Doctoral Dissertation

Studies on Synthesis of Phosphorus-Containing Heterocycles through C-H Bond Cleavage

Yuto Unoh

January 2017

Graduate School of Engineering

Osaka University

Preface and Acknowledgements

This thesis describes the studies that were carried out under the guidance of Professor Masahiro Miura at Department of Applied Chemistry, Graduate School of Engineering of Osaka University from April 2011 to March 2017. This study is concerned with the synthesis of phosphorus-containing heterocycles by C-H bond functionalization.

To complete these studies, there are indispensable contributions from many people with their so kind helps, supports, and encouragements. Here, the author wishes to express my gratitude for them.

First and foremost, the author would particularly like to thank Professor Masahiro Miura for his great guidance and support. With his thoughtful encouragements and suggestion, the author really enjoyed chemistry. In addition, the author also thanks him for providing many chances to join symposiums and study abroad. They are very big stimulus for the life of author.

The author is also very grateful to Professor Nobuaki Kambe and Professor Naoto Chatani for the invaluable discussion and suggestion.

The author deeply appreciates Professor Tetsuya Satoh in Osaka City University for his constant advice and support. The author's academic career is not always smooth. Whenever the author faced difficulties, he always encouraged me with unlimited patience.

It is great pleasure to thank Associate Professor Koji Hirano for his countless instructive and crucial suggestions. His innovative proposals always reminded the author of the new aspects of my research. The author owes lots of gratitude to Assistant professor Yuji Nishii for valuable advice and discussion.

The author also would like to express my appreciation to Ms. Noriko Fujimoto and Ms. Kiyomi Lee for their kind helps and supports.

Special thanks to the former and present members of Miura group: Dr. Naoto Matsuyama, Mr. Yoshiro Oda, Mr. Shinya Ota, Mr. Keisuke Morimoto, Mr. Tomoyuki Yao, Mr. Daisuke Takeda, Mr. Yuto Hashimoto, Mr. Naoki Matsuda, Mr. Masaki Itoh, Mr. Akihiro Nakatani, Mr. Yuya Miki, Mr. Tomonori Iitsuka, Ms. Riko Odani, Mr. Ryosuke Sakae, Ms. Chiharu Suzuki, Mr. Kazutaka Takamatsu, Mr. Sho Tabuchi, Mr. Tomoya Nagata, Mr. Ryosuke Morioka, Mr. Yuki Yokoyama, Mr. Hiroyuki Kaida, Mr. Daiki Nishikawa, Mr. Wataru Miura, Mr. Tomohiro Morita, Mr. Yuhei Itai, Mr. Yuto

Okugawa, Mr. Masanori Shigeno, Ms. Chiaki Yamamoto, Ms. Atifah Najib, Mr. Keita Fukuzumi, Mr. Fumiki Ichioka, Mr. Nobutaka Otomura, Ms. Misaki Terada, Mr. Shotaro Nakamura, Mr. Teppei Noguchi, and Mr. Tomohiro Yasuhisa.

The author is thankful to be spending a precious time with my talented classmates in Osaka University: Ms. Marina Ide, Mr. Kaname Shibata, Ms. Yukari Hayashi, Mr. Takayuki Furukawa, Mr. Tetsuya Miyano, Mr. Masato Okazaki, Mr. Hirofumi Harada, Ms. Ayaka Hosoya, Mr. Makoto Sako, Mr. Masashi Shigenobu, Ms. Haruka Nishiyama, and Mr. Takafumi Higuchi. He was very stimulated and motivated by their activity.

The author's sincere appreciation is extended to technical advisers, Dr. Nobuko Kanehisa for X-ray crystallographic analysis, Ms. Kyoko Inoue for NMR measurement, and Mr. Hiroshi Moriguchi for HRMS measurements.

The author is much obliged to Professor Carsten Bolm at RWTH Aachen for giving a chance to study in his group from September to December 2015. It was so precious experience. The author also would like to thank the Japanese-German Graduate Externship Program coordinators, Professor Kazushi Mashima and Professor Jun Okuda.

The author also thanks people in RWTH Aachen for a lot of kind assistance and support: Dr. Hannah Baars, Dr. Rebekka Anna Bohmann, Dr. Deo Tiwari, Dr. Shunxi Dong, Dr. Anne-Dorothee Steinkamp, Dr. José Hernandéz-Barajas, Ms. Plamena Staleva, Ms. Saumya Dabral, Mr. Carl Dannenberg, Mr. Felix Krauskopf, Mr. Marcus Frings, Mr. Gary Hermann, Dr. Ingo Schiffers, Mr. Julien Engel, Mr. Jian Wen, Mr. Stefan Wiezorek, Ms. Duo Zhang, Ms. Ingrid Voss, Mr. Steffen Mader, Mr. Hsuan Hung Liao, Mr. Adisak Chatupheeraphat, and Dr. Daniel Hack.

The author acknowledges the Japan Society for the Promotion of Science (JSPS) for the financial supports for the research fellowship.

The author is deeply indebted to Ms. Aya Jodoji for hers warmest encouragement and supports over six years.

Finally, the author's sincere gratitude is dedicated to his family, Naoto Unoh, Kyoko Unoh, and Daisuke Unoh in Gifu, for their understanding and encouragement.

Suita, Osaka
January 2017

Yuto Unoh

Contents

Chapter 1

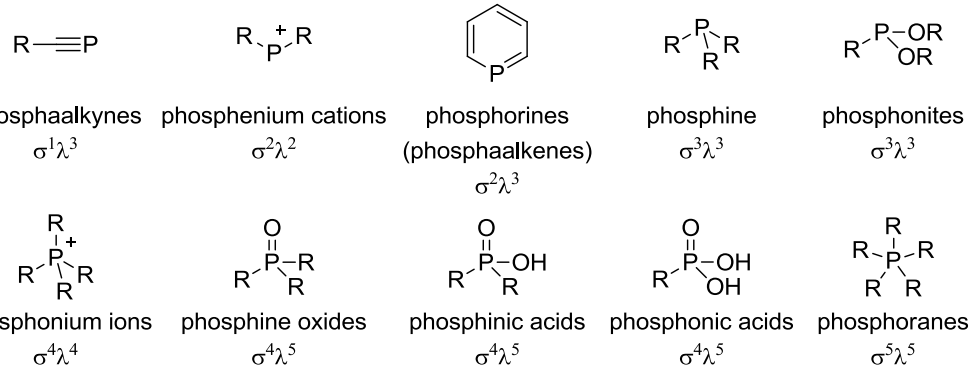
General Introduction

1. Organophosphorus Compounds in Synthetic Organic Chemistry

General

The origin of organophosphorus chemistry[1] goes far back to the 17 century. It is said that the phosphorus element was isolated by the alchemist Hennig Brand, in Hamburg, in 1669 from dried urine.[1d,2] Its name is derived from the Greek "phosphoros", that means light-bearing. Phosphorus is a main group element belonging to group 15, pnictogen in the periodic table. Its oxidation state varies from -3 to +5, and coordination number ranges from 1 to 6. Some representative organophosphorus compounds are illustrated in Figure 1.1, where each compound is assigned with σ (a number of directly attached atoms) and λ (total number of bonds). Most common phosphorus compounds have tricovalent bonds (pyramidal) $\sigma^3\lambda^3$ or pentavalent bonds (tetrahedral) $\sigma^4\lambda^5$.

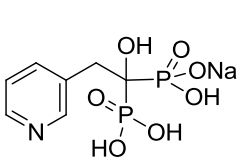
Figure 1.1. Representative Organophosphorus Compounds with Various Coordination Numbers and Oxidation States



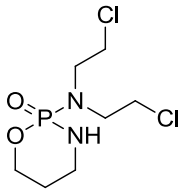
Nowadays, organophosphorus compounds have a wide range of use and application (Figure 1.2). They are utilized as building blocks for pharmaceuticals (anti-cancer, anti-viral, and agent for treatment of bone disease) and agrochemicals (insecticides, pesticides, and herbicides).[1,3] They are also widely used as ligands for transition metal complexes.[4] A huge number of well-designed organophosphines are employed for metal

catalyzed reactions.

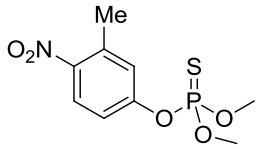
Figure 1.2. Utility of Organophosphorus Compounds



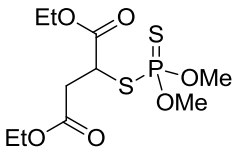
Actonel®
(risedronate, Eisai)
Osteoporosis treatment



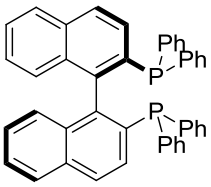
Endoxan®
(Cyclophosphamide, Shionogi)
Anti-cancer



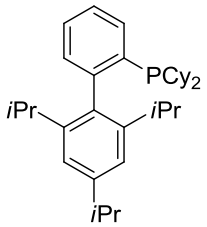
Sumithion®
(Fenitrothion, Sumitomo Chemical)
Insecticide



Malathion
Pesticide



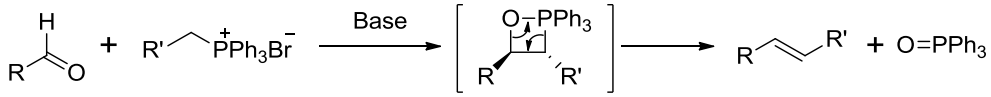
(*S*)-BINAP
Ligand for asymmetric catalysis



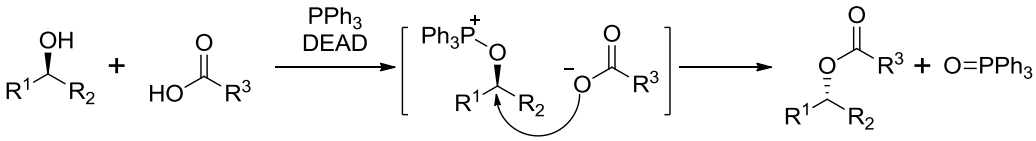
X-Phos
Ligand for C-C and C-X coupling

Furthermore, taking advantages of unique nucleophilicity and oxophilicity of phosphines, some of organophosphorus reagents play significant roles in synthetic chemistry. For example, Wittig reaction (Horner-Wadsworth-Emmons reaction as well) is one of the most popular ways to install an alkene functional group in organic synthesis (Scheme 1.1).[5] Mitsunobu reaction[6] and Appel reaction[7] are representative phosphine-triggered functional group interconversion reactions (Scheme 1.2).

Scheme 1.1. Wittig Reaction



Scheme 1.2. Mitsunobu Reaction



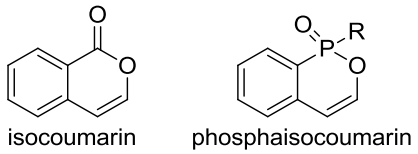
Phosphorus containing heterocycles

Among these organophosphorus compounds, phosphorus-containing heterocycles have particularly attracted attention due to their interesting properties.[1c,8] Lighter congeners, namely, nitrogen-containing heterocycles, (for examples, pyrroles and indoles) are wildly found in natural products, pharmaceuticals and organic materials. In addition, phosphoryl group (P=O bond) could also be regarded as carbonyl (C=O bond) isostere, which is ubiquitous functionality in organic chemistry. The differences between P and N significantly affect biological activity factors and physical properties (stable conformations, solubility, dipole moment, thermal stability, electro- and photo-chemical properties). Therefore, it is highly important to explore physical and biological properties of phosphorus containing heterocycles.

