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REDUCTION BY A MODEL OF NAD(P)H. PHOTO-ACTIVATION OF NADH AND ITS MODEL COMPOUNDS TOWARD THE REDUCTION OF OLEFINS

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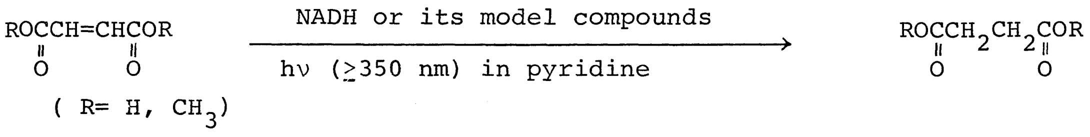
NADH, 1-benzyl-1,4-dihydronicotinamide, and Hantzsch ester reduce dimethyl maleate and fumarate to dimethyl succinate under photo-activation at room temperature. Fumaric acid is also reduced under the same condition. Pyridine is the best solvent for the reaction.

Nicotinamide nucleotides play a vital role in biological oxidation-reductions.[1] Namely, NAD(P)H reduces carbonyl compounds to alcohols. In certain enzymatic systems, NAD(P)H also reduces carbon-carbon double bond in α-ketoolefin structure such as crotonyl-CoA and benzalacetone.[2] In order to understand mechanisms of biochemical reactions and to extend them to organic synthetic chemistry, it is worthy to approach the subject from the view point of organic chemistry.[3] Most studies on the model reaction so far reported, however, have concerned with looking for active substrates and no effort has been done to activate NAD(P)H or its models.[3,4] We, in this communication, wish to report photochemical activation of NADH and its model compounds.



$$\underset{\overset{\|}{O}}{ROC}CH{=}CH\underset{\overset{\|}{O}}{COR} \xrightarrow[h\nu\ (\geq 350\ \text{nm})\ \text{in pyridine}]{\text{NADH or its model compounds}} \underset{\overset{\|}{O}}{ROC}CH_2CH_2\underset{\overset{\|}{O}}{COR}$$

(R= H, CH_3)

Dimethyl fumarate cannot be reduced by 1-benzyl-1,4-dihydronicotinamide (BNAH) or 2,6-dimethyl-3,5-dicarboethoxy-1,4-dihydropyridine (Hantzsch ester), a model for NAD(P)H, without light at room temperature.[5,6] On the other hand, it was found that photo-activated dihydropyridine derivatives resulted in the reduction of dimethyl fumarate and maleate giving dimethyl succinate at room temperature. All samples were degassed and sealed prior to irradiations.[7] A 100W high pressure mercury lamp with a filter solution of 2,3-dihydro-5,7-dimethy-1,4-diazepine perchlorate[8] was used for irradiation. Esters were analyzed on vpc (20% XF-1150 cyanosilycone, 1 m, 120°). Acids were subjected to vpc (20% SE-30, 1 m, 90°) after silylation with N,O-bis(trimethylsilyl)acetamide. A typical example, where a mixture of dimethyl fumarate (72.5 mg, 0.5 mmol) and BNAH(225.1 mg, 1.05 mmol) in pyridine(25 ml) were irradiated with a merry-go-round apparatus, is shown in Figure 1. When acetonitrile was used as a solvent, much slower reduction was observed. Maximum yields of products in other systems are listed in Table 1. It is interesting to note that fumaric acid[9] is also reduced to succinic acid in spite of the expectation that they

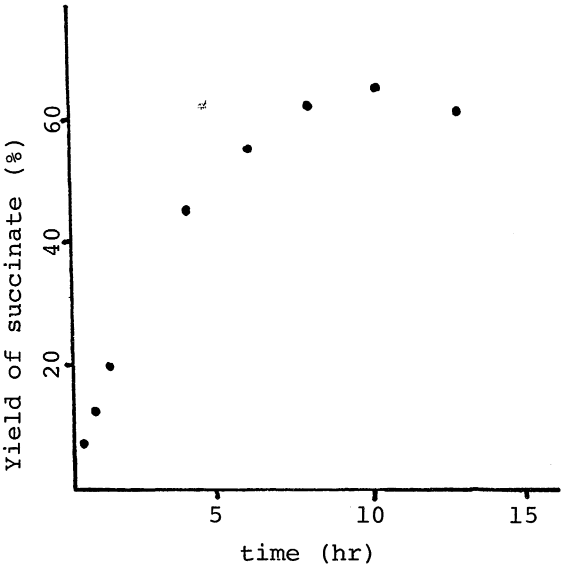
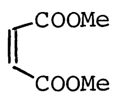
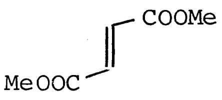
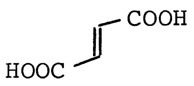


Figure 1. Effect of Photo-irradiation on the Yield of Dimethyl Succinate.

Table 1. Yields of Products in the reduction with NADH or its Model Compounds under Photo-irradiation at Room Temperature

Olefin	Reactant	Solvent	Yields, %
	BNAH	pyridine	60
	BNAH	acetonitrile	0.6
	Hantzsch ester	pyridine	70
	BNAH	pyridine	67
	BNAH	acetonitrile	0.8
	Hantzsch ester	pyridine	70
	NADH	23% aq. pyridine	30
	BNAH	pyridine	45

are in dianion forms in pyridine. Additionally, we obtained an evidence that the present reduction proceeds via direct hydrogen transfer from dihydropyridine derivatives to a substrate, analogously to enzymic systems: reduction of dimethyl fumarate with the 4,4-dideuterio analog of Hantzsch ester gave monodeuterated dimethyl succinate.

Since only NADH or its model compounds absorbs the irradiated light, there is no doubt that the reduction is initiated by photoexcited dihydropyridines.[10] However, we have no evidence to discuss on a special role of pyridine. Photoactivation of NAD(P)H and its models have been reported by Krasnovskii and his coworkers.[11] They found that the photo-excitation of dihydropyridines in aqueous pyridine gave active ($E_0' \approx -0.5$ volt) and stable (more than 1 hr at room temperature) species which reduced methyl viologen in a dark. They assumed that an electron released from the photoexcited dihydropyridine is stabilized by solvation with pyridine.[12] Since the present reaction undergoes only under photo-irradiating condition, the reacting species may be different form that reported by Krasnovskii. In spite of such a difference, we assume that pyridine is playing a similar role in both reactions: to make the dihydropyridines easy to release an electron.[13]

Although NAD(P)H, in enzymic systems, has rarely a chance to be photoactivated, there is a possibility that it is enzymatically activated to the similar state which is responsible to the present reaction.

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