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Phosphorus-Recycling Wittig Reaction: Design and Facile Synthesis of a Fluorous Phosphine and Its Reusable Process in the Wittig Reaction

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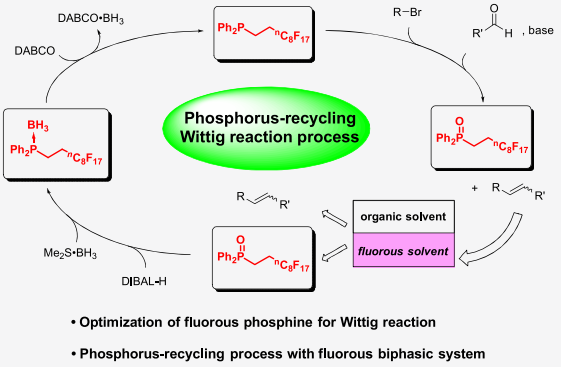
ABSTRACT: This study shows that phosphorus sources can be recycled using the appropriate fluorous phosphine in the Wittig reaction. The designed fluorous phosphine, which has an ethylene spacer between its phosphorus atom and the perfluoroalkyl group, was synthesized from air-stable phosphine reagents. The synthesized phosphine can be used for the Wittig reaction process to obtain various alkenes in adequate yields and stereoselectivity. The concomitantly formed fluorous phosphine oxide was extracted from the reaction mixture using a fluorous biphasic system. The fluorous phosphine was regenerated by reducing the fluorous phosphine oxide with diisobutylaluminum hydride. Finally, a series of gram scale phosphorus recycling processes were performed, which included the Wittig reaction, separation, reduction, and reuse.



INTRODUCTION

Phosphorus is an important element in food production and manufacturing,[1−3] and the sustainable use of phosphorus is essential to our economy because its regeneration through the natural cycle is much slower than the global consumption.[4−9] In organic chemistry, organophosphorus compounds are versatile reagents for the Wittig, Mitsunobu, and Baylis−Hillman reactions and preferred ligands for the transition-metal catalysis.[10−14] Specifically, the Wittig reaction can easily synthesize alkenes from carbonyl compounds and ylides, and the alkenes are vital precursors in organic synthesis. However, this reaction generates equimolar amounts of phosphine oxides, which are typically regarded as waste and removed from the alkenes by silica gel column chromatography.[15] Given the sustainable use of phosphorus compounds, several catalytic Wittig reactions were reported;[16−23] however, the modification of the Wittig reaction, which promotes phosphine recycling, is more beneficial. Polymer-supported phosphines are separated as the phosphine oxides by filtration after the reaction.[24−26] Bergbreiter et al. showed that the polymer-supported phosphine is recyclable and used as a regenerable catalyst and reagent.[27] Polymer-supported phosphines are often used to easily separate and recover transition-metal catalysts.[28] Fluorous phosphines, which are phosphines that include perfluoroalkyl groups, are also easily separated by fluorous biphasic systems (FBS)[29−31] and can potentially be applied for recycling phosphines because some reactions using stoichiometric amounts of fluorous phosphines, such as the Wittig reaction, were reported.[32−36] Although the concept of phosphorus recycling using FBS in the Wittig reaction was shown by Sinou in 2001,[32] the total system including reduction and reuse was not examined.

We previously developed a *P*-fluorous phosphine **1** as a recoverable and reusable ligand for transition-metal-catalyzed cross-coupling reactions.[37−40] *P*-Fluorous phosphine **1**, in which the perfluoroalkyl group (R_f) is directly bound to the phosphorus atom, is prepared and its fluorous affinity enables the reuse of **1**/palladium(II) complexes using a fluorous biphasic system (FBS).[38]

The easy access and considerable fluorous affinity of **1** motivated us to investigate a phosphorus-recycling process including the Wittig reaction (Figure 1a). We propose the following recycling process that includes four steps: (1) the Wittig reaction, (2) the separation of alkenes from phosphine oxides using FBS, (3) the reduction of the phosphine oxides, and (4) the recovery of the phosphines (Figure 1b). For all these processes, the appropriate reaction conditions must be determined. Unfortunately, the Wittig reaction of *P*-fluorous phosphine **1** was unsuccessful because of the inefficient

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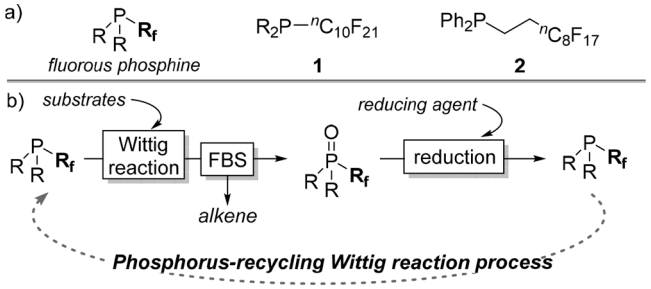


Figure 1. Phosphorus-recycling Wittig reaction process using FBS.

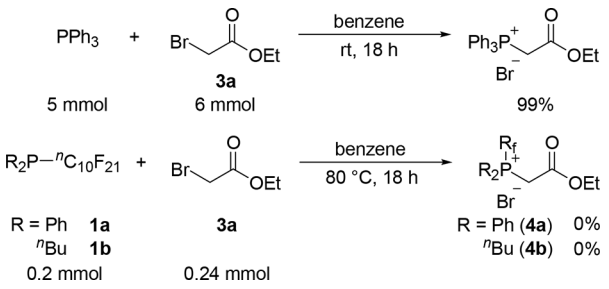
alkylation of *P*-fluorous phosphine **1** with alkyl halides to generate the corresponding phosphonium salts; more specifically, the electron-poor nature of *P*-fluorous phosphine decreases its nucleophilicity. By contrast, fluorous phosphine **2**, which has an ethylene spacer between the phosphorus atom and the perfluoroalkyl group, was successfully subjected to the Wittig reaction with a variety of alkyl halides and aldehydes, producing satisfactory yields of alkenes.

To develop fluorous phosphines that can be applied more widely in the chemistry field, the investigation of all synthetic and recovering processes is of great importance. Both the optimization of the fluorous phosphine synthesis and the separation of the fluorous phosphine oxide from the reaction mixture are required to create a practical synthetic process. Therefore, the overall recycling process as well as the synthesis of **2** was investigated in this study.

RESULTS AND DISCUSSION

We initiated our study synthesizing fluorous phosphonium salts as precursors for fluorous ylides from *P*-fluorous phosphine **1** and alkyl bromide **3a** (Scheme 1).

Scheme 1. Synthesis of Phosphonium Salts from Triphenylphosphine and Fluorous Phosphine 1 with Alkyl Bromide 3a



When a mixture of triphenylphosphine and **3a** was stirred for 18 h at 25 °C, the corresponding phosphonium salt was quantitatively obtained. In contrast to triphenylphosphine, *P*-fluorous phosphine **1a** and **1b** did not react with **3a** even at 80 °C, as shown in Scheme 1. A possible reason for the unsuccessful result was the low nucleophilicity of *P*-fluorous phosphines due to its electron-poor nature. Hence, we synthesized triphenylphosphine selenide and *P*-fluorous phosphine selenides and compared their $^{31}P-^{77}Se$ coupling constants (Figure 2). Phosphine selenide bearing a larger $^{31}P-^{77}Se$ coupling constant exhibits more electron-poor characteristics.[41] Both *P*-fluorous phosphine selenides showed much larger coupling constants than triphenylphosphine selenide. This result suggests that the formation of *P*-fluorous phosphonium salt **4** failed because of the electron-poor property of *P*-fluorous phosphine **1**.

To develop a fluorous phosphine that easily forms a phosphonium salt and performs the Wittig reactions, we next focused on the fluorous phosphine **2** that has an ethylene spacer between its phosphorus atom and the perfluoroalkyl group (Figure 2).[42,43] The ethylene spacer of **2** not only reduces the electron-withdrawal from the perfluoroalkyl group but also acts as an electron-donating group. The $^{31}P-^{77}Se$ coupling constant of **2** was smaller than that of triphenylphosphine selenide. Hence, **2** was a promising fluorous phosphine for the Wittig reaction.

The ease of the fluorous phosphine synthesis is also important for the Wittig reaction because an equimolar amount of phosphines is required to generate the desired products. We previously reported a convenient synthesis method of an alkylphosphine using (2,4,6-trimethylbenzoyl)-phosphine oxide (TMDPO) **5**, alkyl iodide, and distananne **6** under light irradiation.[44−46] This reaction affords trivalent phosphine compounds from TMDPO, which is a shelf-stable pentavalent phosphorus compound. In view of the air-stable nature of the reagent, this method was applied to synthesize **2**. When a mixture of **5**, **6**, and 1*H*,1*H*,2*H*,2*H*-heptadecafluorodecyl iodide dissolved in BTF was irradiated with a xenon lamp (500 W) for 6 h, fluorous phosphine **2** was obtained in 58% yield (Table 1, entry 1). The use of 5 equiv of **5** did not improve the production of **2** (entry 2). Excess amounts of distananne **6** prevented the reaction progress because the light absorption of **5** was restricted from that of **6** (entry 3). It is possible to keep the reaction glassware at 40 °C by irradiating with a xenon lamp while placing a heat-insulating material around it. This reductive alkylation efficiently produced **2** in 79% yield at 40 °C (entry 4). The decrease in the amount of **5** largely influenced this reaction and **2** was formed in 55% yield (entry 5).

