Doctoral Dissertation

Phosphole Synthesis via Carbon–Phosphorus Bond Cleavage and Catalytic Reactions Using a Fluorophosphorane Platform

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Preface and Acknowledgement

The research presented in this thesis was carried out under the direction of Professor Mamoru Tobisu of the Department of Applied Chemistry, Graduate School of Engineering, Osaka University. I was a student in the Functional Organic Chemistry lab. (supervisor: Prof. Toru Amaya and Prof. Toshiyuki Moriuchi) from April 2016 to March 2017 and I then moved to Professor Tobisu's laboratory on his promotion to full professor. I spent the remainder of my career as a Ph.D. student in his group from April 2019 to March 2022. The thesis is concerned with phosphole synthesis via carbon–phosphorus bond cleavage and catalytic reactions using a fluorophosphorane platform.

This thesis could not have been completed without the support of numerous people. Here, I wish to express my sincerest appreciation to all of these people.

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Contents

General Introduction

Organophosphorus compounds are an important class of compounds that are used in numerous applications such as ligands for transition metal catalysts,[1] organic electronic materials,[2] and organocatalysts[3] (Figure 1). Therefore, the development of new methods for the synthesis of organophosphorus compounds has continued to be a subject of intense interest. The key issues in this synthesis are methods used to form a new C–P bond and the type of phosphorus source that is used to accomplish this (Figure 2). The most frequently used method for the synthesis of organophosphorus compounds involves the nucleophilic substitution of a P–X bond with a stoichiometric amount of an organometallic species, such as an organolithium or an organomagnesium reagent.[4] However, there are problems associated with the use of phosphorus reagents that contain a P–X bond, which include toxicity, volatility, and the fact that these reagents are a source of irritation. A low functional group compatibility associated with the organometallic reagents that are used can also be a drawback. The second approach involves the use of compounds bearing a P–H bond, which can be activated by a transition metal catalyst and used for new C–P bond formation reactions via the addition to unsaturated bonds or cross-coupling with aryl halides.[4] Although these catalytic methods address some of the issues associated with methods that involve P–X bond transformations, several problems still remain, including the fact that compounds bearing a P–H bond are unstable. The third emerging approach to the synthesis of organophosphorus compounds involves the direct transformation of C–P bonds.[5] This method is useful because readily available tertiary phosphines can be directly used as starting materials for the synthesis of new organophosphorus compounds. However, such methods that involve C–P bond cleavage have been less explored due to the difficultly in activting an inert C–P bond.

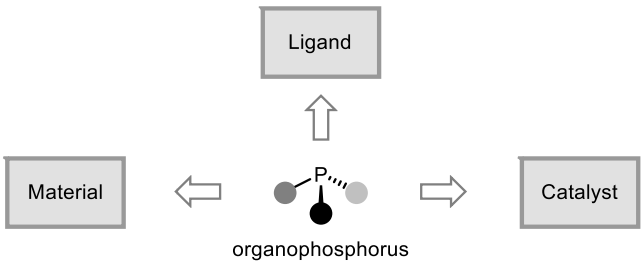


Figure 1. Applications of organophosphorus compounds

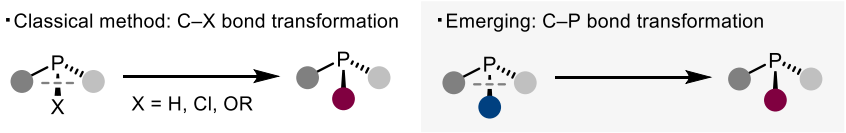


Figure 2. Synthesis of organophosphorus compounds

C−P bond cleavage is frequently encountered as an undesired side reaction in phosphine-ligated metal-catalyzed processes. Several mechanisms for this C−P bond cleavage process have been proposed. One possible mechanism involves the direct oxidative addition of a C−P bond of the phosphine to a low-valent metal to form a P-bridged dimeric intermediate.[6] C−P bond cleavage is also mediated by Ar−Pd−X species, through reductive elimination with the formation of a phosphonium salt and Pd(0), followed by the oxidative addition of a C−P bond of the phosphonium.[7] In the first half of this thesis reaserch, the focus is on development of methods for the synthesis of

dibenzophosphole derivatives via C–P bond cleavage.

Regarding the use of organophosphorus compounds as catalysts, organophosphine catalysis can be classified into four categories (Figure 3).

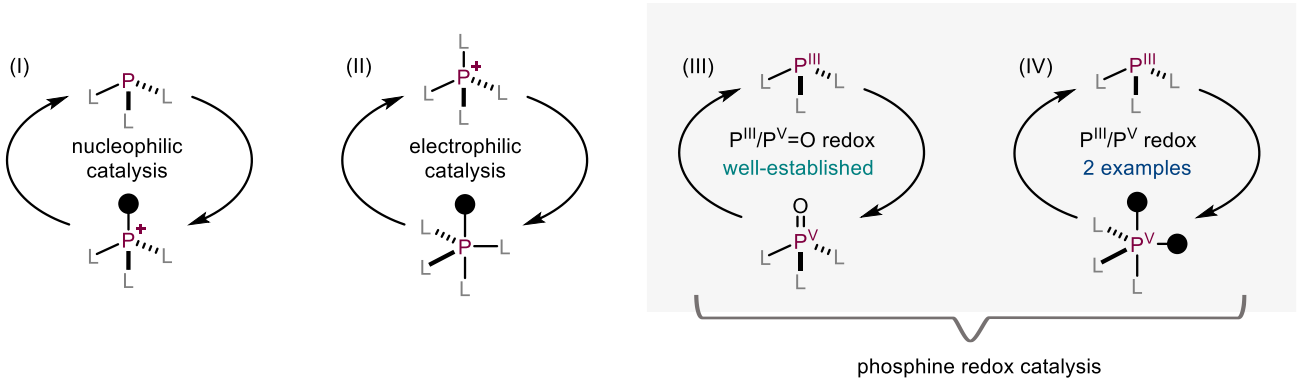
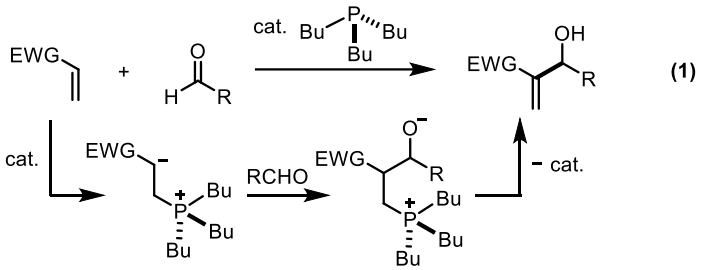


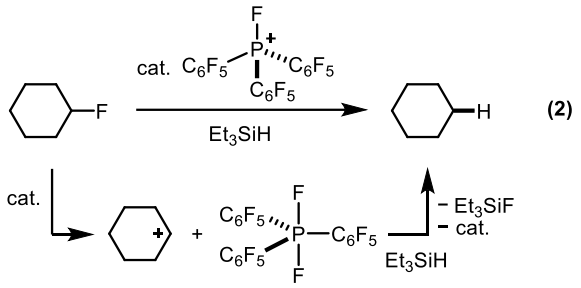
Figure 3. Organophosphine catalysis

Nucleophilic catalysis by a tricoordinate phosphine species comprises the most common type of organophosphine catalysis, wherein neutral tricoordinate phosphines function as electron-pair donors to activate electrophiles to form tetracoordinate phosphonium species. Such reactions are amenable to various subsequent transformations with the regeneration of neutral tricoordinate phosphines (Type I). The Morita-Baylis-Hillman reaction[8] is a typical example of this nucleophilic phosphine catalysis (Scheme 1). In this reaction, the addition of PR_3 to an electron-deficient alkene results in the generation of a Horner zwitterion,[9] the enolate moiety of which then adds to an aldehyde, with the eventual formation of α-hydroxymethylated acrylates via alkoxide-to-enolate proton transfer and *β*-elimination of the phosphine catalyst.



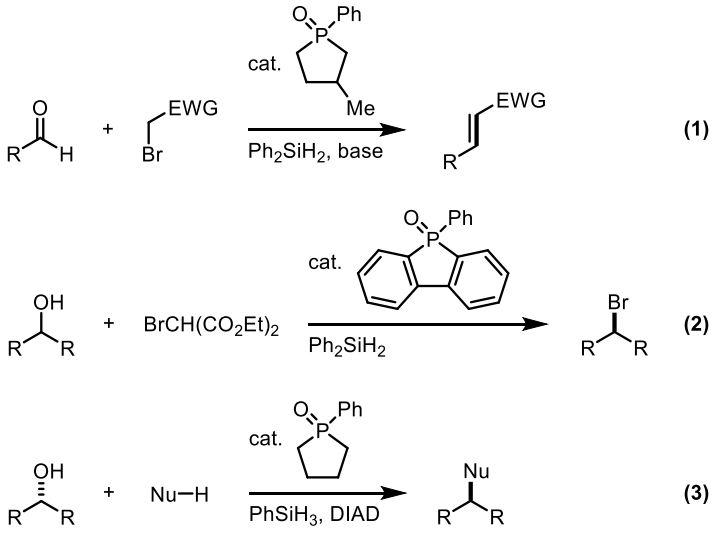
Scheme 1. An example of nucleophilic catalysis (Type I)

The use of Lewis acidic phosphonium cations as electrophilic catalysts via pentacoordinate phosphoranes has also been reported (Type II). Stephan et al. reported that a fluorophosphonium salt can function as an electrophilic catalyst to directly activate a C–F bond of an alkyl fluoride and to effect the catalytic hydrodefluorination of fluoroalkanes when the reaction is carried out in the presence of a hydrosilane derivative (Scheme 2).[10]

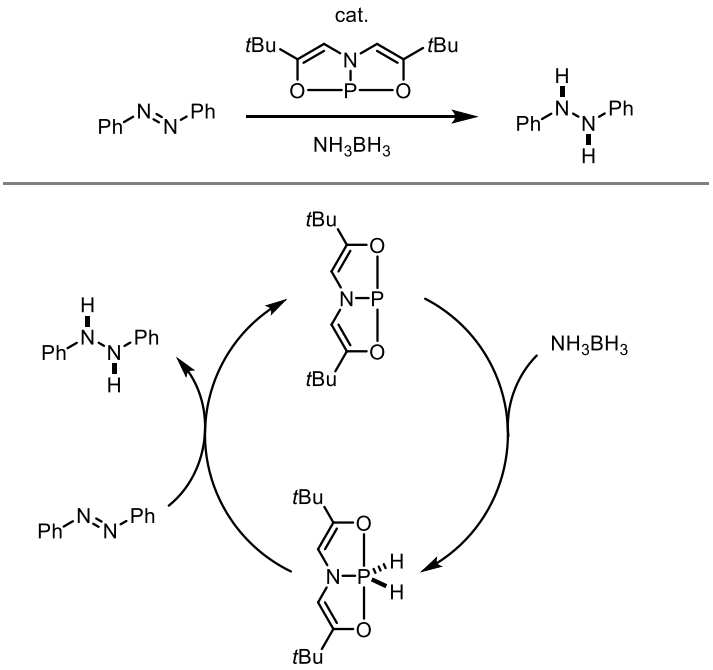


Scheme 2. An example of electrophilic catalysis (Type II)

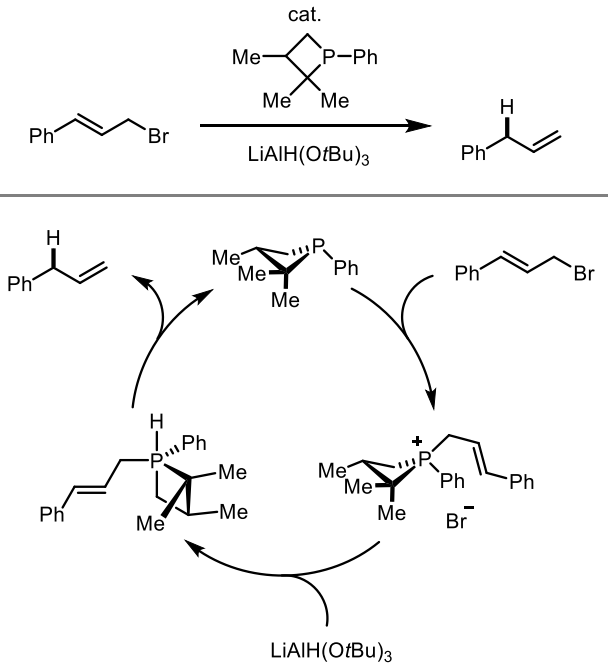
The P(III)/P(V) redox cycle is a competent main group-based manifold for applications in catalytic reactions.[11] Two classes (Type III and IV) of phosphine redox catalysis via a P(III)/P(V) redox cycle have been reported. The reported catalytic reactions based on the P(III)/P(V) couple are primarily limited to oxygen transfer reactions mediated by the reversible interconversion of tricoordinate phosphine/phosphine oxide (P(III)/O=P(V), Type III). O'Brien et al. reported on the first catalytic Wittig reaction using a P(III)/O=P(V) redox cycle, in which a phosphine oxide byproduct was in situ reduced back to the phosphine by a hydrosilane (eq. 1).[12] This strategy has since been employed to promote Appel (eq. 2),[13] and Mitsunobu reactions (eq. 3),[14] as well as other reactions[3] that are thermodynamically driven by the formation of a phosphine oxide.



Pentacoordinate phosphorane-mediated stoichiometric oxidative addition[15] and reductive elimination[16] reactions have also been repoted. A stoichiometric redox cycle based on the pentacoordinate phosphorane was also reported.[17] However, the use of such redox processes in catalytic reactions (Type IV) are limited to two reactions. One of these is the hydrogenation of azobenzene catalyzed by a planer tricoordinate phosphorus compound (Scheme 3).[18] The planar phosphorus catalyst activates ammonia-borane to furnish a pentacoordinate dihydridophosphorane derivative, which mediates the transfer of hydrogen to azobenzene. The other is the reduction of allyl bromides catalyzed by a four-membered phosphacycle (Scheme 4).[19] This allylic reduction proceeds via hydridophosphorane as a key intermediate, which allows for the stereoselective reductive transposition of allyl bromides. In the second half of this thesis,. the author's focus is on the development of tricoordnate phosphine/pentacoordinate phosphorane redox cycles (Type IV) using a fluorophosphorane platform.



Scheme 3. Hydrogenation of azobenzene by a P(III)/P(V) redox cycle (Type IV)



Scheme 4. Reduction of allyl bromides by P(III)/P(V) redox cycle (Type IV)

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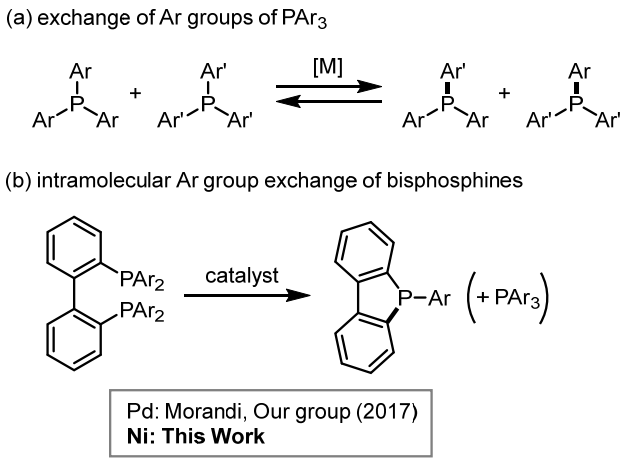
Chapter 1

Nickel-Catalyzed Synthesis of Phosphole Derivatives via the Cleavage of Two Carbon–Phosphorus Bonds

1.1 Introduction

Tertiary phosphines are the essential components of transition metal catalysts in regulating the reactivity and selectivity of the catalytic reactions. In phosphine-ligated metal-catalyzed processes, C–P bond cleavage is frequently encountered as an undesired side reaction.[1] For example, in palladium-catalyzed cross-coupling reactions of aryl halides, the aryl group of a triarylphosphine ligand has been known to be incorporated to the product in place of the aryl group of the aryl halide substrate.[2] Such an undesired reaction proceeds via a C–P bond exchange pathway (Scheme 1a), which can be mediated by several metal species with palladium being most active.[3] Although this intermolecular aryl group exchange has limited synthetic utility due to the reversibility of the reaction,[4] Morandi et al.[5] and our group[6] independently reported an intramolecular variant, which enables the palladium-catalyzed selective synthesis of dibenzophosphole derivatives from readily available bisphosphines (Scheme 1b). We report herein that this intramolecular C–P bond exchange reaction can be catalyzed by nickel. Nickel complexes are much less active in mediating C–P bond exchange reactions,[3b] and there are no general catalytic reactions[7] involving the cleavage of C–P bonds of tertiary phosphines, except for one isolated example using highly strained methylenecyclopropa[*b*]naphthalenes.[8]

Scheme 1. Metal-mediated C–P bond exchange and its application to the catalytic synthesis of phospholes

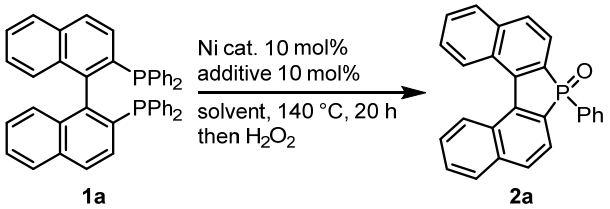


1.2 Results and Discussion

We initially investigated the nickel-catalyzed cyclization of 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP, **1a**) using $Ni(cod)_2$ as a nickel(0) catalyst (Table 1). To our delight, the desired phosphole was formed in 8% without the need for any additives (entry 1). Because phosphole derivatives are sensitive to oxygen, the product was quantified as the air-stable phosphole oxide **2a** after an oxidative workup with H_2O_2. Inspired by the seminal work by Morandi,[5] in which added PhI serves as a cocatalyst to facilitate the formation of a phosphonium salt, a key intermediate, we examined a nickel catalyst in conjunction with an aryl halide. The addition of a catalytic amount of PhI (entry 2) and PhBr (entry 3) increased the yield of **2a** to ca. 20%. We were then able to increase the yield to 79% when PhOTf was used as a cocatalyst (entry 4). The use of DMF (entry 6) allowed the reaction to proceed quantitatively to give **2a** in 84% isolated yield, along with a stoichiometric amount of triphenylphosphine

oxide, thus confirming the fate of the cleaved phosphorus residue. The use of $Ni(OAc)_2$ (entry 7) and $Ni(OTf)_2$ (entry 8) as nickel(II) catalysts failed to promote the reaction.

Table 1. Nickel-catalyzed cyclization of **1a** to **2a**[a]



1a **2a**

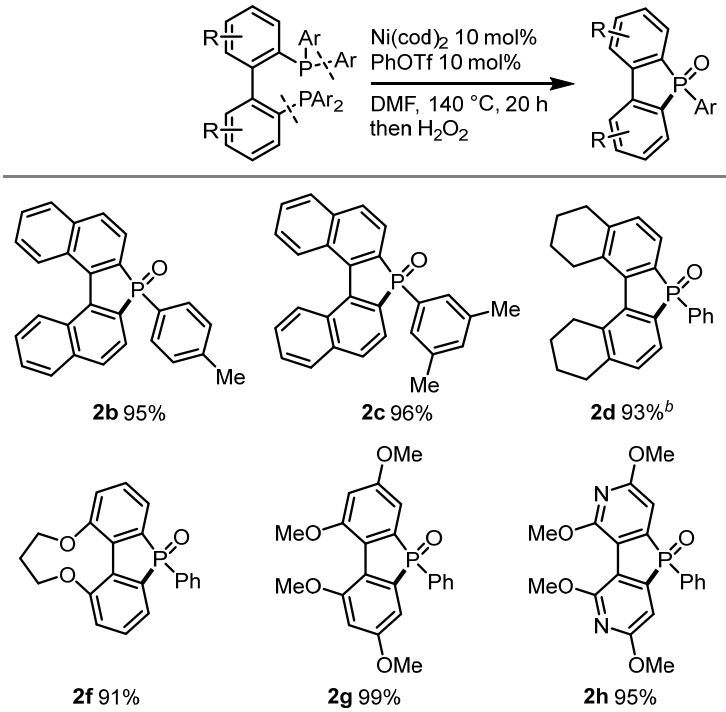
entry	catalyst	additive	solvent	NMR yield of **2a**/ %
1	$Ni(cod)_2$	none	toluene	8
2	$Ni(cod)_2$	PhI	toluene	19
3	$Ni(cod)_2$	PhBr	toluene	23
4	$Ni(cod)_2$	PhOTf	toluene	79
5	$Ni(cod)_2$	PhOTf	1,4-dioxane	61
6	$Ni(cod)_2$	PhOTf	DMF	99 (84)[b]
7	$Ni(OAc)_2$	PhOTf	toluene	trace
8	$Ni(OTf)_2$	PhOTf	toluene	trace

[a] Reaction conditions: **1a** (0.20 mmol), Ni cat. (0.020 mmol), and additive (0.020 mmol) in solvent (1.0 mL) at 140 °C for 20 h. The NMR yield was determined using 1,1,2,2,-tetrachloroethane as an internal standard. [b] Isolated yield.

The scope of this nickel-catalyzed cyclization reaction was examined using a series of commercially available bisphosphine derivatives (Table 2). The scope of the substituent on the phosphorus atom was initially examined. Aryl groups, such as *p*-tolyl (**1b**) and 3,5-xylyl (**1c**), were found to participate in this cyclization to provide the corresponding phosphole derivatives **2b** and **2c** in excellent yields. The cyclization reaction is not limited to a binaphthyl-based skeleton, but a simpler biphenyl system, including **1d**–**1g**, also participated successfully in the reaction. Although these bisphosphines have a diverse range of bite angles, which could potentially affect the efficiency of the reaction, all provided the corresponding phospholes **2d**–**2g** in >90% yields. It was also possible to synthesize heterocyclic (**2h**) and six-membered (**2i**) phosphacycles using the corresponding bisphosphines **1h** and **1i** under these nickel-catalyzed conditions.

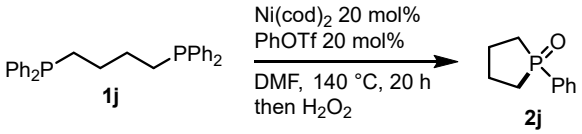
Apart from the earth-abundant nature, the use of nickel in place of palladium provides an opportunity to realize some unique transformations. Since oxidative addition occurs more readily in the presence of nickel than palladium,[9] a nickel catalyst shows superior reactivity to a palladium catalyst in cyclization reactions (Table 3). For example, the cyclization of an alkylene linked bisphosphine such as 1,4-bis(diphenylphosphino)butane (**1j**, DPPB) failed to proceed under palladium-catalyzed conditions.[6,10] However, to our delight, when the $Ni(cod)_2$/PhOTf was used, **1j** underwent cyclization to form the aliphatic phosphacycle **2j** in 50% yield.

Table 2. Reaction scope[a]



[a] Reaction conditions: bisphosphine (0.20 mmol), $Ni(cod)_2$ (0.020 mmol), PhOTf (0.020 mmol) in DMF (1.0 mL) for 20 h at 140 °C. Yields of isolated products are given. [b] 0.10 mmol scale. [c] 3.0 mmol scale. 1.05 g of **2e** was obtained. [d] Run using 0.040 mmol of $Ni(cod)_2$ and PhOTf. [e] Isolated as a mixture of triphenylphosphine oxides (1:1).

Table 3. Comparison between nickel and palladium catalyst[a]



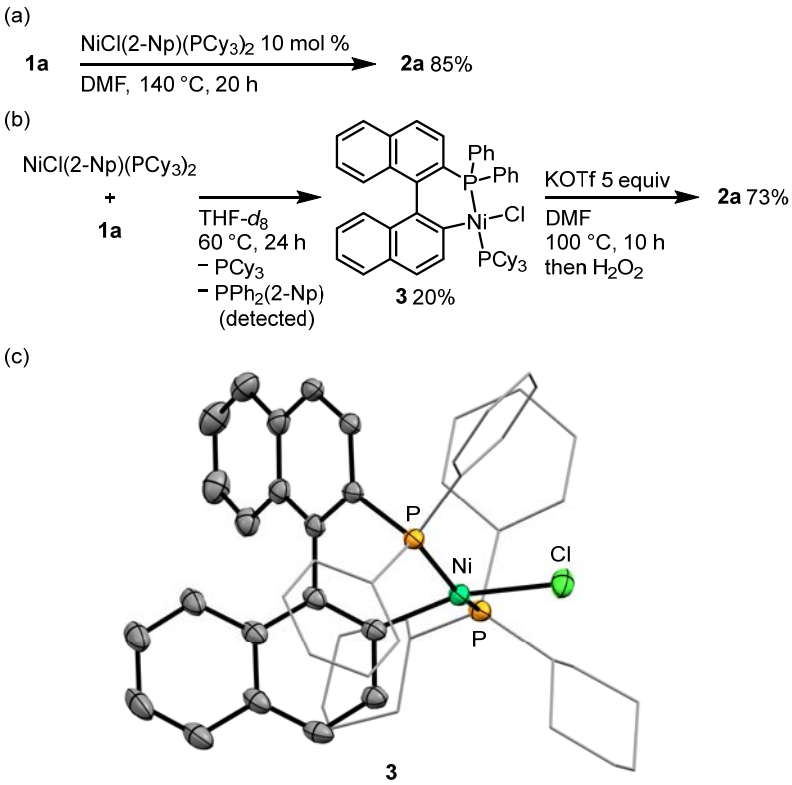
method	catalyst	yield
A	$Ni(cod)_2$/PhOTf	50%
B	$[(allyl)PdCl]_2$	0%
C	$Pd_2(dba)_3$/PhI	0%

[a] Reaction conditions: method A, $Ni(cod)_2$/PhOTf; method B,[6] $[(allyl)PdCl]_2$; method C,[5] $Pd_2(dba)_3$/PhI. Isolated yield. Isolated as a mixture with triphenylphosphine oxide.

The reaction is presumably initiated by the oxidative addition of PhOTf to Ni(0) to form a Ni(OTf)Ph(bisphosphine), which then serves as a catalytically active species. To confirm this possibility, $NiCl(2\text{-Np})(PCy_3)_2$ (2-Np = 2-naphthalenyl)[11] was synthesized as a model of Ni(OTf)Ph(bisphosphine), and its catalytic activity was examined (Scheme 2a). The BINAP **1a** provided the corresponding phosphole **2a** in 85% yield, even in the absence of PhOTf. Stoichiometric experiments were performed to gain additional insights into the reaction mechanism (Scheme 2b). When $NiCl(2\text{-Np})(PCy_3)_2$ was reacted with 1.0 equiv of BINAP **1a** at 60 °C in THF-d_8, ^{31}P NMR signals corresponding to two mutually *trans* phosphine resonances (doublets at 16.6 and 22.8 ppm with J_{PP} = 318 Hz) were observed. Single-crystal X-ray diffraction of the crystalized material revealed that the six-membered phospha-nickelacycle complex **3** was formed via the cleavage of a C–P bond of **1a** (Scheme 2c).

Hartwig[12] reported on a similar phospha-nickelacycle by the reaction of a BINAP-ligated Ni(0) complex with an electron-rich aryl chloride. During the course of the formation of the phospha-nickelacycle **3**, the 2-naphthyldiphenylphosphine [PPh_2(2-Np)], the cleaved phosphorus residue, was also observed by FAB-MS. In addition, a BINAP-ligated Ni(I) complex **4**, which is formed by the bimolecular reductive elimination of 2,2'-binaphthalene from the BINAP-ligated Ni(II) complex, was also formed. The phospha-nickelacycle **3** could be used to catalyze the cyclization of **1a** to form **2a** in 98% yield, even in the absence of PhOTf, whereas the Ni(I) complex **4** showed no catalytic activity. Heating the phospha-nickelacycle **3** in DMF at 100 °C for 10 h afforded **2a** in 73% yield. In this process, the addition of KOTf accelerated the formation of **2a** by approximately two fold, probably by decreasing the electron density of the nickel center through exchanging the ligand from Cl to OTf.[13] These results indicate that reductive elimination to form the cyclic phosphonium salt[14] is the turnover limiting step of this reaction, and the role of a PhOTf cocatalyst is best rationalized to facilitate this C–P bond forming reductive elimination.

Scheme 2. Mechanistic studies



1.3 Conclusion

In conclusion, we report on the nickel-catalyzed cyclization of bisphosphines to diverse phosphacycles via the cleavage of two C–P bonds. The method features nickel-catalyzed C–P bond cleavage, which allows for the transformation of bulky and sp^3 C–P bonds. Detailed studies related to the mechanism of this reaction revealed that the phospha-nickelacycle **3** is a key intermediate.

1.4 Experimental Section

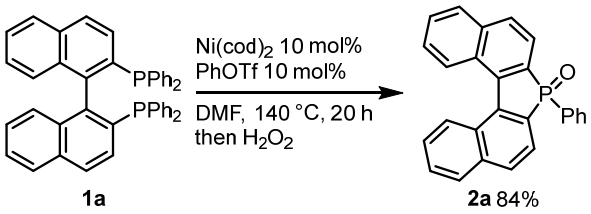
I. General Information

^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a JEOL ECS-400 spectrometer in $CDCl_3$. The chemical shifts in ^{1}H NMR spectra were recorded relative to $CHCl_3$ (δ 7.26). The chemical shifts in ^{13}C NMR spectra were recorded relative to $CDCl_3$ (δ 77.0). The chemical shifts in ^{31}P NMR spectra were recorded relative to H_3PO_4 (δ 0.0). The data is reported as follows: chemical shift (δ) in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, and m = multiplet), coupling constant (Hz), and integration. Infrared spectra (IR) were obtained using a JASCO FT/IR-4200 spectrometer. Absorption is reported in reciprocal centimeters (cm^{-1}) with the following relative intensities: s (strong), m (medium), or w (weak). High resolution mass spectra (HRMS) were obtained using a JEOL JMS-T100LP spectrometer. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed with Biotage Isolera® equipped with Biotage SNAP Ultra. Gel permeation chromatography (GPC) was performed using a LC-9210NEXT HPLC or LC9225NEXT HPLC system. Data collection for X-ray crystal analysis were performed on a Rigaku/XtaLAB Pro P200 Hybrid Photon Counting diffractometer (Cu-Kα, λ = 1.54184 Å for **3** and Mo-Kα, λ = 0.71075 Å for **4**). The structures were solved with direct methods and refined with full-matrix least squares.

II. Materials

All reagents were obtained from commercial suppliers and were used as received. $Ni(cod)_2$ was purchased from Strem Chemicals. Phenyl trifluoromethanesulfonate (CAS: 17763-67-6), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (**1a**, CAS: 98327-87-8), (*S*)-Tol-BINAP (**1b**, CAS: 100165-88-6), (*S*)-Xyl-BINAP (**1c**, CAS: 135139-00-3), (*R*)-SEGPHOS (**1e**, CAS: 244261-66-3), DPEPHOS (**1i**, CAS: 166330-10-5), and DPPB (**1j**, 7688-25-7) were purchased from Tokyo Chemical Industry Co., Ltd. (*R*)-H_8-BINAP (**1d**, CAS: 139139-86-9), (*R*)-C_3-TUNEPHOS (**1f**, CAS: 301847-89-2), (*R*)-Ph-GARPHOS (**1g**, CAS: 1365531-75-4) and (*R*)-P-PHOS (**1h**, CAS: 221012-82-4) were purchased from Sigma-Aldrich Co. $NiCl(2\text{-Np})(PCy_3)_2$ was prepared according to literature procedure.[11]

III. Typical Procedure

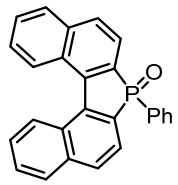


1a **2a** 84%

In a glovebox filled with nitrogen, $Ni(cod)_2$ (5.5 mg, 0.02 mmol), PhOTf (4.5 mg, 0.02 mmol), **1a** (125 mg, 0.20 mmol) and DMF (1 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The vessel was heated at 140 °C for 20 h followed by cooling. An aqueous solution of H_2O_2 (ca. 30%, a few drops) was added, and the mixture was stirred at room temperature for 1 h. The mixture was filtered through a short pad of silica gel, and the pad was washed with EtOAc. The filtrate was evaporated, and the residue was purified by GPC to give **2a** (63 mg, 84%) as a pale yellow solid.

IV. Spectroscopic Data

7-Phenylbenzo[*e*]naphtho[2,1-*b*]phosphindole 7-oxide (2a) [CAS:159211-70-8].



Pale yellow solid (60.9 mg, 84%). R_f 0.34 (SiO_2, EtOAc).

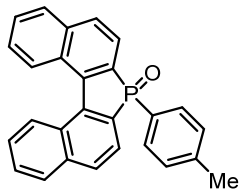
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.35 (td, *J* = 7.6, 3.2 Hz, 2H), 7.47 (td, *J* = 7.6, 1.6 Hz, 1H), 7.54–7.66 (m, 6H), 7.83 (dd, *J* = 9.2, 8.2 Hz, 2H), 7.98 (d, *J* = 7.8 Hz, 4H), 8.21 (d, *J* = 7.3 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 124.4 (d, *J* = 9.6 Hz), 125.8, 127.6, 128.1, 128.7, 128.8, 128.9, 130.2 (d, *J* = 102.6 Hz), 130.5 (br), 131.0, 131.1, 132.3 (d, *J* = 2.9 Hz), 137.3, 141.5 (br).

^{31}P NMR ($CDCl_3$, 161.83 MHz) δ: 35.1.

HRMS (EI+, M^+) Calcd for $C_{26}H_{17}OP$: 376.1017. Found: 376.1015.

7-(4-Methylphenyl)benzo[*e*]naphtho[2,1-*b*]phosphindole 7-oxide (2b).



