Luminescence, Charge-Transfer Complexes, and Photoredox Processes Involving *N*-Alkylnicotinamide/Dihydronicotinamide Surfactants

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Abstract: Various aspects of photophysics, charge-transfer complexes, and photoredox processes involving various *N*-alkylnicotinamide surfactants, RNA^+X^- (R = C_4, C_8, C_{10}, C_{12}, C_{14}, and C_{16}; X = Cl, Br, and I), and their 1,4-dihydro derivatives, RNAH, have been investigated in solution at room temperature. In nonpolar solvents, iodide salts (RNA^+I^-) show typical charge-transfer (CT) bands. The solvent sensitivity of spectral shifts, though significant, is much less pronounced as compared to that of the popular probe "4-carbomethoxypyridinium iodide". The absorption and emission properties of dihydronicotinamides (very similar to those of NADH) are very sensitive to the nature of the solvent. The order of solvent effects is typical of Kosower's *Z* scale or Dimroth's $E_T(30)$ scale and the solvent effects are interpreted as due to H-bonding effects. The dihydronicotinamide derivatives readily form CT complexes with various pyridinium salts (e.g., their own oxidized form, alkylpyridinium halides, simple and surfactant viologen salts). Photoreduction of viologens and two zinc porphyrins using RNAH as donor has been investigated. Finally, sensitized photoreduction of the alkylnicotinamide surfactants to their dihydro derivative using polypyridyl complexes of Rh(III) and Ru(II) is also demonstrated and application of this class of surfactants in biphasic systems is indicated.

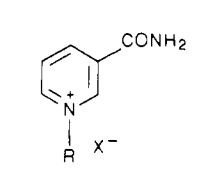
Nicotinamide adenine dinucleotide (NAD^+) is an important cofactor taking part in numerous cellular processes, particularly in the intermediary metabolism and in energy-conversion reactions (e.g., electron transport and oxidative phosphorylation).[1,2] Also there is growing interest among bioorganic chemists to use NADH in enzyme-mediated asymmetric synthesis. Hence various aspects of its chemistry and biochemical mode of action have been subject to detailed scrutiny. Topics under investigation include, for example, the role of the individual chemical fragments (nicotinamide, adenine, and the phosphoribose unit), the mode of reduction (chemical and enzymatic), the structure, the activity of the reduction product, NADH, and the quantitative cycling between the oxidized and reduced forms with the intermediary of enzymes or appropriate catalysts. It has been firmly established that the nicotinamide moiety is the portion that undergoes the reversible redox reactions during the numerous processes involving NAD^+ or $NADP^+$:

$$NAD^+ + H^+ + 2e^- \rightarrow NADH \qquad (1)$$

$$E_0' = (-0.105 - 0.03\ pH),\ vs\ NHE$$

During the reduction of NAD^+ to NADH, a hydride ion (H^-) is transferred from the substrate molecule to the 4-position of the nicotinamide, ultimately leading to the formation of the 1,4-dihydro reduction product. The hydrogen transfer is direct, often stereospecific, and does not involve free protons. Rh(III) complexes containing porphyrin or polypyridyl ligands have been found to be useful catalysts to mediate the reduction of NAD^+ to NADH.[3] The reduced form, NADH, being a good electron donor readily forms charge-transfer complexes with numerous electron acceptors[4] and also takes part in photoredox reactions.[5] NADH has a characteristic luminescence and this has been used to monitor reduction/oxidation processes involving NAD^+ in vivo.[6]

In this study we have attempted to make a systematic investigation of some of the above-cited basic chemistry associated with the nicotinamide chromophore, using a series of surfactant nicotinamides **1** (nicotinamide derivatives in which the pyridinium N is quaternized with long-chain alkyl halides, RNA^+X^- (1-alkyl-3-carbamoylpyridinium halides)) as model compounds. Such modified nicotinamide derivatives enable basic studies on the crucial chromophore to be carried out under a variety of conditions: oxidized/reduced forms as monomers in homogeneous solvents or solubilized in micellar assemblies or as their own micellar aggregates in aqueous media. As has been shown for numerous other molecules, incorporation in a micellar aggregate provides additional control on solute distribution and can enhance efficiencies of photoredox processes and in the formation of charge-transfer complexes.[7] In this context, surfactant viologen derivatives developed earlier[8] represent an important class of



N-alkylnicotinamide (RNA^+X^-)
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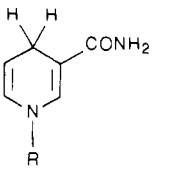

N-alkyl-1,4-dihydronicotinamide (RNAH)
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acceptor molecules with a wide variety of applications. With large differences in the solubility that can arise upon reduction of cationic nicotinamide surfactant (RNA^+X^-) to neutral forms (RNAH), there exists an intriguing possibility of selective extraction of reduced forms in biphasic systems (reduction in the aqueous phase followed by extraction into the organic phase).

Though the synthesis of *N*-alkylnicotinamide has been known for quite sometime,[9] except for some scattered studies, to our knowledge, there has not been any systematic study on this important class of model compounds. In this paper we report on our observations on the following aspects of the chemistry of nicotinamide surfactants: absorption spectral features and solubility of RNA^+X^- in aqueous and nonaqueous media, characterization of the luminescence of the surfactants in the reduced form (RNAH) in various solvents and micellar media, charge-transfer complexes of the surfactants between their oxidized/reduced form and with various pyridinium (alkylpyridinium salts), and bipyridinium (viologen) salts, photoredox reactions involving RNAH as donors, and sensitized photoreduction using rhodium(III) polypyridyls and ruthenium(II) polypyridyl complexes in biphasic systems. Data on the micellar properties of *N*-alkylnicotinamide surfactants (critical micelle concentration and Kraft point temperature) are reported elsewhere.[10]

Experimental Section

Materials. ***N*-Alkylnicotinamide surfactants 1** were synthesized by the reaction of nicotinamide with a series of 1-alkyl halides in solvents such as xylene or DMF (heating under reflux) as described in the literature.[9,11] The product is often insoluble and precipitated during the reflux, which lasted 4–8 h. The solution is cooled, and the precipitate is filtered and washed three times with acetone (only the reactants are soluble in acetone). The product is finally recrystallized from ethanol. C_4, C_8, and C_{10} derivatives were obtained in the form of a shiny, white powder. C_{12}, C_{14}, and C_{16} products appeared slightly brownish and were recrystallized from water to obtain shiny, white powders. The melting point data (°C) for the *N*-alkylnicotinamides are in good agreement with literature values: C_4-Br (170–171); C_8-Br (221–222); C_{10}-Br (223–224), C_{12}-Br (229–230), C_{16}-Br (227); C_{12}-Cl (240–241), C_{16}-Cl (244–245).

***N*-Alkyl-1,4-dihydronicotinamides 2** were obtained by chemical reduction using sodium dithionite as a reductant, following procedures described in the literature.[9,11] In a typical preparation, 4.7 mmol of 1-alkylnicotinamide surfactant is mixed with 4.3 g of sodium bicarbonate in 30 mL of water. Sodium dithionite (3.6 g) was then slowly added in small portions to a well-stirred solution. The solution was kept stirred for 1 h under nitrogen bubbling, during which the dihydronicotinamide product (oily, yellowish) slowly separates out. The product is extracted with several 20-mL portions of $CHCl_3$ and dried with magnesium sulfate. Long-chain *N*-alkyldihydronicotinamides were obtained as yellow powders/needles (C_4 derivative remains a viscous solid). The dihydronicotinamides slowly darken and become sticky in the air at room temperature and are kept cold (freezer) and in the dark. Several chemical/structural studies[11,12] have established unambiguously the reduction product as the 1,4 isomer **2**. In chloroform solutions, *N*-alkyl-1,4-dihydronicotinamides show absorption maximum at 353 nm ($\epsilon \approx 7000\ M^{-1}\ cm^{-1}$) and a broad minimum centered at 284 nm ($\epsilon \approx 600\ M^{-1}\ cm^{-1}$), in good agreement with literature values.

The surfactants SDS (sodium dodecyl sulfate) (Fluka), CTAC (cetyltrimethylammonium bromide) (Kodak), RPy^+Cl^- (*N*-alkylpyridinium chlorides) (Kodak) were p.a. grade chemicals and were used as supplied or after a single recrystallization. $[Rh(bpy)_3]Cl_3$, $[Rh(bpy)_2Cl_2]Cl$, $C_{14}Me\text{-}V^{2+}$, $ZnTMPyP(4)^{4+}$ ((tetrakis(*N*-methyl-4-pyridyl)-porphyrinato)zinc), and $ZnTPPS(4)^{4-}$ ((tetrakis(4-sulfonatophenyl)-porphyrinato)zinc) were all available from our earlier work.[13] $[Ru(bpy)_3]Cl_2$ (Strem) and methyl viologen (Fluka) were commercial samples.

Methods. UV–visible *absorption spectra* were recorded on a Cary 200 spectrophotometer. The *fluorescence spectra* were recorded on a Hitachi Perkin-Elmer spectrofluorimeter. Quantum yields of emission from various dihydronicotinamides were determined relative to quinine sulfate in 1 N H_2SO_4 ($\phi = 0.55$). *Emission lifetimes* were measured on a single photon-counting apparatus using a filtered H_2/N_2 lamp as the excitation source.

Steady state photolysis experiments were carried out on a 450-W Xe-arc lamp fitted with water and the appropriate glass cutoff filters. Solutions in 1-cm quartz cells were thoroughly degassed for at least 15 min with Ar or N_2 prior to irradiation. *Laser flash photolysis* studies were carried out with the 353- or 530-nm laser pulses (pulse width ca. 12 ns) from a Q-switched Nd YAG laser.

