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Importance of Molecular-Level Contacts under Solventless Conditions for Chemical Reactions and Self-Assembly

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It has been shown that solventless reactions are accelerated when the reactants are mixed at molecular level. Accordingly, a solid film obtained by evaporating a solution of reactants mixture underwent facile reaction either upon grinding or upon simply standing. The effectiveness of these methods is evident from comparison with conventional solventless and solution reactions. It was concluded consequently that, once the molecular-level contacts are formed between reactants, the reaction occurs more efficiently under solventless conditions than in solution. Due to this pre-mixing method, efficient synthesis of [2]rotaxanes and rate acceleration of the Wittig reaction were achieved.

The solventless reactions have received increasing attention and show promise for green chemical processes.[1] However, more significantly, from viewpoints of organic synthesis and process chemistry, high efficiency and selectivity are frequently attained under solventless conditions. Many organic reactions proceed faster under solventless conditions than in solution, and we have reported a dramatic rate enhancement for supramolecular self-assembly as well.[2] For example, a platinum cage molecule, which originally had been prepared in H_2O by heating the reactants for 4 weeks at 100 °C,[3] can be obtained in 10 min at ambient temperature by simply grinding the reaction components.[4] Most reactions between solid reactants demand mechanical forces, like grinding in a mortar with a pestle[1] or compounding in a ball mill.[5] The reaction generally proceeds via a liquid or melt phase through an intimate mixture of solid macroscopic particles of the reactants, so that the molecules inside the solid particles are mobile enough for frequent molecular collisions to occur.[6] In a few cases, powdered, solid reactants liquefy simply by coming in contact each other. Once the melt has been formed, reaction occurs very quickly. It has been suggested that the high mobility can also be achieved in co-crystal formation by adding a minor amount of appropriate solvent (2 drops (ca. 0.05 mL) of organic solvent per ca. 200 mg of the solid mixture).[7] On the other hand, it has been reported that formation of voids and cracks are responsible for the reaction between solids in case of no melt being formed.[8]

In our project involving rotaxane chemistry,[9] we have published a preliminary communication on new versions of solventless reaction.[10] Namely, solid reactants are mixed in solution, and subsequently, the solvent is evaporated. Grinding of the resulting solid film drives the reaction more readily than the direct grinding of the solid reaction components, because the reactant amalgam thus formed contains molecular-level contacts. More remarkably, the reaction proceeds simply upon standing the film without any mechanical forces. In these treatments, both threading of the crown-ether beads and *N*-alkylation take place without solvent. A similar rate acceleration has also been observed for carbon–carbon bond formation like the Wittig reaction.[11] Thus, we became interested in gaining more insight into how the blending of reactants affects a reaction under solventless conditions. In this paper, we report a full account on assessment of these pre-mixing methods by comparing relevant protocols for *N*-alkylation reaction of pyridine derivatives and Wittig reaction. In addition, in the context of rotaxane chemistry, we tried to elucidate how easily self-assembly between bead and thread molecules occurs under solventless conditions, because the mobility of these molecules is another key factor in the efficient solventless end-capping method for rotaxane synthesis.[12] This issue also will be discussed in detail.

Results and Discussion

***N*-Alkylation.** In order to assess the effect of mixing, the following five procedures were compared for three *N*-alkylation reactions of pyridine derivatives **1** with bromides **2** (Scheme 1). Procedure A is a typical conventional solventless reaction, in which solid reactants are directly ground at ambient temperature in a mortar with a pestle. In Procedure B, the conventional method is slightly modified by adding a small amount of an organic solvent to the reactant mixture, according to the literature method.[7] In Procedure C, both reactants are dissolved in acetone in a mortar, and then the solvent is evaporated in vacuo in 5 min period. A film, which has been cast on the surface of the mortar, is ground. Alternatively, in Procedure D, the film is merely allowed to stand on the mortar or more conveniently on an inner surface of a flask without grinding. The high concentration solution method, Procedure E, was used as the reference solution protocol, because of its effectiveness for end-capping synthesis of rotaxanes.[13] In Procedure F, a static pressure ($40\,\mathrm{kg\,cm^{-2}}$) was applied to a pellet of the solid reactants mixture for 1 h at ambient temperature to clarify the importance of mechanical forces for intermingling solid reactants. The results of these operations for the three *N*-alkylation reactions, depicted in Scheme 1, are summarized in Table 1. All reactions were carried out using 0.03 mmol of **1** and 0.06 mmol of **2**. The yields were determined by measuring ^{1}H NMR spectra of the reaction mixture or by isolation as PF_6 salts.[14] The typical mechanochemical

