Highly Selective Reduction of Cinnamaldehyde to Cinnamyl Alcohol Using Nanometric Alkali Metal Hydrides

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Under mild reaction conditions, cinnamaldehyde was reduced to cinnamyl alcohol with high selectivity and conversion using nano-LiH or nano-NaH as a reducing agent. Selectivity of 99.8% was obtained as reduced by nano-LiH with conversion of 99.4% in short reaction times.
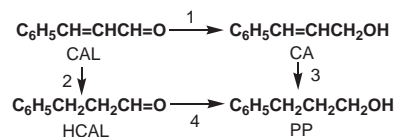
The selective reduction of α,β-unsaturated aldehydes to the corresponding alcohols is of great importance in the synthesis of various fine chemicals as well as of academic interest.[1] Selective reduction reactions are problematic when the C=O and C=C double bonds are conjugated further with the aromatic ring. An example is the selective reduction of cinnamaldehyde. Reduction of α,β-unsaturated aldehydes can be carried out by a variety of methods, including catalytic hydrogenation and the use of reducing agents, such as metal hydrides, dissolving metals and aluminum isopropoxide.[2] During the last few years, various attempts have been done to develop the method for the selective reduction in order to get either cinnamyl alcohol or hydrocinnamaldehyde.[2–14] Platinum catalysts have been frequently studied for the selective hydrogenation of cinnamaldehyde to cinnamyl alcohol, and usually a fairly high pressure was required.[3–8] Liu et al. have reported the use of Pt catalyst for the selective hydrogenation of cinnamaldehyde under 4 MPa pressure. The catalyst efficiency TO (turnover) in an hour was 186 mol cinnamaldehyde/mol Pt.[5] Classical reducing agents, such as $LiAlH_4$, $NaBH_4$, and $Na(i\text{-}PrO)BH$, could reduce C=O bond to get cinnamyl alcohol.[9–11,15] Usually, the selectivity was not higher than 99% with a cinnamaldehyde conversion less than 92% based on either catalysts or reducing agents.[2–12] In our previous study, $PdCl_2$–$0.5Co(OAc)_2$–PPh_3 catalyst could selectively hydrogenate cinnamaldehyde to hydrocinnamaldehyde under mild reaction conditions.[13] This paper reports that cinnamaldehyde can be selectively reduced to cinnamyl alcohol at high selectivity and conversion by the simple nanometric alkali metal hydrides for the first time.

Nano-MH is sensitive to air and moisture, therefore, all manipulations were carried out strictly under dry argon atmosphere using Schlenk technique. Nanometric alkali metal hydrides were synthesized according to the method in our previous report.[16] Transmission electron micrographs (TEM) showed that the average primary particle sizes of LiH, NaH, and KH were 22, 23, and 19 nm and specific surface areas were 125, 90, and 50 m^2/g respectively.[16] The reactions of cinnamaldehyde with nanometric alkali metal hydrides were carried out in tetrahydrofuran (THF) in a well-stirred glass flask. Typical reaction conditions were: THF 10 mL, nano-MH 3 mmol, cinnamaldhyde: according to the mole ratio to MH, refluxing THF, and normal pressure. The hydrolyzed products were analyzed by Shimadzu GC-14A

Scheme 1.

gas chromatograph with a PEG-20M capillary column of 30 m and a FID detector.

The reduction of cinnamaldehyde (CAL) can give rise to three possible products: cinnamyl alcohol (CA), hydrocinnamaldehyde (HCAL), and 3-phenylpropanol (PP). The possible reaction pathways of reduction are shown in Scheme 1.

