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Development of an Efficient and Durable Photocatalytic System for Hydride Reduction of an NAD(P)$^+$ Model Compound Using a Ruthenium(II) Complex Based on Mechanistic Studies

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Abstract: The mechanism of photocatalytic reduction of 1-benzylnicotinamidium cation (**BNA$^+$**) to the 1,4-dihydro form (**1,4-BNAH**) using $[Ru(tpy)(bpy)(L)]^{2+}$ (**Ru-L^{2+}**, where tpy = 2,2′:6′,2′′-terpyridine, bpy = 2,2′-bipyridine, and L = pyridine and MeCN) as a photocatalyst and NEt_3 as a reductant has been clarified. On the basis of this mechanistic study, an efficient and durable photocatalytic system for selective hydride reduction of an NAD(P)$^+$ model compound has been developed. The photocatalytic reaction is initiated by the formation of $[Ru(tpy)(bpy)(NEt_3)]^{2+}$ (**Ru-NEt$_3$$^{2+}$**) via the photochemical ligand substitution of **Ru-L^{2+}**. For this reason, the production rate of 1,4-BNAH using $[Ru(tpy)(bpy)(MeCN)]^{2+}$ (**Ru-MeCN^{2+}**) as a photocatalyst, from which the quantum yield of photoelimination of the MeCN ligand is greater than that of the pyridine ligand from $[Ru(tpy)(bpy)(pyridine)]^{2+}$ (**Ru-py^{2+}**), was faster than that using **Ru-py^{2+}**, especially in the first stage of the photocatalytic reduction. The photoexcitation of **Ru-NEt$_3$$^{2+}$** yields $[Ru(tpy)(bpy)H]^+$ (**Ru-H$^+$**), which reacts with **BNA$^+$** to give 1:1 adduct [Ru(tpy)(bpy)(1,4-BNAH)]$^{2+}$ (**Ru-BNAH^{2+}**). In the presence of excess NEt_3 in the reaction solution, a deprotonation of the carbamoyl group in **Ru-BNAH^{2+}** proceeds rapidly, mainly forming [Ru(tpy)(bpy)(1,4-BNAH-H$^+$)]$^+$ (**Ru-(BNAH-H$^+$)$^+$**). Although photocleavage of the adduct yields **1,4-BNAH** and the cycle is completed by the re-coordination of a NEt_3 molecule to the Ru(II) center, this process competes with hydride abstraction from **Ru-(BNAH-H$^+$)$^+$** by **BNA$^+$** giving **1,4-BNAH** and [Ru(tpy)(bpy)(BNA$^+$-H$^+$)]$^{2+}$. This adduct was observed as the major complex in the reaction solution after the photocatalysis was depressed and is a dead-end product because of its stability. Based on the information about the reaction mechanism and the deactivation process, we have successfully developed a new photocatalytic system using **Ru-MeCN^{2+}** with 2 M of NEt_3 as a reductant, which could reduce more than 59 equivalent amounts of an NAD(P)$^+$ model, 1-benzyl-*N*,*N*-diethylnicotinamidium cation, selectively to the corresponding 1,4-dihydro form in a 6×10^{-4} quantum yield using 436-nm light.

Introduction

Reductions of various kinds of organic compounds using the coenzyme NAD(P)H and model compounds have been well studied for several decades.[1] For example, asymmetric reductions of unsaturated substrates have been reported using NAD(P)H models with a chiral center or chiral centers, and some of their reactions yielded high enantiomeric excesses.[1f,2] From the standpoint of organic synthesis, the stoichiometric requirement of the NAD(P)H model is a problem; therefore, a catalytic system is needed to reduce the oxidized form.[3,4] The system has to provide two types of selectivities: (1) chemoselectivity, where only hydride reduction should occur without producing the corresponding radical coupling products, and (2)

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(1) (a) Yasui, S.; Ohno, A. *Bioorg. Chem.* **1986**, *14*, 70–96. (b) Lavilla, R. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1141–1156. (c) Fox, M. A.; Chanon, M. *Photoinduced electron transfer, Part C*; Elsevier: New York, 1988. (d) Stout, D. M.; Meyers, A. I. *Chem. Rev.* **1982**, *82*, 223–243. (e) Pac, C.; Ishitani, O. *Photochem. Photobiol.* **1988**, *48*, 767–785. (f) Ohno, A. In *Asymmetric Reactions and Processes in Chemistry*, ACS: Washington, D. C., 1982; pp 219−228. (g) Pac, C.; Kaseda, S.; Ishii, K.; Yanagida, S.; Ishitani, O. In *Photochemical Processes in Organized Molecular Systems*; Honda, K., Kitamura, M., Masuhara, H., Ikeda, T., Sisido, M., Winnik, M. A., Eds.; Elsevier: Amusterdam, 1991, pp 177−186.

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(3) (a) Ishitani, O.; Inoue, N.; Koike, K.; Ibusuki, T. *J. Chem. Soc., Chem. Commun.* **1994**, 367–368. (b) Wienkamp, R.; Steckhan, E. *Angew. Chem., Int. Ed.* **1983**, *22*, 497. (c) Polyansky, D.; Cabelli, D.; Muckerman, J. T.; Fujita, E.; Koizumi, T.; Fukushima, T.; Wada, T.; Tanaka, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 4169–4172. (d) Polyansky, D. E.; Cabelli, D.; Muckerman, J. T.; Fukushima, T.; Tanaka, K.; Fujita, E. *Inorg. Chem.* **2008**, *47*, 3958–3968.

