of light dispersion and software that allows scanning of the spectrometer was prepared. Details of this Raman system will be reported elsewhere.[15] Purification procedures of beef heart cytochrome *c* oxidase has been described previously,[16a] but the final step of purification adopted was crystallization,[16b] which removed the fluorescence background in Raman scattering. A deuterated sample was prepared by repeated (three times) filtration through a membrane filter (Amicon YM-5) and dilution by 10-fold (v/v) D_2O buffer.

Figure 1 shows the 840-nm-excited RR spectra of the resting enzyme (A) and its fully reduced form (B). They are distinct from the 600-nm-excited RR spectra reported by others[12] and contain protein modes such as amide I (1656 cm^{-1}), CH_2 scissoring (1447 cm^{-1}), and the side-chain modes of Phe residues (1003 cm^{-1}). A heme mode also appears at 1556 cm^{-1} for the resting form and at 1545 cm^{-1} for the reduced form. This band became stronger when the excitation wavelength was shifted to 735 nm. Although amide II is expected in this frequency region, it is generally weak in Raman scattering and, moreover, the 1556-cm^{-1} band does not disappear in D_2O contrary to the property of amide II. Besides these protein and heme modes, a broad and intense band is observed at 330 cm^{-1} for the resting form. This band disappears in the reduced form while the protein modes show little change upon the redox change. Although a fluorescence band appears in the reduced form in the low-frequency region and the background becomes higher, a weak protein band at 471 cm^{-1} is identified similarly to the oxidized form. Therefore, if the 330-cm^{-1} band were present in the reduced form, it could be observed under this background level. The 330-cm^{-1} band is observable with the mixed-valence enzyme in which cytochrome *a* and Cu_A are oxidized, but not with one with the opposite redox combination. Therefore, it is reasonable to assign the band at 330 cm^{-1} to the moiety associated with the 830-nm absorption, that is, the Cu_A^{II} center.

Figure 2 compares the RR spectra in the 500–300-cm^{-1} region of the resting enzyme in H_2O (A) and D_2O (B). Although this was excited at 845 nm to examine another excitation wavelength, a spectrum similar to Figure 1A, obtained with 840-nm excitation, was observed. The difference spectrum (trace C), which shows one derivative pattern around 353 cm^{-1} and one positive peak at 335 cm^{-1}, indicates the presence of at least three components in the broad band; the 356, 335, and 330-cm^{-1} bands show a frequency shift, an intensity change, and no change in D_2O, respectively.

The visible absorption of blue copper proteins around 600 nm is considered to arise from a sulfur (Cys) to Cu^{II} charge-transfer transition,[17] and accordingly, RR spectra obtained with 600-nm excitation can be attributed mainly to the Cu^{II}–S stretching mode.[8b,10,11] The 830-nm absorption of Cu_A is also considered to arise from a similar transition of the Cu_A center,[13] and hence we tentatively assign the most intense and deuteration insensitive band at 330 cm^{-1} to a mode mainly associated with a Cu^{II}–S(Cys) stretching vibration of Cu_A and the weak and deuteration sensitive band at 356 cm^{-1} to the Cu–N(His) stretching vibration. The Cu–S stretching bands of blue copper proteins with a single cysteine ligand exhibit complicated patterns of D_2O shifts,[8b,11b] which are explained in terms of vibrational mixing of the Cu–S with Cu–N stretching modes. Normal coordinate calculations of the Cu center of blue copper proteins indicate significant mixing of the Cu^{II}–S with the Cu^{II}–N stretching modes.[8b,18] Therefore, it is highly likely that Cu_A-associated RR bands are mixed modes of the Cu–N and Cu–S stretching vibrations. Recently, coordinations of Cys-196, Cys-200, His-204, and His-161[19] or Met-

207[20] of subunit II to Cu_A have been suggested.

