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Stereoselective Photocycloaddition of Alkenes to Naphthalene Rings Assisted by Hydrogen Bonding

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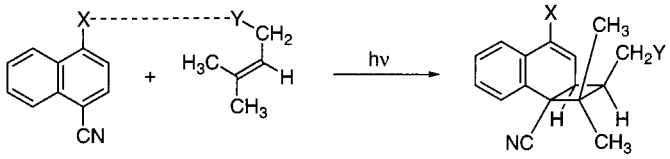
ABSTRACT



Introduction of a hydrogen-bonding substituent to 1-cyanonaphthalene and alkene resulted in the selective formations of *endo*-photocycloadducs. Furthermore, the yield and selectivity were improved as the reaction temperature was lowered.

Photoinduced reactions have been used as key transformations in many organic syntheses to construct organic compounds having unique structures that were barely accessible by other methods.[1] [2 + 2] photocycloaddition of two carbon−carbon double bonds is one such photoreaction. Many synthetic applications of this reaction have been reported, and their stereoselectivities were discussed in terms of the electronic nature of substrates, the steric repulsions between substituents, and the conformational restrictions of intramoleculer reactions.[2]

It can be highly attractive to use hydrogen bonds[3] to control regio- and stereoselectivity, because hydrogen-bonding substituents such as hydroxyl and amino groups frequently interact with other functional groups or heteroatoms. While many thermal reactions are disturbed by hydrogen-bonding substituents, this is not the case in certain photocycloadditions. There are some photoreactions in which the regio- or stereoselectivity is controlled by hydrogen bonds, but all of them have limitations: some of these reactions are such that the reactive or chromophoric site of the reactant participates in the hydrogen bond,[4] and the others are intramolecular reactions.[5] Because hydrogen bonds can be formed independent of photoexcitation and the succeeding reaction, the stereoselectivity of an intermolecular photoreaction might be controlled by introduction of a hydrogen-bonding substituent to an appropriate position of the reac-

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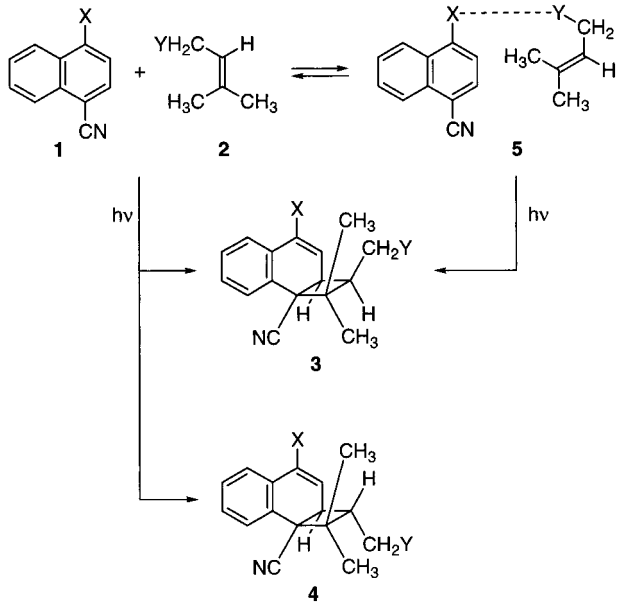
Table 1. Substituent Effect of Photocycloadditions of **1** and **2** in Benzene[a]

	reactants		cycloadducts				
entry	X	Y	**3**	**4**	yield (%)[b]	**3**/**4**	recovery of **1** (%)
1	H (**1a**)	OH (**2a**)	**3aa**	**4aa**	41	0.72	24
2	CH_3 (**1b**)	**2a**	**3ba**	**4ba**	22	0.84	45
3	CH_2OH (**1c**)	**2a**	**3ca**	**4ca**	42	3.3	18
4	CH_2OCH_3 (**1d**)	**2a**	**3da**	**4da**	47	2.4	33
5	**1c**	OCH_3 (**2b**)	**3cb**	**4cb**	22	1.7	62
6	**1d**	**2b**	**3db**	**4db**	18	0.95	40

[a] Irradiations were carried out at room temperature for 20−21 h. [b] Isolated yields of **3** + **4**.

tants. We designed such a photoreaction and report here that excellent selectivity was achieved. As a photoreaction, we chose the [2 + 2] photocycloaddition between 4-substituted 1-cyanonaphthalenes (**1**) and 1-substituted 3-methyl-2-butenes (**2**).[6,7] As shown in Scheme 1, this reaction is suitable

Scheme 1



for investigation of hydrogen-bonding effects because it gave two stereoisomers (**3** and **4**) regioselectively and an attractive interaction between X and Y would form a complex (**5**) in the ground and/or excited states that could give **3** selectively.

