

Catecholalane (1,3,2-Benzodioxaluminole) as a Selective Reducing Agent

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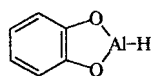
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Catecholalane (1,3,2-Benzodioxaluminole, CA) prepared from catechol and aluminum hydride in tetrahydrofuran (THF) is found to be a selective reducing agent. The systematic study in order to characterize the reducing properties of the reagent under practical conditions (THF, 0 or 25 °C, the quantitative amount of reagent to compound) has been done. The reagent reduces aldehydes, ketones, esters and acid chlorides to the corresponding alcohols, and primary amides to the corresponding amines. Especially noteworthy is that the reagent can convert both aromatic and aliphatic nitriles to the corresponding aldehydes in very high yields.

Introduction

Catecholborane (1,3,2-Benzodioxaborole, CB),¹ reported by Kabalka and his co-workers, appears to be a very useful and unique reducing agent. CB is milder than borane or dialkylborane. This diminished reactivity is a consequence of the lower Lewis acidity of boron in boronic esters, which apparently is a result of electron donation from oxygen.

Similarly, catecholalane (1,3,2-Benzodioxaluminole, CA) seems to exhibit unique reducing properties different from that of the parent aluminum hydride. In fact, CA is found to be an excellent reducing agent for converting both aromatic and aliphatic nitriles into the corresponding aldehydes in very high yields,² but aluminum hydride itself reduces nitriles only to amines.^{3,4} Consequently, a knowledge of the reducing properties of CA is necessary before this reagent should be used for such conversion. Accordingly, we undertook a systematic exploration of the reaction of CA with some representative organic compounds containing the common functional groups under practical conditions (THF, the calculated amount of reagent to compound).

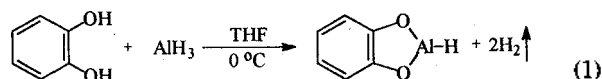


Catecholalane (CA)

In this article, the reducing properties of CA are compared with those of aluminum hydride-triethylamine (AHTEA) complex⁴ as a parent reagent, because the reducing properties of AHTEA appeared to be essentially same as those of aluminum hydride itself.³

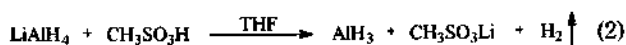
Results and Discussion

Preparation of Catecholalane (CA) Solutions in THF. The reagent is conveniently prepared by a reaction between catechol and aluminum hydride in THF at 0 °C (Eq. 1).



The ²⁷Al NMR spectrum of the solution of CA in THF showed a broad singlet centered at 15 ppm relative to [Al(H₂O)₆]³⁺.

There have been reported some useful methods for preparation of aluminum hydride solutions: the reactions of sodium and lithium aluminum hydrides with methanesulfonic acid or hydrogen chloride.⁴ Among these, the procedure utilizing lithium aluminum hydride and methanesulfonic acid is adopted in the synthesis of aluminum hydride solutions (Eq. 2).



Alcohols, Phenol, Amine, and Thiols. All the alcohols and phenol examined liberated hydrogen instantly and quantitatively in the reaction with a quantitative amount of CA at 0 °C. On the other hand, *n*-hexylamine liberated only 1 equiv of hydrogen rapidly, but the further hydrogen evolution was not observed in the reaction with 2 equiv of CA even at 25 °C. 1-Hexanethiol liberated hydrogen only slowly at 0 °C but rapidly at 25 °C, while the hydrogen evolution from benzenthioal was to be complete in 15 min at 0 °C. These results are summarized in Table 1.