Phosphaisocoumarins

A benzo-fused lactone, isocoumarin (1*H*-2-benzopyran-1-one) is a common substructure in a number of natural products. Since some of isocoumarin derivatives exhibit biological activities, numerous efforts have been made for their synthesis and application.[9] Phosphaisocoumarin is a phosphorus analog of isocoumarin, in which carbonyl group is replaced with phosphoryl group (Figure 1.3). Due to their structural analogy, phosphaisocoumarins are also attracted attention as potentially bioactive building blocks. Actually, some of phosphaisocoumarins are investigated as a new class of inhibitors for pancreatic cholesterol esterase.[10] However,

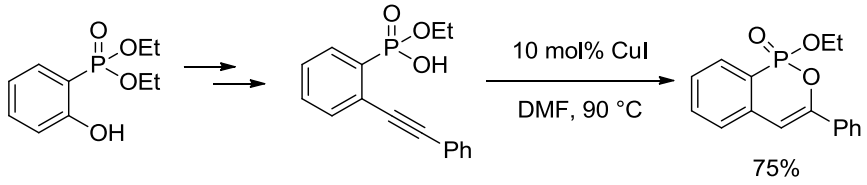
Figure 1.3.



isocoumarin phosphaisocoumarin

despite a number of synthetic methodologies of isocoumarins have been established so far, there are only limited examples of synthesis of phosphaisocoumarins. In 2003, Ding and coworkers reported the synthesis of phosphaisocoumarins by cyclization of *ortho*-alkynyl arylphosphonate derivatives (Scheme 1.3).[11]

Scheme 1.3.

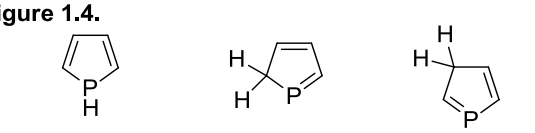


In this method, the alkynyl unit and the phosphoryl unit are installed in a stepwise manner that causes tedious multistep transformations with low atom economy. Therefore, more efficient and straightforward methodologies for the synthesis of phosphaisocoumarins are desired.

Phospholes

Phospholes[12] are five membered unsaturated heterocycles consisting of 4 carbons and 1 phosphorus atom. Among potentially possible isomers (1*H*-phosphole, 2*H*-phosphole, 3*H*-phosphole), 1*H*-phosphole derivatives are extensively studied due to their interesting properties. The 1*H*-phosphole has totally different features against its nitrogen isostere, namely, pyrrole. The pyrrole is a planar and aromatic compound. However, the phosphole is hardly aromatic because the pyramidalized phosphorus center makes the lone pair difficult to

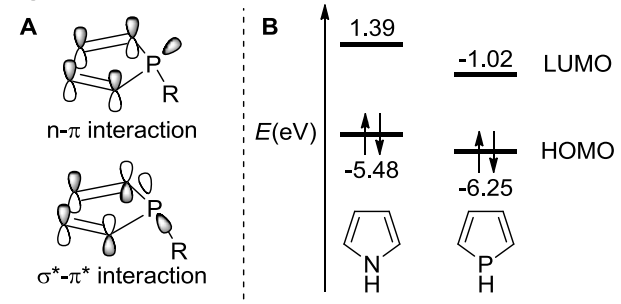
Figure 1.4.



1*H*-phosphole 2*H*-phosphole 3*H*-phosphole

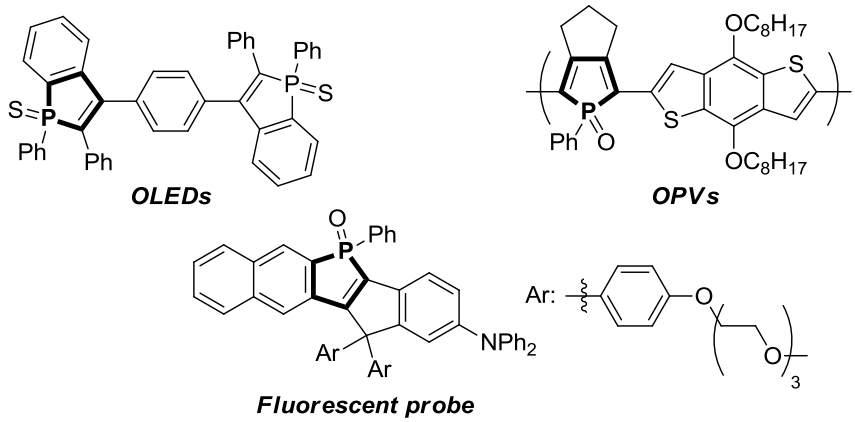
participate in π-conjugation with the butadiene backbone (Figure 1.5A).

Figure 1.5.



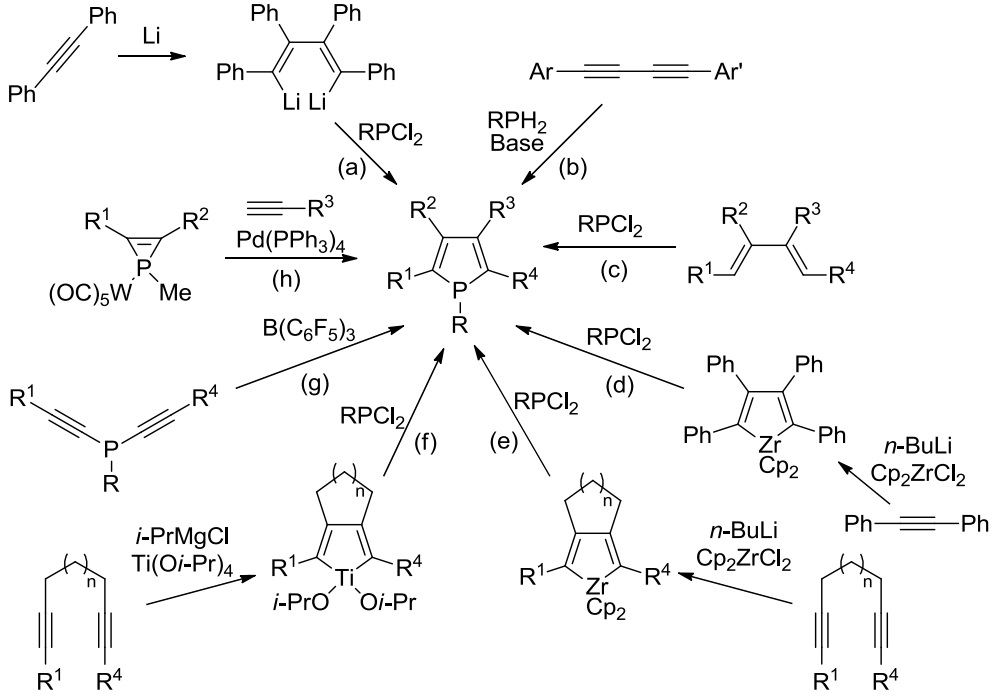
The weak aromaticity is considered to originate from the hyperconjugation of the diene backbone with the exocyclic P-R σ bond. Therefore, the simple phosphole shows cyclopentadiene-like reactivity (i.e. Diels-Alder reaction with dienophiles). In addition, there is an efficient orbital interaction between the π* of the conjugated butadiene and the σ* of exocyclic P-R σ bond, resulting a low lying LUMO level (-1.02 eV for 1*H*-phosphole vs 1.39 eV for pyrrole, calculated at the B3LYP/6-31G* level, Figure 1.5B).[12c] Therefore, the phosphole scaffold has been regarded as an attractive building block in materials chemistry, such as OLEDs (Organic Light Emitting Diodes),[13a] OPVs (Organic Photovoltaics),[13b] and fluorescent probes for bioimaging (Figure 1.6).[13c]

Figure 1.6. Examples of Phosphole-based Organic Materials



Until now, a variety of π-conjugated phospholes, benzo[*b*]phospholes, and dibenzo[*b*]phospholes have been synthesized. Representative methods for construction of these phosphole derivatives are summarized in Scheme 1.4-1.6. The substituted phospholes are synthesized from the reaction of dilithium nucleophiles derived from alkynes and metallic lithium with dichlorophosphine (Scheme 1.4, route a).[14a,b] Alternatively, the reaction of 1,4-diaryl-1,3-diynes with primary phosphines in the presence of a base was also reported (route b).[14c] The reaction of 1,3-dienes with dichlorophosphines, known as the McCormack reaction, is often employed in phosphole synthesis (route c).[14d] The routes d-f in Scheme 1.4 are so-called Fagan-Nugent route and its modified ones. In these methodologies, various phospholes are prepared via metallacyclopentadienes derived from activated metallocene species with alkynes. The original method (route d)[14e] suffers from regioselectivity issues in the case of asymmetrical alkynes. However, introduction of a suitable linker enhances efficiency and selectivity in the reaction (routes e and f)[14f-h]. These methods enable an installing of various functional groups at 2- and 5- positions. The phosphole scaffold is also synthesized from bis(alkynyl)phosphine derivatives (route g). Erker, Itami, and co-workers disclosed that the 1,1-carboboration of a bis(alkynyl)phosphane with $B(C_6F_5)_3$ could proceed to afford the corresponding 3-borylated phosphole.[14i] The boryl moiety could be converted to benzene ring by the subsequent Suzuki-Miyaura coupling. Mathey and co-workers reported the ring expansion reaction of phosphirene tungsten complexes with terminal alkynes catalyzed by $Pd(PPh_3)_4$ (route h).[14j,k]

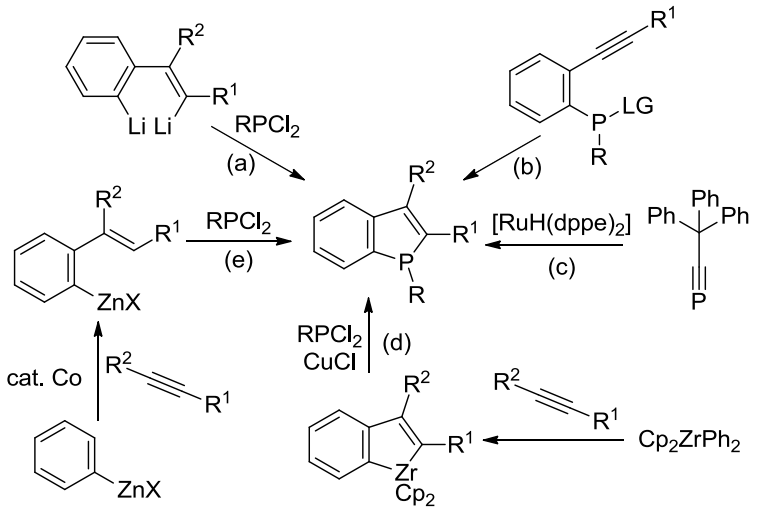
Scheme 1.4. Preparation of Phospholes



Benzo[*b*]phosphole synthesis is summarized in Scheme 1.5.[15] Similar to phosphole synthesis, benzo[*b*]phospholes could be constructed by the reaction of 1,4-dilithium species with dichlorophosphines (route a).[15a-c] The most popular way to synthesize benzo[*b*]phospholes is the cyclization of *ortho*-alkynylarylphosphine derivatives including phosphines,[15d-g] *H*-phosphine oxides,[15h] aminophosphines,[15i,j] and phosphinilidenes[15k,l] (route b). Although less practical in synthesis, the Ru-promoted rearrangement of phosphaalkyne was previously reported (route c).[15m] Ogasawara, Takahashi, and co-workers reported a benzo[*b*]phosphole synthesis by the Fagan-Nugent type approach via a zirconaindene intermediate (Scheme d).[15n] Recently, Yoshikai and co-workers established highly flexible and modular methods based on transition metal-catalyzed carbometallation of alkynes (route e).[15o,p] In this approach, the phosphole ring was constructed by the intramolecular phospha-Friedel-Crafts

reaction.

