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[2+2] Photodimerization of bispyridylethylenes by a controlled shift of the protonation equilibrium

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ABSTRACT

Irradiation of *trans*-4,4′-bispyridylethylene in the presence of 1 equiv of concd HCl produced a *syn* dimer with high selectivity, whereas irradiation in the presence of more than 2 equiv of concd HCl or in the absence of HCl gave a mixture of dimers and by-products with much lower selectivity. This indicated that a suitable amount of acid served as a catalyst for the [2+2] photodimerization of BPEs through cation–π interactions between the pyridinium and pyridine rings.

Introduction

The preorientation of alkenes prior to irradiation is a powerful strategy to achieve high stereoselectivity in solid-state [2+2] photodimerization reactions.[1] As a substrate, *trans*-4,4′-bispyridylethylene (BPE) has often been employed, as the two pyridyl moieties are effective in making complexes with templates,[2] hosts,[3] metal ions,[4] and imprinted polymers,[5] and in the formation of coordination polymers.[6] Irradiation of such systems affords *syn* dimers in high yields. However, except for reports using an inclusion complex with CA[8][3a] and CB[8],[3b] there have been only a few examples of the photodimerization in solution phase due to the difficulties associated with controlling the orientation of molecules in solution. From a synthetic point of view, photochemical reactions in solution phase remain of great importance.

We have reported that cation–π-controlled preorientation is extremely effective in the stereoselective photodimerization of styrylpyridines[7] and azaanthracenes[8] in solution phase. In these reactions, cation–π interactions between pyridinium and aromatic rings lead the molecules to arrange themselves in a head-to-tail fashion, the subsequent irradiation of which affords *syn*HT dimers. These observations prompted us to investigate the photodimerization of BPEs according to the strategy shown in Scheme 1: the protonation equilibrium among **A**–**C** can be shifted toward **B** by adjusting the concentration of an acid, irradiation of which would stereoselectively produce a *syn* dimer.

In this communication, we report that the acid amount is critical to the stereoselectivity in the [2+2] photodimerization of BPEs in solution. In addition, the relationship between the crystal structures and photoreactivities of the BPEs (**1a** and **1b**) and corresponding *N*-methyl (**2a** and **2b**) and *N*,*N*′-dimethyl salts (**3a** and **3b**) were investigated (Fig. 1) to clarify the importance of monocationic species.

Results and discussion

Irradiation of 0.5 M of **1a** in a 1:1 mixture of methanol/water solution with a 450 W high-pressure mercury lamp for 2 h through a Pyrex filter afforded dimers **4a** and **5a**, as well as dipyridylethane **6a**[9] and hydroxymethylated compound **7a**[9] with lower selectivities as shown in Table 1 (entry 1). This lower selectivity is in agreement with that previously reported.[9] On the other hand, in the presence of 0.05 equiv of concd hydrochloric acid, the photochemical reaction resulted in remarkable changes in product distribution (entry 2); the yield of the *syn* dimer **4a** significantly increased, becoming a major product, while that of the *anti* dimer **5a** decreased. Increasing the HCl loading to 0.8 equiv led the highest yield of **2a**, with a *syn*/*anti* ratio of 16.6 (entries 5 and 6). Further addition of HCl from 0.8 to 3.0 equiv caused a gradual decrease in **4a** and increases in **5a**, **6a**, and **7a** (entries 7–9). The addition of 3 equiv of HCl, in particular, resulted in a dramatic decrease in **4a** and increase in **6a**.

Figure 2 shows the plots of product distribution versus HCl loading. This clearly shows that the formation of a *syn* dimer is extremely dependent on HCl concentration, with HCl in the range from 0.1 to 1.5 equiv being particularly effective. This means that a

