

REDUCTION OF α, β -UNSATURATED CARBONYL COMPOUNDS BY A MODEL OF NAD(P)H
WITH CHLOROTRIS(TRIPHENYLPHOSPHINE)RHODIUM¹⁾

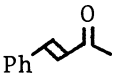

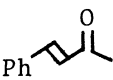

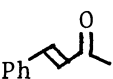

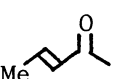

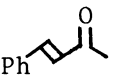

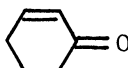
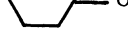
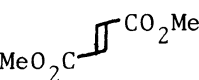

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α, β -Unsaturated carbonyl compounds are reduced to the corresponding saturated carbonyl compounds by a model of NAD(P)H with the aid of a rhodium(I) catalyst.

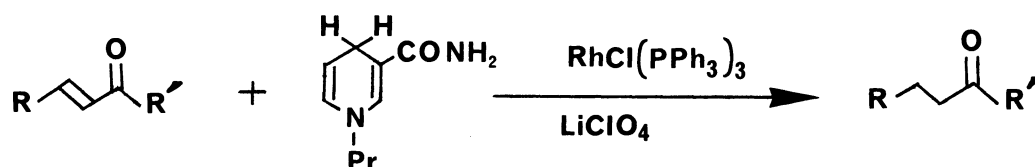
In certain enzymatic systems, NAD(P)H reduces carbon-carbon double bonds in α, β -unsaturated carbonyl compounds such as crotonyl-CoA and coumarate.²⁾ Although a few reports have contributed to the nonenzymatic reductions of olefins, the reductions of carbon-carbon double bonds have been limited to strongly electron-deficient substrates and even benzalacetone has never been reduced.³⁾ We report an extension of a scope of the reduction with an NAD(P)H-model.

In biomimetic reactions, a certain catalyst is necessary to substitute an enzyme, which is an excellent catalyst in biological reactions. The catalysts in biomimetic reductions must be able to ligate both a reductant and a substrate at least at the transition state of the reaction.⁴⁾ We employed chlorotris-(triphenylphosphine)rhodium (1) as a catalyst in the reduction of α, β -unsaturated carbonyl compounds because 1 can ligate an olefinic functional group as well as the dihydronicotinamide moiety.⁵⁾ Indeed, N-propyl-1,4-dihydronicotinamide (PNAH) reduced a variety of α, β -unsaturated carbonyl compounds to the corresponding saturated carbonyl compounds in the presence of catalytic amount of 1. Thus, benzalacetone was reduced to benzylacetone in 61% yield by PNAH in the presence of 10 mol% of 1 under an argon atmosphere. The product corresponding 1,2-reduction could not be detected. Results from other olefins are summarized in Table 1.

Table 1. 1,4-Reduction of α,β -unsaturated carbonyl compounds by PNAH^{a)}

Entry	Substrate	Solvent	Reaction temp /°C	Yield/% ^{b)}	
				Product	Substrate ^{c)}
1		MeOH	60	33	30
2	Ph  H	MeCN	70	60	40
3		MeOH	60	61 ^{d)}	5
4	Ph  Me	MeCN	70	60	20
5		MeOH	60	70	11
6	Ph  Ph	MeCN	70	61	18
7		MeOH	60	30	20
8	Me  Ph	MeCN	70	31	20
9		MeOH	60	5	18
10	Ph  OMe	MeCN	70	5	70
11		MeOH	60	10	63
12		MeCN	70	47	0
13		MeOH	60	4 ^{e)}	0
14	MeO ₂ C 	MeCN	70	4	70

a) Reaction condition: [Substrate] = 0.1 mmol, [PNAH] = 0.15 mmol, [RhCl(PPh₃)₃] = 0.01 mmol, [LiClO₄] = 0.2 mmol, [Solvent] = 2 cm³, 20 h under an argon atmosphere in the dark. b) Determined on GLPC (Silicone OV-330, 70-180 °C, internal standards: 1,4-dimethoxybenzene for entries 1-4 and 7-10; 1,4-diisopropoxybenzene for entries 5 and 6; tetraline for entries 11-14). c) Recovered starting material. d) Isolated yield was 51% in a preparative scale experiment. e) No other product was detected on GLPC.