Table 1 summarizes the substituent effect of the photocycloaddition of **1** to **2** in benzene solution.[8] When X and Y can form a hydrogen bond, the *endo*-isomers (**3**) were preferentially formed over the *exo*-isomers (**4**) (entries 3−5). However, if the combination of X and Y was unable to form a hydrogen bond, no selectivity was observed (entries 1, 2, and 6). While **1d** and **2b** seemed to have dipole moments similar to those of **1c** and **2a**, respectively, photocycloaddition between these compounds showed no *endo*-selectivity (entry 6). Thus, a contribution of dipole interactions to the endo-selectivity should be negligible.

Solvent and temperature effects were investigated in the photocycloaddition of **1c** to **2a** (Table 2).[8] At room temperature, photocycloaddition in benzene (entry 1) and in CH_2Cl_2 (entry 2) gave **3ca** preferentially over **4ca** in the ratio of 3:1. Use of more polar solvents such as CH_3CN (entry 5) and 5% MeOH−95% CH_3CN (entry 6) decreased the selectivity, and no selectivity was observed in MeOH (entry 7). This decrease of selectivity can be explained by the disruption of hydrogen bonds between hydroxyl groups of

Table 2. Solvent and Temperature Effect of Photocycloaddition of **1c** to **2a**[a]

entry	solvent	temp[b]	yield (%)[c]	**3ca**/**4ca**	recovery (**1c**, %)
1	benzene	rt	42	3.3	18
2	CH_2Cl_2	rt	33	3.4	10
3	CH_2Cl_2	−20 °C	28	6.6	trace
4	CH_2Cl_2	−60 °C	73	13	trace
5	CH_3CN	rt	39	1.6	10
6	5% MeOH −95% CH_3CN	rt	32	1.7	20
7	MeOH	rt	28	1.0	17

[a] Irradiations were carried out for 20 h. [b] rt indicates room temperature. [c] Isolated yields of **3ca** + **4ca**.

(6) For [2 + 2] photocycloadditions of 1-cyanonaphthalene with alkenes, see: (a) Pac, C.; Sugioka, T.; Mizuno, K.; Sakurai, H. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 238−243. (b) Pac, C.; Mizuno, K.; Sugioka, T.; Sakurai, H. *Chem. Lett.* **1973**, 187−188. (c) Mizuno, K.; Pac, C.; Sakurai, H. *J. Chem. Soc., Chem. Commun.* **1974**, 648−649. (d) McCullough, J. J.; Miller, R. C.; Fung, D.; Wu, W.-S. *J. Am. Chem. Soc.* **1975**, *97*, 5942−5943. (e) Yang, N. C.; Kim, B.; Chiang, W.; Hamada, T. *J. Chem. Soc., Chem. Commun.* **1976**, 729−730. (f) McCullough, J. J.; Miller, R. C.; Wu, W.-S. *Can. J. Chem.* **1977**, *55*, 2909−2915. (g) Pac, C.; Mizuno, K.; Okamoto, H.; Sakurai, H. *Synthesis* **1978**, 589−590. (h) Yasuda, M.; Pac, C.; Sakurai, H. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 502−507. (i) Albini, A.; Fasani, E.; Giavarini, F. *J. Org. Chem.* **1988**, *53*, 5601−5607. (j) Chow, Y. L.; Buono-Core, G. E.; Zhang, Y.-H.; Liu, X.-Y. *J. Chem. Soc., Perkin Trans. 2* **1991**, 2041−2045. (k) Mella, M.; Fasani, E.; Albini, A. *J. Org. Chem.* **1992**, *57*, 6210−6216. (l) Dopp, D.; Erian, A. W.; Henkel, G., *Chem. Ber.* **1993**, *126*, 239−242. (m) Noh, T.; Kim, D. *Tetrahedron Lett.* **1996**, *37*, 9329−9332. (n) Noh, T.; Kim, D.; Kim, Y.-J. *J. Org. Chem.* **1998**, *63*, 1212−1216.