(4) Lo, H. C.; Leiva, C.; Buriez, O.; Kerr, J. B.; Olmstead, M. M.; Fish, R. H. *Inorg. Chem.* **2001**, *40*, 6705–6716.

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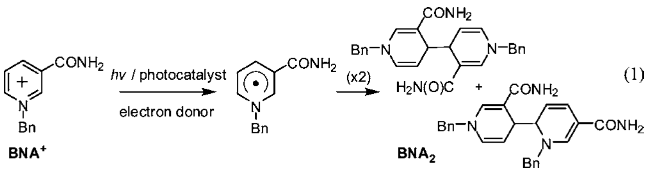
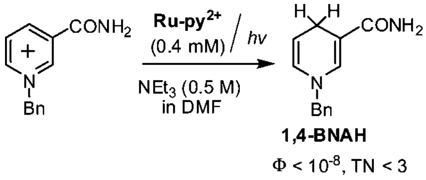
regioselectivity, where the 1,4-dihydro form should be produced without producing the corresponding 1,2- and 1,6-dihydro forms.

In the photosynthesis of green plants, two electrons photochemically collected from water are injected into one molecule of $NADP^+$ by the action of ferredoxin-NADP reductase, which selectively generates the 1,4-dihydro form, i.e., NADPH. This reaction has an important role in the conversion of a photochemical one-electron transfer into the two-electron reduction. The development of artificial photocatalytic systems with this function has been an attractive and important research subject for both constructing artificial photosynthesis and recycling the $NAD(P)^+$/NAD(P)H models under varying mild conditions, including room temperature and weak reductant use. However, there are only a few photocatalytic systems which can reduce $NAD(P)^+$ and/or the models with the two selectivities as described above.[3] Most of the redox photocatalysts drive only one-electron transfer by absorption of one photon and can inject only one electron at a time into the $NAD(P)^+$ model, which is a good electron acceptor as well.[1g] As a typical example, the one-electron reduction potential of 1-benzylnicotinamidium cation (**BNA^+**) is −1.08 V in MeCN vs SCE, and it is difficult to reduce the $NAD(P)^+$ model electrochemically into the dihydro form with a good yield because of the fast dimerization process of the radical (**$BNA^•$**) to give the corresponding dimers (**BNA_2**, eq 1).[5]



(1)

A rare successful system utilizes the combination of $[Ru(tpy)(bpy)(pyridine)]^{2+}$ (**$Ru\text{-}py^{2+}$**, where tpy = 2,2′:6′,2″-terpyridine and bpy = 2,2′-bipyridine) as a photocatalyst and triethylamine (NEt_3) as a reductant, which can selectively catalyze the hydride reduction of **BNA^+** to the corresponding 1,4-dihydro form (**1,4-BNAH**, eq 2).[3a] In this photocatalytic reaction, the regioisomers of the **1,4-BNAH**, i.e., 1,6-dihydro and 1,2-dihydro forms, and the radical coupling products of **BNA_2** are not produced at all. However, both the efficiency ($\Phi < 10^{-8}$) and the durability (turnover number <3) are too low for this system to be utilized to regenerate the NAD(P)H model compound.



(2)

Here, we report the details of the photocatalytic reaction mechanism and the development of a much more efficient and durable photocatalytic system for the hydride reduction of an $NAD(P)^+$ compound ($\Phi = 6 \times 10^{-4}$, TN > 59), based on the mechanistic study.

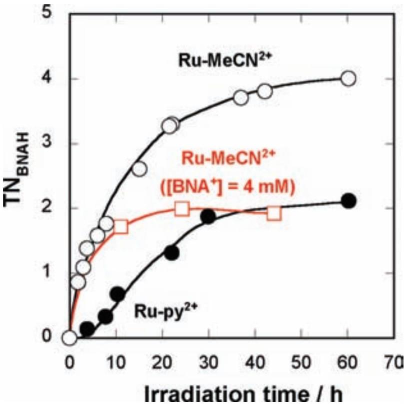
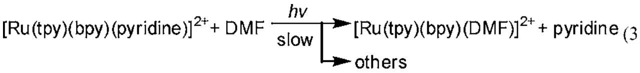


Figure 1. Turnover number (TN) for photocatalytic production of **1,4-BNAH** as a function of irradiation time. A DMF solution containing **$Ru\text{-}py^{2+}$** (●) or **$Ru\text{-}MeCN^{2+}$** (○) (0.4 mM), **BNA^+** (2 mM), and NEt_3 (0.5 M) was irradiated (>500 nm) under an Ar atmosphere. The red line shows the case using a higher concentration of **BNA^+** (4 mM) with **$Ru\text{-}MeCN^{2+}$** (0.4 mM) and NEt_3 (0.5 M).

Result and Discussion

Effect of the Monodentate Ligand. In a typical run, a DMF solution (4 mL) containing a ruthenium complex (0.4 mM), **BNA^+** (2 mM), and NEt_3 (0.5 M) was irradiated with >500-nm light using a high-pressure mercury lamp and a cutoff filter under an Ar atmosphere. In two separate cases using **$Ru\text{-}py^{2+}$** and $[Ru(tpy)(bpy)(MeCN)]^{2+}$ (**$Ru\text{-}MeCN^{2+}$**)[6] as photocatalysts, **1,4-BNAH** was selectively produced and one-electron-reduced dimers (**BNA_2**) were not detected at all. However, the lengths of time to produce **1,4-BNAH** were different in the two cases (Figure 1). Using **$Ru\text{-}py^{2+}$**, the previously reported photocatalyst (eq 2), an induction period of about 5 h was observed for the production of **1,4-BNAH**, which stopped at the turnover number, TN = 2. In the case of **$Ru\text{-}MeCN^{2+}$**, no such induction period was observed, and the rate of **1,4-BNAH** formation was much faster than the one using **$Ru\text{-}py^{2+}$**. The TN increased to 4, and the yield of **1,4-BNAH** was 80% based on **BNA^+** used after irradiation for 60 h. However, the increased concentration of the added **BNA^+** (4 mM) lowered the TN (red line in Figure 1).

