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[4 + 4] Photodimerization of Azaanthracenes in Both Solution and Solid Phase Controlled by Cation−π Interactions

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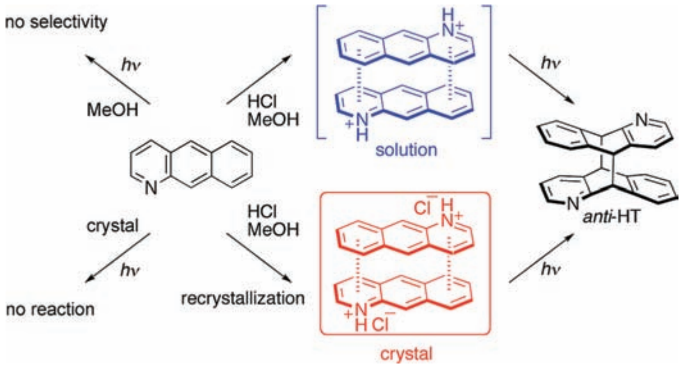
ABSTRACT



Regio- and stereoselective [4 + 4] photodimerization reactions of 1- and 2-azaanthracenes were performed in both methanol solution and solid phases to give *anti*-HT dimers in high yields. In these reactions, intermolecular cation−π interactions between the pyridinium cation and the benzene ring play a key role in preorientation prior to the photodimerization reactions.

Preorientation of alkenes and aromatic compounds prior to irradiation is essential to the success of regio- and stereocontrolled photodimerization reactions.[1] For the preorientation of anthracene derivatives, a variety of approaches have been extensively investigated.[2] For example, topochemical,[3] supramolecular,[4] and biocatalytic[5] approaches, as well as host−guest complex formation using γ-CD[6] and CB8,[7] are effective in arranging the substrate molecules in an orientation suitable for the formation of a particular [4 + 4] photodimer. On the other hand, the [4 + 4] photodimerization of azaanthracenes has received little attention.[8]

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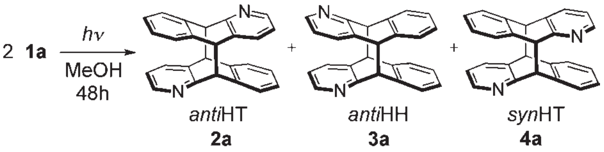
We have previously reported that a cation–π interaction plays a key role in controlling the orientation of 4-styrylpyridines[9] and azachalcones[10] in solution and solid phases, enabling stereoselective [2 + 2] photodimerization. In this letter, we report that a cation–π interaction[11,12] is effective for the preorientation of 1-azaanthracene (**1a**)[13] and 2-azaanthracene (**1b**)[14] in acidic solution and as a HCl salt (Figure 1), irradiation of which leads to [4 + 4] photodimerization to produce *anti*-HT dimers with high selectivities.

1a **1b**

Figure 1. The 1-aza- and 2-azaanthracene photodimerization substrates.

Irradiation of a 0.5 M methanol solution of **1a** with a 450 W high-pressure mercury lamp for 48 h through a Pyrex filter afforded dimers **2a**–**4a** with lower selectivities as shown in Table 1 (entry 1). The concentration of the solution had little effect on the compound ratio (entry 2). In the presence of 1 equiv of concentrated hydrochloric acid, the photochemical reaction resulted in remarkable changes in the product distribution (entry 3); the *anti*-HT dimer **2a** became a major product while **4a** disappeared. Increasing the amount of HCl loading to 3 equiv lead to a dramatic increase in the *anti*-HT dimer **2a** and a decrease in the *anti*-HH dimer **3a** (entry 5). The lowering of the concentration of the solution had a significant effect on selectivity, resulting in a decrease in **2a** (entry 4), which is in contrast to results observed in the absence of HCl (entries 1 and 2). This suggests the contribution of cation–π interactions between the two molecules to the formation of the *syn*-HT dimer.

