

COMMUNICATIONS

LETTERS

Facile and Chemoselective Reduction of Aldehydes and Ketones with Zinc-Modified CyanoborohydrideSunggak Kim[†], Yong Jin Kim, Chang Ho Oh and Kyo Han Ahn*Department of Chemistry, Korea Advanced Institute of Science and Technology, Seoul 131**(Received May 2, 1984)*

Sodium cyanoborohydride is well-known as being useful for imine reduction, carbonyl amination, deoxygenation of aldehydes and ketones, and reductive displacement of halides and tosylates.¹ Although in the past decade considerable efforts have been devoted to modify the usual reducing ability of sodium borohydride by the combination of sodium borohydride and metal salts,² there are only few reports in the literature on the use of sodium cyanoborohydride and metal salts.³

In connection with our studies toward development of new hydride reducing agents,⁴ we have recently reported that zinc-modified cyanoborohydride in diethyl ether reduces tertiary, allyl, and benzyl halides to the corresponding hydrocarbons but the reagent is inert toward primary alkyl, secondary alkyl, vinyl, and aryl halides.⁵ We now wish to describe reducing characteristics of zinc-modified cyanoborohydride toward reduction of aldehydes and ketones.

We have found that the nature of solvent is an important factor for the reduction of aldehydes and ketones. For example, reduction of 4-*t*-butyl-cyclohexanone with the reagent in diethyl ether afforded 4-*t*-butylcyclohexanol in an essentially quantitative yield at room temperature in 4 h, whereas the reaction occurred only to some extent in tetrahydrofuran (73% reduction), in methanol (12% reduction), and dimethoxyethane (6% reduction) under the same condition.

On the basis of the reduction results with 4-*t*-butylcyclohexanone, the remaining reductions were carried out with 0.5 molar equiv of zinc-modified cyanoborohydride in anhydrous diethyl ether at room temperature for 4 h.⁶ As shown in Table 1, cyclic ketones such as 4-methylcyclohexanone and cycloheptanone were completely reduced to the corresponding alcohols under the present conditions. Likewise, acyclic ketones, aldehydes, and α , β -unsaturated ketones were reduced to the corresponding alcohols in excellent yields. It is noteworthy that reduction of α , β -unsaturated ketones like isophorone afforded a 81:11 mixture of the saturated

alcohol and the allylic alcohol with a small amount of the saturated ketone (<5%) unlike selective 1,2 reduction of α , β -unsaturated ketones with zinc borohydride in diethyl ether.⁷

In view of the fact that sodium cyanoborohydride can reduce aldehydes and ketones in methanol only under acidic conditions,⁸ we believe that the zinc-modified cyanoborohydride in diethyl ether is very useful for reduction of aldehydes and ketones under mild conditions.

It is often necessary in organic synthesis to reduce one carbonyl group in a molecule without affecting another carbonyl group. A number of reagents have been devised to show the ability of discrimination between aldehydes and ketones.⁹ Although no selectivity has been found in the reduction of aldehydes and ketones with zinc-modified cyanoborohydride in anhydrous diethyl ether, we have found that the reagent in wet diethyl ether containing 5% water can reduce selectively cyclohexanones in the presence of aromatic aldehydes, acyclic ketones, aromatic ketones, and α , β -unsaturated ketones.

Competition experiments were carried out with a variety of structurally different aldehydes and ketones by use of 0.5 molar equiv of the reagent in diethyl ether containing 5% water for each mole of the substrate at room temperature for 4 h and some experimental results are summarized in Table 2. The results obtained in this study indicate that the general trend cyclohexanones > aliphatic aldehydes > acyclic ketones \approx aromatic aldehydes \approx aromatic ketones \approx α , β -unsaturated ketones was observed as the relative reactivity toward the reagent. Virtually no reduction of acetophenone, *p*-methoxybenzaldehyde, isophorone, and diisopropylketone occurred after 4h sufficient to reduce most 4-methylcyclohexanone. For example, 4-methylcyclohexanone was selectively (93%) reduced in the presence of acetophenone (1%) and 3-pentanone (8%). The reagent reached a limit with relatively reactive aliphatic aldehyde toward most hydride reducing agents. Thus, nonyl aldehyde was reduced to nonyl alcohol (76%), while 4-methylcyclohexanone was converted into the

TABLE 1: Reduction of Aldehydes and Ketones with Zinc-Modified Cyanoborohydride in Et₂O at Room Temperature for 4 h

Compound	Product	Yield, % ^a
4- <i>t</i> -Butylcyclohexanone	4- <i>t</i> -Butylcyclohexanol	99 ^b
4-Methylcyclohexanone	4-Methylcyclohexanol	99
3-Pentanone	3-Pentanol	97
<i>p</i> -Methoxybenzaldehyde	<i>p</i> -Methoxybenzyl alcohol	100
Nonyl aldehyde	Nonyl alcohol	93
Acetophenone	1-Phenylethanol	99
Cycloheptanone	Cycloheptanol	100
Isophorone	Saturated alcohol ^c	81(97) ^d

^a Determined by GLC. ^b a 85:15 mixture of trans and cis isomer
^c The product refers 3,3,5-trimethylcyclohexanol. ^d The figure in a parenthesis indicates the reduction yield containing 11 % of the corresponding allylic alcohol and 5 % of 3,3,5-trimethylcyclohexanone.

TABLE 2: Selective Reduction of Aldehydes and Ketones with Zinc-Modified Cyanoborohydride in Et₂O containing 5 % Water at Room Temperature for 4 h

No.	Starting Mixture	Conversion, % ^a
1	4- <i>t</i> -Butylcyclohexanone	99 ^b
	Acetophenone	1
	4-Methylcyclohexanone	93
2	Acetophenone	1
	3-Pentanone	8
	4-Methylcyclohexanone	93
3	Isophorone	3
	Diisopropyl ketone	1
	4-Methylcyclohexanone	92
4	Nonyl aldehyde	76
	<i>p</i> -Methoxybenzaldehyde	2
5	4-Methylcyclohexanone	94
	Cyclopentanone	8
6	Isophorone	5 ^c
	3-Pentanone	26

^a Determined by GLC. ^b for 12 h. ^c for 24 h.

alcohol (92%).

Although clear conclusions for the effect of a small amount of water under the present conditions await further study, the results obtained here indicate that zinc-modified cyanoborohydride in diethyl ether containing 5% water is very useful for chemoselective reduction of cyclohexanones in the presence of acyclic ketones, aromatic aldehydes, aromatic ketones, and α,β -unsaturated ketones.

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