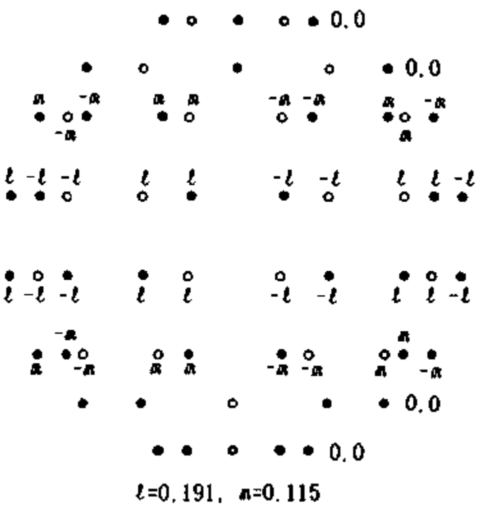

Figure 5. Self this-trapping state $\psi(a_{1u})$. Here the number in each site indicates the value of the wave function $\psi(a_{1u})$.

symmetric.

2. These two states are localized in the equator area.

These features manifest that $\psi(a_{2u})$ and $\psi(a_{1u})$ are the self-trapping electronic bound states associated with the bond distortion induced by the charge transfer.

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Selective Reduction by Lithium Bis- or Tris(dialkylamino)aluminum Hydrides. VII. Reaction of Lithium Tris(dihexylamino)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(dihexylamino)aluminum hydride(LTDHA) with selected organic compounds containing representative functional groups under the standardized conditions (tetrahydrofuran, 0℃) were studied in order to define the reducing characteristics of the reagent for selective reductions. The reducing ability of LTDHA was also compared with those of the parent lithium aluminum hydride(LAH), lithium tris(diethylamino)aluminum hydride(LTDEA), and lithium tris(dibutylamino)aluminum hydride(LTDBA). In general, the reactivity toward organic functionalities is in order of LAH>LTDEA≥LTDBA>LTDHA. LTDHA shows a unique reducing characteristics. Thus, the reagent reduces aldehydes, ketones, esters, epoxides, and tertiary amides readily. Anthraquinone is cleanly reduced to 9,10-dihydro-9,10-anthracenediol without hydrogen evolution, whereas *p*-benzoquinone is inert to LTDHA. In addition to that, disulfides are also readily reduced to thiols without hydrogen evolution. However, carboxylic acids, anhydrides, nitriles, and primary amides are reduced slowly. Especially, this reagent reduces aromatic nitriles to the corresponding aldehydes in good yields.

Introduction

Lithium aluminum hydride (LAH), a very powerful reducing agent, has been widely used for the reduction of functional groups.[2] The introduction of alkoxy groups into lithium aluminum hydride[3,4] modifies its reducing characteristics[5-8] and has made possible a number of selective reductions of considerable utility in synthetic work.[9]

Similarly, the dialkylamino-substituted derivatives of lithium aluminum hydride seem to exhibit reducing properties different from those of the parent reagent and/or the alkoxy derivatives. Recently, we synthesized various dialkylamino-substituted derivatives of lithium aluminum hydride[10] and have been investing the reducing properties of the derivatives.[11,12] In this course, we found that lithium tris(dihexylamino)aluminum hydride(LTDHA) converts aromatic nitriles into aldehydes in excellent yields.[13] Accordingly, it appeared desirable to undertake a systematic exploration of the reaction of LTDHA, one of the class of dialkylamino derivatives, with the standard list of organic compounds containing 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

Procedure for Rates and Stoichiometry. Lithium tris(dihexylamino)aluminum hydride, LTDHA, was prepared readily from the reaction of 1 mole of lithium aluminum hydride with 3 moles of dihexylamine in tetrahydrofuran at room temperature (Eq. 1).[14] The reagent is very stable under the reaction condition.

$$\mathrm{LiAlH_4} + 3n\text{-}\mathrm{Hex_2NH} \xrightarrow[\mathrm{RT,\,6h}]{\mathrm{THF}} \mathrm{Li}(n\text{-}\mathrm{Hex_2N})_3\mathrm{AlH} + 3\mathrm{H_2}\uparrow \quad (1)$$

The ^{27}Al NMR spectrum of LTDHA in THF showed a broad singlet at δ 129 ppm relative to $\mathrm{Al(H_2O)_6}^{3+}$.