Table 1. [4 + 4] Photodimerization of **1a** in MeOH[a]



entry	HCl (eq)	concn (M)	conv (%)	products (%)[a]		
				2a	3a	4a
1	0	0.5	97	52	20	28
2	0	1.0	>99	52	26	22
3	1	1.0	>99	76	24	0
4	3	0.5	>99	79	21	0
5	3	1.0	>99	95	5	0

[a] The conversion and yields were determined by ^{1}H NMR spectra.

^{1}H NMR and X-ray structural analyses were undertaken to determine the structures of the dimers. In the ^{1}H NMR spectra, the methine protons at the bridge head position of **2a** and **3a** appear as two doublets at δ 4.78 and 4.62, and δ 4.77 and 4.61, respectvely, whereas those of **4a** appeared as two singlets. These results show that **2a** and **3a** are *anti* dimers and **4a** is a *syn* dimer. The X-ray structural analysis proved **2a** to be *anti*-HT; therefore, **3a** was assigned as *anti*-HH. The *syn*-HT structure of **4a** was also confirmed by X-ray structural analysis. The chiral space group of $P2_1$ reflects this structure.

To gain insight into the reaction mechanism, product distribution vs reaction time was monitored by ^{1}H NMR spectra (Table S1). Figure 2 shows the plots of the amount of **1a**–**3a** vs reaction time. It is clear that as the irradiation time was increased, the yield of **1a** rapidly decreased and that of **2a** increased accompanied by a small amount of **3a**. Substrate **1a** was almost totally consumed after 48 h of irradiation. These observations indicate the direct formation of the *anti*-HT dimer **2a** through the dimerization of **1a**. As irradiation of the isolated **2a** gave no other isomeric product under the same reaction conditions, this dimerization process is irreversible.

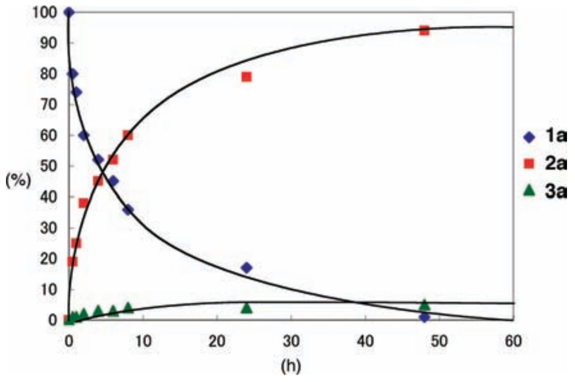


Figure 2. Plots of product yields vs irradiation time.

The selectivity in the photocycloaddition reactions is often explained by orbital interactions.[15] To elucidate the mechanism for the selectivities of **1a** and **1a**·H$^+$, DFT

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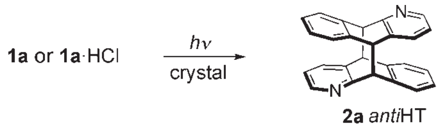
calculations of HOMOs and LUMOs for these molecules were carried out at the B3LYP/6-31G* level (Figure S1).[16] The LUMO of **1a** is symmetric with respect to reflection in the mirror planes lying midway on the long and short axes, suggesting that the orbital interaction for **1a** allows the formation of both HH and HT dimers. This is in agreement with the formation of **2a**–**4a** with lower selectivities (Table 1, entries 1 and 2). On the other hand, the LUMO of **1a**·H^+ is symmetric with respect to reflection in the mirror plane lying midway on the long axis but antisymmetric to that on the short axis, suggesting a preference for the formation of HH products. However the fact that the *anti*-HT dimer **2a** is a major product strongly suggests that the reaction is not controlled by orbital interactions but by cation–π interactions. It should be noted that no HOMO–LUMO interactions were expected for both **1a** and **1a**·H^+; the orbitals at the reactive sites of the HOMOs and LUMOs are antibonding. The disapperance of **4a** may be due to repulsion between the dipoles produced by the protonation of **1a** (Table 1, entries 3–5).

Table 2. Photodimerization of **1a** and **1a**·HCl in Crystal Form[a]



entry	substrate	time (h)	conv (%)	yield (%)[a]
1	**1a**	22	0	0
2	**1a**·HCl·$2H_2O$[b]	0.5	>99	>99
3	**1a**·HCl	4	60	60
4	**1a**·HCl	16	92	92
5	**1a**·HCl	24	>99	>99

[a] The conversion and yields were determined by ^1H NMR spectra. [b] Hydrate crystals dipped in paraffin oil.

