 500-mL flask, fitted with an inlet port, rubber syringe cap, and a magnetic stirring bar and connected to a mercury bubbler *via* a reflux condenser. The flask was cooled to 0 °C and maintained at the temperature using a refrigerating bath circulator. To this solution 29.5 g of methanesulfonic acid (308 mmol, 2.5% excess) was added slowly by means of a hypodermic syringe, while stirring the solution vigorously. After the complete addition, the solution was permitted to stir for 1 h, and then allowed to stand to permit the lithium sulfonate precipitate to settle. The clear, supernatant solution was analyzed for hydride by hydrolyzing an aliquot with 2 N H₂SO₄-THF (1:1) solution to indicate a concentration of 1.10 M (²⁷Al NMR: δ 127).

Preparation of Cyclic Dialkyl-diaminoaluminum Hydride (1, 2) Solution in THF

The preparation of reagent 1 (*N,N'*-dimethylethylenediaminoaluminum hydride) is illustrative. In a 100-mL, round-bottomed flask was placed 30 mL of a 1.10 M solution of AlH₃ in THF (40 mmol) and the solution was kept at 0 °C by using a refrigerating bath circulator. To this solution was added 3.92 g of *N,N'*-dimethylethylenediamine (44 mmol) dropwise with vigorous stirring. After the complete addition, the solution was stirred for 3 h. The concentration of the solution was estimated gasometrically to indicate 0.92 M. ²⁷Al NMR spectrum of the solution showed a doublet ($J_{\text{Al-H}} = 265$ Hz) at δ 106 ppm. IR spectrum of the solution displayed a strong absorption at 1821 cm⁻¹, attributed to the Al-H stretching vibration.

General Procedure Used for Reductions. The following procedure was used for quantitative studies. The reduction of benzoic acid is described as an example of the experimental procedure. To a 50-mL flask fitted with a rubber syringe cap on an inlet port, a magnetic stirring bar, and a bent adapter

connected to a mercury bubbler *via* a reflux condenser 8.7 mL of a solution of 0.92 M reagent **1** (8 mmol) was placed and the solution was maintained at 25 °C. To this solution 0.49 g of benzoic acid (4.0 mmol) in 4 mL of THF was injected slowly. One equiv of hydrogen was evolved immediately. After the complete evolution of hydrogen, a measured quantity of tridecane (*ca.* 2 mmol) as an internal standard was added. After 72 h, a small portion of the reaction mixture was withdrawn and then quenched with 2 N HCl. The aqueous layer was saturated with MgSO₄, and the organic layer was washed with saturated NaCl solution. The organic layer dried over anhydrous K₂CO₃ was subjected to GC analysis to indicate the presence of benzaldehyde in a yield of 85% along with 5% of benzyl alcohol and some unreacted starting benzoic acid.

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