Selective Reduction by Lithium Bis- or Tris(dialkylamino)-aluminum Hydrides. II. Reaction of Lithium Tris(dibutylamino)-aluminum Hydride with Selected Organic Compounds Containing Representative Functional Groups[1]

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The approximate rates and stoichiometry of the reaction of excess lithium tris(dibutylamino)aluminum hydride (LTDBA) with selected organic compounds containing representative functional groups under standardized conditions (tetrahydrofuran, 0℃) were studied in order to characterize the reducing characteristics of the reagent for selective reductions. The reducing ability of LTDBA was also compared with those of the parent lithium aluminum hydride and the alkoxy derivatives. The reagent appears to be much milder than the parent reagent, but stronger than lithium tri-*t*-butoxyaluminohydride in reducing strength. LTDBA shows a unique reducing characteristics. Thus, the reagent reduces aldehydes, ketones, esters, acid chlorides, epoxides, and amides readily. In addition to that, α,β-unsaturated aldehyde is reduced to α,β-unsaturated alcohol. Quinones are reduced to the corresponding diols without evolution of hydrogen. Tertiary amides and aromatic nitriles are converted to aldehydes with a limiting amount of LTDBA. Finally, disulfides and sulfoxides are readily reduced to thiols and sulfides, respectively, without hydrogen evolution.

Introduction

The alkoxy-substituted derivatives of lithium aluminum hydride have appeared to exhibit reducing properties significantly different from those of the parent reagent[2-12]. For example, lithium tri-*t*-butoxyaluminohydride has proven to be a valuable selective reducing agent for transformation of acid chlorides to aldehydes[2,3]. The ethoxy-substituted derivatives have also proven to be valuable for the reduction of nitriles and dimethylamides to the corresponding aldehydes in high yields[8,9].

Similarly, the dialkylamino-substituted derivatives of lithium aluminum hydirde seem to exhibit reducing properties different from those of the parent reagent and/or the alkoxy derivatives. In fact, preliminary observation revealed that the dialkoxyamino derivatives possess unique reducing potentials for the selective reduction of organic functionalities. Accodingly, it appeared desirable to undertake a systematic exploration of the reaction of lithium tris(dibutylamino)aluminum hydride (LTDBA), one of the class of dialkylamino derivatives, with the standard list of organic compounds, comprising the common functional groups, under standardized conditions (tetrahydrofuran, 0℃) in order to define its reducing characteristics and compare to those of various reducing agents.

Results and Discussion

Lithium tris(dibutylamino)aluminum hydride, LTDBA, was prepared readily from the addition of 3 moles of dibutylamine to 1 mole of lithium aluminum hydride in tetrahydrofuran at room temperature (Eq. 1)[13].

$$LiAlH_4 + 3\,n\text{-}Bu_2NH \xrightarrow[RT,\ 6h]{THF} \underset{\text{"LTDBA"}}{Li(n\text{-}Bu_2N)_3AlH} + 3\ H_2\uparrow \qquad (1)$$

The reagent is very stable under the reaction condition. The ^{27}Al-NMR spectrum of LTDBA in THF showed broad singlet at δ 128 ppm relative to $Al(H_2O)_6^{3+}$.

The general procedure for the systematic study on the approximate rates and stoichiometry involved preparation of a reaction mixture of the reagent (1.0 M in reagent) and the compound examined (0.25 M) under study in THF at 0℃. In a few cases, such as anhydrides, the compound undergoing reduction utilized so many equivalents of hydride that it was necessary to increase the hydride/compound ratio. Hydrogen evolution during the reaction was measured by using a gas-buret. At the appropriate reaction intervals, aliquots were withdrawn from the reaction mixture and analyzed for residual hydride by hydrolysis[14]. From the difference in the volume of hydrogen evolution in the two intervals, the hydride used by the compound for reduction was calculated. In this way, it was possible to calculate a value for the number of moles of the hydride utilized for the reduction.

Alcohols, Phenols, Amines, and Thiols (Active Hydrogen Compounds). Primary and secondary alcohols evolved hydrogen rapidly and completely in 1-3 h at 0℃, whereas tertiary alcohol evolved only sluggishly. *n*-Hexylamine also evolved hydrogen only slowly, requiring 72 h for completion. However, surprisingly, benzyl alcohol, phenol and thiols did not react with this reagent at all. In this respect, LTDBA is much less reactive than lithium aluminum hydride which evolves hydrogen immediately from reaction with these active hydrogen compounds[15]. These results are summarized in Table 1.