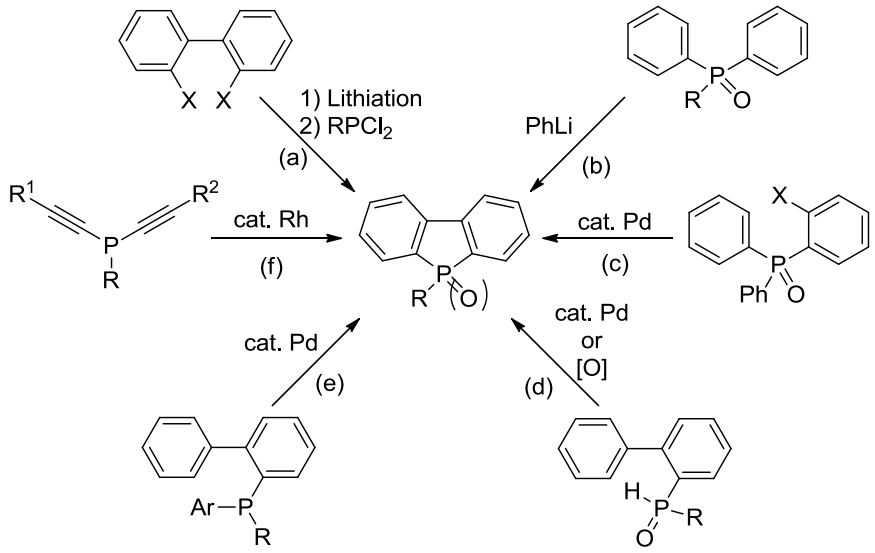
Scheme 1.5. Preparation of Benzo[*b*]phospholes



Several methods for the preparation of dibenzo[*b*]phospholes are shown in Scheme 1.6.[16] The reaction of 2,2'-dilithiobiphenyl with dichlorophosphines is classical but still frequently used (route a).[16a] The cyclization of triphenylphosphine oxides using strong bases such as PhLi is also known as a classical method (route b).[16b,c] There are some reports of dibenzo[*b*]phosphole synthesis utilizing C-H direct coupling strategy. Cui and co-workers reported the Pd-catalyzed C-H/C-X type direct cyclization reaction of *ortho*-haloarylphosphine oxides (route c).[16d] Takai, Kuninobu, and co-workers disclosed the Pd-catalyzed intramolecular C-H/P-H dehydrogenative coupling of biphenylyl-*H*-phosphine oxides (route d).[16e] Alternatively, a radical-based similar transformation is reported. Kawashima and co-workers found the oxidative radical cyclization of the same substrate using an Et_3B/air system.[16f] Chatani, Tobisu, and co-workers reported the Pd-catalyzed intramolecular cyclization of biarylphosphines involving cleavage of C-H and C-P bonds, in which one of the aryl moiety on

phosphorus atom removed as Aryl-H (route e).[16g] Not only the benzene ring substitution approach, but also the benzene ring construction method from bis(alkynyl)phosphines is reported (route f). Tanaka and co-workers reported an enantioselective synthesis of helical dibenzo[*b*]phophole derivatives in the presence of chiral Rh(I)/bisphosphine catalyst system.[16h,i]

Scheme 1.6. Preparation of Dibenzo[*b*]phosphole(oxide)s

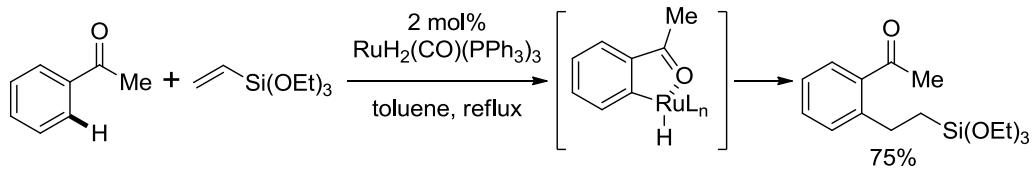


2. C-H Bond Functionalization

Transition metal-catalyzed C-H bond functionalization has been attracted significant attentions as an atom and step economical synthetic strategy.[17] The traditional C-X/C-M (X = halogen, M = metal) type cross coupling reaction requires prefunctionalization such as halogenation and metallation at reaction sites before the coupling reaction.[18] Preparation of such a prefunctionalized substrate sometimes needs tedious multistep transformations with large costs and wastes. Meanwhile, the C-H direct coupling reaction can functionalize generally inactive but ubiquitous C-H bonds directly and thus

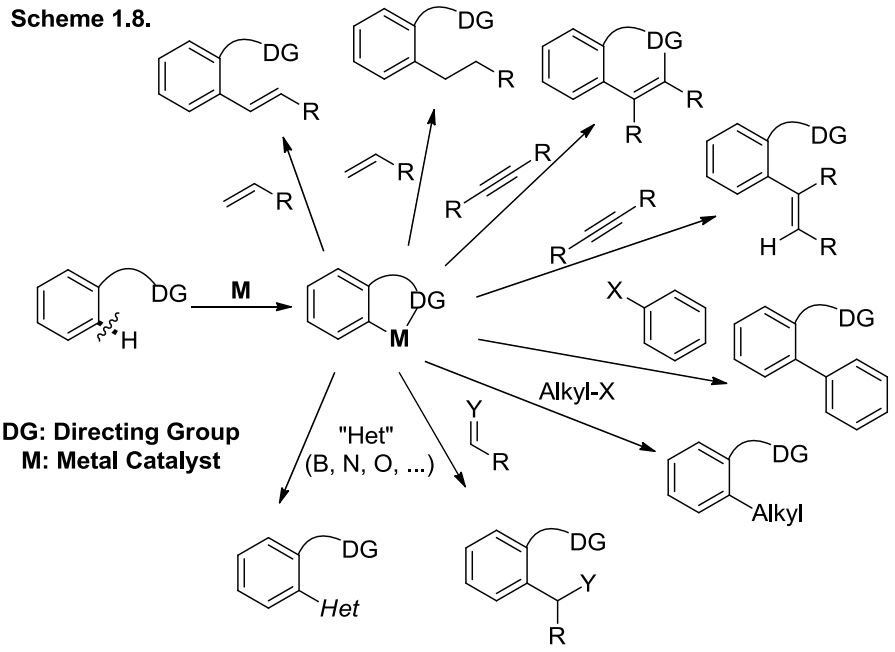
enables more straightforward transformation from simple starting substrates. Since multiple C-H bonds usually exist in hydrocarbons, a directing group is utilized to achieve the regioselective transformation. In this transformation, the directing group interacts with the metal catalyst, and then the neighboring C-H bond cleavage proceeds regioselectively. As pioneering work, Murai, Kakiuchi, Chatani, and co-workers reported the ruthenium-catalyzed C-H alkylation of arenes with alkenes directed by a ketone functionality (Scheme 1.7).[19] In this reaction, the carbonyl group promoted regioselective *ortho* C-H bond cleavage to form a five-membered ruthenacycle intermediate. Subsequently, insertion of an alkene into the Ru-H bond followed by reductive elimination proceeded to furnish alkylated product.

Scheme 1.7.



The directing group strategy is now broadly utilized. The resulting cyclometallated complexes can also react with alkynes, arenes, and various electrophiles to form C-C and C-heteroatom bonds (Scheme 1.8). A variety of directing groups and catalytic systems have been developed so far.

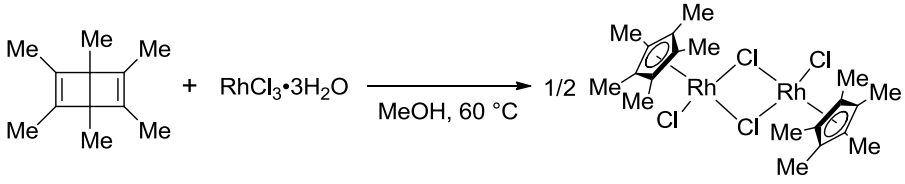
Scheme 1.8.



Cp*Rh(III)-Catalyzed C-H Bond Functionalization

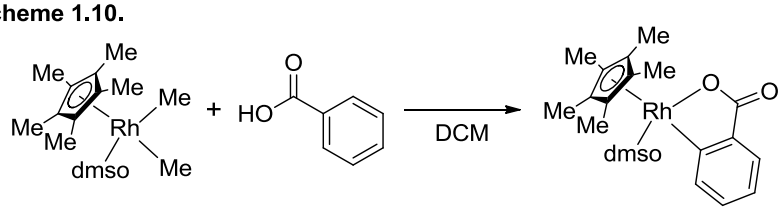
Over the last decade, pentamethylcyclopentadienylrhodium(III) complexes (Cp^*RhX_2) have been widely utilized as efficient catalysts for the directed C-H bond functionalization reactions.[20] The $[Cp^*RhCl_2]_2$ complex was first synthesized by Haszeldine in 1967, from the reaction of Dewar hexamethylbenzene (hexamethylbicyclo [2,2,0] hexa-2,5-diene) with $RhCl_3 \bullet 3H_2O$ in aqueous methanol (Scheme 1.9).[21a] However, they claimed that the product was $[Me_6C_6RhCl]_2^{4+}4Cl^-$. Shortly later, Kang and Maitlis reassigned this compound to be $[Cp^*RhCl_2]_2$.[21b] Now $[Cp^*RhCl_2]_2$ can be easily synthesized from Cp*H with $RhCl_3 \bullet 3H_2O$.[22]

Scheme 1.9.



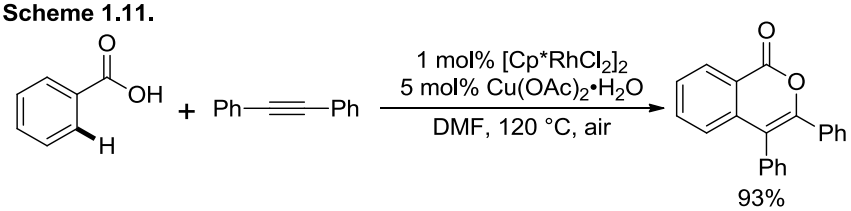
Consequently, Maitlis and others investigated the reactivity of the series of Cp*Rh(III) complexes.[23] In 1987, they disclosed that Cp*Me_2Rh(dmso) can react with benzoic acids to give the corresponding cyclometallated complex under certain conditions (Scheme 1.10).[23c]

Scheme 1.10.



In 2002, Yoshida and co-workers reported the activity of rhodium catalysts toward the direct coupling reaction of benzenes with alkenes.[24] They found that [Cp*$RhCl_2$]$_2$ also had catalytic activity for the oxidative coupling reaction of benzene and pressured ethylene gas in an acidic media in the presence of O_2/Cu(OAc)$_2$.[25] However, until recently, the potential of Cp*Rh(III) complexes as catalysts for the directed C-H bond functionalization had not been fully investigated. The breakthrough was in 2007: Miura, Satoh, and co-workers reported the Cp*Rh(III)-catalyzed oxidative annulation reaction of benzoic acids with internal alkynes via carboxylic acid directed C-H bond cleavage to produce isocoumarin derivatives (Scheme 1.11).[26]

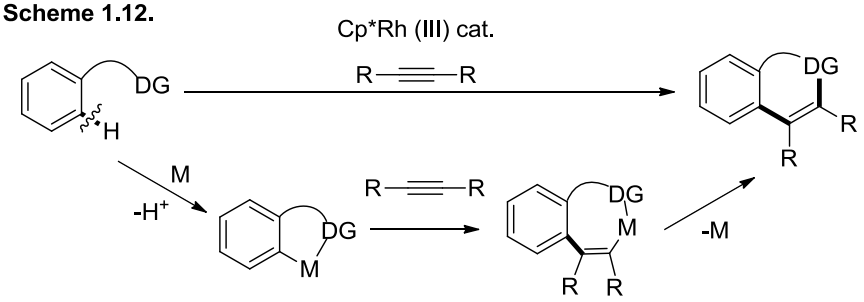
Scheme 1.11.



After this report, various similar annulation reactions of aromatic substrates with alkynes have been reported. A general reaction mechanism is shown in Scheme 1.12.

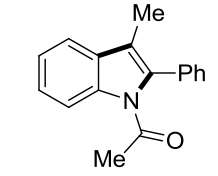
The reaction proceeds through directing group-assisted regioselective C-H bond cleavage, alkyne insertion, and ring closure (usually via reductive elimination) to form heterocyclic product. In this category of reaction, a directing group is incorporated in the forming heterocycle. Therefore new types of directing groups are intensively explored to develop new heterocycle syntheses.

Scheme 1.12.