The method presented in Table 1 provided a 0.1 mmol scale synthesis of **2**. To facilitate the utilization of the fluorous phosphine **2** in the Wittig reaction, the development of a large-scale synthesis method is essential for practical use. Therefore, the synthesis of **2** on a gram scale was further optimized (Scheme 2): (i) PPh_3 (14 mmol, 3.7 g) and fluorous iodide (14 mmol, 8.0 g) were dissolved in toluene and refluxed for 48 h to obtain the corresponding phosphonium salt. The phosphonium salt was then treated with a saturated aqueous NaOH solution at 100 °C to produce the phosphine oxide **2′** in 80% NMR yield.[47,48] (ii) The reduction of **2′** was conducted with diisobutylaluminum hydride (DIBAL-H) as the reducing agent,[49,50] and **2** generated in situ was transformed to the phosphine−borane complex **2″** using an excess of $Me_2S{\cdot}BH_3$ in 90% isolated yield. (iii) Then the phosphine borane **2″** was treated with DABCO for deprotection, and the formed DABCO·BH_3 was removed by filtration under an argon atmosphere.[51] Finally, this procedure provided a 3.6 g scale synthesis of the fluorous phosphine **2**.

The fluorous phosphine **2** is easily transformed into a variety of fluorous phosphonium salts **7** (Table 2). Bromoacetate **3a** efficiently reacted with **2** at 60 °C, and phosphonium salt **7a** was obtained in 99% yield (entry 1). Benzyl bromide **3b** and 2-bromoacetonitrile **3c** also afforded the corresponding phosphonium salts in excellent yields (entries 2 and 3). The reaction of **2** with allyl bromide **3d** and **3e** successfully produced the corresponding phosphonium salts **7d** and **7e** in 96% and 100% yields, respectively (entries 4 and 5). Under

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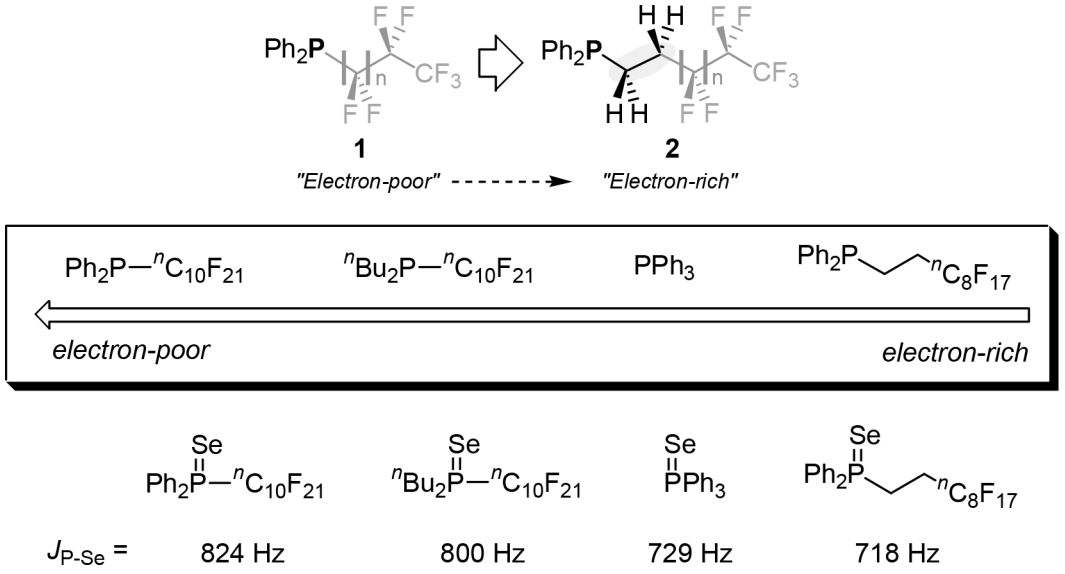
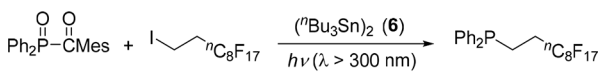


Figure 2. $^{31}P-^{77}Se$ coupling constants of phosphine selenides and the evaluation of the electron property of fluorous phosphine **2**.

Table 1. Optimization of Reaction Conditions to Synthesize Alkylphosphine 2[a]



entry	5 (mmol)	6 (mmol)	yield[b] (%)
1	0.4	0.1	58
2	0.5	0.1	53
3	0.4	0.4	33
4[c]	0.4	0.1	79 (63)
5[c]	0.3	0.1	55

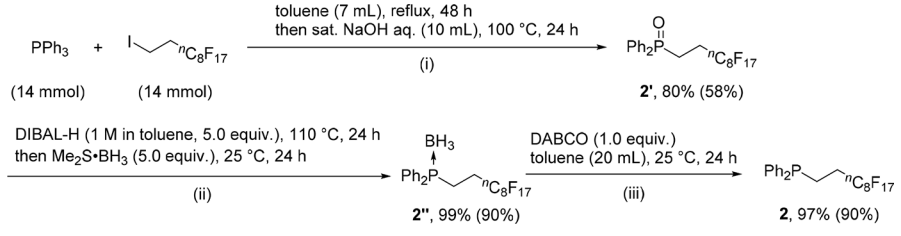
[a]Reaction conditions: **5**, 1*H*,1*H*,2*H*,2*H*-heptadecafluorodecyl iodide (0.1 mmol), distananne **6**, BTF (0.6 mL), xenon lamp (500 W), 6 h, room temperature. [b]Determined by ^{31}P NMR spectroscopy. [c]The reaction mixture was heated at 40 °C.

similar conditions, the alkyl bromide **3f** formed the phosphonium salt **7f** in only 5% yield (entry 6, X = Br). However, the use of the alkyl iodide instead of the alkyl bromide improved the formation of the phosphonium salt **7f**, and **7f** was obtained in 70% yield by prolonging the reaction time to 24 h (entry 6, X = I).

Next, the scope of the Wittig reaction was investigated. Notably, several alkenes were synthesized by one-pot operation from fluorous phosphine **2**, bromoacetate **3a**, and aldehyde **9** via the formation of fluorous phosphonium salt **7a** and its ylide **8a** (Table 3). When a mixture of **7a** (generated from **2** and **3a** as shown in entry 1 of Table 2) and potassium bis(trimethylsilyl)amide was stirred for 6 h at 60 °C, the fluorous ylide **8a** was almost quantitatively generated. Aldehyde **9** was then added to the mixture and stirred for 3 h at 60 °C to afford alkene **10aa** in 96% yield with a good *E*-selectivity (entry 1). The Wittig reaction between **8a** and aryl aldehyde **9b** and **9c** produced the corresponding alkenes in 99% and 90% yield, respectively, with satisfactory stereoselectivity (entries 2 and 3). Interestingly, *α,β*-unsaturated aldehyde **9d** successfully generated *α,β*- and *γ,δ*-unsaturated ester **10ad** in 66% yield (entry 4). This reaction also took place using aliphatic aldehyde **9e** to provide alkene **10ae** in 34% yield with an adequate stereoselectivity (entry 5).

Instead of potassium bis(trimethylsilyl)amide, diisopropylethylamine was used without difficulty in the Wittig reaction (Table 4, see Table S1 in the Supporting Information). The reaction of fluorous phosphonium salt **7** with aldehyde **9** in the presence of diisopropylethylamine easily afforded a variety of alkenes in moderate to excellent yields. For example, the Wittig reaction between **7a** and **9a** formed alkene **10aa** in 93% yield (entry 1). When the Wittig reaction was conducted with PPh_3, which is commonly used as the phosphorus source in the Wittig reaction, **10aa** was obtained under the same reaction condition as Table 4 entry 1 in 88% (*E*/*Z* = 88/12). The yield and the stereoselectivity of the alkene were almost similar. This result demonstrated that the fluorous phosphine **2** could be an effective alternative phosphorus source for the Wittig reaction. The electron-poor aryl aldehyde **9f** provided alkene **10af** in

Scheme 2. Gram-Scale Synthesis of the Fluorous Phosphine 2[a]



[a]The yields were determined by ^{31}P NMR spectroscopy (isolated yields).

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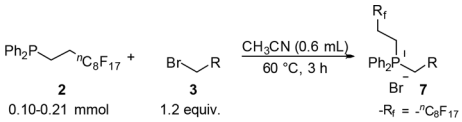
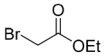
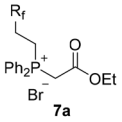
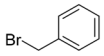
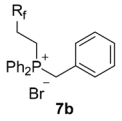
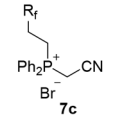
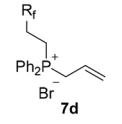
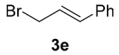
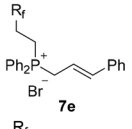
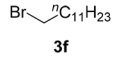
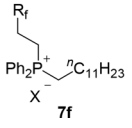
Table 2. Synthesis of Fluorous Phosphonium Salt 7 from Fluorous Phosphine 2 and Alkyl Bromide 3[a]



Entry	3	7	Yield[c]
1	 **3a**	 **7a**	99% (79%)
2	 **3b**	 **7b**	99% (98%)
3	 **3c**	 **7c**	99% (84%)
4	 **3d**	 **7d**	96% (93%)
5	 **3e**	 **7e**	100% (47%)[d]
6	 **3f**	 **7f**	X = Br: 5% X = I: 70% (67%)[e]

[a]Reaction conditions: **2** (0.10−0.28 mmol), alkyl bromide **3** (1.2 equiv), CH_3CN (0.6 mL), 60 °C, 3 h. [b]The scale of **2**: 0.103 mmol (entry 1), 0.100 mmol (entry 2), 0.111 mmol (entry 3), 0.098 mmol (entry 4), 0.100 mmol (entry 5), and 0.13 mmol (entry 6). [c]Determined by ^{31}P NMR spectroscopy (isolated yields). [d]**7e** was highly soluble in organic solvents, and purification by recrystallization provided **7e** in moderate yield. [e]Reaction time: 24 h.