Aldehydes and Ketones. All of the saturated aldehydes and ketones examined took up 1 equiv. of hydride for reduction to the corresponding alcohols rapidly within 1 h. Cinnamaldehyde utilized 1 equiv. of hydride rapidly, but further reduction to the hydrocinnamyl alcohol stage was very

Table 1. Reaction of Lithium Tris(dibutylamino)aluminum Hydride with Representative Active Hydrogen Compounds in Tetrahydrofuran at 0℃

Compounds[a]	Time (hr)	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
1-Hexanol	0.5	0.98	0.98	0.00
	1.0	1.00	1.00	0.00
Benzyl alcohol	3.0	0.01	0.01	0.00
3-Hexanol	0.5	0.87	0.87	0.00
	1.0	0.93	0.93	0.00
	3.0	1.00	1.00	0.00
3-Ethyl-3-pentanol	24.0	0.54	0.54	0.00
	72.0	0.71	0.71	0.00
Phenol	3.0	0.00	0.00	0.00
n-Hexylamine	3.0	0.37	0.37	0.00
	24.0	0.76	0.76	0.00
	72.0	1.00	1.00	0.00
1-Hexanethiol	3.0	0.00	0.00	0.00
Benzenethiol	3.0	0.01	0.01	0.00

[a] 5.0 Mmol of compound was added to 20 mmol of the reagent (0.25 M in compound and 1.0 M in hydride). [b] Mmol/mmol of compound.

Table 2. Reaction of Lithium Tris(dibutylamino)aluminum Hydride with Representative Aldehydes and Ketones in Tetrahydrofuran at 0℃

Compounds[a]	Time (hr)	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
Caproaldehyde	0.5	0.01	1.01	1.00
Benzaldehyde	0.5	0.00	1.00	1.00
2-Heptanone	0.5	0.00	1.00	1.00
Norcamphor	0.5	0.00	0.97	0.97
	1.0	0.00	1.00	1.00
Acetophenone	0.5	0.01	0.92	0.91
	1.0	0.01	1.01	1.00
Benzophenone	0.5	0.00	1.00	1.00
Cinnamaldehyde	0.5	0.00	1.01	1.01
	12.0	0.00	1.48	1.48
	48.0	0.00	1.73	1.73
	120.0	0.00	2.01	2.01

[a,b] See the corresponding footnotes in Table 1.

slow. Lithium aluminumm hydride reduces cinnamaldehyde to hydrocinnamyl alcohol rapidly[15], but lithium tri-*t*-butoxyaluminohydride does not attack the double bond to provide a clean reduction to cinnamyl alcohol[6]. The results are summarized in Table 2.

The stereoselectivity of the reagent on the reduction of cyclic ketones was also studied, and the results and those of lithium aluminum hydride and lithium tir-*t*-butoxyaluminohydride for comparison are summarized in Table 3. The introduction of di-*n*-butylamino group enhances the stereoselectivity to a large extent, compared with the results of the parent reagent and the alkoxy derivative. For example, 3,3,5-trimethylcyclohexanone is reduced by LTDBA to the corresponding less stable isomer (*trans* alcohol) in a ratio of 93% at 0℃, whereas the ratios by lithium aluminum hydride and lithium tri-*t*-butoxyaluminohydride are 52 and 73%, respectively.

Table 3. Stereochemistry in the Reduction of Cyclic Ketones with Lithium Tris(dibutylamino)aluminum Hydride in Tetrahydrofuran at 0℃

Compound	Less stable isomer (%)[a,b]		
	$Li(Bu_2N)_3AlH$	$LiAlH_4$[c]	$Li(t\text{-}BuO)_3AlH$[d]
Cyclohexanone			
2-methyl-	55.5	24	30
3-methyl-	27.5	16	14
4-methyl-	27.5	19	17
4-*t*-butyl-	48.5	9	10
3,3,5-trimethyl-	93	52	73
Norcamphor	90.5	89	93
Camphor	93.5	92	93

[a] Excess reagent used. [b] Quantitative yields. [c] Data taken from ref. 16. [d] Data taken from ref. 16.

