7.57 (d, $J = 7$ Hz, 1H), 7.48 (d, $J = 7$ Hz, 1H), 7.40 (t, $J = 7$ Hz, 1H), 5.00 (d, $J = 3$ Hz, 6H), 3.83 (d, $J = 9$ Hz, 6H), 3.61 (dd, $J' = 10$, $J'' = 3$ Hz, 6H), 3.52 (s, 3H), 3.49 (t, $J = 10$ Hz, 6H), 3.34 (d, $J = 10$ Hz, 6H), 3.31 (s, 18H), 3.26 (s, 18H), 3.24 (s, 18H), 3.19 (t, $J = 10$ Hz, 6H), 3.01 (dd, $J' = 10$, $J'' = 3$ Hz, 6H); ^{13}C NMR (125 MHz, D_2O): $\delta = 169.1$, 165.4, 164.0, 150.7, 150.5, 147.7, 143.8, 141.8, 141.5, 138.5, 133.9, 133.1, 131.7, 129.94, 129.93, 129.7, 128.9, 128.1, 124.9, 123.7, 121.3, 118.5, 117.4, 100.0, 82.4, 81.4, 81.1, 71.4, 71.1, 62.5, 59.0, 57.6, 39.1; UV/Vis (H_2O): $\lambda_{max} = 364$ nm, $\lg\varepsilon = 4.3$; ES-MS (negative): m/z: 964.2 [M^{3-}+Na$^+$].

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[9] UV/Vis titrations in water at 298 K showed that the complex **2**·TM-α-CD has a stability constant of $(5 \pm 1) \times 10^5\,\text{M}^{-1}$ compared to only $(1.1 \pm 0.1) \times 10^4\,\text{M}^{-1}$ for **2**·α-CD. It is difficult to obtain an accurate value of K_1 for **2**·TM-α-CD because a weak complex **2**·2TM-α-CD is also formed, $K_2 \approx 100\,\text{M}^{-1}$. For other work on the stability of azo dye CD complexes, see: N. Yoshida, *J. Chem. Soc. Perkin Trans. 2* **1995**, 2249–2256.

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2-Pyridyldimethylsilyl as a Removable Hydrophilic Group in Aqueous Diels–Alder Reactions[**]

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Jun-ichi Yoshida*

During the last two decades water has been rediscovered as a most intriguing medium for organic synthesis.[1] However, the execution of organic reactions in water is not straightforward since many organic compounds, reagents, and catalysts are insoluble or unstable in it. Therefore, many of the reported aqueous organic reactions have had to rely on the use of organic co-solvents at the expense of the many inherent advantages and unique properties of water, such as hydrophobic effects, hydrogen-bonding interactions, and high polarity.[1]

During the course of our study on the development of multifunctional phase tags for solution-phase synthesis it was found that organic molecules bearing the 2-pyridyldimethylsilyl (2-PyMe$_2$Si) group are miscible with water when HCl is added.[2, 3] Molecular aggregation seems to be involved in their dissolution so as to minimize the energetically unfavorable contact between water molecules and nonpolar carbon chains. In addition, we have also established that the 2-PyMe$_2$Si group can be easily removed from organic molecules by oxidation with H_2O_2 to afford the corresponding alcohols.[4]

We envisioned that if the 2-PyMe$_2$Si group works as a removable hydrophilic group and induces molecular aggregation in water, organic reactions in aqueous molecular aggregates should be possible when the reaction site is located on a hydrophobic side chain of the 2-PyMe$_2$Si-substituted molecule (Figure 1).[5] The advantage of using the 2-PyMe$_2$Si

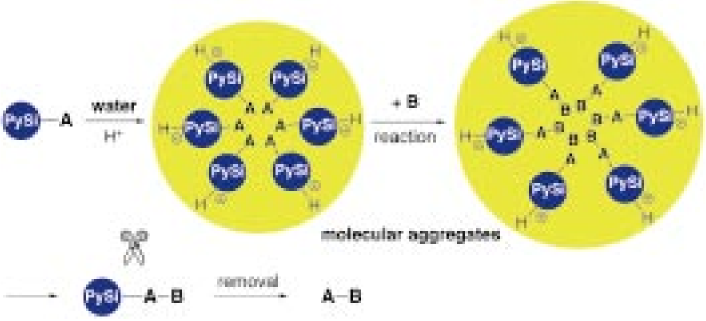

Figure 1. New strategy for aqueous organic reactions using a removable hydrophilic group.