Pale yellow solid (74.3 mg, 95%). R_f 0.50 (SiO_2, EtOAc).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.33 (s, 3H), 7.16 (dd, *J* = 2.3, 8.0 Hz, 2H), 7.49–7.65 (m, 6H), 7.81 (t, *J* = 9.2 Hz, 2H), 7.97 (d, *J* = 8.2 Hz, 4H), 8.20 (d, *J* = 7.3 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.6, 124.4 (d, *J* = 10.5 Hz), 125.8, 126.6 (d, *J* = 105.4 Hz), 127.6, 128.1, 128.8, 129.5, 129.7, 130.5 (br), 131.1, 131.2, 137.3, 142.89, 142.92.

^{31}P NMR ($CDCl_3$, 161.83 MHz) δ: 35.5.

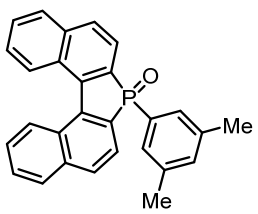
HRMS (EI+, M^+) Calcd for $C_{27}H_{19}OP$: 390.1174. Found: 390.1169.

IR (KBr): 3443 w, 3050 w, 2953 w, 2925 w, 2870 w, 2359 w, 2343 w, 1734 w, 1700 w, 1676 w, 1600 w, 1578 w, 1559 w, 1542 w, 1507 w, 1499 w, 1444 w, 1396 w, 1377 w, 1359 w, 1337 m, 1308 w, 1284 w, 1254 w, 1202 s, 1189 s, 1151 m, 1108 s, 1025 w, 984 w, 961 w, 952 w, 878 w, 839 w, 815 m, 773 w, 749 s, 709 w, 677 m, 667 s, 657 m, 643 m, 634 w, 623 w, 604 w, 592 w, 584 w, 561 m, 526 s, 508 w.

MS, *m/z* (relative intensity, %): 391 (27), 390 (M^+, 100), 389 (54), 327 (12), 326 (18), 298 (14), 297 (39), 281 (15), 252 (24), 250 (14).

m.p. 160 ºC

7-(3,5-Dimethylphenyl)benzo[*e*]naphtho[2,1-*b*]phosphindole 7-oxide (2c).



Pale yellow solid (77.0 mg, 96%). R_f 0.59 (SiO_2, EtOAc).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.22 (s, 6H), 7.10 (s, 1H), 7.22–7.29 (m, 2H), 7.55 (t, *J* = 7.3 Hz, 2H), 7.64 (t, *J*

= 6.9 Hz, 2H), 7.82 (t, *J* = 7.83 Hz, 2H), 7.98 (d, *J* = 7.8 Hz, 4H), 8.22 (d, *J* = 7.3 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.2, 124.4 (d, *J* = 9.6 Hz), 125.7, 127.5, 128.1, 128.5, 128.6, 128.8, 129.58 (d, *J* = 102.6 Hz), 129.60 (d, *J* = 9.6 Hz), 130.1 (br), 134.3 (d, *J* = 2.9 Hz), 137.3, 138.6, 138.7.

^{31}P NMR ($CDCl_3$, 161.83 MHz) δ: 35.9.

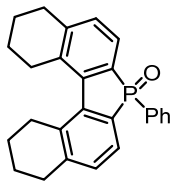
HRMS (EI+, M^+) Calcd for $C_{28}H_{21}OP$: 404.1330. Found: 404.1329.

IR (KBr): 3443 m, 2323 w, 2138 w, 1992 w, 1847 w, 1733 w, 1688 w, 1631 w, 1599 w, 1508 w, 1449 m, 1417 m, 1397 w, 1337 w, 1312 w, 1286 w, 1234 m, 1204 s, 1151 m, 1124 s, 1101 m, 1024 m, 993 m, 887 w, 870 m, 850 m, 815 m, 750 m, 727 w, 704 m, 689 s, 650 m, 626 w, 594 w, 583 m, 569 m, 553 m, 541 m, 530 m, 524 m.

MS, *m/z* (relative intensity, %): 405 (31), 404 (M^+, 100), 403 (51), 341 (10), 340 (12), 298 (17), 297 (43), 281 (17), 252 (25), 250 (14).

m.p. 155 ºC

7-Phenyl-2,3,4,7,10,11,12,13-octahydro-1*H*-benzo[*e*]naphtho[2,1-*b*]phosphindole 7-oxide (2d) [CAS:2148300-95-0].



White solid (35.1 mg, 93%). R_f 0.31 (SiO_2, EtOAc).

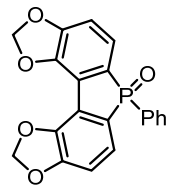
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 1.63 (quint, *J* = 6.9 Hz, 4H), 1.87 (quint, *J* = 6.9 Hz, 4H), 2.77 (t, *J* = 6.0 Hz, 4H), 2.86 (t, *J* = 6.0 Hz, 4H), 7.16 (dd, *J* = 7.3, 3.7 Hz, 2H), 7.33–7.58 (m, 7H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.4, 22.1, 28.8, 30.3, 127.3 (d, *J* = 9.6 Hz), 128.5 (d, *J* = 12.5 Hz), 129.4 (d, *J* = 12.5 Hz), 131.0 (d, *J* = 10.5 Hz), 131.6 (d, *J* = 97.8 Hz), 131.7 (d, *J* = 2.9 Hz), 132.7 (d, *J* = 6.7 Hz), 137.3 (d, *J* = 10.5 Hz), 142.2 (d, *J* = 22.0 Hz), 145.0 (d, *J* = 1.9 Hz).

^{31}P NMR ($CDCl_3$, 161.83 MHz) δ: 33.5.

HRMS (EI+, M^+) Calcd for $C_{26}H_{25}OP$: 384.1643. Found: 384.1640.

6-Phenyl-9,10-dihydro-[1,3]dioxolo[4",5":3',4']benzo[1',2':2,3]phosphindolo[4,5-*b*][1,4]dioxole 6-oxide (2e) [CAS:2127850-05-7].



White solid (66.9 mg, 90%). R_f 0.29 (SiO_2, EtOAc).

Isolated by flash column chromatography using EtOAc as eluent.

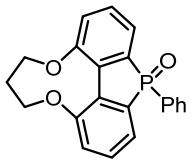
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 6.13 (s, 4H), 6.82 (dd, *J* = 7.8, 2.8 Hz, 2H), 7.23 (dd, *J* = 10.8, 7.8 Hz, 2H), 7.36–7.40 (m, 2H), 7.45–7.49 (m, 1H), 7.63 (ddd, *J* = 12.9, 7.8, 1.4 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 101.7, 109.2 (d, *J* = 14.4 Hz), 119.5 (d, *J* = 25.0 Hz), 125.1 (d, *J* = 10.5 Hz), 126.9 (d, *J* = 110.2 Hz), 128.6 (d, *J* = 12.5 Hz), 130.9 (d, *J* = 10.5 Hz), 131.8 (d, *J* = 107.4 Hz), 131.9, 142.8 (d, *J* = 15.3 Hz), 152.6.

^{31}P NMR ($CDCl_3$, 161.83 MHz) δ: 32.2.

HRMS (EI+, M^+) Calcd for $C_{20}H_{13}O_5P$: 364.0501. Found: 364.0506.

4-Phenyl-10,11-dihydro-9*H*-8,12-dioxa-4-phosphacyclonona[*def*]fluorene 4-oxide (2f) [CAS:2127850-04-6].



White solid (59.2 mg, 91%). R_f 0.20 (SiO_2, EtOAc).

Isolated by flash column chromatography using EtOAc as eluent.

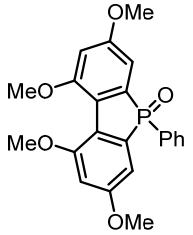
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 1.73 (s, 1H), 2.01 (s, 1H), 4.32 (d, *J* = 11.5 Hz, 2H), 4.60 (t, *J* = 9.6 Hz, 2H), 7.33–7.43 (m, 6H), 7.47–7.55 (m, 3H), 7.63 (dd, *J* = 12.8, 6.9 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 25.9, 76.9, 126.3 (d, *J* = 9.6 Hz), 128.7 (d, 12.5 Hz), 130.6 (d, *J* = 104.5 Hz), 130.9 (d, *J* = 1.9 Hz), 131.1 (d, *J* = 10.5 Hz), 131.4 (d, *J* = 13.4 Hz), 132.2 (d, *J* = 2.9 Hz), 134.8 (d, *J* = 2.9 Hz), 135.2 (d, *J* = 127.5 Hz), 155.4 (d, *J* = 13.4 Hz).

^{31}P NMR ($CDCl_3$, 161.83 MHz) δ: 33.1.

HRMS (EI+, M^+) Calcd for $C_{21}H_{17}O_3P$: 348.0915. Found: 348.0908.

1,3,7,9-Tetramethoxy-5-phenylbenzo[*b*]phosphindole 5-oxide (2g).



Pale yellow solid (74.2 mg, 99%). R_f 0.41 (SiO_2, EtOAc).

Isolated by flash column chromatography using EtOAc as eluent.

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 3.78 (s, 6H), 3.92 (s, 6H), 6.66 (d, *J* = 2.3 Hz, 2H), 6.83 (dd, *J* = 11.9, 2.3 Hz, 2H), 7.36–7.40 (m, 2H), 7.48 (td, *J* = 7.3, 1.6 Hz, 1H), 7.63 (ddd, *J* = 12.8, 7.6, 1.6 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 55.7, 56.8, 106.0, 106.1, 123.1 (d, *J* = 23.0 Hz), 128.7 (d, *J* = 12.5 Hz), 131.0 (d, *J* = 10.5 Hz), 131.1 (d, *J* = 103.5 Hz), 132.0 (d, *J* = 2.9 Hz), 135.9 (d, *J* = 104.5 Hz), 156.4 (d, *J* = 17.3 Hz), 161.0 (d, *J* =16.3 Hz).

^{31}P NMR ($CDCl_3$, 161.83 MHz) δ: 34.8.

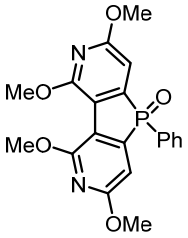
HRMS (EI+, M^+) Calcd for $C_{22}H_{21}O_5P$: 396.1127. Found: 396.1120.

IR (KBr): 3054 w, 3007 w, 2992 m, 2964 m, 2937 m, 2837 m, 1599 s, 1565 s, 1456 s, 1431 s, 1407 m, 1341 s, 1303 s, 1231 s, 1219 m, 1200 s, 1178 s, 1160 s, 1137 s, 1115 m, 1065 s, 1047 s, 998 w, 988 m, 957 w, 945 w, 934 w, 862 s, 849 s, 836 m, 822 s, 760 m, 752 m, 722 s, 707 m, 697 s, 661 m, 629 w, 613 w, 590 m, 569 m, 541 m, 501 m, 491 m, 447 w, 426 w, 419 w.

MS, *m/z* (relative intensity, %): 397 (22), 396 (M^+, 100), 381 (21).

m.p. 200 ºC

1,3,7,9-Tetramethoxy-5-phenylphospholo[3,2-*c*:4,5-*c'*]dipyridine 5-oxide (2h) [CAS:2127850-07-9].



Yellow solid (74.8 mg, 95%). R_f 0.76 (SiO_2, EtOAc).

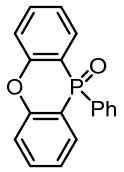
Isolated by flash column chromatography using EtOAc as eluent.

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 3.94 (s, 6H), 4.08 (s, 6H), 6.60 (s, 1H), 6.63 (s, 1H), 7.38–7.43 (m, 2H), 7.50–7.54 (m, 1H), 7.58–7.63 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 53.9, 54.1, 101.9 (d, J = 10.5 Hz), 113.0 (d, J = 22.0 Hz), 128.9 (d, J = 12.5 Hz), 129.1 (d, J = 104.5 Hz), 130.8 (d, J = 10.5 Hz), 132.7 (d, J = 1.9 Hz), 146.5 (d, J = 100.6 Hz), 157.2 (d, J = 15.3 Hz), 162.5 (d, J = 17.3 Hz).

^{31}P NMR ($CDCl_3$, 161.83 MHz) δ: 31.1.

10-Phenyl-10*H*-phenoxaphosphinine 10-oxide (2i) [CAS:1091-27-6].



White solid. R_f 0.34 (SiO_2, EtOAc).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.23–7.25 (m, 2H), 7.34–7.49 (m, 5H), 7.57–7.67 (m, 4H), 7.74 (ddd, J = 13.1, 7.8, 1.6 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 115.3 (d, J = 103.5 Hz), 118.3 (d, J = 5.6 Hz), 124.1 (d, J = 10.5 Hz), 128.5 (d, J = 3.4 Hz), 131.3 (d, J = 5.6 Hz), 131.6 (d, J = 10.5 Hz), 131.8 (d, J = 2.9 Hz), 133.8, 134.0 (d, J = 118.9 Hz), 155.6 (d, J = 2.9 Hz).

^{31}P NMR ($CDCl_3$, 161.83 MHz) δ: -0.1.

HRMS (EI+, M^+) Calcd for $C_{18}H_{13}O_2P$: 292.0653. Found: 292.0655.

Anal. Calcd for $C_{18}H_{13}O_2P$: C, 73.97; H, 4.48, Found: C, 74.10; H, 4.54.

1-Phenylphospholane 1-oxide (2j) [CAS:4963-91-1].

White solid. R_f 0.20 (SiO_2, 3% NEt_3, EtOAc).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 1.91–2.24 (m, 8H), 7.47–7.56 (m, 3H), 7.71–7.77 (m, 2H).

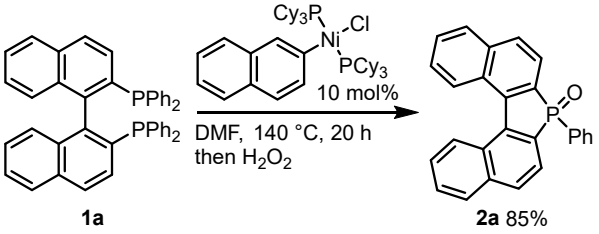
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 25.3 (d, J = 8.6 Hz), 29.7 (d, J = 67.1 Hz), 128.6 (d, J = 11.5 Hz), 129.9 (d, J = 10.5 Hz), 131.6 (d, J = 2.9 Hz), 134.3 (d, J = 90.1 Hz).

^{31}P NMR ($CDCl_3$, 161.83 MHz) δ: 61.0.

HRMS (EI+, M^+) Calcd for $C_{10}H_{13}OP$: 180.0704. Found: 180.0701.

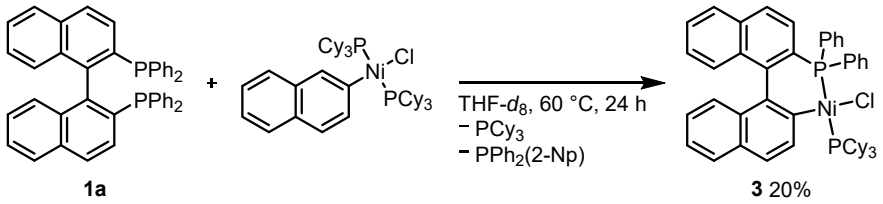
V. Mechanistic Studies

- **Catalytic Experiment Using NiCl(2-Np)(PCy_3)$_2$**



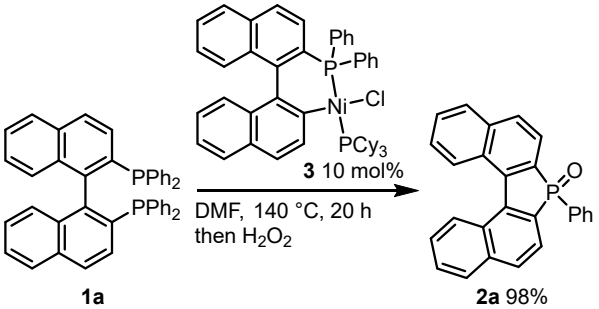
In a glovebox filled with nitrogen, NiCl(2-Np)(PCy_3)$_2$ (15.6 mg, 0.02 mmol), **1a** (125 mg, 0.20 mmol) and DMF (1 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The vessel was heated at 140 °C for 20 h followed by cooling. An aqueous solution of H_2O_2 (ca. 30%, a few drops) was added, and the mixture was stirred at room temperature for 1 h. The yield of **2a** was determined by ^{1}H NMR using 1,1,2,2,-tetrachloroethane as an internal standard.

- **Synthesis of Phospha-Nickelacycle 3 via the Cleavage of Carbon–Phosphorus Bond**



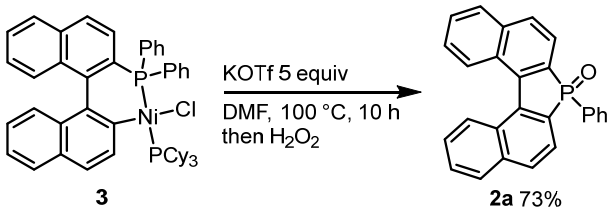
In a glovebox filled with nitrogen, NiCl(2-Np)(PCy_3)$_2$ (7.8 mg, 0.01 mmol), **1a** (6.3 mg, 0.01 mmol) and THF-d_8 (0.6 mL) were added to a J-Young NMR tube and heated at 60 °C for 24 h. The yield of **3** was determined by ^{31}P NMR using hexamethylphosphoric triamide as an internal standard. The resulting solution was filtered through Celite, and dried in vacuo. Pentane (1.0 mL) was added with vigorous stirring and the resulting red suspension was filtrated. The filtrate was dried in vacuo and purified by recrystallization from THF and pentane to afford a red-colored single crystal of **3**. Some of these crystals were suitable for X-ray analysis.

- **Catalytic Experiment Using Phospha-Nickelacycle 3**



In a glovebox filled with nitrogen, **3** (16.1 mg, 0.02 mmol), **1a** (126 mg, 0.20 mmol) and DMF (1 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The vessel was heated at 140 °C for 20 h followed by cooling. An aqueous solution of H_2O_2 (ca. 30%, a few drops) was added, and the mixture was stirred at room temperature for 1 h. The yield of **2a** was determined by ^{1}H NMR using 1,1,2,2,-tetrachloroethane as an internal standard.

- **Reductive Elimination of 2a from Phospha-Nickelacycle 3**



3 **2a** 73%

In a glovebox filled with nitrogen, **3** (16.2 mg, 0.02 mmol), KOTf (18.8 mg, 0.10 mmol) and DMF (1 mL) were added to a 5 mL vial with a Teflon-sealed screwcap and heated at 100 °C for 10 h. An aqueous solution of H_2O_2 (ca. 30%, a few drops) was added, and the mixture was stirred at room temperature for 1 h. The yield of **2a** was determined by ^{1}H NMR using 1,1,2,2,-tetrachloroethane as an internal standard.

1.5 References

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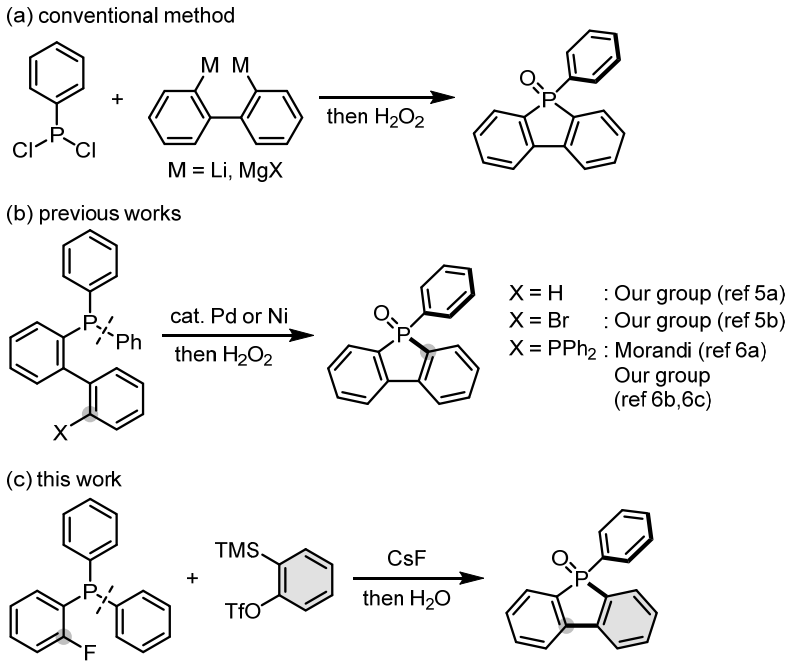
Chapter 2

Aryne-Induced S_NAr/Carbon–Phosphorus Bond Cleavage for the Synthesis of Phosphole Derivatives via a P(V) Intermediate

2.1 Introduction

Dibenzophosphole derivatives have recently attracted significant attention as a promising scaffold for advanced organic materials because of their characteristic optical and electronic properties.[1] The method that is most frequently used for the synthesis of dibenzophospholes involves the nucleophilic substitution of a P–X bond with a stoichiometric amount of an organometallic species, such as an organolithium or an organomagnesium reagent (Scheme 1a).[2] However, there are problems associated with the use of phosphorus reagents that contain a P–X bond, such as toxicity, volatility, and irritation. In addition, the scope of this method is severely limited by the low functional group compatibility and the fact that organometallic reagents are typically sensitive to air/moisture. Therefore, more robust methods that allow access to elaborate derivatives are clearly needed. In view of their widespread availability and stability, triarylphosphines represent favorable starting materials for the synthesis of dibenzophospholes. In 1959, Wittig and co-workers reported on the preparation of a dibenzophosphole by reacting triphenylphosphine with an in situ generated benzyne[3] or phenylsodium.[4] Although this reaction is intriguing and potentially useful, the yields were a maximum of 15%, and the mechanism for the reaction remains unclear. Our group has recently developed synthetic methods for preparing dibenzophospholes from biarylphosphine[5] or bisphosphine[6] derivatives via the cleavage of C–P bonds by transition metal catalysis (Scheme 1b). However, all of these reactions are limited to intramolecular processes, which hampers the rapid construction of diverse products and requires transition metal catalysts. Herein, we report on the transition metal-free, intermolecular annulation for the synthesis of fluorinated dibenzophospholes from triarylphosphine derivatives (Scheme 1c).

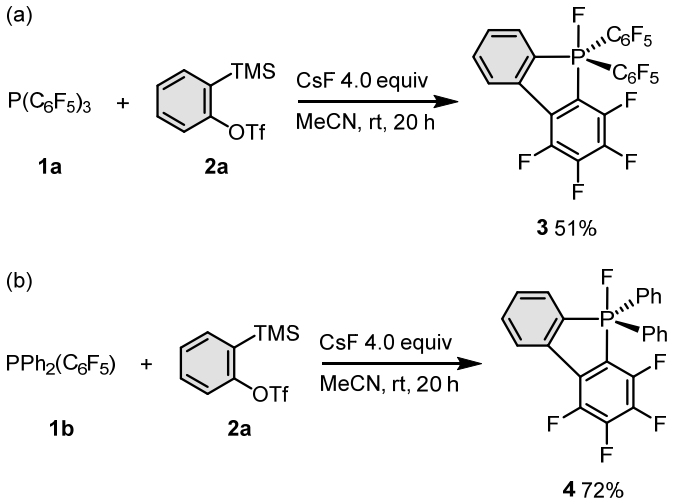
Scheme 1. Dibenzophosphole synthesis via C–P bond cleavage



2.2 Results and Discussion

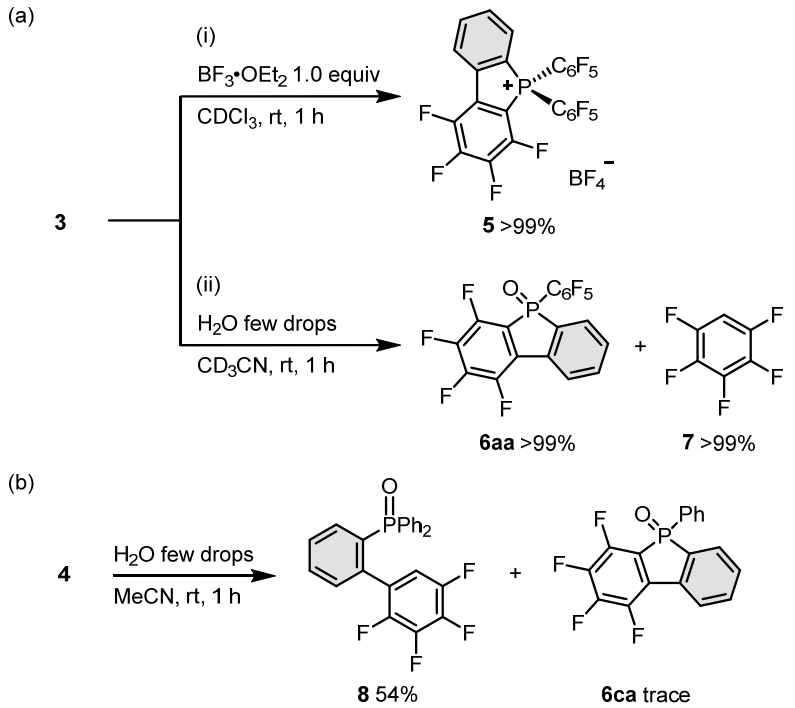
We initially investigated the reaction of tris(pentafluorophenyl)phosphine (**1a**) with benzyne, which was generated in situ from 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2a**, 2.0 equiv) and CsF (4.0 equiv). The pentacoordinate tetraarylfluorophosphorane **3** was unexpectedly obtained in 51% yield, as determined by both ^{19}F and ^{31}P NMR spectroscopies (Scheme 2a). The presence of an apical fluorine atom was confirmed by a doublet at 25.5 ppm ($J_{P–F}$ = 721 Hz) in the ^{19}F NMR spectrum of **3**.[7] The P–F coupling was also observed in ^{31}P NMR spectra as a doublet at –88.5 ppm (J_{P-F} = 721 Hz). When (pentafluorophenyl)diphenylphosphine (**1b**) was reacted with **2a** under identical conditions, the tetraarylfluorophosphorane **4** was obtained in a similar manner (Scheme 2b). The P–F coupling was also observed in ^{19}F (J_{P-F} = 657 Hz) and ^{31}P (J_{P-F} = 657 Hz) NMR spectra of **4**. Although R_4PF type compounds can exist as both four-coordinate ionic (phosphonium fluoride) and pentacoordinate neutral (fluorophosphorane) species,[8] all of the previously reported Ar_4PF compounds were in the form of a phosphonium salt in solution due to an exceptionally weak P–F interaction.[9] To the best of our knowledge, compounds **3** and **4** represent the first example of tetraarylfluorophosphorane derivatives that are stable in solution. The key features of compounds **3** and **4** that permit them to stabilize a P(V) state are: 1) the Lewis acidity of the phosphorus center enhanced by the presence of perfluorinated aryl groups, and 2) the rigid five-membered ring structure, which would favor a trigonal bipyramidal geometry (the endocyclic C–P–C angle is ca. 90°) over a tetrahedral geometry.[10]

Scheme 2. Synthesis of tetraarylfluorophosphorane **3** and **4**



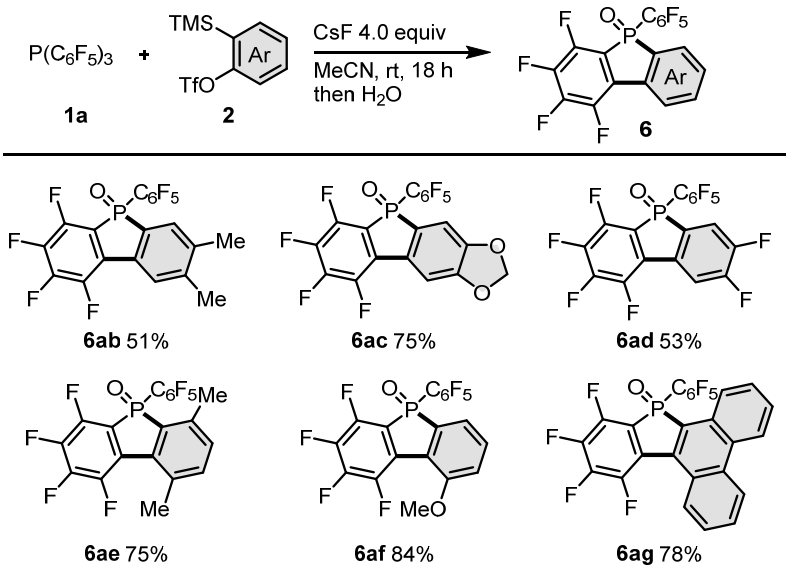
Next, the reactivity of the fluorophosphoranes **3** and **4** was investigated (Scheme 3). Treatment of **3** with BF_3•OEt_2 (1 equiv) afforded the phosphonium salt **5** in quantitative yield, the structure of which was determined to be tetrahedral by X-ray crystallographic analysis (Scheme 3a-i). When the fluorophosphorane **3** was treated with a few drops of H_2O, the dibenzophosphole oxide **6aa** was formed quantitatively via the loss of pentafluorobenzene **7** (Scheme 3a-ii).[11] In contrast, the fluorophosphorane **4** afforded the biphenylphosphosphine oxide **8** (54%) upon treatment with H_2O, with an endocyclic C(fluoroaryl)–P bond being protonated, and only trace amounts of the corresponding dibenzophosphole **6ca** were formed (Scheme 3b). These results indicate that the order of reactivity of the ligand on the phosphorane is as follows: C_6F_5 > endocyclic fluorinated aryl > non-fluorinated aryl, endocyclic non-fluorinated aryl.[12]

Scheme 3. Reactivity of tetraarylfluorophosphoranes



The overall process shown in Scheme 3a-ii is the dearylative annulation of fluorinated phosphines with an aryne. This process should be a useful method for the synthesis of fluorinated dibenzophospholes, since both coupling components are readily available and the reaction proceeds under neutral, ambient conditions without the need for transition metal catalyst. In fact, our annulation method allows the rapid access to a range of fluorinated dibenzophospholes by using different arynes (Table 1). Symmetrical arynes containing substituents at the 4 and 5-positions readily participated in the annulation reaction, irrespective of their electronic nature, to provide the corresponding fluorinated dibenzophospholes (**6ab**–**6ag**). This reaction is tolerant of the steric hindrance of an aryne component, as exemplified by an efficient reaction of the 3,6-disubstituted aryne **2e**. When unsymmetrical methoxy-substituted aryne derived from **2f** was used, the annulation proceeded in a regioselective manner with the formation of phosphole derivatives containing a methoxy group at the 9-position (**6af**). The observed regioselectivity can be rationalized by the electron-withdrawing effect of the methoxy group, which directs the incoming nucleophile to attack at the distal carbon of the aryne.[13] It is possible to synthesize π-extended dibenzophospholes using the corresponding aryne precursors (**2g**). The products that can be synthesized by this protocol should find numerous applications as metarials with lowered LUMO energy levels based on the phosphole skeleton[1] combined with fluorinated aromatic systems,[14] such as *n*-type semiconducting materials.[15]

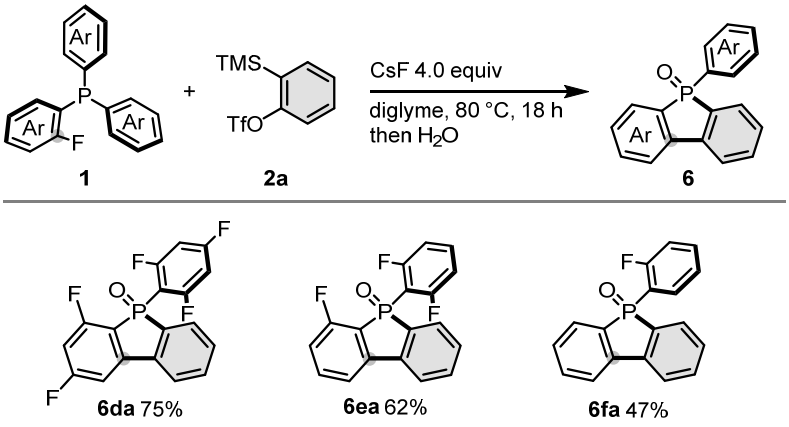
Table 1. Scope of the reaction for arynes[a]



[a] Reaction conditions: **1** (0.2 mmol), aryne (0.4 mmol), CsF (0.8 mmol) and MeCN (1.0 mL) were reacted in a sealed tube at room temperature for 18 h. Yields of isolated products are shown.

The scope with respect to triarylphosphines was next examined (Table 2). This intermolecular annulation is not limited to perfluorinated triarylphosphines, and triarylphosphines with fewer fluorine atoms on the aryl groups (i.e., **1d**–**1f**) were also successfully annulated to provide the corresponding fluorinated dibenzophospholes **6da**–**6fa**.

Table 2. Scope of the reaction for triarylphosphines[a]



[a] Reaction conditions: triarylphosphine (0.2 mmol), **2a** (0.4 mmol), CsF (0.8 mmol) and diglyme (1.0 mL) were reacted in a sealed tube at 80 ºC for 18 h. Yields of isolated products are shown.

2.3 Conclusion

In conclusion, a method for the dearylative anulation of triarylphosphines with arynes is reported. This reaction proceeds through 1) the nucleophilic attack of triarylphosphine to an aryne to form a phosphonium bearing an aryl anion moiety,[16] 2) the intramolecular S_NAr reaction of an aryl fluoride moiety by the generated carbanion to form a pentacoordinate fluorophosphorane, 3) dearylation from the stable fluorophosphorane to form phosphole oxide. The advantages of this method over reported methods include transition metal-free, mild conditions (neutral and room temperature) and intermolecular annulation, allowing the synthesis of various fluorinated dibenzophosphole derivatives in a convergent manner.