Table 4. Reaction of Lithium Tris(dibutylamino)aluminum Hydride with Representative Quinones in Tetrahydrofuran at 0 ℃

Compounds[a]	Time (hr)	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
p-Benzoquinone[c]	0.5	0.00	1.75	1.75
	1.0	0.00	1.90	1.90
	3.0	0.00	2.01	2.01
Anthraquinone[d]	0.5	0.00	1.79	1.79
	1.0	0.00	1.98	1.98
	3.0	0.00	2.00	2.00

[a,b] See the corresponding footnotes in Table 1. [c] Turn to be dark greenish immediately. [d] Dark brown color was formed immediately.

Quinones. LTDBA shows a very interesting characteristics on the reduction of quinones examined. Thus, both *p*-benzoquinone and anthraquinone evolved no hydrogen and utilized 2 equiv. of hydride for reduction in 3 h at 0℃. These results correspond to the reduction to the 1,4-dihydroxycyclohexadiene and 9,10-dihydro-9,10-anthracenediol stages, respectively. In general, the reduction of quinones with common boron and aluminum hydrides yields a mixture containing hydroquinones. Similarly, in the case of lithium tri-*t*-butoxyaluminohydride no hydrogen evolutions is observed during the reduction, but a long reaction time(longer than 24 h) is required for completion[6]. These results are summarized in Table 4.

Carboxylic Acids and Acyl Derivatives. Carboxylic acids evolved hydrogen only incompletely when added to the reagent at 0℃. Moreover, the reduction of the acids was very slow, requiring 3 days for caproic acid and 7 days for benzoic acid to be reduced to the corresponding alcohols (the hydrazine analysis of the reaction mixture did not show any aldehyde formation). Acid anhydrides took up two hy-

Table 5. Reaction of Lithium Tris(dibutylamino)aluminum Hydride with Representative Carboxylic Acids and Acyl Derivatives in Tetrahydrofuran at 0℃

Compounds[a]	Time (hr)	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
Caproic acid	0.5	0.21	1.25	1.04
	3.0	0.25	1.48	1.23
	24.0	0.25	1.94	1.69
	72.0	0.25	2.27	2.02
Benzoic acid	0.5	0.24	0.94	0.70
	3.0	0.29	1.24	0.95
	12.0	0.29	1.41	1.12
	48.0	0.29	1.57	1.28
	168.0	0.29	2.30	2.01
Acetic anhydride[c]	0.5	0.00	2.01	2.01
	3.0	0.00	2.30	2.30
	12.0	0.00	2.56	2.56
	48.0	0.00	2.75	2.75
	120.0	0.00	3.02	3.02
Succinic anhydride[c]	0.5	0.01	1.41	1.40
	3.0	0.01	1.84	1.83
	24.0	0.01	2.15	2.14
	72.0	0.01	2.29	2.29
Phthalic anhydride[c]	0.5	0.00	1.35	1.35
	3.0	0.00	1.72	1.72
	24.0	0.00	2.06	2.06
	72.0	0.00	2.17	2.17
Caproyl chloride	0.5	0.01	1.53	1.52
	1.0	0.01	1.82	1.82
	3.0	0.01	2.03	2.02
Benzoyl chloride	0.5	0.00	1.74	1.74
	1.0	0.00	1.92	1.92
	3.0	0.00	2.01	2.01

[a,b]See the corresponding footnotes in Table 1. [c]Hydride to compound ratio=6 : 1.

drides relatively fast, with the further hydride being taken up only very slowly. Reduction of acid chlorides was completed rapidly to the corresponding alcohols. These results are summarized in Table 5.

Lithium aluminum hydride reduced thes functionalities rapidly[15]. However, lithium tir-*t*-botoxyaluminohydride reduced only acid chlorides completely. Carboxylic acids were not reduced at all and anhydrides consumed only 2 equiv. of hydrides rapidly for reduction[6].

Esters and Lactones. All of the esters examined reacted with LTDBA readily with the uptake of 2 equiv. of hydride per mole of compound to be reduced to the alcohol stage. However, reduction of lactones such as *r*-butyrolactone and phthalide utilized one hydride rapidly, with a second equivalent of hydride being taken up only quite slow. Consequently, the reduction must be proceeding to the lactol stage. In fact, (2,4-dinitrophenyl)hydrazine analysis showed the corresponding aldehyde formation in *ca.* 80% yield. Isopropenyl acetate utilized 2 equiv. of hydride relatively fast, and a third hydride consumption was observed. Apparently the reaction involves the attack on the double bond. The results are summarized in Table 6.