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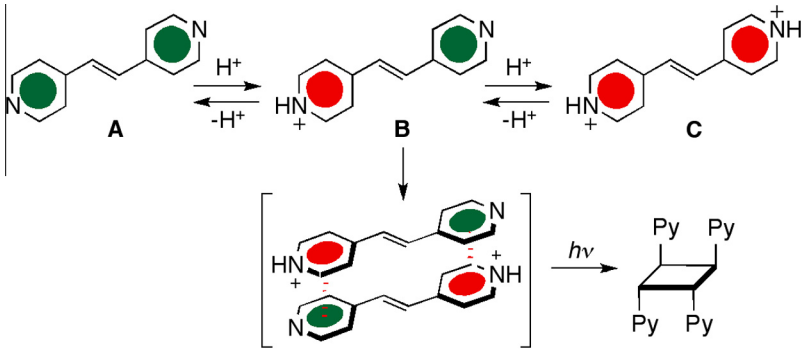


Scheme 1. Photodimerization of BPE through cation–π interactions under a controlled shift of the protonation equilibrium toward **B**.

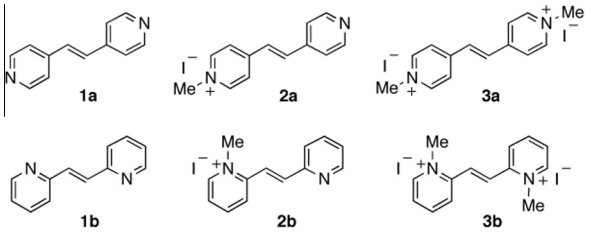
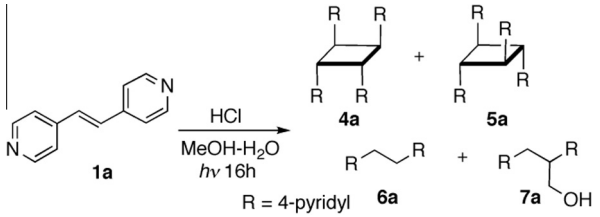


Figure 1. Substrates for photodimerization.

Table 1
Product distribution for photodimerization reaction of **1a** in the presence of HCl[a]



Entry	HCL (equiv)	Conv (%)	Products[b] (%)				Ratio (**4a**/**5a**)
			4a	**5a**	**6a**	**7a**	
1	0	90	37	11	14	38	3.4
2	0.05	>99	68	5	14	13	14.0
3	0.1	>99	74	5	10	11	14.8
4	0.5	>99	80	5	6	9	16.0
5	0.8	>99	83	5	4	8	16.6
6	1.0	>99	80	6	4	10	13.3
7	1.5	>99	78	7	4	12	11.1
8	2.0	>99	68	7	8	18	9.7
9	3.0	>99	19	8	49	24	2.4

[a] A 0.5 M solution was used.
[b] Determined by ^{1}H NMR spectra.

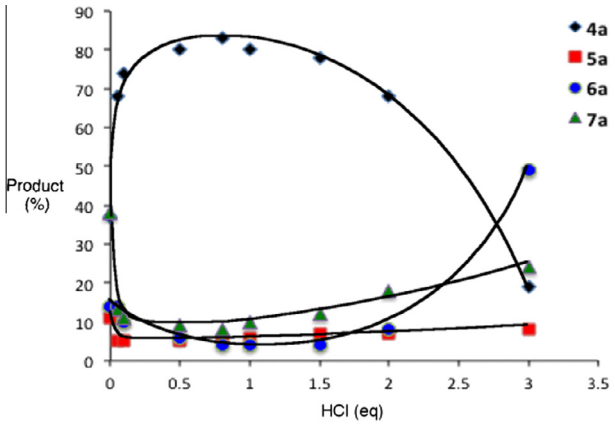


Figure 2. The product distribution for the photodimerization of **1a** versus HCl loading.

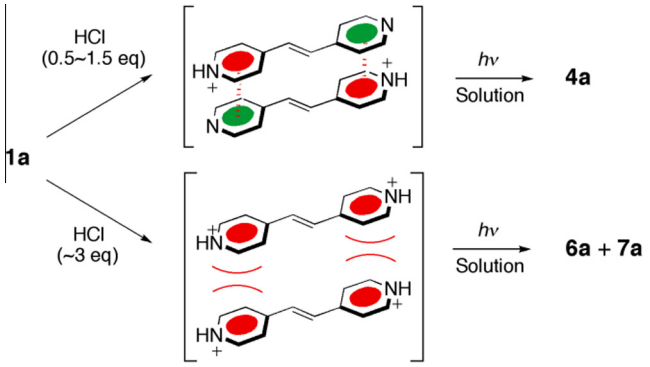
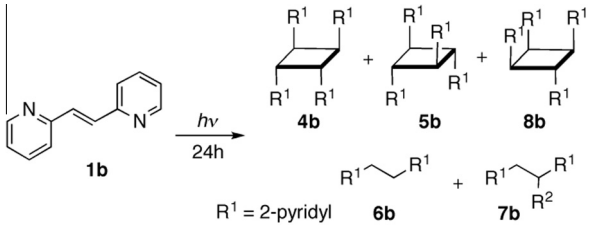