The conversion and selectivity were calculated on the base of GC (gas chromatograph) analysis. As shown in Table 1, exclusive formation of the target molecule (CA) was observed, and the amount of side product (PP) is very small. No hydrocinnamaldehyde was found in the GC analysis. These results show that the reduction of an aldehyde group is much faster than that of carbon–carbon double bond when MH is used as a reducing agent. Cinnamaldehyde reacts with nano-MH to form metal alcoholate, which generates cinnamyl alcohol after hydrolysis. This addition reaction can be regarded as a nucleophilic addition. To the carbonyl carbon, a hydride ion from the nano-MH acts as a nucleophile, which is the same as that in the reaction mechanism using $LiAlH_4$ or $NaBH_4$ as a reducing agent.[10] From Table 1, it can be seen that a selectivity of 99.8% is obtained as reduced by nano-LiH, and 99.4% by nano-NaH, nano-KH exhibits lower selectivity, and the selectivity decreases further with longer reaction time. When nano-LiH is used as a reducing agent, the selectivity for cinnamyl alcohol almost keeps constant (99.8%) with time, while a slight decrease in selectivity in the case of nano-NaH as a reducing agent is observed. The selectivity decreases from 99.4% at 3 min to 99.1% at 30 min. When nano-KH is used as a reducing agent, the selectivity decreases from 98.8% at 3 min to 97.8% at 15 min. Nano-LiH gives the highest conversion of cinnamaldehyde as compared with nano-NaH and nano-KH, but the rate of reaction is the slowest among the three metal hydrides. The conversion can be affected by changing the molar ratio between the nano-LiH and cinnamaldehyde. The conversion increases by changing the ratio from 1.05:1 to 2:1 while the selectivity is unchanged. A maximum selectivity (99.8%) and conversion (99.4%) can be obtained in 60 min at a ratio of LiH/CAL = 2:1.

We have investigated the influence of temperature on the selectivity and reduction rate of cinnamaldehyde to cinnamyl alcohol using nano-NaH as a reducer. The selectivity almost kept constant in the temperature range from 15 to 60 °C. An activation energy of 54 kJ/mol was obtained by the Arrhenius plot us-

Table 1. Selective reduction of cinnamaldehyde to cinnamyl alcohol by nano-MH[a]

MH	MH/CAL /mol ratio	Time /min	Conversion /%	Selectivity/%		
				HCAL	PP	CA
Nano-LiH	1.05:1.0	60	82.5	0	0.1	99.9
Nano-LiH	1.05:1.0	120	93.4	0	0.1	99.8
Nano-LiH	1.05:1.0	240	96.5	0	0.2	99.8
Nano-LiH	1.50:1.0	60	96.9	0	0.2	99.8
Nano-LiH	1.50:1.0	120	98.4	0	0.2	99.8
Nano-LiH	2.00:1.0	60	99.4	0	0.2	99.8
Nano-NaH	1.05:1.0	3	92.5	0	0.6	99.4
Nano-NaH	1.05:1.0	15	95.6	0	0.7	99.3
Nano-NaH	1.05:1.0	30	96.3	0	0.9	99.1
Nano-KH	1.05:1.0	3	84.5	0	1.2	98.8
Nano-KH	1.05:1.0	15	89.4	0	2.2	97.8

[a]Each reaction was carried out in refluxing THF (10 mL) under normal pressure, 3 mmol nanometric alkali metal hydrides.

ing the initial reduction rate.

In order to discuss whether the by-product (PP) was formed via the reaction pathways 1 and 3 or the reaction pathways 2 and 4 or both, hydrocinnamaldehyde and cinnamyl alcohol were used as substrates to react with nano-MH respectively under the same reaction conditions. The results are illustrated in Tables 2 and 3 respectively. Comparing the results in Tables 2 and 1, it can be seen that in the reduction of an aldehyde group, the reduction of unsaturated aldehyde (CAL) is much faster than that of the saturated aldehyde (HCAL). The presence of conjugated double bonds favors the reduction of an aldehyde group. The direct reduction of carbon–carbon double bond in the unsaturated alcohol (CA) is extremely slow as shown in Table 3. The amount of 3-phenylpropanol formed is comparable with that in the reduction of cinnamaldehyde (Table 1). Besides, the reduction of hydrocinnamaldehyde is not so fast. If there were any cinnamaldehyde converted to hydrocinnamaldehyde during the reduction of the former, a small amount of hydrocinnamaldehyde should be left in the reaction mixture. Actually, this was not the case. We could not find any hydrocinnamaldehyde among the reaction products by GC analysis. These results indicate that the formation of by-product (PP) proceeds via the reaction pathways 1 and 3, not via pathways 2 and 4.

