Table 1. Yields of Aldehydes in the Reduction of Primary Carboxamides Through Treatment of N-Diisobutylaluminocarboxamides with Lithium Tris(diethylamino)aluminum Hydride in Tetrahydrofuran at Room Temperature[a]

Class	Amide	Reaction time (h)	Yield of aldehyde (%)[b]
Aliphatic	acetamide	3.0	52
	2-chloroacetamide	3.0	56
	trimethylacetamide	6.0	71
	n-butyramide	3.0	60
	isobutyramide	3.0	64
	methacrylamide	3.0	50
	caproamide	3.0	62 (68)[c]
	octadecaneamide	6.0	70 (72)[c]
	cyclohexane-carboxamide	3.0	63
Aromatic	benzamide	3.0	82 (63)[c] (76)[d]
	o-toluamide	1.0	77
	4-methoxybenzamide	1.0	74
	2-ethoxybenzamide	1.0	70
	2-chlorobenzamide	3.0	71
	2-nitrobenzamide	1.0	36
	nicotinamide	1.0	62

[a] 3 Equiv of LTDEA used. [b] Analyzed with (2,4-dinitrophenyl)hydrazine. [c] 2 Equiv of LTDEA utilized. [d] at 0℃.

amides examined. Aromatic carboxamides ae also readily converted into the corresponding aldehydes in yields more than 70%, except for nitrobenzamides. The nitro group itself appears to be reduced readily. Derivatives containing alkyl, alkoxy or halogeno group are readily accommodated. Nicotinamide is also converted into the corresponding aldehyde in a yield of 62%.

In general, the yields of aldehydes obtained from this system appear to be similar to those obtained from LTDEA itself[2a], however the rate of reduction in this procedue is much faster. Thus, this system requires the reaction time of 1-3 h, but LTDEA itself requires 6-12 h both at room temperature.

The following procedue for the reduction of *o*-toluamide is illustrative. An oven-dried, 50-m*l* flask, fitted with a side arm and a bent adaptor connected to a mercury bubbler, was charged with 3.3 m*l* of 1.5 M solution of *o*-toluamide (0.677 g, 5.0 mmol) in THF. The solution was cooled to 0℃ and 2.0 m*l* of DIBAH-THF solution (2.5 M, 5.0 mmol) was injected dropwise. After the hydrogen evolution was ceased, the reaction mixture was warmed to room temperature and 11 m*l* of LTDEA-THF solution (1.4 M, 1.5 mmol) was added. The mixture was stirred for 1 h at room temperature. Analysis of the reaction mixture with (2,4-dinitrophenyl)hydrazine showed a yield of 77%.

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Mechanism of Aldehyde Synthesis from Ester by Sodium Diethylpiperidinohydroaluminate

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Among several metal hydrides, which are reported to be useful for aldehyde synthesis from carboxylic acid esters[1-5], diisobutylaluminum hydride (DIBAH) has been most generally utilized for the aldehyde synthesis from esters. However the very low temperature (−70℃) required for the DIBAH reduction is still a considerable handicap, especially for larger samples. Recently we have reported that sodium diethylpiperidinohydroaluminate (SDPA) prepared from equimolar sodium diethyldihydroaluminate (SDDA) and piperidine in THF-toluene, is an excellent reagent for the aldehyde synthesis[6]. Thus we could obtain aromatic aldehydes quantitatively even though the yields of aliphatic aldehydes varied depending on the structure (60-90%). In the hope of clarifying the mechanism of the reaction, we studied the reaction of ethyl benzoate with 5 different *sec*-amine derivatives of SDDA (Table 1). As shown in Table 1, the yield of benzaldehyde are heavily dependent on the nature of secondary amino group in these derivatives. Thus replacement of piperidyl group by bulky dibenzylamino or less nucleophilic diphenylamino group resulted in a drastic decrease in yield of benzaldehyde (entry 4 and 6)

This suggests that reaction of equimolar ethyl benzoate and SDPA rapidly forms two unstable intermediates [1] and [2] by the attack of hydride or piperidyl group on sp^2 carbon of ester, and these are quickly transformed into a more stable intermediate, α-piperidyl alkoxoaluminate [3], by the rearrangement involving migration of piperidyl group or hydride as shown in Scheme 1.

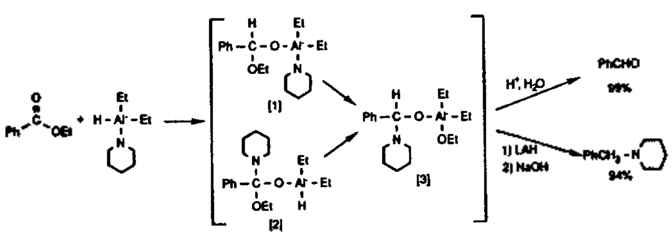
The mechanism is supported by the following facts. (1) Under the same experimental conditions, benzaldehyde was

† This paper is dedicated to Professor Herbert C. Brown on the occasion of his 80th birthday.