Similarly, in the reaction with a quantitative amount of aluminum hydride-triethylamine (AHTEA) complex, the alcohols, phenols and thiols examined all liberated hydrogen instantly and quantitatively at room temperature.⁴ However, *n*-hexylamine liberated 1 equiv of hydrogen rapidly, but the second equiv was evolved relatively slowly to be complete in 3 h at room temperature.⁴

Aldehydes and Ketones. All of the aldehydes and ketones examined were cleanly reduced to the corresponding alcohols with a quantitative amount of hydride within 0.5 h at 0 °C, similar to the reactions with AHTEA.⁴ The results

Table 1. Reaction of Catecholalane with Representative "Active Hydrogen" Compounds in Tetrahydrofuran at 0 °C^a

Compd	Time	Ratio of CA/compd	Hydride used for hydrogen evln ^b
1-hexanol	5 min	1.00	0.99
benzyl alcohol	5 min	1.00	1.01
3-hexanol	5 min	1.00	0.95
	15 min	1.00	0.99
phenol	5 min	1.00	1.00
<i>n</i> -hexylamine	5 min	2.00	0.96
	15 min	2.00	1.00
	5 min ^c	2.00	0.98
	15 min ^c	2.00	1.00
1-hexanethiol	5 min	1.00	0.37
	1.0 h	1.00	0.45
	3.0 h	1.00	0.46
	5 min ^c	1.00	0.94
	0.25 h ^c	1.00	0.96
	1.0 h ^c	1.00	0.96
benzenethiol	5 min	1.00	0.94
	15 min	1.00	0.98

^a0.9 M of the reagent and 2.0 M of the compounds examined in THF were utilized for reactions. ^bMmoles of hydride per mmol of compound. ^cAt 25 °C.

Table 2. Reaction of Catecholalane with Representative Aldehydes and Ketones in Tetrahydrofuran at 0 °C^a

Compd	Time, min	Ratio of CA/compd	Product	Yield, ^b %
caproaldehyde	15	1.00	1-hexanol	100
benzaldehyde	15	1.00	benzyl alcohol	100
2-heptanone	15	1.00	2-heptanol	99
	30	1.00	2-heptanol	100
pinacolone	5	1.00	pinacolyl alcohol	98
	15	1.00	pinacolyl alcohol	100
acetophenone	5	1.00	1-phenylethanol	99
	15	1.00	1-phenylethanol	100
benzophenone	15	1.00	benzhydrol	100

^aSee corresponding footnote in Table 1. ^bGC yields.

are summarized in Table 2.

α,β -Unsaturated Aldehydes and Ketones. Since selective 1,2-reduction of enals and enones is of special interest in organic synthesis, representative enals and enones were tested with the reagent. Reductions of all the enals and enones examined with a quantitative amount of the reagent at 0 °C gave the corresponding 1,2-reduction products in a pure form quantitatively. However, reductions under the elevated reaction temperature (at 25 °C) or with excess reagent gave a mixture of 1,2- and 1,4- reduction products, with the exception of 2-hexenal which was reduced to 2-hexenol cleanly even under such drastic conditions. In general, the regioselectivity in the reduction of enones under such reaction condi-

Table 3. Reaction of Catecholalane with Representative α,β -Unsaturated Aldehydes and Ketones in Tetrahydrofuran^a

Compd	Temp, °C	Time, h	Ratio of CA/compd	Product ratio ^b 1,2:1,4	Yield, ^b %	
2-hexenal	0	0.25	1.00	100:0	98	
		0.5	1.00	100:0	99	
		0.25	2.00	100:0	100	
cinnamaldehyde	25	0.25	2.00	100:0	100	
		0	0.25	2.00	100:0	100
		0	0.25	2.00	98:2	100
2-cyclohexen-1-one	0	0.25	1.00	100:0	96	
		0.5	1.00	100:0	100	
		0.25	2.00	85:15	100	
benzalacetone	0	0.25	1.00	100:0	100	
		0.25	2.00	86:14	100	
		24.0	2.00	72:28	100	
	25	0.25	2.00	75:25	100	
		24.0	2.00	66:34	100	

^aSee corresponding footnote in Table 1. ^bThe product ratios and yields were determined by GC.