The general procedure for the systematic study on the approximate rates and stoichiometry involved preparation of a reaction mixture of the reagent (0.5 M in reagent) and the compound examined (0.125 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. A blank test under identical conditions, but without the compound, was accompanied. At the approximate reaction intervals, aliquots were withdrawn from the reaction mixture and analyzed for residual hydride by hydrolysis.[15] From the difference in the volume of hydrogen evolution in the two intervals, the hydride used by the compound for reaction was calculated. In this way, it was possible to calculate a value for the number of moles of the hydride consumed by the compound to evolve hydrogen and the number of moles of hydride utilized for the reduction.

Alcohols, Amines, and Thiols (Active Hydrogen Compounds). Primary, secondary, and tertiary alcohols all failed to react with LTDHA, and phenol also did not evolve any hydrogen under these conditions. However, *n*-hexylamine reacted with this reagent very sluggishly and evolved only a partial equivalent of hydrogen. Both 1-hexanethiol and benzenethiol also were inert to LTDHA, exactly same as the case of lithium tris(dibutylamino)aluminum hydride(LTDBA).[11] These results are summarized in Table 1.

Aldehyes and Ketones. All of the saturated aldehydes and ketones examined used 1 equivalent of hydride for reduction to the corresponding alcohols rapidly within 1 h. Cinnamaldehyde utilized 1 equivalent of hydride rapidly, followed by a slow reduction of the double bond. Lithium aluminum hydride reduces cinnamaldehyde to hydrocinnamyl alcohol rapidly,[5] while lithium tri-*t*-butoxyaluminohydride does not attack the double bond to provide a clean reduction to cinnamyl alcohol.[6] These results are summarized in Table 2.

Table 1. Reaction of Lithium Tris(dihexylamino)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	6.0	0.00	0.00	0.00
benzyl alcohol	6.0	0.00	0.00	0.00
3-hexanol	6.0	0.00	0.00	0.00
3-ethyl-3-pentanol	6.0	0.00	0.00	0.00
phenol	6.0	0.00	0.00	0.00
n-hexylamine	1.0	0.41	0.41	0.00
	3.0	0.54	0.54	0.00
	6.0	0.57	0.57	0.00
	12.0	0.60	0.60	0.00
1-hexanethiol	6.0	0.00	0.00	0.00
benzenethiol	6.0	0.00	0.00	0.00

[a] 5 mmol of compound was added to 20 mmol of the reagent (0.125 M in compound and 0.5 M in hydride). [b] Mmol per mmol of compound.

Table 2. Reaction of Lithium Tris(dihexylamino)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	0.00	1.00	1.00
benzaldehyde	0.5	0.00	1.01	1.01
2-heptanone	0.5	0.00	1.00	1.00
acetophenone	0.5	0.00	1.01	1.01
benzophenone	0.5	0.00	1.00	1.00
cinnamaldehyde	0.5	0.00	1.28	1.28
	3.0	0.00	1.44	1.44
	12.0	0.00	1.60	1.60
	24.0	0.00	1.71	1.71
	72.0	0.00	1.75	1.75
	120.0	0.00	1.97	1.97

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

The stereoselectivity of the reagent toward cyclic ketones was also studied, and the results and those of lithium aluminum hydride (LAH)[5], lithium tris(diethylamino)aluminum hydride(LTDEA)[12], and lithium tris(dibutylamino)aluminum hydride(LTDBA)[11] for comparison are summarized in Table 3. The introduction of dialkylamino group enhances the stereoselectivity to a large extent. Thus, the stereoselectivity increases with increasing the bulkiness of dialkylamino group. For example, the parent LAH reduces 3,3,5-trimethylcyclohexanone to the corresponding less stable isomer (*trans* alcohol) in a ratio of 52% at 0℃,[5] whereas LTDEA,[12] LTDBA,[11] and LTDHA reduce it in ratios of 87, 93, and 94%, respectively.