To start this photocatalytic reaction, evidence strongly suggests that it is necessary to form $[Ru(tpy)(bpy)(NEt_3)]^{2+}$ (**$Ru\text{-}NEt_3^{2+}$**) by photochemical ligand substitution with the reductant NEt_3.[3a] Therefore, the efficiency of the photochemical ligand substitution of the monodentate ligand should strongly affect whether the induction period is observed. In fact, the efficiency of such a reaction of **$Ru\text{-}py^{2+}$** was low ($\Phi < 10^{-5}$) in DMF, and undesirable side reactions also occurred (eq 3, Figure S1).



$$[Ru(tpy)(bpy)(pyridine)]^{2+} + DMF \xrightarrow[slow]{h\nu} [Ru(tpy)(bpy)(DMF)]^{2+} + pyridine \quad (+\ others) \tag{3}$$

In contrast, the photochemical ligand substitution of the MeCN ligand of **$Ru\text{-}MeCN^{2+}$** with DMF quantitatively proceeded with a much higher quantum yield, $\Phi = 6 \times 10^{-3}$, in DMF (eq 4, Figure S2).[9]

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(5) (a) Schmakel, C. O.; Santhanam, K. S. V.; Elving, P. J. *J. Am. Chem. Soc.* **1975**, *97*, 5083–5092. (b) Jaegfeldt, H. *Bioelectrochem. Bioenerg.* **1981**, *8*, 355–370. (c) Ohnishi, Y.; Kitami, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2674–2677. (d) Kano, K.; Matsuo, T. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3269–3273.

(6) **$Ru\text{-}DMF^{2+}$** also worked as a precursor of the photocatalyst as well as **$Ru\text{-}MeCN^{2+}$**. However, **$Ru\text{-}MeCN^{2+}$** can be more easily synthesized and appropriate to be stored. Therefore, we used **$Ru\text{-}MeCN^{2+}$** in this study.

$$[\mathrm{Ru(tpy)(bpy)(MeCN)}]^{2+} + \mathrm{DMF} \xrightarrow[\text{fast}]{h\nu} [\mathrm{Ru(tpy)(bpy)(DMF)}]^{2+} + \mathrm{MeCN} \quad (4)$$

Since it has been reported that the photochemical ligand substitution reactions of Ru(II) polypyridine complexes proceed through the dissociative mechanism,[7] it is reasonable that **Ru-NEt$_3^{2+}$** efficiently formed as one of the products of the photochemical ligand substitution reaction of **Ru-MeCN^{2+}** in the photocatalytic reaction solution containing 0.5 M of NEt_3 (eq 5), and this is why the production rate of **1,4-BNAH** was faster using **Ru-MeCN^{2+}** compared with **Ru-py^{2+}**.

$$[\mathrm{Ru(tpy)(bpy)(MeCN)}]^{2+} + \mathrm{NEt_3} \xrightarrow{h\nu} [\mathrm{Ru(tpy)(bpy)(NEt_3)}]^{2+} + \mathrm{MeCN} \quad (5)$$

It is also suggested that other deactivation process(es) made the TN low in the presence of excess **BNA$^+$**. Therefore, elucidation of the whole picture of the reaction mechanism, especially the deactivation process(es) of the photocatalyst, is required for substantial improvement of the efficiency and the durability of the photocatalytic system.

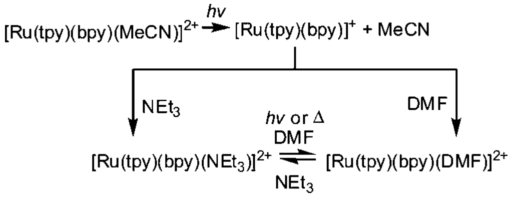
Mechanism. As described above, the coordinative unsaturated species, which is formed by irradiation to **Ru-MeCN^{2+}** in the reaction solution, should react with DMF or NEt_3, yielding **Ru-DMF^{2+}** and **Ru-NEt$_3^{2+}$** in a ratio depending on the concentration of NEt_3 (Scheme 1).[8] The ligand substitution reaction between DMF and NEt_3 probably takes place even in the dark. It has been reported that the equilibrium constants (K) of **Ru-NEt$_3^{2+}$** with $[\mathrm{Ru(tpy)(bpy)(CD_2Cl_2)}]^{2+}$ and $[\mathrm{Ru(tpy)(bpy)(THF)}]^{2+}$ are $(9.8 \pm 1.2) \times 10^3$ and 6.9 ± 2.1, respectively (eq 6).[9]

$$[\mathrm{Ru(tpy)(bpy)(S)}]^{2+} + \mathrm{NEt_3} \overset{K}{\rightleftharpoons} [\mathrm{Ru(tpy)(bpy)(NEt_3)}]^{2+} + \mathrm{S} \quad (=\mathrm{CD_2Cl_2},\ \mathrm{THF}) \quad (6)$$

Although the equilibrium constant between **Ru-NEt$_3^{2+}$** and **Ru-DMF^{2+}** has been unknown, it is possibly smaller compared with the two above constants because of the higher coordination ability of DMF than CD_2Cl_2 and THF. However, since the efficiency of the photochemical ligand substitution of the DMF ligand in **Ru-DMF^{2+}** is relatively high ($\Phi = 8 \times 10^{-2}$),[9] **Ru-NEt$_3^{2+}$** should be also continuously formed by the photochemical ligand substitution of **Ru-DMF^{2+}** when **Ru-NEt$_3^{2+}$** is converted to **Ru-H$^+$** during the photocatalytic reaction (Scheme 1).