Table 4. Stereochemistry in the Reduction of Cyclic Ketones with Catecholalane in Tetrahydrofuran at 0 °C^a

Compd	Time, h	Ratio of CA/compd	Ratio of less stable isomer ^b	Yield, ^b %
2-methylcyclohexanone	0.25	1.00	52 (26.5) ^c	100
3-methylcyclohexanone	0.25	1.00	26	100
4-methylcyclohexanone	0.25	1.00	20	100
4- <i>t</i> -butylcyclohexanone	0.25	1.00	25 (13)	100
3,3,5-trimethylcyclohexanone	0.25	1.00	60	100
norcamphor	0.5	1.00	90	95
	1.0	1.00	90 (93)	99
camphor	0.5	1.00	81	86
	1.0	1.00	81 (90)	88
	24.0	1.00	81	99

^aSee corresponding footnote in Table 1. ^bThe isomer ratio and yields were determined by GC. ^cThe figures in parentheses are the results by aluminum hydride: see ref 3b.

tions is much poorer than that in the reduction of enals. Thus, the regioselectivity in the reduction of enones appears to be fluctuated significantly by the reaction temperature and the amount of reagent used. The results are summarized in Table 3.

Stereochemistry in the Reduction of Cyclic Ketones. The reduction of cyclic and bicyclic ketones by CA was studied. Consequently, it was of interest to explore whether the results with CA would exhibit any significant dif-

Table 5. Reaction of Catecholalane with Representative Carboxylic Acids and Derivatives in Tetrahydrofuran^a

Compd	Temp, °C	Time	Ratio of CA/compd	Product	Yield, ^b %
benzoic acid	0	0.5 h	2.00	benzyl alcohol ^c	12
		24.0 h	2.00	benzyl alcohol ^c	15
		24.0 h	3.00	benzyl alcohol ^c	23
	25	24.0 h	4.00	benzyl alcohol ^c	45
		120.0 h	4.00	benzyl alcohol ^c	52
caproic acid	0	24.0 h	2.00	1-hexanol ^c	19
		24.0 h	3.00	1-hexanol ^c	37
	25	24.0 h	4.00	1-hexanol ^c	58
		120.0 h	4.00	1-hexanol ^c	60
ethyl caproate	0	0.5 h	1.00	1-hexanol	53
		0.25 h	2.00	1-hexanol	100
ethyl benzoate	0	1.0 h	1.00	benzyl alcohol	23
		6.0 h	2.00	benzyl alcohol	71
		72.0 h	2.00	benzyl alcohol	96
		144.0 h	2.00	benzyl alcohol	100
	25	0.5 h	2.00	benzyl alcohol	94
1.0 h		2.00	benzyl alcohol	97	
3.0 h		2.00	benzyl alcohol	100	
caproyl chloride	0	5 min	1.00	1-hexanol	51
		5 min	2.00	1-hexanol	100
benzoyl chloride	0	5 min	1.00	benzyl alcohol	50
		5 min	2.00	benzyl alcohol	100

^aSee corresponding footnote in Table 1. ^bGC yields. ^cAlong with 1 equiv of hydrogen evolution.

ference from those with the parent aluminum hydride.^{3b} The results are summarized in Table 4.

The stereochemical results in reductions by CA are significantly different from those by aluminum hydride itself. For example, the reduction of 2-methylcyclohexanone by aluminum hydride gave 26.5% *cis*-2-methylcyclohexanol, while 52% of the *cis* epimer was produced by CA. However, obviously, there would be no point to the use of CA for the reduction of such simple ketones for stereochemical purpose.

Carboxylic Acids and Derivatives. Carboxylic acids were examined with a theoretical amount or excess of the reagent at 0 or 25 °C. The acids were reduced very sluggishly to the corresponding alcohols after immediate evolution of 1 equiv of hydrogen. On the contrary, aluminum hydride reduces carboxylic acids readily to the corresponding alcohols.³ Ethyl caproate was readily reduced to the corresponding alcohols with a theoretical amount of the reagent at 0 °C, whereas ethyl benzoate was reduced only slowly. However, an elevated reaction temperature (at 25 °C) accelerated the reaction to be complete in 3 h. Acid chlorides were reduced rapidly and cleanly to the corresponding alcohols. The possibility for the partial reduction of esters and acid chlorides to aldehydes was also examined with a limiting amount of the reagent, but no aldehyde formation was apparent. These results are summarized in Table 5.