Quinones. Two examples for quinones were examined

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

Compound	Less stable isomer (%)[a,b]			
	$LiAlH_4$[c]	$Li(Et_2N)_3$-AlH[d]	$Li(Bu_2N)_3$-AlH[e]	$Li(Hex_2N)_3$-AlH
Cyclohexanone				
2-methyl-	24	52	56	58
3-methyl-	16	19	28	29
4-methyl-	19	25	28	30
4-*t*-butyl-	9	43	49	49
3,3,5-trimethyl-	52	87	93	94
Norcamphor	89	91	91	92
Camphor	92	93	94	94

[a] Excess reagent utilized. [b] Quantitative yields of alcohols. [c] Data taken from ref 5. [d] Data taken from ref 12. [e] Data taken from ref 11.

Table 4. Reaction of Lithium Tris(dihexylamino)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	0.00	0.00
	1.0	0.00	0.00	0.00
	24.0	0.00	0.00	0.00
anthraquinone[c]	0.5	0.00	0.25	0.25
	1.0	0.00	0.42	0.42
	3.0	0.00	0.61	0.61
	6.0	0.00	1.03	1.03
	12.0	0.00	1.48	1.48
	24.0	0.00	2.02	2.02

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

Table 5. Reaction of Lithium Tris(dihexylamino)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	0.23	1.32	1.09
	6.0	0.24	1.77	1.53
	24.0	0.24	2.10	1.86
	48.0	0.24	2.25	2.01
benzoic acid	0.5	0.23	1.26	1.03
	6.0	0.25	1.69	1.44
	24.0	0.25	2.05	1.80
	48.0	0.25	2.27	2.02
acetic anhydride[c]	0.5	0.00	1.54	1.54
	6.0	0.00	2.31	2.31
	24.0	0.00	2.56	2.56
	72.0	0.00	2.77	2.77
	120.0	0.00	2.98	2.98
succinic anhydride[c]	0.5	0.01	1.28	1.27
	6.0	0.01	1.77	1.76
	24.0	0.01	2.04	2.03
	72.0	0.01	2.15	2.14
	120.0	0.01	2.22	2.21
phthalic anhydride[c]	0.5	0.00	1.24	1.24
	6.0	0.00	1.76	1.76
	24.0	0.00	2.01	2.01
	72.0	0.00	2.10	2.10
	120.0	0.00	2.16	2.16
caproyl chloride	0.5	0.02	1.50	1.48
	1.0	0.02	1.73	1.71
	3.0	0.02	1.94	1.92
	6.0	0.02	2.04	2.02
benzoyl chloride	0.5	0.01	1.29	1.28
	1.0	0.01	1.57	1.56
	3.0	0.01	1.86	1.87
	6.0	0.01	1.98	1.97
	12.0	0.01	2.02	2.01

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

and the results are summarized in Table 4. No reaction between *p*-benzoquinone and LTDHA was observed. However, anthraquinone consumed 2 equivalents of hydride for reduction without evolution of any hydrogen to indicate a clean reduction to 9,10-dihydro-9,10-anthracenediol. In general, the reduction of quinones with common boron and aluminum hydrides yields a mixture containing hydroquinones. Similarly, in the cases of lithium tri-*t*-butoxyaluminohydride[6] and LTDBA[11] no hydrogen evolution is observed during the reduction.

Carboxylic Acid and Acyl Derivatives. Both caproic acid and benzoic acid examined evolved hydrogen only incompletely when added to the reagent at 0℃ in THF. Moreover, the reduction of the acids was also slow, requiring 2 days to be reduced to the corresponding alcohols (the hydrazine analysis of the reaction mixture did not show any aldehyde formation). Acetic anhydride consumed almost 3 equivalents of hydride slowly, suggesting the reduction to acetaldehyde and ethyl alcohol. Likewise, cyclic anhydrides, such as succinic and phthalic anhydrides, reacted with LTDHA at a very slow rate. Reduction of acid chlorides was completed rapidly to the corresponding alcohols. These results are summarized in Table 5.

Esters and Lactones. All of the esters examined used 2 equivalents of hydride, undergoing reduction to the alcohol stage. The reaction of γ-butyrolactone proceeded relatively fast to the corresponding diol, whereas phthalide utilized one hydride rapidly, with a second equivalent of hydride being taken up quite slowly. Isopropenyl acetate utilized 2 equivalents of hydride very sluggishly. The results are summarized in Table 6.