2.4 Experimental Section

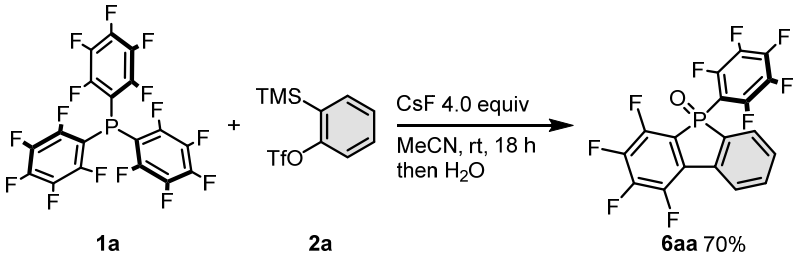
I. General Information

^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectra were recorded on a JEOL ECS-400 spectrometer in $CDCl_3$. The chemical shifts in ^{1}H NMR spectra were recorded relative to $CHCl_3$ (δ 7.26). The chemical shifts in ^{13}C NMR spectra were recorded relative to $CDCl_3$ (δ 77.0). The chemical shifts in ^{19}F NMR spectra were recorded relative to benzotrifluoride (δ –65.64). The chemical shifts in ^{31}P NMR spectra were recorded relative to H_3PO_4 (δ 0.0). The data is reported as follows: chemical shift (δ) in ppm, coupling constant (Hz), and integration. Infrared spectra (IR) were obtained using a JASCO FT/IR-4200 spectrometer. Absorption is reported in reciprocal centimeters (cm^{-1}) with the following relative intensities: s (strong), m (medium), or w (weak). High resolution mass spectra (HRMS) were obtained using a JEOL JMS-T100LP spectrometer. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed with Biotage Isolera® equipped with Biotage SNAP Ultra Cartridge.

II. Materials

All commercially available reagents and solvents were supplied from TCI and Aldrich. Aryne precursors **2b** [CAS:458566-99-9], **2c** [CAS:717903-52-1], **2d** [217813-00-8], **2e** [CAS:780820-44-2] and **2g** [CAS:252054-91-4] were prepared according to a literature procedure.[17] Tris(2-fluorophenyl)phosphine **1f** [CAS:84350-73-2] was prepared according to a literature procedure.[18]

III. Typical Procedure

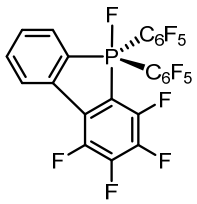


1a **2a** **6aa** 70%

In a glovebox filled with nitrogen, the phosphine **1a** (106 mg, 0.20 mmol), **2a** (97 μL, 0.40 mmol), CsF (122 mg, 0.80 mmol) and MeCN (1.0 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The mixture was stirred at room temperature for 18 h. H_2O was added, and the mixture was stirred at room temperature for an additional 3 h. This mixture was then evaporated to dryness, and the residue was purified by flash column chromatography using hexane/EtOAc = 3/1 as the eluent to give **6aa** as a white solid (61 mg, 70%).

IV. Spectroscopic Data

1,2,3,4,5-Pentafluoro-5,5-bis(perfluorophenyl)-5*H*-5λ^5-benzo[*b*]phosphindole (3).



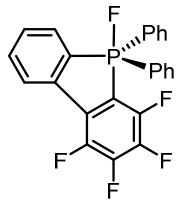
^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.55–7.61 (m, 1H), 7.81 (t, *J* = 7.8 Hz, 1H), 8.21 (t, *J* = 6.4 Hz, 1H), 8.27 (ddd, *J* = 14.0, 8.0, 0.9 Hz, 1H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −161.8 (s, 4F), −155.7 (d, *J* = 23.1 Hz, 1F), −154.8 (d, *J* = 23.1 Hz, 1F), −151.9 (t, *J* = 23.1 Hz, 2F), −142.9 (d, *J* = 34.7 Hz, 1F), −135.7 (s, 1F), −132.0 (s, 4F), 25.5 (dd, *J* = 721, 23.1 Hz, 1F).

^{31}P NMR ($CDCl_3$, 162 MHz) δ: −88.5 (d, *J* = 721 Hz).

HRMS (EI+, M^+) Calcd for $C_{24}H_4F_{15}P$: 607.9811. Found: 607.9815.

1,2,3,4,5-Pentafluoro-5,5-diphenyl-5*H*-5λ^5-benzo[*b*]phosphindole (4).



The procedure for **3** was followed except that **1b** (70.4 mg, 0.20 mmol) was used in a place of **1a**. The yield of **4** was determined to be 72% by ^{19}F NMR.

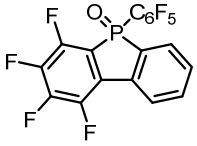
^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.28–7.77 (m, 12H), 8.25 (t, *J* = 6.2 Hz, 1H), 8.35 (dd, *J* = 7.8, 12.8 Hz, 1H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −157.7 (t, *J* = 23.1 Hz, 1F), −157.0 (t, *J* = 23.1 Hz, 1F), −146.6 (t, *J* = 23.1 Hz, 1F), −134.3 (s, 1F), −2.5 (d, *J* = 657 Hz, 1F).

^{31}P NMR ($CDCl_3$, 162 MHz) δ: −70.7 (d, *J* = 657 Hz).

HRMS (CI−, M^+) Calcd for $C_{24}H_{14}F_5P$: 428.0753. Found: 428.0760.

1,2,3,4-Tetrafluoro-5-(perfluorophenyl)benzo[*b*]phosphindole 5-oxide (6aa).



White solid. R_f 0.23 (SiO_2, hexane/EtOAc = 3/1). M.p. 125 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.55 (td, *J* = 7.8, 4.4 Hz, 1H), 7.72 (t, *J* = 7.78 Hz, 1H), 7.97 (dd, *J* = 11.7, 7.8 Hz, 1H), 8.07 (dd, *J* = 7.8, 3.7 Hz, 1H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −160.8 (s, 2F), −154.3 (s, 1F), −146.7 (s, 1F), −146.2 (s, 1F), −142.7 (d, *J* = 23.1 Hz, 1F), −133.2 (s, 2F), −131.8 (s, 1F).

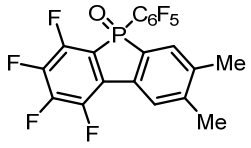
^{31}P NMR ($CDCl_3$, 162 MHz) δ: 18.9.

IR (KBr): 1649 m, 1478 m, 1388 w, 1294 m, 1232 w, 1110 m, 981 s, 873 w, 773 s, 742 m, 727 m, 640 m, 588 w, 554 m, 452 s.

MS, *m/z* (relative intensity, %): 438 (M^+, 46), 272 (15), 271 (100), 255 (39), 244 (28).

HRMS (EI+, M^+) Calcd for $C_{18}H_4F_9OP$: 437.9856. Found: 437.9861.

1,2,3,4-Tetrafluoro-7,8-dimethyl-5-(perfluorophenyl)benzo[*b*]phosphindole 5-oxide (6ab).



Pale yellow solid (47.8 mg, 51%). R_f 0.28 (SiO_2, hexane/EtOAc = 3/1). M.p. 200 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.34 (s, 3H), 2.40 (s, 3H), 7.69 (d, *J* = 11.9 Hz, 1H), 7.81 (d, *J* = 4.1 Hz, 1H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −161.1 (s, 2F), −155.5 (t, *J* = 23.1 Hz, 1F), −147.4 (s, *J* = 23.1 Hz, 1F), −146.8 (s, 1F), −143.4 (d, *J* = 23.1 Hz, 1F), −133.4 (s, 2F), −132.4 (s, 1F).

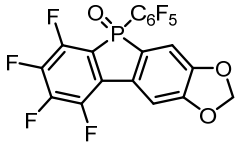
^{31}P NMR ($CDCl_3$, 162 MHz) δ: 19.1.

IR (KBr): 1644 s, 1603 w, 1523 s, 1496 s, 1477 s, 1296 s, 1239 s, 1142 w, 1101 s, 1054 s, 980 s, 887 w, 871 w, 825 m, 724 m, 642 m, 602 s.

MS, *m/z* (relative intensity, %): 467 (17), 466 (M^+, 73), 300 (14), 299 (100), 283 (20), 237 (16).

HRMS (EI+, M^+) Calcd for $C_{20}H_8F_9OP$: 466.0169. Found: 466.0166.

6,7,8,9-Tetrafluoro-5-(perfluorophenyl)benzo[2,3]phosphindolo[5,6-*d*][1,3]dioxole 5-oxide (6ac).



White solid (73.1 mg, 75%). R_f 0.20 (SiO_2, hexane/EtOAc = 3/1). M.p. 198 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.15 (dd, *J* = 9.6, 0.9 Hz, 2H), 7.31 (d, *J* = 11.0 Hz, 1H), 7.48 (d, *J* = 3.2 Hz, 1H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −160.9 (t, *J* = 23.1 Hz, 2F), −155.7 (t, *J* = 23.1 Hz, 1F), −147.0 (t, *J* = 23.1 Hz, 1F), −146.520 (s, 1F), −144.5 (d, *J* = 34.7 Hz, 1F), −133.3 (d, *J* = 23.1 Hz, 2F), −132.2 (s, 1F).

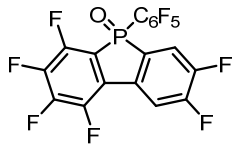
^{31}P NMR ($CDCl_3$, 162 MHz) δ: 17.5.

IR (KBr): 2921 w, 1640 m, 1599 w, 1494 s, 1393 m, 1336 w, 1279 s, 1230 s, 1106 s, 1044 s, 907 m, 729 m, 557 s.

MS, *m/z* (relative intensity, %): 483 (21), 482 (M^+, 100), 481 (14), 316 (15), 315 (97), 299 (12), 229 (16), 141 (12).

HRMS (EI+, M^+) Calcd for $C_{19}H_4F_9O_3P$: 481.9754. Found: 481.9745.

1,2,3,4,7,8-Hexafluoro-5-(perfluorophenyl)benzo[*b*]phosphindole 5-oxide (6ad).



Pale yellow solid (24.4 mg, 53%). R_f 0.49 (SiO_2, hexane/EtOAc = 3/1). M.p. 152 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.78 (ddd, *J* = 11.9, 8.0, 7.8 Hz, 1H), 7.88 (ddd, *J* = 10.0, 6.5, 3.7 Hz, 1H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −160.2 (s, 2F), −152.9 (t, *J* = 23.1 Hz, 1F), −145.5 (t, *J* = 23.1 Hz, 23.1 Hz, 1F), −145.0 (s, 1F), −143.1 (d, *J* = 23.1 Hz, 1F), −133.6 (s, 1F), −133.2 (d, *J* = 23.1 Hz, 2F), −130.1 (s, 1F), −126.8 (s, 1F).

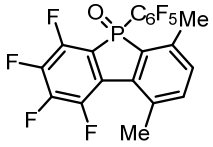
^{31}P NMR ($CDCl_3$, 162 MHz) δ: 16.3.

IR (KBr): 2361 w, 1644 w, 1599 w, 1481 s, 1436 m, 1390 w, 1299 s, 1230 s, 1106 s, 1054 s, 984 s, 883 w, 779 m, 612 m, 458 m.

MS, *m/z* (relative intensity, %): 474 (M^+, 39), 308 (14), 307 (100), 291 (37), 260 (24), 47 (12).

HRMS (EI+, M^+) Calcd for $C_{18}H_2F_{11}OP$: 473.9668. Found: 473.9674.

1,2,3,4-Tetrafluoro-6,9-dimethyl-5-(perfluorophenyl)benzo[*b*]phosphindole 5-oxide (6ae).



White solid (70.4 mg, 75%). R_f 0.31 (SiO_2, hexane/EtOAc = 3/1). M.p. 164 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.52 (s, 3H), 2.63 (d, *J* = 11.9 Hz, 3H), 7.18 (dd, *J* = 7.7, 5.7 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −161.1 (s, 2F), −154.4 (t, *J* = 23.1 Hz, 1F), −147.0 (t, *J* = 23.1 Hz, 1F), −145.8 (t, *J* = 23.1 Hz, 1F), −133.9 (d, *J* = 23.1 Hz, 2F), −133.6 (s, 1F), −128.2 (s, 1F).

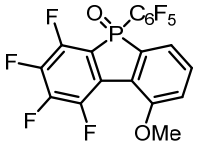
^{31}P NMR ($CDCl_3$, 162 MHz) δ: 18.4.

IR (KBr): 3003 s, 2461 w, 1645 s, 1479 s, 1392 m, 1298 s, 1222 m, 1103 s, 984 m, 930 m, 876 w, 822 m, 764 s, 663 m, 456 m.

MS, *m/z* (relative intensity, %): 466 (18), 447 (31), 446 (M^+, 100), 431 (19), 379 (12), 378 (11), 360 (11), 237 (13), 47 (12).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{20}H_9F_9OP$: 467.0241. Found: 467.0245.

1,2,3,4-Tetrafluoro-9-methoxy-5-(perfluorophenyl)benzo[*b*]phosphindole 5-oxide (6af).



White solid (78.6 mg, 84%). R_f 0.49 (SiO_2, hexane/EtOAc = 1/1). M.p. 149 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.99 (s, 3H), 7.23–7.25 (m, 1H), 7.51–7.54 (m, 2H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −161.1 (s, 2F), −155.2 (s, 1F), −147.0 (t, *J* = 23.1 Hz, 1F), −145.0 (t, *J* = 23.1 Hz, 1F), −133.5 (s, 1F), −133.2 (s, 2F), −124.9 (s, 1F).

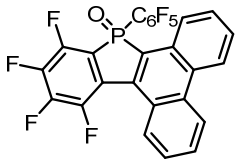
^{31}P NMR ($CDCl_3$, 162 MHz) δ: 18.4.

IR (KBr): 1644 w, 1584 w, 1521 m, 1476 s, 1389 m, 1297 m, 1235 m, 1104 m, 1032 m, 983 m, 883 w, 725 w, 561 w, 455 m.

MS, *m/z* (relative intensity, %): 469 (16), 468 (M^+, 88), 302, (18), 301 (100), 286 (14), 285 (22), 258 (22), 207 (11), 205 (13), 161 (14), 73 (13), 47 (11).

HRMS (EI+, M^+) Calcd for $C_{19}H_6F_9O_2P$: 467.9962. Found: 467.956.

10,11,12,13-Tetrafluoro-9-(perfluorophenyl)tribenzo[*b,e,g*]phosphindole 9-oxide (6ag).



Yellow solid (66.6 mg, 78%). R_f 0.43 (SiO_2, hexane/EtOAc = 3/1). M.p. 121 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.71 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.76–7.81 (m, 2H), 7.90 (t, *J* = 7.3 Hz, 1H), 8.38 (d, *J* = 8.2 Hz, 1H), 8.46 (t, *J* = 7.3 Hz, 1H), 8.75 (d, *J* = 8.7 Hz, 1H), 8.81 (d, *J* = 8.2 Hz, 1H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −160.7 (d, *J* = 23.1 Hz, 2F), −153.3 (d, *J* = 23.1 Hz, 1F), −146.4 (t, *J* = 23.1 Hz, 1F), −145.0 (d, *J* = 23.1 Hz, 1F), −133.5 (d, *J* = 23.1 Hz, 2F), −132.2 (s, 1F), −125.4 (s, 1F).

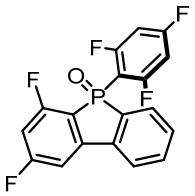
^{31}P NMR ($CDCl_3$, 162 MHz) δ: 20.2.

IR (KBr): 2360 m, 1520 m, 1496 s, 1477 s, 1299 w, 1231 w, 1101 m, 1072 w, 983 m, 944 w, 759 m, 517 m, 454 m.

MS, *m/z* (relative intensity, %): 539 (30), 538 (97), 472 (27), 471 (100), 470 (22), 452 (22), 421 (12), 371 (12), 324 (59), 304 (11), 293 (10).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{28}H_9F_9OP$: 539.0241. Found: 539.0248.

2,4-Difluoro-5-(2,4,6-trifluorophenyl)benzo[b]phosphindole 5-oxide (6da).



White solid (54.4 mg, 75%). R_f 0.29 (SiO_2, hexane/EtOAc = 1/1). M.p. 251 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ:.6.68–6.71 (m 2H), 6.77–6.86 (m, 1H), 7.18–7.32 (m, 1H), 7.46–7.53 (m, 1H), 7.61–7.66 (m, 1H), 7.72–7.76 (m, 1H), 7.94–8.00 (m, 1H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −102.9 (s, 1F), −101.9 (s, 1F), −101.8 (s, 1F), −100.1 (s, 2F).

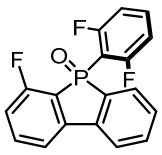
^{31}P NMR ($CDCl_3$, 162 MHz) δ: 19.0.

IR (KBr): 3049 m, 1608 s, 1474 m, 1361 w, 1294 w, 1226 s, 1104 s, 1003 m, 867 m, 774 m, 727 m, 671 s, 628 w, 518 s, 480 s.

MS, *m/z* (relative intensity, %): 366 (M^+, 45), 236 (13), 235 (100), 219 (63), 188 (25), 150 (13), 81 (16).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{18}H_9F_5OP$: 367.0306. Found: 367.0309.

5-(2,6-Difluorophenyl)-4-fluorobenzo[*b*]phosphindole 5-oxide (6ea).



White solid (40.7 mg, 62%). R_f 0.31 (SiO_2, hexane/EtOAc = 1/2). M.p. 178 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.92 (td, *J* = 8.5, 3.9 Hz, 2H), 7.04–7.10 (m, 1H), 7.42–7.51 (m, 2H), 7.58–7.64 (m, 3H), 7.80 (d, *J* = 7.8, 3.2 Hz, 1H), 8.01 (d, *J* = 10.8, 7.6 Hz, 1H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −107.3 (s, 1F), −103.3 (s, 1F).

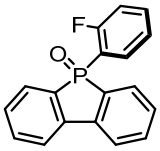
^{31}P NMR ($CDCl_3$, 162 MHz) δ: 21.1.

IR (KBr): 3089 w, 1613 s, 1568 s, 1479 s, 1458 s, 1442 s, 1266 s, 1238 s, 1213 s, 1159 m, 1119 s, 986 m, 874 w,806 s, 760 s, 705 m, 607 s, 525 s.

MS, *m/z* (relative intensity, %): 331 (11), 330 (M^+, 57), 218 (14), 217 (100), 202 (11), 201 (91), 170 (30), 169 (10), 151 (20), 150 (21), 139 (13), 132 (14), 75 (14), 63 (23).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{18}H_{11}F_3OP$: 331.0494. Found: 331.0494.

5-(2-Fluorophenyl)benzo[*b*]phosphindole 5-oxide (6fa).



Pale yellow solid (27.0 mg, 47%). R_f 0.26 (SiO_2, hexane/EtOAc = 1/1). M.p. 152 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.96 (td, *J* = 8.9, 5.3 Hz, 1H), 7.27-7.31 (m, 1H), 7.41 (tdd, *J* = 7.4, 3.9, 1.0 Hz, 2H), 7.49–7.55 (m, 1H), 7.60 (tt, *J* = 7.6, 1.4 Hz, 2H), 7.78–7.85 (m, 4H), 7.99–8.06 (m, 1H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −106.1.

^{31}P NMR ($CDCl_3$, 162 MHz) δ: 27.6.

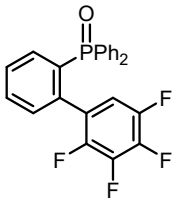
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 116.0 (dd, *J* = 22.0, 5.8 Hz), 118.7 (dd, *J* = 101, 18.2 Hz), 121.3 (d, *J* = 10.5 Hz), 124.5 (dd, *J* = 10.5, 2.9 Hz), 129.3 (d, *J* = 11.5 Hz), 129.8 (d, *J* = 9.6 Hz), 131.8 (d, *J* = 111.2 Hz), 133.6, 134.3 (dd, *J* = 9.1, 2.9 Hz), 134.7 (d, *J* = 8.6 Hz), 141.7 (d, *J* =23.0 Hz), 163.3 (d, *J* = 252 Hz).

IR (KBr): 3061 w, 1601 m, 1474 m, 1442 m, 1267 m, 1210 s, 1137 m, 1078 m, 966 w, 827 m, 758 s, 724 s, 671 m, 566 s, 499 s.

MS, *m/z* (relative intensity, %): 295 (18), 294 (M^+, 90), 293 (11), 248 (13), 247 (75), 246 (33), 244 (12), 227 (29), 226 (18), 200 (14), 199 (92), 184 (11), 183 (82), 170 (17), 153 (13), 152 (100), 151 (27), 150 (12), 126 (11), 114 (12), 113 (15), 101 (10), 76 (11), 75 (28), 74 (11), 51 (14), 50 (13).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{18}H_{13}FOP$: 295.0682. Found: 295.0683.

Diphenyl(2',3',4',5'-tetrafluoro-[1,1'-biphenyl]-2-yl)phosphine oxide (8).



Pale yellow solid (45.8mg, 54%). R_f 0.51 (SiO_2, hexane/EtOAc = 1/1). M.p. 182 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.10 (dtd, *J* = 12.8, 6.0, 2.3 Hz, 1H), 7.29–7.61 (m, 12H), 7.72 (br, 2H).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −160.1 (t, *J* = 23.1 Hz, 1F), −159.2 (s, 1F), −143.5 (s, 1F), −140.8 (s, 1F).

^{31}P NMR ($CDCl_3$, 162 MHz) δ: 27.3.

IR (KBr): 3061 w. 1588 w, 1527 m, 1482 m, 1436 m, 1371 m, 1264 w, 1193 m, 1119 m, 1070 m, 990 m, 859 m, 721 s, 696 s, 542 s, 426 m.

MS, *m/z* (relative intensity, %): 426 (M^+, 42), 425 (19), 407 (31), 349 (35), 333 (19), 283 (10), 282 (15), 271 (25), 255 (14), 224 (18), 206 (10), 205 (13), 204 (62), 203 (24), 201 (20), 199 (11), 183 (19), 154 (12), 152 (16), 78 (19), 77 (100), 51 (74), 47 (26).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{24}H_{16}F_4OP$: 427.0869. Found: 427.0870.

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Chapter 3

Phosphine-Catalyzed Carbofluorination of Alkynes via a P(V) Intermediate

3.1 Introduction

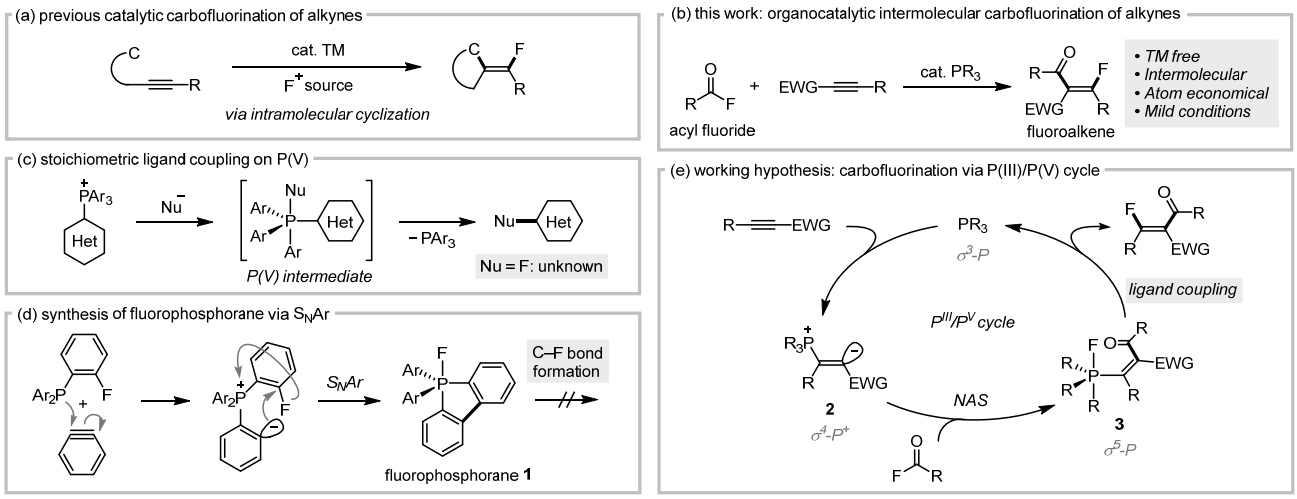
Fluorinated molecules occupy an important place in the pharmaceutical, medicinal, agrochemical and material sciences.[1] Among the various fluorinated motifs, monofluoroalkene derivatives are of particular interest, partly because of their utility as a peptide bond isostere.[2] Therefore, novel, straightforward methods for the synthesis of monofluoroalkenes via C–F bond formation are in great demand.[3] The carbofluorination of alkynes, which proceeds via the concomitant formation of C–C and C–F bonds, is a powerful method for the synthesis of monofluoroalkenes. Although some methods for the catalytic carbofluorination of alkynes have recently been developed,[4] these methods are restricted to intramolecular reactions in which transition-metal catalysts and electrophilic F^+ reagents, such as Selectfluor and NFSI (Scheme 1a) are used. Herein we report on the phosphine-catalyzed intermolecular carbofluorination of alkynes via the C–F bond-forming ligand coupling of a P(V) intermediate (Scheme 1b).

In recent years, ligand coupling on P(V) species[5] has attracted renewed interest as an alternative to transition-metal mediated cross-coupling reactions. For example, McNally and coworkers reported on the ligand coupling of pyridine derivatives on a P(V) species which was generated by the reaction of heterocyclic phosphonium salts with heteronucleophiles[6] (Scheme 1c) and heterobiaryl synthesis[7] via a P(V) intermediate. Vilotijevic and coworker also reported on a related phosphine-mediated C2-functionalization of benzothiazole derivatives.[8] Despite the significant advances in P(V)-mediated reactions over the past years, a P(V)-mediated C–F bond-formation reaction have not been achieved.[9]

Quite recently, we reported on the first synthesis of a stable tetraarylfluorophosphorane by the reaction of fluorine-substituted phosphines with an aryne via tandem nucleophilic addition and nucleophilic aromatic substitution (Scheme 1d).[10]

Phosphine-mediated C–F bond formation would be possible if the ligand coupling from the fluorophosphorane **1** were to take place. However, all of our attempts to achieve ligand coupling of **1** were unsuccessful. We envisaged that increasing the electrophilicity of the equatorial ligand in the fluorophosphorane derivative would permit this unprecedented C–F bond forming ligand coupling on P(V) to be successful. Based on this hypothesis, we designed phosphine-catalyzed carbofluorination of alkynes via a P(III)/P(V) manifold (Scheme 1e). It is well known that phosphines add, not only to an aryne, but also to an electron-deficient alkyne such as an alkynoate to form a carbanion species.[11] If the resulting carbanion **2** is sufficiently nucleophilic to react with an acyl fluoride, the fluorophosphorane **3** would be formed by nucleophilic acyl substitution (NAS). The fluorophosphorane **2** has an equatorial ligand bearing electron-withdrawing groups, which we hypothesized would facilitate ligand coupling to form a C–F bond with the regeneration of the phosphine catalyst.

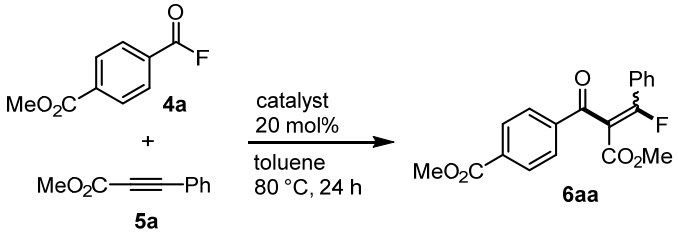
Scheme 1. Carbofluorination of alkynes: background and working hypothesis



3.2 Results and Discussion

To verify the feasibility of our hypotheses, we initially examined the reaction between the acyl fluoride **4a** and alkynoate **5a** using different phosphines (Table 1). Intensive screening resulted in identifying PCy_3 as a uniquely effective catalyst, whereas other phosphines, amines (DMAP and DABCO) and N-heterocyclic carbenes failed to promote this carbofluorination. Thus, the reaction of **4a** (1.5 equiv) with **5a** in the presence of PCy_3 (30 mol%) in toluene at room temperature afforded the monofluoroalkene **6aa** in 74% isolated yield. A ^{19}F NMR analysis indicated that the carbofluorination product was formed as a 1:1.2 mixture of *E*:*Z* isomers. The isomers interconverted by the reversible addition–elimination of PCy_3 under the catalytic conditions used (see Scheme S1),[12] and therefore the ratio of isomers were determined under thermodynamic control.[13,14] In addition to the fact that this reaction represents the first intermolecular carbofluorination, it features the use of acyl fluorides both as acylating and fluorinating reagents in an atom-economical manner, which is also unprecedented.

Table 1. Catalyst optimization for carbofluorination between **4a** and **5a**[a]



entry	catalyst	yield (%)	
1	PCy_3	52	*E*:*Z* = 1:1.2
2[b]	PCy_3	76 (74)	*E*:*Z* = 1:1.2
3	$PCyp_3$	4	
4	dcype	6	
5	P^nBu_3, P^tBu_3, PAd_3, $PAd_2{}^nBu$, $PPhMe_2$, $PPhCy_2$	0	
6	DMAP, DABCO	0	
7	IPr	0	

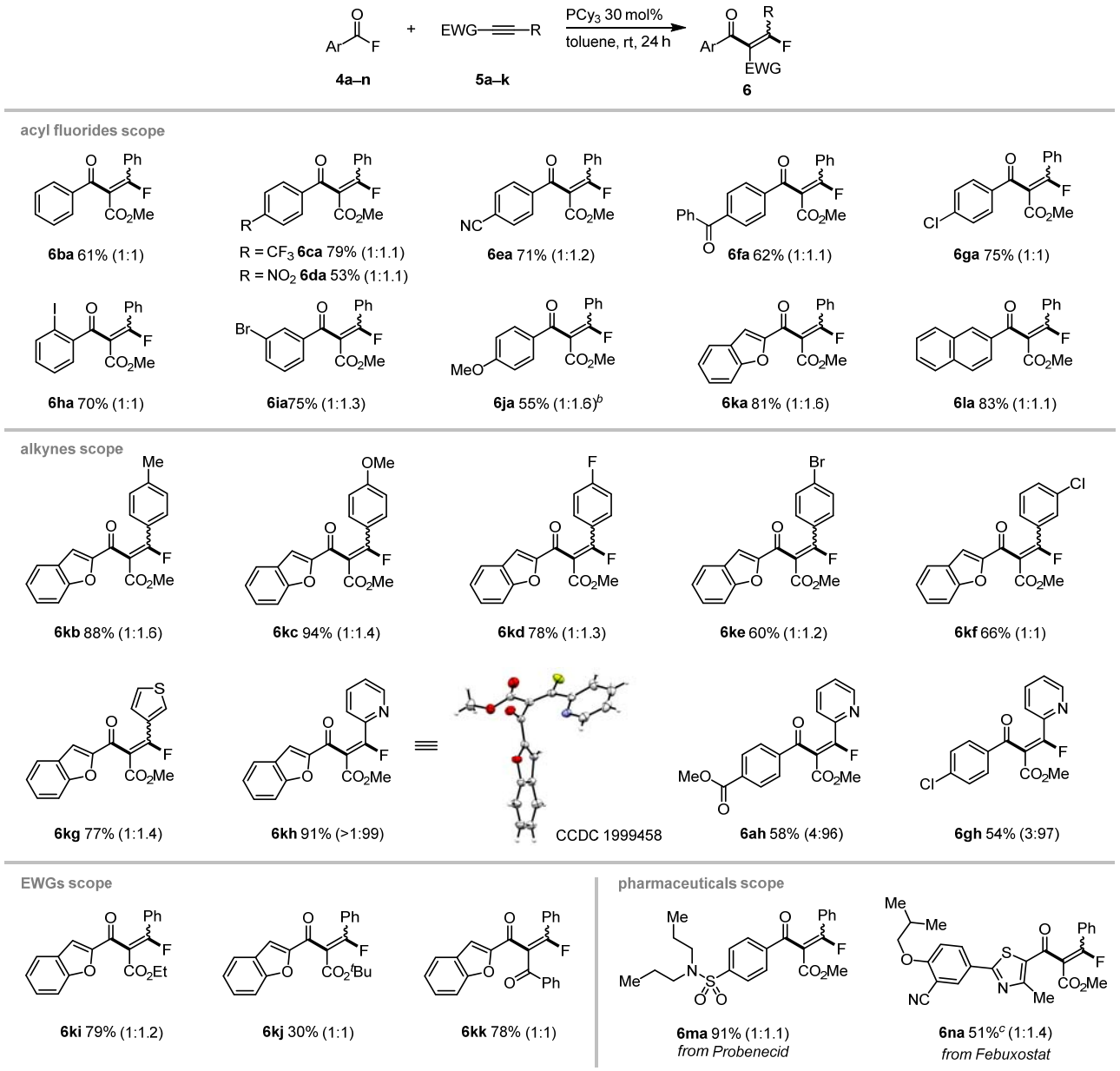
[a] **4a** (0.30 mmol), **5a** (0.20 mmol), catalyst (0.04 mmol) and toluene (1.0 mL) in sealed tube at 80 ºC for 24 h. [b] Reaction conducted at room temperature in the presence of PCy_3 (0.06 mmol). Yield of isolated products are

shown in parentheses. *E*:*Z* ratios were determined by ^{19}F NMR analysis.

With the optimized reaction conditions in hand, we subsequently examined the scope of the carbofluorination reactions (Scheme 2). Regarding acyl fluorides, electron-neutral (**4b**) as well as electron-deficient substrates bearing trifluoromethyl (**4c**), nitro (**4d**), cyano (**4e**), and benzoyl (**4f**) groups readily participated in this reaction to produce the corresponding monofluoroalkenes. Halogens such as *p*-chloro (**4g**), *o*-iodo (**4h**) and *m*-bromo (**4i**) groups were compatible, allowing the resulting monofluoroalkenes to be amenable to further structural elaboration via common C–X bond functionalization reactions. The electron-rich substrate (**4j**) also participated in this reaction, although it required a longer reaction time (72 h). Acyl fluorides bearing heteroaryl (**4k**) and π-extended aryl (**4l**) groups also underwent the carbofluorination successfully. Alkynoates bearing methyl (**5b**), methoxy (**5c**), fluoro (**5d**), bromo (**5e**), chloro (**5f**) groups reacted to afford the corresponding monofluoroalkenes. Although alkynoates bearing alkyl groups, such as *n*-pentyl, cyclopropyl and *t*-butyl groups, failed to form the corresponding carbofluorinated product, the 3-thienyl (**5g**) and 2-pyridyl substituted alkynoate (**5h**) were compatible. Interestingly, when **5h** was used, products **6kh**, **6ah** and **6gh** with a high *Z* selectivity were obtained. This carbofluorination proceeded when alkynes bearing a different electron-withdrawing group such as ethyl ester (**5i**), *t*-butyl ester (**5j**) and benzoyl (**5k**) groups were used instead of the methyl ester **5a**, affording the corresponding coupling products **6ki**–**6kk**. This organocatalyic carbofluorination can be used in the late-stage functionalization of pharmaceuticals containing a carboxylic acid functionality, such as probenecid and febuxostat to form the corresponding monofluoroalkene derivatives **6ma** and **6na**.