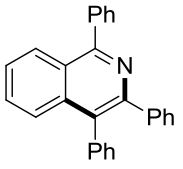


Representative examples are summarized in Scheme 1.13.[27] A number of oxygen-, nitrogen-, and sulfur-containing heterocycles are synthesized by this method.

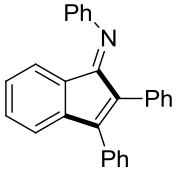
Scheme 1.13. Cp*Rh(III)-catalyzed Synthesis of Heterocycles



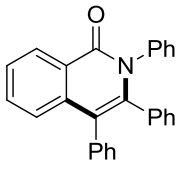
79%
Fagnou (2008)[27a]



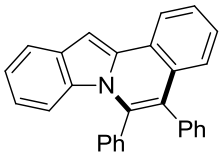
90%
Satoh and Miura (2009)[27b]



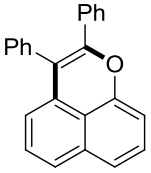
76%
Satoh and Miura (2009)[27b]



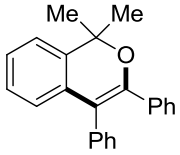
66%
Satoh and Miura (2010)[27c]
Rovis (2010)[27d]
Xingwei Li (2010)[27e]
Fagnou (2011)[27f]



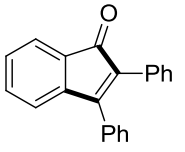
96%
Satoh and Miura (2010)[27g]



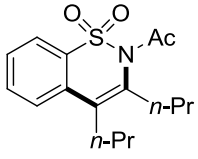
73%
Satoh and Miura (2010)[27h]



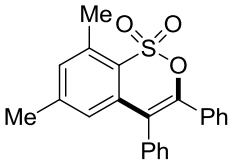
82%
Satoh and Miura (2011)[27i]



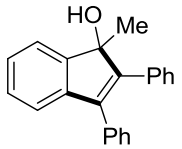
76%
Shi (2011)[27l]



99%
Cramer (2012)[27m]



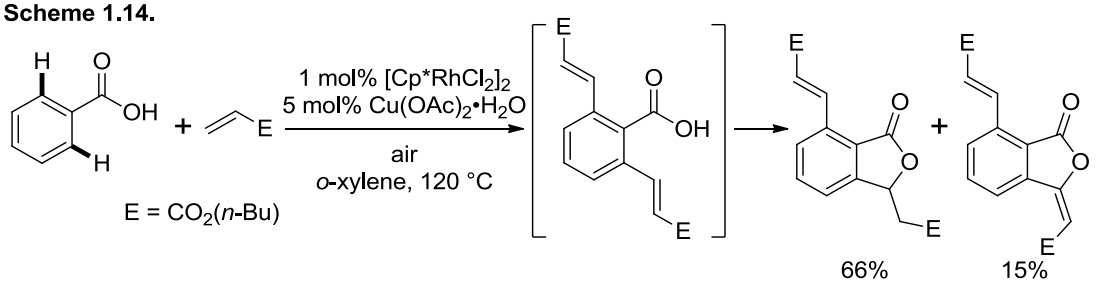
86%
Xingwei Li (2014)[27n]



91%
Glorius (2011)[27j]
Cheng (2011)[27k]

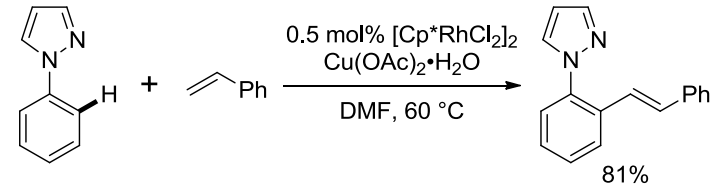
In addition to the annulative heterocycle syntheses, it was shown that the Cp*Rh catalysts are highly efficient for the directed alkenylation and arylation. For examples, Miura, Satoh, and co-workers reported the Rh-catalyzed direct alkenylation of benzoic acids with acrylates (Scheme 1.14).[26]

Scheme 1.14.



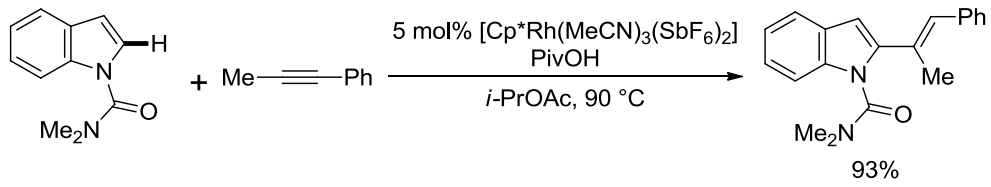
Soon later, the same group reported the pyrazole-directed oxidative alkenylation with styrenes (Scheme 1.15).[28]

Scheme 1.15.



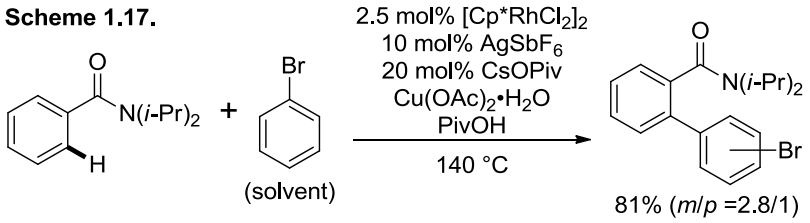
Many examples of similar directed oxidative alkenylation of arenes with alkenes have been reported to date. As an alternative approach for direct alkenylation, Fagnou and co-workers disclosed a non-oxidative alkenylation using alkynes (i.e. hydroarylation) (Scheme 1.16).[29]

Scheme 1.16.



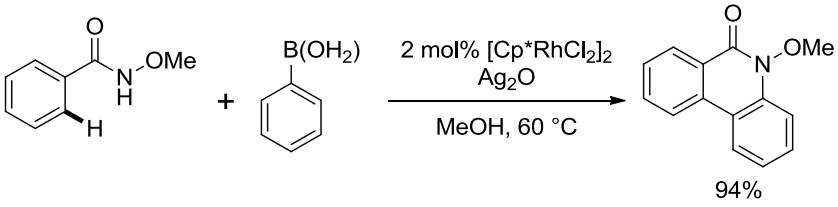
The direct arylation reaction was developed relatively recently. For examples, Glorius and co-workers reported the dehydrogenative coupling of benzamides with bromoarenes as solvents (Scheme 1.17).[30]

Scheme 1.17.



Cheng and co-workers reported the C-H arylation of hydroxamic acid drivatives with arylboron reagents (Scheme 1.18).[31]

Scheme 1.18.

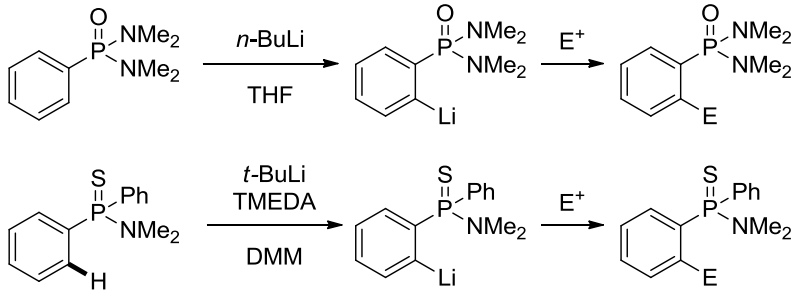


Based on these concepts, additional improvements are developed day by day.[32] Now, the Cp*Rh(III) catalysts have become an important key player in C-H functionalization chemistry field.

Phosphorus-Containing Directing Group

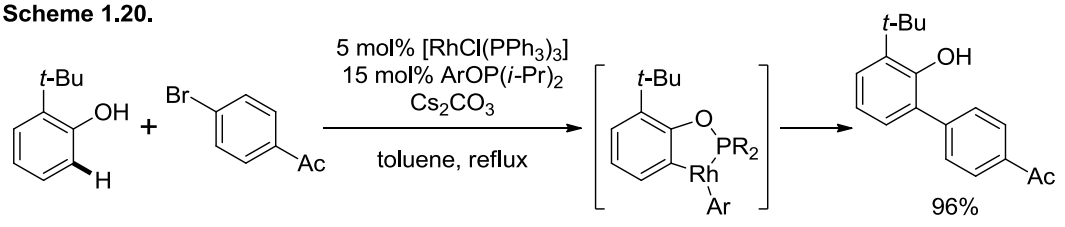
When the author initiated the research project of this thesis, phosphorus-containing groups were rarely utilized as directing groups in synthetic organic chemistry. Phosphoryl and thiophosphoryl groups were used in directed *ortho* metalation (DoM) reactions in the presence of organolithium reagents, in which the resulting lithiated intermediates were subjected to further transformations (Scheme 1.19).[33]

Scheme 1.19.

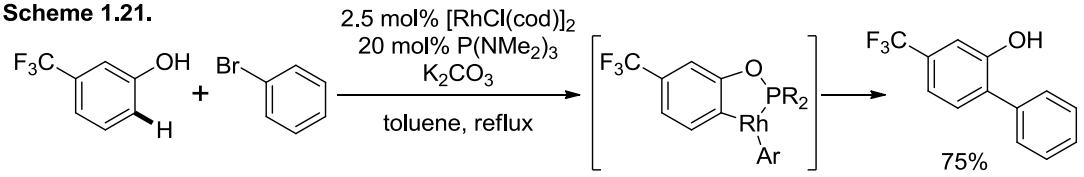


Examples of catalytic transformation involving phosphorus directing groups were limited.[34] In 2003, Bedford (Scheme 1.20)[34b] and Oi (Scheme 1.21)[34c] independently reported the Rh(I)-catalyzed *ortho* C-H arylation of phenols via in situ generated arylphosphites. The phosphite groups act as a transient directing group, hence these transformations are formally direct *ortho* arylation of phenols.

Scheme 1.20.

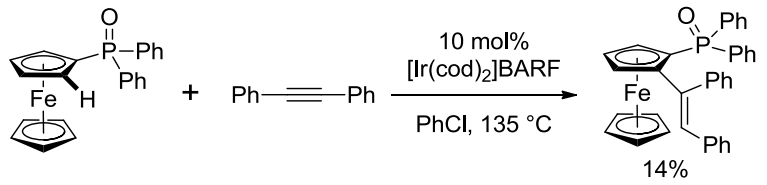


Scheme 1.21.



Shibata and coworkers reported the Ir(I)-catalyzed phosphine oxide-directed C-H alkenylation of ferrocene with diphenylacetylene, albeit in a low product yield (Scheme 1.22).[35]

Scheme 1.22.



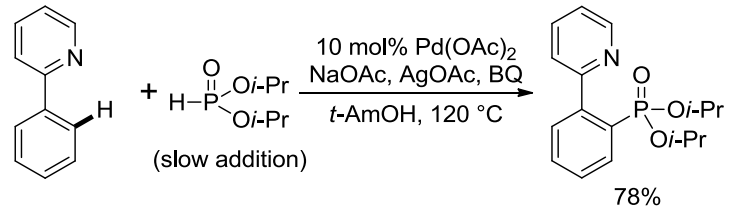
Although it is well known that phosphines and related phosphoryl groups have coordinating ability toward metal center, utilization of them as directing groups in C-H bond functionalization was still rare, and development of more practical methods has been highly desired.