We have recently reported that the formation of **Ru-H$^+$** proceeds quantitatively with a quantum yield of 3.4×10^{-3} via excitation of **Ru-NEt$_3^{2+}$** in a THF solution containing 2 M of NEt_3.[9] Irradiation with 436-nm light to a DMF solution containing **Ru-MeCN^{2+}** and NEt_3 (2 M) also made **Ru-H$^+$**, but the yield was 42% for 1-h irradiation (eq 7). The formation rate of **Ru-H$^+$** ($\Phi_{\mathrm{Ru-H}} = 1.1 \times 10^{-3}$) was about 3 times lower than that in the THF solution (Figure S3), probably because of the lower concentration of **Ru-NEt$_3^{2+}$** in the DMF solution compared with the THF solution.[10] Therefore, it is reasonable that **Ru-H$^+$** was also produced via the photochemical ligand substitution of the MeCN ligand with NEt_3 (Scheme 1) followed by the photochemical conversion of **Ru-NEt$_3^{2+}$** (eq 8) in the photocatalytic reaction solution.

Scheme 1. Photochemical, Ligand Substitution Reaction of **Ru-MeCN^{2+}** and Equilibrium between the Products in the Reaction Solution



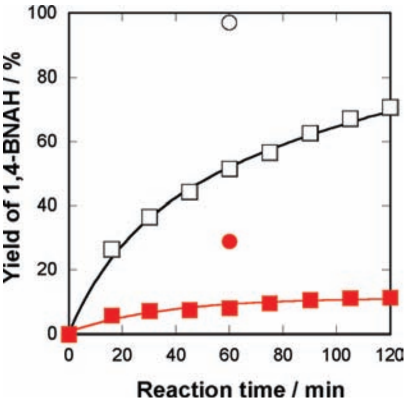


Figure 2. Formation yields of **1,4-BNAH** from the adducts. The circles show photochemical formation of **1,4-BNAH** for 45 min of irradiation with 436-nm light under an Ar atmosphere after **Ru-H$^+$** (8 mM) and **BNA$^+$** (8 mM) were mixed in DMF containing 0.5 M of NEt_3 (●) and in the absence of NEt_3 (○). Sample preparation and NMR measurement required a total of 15 min. The squares show **1,4-BNAH** formation in the dark under an Ar atmosphere in the DMF solutions containing 0.5 M of NEt_3 (■) and in the absence of NEt_3 (□). The yields of **1,4-BNAH** were based on **Ru-H$^+$** used.

$$[\mathrm{Ru(tpy)(bpy)(MeCN)}]^{2+} \xrightarrow[\text{2 M NEt}_3\text{ in DMF}]{h\nu\ \text{(436 mn), 1 h}} [\mathrm{Ru(tpy)(bpy)H}]^{+} \quad (42\%) \quad (7)$$

$$[\mathrm{Ru(tpy)(bpy)(NEt_2)}]^{2+} \xrightarrow[\text{2 M NEt}_3\text{ in DMF}]{h\nu} [\mathrm{Ru(tpy)(bpy)H}]^{+} \quad (8)$$

We have also reported that **Ru-H$^+$** reacts with **BNA$^+$** in a DMF solution to give a 1:1 adduct (**Ru-BNAH^{2+}**), of which the carbamoyl group coordinates to the Ru(II) center.[11] Because the formation of **Ru-BNAH^{2+}** is fast ($k_2 = 1.7 \times 10^3\ \mathrm{M^{-1}\ s^{-1}}$ at 27 °C in DMF), the same reaction should proceed during the photocatalytic reaction. The adduct quantitatively cleaved to **1,4-BNAH** and the solvento complex **Ru-DMF^{2+}** slowly in a DMF solution in the dark for a period of several hours (eq 9).[11] It was found, on the other hand, that the cleavage of **Ru-BNAH^{2+}** was accelerated by irradiation (Figure 2) and yielded **1,4-BNAH** and **Ru-DMF^{2+}** quantitatively. No regioisomers of **1,4-BNAH** and one-electron-reduced dimers formed during irradiation.

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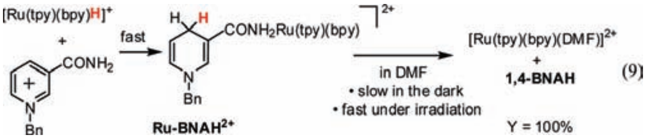
(7) Hecker, C. R.; Fanwick, P. E.; McMillin, D. R. *Inorg. Chem.* **1991**, *30*, 659–666.

(8) PF_6^-, which has a very weak coordination ability, is used as a counter anion of both **Ru-MeCN^{2+}** and **BNA$^+$**.