To gain additional insights into the reaction mechanism, some control experiments were performed (Scheme 3). Apart from the mechanism shown in Scheme 1e, an alternative pathway that is initiated by the reaction of PCy_3 with the acyl fluoride is also possible. This would lead to the formation of an acylphosphonium fluoride, which could function as a fluoride ion source to induce the subsequent addition to the alkynoate to form the fluoroallenoate **7** as a key intermediate.[15] However, external fluoride sources, such as CsF and tetrabutylammonium difluorotriphenylsilicate (TBAT) failed to promote the carbofluorination of **4a** and **5a**, thus excluding the alternative fluoride-mediated mechanism (Scheme 3a). In an attempt to observe the postulated fluorophosphorane intermediate **3**, the reaction of **4a** and **5a** in toluene-d_8 using 1.0 equiv of PCy_3 was monitored by ^{19}F NMR spectroscopy (Scheme 3b). However, no resonances assignable to P(V) species were observed and **6ba** was formed in 43% yield (*E*:*Z* = 1.6:1), indicating that the rate of ligand coupling of **3** is rapid compared with that of the formation of **3**. When the same reaction was conducted in CD_3CN, instead of toluene-d_6, **6ba** was not formed in an appreciable amount and instead, PCy_3F_2 (**8**) and the hydroacylated product **9** were produced in 28% and 34% yields, respectively. R_4PF-type compounds can exist as both four-coordinate ionic (phosphonium fluoride) and five-coordinate neutral (fluorophosphorane) species, wherein a phosphonium fluoride form is more stable in polar solvents.[16] Therefore, the fluorophosphorane **3** ionizes in CD_3CN thus making it susceptible to undergoing decomposition,[9,17] which would eventually lead to the formation of **8** and **9** via protonation. These results suggest that phosphonium fluoride is not a competent intermediate for C–F bond formation.

Scheme 2. Scope of the phosphine-catalyzed carbofluorination of alkynoates[a]

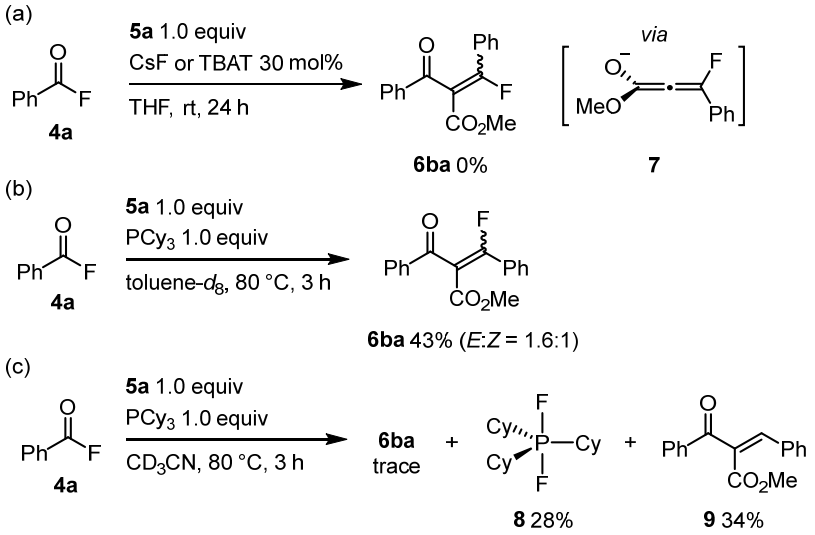


[a] Acyl fluoride (0.30 mmol), alkyne (0.20 mmol), PCy_3 (0.06 mmol) and toluene (1.0 mL) in a sealed tube at room temperature for 24 h. Yields of isolated products are shown. *E*:*Z* ratios were determined by ^{19}F NMR analysis and are shown in parentheses. [b] Run for 72 h. [c] Reaction at 50 ºC.

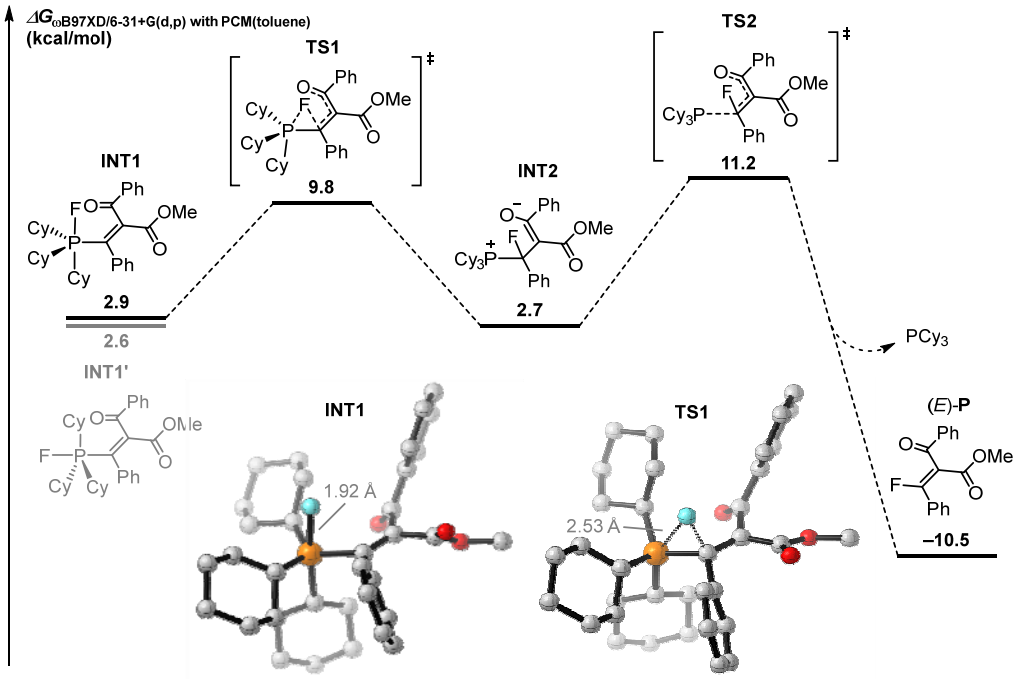
To further verify the intermediacy of fuluorophosphorane **3** in the PCy_3-catalyzed carbofluorination, DFT calculations (ωB97X-D/6-31+G(d,p) with PCM (toluene)) were conducted for the C–F bond-forming ligand coupling process (Scheme 4). **INT1** and **INT1'** are the most stable fluorophosphoranes among the suite of isomers, having a trigonal bipyramidal geometry in which fluorine occupies the apical position.[9,10] Since **INT1** and **INT1'** have nearly the same energy (ΔG = −0.3 kcal/mol), they can be interconverted each other. C–F bond formation from the **INT1** occurs in a stepwise fashion, similar to the C–C bond-forming ligand coupling of a P(V) intermediate.[7a] In the C–F bond forming step, an apical P–F bond breaks, allowing the fluorine atom to migrate to the equatorial β-carbon (**TS1**) to form the zwitterionic intermediate **INT2**. In the C–P bond breaking step, fluorinated product (*E*)-**P** is generated by the dissociation of PCy_3. This energy diagram indicates that the process from **INT1** to (*E*)-**P** is a reversible process (highest activation barrier for the reverse reaction: $\Delta G^{\ddagger}$ = 21.7

kcal/mol), which leads to the *E*/*Z* isomerization of the product. Considering that the addition of a phosphine to an alkyne has a high activation barrier (~19 kcal/mol),[14] the ligand coupling process (~8.5 kcal/mol) would be relatively facile. This view is consistent with the failure to observe a fluorophosphorane intermediate, such as **INT1** (Scheme 3b).

Scheme 3. Control experiments



Scheme 4. Calculated energy diagrams for the ligand coupling of a phosphorane intermediate [a]



[a] The Gibbs free energies of intermediates and transition states are presented relative to the sum of the energies of starting materials.

3.3 Conclusion

In conclusion, we report on the first catalytic intermolecular carbofluorination reaction. This reaction operates

under mild conditions and in the absence of metals, thus showing a wide functional group tolerance. DFT calculations revealed that a C–F bond is formed via ligand coupling on a phosphorus, which has not been achieved to date.[9]

3.4 Experimental Section

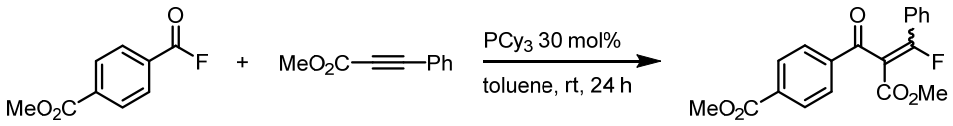
I. General Information

^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a JEOL ECS-400 spectrometer in $CDCl_3$. The chemical shifts in ^{1}H NMR spectra were recorded relative to $CHCl_3$ (δ 7.26). The chemical shifts in ^{13}C NMR spectra were recorded relative to $CDCl_3$ (δ 77.0). The chemical shifts in ^{19}F NMR spectra were recorded relative to benzotrifluoride (δ –65.64). The data is reported as follows: chemical shift (δ) in ppm, coupling constant (Hz), and integration. Infrared spectra (IR) were obtained using a JASCO FT/IR-4200 spectrometer. Absorption is reported in reciprocal centimeters (cm^{-1}) with the following relative intensities: s (strong), m (medium), or w (weak). High resolution mass spectra (HRMS) were obtained using a JEOL JMS-T100LP spectrometer. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed with Biotage Isolera® equipped with Biotage SNAP Ultra or SNAP Isolute NH_2 Cartridge. Data collection for X-ray crystal analysis were performed on a Rigaku/XtaLAB Pro P200 Hybrid Photon Counting diffractometer (Cu-Kα, λ = 1.54184 Å). The structures were solved with direct methods and refined with full-matrix least squares.

II. Materials

All commercially available reagents and solvents were supplied from TCI and Aldrich. Acyl fluoride **4a** [CAS:709-69-3], **4c** [CAS:368-94-5], **4d** [CAS:403-50-9], **4e** [CAS:77976-02-4], **4f** [CAS:2254447-01-1], **4g** [CAS:456-21-3], **4j** [CAS:701-53-1], **4k** [CAS:2141982-54-7], **4l** [CAS:37827-83-1], **4m** [CAS:2248551-77-9] were prepared according to a literature procedure.[18,19] Alkyne **5b** [CAS:7515-16-4], **5c** [CAS:7515-17-5], **5d** [CAS:42122-44-1], **5e** [CAS:42122-27-0], **5f** [CAS: 7572-40-9], **5g** [CAS:1340531-00-1], **5h** [CAS: 93139-50-5] were prepared according to a literature procedure.[20,21]

III. Typical Procedure

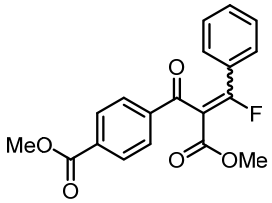


4a **5a** **6aa** 74% (*E*:*Z* = 1:1.2)

In a glovebox filled with nitrogen, the acyl fluoride **4a** (54.6 mg, 0.30 mmol), alkyne **5a** (32.0 mg, 0.20 mmol), PCy_3 (16.8 mg, 0.06 mmol) and toluene (1.0 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The mixture was stirred at room temperature for 24 h. This mixture was then evaporated to dryness, and the residue was purified by flash column chromatography using hexane/EtOAc = 9/1 as the eluent to give **6aa** as a colorless oil (50.7 mg, 74%, *E*:*Z* = 1:1.2).

IV. Spectroscopic Data

Methyl 4-(3-fluoro-2-(methoxycarbonyl)-3-phenylacryloyl)benzoate (6aa).



Colorless oil 50.7 mg (*E*:*Z* = 1:1.2, 74%). R_f 0.41 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.65 (s, 3H), 3.75 (s, 3H), 3.90 (s, 3H), 3.94 (s, 3H), 7.22–7.28 (m, 2H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.40–7.50 (m, 4H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.67 (d, *J* = 7.3 Hz, 2H), 7.94 (dt, *J* = 8.2, 1.8 Hz, 2H), 8.01–8.05 (m, 4H), 8.15 (dt, *J* = 8.2, 1.8 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.5 (3C), 52.6, 113.9 (d, *J* = 8.6 Hz), 114.6 (d, *J* = 25.9 Hz), 126.9, 128.28, 128.31, 128.34, 128.6, 128.8, 128.9, 129.0, 129.1, 129.87, 129.94, 132.06, 132.14, 134.36, 134.43, 139.6 (d, *J* = 3.8 Hz), 139.9, 162.8, 164.1 (d, *J* = 17.3 Hz), 166.0 (d, *J* = 12.5 Hz), 166.6 (d, *J* = 286 Hz), 167.5 (d, *J* = 270 Hz), 189.3 (d, *J* = 2.9 Hz), 190.5 (d, *J* = 7.7 Hz).

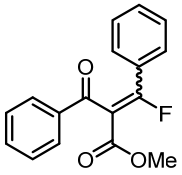
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −84.0, −78.4.

IR (ATR): 1722 m, 1681 m, 1636 w, 1435 w, 1326 w, 1277 s, 1221 s, 1192 w, 1104 m, 1063 m, 979 w, 872 w, 778 s, 694 m.

MS, *m/z* (relative intensity, %): 343 (23), 342 (M^+, 97), 341 (88), 311 (19), 164 (21), 163 (100), 155 (14), 139 (56), 135 (48), 120 (33), 104 (20), 103 (27), 76 (24), 75 (14), 59 (14).

HRMS (EI+, M^+) Calcd for $C_{19}H_{15}FO_5$: 342.0898. Found: 342.0899.

Methyl 2-benzoyl-3-fluoro-3-phenylacrylate (6ba).



Colorless oil 38.3 mg (*E*:*Z* = 1:1, 61%). R_f 0.43 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.64 (d, *J* = 1.4 Hz, 3H), 3.73 (d, *J* = 0.92 Hz, 3H), 7.25 (t, *J* = 7.8 Hz, 2H), 7.31–7.70 (m, 11H), 7.60 (td, *J* = 7.1, 1.4 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 2H), 7.90 (d, *J* = 8.2 Hz, 2H), 8.00 (d, *J* = 7.8 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.4, 52.5, 114.1 (d, *J* = 7.7 Hz), 114.9 (d, *J* = 26.8 Hz), 126.9, 128.20, 128.22, 128.3, 128.5, 128.7, 128.8, 128.9, 129.2, 129.3, 131.8, 131.9, 133.9 (d, *J* = 3.8 Hz), 136.4 (d, *J* = 2.9 Hz), 136.5, 142.8, 163.0, 164.3 (d, *J* = 18.2 Hz), 165.9 (d, *J* = 285 Hz), 167.0 (d, *J* = 268 Hz), 189.7 (d, *J* = 2.8 Hz), 191.0 (d, *J* = 6.7 Hz).

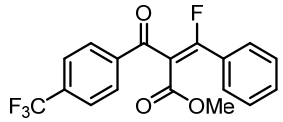
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −85.8, −79.0.

IR (ATR): 1732 m, 1674 m, 1448 w, 1232 s, 1061 m, 979 w, 804 w, 765 w, 690 s, 609 w.

MS, *m/z* (relative intensity, %): 284 (M^+, 19), 283 (19), 139 (15), 105 (100), 77 (53), 51 (13).

HRMS (EI+, M^+) Calcd for $C_{17}H_{13}FO_3$: 284.0843. Found: 284.0850.

Methyl (*E*)-3-fluoro-3-phenyl-2-(4-(trifluoromethyl)benzoyl)acrylate (*E*-6ca).



Colorless oil. R_f 0.45 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.68 (s, 3H), 7.49 (t, J = 7.3 Hz, 2H), 7.57 (t, J = 7.3 Hz, 1H), 7.68 (d, J = 7.3 Hz, 2H), 7.78 (d, J = 8.2 Hz, 2H), 8.10 (d, J = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.6, 114.4 (d, J = 24.9 Hz), 123.5 (d, J = 273 Hz), 126.9, 128.4, 128.8, 128.9, 129.4, 134.9 (d, J = 32.6 Hz), 139.4, 143.6, 164.1 (d, J = 18.2 Hz), 167.7 (d, J = 270 Hz), 188.9 (d, J = 18.2 Hz).

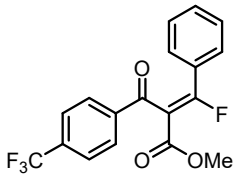
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −77.7 (s, 1F), −65.6 (s, 3F).

IR (ATR): 1719 m, 1685 m, 1598 m, 1573 m, 1448 m, 1411 m, 1322 s, 1276 s, 1168 s, 1126 s, 1065 s, 1016 m, 911 w, 852 m, 775 m, 689 m.

MS, *m/z* (relative intensity, %): 352 (M^+, 43), 351 (50), 173 (100), 145 (89), 139 (52), 120 (14), 95 (14), 75 (11), 59 (12).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{18}H_{13}F_4O_3$: 353.0806. Found: 353.0803.

Methyl (*Z*)-3-fluoro-3-phenyl-2-(4-(trifluoromethyl)benzoyl)acrylate (*Z*-6ca).



White solid. R_f 0.53 (SiO_2, Hexane/EtOAc = 3/1). M.p. 90 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.77 (s, 3H), 7.29 (t, J = 7.8 Hz, 2H), 7.36–7.45 (m, 3H), 7.66 (d, J = 8.2 Hz, 2H), 8.00 (d, J = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.6, 113.7 (d, J = 8.6 Hz), 123.4 (d, J = 273 Hz), 125.9 (d, J = 3.8 Hz), 128.3, 128.4, 128.8, 129.5, 132.2, 134.9 (q, J = 32.6 Hz), 139.2, 162.8, 166.7 (d, J = 286 Hz), 190.1 (d, J = 6.7 Hz).

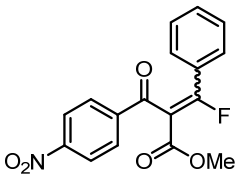
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −82.8 (s, 1F), −65.6 (s, 3F).

IR (KBr): 1735 s, 1672 s, 1649 s, 1598 w, 1577 w, 1509 m, 1448 m, 1433 m, 1412 m, 1325 s, 1291 s, 1238 s, 1164 s, 1134 s, 1112 s, 1065 s, 1016 m, 988 s, 936 w, 900 s, 870 m, 852 m, 775 s, 753 m, 698 s, 624 m, 566 m, 519 m, 485 m.

MS, *m/z* (relative intensity, %): 352 (M^+, 42), 351 (49), 173 (100), 145 (94), 139 (54), 120 (16), 95 (15), 75 (12), 59 (13).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{18}H_{12}F_4O_3$: 353.0806. Found: 353.0801.

Methyl 3-fluoro-2-(4-nitrobenzoyl)-3-phenylacrylate (6da).



Colorless oil 37.5 mg (*E*:*Z* = 1:1.1, 53%). R_f 0.41, 0.47 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.67 (s, 3H), 3.76 (s, 3H), 7.23–7.30 (m, 3H), 7.34–7.43 (m, 3H), 7.49 (d, J = 7.8,

1H), 7.56 (td, *J* = 7.3, 1.4 Hz, 1H), 7.66 (d, *J* = 7.3 Hz, 2H), 8.01 (d, *J* = 8.7 Hz, 2H), 8.12 (d, *J* = 8.7 Hz, 2H), 8.20 (d, *J* = 8.7 Hz, 2H), 8.33 (d, *J* = 8.7 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 52.6, 52.7, 113.5 (d, *J* = 9.6 Hz), 114.2 (d, *J* = 24.0 Hz), 123.9, 124.0, 126.8, 128.3, 128.4, 128.8, 128.9, 130.0, 130.1, 132.4, 132.4, 140.9 (d, *J* = 3.8 Hz), 141.3, 144.1, 150.4, 150.6, 162.6, 163.9 (d, *J* = 17.3 Hz), 167.2 (d, *J* = 287 Hz), 168.0 (d, *J* = 272 Hz), 188.4 (d, *J* = 2.9 Hz), 189.6 (d, *J* = 7.7 Hz).

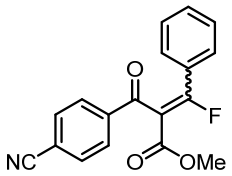
^{19}F NMR ($CDCl_3$, 376 MHz) *δ*: −82.1, −77.6.

IR (ATR): 1734 m, 1684 m, 1525 s, 1436 w, 1319 m, 1236 m, 1065 w, 847 w, 768 w, 694 m.

MS, *m/z* (relative intensity, %): 330 (12), 329 (63), 328 (M^+, 84), 150 (100), 139 (70), 129 (11), 120 (46), 105 (18), 104 (61), 92 (35), 76 (51), 75 (24), 59 (20), 50 (20).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{17}H_{13}FNO_5$: 330.0772. Found: 330.0768.

Methyl 2-(4-cyanobenzoyl)-3-fluoro-3-phenylacrylate (6ea).



Colorless oil 51.9 mg (*E*:*Z* = 1:1.2, 71%). R_f 0.33 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.65 (s, 3H), 3.75 (s, 3H), 7.24–7.29 (m, 3H), 7.34–7.41 (m, 3H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.63–7.67 (m, 4H), 7.79 (d, *J* = 8.7 Hz, 2H), 7.94 (d, *J* = 8.7 Hz, 2H), 8.05 (d, *J* = 8.7 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 52.6, 52.7, 113.4 (d, *J* = 9.6 Hz), 114.1 (d, *J* = 24.0 Hz), 116.8 (d, *J* = 3.8 Hz), 117.6, 117.8, 128.3, 128.4, 128.7, 128.8, 128.9, 129.4, 129.5, 130.0, 132.3, 132.4, 132.5, 132.6, 139.4 (d, *J* = 3.8 Hz), 139.7, 143.9, 162.6, 163.9 (d, *J* = 17.3 Hz), 167.0 (d, *J* = 287 Hz), 167.9 (d, *J* = 271 Hz), 188.5 (d, *J* = 2.9 Hz), 189.8 (d, *J* = 6.7 Hz).

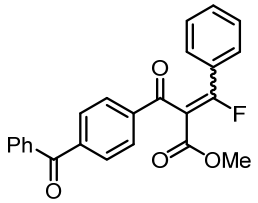
^{19}F NMR ($CDCl_3$, 376 MHz) *δ*: −82.4, −77.8.

IR (ATR): 1732 m, 1683 m, 1330 m, 1289 m, 1235 s, 1098 m, 1064 m, 982 w, 866 w, 771 s, 695 w.

MS, *m/z* (relative intensity, %): 309 (M^+, 37), 308 (44), 139 (40), 131 (10), 130 (100), 120 (13), 102 (62), 75 (15), 51 (11).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{18}H_{13}FNO_3$: 310.0874. Found: 310.0873.

Methyl 2-(4-benzoylbenzoyl)-3-fluoro-3-phenylacrylate (6fa).



Colorless oil 46.2 mg (*E*:*Z* = 1:1.1, 62%). R_f 0.31 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.68 (s, 3H), 3.78 (s, 3H), 7.28 (t, *J* = 7.8 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.43–7.65 (m, 11H), 7.69 (d, *J* = 7.8 Hz, 2H), 7.73–7.85 (m, 6H), 7.90 (d, *J* = 8.2 Hz, 2H), 8.00 (d, *J* = 8.7 Hz, 2H), 8.10 (d, *J* = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 52.5, 52.6, 113.9 (d, *J* = 8.6 Hz), 114.6 (d, *J* = 25.9 Hz), 126.9, 128.3, 128.36,

128.44, 128.7, 128.8, 128.9. 129.0, 129.1, 129.2, 129.6 (d, J = 25.9 Hz), 130.0, 130.06, 130.08, 130.12, 132.07, 132.14, 133.0, 133.1, 136.6, 136.7, 138.9 (d, J = 3.8 Hz), 139.1, 141.8, 141.9, 162.9, 164.1 (d, J = 17.3 Hz), 166.5 (d, J = 286 Hz), 167.5 (d, J = 270 Hz), 189.3 (d, J = 2.9 Hz), 190.5 (d, J = 7.7 Hz), 195.8 (d, J = 7.7 Hz).

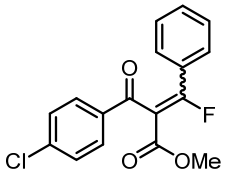
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −84.0, −78.3.

IR (ATR): 1733 m, 1656 s, 1600 w, 1447 w, 1315 m, 1275 s, 1233 s, 1113 w, 1063 m, 924 m, 868 m, 771 s, 729 m, 661 m.

MS, *m/z* (relative intensity, %): 388 (M^+, 27), 387 (23), 210 (11), 209 (76), 153 (17), 152 (23), 151 (11), 139 (32), 105 (100), 104 (24), 77 (85), 76 (31), 59 (13), 51 (18).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{24}H_{18}FO_4$: 389.1184. Found: 389.1178.

Methyl 2-(4-chlorobenzoyl)-3-fluoro-3-phenylacrylate (6ga).



Colorless oil 48.1 mg (E:Z = 1:1, 75%). R_f 0.46, 0.51 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.66 (s, 3H), 3.76 (s, 3H), 7.23–7.50 (m, 11H), 7.54 (t, J = 7.8 Hz, 1H), 7.67 (d, J = 7.8 Hz, 2H), 7.84 (dt, J = 8.7, 2.1 Hz, 2H), 7.94 (d, J = 8.7 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.4, 52.5, 113.7 (d, J = 8.6 Hz), 114.5 (d, J = 25.9 Hz), 126.9, 128.2, 128.3 (2C), 128.7, 128.8, 128.9, 129.2, 130.6, 130.7, 132.0, 132.1, 134.8 (d, J = 3.8 Hz), 134.9, 140.4, 143.2, 162.9, 164.1 (d, J = 18.2 Hz), 166.1 (d, J = 285 Hz), 167.2 (d, J = 269 Hz), 188.6 (d, J = 2.8 Hz), 189.8 (d, J = 7.7 Hz).

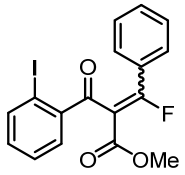
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −84.9, −78.7.

IR (ATR): 1732 m, 1676 m, 1586 m, 1435 w, 1400 w, 1328 m, 1284 m, 1232 s, 1090 m, 1063 m, 981 w, 859 w, 772 s, 694 m.

MS, *m/z* (relative intensity, %): 319 (15), 318 (M^+, 30), 317 (31), 141 (43), 140 (13), 139 (100), 120 (12), 113 (18), 111 (56), 75 (30).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{17}H_{13}{}^{35}ClFO_3$: 319.0532. Found: 319.0543.

Methyl 3-fluoro-2-(2-iodobenzoyl)-3-phenylacrylate (6ha).



Pale yellow oil 53.0 mg (E:Z = 1:1, 70%). R_f 0.41 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.72 (s, 3H), 3.80 (s, 3H), 6.98 (td, J = 7.8, 1.4 Hz, 1H), 7.16 (td, J = 7.8, 1.4 Hz, 1H), 7.22 (td, J = 7.8, 1.4 Hz, 1H), 7.26–7.38 (m, 2H), 7.41–7.64 (m, 11H), 7.84 (dd, J = 7.8, 1.4 Hz, 1H), 7.95 (dd, J = 7.8, 1.4 Hz, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.6, 52.8, 91.7, 94.6, 115.5 (d, J = 10.5 Hz), 116.3 (d, J = 18.2 Hz), 127.7, 128.1, 128.3, 128.39, 128.44, 128.5, 128.69, 128.74, 129.2, 129.4 (d, J = 26.8 Hz), 129.5 (d, J = 25.9Hz), 130.9, 132.0, 132.2, 132.4, 132.8, 140.6, 141.7, 163.4, 165.0 (d, J = 15.3 Hz), 167.6 (d, J = 278 Hz), 168.4 (d, J = 285 Hz),

191.1 (d, J = 8.6 Hz), 191.2.

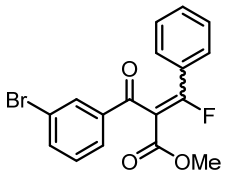
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −80.4, −80.1.

IR (ATR): 1719 w, 1654 m, 1601 m, 1439 m, 1341 m, 1279 m, 1243 s, 1147 m, 1105 m,1018 w, 990 w, 912 w, 702 m, 623 w.

MS, *m/z* (relative intensity, %): 284 (19), 283 (100), 231 (48), 203 (28), 163 (11), 139 (23), 135 (15), 120 (18), 76 (59), 75 (14), 59 (16), 50 (24).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{17}H_{13}FIO_3$: 410.9888. Found: 410.9881.

Methyl 2-(3-bromobenzoyl)-3-fluoro-3-phenylacrylate (6ia).



Colorless oil 70.0 mg (E:Z = 1:1.3, 89%). R_f 0.41 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.69 (s, 3H), 3.78 (s, 3H), 7.27–7.34 (m, 3H), 7.37–7.53 (m, 6H), 7.56 (d, J = 7.3 Hz, 1H), 7.64 (d, J = 8.2 Hz, 1H), 7.70 (d, J = 7.3 Hz, 2H), 7.76 (d, J = 8.2 Hz, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.93 (dd, J = 7.8, 0.9 Hz, 1H), 8.05 (s, 1H), 8.15 (s, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.7, 52.8, 113.8 (d, J = 8.6 Hz), 114.5 (d, J = 25.9 Hz), 123.2, 127.0, 128.97, 128.04, 128.4, 128.5, 128.8, 129.0, 129.1, 130.47, 130.51, 132.1, 132.15, 132.24, 132.3, 136.8, 136.9, 138.3 (d, J = 2.9 Hz), 138.5, 143.6, 163.0, 164.2 (d, J = 17.3 Hz), 166.7 (d, J = 286 Hz), 167.6 (d, J = 270 Hz), 188.6 (d, J = 3.8 Hz), 189.8 (d, J = 7.7 Hz).

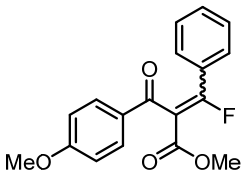
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −84.0, −78.1.

IR (ATR): 1733 m, 1681 m, 1567 w, 1435 w, 1311 m, 1286 m, 1234 s, 1099 m, 1064 m, 692 s.

MS, *m/z* (relative intensity, %): 310 (17), 309 (12), 145 (23), 139 (34), 131 (100), 120 (15), 115 (20), 105 (22), 103 (49), 102 (15), 77 (55), 76 (13), 75 (14), 59 (13), 50 (11).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{17}H_{13}{}^{79}BrFO_3$: 363.0027. Found: 363.0028.

Methyl 3-fluoro-2-(4-methoxybenzoyl)-3-phenylacrylate (6ja).



Colorless oil 31.6 mg (E:Z = 1:1.6, 55%). R_f 0.31 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.66 (s, 3H), 3.75 (s, 3H), 3.83 (s, 3H), 3.89 (s, 3H), 6.87 (d, J = 8.7 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H), 7.23–7.30 (m, 2H), 7.35 (t, J = 7.3 Hz, 1H), 7.43–7.50 (m, 4H), 7.53 (t, J = 7.3 Hz, 1H), 7.67 (d, J = 7.3 Hz, 2H), 7.90 (d, J = 8.7 Hz, 2H), 8.00 (d, J = 8.7 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.4, 52.5, 55.5, 55.6, 114.1 (2C), 128.1, 128.2, 128.5, 128.97, 128.7, 128.9, 129.46, 129.55, 129.8 (d, J = 9.6 Hz), 130.1 (d, J = 13.4 Hz), 131.66, 131.74, 131.80, 131.85, 132.8, 163.2, 164.2 (d, J = 11.5 Hz), 164.4 (d, J = 18.2 Hz), 165.2 (d, J = 283 Hz), 166.4 (d, J = 267 Hz), 188.2 (d, J = 2.9 Hz), 189.4 (d, J = 5.8 Hz).

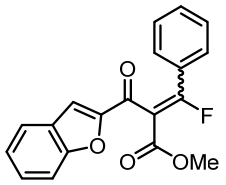
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −87.5, −79.8.

IR (ATR): 1729 m, 1666 m, 1596 s, 1574 m, 1509 w, 1435 w, 1314 m, 1254 s, 1169 m, 1113 w, 1061 m, 1026 m, 980 m, 903 w, 842 w, 693 w.

MS, *m/z* (relative intensity, %): 314 (M^+, 3), 135 (100), 107 (13), 92 (18), 77 (28).

HRMS (EI+, $[M]^+$) Calcd for $C_{18}H_{15}FO_4$: 314.0954. Found: 314.0947.

Methyl 2-(benzofuran-2-carbonyl)-3-fluoro-3-phenylacrylate (6ka).



Colorless oil 49.7 mg (*E*:*Z* = 1:1.6, 81%). R_f 0.34 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.69 (s, 3H), 3.79 (s, 3H), 7.25–7.37 (m, 6H), 7.43–7.66 (m, 12H), 7.70 (d, *J* = 7.3 Hz, 1H), 7.73 (d, *J* = 8.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.5, 52.6, 112.5, 112.6, 114.3 (d, *J* = 24.9 Hz), 115.9, 116.2, 123.5, 124.1, 126.7, 126.9, 128.25, 128.28, 128.33, 128.7, 128.88, 128.95, 129.01, 129.1, 129.4, 129.7 (d, *J* = 25.9 Hz), 130.2, 132.1, 132.1, 152.0, 152.1, 156.1, 156.2, 162.6, 164.0 (d, *J* = 16.3 Hz), 167.3 (d, *J* = 286 Hz), 168.4 (d, *J* = 272 Hz), 178.7 (d, *J* = 2.9 Hz), 180.0 (d, *J* = 7.7 Hz).