Next, the solid-state reaction of **1a** was carried out. When the powdered crystals of **1a**, placed between two Pyrex plates, were irradiated with a 250 W high-pressure mercury lamp for 24 h, no product was obtained (Table 2, entry 1). On the other hand, irradiation of **1a**·HCl·$2H_2O$ produced **2a** in quantitative yield, which was confirmed by the ^1H NMR spectrum (entry 2).

It is interesting to note that irradiation of the anhydrate obtained by heating at 100 °C under a vacuum for 15 h also produced **2a**, although the reaction rate is much slower than that of the hydrate. This suggests that the head-to-tail column structure is retained in the anhydrate (entries 3–5).

To elucidate the reason of differences in the product selectivities dependent on the cationic charge of the pyridine, the X-ray packing diagrams of **1a** and **1a**·HCl·$2H_2O$ were compared. Figure 3 shows X-ray packing diagrams for **1a** and **1a**·HCl·$2H_2O$ and the two neighboring molecules extracted from them. The molecules of **1a** orient themselves in a nonparallel manner, indicating the absence of any π–π interactions between them (Figure 3a). As shown in Figure 3c, the separation of 4.64 and 5.83 Å for the two neighboring double bonds is much longer than that of Schmidt's requirement.[3a] On the other hand, the molecules of **1a**·HCl·$2H_2O$ are arranged parallel to each other in a head-to-tail orientation, forming columns along the *b* axis (Figure 3b). Channels are formed between the columns, and these are occupied by water molecules and chloride anions. These are linked to one another by hydrogen bonds, assisting in the formation of head-to-tail columns. These characteristic structural features are very close to those observed in styrylpyridine crystals.[9] The separation between the double bonds of the neighboring two molecules is 3.45 Å, which is much shorter than that for **1a** (Figure 3d). The close contact between the two molecules in **1a**·HCl·$2H_2O$ could be a result of the cation–π interactions of the pyridinium ring and the phenyl ring, which would account for the excellent selectivity.

To show the generality of the effectiveness of the pyridinium–π interactions for the preorientation of azaanthracenes prior to photodimerization, [4 + 4] photodimerization of 2-azaanthracene (**1b**) was carried out in both solution and solid phase. Irradiation of **1b** in MeOH

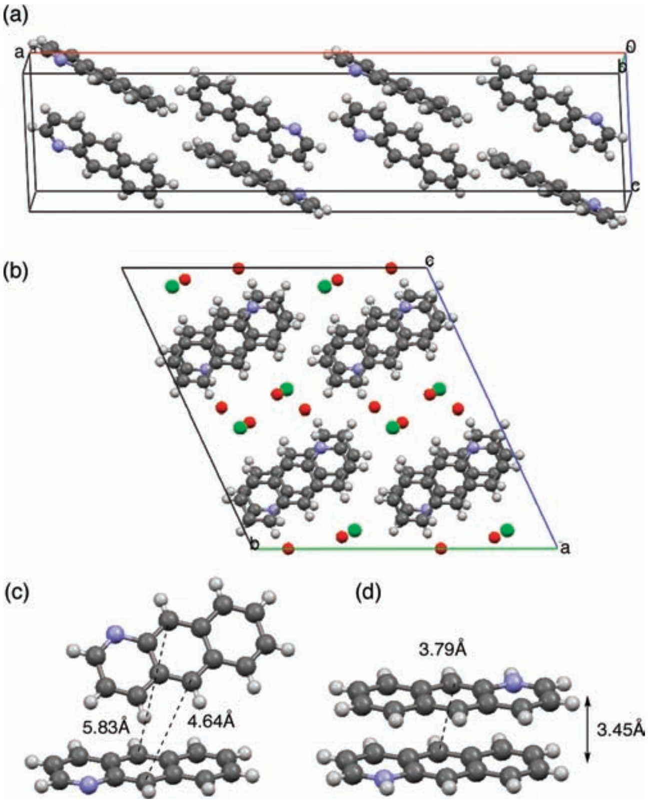


Figure 3. X-ray packing diagrams for (a) **1a** and (b) **1a**·HCl·$2H_2O$, and X-ray structures of two neighboring molecules for (c) **1a** and (d) **1a**·HCl·$2H_2O$.

