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Registry No. **1a**, 13139-15-6; **1b**, 13139-16-7; **1c**, 45170-31-8; **1d**, 53363-89-6; **2a**, 543-27-1; **5a**, 37571-12-3; **5b**, 23010-53-9; **5c**, 86632-69-1; **5c** ($R^1 = PhCH_2OCl(O)$), 86632-70-4; **6a**, 86645-64-9; H-Lys(Z)-OMe, 24498-31-5; H-Lys(Z)-OCH_2Ph, 24458-14-8; Z-MeVal, 42417-65-2; Z-Gly-Val, 33912-87-7; Z-Gly-Phe, 1170-76-9; Z-Gly-Val-Lys(Z)-OCH_2Ph, 86632-71-5; Z-Gly-Phe-Lys(Z)-OCH_2Ph, 86632-72-6; triethylamine, 121-44-8; *N*-methylmorpholine, 109-02-4; *N*-methylpiperidine, 626-67-5.

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Formation of a Novel Type of Adduct between an NADH Model and Carbonyl Compounds by Photosensitization Using Ru(bpy)$_3^{2+}$[1]

Summary: The Ru(bpy)$_3^{2+}$-photosensitized reaction of 1-benzyl-1,4-dihydronicotinamide with several aromatic carbonyl compounds gave 1:1 adducts of the 4-substituted dihydronicotinamide structure in moderate to good yields along with less efficient reduction or no reduction to the corresponding alcohols; di-2-pyridyl ketone was exclusively reduced to the alcohol.

Sir: Reactions of 1,4-dihydropyridines have received much attention in relation with biological processes involving NAD(P)H.[2] Although extensive studies are focused on reductions of unsaturated substrates from mechanistic and synthetic points of view, addition of nucleophiles to the C_5–C_6 double bond of NADH models has also been well documented.[3] Reactions of NADH models with aromatic carbonyl compounds in aqueous solution lead to addition of both water and substrate molecules to the C_5–C_6 bond, giving 1:1:1 adducts.[4-6] The adduct formation was suggested to be of mechanistic importance in relation with reduction of carbonyl compounds.[5,6] We report here that the photosensitized reactions of 1-benzyl-1,4-dihydronicotinamide (BNAH) with aromatic carbonyl compounds **1a–f** by Ru(bpy)$_3^{2+}$ (bpy = 2,2′-bipyridine) afford a novel type of 1:1 adducts **3a–e** unlike the products of dark reactions. This type of adduct formation has only a few precedents in reactions with olefins.[7,8]

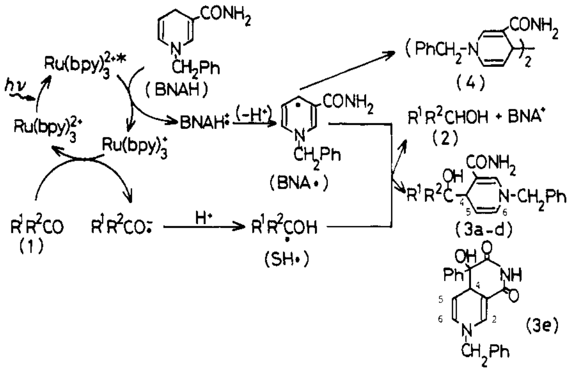
Deaerated metanolic solutions containing Ru(bpy)$_3$Cl$_2$·6H$_2$O (1×10^{-3} M), BNAH (0.1 M), and **1a–f** (0.05 M) were irradiated at >470 nm under cooling with water.[9] The progress of the reactions was followed by VPC, and the products were isolated by column chromatography on basic alumina; Table I summarizes the results. In cases **3a–d**, 1:1 mixtures of the diastereoisomers were obtained, from which each isomer was separated by repeated chromatography. Each of the isomers **3a**, **3b** and **3d** was isolated as a crystalline material while the other isomers and both isomers of **3c** remained oily. On the other hand, **3e** was isolated as a single crystalline isomer of the cyclic imide. In case **1f**, the reduction of **2f** quantitatively occurred without formation of any adduct. The structuers of **3a–e** were deduced from the spectroscopic properties.[10]

Table I. Product Yields in the Ru(bpy)$_3^{2+}$-Photosensitized Reactions of BNAH with 1a–f (R^1R^2CO)[a]

			time,[b]	isolated yields, %		
	R^1	R^2	h	2[c]	3[c,d]	4[e]
1a	C_6H_5	H	15	0	85[f]	<1
1b	p-C_6H_4CN	H	20	16	56[g]	8
1c	2-pyridyl	H	20	20	33[h]	53
1d	C_6H_5	CF_3	15	<4	44[i]	9
1e	C_6H_5	CO_2Me	15	24	60[j]	9
1f	2-pyridyl	2-pyridyl	6	>90	0	50

[a] Methanolic solutions were irradiated at >470 nm under cooling with water (⩽20 °C) where thermal reactions were negligible. [b] Irradiation time required for the complete disappearance of 1a–f. [c] Based on the 1a–f used. [d] Equimolar mixtures of the diastereoisomers except for 3e. [e] Based on the BNAH used. [f] mp 158.5–159 °C dec and oil. [g] mp 164.5–165 °C dec and oil. [h] Both isomers are oily. [i] mp 176.5–177.5 °C dec and oil. [j] A single isomer; mp 223–224 °C dec.