3. Direct C(sp^2)-P Bond Formation

There are many methods to make C(sp^2)-P bond. Nucleophilic substitution reaction of halophosphines with organometal species such as RMgX or RLi is the most general method for a C-P bond formation.[1] On the other hand, the direct C-P bond formation with the cleavage of C-H bond is one of the most ideal transformations from the viewpoint of atom and step economy. However, due to the strong coordinating property of phosphorus functions to transition metals, metal-catalyzed direct C-P coupling is generally considered to be difficult. In fact, there are only a few examples of the transition-metal catalyzed directed intermolecular C(sp^2)-H phosphonation reaction so

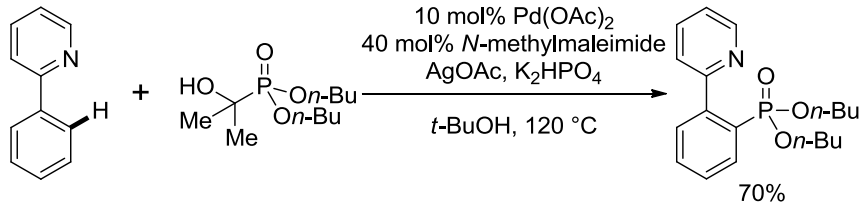
far.[36] In 2013, Yu and co-workers reported the palladium catalyzed C-H phosphonation of 2-arylpyridines with *H*-phosphonates and *H*-phosphine oxides (Scheme 1.23).[36b] To avoid over coordination of the *H*-phosphonate, this reagent was carefully added dropwise to keep its low concentration.

Scheme 1.23.



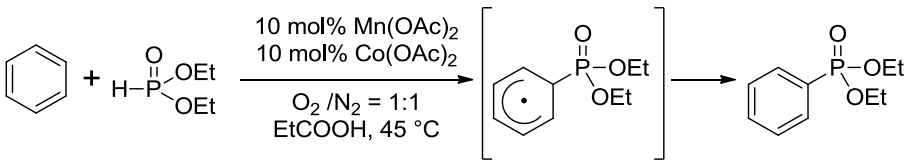
In 2014, Murakami and co-workers reported a similar transformation using α-hydroxyalkylphosphonate as a coupling partner which generates the corresponding *H*-phosphonate in situ by the action of base (Scheme 1.24).[36c] Intramolecular variants are already noted in the phosphole synthesis section.[16e,g]

Scheme 1.24.



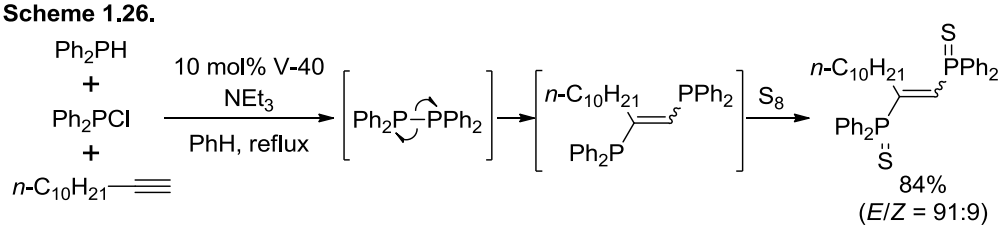
Conversely, addition of P-centered radical species into (hetero)arenes and alkynes to form C(sp^2)-P bond is well established.[37,38] The P radicals can be generated in the presence of radical initiators or metal oxidants. For examples, Ishii and co-workers reported the radical type phosphonation of simple arenes with dialkyl phosphites catalyzed by the $Mn(OAc)_2/Co(OAc)_2/O_2$ system (Scheme 1.25).[37a]

Scheme 1.25.



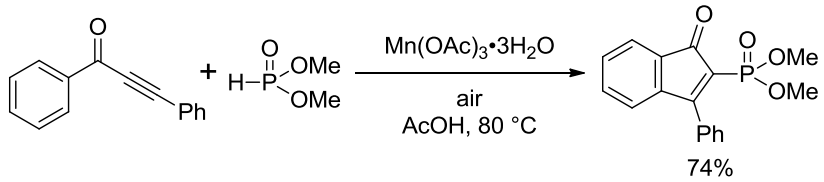
Oshima and co-workers disclosed the radical type addition of diphosphanes generated in situ into terminal alkynes to afford vicinal alkenyl diphosphine derivatives (Scheme 1.26).[37b]

Scheme 1.26.



Zhang and co-workers reported the addition/cyclization of a dialkyl phosphoryl radical with alkynes to afford 2-phosphonylindenones in the presence of $Mn(OAc)_3•2H_2O$ (Scheme 1.27).[37c]

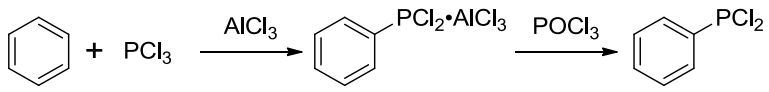
Scheme 1.27.



Friedel-Crafts reaction is exceedingly classical but highly useful for $C(sp^2)$-H functionalization. The phosphorus variant, namely, phospha-Friedel-Crafts (PFC) reaction also has a long history. In 1876, Michaelis discovered that $PhPCl_2$ could be synthesized by the aluminum chloride-catalyzed reaction of benzene with PCl_3 (Scheme

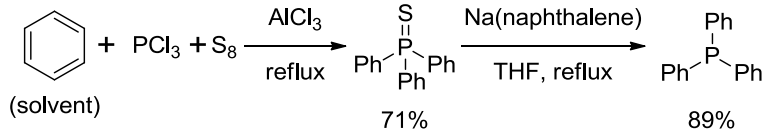
1.28).[39a] It is also known that this transformation is also possible without the $AlCl_3$ catalyst at higher temperature (600 °C), and thus, the later non-catalytic process is employed in the commercial production of $PhPCl_2$.[1a]

Scheme 1.28.



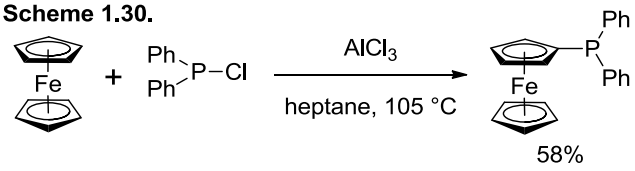
Several synthetic studies of organophosphorus compounds based on PFC chemistry have so far been carried out. Olah and co-workers disclosed that the PFC reaction of $S{=}PCl_3$ with benzene was efficient for the synthesis of $S{=}PPh_3$, while the reaction of PCl_3 with benzene gave only a mixture of $PhPCl_2$ and Ph_2PCl (Scheme 1.29).[39b]

Scheme 1.29.



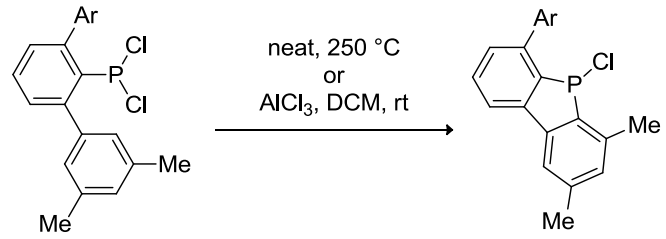
Xiao and co-workers utilized the PFC reaction for the synthesis of ferrocenylphosphine ligands (Scheme 1.30).[39c]

Scheme 1.30.



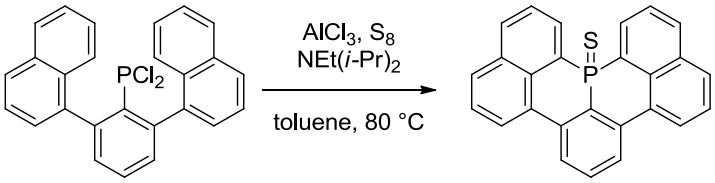
Wehmschulte and co-workers reported an intramolecular PFC reaction to afford dibenzo[*b*]phosphole framework (Scheme 1.31).[39d] They showed this transformation required high temperature (250 °C) without any catalyst, while no heating was necessary in the presence of $AlCl_3$.

Scheme 1.31.



Recently, Nakamura, Hatakeyama, and co-workers synthesized uniquely fused phosphorus-containing heterocycles using the PFC reaction of a P(V) intermediates (Scheme 1.32).[39e,f]

Scheme 1.32.



As noted, the typical PFC reaction requires a stoichiometric amount of Lewis acid and harsh conditions. Additionally, it is limited to electron-rich substrates or intramolecular cases. Properties of phosphenium species, that is considered as a reactive intermediate in the PFC reaction, are well studied since they are interesting as phosphorus analogues of carbenes.[40] However, the PFC reaction should be further developed for the efficient synthesis of various phosphorus compounds.

Aim of This Thesis

So far, a number of phosphorus containing heterocycles have been synthesized based on the traditional synthetic ways including long step sequences under narrow functional group compatibility conditions. From the viewpoint of diversity-oriented synthesis, more efficient and straightforward synthetic methodologies are desired. In this doctoral

thesis, the author would like to focus on development of new synthetic methods of phosphorus-containing heterocycles, especially for phosphaisocoumarins and (di)benzo[*b*]phosphole derivatives based on the C-H bond functionalization strategy. This thesis consists of following 5 chapters.

Chapter 2 deals with the Rh(III)-catalyzed synthesis of phosphaisocoumarins via C-H bond cleavage. This reaction proceeds through *ortho*-selective C-H bond cleavage with the assistance of phosphinoxy directing group and insertion/annulation of internal alkynes.

Chapter 3 shows a new Ag(I) or Mn(III)-mediated synthesis of benzo[*b*]phosphole derivatives via oxidative radical cyclization. In this reaction, a variety of functionalized benzo[*b*]phospholes are prepared in one step from readily available *H*-phosphine oxides and internal alkynes.

Chapter 4 involves the Rh(III)-catalyzed direct coupling of arylphosphine derivatives with heterobicyclic alkenes. A variety of biarylphosphine derivatives are synthesized from simple arylphosphine oxides and oxabicyclic alkenes via the direct coupling and ring-opening aromatization. In addition, fused dibenzo[*b*]phosphole derivatives are prepared from arylthiophosphinamides via direct coupling and subsequent phospha-Friedel-Crafts reaction in a one-pot manner.

Chapter 5 makes mention with the regioselective synthesis of benzo[*b*]phosphole derivatives via Rh(III)-catalyzed C-H alkenylation and formal phospha-Friedel-Crafts cyclization. A number of benzo[*b*]phosphole derivatives are synthesized from arylthiophosphinamides and internal alkynes via a C-H alkenylation-desulfurization-cyclization sequence in a semi-one-pot manner.

Chapter 6 presents the transition metal free electrophilic phosphination/cyclization of alkynes promoted by triflic anhydride (Tf_2O). An electrophilic phosphenium cation generated in situ from secondary phosphine oxides with Tf_2O couples with alkynes to give phosphinated alkenes and (hetero)cyclic compounds.

References and Notes

(1) For books, see: (a) Quin, L. D. *A Guide to Organophosphorus Chemistry*; Wiley Interscience: New York, **2000**. (b) Murphy, P. J. *Organophosphorus Reagents*; Oxford University Press: Oxford, U.K., **2004**. (c) Alvarez-Builla, J.; Vaquero, J. J.; Barluenga, J. *Modern Heterocyclic Chemistry Vol. 1*; Wiley-VCH: Weinheim, Germany, **2011**. (d) Timperley, C. M. *Best Synthetic Method: Organophosphorus (V) Chemistry*; Academic Press: Amsterdam, **2014**.

(2) Krafft, F. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 660.

(3) For selected reviews, see: (a) Westheimer, F. H. *Science* **1987**, *235*, 1173. (b) Seto, H.; Kuzuyama, T. *Nat. Prod. Rep.* **1999**, *16*, 589. (c) Moonen, K., Laureyn, I., and Stevens, C. V. *Chem. Rev.* **2004**, *104*, 6177. (d) Demmer, C. S.; Krogsgaard-Larsen, N.; Bunch, L. *Chem. Rev.* **2011**, *111*, 7981. (e) Queffelec, C.; Petit, M.; Janvier, P.; Knight, D. A.; Bujoli, B. *Chem. Rev.* **2012**, *112*, 3777.