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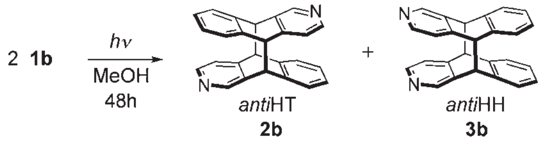
Table 3. [4 + 4] Photodimerization of **1b** in MeOH[a]



entry	HCl (eq)	concn (M)	conv (%)	products (%)[a]	
				2b	**3b**
1	0	1.0	>99	62	38
2	3	1.0	>99	77	23
3	5	1.0	>99	84	16

[a] The conversion and yields were determined by ^{1}H NMR spectra.

Table 4. Photodimerization of **1b** and **1b**·HCl in Crystal Form

$$\mathbf{1b} \text{ or } \mathbf{1b}\cdot\text{HCl} \xrightarrow[\text{crystal}]{h\nu} \mathbf{2b} + \mathbf{3b}$$

entry	substrate	time (h)	conv (%)	products (%)[a]	
				2b	**3b**
1	**1b**	22	0	0	0
2	**1b**·HCl·2H_2O[b]	30	89	89	11
3	**1b**·HCl	48	63	>99	0

[a] The conversion and yields were determined by ^{1}H NMR spectra. [b] Hydrate crystals dipped in paraffin oil.

for 48 h produced the *anti*-HT dimers **2b** and **3b** in 62% and 38% yields, respectively (Table 3, entry 1). The X-ray structural analysis and the ^{1}H NMR spectra proved that the structures of **2b** and **3b** are *anti*-HT and *anti*-HH, respectively. As the amount of HCl was increased, the yield of the *anti*-HT **2b** was increased, a result similar to that observed for **1a** (entries 2 and 3), which can also be explained by the contribution of cation−π interactions.

The irradiation of powdered 2-azaanthracene crystals gave no dimer (Table 4, entry 1), whereas the irradiation of **1b**·HCl·2H_2O gave the *anti*-HT dimers **2b** in 89% yield accompanied by a small amount of **3b** (entry 2). On the other hand, irradiation of anhydrate obtained by dehydration of **1b**·HCl·2H_2O produced **2b** with high selectivity (entry 3).

The preference for a head-to-tail orientation among pyridinium compounds has also been observed in a *N*-methylnicotinium salt[12] and a 4-styrylpyridinium salt.[9,12] These characteristic features are speculated to be the result of stabilization by cation−π interactions, a hypothesis supported by the significantly larger $Py^+\cdots Ar$ interaction energy (−8.34 kcal/mol) than that for the $Py\cdots Ar$ interaction (−3.04 kcal/mol).[17] It has been reported that the X-ray structure of acridizinium,[18] which is structurally related to **1a**·H^+, also shows a head-to-tail orientation. This also may be due to cation−π interactions similar to the case of **1a**·H^+.

In summary, we clarified that the irradiation of azaanthracenes produced dimers in both solution and solid phase. In solution, the addition of HCl dramatically improved the selectivities of *anti*-HT dimers. In the solid state, although both **1a** and **1b** are photostable, the corresponding HCl salts quantitatively produced *anti*-HT dimers. These results clearly show that only protonation of the pyridine moiety is critical for the preorientation of azaanthracenes through cation−π interactions, thereby providing excellent selectivities in the [4 + 4] photodimerization reactions.

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Supporting Information Available. Crystallographic data for **1a**, **1a**·HCl, **2a**·2HCl, **2b**·2HCl, and **4a**. Experimental procedure of photodimerization. Details for DFT calculations. Spectral data and ^{1}H NMR spectra for **2a**, **2b**, **3a**, **3b**, and **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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