Scheme I



The luminescence of Ru(bpy)$_3^{2+}$ was quenched by BNAH[7] but not at all by **1a–f**. as discussed in a previous paper,[7] the photosensitized reactions are initiated by electron transfer from BNAH to excited Ru(bpy)$_3^{2+}$ followed by one-electron reduction of **1a–f** (Scheme I); Ru(bpy)$_3^{2+}$ can mediate one-electron transfer from BNAH to **1a–f** upon photoexcitation. The followup processes involve BNA· and HS· as intermediates which are formed by facile deprotonation of the cation radical of BNAH[11,12] and by protonation to the anion radical of **1a–f**, respectively, a

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[9] A filter solution containing potassium chromate (30 g/L), sodium nitrate (300 g/L), and sodium hydroxide (10 g/L) was used in order to avoid direct photoexcitation of BNAH. It was confirmed that no reaction occurs in the absence of Ru(bpy)$_3^{2+}$ as well as in the dark.

[10] Sufficient analytical data were obtained for the crystalline compounds. Details of IR, UV, mass spectral, and ^{13}C NMR data that unambiguously support the assigned structures will be published in a full paper.

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process of formal proton transfer. In other words, the photosensitized reactions involve formal electron–proton transfer from BNAH to **1a–f**. Radical-coupling reactions between BNA· and HS· afford **3a–e**, while competitive electron transfer can occur to give **2b–e** in cases where R^1 or R^2 is an electron-withdrawing group. The exclusive reduction of **1f** to **2f** can thus be easily understood, since the two pyridyl groups sterically inhibit the radical-coupling reaction but favor the one-electron reduction of HS· because of the electron-withdrawing nature.

In contrast, thermal reactions in the dark did not give **3a–e** at all.[13] It is known that little reaction occurs with **1a** in the dark.[14] Thermal reactions with **1b** as well as with **1c** gave complex mixtures without the formation of **2b** and **2c**, while quantitative formation of **2d** and **2e** was observed in the cases of **1d** and **1e**, observations in accord with the reported results on thermal reactions of NADH models with **1c–e**.[4,5,15] It is of mechanistic interest to note that the thermal reactions reveal no parallelism with photosensitized reactions at all. On the basis of the photosensitized reactions, it can be expected that the involvement of sequential electron–proton transfer in thermal reactions[16] would yield **3** unless there were specific interactions between the radical species in a solvent cage that inhibit the radical-coupling reaction. In other words, a simple mechanism involving sequential electron–proton–electron transfer without any specific interaction between radical intermediates is inadequate to describe thermal reductions of carbonyl compounds by BNAH and probably by other similar NADH models. Therefore, a direct hydride-transfer mechanism or sequential transfer of an electron and a hydrogen atom may be the best choice. Finally, it should be noted that the photosensitized reaction can provide a synthetic tool for the preparation of **3**.

Registry No. **1a**, 100-52-7; **1b**, 105-07-7; **1c**, 1121-60-4; **1d**, 434-45-7; **1e**, 15206-55-0; **1f**, 19437-26-4; **3a** (isomer 1), 86668-15-7; **3a** (isomer 2), 86668-16-8; **3b** (isomer 1), 86668-17-9; **3b** (isomer 2), 86668-17-9; **3c** (isomer 1), 86668-19-1; **3c** (isomer 2), 86668-20-4; **3d** (isomer 1), 86668-21-5; **3d** (isomer 2), 86668-22-6; **3e**, 86668-23-7; $Ru(bpy)_3^{2+}$, 15158-62-0; BNAH, 952-92-1; NADH, 18940-08-4.

Supplementary Material Available: ^1H NMR data of **3a–e** (1 page). Ordering information is given on any current masthead page.

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[13] Methanolic solutions were heated at 60 °C for 24–100 h. Concentrations of reactants were set to be identical with those employed in the photosensitized reactions. It was confirmed that $Ru(bpy)_3^{2+}$ at 1×10^{-3} M exerts no effect on the thermal reactions at all.

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