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Mechanistic Difference in Photoreduction of Phenacyl Halides by NADH Model Compounds

Shunichi FUKUZUMI,* Seiji MOCHIZUKI, and Toshio TANAKA
Department of Applied Chemistry, Faculty of Engineering,
Osaka University, Suita, Osaka 565

Photoreduction of phenacyl halides by an NADH model compound, 10-methylacridan ($AcrH_2$), in MeCN proceeds via photoinduced electron transfer from the singlet excited state of $AcrH_2$ to phenacyl halides without the contribution of radical chain reactions, while the photoreduction by another NADH model compound, 1-benzyl-1,4-dihydronicotinamide (BNAH), proceeds via photoinduced radical chain reactions. The origin of the mechanistic difference between $AcrH_2$ and BNAH has been discussed.

Photochemistry of reduced nicotinamide adenine dinucleotide (NADH) and NADH model compounds has recently attracted increasing interest since the excited states of NADH and NADH model compounds, being much stronger reductants than the ground states, can reduce a variety of substrates.1) Photoreduction of substrates by NADH model compounds has been reported to proceed via either photoinduced radical chain reactions2) or direct photoreduction without the contribution of radical chain reactions.3) Such a mechanistic difference would be difficult to understand without a systematic comparison of different mechanisms under the comparable conditions. We wish to report herein that photoreduction of phenacyl halides by two different types of NADH model compounds [10-methylacridan ($AcrH_2$) and 1-benzyl-1,4-dihydronicotinamide (BNAH)] proceeds via different mechanistic pathways, providing nice opportunity to understand the origin of the mechanistic difference.

Irradiation of a deaerated acetonitrile (MeCN) solution containing $AcrH_2$ and phenacyl halide ($PhCOCH_2X$: X = Br, Cl) with monochromatized light of λ 320 nm4) results in the conversion of $AcrH_2$ and $PhCOCH_2X$ into $AcrH^+X^-$ and $PhCOCH_3$, respectively (Eq. 1) as shown in Table 1. When $AcrH_2$ is replaced by the 9,9'-

$$AcrH_2 + PhCOCH_2X \xrightarrow{h\nu} AcrH^+ + X^- + PhCOCH_3 \qquad (1)$$

dideuterated analogue ($AcrD_2$) in thoroughly dried MeCN, phenacyl bromide is converted to monodeuterated acetophenone ($PhCOCH_2D$). However, no deuterium has been incorporated into acetophenone when H_2O (0.10 mol dm^{-3}) was added to the $AcrD_2$-phenacyl bromide system (Table 1). The use of 10-methyl-d_3-acridan ($AcrH_2$-CD_3) instead of $AcrD_2$ results in no incorpolation of deuterium into acetophenone, either (Table 1). Thus, the photoreduction of phenacyl halides by $AcrH_2$ involves the transfer of a hydrogen from the 9-methylene position of $AcrH_2$ to phenacyl

Table 1. Photoreduction of Phenacyl Halides by NADH Model Compounds in Acetonitrile[a]

NADH model compound[b]	Phenacyl halide[c]	Time / h	Product yield / %[d]	
$AcrH_2$	$PhCOCH_2Br$	20	$AcrH^+$ (86)	$PhCOCH_3$ (84)
$AcrH_2$	$PhCOCH_2Cl$	29	$AcrH^+$ (86)	$PhCOCH_3$ (86)
$AcrD_2$	$PhCOCH_2Br$	15	$AcrD^+$ (60)	$PhCOCH_2D$ (60)
$AcrD_2$[e]	$PhCOCH_2Br$	12	$AcrD^+$ (53)	$PhCOCH_3$ (53)
$AcrH_2$-CD_3	$PhCOCH_2Cl$	15	$AcrD^+$ (61)	$PhCOCH_3$ (60)
BNAH[f]	$PhCOCH_2Br$	0.5	BNA^+ (50)	$PhCOCH_3$ (47)

[a] The irradiation wavelength is 320 nm unless otherwise noted. [b] 0.10 mol dm^{-3}. [c] 0.30 mol dm^{-3}. [d] Determined by ^1H NMR. [e] In the presence of H_2O (0.10 mol dm^{-3}). [f] The irradiation wavelength is > 360 nm.

halides.[5] The transferred hydrogen can be readily exchanged with H_2O.

The quantum yields for photoreduction of phenacyl halides by $AcrH_2$ and $AcrD_2$ were determined under irradiation of light (λ = 320 or 340 nm),[4] using ferrioxalate actinometry.[6] The quantum yields are constant with change of the $AcrH_2$ concentration as shown in Fig. 1. On the other hand, the quantum yield increased with an increase in the phenacyl halide concentration to approach a limiting value (Φ_∞) in the high concentrations as given by Eq. 2. The quantum yields of $AcrD_2$

$$\Phi^{-1} = \Phi_\infty^{-1}[1 + (K_{obs}[PhCOCH_2X])^{-1}] \qquad (2)$$

were essentially the same as those of $AcrH_2$ and thus no kinetic isotope effect has been observed. The K_{obs} values of phenacyl bromide and phenacyl chloride were determined as 4.4 x 10^2 and 3.3 x 10^2 dm^3 mol^{-1}, respectively from the slopes and intercepts of the linear plots of Φ^{-1} vs. $[PhCOCH_2X]^{-1}$ according to Eq. 2. The K_{obs} values agree well with those obtained from fluorescence quenching of $AcrH_2$ by electron transfer from $^1AcrH_2^*$ to phenacyl bromide and phenacyl chloride (4.2 x 10^2 and 3.2 x 10^2 dm^3 mol^{-1}, respectively).