Epoxides. The results of reducing three epoxides are summarized in Table 6. All of the epoxides examined were

Table 6. Reaction of Catecholalane with Representative Epoxides in Tetrahydrofuran^a

Compd	Temp, °C	Time, h	Ratio of CA/compd	Product	Yield, ^b %
1,2-butylene oxide	0	0.25	1.00	1-butanol	15
				2-butanol	85
	25	0.25	1.00	1-butanol	17
				2-butanol	83
styrene oxide	0	0.25	1.00	1-phenylethanol	20
				2-phenylethanol	80
	25	0.25	1.00	1-phenylethanol	4
				2-phenylethanol	96
cyclohexene oxide	0	0.25	1.00	cyclohexanol	99

^aSee corresponding footnote in Table 1. ^bGC yields.

rapidly reduced with a quantitative amount of CA. The reaction of 1,2-butylene oxide gave the *S_N2*-type of ring-opened product primarily in a 15 : 85 ratio. In contrast, the hydride attack on styrene oxide, an aromatic epoxide, occurs primarily at the more hindered carbon to afford a mixture of 20% 1-phenylethanol and 80% 2-phenylethanol at 0 °C, and at 25 °C the ratio of 2-phenylethanol increased to 96%.

The results obtained with CA are quite different from those with AHTEA. The reaction of aliphatic epoxides with AHTEA gives the *S_N2*-type of ring-opened products exclusively, whereas the reaction of styrene oxide, an aromatic one, proceeds to afford a mixture of 77% 1-phenylethanol and 23% 2-phenylethanol.³ It is noteworthy to point out the anti-Markovnikov reductive opening of epoxides: the reaction of aryl epoxides with $\text{BH}_3 \cdot \text{BF}_3$ proceeds to the hydride attack at the aryl-bound carbon exclusively.⁵ In the reaction of aliphatic trisubstituted epoxides with $\text{KPh}_3\text{BH} \cdot \text{Ph}_3\text{B}$ (1 : 1),⁶ the hydride attack occurs at the more hindered carbon. A similar trend has been observed with $\text{BH}_3 \cdot \text{LiBH}_4$ (1 : 1)⁷ and $\text{NaBH}_3\text{CN} \cdot \text{BF}_3$.⁸

Amides and Nitriles. Primary amides with 3 equiv of the reagent liberated hydrogen less than 1 equiv rapidly, but the reduction proceeded slowly to be complete in 24 h to give the corresponding amines. In order to test the possible formation of aldehydes, we treated them with a limiting amount of the reagent (2 equiv). However, only the corresponding amines were formed in around 50% yields. On the other hand, the reduction of *N,N*-dimethylbenzamide, a tertiary amide, with a limiting amount of the reagent provided a mixture of benzaldehyde and *N,N*-dimethylbenzylamine.

The most striking feature of CA seems to be the reaction of nitriles. Both capronitrile and benzonitrile utilized only 1 equiv of hydride slowly to be reduced to the corresponding aldehydes in very high yields. A full scope of the aldehyde synthesis from aromatic and aliphatic nitriles of various structure with this reagent has already been appeared in the literature.² Aluminum hydride can only reduce amides and nitriles to the corresponding amines. The results are summarized in Table 7.