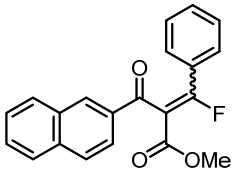
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −82.8, −77.6.

IR (ATR): 1731 m, 1660 s, 1548 s, 1435 w, 1333 m, 1237 s, 1173 m, 1113 m, 1064 m, 989 m, 958 w, 838 w, 751 s, 693 s.

MS, *m/z* (relative intensity, %): 324 (M^+, 13), 323 (21), 308 (21), 307 (100), 264 (23), 248 (11), 237 (15), 236 (32), 207 (12), 148 (33), 145 (80), 139 (23), 133 (27), 120 (21), 105 (16), 89 (94), 63 (30), 59 (16).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{19}H_{14}FO_4$: 325.0871. Found: 325.0872.

Methyl 2-(2-naphthoyl)-3-fluoro-3-phenylacrylate (6la).



Colorless oil 53.1 mg (*E*:*Z* = 1:1.1, 83%). R_f 0.37 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.68 (s, 3H), 3.75 (s, 3H), 7.24 (t, *J* = 7.8 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 1H), 7.47–7.66 (m, 10H), 7.74 (d, *J* = 6.9 Hz, 2H), 7.82–8.04 (m, 7H), 8.11 (dd, *J* = 8.5, 1.6 Hz, 1H), 8.45 (s, 1H), 8.51 (s, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.4, 52.5, 114.2 (d, *J* = 7.7 Hz), 115.0 (d, *J* = 26.8 Hz), 124.12, 124.14, 126.9, 127.76, 127.83, 128.1, 128.2, 128.3, 128.6 (2C), 128.77, 128.85, 128.90, 128.93, 128.95, 129.0, 129.4 (d, *J* = 25.9 Hz), 129.69, 129.74, 130.1 (d, *J* = 26.8 Hz), 131.8, 131.9, 132.4, 132.5, 133.9, 134.0, 135.9, 136.0, 163.1, 164.3, 165.9 (d, *J* = 285 Hz), 167.0 (d, *J* = 268 Hz), 189.7 (d, *J* = 2.9 Hz), 190.8 (d, *J* = 6.7 Hz).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −86.0, −79.2.

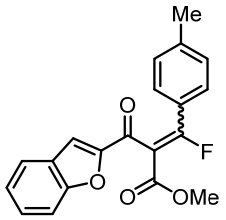
IR (ATR): 1731 m, 1670 m, 1625 s, 1434 w, 1353 w, 1311 m, 1226 s, 1196 m, 1111 m, 1062 m, 989 w, 906 w, 825

w, 772 s, 693 m.

MS, *m/z* (relative intensity, %): 334 (M^+, 15), 156 (12), 155 (98), 139 (16), 128 (12), 127 (100), 126 (14), 77 (14).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{21}H_{16}FO_3$: 335.1078. Found: 335.1076.

Methyl 2-(benzofuran-2-carbonyl)-3-fluoro-3-(*p*-tolyl)acrylate (6kb).



Pale yellow oil 62.3 mg (*E*:*Z* = 1:1.6, 88%). R_f 0.41 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.25 (s, 3H), 2.42 (s, 3H), 3.68 (s, 3H), 3.77 (s, 3H), 7.08 (d, J = 8.2 Hz, 2H), 7.24–7.34 (m, 4H), 7.40–7.54 (m, 7H), 7.56–7.65 (m, 4H), 7.71 (d, J = 8.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 21.47, 21.67, 52.42, 52.53, 112.52, 112.56, 113.62 (d, J = 24.9 Hz), 115.77, 116.21, 123.49, 123.53, 124.02, 124.04, 126.33 (d, J = 25.9 Hz), 126.74, 126.79, 126.94, 127.00, 128.25, 128.32, 128.80, 128.88, 128.97, 129.02, 129.48, 142.96, 143.00, 152.12, 152.19, 156.12, 162.75, 164.21 (d, J = 17.3 Hz), 167.58 (d, J = 286 Hz), 168.78 (d, J = 272 Hz), 178.88 (d, J = 3.8 Hz), 180.29 (d, J = 8.6 Hz).

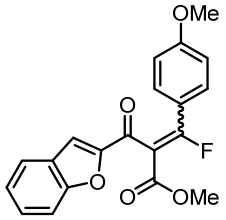
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −83.0, −77.6.

IR (ATR): 1732 m, 1661 m, 1609 m, 1549 s, 1436 w, 1333 m, 1238 m, 1174 m, 1105 m, 1065 m, 991 w, 824 m, 771 m, 669 w.

MS, *m/z* (relative intensity, %): 337 (41), 294 (13), 278 (12), 207 (11), 178 (24), 148 (35), 145 (85), 169 (20), 135 (25), 133 (33), 107 (21), 89 (100), 63 (28), 59 (19), 44 (12).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{20}H_{16}FO_4$: 339.1027. Found: 339.1031.

Methyl 2-(benzofuran-2-carbonyl)-3-fluoro-3-(4-methoxyphenyl)acrylate (6kc).



Yellow oil 62.1 mg (*E*:*Z* = 1:1.4, 94%). R_f 0.26 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.70 (s, 3H), 3.74 (s, 3H), 3.77 (s, 3H), 3.88 (s, 3H), 6.79 (d, J = 8.7 Hz, 2H), 6.98 (d, J = 9.2 Hz, 2H), 7.25–7.35 (m, 3H), 7.41–7.56 (m, 7H), 7.59 (t, J = 4.1 Hz, 1H), 7.64 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 8.7 Hz, 1H), 7.72 (d, J = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.4, 52.5, 55.3, 55.4, 111.1, 111.6, 111.7, 122.5, 112.6, 113.7, 114.2, 115.6, 116.2, 121.2 (d, J = 26.8 Hz), 121.9 (d, J = 26.8 Hz), 122.1, 123.5, 124.0, 126.1, 126.8, 128.7, 128.9, 130.3 (d, J = 6.7 Hz), 131.1 (d, J = 6.7 Hz), 152.21, 152.24, 156.08, 156.13, 162.5, 162.7, 162.9, 164.5 (d, J = 16.3 Hz), 167.5 (d, J = 285 Hz), 168.7 (d, J = 270 Hz), 179.1 (d, J = 2.9 Hz), 180.6 (d, J = 7.7 Hz).

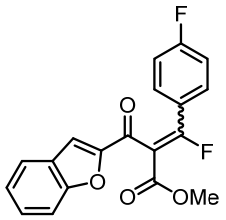
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −83.0, −77.6.

IR (ATR): 1732 m, 1604 s, 1550 m, 1511 m, 1437 w, 1335 m, 1303 m, 1259 s, 1173 s, 1106 w, 839 m.

MS, *m/z* (relative intensity, %): 338 (11), 337 (43), 294 (14), 278 (12), 178 (22), 169 (21), 148 (34), 145 (84), 135 (27), 133 (30), 132 (11), 107 (21), 89 (100), 63 (29), 59 (18).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{20}H_{16}FO_5$: 355.0976. Found: 355.0964.

Methyl 2-(benzofuran-2-carbonyl)-3-fluoro-3-(4-fluorophenyl)acrylate (6kd).



Pale yellow oil 56.5 mg (*E*:*Z* = 1:1.3, 78%). R_f 0.45 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.70 (s, 3H), 3.79 (s, 3H), 6.99 (t, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 2H), 7.27–7.36 (m, 2H), 7.45–7.59 (m, 9H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.71–7.76 (m, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 52.56, 52.63, 112.52, 112.58, 113.40 (d, *J* = 9.6 Hz), 114.21 (d, *J* = 24.9 Hz), 115.50, 115.72, 115.81, 116.04, 116.27, 116.31, 123.53 (d, *J* = 3.8 Hz), 124.16 (d, *J* = 4.8 Hz), 125.32 (dd, *J* = 26.4, 2.9 Hz), 125.94 (dd, *J* = 26.4, 2.9 Hz), 126.69, 126.91, 128.94, 129.13, 130.78 (dd, *J* = 8.6, 5.8 Hz), 131.60 (dd, *J* = 8.6, 5.8 Hz), 151.94, 151.99, 156.15(2C), 162.49, 163.87 (d, *J* = 17.3 Hz), 164.60 (d, *J* = 255 Hz), 164.78 (d, *J* = 255 Hz), 166.21 (d, *J* = 286 Hz), 167.49 (d, *J* = 271 Hz), 178.57 (d, *J* = 2.9 Hz), 179.92 (d, *J* = 7.7 Hz).

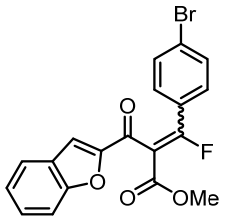
^{19}F NMR ($CDCl_3$, 376 MHz) *δ*: −108.5, −108.3, −82.5, −77.0.

IR (ATR): 1732 m, 1662 m, 1603 m, 1549 s, 1507 s, 1437 w, 1333 m, 1232 s, 1161 m, 1114 m, 1067 m, 992 w, 844 s, 669 w.

MS, *m/z* (relative intensity, %): 342 (M^+, 10), 325 (34), 282 (12), 254 (18), 157 (20), 148 (26), 145 (68), 138 (20), 133 (23), 123 (14), 89 (100), 63 (29), 62 (11), 59 (17).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{19}H_{13}F_2O_4$: 343.0776. Found: 343.0777.

Methyl 2-(benzofuran-2-carbonyl)-3-(4-bromophenyl)-3-fluoroacrylate (6ke).



Pale yellow oil 53.0 mg (*E*:*Z* = 1:1.2, 60%). R_f 0.46 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.70 (s, 3H), 3.79 (s, 3H), 7.27–7.36 (m, 2H), 7.38–7.68 (m, 15H), 7.73 (dd, *J* = 9.2, 0.9 Hz, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 52.6, 52.7, 112.56, 112.60, 113.9 (d, *J* = 9.6 Hz), 114.7 (d, *J* = 24.9 Hz), 115.9, 116.4, 123.5, 123.6, 124.17, 124.23, 126.7, 126.90, 126.99, 127.05, 128.1 (d, *J* = 25.9 Hz), 128.6 (d, *J* = 26.8 Hz), 129.0, 129.2, 129.68, 129.75, 130.5, 130.6, 131.6, 132.1, 151.89, 151.93, 156.17, 156.19, 166.0 (d, *J* = 285 Hz), 167.4 (d, *J* = 271 Hz), 178.4 (d, *J* = 3.8 Hz), 179.7 (d, *J* = 7.7 Hz).

^{19}F NMR ($CDCl_3$, 376 MHz) *δ*: −84.2, −78.6.

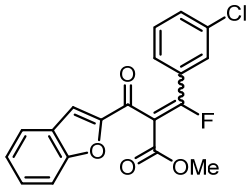
IR (ATR): 1669 m, 1648 m, 1613 m, 1584 m, 1550 s, 1439 w, 1335 m, 1282 s, 1256 s, 1213 m, 1173 m, 1137 w,

1113 m, 1010 m, 832 m, 752 s.

MS, *m/z* (relative intensity, %): 333 (39), 262 (17), 165 (11), 148 (19), 146 (20), 145 (72), 133 (30), 131 (11), 89 (100), 77 (12), 63 (29), 59 (18).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{19}H_{13}{}^{79}BrFO_4$: 402.9987. Found: 402.9989.

Methyl 2-(benzofuran-2-carbonyl)-3-(3-chlorophenyl)-3-fluoroacrylate (6kf).



Pale yellow oil 43.2 mg (*E*:*Z* = 1:1, 66%). R_f 0.46 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.71 (s, 3H), 3.80 (s, 3H), 7.22 (t, *J* = 7.8 Hz, 1H), 7.27–7.63 (m, 14H), 7.65–7.70 (m, 2H) 7.74 (d, *J* = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.7, 52.8, 112.6, 112.7, 116.0, 116.4, 123.59, 123.62, 124.21, 124.23, 126.64, 126.69, 126.8 (d, *J* = 19.2 Hz), 127.26, 127.30, 128.1, 128.2, 129.0, 129.2, 129.6, 130.0, 130.5 (d, *J* = 21.1 Hz), 131.0 (d, *J* = 25.6 Hz), 131.4 (d, *J* = 26.8 Hz), 132.12, 132.15, 134.4, 134.9, 151.90, 151.94, 156.20, 156.22, 162.3, 163.6 (d, *J* = 17.2 Hz), 165.5 (d, *J* = 286 Hz), 166.7 (d, *J* = 272 Hz), 178.2 (d, *J* = 2.9 Hz), 179.5 (d, *J* = 7.7 Hz).

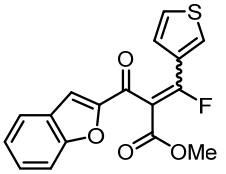
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −83.9, −78.6.

IR (ATR): 1552 w, 1547 w, 1254 w, 1220 m, 908 w, 775 s, 708 w, 665 w, 572 w, 508 w.

MS, *m/z* (relative intensity, %): 343 (11), 341 (44), 323 (12), 291 (28), 270 (18), 236 (18), 154 (13), 148 (22), 146 (11), 145 (82), 133 (35), 89 (100), 63 (43), 59 (22).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{19}H_{13}ClFO_4$: 359.0481. Found: 359.0481.

Methyl 2-(benzofuran-2-carbonyl)-3-fluoro-3-(thiophen-3-yl)acrylate (6kg).



Yellow oil 56.6 mg (*E*:*Z* = 1:1.4, 77%). R_f 0.44 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.73 (s, 3H), 3.76 (s, 3H), 7.15 (dd, *J* = 5.5, 1.4 Hz, 2H), 7.20–7.24 (m, 1H), 7.27–7.34 (m, 2H), 7.36–7.40 (m, 1H), 7.46–7.60 (m, 7H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.80 (dd, *J* = 3.3, 1.4 Hz, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.4, 52.6, 111.4 (d, *J* = 8.6 Hz), 112.6, 115.7, 116.5, 123.5, 123.6, 124.1, 124.2, 125.8, 126.2, 126.3, 126.8, 126.9, 127.1, 127.46, 127.52, 128.8, 129.1, 130.0 (d, *J* = 29.7 Hz), 130.80 (d, *J* = 7.7 Hz), 130.83 (d, *J* = 28.8 Hz), 132.3 (d, *J* = 8.6 Hz), 152.08, 152.13, 156.1, 156.3, 162.2 (d, *J* = 281 Hz), 162.6, 163.2 (d, *J* = 263 Hz), 163.9 (d, *J* = 18.2 Hz), 178.8 (d, *J* = 4.8 Hz), 180.1 (d, *J* = 7.7 Hz).

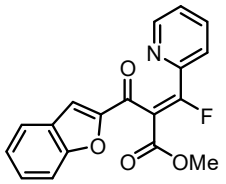
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −87.0, −82.2.

IR (ATR): 1729 m, 1661m, 1613 m, 1549 s, 1435 w, 1299 m, 1217 m, 1173 m, 1146 w, 1111 m, 1006 w, 958 w, 887 w, 841 w, 803 w, 680 w.

MS, *m/z* (relative intensity, %): 313 (14), 298 (31), 270 (17), 243 (21), 242 (26), 145 (62), 133 (15), 126 (15), 89 (100), 63 (40), 45 (17).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{17}H_{12}FO_4S$: 331.0446. Found: 331.0441.

Methyl (*Z*)-2-(benzofuran-2-carbonyl)-3-fluoro-3-(pyridin-2-yl)acrylate (6kh).



White solid 56.6 mg (91%). R_f 0.49 (SiO_2, Hexane/EtOAc = 1/1). M.p. 115 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.78 (s, 3H), 7.18–7.23 (m, 1H), 7.26 (t, J = 7.3 Hz, 1H), 7.40–7.45 (m, 2H), 7.54 (d, J = 8.7 Hz, 1H), 7.63 (d, J = 7.3 Hz, 1H), 7.73–7.81 (m, 2H), 8.29 (d, J = 4.6 Hz, 1H).

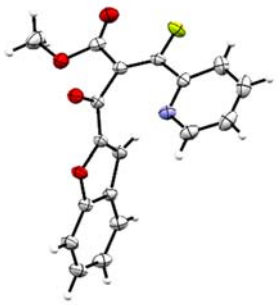
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.56, 112.4, 113.0, 113.5 (d, J = 3.8 Hz), 121.9 (d, J = 4.8 Hz), 123.1, 123.7, 125.6, 127.1, 127.9, 137.0, 147.3 (d, J = 34.5 Hz), 148.8 (d, J = 4.8 Hz), 153.2 (d, J = 4.8 Hz), 155.6, 162.4, 162.8 (d, J = 282 Hz), 179.0 (d, J = 6.7 Hz).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −106.

IR (ATR): 1730 m, 1671 s, 1612 w, 1556 m, 1434 m, 1337 m, 1295 w, 1237 s, 1173 w, 1134 m, 1089 m, 994 w, 958 w, 887 w, 850 w, 650 w, 617 w.

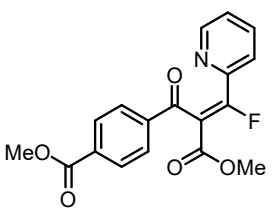
MS, *m/z* (relative intensity, %): 296 (18), 267 (12), 266 (68), 238 (36), 209 (11), 177 (20), 149 (20), 145 (41), 140 (22), 121 (13), 89 (100), 78 (15), 63 (39), 59 (13), 51 (16).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{18}H_{13}FNO_4$: 326.0823. Found: 326.0821.



Ellipsoids set at a 50% probability. monoclinic, space group $P2_1/c$ (no. 14), a = 6.91739(14) Å, b = 23.4940(4) Å, c = 9.63136(19) Å, β = 104.644(2)°, V = 1514.42(5) Å^3, T = 123 K, Z = 4, R_1 (wR2) = 0.0379 (0.1075) for 899 parameters and 19566 unique reflections. GOF = 1.048. CCDC 1999458.

Methyl (*Z*)-4-(3-fluoro-2-(methoxycarbonyl)-3-(pyridin-2-yl)acryloyl)benzoate (6ah).



Pale yellow oil 36.3 mg (58%). R_f 0.54 (SiO_2, Hexane/EtOAc = 1/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.75 (s, 3H), 3.91 (s, 3H), 7.17–7.22 (m, 1H), 7.74–7.77 (m, 2H), 8.00 (d, J = 8.2

Hz, 2H), 8.07 (d, J = 8.2 Hz, 2H), 8.14 (d, J = 4.6 Hz, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.36, 52.55, 114.0, 121.7 (d, J = 3.8 Hz), 125.6, 128.3, 129.7, 133.4, 137.1, 140.9 (d, J = 3.8 Hz), 147.2 (d, J = 35.5 Hz), 148.4 (d, J = 4.8 Hz), 161.7 (d, J = 281 Hz), 162.6, 166.3, 188.7 (d, J = 5.8 Hz).

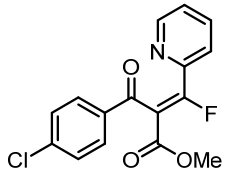
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −108.

IR (ATR): 1721 s, 1683 m, 1644 w, 1578 w, 1435 m, 1340 w, 1276 s, 1221 s, 1103 m, 873 w, 714 w, 613 w.

MS, *m/z* (relative intensity, %): 327 (13), 315 (19), 314 (91), 312 (16), 300 (40), 284 (33), 265 (32), 256 (26), 237 (12), 209 (13), 208 (55), 196 (17), 197 (13), 164 (11), 163 (100), 149 (11), 140 (47), 136 (11), 135 (73), 130 (18), 121 (24), 120 (32), 119 (21), 116 (15), 112 (12), 104 (45), 103 (62), 98 (16), 94 (21), 92 (20), 89 (20), 78 (33), 77 (45), 76 (88), 75 (51), 74 (12), 63 (12), 51 (32), 50 (49).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{18}H_{15}FNO_5$: 344.0923. Found: 344.0925.

Methyl (*Z*)-2-(4-chlorobenzoyl)-3-fluoro-3-(pyridin-2-yl)acrylate (6gh).



White solid 30.3 mg (54%). R_f 0.57 (SiO_2, Hexane/EtOAc = 1/1). M.p. 141 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.76 (s, 3H), 7.20–7.24 (m, 1H), 7.38 (d, J = 8.2 Hz, 2H), 7.75–7.77 (m, 2H), 7.63 (dd, J = 4.6, 0.9 Hz, 2H), 7.90 (d, J = 8.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.56, 114.0 (d, J = 2.9 Hz), 121.8 (d, J = 3.8 Hz), 125.5, 128.8, 129.9, 136.0 (d, J = 3.8 Hz), 137.0, 139.0, 147.3 (d, J = 35.5 Hz), 148.6 (d, J = 4.8 Hz), 161.6 (d, J = 280 Hz), 162.6, 188.3 (d, J = 5.8 Hz).

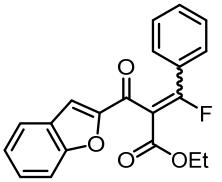
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −108.

IR (ATR): 1731 m, 1682 s, 1639 w, 1581 m, 1435 m, 1339 m, 1234 s, 1134 w, 1088 m, 899 w, 868 w, 841 w, 613 w.

MS, *m/z* (relative intensity, %): 303 (25), 292 (34), 291 (16), 290 (84), 276 (16), 262 (19), 261 (13), 260 (47), 243 (12), 241 (23), 234 (10), 232 (27), 209 (17), 208 (43), 197 (12), 196 (11), 141 (30), 140 (38), 139 (93), 130 (11), 121 (15), 113 (30), 112 (13), 111 (100), 94 (17), 78 (20), 76 (15), 75 (53), 59 (15), 51 (25), 50 (12).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{16}H_{12}{}^{35}ClFNO_3$: 320.0484. Found: 320.0486.

Ethyl 2-(benzofuran-2-carbonyl)-3-fluoro-3-phenylacrylate (6ki).



Pale yellow oil 54.9 mg (*E*:*Z* = 1:1.2, 79%). R_f 0.39 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.10 (t, J = 7.3 Hz, 3H), 1.22 (t, J = 7.3 Hz, 3H), 4.17 (q, J = 7.3 Hz, 2H), 4.27 (t, J = 7.3 Hz, 2H), 7.25–7.37 (m, 6H), 7.43–7.66 (m, 12H), 7.70 (d, J = 7.3 Hz, 1H), 7.73 (d, J = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 13.7, 14.0, 61.6, 61.7, 112.5, 112.6, 115.8 (d, J = 28.8 Hz), 123.5, 124.1, 126.7,

126.9, 128.2, 128.28, 128.33, 128.7, 128.80, 128.84, 128.88, 128.95, 129.01, 129.1, 129.3, 129.8 (d, J = 25.9 Hz), 130.1, 132.0, 152.09, 152.14, 152.2, 156.02, 156.05, 162.2, 163.6 (d, J = 16.3 Hz), 167.2 (d, J = 285 Hz), 168.2 (d, J = 272 Hz), 178.7 (d, J = 2.9 Hz), 180.1 (d, J = 7.7 Hz).

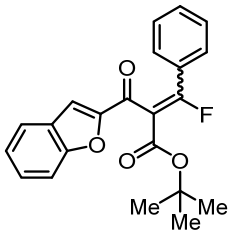
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −83.1, −78.3.

IR (ATR): 1674 s, 1550 s, 1446 w, 1279 s, 1178 m, 1112 m, 1019 m, 963 w, 837 w, 752 s, 716 w, 691 m.

MS, *m/z* (relative intensity, %): 338 (M^+, 11), 337 (12), 322 (19), 321 (80), 293 (19), 291 (10), 264 (24), 248 (12), 237 (14), 236 (28), 149 (16), 146 (11), 145 (M^+, 100), 134 (33), 133 (11), 125 (15), 105 (26), 101 (15), 89 (69), 63 (20), 77 (12).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{20}H_{16}FO_4$: 339.1038. Found: 339.1039.

tert-Butyl 2-(benzofuran-2-carbonyl)-3-fluoro-3-phenylacrylate (6kj).



Pale yellow oil 23.2 mg (E:Z = 1:1, 30%). R_f 0.50 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.32 (s, 9H), 1.42 (s, 9H), 7.26–7.70 (m, 19H), 7.73 (d, J = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 27.6, 27.9, 82.8, 82.9, 112.48, 112.53, 115.1, 115.2, 115.7 (d, J = 10.5 Hz), 116.4 (d, J = 22.0 Hz) 123.5, 124.0, 126.8, 127.0, 128.2, 128.3, 128.4, 128.63, 128.66, 128.74, 128.99, 129.04, 129.8 (d, J = 22.0 Hz), 130.0 (d, J = 22.0 Hz), 131.8, 152.3, 152.47, 152.51, 155.91, 155.93, 161.2, 162.7 (d, J = 16.3 Hz), 166.7 (d, J = 284 Hz), 168.2 (d, J = 273 Hz), 179.0 (d, J = 1.9 Hz), 180.4 (d, J = 7.7 Hz).

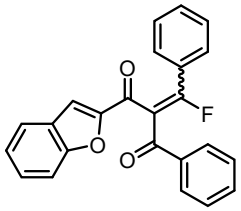
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −84.6, −80.5.

IR (ATR): 1727 m, 1673 m, 1612 m, 1550 s, 1475 w, 1446 w, 1368 m, 1331m, 1294 m, 1157 s, 1112 m, 1063 m, 965 w, 858 w, 835 m, 772 m, 749 s, 693 m.

MS, *m/z* (relative intensity, %): 266 (51), 265 (86), 249 (15), 247 (18), 246 (63), 237 (12), 219 (20), 218 (100), 189 (48), 129 (95), 121 (14), 118 (17), 109 (31), 102 (14), 101 (87), 94 (32), 89 (55), 77 (19), 75 (56), 74 (15), 63 (47), 62 (17), 51 (35), 50 (13), 41 (13).

HRMS (EI+, M^+) Calcd for $C_{22}H_{19}FO_4$: 366.1262. Found: 366.1262.

1-(Benzofuran-2-yl)-2-(fluoro(phenyl)methylene)-3-phenylpropane-1,3-dione (6kk).



Yellow oil 58.5 mg (E:Z = 1:1, 78%). R_f 0.31 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.21–7.55 (m, 19H), 7.58–7.65 (m, 5H), 7.69–7.73 (m, 2H), 7.99–8.03 (m, 2H), 8.12 (d, J = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 112.3, 112.5, 116.7, 117.3, 120.8 (d, J = 21.1 Hz), 121.0 (d, J = 18.2 Hz), 123.6,

124.0, 126.8, 127.0, 128.19, 128.25, 128.38, 128.44, 128.53, 128.68 (2C), 128.71, 128.8, 128.9, 129.56 (d, J = 26.8 Hz), 129.61 (d, J = 27.8 Hz), 129.63, 129.8, 131.8, 133.9, 136.47, 136.51, 137.0, 151.88, 151.92, 151.99, 155.98, 156.04, 164.1 (d, J = 271 Hz), 164.3 (d, J = 274 Hz), 179.0 (d, J = 2.9 Hz), 180.4 (d, J = 10.5 Hz), 190.3 (d, J = 1.9 Hz), 191.4 (d, J = 8.6 Hz).

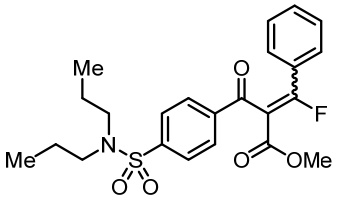
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −89.0, −86.8.

IR (ATR): 1594 m, 1577 m, 1540 m, 1447 m, 1274 s, 1247 m, 1167 m, 1143 m, 1109 m, 1027 w, 885 w, 746 s.

MS, *m/z* (relative intensity, %): 370 (M^+, 15), 353 (28), 237 (18), 236 (19), 209 (35), 145 (25), 105 (100), 89 (30), 77 (95), 236 (28), 51 (13).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{24}H_{16}FO_3$: 371.1089. Found: 371.1074.

Methyl 2-(4-(*N*,*N*-dipropylsulfamoyl)benzoyl)-3-fluoro-3-phenylacrylate (6ma).



Pale yellow oil 77.4 mg (*E*:*Z* = 1:1.1, 91%). R_f 0.37 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.80 (t, J = 7.8 Hz, 6H), 0.84 (t, J = 7.8 Hz, 6H), 1.47 (sext, J = 7.8 Hz, 4H), 1.53 (sext, J = 7.8 Hz, 4H), 3.02 (t, J = 7.8 Hz, 4H), 3.09 (t, J = 7.8 Hz, 4H), 3.64 (s, 3H), 3.75 (s, 3H), 7.22–7.26 (m, 2H), 7.30–7.40 (m, 3H), 7.42–7.48 (m, 2H), 7.53 (t, J = 7.8 Hz, 1H), 7.64 (d, J = 7.8 Hz, 2H), 7.76 (d, J = 8.2 Hz, 2H), 7.90 (d, J = 8.2 Hz, 2H), 7.94 (d, J = 8.2 Hz, 2H), 8.06 (d, J = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 11.0, 11.1, 21.8, 21.9, 49.7, 49.9, 52.5, 52.6, 113.6 (d, J = 9.6 Hz), 114.3 (d, J = 24.9 Hz), 126.8, 127.2, 127.30, 127.34, 128.28, 128.31, 128.34, 128.6, 129.6, 129.7, 132.17, 132.24, 139.0 (d, J = 2.9 Hz), 139.3, 144.57, 144.63, 162.8, 164.0 (d, J = 17.3 Hz), 166.8 (d, J = 286 Hz), 167.7 (d, J = 271 Hz), 188.7 (d, J = 3.8 Hz), 190.0 (d, J = 7.7 Hz).

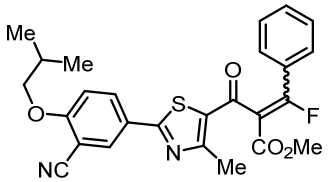
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −83.2, −78.1.

IR (ATR): 1734 m, 1683 m, 1447 w, 1397 w, 1335 m, 1234 m, 1156 s, 1088 m, 1063 w, 986 m, 868 w, 693 s, 605 m, 567 m.

MS, *m/z* (relative intensity, %): 444 (12), 419 (24), 418 (100), 400 (13), 251 (14), 72 (12), 61 (10).

HRMS (FAB+, M^+) Calcd for $C_{23}H_{26}FNO_5S$: 447.1516. Found: 447.1597.

Methyl 2-(2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carbonyl)-3-fluoro-3-phenylacrylate (6na).



Colorless oil 48.9 mg (*E*:*Z* = 1:1.4, 51%). R_f 0.27 (SiO_2, Hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.08 (d, J = 5.5 Hz, 6H), 1.09 (d, J = 5.5 Hz, 6H), 2.13–2.27 (m, 2H), 2.70 (s, 3H), 2.81 (s, 3H), 3.71 (s, 3H), 3.83 (s, 3H), 3.88 (d, J = 6.9 Hz, 2H), 3.90 (d, J = 6.4 Hz, 2H), 6.98 (d, J = 9.2 Hz, 1H), 7.02 (d, J = 9.2 Hz, 1H), 7.29–7.38 (m, 2H), 7.42 (t, J = 7.3 Hz, 1H), 7.49 (t, J = 7.3 Hz, 1H), 7.55 (d, J = 7.3 Hz,

2H), 7.67 (d, J = 7.3 Hz, 2H), 7.88 (s, 1H), 7.99–8.06 (m, 2H), 8.10–8.15 (m, 2H), 8.21 (d, J = 2.3 Hz, 1H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 18.18, 18.20, 19.0 (2C), 28.1 (2C), 52.64, 52.67, 75.7 (2C), 103.0 (2C), 112.55, 112.60, 115.2, 115.3, 116.6 (d, J = 25.9 Hz), 125.5, 125.7, 128.2, 128.3, 128.8, 128.9, 129.0, 129.6 (d, J = 25.9 Hz), 130.1, 130.9, 132.18, 132.22, 132.28, 132.32, 132.68, 132.74, 160.9, 161.1, 161.3, 162.4, 162.8, 163.4, 163.6, 166.1 (d, J = 266 Hz), 167.5 (d, J = 269 Hz), 168.66, 168.69, 181.1 (d, J = 3.8 Hz), 182.6 (d, J = 6.7 Hz).

^{19}F NMR ($CDCl_3$, 376 MHz) δ: −85.6, −77.8.

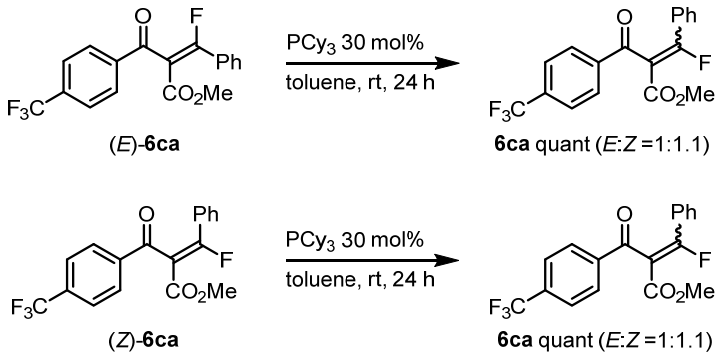
IR (ATR): 1732 w, 1636 w, 1604 w, 1508 w, 1427 w, 1324 m, 1285 m, 1221 s, 1117 w, 1065 w, 1011 w, 778 s, 694 w.

MS, *m/z* (relative intensity, %): 478 (M^+, 19), 390 (38), 389 (47), 243 (34), 242 (33), 215 (15), 139 (55), 120 (11), 115 (12), 105 (17), 71 (100), 70 (52), 59 (28), 57 (53), 45 (39), 41 (93).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{26}H_{24}FN_2O_4S$: 479.1446. Found: 479.1442.

