the compounds in accord with the structure. Selected physical and spectral data are as follows. (2R, 3S)-2,3-Isopropylidenedioxy-1-octanol (**3**): ^{1}H-NMR(80 MHz, $CDCl_3$) δ 0.92 (t, 3H), 1.38(s, 3H), 1.48(s, 3H), 1.22-1.59(m, 8H), 3.62(d, 2H), 4.13(m, 2H). IR(neat) 3450, 1045 cm^{-1}, $[\alpha]_D^{21}$ = +30.36° (c = 0.20, $CHCl_3$). TLC, SiO_2, R_f = 0.72 (hexanes/EtOAc 1:1). (2S, 3S)-2,3-Isopropylidenedioxy-1-iodooctane (**4**): ^{1}H-NMR(80 MHz, $CDCl_3$) δ 0.89(t, 3H), 1.18-1.78(m, 14H), 3.26(d, 2H, J = 5 Hz), 3.49-3.80(m, 2H), IR(neat) 1380, 1230, 1045cm^{-1}. TLC, SiO_2, R_f = 0.72 (hexanes/EtOAc 3:1). (S)-1-Octen-3-ol(**5**): ^{1}H-NMR(80 MHz, $CDCl_3$) δ 0.90(t, 3H), 1.09-1.83(m, 8H), 4.36(m, 1H), 5.16(d, 1H, J = 6 Hz), 5.32(d, 1H, J = 12 Hz), 5:82(ddd, 1H, J_1 = 12 Hz, J_2 = 9 Hz, J_3 = 5 Hz). IR(neat) 3450 cm^{-1} $[\alpha]_D^{24}$ = +9.0° (c = 4.0, $CHCl_3$). TLC, SiO_2, R_f = 0.49 (hexanes/EtOAc 3:1). (S)-[(1,1-Dimethyl)ethyldiphenylsilyloxy]-1-octene (**6**): ^{1}H-NMR (100 MHz, $CDCl_3$) δ 0.90(t, 3H), 110-1.50(m, 17H), 4.10(m, 1H), 4.92(d, 1H, J = 6 Hz), 5.05(d, 1H, J = 12 Hz), 5.80(ddd, 1H, J_1 = 12 Hz, J_2 = 9 Hz, J_3 = 5 Hz). $[\alpha]_D^{24}$ = +28.0° (c = 4.0, $CHCl_3$). TLC, SiO_2, R_f = 0.69(hexanes/EtOAc 3:1). (S)-2-[(1,1-Dimethyl)ethyldiphenylsilyloxy]-1-heptanol (**7**): ^{1}H-NMR (100 MHz, $CDCl_3$) δ 0.80(t, 3H), 1.10(s, 9H), 1.20-1.60(m, 8H), 4.00(m, 1H), 7.40(m, 5H), 7.65(m, 5H), 9.60(d, 1H). IR(neat) 2962, 2873, 1715 cm^{-1}. $[\alpha]_D^{25}$ = +6.3° (c = 1.2, benzene). TLC, SiO_2 R_f = 0.59 (hexanes/EtOAc 4:1). (2E)-4-[(1,1-Dimethyl) ethyldiphenylsilyloxy]-2-nonen-1-al (**8**): ^{1}H-NMR(100 MHz, $CDCl_3$) δ 0.82(t, 3H, J = 6.7 Hz), 1.09(s, 9H), 1.30-2.00(m, 8H), 4.00(q, 1H), 6.22(ddd, 1H, J_1 = 15 Hz, J_2 = 7.5 Hz, J_3 = 1.4 Hz), 6.70(dd, 1H, J_1 = 15 Hz, J_2 = 5.0 Hz), 7.33(m, 5H) 7.68(m, 5H), 9.50(d, 1H, J = 8.0 Hz). IR(neat) 3060, 3040, 2960, 2940, 2840, 1675 cm^{-1}, $[\alpha]_D^{25}$ = −19° (c = 0.4, $CHCl_3$). TLC, SiO_2 R_f = 0.50(hexanes/EtOAc 5:1). Methyl-(13S)-[(1,1-dimethyl)ethyldiphenylsilyloxy]-(9Z, 11E)-9,11-octadecadienoate (**9**): ^{1}H-NMR(270 MHz, $CDCl_3$) δ 0.90(t, 3H), 1.00-1.90(m, 18H), 2.02(q, 2H), 2.32(t, 2H), 3.67(s, 3H), 4.18(q, 1H), 5.35 (dt, 1H, J_1 = 8.5 Hz, J_2 = 7.5 Hz), 5.56(dd, 1H, J_1 = 15 Hz, J_2 = 7.5 Hz), 5.87(t, 1H, J = 10 Hz), 6.20(dd, 1H, J_1 = 15 Hz, J_2 = 10 Hz), 7.33(m, 5H), 7.70(m, 5H), IR(neat) 3050, 3020, 1740cm^{-1}. $[\alpha]_D^{25}$ = −16° (c = 0.07, $CHCl_3$). TLC, SiO_2, R_f = 0.50 (hexanes/EtOAc 5:1). Methyl-(13S)-hydroxy-(9Z),(11E)-octadecadienoate(**10**): ^{1}H-NMR(270 MHz, $CDCl_3$) δ 0.90(t, 3H), 1.10-1.50(m, 3H), 1.60-1.90(m, 6H), 2.10(q, 2H, J = 7Hz), 2.42(t, 2H, J = 7Hz), 3.71(s, 3H), 4.20(q, 1H), 5.40(dt, 1H, J_1 = 8.5Hz, J_2 = 7.5Hz), 5.60(dd, 1H, J_1 = 15Hz, J_2 = 7.5Hz), 5.90(t, 1H, J = 10Hz), 6.30(dd, 1H, J_1 = 15Hz, J_2 = 10Hz). IR(neat) 3400, 1735cm^{-1}, $[\alpha]_D^{25}$ = +6.4° (c = 10, $CHCl_3$). TLC, SiO_2, R_f = 0.30(hexanes/EtOAc 5:1).