Photoreduction of RNA^+X^- to RNAH. Procedure I (Using Rhodium(III) Polypyridyl and TEOA Alone). Photolyses were carried out on 5 mL of an aqueous solution (pH adjusted to 8.0 or with a 0.05 M phosphate buffer) that contained 3.0×10^{-4} M $Rh(bpy)_3Cl_3$ (or equivalently $Rh(bpy)_2Cl_3$) as the sensitizer, 0.03 M triethanolamine (TEOA) as the electron donor, and 5.0×10^{-3} M *N*-dodecylnicotinamide surfactant ($C_{12}NA + Cl^-$). The deaerated mixture was illuminated under continuous stirring on a 450-nm Xe-arc lamp (light filtered through a 10-cm water filter and 300-nm Corning glass cutoff filters). After various irradiation times (a few hours), 5 mL of $CHCl_3$ was added and the solution was well shaken. The organic layer was then separated and repeatedly washed with aqueous solution (pH 8.0) to remove coextracted RNA^+Cl^- (at least three times, each time with 10 mL). The formation of RNAH was followed by its characteristic absorption and emission spectral features. A turnover number with respect to the Rh(III) complex of ≥5 is readily obtained after an irradiation of about 3 h. Examination of the absorption spectra of the photolysis solution after prolonged photolysis showed conversion of $[Rh(bpy)_3]Cl_3$ (or equivalently $[Rh(bpy)_2Cl_2]Cl$) to its diaquo form, $[Rh(bpy)_2(H_2O)_2]Cl$. (Absorption spectral details in H_2O: $[Rh(bpy)_2Cl_2]Cl$, 311 nm ($\epsilon = 2.32 \times 10^4\ M^{-1}\ s^{-1}$), 252 nm ($\epsilon = 1.90 \times 10^4\ M^{-1}\ s^{-1}$); $[Rh(bpy)_3]Cl_3$, 320 nm ($\epsilon = 4.25 \times 10^4\ M^{-1}\ s^{-1}$), 306 nm ($\epsilon = 3.93 \times 10^4\ M^{-1}\ s^{-1}$); and $[Rh(bpy)_2(H_2O)_2]Cl$, pH 11, 311 nm ($\epsilon = 2.87 \times 10^4\ M^{-1}\ s^{-1}$), 301 nm ($\epsilon = 2.54 \times 10^4\ M^{-1}\ s^{-1}$).) Control photolysis experiments on solutions that did not contain either the Rh(III) complex or the amine donor did not result in the reduction of RNA^+ to RNAH. The photolysis mixture and the $CHCl_3$ extract were found to be very sensitive to the nature of the buffer used. Most of our experiments were carried out with aqueous solutions adjusted to the required pH or with phosphate buffer. Significant spectral changes of the reaction mixture were observed *in the dark* with tris salts as buffer, and hence tris buffers are to be avoided.

Procedure II (Using Rhodium(III) Polypyridyl, $Ru(bpy)_3^{2+}$, and TEOA). Experiments were carried out on similar lines to that described above, but the photolysis solutions were irradiated with visible light ($\lambda \geq 400$ nm).

Results and Discussion

In order to obtain a comprehensive picture on the chemistry and utility of various *N*-alkylnicotinamide and *N*-alkyldihydronicotinamide surfactants, their properties have been determined on various domains. Studies on the oxidized/reduced forms of the surfactants are presented first followed by studies on the charge-transfer complexes formed in their solution mixtures, on sensitized photoreduction using rhodium(III) and ruthenium(II) polypyridyl complexes, and finally on their potential applications in biphasic systems.

I. Ground State Absorption Spectral Features and Solvent Sensitivity of *N*-Alkylnicotinamide Surfactants. An important feature of the *N*-alkyl surfactants is their ability to form micellar aggregates in aqueous solution. Elsewhere we have reported data on the micellar properties (critical micellar concentration, temperature).[10] It is worth pointing out here that the critical micellar temperatures of these surfactants are significantly higher (by 25 °C) as compared to that of the corresponding simple *N*-alkylpyridinium surfactants, though the critical micellar concentrations are very similar.

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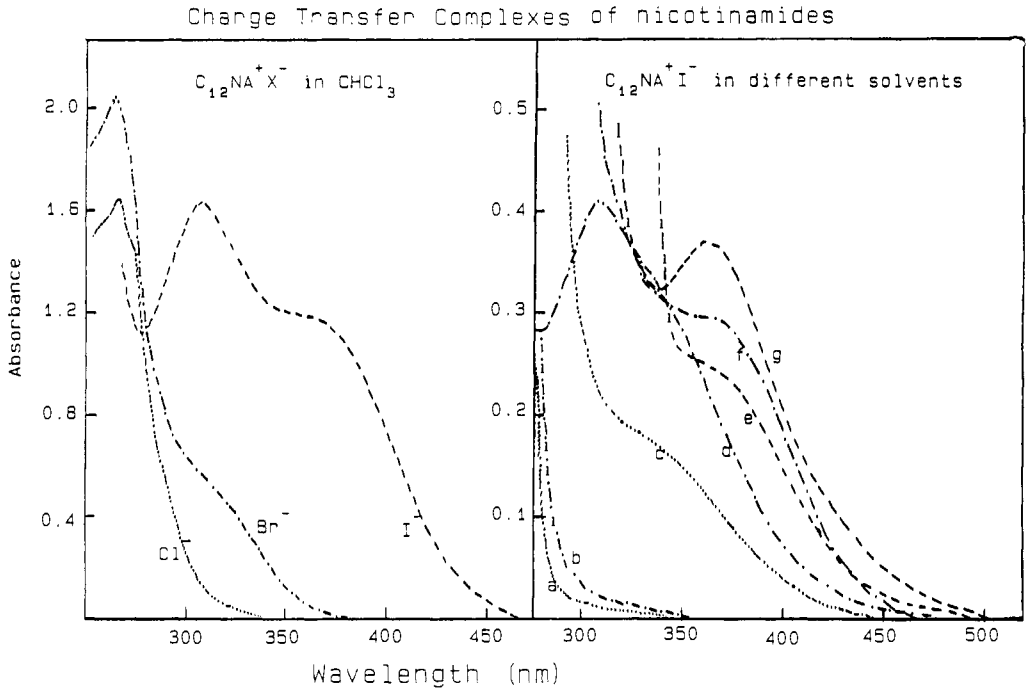

Figure 1. Absorption spectral features of charge-transfer complexes of *N*-alkylnicotinium halide surfactants in solution: left, absorption spectra of $C_{12}NA^+Cl^-$ in $CHCl_3$; right, absorption spectra of $C_{12}NA^+I^-$ in various solvents such as (a) H_2O, (b) CH_3OH, (c) *i*-PrOH, (d) *n*-BuOH, (e) CH_3COCH_3, (f) $CHCl_3$, and (g) THF.

The absorption spectra of *N*-alkylnicotinamide surfactants in aqueous solution are characterized by an absorption maximum located around 265 nm with ϵ values in the range of 4.0×10^3 M^{-1} cm^{-1}. Table I presents a summary of the absorption maxima along with the ϵ values for various nicotinamide surfactants. For comparison, the table also includes corresponding data on NAD^+, $NADP^+$, nicotinamide, and alkylpyridinium chlorides in water. The absorption maximum of *N*-alkylnicotinamide surfactants are red-shifted by ca. 5 nm with respect to those of alkylpyridinium chlorides. Incorporation of RNA^+Br^- into ionic micelles such as CTAB causes a further red-shift of ca. 6 nm. In NAD^+ and $NADP^+$, the chromophore largely responsible for the absorption in the 250–280-nm region is adenine and not nicotinamide.

The chloride salts of *N*-alkylnicotinamides are rather insensitive to changes in the solvent polarity, being present as fully ionized species in solution. Iodide salts and to a lesser extent the bromide salts are sensitive to polarity. As has been shown earlier by Kosower et al. for the simple alkylpyridinium salts,[14] in nonpolar solvents, the absorption spectra of nicotinamide halide salts show new broad absorption features corresponding to the formation of *charge-transfer (CT) complexes* in the ground state:

$$R\text{–}Pyr\text{–}I \rightarrow R\text{–}Pyr^{\delta+}\text{–}I^{\delta-} \qquad (2)$$

Figure 1 presents a series of absorption spectra showing the influence of a halide counterion on the charge-transfer absorption of C_{12}-nicotinamide surfactant salts in chloroform (left) and, for the iodide salts, the influence of various solvents (right). In solvents such as chloroform, tetrahydrofuran, or acetone, the charge transfer absorption band has a broad maximum centered around 360 nm. With solvents of increasing *Z* value[14] (increasingly polar), the CT absorption blue-shifts and decreases in intensity. Studies with various nicotinamide surfactants of increasing chain length (C_4–C_{16}) showed that the charge-transfer bands are independent of the surfactant chain length.

In general the behavior of CT bands of nicotinamide surfactants are very similar to that of the widely studied 4-carbomethoxypyridinium iodide, though the extent of spectral shifts are much smaller with nicotinamide halide surfactants (for example, the CT band is located at 342, 375, 417, and 449 nm in CH_3OH, 2-PrOH, DMF, and $CHCl_3$, respectively). It may be recalled that Kosower et al.[14] have proposed the practical utility of the large solvent-dependent spectral shifts in *N*-alkylpyridinium iodides as potential probes of solvent polarity. Ray and Mukerjee[15] in fact have used such absorption spectral shifts of dodecylpyridinium iodide in micellar media to deduce approximate polarity of micellar interface region and even for the measurement of cmc.