Epoxides. All of the epoxides examined consumed 1 equivalent of hydride relatively fast to give the S_N2-type ring-opened products exclusively, like the cases of LTDBA[11] and LTDEA[12]. Thus, the reaction proved to be quite selective,

Table 6. Reaction of Lithium Tris(dihexylamino)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	2.00	2.00
	1.0	0.00	2.00	2.00
ethyl benzoate	0.5	0.00	2.01	2.01
	1.0	0.00	2.01	2.01
phenyl acetate	0.5	0.00	2.00	2.00
	1.0	0.00	2.00	2.00
γ-butyrolactone	0.5	0.02	1.20	1.18
	1.0	0.08	1.47	1.39
	3.0	0.08	1.70	1.62
	6.0	0.08	2.11	2.03
phthalide	0.5	0.03	1.05	1.02
	3.0	0.03	1.14	1.11
	12.0	0.03	1.21	1.18
	24.0	0.03	1.24	1.21
	48.0	0.03	1.25	1.22
isopropenyl acetate	0.5	0.05	0.74	0.69
	3.0	0.05	1.21	1.16
	12.0	0.05	1.47	1.43
	24.0	0.05	1.64	1.59
	48.0	0.05	1.75	1.70
	120.0	0.05	2.02	1.97

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

Table 7. Reaction of Lithium Tris(dihexylamino)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	0.5	0.00	0.97	0.97
	1.0	0.00	0.98	0.98
	3.0[c]	0.00	1.00	1.00
styrene oxide	0.5	0.00	0.73	0.73
	1.0	0.00	0.89	0.89
	3.0[d]	0.00	1.00	1.00
cyclohexene oxide	0.5	0.00	0.76	0.76
	1.0	0.00	0.83	0.83
	3.0[e]	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.

with hydride undergoing transfer to less substituted carbon atom of the epoxide ring. These results are summarized in Table 7.

Amides and Nitriles. Both primary amides examined, such as caproamide and benzamide, evolved hydrogen partially, and the subsequent reduction was very sluggish. On the other hand, typical disubstituted amides, such as *N,N*-dimethylcaproamide and *N,N*-dimethylbenzamide, took up 2 equivalents of hydride rapidly. In the reduction of nitriles, we can find a very interesting feature. The typical aliphatic nitrile, capronitrile, reacted with the reagent without hydrogen evolution very slowly, whereas aromatic nitrile, such as benzonitrile, used the first hydride rapidly and the subsequent second hydride very sluggishly. These results are summarized in Table 8.

Table 8. Reaction of Lithium Tris(dihexylamino)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	0.11	0.40	0.29
	3.0	0.11	0.61	0.50
	12.0	0.11	0.83	0.72
	24.0	0.11	0.91	0.80
	48.0	0.11	0.94	0.83
	120.0	0.11	1.08	0.97
benzamide	0.5	0.21	0.40	0.19
	3.0	0.21	0.67	0.46
	12.0	0.21	0.86	0.65
	24.0	0.21	0.93	0.72
	72.0	0.21	1.02	0.81
	120.0	0.21	1.10	0.89
	168.0	0.21	1.17	0.96
N,N-dimethyl-caproamide	0.5	0.00	1.38	1.38
	1.0	0.00	1.70	1.70
	3.0	0.00	2.00	2.00
N,N-dimethyl-benzamide	0.5	0.00	1.44	1.44
	1.0	0.00	1.78	1.78
	3.0	0.00	2.01	2.01
capronitrile	0.5	0.00	0.05	0.05
	3.0	0.00	0.24	0.24
	12.0	0.00	0.38	0.38
	24.0	0.00	0.45	0.45
	72.0	0.00	0.61	0.61
	120.0	0.00	0.78	0.78
benzonitrile	0.5[c]	0.02	1.04	1.02
	6.0	0.02	1.07	1.05
	12.0	0.02	1.10	1.08
	24.0	0.02	1.16	1.14
	48.0	0.02	1.18	1.16
	120.0	0.02	1.22	1.20

[a,b] See the corresponding footnotes in Table 1, [c] 99% of benzaldehyde was obtained when treated with 1 equivalent of reagent at 0℃.