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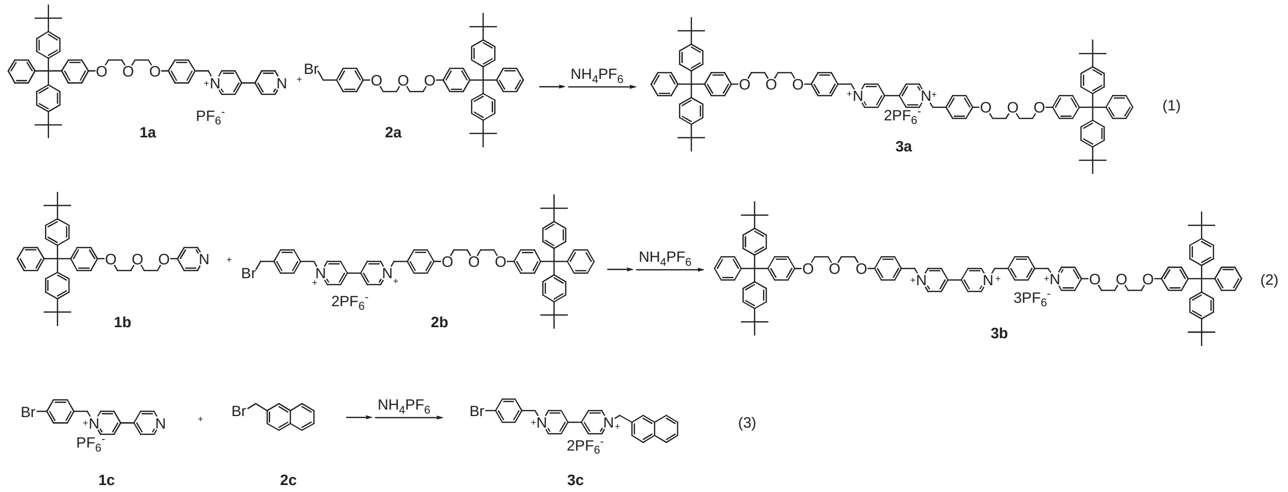


Scheme 1.

Table 1. Solventless *N*-Alkylation under Various Conditions

	Yiled/%[a)]		
	3a	**3b**	**3c**
Procedure A[b)]	40	60	60
Procedure B[c)]	78(73)	80(72)[d)]	73
Procedure C[e)]	79(78)[f)]	82(76)[g)]	82(73)[h)]
Procedure D[i)]	85(77)	80(74)	81(75)[j)]
Procedure E[k)]	83(79)	85(80)	86(77)
Procedure F	0	0	0

a) Determined by NMR; Isolated yileds are given in parentheses. b) Reaction conditions: for **3a**, **3c**: **1** (0.03 mmol); **2** (0.06 mmol); grinding for 1.5 h at r.t.: for **3b**: **1b** (0.06 mmol); **2b** (0.03 mmol); grinding for 1.5 h at r.t. c) Reaction conditions: for **3a**, **3c**: **1** (0.03 mmol); **2** (0.06 mmol); anisole (0.02 mL); grinding for 30 min at r.t.: for **3b**: **1b** (0.06 mmol); **2b** (0.03 mmol); anisole (0.02 mL); grinding for 30 min at r.t. d) 40 min. e) Reaction conditions: for **3a**, **3c**: **1** (0.03 mmol); **2** (0.06 mmol); acetone (0.2 mL); grinding at r.t. after evaporation: for **3b**: **1b** (0.06 mmol); **2b** (0.03 mmol); grinding at r.t. after evaporation. f) Grinding for 30 min. g) Grinding for 50 min. h) Grinding for 15 min. i) Reaction conditions: for **3a**, **3c**: **1** (0.03 mmol); **2** (0.06 mmol); acetone (0.2 mL); standing for 2 h at r.t. after evaporation: for **3b**: **1b** (0.06 mmol); **2b** (0.03 mmol); acetone (0.2 mL); standing for 2 h at r.t. after evaporation. j) Standing for 40 min. k) Reaction conditions: for **3a**, **3c**: **1** (0.03 mmol); **2** (0.06 mmol); acetone (0.2 mL); stirring for 2 days at r.t.: for **3b**: **1b** (0.06 mmol); **2b** (0.03 mmol); acetone (0.2 mL); stirring for 2 days at r.t.

treatment, i.e., Procedure A, did not go to completion, and the desired products **3** were obtained only in 40–60% yields. After being ground for 1.5 h, most of the reactants mixture stayed powdery, although small yellow pasty spots appeared, on which presumably a biased pressure was applied locally. The yield of the alkylation product was increased using Procedure B. The reaction mixture of **1a**/**2a** or **1b**/**2b** formed a melt upon addition of 0.02 mL of anisole and became to a yellow paste by grinding for 5 min. Further grinding for 10 min caused the mixture to solidify, and the reaction was complete in 30–40 min. When acetone was used in place of anisole, the reaction mixture solidified immediately upon grinding probably on account of rapid vaporization of the acetone, and the reaction was not complete after 1.5 h. On the other hand, this protocol was not effective for reaction (3). The reactants mixture did not converted into a molten state by adding anisole, acetone or acetophenone, and grinding of this heterogeneous mixture did not cause the reaction to go to completion, yet a 73% yield of **3c** was obtained. Apparently, the choice of suitable solvent and reactants is crucial for this method.