The frequency of the Cu–S stretching band of Cu_A is distinctly low compared with the corresponding frequencies of blue copper proteins (350–450 cm^{-1}). This might be explained by the longer Cu_A–S bond as revealed by EXAFS.[6] It is observed from the MCD, EXAFS, and sequence analysis[21] that, among various copper proteins so far characterized, only nitrous oxide reductase has the Cu_A type copper,[21] and in fact, the present RR spectrum bears close similarity to that of nitrous oxide reductase.[22]

The function of Cu_A of cytochrome *c* oxidase is considered to be delivery of electrons, together with Cyt *a*, from cytochrome *c* to a Cyt a_3–Cu_B center,[1,23] and possibly service as a gate of a proton pump.[24] However, the mechanism still remains to be experimentally clarified. The present technique combined with the flow apparatus for time-resolved measurements[25] is expected to provide a new means for studying the Cu_A site of cytochrome *c* oxidase.

(20) Covello, P. S.; Gray, M. W. *FEBS Lett.* **1990**, *268*, 5–7.
(21) Scott, R. A.; Zumft, W. G.; Coyle, C. L.; Dooley, D. M. *Proc. Natl. Acad. Sci. U.S.A.* **1989**, *86*, 4082–4086, 9278.
(22) Dooley, D. M.; Moog, R. S.; Zumft, W. G. *J. Am. Chem. Soc.* **1987**, *109*, 6730–6735.
(23) Saraste, M. *Q. Rev. Biophys.* **1990**, *23*, 331–366.
(24) Chan, S. 1.; Li, P. M. *Biochemistry* **1990**, *29*, 1–12.
(25) Ogura, T.; Yoshikawa, S.; Kitagawa, T. *Biochemistry* **1989**, *28*, 8022–8027.

Photosensitized Decarboxylative Michael Addition through *N*-(Acyloxy)phthalimides via an Electron-Transfer Mechanism

Keiji Okada,* Kazushige Okamoto, Naoto Morita, Katsura Okubo, and Masaji Oda*

Department of Chemistry, Faculty of Science Osaka University, Toyonaka, Osaka 560, Japan

Although photosensitized electron-transfer reactions have recently attracted considerable attention in organic photochemistry, application of this methodology to organic synthesis has been limited to fewer examples. We have recently reported a method of photodecarboxylation using *N*-(acyloxy)phthalimides which can be readily obtained from carboxylic acids.[1] This method may be applicable to decarboxylative radical type Michael addition. Hitherto, an elegant decarboxylative radical addition to electron-deficient olefins has been reported by Barton and his co-workers.[2] However, in their method, the 2-pyridylthio group is always introduced to the α-position of the electron-deficient group because of the high affinity of alkyl radicals toward the sulfur atom of the thiocarbonyl group. In order to introduce hydrogen to this position (Michael addition), we have examined several redox systems using *N*-(acyloxy)phthalimides. We now report a new and efficient radical chain method for this conversion using the redox combination of $Ru(bpy)_3Cl_2$ and 1-benzyl-1,4-dihydronicotinamide (BNAH) in aqueous solvents with visible-light excitation.

Irradiation of a THF–water (7:3, 40 mL) solution of $Ru(bpy)_3Cl_2$ (ca. 10 mg), *N*-(acyloxy)phthalimide (**1a**, 0.58 mmol),

(15) Takahashi, S.; Ogura, T.; Kitagawa, T., to be published.
(16) (a) Yoshikawa, S.; Choc, M. G.; O'Toole, M. C.; Caughey, W. S. *J. Biol. Chem.* **1977**, *252*, 5498–5508. (b) Yoshikawa, S.; Tera, T.; Takahashi, Y.; Tsukihara, T.; Caughey, W. S. *Proc. Natl. Acad. Sci. U.S.A.* **1988**, *85*, 1354–1358.
(17) Gray, H. B.; Solomon, E. I. In *Copper Proteins*; Spiro, T. G., Ed.; Wiley: New York, 1981; pp 1–39.
(18) Thamann, T. J.; Frank, P.; Willis, L. J.; Loehr, T. M. *Proc. Natl. Acad. Sci. U.S.A.* **1982**, *79*, 6396–6400.
(19) Holm, L.; Saraste, M.; Wikström, M., *EMBO J.* **1987**, *6*, 2819–2823.