There was observed that the rate in the reduction of aliphatic nitriles by LTDHA 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 selectively

$$\mathrm{ArC{\equiv}N} \xrightarrow{\mathrm{LTDHA}} \xrightarrow{\mathrm{H_3O^+}} \mathrm{ArCHO} \qquad (2)$$

in the presence of aliphatic nitriles intact (Eq. 2). The results

Table 9. Reaction of Lithium Tris(dihexylamino)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	0.5	0.00	1.41	1.41
	3.0	0.00	1.74	1.74
	12.0	0.00	2.01	2.01
	24.0	0.00	2.03	2.03
nitrobenzene	0.5	0.49	1.72	1.23
	1.0	0.55	2.05	1.50
	6.0	0.55	2.54	1.99
	12.0	0.55	2.56	2.01
	24.0	0.55	2.57	2.02
azobenzene	0.5	0.00	0.06	0.06
	3.0	0.00	0.22	0.22
	12.0	0.00	0.32	0.32
	24.0	0.00	0.33	0.33

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

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

Compounds[a]	Time (hr)	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
cyclohexanone oxime	0.5	0.21	0.33	0.12
	1.0	0.21	0.38	0.17
	6.0	0.21	0.47	0.26
	24.0	0.21	0.56	0.35
	48.0	0.21	0.58	0.37
phenyl isocyanate	0.5	0.00	0.09	0.09
	1.0	0.00	0.18	0.18
	6.0	0.00	0.35	0.35
	24.0	0.00	0.54	0.54
	48.0	0.00	0.63	0.63
pyridine	0.5	0.01	0.09	0.08
	1.0	0.01	0.13	0.12
	6.0	0.01	0.18	0.17
	24.0	0.01	0.25	0.24
	48.0	0.01	0.25	0.24
4-picoline *N*-oxide	0.5	0.00	0.39	0.39
	3.0	0.00	0.79	0.79
	12.0	0.00	0.92	0.92
	24.0	0.00	1.13	1.13

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

for this partial reduction of various nitriles to the corresponding aldehydes have been published.[13]

Nitro Compounds and Their Derivatives. 1-Nitropropane utilized 2 equivalents of hydride without hydrogen evolution to proceed to the amine stage at a moderate rate. Nitrobenzene likewise used readily 2 equivalents of hydride with a partial evolution of hydrogen. On the other hand, azobenzene showed very slow reactivity toward this reagent, with no hydrogen evolution. These results are similar to those of LTDBA,[11] and summarized in Table 9.

Table 11. Reaction of Lithium Tris(dihexylamino)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 disulfide	0.5	0.00	1.03	1.03
	1.0	0.00	1.03	1.03
diphenyl disulfide	0.5	0.00	0.92	0.92
	1.0	0.00	1.01	1.01
	3.0	0.00	1.01	1.01
dimethyl sulfoxide	0.5	0.00	0.05	0.05
	1.0	0.00	0.14	0.14
	6.0	0.00	0.34	0.34
	24.0	0.00	0.43	0.43
	48.0	0.00	0.47	0.47
diphenyl sulfone	0.5	0.00	0.00	0.00
	6.0	0.00	0.00	0.00
methanesulfonic acid	0.5	0.23	0.23	0.00
	6.0	0.24	0.24	0.00
	24.0	0.25	0.25	0.00
	72.0	0.26	0.26	0.00
p-toluenesulfonic acid monohydrate	0.5	0.72	0.72	0.00
	1.0	0.94	0.94	0.00
	3.0	1.01	1.01	0.00
	96.0	1.01	1.01	0.00

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

Other Nitrogen Compounds. Cyclohexanone oxime underwent partial hydrogen evolution with the reduction process being very slow. Phenyl isocyanate was reduced slowly, utilizing 1 equivalent of hydride, corresponding to reduction to the formanilide stage. LTDHA showed very little reactivity toward pyridine and 4-picoline *N*-oxide. The results are summarized in Table 10.