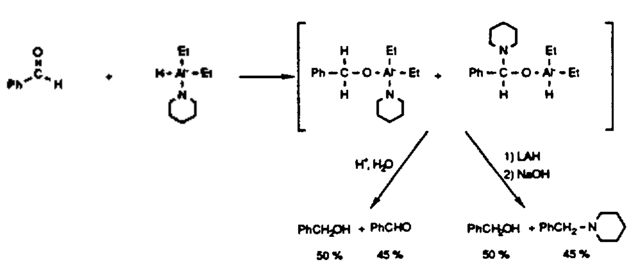
Table 1. Reaction of *sec*-Amine Derivatives of Sodium Diethyldihydroaluminate with Ethyl Benzoate

entry	hydride	product[a,b]	
		benzaldehyde	benzyl alcohol
1	$Na^{+}\ H\text{-}\overset{Et}{\underset{Et}{Al^{-}}}\text{-}N\bigcirc$	99%	trace
2	$Li^{+}\ H\text{-}\overset{Et}{\underset{Et}{Al^{-}}}\text{-}N\bigcirc$	95%	trace
3	$Na^{+}\ H\text{-}\overset{Et}{\underset{Et}{Al^{-}}}\text{-}NEt_2$	95%	4%
4	$Na^{+}\ H\text{-}\overset{Et}{\underset{Et}{Al^{-}}}\text{-}N(CH_2Ph)_2$	48%	23%
5	$Na^{+}\ H\text{-}\overset{Et}{\underset{Et}{Al^{-}}}\text{-}H$	22%	42%
6	$Na^{+}\ H\text{-}\overset{Et}{\underset{Et}{Al^{-}}}NPh_2$	trace	50%

[a] 1.1 Eq of H^- was added to ethylbenzoate in THF-toluene at 0℃ and the reduction was carried out for 1.0 h. [b] Analyzed by GC.



Scheme 1



Scheme 2

reduced only partially and 1-benzylpiperidine was obtained by treating the reaction mixture with lithium aluminum hydride (LAH). This shows that the sp^2 carbon of benzaldehyde was competitively attacked by hydride and piperidyl group of SDPA (Scheme 2). (2) A 94% yield of 1-benzylpiperidine was realized by the reduction of the reaction mixture of equimolar SDPA and ethyl benzoate with LAH (Scheme 1). (3) The reduction of 1-benzoylpiperidine with equimolar SDPA gave 98% yield of benzaldehyde in 3 h at 0℃. This shows the intermediate [3] is very stable under the reaction conditions. It is not clear at this time whether the step [1]→[3] and the step [2]→[3] involve the formation of benzaldehyde and 1-benzoylpiperidine[7] or not. However the lower yield of benzaldehyde and increased yield of benzyl alcohol realized with bulky dibenzylamino derivative and less nucleophilic diphenylamino derivative (entry 4 and 6) could be rationalized by the predominant formation of [1] over [2] and the successful competitive reduction of [1] by another hydride (probably through benzaldehyde) over the step [1]→[3].

Experimental

Preparation of *sec*-Amine Derivatives of SDDA. Reaction of SDDA with 2.0 mol equiv. of piperidine, diethylamine (at 0℃), dibenzylamine or diphenylamine (at room temperature) evolves only one mol equiv. of hydrogen rapidly in THF-toluene and no further hydrogen evolution is apparent. Therefore the *sec*-amine derivatives of SDDA were prepared as described below for SDPA. A 100 m*l* flask fitted with a rubber septum on an inlet port and magnetic stirring bar was thoroughly dried in an oven and cooled down under nitrogen. Into the flask, 30 m*l* (60 mmol) of 2 M SDDA solution in toluene and 60 m*l* of THF were introduced. The solution was cooled to 0℃, and then 6.52 m*l* (66 mmol) of distilled piperidine was added with vigorous stirring. Stirring was continued for an additional 3 h for complete hydrogen evolution. The SDPA solution thus prepared was 0.88 M in hydride as standardized by hydrolyzing with t-BuOH-THF (1 : 1 mixture). Lithium derivative was prepared by the addition of equimolar lithium chloride to SDPA solution and used as such without elimimating NaCl.

Reduction of Benzaldehyde with SDPA. Into a 50 m*l* flask, similarly equipped as above, 11.4 m*l* of 0.88 M SDPA (10 mmol) and 3.6 m*l* of THF were placed in the flask and the reaction was started by adding 5 m*l* of 0.5 M (2.5 mmol) benzaldehyde solution in THF containing 2.5 mmol of naphthalene as an internal standard. The hydrolysis of aliquots at 0.5 h, 1.0 h and 3.0 h revealed that 0.49, 0.49 and 0.49 equiv. of hydride were consumed respectively for reduction per mol of compound. And GC analysis showed 45% benzaldehyde and 50% benzyl alcohol. However, when this readion mixture was reacted with excess LAH for 3 h at room temperature, the products were 1-benzylpiperidine (45%) and benzyl alcohol (50%).