Sulfur Compounds and Alkenes. Di-*n*-butyl disulfide

Table 7. Reaction of Catecholalane with Representative Amides and Nitriles in Tetrahydrofuran^a

Compd	Temp, °C	Time, h	Ratio of CA/compd	Product	Yield, ^b %
caproamide	0	6.0	2.00	hexylamine ^c	51
	25	6.0	2.00	hexylamine ^d	60
		24.0	3.00	hexylamine ^e	98
benzamide	0	6.0	2.00	benzylamine ^f	48
	25	6.0	2.00	benzylamine ^g	57
		24.0	3.00	benzylamine ^h	99
<i>N,N</i> -dimethylbenzamide	0	24.0	1.00	benzaldehyde	33
		3.0	2.00	benzaldehyde	15
	25	3.0	1.00	<i>N,N</i> -dimethylbenzylamine	72
			2.00	benzaldehyde	20
		24.0	1.00	<i>N,N</i> -dimethylbenzylamine	32
			2.00	benzaldehyde	21
capronitrile	0	72.0	2.00	hexanal	81
	25	24.0	2.00	hexanal	96
		96.0	1.00	benzaldehyde	33
benzonitrile	0	96.0	1.50	benzaldehyde	53
		72.0	2.00	benzaldehyde	94
		96.0	2.00	benzaldehyde	99
		24.0	2.00	benzaldehyde	99, 94 ⁱ

^a See corresponding footnote in Table 1. ^b GC yields. ^c Along with 0.91 equiv of hydrogen evolution. ^d Along with 0.93 equiv of hydrogen evolution. ^e Along with 0.95 equiv of hydrogen evolution. ^f Along with 0.88 equiv of hydrogen evolution. ^g Along with 0.92 equiv of hydrogen evolution. ^h Along with 0.96 equiv of hydrogen evolution. ⁱ Yield based on 2,4-dinitrophenylhydrazone.

Table 8. Reaction of Catecholalane with Representative Sulfur Compounds and Alkenes in Tetrahydrofuran^a

Compd	Temp, °C	Time h	Ratio of CA/compd	Hydride used for redn	Product	Yield, ^b %
di- <i>n</i> -butyl disulfide	0	24.0	2.00	0.16	1-butanethiol	12
	25	24.0	2.00	0.20 ^c	1-butanethiol	15
diphenyl disulfide	0	1.0	2.00	0.94 ^d	benzenethiol	92
		3.0	2.00	1.01 ^e	benzenethiol	99
phenyl <i>n</i> -propyl sulfide	25	3.0	1.00	0.00		
1-octene	0	6.0	1.00	0.00		
1-methyl-1-cyclohexene	0	6.0	1.00	0.00		

^a See corresponding footnote in Table 1. ^b GC yields. ^c Along with 0.09 equiv of hydrogen evolution. ^d Along with 0.48 equiv of hydrogen evolution. ^e Along with 0.60 equiv of hydrogen evolution.

was reduced very sluggishly even at 25 °C, whereas diphenyl disulfide was readily reduced by 2 equiv of CA with evolution of 0.6 equiv of hydrogen slowly, yielding 2 equiv of benzenethiol in 3 h at 0 °C. Sulfide, such as phenyl propyl sulfide, and alkenes are essentially inert to this reagent. These results are summarized in Table 8.

Conclusion

The reducing properties of catecholalane (1,3,2-benzodioxaluminole, CA) in tetrahydrofuran toward various organic compounds containing representative functional groups under practical conditions (tetrahydrofuran, 0 or 25 °C, the qua-

ntitative amount of reagent to compound) have been investigated. The reagent possesses unique reducing characteristics quite different from those of the parent aluminum hydride. Especially, the ready conversion of both aromatic and aliphatic nitriles to the corresponding aldehydes by the reagent is noteworthy. This systematic study permits quantitative and ready use of the reagent in organic synthesis with high convenience and efficiency, with the possibility of converting the structure of the parent aluminum hydride reagent to other derivatives of an improved selectivity.