(4) For selected reviews, see: (a) van Leeuwen, P. W. N. M.; Kamer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem. Rev.* **2000**, *100*, 2741. (b) Helmchen, G.; Pfaltz, A. *Acc. Chem. Res.* **2000**, *33*, 336. (c) McCarthy, M.; Guiry, P. J. *Tetrahedron* **2001**, *57*, 3809. (d) Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029. (e) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461. (f) Birkholz, M.-N.; Freixa, Z.; van Leeuwen, P. W. N. M. *Chem. Soc. Rev.* **2009**, *38*, 1099. (g) Fernandez-Perez, H.;

Etayo, P.; Panossian, A.; Vidal-Ferran, A. *Chem. Rev.* **2011**, *111*, 2119. (h) Pereira, M. M.; Calvete, M. J. F.; Carrilho, R.; Abreu, A. R. *Chem. Soc. Rev.* **2013**, *42*, 6990. (i) Genet, J.-P.; Ayad, T.; Ratovelomanana-Vidal, V. *Chem. Rev.* **2014**, *114*, 2824. (j) Verendel, J. J.; Pamies, O.; Dieguez, M.; Andersson, P. G. *Chem. Rev.* **2014**, *114*, 2130. (k) Fu, W.; Tang, W. *ACS Catal.* **2016**, *6*, 4814.

(5) (a) Wittig, G.; Geissler, G. *Liebigs Ann. Chem.* **1953**, *580*, 44. (b) Horner, L.; Hoffmann, H. M. R.; Wippel, H. G. *Ber.* **1958**, *91*, 61. (c) Wadsworth, W. S., Jr.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733. (d) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863. (e) Cristau, H.-J. *Chem. Rev.* **1994**, *94*, 1299. (f) O'Brien, C. J.; Tellez, J. L.; Nixon, Z. S.; Kang, L. J.; Carter, A. L.; Kunkel, S. R.; Przeworski, K. C.; Chass, G. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 6836. (g) Byrne, P. A.; Gilheany, D. G. *Chem. Soc. Rev.* **2013**, *42*, 6670.

(6) (a) Mitsunobu, O.; Yamada, M.; Mukaiyama, M.; *Bull. Chem. Soc. Jpn.* **1967**, *40*, 935. (b) Mitsunobu, O. *Synthesis* **1981**, 1. (c) But, T. Y. S.; Toy, P. H. *Chem.—Asian J.* **2007**, *2*, 1340. (c) Swamy, K. C. K.; Kumar, N. N. B.; Balaraman, E.; Kumar, K. V. P. P. *Chem. Rev.* **2009**, *109*, 2551. (d) O'Brien, C. J. PCT Int. Appl. WO2010/118042A2, **2010**.

(7) (a) Appel, R. *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 801. (b) van Kalkeren, H. A.; Leenders, S. H. A. M.; Hommersom, C. R. A.; Rutjes, F. P. J. T.; van Delft, F. L. *Chem.—Eur. J.* **2011**, *17*, 11290.

(8) (a) Nyulászi, L. *Chem. Rev.* **2001**, *101*, 1229. (b) Kollar, L.; Keglevich, G. *Chem. Rev.* **2010**, *110*, 4257.

(9) (a) Barry, R. *D. Chem. Rev.* **1964**, *64*, 229. (b) Yao, T.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 5936. (c) Pal, S.; Chatare, V.; Pal, M. *Curr. Org. Chem.* **2011**, *15*, 782.

(10) Li, B.; Zhou, B.; Lu, H.; Ma, L.; Peng, A.-Y. *Eur. J. Med. Chem.* **2010**, *45*, 1955.

(11) (a) Peng, A.-Y.; Ding, Y.-X. *J. Am. Chem. Soc.* **2003**, *125*, 15006. (b) Peng, A.-Y.; Ding, Y.-X. *Org. Lett.* **2004**, *6*, 1119. (c) Wei, P.; Ding, Y.-X. *Synlett.* **2005**, 599.

(12) For reviews of phospholes, see: (a) Mathey, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1578. (b) Baumgartner, T.; Reau, R. *Chem. Rev.* **2006**, *106*, 4681. (c) Matano, Y.; Imahori, H. *Org. Biomol. Chem.* **2009**, *7*, 1258. (d) Stolar, M.; Baumgartner, T. *Chem.—Asian J.* **2014**, *9*, 1212. (e) Baumgartner, T. *Acc. Chem. Res.* **2014**, *47*, 1613. (f) Fourmy, K.; Nguyen, D. H.; Dechy-Cabaret, O.; Gouygou, M. *Catal. Sci. Technol.* **2015**, *5*, 4289. (g) Duffy, M. P.; Delaunay, W.; Bouit, P.-A.; Hissler, M. *Chem. Soc. Rev.* **2016**, *45*, 5296. (h) Shameem, M. A.; Orthaber, A. *Chem.—Eur. J.* **2016**, *22*, 10718.

(13) (a) Tsuji, H.; Sato, K.; Sato, Y.; Nakamura, E. *J. Mater. Chem.* **2009**, *19*, 3364. (b) Matano, Y.; Ohkubo, H.; Miyata, T.; Watanabe, Y.; Hayashi, Y.; Umeyama, T.; Imahori, H. *Eur. J. Inorg. Chem.* **2014**, 1620. (c) Wang, C.; Fukazawa, A.; Taki, M.; Sato, Y.; Higashiyama, T.; Yamaguchi, S. *Angew.*

Chem., Int. Ed. **2015**, *54*, 15213.

(14) (a) Leavitt, F. C.; Manuel, T. A.; Johnson, F. *J. Am. Chem. Soc.* **1959**, *81*, 3163. (b) Leavitt, F. C.; Manuel, T. A.; Johnson, F.; Matternas, L. U.; Lehman, D. S. *J. Am. Chem. Soc.* **1960**, *82*, 5099. (c) Märkl, G.; Potthast, R. *Angew. Chem., Int. Ed.* **1967**, *6*, 86. (d) Breque, A.; Mathey, F.; Savignac, P. *Synthesis* **1981**, *1981*, 983. (e) Fagan, P. J.; Nugent, W. A. *J. Am. Chem. Soc.* **1988**, *110*, 2310. (f) Fagan, P. J.; Nugent, W. A.; Calabrese, J. C. *J. Am. Chem. Soc.* **1994**, *116*, 1880. (g) Matano, Y.; Miyajima, T.; Nakabuchi, T.; Matsutani, Y.; Imahori, H. *J. Org. Chem.* **2006**, *71*, 5792. (h) Matano, Y.; Nakashima, M.; Imahori, H. *Angew. Chem., Int. Ed.* **2009**, *48*, 4002. (i) Möbus, J.; Bonnin, Q.; Ueda, K.; Fröhlich, R.; Itami, K.; Kehr, G.; Erker, G. *Angew. Chem., Int. Ed.* **2012**, *51*, 1954. (j) Marinetti, A.; Mathey, F. *Tetrahedron Lett.* **1987**, *28*, 5021. (k) Marinetti, A.; Mathey, F. *J. Am. Chem. Soc.* **1985**, *107*, 4700.

(15) (a) Rausch, M. D.; Klemann, L. P. *J. Am. Chem. Soc.* **1967**, *89*, 5732. (b) Kurita, J.; Ishii, M.; Yasuike, S.; Tsuchiya, T. *J. Chem. Soc., Chem. Commun.* **1993**, 1309. (c) Matano, Y.; Hayashi, Y.; Suda, K.; Kimura, Y.; Imahori, H. *Org. Lett.* **2013**, *15*, 4458. (d) Märkl, G.; Jin, G. Y. ; Berr, K.-P. *Tetrahedron Lett.*, **1993**, 34, 3103. (e) Tsuji, H.; Sato, K.; Ilies, L.; Itoh, Y.; Sato, Y.; Nakamura, E. *Org. Lett.* **2008**, *10*, 2263. (f) Xu, Y.-Z.; Wang, Z.-H.; Gan, Z.-J.; Xi, Q.-Z.; Duan, Z.; Mathey, F. *Org. Lett.* **2015**, *17*, 1732. (g) Zhou, Y.; Gan, Z.; Su, B.; Li, J.; Duan, Z.; Mathey, F. *Org. Lett.* **2015**, *17*, 5722. (h) Sanji, T.; Shiraishi, K.; Kashiwabara, T.; Tanaka, M. *Org. Lett.* **2008**, *10*, 2689. (i) Fukazawa, A.; Hara, M.; Okamoto, T.; Son, E.-C.; Xu, C.; Tamao, K.; Yamaguchi, S. *Org. Lett.* **2008**, *10*, 913. (j) Fukazawa, A.; Ichihashi, Y.; Kosaka, Y.; Yamaguchi, S. *Chem.—Asian J.* **2009**, *4*, 1729. (k) Wei, X.; Lu, Z.; Zhao, X.; Duan, Z.; Mathey, F. *Angew. Chem., Int. Ed.* **2015**, *54*, 1583. (l) Zhao, X.; Lu, Z.; Wang, Q.; Wei, D.; Lu, Y.; Duan, Z.; Mathey, M. *Organometallics*, **2016**, *35*, 3440. (m) Cordaro, J. G.; Stein, D.; Grützmacher, H. *J. Am. Chem. Soc.* **2006**, *128*, 14962. (n) Ogasawara, M.; Arae, S.; Watanabe, S.; Subbarayan, V.; Sato, H.; Takahashi, T. *Organometallics* **2013**, *32*, 4997. (o) Wu, B.; Santra, M.; Yoshikai, N. *Angew. Chem., Int. Ed.* **2014**, *53*, 7543. (p) Wu, B.; Chopra, R.; Yoshikai, N. *Org. Lett.* **2015**, *17*, 5666.

(16) (a) Wittig, G.; G. Geissler, *Justus Liebigs Ann. Chem.* **1953**, *580*, 44. (b) Ogawa, S.; Tajiri, Y.; Furukawa, N. *Bull. Chem. Soc. Jpn.*, **1991**, *64*, 3182. (c) Byrne, P. A.; Gilheany, D. G. *J. Am. Chem. Soc.* **2012**, *134*, 9225. (d) Cui, Y.; Fu, L.; Cao, J.; Deng, Y.; Jiang, J. *Adv. Synth. Catal.* **2014**, *356*, 1217. (e) Kuninobu, Y.; Yoshida, T.; Takai, K. *J. Org. Chem.* **2011**, *76*, 7370. (f) Furukawa, S.; Haga, S.; Kobayashi, J.; Kawashima, T. *Org. Lett.* **2014**, *16*, 3228. (g) Baba, K.; Tobisu, M.; Chatani, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 11892. (h) Fukawa, N.; Osaka, T.; Noguchi, K.; Tanaka, K. *Org. Lett.* **2010**, *12*, 1324. (i) Sawada, Y.; Furumi, S.; Takai, A.; Takeuchi, M.; Noguchi, K.; Tanaka, K. *J.*

Am. Chem. Soc. **2012**, *134*, 4080. See also; (j) Saito, K.; Chikkade, P. K.; Kanai, M.; Kuninobu, Y. *Chem.—Eur. J.* **2015**, *21*, 8365.

(17) Selected recent reviews, see: (a) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013. (b) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335. (c) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev.* **2009**, *38*, 2447. (d) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074. (e) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (f) Satoh, T.; Miura, M. *Synthesis* **2010**, 3395. (g) Sun, C.-L.; Li, B.-J.; Shi, Z.- J. *Chem. Commun.* **2010**, *46*, 677. (h) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (i) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (j) Lapointe, D.; Fagnou, K. *Chem. Lett.* **2010**, *39*, 1118. (k) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. (l) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780. (m) Kuninobu, Y.; Takai, K. *Chem. Rev.* **2011**, 111, 1938. (n) Wencel-Delord, J.; Droge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740. (o) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (p) Mitchell, E. A.; Peschiulli, A.; Lefevre, N.; Meerpoel, L.; Maes, B. U. W. *Chem.—Eur. J.* **2012**, *18*, 10092. (q) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788. (r) Miura, M.; Satoh, T.; Hirano, K. *Bull. Chem. Soc. Jpn.* **2014**, *87*, 751. (s) Chen, Z.; Wang, B.; Zhang, J.; Yu, W.; Liu, Z.; Zhang, Y. *Org. Chem. Front.* **2015**, *2*, 1107. (t) Boyarskiy, V. P.; Ryabukhin, D. S.; Bokach, N. A.; Vasilyev, A. V. *Chem. Rev.* **2016**, *116*, 5894. (u) Gulías, M.; Mascareñas, J. L. *Angew. Chem., Int. Ed.* **2016**, *55*, 11000. (v) Hartwig, J. F. *J. Am. Chem. Soc.* **2016**, *138*, 2. (w) Davies, H. M. L.; Morton, D. *J. Org. Chem.* **2016**, *81*, 343.