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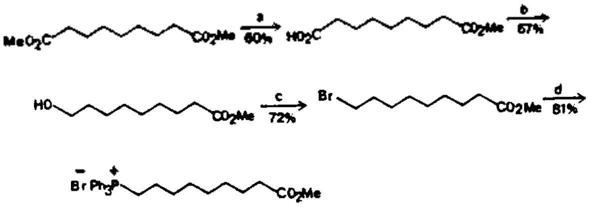
16. 8-Carbomethoxyoctyltriphenylphosphonium bromide was prepared from 1,9-non-anoic acid dimethy ester in four steps as follows.



(a) KOH, EtCH, rt, 4h, (b) $ClCO_2Et$, Et_3N, THF, 0°C, 1h, then $NaBH_4$, MeOH, rt, 2h, (c) PBr_3, ether, pyridine, rt, 12h (d) Ph_3P, CH_3CN, reflux, 48 h.

Solvent Effects on the Reactions of 1-Benzyl-1,4-dihydronicotinamide in Ethanol/Water Mixed Solvent

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1,4-Dihydronicotinamides like 1-benzyl-1,4-dihydronicotinamide (BNAH) have been the subject of intense study as model compounds of coenzyme reduced nicotinamide adenine dinucleotide (NADH).[1] The net change of NADH and NADH model compound in the reduction reaction is the transfer of a hydride (H^-) equivalent from dihydronicotinamide moiety to the substrate. However, the detailed mechanism of the reduction is still much of the controversy whether the reaction is an one-step hydride transfer[2-5] or a three-step electron-proton-electron transfer mechanism.[6-9] For oxidation of NADH model compounds by cupric ion[10] and ferrocenium salts[4], the possibility of the mechanism in which the reactions proceed via complex formation between the reactants was proposed.

The effects of reaction medium on the reaction rate gives information about the reaction mechanism.[11] In biomimetic transformation such as reactions of NADH analogs, the medium effect is particularly important with respect to the reaction environment in biochemical systems. It has been noted that the rates of the reduction of acridinium ions[2,12] and trifluoroacetophenone[13,14] by 1,4-dihydronicotinamides are sensitive to the polarity of medium. In this communication, we wish to report the solvent effects on the acid (HCl)-catalyzed hydration reaction as well as cupric, ferricyanide, and acridinium ion oxidation reactions of BNAH.