Table 6. Reaction of Lithium Tris(dibutylamino)aluminum Hydride with Representative Esters and Lactones in Tetrahydrofuran at 0℃

Compounds[a]	Time (hr)	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
Ethyl caproate	0.5	0.00	1.70	1.70
	1.0	0.00	1.87	1.87
	3.0	0.00	2.01	2.01
Ethyl benzoate	0.5	0.00	1.83	1.83
	1.0	0.00	1.95	1.95
	3.0	0.00	2.00	2.00
Phenyl acetate	0.5	0.00	1.33	1.33
	1.0	0.00	1.58	1.58
	3.0	0.00	1.82	1.82
	6.0	0.00	2.00	2.00
r-Butyrolactone	0.5	0.00	1.05	1.05
	3.0	0.00	1.16	1.16
	12.0	0.00	1.29	1.29
	48.0	0.00	1.40	1.40
Phthalide	0.5	0.00	1.04	1.04
	24.0	0.00	1.05	1.05
Isopropenyl acetate	0.5	0.00	1.76	1.76
	3.0	0.00	1.97	1.97
	24.0	0.00	2.25	2.25
	72.0	0.00	2.44	2.44
	168.0	0.00	2.81	2.81

[a,b]See the corresponding footnotes in Table 1.

Table 7. Reaction of Lithium Tris(dibutylamino)aluminum Hydride with Representative Epoxides in Tetrahydrofuran at 0℃

Compounds[a]	Time (hr)	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
1,2-Butylene oxide[c]	0.5	0.00	1.01	1.01
Styrene oxide[d]	0.5	0.00	1.02	1.02
Cyclohexene oxide	0.5	0.00	1.00	1.00
1-Methylcyclohexene oxide[e]	0.5	0.00	0.98	0.98
	0.5	0.00	1.01	1.01

[a,b]See the corresponding footnotes in Table 1. [c]Only 2-butanol was detected. [d] 1-Phenylethanol (99%) and trace of 2-phenylethanol. [e]Only 1-methylcyclohexanol was detected.

Lithium aluminum hydride reacted with esters and lactones exceedingly rapidly[15]. On the other hand, lithium tri-*t*-butoxyaluminohydride failed to reduce ethyl benzoate and reacted only sluggishly with ethyl caproate. Lactones reacted with the alkoxy derivative faster than LTDBA, utilizing more than 1 equiv. of hydride slowly[6].

Epoxides. Unexpectedly, the reaction with the epoxides examined proceeded exceedingly rapidly, an uptake of 1 equiv. of hydride being realized in 1 h or less, at a rate comparble to that with lithium aluminum hydride[15]. The reaction also proved to be very selective, with the hydride undergiong transfer to the less substituted carbon atom. The results are summarized in Table 7.

Table 8. Reaction of Lithium Tris(dibutylamino)aluminum Hydride with Representative Amides and Nitriles in Tetrahydrofuran at 0℃

Compounds[a]	Time (hr)	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
Caproamide	0.5	0.03	1.41	1.38
	3.0	0.03	1.91	1.88
	6.0	0.03	2.03	2.00
Benzamide	0.5	0.00	1.01	1.01
	3.0	0.00	1.35	1.35
	12.0	0.00	1.90	1.90
	24.0	0.00	2.01	2.01
N,N-Dimethyl	0.5	0.02	1.96	1.94
caproamide	1.0	0.02	2.03	2.01
N,N-Dimethyl	0.5	0.00	1.98	1.98
benzamide	1.0	0.00	2.00	2.00
Capronitrile	0.5	0.00	1.10	1.10
	1.0	0.00	1.33	1.33
	6.0	0.00	1.69	1.69
	24.0	0.00	2.00	2.00
Benzonitrile	0.5	0.00	2.00	2.00

[a,b] See the corresponding footnotes in Table 1.

The reaction of lithium tri-*t*-butoxyaluminohydride with epoxides was much slower than that of LTDBA, requiring more than 24 h, but the selectivity in the opening of the epoxide ring appears to be similar[6].