By contrast, Procedure C constantly gave good yields of the *N*-alkylation products **3** after grinding for 15–50 min. No melt was formed during the manipulation. With Procedure D, the reaction proceeded smoothly even without mechanical forces, although the reaction time was longer than in Procedure C. No change was observed again in the appearance of the film, except for a slight deepening of the yellow color. It was confirmed by monitoring ^{1}H NMR spectra of reaction (1) that the reaction actually proceeded in the solid film without grinding (Fig. 1). In a fresh film which was obtained by mixing **1a** and **2a** in solution followed by evaporation (5 min after the start of mixing), the reaction started to occur to some extent since **1a** was detected in 75% yield.[15] The amount of **1a** was 67% after 30 min, 43% after 1 h, and 9.2% after 1.5 h. The reaction was nearly complete after 2 h with 2% of **1a** remaining. Apparently, the reaction occurred without external mechanical forces, probably because of the close contacts between or facile movement of the reactants molecules in the solid. To check if any acetone remained in the film or not, freshly prepared film in reaction (3) was extracted with $CDCl_3$. The ^{1}H NMR spectrum of this solution exhibited no signal attributable to acetone, an implication of no intervention of the acetone between the reactant molecules in the film.

For comparison, the same reaction was conducted in solution (Procedure E). This procedure furnished comparative yields of **3** after stirring an acetone solution (0.2 mL) of **1** (0.06 mmol) and **2** (0.03 mmol) at ambient temperature.[16] Unfortunately, however, it took 2 days to reach the maximum yield, and TLC analyses showed that the starting compounds remained after shorter reaction times.

The importance of the molecular-level mixing was supported by the following experiments. A pellet of the well-shaken