80% yield (entry 2). In the reaction between **7b** (generated from **2** and **3b**) and benzaldehyde **9g**, alkene **10bg** was obtained with satisfactory stereoselectivity (entry 3). The method was applied to synthesize acrylonitriles **10ca** and **10cf**, and **10ca** was isolated in excellent yield (entry 4) and the yield of **10cf** was reduced during the isolation procedure because it was relatively easy to oligomerize (entry 5). The Wittig reaction between **7e** (generated from **2** and **3e**) and several substituted benzaldehydes produced the dienes **10ea**, **10ef**, **10eh**, and **10ei** in moderate to adequate yields with excellent *E*-selectivity (entries 6−9). Noteworthy is that the sterically hindered aldehyde **9i** attained diene **10ei** (entry 9) in acceptable yields. When the Wittig reactions shown in Tables 3 and 4 were conducted, the fluorous phosphine oxide **2′** was quantitatively recovered in all cases, as indicated by ^{31}P NMR measurement.

In the Wittig reactions summarized in Tables 3 and 4, stoichiometric amounts of fluorous phosphine oxide **2′** were concomitantly generated with the desired alkene **10** (Table 5 a)). Fluorous phosphine oxide **2′** is soluble in both fluorous and organic solvents. By contrast, other organic compounds, such as alkenes and aldehydes, do not sufficiently dissolve in fluorous solvents. Thus, fluorous phosphine oxide **2′** can be selectively extracted using FBS (Table 5 b)). However, the solubility of fluorous phosphine oxides such as **2′** in fluorous solvents is generally lower than that of the corresponding fluorous phosphines such as **2** because of the high polarity of the P−O bond. To use the fluorous/organic extraction method to separate alkenes and **2′**, the partition coefficient for **2′** between several organic and fluorous solvents was determined (Table 5). A solvent that easily dissolves alkenes and other organic compounds but not **2′** is desirable. Fluorous phosphine oxide **2′** was dissolved in methanol (entry 1) and acetonitrile (entry 2) with ease; thus, the partition of **2′** to the fluorous solvent was inefficient. The benzene/*n*-hexane (= 1/5) solution had a moderate partition coefficient but the solubility of alkenes such as **10aa** was insufficient (entry 3). In addition, the phase separation between FC-72 and the benzene/*n*-hexane solution was noticeably slow. The addition of a small amount of water to acetonitrile (CH_3CN/H_2O = 19/1) efficiently improved the phase separation of FBS (entry 4). As the phase separation between organic solvents and Novec 7100 was inefficient, a mixed solution of two fluorous solvents was used next to provide a better phase separation. Because the partition coefficient determined for a mixed solution of FC-72 and fluorous solvent **11a** was still low (entry 5), the use of a mixed solution of FC-72 and fluorous solvent **11b** improved the partitioning of **2′** to the fluorous phase (entry 6). These results confirmed that **2′** efficiently dissolves in fluorous ethers. Thus, using the FC-72/Novec 7100 (= 1/4) solution provided an effective partitioning of **2′** to the fluorous solvent (entry 7). The use of CH_3CN/H_2O = 9/1 as the organic solvent significantly enhanced the partition coefficient to 1/1.97; however, the alkene was also soluble in the fluorous solution (entry 8). Further decreasing the ratio of Novec 7100 in the fluorous solvent improved the recovery of alkenes from the organic solution (see Table S2 and Table S3 in the Supporting Information).

Hence, we examined the extraction of fluorous phosphine oxide using an FBS with FC-72/Novec and CH_3CN/H_2O in the Wittig reaction as shown in entry 9 of Table 5. The reaction mixture was concentrated under reduced pressure, and fluorous phosphine oxide **2′** was extracted from the residue using the FBS (Figure 3). After the residue was diluted with 5 mL of the organic solution (CH_3CN/H_2O = 9/1) and extracted twice with 10 mL of the fluorous solution (FC-72/Novec 7100 = 1/1), **2′** was recovered from the fluorous solution in 90% yield. Alkene **10aa** was also obtained from the organic solution in 67% yield, which was almost 80% of the alkene generated from the Wittig reaction. This result demonstrated that the selected FBS effectively separated alkenes and fluorous phosphine oxides.

With the optimized fluorous biphasic system using **2** for the Wittig reaction in hand, a phosphine recycling process as part of the Wittig reaction was also investigated (Table 6). This process included four steps: (i) the Wittig reaction with **2**, **3a**, **9a**, and $^{i}Pr_2NEt$; (ii) extraction of **2** from the reaction mixture by FBS; (iii) reduction of **2′** with DIBAL-H and in situ complex formation with **2** generated by $Me_2S{\cdot}BH_3$; and (iv) deprotection of **2′′** with DABCO. In the first cycle of the process, the fluorous phosphine **2** (1 g scale) was used as the phosphorus source, and **10aa** was obtained in 96% yield along with the phosphine oxide **2′** recovered in 100% yield determined by ^1H and ^{31}P NMR. After the separation of **2′** from the reaction mixture using FBS with the conditions of

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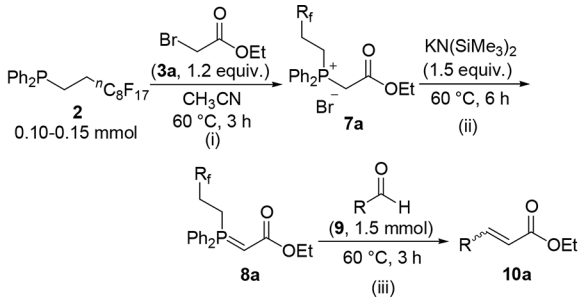
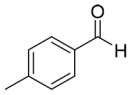
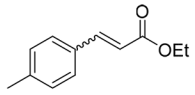
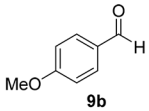
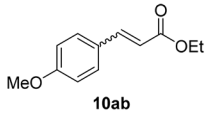
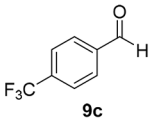
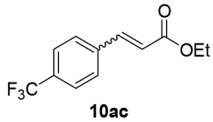
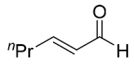
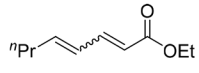
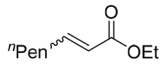
Table 3. One-Pot Wittig Reaction Using Fluorous Phosphine 2, Bromoacetate 3a, and Aldehydes 9[a,b]



Entry	9	10a	Yield[c]
1	 9a	 10aa	96% (94%) [*E*/*Z* = 87/13]
2	 9b	 10ab	99% (90%) [*E*/*Z* = 88/12]
3	 9c	 10ac	90% (56%) [*E*/*Z* = 83/17]
4	 9d	 10ad	66% (38%) [*E*/*Z* = 79/21]
5	 9e	 10ae	34% (13%) [*E*/*Z* = 86/14]

[a]Reaction conditions: (i) **2** (0.10−0.15 mmol), **3a** (1.2 equiv), CH_3CN (0.6 mL), 60 °C, 3 h, (ii) $KN(SiMe_3)_2$ (1.5 mmol), 60 °C, 6 h, (iii) **9** (1.5 equiv), 60 °C, 3 h. [b]The scale of **2**: 0.10 mmol (entry 1), 0.12 mmol (entry 2), 0.14 mmol (entry 3), 0.12 mmol (entry 4), and 0.15 mmol (entry 5). [c]Determined by ^1H NMR spectroscopy based on **2**. Isolated yields are shown in parentheses.

Table 5 entry 9, **10aa** and **2′** were obtained in 76% and 86% yields from the organic layer and the fluorous layer, respectively. Then **2′** recovered from the fluorous layer was converted into **2′′** in 73% yield, and **2** was recovered in 87% yield via deboronation of **2′′** with DABCO. The second cycle of this process was also conducted, and the results are shown in Table 6. The phosphine source was recovered in excellent yields, and these results strongly indicate that phosphorus can actually be recycled in the Wittig reaction using this phosphorus compound **2** with FBS.

CONCLUSIONS

In conclusion, the phosphorus-recycling Wittig reaction process was demonstrated on the gram scale. The phosphine synthesized from air-stable phosphine reagents was a fluorous phosphine with an ethylene spacer between the phosphorus atom and the perfluoroalkyl group. The designed phosphine supported the Wittig reaction to produce various alkenes in adequate yields, and it had a high enough solubility in the fluorous phase. The corresponding phosphine oxide was reduced with DIBAL-H for reuse as the fluorous phosphine in the Wittig reaction. We anticipate that this phosphorus-recycling Wittig reaction will reduce the global consumption of phosphorus. Further investigations to wider utilization of this fluorous phosphine recycling system are currently underway.