Amides and Nitriles. Primary amides, such as caproamide and benzamide, were reduced relatively fast to the corresponding amines without evolution of hydrogen in 6 and 24 h at 0℃, respectively. Surprisingly, tertiary amides took up 2 equiv. of hydride rapidly. Finally, aliphatic nitrile such as capronitrile utilized 2 equiv. of hydride slowly without hydrogen evolution, whereas aromatic nitrile such as benzonitrile was reduced rapidly. these results are summarized in Table 8.

There was observed that the rate in the reduction of aliphatic nitriles by LTDBA with a limiting amount (*i.e.*, the ratio of reagent to compound is 1 : 1) is quite slow, whereas that of aromatic nitrile is rapid at 0℃. These results indicate that this reagent with a limiting amount can convert aromatic nitriles to aldehydes, while aliphatic nitriles being intact. Preliminary examination revealed that aromatic nitriles are readily transformed into the corresponding aldehydes in high yields even at room temperature. These results will be reported shortly.

It is noteworthy that LTDBA reduces these derivatives at a faster rate than lithium aluminum hydride. In spite of such a faster reaction, LTDBA does not evolve any hydrogen in the reduction of capronitrile. This unique selectivity would enhance the usefulness for this reagent. Lithium tri-*t*-butoxyaluminohydride dose not reduce these compounds under the reaction condition.

Nitro Compounds and Their Derivatives. 1-Nitropropane consumed 2 equiv. of hydride rapidly without evolution of hydrogen, but no further reduction was observed. Nitrobenzene likewise utilized 2 equiv. of hydride readily with a partial evolution of hydrogen. The reduction of nitrobenzene by lithium aluminum hydride to azobenzene stage consumes 4 equiv. of hydride, with 2 equiv. of hydride being utilized for reduction and 2 for hydrogen evolution. Therefore, the reaction by this reagent utilizing 2 equiv. of hydride for reduction corresponds to a reduction to the azobenzene stage. The reason for the only partial evolution of hydrogen is not clear, but we can assume that the reagent reacts with an unknown intermediate to evolve such amount of hydrogen, before the intermediate being rearranged to the azobenzene stage. On the other hand, azobenzene was reduced quite sluggishly without evolution of hydrogen, requiring 5 days for reduction to the hydrazobenzene stage. Azoxybenzene also reacted very slowly. These results are summarized

Table 9. Reaction of Lithium Tris(dibutylamino)aluminum Hydride with Representative Nitro Compounds and Their Derivatives in Tetrahydrofuran at 0℃

Compounds[a]	Time (hr)	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
1-Nitropropane[c]	0.5	0.01	1.68	1.67
	1.0	0.01	1.89	1.88
	3.0	0.01	2.01	2.00
	6.0	0.01	2.03	2.02
Nitrobenzene[d]	0.5	0.49	2.34	1.85
	1.0	0.49	2.43	1.94
	3.0	0.49	2.51	2.02
	6.0	0.49	2.54	2.02
Azobenzene[e]	0.5	0.00	0.15	0.15
	12.0	0.00	0.55	0.55
	120.0	0.00	1.02	1.02

[a,b] See the corresponding footnotes in Table 1. [c] A brown color formed immediately. [d] A brown color turned to light brown slowly. [e] Solution became reddish brown, then turned to be dark brown.

Table 10. Reaction of Lithium Tris(dibutylamino)aluminum Hydride with Other Nitrogen Compounds in Tetrahydrofuran at 0℃

Compounds[a]	Time (hr)	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
Cyclohexanone	0.5	0.00	0.72	0.72
oxime	1.0	0.00	0.81	0.81
	6.0	0.00	0.90	0.90
	24.0	0.00	1.01	1.01
Phenyl	0.5	0.00	0.87	0.87
isocyanate	1.0	0.00	0.95	0.95
	3.0	0.00	1.01	1.01
Pyridine	0.5	0.00	0.54	0.54
	3.0	0.00	0.85	0.85
	12.0	0.00	1.12	1.12
	120.0	0.00	1.70	1.70
4-Picoline	1.0	0.00	0.63	0.63
N-oxide	3.0	0.00	0.95	0.95
	12.0	0.00	1.25	1.25

[a,b] See the corresponding footnotes in Table 1.