Table I. Absorption Spectral Data on 1-Alkylnicotinamide Surfactants and Related Compounds in Solution

surfactant	abs in water: λ_{max}, nm (ϵ, $\times 10^3$ M^{-1} cm^{-1})	abs in ethanol: λ_{max}, nm (ϵ, $\times 10^3$ M^{-1} cm^{-1})
	Nicotinamide Surfactants	
$C_4NA^+Br^-$	265 (3.77) (pH 3.0)	265? (4.35)
$C_4NA^+Br^-$	265 (3.83) (pH 7.0)	
$C_4NA^+Br^-$	265 (3.82) (pH 11.0)	
$C_8NA^+Br^-$	265 (3.05)	266 (4.20)
$C_{10}NA^+Br^-$	266 (4.07)	266 (4.35)
$C_{12}NA^+Cl^-$	266 (4.07)	266 (4.20)
$C_{12}NA^+Cl^-$	265 (4.68)	266 (4.91)
$C_{16}NA^+Cl^-$	266 (3.66)	266 (4.91)
$C_{16}NA^+Cl^-$	266 (4.70)	266 (3.94)
	Reference Compounds	
nicotinamide	264 (2.67) (pH 3.0)	
nicotinamide	263 (2.50) (pH 11.0)	
$BzNA^+Br^-$		264 (4.27)
β-NAD^+	260 (17.6) (pH 7.0)	
β-$NADP^+$	260 (18.0) (pH 7.0)	
$C_{12}Pyr^+Cl^-$	260 (4.07)	260 (4.41)
$C_{16}Pyr^+Cl^-$	260 (4.23)	260 (4.27)

II. Photophysics of *N*-Alkyldihydronicotinamides and of NADH. Dihydro derivatives (1,4 isomers) of *N*-alkylnicotinamide surfactants are readily prepared via chemical reduction with sodium dithionite under alkaline conditions, following the procedure initially proposed by Karrer et al. in the thirties:[9] *N*-alkyldihydronicotinamides are obtained as yellow solids. Unless kept in the dark and the cold, the dihydronicotinamides slowly darken and become waxy. Only the C_4 derivative was found to be moderately soluble in water (solubility ca. 10^{-3} M). All the dihydronicotinamide surfactants are soluble in various organic

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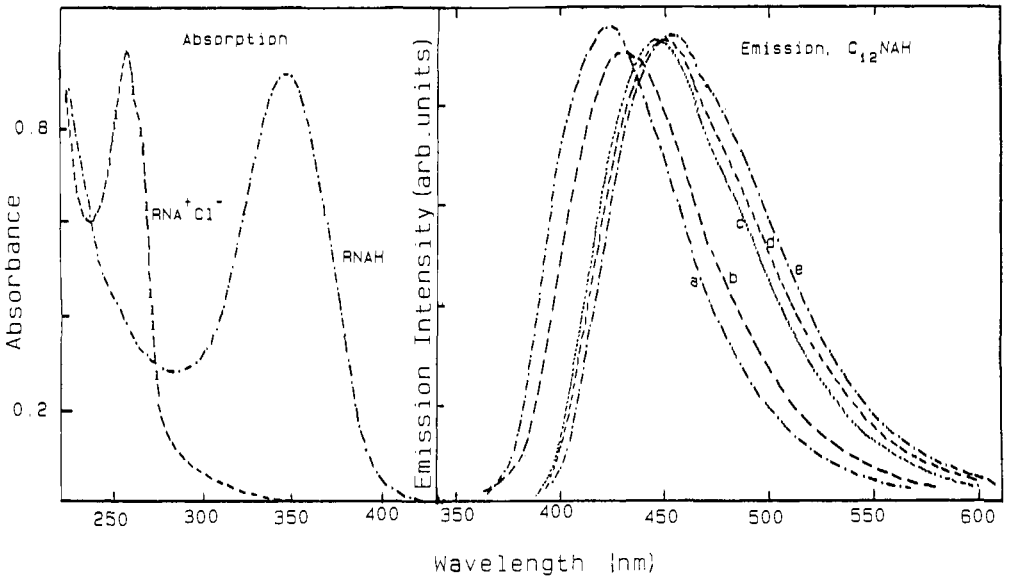

Figure 2. Absorption/emission spectra of RNA^+Cl^- and RNAH in various solvents: left, absorption spectra of $C_4NA^+Cl^-$ and C_4NAH in water; right, emission spectra of $C_{12}NAH$ in (a) ethyl acetate, (b) dioxane, (c) EtOH, (d) CH_3OH, and (e) $CH_3OH:H_2O$ (2:1, v/v).

solvents though the long-term stability of such solutions was very limited.

In solution the 1,4-dihydronicotinamides are characterized by an absorption spectrum with a maximum around 340–360 nm. (e.g., ϵ_{355} for C_4NAH = 7000 M^{-1} cm^{-1}). In aqueous or nonaqueous solutions, dihydronicotinamide surfactants show room-temperature emission (fluorescence) similar to that observed with NADH. The distinct absorption/emission properties of the 1,4-dihydronicotinamide derivatives have been used extensively in biochemical studies of NADH to monitor the interconversions "in vivo" and in the formation of enzyme–cofactor complexes.[16] In spite of their importance, there have been only a few spectroscopic, photophysical studies devoted to the characterization of the absorption and emission.[17]

In aqueous solution, the stability of *N*-alkyldihydronicotinamides is restricted to neutral or alkaline solutions. In acid solutions, rapid protonation causes irreversible secondary reactions. (The process is characterized by loss of the absorption at 340 nm and the fluorescence emission. A product with an absorption maximum around 290 nm is formed. This "primary acid-modification compound", identified as the 6-hydroxy-1,4,5,6-tetrahydro derivative, is unstable in acid and undergoes a much slower so-called "secondary acid reaction".[18a,b]) Hence all our studies in aqueous solution (including those in micellar media) were restricted to pH 8.0–9.0.

The absorption/emission spectra of *N*-alkyldihydronicotinamides are very sensitive to the nature of the solvent. Figure 2 presents illustrative absorption/emission spectra for the C_{12} derivative in different solvents. The emission spectra are rather broad and featureless. Table II presents a summary of the data on the absorpion and emission spectral features (emission maxima, quantum yields, and lifetimes) measured in solution at room temperature. Emission quantum yields were measured relative to quinine sulfate in 1 N H_2SO_4 as a standard (ϕ = 0.55) and

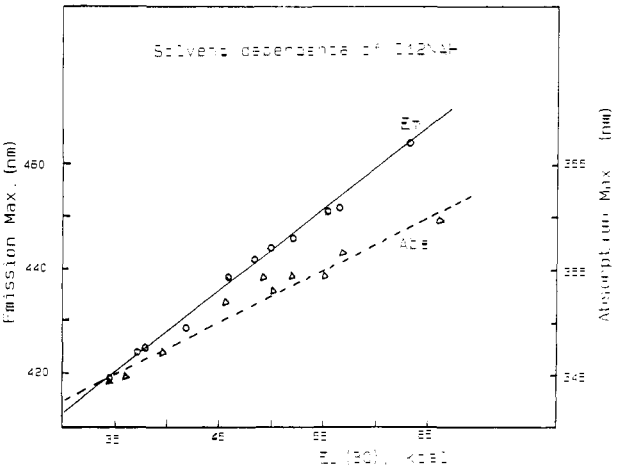

Figure 3. Variation in the absorption/emission spectral maxima of $C_{12}NAH$ with solvent polarity scale $E_T(30)$.

emission lifetimes were measured on a single photon-counting unit using correlation techniques.

Examination of the spectral data presented in Table II reveals several interesting features of the absorption/emission properties of the dihydronicotinamide chromophore:

(i) In the limited number of solvents that we have examined, the absorption and emission spectral maxima show increasing red-shift with solvents in the following order: toluene, THF, ethyl acetate, acetone, dioxane, acetonitrile, chloroform, isopropyl alcohol, 1-butanol, ethanol, methanol, ethylene glycol, and water. In general, the solvent order roughly follows the solvent ordering in Kosower's *Z* scale or the $E_T(30)$ scales of Dimroth.[18c] Figure 3 presents such a correlation of the absorption/emission maxima for the $C_{12}NAH$ derivative with $E_T(30)$ scale. (Since the $E_T(30)$ scale and Kosower's *Z* scale have the same origin as the solvent effects and show mutual linear correlations,[18c] RNAH absorption/emission maxima also show linear variation with *Z* scales as well.) The most likely cause of the solvent effects observed is H-bonding effects of the solvent with the chromophore (in particular at the 3-carbamoyl substituent position). Possibly direct photoionization from the singlet excited state also occurs (cf. discussion).

(ii) The red-shifts in the emission spectra are more pronounced than the corresponding shifts in absorption; i.e., the Stokes shift increases along the solvent series.

(iii) The emission intensities are rather moderate (ϕ_{em} is a few percent). Along the solvent series cited above, the emission

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Table II. Emission Properties of *N*-Alkyl-1,4-dihydronicotinamide in Various Organic Solvents and in Micellar Media

solvent	$E_T(30)$	Z	$\lambda_{max(abs)}$, nm (ϵ, M^{-1} cm^{-1})	$\lambda_{max(em)}$, nm	ϕ_{fl}, %	τ_{fl}, ns
			C_4NAH			
$CHCl_3$	46.0	71.3	354	439	2.5	0.85
H_2O	63.1	94.6	360	461	3.0?	0.39
			C_8NAH			
THF	37.4	58.8	342	425	1.04	
CH_3CN	39.1	63.2	347	435	2.60	
$CHCl_3$	46.0	71.3	353	437	2.65	
			$C_{12}NAH$			
toluene	33.9	54.0	343	419	2.36	
THF	37.4	58.8	340	424	1.31	0.61
EtAc	38.1	64.0	342	425	1.33	
acetone	42.2	65.7		429		
dioxane	36.0	64.6	345	432	2.16	
CH_3CN	39.1	63.2	347	434	2.76	
$CHCl_3$	46.0	71.3	352	439	3.35	0.79
i-PrOH	48.6	76.3	355	442	3.93	
n-BuOH	50.2	77.7	353	444	4.34	1.16
EtOH	51.9	79.6	354 (7000)	446	4.05	1.21
CH_3OH	5.5	83.6	354	451	3.73	0.93
$Et(OH)_2$	56.3	85.1	358	452		
CH_3OH/H_2O			358	456	3.28	
H_2O	63.1	94.6				
CTAC (0.05 M)			347	438?		
CPyC (0.1 M)			353	?		
SDS (0.05 M)			354	456		
			$C_{16}NAH$			
$CHCl_3$	46.0	71.3	354	438	3.9	0.91
			NADH[a]			
H_2O			340 (6200)	470	1.9	0.4
PG			340 (6400)	450	8.0	1.24
			BzNAH[b]			
CH_3CN			348 (6000)	443		0.76
CH_3OH			352 (6350)	457		0.93
EtOH			355 (7240)			
SDS (0.02 M)			354 (6900)	466		0.6
CTAB (0.02 M)			355 (6900)	457		0.9

[a] Reference 18. [b] Reference 19.

quantum yield goes through a maximum with maximal intensities obtained in hydroxylic solvents such as isopropyl alcohol or 1-butanol. The emission lifetimes are short, often less than 1 ns. The emission decay were largely exponential (to about 98–99%). The variation in the emission quantum yield is more linear with the ratio of the theoretical and experimentally measured lifetimes [τ_{calcd}/τ_{expt}] than with the experimentally measured lifetimes (τ_{expt}). The theoretical emission lifetime of the chromophore can be estimated by using the Strickler–Berg equation.