EXPERIMENTAL SECTION

General Remarks. Unless otherwise stated, all starting materials and catalysts were purchased from commercial sources and used without further purification. All solvents were distilled and degassed with nitrogen before use. The fluorinated solvents (FC-72, Novec 7100, **11a**, **11b**) were also procured from commercial suppliers (3 M Japan Limited) and used without further purification. ^1H NMR spectra were recorded on a JEOL JNM-ECS400 (400 MHz) FT NMR system or a JEOL JNM-ECX400 (400 MHz) FT NMR system using $CDCl_3$ with Me_4Si as an internal standard. ^{13}C NMR spectra were recorded on a JEOL JNM-ECX400 (100 MHz) FT NMR or a JEOL JNM-ECS400 (100 MHz) FT NMR system in $CDCl_3$. ^{19}F NMR spectra were obtained with a JEOL JNM-ECX400 (376 MHz) FT NMR or a JEOL JNM-ECS400 (376 MHz) FT NMR system with $CDCl_3$ as a solvent. ^{31}P NMR spectra were analyzed on a JEOL JNM-ECX400 (162 MHz) FT NMR or a JNM-ECS400 (162 MHz) FT NMR system using $CDCl_3$ with an 85% H_3PO_4 solution as an external standard. ^{11}B NMR spectra were measured on a JEOL JNM-ECX400 (162 MHz) FT NMR or a JEOL JNM-ECS400 (128 MHz) FT NMR system with $CDCl_3$ and $BF_3{\cdot}OEt_2$ as an external standard. IR spectra were reported in wavenumbers (cm^{-1}). High-resolution mass spectroscopy (HRMS) was conducted on a Bruker micrOTOF II ESI/TOF analyzer.

Synthesis of Fluorous Phosphine 2 from TMDPO, Fluorous Iodide, and $(^nBu_3Sn)_2$ under Photoirradiation (Table 1 Entry 4). TMDPO **5** (0.4 mmol), 1*H*,1*H*,2*H*,2*H*-heptadecafluorodecyl iodide (0.1 mmol), and $(^nBu_3Sn)_2$ **6** (0.1 mmol) in (1,1,1-trifluoromethyl)benzene (BTF) (0.6 mL) were placed into a sealed

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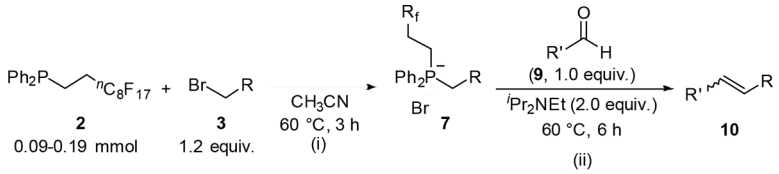
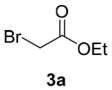
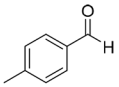
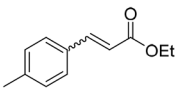
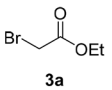
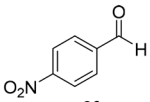
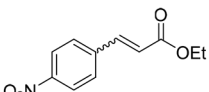
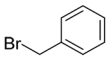
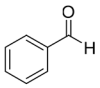
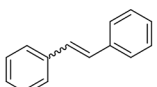
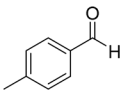
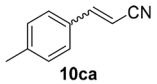
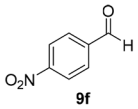
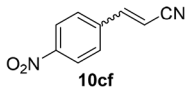
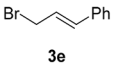
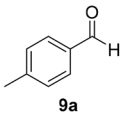
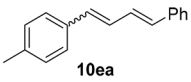
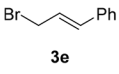
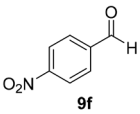
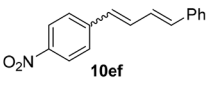
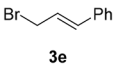
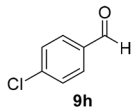
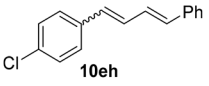
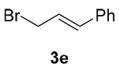
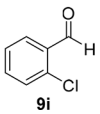
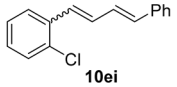
Table 4. Synthesis of Various Alkenes from Fluorous Phosphine 2, Alkyl Bromides 3, and Aldehydes 9[a]



Entry	3	9	10	Yield[c]
1	 **3a**	 **9a**	 **10aa**	93% (91%) [*E*/*Z* = 87/13]
2	 **3a**	 **9f**	 **10af**	80% (63%) [*E*/*Z* = 84/16]
3	 **3b**	 **9g**	 **10bg**	(81%) [*E*/*Z* = 90/10]
4	 **3c**	 **9a**	 **10ca**	93% (97%) [*E*/*Z* = 73/27]
5	 **3c**	 **9f**	 **10cf**	86% (44%[d]) [*E*/*Z* = 70/30]
6	 **3e**	 **9a**	 **10ea**	47% (29%[d]) [*E*/*Z* = 94/6]
7	 **3e**	 **9f**	 **10ef**	55% (51%[d]) [*E*/*Z* = 100/0]
8	 **3e**	 **9h**	 **10eh**	82% (78%[d]) [*E*/*Z* = 97/3]
9	 **3e**	 **9i**	 **10ei**	82% (78%[d]) [*E*/*Z* = 99/1]

[a]Reaction conditions: (i) **2** (0.09−0.19 mmol)[b], **3** (1.2 equiv), CH_3CN (0.6 mL), 60 °C, 3 h. (ii) **9** (1.0 equiv), $^iPr_2NEt$ (2.0 equiv), 60 °C, 6 h. [b]The scale of **2**: 0.12 mmol (entry 1), 0.16 mmol (entry 2), 0.09 mmol (entry 3), 0.15 mmol (entry 4), 0.13 mmol (entry 5), 0.13 mmol (entry 6), 0.12 mmol (entry 7), 0.16 mmol (entry 8), and 0.19 mmol (entry 9) [c]Determined by ^1H NMR spectroscopy. Isolated yields are shown in parentheses. [d]Only the *E*-isomer was isolated.

NMR tube (Pyrex grass) under an argon atmosphere, and the mixture was irradiated with a xenon lamp (500 W) for 6 h. After the reaction was completed, the resulting mixture was extracted with FBS (FC-72/MeOH = 1/1, 10 mL × 3) under an argon atmosphere to produce a pure product **2**.

Gram-Scale Synthesis of Fluorous Phosphine 2 from PPh_3 and Fluorous Iodide (Scheme 2). (i) Synthesis of phosphine oxide **2′**: PPh_3 (14 mmol), 1*H*,1*H*,2*H*,2*H*-heptadecafluorodecyl iodide (14 mmol), and toluene (7 mL) were added to a 100 mL round-bottom flask and the reaction mixture refluxed for 48 h under an argon atmosphere. Then, the solvent was concentrated under reduced pressure and a saturated aqueous NaOH (10 mL) solution added to the resulting residue. The solution was heated for 24 h at 100 °C and the solution neutralized with 3 M aqueous HCl (30 mL). The resulting mixture was extracted with CH_2Cl_2 (10 mL) in triplicate, and the organic layer washed with brine (10 mL) and dried with anhydrous $MgSO_4$. The solution was filtered and the filtrate concentrated under reduced pressure. Finally, the residue was purified by silica-gel chromatography (AcOMe/isohexane = 1:1) to obtain **2′**.

*(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecyl)-diphenylphosphine oxide (**2′**):* white solid, 5.27 g, 58%; mp 123.3−124.1 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78−7.73 (m, 4H), 7.60−

https://dx.doi.org/10.1021/acs.joc.0c01926
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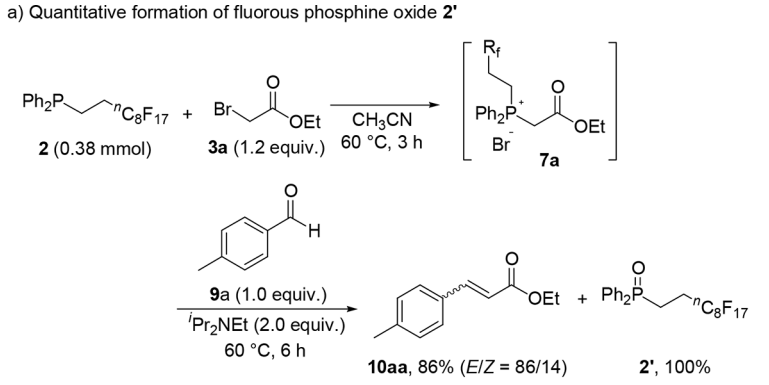
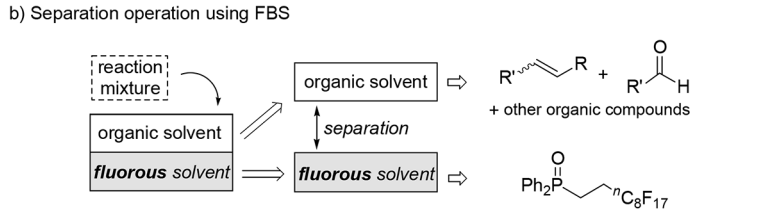
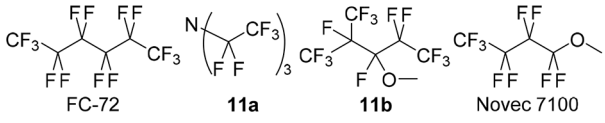
Table 5. Partition Coefficients of 2′ between Several Organic and Fluorous Solvents





Entry	Organic solvent	Fluorous solvent	Partition coefficient of **2'**[a]
1	MeOH	FC-72	1/0.07
2	CH_3CN[b]	FC-72	1/0.08
3	Benzene/^{n}hexane = 1/5	FC-72	1/0.58
4	CH_3CN/H_2O = 19/1	FC-72	1/0.09
5	CH_3CN/H_2O = 19/1	FC-72/**11a** = 1/4	1/0.09
6	CH_3CN/H_2O = 19/1	FC-72/**11b** = 1/4	1/0.48
7	CH_3CN/H_2O = 19/1	FC-72/Novec 7100 = 1/4	1/0.79
8	CH_3CN/H_2O = 9/1	FC-72/Novec 7100 = 1/4	1/1.97
9[c]	CH_3CN/H_2O = 9/1	FC-72/Novec 7100 = 1/1	1/1.07



[a]Partition coefficients of organic solvent/fluorous solvent; values determined by gravimetric method. [b]Solvent was cooled to −30 °C. [c]The organic solvent (2 mL) and the fluorous solvent (4 mL) were used.

