CHEMISTRY LETTERS, pp. 1447-1450, 1974. Published by the Chemical Society of Japan

AMINOALUMINUM HYDRIDE AS NEW REDUCING AGENTS. I.

SELECTIVE REDUCTION OF CARBOXYLIC ACIDS TO ALDEHYDES

Masayoshi MURAKI(1) and Teruaki MUKAIYAMA
Laboratory of Organic Chemistry, Tokyo Institutes of Technology
Ookayama, Meguro-Ku, Tokyo 152

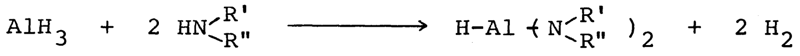
A new method for the preparation of aldehydes from carboxylic acids by use of diaminoaluminum hydride is described. Reducing agents, diaminoaluminum hydrides, were prepared from aluminum hydride and two moles of various secondary amines. It was found that bis(4-methylpiperazinyl)aluminum hydride is the most suitable reducing agent, which reduces carboxylic acids to the corresponding aldehydes at room temperature or under reflux in good yields.

Many methods have been reported for the preparation of aldehydes from carboxylic acid derivatives such as esters, amides, and halides. However, little work has been reported on the selective reduction of free carboxylic acids to aldehydes except that by use of lithium in methylamine(2) and thexylborane(3). We now report a convenient method for the reduction of free carboxylic acids to aldehydes by use of bis(4-methylpiperazinyl)aluminum hydride (Ia).

Recently, it was shown in reviews by Málek and Černý(4), and by Rerick(5) that lithium alkoxyaluminum hydrides prepared from lithium aluminum hydride and alcohols were mild reducing agents which made possible the reduction of carboxylic acid derivatives to aldehydes. However, the reduction of carboxylic acids with lithium trimethoxyaluminum hydride(6) or aluminum hydride(7) in stoichiometric ratio gave alcohols and no or, if any, only trace amounts of aldehydes. No reaction takes place when lithium tri-t-butoxyaluminum hydride(6) was used in the reduction of carboxylic acid.

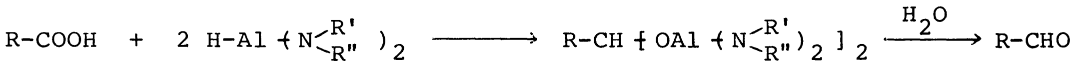
It was found by the present experiment that diaminoaluminum hydrides (I) or lithium diaminoaluminum hydrides (II) especially Ia are very effective for the reduction of carboxylic acids to the corresponding aldehydes after screening various alkoxy, mercapto or amino groups substituted aluminum hydrides or lithium aluminum hydrides.

Aluminum hydride in tetrahydrofuran (THF) reacts readily with two moles of secondary amines such as N-methylpiperazine, morpholine, di-n-propylamine, N-methylaniline, and forms I at room temperature with the liberation of two moles of hydrogen. In the case of diacid bases, the reducing agents were prepared by treating equimolar amounts of piperazine or sym-dimethylethylenediamine and aluminum hydride.



$$AlH_3 + 2\ HN\begin{smallmatrix}R'\\R''\end{smallmatrix} \longrightarrow H\text{-}Al(N\begin{smallmatrix}R'\\R''\end{smallmatrix})_2 + 2\ H_2$$

Treatment of a mixture of one mole of carboxylic acid with two to four moles of the reagent I in THF either stirring for 1-2 days at room temperature or refluxing for 3-6 hours, followed by hydrolysis afforded the corresponding aldehyde.



$$R\text{-}COOH + 2\ H\text{-}Al(N\begin{smallmatrix}R'\\R''\end{smallmatrix})_2 \longrightarrow R\text{-}CH[OAl(N\begin{smallmatrix}R'\\R''\end{smallmatrix})_2]_2 \xrightarrow{H_2O} R\text{-}CHO$$

Among the secondary amines examined, alicyclic amines, especially N-methylpiperazine gave more favorable result for the preparation of aldehydes than alkyl or aromatic amines. Further, it was shown that the yield of aldehyde by using various secondary amines decreases in the following order.

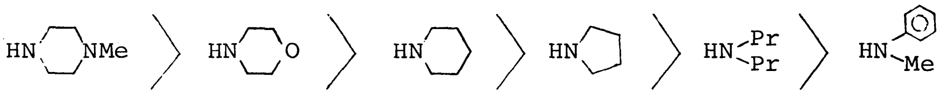
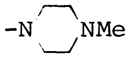
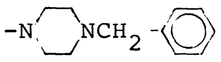
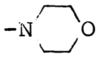
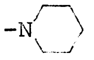
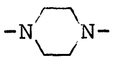


Table 1. Yields of Aldehydes and Alcohols in the Reduction of Carboxylic Acids by I.

Diaminoaluminum Hydride H-Al(X)$_2$	β-Phenylpropionic acid		Benzoic acid	
	a) aldehydes (%)	b) alcohols (%)	a) aldehydes (%)	b) alcohols (%)
Ia, X= 	70	3	86	4
Ib, X= 	52	14		
Ic, X= 	51	7	46	5
Id, X= 	28	3	38	4
Ie, X$_2$= 	53	16		

a) By analysis with 2,4-dinitrophenylhydrazine.