(iv) Similar values obtained for various alkyl chain derivatives suggests that the absorption/emission properties are insensitive to the presence of the alkyl chain. Also, in a few cases where direct comparison can be made, the absorption/emission spectral features of dihydro-*N*-alkylnicotinamide surfactants show a strong resemblance to those of NADH[17] and benzyldihydronicotinamide.[17] It is likely that in NADH also such solvent effects are expected, though the limited stability of NADH in organic solvents restricts direct examination. Nevertheless, the data strongly suggest that the dihydronicotinamide chromophore is very sensitive to the solvent environment.

The emission properties of NADH have been subject to some analysis. The increased emission quantum yield and lifetime in 1,2-propanediol as compared to that in water[17a] has been interpreted as due to different conformations of NADH in these solvent media ("in water, NADH behaves as a molecule in which adenine and dihydronicotinamide are proximate whereas in nonaqueous media NADH resembles a model in which the terminal heterocycles are remote"). The heterogeneity in lifetimes of dinucleotides such as NADH in aqueous solution at room temperature (as compared to a mononucleotide such as NMNH) observed recently has been explained as possibly due to "different folded and unfolded conformations in dynamic equilibrium". The strong solvent effects on the absorption/emission properties of model compounds, similar to that observed with NADH, strongly raises doubts about the interactions of adenine and the dihydronicotinamide chromophore as the possible cause of the observed solvent effects in the latter. It is very likely that photoionization from the excited state occurs. Photoionization is a fairly common mechanism in aqueous solutions of molecules containing electron-donating groups.[19]

There have recently been a few 347-nm laser flash photolysis studies (ns,[20a] ps[20b]) of NADH and the simple model compound *N*-propyl-1,4-dihydronicotinamide (PrNAH) in aqueous solutions. In both the compounds, rapid formation of a solvated electron (e^-_{aq}) via photoionization has been observed (the electron rise time was ca. 40 ps and the quantum yield (ϕ_e-) was 0.48). The low photodecomposition yield (ϕ_{ph} = 0.1) as compared to the quantum yield of the hydrated electron suggests that large amounts of $RNAH^+$ recombine with the electron to re-form RNAH. Interestingly, the electron ejection time (rise time) was found to be significantly longer (by 4 times) than the exciting pulse. It has been proposed that at least two distinct excited-state species (two possible conformers?) are involved (eq 3):

$$S_0 \rightarrow S_1^* \text{ (or } S_n) \rightarrow S^{\#} \rightarrow S^+ + e^-_{aq} \rightarrow S_1 \rightarrow S_0 \quad (3)$$

Present studies confirm the earlier observations that "the strong

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similarity in the photophysical behavior of model compounds RNAH with NADH suggest that the conformational differences of NADH must be confined to the nicotinamide chromophore".

III. Charge-Transfer Complexes of *N*-Alkyl-1,4-dihydronicotinamides with Pyridinium and Bipyridinium Salts and Their Photochemistry. 1,4-Dihydronicotinamides, being good electron donors, readily form CT complexes with a variety of electron acceptors such as pyridinium or bipyridinium ("viologens") halides. In addition to enlarging the chemistry of charge-transfer complexes in the ground state, there has been a sustained interest in studying such bimolecular interactions to help understand reactions of NADH such as hydrogen and isotope exchange. The formation of charge-transfer complexes can be seen by the appearance of new long-wavelength absorptions. A solution mixture of MV^{2+} and RNAH, for example, is colorless at low concentrations but appears reddish brown at high concentrations. In homogeneous media such as water or methanol, the formation of CT complexes is a very inefficient process (K_{CT} is typically in the range of 2–4 M^{-1}).[4] Deployment of microheterogeneous systems allows efficient control of the distribution of solutes. Indeed considerable enhancements in the CT complexation have been obtained in organized systems such as cyclophanes and polymers.[21]

With the series of *N*-alkyldihydronicotinamides, we have examined the features of such charge-transfer complexes under a variety of conditions, using different pyridinium ($RPyr^+X^-$), nicotinamide (RNA^+X^-), and viologen (RV^{2+}) surfactants as acceptors. The appropriate choice of the donor/acceptor concentrations (below or above the cmc) or solvent (water or other organic solvents) allows study of the CT complex formation in homogeneous and micellar media: (a) formation of CT complexes in neat solvents, e.g., C_4NAH and $C_{12}NAH$ with $C_{12}Pyr^+Cl^-$ and $C_{12}NA^+Cl^-$ in methanol; (b) CT complexation between various surfactant derivatives of donors and acceptors and its consequences in host micelles of SDS or CTAC; (c) CT complexation between various surfactant derivatives of donors and acceptors and its consequences in functional micelles (viz., host micelles composed of *N*-alkylnicotinium halides, simple *N*-alkylpyridinium halides, or surfactant viologens). In all the cases, the complexation process can be monitored quantitatively either via new CT absorption or via quenching of RNAH fluorescence. In this report we will restrict ourselves to a general description of the charge-transfer complexes of nicotinamides and dihydronicotinamides and postpone to a latter report a more detailed quantitative study of these complexes in organized media and their applications.

CT Complexes in Neat Solvents. As has been noted earlier for shorter alkyl chain/aryl substituted NAH derivatives, the complex formation is indeed very inefficient. One needs to mix donor and acceptor molecules at concentrations ≥0.01 M to observe CT complexes. In the CT complexes with nicotinamide or simple pyridinium surfactants, the absorption raises monotonically from ca. 600 nm without any clear maxima. Quantitative analysis of the new absorption according to Benesi–Hildebrand (eq 4) yields *K*.

$$\Delta A/[\text{Acc}] = K\epsilon[\text{D}] - K\Delta A \qquad (4)$$

For a given RNAH derivative, the efficiency of various pyridinium salts to act as acceptors increases in the following order: bipyridinium salts ("viologens") > *N*-alkylnicotinamides > simple *N*-alkylpyridinium salts. [Representative E_0' values (in water, relative to NHE, at pH 7.0):[22] MV^{2+}/MV^+ (−0.450 V), benzyl viologen (−0.34 V), bzylNAH/$BzNA^+$ (−0.361 V), C_3NAH/C_3NA^+ (−0.387 V), NADH/NAD^+ (−0.315 V).] Thus the CT complex formation is highly favored and more efficient with viologens than with the pyridinium surfactants, and RNA^+X^- derivatives show intermediate behavior. With viologen salts, the CT complex is significantly stabilized (lower in energy), so one can observe distinct CT absorption maxima in the 450–500-nm region, well separated from the RNAH absorptions. In methanol, the CT complexes of $C_{12}NAH$ have been found to have the following features [K_{CT} (in M^{-1}), λ_{max} (ϵ in M^{-1} cm^{-1})]: $C_{12}NAH/C_{12}Pyr^+Cl^-$, 1.8, 440 nm (240); $C_{12}NAH/C_{12}NA^+Cl^-$, 1.5, 440 nm (142); and $C_{12}NAH/MV^{2+}$, 2.75, 440 nm (310).

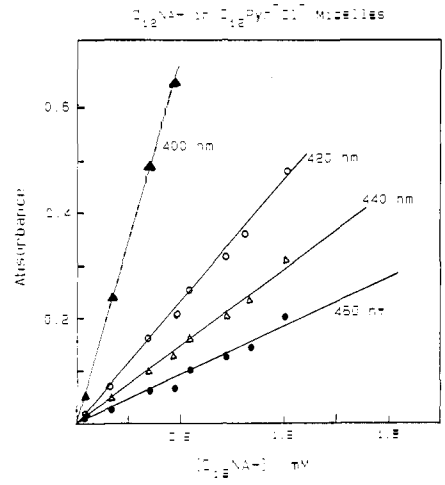

Figure 4. Dependence of the charge transfer complex absorption on the concentration of $C_{12}NAH$ in aqueous micellar solutions of $C_{12}Pyr^+Cl^-$ (0.05 M).

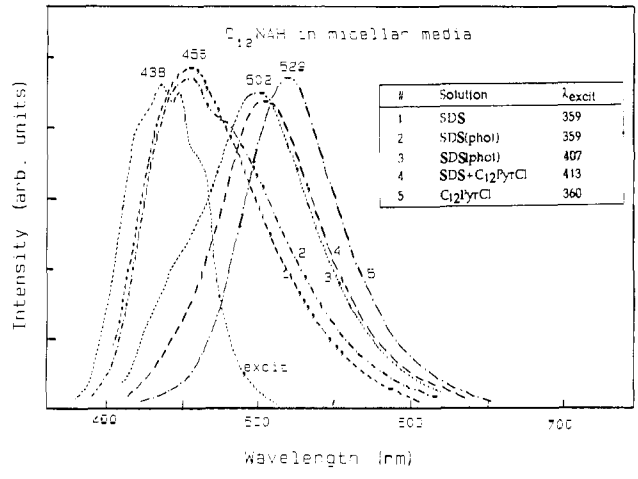

Figure 5. Emission spectra of $C_{12}NAH$ in SDS, in $C_{12}Pyr^+Cl^-$ micelles, and in mixed micelles of SDS–$C_{12}Pyr^+Cl^-$: (1) emission from $C_{12}NAH$ in freshly prepared SDS (0.05 M) solutions; (2) emission from photolyzed $C_{12}NAH$–SDS solutions; (3) emission from photolyzed $C_{12}NAH$–SDS solutions; (4) emission of $C_{12}NAH$ in mixed micelles of SDS (0.05 M)–$C_{12}Pyr^+Cl^-$ (0.02 M); and (5) emission of $C_{12}NAH$ in $C_{12}Pyr^+Cl^-$ (0.02 M) micelles [cf. insert for excitation wavelength in each case].

CT Complexes in Micellar Media. In neat solvents a low K_{CT} value (2–4 M^{-1}) necessitates, for donor RNAH concentrations of ca. 10^{-4} M, a 1000-fold excess of acceptor (>0.1 M) for total complexation. In functional micellar systems these conditions can be readily met. As shown in Figure 4, in functional micellar systems, one can observe a linear increase in the CT absorptions with the increasing concentration of RNAH indicating total complexation. The complexation appears to be quantitative even for high loading of donors. Thus, in aqueous functional micellar assemblies composed of alkylpyridinium or alkylnicotinamide surfactants, the formation of the CT complex is very efficient and quantitative.