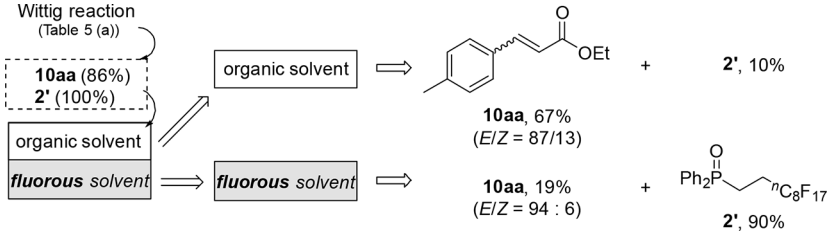


Figure 3. Separation scheme using an FBS ((FC-72/Novec 7100)/(CH_3CN/H_2O)) after the Wittig reaction.

7.56 (m, 2H), 7.54−7.49 (m, 4H), 2.55−2.46 (m, 2H), 2.44−2.34 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 132.4 (d, J = 2.9 Hz), 131.6 (d, J = 100.6 Hz), 130.8 (d, J = 9.6 Hz), 129.1 (d, J = 12.5 Hz), 24.3 (m), 21.1 (d, J = 71.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.6 (s, 3F), −114.6 (s, 2F), −121.6 (s, 2F), −121.8 (s, 4F), −122.6 (s, 2F), −123.0 (s, 2F), −126.0 (s, 2F); ^{31}P NMR (162 MHz, $CDCl_3$)

https://dx.doi.org/10.1021/acs.joc.0c01926
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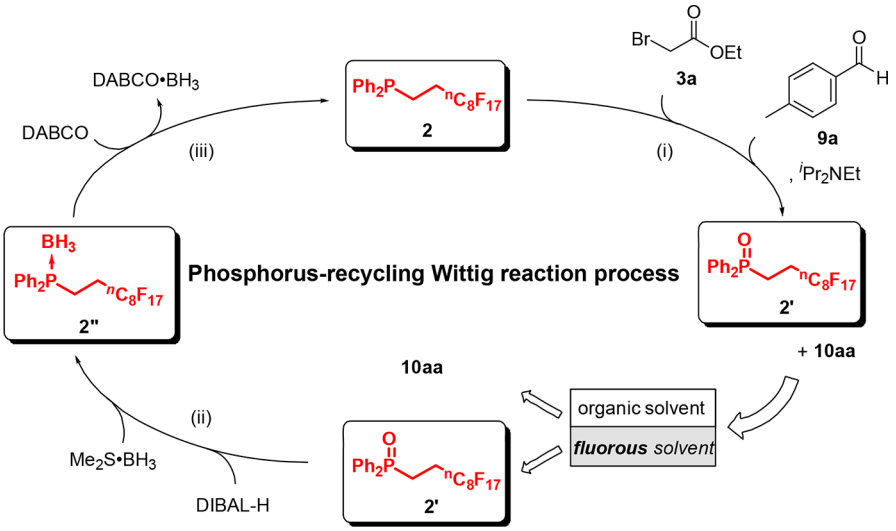
Table 6. Gram-Scale Phosphorus-Recycling Wittig Reaction Process[a]



cycle	**10aa** before separation	**10aa** after separation	**2′** before separation	**2′** after separation	**2′**→**2″**	**2″**→**2**
1	96%[b]	76%[b]	100%[b]	86%[b]	99%[b]	100%[b]
	(*E*/*Z* = 84/16)	(*E*/*Z* = 86/14)			(73%)[c]	(87%)[c]
2	90%[b]	68%[b]	100%[b]	90%[b]	90%[b]	100%[b]
	(*E*/*Z* = 84/16)	(*E*/*Z* = 87/13)			(75%)[c]	

[a]Reaction conditions: (i) **2** (first cycle: 1.8 mmol, 1.14 g; second cycle: recovery from the previous cycle), **3a** (1.2 equiv), CH_3CN (10 mL), 60 °C, 3 h. Then **9a** (1.0 equiv), $^iPr_2NEt$ (2.0 equiv), 60 °C, 6 h. (ii) **2′** obtained from the first step, DIBAL-H (1 M in toluene, 5.0 equiv), reflux, 24 h. Then, $Me_2S{\cdot}BH_3$ (5.0 equiv), 25 °C, 24 h. (iii) Borane complex **2″** obtained from the second step, DABCO (1.0 equiv), toluene (10 mL), 25 °C, 24 h. [b]Yields were determined by ^{31}P NMR and ^1H NMR. [c]Isolated yields.

δ 31.2; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{14}F_{17}PONa$ $[M + Na]^+$ 671.0409, found 671.0402.

(ii) **2″** was synthesized via reduction of **2′** and reacted with $Me_2S{\cdot}BH_3$: **2′** (7.7 mmol) was transferred to a 500 mL three-necked round-bottom flask, and DIBAL-H (1 M in toluene, 5.0 equiv) was added dropwise at 0 °C under an argon atmosphere. After the addition, the mixture was refluxed for 24 h under an argon atmosphere. Then $Me_2S{\cdot}BH_3$ (5.0 equiv) was slowly added to the reaction vessel at 25 °C and stirred for 24 h under an argon atmosphere. Afterward, EtOH (40 mL) and 30 wt % aqueous K_3PO_4 (40 mL) were carefully added and the mixture extracted three times with Et_2O (40 mL). The organic layer was washed twice with H_2O (20 mL) and brine (10 mL) and dried with anhydrous $MgSO_4$. The solution was filtered, and the filtrate concentrated under reduced pressure. The residue was dissolved in a combined solvent (CH_2Cl_2/isohexane = 1:1) and filtered over silica gel. Finally, the solvent was concentrated under reduced pressure to obtain a pure product **2″**.

(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecyl)-diphenylphosphine borane (2″): light yellow solid, 4.49 g, 90%; mp 69.5–70.7 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72–7.67 (m, 4H), 7.56–7.46 (m, 6H), 2.50–2.43 (m, 2H), 2.38–2.22 (m, 2H), 1.41–0.68 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 132.1 (d, *J* = 9.6 Hz), 131.9 (d, *J* = 1.9 Hz), 129.3 (d, *J* = 10.5 Hz), 127.9 (d, *J* = 56.6 Hz), 25.7 (m), 17.2 (d, *J* = 39.3); ^{11}B NMR (128 MHz, $CDCl_3$) δ −41.5 (br); ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.7 (s, 3F), −114.6 (s, 2F), −121.7 (s, 2F), −121.8 (s, 4F), −122.6 (s, 2F), −122.9 (s, 2F), −126.1 (s, 2F); ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.9 (d, *J* = 43.4 Hz); HRMS (ESI) *m*/*z* calcd for $C_{22}H_{17}BF_{17}NaP$ $[M + Na]^+$ 669.0787, found 669.0778.

(iii) Deprotection of phosphine borane **2″** using DABCO: **2″** (6.4 mmol), DABCO (1.0 equiv), and toluene (20 mL) was transferred into a 100 mL Schlenk flask under an argon atmosphere. The mixture was then stirred for 24 h at 25 °C. After the reaction was completed, the solvent was removed under reduced pressure and the residue dissolved in toluene (5 mL). The solution was filtered with a long-length Sep-Pak under an argon atmosphere and the filtrate concentrated under reduced pressure to obtain a pure product **2**.

(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecyl)-diphenylphosphane (2): white solid, 3.63 g, 90%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.44 (m, 4H), 7.37 (q, *J* = 1.5 Hz, 6H), 2.28 (m, 2H), 2.09–2.21 (m, 2H)-; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 137.0 (d, *J* = 11.5 Hz), 132.7 (d, *J* = 19.2 Hz), 129.0 (d, *J* = 38.3 Hz), 128.8, 28.2 (m), 18.3 (d, *J* = 12.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.7 (s, 3F), −114.4 (s, 2F), −121.6 (s, 2F), −121.8 (s, 4F), −122.6 (s, 2F), −123.0 (s, 2F), −126.0 (s, 2F); ^{31}P NMR (162 MHz, $CDCl_3$) δ −15.6; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{14}F_{17}PONa$ $[M + O + Na]^+$ 671.0409, found 671.0402.

