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NAD(P)$^+$-NAD(P)H MODEL. 40. EFFECT OF WATER ON THE RATE OF REDUCTION

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Summary: Effect of water on catalytic activity of magnesim ion in the reduction with an NAD(P)H-model has been studied. It is concluded that small amount of water does not affect the catalytic activity.

Since our finding that magnesium ion accelerates the rate of reduction of α-keto esters and certain carbonyl compounds with NAD(P)H-models in dry acetonitrile (*1*,*2*), the role of magnesium ion in the reduction has been studied extensively. We came to the conclusion that magnesium ion assists the transfer of one electron from the model to a substrate and stabilizes the charge-transfer intermediate. Proton and another one-electron transfers take place to complete the reduction (*3*,*8*).

Recently, Powell and Bruice reinvestigated the reduction of N-methylacridinium ion from the view point of kinetic and product isotope effects (*9*). Their conclusion is that N-methylacridane, the reduction product, reduces oxidized-form of the model compound resulting in the scrambling of isotopes. They also presumed that magnesium ion is not involved in the reduction directly.

Discussions in our previous papers (*5*,*6*) mainly based on the variation in kinetic isotope effect and product isotope effect was used only to indicate the upper limit of the kinetic isotope effect. In addition, the reduction of carbonyl compounds are, no doubt, free from the isotopic scrambling. Therefore, Powell and Bruice's observation does not affect our conclusion obtained from the study on isotope effect.

On the other hand, it should be further confirmed whether magnesium ion is directly involved in the reduction or it acts as a drying agent, because it is true that *dry* acetonitrile is contaminated by trace amount of water. Since it is impossible to obtain *absolutely dry* acetonitrile, we studied the effect of *added* water on the rate of reduction of *m*-nitro-α,α,α-trifluoroacetophenone (1), a substrate which is strongly hydrated (*10*), with N-propyl-1,4-dihydronicotinamide (PNAH) in acetonitrile. The results are summarized in Table 1.

Water-content in the reaction mixture in a 1 cm UV-cell was measured on GLC (30% β,β'-oxydipropionitrile, 1 m, 40°C).

Increased amount of water retards the reduction. This is probably due to the hydration onto the substrate (*10*). However, the addition of magnesium ion

(1.9×10^{-2} *M*) accelerates the reaction and the accelerating effect remains the same extent regardless the amount of water at least up to its concentration of 1.09 *M*. The result suggests that magnesium ion *does* act as a catalyst and the catalytic effect is not affected largely by certain extent of hydration, even if it is hydrated.

If the result stemed from the fact that all the added water was absorbed by 1.9×10^{-2} *M* magnesium ion, the rate constant for the system of 1.9×10^{-2} *M* magnesium ion should be as large as or larger than that for the system without both added water and magnesium ion. Further increase in the concentration of magnesium ion (3.8×10^{-2} *M*) results in the increase in the rate, which also supports the idea that not all of added water can be absorbed by magnesium ion of 1.9×10^{-2} *M*. The rate increase accompanied by further increase in the concentration of magnesium ion from 1.9×10^{-2} *M* to 3.8×10^{-2} *M* is larger for the system with 1.09 *M* water than that with 4.2×10^{-2} *M* water. Probably, the result comes from the fact that a part of *hydrated* magnesium ion losts or diminishes its catalytic activity.

Thus, the present result clearly shows that magnesium ion is directly involved in the reaction to accelerate the rate, although catalytic efficiency of hydrated and unhydrated magnesium ions are not clear.

Table 1. Reduction of *m*-Nitro-α,α,α-trifluoroacetophenone in Wet Acetonitrile

10^2[Mg(ClO_4)$_2$], *M*	10k, M^{-1}min^{-1} [a]		
[H_2O], *M*	0	1.9	3.8
0.042[b]	3.59 ± 0.034	7.77 ± 0.051	9.48 ± 0.007
1.09[c]	0.638 ± 0.0010	1.34 ± 0.023	2.21 ± 0.028
2.14[d]	——[e]	——[e]	~0

[a] At 50°C. [Substrate] = 2.5×10^{-2} *M*. [PNAH] = 2.5×10^{-4} *M*. Errors are standard deviations. Rates were corrected for auto-decomposition of PNAH.
[b] 0.075% v/v. The driest solvent available. [c] 2.0% v/v. [d] 4.0% v/v.
[e] Reaction is too slow to be followed.

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