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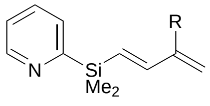
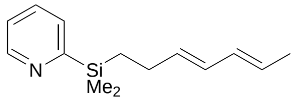
group is apparent, as it can be readily removed from the molecules when required either by desilylation or oxidation. We chose an intermolecular Diels–Alder reaction of the 2-PyMe$_2$Si-substituted 1,3-dienes **1**–**3** to evaluate our strategy of using a removable hydrophilic group in aqueous organic reactions.[1, 6–9]



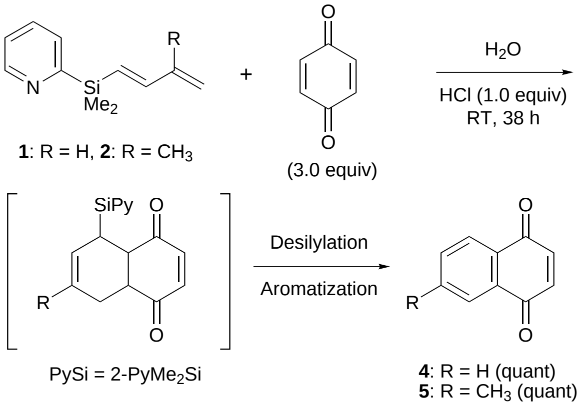
1: R = H, **2**: R = CH$_3$



3

First, the solution behavior of the 2-PyMe$_2$Si-substituted 1,3-dienes **1**–**3** in water was examined by dynamic light-scattering experiments on aqueous solutions (containing 1.0 equiv of HCl) of these dienes. These experiments revealed the presence of molecular aggregates of **1**–**3** with average hydrodynamic radii of 197, 138, and 307 nm, respectively. However, the determination of the exact structure of the molecular aggregates must await further investigations. The large radii observed can probably be attributed to nonordered structures of molecular aggregates in aqueous solution. The detection of molecular aggregates led us to explore aqueous reactions of **1**–**3**, irrespective of the structures of their molecular aggregates.

The Diels–Alder reactions of **1** and **2** with *p*-benzoquinone occurred at room temperature in water with simultaneous desilylation and aromatization to afford, respectively, naphthoquinones **4** and **5** quantitatively [Eq. (1)]. In these cases, an additional chemical operation to remove the 2-PyMe$_2$Si group was unnecessary.



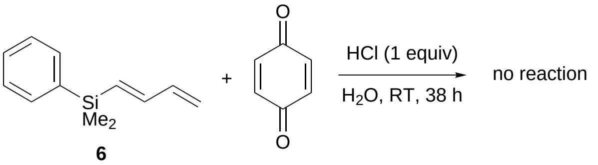
(1)

Several control experiments were conducted to assess the effect of the 2-PyMe$_2$Si group (Table 1). Decreasing the amount of HCl added slowed down the reaction enormously and only a trace amount of **4** was formed (entries 2 and 3). We contend that at least one equivalent of HCl is required for the 2-PyMe$_2$Si-substituted diene to form molecular aggregates and that the reaction probably occurs in the interior of aggregates where there are enhanced hydrophobic interactions,[10] and not in the aqueous bulk phase.[6] The use of H_2SO_4 also gave rise to a rate enhancement, but not as dramatic as with HCl (entry 4). The reaction carried out in organic solvent resulted in a much lower yield of the product (entries 5 and 6), which indicates the rate acceleration occurs in water. In contrast, the reaction with the PhMe$_2$Si-substituted diene **6** gave no Diels–Alder adduct at all in water [Eq. (2)].

Table 1. Aqueous Diels–Alder reactions of **1** with *p*-benzoquinone.[a]

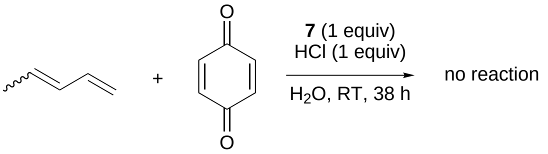
Entry	Solvent	Additive (equiv)	Time [h]	Yield of **4** [%][b]
1	H_2O	HCl (1.0)[c]	38	quant
2	H_2O	HCl (0.2)	47	2
3	H_2O	–	89	4
4	H_2O	H_2SO_4 (1.0)	38	73
5	Et_2O/toluene	HCl (1.0)	38	22
6	Et_2O/toluene	–	38	6

[a] All reactions were performed at room temperature using **1** (1.0 equiv, 1.0 M concentration) and *p*-benzoquinone (3.0 equiv). [b] Yields of isolated product. [c] The addition of 2.0 equivalents of HCl did not affect the rate and yield.