General Procedure for the Synthesis of Fluorous Phosphonium Salts (7). Fluorous phosphine **2** (the scale of **2**: 0.103 mmol (entry 1), 0.100 mmol (entry 2), 0.111 mmol (entry 3), 0.098 mmol (entry 4), 0.100 mmol (entry 5), and 0.130 mmol (entry 6)) and alkyl bromide **3** (1.2 equiv) in degassed dry CH_3CN (0.6 mL) were placed into a 10 mL Pyrex Schlenk tube equipped with a stir bar under an argon atmosphere, and the mixture was heated for 3 h at 60 °C in an oil bath. After the reaction was completed, the solvent was concentrated under reduced pressure. The residue was washed three times with Et_2O (10 mL) and the resulting solid recrystallized using $CHCl_3$ and isohexane. The precipitation was filtered to provide the corresponding fluorous phosphine salt **7**.

*(2-Ethoxy-2-oxoethyl)(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)diphenylphosphonium bromide (**7a**):* light yellow solid, 65.2 mg, 79%; mp 71.4–72.0 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03–8.08 (m, 4H), 7.82 (m, 2H), 7.71–7.73 (m, 4H), 5.47 (t, *J* = 12.1 Hz, 2H), 3.96–4.08 (m, 4H), 2.46 (s, 2H), 1.05–1.11 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.7, 134.0, 133.7 (d, *J* = 10.5 Hz), 130.5 (d, *J* = 13.4 Hz), 116.2 (d, *J* = 85.8 Hz), 63.0, 32.0 (d, *J* = 56.6 Hz), 24.9 (t, *J* = 20.9 Hz), 15.6 (d, *J* = 56.6 Hz), 13.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.8 (s, 3F), −113.4 (s, 2F), −121.6 (s, 2F), −121.9 (s, 4F), −122.6 (s, 2F), −122.7 (s, 2F), −126.1 (s, 2F); ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.3; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{21}F_{17}O_2P$ $[M]^+$ 719.1008, found 719.0983.

*Benzyl(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-diphenylphosphonium bromide (**7b**):* light yellow solid, 79.0 mg, 98%; mp 153.5–154.1 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97–7.92

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(m, 4H), 7.78 (m, 2H), 7.65 (d, J = 6.8 Hz, 4H), 7.09−7.05 (m, 5H), 5.42 (d, J = 15.2 Hz, 2H), 3.70 (m, 2H), 2.36 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 135.2 (d, J = 2.8 Hz), 134.1 (d, J = 9.6 Hz), 130.9 (d, J = 4.8 Hz), 130.3 (d, J = 12.5 Hz), 128.8 (d, J = 2.9 Hz), 128.2 (d, J = 3.8 Hz), 127.2 (d, J = 8.6 Hz), 115.8 (d, J = 83.4 Hz), 30.4 (d, J = 46.0 Hz), 24.6 (t, J = 22.9 Hz), 13.7 (d, J = 55.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.8 (s, 3F), −113.7 (s, 2F), −121.7 (s, 2F), −121.9 (s, 4F), −122.6 (s, 2F), −122.8 (s, 2F), −126.1 (s, 2F); ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.9; HRMS (ESI) m/z calcd for $C_{29}H_{21}F_{17}P$ $[M]^+$ 723.1109, found 723.1103.

*(Cyanomethyl)(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)diphenylphosphonium bromide (**7c**):* yellow solid, 71.0 mg, 84%; mp 83.3−84.0 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11−8.10 (m, 4H), 7.87 (m, 2H), 7.86−7.76 (m, 4H), 6.22 (d, J = 15.2 Hz, 2H), 4.28 (m, 2H), 2.40 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 136.4, 134.2 (d, J = 10.5 Hz), 130.9 (d, J = 13.4 Hz), 113.9 (d, J = 85.3 Hz), 111.2 (d, J = 9.6 Hz), 24.7, 17.2 (d, J = 53.7 Hz), 15.6 (d, J = 54.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.8 (s, 3F), −113.5 (s, 2F), −121.7 (s, 2F), −122.0 (s, 4F), −122.6 (s, 2F), −126.8 (s, 2F), −126.2 (s, 2F); ^{31}P NMR (162 MHz, $CDCl_3$) δ 29.4; HRMS (ESI) m/z calcd for $C_{24}H_{16}F_{17}NP$ $[M]^+$ 672.0749, found 672.0749.

*Allyl(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-diphenylphosphonium bromide (**7d**):* light yellow solid, 68.5 mg, 93%; mp 72.8−74.1 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, J = 12.4, 7.3 Hz, 4H), 7.81−7.84 (m, 2H), 7.71−7.76 (m, 4H), 5.58 (m, 2H), 5.31−5.35 (m, 1H), 4.76 (dd, J = 16.3, 4.8 Hz, 2H), 3.78−3.85 (m, 2H), 2.54−2.35 (2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 135.3, 133.8 (d, J = 9.6 Hz), 130.5 (d, J = 12.5 Hz), 126.0 (d, J = 13.4 Hz), 123.1 (d, J = 10.5 Hz), 116.1 (d, J = 83.4 Hz), 28.1 (d, J = 48.9 Hz), 24.6, 14.5 (d, J = 54.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.8 (s, 3F), −113.5 (s, 2F), −121.7 (s, 2F), −121.9 (s, 4F), −122.6 (s, 2F), −122.7 (s, 2F), −126.1 (s, 2F); ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.8; HRMS (ESI) m/z calcd for $C_{25}H_{19}F_{17}P$ $[M]^+$ 673.0953, found 673.0953.

*Cinnamyl(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)diphenylphosphonium bromide (**7e**):* light orange solid, 38.9 mg, 47%; mp 69.6−71.8 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07−8.03 (m, 4H), 7.80−7.74 (m, 2H), 7.73−7.71 (m, 4H), 7.11 (d, J = 3.6 Hz), 5.86−5.81 (m, 1H), 5.06−5.00 (m, 2H), 3.90−3.83 (m, 2H), 2.54−2.39 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 139.9 (d, J = 13.4 Hz), 135.6, 135.3, 134.0 (d, J = 8.6 Hz), 130.5 (d, J = 12.4 Hz), 128.5, 128.3, 126.5, 116.1 (d, J = 82.0 Hz), 113.7 (d, J = 11.4 Hz), 28.0 (d, J = 47.7 Hz), 24.7 (m), 14.9 (d, J = 59.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.7 (s, 3F), −113.4 (s, 2F), −121.6 (s, 2F), −121.8 (s, 4F), −122.5 (s, 2F), −122.7 (s, 2F), −126.1 (s, 2F); ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.0; HRMS (ESI) m/z calcd for $C_{31}H_{23}F_{17}P$ $[M]^+$ 749.1266, found 749.1265.

*Dodecyl(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)diphenylphosphonium iodide (**7f**):* white solid, 80.5 mg, 67%; mp 81.2−82.3 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, J = 12.4, 7.3 Hz, 4H), 7.89−7.85 (m, 2H), 7.79−7.75 (m, 4H), 3.74−3.67 (m, 2H), 3.54−3.50 (m, 2H), 2.47−2.32 (m, 2H), 1.53−1.53 (m, 4H), 1.26−1.19 (m, 16H), 0.86 (t, J = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 135.5, 133.4 (d, J = 9.6 Hz), 130.8 (d, J = 12.5 Hz), 116.2 (d, J = 83.4 Hz), 31.9, 30.4, 30.3, 29.6, 29.5, 29.3, 29.2, 29.1, 24.6 (m), 22.7, 22.6, 22.2 (d. J = 4.8 Hz), 15.0 (d, J = 53.7 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.9 (s, 3F), −113.4 (s 2F), −121.7 (s, 2F), −122.0 (s, 4F), −122.6 (s, 2F), −122.8 (s, 2F), −126.2 (s, 2F); ^{31}P NMR (162 MHz, $CDCl_3$) δ 29.8; HRMS (ESI) m/z calcd for $C_{34}H_{40}F_{17}P$ $[M + H]^+$ 802.2596, found 802.2515.

General Procedure for One-Pot Wittig Reactions Using 2, 3, and 7 (10, Table 3). Fluorous phosphine **2** (the scale of **2**: 0.10 mmol (entry 1), 0.12 mmol (entry 2), 0.14 mmol (entry 3), 0.12 mmol (entry 4), and 0.15 mmol (entry 5)) and bromoacetate **3a** (1.2 equiv) in degassed dry CH_3CN (0.6 mL) were placed into a 10 mL Pyrex Schlenk tube equipped with a stirrer bar under an argon atmosphere, and the mixture was heated for 3 h at 60 °C in an oil bath. $KN(SiMe_3)_3$ (1.5 equiv) was slowly added to the reaction mixture at 0 °C and heated for 6 h at 60 °C in an oil bath. After the reaction, aldehyde **9** (1.0 equiv) was carefully added to the reaction vessel at 0 °C and the content stirred for 3 h at 60 °C. Finally, the solvent was removed under reduced pressure and the residue purified by preparative thin-layer chromatography (AcOMe/isohexane) to generate product **10**.