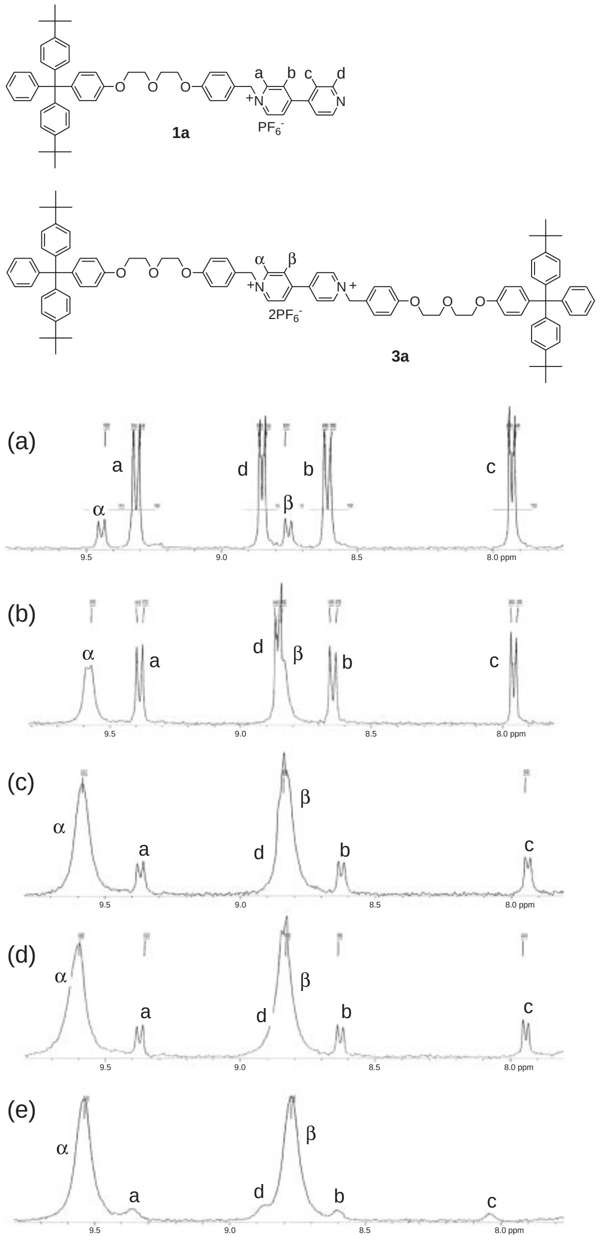


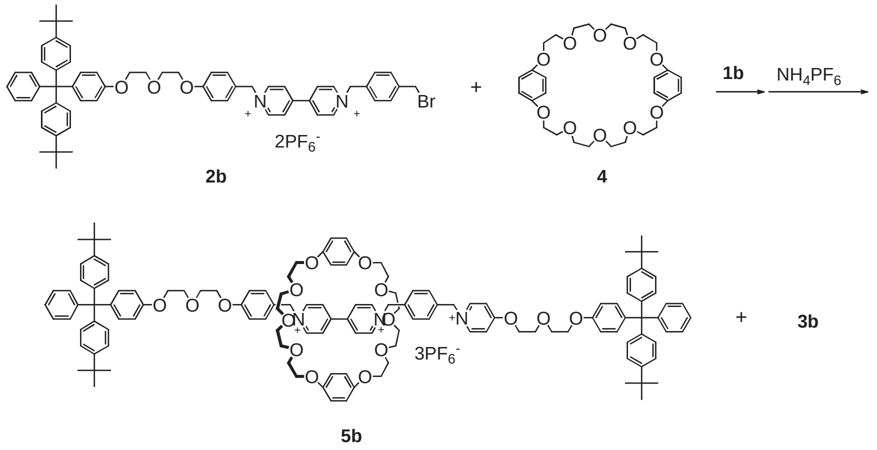
Fig. 1. Monitoring of reaction between **1a** and **2a** by the pre-mixing method D. (a) After 5 min. (b) After 30 min. (c) After 1 h. (d) After 1.5 h. (e) After 2 h.

powdery mixture composed of **1** and **2** was subjected to a static pressure (40 kg cm^{-2}) for 1 h (Procedure F). No reaction occurred at all in all cases, indicating that the molecule-to-molecule contacts are crucial for the reaction to occur. Obviously, the contacts are best attained by mixing in solution followed by evaporation (Procedures C and D) and next best by adding a small amount of suitable solvent to a solid reactants mixture (Procedure B), whereas the mechanical forces are modestly useful (Procedure A). In Procedure B, anisole, though having a rather high boiling point, was not detected after grinding for 10 min, and thus the reaction mostly proceeded under solventless conditions. Acetone vaporized before the molecular-level contacts could form sufficiently. Consequently, pre-mixing protocols are highly dependent on the solvent. In Procedure A, grinding may help change relatively intimate solid reactants to a molten state. The formation of voids and cracks[8] is presumably facilitated by mechanical forces for the solid reactants in case of no molten mixture being formed.

End-Capping Synthesis of [2]Rotaxanes. Because of their high efficiency as found above, Procedures B and D were applied to the end-capping synthesis of [2]rotaxane **5b** (Scheme 2). First, **2b** (0.03 mmol) and crown ether **4** (0.06 mmol) were ground in the presence of anisole (0.02 mL) for 20 min. To this mixture were added **1b** (0.06 mmol) and anisole (0.02 mL). Grinding the mixture for 1.5 h afforded, after treatment with NF_4PF_6, the desired rotaxane **5b** in 72% yield together with **3b** in 17% yield (Procedure B-1). When the three components with the same ratio and anisole (0.06 mL) were mixed simultaneously, **5b** and **3b** were obtained in 75 and 13% yields, respectively after grinding for 2 h (Procedure B-2). No appreciable difference was observed between these two procedures, suggesting that the threading between **2b** and **4** is fast and exerts no influence on the ratio of **5b** and **3b**. It should be noted that the high concentration solution method (Procedure E) gave a similar outcome, yet a much longer reaction time (3 days) was needed. Procedure D was carried out using a mixture of acetone and CH_2Cl_2 because **4** is not soluble in acetone. Thus, **1b** (0.06 mmol), **2b** (0.03 mmol), and **4** (0.06 mmol) were dissolved in a mixture of acetone (0.1 mL)/CH_2Cl_2 (0.1 mL). The film which had been cast from this solution was allowed to stand for 4 h to afford **5b** in 85% yield together with **3b** in 8% yield. The yield of **5b** by using this procedure was higher than those by using Procedures B and E. More significantly, the ratio of **5b**/**3b** increased, an implication that the difference in relative rate of the threading reaction over *N*-alkylation is larger for Procedure D than for the others.

The advantage of the pre-mixing protocol was also confirmed in the synthesis of [2]rotaxane **5a** (Scheme 3). However, even Procedure D resulted in a lower yield of **5a** than that of **5b** in the previous case. This is reasonable because **2b** innately has a dipyridinium moiety that can interact with **4** to facilitate the threading prior to the *N*-alkylation. It is apparent from these results that the self-assembly of the thread and bead can take place as easily as or more easily than the *N*-alkylation in the solid film.