Experimental Section

All glassware used in experiments was predried thorough-

ly in a drying oven and cooled under a dry nitrogen atmosphere. Hypodermic syringes were used to transfer solutions. All reactions were carried out under a static pressure of nitrogen in flasks fitted with septum-covered sidearms with use of standard techniques for handling air-sensitive materials.⁹

Materials. Most of the organic compounds utilized in this study were commercial products of the highest purity. They were further purified by distillation or recrystallization when necessary. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl and stored under dry nitrogen. Lithium aluminum hydride was obtained from the Aldrich Chemical Co. and used directly without further purification. Hydrogen chloride in diethyl ether was purchased from the Aldrich Chemical Co. or synthesized from hydrochloric acid and sulfuric acid using an automatic gasimeter.⁹

Instruments. GC analyses were carried out on a Donam DS 6200 FID chromatograph equipped with a Youngin D520 B computing integrator, using 10% Carbowax 20 M, cross-linked Methyl Silicone, and Carbowax TPA capillary columns. All GC yields were determined with use of a suitable internal standard and authentic mixtures. NMR spectrometer used was a Bruker AMX 300 for ²⁷Al NMR spectrum and chemical shifts are recorded relative to [Al(H₂O)₆]³⁺.

Preparation of Lithium Aluminum Hydride in Tetrahydrofuran. An oven-dried, 2-L, round-bottom flask with sidearm, equipped with a magnetic stirring bar and an adapter, was attached to a mercury bubbler. The flask was flushed with dry nitrogen and then maintained under a static pressure of nitrogen. The flask was charged with ca. 29 g of lithium aluminum hydride (ca. 720 mmol) and 600 mL of THF. The slurry was stirred for 7 days at room temperature and then allowed to stand to permit the undissolved materials to settle. The concentration of lithium aluminum hydride in THF measured by hydrolysis was 1.2 M. This solution was used for further reactions.

Preparation of Aluminum Hydride in Tetrahydrofuran. By means of a double-ended needle and a mass cylinder, 500 mL of 1.2 M lithium aluminum hydride thus prepared was introduced into a 2-L flask, fitted with an inlet port and magnetic stirring bar and connected to a mercury bubbler via a reflux condenser. The solution was cooled to 0 °C, and 59.1 g of methanesulfonic acid (615 mmol, 2.5% excess) was added slowly with vigorous stirring. The solution was permitted to stir for 1 h and then allowed to stand at 0 °C to permit the salt precipitate to settle. The clear supernatant solution was removed by a syringe. The ²⁷Al NMR spectrum of the solution showed a broad singlet centered at δ 127. The concentration of aluminum hydride in THF was 1.1 M. This solution was used for further reactions.

Preparation of Catecholalane (1,3,2-Benzodioxaluminumole, CA) in Tetrahydrofuran. To 400 mL of 1.1 M aluminum hydride in THF (440 mmol) thus prepared, was added 49.7 g of catechol (451 mmol, 2.5% excess), dissolved in 80 mL of THF, at 0 °C with vigorous stirring. The concentration of the solution was 0.9 M. The ²⁷Al NMR spectrum of CA in THF showed a broad singlet at δ 15. The solution was stored under nitrogen for 1 month at 0 °C, and aliquots were removed for analysis. There was not observed any change in concentration.

General Procedure Used for Hydride Reductions.

The following procedure was used for quantitative studies. The reduction of 1,2-butylene is described as an example of the experimental procedure. The CA solution, 10 mL of 0.9 M (9 mmol), was introduced into a dried, 50-mL flask fitted with a rubber syringe cap on an inlet port, a magnetic stirring bar, and a bent adapter connected to a mercury bubbler through a reflux condenser. The flask was immersed in a water bath, the stirred solution was maintained at 25 °C, and 0.72 g of 1,2-butylene oxide (10 mmol) in 5 mL of THF was injected slowly. After 15 min, the reaction mixture was treated with 3 N HCl. Dodecane was added as an internal standard. The gas chromatographic analysis with use of a capillary column (25 m) of 10% Carbowax 20 M showed 17% 1-butanol and 83% 2-butanol.

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