Table 11. Reaction of Lithium Tris(dibutylamino)aluminum Hydride with Representative Sulfur Derivatives in Tetrahydrofuran at 0℃

Compounds[a]	Time (hr)	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
Di-*n*-butyl	0.5	0.01	1.01	1.00
disulfide	3.0	0.01	1.01	1.00
Dipheny	0.5	0.00	1.02	1.02
disulfide	1.0	0.00	1.02	1.02
Dimethyl	0.5	0.00	0.48	0.48
sulfoxide	1.0	0.00	0.60	0.60
	6.0	0.00	0.91	0.91
	12.0	0.00	1.00	1.00
Diphenyl	0.5	0.00	0.63	0.63
sulfone	3.0	0.00	0.81	0.81
	6.0	0.00	0.88	0.88
	24.0	0.00	1.00	1.00
Methane-	3.0	0.31	0.31	0.00
sulfonic acid	72.0	0.60	0.60	0.00
p-Toluene-	0.5	0.64	0.64	0.00
sulfonic acid	12.0	0.84	0.84	0.00
monohydrate	48.0	0.91	0.91	0.00
	120.0	1.00	1.00	0.00

[a,b] See the corresponding footnotes in Table 1.

in Table 9.

Lithium aluminum hydride reduced these compounds readily[6], whereas lithium tri-*t*-butoxyaluminohydride did not react with these derivatives[15].

Other Nitrogen Compounds. Cyclohexanone oxime liberated no hydrogen, but utilized 1 equiv. of hydride for reduction in 24 h at 0℃, apparently being reduced to the corresponding N-hydroxyamine. Phenyl isocyanate was rapidly reduced, utilizing 1 equiv. of hydride, corresponding to reduction to the formanilide stage. Pyridine and 4-picolin N-oxide underwent a moderate reduction without hydrogen evolution, apparantly the pyridine ring being attacked. The results are summarized in Table 10.

Lithium aluminum hydride readily reduced cyclohexanone oxime to cyclohexylamine, and phenyl isocyanate to N-methylaniline[6], but the alkoxy derivative showed a low reactivity toward these compounds[15].

Sulfur Compounds. LTDBA shows a very interesting characteristics in the reductions of sulfur compounds; the reagent reduced disulfide and sulfoxides to thiols and sulfides, respectively, at an exceedingly fast rate at 0℃ without evolution of any hydrogen. Lithium aluminum hydride also reduced these compounds rapidly, but evolved an equivalent hydrogen concurrently[6]. Dimethyl sulfoxide was reduced slowly. Methansulfonic acid and *p*-toluenesulfonic acid monohydrate liberated hydrogen very slowly; the former was not completed even in 3 days and the latter evolved only *ca.* 1 equiv. of hydrogen even in 5 days at 0℃. Lithium tri-*t*-butoxyaluminohydride showed a lower reactivity toward disulfides and sulfoxides, but evolved hydrogen with sulfonic acids readily[15]. The results are summarized in Table 11.

Conclusion

The reducing properties of lithium tris(dibutylamino)aluminum hydride(LTDBA) in tetrahydrofuran are now broadly characterized. The reducing power of the reagent appears to be some where between lithium aluminum hydride and lithium tri-*t*-butoxyaluminohydride. The reducing properties of LTDBA are quite different from those of the alkoxy deirvatives. Consequently, this new class of reagents should widen their role in the selective reduction area. A variety of examples in the selective reduction of organic functionalities achieved by these amino derivatives will follow in series.

Experimental Section

All glassware was predried at 140℃ for several hours, assembled hot, dried further with a flame, and cooled under a stream of nitrogen. All reactions were carried out under a static pressure of dry nitrogen in flasks fitted with a septum-covered side arm with use a standard technique for handling air-sensitive material[14]. Terahydrofuran(THF) was dried over a 4 Å molecular sieve and distilled over sodium-benzophenone ketyl prior to use. ^{27}Al-NMR spectra were recorded on a Bruker WP 80 SY Spectrometer, and chemical shifts are reported relative to $Al(H_2O)_6^{3+}$. GC analyses were performed using a Hewlett-Packard 5790 FID chromatography with use of 12 ft.×0.125 in. column of 15% THEED on a 100-120 mesh Supelcoport or of 10% Carbowax 20 M on 100-120 mesh Supelcoport.