Lithium aluminum hydride readily reduced cyclohexanone oxime to cyclohexylamine, and phenyl isocyanate to *N*-methylaniline,[5] but the alkoxy derivative showed a low reactivity toward these compounds.[6]

Sulfur Compounds. LTDHA like the cases of LTDBA[11] and LTDEA[12] shows a very interesting characteristics in the reduction of sulfur compounds: the reagent reduced disulfide to thiols at a very fast rate, and sulfoxides to sulfides very solwly, without evolution of any hydrogen (Eq. 3). Lithium aluminum hydride also reduced these compounds rapidly, but

$$\text{R-S-S-R} \xrightarrow{\text{LTDHA}} \xrightarrow{H_3O^+} \text{2RSH} \qquad (3)$$

evolved an equivalent hydrogen concurrently.[5] Diphenyl sulfone was inert to this reagent. Methanesulfonic acid and *p*-toluenesulfonic acid monohydrate liberated hydrogen very slowly: the former was not complete even in 3 days and the latter evolved only 1 equivalent of hydrogen rapidly without further hydrogen evolution. Lithium tri-*t*-butoxyaluminohydride showed a lower reactivity toward disulfides and sulfoxides, but evolved hydrogen with sulfonic acids readily.[6] These results are summarized in Table 11.

Conclusion

The reducing properties of lithium tris(dihexylamino)aluminum hydride (LTDHA) in tetrahydrofuran are now fully characterized with the standard list of organic compounds containing representative functional groups. The reagent appears to be milder reducing agent than lithium aluminum hydride,[5] lithium tris(diethylamino)aluminum hydride,[12] and lithium tris(dibutylamino)aluminum hydride,[11] but stronger than lithium tri-*t*-butoxyaluminohydride.[6] Especially, LTDHA reduces aromatic nitriles to the corresponding aldehydes in good yields. This unique reducing characteristics should find very useful applications in organic synthesis.

Experimental Section

All glassware was predried at 140℃ for several hours, assembled hot, dried further with a flame, and cooled under the stream of nitrogen. All reaction were carried out under the static pressure of dry nitrogen in flasks fitted with a septum-covered side arm with use a standard technique for handling air-sensitive materials.[15] Tetrahydrofuran (THF) was dried over sodium-benzophenone ketyl prior to use. ^{27}Al NMR spectra 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 100-200 mesh Supelcoport or 10% Carbowax 20 M on 100-200 mesh Supelcoport.

Preparation of Lithium Tris(dihexylamino)aluminum Hydride (LTDHA). An oven-dried, 500-mL, 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 charged 100 mL of $LiAlH_4$-THF (2.0 M, 200 mmol), and followed by dropwise addition of 116.78 g of dihexylamine (630 mmol) *via* a double-ended needle with vigorous stirring. The mixture was stirred for 6 h at room temperature until the hydrogen evolution was completed. The resulting clear solution was standardized by hydrolyzing an aliquot with 2 N H_2SO_4-THF mixture to be 0.80 M, and kept under nitrogen at 0℃. The THF solution of LTDHA was characterized by a characteristic absorption in the IR at around 1,635 cm^{-1} ($\nu_{Al\text{-}H}$) and by a broad singlet at δ 129 ppm in ^{27}Al NMR.

General Procedure for Determination of Rates and Stoichiometry. To a 100 mL flask fitted with a side arm and a condenser leading to a gas-buret was added 25 mL (20 mmol) of a 0.80 M THF solution of LTDHA. The flask was immersed into an ice bath and the reaction mixture was diluted with 15 mL of THF containing a mmol of the compound to be examined. This makes the mixture 0.5 M in hydride and 0.125 M in the compound under investigation. At approximate time intervals, 4 mL 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 25 mL of 0.80 M LTDHA in THF, and follwed by addition of 15 mL of THF solution containing 0.60 g (5 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 LTDHA was performed for 3.0 h at 0℃. The reaction mixture 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, no further identification of the product was performed.

General Procedure for Stereoselectivity Study. The reduction of 3,3,5-trimethylcyclohexanone is described as representative. To a 10 mL vial capped by a rubber septum was added 3.8 mL of a solution of LTDHA in THF (0.80 M, 3 mmol). The vial was kept at 0℃, and to this was added 1 mL 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.

