

## Reduction of Organic Compounds with Sodium Borohydride-Copper(II) Sulfate System

Sung-eun Yoo,\* Sang-hee Lee

Korea Research Institute of Chemical Technology, P.O. Box 9, Daedeog Danji, Chungnam, South Korea

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**Abstract:** The reduction of various functional groups was investigated using sodium borohydride-copper(II) sulfate. Ketones, aliphatic esters, olefins, nitriles and aliphatic and aromatic nitro groups were reduced, but amides, aliphatic and aromatic carboxylic acids were inert. Rate of reaction was different for the various functional groups, allowing selective reductions to be performed.

Sodium borohydride is well known as one of the most excellent reducing agents for ketones and aldehydes but when used alone its reducing power is rather limited. However, reducing reagents formed by combining sodium borohydride and transition-metal salts have an enhanced reducing power to reduce various functional groups which are not generally reducible with sodium borohydride alone. For this purpose cerium chloride<sup>1</sup>, cobalt chloride<sup>2,3,4</sup>, titanium chloride<sup>5</sup>, samarium chloride<sup>6</sup> and other metal salts<sup>7,8</sup> have been used with NaBH<sub>4</sub>. It has been reported that sodium borohydride with copper acetylacetonate could reduce the aromatic nitro compounds to the corresponding amines<sup>9</sup>. But in general, NaBH<sub>4</sub>-Cu<sup>++</sup> system has been rarely studied than previously mentioned NaBH<sub>4</sub>-metal salt systems. Herein we would like to report a simple and efficient reduction condition of sodium borohydride and readily available cupric sulfate. The reaction can be carried out in alcoholic solvents as well as in the mixture of alcoholic solvent and water which makes the workup process quite simple. We found that under this condition the reducing power increases substantially to reduce various functional groups such as nitro, ester, nitrile and even olefin. Furthermore the selectivity among functional groups is substantially enhanced to reduce a certain group in the presence of other functional groups.

In a typical experiment, the starting material is dissolved in ethanol. The solution of cupric sulfate (2 molar aqueous solution, 10 mole %) is added. After the reaction mixture is cooled to 0°C, sodium borohydride (5 moles) is added portionwise. Then the reaction mixture is stirred at room temperature or at the specified reaction temperature. The reaction mixture is then diluted with ethyl acetate and the ethyl acetate layer is washed with water, dried and concentrated to give the crude product which is purified by silica gel column chromatography<sup>10</sup>.

As shown in Table 1, the NaBH<sub>4</sub>-CuSO<sub>4</sub> system is capable of reducing various functional groups. Thus the aromatic and aliphatic nitro groups can be reduced to the corresponding amines (entry 1, 2 & 4). The aromatic nitro groups is reduced much more rapidly than the aliphatic nitro group (entry 1 & 3 vs entry 2). The reduction of nitro group is fairly fast but slower than the reduction of ketones as expected

Table 1.