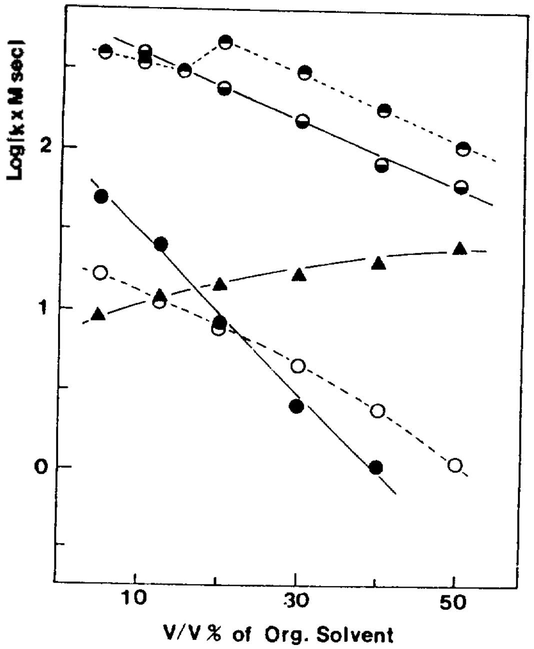
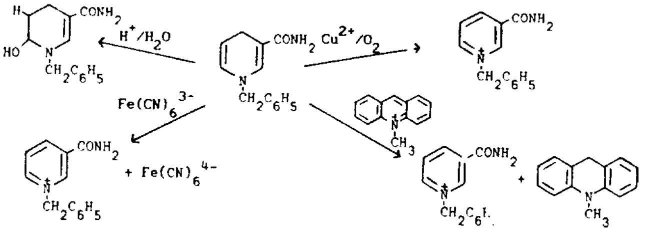


Figure 1. Logarithm of the second-order rate constants for HCl-catalyzed hydration (○), cupric ion oxidation (▲), ferricyanide ion oxidation (●), and N-methylacridinium ion oxidation (◒, ◓) reactions of 1-benzyl-1,4-dihydronicotinamide in ethanol/water and CH_3CN/water mixed solvent as functions of the content (v/v %) of the organic cosolvents. (◒) is taken in CH_3CN/water medium and others were taken in ethanol/water medium.



Since different mechanisms have been proposed for these reactions, it is hoped that the difference in reaction mechanism is revealed in difference in solvent effects on the reaction rate.

The reactions were studied in the appropriate solvent mixtures using the experimental procedures employed in a previous report[15]: for acridinium ion oxidation reaction which was carried out with equimolar mixture of BNAH and N-methylacridinium iodide (MAI), the disappearance of MAI monitored spectroscopically at 415 nm followed second-order kinetics; the other reactions were followed by the disappearance of BNAH at 354 nm and analyzed by pseudo first-order kinetics.[16] Over a wide range of ethanol content (5-50 v/v %) in aqueous ethanol media, the experimental data obeyed the respective kinetic equations properly and the second-order rate constants for the reactions of BNAH were evaluated. In all cases, the rates of reactions are varied sensitively with solvent composition (Figure 1).

The HCl-catalyzed hydration rate constant of BNAH is smaller when the ethanol content in ethanol/water mixed solvent is higher. It is 15-fold smaller in 50% ethanol than in 5% ethanol in water. This agrees fairly well with the report of 11-fold slower reaction rate in 49% ethanol than in strictly aqueous solution.[17] The rate-determining step of the hydration reaction of dihydropyridine derivatives is known to be the initial protonation of the substrates. Lower polarity of medium typically decreases acidity of uncharged acids like HCl,[18] and the rate decrease upon increasing the fraction of ethanol in ethanol/water medium reflects this.

Cupric ion (Cu^{2+}) oxidizes 1,4-dihydronicotinamide and the resulting cuprous ion (Cu^+) is reoxidized by the dissolved dioxygen in the reaction medium.[10] The rate constant for the cupric ion oxidation of BNAH increases with ethanol content in water. The enhancement in the rate constant is 2.7-fold as the ethanol content increases from 5% to 50%. For the reaction, we proposed a concerted two-electron transfer route involving dihydronicotinamide/Cu^{2+} complex.[10] Electric charge is dispersed by the electron-transfer from dihydronicotinamide moiety to Cu^{2+} in the complex. Hence the transition state is less destabilized than the initial state in less polar medium. The observed rate enhancing effect of ethanol for the reaction in aqueous media accords well with Hughes-Ingold rule[19] which predicts dispersion of charge results in faster reaction rate in less polar medium. Alternatively, the effect of ethanol on the rate of the cupric ion oxidation of BNAH in aqueous medium can be interpreted in terms of stability of the BNAH/Cu^{2+} complex. As the content of water is less, the Cu^{2+} is less hydrated and the formation constant for the complex is larger. This may lead to a higher rate of the oxidation reaction of BNAH by Cu^{2+}.