As expected, in functional micellar assemblies with pyridinium, nicotinamide, or bipyridinium surfactants, the normal RNAH fluorescence is heavily quenched. Surprisingly, the features of the emission spectra were found to be strongly dependent on the

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excitation wavelength. Careful examination of the emission/excitation spectra at several wavelengths (in functional micelles composed of pyridinium or nicotinamide surfactants or in mixed micelles of CTAC/RPyr$^+$X$^-$) showed that the normal RNAH emission is accompanied by the appearance of a new emission with maxima in the 500–520-nm region. Figure 5 presents typical "normal" RNAH fluorescence along with the "new/anomalous" emission observed upon excitation of the D–A solutions in the 400–500-nm region (i.e., outside the region of RNAH absorptions). To our knowledge, the appearance of such new emission during the formation of CT complexes of nicotinamide derivatives has not been reported.

Examination of the excitation spectrum for this new/anomalous emission (spectrum also shown in Figure 5) raises doubts about the possible assignments of the new emission as due to the CT complexes. In contrast to the smooth, structureless rising absorptions of the CT complexes (as seen in the absorption spectra), excitation spectra invariably are structured (show two distinct maxima at 438 and 448 nm). A plausible assignment for the new emission can be a "photoproduct". For example, C_{12}NAH in normal (SDS or CTAC) micelles shows only the normal RNAH fluorescence. No new emissions are observed unless the solutions are intentionally photolyzed. Reabsorption of normal fluorescence by CT bands complicates analysis.

Photosensitivity of the Charge-Transfer Complexes ("Photoreduction of Viologens"). As mentioned earlier, excitation of ground-state charge-transfer complexes leads to the quenching of the emission of the dihydronicotinamide chromophore. In principle, the quenching process can be purely static or concurrently dynamic. In the absence of any further chemistry, binding constants determined either via monitoring of CT absorption or quenching of RNAH fluorescence yield very similar values. With the CT complexes of simple pyridinium surfactants, this is the case.

However, with excellent acceptors such as methyl viologen, orange or reddish brown colored solutions are very sensitive to photolysis. In degassed solutions, one can readily observe the photoinduced formation of blue-violet reduced viologen radicals (reaction 5):

$$\mathrm{RNAH^*} + 2\mathrm{R'V^{2+}} \rightarrow \mathrm{RNA^+} + 2\mathrm{R'V^+} + \mathrm{H^+} \qquad (5)$$

Figure 6 presents absorption spectral changes for two cases corresponding to such photoinduced reduction of viologens: (a) reduction of simple dimethyl viologen (MV^{2+}) upon irradiation of C_4NAH in aqueous solutions and (b) reduction of a surfactant viologen $C_{14}MV^{2+}$ by irradiation of C_{12}NAH in aqueous micellar solutions of CTAC. Steady-state photolysis of the CT complexes leads to net formation of viologen radicals with consumption of RNAH in a 2:1 stoichiometry, as demanded by eq 5.

As has been noted earlier for the photoreduction of MV^{2+} by benzyldihydronicotinamide in aqueous solutions,[17e] in both cases examined, formation of blue viologen radicals are observed upon photolysis at the RNAH absorption band (maximum at 360 nm). However, in this study we have noted that the *photoreduction of viologen to their one electron reduced radicals is still observed if one carries out the photolysis in the region of charge-transfer absorption as well, i.e., with visible light* ($\lambda > 400$ *nm*)! Due to the very low absorption coefficients of the CT absorptions ($\epsilon \leq 400$ M^{-1} cm^{-1}), the process is readily observed only in solutions that contain high concentrations of donors and acceptors. The reduction of viologens via photolysis of their charge-transfer complexes with dihydronicotinamides is reminiscent of similar photoreductions reported for the ion-pair complexes of viologens with donors such as EDTA.[23] The visible-light sensitivity of the charge-transfer complexes with RNAH is more pronounced than in the ion-pair complexes with EDTA.

Returning to Figure 6, even though the photochemistry is the same in both of the cases shown, they illustrate the possibility of carrying out the same reaction in two different microenvironments

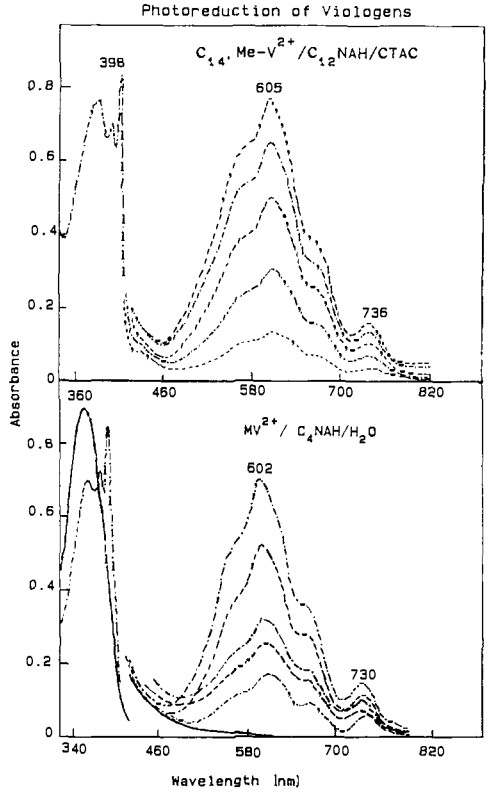

Figure 6. Absorption spectral changes observed during photolysis of RNAH in the presence of viologen derivatives in aqueous and micellar media: bottom (a), photolysis of degassed solution of C_4NAH (1.5×10^{-4} M)–MV^{2+} (2.0×10^{-3} M) in H_2O, pH 8.5, $\lambda \geq 340$ nm; top (b), photolysis of C_{12}NAH (2.0×10^{-4} M)–C_{14}Me-V^{2+} (1.0×10^{-3} M) in degassed micellar solutions of CTAC (0.02 M), pH 8.5, $\lambda \geq 340$ nm.

with associated features and restraints. Photoreduction of viologen in case b is purely "intramicellar" as compared to pure aqueous phase reduction in case a. In case b, for example, with micelle-bound donor C_{12}NAH and acceptor $C_{14}MV^{2+}$, one can readily control their loading and hence their interactions. For example, it is known that the reduced viologen radical $C_{14}MV^+$ is very hydrophobic and readily dimerizes in aqueous solutions at concentrations as low as 10^{-5} M. With acceptor molecules well separated from one another, as in the case shown in Figure 6, *in micellar media, dimerization effects are not observed at "total" viologen radical concentrations as high as* 10^{-4} *M*. An added advantage of the "electrically neutral" long-chain dihydronicotinamides, RNAH, is that they can be solubilized easily in all types of organized assemblies: cationic, anionic, or neutral. The two cases illustrate the potential utility of this class of long-chain derivatives of dihydronicotinamides as electron donors for different forms of organized media.

Models for the analysis of dynamic quenching of fluorescence in the presence of charge-transfer complexation (static quenching) have been described in the literature.[24] While the extreme cases (predominantly dynamic or static) are easier to analyze, experimental establishment of the relative importance of each of the two processes is not straightforward. In principle, time resolved transient absorption studies with equipment capable of time resolution considerably shorter than the excited-state lifetime can provide direct experimental data on the yields of static (initial/end of pulse yield) and dynamic quenching (that which grows on time scales of accelerated excited-state decay). The subnanosecond excited-state lifetime of RNAH ($\tau = 0.39$ ns for C_4NAH in water) necessitates time-resolved absorption measurements on a picosecond time domain. We plan to carry out such studies in the near future. A 20-ns laser pulse used in the laser-photolysis studies

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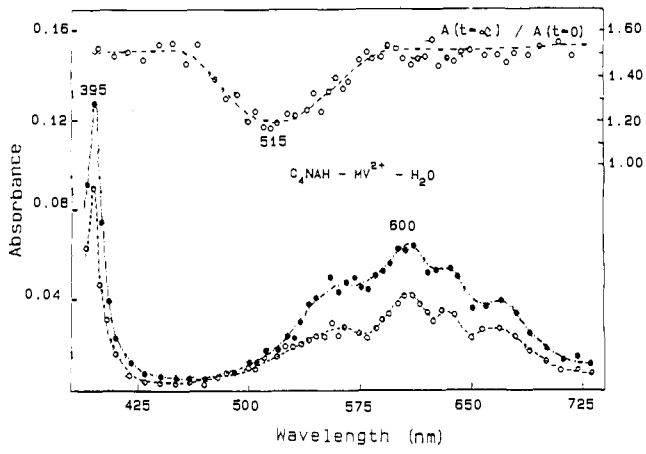

Figure 7. Bottom: transient absorption changes (difference spectra) observed during 353-nm Nd-laser photolysis of degassed aqueous solutions containing C_4NAH (2.0×10^{-4} M) and MV^{2+} (6.5×10^{-3} M). The open circles (○) represent the spectrum recorded immediately after the laser pulse excitation (ca. 20 ns). The filled circles (●) represent the spectrum recorded at $t = 4$ μs. Top: the variation in the absorbance ratio $[I(t = 4\ \mu s)/I(t = 0)]$ with wavelength is shown.

of Martens et al.[25] on this system does not resolve this question.

The mechanism of formation of 2 equiv of reduction products for every photon absorped by RNAH is very similar to that shown earlier for irreversible donors such as EDTA[26] and triethanolamine (TEOA)[13c,27] in alkaline solutions. The oxidized donor (DH^+) formed in the primary electron-transfer step loses a proton to generate a strongly reducing radical (D•), which in turn reduces a second acceptor molecule (reactions 6–8):

$$DH^* + A \rightarrow DH^+ + A^- \quad (6)$$

$$DH^+ \rightarrow D^\bullet + H^+ \quad (7)$$

$$D^\bullet + A \rightarrow D^+ + A^- \quad (8)$$

We have studied the mechanism of reduction of C_4NAH by MV^{2+} in aqueous solution by nanosecond laser flash photolysis and have confirmed the occurrence of such a sequence in aqueous solution. [Given the fact that oxygen solubility in CH_3OH is fairly high (2.1 mM) and oxygen reacts very rapidly with reduced viologen radical ($MV^{\bullet+}$), we are surprised that earlier flash-photolysis studies of MV^{2+} reduction by benzyl viologen (BzNAH) in CH_3OH[27] have been carried out on nondeoxygenated solutions!] The pK_a value of the oxidized donor radical (DH^+) is particularly of interest, and hence we examined the pH dependence of the reaction. The pK_a for the deprotonation step (eq 9) has been estimated to be ca. 6.5 for EDTA[26] and ca. 8.5 for TEOA.[27]

Figure 7 presents transient absorption spectra recorded at two different times following 353-nm laser-pulse excitation of degassed C_4NAH–MV^{2+} solutions at pH 9.0. The spectra are dominated by two distinct maxima (395 and 600 nm), characteristic of $MV^{\bullet+}$ radicals. Kinetic monitoring of the absorption changes at the viologen radical absorption maxima (602 nm) showed that a certain amount of $MV^{\bullet+}$ is observed immediately with the pulse, followed by a slow growth of $MV^{\bullet+}$ absorptions over a few microseconds. As the concentration of MV^{2+} is much larger than the concentration of D• radicals produced in each pulse (via reaction 7), the secondary growth shows pseudo-first-order kinetics. The rate of growth of secondary $MV^{\bullet+}$ and the final yields were both pH dependent. Figure 8 presents typical $MV^{\bullet+}$ growth curves at several pH values (monitored at 602 nm) and also the pH dependence of the initial to final $MV^{\bullet+}$ absorbance ratio, $[\Delta A_\infty/\Delta A_0]$ and half-life for the secondary growth of $MV^{\bullet+}$ radical. With increasing pH, the growth rate and yield increases. The initial to final yields of $MV^{\bullet+}$ reaches a value of 2.0 at pH values ≥11.0. At pH 9.0, for example (the case shown in Figure 10), this ratio is about 1.50 ± 0.03. The pK_a of the deprotonation step for the oxidized $RNAH^+$ radical is probably around 8.0. Unfortunately, thermal instability of RNAH in acidic aqueous solutions did not allow following the $MV^{\bullet+}$ yield curve to pH values below 6.0.