(1) (a) Okada, K.; Okamoto, K.; Oda, M. *J. Am. Chem. Soc.* **1988**, *110*, 8736. (b) Okada, K.; Okamoto, K.; Oda, M. *J. Chem. Soc., Chem. Commun.* **1989**, 1636.
(2) (a) Barton, D. H. R.; Crich, D.; Kretzschmar, G. *Tetrahedron Lett.* **1984**, *25*, 1055. (b) Barton, D. H. R.; Togo, H.; Zard, S. Z. *Tetrahedron* **1985**, *41*, 5507. (c) Barton, D. H. R.; Crich, D.; Kretzschmar, G. *J. Chem. Soc., Perkin Trans. 1* **1986**, 39. (d) Barton, D. H. R.; da Silva, E.; Zard, S. Z. *J. Chem. Soc., Chem. Commun.* **1988**, 285.

Table I. Photosensitized Decarboxylative Michael Addition of N-(Acyloxy)phthalimides to Electron-Deficient Olefins

| R; a: t-Bu—⟨⟩—$(CH_2)_3$- | b: $(PhCH_2)_2CH$- | c: 1-adamantyl |
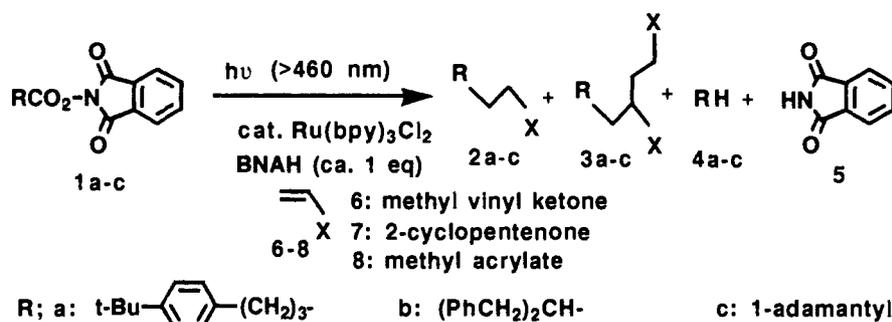
run	R	olefin (equiv)	solvent[a]	2 (%)	3 (%)	4 (%)
1	a	6 (1.0)	$THF-H_2O$	68	5	18
2	b	6 (1.0)	$THF-H_2O$	68	3	11
3	c	6 (1.9)	$THF-H_2O$	68	10	0
4	a	7 (5.4)	t-$BuOH-H_2O$	41	0	16
5	b	7 (4.8)	t-$BuOH-H_2O$	58	0	17
6	c	7 (5.0)	t-$BuOH-H_2O$	69	0	1
7	a	8 (1.1)	t-$BuOH-H_2O$	49	6	7
8	b	8 (1.1)	$THF-H_2O$	45	0	11
9	c	8 (1.1)	$THF-H_2O$	50	0	1

[a] In aqueous solvents containing 30% of water.

Scheme I
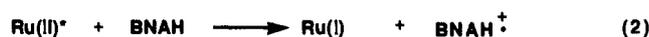
BNAH (0.63 mmol), and methyl vinyl ketone (0.60 mmol) with visible light (>460 nm from a 500-W Xenon lamp) for 2 h under a nitrogen atmosphere produced the expected Michael addition product (2a, 68%) and phthalimide (89%) along with a small amount of the hydrocarbon (4a, 18%) and the 1:2 adduct (3a, 5%) of the alkyl radical and methyl vinyl ketone.[3] Under the conditions, incident light is absorbed only by the Ru sensitizer and no reaction takes place without $Ru(bpy)_3Cl_2$ and/or BNAH.[4] The reaction similarly proceeds for secondary (1b) and tertiary (1c) carboxylic acid derivatives with several electron-deficient olefins (Table I). The quantum yields for addition to methyl vinyl ketone are over unity (1.3 for 1a, 2.3 for 1b, and 1.2 for 1c)[5] and clearly demonstrate the participation of radical chain processes.

