Preparation of Potassium Diisobutylalkoxyaluminum Hydrides from Diisobutylalkoxyalanes. A New Class of Reducing Agents

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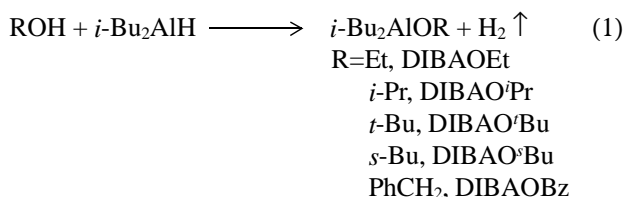*Department of Chemistry, Yeungnam University, Kyongsan 712-749, Korea*
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Trisubstituted borohydrides such as trialkylborohydrides, trialkoxyborohydrides and mixed alkoxyalkylborohydrides constitute a highly attractive class of reducing agents in organic synthesis. Trialkylborohydrides have proven to be powerful selective reducing agents.[1] On the other hand, trialkoxyborohydrides proved to be very mild reducing agents,[2] whereas mixed alkoxyalkylborohydrides showed their unique reducing charcateristics.[3]

Similarly, trisubstituted aluminum hydride such as diethylpiperinoaluminum hydride, a dialkylaminoaluminum hydride, has proven to be a selective reducing agent.[4] However, the investigation of any dialkylalkoxyaluminum hydride is still missing. Accordingly, development of a general procedure for the syntheses of such mixed alkylalkoxyaluminum hydrides has been of considerable interest. Herein, we wish to report a general procedure for the synthesis of potassium diisobutylalkoxyaluminum hydrides in tetrahydrofuran (THF) with various alkoxy group of different steric environments and their selectivities in the reduction of carbonyl compounds.

Diisobutylalkoxyalanes (DIBAOR) were prepared from the corresponding alcohols and diisobutylaluminum hydride (DIBAH) in THF at 0 °C (Eq. 1). The reaction of alcohols with

$$ROH + i\text{-}Bu_2AlH \longrightarrow i\text{-}Bu_2AlOR + H_2 \uparrow \qquad (1)$$

$$\begin{aligned}
R=Et, &\ DIBAOEt \\
i\text{-}Pr, &\ DIBAO^iPr \\
t\text{-}Bu, &\ DIBAO^tBu \\
s\text{-}Bu, &\ DIBAO^sBu \\
PhCH_2, &\ DIBAOBz
\end{aligned}$$

DIBAH[5] at 0 °C is summarized in Table 1. The course of the reaction was monitored by calculating the moles of hydrogen evolved. DIBAH reacted readily with alcohols at 0
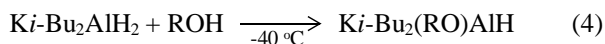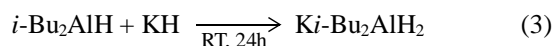
Table 1. Reaction of Diisobutylaluminum Hydride (DIBAH) with Alcohols in Tetrahydrofuran at 0 °C[a]

Alcohol	Reaction time (h)[b]		
	0.25	0.5	1.0
Ethyl alcohol	1.01	1.01	
i-Propyl alcohol	0.99	1.00	1.00
s-Butyl alcohol	0.97	1.01	1.01
t-Butyl alcohol	0.95	1.01	1.01
Benzyl alcohol	1.00	1.00	

[a]Reaction with 1 equivalent of alcohol. The mixture is *ca*. 1 M in THF.
[b]Mmol of hydrogen evolved per mmol of DIBAH.

°C. The ^{27}Al NMR of diisobutylalkoxyalanes in THF revealed a broad singlet at δ 150 for DIBAOEt, δ 162 for DIBAO^{i}Pr, δ 160 for DIBAO^{s}Bu, δ 165 for DIBAO^{t}Bu and δ 160 for DIBAOBz, relative to $[Al(H_2O)_6]^{3+}$.

