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DITHIOL-FERROUS CHLORIDE CATALYZED SELECTIVE REDUCTION OF ALKYNES WITH SODIUM BOROHYDRIDE

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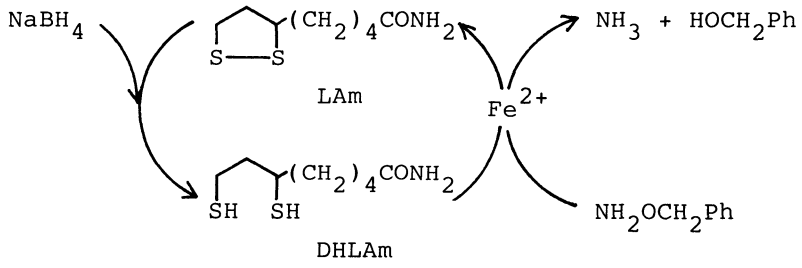
Simple dithiols-ferrous chloride or lipoamide-ferrous chloride were found to be effective catalysts for the selective reduction of substituted alkynes to alkenes with sodium borohydride presumably by forming active dithiol-Fe(II) complexes.

We have previously reported the reduction of hydroxylamines,[1] azobenzene, and nitrobenzene[2] by dihydrolipoamide (DHLAm) and Fe(II), and also reported the catalytic reduction of hydoxylamine derivatives with sodium borohydride ($NaBH_4$) in the presence of lipoamide (LAm) and ferrous ammonium sulfate in buffer (pH 9.8)-EtOH solution (Scheme 1).[3] These reactivities are of interest in relation to those of nonheme-iron proteins such as ferredoxines and their models.[4-6]

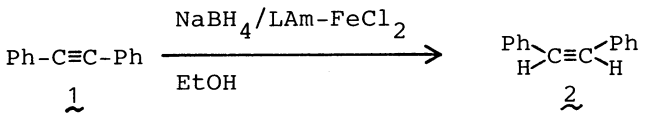


Scheme 1.

In this letter, simple dithiols-Fe(II) or LAm-Fe(II) catalyzed reduction of substituted alkynes with $NaBH_4$ is described.

A LAm-Fe(II) catalyzed reduction of diphenylacetylene was attempted in various conditions (Table 1). Diphenylacetylene (1) was not reduced at all by the $NaBH_4$/LAm-Fe(II) system in aqueous media, whereas, in anhydrous EtOH, 1 was reduced with

$NaBH_4$ to cis-stilbene (2) in 75% yield in the presence of catalytic amounts of LAm and ferrous chloride ($FeCl_2$) for 8 h at 35 °C under argon. The reduction did



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not occur in the presence of LAm or $FeCl_2$ alone as a catalyst. $FeCl_3$ was also effective but ferric acetylacetonate showed lower reactivity for the reduction.

Some alkynes were reduced by the $NaBH_4$/LAm-$FeCl_2$ system (Table 2).

Table 1. LAm-Fe^{2+} catalyzed reduction of diphenylacetyrene 1 with $NaBH_4$[a)]

Catalyst			Solvent	Yield of cis-stilbene 2/%[b)]
LAm/mM	Fe^{n+}	/mM		
10	$FeSO_4(NH_4)_2SO_4$	10	buffer[c)]-EtOH	0
10	$FeCl_2$	10	buffer[c)]-EtOH	0
10	$FeCl_2$	10	EtOH	64
7.5	$FeCl_2$	10	EtOH	75
0	$FeCl_2$	10	EtOH	7
10	$FeCl_2$	0	EtOH	0
10	$FeCl_3$	10	EtOH	73
10	$Fe(acac)_3$	10	EtOH	29

a) Reaction conditions:[$NaBH_4$] = 500 mM, [PhC≡CPh] = 100 mM, 35 °C, 8 h, under argon. b) Determined by GLC. c) 0.1 M Carbonate buffer (pH 9.8).

Table 2. Reduction of alkynes with $NaBH_4$/LAm-$FeCl_2$[a)]

Substrate	Conversion/%	Product (yield/%)[b)]
Ph-C≡C-Ph	65	Cis-stilbene (64), trans-stilbene (1)
Ph-C≡C-CH_3	40	Cis-1-phenyl-1-propene (40)
Ph-C≡C-H	93	Styrene (85), ethylbenzene (8)
Ph-C≡C-COOEt	84	Cis-ethyl cinnamate (7), trans-ethyl cinnamate (16), cis-cinnamyl alcohol (39) ethyl 3-phenylpropanoate (22)
Ph-C≡C-$CONHCH_2Ph$	100	Cis-N-benzylcinnamide (38), trans-N-benzylcinnamide (62)
Ph-C≡C-CH=CH-Ph	56	Diphenylbutadiene (56)
$CH_3(CH_2)_4C{\equiv}C(CH_2)_4CH_3$	22	Cis-6-dodecene (22)

a) Reaction conditions:[$NaBH_4$] = 500 mM, [Substrate] = 100 mM, [LAm] = 10 mM, [$FeCl_2$] = 10 mM, 35 °C, 8 h, under argon. b) Determined by GLC.