Preparation of lithium tris(dibutylamino)aluminum Hydride(LTDBA) in THF. An oven-dried, 500 m*l* round-bottomed flask with a side arm, equipped with a condenser leading to a mercury bubbler was flushed with dry nitrogen and maintained under a static pressure of nitrogen. To this flask was added 100 m*l* of $LiAlH_4$-THF (2.0 M, 200 m*l*), and followed by slow addition of 82.25 g of dibutylamine (0.63 mol) *via* a double-ended needle with vigorous stirring. The mixture was stirring for about 6 h at room temperature until the hydrogen evolution was ceased. The resulting clear solution was standardized by hydrolyzing an aliquot with 2 N H_2SO_4-THF (1 : 1) mixture to be 1.60 M, and kept under nitrogen at 0℃. The THF solution of LTDBA was characterized by a characteristic absorption in the IR at around 1650 cm^{-1} (ν_{Al-H}) and by a broad singlet at δ 128 ppm in ^{27}AlNMR.

General Procedure for Determination of Rates and Stoichiometry. To a 100 m*l* flask fitted with a side arm and a condenser leading to a gas buret was added 24 m*l* (36 mmol) of a 1.50 M THF solution of LTDBA. The flask was immersed into an ice bath and the reaction mixture was diluted with 12 m*l* of THF containing a mmol of the compound to be examined. This makes the mixture 1 M in hydride and 0.25 M in the compound under investigation. At appropriate time intervals, 4 m*l* of aliquots were withdrawn and quenched in a 2 N H_2SO_4-THF hydrolyzing mixture. The hydrogen evolved by the compound was collected in a gas buret and measured the volume of hydrogen.

The reaction of 2-heptanone is described as a representative. In an usual set-up was placed 24 m*l* of 1.50 M LTDBA in THF, and followed by addition of 12 m*l* of THF solution containing 1.03 g (9 mmol) of 2-heptanone at 0℃. No hydrogen was evolved. After 3 h, the analysis showed no difference in the residual hydride, which indicates that the reaction was completed. The results are summarized in Table

2.

Reduction of Styrene Oxide. The following experiment illustrates the technique utilized in cases where the reaction mixture was subjected to identification of products.

Utilizing the above general procedure, the reduction of styrene oxide with LTDBA was performed for 0.5 h at 0℃. The reaction mixtrue was then hydrolyzed with 2 N HCl and the organic layer was taken up in ether. The GC analysis showed the presence of 99% of 1-phenylethanol and trace of 2-phenylethanol.

In cases where a single product in the reaction mixture was apparent, we did not perform the product identification further.

Genaral Procedure for Stereoselectivity Study. The reduction of 3,3,5-trimethylcyclohexanone is descirbed as representative. To a 10 m*l* vial capped by a rubber septum was added 2 m*l* of a solution of LTDBA in THF (1.50 M, 3 mmol). The vial was kept at 0℃, and to this was added 1 m*l* of a 2 M compound (2 mmol) in THF. The reaction mixture was stirred for 3 h at that temperature and then hydrolyzed by 3 N H_2SO_4. The aqueous layer was saturated with anhydrous magnesium sulfate, and the organic layer was subjected to GC analysis. The results are summarized in Table 3.

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Ruthenium Catalyzed Synthesis of 1-Substituted Perhydroazocines from Primary Amines and 1,7-Heptanediol

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The reaction of primary aromatic amines with 1,7-heptanediol in the presence of a catalytic amount of ruthenium complex in dioxane at 180℃ for 24 hours gave the corresponding 1-substituted perhydroazocines in moderate yield.

Introduction

A large variety of methods are known for building up pipiperidine,[1] and perhydroazepine[2] rings, which are often present in natural products. In these methods, substrates such as 1,5- and 1,6-dihaloalkanes or 1,6-dihalogenoamines are used as the starting materials and hetero-rings are usually closed intramolecularly at the nitrogen atom.

We have previously reported the synthesis of 1-substituted pyrrolidines,[3] piperidines,[4] and perhydroazepines[5] from succinaldehyde, glutaraldehyde or adipaldehyde, and primary amines, respectively with tetracarbonylhydridoferrate, $HFe(CO)_4^-$, as a selective reducing agent. These reactions, however, required stoichiometric amounts of $HFe(CO)_4^-$.[6]

Watanabe *et al.*[7] have recently developed organic synthesis involving dehydrogenation of an alcohol by a ruthenium cata-