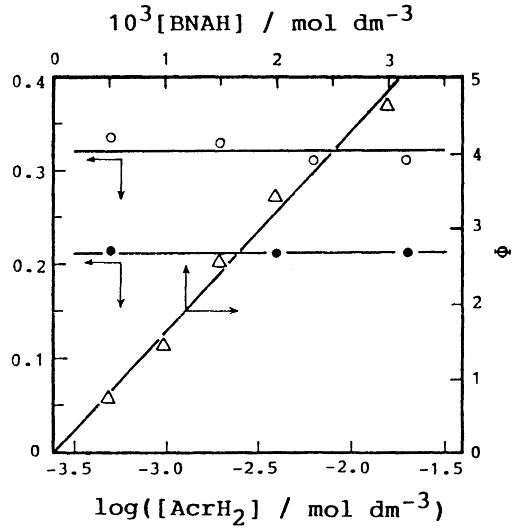
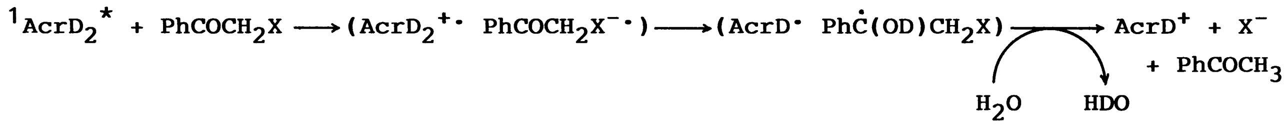


Fig. 1. Dependence of the quantum yields (Φ) on the $AcrH_2$ concentration for photoreduction of $PhCOCH_2Br$ (○) and $PhCOCH_2Cl$ (●) by $AcrH_2$ in MeCN under irradiation of light (λ 340 nm); $[PhCOCH_2X]$ = 1.0 x 10^{-3} mol dm^{-3}, and on the BNAH concentration for photoreduction of $PhCOCH_2Br$ by BNAH (△) in MeCN under irradiation of light (λ 370 nm); $[PhCOCH_2Br]$ = 5.0 x 10^{-2} mol dm^{-3}.

Based on the above results, the mechanism of the photoreduction of phenacyl halides by $AcrH_2$ may be given by Scheme 1, where photoinduced electron transfer



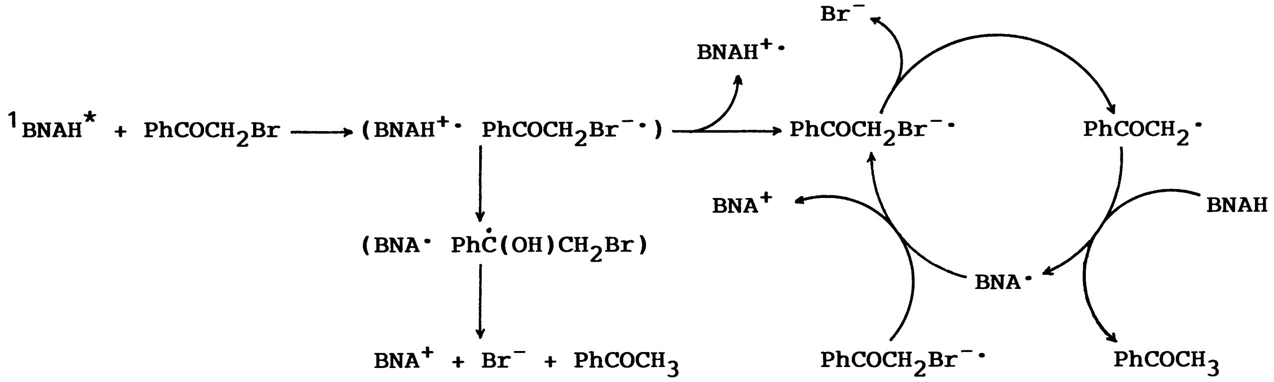
Scheme 1.

from $^1AcrH_2^*$ to $PhCOCH_2X$ occurs to give a radical ion pair ($AcrH_2^{+\cdot}$ $PhCOCH_2X^{-\cdot}$) which may disappear by fast proton transfer from $AcrH_2^{+\cdot}$ to $PhCOCH_2X^{-\cdot}$ to yield $AcrH^{\cdot}$ and $Ph\dot{C}(OH)CH_2X$, accompanied by the exchange of proton with water. This may be the reason why no deuterium has been incorporated into acetophenone in the presence of water (Table 1). The subsequent facile electron transfer from $AcrH^{\cdot}$ to $Ph\dot{C}(OH)CH_2X$, accompanied with dehalogenation, yields the final products, $AcrH^+$ and $PhCOCH_3$. No kinetic isotope effect has been observed since the photoinduced electron transfer from $^1AcrH_2^*$ to phenacyl halides may be the rate-determining step.