In the 380–740-nm region the product absorptions are predominantly due to MV^+. The initial (end of laser pulse) absorption spectrum is in fact a composite of absorptions due to $MV^{\bullet+}$ and the oxidized $DH^{\bullet+}$ radical. Since no information is yet available on the absorption spectral features of $DH^{\bullet+}$ radical, the absorption ratio of initial to final (plateau) absorption was examined over the entire range (the ratio curve shown in the top of the Figure 7). It appears that $DH^{\bullet+}$ radical has a weak absorption with a maximum at 515 nm ($\epsilon \leq 3000\ M^{-1}\ cm^{-1}$). There have been a few pulse-radiolysis studies[28] on the one-electron adduct of various 3- and 4-substituted *N*-alkylpyridinyl compounds (including nicotinamide). The product D• radical, the deprotonated form of the $DH^{\bullet+}$ radical, has been reported to have two maxima at 300 and 400 nm, respectively.

The extent of complexation of BzNAH with MV^{2+} has been analyzed in SDS micelles by Martens and Verhoeven[17c] via Scatchard plots of CT absorption and by Itoh et al.[4f] in polymers via fluorescence. According to the procedure outlined by Itoh et al., we have analyzed the MV^{2+} quenching of solubilized $C_{12}NAH$ fluorescence in SDS micelles by steady-state measurements. Figure 9 presents two plots showing the (i) variation of $[I_0/I]$ values with the total quencher concentration, [Q], and (ii) variation of $[I_0/I_0 - I]$ values with 1/[Q]. The overall quenching constant (K') value of 333 M^{-1} derived for the $C_{12}NAH$–MV^{2+} pair in SDS micelles is in the same range of K = 315 M^{-1} obtained for the BzNAH–MV^{2+} pair also in SDS micelles.

IV. Photoredox Reactions Involving Dihydro-*N*-alkylnicotinamides. The ability of NADH to act as electron donor in ground- and excited-state processes has been examined, particularly the role of NADH to act as a $1e^-$ vs $2e^-$ donor.[29,30] Various systems studied include, for example, (a) reductive quenching of porphyrins (reaction 9)

$$S^* + NADH \rightarrow SH^- + NAD^+ \quad (9)$$

where S = SnTMPyP[29a] and ZnTMPyP[29b], (b) photoreduction of viologens by photoexcited NADH (a reaction already discussed in the earlier section) (reaction 10)

$$2MV^{2+} + NADH \rightarrow 2MV^+ + NAD^+ + H^+ \quad (10)$$

and (c) regeneration of photooxidized sensitizer dyes (reaction 11)

$$S^+ + NADH \rightarrow S + NAD^+ + H^+ \quad (11)$$

where S = ZnTPPS,[29c] chlorophyll *a*,[29d] and $Ru(bpy)_3^{2+}$,[29e] and thermal (dark) reduction of dyes (reaction 16)

$$2S + NADH \rightarrow SH^- + NAD^+ \quad (12)$$

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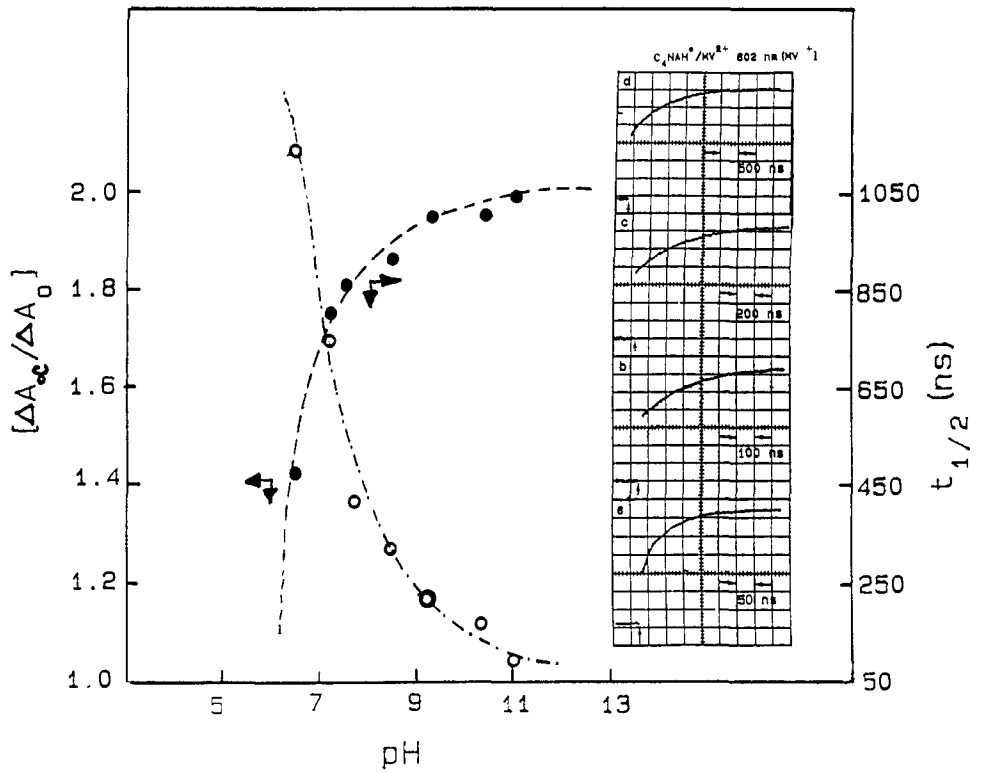


Figure 8. pH dependence of the final to initial absorption ratio $[\Delta A_\infty/\Delta A_0]$ (λ = 602 nm) and the half-life for the secondary growth of $MV^{\bullet+}$ measured during the laser photolysis of C_4NAH–MV^{2+} solutions. Insert: the kinetic traces of $MV^{\bullet+}$ absorbance changes with time, recorded at several pH values (11.0 (a), 10.5 (b), 9.6 (c), 8.5 (d)) are presented.

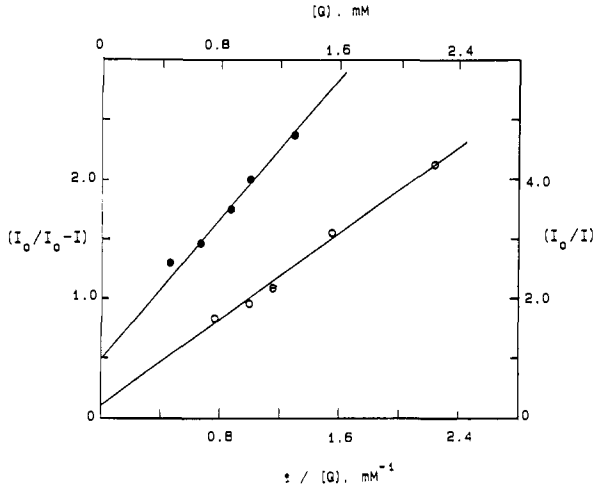


Figure 9. Analysis of MV^{2+} quenching of $C_{12}NAH$ fluorescence in SDS micelles; fluorescence monitored at 455 nm: right, $[I_0/(I_0 - I)]$ vs $1/[Q]$; left, $[I_0/I]$ vs [Q].

where S = methylene blue.[29f] The mechanism of action of NADH continues to be controversial[30]—whether the reactions involve a direct hydride (H^-) transfer, hydrogen atom transfer accompanied by electron transfer, *or* a sequential transfer of e^-, H^+, e^-.

In continuation of our interest in the photochemistry and redox chemistry of water-soluble porphyrins, in this study we have examined the photoreduction of two zinc porphyrins ($ZnTMPyP^{4+}$ and $ZnTPPS^{4-}$) using various long-chain RNAH derivatives as donors. While C_4NAH can be used as a donor in aqueous solution, it was pointed out in the earlier section that one particular, potentially useful application of the long-chain dihydronicotinamide (RNAH) derivatives is as *neutral, hydrophobic electron donors for organized assemblies such as micelles and vesicles and monolayers, of both cationic and anionic type.* It is well known[31b] that irradiation of porphyrins in the presence of suitable electron donors leads to the photoreduction of the porphyrins to their dihydro derivatives, phlorin or chlorin (reaction 13):

$$MP + RNAH + H^+ \rightarrow MPH_2 + RNA^+ \qquad (13)$$

Formation of either phlorin or chlorin (or a mixture) depends largely on the nature of the porphyrin and the conditions of reduction. Recently we investigated the mechanism of such photoreductions using EDTA as a donor by using the technique of laser photolysis.[29b]

Visible-light irradiation ($\lambda > 500$ nm) of the cationic porphyrin ZnTMPyP in degassed aqueous solutions in the presence of C_4NAH leads to very efficient reduction of the porphyrin to a product, which by its absorption spectral features and sensitivity to molecular oxygen is identified as phlorin (MPH_2). Irradiation of the anionic ZnTPPS under similar conditions leads to inefficient photoreduction of the porphyrin to its chlorin (MPH_2). Laser-flash photolytic monitoring of the triplet-state quenching of the two porphyrins by C_4NAH has established that the relative efficiencies of reduction are due to large differences in the two quenching rate constants:

$$^3MP^* + D \rightarrow MP^- + D^+ \qquad (14)$$

In water (pH 8.0), the quenching rate constant k_q is 3.0×10^9 M^{-1} s^{-1} and 4.1×10^6 M^{-1} s^{-1} for $ZnTMPyP^{4+}$ and $ZnTPPS^{4-}$, respectively. The differences in the rate constants can be rationalized in terms of the redox potentials of the two porphyrin triplets. It is known that[8a] the triplet state of ZnTMPyP is a better oxidant than that of ZnTPPS: $E°(^3ZnP^*/ZnP^-) = 0.78$ V and 0.45 V for ZnTMPyP and ZnTPPS, respectively.