In this study, commercial-NaH (Serva Feinbiochemica) was also used as a reducing agent for the same reaction. Under the same reaction conditions, the conversion of cinnamaldehyde was extremely slow, only 1.4% as compared with 92.5% conversion when nano-NaH was used as a reducing agent. The difference in reaction rates between these two forms of NaH is com-

Table 2. Reduction of hydrocinnamaldehyde to 3-phenylpropanol using nano-MH as reducer[a]

Nano-MH	Time/min	Yield of 3-phenylpropanol/%
Nano-LiH	30	32.9
Nano-LiH	120	57.4
Nano-NaH	15	35.6
Nano-NaH	30	64.0
Nano-KH	15	58.1

[a]Each reaction was carried out in refluxing THF (10 mL) under normal pressure, 3 mmol nanometric alkali metal hydrides, MH/HCAL (molar ratio) = 1.05:1.0.

Table 3. Reduction of cinnamyl alcohol to 3-phenylpropanol using nano-MH as reducer[a]

Nano-MH	Time/min	Yield of 3-phenylpropanol/%
Nano-LiH	240	0.2
Nano-NaH	30	0.9
Nano-KH	15	2.4

[a]Each reaction was carried out in refluxing THF (10 mL) under normal pressure, 3 mmol nanometric alkali metal hydrides, MH/HCAL (molar ratio) = 1.05:1.0.

parable to the difference of their specific surface areas, since in a liquid–solid phase reaction, the rate of reaction is directly proportional to the surface area of the solid phase. The specific surface area of commercial NaH is around $1.4 \, m^2/g$, which is approximately two orders of magnitude smaller than that of the nano-NaH (around $90 \, m^2/g$).

The reduction of crotonaldehyde has also been studied using nano-NaH, but the result was not satisfactory due to the side reactions. In this case, by-products with high molecular weight were obtained.

In conclusion, under mild reaction conditions, cinnamaldehyde was selectively reduced to cinnamyl alcohol by nano-LiH, nano-NaH with high conversions in short reaction times. To our knowledge, besides mild reaction conditions, the high selectivity to cinnamyl alcohol as well as the high conversion is by far the best selectivity published for this reaction.

References
1 M. Boudart, *Nature* **1994**, *372*, 320.
2 R. K. Mackie, D. M. Smith, R. A. Aitken, *Guidebook to Organic Synthesis*, 3rd ed., Pearson Education Limited, Essex, **1999**, pp. 166–168.
3 A. B. da Silva, E. Jordao, M. J. Mendes, P. Fouilloux, *Appl. Catal., A* **1997**, *148*, 253.
4 S. Galvagno, Z. Poltarzewski, A. Donato, G. Neri, R. Pietropaolo, *J. Chem. Soc., Chem. Commun.* **1986**, 1729.
5 W.-Y. Yu, H.-F. Liu, M.-H. Liu, Q. Tao, *J. Mol. Catal. A: Chem.* **1999**, *138*, 273.
6 M. Arai, K. Usui, Y. Nishiyama, *J. Chem. Soc., Chem. Commun.* **1993**, 1853.
7 M. Hernandez, P. Kalck, *J. Mol. Catal. A: Chem.* **1997**, *116*, 131.
8 C. S. Narasimhan, V. M. Deshpande, K. Ramnarayan, *J. Chem. Soc., Chem. Commun.* **1988**, 99.
9 H. O. House, *Modern Synthetic Reactions*, 2nd ed., Benjamin/Cummings, Publishing Co., California, **1972**, pp. 89–91.
10 A. S. Wingrove, R. L. Caret, *Organic Chemistry*, Harper & Row Publishers, New York, **1981**, pp. 859–860.
11 H. C. Brown, J. S. Cha, B. Nazer, S.-C. Kim, S. Krishnamurthy, C. A. Brown, *J. Org. Chem.* **1984**, *49*, 885.
12 F. Kazemi, A. R. Kiasat, *Synth. Commun.* **2002**, *32*, 2255.
13 Y.-K. Zhang, S.-J. Liao, Y. Xu, D.-R. Yu, *Appl. Catal., A* **2000**, *192*, 247.
14 K. Tanemura, T. Suzuki, Y. Nishida, K. Satsumabayashi, T. Horaguchi, *Synth. Commun.* **2005**, *35*, 867.
15 B. Zeynizadeh, T. Behyar, *Bull. Chem. Soc. Jpn.* **2005**, *78*, 307.
16 Y.-P. Zhang, S.-J. Liao, Y. Xu, *J. Mol. Catal.* **1993**, *84*, 211.