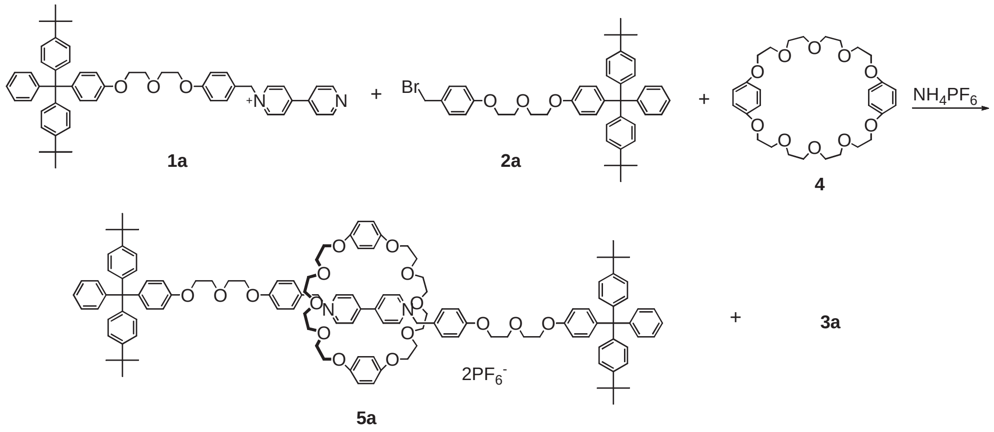
Wittig Reaction. An evaluation of Procedures A, C, D, and E, for Wittig reactions of solid reactants is summarized in Table 2. Obviously, solventless protocols (Procedures A, C, and D) always gave rise to better outcomes in terms of reaction rate and yield than the solution reactions (Procedure E). In particular, Procedure C worked best, except Entry 4, indicating the effectiveness of combination of film casting and grinding. However, the relative significance between these two effects is not straightforward. Comparison of Procedures A and D shows that the former is more effective in Entries 1 and 4, whereas the reverse is true in Entries 2, 3, 5, and 6. Notably, no reaction occurred by using Procedure A in Entries 5 and 6, implying that the affinity of the surface of the solid particles plays a pivotal role. The same reactions did not go to completion in Procedure C. This is attributed to disruption of the molecule-to-molecule contacts once formed by grinding as well as the low reactivity. The importance of the molecular-



Procedure B-1 (2 h)	72%	17%
Procedure B-2 (2 h)	75%	13%
Procedure D (4 h)	85%	8%
Procedure E (3 days)	78%	11%

[a] For the reaction conditions, see the text.

Scheme 2.



Procedure B	40%	36%
Procedure D	64%	20%
Procedure E	56%	32%

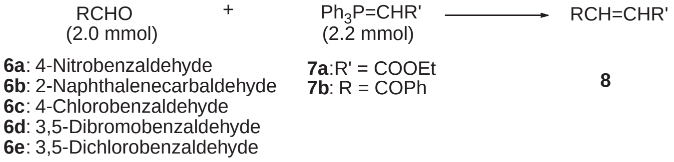
Scheme 3.

level homogeneity is apparent from the solvent effect in Procedure D. A large amount of CH_3CN (70 mL) was employed as a solvent for reaction between **6a** (2.0 mmol) and **7b** (2.2 mmol) because of poor solubility of **7b**. When the resulting homogeneous solution was concentrated to dryness, a white precipitate of **7b** appeared first, whereas yellow **6a** remained in solution. Complete removal of the solvent resulted in a light yellow film with white spots. Standing this film at room temperature for 24 h afforded only a 53% yield of **8b**.

In conclusion, the superiority of the molecular-level interactions of reactants to the solid particle-to-particle contacts are evident from the high efficiency of Procedures B, C, and D, although it was not clear in case of Procedure B if a homogeneous state emerges or if some solid particles remain. In any case, once the molecular-level contacts are realized, the solventless conditions are more advantageous than the solution conditions, because the contacts are preserved more easily due to lack of thermal movements as in the case of solution conditions. In addition, the desolvation energy, which is inevitable in solution reaction,[17] is avoided. A further notable feature is the facile threading, which not only represents the usefulness of the solventless treatment in supramolecular chemistry but also implies that molecules move rather facilely in a solid mixture.