Figure 3. Differences in the orientation behavior between mono- and dications in solution.

Table 2
Product distribution for photodimerization reaction of **1b** in the presence of HCl



Entry	Solv[a]	HCL (equiv)	Conv (%)	Products[b] (%)				
				4b	**5b**	**6b**	**7b**	**8b**
1	MeOH	0	67	52	13	7	28[c]	0
2	MeOH	1.0	94	32	1	3	61[c]	3
3	*i*-PrOH	1.0	83	56	1	11	22[d]	10
4	H_2O	1.0	92	71	1	0	0[e]	28
5	H_2O	2.5	95	26	2	5	9[e]	59

[a] A 0.5 M solution was used.
[b] Determined by ^{1}H NMR spectra.
[c] $R^2 = CH_2OH$.[9]
[d] $R^2 = C(CH_3)_2OH$.[10]
[e] $R^2 = OH$.[11]

controlled shift of the protonation equilibrium toward monocation species enables cation–π interactions between the pyridinium and the pyridine rings, as shown in Figure 3. This working model also explains the observed increase in the ratio of **4a** to **5a** with increases in HCl loading. On the other hand, for fully protonated pyridinium dications, the attractive force is no longer reduced and a repulsive force arises, leading to the increase in **6a** and **7a** as a result of lowered dimerization rates, as shown in Figure 3.

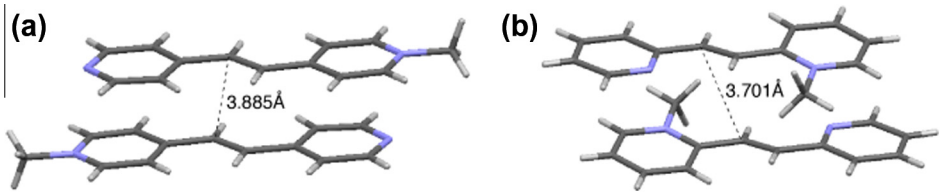


Figure 4. The crystal structures for (a) **2a** and (b) **2b**.

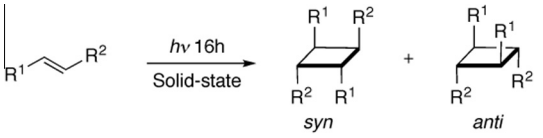
The contribution of the cation–π interaction between the monocations was determined by studying the concentration dependence of the ^{1}H NMR chemical shifts. As the concentration of **1a**·HCl was increased from 1.0 to 30 mM in $CDCl_3$, the α-proton of the pyridinium ring of **1a**·HCl was shifted from δ 8.70 to δ 8.78, whereas no shift was observed for the corresponding α-proton of **1a**, suggesting the contribution of the cation–π interaction in the HCl salt at higher concentrations (see, Supplementary data).

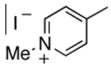
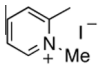
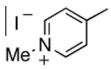
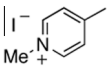
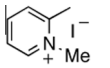
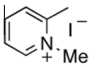
To show the generality of the importance of the monocation in *syn* selectivity, [2+2] photodimerization of 2,2′-bispyridylethylene (**1b**) was carried out (Table 2). Irradiation of a 0.5 M MeOH solution of **1b** for 24 h produced a mixture of *syn* and *anti* dimers with low selectivity (entry 1). On the other hand, the addition of 1.0 equiv of HCl, significantly improved the syn selectivity, similar to that observed for **1a**, although **7b** was obtained as a major product (entry 2). To reduce the yield of byproduct **7b**, a change in solvent from MeOH to *i*-PrOH was effective to yield **4b** as a major product.[12] The use of H_2O as a solvent significantly improved the yield of **4b** (entry 4). In the presence of 2.5 equiv of HCl, the yield of **4b** was significantly decreased with increase of **8b** (entry 5).

