CHEMISTRY LETTERS, pp. 2165-2166, 1990.

A Novel Photocyclization Reaction of Lysine-Anthraquinone Molecules

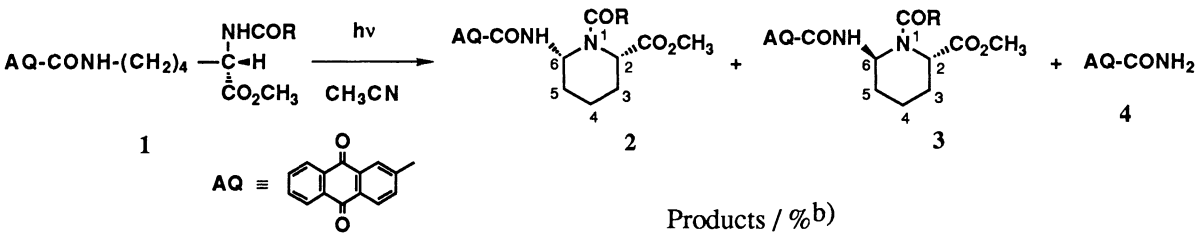
Kazuhiro MARUYAMA,* Masakazu HASHIMOTO, and Hitoshi TAMIAKI
Department of Chemistry, Faculty of Science, Kyoto University, Kyoto 606

N^{α}-Acetyl-N^{ε}-(2-anthraquinonyl)-L-lysine methyl ester underwent a photocyclization reaction in an acetonitrile solution to produce piperidine derivatives. The cyclization might proceed via a novel process that carbon-centered radical formed at the ε-position attacked the α-amido group in the molecule, followed by the formation of C-N bond.

In natural systems, a variety of bio-active quinones function in proteins, for example, ubiquinone-n in photosynthetic reaction center, vitamin K, and so on.[1] Interactions between quinones and proteins are of importance and have attracted much attention. We first synthesized lysine-linked-anthraquinone molecules and have investigated their photoreactions. In this paper, we report a novel photocyclization of the molecules and its reaction pathway.

Irradiation of an acetonitrile solution (400 ml) containing N^{α}-acetyl-N^{ε}-(2-anthraquinonyl)-L-lysine methyl ester (**1a**, 0.8 mmol) through an aqueous $CuSO_4$ solution filter with a high pressure mercury arc lamp for 6 h under argon afforded (2S,6S)-1-acetyl-6-(2-anthraquinonylamino)-2-(methoxycarbonyl)piperidine (**2a**, 20%), (2S,6R)-1-acetyl-6-(2-anthraquinonylamino)-2-(methoxycarbonyl)piperidine (**3a**, 17%), and 2-anthraquinone carboxamide (**4a**, 26%) as isolable products after column chromatography (see Table 1). Similarly, N^{α}-t-butoxycarbonyl substituted molecule **1b** gave **2b**, **3b**, and **4a**.

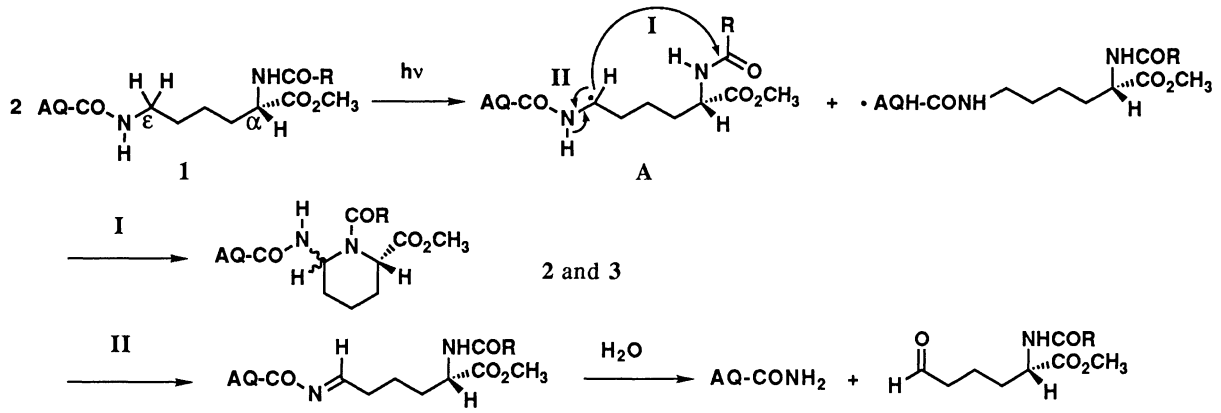
Table 1. Photochemical Reaction of Lysine-Anthraquinone Molecules[a]