Potassium diisobutylalkoxyaluminum hydrides were prepared from the corresponding diisobutylalkoxyalanes and commercially available potassium hydride (35 wt. % dispersion in mineral oil), after removing the oil by washing the reagent with THF (Eq. 2). Reactions were generally carried

$$KH + i\text{-}Bu_2AlOR \xrightarrow[\Delta]{THF} K i\text{-}Bu_2(RO)AlH \qquad (2)$$
$$KDIBAH(OR)$$
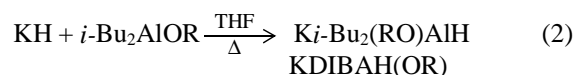
out by adding diisobutylalkoxyalane to potassium hydride (100% excess over the stoichiometric amount) suspended in sufficient THF to produce a nearly 1.0 M potassium diisobutylalkoxyaluminum hydride solution. The formation of potassium diisobutylalkoxyaluminum hydrides was quite slow : it required refluxing in THF for 2 days.

Alternatively, potassium diisobutylalkoxyaluminum hydrides can be prepared from the reaction of potassium diisobutylaluminum hydride with the correspounding alcohols at -40 °C (Eq. 4). The potassium diisobutylaluminum hydrides were prepared from the reaction of DIBAH with 50% excess potassium hydride at room temperature (Eq. 3).

$$i\text{-}Bu_2AlH + KH \xrightarrow[RT, 24h]{} K i\text{-}Bu_2AlH_2 \qquad (3)$$

$$K i\text{-}Bu_2AlH_2 + ROH \xrightarrow[-40\ °C]{} K i\text{-}Bu_2(RO)AlH \qquad (4)$$

The diisobutylalkoxyaluminum hydrides thus prepared in THF were characterized by IR and ^{27}Al NMR spectroscopy and the results are summarized in Table 2. Solution of the potassium diisobutylalkoxyaluminum hydrides in THF displays typical absorption in the IR: a strong absorption around 1600 cm^{-1}, attributed to the Al-H stretching vibration. The ^{27}Al NMR spectra of the THF solutions of potassium diisobutylalkoxyaluminum hydride exhibit broad singlet peaks around δ 130-145 downfield region relative to $[Al(H_2O)_6]^{3+}$ as reference. All the potassium diisobutylalkoxyaluminum hydrides examined were stable to disproportionation for an extended period of time, when the THF solutions of the aluminum hydride regents were maintained under a positive pressure of nitrogen at 0 °C. During the period, moreover, no significant change in the hydride con-

Table 2. Infrared and ^{27}Al NMR Spectra of Potassium Diisobutylalkoxyaluminum Hydride in Tetrahydrofuran

Potassium diisobutylmonoalkoxyaluminum hydride	IR ν_{Al-H}	^{27}Al NMR[a] δ, ppm
Potassium diisobutylethoxyaluminum hydride	1600	140(br,s)
Potassium diisobutyl*iso*-propoxyaluminum hydride	1615	131(br,s)
Potassium diisobutyl*sec*-butoxylaluminum hydride	1620	128(br,s)
Potassium diisobutyl*tert*-butoxylaluminum hydride	1610	145(br,s)
Potassium diisobutylbenzyloxyaluminum hydride	1595	143(br,s)

[a]Chemical shifts are relative to [Al(H$_2$O)$_6$]$^{3+}$.

Table 3. Reaction of Potassium Diisobutylalkoxyaluminum Hydrides with Representative Carbonyl Compounds in Tetrahydrofuran under Reflux[a,b]

Compound	Time (h)	KDIBAH (OEt)	KDIBAH (O^{i}Pr)	KDIBAH (O^{t}Bu)
Benzaldehyde	72[c]	52	42	40
	12	85	83	80
	24	100	98	96
	48		100	100
Caproaldehyde	72[c]	52	48	40
	12	86	84	75
	24	100	100	96
	48			100
2-Heptanone	72[c]	20	15	13
	12	68	66	60
	24	92	90	80
	48	100	98	90
	72			98
	96			100
4-Methylcyclohexanone	24	99	98	73
	48	100	100	80
	72			100
2-Cyclohexen-1-one	96	90	89	85
	120	98	95	92
	144			96
	168			100

[a]Two equivalents of reagent were utilized. Reaction mixtures were *ca.* 1 M in substrates. [b]Determined by GC using suitable internal standard. [c]At 25 °C.

centration was observed.