(18) For earlier examples see: (a) Kochi, J. K.; Tamura, M. *J. Am. Chem. Soc.* **1971**, *93*, 1487. (b) Tamao, K.; Sumitani, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 4374. (c) Corriu, R. J. P.; Massse, J. P. *J. Chem. Soc., Chem. Commun.* **1972**, 144. (d) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (e) Heck, R. F.; Nolley, Jr., J. P. *J. Org. Chem.* **1972**, *37*, 2320. (f) Yamamura, M.; Moritani, I.; Murahashi, S. *J. Organomet. Chem.* **1975**, *91*, C39. (g) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron lett.* **1975**, *50*, 4467. (h) King, A. O.; Okukado, N.; Negishi, E. *J. Chem. Soc., Chem. Commun.* **1977**, 683. (i) Kosugi, M. Sasazawa, K.; Shimizu, Y.; Migita, T. *Chem. Lett.* **1977**, 301. (j) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 3636. (k) Miyaura, N.; Suzuki, A. *J. Chem. Soc., Chem. Commun.* **1979**, 866. (l) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918.

(19) (a) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529. (b) Kakiuchi, F.; Murai, S. *Acc. Chem. Res.* **2002**, *35*, 826.

(20) (a) Satoh, T.; Miura, M. *Chem.—Eur. J.* **2010**, *16*, 11212. (b) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814. (c) Patureau, F. W.; Wencel-Delord, J.;

Glorius, F. *Aldrichimica Acta* **2012**, *45*, 31. (d) Chiba, S. *Chem. Lett.* **2013**, *41*, 1554. (e) Yang, Y.; Li, K.; Cheng, Y.; Wan, D.; Li, M.; You, J. *Chem. Commun.* **2016**, *52*, 2872.

(21) (a) Booth, B. L.; Haszeldine, R. N.; Hill, M. *Chem. Commun.(London)* **1967**, 1118. (b) Kang, J. W.; Maitlis, P. M. *J. Am.Chem. Soc.* **1968**, *90,* 3259.

(22) Fujita, K.; Takahashi, Y.; Owaki, M.; Yamamoto, K.; Yamaguchi, R. *Org. Lett.* **2004**, *6*, 2785.

(23) (a) Kang, J. W.; Moseley, K.; Maitlis, P. M. *J. Am. Chem. Soc.* **1969**, *91*, 5970. (b) Kang, J. W.; Mosley, K.; Maitlis, P. M. *Chem. Commun.(London)* **1968**, 1304. (c) Kisenyi, J. M.; Sunley, G. J.; Cabeza, J. A.; Smith, A. J.; Adams, H.; Salt, N. J.; Maitlis, P. M. *J. Chem. Soc., Dalton Trans.* **1987**, 2459.

(24) (a) Matsumoto, T.; Periana, R. A.; Taube, D. J.; Yoshida, H. *J. Catal.* **2002**, *206*, 272. (b) Matsumoto, T.; Yoshida, H. *Chem. Lett.* **2000**, *29*, 1064.

(25) For a related process catalyzed by palladium; (a) Fujiwara, Y.; Moritani, I.; Danno, S.; Asano, R.; Teranishi, S. *J. Am. Chem. Soc.* **1969**, *91,* 7166. (b) Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992. (c) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 633.

(26) (a) Ueura, K.; Satoh, T.; Miura, M. *Org. Lett.* **2007**, *9*, 1407. (b) Ueura, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2007**, *72*, 5362.

(27) (a) Stuart, D. R.; Bertrand-Laperle, M.; Burgess, K. M. N.; Fagnou, K. *J. Am. Chem. Soc.* **2008**, *130,* 16474. (b) Fukutani, T.; Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *Chem.Commun.* **2009**, 5141. (c) Mochida, S.; Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *Chem. Lett.* **2010**, *39*, 744. (d) Hyster, T. K.; Rovis, T. *J. Am. Chem. Soc.* **2010**, *132*, 10565. (e) Song, G.; Chen, D.; Pan, C.-L.; Crabtree, R. H.; Li, X. *J. Org. Chem.* **2010**, *75*, 7487. (f) Guimond, N.; Gorelsky, S. I.; Fagnou, K. *J. Am. Chem. Soc.* **2011**, *133*, 6449. (g) Morimoto, K.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2010**, *12*, 2068. (h) Mochida, S.; Shimizu, M.; Hirano, K.; Satoh, T.; Miura, M. *Chem.—Asian J.* **2010**, *5*, 847. (i) Morimoto, K.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2011**, *76*, 9548. (j) Patureau, F. W.; Besset, T.; Kuhl, N.; Glorius, F. *J. Am. Chem. Soc.* **2011**, *133*, 2154. (k) Muralirajan, K.; Parthasarathy, K.; Cheng, C.-H. *Angew. Chem., Int. Ed.* **2011**, *50*, 4169. (l) Li, B.-J.; Wang, H.-Y.; Zhu, Q.-L.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2012**, *51*, 3948. (m) Pham, M. V.; Ye, B.; Cramer, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 10762. (n) Qi, Z.; Wang, M.; Li, X. *Chem. Commun.* **2014**, *50*, 9776.

(28) Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74,* 7094.

(29) Schipper, D. J.; Hutchinson, M.; Fagnou, K. *J. Am. Chem. Soc.* **2010**, *132*, 6910.

(30) Wencel-Delord, J.; Nimphius, C.; Patureau, F. W.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51,*

2247.

(31) Karthikeyan, K.; Haridharan, R.; Cheng, C.-H. *Angew. Chem., Int. Ed.*, **2012**, *51*, 12343.

(32) (a) Hyster, T. K.; Knörr, L.; Ward, T. R.; Rovis, T. *Science* **2012**, *338*, 500. (b) Newton, C. G.; Kossler, D.; Cramer, N. *J. Am. Chem. Soc.* **2016**, *138*, 3935. (c) Song, G.; Li, X. *Acc. Chem. Res.* **2015**, *48*, 1007. (d) Yoshino, T.; Ikemoto, H.; Matsunaga, S.; Kanai, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 2207. (e) Yoshikai, N. *ChemCatChem* **2015**, *7*, 732. (f) Wei, D.; Zhu, X.; Niu, J.-L.; Song, M.-P. *ChemCatChem* **2016**, *8*, 1242.

(33) For a review, see: Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.

(34) (a) Lewis, L. N.; Smith, J. F. *J. Am. Chem. Soc.* **1986**, *108*, 2728. (b) Bedford, R. B.; Coles, S. J.; Hursthouse, M. B.; Limmert, M. E. *Angew. Chem., Int. Ed.* **2003**, *42*, 112. (c) Oi, S.; Watanabe, S.-i.; Fukita, S.; Inoue, Y. *Tetrahedron Lett.* **2003**, *44*, 8665. (d) Bedford, R. B.; Limmert, M. E. *J. Org. Chem.* **2003**, *68*, 8669. (e) Lewis, J. C.; Wu, J.; Bergman, R. G.; Ellman, J. A. *Organometallics* **2005**, *24*, 5737.

(35) Takebayashi, S.; Shibata, T. *Organometallics* **2012**, *31*, 4114.

(36) (a) Hou, C.; Ren, Y.; Lang, R.; Hu, X.; Xia, C.; Li, F. *Chem. Commun.* **2012**, *48*, 5181. (b) Feng, C. G.; Ye, M.; Xiao, K. J.; Li, S.; Yu, J. Q. *J. Am. Chem. Soc.* **2013**, *135*, 9322. (c) Li, C.; Yano, T.; Ishida, N.; Murakami, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 9801. (d) Hong, G.; Mao, D.; Wu, S.; Wang, L. *J. Org. Chem.* **2014**, *79*, 10629. (e) Min, M.; Kang, D.; Jung, S.; Hong, S. *Adv. Synth. Catal.*, **2016**, *358*, 1296.

(37) (a) Kagayama, T.; Nakano, A.; Sakaguchi, S.; Ishii, Y. *Org. Lett.* **2006**, *8*, 407. (b) Sato, A.; Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 1694. (c) Zhou, J.; Zhang, G.-L.; Zou, J.-P.; Zhang, W. *Eur. J. Org. Chem.* **2011**, *2011*, 3412.

(38) For selected reviews, see: (a) Leca, D.; Fensterbank, L.; Lacote, E.; Malacria, M. *Chem. Soc. Rev.* **2005**, *34*, 858. (b) Yorimitsu, H. *Beilstein J. Org. Chem.* **2013**, *9*, 1269. (c) Kawaguchi, S.; Ogawa, A. *Synlett* **2013**, *24*, 2199. (d) Pan, X.-Q.; Zou, J.-P.; Yi, W.-B.; Zhang, W. *Tetrahedron* **2015**, *71*, 7481.

(39) (a) Michaelis, M. *Ber.* **1879**, *12*, 1009. (b) Olah, G. A.; Hehemann, D. *J. Org. Chem.* **1977**, *42*, 2190. (c) Baillie, C.; Zhang, L.; Xiao, J. *J. Org. Chem.* **2004**, *69*, 7779, (d) Diaz, A. A.; Young, J. D.; Khan, M. A.; Wehmschulte, R. J. *Inorg. Chem.* **2006**, *45*, 5568. (e) Hatakeyama, T.; Hashimoto, S.; Nakamura, M. *Org. Lett.* **2011**, *13*, 2130. (g) Hashimoto, S.; Nakatsuka, S.; Nakamura, M.; Hatakeyama, T. *Angew. Chem., Int. Ed.* **2014**, *53*, 14074.

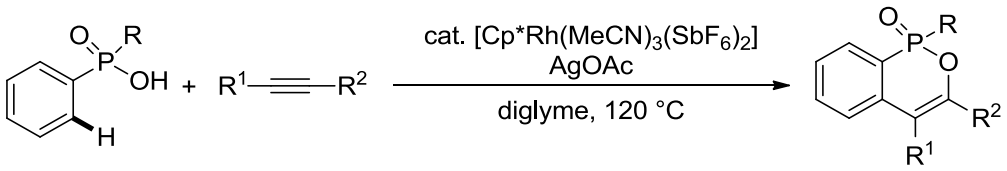
(40) For reviews on phosphenium species, see: (a) Cowley, A. H.; Kemp, R. A. *Chem. Rev.* **1985**, *85*, 367. (b) Gudat, D. *Coord. Chem. Rev.* **1997**, *163*, 71. (c) Gudat, D. *Acc. Chem. Res.* **2010**, *43*,

1307.

Chapter 2

Synthesis of Phosphaisocoumarins by Rh(III)-catalyzed Direct Coupling of Arylphosphinic Acids with Alkynes

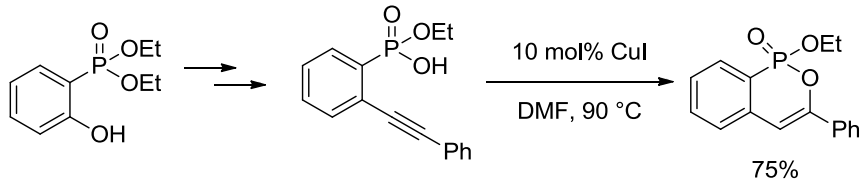
A synthesis of phosphaisocoumarins by the Cp*Rh(III)-catalyzed oxidative coupling of arylphosphinic acid derivatives with alkynes is described. The straightforward transformation is achieved by regioselective C-H bond functionalization. The P(=O)–OH groups effectively act as the directing group for the *ortho*-C–H bond cleavage.