Product distribution was monitored by ^{1}H NMR spectra to clarify its irradiation time dependence (see, Supplementary data). As irradiation time was increased, the yield of **1b** rapidly decreased and that of the *syn* dimer **4b** increased, whereas that of **5b** was almost unchanged. After irradiation for 11 h, **1b** was almost completely consumed. These observations indicate that **4b** was directly produced through the dimerization of **1b** without any isomerization of the other products, similar to process observed for **1a** (Fig. 3). Irradiation of the isolated **4b** was unchanged under the same reaction conditions, showing that this dimerization process is irreversible. It has been known that the quantum efficiency of *E*/*Z* isomerization of bispyridylethylene is much lower than that of stilbene.[13] In addition, the efficiency in 4,4-BPE is much lower than that in 2,2-BPE.[13] Therefore, the *E*/*Z* isomerization would not be observed for the photochemical reaction of 4,4-BPE. On the other hand, it has also been reported that a polar solvent enhances the *E*/*Z* isomerization of BPE,[10] suggesting that the dimer **8b** would be produced from the [2+2] photocyclization reaction between (*E*)-**1b** and (*Z*)-**1b** formed by photoisomerization, which is similar to the mechanism for the photodimerization of (*Z*)-styrylpyridines.[14] Although it was reported that isomerization of **4b** to **8b** proceeds in the presence of HCl,[4i] the isolated **4b** did not undergo isomerization under the present reaction conditions.

To investigate the role of the cationic charge of the molecules on their orientation, a comparison among X-ray crystal structures of bispyridylethylenes (**1a**[15] and **1b**[15]), *N*-methyl salts (**2a**[16] and **2b**[15]) and *N*,*N*′-dimethyl salts (**3a**[15] and **3b**[15]) was carried out (see, Supplementary data). As the preparation of single crystals of mono-hydrochloride is difficult due to it having two pyridyl moieties, *N*-methyl salts were employed for comparison instead of hydrochloride salts. The pyridine rings between neighboring molecules for **1a** and **1b**, and the pyridinium rings between neighboring molecules for **3a** and **3b** were located apart from each other (**1a**: 5.772 Å; **1b**: 5.654 Å; **3a**: 6.281 Å; **3b**: 7.023 Å). On the other hand, the molecules of **2a** and **2b** were arranged head-to-tail and face-to-face (Fig. 4). The distances between the neighboring double bonds were 3.885 Å and 3.701 Å, respectively. As expected from the crystal structures of **2a** and **2b**, they were photoreactive and gave the corresponding *syn* dimers[15,17] in quantitative yields. On the other hand, the compounds **1a**, **1b**, **3a**, and **3b** were all basically photostable (Table 3).[18] The fact that head-to-tail column structures were observed only in the mono-methyl salts **2a** and **2b** supports the existence of an attractive interaction between the pyridinium and pyridine rings.

Table 3
Solid-state photodimerization reactions of **1a**, **1b**, **2a**, **2b**, **3a**, and **3b**



Compd	R^1	R^2	Product[a] (%)
1a			*syn* (1.6%) + *anti* (0.4%)
1b			*syn* (1.6%) + *anti* (9%)
2a			*syn* (>99%)
2b			*syn* (>99%)
3a			No reaction
3b			No reaction

[a] Determined by ^{1}H NMR spectra.

Conclusion

In summary, we clarified that the HCl loading is critical to the product distribution in the [2+2] photodimerization of *trans*-BPEs. Irradiation in the presence of 1 equiv of concd HCl produced the *syn* dimer with high selectivity, whereas in the absence or in the presence of more than 2 equiv of concd HCl a mixture of dimers was obtained with much lower selectivity, strongly suggesting the contribution of the cation–π interaction between the pyridinium and pyridine rings. This indicated that a suitable amount of acid served as a catalyst for the [2+2] photodimerization of BPEs through cation–π interactions.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.05.075.

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