The reactivity of this series of agents toward representative carbonyl compounds was examined, and results are listed in Table 3. Generally, all the derivatives appear to be extremely mild reducing agents. The reaction of representative carbonyl compounds with these reagents are quite slow at room temperature : the reaction requires a drastic condition, where the reaction mixture in THF is under reflux, to be completed. However, the relative reactivity of these reagents is in the order of KDIBH(OEt) > KDIBAH(O^{i}Pr) > KDIBAH(O^{t}Bu). Apparently, such a reactivity order arises from the size of the alkoxy substituent.

The reductions of enals and enones were carried out by the addition of two equivalents of KDIBAH(OR) to the carbonyl compounds in THF under reflux and the products were analyzed by GC (Table 4). Reduction of simple conjugated aldehydes, such as crotonaldehyde and cinnamaldehyde, afforded entirely the corresponding allylic alcohols, resulting only from 1,2-reduction. In the case of cyclic enones, such as 2-cyclohexen-1-one and isophorone, the reaction also proceeded cleanly in a 1,2-sense to give the corresponding allylic alcohols.

The stereoselectivity of these trisubstituted aluminum hydrides toward representative cyclic ketones was studied, and the results are summarized in Table 5. The reactivity of

Table 5. Stereoselective Reaction of Potassium Diisobutylalkoxyaluminum Hydrides with Cyclic Ketones in Tetrahydrofuran under Reflux[a]

Ketone	R in Ki-Bu$_2$(RO)AlH[b,c]		
	Et	*i*-Pr	*t*-Bu
2-Methylcyclohexanone	75(90)	72(90)	65(80)
3-Methylcyclohexanone	81(100)	79(100)	71(80)
4-Methylcyclohexanone	80(100)	79(100)	73(80)
4-*t*-Butylcyclohexanone	83(100)	91(100)	72(70)
	80[d](30)[d]	87[d](29)[d]	
3,3,5-Trimethylcyclohexanone	84(95)	84(95)	87(70)
Norcamphor	86(55)	84(50)	92(35)
Camphor	90(40)	92(40)	92(30)

[a]Two equtvalents of reagent to ketone utilized. [b]Reacted for 48 h. [c]The figures are ratios of the more stable isomers. The figures in parentheses are yields of alcohols (both isomers). [d]Reacted at 25 °C.

Table 4. Reduction of α,β-Unsaturated Alehydes and Ketones with Potassium Diisobutylalkoxyaluminum Hydrides in Tetrahydrofuran under Reflux[a,b]

Compound	Time(h)	KDIBAH(OEt)		KDIBAH(O^{i}Pr)		KDIBAH(O^{t}Bu)	
		Product ratio (1,2 : 1,4)	Yield (%)	Product ratio (1,2 : 1,4)	Yield (%)	Product ratio (1,2 : 1,4)	Yield (%)
Crotonaldehyde	72	100 : 0	100	100 : 0	100	100 : 0	98
	96					100 : 0	100
Cinnamaldehyde	120	100 : 0	100	100 : 0	99	100 : 0	98
2-Cyclohexen-1-one	120	100 : 0	98	100 : 0	95	100 : 0	92
	168					100 : 0	100
Isophorone	192	100 : 0	99	100 : 0	99	100 : 0	90

[a,b]See the corresponding footnotes in Table 3.

these aluminum hydrides toward cyclic ketones are quite sluggish: it required refluxing in THF for 2~5 days to be completed. The stereoselectivities achieved by these reagents are somewhat extraordinary. Thus, the reagents converted cyclic ketones to the thermodynamically more stable alcohols. This is in contrast to the case of trisubstituted borohydrides[1~3] : usually, the trisubstituted borohydrides converted cyclic ketones to the thermodynamically less stable alcohols. However, these aluminum hydrides do not show high stereoselectivity in the reduction of cyclic ketones, compared to that achieved by *Al*-isopropoxydiisobutylalane (DIBAO^{i}Pr).[6]

The reaction of excess potassium hydride with diisobutylalkoxyalanes provides the corresponding potassium diisobutylalkoxyaluminum hydrides (KDIBAH(OR)), a new class of trisubstituted aluminum hydrides. These aluminum hydrides examined are stable to disproportionation. The reactivity of these reagents appears to be far much milder than that of simple aluminum hydrides: even aldehydes can be reduced effectively in refluxing THF. However, they showed a clean 1,2-reduction of α,β-unsaturated aldehydes and ketones to the corresponding allylic alcohols under such a drastic conditions. They also showed quite different stereoselectivity in the reduction of cyclic ketones, compared to that achieved by trisubstituted borohydrides. We plan to investigate the full scope of the reducing characteristics of these in order to find its application in origanic synthesis. Therefore, a series of reports will be followed