Photoreduction of porphyrins by dihydronicotinamide is an interesting system to distinguish the two possible pathways (hydride transfer vs e^-, H^+, e^- transfer) for the mechanism of action of RNAH as a two-electron donor. Porphyrin reduction in general goes through two principal intermediates: porphyrin anion (MP^-) and phlorin anion (PH^-). With electron donors such as EDTA, the latter intermediate, PH^- (equivalent to a hydride adduct of

(31) Lovesay, A. C.; Ross, W. C. J. *J. Chem. Soc. B* **1969**, 192.

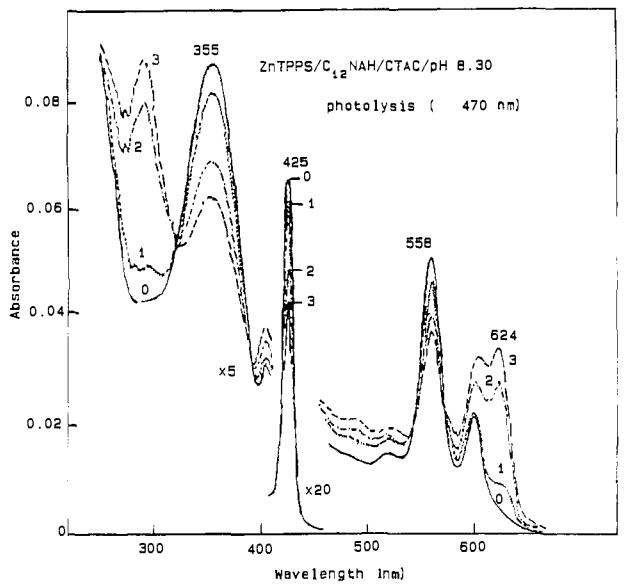


Figure 10. Absorption spectral changes observed during visible-light photolysis of $ZnTPPS^{4-}$ porphyrin in the presence of $C_{12}NAH$ (6.5×10^{-5} M) in CTAC micelles (0.02 M).

the porphyrin), is formed via disproportionation of the porphyrin anion (P^-) and subsequent protonation of the dianion (P^{2-}). The porphyrin anion (P^-) and phlorin anion (PH^-) both have distinct absorption spectra that allow unequivocal monitoring of the early reduction product using RNAH. We examined the photoreduction of ZnTMPyP by C_4NAH by laser photolysis, along the lines of EDTA (extensive details on the spectra and mechanism of reduction were published recently[29b]) with the above viewpoint. In short, MP^- was formed as the first product which subsequently generates MPH^-. Hence, at least with two photoredox systems that we have examined (reduction of viologen using RNAH* in section III and of excited zinc porphyrin by RNAH here in section IV), the experimental results favor a e^-, H^+, e^- sequence.

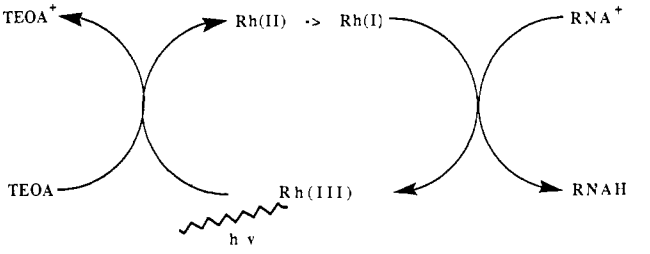
With a long-chain dihydronicotinamide derivative and ionic/water-soluble porphyrins, one can readily construct a functionalized photoredox assembly: $C_{12}NAH/ZnTPPS^{4-}$ pair in cationic micelles of CTAC (The anionic zinc porphyrin associates readily with cationic micelles for electrostatic reasons). With such a functionalized system, the photoreduction of even ZnTPPS by RNAH becomes very efficient. Figure 10 presents steady-state spectral changes showing the formation of zinc chlorin ($ZnPH_2$) during the visible light photolysis of $C_{12}NAH/ZnTPPS$ in CTAC micelles. The photoreduction in the corresponding aqueous system under similar conditions is very inefficient. Laser-photolysis studies have confirmed efficient quenching of ZnTPPS triplets by C_{12}-NAH (at low loading, i.e., [quencher]/[micelle] ≤ 0.05, the apparent quenching rate constant (k_q) is 2.18×10^5 s^{-1} at $C_{12}NAH$ = 10^{-4} M in 0.02 M). (As a rate constant for an intramicellar process, k_q has the units of a first-order rate constant). As the triplet quenching by RNAH is an intramicellar process, at high loading the quenching becomes nonlinear.

V. Photosensitized Reduction of Surfactant Nicotinamides to Their Dihydro Derivatives in Biphasic Systems. The reduction of NAD^+ to NADH (1,4 isomer form in particular) is a complex, stereospecific process involving transfer of two electrons and a proton (reaction 15). Assisted by enzymes, the reduction occurs very efficiently as a one-step process. The high cost of cofactors

$$NAD^+ + H^+ + 2e^- \rightarrow NADH \quad (15)$$

mediating the redox reaction catalyzed by the enzymes exclude their use in stoichiometric quantities and there have been sustained efforts to design a system that efficiently regenerates NADH from NAD^+. The enzymatic activity of the NADH produced is assessed by the efficiency of the reduction of various ketones in the presence of enzymes such as liver alcohol dehydrogenase.

Scheme I



Sequential one-electron reduction (reactions 16 and 17) invariably leads to formation and rapid dimerization of the free-radical intermediate (NAD•). Also the possible formation of other

$$NAD^+ + e^- \rightarrow NAD^\bullet \rightarrow NADH \quad (16)$$

$$2NAD^\bullet \rightarrow (NAD)_2 \quad (17)$$

enzymatically inactive isomers in chemical or electrochemical means makes the reduction more delicate than the reverse process of reoxidation of NADH to NAD^+.[31] Chemical reduction using dithionite probably is the simplest and most direct process that yields the desired 1,4-dihydro derivative. Utilization of various Rh(III) complexes (for example, octaethylporphyrin, rhodium polypyridyl, bis(phosphine) complexes) in hybrid chemical/enzymatic, electrochemical, and photochemical systems have produced very encouraging results.[3,32]

In this study, we examined the sensitized photoreduction of *N*-alkylnicotinamide surfactants in aqueous solutions to their 1,4-dihydro derivatives (pH 9.0 buffer) [at surfactants invariably below their cmc] using rhodium(III) polypyridyl and ruthenium(II) polypyridyl complexes as sensitizers and TEOA as "sacrificial" electron donor. Schemes I and II below outline the principal reactions that occur upon photolysis. It should be noted that the primary photoredox reactions involved in these schemes have been studied earlier, and the mechanisms are fairly well-established.[33] In Scheme I, UV excitation of $[Rh^{III}(bpy)_2(X)_2]^+$ (or equivalently of $[Rh^{III}(bpy)_3]^{3+}$) leads to the formation of LF excited state (reaction 18):

$$[Rh^{III}(bpy)_2(X)_2]^+ \rightarrow [Rh^{III}(bpy)_2(X)_2]^{+*} \quad (18)$$

The LF state undergoes a photoredox-quenching reaction with electron donors such as TEOA to form $[Rh^{II}(bpy)_2(X)_2]$ (reaction 19)

$$[Rh^{III}(bpy)_2(X)_2]^{+*} + TEOA \rightarrow [Rh^{II}(bpy)_2(Cl)_2] + TEOA_{ox} \quad (19)$$

Rh(II) complexes are labile and undergo rapid ligand loss and disproportionation to yield $[Rh^{I}(bpy)_2]^+$ as the principal product (reaction 20)

$$2[Rh^{II}(bpy)_2(X)_2] \rightarrow [Rh^{I}(bpy)_2]^+ + 2X^- + [Rh^{III}(bpy)_2(X)_2]^+ \quad (20)$$

Rh(I) complexes finally reduce RNA^+ directly to the 1,4-dihydro derivatives in a thermal step (reaction 21):

$$[Rh^{I}(bpy)_2]^+ + RNA^+ + 2H_2O \rightarrow [Rh^{III}(bpy)_2(OH)_2]^+ + RNAH + H^+ \quad (21)$$

In Scheme II, reactions 18 and 19 are replaced by the reduc-

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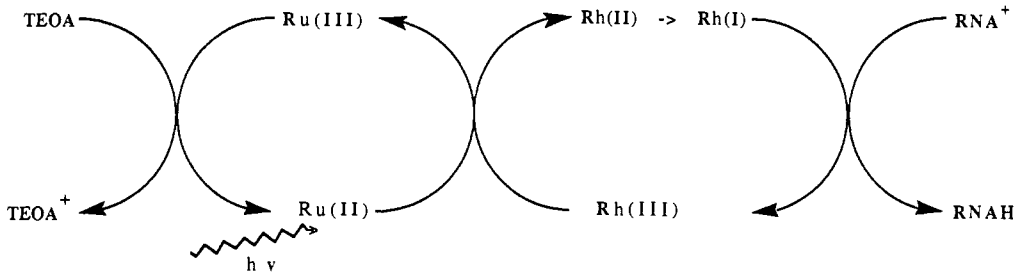
Scheme II



tive-quenching reaction of $Ru^{II}(bpy)_3^{2+}$ by $Rh^{III}(bpy)_3^{3+}$ (reaction 22) and thermal regeneration of $Ru(bpy)_3^{2+}$ (reaction 23):

$$Ru^{II}(bpy)_3^{2+*} + [Rh^{III}(bpy)_2(X)_2]^+ \rightarrow [Rh^{II}(bpy)_2(Cl)_2] + Ru^{II}(bpy)_3^{3+} \quad (22)$$

$$Ru^{II}(bpy)_3^{3+} + TEOA \rightarrow Ru^{II}(bpy)_3^{2+} + TEOA_{ox} \quad (23)$$

Electrochemical and sensitized photoreduction of NAD^+ to NADH using rhodium(III) polypyridyl complexes have, in fact, been demonstrated earlier.[3a,b,34] Our interests in examining Schemes I and II have been for two principal reasons: Firstly, to assess the generality of such schemes for other derivatives of nicotinamide. Secondly, to exploit the large differences in the solubility (hydrophobicity) of the oxidized/reduced form of nicotinamide surfactants to achieve selective extraction of the reduced form in biphasic systems.