V. Isomerization Experiments

Scheme S1. Isomerization experiment



In a glovebox filled with nitrogen, (*E*)-**6ca** or (*Z*)-**6ca** (68.5 mg, 0.20 mmol), PCy_3 (16.8 mg, 0.06 mmol) and toluene (1.0 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The mixture was stirred at room temperature for 24 h. Yields were determined by ^{19}F NMR spectroscopy using benzotrifluoride as an internal standard (quant). Geometrically pure (*E*)-**6ca** and (*Z*)-**6ca** both gave a mixture of isomers with identical *E*/*Z* ratios (1:1.1).

VI. Control Experiments

Fluoride-Initiated Reaction

In a glovebox filled with nitrogen, the benzoyl fluoride **4b** (54.6 mg, 0.30 mmol), alkynoate **5a** (32.0 mg, 0.20 mmol), THF (1.0 mL), and CsF (9.1 mg, 0.06 mmol) or TBAT (32.4 mg, 0.06 mmol) as a fluoride initiator were added to a 5 mL vial with a Teflon-sealed screwcap. The mixture was stirred at room temperature for 24 h. Although reactions were monitored by ^{19}F NMR spectroscopy, no reaction occurred.

Stoichiometric Reaction in Toluene

In a glovebox filled with nitrogen, the benzoyl fluoride **4b** (24.8 mg, 0.20 mmol), alkynoate **5a** (32.0 mg, 0.20 mmol), PCy_3 (16.8 mg, 0.06 mmol) and toluene (1.0 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The mixture was stirred at room temperature for 24 h. Yield and *E*:*Z* ratio of **6ba** were determined by ^{19}F NMR spectroscopy using benzotrifluoride as an internal standard (43%, *E*:*Z* = 1.6:1).

Stoichiometric Reaction in MeCN

The procedure of **Stoichiometric Reaction in Toluene** was followed except that MeCN was used in a place of toluene. Yield of **8** was determined by ^{19}F NMR spectroscopy using benzotrifluoride as an internal standard (28%). Then, this mixture was then evaporated to dryness, and the residue was purified by flash column chromatography using hexane/EtOAc = 9/1 as the eluent to give **9** as a colorless oil (18.1 mg, 34%).

3.5 References

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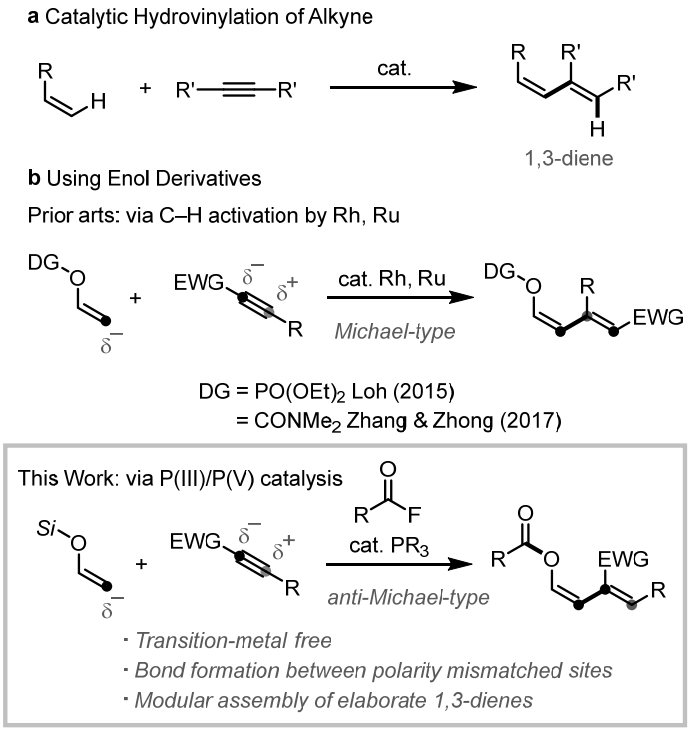
Chapter 4

Phosphine-Catalyzed Hydrovinylation of Alkynes via a P(V) Intermediate

4.1 Introduction

The 1,3-diene motif is frequently found in complex natural products and biologically active molecules,[1] and also serve as a versatile synthetic precursor for a variety of important organic transformations.[2,3] Among the methods reported to date,[4] the catalytic hydrovinylation of alkynes is a straightforward approach and has been a subject of considerable research interest (Scheme 1a).[5,6] The hydrovinylation of alkynes using enol derivatives is of particular interest because the resulting conjugate dienolate derivatives can be used in a variety of useful synthetic transformations.[7,8] However, despite the potential synthetic impact, the catalytic hydrovinylation of alkynes using enol derivatives has not been accomplished, except for the following two examples. Loh[9] and Zhang[10] independently reported that enol derivatives bearing a directing group on the oxygen atom can add across alkynes via transition metal-catalyzed vinylic C–H bond activation (Scheme 1b, top). In these reactions, a new C–C bond can be forged between the nucleophilic carbon of an enol and the electrophilic β-carbon of an alkyne when electron-deficient alkynes are used (Michael-type addition). Herein, we report on a phosphine-catalyzed formal hydrovinylation reaction by the three-component coupling of acyl fluorides, silyl enol ethers, and alkynoates. This reaction involves the alkenylation of a vinylic C–H bond and the acylation of an Si–O bond of silyl enol ethers occur in one reaction sequence (Scheme 1b, bottom). Notably, the C–C bond formation involves umpolung, which allows for connection between polarity mismatched sites to afford an anti-Michael-type adduct. This regioselectivity is complementary to that observed in the transition metal-catalyzed hydrovinylation of alkynes using enol derivatives.[9,10]

Scheme 1. Catalytic hydrovinylation of alkyne using enol derivatives

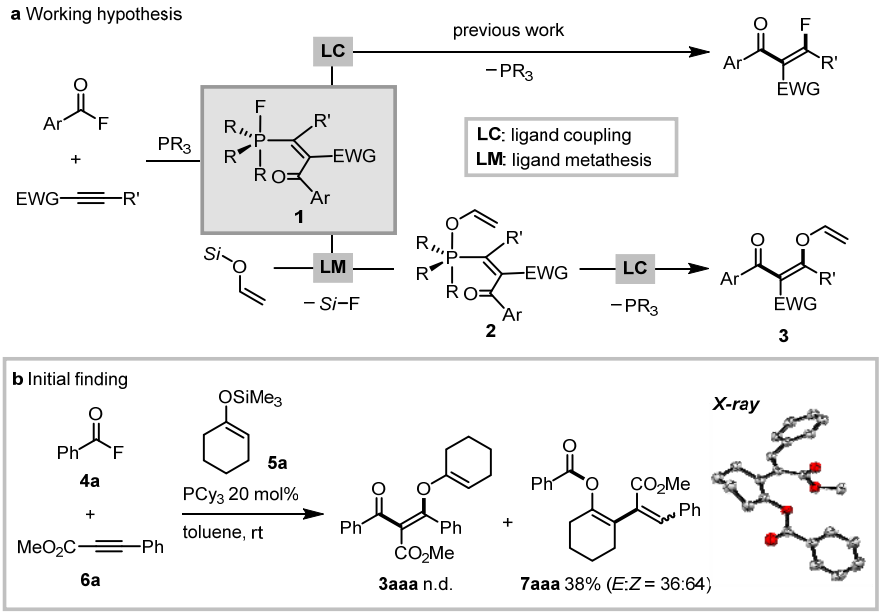


The use of p-block elements as surrogates for transition metal catalysts has attracted considerable interest in terms of both the fundamental aspects of main group elements in uncommon oxidation states and concerns related to the shortage of some metallic elements.[11–16] The P(III)/P(V) redox cycle is a competent main group-based manifold for applications in catalytic reactions. However, the reported examples of catalytic reactions based on the P(III)/P(V) couple are primarily limited to oxygen transfer reactions mediated by the reversible interconversion of phosphine/phosphine oxide (*i.e.*, P(III)/O=P(V) cycle).[14,17] In a P(III)/O=P(V) cycle, the catalyst regeneration step (O=P(V) to P(III)) is irrelevant to the product formation, and a sacrificial reducing agent is essential. It would appear that the P(III)/P(V) manifold could be used for a wider range of catalytic reactions in view of a number of studies on the stoichiometric redox reactivity of organophosphorus compounds in mediating formal oxidative addition or reductive elimination processes through a pentacoordinate phosphorane intermediate as a P(V) species.[11,18,19] However, examples reported thus far are limited to hydrogenation,[20] reduction of allyl bromides,[21] and acylfluorination of alkynes.[22] This work allows the P(III)/P(V) redox cycle to be extended to a phosphine-catalyzed formal hydrovinylation reaction by the three-component coupling of acyl fluorides, silyl enol ethers, and alkynoates.

4.2 Results and Discussion

Quite recently, we reported on the phosphine-catalyzed intermolecular addition of acyl fluorides across triple bonds in electron-deficient alkynes (Scheme 2a).[22] In this reaction, a pentacoordinate fluorophosphorane **1** is involved as the key intermediate, and a C–F bond is formed via ligand coupling (LC) on **1**, an alternative to reductive elimination on transition metal complexes. We envisioned that a three-component coupling would be possible if ligand metathesis (LM) between a fluoride on the phosphorus center of **1** and an organometallic nucleophile were to take place, in a manner similar to the transmetalation reaction on transition metal complexes (Scheme 2b).[19] Silyl enol ethers were chosen as a feasible nucleophile because they can be readily prepared from a range of carbonyl compounds by reliable protocols and exhibit temperate reactivity as an enolate equivalent amenable to various catalysis manifolds. We anticipated that ligand metathesis would generate the phosphorane **2**, which would eventually lead to the formation of densely functionalized alkene **3** via ligand coupling. The three-component coupling of benzoyl fluoride (**4a**), silyl enol ether **5a**, and methyl phenylpropiolate (**6a**) was initially examined. Although, the expected three-component coupling product **3aaa** was not observed, the 1,3-diene **7aaa**, which can be viewed as a formal hydrovinylation product, was obtained in 38% yield (*E*:*Z* = 36:64). X-ray crystallographic analysis unambiguously determined that the alkenylation of a vinylic C–H bond and *O*-acylation of silyl enol ether simultaneously occurred with C–C bond formation between the polarity mismatched sites. Intrigued by the unusual bond connection mode and the rapid assembly of elaborate 1,3-dienes from simple building blocks, we embarked on a study of this synthetic transformation in more detail. Increasing the catalyst loading to 30 mol% improved the yield of **7aaa** to 43% (Figure 2c, entry 1). Since we identified the 1,3-diketone **8aa** and the vinyl ester **9aa** as major byproducts (see Scheme 1-(i) for the structure of **8aa** and **9aa**), which were formed by the direct addition of **5a** to **4a**, the slow addition of **4a** was examined. The dropwise addition of **4a** (7 μL/h, 2.0 equiv) to a mixture of **5a** (2.0 equiv), **6a** and PCy_3 afforded the 1,3-diene **7aaa** in 84% isolated yield (*E*:*Z* = 37:63) (entry 2). Alternatively, increasing the amount of **4a** and **5a** (3.0 equiv each) also improved the yield of 1,3-diene **7aaa** without the dropwise addition of **4a** (entry 3). Other phosphines, such as P^tBu_3, $PPhMe_2$ and PPh_3, and amines (DMAP and DABCO) failed to promote this three-component coupling.

Scheme 2. Reaction development based on fluorophosphorane **1**



entry	catalyst	yield (%)[b]	*E*:*Z*[c]
1	PCy_3	43	33:67
2[d]	PCy_3	90 (84)[e]	37:63
3[f]	PCy_3	55	37:63
4	$PCyp_3$	24	48:52
5	P^nBu_3	16	82:18

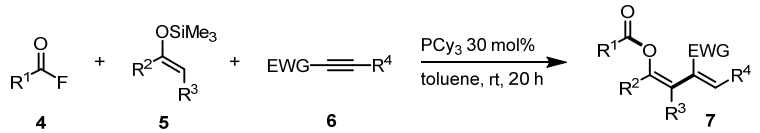
Ineffective catalysts
P^tBu_3, PAd_3, $PAd_2{}^nBu$, $PPhMe_2$, PPh_3
DMAP, DABCO

[a] Reaction conditions: **4a** (0.30 mmol), **5a** (0.30 mmol), **6a** (0.20 mmol), catalyst (0.06 mmol), and toluene (1.0 mL) in a sealed tube at room temperature for 20 h. [b] Determined by ^{1}H NMR. [c] Determined by ^{1}H NMR analysis. [d] Dropwise addition of **4a** (0.40 mmol) at 7 μL/h to the mixture of **5a** (0.40 mmol), **6a** (0.20 mmol), and PCy_3 (0.06 mmol) in toluene (1.0 mL), then at room temperature for 14 h. [e] Yield of the isolated product. [f] **4a** (0.60 mmol), **5a** (0.60 mmol), **6a** (0.20 mmol), PCy_3 (0.06 mmol), and toluene (1.0 mL) in a sealed tube at room temperature for 20 h.

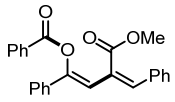
With the optimized reaction conditions in hand, we subsequently examined the scope of the three-component coupling (Table 1). The silyl enol ether **5b**, which was prepared from acetophenone, participated in this reaction to produce **7aba**, in which the C–H bond *cis* to the siloxy group in **5b** was exclusively alkenylated. Regarding the stereochemistry of an alkene moiety derived from **6a**, the *E* configuration was dominated [(*Z*,*E*):(*Z*,*Z*) = 18:82]. The structure of (*Z*,*Z*)-**7aba** was confirmed by a single-crystal X-ray analysis. Silyl enol ethers bearing methyl (**5c**), methoxy (**5d**), and cyano (**5e**) groups readily participated in this reaction. Halogen groups such as chloro (**5f**) and bromo (**5g**) were compatible, allowing the resulting 1,3-diene to be amenable to further structural elaboration via common C–X bond functionalization reactions. Substrates containing heteroarenes such as furan (**5h**) and thiophene (**5i**) also successfully underwent the three-component coupling. The silyl enol ether **5j**, which was prepared from acetone, participated in this reaction to produce **7aja** with a high stereoselectivity [(*Z*,*E*):(*Z*,*Z*) = 9:91]. Five-membered (**5k**), six-membered (**5l**, **5m**, **5n**), and seven-membered (**5o**, **5p**) cyclic silyl enol ethers all reacted to afford the corresponding 1,3-diene derivative. Aromatic alkynoates bearing methyl (**6b**), methoxy (**6c**), fluoro (**6d**), and thienyl groups (**6e**, **6f**) were also viable substrates for this three-component coupling with high *Z*-selectivity. The three-component coupling can also be applied successfully to non-aromatic alkynoates bearing cyclopropyl (**6g**) and *n*-pentyl (**6h**) groups. This three-component coupling also proceeded when alkynoates bearing a different ester moiety such as ethyl (**6i**), *t*-butyl (**6j**), and allyl (**6k**) esters were used. It was also possible to use several acyl fluorides, such as those bearing cyano (**4b**), chloro (**4c**), iodo (**4d**), and π- extended aryl (**4e**) groups to afford the corresponding products **7bba**–**7eba**. The structural elaboration of pharmaceuticals containing a carboxylic acid functionality into the corresponding 1,3-dienes is possible through acid fluoride formation

followed by the three-component coupling (*i.e.*, the conversion of probenecid into **7fba**).

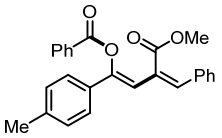
Table 1. Scope of the phosphine-catalyzed three-component coupling [a]



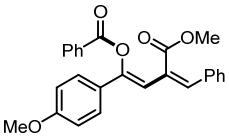
silyl enol ethers scope



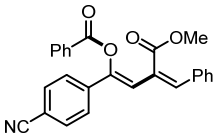
7aba[b] 79% (18:82)
76%[c] (20:80)
62%[d] (18:82)



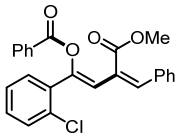
7aca[b] 61% (15:85)



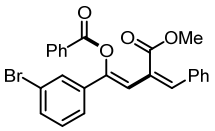
7ada[b] 62% (18:82)



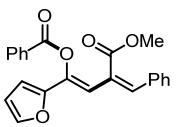
7aea[b] 53% (22:78)



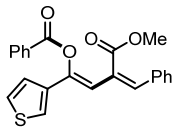
7afa[b] 75% (18:82)



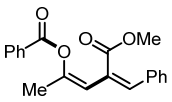
7aga[b] 90% (21:79)



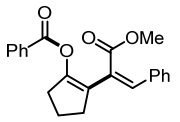
7aha[b] 58% (22:78)



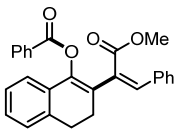
7aia[b] 56% (17:83)



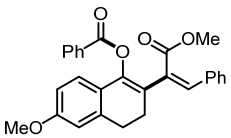
7aja[b] 43% (9:91)



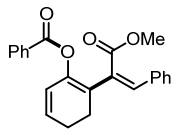
7aka 88% (7:93)



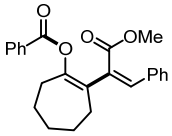
7ala[b] 59% (7:93)



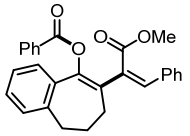
7ama[b] 41% (>1:99)



7ana 60% (9:91)

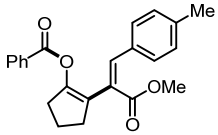


7aoa 65% (25:75)

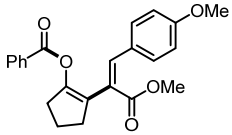


7apa[b] 45% (18:82)

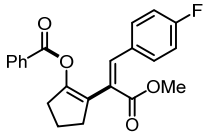
alkynes scope



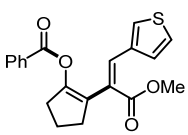
7akb 76% (8:92)



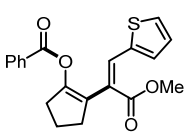
7akc 73% (7:93)



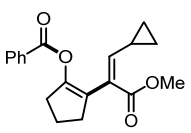
7akd 66% (>1:99)



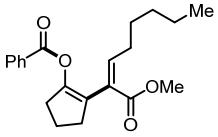
7ake 71% (10:90)



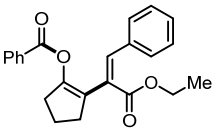
7akf 41% (6:94)



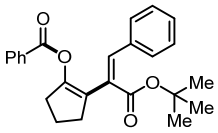
7akg 73% (15:85)



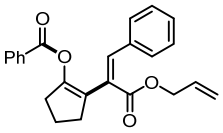
7akh 30% (>1:99)



7aki 74% (6:94)

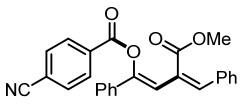


7akj 41% (7:93)

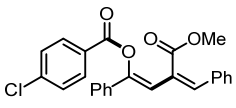


7akk 61% (11:89)

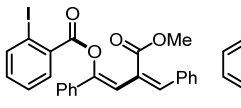
acyl fluorides scope



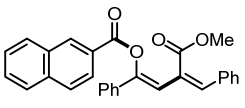
7bba[b] 51% (30:70)



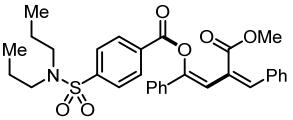
7cba[b] 55% (22:78)



7dba[b] 46% (13:87)



7eba[b] 81% (15:85)



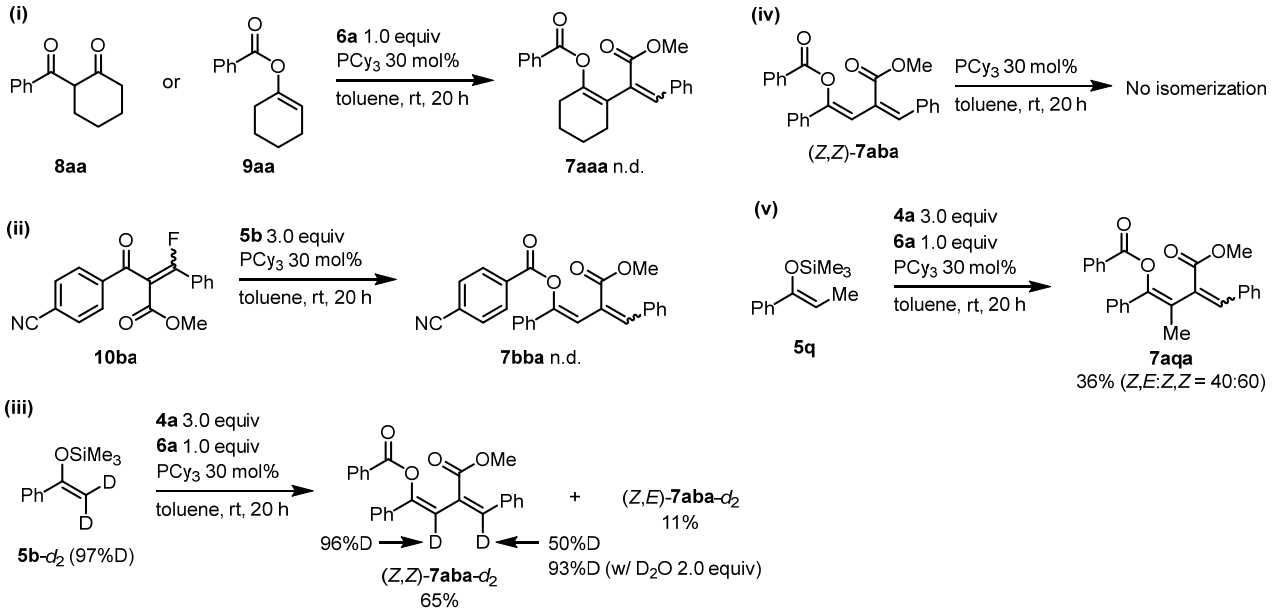
7fba[b] 86% (30:70)

[a] Reaction conditions: dropwise addition of **4a** (0.40 mmol) at 7 μL/h to a mixture of **5a** (0.40 mmol), **6a** (0.20 mmol), and PCy_3 (0.06 mmol) in toluene (1.0 mL), then at room temperature for 14 h. Yields of isolated products are shown. The (*Z*,*E*):(*Z*,*Z*) ratios that were determined by ^1H NMR analysis are shown in parentheses. [b] **4a** (0.60 mmol), **5a** (0.60 mmol), **6a** (0.20 mmol), PCy_3 (0.06 mmol), and toluene (1.0 mL) at room temperature for 20 h. [c] Run on a 5.50 mmol scale. 1.62 g of product was obtained. [d] Run for 48 h in the presence of PCy_3 (0.02 mmol).

To gain insights into the reaction mechanism, several control experiments were performed (Scheme 1). In this three-component coupling between **4a**, **5a**, and **6a**, 1,3-diketone **8aa** and vinyl ester **9aa** were observed as

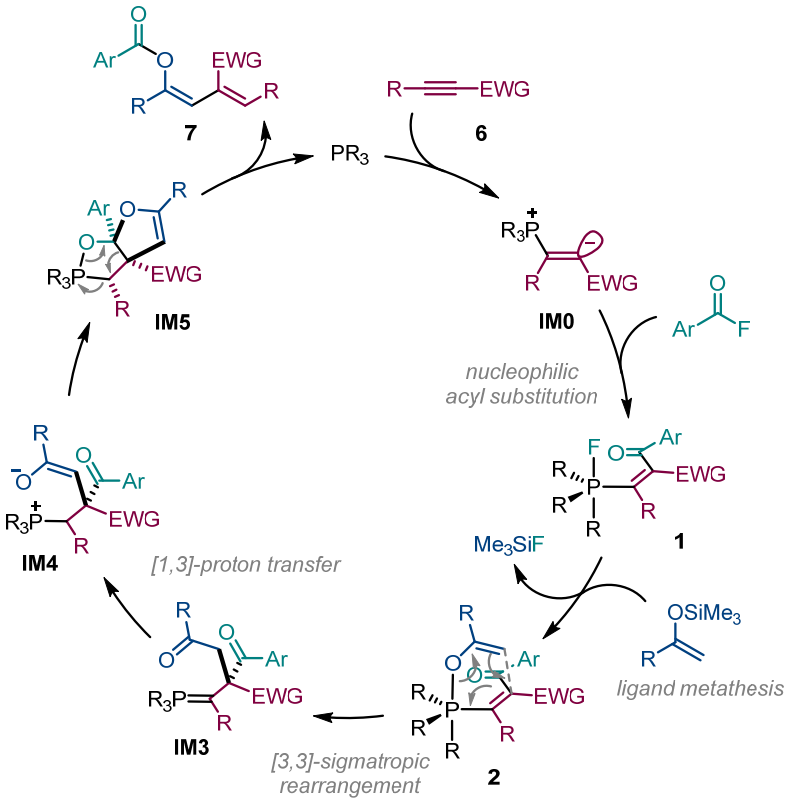
byproducts, which are likely formed by the direct reaction between **4a** and **5a**. To examine the involvement of **8aa** and **9aa** as a viable intermediate in this three-component coupling, the PCy_3-catalyzed reaction of **8aa** (or **9aa**) with **6a** was conducted. However, the expected 1,3-diene **7aaa** was not formed, excluding the intermediacy of **8aa** and **9aa** (Scheme 1-(i)). Monofluoroalkene **10ba**, which can also be formed by phosphine-catalyzed carbofluorination[22] between acyl fluoride **4b** and alkynoate **6a**, is a potential intermediate in this three-component coupling. However, the desired product **7bba** was not formed from **10ba** under these reaction conditions, ruling out the involvement of **10ba** (Scheme 1-(ii)). Deuterium labeling experiments were performed to investigate the origin of the vinylic hydrogen atoms (Scheme 1-(iii)). The three-component coupling of **4a**, **6a**, and the deuterium labeled silyl enol ether **5b**-d_2 (97%D) afforded **7aba**-d_2 under the standard reaction conditions, with deuterium atoms incorporated at the 4-position (50%D), in addition to the 2-position (96%D). Although the deuterium content at the 4-position was 50%, the majority of the cleaved deuterium atoms are incorporated into the product. When this labeling experiment was carried out in the presence of 2.0 equiv of deuterium oxide (D_2O), the deuterium content of **7aba**-d_2 at the 4-position increased to 93%. This result indicates that the decrease in the deuterium content at the 4-position is due to exchange with trace amounts of water that are present in the system.[25] Regarding the stereochemistry of the alkene moiety derived from the alkyne, (*Z*)-isomers were predominantly formed, even though the corresponding (*E*)-isomers were thermodynamically more stable (For example, (*Z*,*E*)-**7aba** is more stable than (*Z*,*Z*)-**7aba** by 1.8 kcal/mol). In fact, the exposure of the geometrically pure (*Z*,*Z*)-**7aba** to the catalytic conditions did not induce any isomerization, indicating that the (*Z*,*Z*)-isomer is a kinetically favored product (Scheme 1-(iv)). Regarding the stereochemistry of the alkene moiety derived from the silyl enol ethers, the vinylic C–H bond that is *cis* to the siloxy group is exclusively alkenylated. However, when the (*Z*)-silyl enol ether **5q** was used as a substrate, 1,3-dienes with a (*Z*)-geometry with respect to the enol moiety was formed exclusively. The structure of (*Z*,*Z*)-**7aqa** was confirmed by a single-crystal X-ray analysis. These results indicate that this three-component coupling involves a stereoconvergent process with respect to the geometry of the enol moiety (Scheme 1-(v)).

Scheme 3. Control experiments



A proposed reaction pathway is depicted in Scheme 4. The catalytic reaction starts with the addition of PR_3 to an alkynoate to generate the carbanion **IM0**, which subsequently undergoes nucleophilic acyl substitution with an acyl fluoride to form the fluorophosphorane **1**.[22] Ligand metathesis between **1** and the silyl enol ether driven by the formation of a stable Si–F bond proceeds to afford alkoxyphosphorane **2**, in preference to the ligand coupling of **1**, to form a C–F bond. The [3,3]-sigmatropic rearrangement of **2** forges a new carbon–carbon bond between the α-carbon of the silyl enol ether and α-carbon of an electron-deficient alkyne to afford the phosphonium ylide **IM3**. The ylide moiety in **IM3** deprotonates the α-hydrogen derived from the silyl enol ether to generate the enolate **IM4**. This [1,3]-proton transfer could be mediated by a trace amount of endogenous water in the system,[25] which also explains the decrease in the deuterium content at the 4-position of the product in the labelling experiment (Scheme 3-(iii)). The enolate moiety in **IM4** subsequently adds to the carbonyl group derived from the acyl fluoride, and the resulting alkoxide anion attacks the phosphorus center to generate the bicyclic phosphorane intermediate **IM5**. The intermediate **IM5** then collapses to the final 1,3-diene **7** with the regeneration of PR_3. The (*Z*)-geometry of the enolate moiety in **IM4** is essential for the cyclization to occur to form **IM5**, which is consistent with the fact that the both (*E*) and (*Z*)-enolates converge into 1,3-dienes with a (*Z*)-enol moiety.

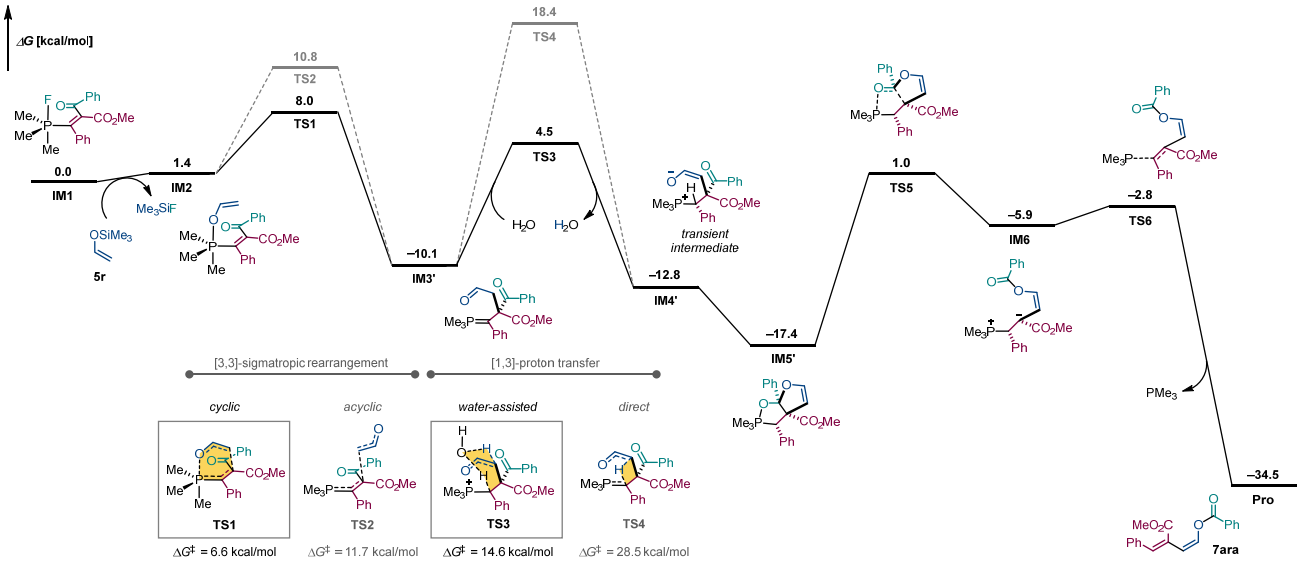
Scheme 4. Proposed mechanism



Density functional theory (DFT) calculations were carried out using PMe_3 as a model catalyst in order to examine the feasibility of the proposed mechanism after the formation of **1**[22] (Scheme 5). Ligand metathesis between **IM1** and the silyl enol ether is endoergonic by 1.4 kcal/mol to generate phosphorane **IM2**, which undergoes the [3,3]-sigmatropic rearrangement to form the phosphonium ylide **IM3'** with a reasonable activation barrier ($\Delta G^{\ddagger}$ = 6.6 kcal/mol). An alternative pathway involving the addition of enolate to vinylphosphonium[26] via an acyclic open transition state (*i.e.*, **TS2**) was found to be energetically less favored ($\Delta G^{\ddagger}$ = 11.7 kcal/mol). The

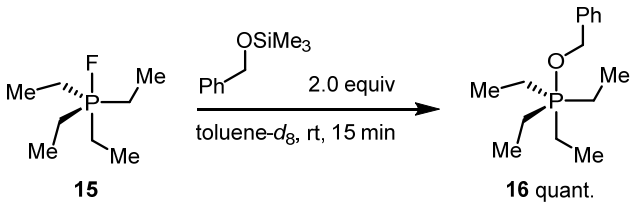
subsequent [1,3]-proton transfer step (*i.e.*, **IM3'** → **IM4'**) requires a high energy transition state (**TS4**, $\Delta G^{\ddagger}$ = 28.5 kcal/mol) when proton migrates directly. The activation barrier is significantly lowered when water is considered to be the proton shuttle (**TS3**, $\Delta G^{\ddagger}$ = 14.6 kcal/mol), a finding that is consistent with the results of the labelling experiment (Scheme 3-(iii)). DFT calculations revealed that the intermediate **IM4'** behaves as a short-lived transient intermediate and is converted to bicyclic phosphorane **IM5'** with no appreciable energetic barrier. The regeneration of the phosphine catalyst was found to proceed through two steps via **IM6** with an activation barrier of 18.4 kcal/mol, which is reasonable for reactions that proceed at room temperature. The energy diagram also indicates that the process from **IM6** to the product is irreversible ($\Delta G^{\ddagger}$ for the product to **IM6**: 31.7 kcal/mol), which is consistent with the geometrical stability of (*Z*,*Z*)-**7aba** under the catalytic conditions (Scheme 3-(iv)).