Experimental Section

All glassware used was predried in an oven, assembled hot, and cooled with a stream of nitrogen. All reactions were carried out under nitrogen atmosphere. Experimental techniques used in handling air-sensitive materials are described elsewhere.[7] Tetrahydrofuran (THF) was dried over a 4 Å molecular sieve and distilled from sodium-benzophenone ketyl just prior to use. Diisobutylaluminum hydride (DIBAH) was from the Aldrich Chemical Co. and was standardized by measurement of the H_2 produced by hydrolysis prior to use. Potassium hydride was purchased from the Aldrich Chemical Co. and was freed from the mineral oil according to the published procedure.[8] GC analyses were performed on a Donam DS 6200 FID Chromatograph. ^{27}Al NMR spectra were recorded on a Bruker AMX-300 Spectrometer.

Preparation KDIBAH(OR) in THF. The following procedure for the preparation of KDIBAH(OEt) is illustrative. An oven-dried, 250-mL, round-bottomed flask with side arm, condenser tube, and adaptor was attached to a mercury bubbler. The flask was flushed with dry nitrogen and maintained under a static pressure of nitrogen and was charged with 17.8 mL of DIBAH (14.2 g, 100 mmol) and 80 mL of THF. It was cooled to 0 °C, and 5.9 mL of ethyl alcohol (4.6 g, 100 mmol) was added dropwise with vigorous stirring. After completion of addition, the reaction mixture was further stirred for 1 h at room temperature. The ^{27}Al NMR of

the solution showed a broad singlet at δ 150 relative to $[Al(H_2O)_6]^{3+}$.

To another 250-mL flask described above was added 8 g of KH (200 mmol) as an oil dispersion with the aid of a syringe. The mineral oil was removed by washing the reagent with THF (3×10 mL). To this oil-free KH was added all the THF solution of diisobutylethoxyalane thus prepared above *via* a double-ended needle while the mixture was stirred vigorously. After completion of addition, the reaction mixture was brought to gentle reflux over the excess KH. The ^{27}Al NMR spectrum of the mixture after 48 h showed a broad singlet at δ 140, indicating the formation of pure potassium diisobutylethoxyaluminum hydride. The concentration of reagent was estimated gasometrically by hydrolyzing an aliquot to give 1.02 M.

Reaction of α,β-Unsaturated Carbonyl compounds. The following procedure for the reduction of crotonaldehyde with KDIBAH(OEt) is representative. An oven-dried, 25-mL flask equipped with a rubber septum, a magnetic stirring bar, and a reflux condenser connected to a mercury bubbler, was charged with 9.8 mL of a stock solution of KDIBAH(OEt) (1.02 M, 10 mmol) and 0.06 mL of *n*-tridecane (2.5 mmol) as an internal standard. To this solution was added 0.42 mL of freshly-distilled crotonaldehyde (0.35 g, 5 mmol), and the reaction mixture was heated to gentle reflux by using an oil bath. At the appropriate reaction time, an aliquot was withdrawn and hydrolyzed with 3 N HCl. The aqueous layer was then saturated with K_2CO_3 and the organic layer was dried over $MgSO_4$. GC analysis showed the presence of crotyl alcohol as a sole product in yield of 100% at 72 h.

General procedure for stereoselective Reaction. The reaction of 2-methylcyclohexanone with KDIBAH(OEt) is representative. To a 50-mL round-bottomed flask equipped as above was added a 2-mL solution of the reagent in THF. To this was added 1.0 mL of a 2-methylcyclohexanone solution in THF (1.0 M in ketone). The flask was immersed into an oil bath and the reaction mixture was heated to reflux for 48 h. It was then hydrolyzed by addition of 3 N HCl. The aqueous layer was saturated with anhydrous K_2CO_3, and the organic layer was analyzed by GC equipped with a 10% Carbowax 20 M capillary column (25 m). The results are summarized in Table 5.

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