We envision the reaction mechanism shown in Scheme I. The initial process of this reaction would be electron transfer from BNAH to the triplet state of $Ru(bpy)_3^{2+}$ (eqs 1 and 2).[6,7] The oxidized BNAH deprotonates to give BNA* (eq 3).[8] The produced $Ru(bpy)^+$ can reduce 1 to give the anion radical (eq 4),[9] which gives alkyl radical according to our previous studies (eq 5).[1] The alkyl radical adds to the electron-deficient olefins to give radical 9, which has a radical center at the α-position of the electron-withdrawing group (eq 6). The radical 9 may abstract hydrogen from BNAH (eq 7) or may be reduced by BNA*.[6a,b] The occurrence of the former process was established by a deuterium-labeling experiment. Thus, similar irradiation using 1a and BNAH-$4,4$-d_2 in the presence of methyl acrylate in $THF-H_2O$ or CH_3CN-H_2O (7:3) produced 2a with deuterium incorporation at the α-position of the carbomethoxy group in 68% or 79% yield, respectively.[10] The BNA* would reduce 1 to regenerate the anion radical of 1 (eq 8),[9] and the radical chain process is initiated.

This method is applicable to several functionalized substrates and radical cyclizations (supplementary material).

Supplementary Material Available: Expanded Table I recording photosensitized decarboxylation Michael additions of N-(acyl-oxy)phthalimides to electron-deficient olefins (2 pages). Ordering information is given on any current masthead page.

(3) 1-Benzyl-3-carbamoylpyridinium chloride was isolated (64%) by re-crystallization of the acidified (hydrochloric acid) water-soluble components of the photolysate.

(4) Irradiation with a shorter wavelength (>330 nm) of BNAH (λ_{max} = 352 nm) without $Ru(bpy)_3Cl_2$ (λ_{max} = 453 nm) under similar conditions slowly gave the same products in similar yield. The mechanism of this uncatalyzed reaction would involve electron transfer of the short-lived excited state of BNAH to 1. See: Martens, F. M.; Vorhoeven, J. W.; Gase, R. A.; Pandit, U. K.; de Boer, Th. J. *Tetrahedron* 1978, *34*, 443.

(5) Quantum yields were determined by using a U-shaped glass tube in which solid BNAH (corresponding to 50 mM) and an aqueous THF solution of 1 (10 mM), 6 (10 mM), and $Ru(bpy)_3Cl_2$ (4.5 mM) were separately degassed and mixed in the dark before irradiation; Reinecke's salt actinometer at 545 nm; Wegner, E. E.; Adamson, A. W. *J. Am. Chem. Soc.* 1966, *88*, 394.

(6) (a) Pac, C.; Ihama, M.; Yasuda, M.; Miyauchi, Y.; Sakurai, H. *J. Am. Chem. Soc.* 1981, *103*, 6495. (b) Pac, C.; Miyauchi, Y.; Ishitani, O.; Ihama, M.; Yasuda, M.; Sakurai, H. *J. Org. Chem.* 1984, *49*, 26. (c) Ishitani, O.; Ihama, M.; Miyauchi, Y.; Pac, C. *J. Chem. Soc., Perkin Trans. 1* 1985, 1527. (d) Ishitani, O.; Yanagida, S.; Takamuku, S.; Pac, C. *J. Org. Chem.* 1987, *52*, 2790.

(7) (a) van Bergan, T. J.; Hedstrand, D. M.; Kruizinga, W. H.; Kellogg, R. M. *J. Org. Chem.* 1979, *44*, 4953. (b) Bock, C. R.; Connor, J. A.; Gu-tierrez, A. R.; Meyer, T. J.; Whitten, D. G.; Sullivan, B. P.; Nagle, J. K. *J. Am. Chem. Soc.* 1979, *101*, 4815. (c) Fukuzumi, S.; Koumitsu, S.; Hironaka, K.; Tanaka, T. *J. Am. Chem. Soc.* 1987, *109*, 305. (d) Fukuzumi, S.; Tanaka, T. In *Photoinduced Electron Transfer*; Fox, M. A., Chanon, M., Eds.; El-sevier: New York, 1988; Part C, pp 578–635 and references cited therein.

(8) (a) Martens, F. M.; Vorhoeven, J. W. *Recl. Trav. Chim. Pays-Bas* 1981, *100*, 228. (b) Martens, F. M.; Vorhoeven, J. W. *J. Photochem.* 1983, *22*, 99.

(9) Although the free energy changes of these electron-transfer processes are 0 to a little endothermic,[1a,7b,c] the processes would be feasible at room temperature.

(10) Similar irradiation using BNAH in $THF-D_2O$ gave no deuterated adduct.