(7) For [2 + 2] photocycloadditions of 1-cyano-4-methylnaphthalene with alkenes, see: (a) McCullough, J. J.; MacInnis, W. K.; Lock, C. J. L.; Faggiani, R. *J. Am. Chem. Soc.* **1980**, *102*, 7780−7782. (b) McCullough, J. J.; MacInnis, W. K.; Lock, C. J. L.; Faggiani, R. *J. Am. Chem. Soc.* **1982**, *104*, 4644−4658.

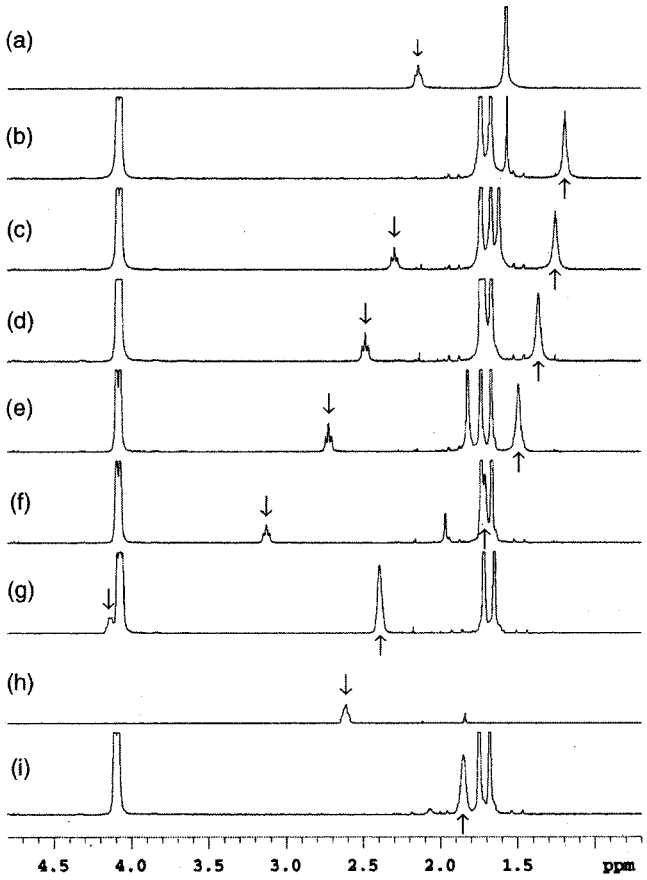


Figure 1. Variable-temperature ^{1}H NMR spectrum of **1c** and **2a** (300 MHz, CD_2Cl_2). ↓ and ↑ indicate the resonances of hydroxylic protons of **1c** and **2a**, respectively. (a) **1c** (27 mM) at +20 °C. (b) **2a** (60 mM) at +20 °C (c−g) A mixture of **1c** (27 mM) and **2a** (48 mM) at +20 °C (c), 0 °C (d), −20 °C (e), −40 °C (f), and −60 °C (g). (h) **1c** (27 mM) at −60 °C. (i) **2a** (60 mM) at −60 °C.

1c and **2a** by the polar solvent: the hydrogen bonds were weakened in polar aprotic solvents and completely disrupted in protic solvents. The effect of temperature was examined in CH_2Cl_2. Lowering the reaction temperature to −20 °C increased the ratio of **3ca**:**4ca** (entry 3), and irradiation at −60 °C gave a highly selective formation of *endo*-isomer (**3ca**:**4ca** = 13:1) in a high yield (73%) (entry 4).