Photolysis studies typically involved irradiation of degassed aqueous solution mixtures of RNA^+Cl^-, $[Rh^{III}(bpy)_2(Cl)_2]^+$, and TEOA with or without $Ru(bpy)_3^{2+}$ for selected periods of time, followed by extraction of the reduced nicotinamide using $CHCl_3$. The formation of the 1,4-dihydronicotinamide product was followed in the $CHCl_3$ extract via its characteristic absorption (maximum at 353 nm) and emission (maximum 438 nm). Photolysis studies conforming to Schemes I and II have confirmed the occurrence of sensitized reduction to neutral RNAH species in both the schemes.

The initial $CHCl_3$ extract also carried some of the oxidized form of nicotinamide surfactant (RNA^+X^- salts have limited solubilities in organic solvents such as $CHCl_3$) and these are readily removed by repeated washing with water (pH 9.0 buffer). Dihydronicotinamides are very sensitive to the solution pH, undergoing acid-induced degradation if the pH falls below 9.0. As mentioned earlier, the degradation product has an absorption maximum at 315 nm. Thus all *photolysis and washings of $CHCl_3$ extract need to be performed in mildly alkaline buffer solutions of pH 9.0–10.0.*

Moderate absorptions in the 250–350-nm region in the $CHCl_3$ extract (instead of a valley with an absorption minimum at 286 nm of RNAH in dry $CHCl_3$ solutions; cf. Figure 7) can also suggest possible formation of 1,6-dihydronicotinamides or dimers as additional products. (*N*-benzyl-1,6-dihydronicotinamide, for example, is reported[31] to have absorption maxima at 358 ($\epsilon \approx 5620$ M^{-1} cm^{-1}) and at 267 nm ($\epsilon \approx 6180$ M^{-1} cm^{-1}) in ethanol.) Similarly, absorption maxima at 259 and 340 nm have been reported[34] for the NAD dimer produced upon $1e^-$ reduction in aqueous solutions. It should be pointed out that the degradation product is formed during the wash with aqueous solution and is not a direct photoproduct. In comparative studies using authentic RNAH luminescence as a standard, over 80% of the "355-nm" absorption is believed to be due to the desired 1,4 isomer. Hence formation of the 1,2 isomer is inefficient, though nonnegligible. Weinkamp and Steckhan[3] have estimated the formation of NAD dimer to the extent of 0.9% in the $Rh(bpy)_3^{3+}$-mediated reduction of NAD^+.

In regard to the quantum yield for the formation of RNAH, a preliminary estimate is $\phi \approx 0.002$. The quantum yield for the formation of the Rh(II) complex in the primary photochemical step however is fairly high, and the values have been reported earlier both for the direct excitation of the rhodium(III) bipyridyl complex and for the excitation of the Ru complex.[33a,b] Clearly the low quantum yield for the formation of the RNAH product reflects the cumulative inefficiencies of the several secondary (dark) steps that generate the key Rh(I) complex (e.g., loss of the ligand in the Rh(II) complex and the disproportionation reactions) and also of the steps (multiple?) that lead to the reduction of RNA^+ to the desired dihydro isomer.

Overall, the sensitized photoreduction of nicotinamide surfactants as shown above is a significant improvement in the "designing of photochemical processes in biphasic systems, wherein the photoredox reactions can take place in one phase with the possibility of accumulating one of the desired products in the other phase". In regard to the optimal choice of chain length, it can be noted that with increasing chain length the cmc of the oxidized form of the surfactant (RNA^+X^-) and the solubility of the reduced form (RNAH) both decrease in aqueous solution (the solubility in organic solvents also increases correspondingly). Hence it is desirable to use a moderate chain length—such as C_{12}. Still longer chain surfactants have a higher Kraft point than room temperature—this can necessitate usage of elevated temperatures. Also the concentration range of RNA^+X^- available for usage as monomer before micelle formation occurs also decreases.

In regard to the practical utility of these model compounds as "real" substitutes for $NADH/NAD^+$, the ability of these compounds to act on enzymes such as liver alcohol dehydrogenase (LADH) without inhibitory effects on the enzyme needs to be examined. It is likely that these simple model compounds lacking the necessary structural components required to orient the substrate and the coenzyme in the active site of the enzymes (adenine, ribosyl phosphate) cannot act directly on the enzyme. The next best option would be whether these RNAH molecules can regenerate NADH from NAD^+. The studies of Taylor and Jones[22d] are very pertinent in this context. Prompted by the observations that the $NADH/NAD^+$ couple undergoes C_4-H exchange reactions with simple pyridinium salts to yield 1,4-dihydropyridines, these authors examined, on a practical scale, enzyme (LADH) assisted conversion of cyclohexanone to cyclohexanol in a solution that contained catalytic amounts of the cofactor NADH but with an auxiliarly "in situ" system (RNAH) that is capable of regenerating NADH in its active form (reactions 24 and 25):

$$>C{=}O + NADH \rightarrow >CHOH + NAD^+ \quad (24)$$

$$RNAH + NAD^+ = RNA^+ + NADH \quad (25)$$

Simple model compounds such as benzyl nicotinamide and C_3N-AH were found to efficiently recycle the coenzyme NADH upto 21-fold, without any inhibitory effect on the enzyme.

Conclusions

With a series of *N*-alkylnicotinamide surfactants of chain length C_4 to C_{16} and their corresponding 1,4-dihydronicotinamides, it has been possible to study the aggregation properties and the basic chemistry of this interesting series of compounds. In almost all of the key areas, the long chain derivatives of nicotinamide and dihydronicotinamide truly reproduce the chemistry of the $NADH/NAD^+$ couple. In some cases (e.g. photophysics) the

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present results raise questions about the existing explanations and models for the NADH/NAD^+ couple's action. On the question of NADH's role as a hydride donor vs the e^-, H^+, e^- transfer sequence, at least in the two photoredox processes of RNAH examined, laser-photolysis studies tend to support the latter mechanism.

Thus in addition to providing a better understanding to the important chemistry exhibited by NADH/NAD^+, these compounds have several unique features that allow practical applications in many areas. One can cite, for example, their use as neutral donors for various forms of organized assemblies and biphasic systems and as agents to regenerate NADH in an inexpensive way. In applications of photochemical solar-energy conversion, due to the retention of their chemical identity in the oxidized form, these RNAH molecules can certainly serve as more useful donors than the commonly used "irreversible" donors such as EDTA and tertiary amines.

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Solvent Effects on the Thermochemistry of Free-Radical Reactions[1]

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Abstract: Heats of the reaction $H_2O_2 + 2RH \rightarrow 2H_2O + 2R^\bullet$ were measured in water for a variety of organic substrates by using photoacoustic calorimetry. The values obtained were substantially lower than those calculated from gas-phase data and the difference was due entirely to the change in solvation energy associated with the conversion of 1 equiv of hydrogen peroxide to 2 of water. The solvation energies of $R^\bullet$ and RH were the same and their contributions to the measured heats of reaction therefore cancelled. The results suggest that solution data, measured in extremely polar solvents, can be converted to their gas-phase equivalents (and vice versa) by considering only the heats of solvation of very small, polar molecules that participate in a given reaction. Moderately large organic molecules and their corresponding radicals are solvated to the same extent—even in water.

A knowledge of the thermochemistry for free-radical reactions is of vital importance from practical, mechanistic, and theoretical perspectives.[3] Much of the thermochemical data that is now available to us comes from gas-phase measurements.[4,5] However, a very large proportion of free-radical reactions are carried out in the liquid phase and there has been a nagging doubt as to whether gas-phase data were applicable in this situation because of solvation effects.

The concerns have, to some extent, been mitigated by measurements of homolytic bond dissociation energies in solutions[6] that have generally been in good agreement with gas-phase data.[7] Indeed, in some instances[6] solution data have paved the way for revisions and improvements to gas-phase results. However, essentially all of these measurements have been made in nonpolar solvents where differences in the solvation of reaction products versus starting materials might be expected to be small.

Recently, Katritzky[8] proposed that differential solvation of reactants versus products might indeed be important in polar solvents when the radicals formed in a reaction had larger dipole moments than their precursors. The hypothesis was based on a theoretical treatment and was immediately countered by experimental work.[9] However, in the light of this continuing uncertainty, we decided to tackle the problem of solvation effects by going to an extreme case and by measuring heats of free-radical reactions and bond strengths in a very polar solvent—water.

Experimental Section

Hydrogen peroxide was used extensively in these experiments and a major consideration in the selection of materials and equipment was therefore to ensure that metal ion contamination was minimized.[10]

Materials. Water was distilled and deionized by using a Milli Q water system (Millipore) or was commercially available in a glass-distilled grade (BDH Omnisolv). The hydrogen peroxide used in this work was a 30% solution in water that was subsequently diluted to the requisite concentration. *o*-Hydroxybenzophenone and 2,4-dihydroxybenzophenone were purified by multiple recrystallizations from ethanol or ethanol–water mixtures. All other materials were commercially available in high purity and were used as received.

Apparatus. The photoacoustic calorimeter used in this work has been described in detail elsewhere.[11] Briefly, pulses from a nitrogen laser (Molectron UV24, 337.1 nm, pulse width 10 ns, output 10 mJ/pulse, repetition rate 5 Hz) were used to photolyze solutions contained in a standard quartz flow cell (Hellma 171 QS). The laser light was attenuated by using an iris so that only a fine beam passed through the sample cell. Variations in laser power were monitored by splitting out a small fraction of the attenuated light to a reference detector.

Each pulse initiated free-radical reactions within the sample cell along the trajectory of the photolyzing beam, and the heat evolved in these

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