Although the pre-mixing protocols may not be solventless in a strict sense if the prior dissolution step is counted, the reac-

Table 2. Wittig Reaction under Various Conditions



Entry	6	7	8	Yield of **8**/%[a)]			
				Procedure A	Procedure C[b)]	Procedure D[c)]	Procedure E[d)]
1	**6a**	**7a**	**8a**	95 (30 min)	92 (5 min)	93 (1 h)	92[e)] (24 h)
2	**6a**	**7b**	**8b**	65[e)] (1 h)	92 (20 min)	92 (1 h)	93 (3 h)
3	**6b**	**7a**	**8c**	94 (50 min)	94 (5 min)	93 (15 min)	93 (5.5 h)
4	**6c**	**7a**	**8d**	91 (5 min)	92 (5 min)	93 (10 min)	91[e)] (24 h)
5	**6d**	**7b**	**8e**	nr[f)]	52[e)] (1 h)	84 (1.5 h)	86 (3.5 h)
6	**6e**	**7b**	**8f**	nr[f)]	80[e)] (1 h)	87[e)] (24 h)	85 (8 h)

a) Isolated yileds after column chromatography. Reaction times are given in parentheses. b) **6**: 2 mmol; **7**: 2.2 mmol; CH_2Cl_2: 4 mL; evaporation by rotary evaporator followed by pumping in vacuo (5 min); grinding. The time for grinding after evaporation is given in parentheses. c) **6**: 2 mmol; **7**: 2.2 mmol; CH_2Cl_2: 4 mL; evaporation by rotary evaporator followed by pumping in vacuo (5 min); standing. The time for standing after evaporation is given in parentheses. Time for standing after evaporation in parentheses. d) **6**: 2 mmol; **7**: 2.2 mmol; CH_2Cl_2: 1 mL; stirring at 27 °C. e) The aldehyde remained, but no further reaction occurred even upon prolonged reaction. f) No reaction.

tion itself proceeds under solventless conditions. In a practical sense, however, reactants in solution can be charged into a reactor much more conveniently than a solid reactants mass. We showed the usefulness of the new protocol via simple *N*-alkylation and the Wittig reaction in addition to self-assembly. Further applications to other reactions are now in progress in our laboratories.

Experimental

General Remarks. All reactions were carried out under an atmosphere of nitrogen with freshly distilled solvents, unless otherwise noted. All solvents were distilled from CaH_2. Silica gel (Daiso gel IR-60) was used for column chromatography. NMR spectra were recorded at 25 °C on JEOL Lambda 300 and JEOL Lambda 500 instruments and calibrated with tetramethylsilane (TMS) as an internal reference. Pelletized mixture of starting compounds was compressed by using Riken Power P-18.

Starting compounds **2c** was commercially available, and crown ether **4** was prepared according to the reported procedure.[18] Pyridine derivatives **1a**–**1c** and benzyl bromide derivatives **2a** and **2b** were prepared by conventional methods.[19] Experimental details are described in the Supporting Information.

Preparation of 3a (Procedure A, Representative). In a mortar, **1a** (27.8 mg, 0.03 mmol) and **2a** (42.3 mg, 0.06 mmol) were placed, and the mixture was ground with a pestle for 1.5 h at r.t. The mixture was dissolved in acetone (5 mL), $CHCl_3$ (2 mL), and water (1 mL). To the resulting solution was added NH_4PF_6 (97.8 mg, 0.6 mmol). The organic layer was separated and evaporated. Column chromatography of this mixture on silica gel (70:16:11:3 $CH_3OH/CH_2Cl_2/CH_3NO_2/NH_4Cl$ (2 mol dm^{-3}) furnished **3a** (20.4 mg, 40%).[19] Compounds **3b** and **3c** were obtained similarly. **3b**: ^{1}H NMR (300 MHz, CD_3COCD_3): δ 9.46 (d, $J = 5.1$ Hz, 4H), 8.93 (d, $J = 7.2$ Hz, 2H), 8.80–8.76 (m, 4H), 7.78–7.62 (m, 8H), 7.34–7.06 (m, 32H), 6.87–6.81 (m, 4H), 6.20 (s, 2H), 6.10 (s, 2H), 5.88 (s, 2H), 4.63 (m, 2H), 4.20–4.13 (m, 6H), 4.00 (m, 2H), 3.88 (m, 6H), 1.30 (s, 36H); ^{13}C NMR (75.5 MHz, CD_3COCD_3): δ 149.3, 148.3, 147.0, 146.0, 132.8, 132.1, 131.7, 131.4, 131.2, 130.7, 128.6, 128.4, 128.3, 128.2, 126.7, 125.2, 125.1, 116.3, 115.3, 114.3, 114.1, 71.6, 70.5, 69.5, 68.6, 64.3, 34.9, 31.6; MS (MALDI-TOF) found *m/z* 1788.86 $[M - PF_6]^+$, calcd for $C_{104}H_{112}F_{12}N_3O_6P_2$ *m/z* 1788.78. **3c**: ^{1}H NMR (300 MHz, CD_3COCD_3): δ 9.60 (d, $J = 6.9$ Hz, 2H), 9.53 (d, $J = 6.9$ Hz, 2H), 8.86 (d, $J = 6.9$ Hz, 4H), 8.25 (s, 1H), 8.06–7.95 (m, 3H), 7.74–7.61 (m, 7H), 6.36 (s, 2H), 6.19 (s, 2H); ^{13}C NMR (75.5 MHz, CD_3COCD_3): δ 151.4, 146.9, 134.2, 133.5, 133.4, 132.3, 131.4, 130.5, 130.4, 129.2, 128.7, 128.6, 128.5, 128.3, 127.9, 126.7, 124.7, 65.9, 64.9; MS (MALDI-TOF) found *m/z* 611.62 $[M - PF_6]^+$, calcd for $C_{28}H_{23}BrF_6N_2P$ *m/z* 611.07.

