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Site-Selective Photocyclization of Acetylglycine-Anthraquinone Molecules

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5-[(*N*-Acetylglycyl)amino]pentyl, 5-[(*N*-acetylglycyl-α-methylalanyl)amino]pentyl, and 5-[(*N*-acetylglycyl-α-methylalanyl-α-methylalanyl)amino]pentyl anthraquinone-2-carboxylate underwent a photocyclization in an acetonitrile solution to produce efficiently large-sized ring-closure compounds as isolable products. In the photocyclization, high site-selectivity in the carbonyl groups of anthraquinone moiety was first observed.

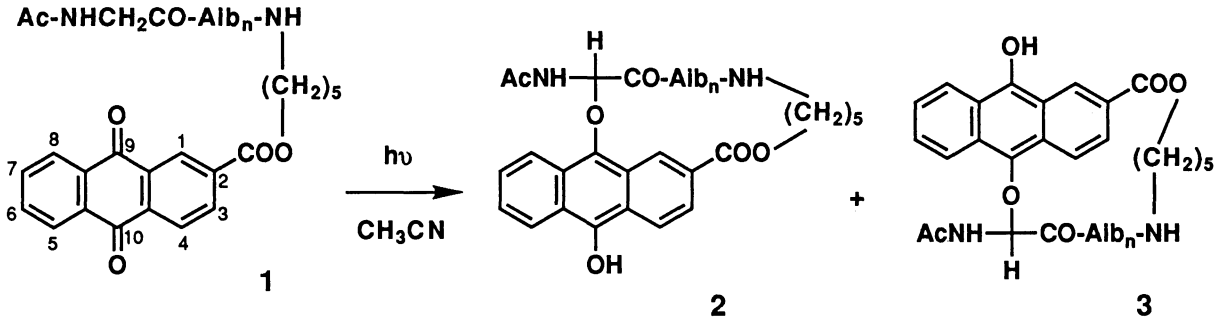
In enzyme-catalyzed reactions, a substrate is tightly held next to a reactant by several interactions in an enzyme-substrate complex and high site-selectivity could be realized. To mimic such a biochemical process, molecules covalently linked with a reagent and a substrate have been examined.[1] Intramolecular photoinduced hydrogen abstraction from linear methylene chains by benzophenone or anthraquinone were studied by Breslow, Winnik[2] and Tanimoto[3] *et al.* But these authors failed to isolate each coupling product because of the complexity of the reaction mixtures. To avoid the complexity of photoreactions and separate each photoproduct, we adopted an active methylene group, a glycine residue as a hydrogen donor[4] and an anthraquinone as a photosensitive hydrogen acceptor.[5] In this paper, we report photocyclization of acetylglycine-anthraquinone molecules and their high site-selectivity.

An acetonitrile solution (100 ml) of 5-[(*N*-acetylglycyl)amino]pentyl anthraquinone-2-carboxylate (**1a**, 0.1 mmol) was saturated with argon and irradiated with a 300-W high-pressure mercury arc lamp through an aqueous $CuSO_4$ solution filter for 30 min at room temperature. The reaction mixture was purified by flash column chromatography on silica gel (dichloromethane–methanol) and 15-membered ring-closure product **2a** was exclusively given in a yield of 41% (Table 1). Similarly, 5-[(*N*-acetylglycyl-α-methylalanyl)amino]pentyl anthraquinone-2-carboxylate (**1b**) gave two isomers, 18-membered ring **2b** and 19-membered ring **3b** in yields of 18 and 23% respectively, and 5-[(*N*-acetylglycyl-α-methylalanyl-α-methylalanyl)amino]pentyl anthraquinone-2-carboxylate (**1c**) gave dominantly 22-membered ring **3c** in a yield of 13% (see Table 1).

The structures of photoproducts were determined on the basis of their spectral data. ^{1}H NMR, IR, MS and fluorescence spectra indicated that products **2** and **3** were intramolecular coupling compounds and had an anthracene structure. The NOESY (Nuclear Overhauser and Exchange Spectroscopy) spectra showed clearly that product **2** was given by cyclization between the α-carbon of the glycine residue and the 9-carbonyl oxygen and product **3** between the α-carbon and the 10-carbonyl oxygen.

The site-selectivity in two carbonyl groups of anthraquinone might depend upon the length of the spacer between acetylglycyl and anthraquinone moiety. The anthraquinone group has two reactive carbonyl groups (9- and 10-positions) and the distance between glycine site and each carbonyl group is different in the molecule **1**. As the spacer length increased, the cyclization site was shifted from the carbonyl group at the 9-position (**2**) to

Table 1. Photochemical Reaction of Acetylglycine-Anthraquinone Molecules



1 2 3

Alb ≡ $NHC(CH_3)_2CO$ (α-methylalanine)

	n	Yield / %[a] 2	3	Conversion of 1 / %
1a	0	41	0	83
1b	1	18	23	70
1c	2	trace	13	36

a) Isolated yield based on consumed **1**.

that of the 10-position (**3**). In the biradical produced by intramolecular photoinduced hydrogen abstraction of molecule **1a**, the carbon-centered radical at the glycine site is much closer to the oxygen-centered radical at the 9-position than that at the 10-position and bonded efficiently to only the former position. Insertion of one α-methylalanyl (≡ Aib) residue to the spacer of **1a** as in **1b** makes it possible that the C-radical interacts with both the O-radicals at the 9- and 10-carbonyl groups. One more insertion of Aib residue as in **1c** induces little interaction of the CH• with the 9-C–O• and dominant coupling of the CH• with the 10-C–O•. In spite of conformationally large freedom of the linkage (the flexible linear methylene chain and the relatively rigid homo-oligomer of Aib), the position of the cyclization was changed systematically, to give clear information about the dependency of photoreactivity on the structure of the spacer. Therefore, this simple system might be helpful for the conformational analysis of a flexible molecule in a solution and the selective functionalization of a molecule with many reactive sites.

References

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