Ferricyanide oxidation rate of BNAH is slower as the reaction medium is richer in ethanol. The reaction exhibits the greatest solvent effect among reactions investigated and the rate is as much as 250-fold slower in 50% ethanol than in 5% ethanol aqueous medium. Based on the inhibitory effect of ferrocyanide for the reaction,[3,9] Bruice *et al.* concluded that the reaction undergoes electron-proton-electron transfer mechanism and general base-catalyzed deprotonation from dihydropyridinium cationic radical intermediate is the rate determining step.[9] Decrease in the concentration of water, which is the general base in the deprotonation step, in ethanol-rich medium can partly explain the solvent effect of this reaction. However the observed solvent effect is too large to be accounted for only by this. A plausible explanation for the drastic solvent effect is shift of the equilibrium of the initial electron-transfer reaction between BNAH and $Fe(CN)_6^{3-}$ to produce the dihydropyridinium cationic radical and $Fe(CN)_6^{4-}$. Obviously, the products are more highly charged than the reactants, and thus the equilibrium concentration of the dihydropyridinium cationic radical is less in less polar medium resulting in slower overall reaction rate.

Except the small variation near 20% ethanol in water, the second-order rate constant for the disappearance of BNAH by MAI decreases as the aqueous medium contains more ethanol. This trend is also observed in CH_3CN/water medium (Figure 1). The parallelism between the reaction rate and solvent polarity agrees with a previous report.[12]

Van Laar *et al.* claimed that the oxidation reaction of BNAH by MAI exhibits a biphasic kinetic behavior and attributed this to the formation of a covalent adduct between the reactants.[2] This was strongly refuted by Bunting *et al.*[20] We also could not observe any evidence for the biphasic behavior, in support of the argument of the latter authors. It is known that BNAH and MAI form charge-transfer complex with the association constant less than 3 M^{-1} in methanol.[20] Under our experimental conditions, [BNAH] = [MAI] = 5.0×10^{-5} M and aqueous ethanol solvent, the concentration of the complex is too small to affect the kinetic measurement: even if the complex is the active reaction intermediate, the second-order kinetics is still valid when the association constant is small.[10]

Retardation of the reaction between BNAH and MAI by the presence of higher fraction of ethanol in the ethanol/water medium is regarded as an indication of a higher degree of charge localization in the rate-determining transition state, as compared to the acridinium ion. This implies virtually full unit positive charge generation on the nicotinamide moiety in the transition state. This is consistent with the conclusion drawn from isotope and substituent effects on the reactions of 1,4-dihydronicotinamide with MAI.[20]

We do not have clear explanation for the biphasic behavior in k_{MAI} vs ethanol content in ethanol/water mixed solvent (Figure 1). However, two possibilities are suggested for this. One is the peculiar composition dependence of the properties of ethanol/water mixture: for example, viscosity of the mixture shows a maximum at water mole fraction of about 0.8.[21] Combination of the viscosity effect with aforementioned polarity effect on the reaction rate may give the kinetic biphasic behavior. Similar to this, it was shown that the effective radius for mutual diffusion of (solvated electron + charged solutes) is minimum at ethanol mole fraction of about 0.1 (27 v/v %).[21] The other possibility is the switching of reaction mechanism from electron-proton-electron transfer to hydride transfer, suggested for the reaction in CH_3CN/water mixed solvent.[20] If the second explanation is held, our results in CH_3CN/water mixed solvent, which show monotonic decrease of k_{MAI} with the content of CH_3CN, do not give any evidence for the change in the mechanism of the reaction over the experimental range of the solvent composition of the mixed solvent.

In conclusion, it has been shown that the reactions of BNAH exhibit the drastic solvent effects in ethanol/water mixed solvent. The results are interpreted in the framework of the existing mechanisms of the reactions. Further studies on a variety of NADH analogs and solvent effects on the chemistry of NADH analogs which is relevant to the mechanisms are currently underway.

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Regeneration of Carbonyl Compounds from Oximes and Hydrazones *Via* an Exchange Reaction Using 1,1,1-trifluoro-2,4-pentanedione[1]

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Derivatives of carbonyl compounds such as oximes and hydrazones have been used in the purification and characterization of aldehydes and ketones, and also employed as important intermediates[2] in organic synthesis, particularly in C-C bond forming reactions. Most of the known methods of