Preparation of 3a (Procedure B, Representative). In a mortar, **1a** (27.8 mg, 0.03 mmol), **2a** (42.3 mg, 0.06 mmol), and anisole (0.02 mL) were placed, and the mixture was ground with a pestle for 30 min at r.t. The mixture was dissolved in acetone (5 mL), $CHCl_3$ (2 mL), and water (1 mL). To the resulting solution was added NH_4PF_6 (97.8 mg, 0.6 mmol). The organic layer was separated and evaporated. ^{1}H NMR spectrum of this crude mixture indicated formation of **3a** in 78% yield. Column chromatography of this mixture on silica gel (70:16:11:3 $CH_3OH/CH_2Cl_2/CH_3NO_2/NH_4Cl$ (2 mol dm^{-3}) furnished **3a** (37.2 mg, 73%).

Preparation of 3a (Procedure C, Representative). In a mortar, **1a** (27.8 mg, 0.03 mmol) and **2a** (42.3 mg, 0.06 mmol) were dissolved in acetone (0.2 mL). The acetone solution became yellow film after 5 min of standing in open air, followed by evaporation in vacuo. The film was ground with a pestle for 30 min at r.t. The mixture was dissolved in acetone (5 mL), $CHCl_3$ (2 mL), and water (1 mL). To the resulting solution was added NH_4PF_6 (97.8 mg, 0.6 mmol). The organic layer was separated and evaporated. ^{1}H NMR spectrum of this crude mixture indicated formation of **3a** in 79% yield. Column chromatography of this mixture on silica gel (70:16:11:3 $CH_3OH/CH_2Cl_2/CH_3NO_2/NH_4Cl$ (2 mol dm^{-3}) gave **3a** (39.7 mg, 78%).

Preparation of 3a (Procedure D, Representative). In a mortar, **1a** (27.8 mg, 0.03 mmol) and **2a** (42.3 mg, 0.06 mmol) were dissolved in acetone (0.2 mL). The acetone solution became a yellow film after 5 min of standing in open air, followed by evaporation in vacuo. The film was kept standing in open air for 2 h at r.t.

The mixture was dissolved in acetone (5 mL), $CHCl_3$ (2 mL), and water (1 mL). To the resulting solution was added NH_4PF_6 (97.8 mg, 0.6 mmol). The organic layer was separated and evaporated. ^1H NMR spectrum of this crude mixture indicated formation of **3a** in 85% yield. Column chromatography of this mixture on silica gel (70:16:11:3 $CH_3OH/CH_2Cl_2/CH_3NO_2/NH_4Cl$ (2 mol dm^{-3}) gave **3a** (39.2 mg, 77%).

Preparation of 3a (Procedure E, Representative). In a 1-mL vial, **1a** (27.8 mg, 0.03 mmol) and **2a** (42.3 mg, 0.06 mmol) were dissolved in acetone (0.2 mL), and the vial was sealed with a plastic cap. The acetone solution was kept standing for 2 days at r.t. The mixture was dissolved in acetone (5 mL), $CHCl_3$ (2 mL), and water (1 mL). To the resulting solution was added NH_4PF_6 (97.8 mg, 0.6 mmol). The organic layer was separated and evaporated. ^1H NMR spectrum of this crude mixture indicated formation of **3a** in 83% yield. Column chromatography of this mixture on silica gel (70:16:11:3 $CH_3OH/CH_2Cl_2/CH_3NO_2/NH_4Cl$ (2 mol dm^{-3}) gave **3a** (40.2 mg, 79%).

Attempted Preparation of 3a (Procedure F, Representative). In a 1-mL vial were placed **1a** (27.8 mg, 0.03 mmol) and **2a** (42.3 mg, 0.06 mmol), and the mixture was shaken. The mixture was pelletized and compressed in 40 kg cm^{-2} for 1 h at r.t. The mixture was dissolved in acetone (5 mL), $CHCl_3$ (2 mL), and water (1 mL). To the resulting solution was added NH_4PF_6 (97.8 mg, 0.6 mmol). The organic layer was separated and evaporated. ^1H NMR spectrum of this crude mixture indicated no formation of **3a**.