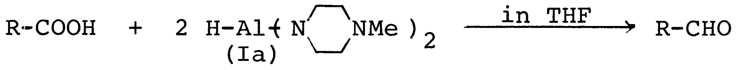
b) Calculated by the ratio of aldehyde to alcohol by means of gas chromatography.

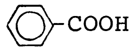
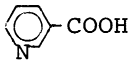
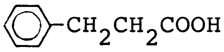
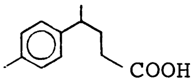
The results of reduction of β-phenylpropionic or benzoic acid with Ia-e are summarized in Table 1.

Typical procedure : N-methylpiperazine (14.1 g, 141 mmol) was added to a 0.71 M solution of aluminum hydride in anhydrous THF⁷⁾ (97 ml, 69 mmol) over a period of 15 min in an ice-bath under argon. After stirring for 2 hr at room temperature, 0.52 M of clear solution of Ia, resulted. The concentration was estimated by analysis of hydride (by hydrolysis). Twenty-three ml of the above reagent solution was added to a solution of palmitic acid (785 mg, 3.1 mmol) in THF in an ice-bath over a period of 5 min. The solution was refluxed for 6 hr. Then, water (0.7 g) was added to the solution in an ice-bath. Crystals were filtered off and extracted repeatedly with hot THF. The filtrate and extracts were condensed in vacuo and the residue was dissolved in ether, washed with water, are dried over Na_2SO_4. Evaporation of the ethereal phase gave a crude oil of 1.2 g, which was purified by column chromatography of silica-gel to afford pure palmitic aldehyde 560 mg (77 %), mp 32-34°C.

The yields of aldehydes in the reduction of various carboxylic acids with the reducing agent Ia are summarized in Table 2. The yields appear to be equally satisfactory both for aliphatic and aromatic derivatives and for hetero-cyclic derivatives.

Table 2. Yields of Aldehydes in the Reduction of Carboxylic Acids by Ia.

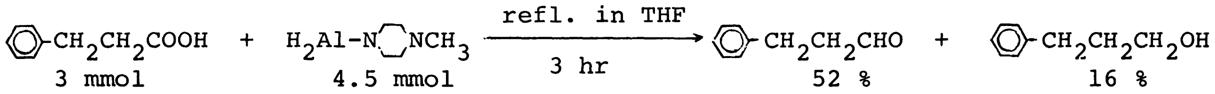


Carboxylic Acids	Conditions	Aldehydes (%)	
		a)	b)
n-$C_5H_{11}COOH$	refl. 6hr	72	63
n-$C_7H_{15}COOH$	refl. 20hr	75	69
n-$C_{15}H_{31}COOH$	refl. 6hr		77
	refl. 3hr	86	
	r.t. 2day		75
	refl. 3hr	75	70
	refl. 10hr		68

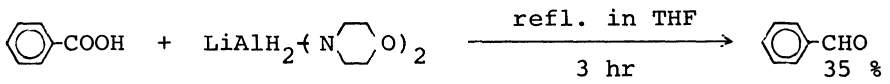
a) By analysis with 2,4-dinitrophenylhydrazine.

b) By isolation.

The reduction of carboxylic acids with monoaminoaluminum hydrides was not so satisfactory as compared with I because of an increase in yields of by-products alcohols.



The reducing agents II, prepared from lithium aluminum hydride and two moles of secondary amines, also reduced carboxylic acids to give corresponding aldehydes. The reduction by lithium dimorpholinoaluminum hydride gave aldehydes in low yields with small amounts of alcohols.



The reduction of carboxylic acids with aluminum hydride in stoichiometric ratio gave only trace amounts of aldehydes. When an excess amount of Ia was used in the above experiment, aldehydes were produced in good yields in company with small amounts of alcohols.

It is noted that Ia reduces carboxylic acids to aldehydes very easily, but very small amounts of alcohols are produced even when the reduction is carried out under refluxing. This new aldehyde synthesis should provide a convenient alternative route for proceeding from free carboxylic acid to the corresponding aldehyde.

REFERENCES

1) Present address; Organic Chemistry Research Laboratory, Tanabe Seiyaku Co. Ltd., 2-2-50, Kawagishi, Toda, Saitama 335.

2) A.O. Bedenbaugh, J.H. Bedenbaugh, W.A. Bergin, and J.D. Adkins, J. Amer. Chem. Soc., 92, 5774 (1970).

3) H.C. Brown, P. Heim, and N.M. Yoon, J. Org. Chem., 37, 2942 (1972).

4) J. Málek and M. Černý, Synthesis, 217 (1972).

5) M.N. Rerick, "Reduction: Techniques and Applications in Organic Synthesis," ed. by R.L. Augustine, Marcel Dekker, Inc., New York, 1968, Chapter 1.

6) H.C. Brown and P.M. Weissman, J. Amer. Chem. Soc., 87, 5614 (1965).

7) H.C. Brown and N.M. Yoon, ibid., 88, 1464 (1966).

(Received October 4, 1974)