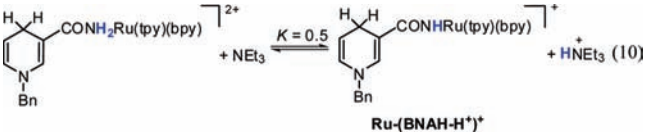
(9) Matsubara, Y.; Konno, H.; Kobayashi, A.; Ishitani, O. *Inorg. Chem.* **2009**, *48*, 10138–10145.

(10) Irradiation to a THF solution containing **Ru-DMF^{2+}** and 2 M of NEt_3 for 2 h produced **Ru-H$^+$** quantitatively.[9] However, THF is not a suitable solvent for the photocatalytic reaction because an irreversible reaction slowly took place in the solution even when the solution was kept in the dark, and the product(s) did not have any photocatalytic ability.

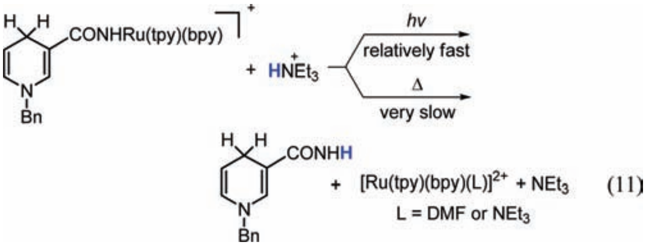
(11) Kobayashi, A.; Takatori, R.; Kikuchi, I.; Konno, H.; Sakamoto, K.; Ishitani, O. *Organometallics* **2001**, *20*, 3361–3363.



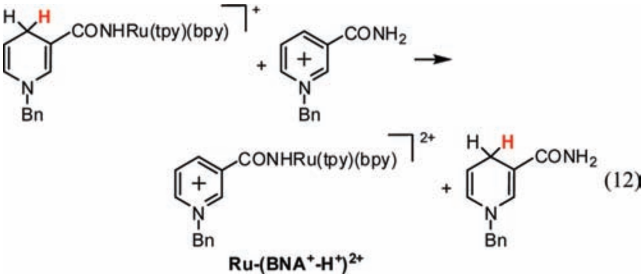
On the other hand, in the presence of NEt_3 (0.5 M), the rate of the splitting of the adduct was much slower in the dark than that in the absence of NEt_3 (Figure 2). It is likely that this is due to the deprotonation from the carbamoyl group in **Ru-BNAH**$^{2+}$ by NEt_3, giving another 1:1 adduct **Ru-(BNAH-H**$^+$**)**$^+$ (eq 10) because the acid−base equilibrium constant, which has been reported as 0.5,[12,13] indicates that most of the formed **Ru-BNAH**$^{2+}$ is converted to **Ru-(BNAH-H**$^+$**)**$^+$ (>99.8%) in the reaction solution containing 0.5 M of NEt_3 (see Supporting Information). Photochemical splitting of **Ru-(BNAH-H**$^+$**)**$^+$ also takes place to make **1,4-BNAH** (eq 11). However, its production rate was slower compared with that of **Ru-BNAH**$^{2+}$ (Figure 2).



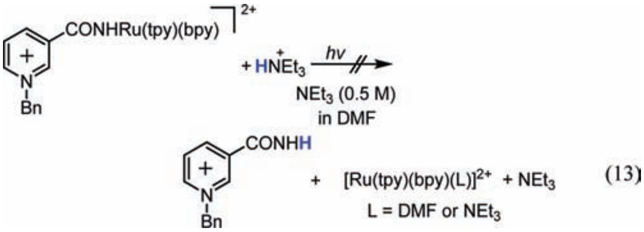
Photocleavage of **Ru-(BNAH-H**$^+$**)**$^+$ was slower than that of **Ru-BNAH**$^{2+}$ (eq 11) as described above. This is understandable because most photochemical ligand substitution of ruthenium polypyridyl complexes takes place via thermal transition from the ^{3}MLCT state to the ^{3}d−d state.[7,14] The efficiency of such a photochemical ligand substitution should decrease when the d−d splitting is enlarged by coordination of the deprotonated carbamoyl group, where σ donor ability is greater than that of the protonated one and, consequently, the energy gap between the ^{3}MLCT state and the ^{3}d−d state should also be greater.



Although **Ru-(BNAH-H**$^+$**)**$^+$ is relatively stable in the absence of oxidants such as O_2 and **BNA**$^+$ in the dark, it is more easily oxidized by the oxidant compared with **Ru-BNAH**$^{2+}$ and free **1,4-BNAH** (eq 12) because of its lower oxidation potential (E_p^{ox} = −0.04 V vs $Ag/AgNO_3$ for **Ru-(BNAH-H**$^+$**)**$^+$, 0.55 V for **Ru-BNAH**$^{2+}$ (without NEt_3), and 0.32 V for **1,4-BNAH** in MeCN with 0.2 M of NEt_3).[13] The ESI mass spectrum of the reaction solution after 37 h of irradiation, when the production of **1,4-BNAH** almost stopped (see Figure 1), showed the main peak corresponding to **Ru-(BNA**$^+$**-H**$^+$**)**$^{2+}$ (m/z = 351.3, calced 351.6), which is the deprotonated 1:1 adduct of the Ru moiety and deprotonated **BNA**$^+$, with small peaks at m/z = 848.4 ([**Ru-(BNA**$^+$**-H**$^+$**)** + PF_6]$^+$), 261.4 ([Ru(tpy)(bpy)(MeOH)]$^{2+}$; MeOH was the eluent), and 281.5 ([**Ru-DMF**]$^{2+}$) (Figure S4). Therefore, **Ru-(BNAH-H**$^+$**)**$^+$ with strong reducing power should transfer the hydride to free **BNA**$^+$ during the photocatalytic reaction, making free **1,4-BNAH** and **Ru-(BNA**$^+$**-H**$^+$**)**$^{2+}$ (eq 12).[13]



During the photocatalytic reaction, therefore, this hydride transfer reaction competes with the photochemical cleavage of **Ru-(BNAH-H**$^+$**)**$^+$ (eq 11) because of the presence of an excess amount of **BNA**$^+$ in the photocatalytic reaction solution. A main deactivation process in the photocatalytic reaction should be the formation of **Ru-(BNA**$^+$**-H**$^+$**)**$^{2+}$ because **Ru-(BNA**$^+$**-H**$^+$**)**$^{2+}$ did not cleave at room temperature, even after irradiation for 12 h in a DMF solution containing NEt_3 (eq 13).