Scheme 5. Computed energy profile of the three-component coupling from a fluorophosphorane intermediate



To further verify the intermediacy of alkoxyphosphorane, a stoichiometric reaction between isolable fluorophosphorane **15**[27] and silyl alkoxide was performed (Scheme 6). The ligand metathesis proceeded immediately, quantitatively giving alkoxyphosphorane **16**, which has a pentacoordinate geometry[28] determined by VT-NMR experiments.

Scheme 6. Experimental observation of ligand metathesis



4.3 Conclusion

In conclusion, we report on the phosphine-catalyzed three-component coupling of acyl fluorides, silyl enol ethers, and alkynes, which provides straightforward access to a variety of densely functionalized 1,3-dienes. This reaction operates under mild conditions and in the absence of transition metals, therefore permitting a wide functional group tolerance. The key feature of this reaction is ligand metathesis on the fluorophosphorane platform, which allows for the bond formation between polarity mismatched sites to form anti-Michael-type adducts. This study

demonstrates the potential utility of a P(III)/P(V) manifold as a viable alternative to transition metal-mediated catalytic cycles consisting of oxidative addition, transmetalation and reductive elimination.

4.4 Experimental Section

I. General Information

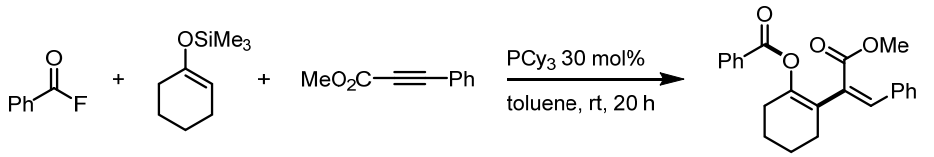
^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a JEOL ECS-400 spectrometer in $CDCl_3$. The chemical shifts in ^{1}H NMR spectra were recorded relative to $CHCl_3$ (δ 7.26) or toluene-d_8 (δ 6.97). The chemical shifts in ^{13}C NMR spectra were recorded relative to $CDCl_3$ (δ 77.0) or CD_2Cl_2 (δ 53.8). The chemical shifts in ^{19}F NMR spectra were recorded relative to benzotrifluoride (δ –65.64). The data is reported as follows: chemical shift (δ) in ppm, coupling constant (Hz), and integration. Infrared spectra (IR) were obtained using a JASCO FT/IR-4200 spectrometer. Absorption is reported in reciprocal centimeters (cm^{-1}) with the following relative intensities: s (strong), m (medium), or w (weak). High resolution mass spectra (HRMS) were obtained using a JEOL JMS-T100LP spectrometer. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed with Biotage Isolera® equipped with Biotage SNAP Ultra or SNAP Isolute NH_2 Cartridge. Data collection for X-ray crystal analysis were performed on a Rigaku/XtaLAB Pro P200 Hybrid Photon Counting diffractometer (Cu-Kα, λ = 1.54184 Å). The structures were solved with direct methods and refined with full-matrix least squares.

II. Materials

All commercially available reagents and solvents were supplied from TCI and Aldrich. Acyl fluorides **4b** [CAS:77976-02-4], **4c** [CAS:2254447-01-1], **4d** [CAS:1064679-44-2], **4e** [CAS:37827-83-1], **4f** [CAS:2248551-77-9] were prepared according to a literature procedure.[29,30] Alkynes **6b** [CAS:7515-16-4], **6c** [CAS:7515-17-5], **6d** [CAS:42122-44-1], **6e** [CAS:1340531-00-1], **6f** [CAS:6824-26-6], **6g** [CAS:80866-48-4], **6j** [CAS:93139-50-5], **6k** [CAS:29577-34-2] were prepared according to a literature procedure.[31,32] **15** [CAS: 41925-21-7] was also prepared according to a literature procedure.[27a]

III. Typical Procedure

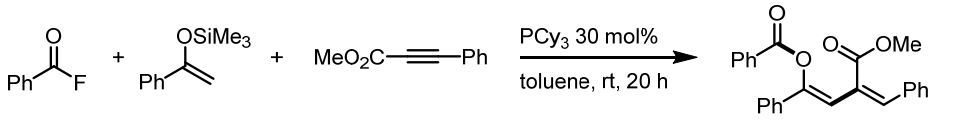
- **Procedure A**



4a **5a** **6a** **7aaa** 84% (*E*:*Z* = 37:63)

In a glovebox filled with nitrogen, the silyl enol ether **5a** (76.6 μL, 0.40 mmol), alkyne **6a** (32.0 mg, 0.20 mmol), PCy_3 (16.8 mg, 0.06 mmol) and toluene (1.0 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The acyl fluoride **4a** (43.2 μL, 0.40 mmol) was added to the reaction mixture at a rate of 7 μL/h, and the mixture was then stirred at room temperature for 9 h. This mixture was then evaporated to dryness, and the residue was purified by flash column chromatography using hexane/EtOAc = 9/1 as the eluent to give **7aaa** as a white solid (58.2 mg, 84%, *E*:*Z* = 37:63).

• **Procedure B**

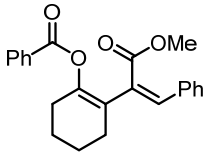


4a **5b** **6a** **7aba** 79% (*Z*,*E*:*Z*,*Z* = 18:82)

In a glovebox filled with nitrogen, the acyl fluoride **4a** (64.8 μL, 0.60 mmol), silyl enol ether **5b** (123 μL, 0.6 mmol), the alkyne **6a** (32.0 mg, 0.20 mmol), PCy_3 (16.8 mg, 0.06 mmol) and toluene (1.0 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The mixture was stirred at room temperature for 20 h. The resulting mixture was then evaporated to dryness, and the residue was purified by flash column chromatography using hexane/EtOAc = 9/1 as the eluent to give **7aba** as a white solid (60.4 mg, 79%, *Z*,*E*:*Z*,*Z* = 18:82).

IV. Spectroscopic Data

(*Z*)-2-(3-Methoxy-3-oxo-1-phenylprop-1-en-2-yl)cyclohex-1-en-1-yl benzoate (7aaa).



Procedure A.

White solid 58.2 mg (84%, *E*:*Z* = 37:63). R_f 0.26 (SiO_2, Hexane/EtOAc = 9/1). M.p. 135 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.80–1.88 (m, 4H), 2.41–2.48 (m, 4H), 3.16 (s, 3H), 6.75 (s, 1H), 7.17–7.27 (m, 5H), 7.42 (t, *J* = 7.3 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 8.03 (d, *J* = 7.3 Hz, 2H).

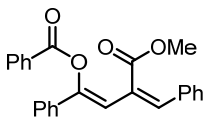
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 22.4, 22.6, 27.9, 28.1, 51.7, 121.1, 127.8, 128.0, 128.2, 128.4, 129.5, 130.1, 131.5, 132.5, 133.4, 135.9, 147.0, 164.2, 169.8.

IR (KBr): 2950 w, 2933 m, 2858 w, 1736 s, 1712 s, 1655 m, 1600 w, 1451 m, 1430 m, 1384 w, 1316 m, 1262 m, 1208 m, 1176 w, 1105 s, 1069 m, 1023 m, 748 m, 706 s, 691 s, 579 w.

MS, *m/z* (relative intensity, %): 362 (M^+, 2), 257 (35), 225 (18), 141 (14), 128 (10), 115 (13), 106 (61), 105 (100), 91 (10), 77 (86), 51 (13).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{23}H_{23}O_4$: 363.1591. Found: 363.1593.

(1*Z*,3*Z*)-3-(Methoxycarbonyl)-1,4-diphenylbuta-1,3-dien-1-yl benzoate (7aba).



Procedure B.

White solid 60.4 mg (79%, *Z*,*E*:*Z*,*Z* = 18:82). R_f 0.23 (SiO_2, Hexane/EtOAc = 9/1). M.p. 135 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.28 (s, 3H), 6.55 (d, *J* = 0.9 Hz, 1H), 6.84 (s, 1H), 7.23–7.37 (m, 8H), 7.51–7.54 (m, 4H), 7.65 (t, *J* = 7.8 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.1, 116.0, 124.8, 128.1, 128.5 (overlapped two peaks), 128.7 (overlapped two peaks), 128.8, 129.0, 129.8, 130.3, 133.9, 134.7, 135.0, 135.1, 147.0, 164.0, 169.2.

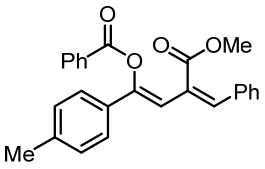
IR (KBr): 3061 w, 3020 w, 2948 w, 1742 s, 1718 s, 1638 m, 1601 m, 1592 m, 1573 w, 1490 m, 1445 m, 1376 m,

1318 w, 1248 s, 1221 s, 1180 m, 1158 s, 1086 s, 1068 s, 1026 m, 970 w, 925 w, 891 s, 765 s, 712 s, 701 s, 662 s, 595 w, 470 m.

MS, *m/z* (relative intensity, %): 384 (M^+, 1), 105 (100), 77 (37).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{25}H_{21}O_4$: 385.1434. Found: 385.1443.

(1*Z*,3*Z*)-3-(Methoxycarbonyl)-4-phenyl-1-(p-tolyl)buta-1,3-dien-1-yl benzoate (7aca).



Procedure B.

Pale yellow solid 48.6 mg (61%, *Z*,*E*:*Z*,*Z* = 15:85). R_f 0.20 (SiO_2, Hexane/EtOAc = 9/1). M.p. 114 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.34 (s, 3H), 3.27 (s, 3H), 6.50 (s, 1H), 6.81 (s, 1H), 7.14 (d, J = 8.2 Hz, 2H), 7.24–7.31 (m, 5H), 7.40 (d, J = 8.2 Hz, 2H), 7.51 (t, J = 7.8 Hz, 2H), 7.64 (t, J = 7.8 Hz, 1H), 8.18 (d, J = 7.8 Hz, 2H).

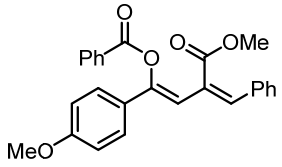
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 21.3, 52.1, 115.1, 124.7, 128.1, 128.4, 128.5, 128.7, 128.9, 129.5, 129.9, 130.3, 131.9, 133.8, 134.5, 135.2, 139.1, 147.1, 164.0, 169.3.

IR (KBr): 2945 w, 1742 s, 1717 s, 1635 m, 1599 m, 1510 w, 1490 m, 1435 m, 1375 m, 1310 w, 1244 s, 1159 s, 1085 s, 1068 s, 1028 m, 971 w, 926 w, 888 m, 848 w, 817 s, 764 m, 708 s, 652 m, 598 w, 524 m, 473 m, 418 m.

MS, *m/z* (relative intensity, %): 398 (M^+, 3), 293 (10), 267 (13), 182 (26), 119 (25), 106 (15), 105 (100), 91 (16), 77 (50).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{26}H_{23}O_4$: 399.1591. Found: 399.1595.

(1*Z*,3*Z*)-3-(Methoxycarbonyl)-1-(4-methoxyphenyl)-4-phenylbuta-1,3-dien-1-yl benzoate (7ada).



Procedure B.

Pale yellow solid 51.6 mg (62%, *Z*,*E*:*Z*,*Z* = 18:82). R_f 0.11 (SiO_2, Hexane/EtOAc = 9/1). M.p. 160 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.27 (s, 3H), 3.80 (s, 3H), 6.45 (s, 1H), 6.80 (s, 1H), 6.87 (d, J = 8.7 Hz, 2H), 7.22–7.30 (m, 5H), 7.45 (d, J = 8.7 Hz, 2H), 7.52 (t, J = 7.3 Hz, 2H), 7.64 (t, J = 7.3 Hz, 1H), 8.19 (d, J = 7.3 Hz, 2H).

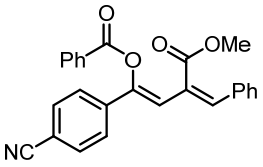
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.1, 52.3, 114.16, 114.24, 126.3, 127.2, 128.0, 128.3, 128.4, 128.7, 128.9, 129.9, 130.3, 133.8, 134.1, 135.2, 146.9, 160.2, 164.1, 169.4.

IR (KBr): 3003 w, 2944 w, 1747 s, 1732 s, 1634 m, 1600 s, 1575 m, 1510 m, 1454 m, 1430 m, 1373 m, 1313 m, 1249 s, 1121 w, 1066 m, 1023 m, 967 w, 930 w, 882m, 823 s, 763 m, 704 s, 654 m, 597 m, 467 m.

MS, *m/z* (relative intensity, %): 414 (M^+, 1), 135 (16), 105 (100), 77 (36).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{26}H_{23}O_5$: 415.1540. Found: 415.1532.

(1*Z*,3*Z*)-1-(4-Cyanophenyl)-3-(methoxycarbonyl)-4-phenylbuta-1,3-dien-1-yl benzoate (7aea).



Procedure B.

White solid 40.0 mg (53%, *Z*,*E*:*Z*,*Z* = 22:78). R_f 0.09 (SiO_2, Hexane/EtOAc = 9/1). M.p. 115 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.28 (s, 3H), 6.64 (d, J = 0.9 Hz, 1H), 6.91 (s, 1H), 7.27–7.33 (m, 5H), 7.54 (t, J = 7.6 Hz, 2H), 7.58–7.65 (m, 4H), 7.68 (tt, J = 7.6, 1.4 Hz, 1H), 8.17 (dd, J = 7.6, 1.4 Hz, 2H).

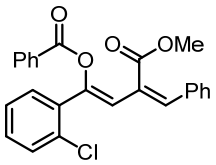
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.3, 112.1, 118.5, 119.0, 128.19, 128.23, 128.6, 128.8, 129.0, 129.2, 130.1, 130.3, 132.5, 134.3, 134.6, 137.1, 139.1, 144.8, 163.9, 168.8.

IR (KBr): 2224 w, 1735 s, 1598 w, 1451 w, 1438 w, 1246 s, 1155 m, 1080 m, 1064 s, 826 w, 757 w, 713 m, 591 w, 462 w, 437 w.

MS, *m/z* (relative intensity, %): 409 (M^+, 1), 105 (100), 77 (23).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{26}H_{20}NO_4$: 410.1387. Found: 410.1396.

(1*Z*,3*Z*)-1-(2-Chlorophenyl)-3-(methoxycarbonyl)-4-phenylbuta-1,3-dien-1-yl benzoate (7afa).



Procedure B.

White solid 60.7 mg (75%, *Z*,*E*:*Z*,*Z* = 18:82). R_f 0.20 (SiO_2, Hexane/EtOAc = 9/1). M.p. 52 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.29 (s, 3H), 6.24 (s, 1H), 6.79 (s, 1H), 7.23–7.30 (m, 7H), 7.35–7.37 (m, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.57–7.60 (m, 2H), 8.10 (d, J = 7.6 Hz, 2H).

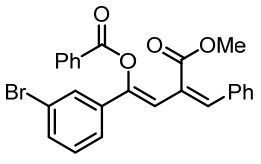
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.1, 120.3, 126.8, 128.2, 128.52, 128.58, 128.61, 128.7, 128.5, 130.0, 130.29, 130.33, 130.7, 132.3, 133.8, 134.5, 134.9, 135.5, 145.1, 163.7, 169.1.

IR (KBr): 3060 w, 2949 w, 1739 s, 1645 w, 1600 w, 1472 w, 1434 m, 1387 w, 1243 s, 1151 m, 1084 m, 1058 m, 1025 m, 968 w, 755m, 712 s, 472 m, 429 w.

MS, *m/z* (relative intensity, %): 418 (M^+, 2), 313 (18), 139 (22), 111 (11), 106 (28), 105 (100), 77 (76).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{25}H_{20}{}^{35}ClO_4$: 419.1045. Found: 419.1043.

(1*Z*,3*Z*)-1-(3-Bromophenyl)-3-(methoxycarbonyl)-4-phenylbuta-1,3-dien-1-yl benzoate (7aga).



Procedure B.

White solid 83.4 mg (90%, *Z*,*E*:*Z*,*Z* = 21:79). R_f 0.17 (SiO_2, Hexane/EtOAc = 9/1). M.p. 155 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.27 (s, 3H), 6.53 (s, 1H), 6.86 (s, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.25–7.32 (m, 5H), 7.40–7.45 (m, 2H), 7.53 (t, J = 7.6 Hz, 2H), 7.64–7.68 (m, 2H), 8.17 (d, J = 7.6 Hz, 2H).

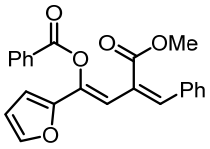
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.2, 117.2, 122.9, 123.4, 127.8, 128.2, 128.5 (overlapped two peaks), 128.7, 128.8, 129.4, 130.2, 130.3, 131.9, 134.1, 134.9, 135.9, 137.0, 145.4, 163.9, 169.0.

IR (KBr): 1737 s, 1719 s, 1639 w, 1599 w, 1559 w, 1492 w, 1451 m, 1435 m, 1245 s, 1175 w, 1152 m, 1080 s, 1065 s, 1026 m, 970 w, 887 w, 774 m, 759 m.

MS, *m/z* (relative intensity, %): 463 (M^+, 0.1), 106 (7), 105 (100), 77 (25).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{25}H_{20}{}^{79}BrO_4$: 463.0540. Found: 463.0533.

(1*Z*,3*Z*)-1-(Furan-2-yl)-3-(methoxycarbonyl)-4-phenylbuta-1,3-dien-1-yl benzoate (7aha).



Procedure B.

White solid 43.4 mg (58%, *Z*,*E*:*Z*,*Z* = 22:78). R_f 0.20 (SiO_2, Hexane/EtOAc = 9/1). M.p. 60 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.27 (s, 3H), 6.34 (d, J = 3.4 Hz, 1H), 6.40 (dd, J = 3.4, 1.8 Hz, 1H), 6.63 (s, 1H), 6.81 (s, 1H), 7.22–7.30 (m, 5H), 7.42 (d, J = 1.8 Hz, 1H), 7.52 (t, J = 7.6 Hz, 2H), 7.65 (t, J = 7.6 Hz, 1H), 8.17 (d, J = 7.6 Hz, 2H).

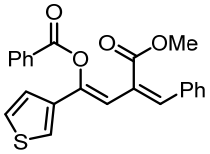
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.1, 108.4, 111.8, 114.2, 128.1, 128.5 (overlapped two peaks), 128.6, 128.7, 129.2, 130.3, 134.0, 134.8, 135.0, 137.9, 143.3, 148.7, 164.0, 169.2.

IR (KBr): 2952 w, 1736 s, 1638 m, 1600 m, 1492 w, 1451 m, 1436 m, 1243 s, 1160 w, 1083 m, 1064 m, 1023 m, 800 w, 754 m, 708 s, 499 w, 447 w, 407 m.

MS, *m/z* (relative intensity, %): 374 (M^+, 1), 105 (100), 77 (28).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{23}H_{19}O_5$: 375.1227. Found: 375.1234.

(1*Z*,3*Z*)-3-(Methoxycarbonyl)-4-phenyl-1-(thiophen-3-yl)buta-1,3-dien-1-yl benzoate (7aia).



Procedure B.

White solid 43.6 mg (56%, *Z*,*E*:*Z*,*Z* = 17:83). R_f 0.17 (SiO_2, Hexane/EtOAc = 9/1). M.p. 87 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.27 (s, 3H), 6.50 (s, 1H), 6.81 (s, 1H), 7.24–7.32 (m, 8H), 7.52 (t, J = 7.6 Hz, 2H), 7.65 (t, J = 7.6 Hz, 1H), 8.19 (d, J = 7.6 Hz, 2H).

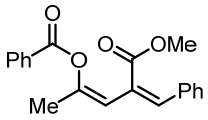
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.1, 115.4, 122.1, 124.6, 126.7, 128.1, 128.4, 128.5, 128.7, 128.8, 129.5, 130.3, 133.9, 134.5, 135.1, 136.7, 143.2, 164.1, 169.2.

IR (KBr): 3106 m, 3024 w, 2949 m, 1749 s, 1633 m, 1598 s, 1492 m, 1450 s, 1435 s, 1389 m, 1317 w, 1258 m, 1146 w, 1063 s, 1016 s, 973 w, 912 w, 840 w, 781 m.

MS, *m/z* (relative intensity, %): 390 (M^+, 1), 111 (12), 105 (100), 77 (29).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{23}H_{19}O_4S$: 391.0999. Found: 391.0998.

(2*Z*,4*Z*)-4-(Methoxycarbonyl)-5-phenylpenta-2,4-dien-2-yl benzoate (7aja).



Procedure B.

Colorless oil 27.6 mg (43%, *Z*,*E*:*Z*,*Z* =9:91). R_f 0.23 (SiO_2, Hexane/EtOAc = 9/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.17 (s, 3H), 3.22 (s, 3H), 5.84 (s, 1H), 6.62 (s, 1H), 7.20–7.29 (m, 5H), 7.47 (t, J = 7.6 Hz, 2H), 7.61 (tt, J = 7.6, 1.4 Hz, 1H), 8.08 (dd, J = 7.6, 1.4 Hz, 2H).

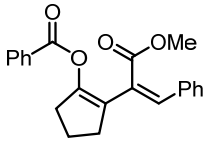
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 20.3, 52.0, 115.9, 127.9, 128.2, 128.4, 128.5, 129.1, 129.4, 130.1, 132.8, 133.6, 135.2, 147.2, 163.8, 169.3.

IR (KBr): 3062 w, 2952 w, 1733 s, 1600 w, 1494 w, 1452 m, 1435 m, 1377 w, 1325 w, 1247 s, 1164 m, 1087 m, 1066 m, 1025 w, 930 w, 755 w, 709 s.

MS, *m/z* (relative intensity, %): 322 (M^+, 0.4), 105 (100), 77 (27), 43 (11).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{20}H_{19}O_4$: 323.1278. Found: 323.1284.

(*Z*)-2-(3-Methoxy-3-oxo-1-phenylprop-1-en-2-yl)cyclopent-1-en-1-yl benzoate (7aka).



Procedure A.

White solid 58.9 mg (88%, *E*:*Z* = 7:93). R_f 0.29 (SiO_2, Hexane/EtOAc = 9/1). M.p. 141 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.10 (quin, J = 7.3 Hz, 2H), 2.71 (t, J = 8.3 Hz, 2H), 2.83 (t, J = 7.3 Hz, 2H), 3.32 (s, 3H), 6.54 (s, 1H), 7.21–7.30 (m, 5H), 7.47 (t, J = 7.3 Hz, 2H), 7.60 (t, J = 7.3 Hz, 1H), 8.08 (d, J = 7.3 Hz, 2H).

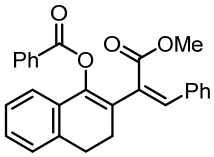
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 19.5, 30.2, 32.4, 52.1, 122.5, 127.9, 128.1, 128.4, 128.5, 128.9, 129.2, 130.1, 130.2, 133.7, 135.4, 148.8, 163.6, 169.8.

IR (KBr): 2196 w, 2847 w, 1735 s, 1725 s, 1653 m, 1600 m, 1493 w, 1438 m, 1299 m, 1246 s, 1171 s, 1089 s, 1019 m, 980 m, 903 w, 761 m, 711 s, 624 w.

MS, *m/z* (relative intensity, %): 348 (M^+, 1), 105 (100), 77 (30).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{22}H_{21}O_4$: 349.1434. Found: 349.1436.

(*Z*)-2-(3-Methoxy-3-oxo-1-phenylprop-1-en-2-yl)-3,4-dihydronaphthalen-1-yl benzoate (7ala).



Procedure B.

White solid 47.8 mg (59%, *E*:*Z* = 7:93). R_f 0.20 (SiO_2, Hexane/EtOAc = 9/1). M.p. 166 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.81 (t, *J* = 6.9 Hz, 2H), 3.04 (t, *J* = 6.9 Hz, 2H), 3.20 (s, 3H), 6.92 (s, 1H), 7.06–7.13 (m, 2H), 7.15–7.29 (m, 4H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.61 (t, *J* =7.8 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 2H).

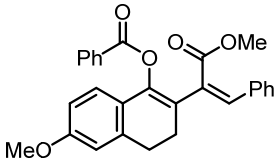
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 27.0, 27.7, 51.9, 121.8, 123.1, 126.6, 127.3, 128.0, 128.1, 128.3 (overlapped two peaks), 128.6, 128.9, 130.3, 130.5, 132.3, 132.6, 133.7, 135.6, 136.4, 143.3, 164.1, 169.5.

IR (KBr): 2945 w, 1737 s, 1719 s, 1598 m, 1486 w, 1450 m, 1434 m, 1389 w, 1293 m, 1259 s, 1244 s, 1177 m, 1127 m, 1087 s, 1021 m, 759 s, 705 s, 626 w, 497 m, 426 w.

MS, *m/z* (relative intensity, %): 410 (M^+, 2), 305 (13), 273 (12), 105 (100), 77 (34).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{27}H_{23}O_4$: 411.1591. Found: 411.1586.

(*Z*)-6-Methoxy-2-(3-methoxy-3-oxo-1-phenylprop-1-en-2-yl)-3,4-dihydronaphthalen-1-yl benzoate (7ama).



Procedure B.

Yellow solid 36.1 mg (41%, *E*:*Z* = >1:99). R_f 0.11 (SiO_2, Hexane/EtOAc = 9/1). M.p. 163 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.80 (br, 2H), 3.03 (br, 2H), 3.18 (s, 3H), 3.79 (s, 3H), 6.64 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.76 (d, *J* = 2.5 Hz, 1H), 6.88 (s, 1H), 6.70 (d, *J* = 8.6 Hz, 1H), 7.20–7.29 (m, 5H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 8.17 (d, *J* = 7.6 Hz, 2H).

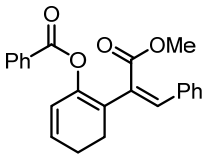
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 26.9, 28.1, 51.9, 55.3, 111.5, 113.5, 120.4, 123.3, 123.5, 128.0 (overlapped two peaks), 128.3, 128.6, 128.9, 130.3, 131.6, 132.4, 133.7, 135.8, 138.5, 143.3, 159.7, 164.1, 169.7.

IR (KBr): 3020 w, 2945 m, 2846 w, 1739 s, 1720 s, 1596 s, 1571 m, 1501 m, 1468 m, 1435 m, 1384 m, 1347 w, 1315 m, 1298 w, 1242 m, 1176 m, 1119 m, 1092 s.

MS, *m/z* (relative intensity, %): 440 (M^+, 4), 335 (13), 303 (15), 105 (100), 77 (32).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{28}H_{25}O_5$: 411.1697. Found: 441.1698.

(*Z*)-2-(3-Methoxy-3-oxo-1-phenylprop-1-en-2-yl)cyclohexa-1,5-dien-1-yl benzoate (7ana).



Procedure A.

Colorless oil 44.0 mg (60%, *E*:*Z* = 9:91). R_f 0.20 (SiO_2, Hexane/EtOAc = 9/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.44–2.50 (m, 2H), 2.69 (t, *J* = 9.4 Hz, 2H), 3.17 (s, 3H), 5.86 (dt, *J* =9.6, 1.8 Hz, 1H), 6.09 (dt, *J* = 9.6, 4.6 Hz, 1H), 6.80 (s, 1H), 7.20–7.30 (m, 5H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.58 (t, *J* = 7.6 Hz, 1H), 8.07 (d, *J* = 7.6 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 22.8, 25.8, 51.9, 118.5, 124.2, 127.9, 128.0, 128.3, 128.4, 129.0, 130.2 (overlapped two peaks), 131.2, 132.2, 133.6, 135.8, 143.4, 164.1, 169.8.

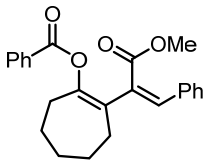
IR (KBr): 3061 w, 2951 w, 1737 s, 1714 s, 1637 w, 1600 m, 1582 w, 1493 w, 1450 m, 1432 m, 1383 w, 1316 w,

1268 s, 1250 s, 1213 m, 1112 m, 1061 m, 1023 m, 712 s, 593 w.

MS, *m/z* (relative intensity, %): 360 (M^+, 1), 255 (13), 223 (10), 105 (100), 77 (33).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{23}H_{21}O_4$: 361.1434. Found: 361.1435.

(*E*/*Z*)-2-(3-Methoxy-3-oxo-1-phenylprop-1-en-2-yl)cyclohept-1-en-1-yl benzoate (7aoa).



Procedure A.

Colorless oil 50.7 mg (65%, *E*:*Z* = 25:75). R_f 0.31 (SiO_2, Hexane/EtOAc = 9/1).

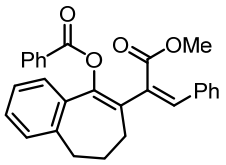
^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.72–1.84 (m, 12H, major and minor), 2.25–2.57 (m, 8H, major and minor), 3.25 (s, 3H, major), 3.78 (s, 3H, minor), 6.75 (s, 1H, major), 7.15–7.58 (m, 17H, major and minor), 7.46 (s, 1H, minor), 7.80 (d, *J* = 7.3 Hz, 2H, minor), 8.01 (d, *J* = 7.3 Hz, 2H, major).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 24.8, 26.2, 31.6, 31.9, 34.1, 51.6, 127.1, 128.0, 128.1, 128.3, 129.7, 129.8, 130.0, 133.0, 133.3, 135.9, 138.5, 151.0, 164.6, 169.4.

IR (KBr): 3097 w, 2951 m, 2846 m, 1726 s, 1649 s, 1601 m, 1452 m, 1438 s, 1397 w, 1313 m, 1267 m, 1208 m, 1129 w, 1089 s, 1020 m, 1002 w, 855 m.

MS, *m/z* (relative intensity, %): 376 (M^+, 1), 271 (17), 106 (14), 105 (100), 77 (43).

(*Z*)-8-(3-Methoxy-3-oxo-1-phenylprop-1-en-2-yl)-6,7-dihydro-5*H*-benzo[7]annulen-9-yl benzoate (7apa).



Procedure B.

Colorless oil 38.5 mg (59%, *E*:*Z* = 18:82). R_f 0.26 (SiO_2, Hexane/EtOAc = 9/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.25–2.37 (m, 4H), 2.99 (t, *J* = 6.6 Hz, 2H), 3.28 (s, 3H), 6.95 (s, 1H), 7.17–7.37 (m, 9H), 7.43 (t, *J* =7.3 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 8.07 (d, *J* = 7.3 Hz, 2H).

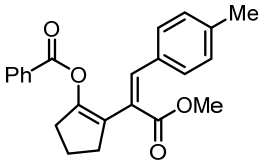
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 28.4, 31.8, 34.6, 51.8, 125.1, 125.6, 126.1, 128.1, 128.2, 128.5, 128.7, 128.9, 129.1, 129.3, 130.1, 133.1, 133.5, 135.6, 136.3, 139.8, 141.5, 143.9, 164.5, 169.6.

IR (KBr): 2945 w, 2857 w, 1736 s, 1599 w, 1490 w, 1450 m, 1434 w, 1244 s, 1215 m, 1152 w, 1113 m, 1092 m, 1059 w, 1021 w, 763 m, 709 m.

MS, *m/z* (relative intensity, %): 424 (M^+, 4), 319 (11), 105 (100), 77 (27).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{28}H_{25}O_4$: 425.1747. Found: 425.1747.

(*Z*)-2-(3-Methoxy-3-oxo-1-(*p*-tolyl)prop-1-en-2-yl)cyclopent-1-en-1-yl benzoate (7akb).



Procedure A.

White solid 57.5 mg (76%, *E*:*Z* = 8:92). R_f 0.31 (SiO_2, Hexane/EtOAc = 9/1). M.p. 133 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.09 (quin, *J* = 7.3 Hz, 2H), 2.31 (s, 3H), 2.70 (t, *J* = 7.3 Hz, 2H), 2.82 (t, *J* = 7.3 Hz, 2H), 3.33 (s, 3H), 6.50 (s, 1H), 7.08 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.60 (t, *J* = 7.6 Hz, 1H), 8.08 (dd, *J* = 7.6, 1.1 Hz, 2H).

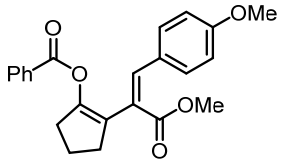
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 19.5, 21.2, 30.2, 32.4, 52.1, 122.6, 127.9, 128.2, 128.5, 129.0, 129.2, 130.1, 130.2, 132.5, 133.6, 138.1, 148.4, 163.6, 167.0.

IR (KBr): 2951 m, 2921 w, 1732 s, 1687 w, 1654 m, 1600 m, 1491 w, 1450 m, 1438 m, 1387 w, 1314 m, 1266 s, 1201 s, 1090 s, 1039 m, 979 m, 878 m, 813 m, 715 s, 542 w, 498 m, 418 w.

MS, *m/z* (relative intensity, %): 362 (M^+, 2), 105 (100), 77 (25).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{23}H_{23}O_4$: 363.1591. Found: 363.1585.

(*Z*)-2-(3-Methoxy-1-(4-methoxyphenyl)-3-oxoprop-1-en-2-yl)cyclopent-1-en-1-yl benzoate (7akc).



Procedure A.

White solid 57.9 mg (73%, *E*:*Z* = 7:93). R_f 0.20 (SiO_2, Hexane/EtOAc = 9/1). M.p. 109 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.09 (quin, *J* = 7.3 Hz, 2H), 2.70 (t, *J* = 7.3 Hz, 2H), 2.82 (t, *J* = 7.3 Hz, 2H), 3.34 (s, 3H), 3.79 (s, 3H), 6.47 (s, 1H), 6.81 (d, *J* = 8.7 Hz, 2H), 7.20 (d, *J* = 8.7 Hz, 2H), 7.47 (t, *J* = 7.3 Hz, 2H), 5.60 (t, *J* = 7.3 Hz, 1H), 8.09 (d, *J* = 7.3 Hz, 2H).

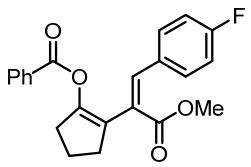
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 19.5, 30.3, 32.4, 52.1, 55.2, 113.9, 122.7, 127.2, 128.0, 128.5, 129.0, 129.5, 129.7, 130.2, 133.6, 148.0, 159.5, 163.6, 170.1.