Synthesis of Benzaldehyde and Benzylpiperidine by the Reduction of Ethyl Benzoate with SDPA. Into a 50 m*l* flask, similarly equipped as above, were introduced 2.8 m*l* of THF and 1.0 m*l* (1.0 mmol) of ethyl benzoate solution in THF containing mesitylene as an internal stnadard, followed by 1.25 m*l* (1.1 mmol) of 0.88 M solution of SDPA in THF-Toluene (1 : 1). The solution was maintained at 0℃ with stirring. After 0.5 h, the mixture was divided in two portions. One portion was hydrolyzed with 5 m*l* of 2 N HCl, treated with NaCl, and extracted with ether. The ether layer was dried over anhydrous magnesium sulfate, and analyzed by GC (99% yield of benzaldehyde). The other portion was introduced to excess LAH at room temperature. After 3.0 h, the mixture was hydrolyzed with NaOH solution, and salt-

ed out with NaCl. The ether layer which was dried over anhydrous magnesium sulfate, showed a 94% yield of 1-benzylpiperdine by GC analysis.

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Table 1. Reaction of *N,N*-Dimethylhexanamide and *N,N*-Dimethylbenzamide with Sodium Diethyldihydroaluminate (SDDA)[a]

tertiary amide	temp ℃	hydride /comp.[b]	time h	yield, %[c] aldehyde	alcohol	amine	amide
N,N-dimethyl hexanamide	0	1.5	1.0	77	8	0	15
			3.0	79	9	0	11
	0	2	0.5	82	12	0	6
			1.0	85	13	0	2
	0	5	1.0	63	30	7	0
			3.0	58	29	13	0
	25	2	0.5	90	10	0	0
	reflux	5	1.0	10	16	70	0
			3.0	0	12	85	0
N,N-dimethyl benzamide	0	1.5	1.0	88	2	0	8
			3.0	92	3	0	4
	0	2	0.5	92	6	0	0
			1.0	95	4	0	0
	0	5	1.0	71	20	4	0
			3.0	68	28	4	0
	25	2	0.5	92	5	0	0
	reflux	5	1.0	13	27	60	0
			3.0	0	22	78	0

[a] Reactions were carried out by adding one mmol of SDDA in 0.5 m*l* toluene to one mmol of amide in 1.5 m*l* THF (0.5 M in compound). [b] Mole of hydride per mole of compound. [c] Yields were estimated by GLPC.

A New Aldehyde Synthesis from Tertiary Carboxamides with Sodium Diethyldihydroaluminate

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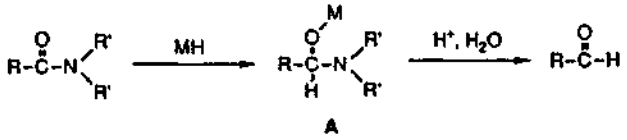
Reduction of tertiary carboxamides to the corresponding aldehydes is one of the most important and highly desirable means in organic synthesis and numerous methods have been reported, among which reduction with lithium aluminum hydride[1] has been sucessful for 1-acylcarbazole[2], 1-acyl-3,5-dimethylpyrazoles[3], 1-acylimidazoles[4], 1-acylaziridines[5] and *N*-ethylanilides[6]. Partial reduction of *N,N*-dimethylcarboxamides with sodium aluminum hydride[7], lithium di- or triethoxylaluminum hydride[8] and aminoaluminum hydride[9] was also reported to be a useful method for preparation of aldehydes.

Recently we have studied the reducing characteristics of sodium diethyldihydroaluminate (SDDA) systematically, and found that SDDA is a promising selective reducing agent[10]. Thus even with excess SDDA (5 equiv. of hydride), *N,N*-dimethylhexanamide and *N,N*-dimethylbenzamide gave 63% and 71% yields of the corresponding aldehydes respectively in 1 h at 0℃. However with excess hydride at 65℃, the major reduction products were corresponding amines. As shown in Table 1, these dimethylamides were conveniently reduced to the corresponding aldehydes in excellent yields in 0.5-1.0 h at room temperature using equimolar SDDA (2 equiv. of hydride). Therefore, in order to test the generality of this aldehyde synthesis, twenty three representative tertiary amides and two secondary amides were reduced at 25℃ for shorter period of time (usually 0.5-1.0 h) with limited amount of SDDA. The results are summarized in Table 2.

As shwon in Table 2, *N,N*-dimethylamides of less hindered aliphatic acids such as hexanoic acid and isovaleric acid or equally less hindered amides such as 1-hexanoyl pyrrolidine and 1-hexanoyl piperidine were readily reduced to the corresponding aldehydes in 83-90% yields, however, *N,N*-dimethylamides of hindered acids such as cyclohexanecarboxylic



acid and pivalic acid gave only fairly good yields (74% and 63%), and *N,N*-diethylhexanamide and *N,N*-diisopropylhexanamide gave poor yields of aldehyde (46% and 35%). Apparently the tetrahedral intermediate [**A**] is destabilized as R and R' groups become bulkier. The reaction of these bulky amides was slower at our standard conditions (25℃, H/co-