1 2 3 4

	R	Products / %[b] 2	3	4	Conversion / %
1a	CH_3	20	17	26	35
1b	$(CH_3)_3CO$	13	15	trace	56

a) Irradiation time was 6 h. b) Isolated yield based on a starting molecule consumed.



Scheme 1. A plausible reaction pathway.

The structure of products were assigned from their spectral data, elemental analyses and chemical transformation.[2] ^{1}H NMR, ^{13}C NMR, and IR spectra showed that photoproducts **2** and **3** had piperidine structures. They were diastereomers each other and their ^{1}H NMR and IR spectra showed that **2** had an intramolecular hydrogen bonding between the C=O at the 2-position and the NH at the 6-position, but **3** had not. Therefore, it could be concluded that both substituents at the 2- and 6-positions in **2** occupied the axial positions (cis-isomer), and **3** trans-isomer.[3]

As shown in Scheme 1, the following reaction pathway is plausible. The first step of the photoreaction is a hydrogen abstraction by photoexcited anthraquinone[4] from the ε-methylene site to afford the radical **A**. Since the quantum yield measured by decreasing **1a** was reduced with decreasing concentration, the initial hydrogen abstraction would be intermolecular. In view of dissociation bond energy, abstraction of α-hydrogen atom could also be happened, but it should be suppressed by steric hindrance. The radical in **A** intramolecularly attacks the α-amido carbonyl group followed by rearrangement (alkyl migration[5] from carbonyl carbon to the neighboring nitrogen) to form finally C-N bond (path I).[6] On the other hand, the radical **A** could be stabilized by dehydrogenation to produce imine (Path II), followed by formation of **4** via hydrolysis.[7]

In general, it is known that carbon-centered radical is trapped by olefin, carbonyl group, cyano group,and so on.[8] In the present case, however, carbon-centered radical attacks amido group, followed by C-N bond formation. It is a novel process and the first example to our knowledge.

References

1) J. Deisenhofer and H. Michel, *Angew. Chem., Int. Ed. Engl.*, **28**, 829 (1989); J. W. Suitte, *Ann. Rev. Biochem.*, **54**, 459 (1985).
2) Authentic compound **4a** was synthesized by the amidation of anthraquinone-2-carboxylic acid with NH_3 aq.
3) At the α-carbon (C-2), no racemization could be observed. Trans-isomer **3** was mixture of two conformers (axial-equatorial and equatorial-axial).
4) K. Maruyama and A. Osuka, "The Chemistry of the Quinonoid Compounds," ed by S. Patai and Z. Rappoport, John Wiley & Sons, New York (1988), Vol. 2, Chap. 13, pp. 759-878.
5) D. C. Nonhebel and J. C. Walton, "Free-radical Chemistry," Cambridge (1974), Chap. 13, pp. 498-532.
6) Direct attack to the nitrogen atom of α-amido group (partial double bond C⁼⁼N) could not be excluded.
7) Aldehyde parts could not be isolated because of their instabilities under the photoreaction conditions. Distilled acetonitrile for photoreaction could not be free from water which induced hydrolysis.
8) "Organic Reaction Mechanisms," ed by A. C. Knipe and W. E. Watts, John Wiley & Sons, New York (1971-1988).

(Received August 24, 1990)