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REDUCTION BY A MODEL OF NAD(P)H. VIII. EFFECTS OF METAL ION ON THE COURSE AND STEREOCHEMISTRY OF THE BIOMIMETIC REDUCTION OF OLEFIN

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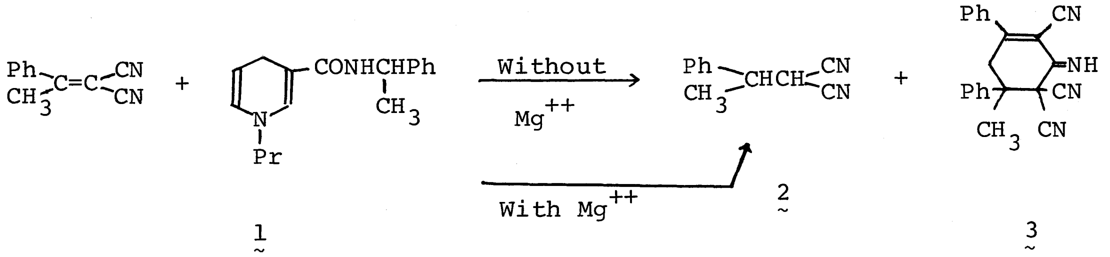
Asymmetric reduction of an olefin is achieved with a chiral NAD(P)H-model compound in the presence of magnesium perchlorate which represses a side reaction catalyzed by a base.

Although not many, there are several enzymes that reduce olefins by the aid of NAD(P)H.2) For example, benzylideneacetone is reduced to benzylacetone by α,β-unsaturated ketone reductase-NADPH system.3) Non-enzymatic reduction of electron-defficient carbon-carbon double bonds with NAD(P)H-model compounds has been achieved at elevated temperatures4) or under acidic5) or photo-irradiating6) conditions. We wish now to disclose the effect of metal ion and the stereochemistry in the biomimetic reduction of a prochiral olefin, (α-methylbenzylidene)malononitrile, with optically active or inactive N-α-methylbenzyl-1-propyl-1,4-dihydronicotinamide (1) under the neutral and anaerobic conditions at room temperature.

The reaction of the olefin with the racemate of compound 1 at 30°C afforded (α-methylbenzyl)malononitrile (2) and a cyclic dimer (3) in 48 and 47% yields, respectively. The cyclic dimer is identical with the compound reported as an unidentified material obtained from the reaction of this olefin with small amount of diethylamine.7) On the other hand, the presence of magnesium perchlorate in the reaction mixture prevented the formation of compound 3 completely and the yield of 2 increased to 83% (Table 1). Thus, it is inferred that the magnesium ion decreases the basic property of the NAD(P)H-model compound,8) probably through coordination.



(α-Methylbenzylidene)malononitrile was also subjected to asymmetric reduction with *R*-configurational isomer of **1**. The reduction in the presence of magnesium perchlorate resulted in the formation of *R*-(+)-**2** in 8% enantiomer excess,[9)] whereas the racemic product was obtained in the absence of the magnesium salt. A similar trend has been observed when α,α,α-trifluoroacetophenone was reduced with the optically active **1**.[10)]

Table 1. Reduction of (α-Methylbenzylidene)malononitrile in 50 ml of Acetonitrile at 30°C.[a)]

Model compound	$Mg(ClO_4)_2$, mmol	Reaction Time, hr	Isolated Yields, %		
			Olefin[c)]	**2**	**3**
BNAH[b)]	0	24	0	48	47
BNAH	4	24	10	83	0
R-**1**	0	48	0	24[d)]	-[e)]
R-**1**	4	48	36	64[f)]	0

a) With each 4 mmol of compound **1** and olefin. b) 1-Benzyl-1,4-dihydronicotinamide. c) Recovered. d) Racemate. e) Small amount of **3** together ambiguous products. f) 8% excess of the *R*-isomer.

References and Notes

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7) a) D.M.W. Anderson, F. Bell, and J.L. Duncan, *J. Chem. Soc.*, 4705(1961): b) The structure of compound **3** was confirmed on the basis of the following data; mp. 209-210°C, NMR(δ from TMS in CD_2Cl_2)1.78(s, 3H), 3.30(ABq, 2H, J=18Hz, $\delta_{AB}\nu_0$=31Hz, two signals at down-field splitting with J=ca.1Hz), 6.5(broad s, 1H), and 7.2-7.6(m, 10H); mass spectrum m/e 337(M^++1), 336(M^+): c) The head-to-tail adduct may be excluded, see, S. Hayashi, T. Anni, and T. Tamao, *Bull. Chem. Soc. Jap.*, 48, 3318(1975): d) Amine tautomer of **3** can not be observed in NMR spectrum, see M.R.S. Weir and J.B. Hyne, *Can, J. Chem.*, 41, 2905(1963).
8) This property can be suggested by the fact that the reaction of fumaronitrile with BNAH in ethanol gives ethoxysuccinonitrile, Michael-type adduct, in 72% yield together with succinonitrile in 12% yield.
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