The branching ratio between splitting of **Ru-BNAH**$^{2+}$ and **Ru-(BNAH-H**$^+$**)**$^+$ and its oxidation by **BNA**$^+$, $(\alpha + \beta):(1 - \alpha - \beta)$, in the photocatalytic reaction solution (Scheme 2) can be calculated using eq 14 (n is the number of the reaction cycles) and TN. When the initial concentration of **BNA**$^+$ was 2 mM, $\alpha + \beta$ was 0.75. On the other hand, $\alpha + \beta$ was decreased to 0.5 when the initial concentration of **BNA**$^+$ was twice as much (4 mM). This is understandable become the oxidation rate of **Ru-(BNAH-H**$^+$**)**$^+$ should be proportional to the concentration of **BNA**$^+$.

$$\mathrm{TN} = 1 + \sum_{n=1}^{\infty} (\alpha + \beta)^n \tag{14}$$

Now we can conclude that the mechanism of the photocatalytic hydride reduction of **BNA**$^+$ with [Ru(tpy)(bpy)(MeCN)]$^{2+}$ as a photocatalyst and NEt_3 as a reductant is as shown in Scheme 2. (1) The reaction is initiated by the photochemical formation of **Ru-NEt$_3$**$^{2+}$ via the elimination of the MeCN ligand followed by the coordination of NEt_3 to the Ru(II) center. Although **Ru-DMF**$^{2+}$ also formed competitively, it can be converted to **Ru-NEt$_3$**$^{2+}$ photochemically and thermally. (2) **Ru-NEt$_3$**$^{2+}$ is photochemically converted to **Ru-H**$^+$. (3) **Ru-H**$^+$ reacts with

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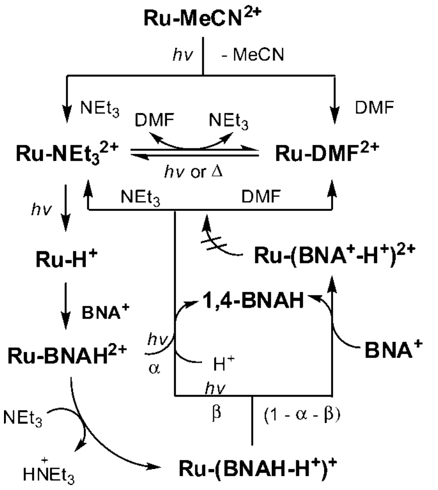
(12) Addition of 0.2 M of piperidine (pK_a = 18.9 in acetonitrile: Coetzee, J. F.; Padmanabhan, G. R. *J. Am. Chem. Soc.* **1965**, *87*, 5005–5010) which is a stronger base than NEt_3 (pK_a = 18.5), into the DMF solution containing **Ru-BNAH**$^{2+}$ caused almost total (∼100%) complex conversion to **Ru-(BNAH-H**$^+$**)**$^+$.[13] In this solution, **Ru-(BNAH-H**$^+$**)**$^+$ did not cleave to **1,4-BNAH** and the solvento complex at room temperature in the dark for several hours. Because in the reaction condition of Figure 2, 3% of **Ru-BNAH**$^{2+}$ remained in the solution, **1,4-BNAH** mostly formed from **Ru-BNAH**$^{2+}$.

(13) Kobayashi, A.; Konno, H.; Sakamoto, K.; Sekine, A.; Ohashi, Y.; Iida, M.; Ishitani, O. *Chem.*—*Eur. J.* **2005**, *11*, 4219–4226.

(14) Campagna, S.; Puntoriero, F.; Nastasi, F.; Bergamini, G.; Balzani, V. *Top. Curr. Chem.* **2007**, *280*, 117–214.

Scheme 2. Mechanism of the Photocatalytic Reduction of **BNA$^+$** Using **Ru-MeCN^{2+}**[a]



[a] α:β:(1 − α − β) denotes the branching ratio among splitting of **Ru-BNAH^{2+}**, splitting of **Ru-(BNAH-H$^+$)$^+$**, and oxidation of **Ru-(BNAH-H$^+$)$^+$** by **BNA$^+$**.

BNA$^+$, giving the 1:1 adduct **Ru-BNAH^{2+}**, most of which is converted to the deprotonated form **Ru-(BNAH-H$^+$)$^+$** by NEt_3. Photocleavage of both **Ru-BNAH^{2+}** and **Ru-(BNAH-H$^+$)$^+$** yields not only **1,4-BNAH** but also **Ru-NEt$_3$$^{2+}$** and **Ru-DMF^{2+}** by coordination of NEt_3 or DMF to the Ru(II) center. Although **1,4-BNAH** is also produced by the reduction of **BNA$^+$** with **Ru-(BNAH-H$^+$)$^+$**, the photocatalytic reaction is inhibited by accumulation of another product **Ru-(BNA$^+$-H$^+$)$^{2+}$** due to its thermal and photochemical stability.