IR (KBr): 3015 w, 2968 m, 2848 m, 1736 s, 1637 m, 1598 s, 1511 s, 1442 m, 1392 w, 1209 m, 1262 s, 1189 s, 1120 w, 1090 s, 10223 s, 903 w, 828 s, 765 w, 705 s.

MS, *m/z* (relative intensity, %): 378 (M^+, 3), 241 (22), 171 (12), 105 (100), 77 (33).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{23}H_{23}O_5$: 379.1540. Found: 379.1538.

(*Z*)-2-(1-(4-Fluorophenyl)-3-methoxy-3-oxoprop-1-en-2-yl)cyclopent-1-en-1-yl benzoate (7akd).



Procedure A.

White solid 48.4 mg (66%, *E*:*Z* = >1:99). R_f 0.29 (SiO_2, Hexane/EtOAc = 9/1). M.p. 83 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.10 (quin, J = 7.3 Hz, 2H), 2.70 (t, J = 7.3 Hz, 2H), 2.83 (t, J = 7.3 Hz, 2H), 3.32 (s, 3H), 6.49 (s, 1H), 6.97 (tt, J = 8.7, 1.8 Hz, 2H), 7.22–7.25 (m, 2H), 7.47 (t, J = 7.3 Hz, 2H), 7.61 (tt, J = 7.3, 1.3 Hz, 1H), 8.08 (d, J = 7.3 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 19.5, 30.2, 32.4, 52.1, 115.5 (d, J = 21.1 Hz), 122.4, 128.6, 128.8, 128.9, 129.1, 129.7 (d, J = 8.6 Hz), 130.2, 131.6 (d, J = 3.8 Hz), 133.7, 148.9, 162.4 (d, J = 248.2 Hz), 163.6, 169.6.

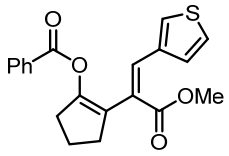
^{19}F NMR ($CDCl_3$, 376 MHz) δ: −116.0.

IR (KBr): 2953 w, 1732 s, 1651 w, 1599 w, 1508 w, 1440 w, 1308 w, 1264 m, 1206 m, 1090 m, 1069 w, 875 w, 841 w, 714 m, 465 m, 448 s, 417 s.

MS, *m/z* (relative intensity, %): 366 (M^+, 1), 106 (11), 105 (100), 77 (28).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{22}H_{20}FO_4$: 367.1340. Found: 367.1334.

(*Z*)-2-(3-Methoxy-3-oxo-1-(thiophen-3-yl)prop-1-en-2-yl)cyclopent-1-en-1-yl benzoate (7ake).



Procedure A.

White solid 54.8 mg (71%, *E*:*Z* = 10:90). R_f 0.29 (SiO_2, Hexane/EtOAc = 9/1). M.p. 160 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.09 (quin, J = 7.3 Hz, 2H), 2.68 (t, J = 7.3 Hz, 2H), 2.82 (t, J = 7.3 Hz, 2H), 3.38 (s, 3H), 6.49 (s, 1H), 7.01 (d, J = 5.0 Hz, 1H), 7.23–7.25 (m, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.61 (t, J = 7.6 Hz, 1H), 8.09 (d, J = 7.6 Hz, 2H).

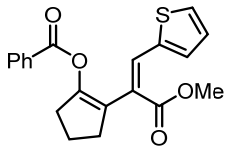
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 19.4, 30.0, 32.4, 52.2, 122.4, 123.7, 124.9, 125.9, 126.9, 127.6, 128.6, 128.9, 130.2, 133.7, 136.6, 148.5, 163.6, 170.0.

IR (KBr): 2952 w, 2848 w, 1724 s, 1651 m, 1600 m, 1451 m, 1439 m, 1309 m, 1246 s, 1189 m, 1086 s, 1019 m, 1002 w, 879 m, 836 w, 781 m, 709 s, 631 m, 453 w.

MS, *m/z* (relative intensity, %): 354 (M^+, 2), 217 (11), 106 (28), 105 (100), 77 (61).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{20}H_{19}O_4S$: 355.0999. Found: 355.1003.

(*Z*)-2-(3-Methoxy-3-oxo-1-(thiophen-2-yl)prop-1-en-2-yl)cyclopent-1-en-1-yl benzoate (7akf).



Procedure A.

Pale yellow solid 29.8 mg (41%, *E*:*Z* = 6:94). R_f 0.31 (SiO_2, Hexane/EtOAc = 9/1). M.p. 157 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.09 (quin, J = 7.6 Hz, 2H), 2.68 (t, J = 7.6 Hz, 2H), 2.83 (t, J = 7.6 Hz, 2H), 3.45 (s, 3H), 6.61 (s, 1H), 6.97 (dd, J = 4.8, 3.4 Hz, 1H), 7.06 (d, J = 3.4 Hz, 1H), 7.27 (d, J = 4.8 Hz, 1H), 4.89 (t, J = 7.6 Hz, 2H), 7.62 (tt, J = 7.6, 1.4 Hz, 1H), 8.09 (dd, J = 7.6, 1.4 Hz, 2H).

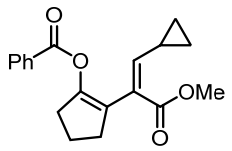
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 19.4, 30.0, 32.4, 52.4, 122.3, 122.5, 126.3, 127.21, 127.25, 128.6, 128.9, 129.4, 130.2, 133.7, 138.3, 148.7, 163.6, 169.4.

IR (KBr): 3097 m, 2952 m, 2908 w, 1725 s, 1650 s, 1600 m, 1452 s, 1438 s, 1399 w, 1362 w, 1305 w, 1268 m, 1207 m, 1173 m, 1129 w, 1089 m, 1038 m.

MS, *m/z* (relative intensity, %): 354 (M^+, 1), 105 (100), 77 (26).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{20}H_{19}O_4S$: 355.0999. Found: 355.0996.

(*Z*)-2-(1-Cyclopropyl-3-methoxy-3-oxoprop-1-en-2-yl)cyclopent-1-en-1-yl benzoate (7akg).



Procedure A.

Colorless oil 46.0 mg (73%, *E*:*Z* = 15:85). R_f 0.29 (SiO_2, Hexane/EtOAc = 9/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.46–0.50 (m, 2H), 0.88 (td, *J* = 7.3, 4.7 Hz, 2H), 1.72–1.81 (m, 1H), 2.02 (quin, *J* = 7.3 Hz, 2H), 2.50 (t, *J* = 7.3 Hz, 2H), 2.75 (t, *J* = 7.3 Hz, 2H), 3.44 (s, 3H), 5.08 (d, *J* = 11.0 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 8.06 (d, *J* = 7.6 Hz, 2H).

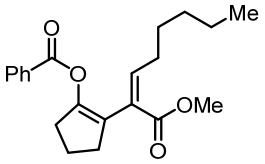
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 8.6, 12.0, 19.6, 30.4, 31.9, 51.7, 122.3, 126.6, 128.5, 129.1, 130.0, 133.5, 141.6, 145.6, 163.8, 169.0.

IR (KBr): 3006 w, 2952 w, 1725 s, 1602 w, 1451 m, 1436 w, 1316 w, 1251 m, 1201 m, 1175 m, 1093 m, 1051 w, 1023 m, 946 w, 711 s.

MS, *m/z* (relative intensity, %): 312 (M^+, 1), 106 (11), 105 (100), 77 (31).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{19}H_{21}O_4$: 313.1434. Found: 313.1433.

(*Z*)-2-(1-Methoxy-1-oxooct-2-en-2-yl)cyclopent-1-en-1-yl benzoate (7akh).



Procedure A.

Colorless oil 19.9 mg (30%, *E*:*Z* = >1:99). R_f 0.49 (SiO_2, Hexane/EtOAc = 9/1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.85 (t, *J* = 6.9 Hz, 3H), 1.23–1.29 (m, 4H), 1.39 (quin, *J* = 7.3 Hz, 2H), 2.03 (quin, *J* = 7.6 Hz, 2H), 2.12 (q, *J* = 7.3 Hz, 2H), 2.56 (t, *J* = 7.6 Hz, 2H), 2.76 (t, *J* = 7.6 Hz, 2H), 3.38 (s, 3H), 5.69 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 8.07 (d, *J* = 7.6 Hz, 2H).

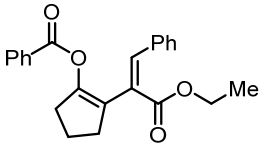
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 13.9, 19.5, 22.4, 28.9, 29.4, 30.1, 31.3, 31.9, 51.6, 122.2, 128.5, 129.0, 129.1, 130.1, 133.6, 135.1, 146.3, 163.7, 169.1.

IR (KBr): 2954 m, 2858 w, 1734 s, 1602 w, 1452 m, 1316 w, 1262 s, 1252 s, 1175 w, 1093 w, 1068 w, 1023 w, 711 s.

MS, *m/z* (relative intensity, %): 342 (M^+, 1), 106 (16), 105 (100), 77 (33).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{21}H_{27}O_4$: 343.1904. Found: 343.1892.

(*Z*)-2-(3-Ethoxy-3-oxo-1-phenylprop-1-en-2-yl)cyclopent-1-en-1-yl benzoate (7aki).



Procedure A.

White solid 51.2 mg (74%, *E*:*Z* = 6:94). R_f 0.29 (SiO_2, Hexane/EtOAc = 9/1). M.p. 128 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.88 (t, *J* = 7.3 Hz, 3H), 2.10 (quin, *J* = 7.3 Hz, 2H), 2.71 (t, *J* = 7.3 Hz, 2H), 2.83 (t, *J* = 7.3 Hz, 2H), 3.73 (q, *J* = 7.3 Hz, 2H), 6.54 (s, 1H), 7.22–7.28 (m, 5H), 7.46 (t, *J* = 7.3 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 8.08 (d, *J* = 7.3 Hz, 2H).

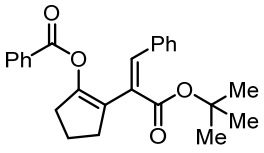
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 13.4, 19.5, 30.2, 32.4, 61.2, 122.5, 128.0, 128.1, 128.3, 128.5, 129.0, 129.6, 129.9, 130.1, 133.7, 135.5, 148.7, 163.6, 169.3.

IR (KBr): 3060 w, 2988 m, 2849 m, 1734 s, 1718 s, 1648 m, 1598 m, 1496 w, 1448 m, 1385 w, 1300 m, 1246 s, 1174 s, 1090 s, 1018 s, 920 w, 855 w, 758 m, 855 w, 758 m, 713 s, 623 w, 572 m, 449 w.

MS, *m/z* (relative intensity, %): 362 (M^+, 1), 105 (100), 77 (23).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{23}H_{23}O_4$: 363.1591. Found: 363.1590.

(*Z*)-2-(3-(*tert*-Butoxy)-3-oxo-1-phenylprop-1-en-2-yl)cyclopent-1-en-1-yl benzoate (7akj).



Procedure A.

White solid 31.6 mg (41%, *E*:*Z* = 7:93). R_f 0.37 (SiO_2, Hexane/EtOAc = 9/1). M.p. 122 ºC.

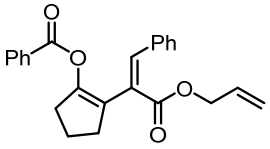
^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.08 (s, 9H), 2.06 (quin, *J* = 7.3 Hz, 2H), 2.69 (t, *J* = 7.3 Hz, 2H), 2.80 (t, *J* = 7.3 Hz, 2H), 6.66 (s, 1H), 7.21–7.32 (m, 5H), 7.43 (t, *J* = 7.3 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 8.08 (d, *J* = 7.3 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 19.4, 27.7, 31.1, 32.5, 81.8, 122.0, 127.6, 128.0, 128.3, 128.4, 129.5, 130.3, 130.7, 131.4, 133.4, 136.2, 148.3, 164.0, 167.5.

IR (KBr): 3071 w, 2935 m, 2851 m, 1734 s, 1651 s, 1599 m, 1494 m, 1451 s, 1393 m, 1367 m, 1317 w, 1261 m, 1179 w, 1144 w, 1093 w.

HRMS (DART+, $[M+H]^+$) Calcd for $C_{25}H_{27}O_4$: 391.1904. Found: 391.1904.

(*Z*)-2-(3-(Allyloxy)-3-oxo-1-phenylprop-1-en-2-yl)cyclopent-1-en-1-yl benzoate (7akk).



Procedure A.

White solid 43.8 mg (61%, *E*:*Z* = 11:89). R_f 0.43 (SiO_2, Hexane/EtOAc = 9/1). M.p. 98 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.10 (quin, *J* = 7.6 Hz, 2H), 2.71 (t, *J* = 7.6 Hz, 2H), 2.84 (t, *J* = 7.6 Hz, 2H), 4.17

(d, *J* = 6.0 Hz, 2H), 4.90 (dd, *J* = 16.3, 1.4 Hz, 1H), 4.98 (dd, *J* =10.5, 1.4 Hz, 1H), 5.53 (ddt, *J* = 16.3, 10.5, 6.0 Hz, 1H), 6.55 (s, 1H), 7.22–7.28 (m, 5H), 7.47 (t, *J* = 7.9 Hz, 2H), 7.60 (t, *J* = 7.9 Hz, 1H), 8.08 (dd, *J* = 7.9, 1.3 Hz, 2H).

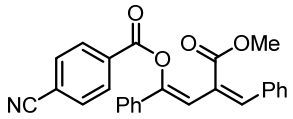
^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 19.5, 30.2, 32.4, 65.9, 118.9, 122.5, 128.0, 128.1, 128.4, 128.5, 129.0, 129.3, 130.2 (overlapped two peaks), 131.0, 133.7, 135.4, 148.8, 163.5, 169.0.

IR (KBr): 2951 w, 1736 s, 1650 m, 1600 w, 1494 w, 1446 m, 1397 m, 1316 m, 1253 m, 1204 w, 1094 s, 1038 m, 977 w, 946 m, 846 w, 800 w, 756 m, 710 s, 696 s, 618 w, 563 w.

MS, *m/z* (relative intensity, %): 374 (M^+, 0.5), 105 (100), 77 (25).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{24}H_{23}O_4$: 375.1591. Found: 375.1593.

(1*Z*,3*Z*)-3-(Methoxycarbonyl)-1,4-diphenylbuta-1,3-dien-1-yl 4-cyanobenzoate (7bba).



Procedure B.

White solid 42.1 mg (51%, *Z*,*E*:*Z*,*Z* = 30:70). R_f 0.40 (SiO_2, Hexane/EtOAc = 3/1). M.p. 148 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.30 (s, 3H), 6.56 (s, 1H), 6.86 (s, 3H), 7.25–7.34 (m, 8H), 7.47–7.49 (m, 2H), 7.83 (d, *J* = 8.2 Hz, 2H), 8.28 (d, *J* = 8.2 Hz, 2H).

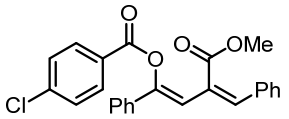
^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 52.1, 116.2, 117.3, 117.7, 124.7, 128.1, 128.6, 128.7, 128.8, 129.3 (overlapped two peaks), 130.6, 132.5, 132.7, 134.2, 134.9, 135.8, 146.5, 162.5, 169.2.

IR (KBr): 2229 m, 1756 s, 1729 s, 1635 w, 1490 w, 1444 m, 1432 m, 1372 w, 1250 s, 1209 w, 1152 m, 1071 s, 1018 m, 883 w, 851 w, 761 s, 697 s, 662 m, 560 w, 525 m.

MS, *m/z* (relative intensity, %): 409 (M^+, 2), 279 (13), 247 (11), 131 (11), 130 (99), 115 (14), 105 (100), 102 (45), 77 (53), 51 (12).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{26}H_{20}NO_4$: 410.1387. Found: 410.1388.

(1*Z*,3*Z*)-3-(Methoxycarbonyl)-1,4-diphenylbuta-1,3-dien-1-yl 4-chlorobenzoate (7cba).



Procedure B.

White solid 45.8 mg (55%, *Z*,*E*:*Z*,*Z* = 22:78). R_f 0.29 (SiO_2, Hexane/EtOAc = 9/1). M.p. 141 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.32 (s, 3H), 6.55 (s, 1H), 6.84 (s, 1H), 7.25–7.37 (m, 8H), 7.48–7.51 (m, 4H), 8.12 (d, *J* = 8.7 Hz, 2H).

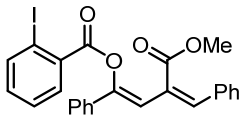
^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 52.2, 116.1, 124.7, 127.2, 128.1, 128.5, 128.6, 128.8, 129.1 (overlapped two peaks), 129,6, 131.6, 134.5, 135.0, 135.3, 140.5, 146.7, 163.2, 169.2.

IR (KBr): 3041 w, 2951 w, 1743 s, 1643 m, 1593 s, 1489 s, 1444 m, 1433 m, 1377 m, 1312 w, 1237 w, 1248 m, 1212 m, 1177 m, 1147 m, 1089 s, 1015 m, 976 m, 927 w, 893 m, 854 s.

MS, *m/z* (relative intensity, %): 418 (M^+, 1), 141 (31), 139 (100), 111 (17), 105 (25), 77 (20).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{25}H_{20}{}^{35}ClO_4$: 419.1045. Found: 419.1055.

(1*Z*,3*Z*)-3-(Methoxycarbonyl)-1,4-diphenylbuta-1,3-dien-1-yl 2-iodobenzoate (7dba).



Procedure B.

White solid 51.0 mg (46%, *Z*,*E*:*Z*,*Z* = 13:87). R_f 0.48 (SiO_2, Hexane/EtOAc = 3/1). M.p. 100 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.25 (s, 3H), 6.49 (s, 1H), 6.81 (s, 1H), 7.20–7.37 (m, 9H), 7.49 (t, J = 7.8 Hz, 1H), 7.54 (d, J = 7.3 Hz, 2H), 8.01 (d, J = 7.8 Hz, 1H), 8.24 (dd, J = 7.8, 1.4 Hz, 1H).

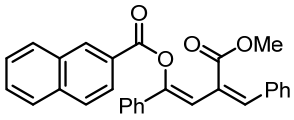
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.0, 95.7, 116.2, 124.9, 128.1, 128.50, 128.53, 128.7, 129.0, 129.6, 130.3, 131.8, 132.4, 133.8, 134.5, 135.0, 135.1, 142.5, 146.9, 162.7, 169.2.

IR (KBr): 3059 w, 2948 w, 1748 s, 1715 s, 1580 m, 1493 m, 1433 m, 1266 m, 1230 s, 1203 m, 1127 m, 1080 s, 1043 m, 1014 m, 908 w, 760 m, 738 s, 692 m, 640 w, 526 w, 445 w.

MS, *m/z* (relative intensity, %): 510 (M^+, 1), 231 (100), 203 (18), 115 (14), 105 (63), 77 (58), 76 (41), 73 (13), 50 (13), 44 (11).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{25}H_{20}IO_4$: 511.0401. Found: 511.0398.

(1*Z*,3*Z*)-3-(Methoxycarbonyl)-1,4-diphenylbuta-1,3-dien-1-yl 2-naphthoate (7eba).



Procedure B.

White solid 71.7 mg (81%, *Z*,*E*:*Z*,*Z* = 15:85). R_f 0.49 (SiO_2, Hexane/EtOAc = 3/1). M.p. 161 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.23 (s, 3H), 6.57 (d, J = 0.9 Hz, 1H), 6.5 (s, 1H), 7.21–7.36 (m, 8H), 7.53–7.65 (m, 4H), 7.91 (d, J = 8.2 Hz, 1H), 7.94 (d, J = 8.7 Hz, 1H), 8.00 (d, J = 7.8 Hz, 1H), 8.16 (dd, J = 8.7, 1.8 Hz, 1H), 8.78 (s, 1H).

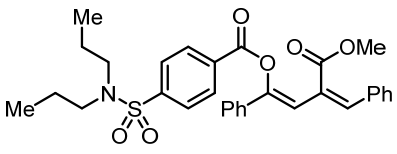
^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.2, 116.1, 124.9, 125.4, 126.0, 127.0, 127.8, 128.1, 128.5 (overlapped two peaks), 128.6, 128.7, 128.8, 129.0, 129.6, 129.9, 132.1, 132.5, 134.7, 135.0, 135.1, 135.9, 147.1, 164.2, 169.3.

IR (KBr): 2952 w, 1743 s, 1725 s, 1630 s, 1597 m, 1506 w, 1491 m, 1467 m, 1446 m, 1436 m, 1381 s, 1270 s, 1261 m, 1214 m, 1185 s, 1156 s, 1132 m, 1073 s, 1030 w, 948 m, 926 w, 896 m, 835 w.

MS, *m/z* (relative intensity, %): 434 (M^+, 1), 156 (12), 155 (100), 127 (51), 105 (16), 77 (19).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{29}H_{23}O_4$: 435.1591. Found: 435.1594.

(1*Z*,3*Z*)-3-(Methoxycarbonyl)-1,4-diphenylbuta-1,3-dien-1-yl 4-(*N*,*N*-dipropylsulfamoyl)benzoate (7fba).



Procedure B.

White solid 97.2 mg (86%, *Z*,*E*:*Z*,*Z* = 30:70). R_f 0.37 (SiO_2, Hexane/EtOAc = 3/1). M.p. 148 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.88 (t, J = 7.3 Hz, 6H), 1.57 (sext, J = 7.3 Hz, 4H), 3.13 (t, J = 7.3 Hz, 4H), 3.28 (s, 3H), 6.56 (s, 1H), 6.86 (s, 1H), 7.25–7.39 (m, 8H), 7.50 (dd, J = 7.8, 1.8 Hz, 2H), 7.95 (d, J = 8.2 Hz, 2H), 8.29 (d, J = 8.7 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 11.1, 21.9, 49.9, 52.1, 116.2, 124.8, 127.3, 128.1, 128.5, 128.7, 128.8, 129.2, 129.4, 130.8, 132.1, 134.3, 134.9, 135.7, 145.2, 146.6, 162.8, 169.2.

IR (KBr): 2962 m, 2872 m, 1746 s, 1733 s, 1596 s, 1733 s, 1596 w, 1491 w, 1468 m, 1395 m, 1342 m, 1249 m, 1209 w, 1172 m, 1154 s, 1078 s, 1002 s, 903 w, 869 w, 858 w, 776 m, 757 s, 689 s.

MS, *m/z* (relative intensity, %): 547 (M^+, 8), 279 (29), 270 (11), 269 (15), 268 (100), 105 (41), 104 (10).

HRMS (EI+, M^+) Calcd for $C_{31}H_{33}NO_6S$: 547.2029. Found: 547.2028.

V. Control Experiments

• Using 1,3-Diketone 8aa

In a glovebox filled with nitrogen, 1,3-diketone **8aa** (60.7 mg, 0.30 mmol), alkyne **6a** (32.0 mg, 0.20 mmol), PCy_3 (16.8 mg, 0.06 mmol) and toluene (1.0 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The mixture was stirred at room temperature for 20 h. No reaction occurred.

• Using Enol Ester 9aa

In a glovebox filled with nitrogen, enol ester **9aa** (60.7 mg, 0.30 mmol), alkyne **6a** (32.0 mg, 0.20 mmol), PCy_3 (16.8 mg, 0.06 mmol) and toluene (1.0 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The mixture was stirred at room temperature for 20 h. No reaction occurred.

Monofluoroalkene **10ba**, which can also be formed by phosphine-catalyzed carbofluorination between acyl fluoride **4b** and alkynoate **6a**, is a potential intermediate in this three-component coupling. However, the desired product **7bba** was not formed from **10ba** under these reaction conditions, ruling out the involvement of **10ba**.

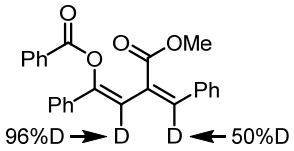
• Using Monofluoroalkene 10ba

In a glovebox filled with nitrogen, monofluoroalkene **10ba** (36.7 mg, 0.10 mmol, E:Z = 45:55), silyl enol ether **5b** (61.4 μL, 0.30 mmol), PCy_3 (8.4 mg, 0.03 mmol) and toluene (0.5 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The mixture was stirred at room temperature for 20 h. No reaction occurred.

• Deuterium-Labeling Experiment

In a glovebox filled with nitrogen, the acyl fluoride **4a** (64.8 μL, 0.60 mmol), silyl enol ether **5b**-d_2 (117 mg, 0.60 mmol), alkyne **6a** (32.0 mg, 0.20 mmol), PCy_3 (16.8 mg, 0.06 mmol) and toluene (1.0 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The mixture was stirred at room temperature for 20 h. Yield of **7aba**-d_2 was determined by ^{1}H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard (76%, Z,E:Z,Z = 15:85). Deuterium content of (Z,Z)-**7aba**-d_2 at the 2,4-positions were determined by ^{1}H NMR spectroscopy. Deuterium content of (Z,E)-**7aba**-d_2 were not able to determined due to overlapping with other peaks in the aromatic region.

(1*Z*,3*Z*)-3-(methoxycarbonyl)-1,4-diphenylbuta-1,3-dien-1-yl-2,4-d_2 benzoate (7aba-d_2).



Procedure B.

White solid (76%, *E*:*Z* = 15:85). R_f 0.23 (SiO_2, Hexane/EtOAc = 9/1). M.p. 136 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.27 (s, 3H), 6.53 (s, 0.04H), 6.82 (s, 0.5H), 7.23–7.35 (m, 8H), 7.50 (t, J = 7.6 Hz, 4H), 7.63 (t, J = 7.6 Hz, 1H), 8.18 (d, J = 7.6 Hz, 2H).

^{2}H NMR ($CHCl_3$, 400 MHz) δ: 6.58 (s, 1D), 6.87 (s, 0.5D).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 52.1, 115.7 (br), 124.8, 128.1, 128.5 (overlapped two peaks), 128.7 (overlapped two peaks), 128.8, 129.0, 129.7, 130.3, 133.9, 134.6, 134.9 (br), 135.0, 135.1, 146.9, 164.0, 169.2.

IR (KBr): 3060 w, 2948 w, 1742 s, 1718 s, 1626 m, 1600 m, 1573 w, 1490 m, 1434 m, 1369 m, 1317 w, 1265 m, 1200 m, 1168 m, 1086 s, 1071 s, 1026 m, 999 w.

MS, *m/z* (relative intensity, %): 386 (M^+, 0.4), 105 (100), 77 (34).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{25}H_{18}O_4D_2$: 386.14816. Found: 386.14914.

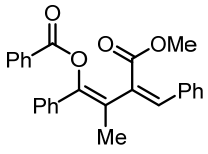
• Isomerization of (*Z*,*Z*)-7aba

In a glovebox filled with nitrogen, (*Z*,*Z*)-**7aba** (38.4 mg, 0.10 mmol), PCy_3 (8.4 mg, 0.03 mmol) and toluene (0.5 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The mixture was stirred at room temperature for 20 h. No reaction occurred.

• Using Silyl Enol Ether 5q

In a glovebox filled with nitrogen, the acyl fluoride **4a** (64.8 μL, 0.60 mmol), silyl enol ether **5q** (123.8 mg, 0.60 mmol), alkyne **6a** (32.0 mg, 0.20 mmol), PCy_3 (16.8 mg, 0.06 mmol) and toluene (1.0 mL) were added to a 5 mL vial with a Teflon-sealed screwcap. The mixture was stirred at room temperature for 20 h. This mixture was then evaporated to dryness, and the residue was purified by flash column chromatography using hexane/EtOAc = 9/1 as the eluent to give **7aqa** as a white solid (29.1 mg, 36%, *Z*,*E*:*Z*,*Z* = 40:60). (*Z*,*Z*)-isomer was isolated by recrystallization from $CHCl_3$ and hexane. Some of these crystals were suitable for X-ray analysis.

(1*Z*,3*Z*)-3-(Methoxycarbonyl)-2-methyl-1,4-diphenylbuta-1,3-dien-1-yl benzoate (7aqa).



Procedure A.

White solid 29.1 mg (36%, *Z*,*E*:*Z*,*Z* = 40:60). R_f 0.20 (SiO_2, Hexane/EtOAc = 9/1). M.p. 251 ºC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.14 (s, 3H), 3.24 (s, 3H), 6.94 (s, 1H), 7.21–7.43 (m, 10H), 7.52–7.56 (m, 3H), 8.04 (d, J = 7.3 Hz, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ: 18.1, 51.8, 121.9, 128.1 (overlapped two peaks), 128.1, 128.2, 128.4, 128.6, 129.0, 129.3, 130.1, 133.3, 133.4, 133.9, 135.6, 135.8, 145.0, 164.3, 169.6.

IR (KBr): 3029 w, 2950 m, 1744 s, 1717 m, 1616 w, 1596 m, 1488 m, 1434 m, 1390 m, 1366 m, 1314 w, 1241 s, 1179 m, 1094 s, 1060 m, 957 m, 928 w, 879 m, 836 w.

MS, *m/z* (relative intensity, %): 398 (M^+, 1), 105 (100), 77 (29).

HRMS (DART+, $[M+H]^+$) Calcd for $C_{26}H_{23}O_4$: 399.1591. Found: 399.1592.

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Conclusion

The reaserch reported in this thesis focused on the development of organophosphorus synthesis via C–P bond cleavage and catalytic reactions using a fluorophosphorane platform.

In chapter 1, nickel-catalyzed cyclization of bisphosphines to diverse phosphole derivatives via the cleavage of two C–P bonds was described. The method features nickel-catalyzed C–P bond cleavage, which allows for the transformation of stable sp^3 C–P bonds. Detailed studies related to the mechanism of this reaction revealed that the phospha-nickelacycle is a key intermediate.

In chapter 2, a method for the aryne-mediated dearylative anulation of triarylphosphines to diverse phosphole derivatives was described. Detailed studies related to the mechanism of this reaction revealed that the fluorophosphorane is a key intermediate. The advantages of this method over reported methods include transition metal-free, mild conditions and intermolecular annulation, allowing the synthesis of various fluorinated dibenzophosphole derivatives in a convergent manner.

In chapter 3, phosphine-catalyzed carbofluorination of alkynes via a fluorophosphorane was described. The method features first example of intermolecular carbofluorination of alkynes and operates under mild conditions and in the absence of metals, thus showing a wide functional group tolerance. DFT calculations revealed that a C–F bond is formed via ligand coupling on a fluorophosphorane intermediate.

In chapter 4, phosphine-catalyzed hydrovinylation of alkynes via a fluorophosphorane was described. The key feature of this reaction is ligand metathesis on the fluorophosphorane platform, which allows for the bond formation between polarity mismatched sites to form anti-Michael-type adducts. This study demonstrates the potential utility of a P(III)/P(V) manifold as a viable alternative to transition metal-mediated catalytic cycles consisting of oxidative addition, transmetalation and reductive elimination.

List of Publications

1. **Fujimoto, H.**; Kusano, M.; Kodama, T.; Tobisu, M.
Cyclization of Bisphosphines to Phosphacycles via the Cleavage of Two Carbon–Phosphorus Bonds by Nickel Catalysis.
Org. Lett. **2019**, *21*, 4177–4181.
2. **Fujimoto, H.**; Kusano, M.; Kodama, T.; Tobisu, M.
Aryne-Induced S_NAr/Dearylation Strategy for the Synthesis of Fluorinated Dibenzophospholes from Triarylphosphines via a P(V) intermediate.
Org. Lett. **2020**, *22*, 2293–2297.
3. **Fujimoto, H.**; Kodama, T.; Yamanaka, M.; Tobisu, M.
Phosphine-Catalyzed Intermolecular Acylfluorination of Alkynes via a P(V) Intermediate.
J. Am. Chem. Soc. **2020**, *142*, 17323–17328.
4. **Fujimoto, H.**; Kusano, M.; Kodama, T.; Tobisu, M.
Three-Component Coupling of Acyl Fluorides, Silyl Enol Ethers, and Alkynes by P(III)/P(V) Catalysis.
J. Am. Chem. Soc. **2021**, *143*, 18394–18399.

Supplementary List of Publications

1. Amaya, T.; **Fujimoto, H.**; Tanaka, T.; Moriuchi, T.
Synthesis and Isomerization Behavior of a Macrocycle with Four Photoresponsive Moieties.
Org. Lett. **2018**, *20*, 2055–2058.
2. Amaya, T.; **Fujimoto, H.**; Moriuchi, T.
Iron(III) nitrate-induced aerobic and catalytic oxidative cleavage of olefins.
Tetrahedron Lett. **2018**, *59*, 2657–2660.
3. Nishizawa, A.; Takahira, T.; Yasui, K.; **Fujimoto, H.**; Iwai, T.; Sawamura, M.; Chatani, N.; Tobisu, M.
Nickel-Catalyzed Decarboxylation of Aryl Carbamates for Converting Phenols into Aromatic Amines.
J. Am. Chem. Soc. **2019**, *141*, 7261–7265.
4. Yasui, K.; Kamitani, M.; **Fujimoto, H.**; Tobisu, M.
The Effect of the Leaving Group in N-Heterocyclic Carbene-Catalyzed Nucleophilic Aromatic Substitution Reactions.
Bull. Chem. Soc. Jpn. **2020**, *93*, 1424–1429.
5. Yasui, K.; Kamitani, M.; **Fujimoto, H.**; Tobisu, M.
N-Heterocyclic Carbene-Catalyzed Truce–Smiles Rearrangement of *N*-Arylacrylamides via the Cleavage of Unactivated C(aryl)–N Bonds.
Org. Lett. **2021**, *23*, 1572–1576.
6. Tobisu, M.; Kodama, T.; **Fujimoto, H.**
Synthetic Applications of C–O and C–E Bond Activation Reactions.
Comprehensive Organometallic Chemistry IV. **2021** (DOI: 10.1016/B978-0-12-820206-7.00089-5).