General Procedure for One-Pot Wittig Reactions Using 2, 3, and 7 (10, Table 4). Fluorous phosphine **2** (the scale of **2**: 0.12 mmol (entry 1), 0.16 mmol (entry 2), 0.09 mmol (entry 3), 0.15 mmol (entry 4), 0.13 mmol (entry 5), 0.13 mmol (entry 6), 0.12 mmol (entry 7), 0.16 mmol (entry 8), 0.19 mmol (entry 9)) and alkyl bromide **3a** (1.2 equiv) in degassed dry CH_3CN (0.6 mL) were placed into a 10 mL Pyrex Schlenk tube equipped with a stirrer bar under an argon atmosphere, and the mixture was heated for 3 h at 60 °C in an oil bath. $^iPr_2NEt$ (2.0 equiv) and aldehyde **9** (1.0 equiv) were added to the reaction mixture, which was then heated for 6 h at 60 °C in an oil bath. After the reaction was completed, the solvent was removed under reduced pressure. Finally, the residue was purified by preparative thin-layer chromatography (AcOMe/isohexane) to provide product **10**.

*Ethyl 3-(4-methylphenyl)acrylate (**10aa**, Table 4):* colorless oil, 19.8 mg, 91%. [*E*-Isomer (CAS no. 24393-49-5)]:[52] ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 16.0 Hz, 1H), 7.42 (d, J = 7.8 Hz, 2H), 7.19 (d, J = 7.8 Hz, 2H), 6.39 (d, J = 16.0 Hz, 1H), 4.26 (q, J = 7.2 Hz, 2H), 2.37 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.0, 144.4, 140.4, 131.6, 129.4, 127.9, 117.0, 60.2, 21.3, 14.2. [*Z*-Isomer (CAS no. 97585-04-1)]:[53] ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.2 Hz, 2H), 7.16 (d, J = 8.2 Hz, 2H), 6.90 (d, J = 12.8 Hz, 1H), 5.89 (d, J = 12.8 Hz, 1H), 4.18 (q, J = 7.0 Hz, 2H), 2.36 (s, 3H), 1.26 (t, J = 7.3 Hz, 3H).

*Ethyl 3-(4-methoxyphenyl)acrylate (**10ab**):* light yellow oil, 22.5 mg, 90%. [*E*-Isomer (CAS no. 24393-56-4)]:[54] ^1H NMR (400 MHz, $CDCl_3$); δ 7.64 (d, J = 16.0 Hz, 1H), 7.47 (d, J = 8.7 Hz, 2H), 6.90 (d, J = 8.7 Hz, 2H), 6.31 (d, J = 16.0 Hz, 1H), 4.25 (q, J = 7.2 Hz, 2H), 3.84 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.4, 161.4, 144.3, 129.8, 127.3, 115.8, 114.4, 60.4, 55.5, 14.5. [*Z*-Isomer (CAS no. 51507-22-3)]:[55] ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 9.2 Hz, 2H), 6.83−6.86 (m, 3H), 5.82 (d, J = 12.8 Hz, 1H), 4.19 (q, J = 7.2 Hz, 2H), 3.83 (s, 1H), 1.28 (t, J = 7.1 Hz, 1H).

*Ethyl 3-(4-(trifluoromethyl)phenyl)acrylate (**10ac**):* colorless solid, 19.3 mg, 56%. [*E*-Isomer (CAS no. 128408-03-7)]:[56] ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 16.0 Hz, 1H), 7.59−7.66 (overlapped with *Z*-isomer, m, 4H), 6.51 (d, J = 16.0 Hz, 1H), 4.29 (q, J = 7.2 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.5, 142.8, 141.5, 137.9, 129.8, 128.2, 126.0, 122.5, 122.2, 121.0, 60.9, 14.4. [*Z*-Isomer (CAS no. 528521-90-6)]:[57] ^1H NMR (400 MHz, $CDCl_3$) δ 7.59−7.66 (overlapped with *E*-isomer, m, 4H), 6.98 (d, J = 12.4 Hz, 1H), 6.06 (d, J = 12.8 Hz, 1H), 4.17 (q, J = 7.2 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H).

*Ethyl octa-2,4-dienoate (**10ad**):* colorless oil, 7.7 mg, 38%. [*E*-Isomer (CAS no. 60388-61-6)]:[58] ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (dd, J = 14.7, 10.5 Hz, 1H), 6.08−6.21 (m, 2H), 5.79 (d, J = 15.1 Hz, 1H), 4.17−4.23 (m, 2H), 2.15 (q, J = 6.9 Hz, 2H), 1.44−1.49 (m, 2H), 1.29 (t, J = 7.6 Hz, 3H), 0.92 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.4, 145.2, 144.6, 128.6, 119.3, 60.3, 35.1, 22.0, 14.4, 13.7.

*Ethyl oct-2-enoate (**10ae**):* light yellow oil, 3.3 mg, 13%. [*E*-Isomer (CAS no. 7367-82-6)]:[59] ^1H NMR (400 MHz, $CDCl_3$) δ 6.93−7.00 (m, 1H), 5.81 (dd, J = 15.6, 1.4 Hz, 1H), 4.18 (overlapped with *Z*-isomer, m, 2H), 2.16−2.22 (m, 2H), 1.42−1.49 (overlapped with *Z*-isomer, m, 2H), 1.34−1.24 (overlapped with *Z*-isomer, m, 6H), 0.87−0.91 (overlapped with *Z*-isomer, m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.9, 149.6, 121.3, 60.2, 32.2, 31.4, 27.8, 22.5, 14.4, 14.0. [*Z*-Isomer (CAS no. 42778-93-8)]:[60] ^1H NMR (400 MHz, $CDCl_3$) δ 6.18−6.25 (m, 1H), 5.75 (dt, J = 11.4, 1.6 Hz, 1H), 4.18 (overlapped with *E*-isomer, m, 2H), 2.61−2.67 (m, 2H), 1.42−1.49 (overlapped with *E*-isomer, m, 2H), 1.34−1.24 (overlapped with *E*-isomer, 7H), 0.87−0.91 (overlapped with *E*-isomer, m, 3H).

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*Ethyl 3-(4-nitrophenyl)acrylate (**10af**):* white solid, 22.2 mg, 63%. [*E*-Isomer (CAS no. 24393-61-6)][61] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20−8.26 (overlapped with *Z*-isomer, m, 2H), 7.67−7.73 (overlapped with *Z*-isomer, m, 3H), 6.56 (d, J = 15.9 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.9, 148.3, 141.4, 140.4, 128.5, 124.0, 122.4, 60.8, 14.1. [*Z*-Isomer (CAS no. 51507-21-2)]:[62] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20−8.26 (overlapped with *E*-isomer, m, 2H), 7.67−7.73 (overlapped with *E*-isomer, m, 2H), 7.02 (d, J = 12.7 Hz, 1H), 6.13 (d, J = 12.7 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H) 1.25 (t, J = 7.0 Hz, 3H).

*1,2-Diphenylethene (**10bg**):* white solid, 13.1 mg, 81%. [*E*-Isomer (CAS no. 103-30-0)]:[63] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 7.8 Hz, 4H), 7.34−7.38 (m, 4H), 7.22−7.28 (m, 2H), 7.11 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.4, 128.8, 127.7, 126.6. [*Z*-Isomer (CAS no. 645-49-8)]:[64] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.52 (overlapped with *E*-isomer, m, 10H), 6.60 (s, 2H).

*(E)-3-(4-Methylphenyl)-prop-2-enyl nitrile (**10ca**):* white solid, 21.4 mg, 97%. [*E*-Isomer (CAS no. 28446-70-0)]:[65] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.40 (m, 3H), 7.21−7.27 (m, 2H), 5.83 (d, J = 16.9 Hz, 1H), 2.39 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.6, 141.9, 130.9, 129.8, 127.4, 118.5, 95.1, 21.6. [*Z*-Isomer (CAS no. 35121-92-7)]:[66] ^{1}H NMR (400 MHz, $CDCl_3$) δ7.71 (d, J = 8.2 Hz, 2H), 7.24−7.20 (overlapped with *E*-isomer, m, 2H), 7.09 (d, J = 11.9 Hz, 2H), 5.38 (d, J = 12.4 Hz, 1H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 148.7, 141.9, 129.9, 129.7, 129.1, 118.5, 93.8, 21.7.

*(E)-3-(4-Nitrophenyl)acrylonitrile (**10cf**):* light yellow solid, 9.9 mg, 44%. [*E*-Isomer (CAS no. 29246-70-6)]:[67] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 8.7 Hz, 2H), 7.64 (d, J = 8.7 Hz, 2H), 7.47 (d, J = 16.5 Hz, 1H), 6.06 (d, J = 16.5 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 149.2, 147.8, 139.3, 128.2, 124.5, 117.1, 101.1.

*1-Methyl-4-((3E)-4-phenylbuta-1,3-dien-1-yl)benzene (**10ea**):* white solid, 8.2 mg, 29%. [*E*-Isomer (CAS no. 37985-11-8):][68] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 7.8 Hz, 2H), 7.30−7.35 (m, 4H), 7.22 (t, J = 7.3 Hz, 1H), 7.14 (d, J = 7.8 Hz, 2H), 6.87−6.98 (m, 2H), 6.61−6.68 (m, 2H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.6, 137.6, 134.9, 132.9, 132.3, 129.5, 129.5, 128.7, 128.4, 127.5, 126.4 (overlapped), 21.4.