Development of a Durable and Efficient Photocatalytic System. On the basis of the information about the reaction mechanism as described above, we tried to develop a photocatalytic system with not only higher efficiency but also much better durability, as follows: (1) **Ru-MeCN^{2+}** was used as a starting complex which can be efficiently converted to **Ru-NEt$_3$$^{2+}$** by irradiation; (2) to increase the content of **Ru-NEt$_3$$^{2+}$** as precursor of **Ru-H$^+$**, the concentration of NEt_3 was increased 4 times, i.e., 2 M;[15] and (3) to block the deprotonation from the adduct, which causes the depression of the cleavage of **Ru-BNAH^{2+}** and the formation of the deactivation complex, 1-benzyl-*N*,*N*-diethylnicotinamidium cation (**BNEt$_2$A$^+$**) was used as an NAD(P)$^+$ model compound, with higher concentration (20 mM) (eq 15).[16]

As a typical run, Figure 3 shows the production of 1-benzyl-*N*,*N*-diethyl-1,4-dihydronicotinamide (**1,4-BNEt$_2$AH**) by irradiation to a DMF solution containing both PF_6^- salts of **Ru-MeCN^{2+}** (0.4 mM) and **BNEt$_2$A$^+$** (20 mM) and NEt_3 (2 M). There was no induction period for the formation of **1,4-BNEt$_2$AH**, whose quantum yield was 6×10^{-4} and tremendously higher than that of the previously reported system using **Ru-py^{2+}**, **BNA$^+$**, and 0.5 M of NEt_3 (Figure 1), especially in the first stage of the photocatalytic reactions.[3a] After irradiation for 24 h, 76% of **BNEt$_2$A$^+$** was reduced to **1,4-BNEt$_2$AH** (TN = 38) without other isomers and one-electron-reduced dimers. Analysis of the irradiated solution with GC-FID after an addition of a small amount of water clearly showed that the same amount of diethylamine formed as **1,4-BNEt$_2$AH** produced (eq 15). Diethylamine should be produced with formaldehyde via a hydrolysis of the two-electron oxidation product of NEt_3 (eq 16).[17] Moreover, it is noteworthy that this photocatalytic system has long durability. Although the TN of **1,4-BNEt$_2$AH** formation was 38 for the 24-h irradiation, addition of 20 mM of **BNEt$_2$A$^+$** to the irradiated solution and re-irradiation for 24 h increased the TN to 59 (Figure 3). Only a very small amount of **1,4-BNEt$_2$AH** was produced without irradiation or in the absence of **Ru-MeCN^{2+}**.[16]

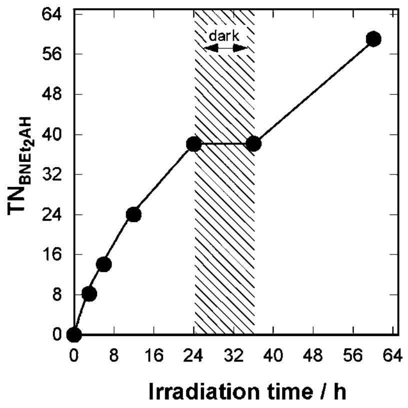
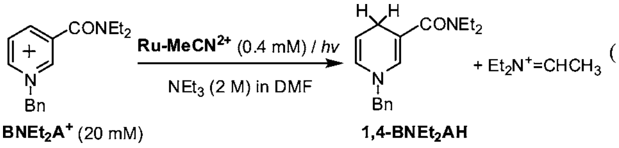


Figure 3. Photocatalytic formation of **1,4-BNEt$_2$AH**. A DMF solution containing **Ru-MeCN^{2+}** (0.4 mM), **BNEt$_2$A$^+$** (20 mM), and NEt_3 (2 M) was irradiated (>500 nm) under an Ar atmosphere. After the solution was irradiated for 24 h and then kept in the dark for 12 h, **BNEt$_2$A$^+$** (20 mM) was added to the solution, and then the solution was irradiated again.



(15)

$$NEt_3 \xrightarrow{2e^- + H^+} Et_2N^+{=}CHCH_3 \xrightarrow{H_2O} Et_2NH + CH_3CHO + H^+ \qquad (16)$$

Conclusion

The mechanism of reduction of **BNA$^+$** using $[Ru(tpy)(bpy)(MeCN)]^{2+}$ as a photocatalyst and NEt_3 as a reductant has been clarified. Based on this mechanistic investigation, a much more efficient and durable photocatalytic system for hydride reduction, which can reduce the NAD(P)$^+$ model to the corresponding 1,4-dihydro form with $\Phi = 6 \times 10^{-4}$ and TN $\geq$ 59, compared with the previously reported system ($\Phi < 10^{-8}$, TN < 3), has been successfully developed. This photocatalytic system can accumulate the NAD(P)H model in the reaction solution without its photochemical reoxidation because the photocatalytic reaction does not proceed via intermolecular electron transfer.

Experimental Section

General Procedures. UV−vis absorption spectra were recorded using a JASCO V-565 or MCPD-2000 (Otsuka Electronic Co.)

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(15) The solubility of the NAD(P)$^+$ model compound is too low in a DMF solution containing NEt_3 of a higher concentration than 2 M.