Alkyl or phenyl subtituted alkynes gave cis-alkenes selectively. Alkynes which have electron withdrowing groups such as ester or amide group could be reduced easily. But these derivatives were reduced to give mixtures of cis- and trans-alkenes under present basic conditions.

The ratio of the LAm to $FeCl_2$ gave an important effect on the product yields. A maximum yield was obtained at nearly equimolar amount of LAm and $FeCl_2$, and excess LAm inhibited the reaction (Fig. 1), which suggested that DHLAm, produced in situ by the reduction of LAm with $NaBH_4$, formed an active 1:1 complex to be effective in the reduction of alkynes.

Various thiols-$FeCl_2$ catalyzed reduction of diphenylacetylene 1 with $NaBH_4$ was examined (Table 3). Dithiols which form stable chelates with metal ions[7] showed higher activity as

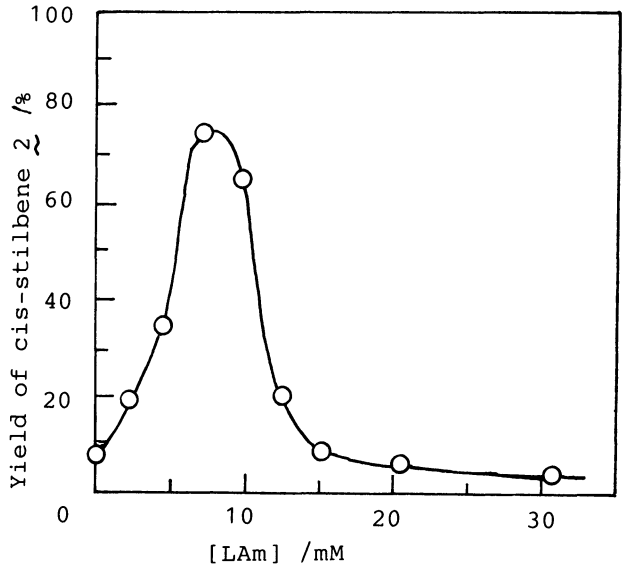
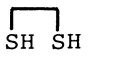
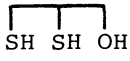
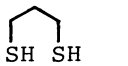
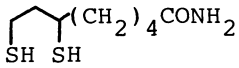
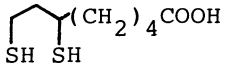
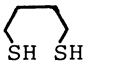
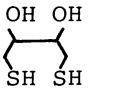
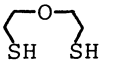
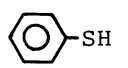


Fig. 1. Effect of the concentration of LAm on the reduction of acetylene 1 by $NaBH_4$/LAm-$FeCl_2$: [$NaBH_4$] = 500 mM, [1] = 100 mM, [$FeCl_2$] = 10 mM, EtOH, 35 °C under argon.

Table 3. Reduction of acetylene 1 with $NaBH_4$/thiol-$FeCl_2$[a)]

Thiol	Cis-stilbene/%
	70
	11
	39
	64
	15
	6
	4
	2
	8

a) Reaction conditions: [Dithiol] = 10 mM, Other conditions are the same as those in Table 1.

the catalyst. Dithiols with carboxyl or hydroxyl groups showed lower activity for the reaction.

These results suggested that the reduction proceeded by coordination of alkynes to an active dithiol-Fe(II) complex, followed by electron or hydride transfer in the complex and regeneration of the active complex by $NaBH_4$ to form a catalytic cycle. Excess thiols, other coordinating groups such as carboxyl and hydroxyl groups in the dithiols, or water might inhibit the coordination of substrate 1 to active dithiol-Fe(II) (1:1) complexes.

It is interesting that such simple thiols-Fe(II) are active for the reduction of acetylenes as other complicated non-heme iron protein model systems.[8)]

Because of availability, simplicity in handling and effectiveness for the selective reduction of both aryl and alkyl substituted alkynes with functional groups under mild conditions, the $NaBH_4$/dithiol-$FeCl_2$ reduction system is predominant to the ferredoxin model [8)] or other reduction systems.[9,10)]

References

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