*1-Nitro-4-((3E)-4-phenylbuta-1,3-dien-1-yl)benzene (**10ef**):* yellow solid, 15.3 mg, 51%. [*E*-Isomer (CAS no. 27370-90-7)]:[69] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 8.7 Hz, 2H), 7.47 (d, J = 7.3 Hz, 2H), 7.36 (t, J = 7.3 Hz, 2H), 7.28 (t, J = 7.3 Hz, 1H), 7.10 (dd, J = 15.6, 10.5 Hz, 1H), 6.97 (dd, J = 15.6, 10.5 Hz, 1H), 6.80 (d, J = 15.6 Hz, 1H), 6.70 (d, J = 15.1 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 146.6, 144.0, 136.8, 136.2, 133.9, 130.2, 128.9, 128.5, 128.4, 126.8, 126.7, 124.2.

*1-Chloro-4-((3E)-4-phenylbuta-1,3-dien-1-yl)benzene (**10eh**):* white solid, 30.2 mg, 78%. [*E*-Isomer (CAS no. 37985-13-0)]:[70] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 7.8 Hz, 2H), 7.22−7.36 (m, 7H), 6.87−6.96 (m, 2H), 6.55−6.72 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.3, 136.0, 133.5, 133.2, 131.5, 129.9, 129.0, 128.9, 128.8, 127.8, 127.6, 126.5.

*1-Chloro-2-((3E)-4-phenylbuta-1,3-dien-1-yl)benzene (**10ei**):* white solid, 35.8 mg, 78%. [*E*-Isomer (CAS no. 69286-52-8)]:[71] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.2 Hz, 1H), 7.45 (s, 2H), 7.34 (dd, J = 12.8, 7.8 Hz, 3H), 7.20−7.26 (m, 2H), 7.12−7.17 (m, 1H), 6.89−7.09 (m, 3H), 6.70 (d, J = 15.1 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.2, 135.4, 134.1, 133.3, 131.7, 130.0, 129.3, 128.8, 128.5, 127.9, 126.9, 126.7, 126.3.

Determination of Partition Coefficients of Fluorous Phosphine Oxide 2′ Using FBS (Table 5). The fluorous phosphine oxide **2′** dissolved in an organic solvent (2 mL) and the fluorous solvent (2 mL) were added to a separating funnel. The solution was vigorously shaken and then the resulting organic and fluorous phase separated. The solvents were removed under reduced pressure and the partition coefficients determined by the ratio of the recovered weight of **2′** between the organic phase and the fluorous phase (see the Supporting Information).

Separation of Alkenes from Phosphine Oxides 2′ Using FBS (Figure 3). Fluorous phosphine **2** (0.4 mmol) and alkyl bromide **3a** (1.2 equiv) in degassed dry CH_3CN (0.6 mL) were placed into a 10 mL Pyrex Schlenk tube equipped with a stirrer bar under an argon atmosphere; the mixture was then heated for 3 h at 60 °C. ^{i}Pr$_2$NEt (2 equiv) and aldehyde **9a** (0.4 mmol) were added to the reaction mixture, which was then heated for 6 h at 60 °C. The solvent was removed under reduced pressure, and the residue diluted with 5 mL of the organic solution (CH_3CN/H_2O = 9/1) and extracted with the fluorous solution (FC-72/Novec 7100 = 1/1, 10 mL× 2) to obtain **10aa** (67%) from the organic phase and fluorous phosphine oxide **2′** (90%) from the fluorous solvent. The yields were determined by ^{1}H NMR spectroscopy using 1,3,5-trioxane as the internal standard.

Gram-Scale Phosphorus-Recycling Wittig Reaction Process (Table 6). (i) (**First Cycle**) Wittig reaction using the fluorous phosphine **2**: Fluorous phosphine **2** (1.8 mmol, 1.14 g) and alkyl bromide **3a** (1.2 equiv) in degassed dry CH_3CN (10 mL) were placed into a 30 mL Pyrex Schlenk tube equipped with a stirrer bar under an argon atmosphere, and the mixture was heated for 3 h at 60 °C in an oil bath. ^{i}Pr$_2$NEt (2 equiv) and aldehyde **9a** (1 equiv) were added to the reaction mixture, which was heated for 6 h at 60 °C in an oil bath. After the reaction was completed, the solvent was removed under reduced pressure and the yields of **10aa** and **2′** determined by ^{1}H and ^{31}P NMR spectroscopy.

(ii) Extraction of the phosphine oxide **2′** from the reaction mixture using FBS: The resulting residue from step (i) was dissolved into 10 mL of the organic solution (CH_3CN/H_2O = 9/1) and extracted with the fluorous solution (FC-72/Novec 7100 = 1/1, 20 mL × 2) to obtain **10aa** (76%) from the organic phase and fluorous phosphine oxide **2′** (86%) from the fluorous solvent.

(iii) Reduction of **2′** with DIBAL-H and following protection by $Me_2S{\cdot}BH_3$: **2′** recovered from the fluorous layer was transferred to a 500 mL three-necked round-bottom flask, and DIBAL-H (1 M in toluene, 5.0 equiv) was added dropwise at 0 °C under an argon atmosphere. After the addition was completed, the mixture was refluxed for 24 h under an argon atmosphere. Then $Me_2S{\cdot}BH_3$ (5.0 equiv) was slowly added to the reaction vessel at 25 °C and stirred for 24 h under an argon atmosphere. Then EtOH (10 mL) and 30 wt % K_3PO_4 aq (10 mL) were carefully added, respectively, and the mixture extracted three times with Et_2O (20 mL). The organic layer was washed twice with H_2O (20 mL) and brine (10 mL) and dried with anhydrous $MgSO_4$. The solution was filtered and the filtrate concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluent: CH_2Cl_2/isohexane = 1:5) to obtain the pure product **2′′** in a 73% isolated yield (735.0 mg, white solid).

(iv) Deprotection of phosphine borane **2′′** using DABCO: **2′′** (recovered from step (iii), 735.0 mg), DABCO (1.0 equiv), and toluene (10 mL) were transferred into a 100 mL Schlenk flask under an argon atmosphere and the mixture stirred for 24 h at 25 °C. After the reaction was completed, the resulting solution was filtered with a long-length Sep-Pak under an argon atmosphere and the filtrate concentrated under reduced pressure to obtain a pure product **2** in 87% isolated yield (625.6 mg, white solid).

(v) (**Second Cycle**) Wittig reaction using the fluorous phosphine **2**: Fluorous phosphine **2** (0.99 mmol, 625.6 mg, recovered from the first cycle) and alkyl bromide **3a** (1.2 equiv) in degassed dry CH_3CN (10 mL) were placed into a 30 mL Pyrex Schlenk tube equipped with a stirrer bar under an argon atmosphere, and the mixture was heated for 3 h at 60 °C in an oil bath. ^{i}Pr$_2$NEt (2 equiv) and aldehyde **9a** (1 equiv) were added to the reaction mixture, which was heated for 6 h at 60 °C in an oil bath. After the reaction was completed, the solvent was removed under reduced pressure and the yields of **10aa** and **2′** determined by ^{1}H and ^{31}P NMR spectroscopy.

(vi) Extraction of the phosphine oxide **2′** from the reaction mixture using FBS: The resulting residue from step (v) was dissolved into 10 mL of the organic solution (CH_3CN/H_2O = 9/1) and extracted with the fluorous solution (FC-72/Novec 7100 = 1/1, 20 mL × 2) to obtain **10aa** (68%) from the organic phase and fluorous phosphine oxide **2′** (90%) from the fluorous solvent.

(vii) Reduction of **2′** with DIBAL-H and following protection by $Me_2S{\cdot}BH_3$: **2′** recovered from the fluorous layer was transferred to a

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200 mL three-necked round-bottom flask, and DIBAL-H (1 M in toluene, 5.0 equiv) was added dropwise at 0 °C under an argon atmosphere. After the addition was completed, the mixture was refluxed for 24 h under an argon atmosphere. Then $Me_2S{\cdot}BH_3$ (5.0 equiv) was slowly added to the reaction vessel at 25 °C and stirred for 24 h under an argon atmosphere. Then, EtOH (10 mL) and 30 wt % K_3PO_4 aq (10 mL) were carefully added, respectively, and the mixture wasextracted three times with Et_2O (20 mL). The organic layer was washed twice with H_2O (20 mL) and brine (10 mL) and dried with anhydrous $MgSO_4$. The solution was filtered and the filtrate concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluent: CH_2Cl_2/isohexane = 1:5) to obtain the pure product **2′′** in a 75% isolated yield (429.0 mg, white solid).

(viii) Deprotection of phosphine borane **2′′** using DABCO: **2′′** recovered from step (vii), DABCO (1.0 equiv), and toluene (10 mL) were transferred into a 100 mL Schlenk flask under an argon atmosphere, and the mixture was stirred for 24 h at 25 °C. After the reaction was completed, the resulting solution was filtered with a long-length Sep-Pak under an argon atmosphere and the filtrate concentrated under reduced pressure. The yield of **2** was determined by ^1H and ^{31}P NMR spectroscopy.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c01926.

Reaction optimization; ^1H NMR, ^{13}C NMR, ^{19}F NMR, ^{11}B NMR, and ^{31}P NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

This work is dedicated to Prof. Ilhyong Ryu (Osaka Prefecture University; National Chiao Tung University) on the occasion of his 70th birthday.

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