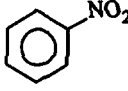
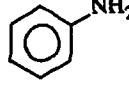
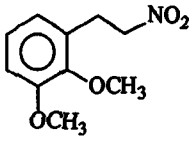
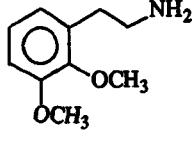
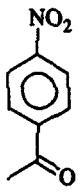
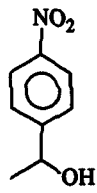
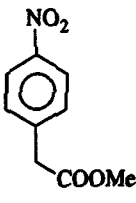
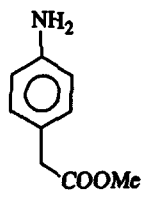
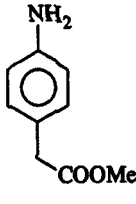
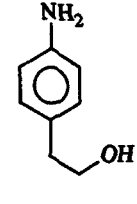
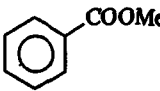
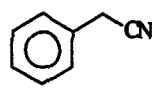
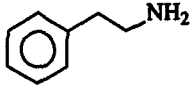
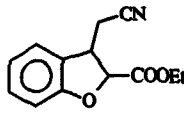
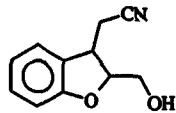
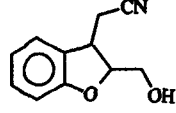
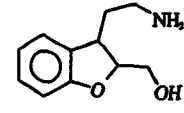
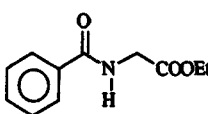
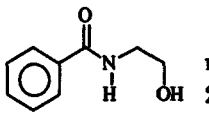
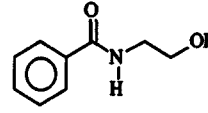
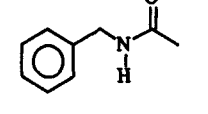
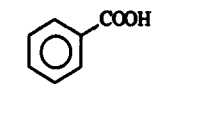
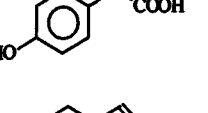
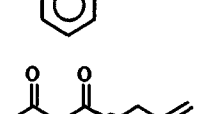
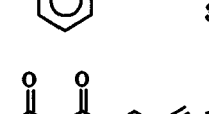
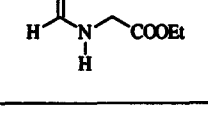
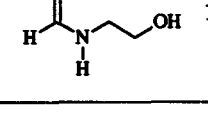
Entry	Substrate	Product	Condition	Yield
1			rt 10 min.	94
2			reflux 30 min.	80
3			0°C 5 min.	100
4			rt 10 min.	90
5			rt 20 min.	84
6			reflux 2 hrs	*
7			reflux 2 hrs	74
8			rt 20 min.	87
9			reflux 2 hrs	69

Table 1. continued

Entry	Substrate	Product	Condition	Yield
10			rt 20 min.	82
11			reflux 2 hrs	*
12			reflux 2 hrs	*
13			reflux 2 hrs	*
14			reflux 2 hrs	*
15			reflux 3 hrs	98
16			reflux 1 hr	65

\* No reaction under this condition

(entry 3). But the reduction of the aromatic nitro groups is faster than that of the aliphatic esters (entry 4). The aliphatic esters can be reduced (entry 5,8,10 & 16) but under this condition the aromatic esters are inert (entry 6). Nitriles can be reduced to give the corresponding amines but the reduction requires a higher reaction temperature (entry 7 & 9). Therefore the selective reduction of esters is possible in the presence of the nitrile group (entry 8). The aromatic and aliphatic carboxylic acids and amides are not reduced under the condition (entry 11, 12, 13 & 14)<sup>1</sup>. Therefore it

is possible to reduce the ester groups selectively in the presence of these functional groups (entry 10). Interestingly under this condition olefins can be reduced to the corresponding saturated hydrocarbons but the reaction requires generally a higher reaction temperature (entry 15 & 16).

In conclusion, the  $\text{NaBH}_4\text{-CuSO}_4$  system was found to be quite powerful to reduce various functional groups and in many cases with good selectivities. Under this condition the following functional groups can be reduced in the order shown; ketones > aromatic nitro groups > aliphatic esters > aliphatic nitro groups > nitriles > olefins.

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#### References and Notes

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- (10) All products were characterized by NMR and mass spectroscopy.
- (11) Carboxylic acids and amides have been successfully reduced to the corresponding alcohols and amines respectively in the  $\text{NaBH}_4$ -titanium chloride system (see ref.5). However our finding, that these functional groups are inert in the  $\text{NaBH}_4\text{-CuSO}_4$  system, strongly suggests that the reducing power of  $\text{NaBH}_4$  is greatly dependent on the transition metal being used.