(16) **BNA$^+$** is slowly reduced by NEt_3 in the dark, yielding not only **1,4-BNAH** but also its isomers: Ohnishi, Y. *Tetrahedron Lett.* **1977**, *24*, 2109–2112 and Ohno, A.; Ushida, S.; Oka, S. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 506–509. In the case of **BNEt$_2$A$^+$**, however, formation of the corresponding dihydro form was much slower. Less than 3% of 20 mM of **BNEt$_2$A$^+$** was reduced to the **1,4-BNEt$_2$AH** for 24 h in a DMF solution containing NEt_3 (2 M).

(17) (a) Castedo, L.; Riguera, R.; Vazquez, M. P. *J. Chem. Soc., Chem. Commun.* **1983**, 301–302. (b) Cohen, S. G.; Stein, N. M. *J. Am. Chem. Soc.* **1971**, *93*, 6542–6551. (c) Russell, C. D. *Anal. Chem.* **1963**, *35*, 1291–1292. (d) Smith, P. J.; Mann, C. K. *J. Org. Chem.* **1969**, *34*, 1821–1826.

spectrometer. Electrospray ionization mass (ESI-MS) spectra were obtained by a Shimazu LCMS-2010A system with HPLC-grade methanol as a mobile phase. The reduced products of the NAD(P)$^+$ model compounds were analyzed using a HPLC system with a Nomura ODS-UG-5 column, a Shimazu ST-50 pump with a Rheodyne 7125 injector, and a Shimazu UV-50 detector (detected wavelength: 340 nm for **1,4-BNEt$_2$AH**; 360 nm for **1,4-BNAH**). Mixed solutions of MeOH/KH_2PO_4−NaOH buffer (PH 7, 0.05 M, 3:2 v/v for **1,4-BNEt$_2$AH** and 1:1 v/v for **1,4-BNAH**) were used as eluent. Diethylamine was analyzed using a Shimazu GC-17A gas chromatograph with a flame ionization detector (FID) and an InertCap for Amines capillary column (GL Sciences Inc. GC69249) after addition of water to the reaction solution.

Materials. Dimethylformamide (DMF) was dried over 4-Å molecular sieves and distilled at reduced pressure before use. Triethylamine (NEt_3) was dried over potassium hydroxide and distilled under an argon atmosphere before use. Other purchased chemicals were reagent grade and used without further purification. [Ru(tpy)(bpy)(pyridine)]$(PF_6)_2$,[7] [Ru(tpy)(bpy)(MeCN)]$(PF_6)_2$,[7] [Ru(tpy)(bpy)H]$(PF_6)\cdot 0.5H_2O$,[18] hexafluorophosphate salts of the NAD(P)$^+$ model compounds (**BNA**$^+$[19] and **BNEt$_2$A**$^+$[20]), and the corresponding 1,4-dihydro forms (**1,4-BNAH**[19] and **1,4-BNEt$_2$AH**[20]) were prepared according to the reported methods. The 1:1 adduct [Ru(tpy)(bpy)(1,4-BNAH)]$^{2+}$ was synthesized by the *in situ* preparation method.[13]

Photocatalytic Reductions. A DMF−NEt_3 mixed solution (4 mL) containing a ruthenium complex (0.4 mM) and an NAD(P)$^+$ model compound (2 mM) was bubbled with argon for 15 min in a Pyrex test tube (i.d. = 8 mm), and then the test tube was sealed using a rubber septum (Aldrich Z553921). The solution was irradiated by a 500 W high pressure Hg lamp (Eikosha Co.) combined with an uranyl glass and a K_2CrO_4 (30 wt %, light-pass length: 1 cm) solution filter (>500 nm) with a merry-go-round irradiation apparatus. The quantum yield was measured using the same reaction solution which was placed in a quartz cuvette (10 × 10 × 40 mm), kept at 25 ± 1 °C using a temperature control unit, and irradiated at 436 nm using a 500-W high-pressure Hg lamp (USHIO Inc.) combined with a band-pass filter (436 ± 5 nm, Asahi Spectra Co.). The incident light intensity into the solution was 0.16 ± 0.02 μeinstein s^{-1}, which was determined using a $K_3Fe(C_2O_4)_3$ actinometer.[21]

Photochemical Formation of the Hydrido Complex. A DMF solution (4 mL) containing [Ru(tpy)(bpy)(MeCN)]$(PF_6)_2$ (0.05 mM) and NEt_3 (2 M) was bubbled with argon for 15 min in a quartz cuvette and then the cuvette was sealed with the rubber septum. The solution was kept at 25 ± 1 °C and irradiated at 436 nm using the same apparatus as described above. The yield of [Ru(tpy)(bpy)H]$^+$ was analyzed by the reported procedure.[9]

Photoreaction of [Ru(tpy)(bpy)(1,4-BNAH)]$^{2+}$ and [Ru(tpy)(bpy)(1,4-BNAH-H$^+$)]$^+$. [Ru(tpy)(bpy)H]PF_6 (0.4 mM) and (**BNA**)PF_6 (0.4 mM) were dissolved in 0.5 mL of DMF-d_7, and quickly transferred to a NMR tube under a nitrogen atmosphere. The solution was bubbled with argon for 3 min, and then the NMR tube was sealed using a rubber septum. Just after these procedures, which required about 15 min, the solution was irradiated using a high-pressure Hg lamp with an uranyl glass and the K_2CrO_4 solution filter (>500 nm). The NMR spectrum of the sample was measured within 20 min after the irradiation.

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Supporting Information Available: Figure S1−S4. This material is available free of charge via the Internet at http://pubs.acs.org.

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