Preparation of 5b (Procedure D, Representative). In a mortar, **1b** (36.8 mg, 0.06 mmol), **2b** (37.7 mg, 0.03 mmol), and **4** (32.2 mg, 0.06 mmol) were dissolved in acetone (0.1 mL) and CH_2Cl_2 (0.1 mL). The solution became a red film after 5 min of standing in open air. The film was kept standing in open air for 4 h at r.t. The mixture was dissolved in acetone (10 mL) and water (2 mL). To the resulting solution was added NH_4PF_6 (97.8 mg, 0.6 mmol). The organic layer was separated and evaporated. ^1H NMR spectrum of this crude mixture indicated formation of **5b** in 85% yield. Column chromatography of this mixture on silica gel (70:16:11:3 $CH_3OH/CH_2Cl_2/CH_3NO_2/NH_4Cl$ (2 mol dm^{-3}) gave yellow solid. The resulting solid was dissolved in acetone (10 mL) and water (2 mL). To the resulting solution was added NH_4PF_6 (97.8 mg, 0.6 mmol). The organic layer was separated, and the solvent was evaporated to afford **5b** (58.6 mg, 79%): ^1H NMR (300 MHz, CD_3COCD_3): δ 9.23 (d, $J = 6.6$ Hz, 2H), 9.18 (d, $J = 6.6$ Hz, 2H), 8.93 (d, $J = 7.3$ Hz, 2H), 8.30–8.25 (m, 4H), 7.89 (d, $J = 8.4$ Hz, 2H), 7.79–7.72 (m, 4H), 7.61 (d, $J = 7.5$ Hz, 2H), 7.33–7.06 (m, 34H), 6.85–6.80 (m, 4H), 6.17 (s, 2H), 6.05 (s, 8H), 5.90 (s, 2H), 4.54 (m$_c$, 2H), 4.22 (m$_c$, 2H), 4.14–4.08 (m, 4H), 3.96–3.65 (m, 40H), 1.294 (s, 36H); ^{13}C NMR (75.5 MHz, CD_3COCD_3): δ 171.9, 161.1, 157.8, 157.7, 152.9, 149.2, 149.1, 148.2, 146.8, 146.7, 146.4, 145.0, 140.2, 140.1, 136.6, 135.3, 132.9, 132.8, 132.3, 131.6, 131.5, 131.4, 130.7, 128.2, 128.1, 126.6, 126.5, 126.3, 126.1, 125.1, 125.0, 116.1, 115.5, 115.1, 114.1, 114.0, 71.5, 71.3, 71.0, 70.7, 70.5, 70.4, 70.3, 69.4, 68.6, 68.3, 68.1, 68.0, 65.3, 65.0, 64.2, 62.7, 34.8, 31.6; MS (MALDI-TOF) found m/z 2180.78 $[M - 2PF_6]^+$, calcd for $C_{132}H_{152}F_6N_3O_{16}P$ m/z 2180.08. Compound **5a**[19] was prepared similarly.

Wittig Reaction (Procedure D, Representative). In a round-bottom flask were placed **6a** (302.2 mg, 2.0 mmol) and **7a** (766.4 mg, 2.2 mmol), and CH_2Cl_2 (4 mL) was added. The clear solution was evaporated at 27 °C for 5 min, and, during evaporation, a solid film formed. After the film had been kept in vacuo at rt for 1 h, a portion of the film was dissolved in $CDCl_3$. Analysis of the film by ^1H NMR showed complete consumption of **6a**. The crude products were subjected to column chromatography on silica gel (30% AcOEt/hexane) to give **8a** in a pure form (93% yield). **8a**: ^1H NMR (500 MHz, $CDCl_3$, $E{:}Z = 99{:}1$) E-isomer: δ 1.36 (t, $J = 7.1$ Hz, 3H), 4.30 (q, $J = 7.1$ Hz, 2H), 6.55 (d, $J = 16.1$ Hz, 1H), 7.68 (d, $J = 8.9$ Hz, 2H), 7.71 (d, $J = 16.1$ Hz, 1H), 8.25 (d, $J = 8.9$ Hz, 2H); Z-isomer: δ 1.25 (t, $J = 7.1$ Hz, 3H), 4.17 (q, $J = 7.1$ Hz, 2H), 6.13 (d, $J = 12.6$ Hz, 1H), 7.02 (d, $J = 12.6$ Hz, 1H), 7.68 (d, $J = 8.9$ Hz, 2H), 8.25 (d, $J = 8.9$ Hz, 2H).

Supporting Information

Preparation of **1a**–**1c** and **2a** and **2b**. This material is available free of charge on the web at http://www.csj.jp/journals/bcsj/.

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