(2)

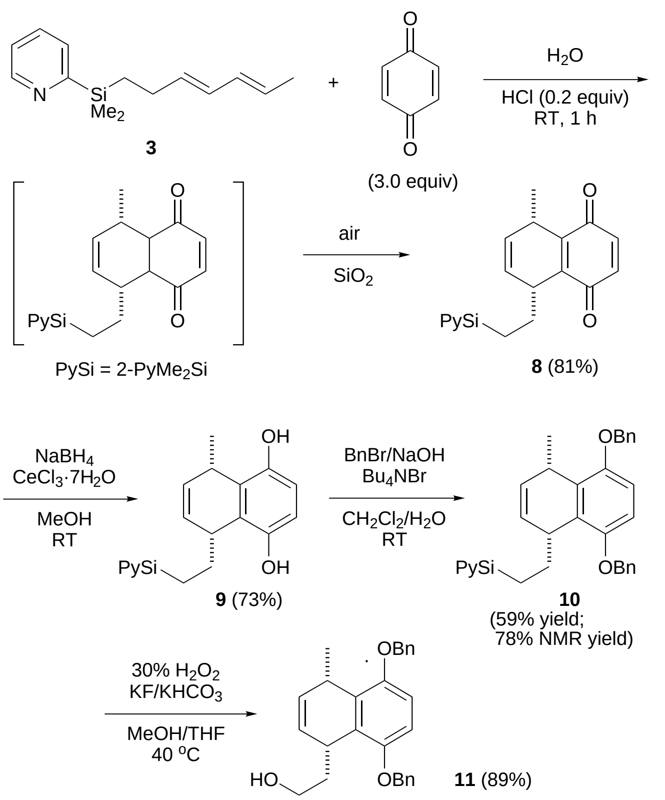
Next, we examined the aqueous reaction of 1,3-pentadiene with *p*-benzoquinone in the presence of protonated 2-pyridyldimethyloctylsilane (**7**) as a surfactant. The hard-to-dissolve 1,3-pentadiene dissolved in water when **7** and HCl were added. Thereafter, *p*-benzoquinone was added to the solution. However, in sharp contrast with the reaction of **1** or **2**, no cycloadduct was observed at room temperature [Eq. (3)]. It is apparent that the use of a reacting surfactant has an advantage in terms of reactivity over the combined use of an external surfactant.[6b, 11]



(3)

The aqueous Diels–Alder reaction of **3** with *p*-benzoquinone was complete within one hour to give the cycloadduct **8** (Scheme 1).[12] In this case a catalytic amount of HCl (0.2 equiv) was enough to promote the reaction. Interestingly, the formation of molecular aggregates (average hydrodynamic radii: 65 nm) was observed even at the end of the reaction. Moreover, the rate acceleration in water was again observed (12 % yield of **8** in Et_2O/toluene).

The transformation of **8** was examined to test the chemical stability and removability of the 2-PyMe$_2$Si group (Scheme 1). The reduction of **8** afforded the substituted hydroquinone **9** in 73 % yield. The protection of the phenolic hydroxyl groups with benzyl groups afforded **10** in 59 % yield (78 % by NMR spectroscopy). Importantly, the 2-PyMe$_2$Si group was unaf-



Scheme 1. Aqueous Diels–Alder reaction of **3** and removal of the 2-PyMe$_2$Si group. Bn = benzyl.

fected throughout these transformations, which indicates the reasonable chemical stability of this group. Finally, the oxidation of **10** with H_2O_2 afforded **11** in 89% yield without affecting the C–C double bond or eroding the stereochemistry at the allylic carbon atoms.

In summary, we have demonstrated the "proof-of-principle" of our strategy for aqueous organic reactions by utilizing the 2-PyMe$_2$Si group as a removable hydrophilic group. Importantly, the strategy described herein should not be limited to aqueous Diels–Alder reactions but could in principle be applied to other aqueous organic reactions as well.

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[12] The cycloadduct formed initially was easily air-oxidized to **8** when subjected to chromatography on silica gel.

The Combination of Spontaneous Resolution and Asymmetric Catalysis: A Model for the Generation of Optical Activity from a Fully Racemic System[**]

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Dedicated to Professor Henri Kagan
on the occasion of his 70th birthday

Considerable efforts have been devoted to the development of new chiral ligands owing to the growing importance of transition metal catalyzed asymmetric synthesis.[1] Among these chiral ligands, diphosphanes have played a dominant role, in particular those possessing C_2 symmetry.[2] We were interested in the possibilities offered by 1,1′-diphenyl-3,3′,4,4′-tetramethyl-2,2′-biphosphole (**1**) (BIPHOS), first synthesized by Mathey et al. in 1986.[3] This diphosphane combines the axial chirality generated by the biphosphole framework with the central chiralities of the phosphorus atoms. This implies the existence of six stereoisomers, corresponding to three pairs of enantiomers, which are in a fast equilibrium in

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