The contribution of the hydrogen bond to the *endo*-selectivity was also examined by low-temperature ^{1}H NMR (Figure 1). It is known that hydroxylic protons move downfield when they participate in hydrogen bonding and that the change in chemical shift is proportional to the extent of hydrogen bonding.[3,9] At 20 °C, mixing of **1c** and **2a** led to downfield shifts of their hydroxylic proton resonances, indicating that the types of hydrogen bonds in **6** and **7** were favored over those in **8** and **9** (Figure 2). When the mixture was cooled, the hydroxylic proton resonances shifted to a lower field, and the extent of their shifts at −60 °C was

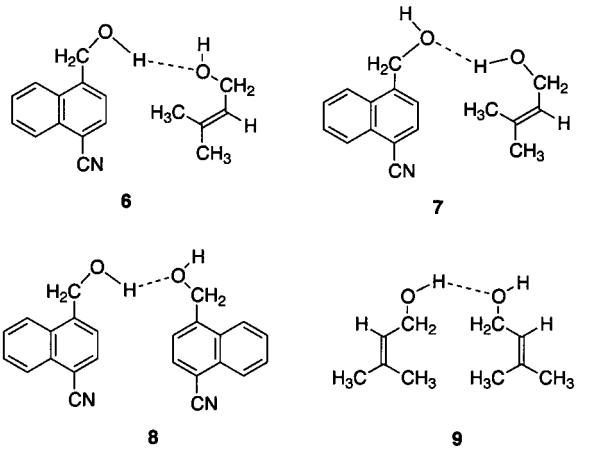


Figure 2.

larger than those of individual solutions. This result suggests that lowering the temperature increased the dominance of **6** and **7** in the ground state and that photocycloadditions via such a hydrogen-bonded complex gave the *endo*-adducts selectively.

In conclusion, we examined the stereoselectivity in the photocycloaddition of **1** and **2** and demonstrated that introduction of a hydroxyl group to these molecules gave *endo*-cycloadducts with excellent selectivity in high yields. We also revealed that the formation of a hydrogen bond in the ground state is essential in this selectivity.

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(8) All photoreactions in Tables 1 and 2 were carried out with a 300 W high-pressure mercury lamp through a Pyrex filter in a deoxyganated solution of **1** (50 mM) and **2** (0.5 M) for the appropriate times. Then the reaction mixture was concentrated, and flash column chromatography on silica gel gave **1** and a mixture of cycloadducts (**3** and **4**). The ratio of **3** to **4** was determined by the relative peak areas of ^{1}H NMR of the isolated mixture. The stereochemistry of **3cb** and **4cb** were determined by NOE studies and finally confirmed by X-ray analysis. Analytical data of **3cb**: colorless cubes (benzene−hexane); mp 100.0−101.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 23 °C, TMS) δ = 7.40−7.37 (m, 1H), 7.32−7.20 (m, 3H), 5.90 (d, ^3J = 4.4 Hz, 1H), 4.53 (td, ^3J = 5.8 Hz, ^4J = 1.4 Hz, ^5J = 1.4 Hz, 2H), 3.69 (ddt, ^3J = 9.8, 4.1 Hz, ^5J = 1.6 Hz, 1H), 3.51 and 3.47 (ABq, ^2J = 9.6 Hz, each parts d with ^3J = 8.2 and 7.4 Hz, 2H), 3.33 (s, 3H), 3.06 (ddd, ^3J = 9.9, 8.2, 7.4 Hz, 1H), 1.53 (t, ^3J = 5.8 Hz, 1H), 1.43 (s, 3H), 0.83 (s, 3H). Anal. Calcd for $C_{18}H_{21}NO_2$: C 76.30, H 7.47, N 4.94. Found: C 76.42, H 7.58, N 4.91. Analytical data of **4cb**: colorless cubes (AcOEt); mp 171.0−172.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 23 °C, TMS) δ = 7.45−7.42 (m, 1H), 7.34−7.25 (m, 2H), 7.20−7.17 (m, 1H), 5.99 (d, ^3J = 5.8 Hz, 1H), 4.52 (d, ^3J = 5.8 Hz, 2H), 3.57 and 3.52 (ABq, ^2J = 9.6 Hz, each parts d with ^3J = 7.4 and 7.1 Hz, 2H), 3.34 (s, 3H), 3.25 (dd, ^3J = 7.7 and 5.5 Hz, 1H), 2.30 (q, ^3J = 7.4 Hz, 1H), 1.51 (t, ^3J = 6.0 Hz, 1H), 1.48 (s, 3H), 0.94 (s, 3H). Anal. Calcd for $C_{18}H_{21}NO_2$: C 76.30, H 7.47, N 4.94. Found: C 76.41, H 7.58, N 5.01.

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