# Aqueous Photo-Dimerization Using 2-Pyridylsilyl Group as a Removable Hydrophilic Group

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The [2 + 2] photo-dimerization of 2-pyridylsilyl-substituted stilbene derivatives was investigated and exclusive dimer production was observed in aqueous dilute solution. This result is explained in terms of the local concentration effect of substrates in water. The transformation of obtained photo-dimer was also investigated.

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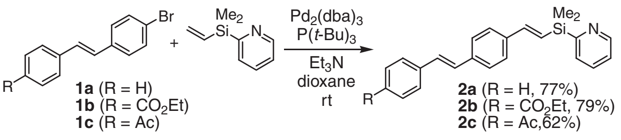
Aqueous organic reactions have been recognized as important processes because of their efficiencies and unique properties of water.[1] Although the low solubility of usual organic compounds in water has been an inevitable problem in aqueous organic reactions, this can be partly overcome by introducing a hydrophilic group to substrate molecules. In view of the synthetic flexibility, the use of "removable hydrophilic group" is extremely attractive for aqueous organic reactions.[2,3]

During the course of our study using 2-pyridyldimethylsilyl group (2-PyMe$_2$Si) as a removable hydrophilic group in aqueous organic reactions, we observed dramatic rate acceleration in the aqueous Diels–Alder reaction using 2-PyMe$_2$Si-substituted 1,3-dienes.[4] This result encouraged us to examine the aqueous [2 + 2] photo-dimerization of alkenes, which is also cycloaddition that could be accelerated in water. As a pioneering work of aqueous photo-dimerization, Morrison reported that coumarin dimerizes at much lower concentration in water than in organic solvents.[5] In this case, the improvement of quantum yield was observed by a 100-fold. Ramamurthy and Syamala observed an efficient photo-dimerization of stilbene derivatives in water. They assumed the accelerated efficiency is ascribed to the hydrophobic association of stilbene molecule in water (local concentration effect).[6] Thus, we prepared 2-PyMe$_2$Si-substituted stilbene derivatives and examined their photo-dimerization in water. Moreover, the removal of 2-PyMe$_2$Si group from the obtained dimer was achieved by the palladium-catalyzed Hiyama-type silicon-based cross-coupling reaction.

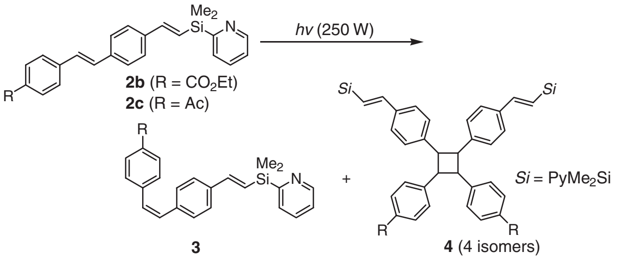
The 2-PyMe$_2$Si-substituted stilbene derivatives **2a**–**2c** were prepared by the Mizoroki–Heck reaction of 2-pyridyldimethylvinylsilane[7] with bromostilbene derivatives **1a**–**1c** under the influence of Pd$_2$(dba)$_3$/P($t$-Bu)$_3$ catalyst (5 mol %)[8] and Et$_3$N in dioxane. The reactions proceeded smoothly at room temperature to furnish the 2-PyMe$_2$Si-substituted stilbene derivatives **2a**–**2c** in good yields (Scheme 1).

With these substrates in hand, we examined their photo-dimerization in water.[9] For comparison, we conducted the reaction in toluene as well. Whereas **2a** did not give any [2 + 2] dimers upon irradiation, **2b** and **2c** were found to give the expected dimers **4** together with the olefin isomerization products **3** (Table 1).



**Scheme 1.**

**Table 1.** Aqueous photo-dimerization of stilbene derivatives **2a**



| Entry | 2 | Solvent | Time /h | Recovered **2**/% | **3** /% | **4** /% |
|---|---|---|---|---|---|---|
| 1[b] | **2b** | $H_2O$ | 20 | 60 | 7 | 33 |
| 2 | **2b** | toluene | 20 | 23 | 41 | 36 |
| 3[b] | **2c** | $H_2O$ | 20 | 29 | 13 | 58 |
| 4[c] | **2c** | toluene | 12 | 26 | 74 | 0 |
| 5[d] | **2c** | toluene | 20 | 37 | 40 | 23 |
| 6[e] | **2c** | toluene | 20 | 7 | 5 | 88 |

[a]Unless otherwise stated, the reactions were carried out at 0.005 M. [b]1.0 equiv. of HCl was added. [c]The reaction reached the steady state within 12 h. [d]0.025 M. [e]0.25 M.

The reaction of **2b** gave the [2 + 2] dimer **4b** (33%) and isomerization products **3b** (7%) after irradiation for 20 h (Entry 1). Although the reaction in toluene gave the dimer **4b** in a similar amount (36%), significant amount of **3b** (41%) was formed (Entry 2). This trend became more significant when **2c** was used as a substrate. While the reaction in aqueous HCl gave the dimer **4c** in 58% yield (Entry 3), the reaction in toluene produced solely the olefin isomerization product **3c** (Entry 4). The expected dimer was not formed at this concentration (0.005 M). These results indicate that photo-dimerization could also be facilitated in water. In addition, the solvent effect in olefin isomerization might be also worthy of noting. As for accelerated photo-dimerization in aqueous solution, the local concentration effect, as Ramamurthy proposed,[6] seems to be responsible for the preferential dimerization in water. In accord with this assumption, the photo-dimerization of **2c** did occur in toluene at higher concentration (Entries 5 and 6).