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Selective Reduction of α,β-Unsaturated Ketones with Borohydride Exchange Resin-$CuSO_4$ in Methanol

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Borohydride exchange resin (BER)-$CuSO_4$ system readily reduces α,β-unsaturated ketones to the corresponding saturated alcohols quantitatively. This reduction tolerates many functional groups such as carbon-carbon multiple bonds, chlorides, epoxides, esters, amides and nitriles.

Introduction

Although many metal hydride systems are reported to be effective on the selective reduction of α,β-unsaturated ketones to the saturated ketones[1] or to the corresponding allylic alcohols,[2] the clean one step reduction to the saturated alcohols is rare. Only a few borohydrieds are reported to be effective on specific enones.[3] Other reagents are hydrogenation over Rh/Al_2O_3,[4] hydrogenation with $LaNi_5H_6$,[5] hydrogenation over Nic in ethanol,[6] and lithium metal in liquid ammonia.[7] Recently we have found borohydride exchange resin (BER)-$CuSO_4$-MeOH[8,9] system reacts slowly with terminal olefins and is inert to many other functional groups, however reacts rapidly with α,β-unsaturated ketones to give the corresponding saturated alcohols. BER is a quaternary ammonium borohydride supported on an anion exchange resin,[8] and unlike $NaBH_4$-MeOH system, BER-MeOH system decomposes slowly at room temperature in the presence of copper. In this paper, we wish to report BER-$CuSO_4$ system is capable of reducing enones almost quantitatively with excellent chemoselectivity.

Results and Discussion

Preparation and Stability of BER-$CuSO_4$ System in Methanol. Borohydride exchange resin was prepared as described previously.[8] When BER was added to copper sulfate solution in methanol, the resin turned black, presumably by copper coating. The stabilities of BER in methanol was studied in the presence and absence of a catalytic amount of copper, and compared with those of $NaBH_4$ in Figure 1. As shown in Figure 1, this polymeric quarternary ammonium borohydride, BH_4^- being attached on the surface of resin (BER) is much more stable in methanol than $NaBH_4$ itself, both in the presence and absence of copper. Thus in the presence of 2.0 mol% of $CuSO_4$, $NaBH_4$ decomposed completely in 5 min, whereas BER retained *ca.* 60% of hydride after 1.0 h at room temperature. Therefore $NaBH_4$ reduction in methanol had to be carried out by adding solid $NaBH_4$ portionwise especially in the presence of transition metal salts.[9,10]

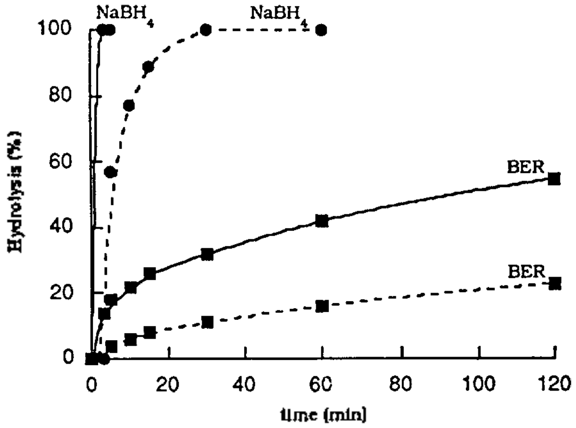

Figure 1. Rate of Hydrolysis of BER and $NaBH_4$ in Methanol in the Presence (solid line) and Absence (dotted line) of $CuSO_4$ (2.0 mol%).

Standard Procedure. Procedure adapted was to add substrate (1.0 mmol) to the mixture of BER (5.0 mmol) and $CuSO_4$ (0.1 mmol) in methanol (20 mL). The reductions were usually completed in 1 h at room temperature, and the products were analyzed by Glpc. When the reduction was slow at the standard conditions, reduction was accelerated by increasing the reagents. In the case of preparative runs, substrate (10.0 mmol) was reacted with BER (50.0 mmol)-$CuSO_4$ (1.0 mmol) and after the reduction, BER-Cu was filtered and methanol was evaporated to get nearly pure product.