Another NADH model compound, BNAH, can also reduce phenacyl bromide under irradiation of visible light of $\lambda > 360$ nm in dry MeCN to yield BNA^+ and acetophenone (Table 1, Eq. 2).$^{6)}$ In contrast with the case of $AcrH_2$, the quantum yield

$$BNAH + PhCOCH_2Br \xrightarrow{h\nu} BNA^+ + Br^- + PhCOCH_3 \qquad (2)$$

of BNAH increases linearly with increasing the BNAH concentration to exceed unity (Fig. 1). When BNAH was replaced by the 4-monodeuterated analogue (BNAH-4-d_1), the quantum yield became 1.6-fold smaller. From the ratio of the quantum yields of BNAH to BNAH-4-d_1 is obtained the kinetic isotope effect $\Phi_H/\Phi_D = 4.0 \pm 0.6$.$^{7)}$ The large quantum yields exceeding unity, combined with the kinetic isotope effect indicate that the photoreduction of phenacyl bromide by BNAH proceeds by photoinduced radical chain mechanism as shown in Scheme 2. In the initiation step,



Scheme 2.

electron transfer from $^1BNAH^*$ to phenacyl bromide occurs with the diffusion rate constant.$^{8)}$ The proton transfer from $BNAH^{+\cdot}$ to $PhCOCH_2Br^{-\cdot}$ may follow the photoinduced electron transfer as the case of $AcrH_2$. However, the proton transfer step from $BNAH^{+\cdot}$ may be slower than that from $AcrH_2^{+\cdot}$ since the pK value of $BNAH^{+\cdot}$ (3.6)$^{9)}$ is larger than that of $AcrH_2^{+\cdot}$ (2.0).$^{9)}$ In such a case, the fission of carbon-halogen bond of $PhCOCH_2Br^{-\cdot}$ caused by an intramolecular electron transfer form the carbonyl oxygen to Br of $PhCOCH_2Br^{-\cdot}$ may compete well with the proton transfer, resulting in the formation of the carbon center radical, $PhCOCH_2^{\cdot}$. The

$PhCOCH_2\cdot$ radical may abstract a hydrogen atom from BNAH to yield $PhCOCH_3$ and $BNA\cdot$ This step may be the rate-determining step and responsible for the linear dependence of Φ on the BNAH concentration as well as the observation of the kinetic isotope effect ($\Phi_H/\Phi_D = 4.0$). Since $BNA\cdot$ is known to be a much stronger one-electron reductant than $AcrH\cdot$,[9] electron transfer from $BNA\cdot$ to $PhCOCH_2Br$ may occur to yield BNA^+, accompanied by regeneration of $PhCOCH_2Br^{-\cdot}$ (Scheme 2).

The mechanistic difference between the NADH model compounds, $AcrH_2$ and BNAH, may be ascribed to the difference in pK of the corresponding radical cations between $AcrH_2^{+\cdot}$ and $BNAH^{+\cdot}$ and also the difference in the one-electron oxidation potentials (E^0_{ox}) between $AcrH\cdot$ and $BNA\cdot$. The smaller pK value of $AcrH_2^{+\cdot}$ than $BNAH^{+\cdot}$ will suppress the formation of free radicals $PhCOCH_2\cdot$, which initiate the chain reactions, by the facile proton transfer from $AcrH_2^{+\cdot}$ to $PhCOCH_2X^{-\cdot}$ and the more positive E^0_{ox} value of $AcrH\cdot$ (0.43 V)[9] than $BNA\cdot$ (-1.1 V)[9] will make it difficult for $AcrH\cdot$, escaped from the cage, to reduce phenacyl halides, which is the essential process to constitute the radical chain reactions (Scheme 2).

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4) The longer irradiation wavelength than λ_{max} of $AcrH_2$ (285 nm) has been chosen in order to avoid the excitation of the absorption band due to $PhCOCH_2X$.

5) The photoreduction of benzophenone by $AcrH_2$ has been reported to occur via electron transfer from $AcrH_2$ to the triplet excited state of benzophenone, followed by proton transfer from 10-methyl position rather than the 9-methylene position of $AcrH_2^{+\cdot}$ to the radical anion of benzophenone; see: L. E. Manring and K. S. Peters, J. Am. Chem. Soc., 107, 6452 (1985).

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7) The Φ_H/Φ_D value is obtained by the relation, $\Phi_H/\Phi_D = [2\Phi(BNAH\text{-}d_1)/\Phi(BNAH) - 1]^{-1}$ in which the secondary kinetic isotope effect is assumed to be unity.

8) The rate constant of electron transfer from $^1BNAH^*$ to $PhCOCH_2Br$ was determined as 2×10^{10} $dm^3\ mol^{-1}\ s^{-1}$ from the fluorescence quenching of $^1BNAH^*$ (τ 1.7 ns) by $PhCOCH_2Br$.

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