The isomer distribution of photo-dimer **2c** was examined in detail. The all possible isomers [*syn* head-to-head (H-H) (**4cA**), *syn* head-to-tail (H-T) (**4cB**), *anti* H-H (**4cC**), and *anti* H-T (**4cD**)] were found and assigned by the NOE experiments and by the comparison with known stilbene dimers reported in the literature (Figure 1).[10] We found that syn isomers (**4cA** and

**4cB**) were obtained exclusively in both aqueous (93% *syn*, 0.005 M) and toluene (88% *syn*, 0.25 M) solutions.

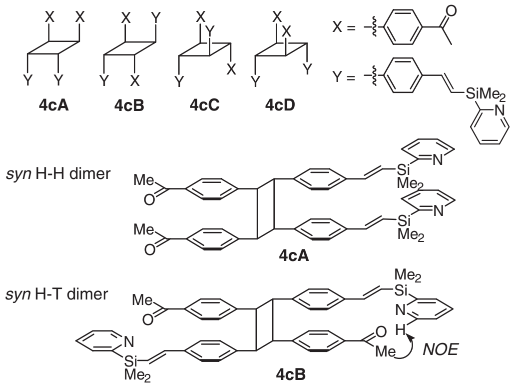
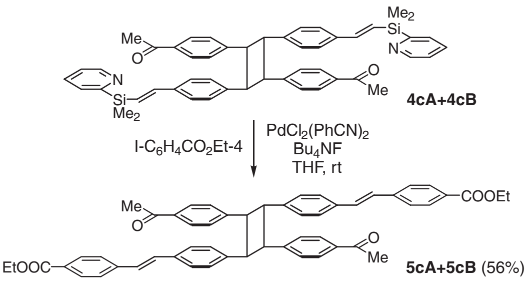


**Figure 1.**

We initially assumed that the *syn* H-H dimer (**4cA**) would be obtained as a major product if 2-PyMe$_2$Si group worked as a hydrophilic group, which induces a H-H orientation of stilbene derivatives at the surface of their aggregates in water.[11] Contrary to our assumption, the aqueous reaction gave the syn H-T dimer (**4cB**) preferentially (**4cA**/**4cB** = 16/84). Since the H-T dimer was also produced preferentially in toluene (**4cA**/**4cB** = 38/62), the observed head-to-tail selectivity may be primarily attributed to the inherent stereoelectronic nature of this substrate (e.g., the steric repulsion between the 2-PyMe$_2$Si groups). These results suggest that the photo-dimerization exclusively takes place at the interior of large aggregates, where there must be little orientation effect. Thus, the effect of water can be regarded as additive for this selectivity. Nevertheless, the enhanced selectivity may be worthy of noting and we assume the followings as the plausible explanations for the selectivity enhancement: (i) the electronic repulsion between pyridinium ions in water; and (ii) the attractive hydrogen bonding between the oxygen atom of the acetyl group and the pyridinium proton in acidic aqueous solutions.

The removal of 2-PyMe$_2$Si group from the photo-dimer **4c** was achieved by the Hiyama coupling.[12] This reaction also serves as a method for the extension of $\pi$-system by introducing aromatic groups. Thus, the treatment of **4c** with 4-iodobenzoic acid ethyl ester (2.4 equiv.) under the influence of PdCl$_2$(PhCN)$_2$ catalyst (10 mol %) and Bu$_4$NF (1.4 equiv.) furnished the coupling product **5c** in 56% yield (Scheme 2).[13]



**Scheme 2.**

In summary, the observations described here indicated that the use of 2-PyMe$_2$Si group as a removable hydrophilic group is quite effective for the aqueous photo-dimerization of stilbene derivatives. The acceleration at lower concentration is attributed to the local concentration effect. It is also noteworthy that the photo-dimer thus obtained could be transformed into a more extended $\pi$-system using Hiyama coupling by the agency of 2-PyMe$_2$Si group.

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9 As stated in our previous papers,[4] we typically add an equimolar amount of HCl to render 2-PyMe$_2$Si-substituted molecules soluble in water. The application of this procedure to stilbene derivatives **2** gave rise to homogeneous emulsion, which was used for aqueous photodimerization.

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11 In the case of aqueous solutions of 2-PyMe$_2$Si-substituted 1,3-dienes, large molecular aggregates were observed. These large aggregates probably stem from nonordered structures as stated in reference 4.

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13 Cross-coupling product **5cB**. $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 1.41 (t, $J = 7.2$ Hz, 6H), 2.53 (s, 6H) , 4.38 (q, $J = 7.2$ Hz, 4H), 4.56 (s, 4H), 7.03 (d, $J = 16.8$ Hz, 2H), 7.10 (d, $J = 16.4$ Hz, 2H), 7.11 (dm, $J = 8.4$ Hz, 4H), 7.22 (dm, $J = 8.4$ Hz, 4H), 7.34 (dm, $J = 8.0$ Hz, 4H), 7.51 (dm, $J = 8.4$ Hz, 4H), 7.77 (dm, $J = 8.8$ Hz, 4H), 8.00 (dm, $J = 8.4$ Hz, 4H). $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 14.5, 26.6, 47.5, 47.8, 60.9, 126.1, 126.6, 127.3, 128.07, 128.17, 128.20, 129.2, 129.8, 130.5, 134.9, 135.1, 139.7, 141.5, 145.8, 166.1, 197.3. HRMS-FAB ($m/z$): [M+H]$^+$ calcd for C$_{54}$H$_{48}$O$_6$ 793.3529, found 793.3528.

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