It is noteworthy that the present reduction is applicable not only to aromatic compounds but also to aliphatic ones. For example, 2-cyclohexen-1-one was reduced to cyclohexanone in 47% yield. This selective reduction shows a sharp contrast with the reduction of enones with an NAD(P)H-model catalyzed by a Lewis acid, in which an enone was reduced to an allylic alcohol selectively.⁶⁾

The present system is effective to α,β -unsaturated ketones but not to α,β -unsaturated esters, and shows again a remarkable difference from the photoirradiated reduction of olefins by an NAD(P)H model.^{3c,d)} In the latter system, dimethyl fumarate was reduced smoothly to dimethyl succinate but benzalacetone was not reduced to benzylacetone.

It is well known that ruthenium(II)⁷⁾ or rhodium(I)⁸⁾ complexes catalyze hydrogen transfer reaction from alcohols or amines to olefins. However, the present reduction by an NAD(P)H model (MR) seems different in the mechanism from hydrogen transfer reactions so far reported (HT) because the feature of these two reactions are different in the following points.

1. HT proceeds only at elevated temperatures (170-200 °C) but MR proceeds smoothly at moderate temperatures (60-70 °C).
2. HT prefers a nonpolar solvent. The reduction in a coordinative solvent such as acetonitrile proceeds very slowly, while the MR reaction nicely proceeds in acetonitrile and no MR reaction proceeds in hexane.
3. In HT, the reductant is required in excess or is employed as a solvent, but only slightly excess (1.5 mol equiv.) of PNAH is enough for MR to give a good result.
4. Both rhodium(I) and ruthenium(II) are excellent catalysts in HT, but ruthenium(II) does not work as a catalyst in MR. Namely, benzalacetone is reduced to give benzylacetone in less than 5% yield when Ru(II) is employed as a catalyst.
5. Benzyl alcohol and indoline are good reductants in HT, but not in MR.

Evidence to propose a detailed mechanism for the present reduction has not been obtained at present. However, the salt effect observed in the reduction may provide information: the reduction was accelerated by the addition of equimolar amount of lithium perchlorate. It is highly probable that lithium ion

polarizes the carbon-rhodium bond in the model-Rh-olefin ternary complex or stabilizes the ionic reaction product (enolate ion). Acceleration by lithium perchlorate was also observed in the reduction of allylic acetates.⁹⁾

Further studies to extend the substrate and to elucidate the mechanism are in progress in our laboratory.

References

- 1) NAD(P)⁺-NAD(P)H Model. Part 51.
- 2) G. Weeks and S. J. Wakil, *Method. Enzymol.*, 14, 66 (1969); C. C. Levy and G. D. Weinstein, *Biochemistry*, 3, 1944 (1964).
- 3) Reductions of strongly electron-deficient olefins with NAD(P)H-models have been reported. a) B. E. Norcross, P. E. Klinedinst Jr., and F. M. Westheimer, *J. Am. Chem. Soc.*, 84, 797 (1962); b) Y. Ohnishi, M. Kagami, T. Numakunai, and A. Ohno, *Chem. Lett.*, 1976, 915; c) Y. Ohnishi, M. Kagami, and A. Ohno, *ibid.*, 1975, 125; d) C. Pac, M. Ihama, M. Yasuda, Y. Miyauchi, and H. Sakurai, *J. Am. Chem. Soc.*, 103, 6495 (1981).
- 4) A. Ohno, H. Yamamoto, and S. Oka *J. Am. Chem. Soc.*, 103, 2041 (1981); A. Ohno, T. Kimura, H. Yamamoto, S. G. Kim, S. Oka, and Y. Ohnishi, *Bull. Chem. Soc. Jpn.*, 50, 1535 (1977).
- 5) S. G. Davies, "Organotransition Metal Chemistry; Applications to Organic Synthesis," Pergamon Press, London (1982), p. 13.
- 6) A. Ohno, Y. Ishihara, S. Ushida, and S. Oka, *Tetrahedron Lett.*, 23, 3185 (1982).
- 7) Y. Sasson and B. Jochanon, *Tetrahedron Lett.*, 1971, 2167; Y. Sasson and B. Jochanon, *J. Org. Chem.*, 40, 1887 (1975).
- 8) T. Nishiguchi, K. Tachi, and K. Fukuzumi, *J. Org. Chem.*, 40, 237 (1975).
- 9) K. Nakamura, A. Ohno, and S. Oka, *Tetrahedron Lett.*, 24, 3335 (1983).

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