Introduction

As described in Chapter 1, phosphorus-containing heterocycles have attracted much attention as new building blocks of biologically active compounds as well as organic functional molecules. Among them, phosphaisocoumarins, phosphorus analogs of isocoumarins, have exhibited their potential as a new class of inhibitor for pancreatic cholesterol esterase.[1] However, synthetic approaches to the phosphaisocoumarin framework are limited. As a recent example, Ding and co-workers reported their synthesis via Sonogashira coupling and subsequent copper-catalyzed cyclization of resulting *ortho*-alkynylphenylphosphonic acids (Scheme 2.1).[2] While interesting, the sequence involves multi-steps. Therefore, development of more efficient and straightforward synthetic methods for these molecules is desired.

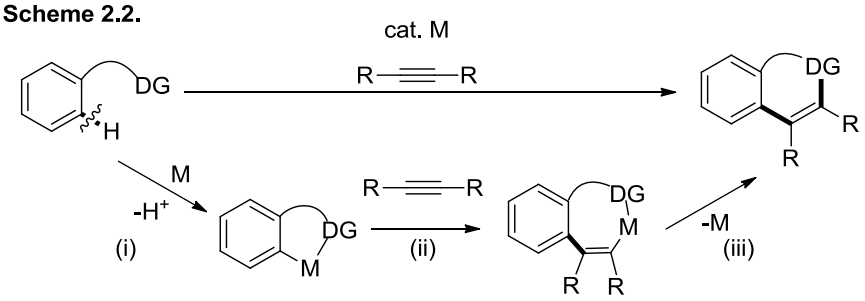
Scheme 2.1.



Transition-metal-catalyzed regioselective C–H functionalizations with the aid of directing groups (−DG) have been recognized as important and environmentally benign synthetic tools, because these procedures provide atom- and step-economical routes to complex target molecules from simple starting materials.[3] Particularly, the oxidative annulation reactions of aromatic substrates possessing a directing group with internal alkynes through (i) chelation-directed C–H bond cleavage, (ii) alkyne insertion, and (iii) annulation allow the straightforward syntheses of benzannulated heterocycles from

readily available monofunctionalized aromatic substrates (Scheme 2.2).

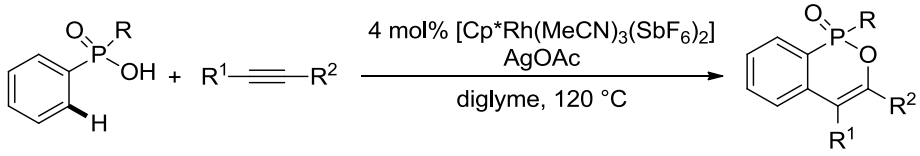
Scheme 2.2.



As an early example, Miura, Satoh, and co-workers reported the rhodium-catalyzed oxidative coupling of benzoic acids with alkynes to produce isocoumarin derivatives (DG = COO(H) in Scheme 2.2).[4] After the discovery, similar annulations of various aromatic substrates have also been developed by them[5] and others.[6] It seems to be possible to achieve the straightforward synthesis of phosphaisocoumarins by this oxidative annulation approach via P–OH directed C–H functionalization. However, the utilization of P–OH groups as directing groups has been scarcely explored.

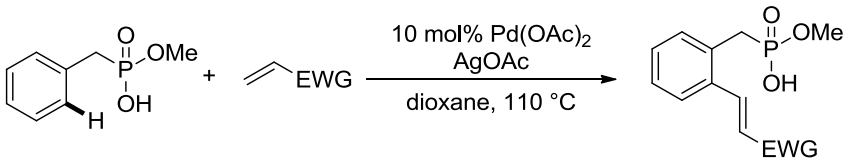
In this Chapter 2, new findings for the synthesis of phosphaisocoumarin derivatives by Cp*Rh(III)-catalyzed oxidative annulation reaction of arylphosphinic acids with internal alkynes are described (Scheme 2.3; published online 17 June 2013).

Scheme 2.3.



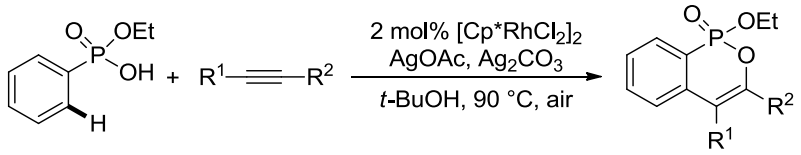
During the course of this study, Kim and co-workers reported the palladium-catalyzed oxidative coupling of benzylphosphonic acids and arylphosphate diesters with alkenes (Scheme 2.4).[7]

Scheme 2.4.



Furthermore, Lee and co-workers reported a Rh(III)-catalyzed similar annulation reaction of arylphosphonic acid monoesters (Scheme 2.5; published online 21 June 2013).[8]

Scheme 2.5.

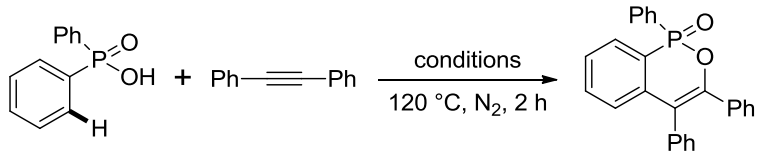


Results and discussion

The results of optimization study are summarized in Table 2.1. In an initial attempt, diphenylphosphinic acid (**1a**) (0.25 mmol) was treated with 1 equiv of diphenylacetylene (**2a**) (0.25 mmol) in the presence of $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (0.01 mmol) and AgOAc (1 mmol) as catalyst and oxidant, respectively, in DMF (3 mL) at 120 °C for 2 h under N_2. As a result, the oxidative annulation proceeded to afford 1,3,4-triphenyl-1*H*-2,1-benzoxaphosphorin-1-oxide (**3a**) in 34% yield (entry 1). Solvent screening showed diglyme was the most effective solvent (entries 2-4). Ag_2CO_3 and $Cu(OAc)_2•H_2O$ were not efficient oxidants for this reaction (entries 5, 6). Increasing the amount of **2a** (0.375 mmol) led to enhancement of the product yield to 94% (entry 7). The use of $[Cp^*RhCl_2]_2$ (0.005 mmol) as catalyst in place of $[Cp^*Rh(MeCN)_3][SbF_6]_2$ reduced the reaction efficiency (entry 8). With a slightly decreased amount of AgOAc

(0.75 mmol), **3a** was obtained almost quantitatively (entry 9). However, further decrease in the amount of AgOAc reduced the product yield (entry 10).

Table 2.1. Optimization Study of the Reaction of Diphenylphosphinic Acid (1a) with Diphenylacetylene (2a)



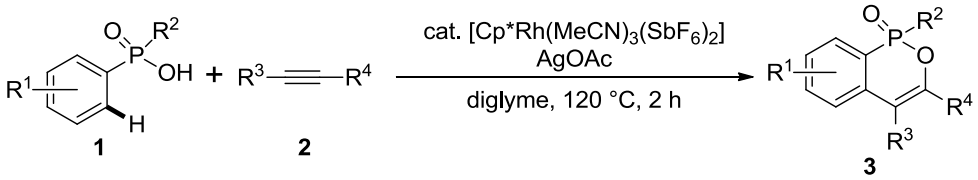
1a **2a** **3aa**

entry	cat. (mol%)	oxidant (equiv.)	**1**:**2** (mmol)	solvent	yield of **3aa** (%)[a]
1	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	AgOAc (4.0)	0.25:0.25	DMF	34
2	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	AgOAc (4.0)	0.25:0.25	*o*-xylene	trace
3	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	AgOAc (4.0)	0.25:0.25	dioxane	71
4	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	AgOAc (4.0)	0.25:0.25	diglyme	79 (73)
5	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	Ag_2CO_3 (2.0)	0.25:0.25	diglyme	trace
6	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	$Cu(OAc)_2 \cdot H_2O$ (4.0)	0.25:0.25	diglyme	10
7	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	AgOAc (4.0)	0.25:0.375	diglyme	94
8	$[Cp^*RhCl_2]_2$ (2)	AgOAc (4.0)	0.25:0.375	diglyme	68
9	***$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)***	***AgOAc (3.0)***	***0.25:0.375***	***diglyme***	***99 (95)***
10	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	AgOAc (2.0)	0.25:0.375	diglyme	78

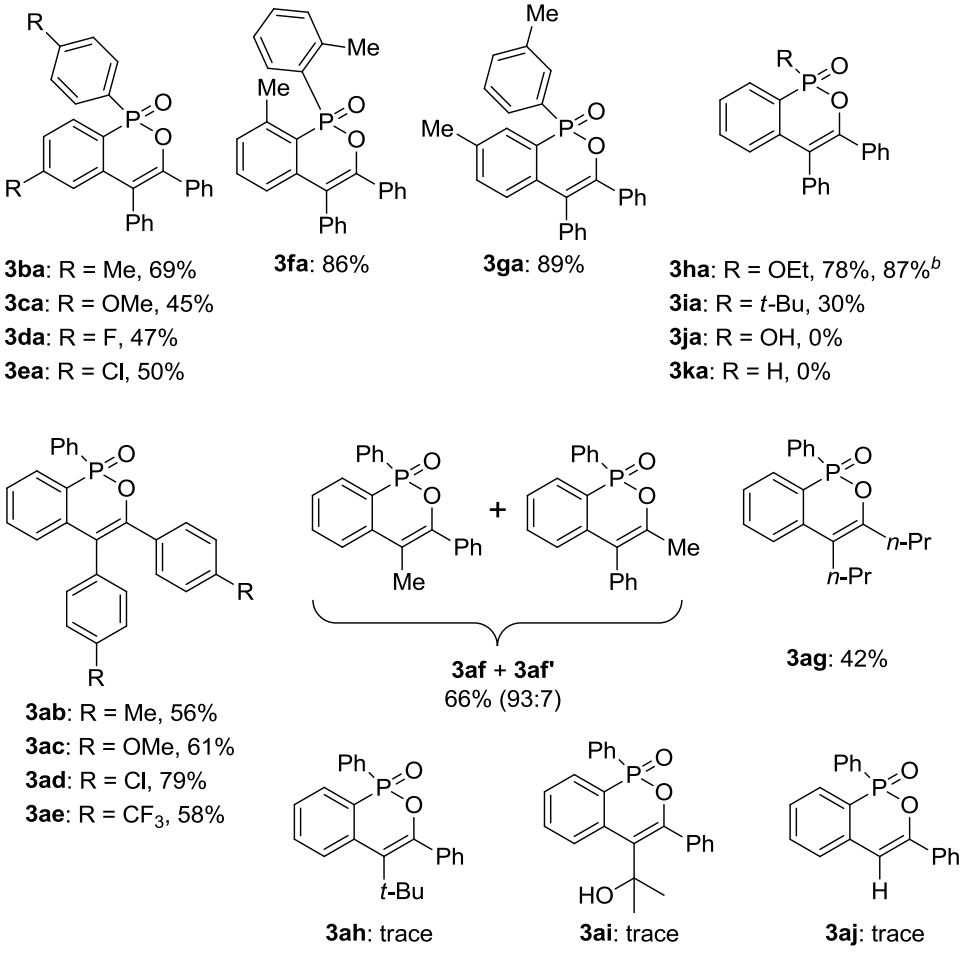
[a] GC yield. Isolated yield is given in parentheses.

Under the optimized conditions, the reactions of various phenylphosphinic acids **1** with alkynes **2** were next examined. Bis(*para*-disubstituted phenyl)phosphinic acids **1b-1e** underwent the coupling with **2a** to afford the corresponding phosphaisocoumarins **3ba-3ea**. In these cases, 1:2 coupling products were also detected by GC-MS. Therefore, the yields of desired 1:1 coupling product **3** seem to somewhat decrease for the overreaction. As expected, the use of sterically hindered bis(*ortho*-methylphenyl)phosphinic acid (**1f**) was found to suppress the overreaction to give **3fa** selectively in 86% yield. In the case of *meta*-methyl-substituted **1g**, the coupling reaction took place at the less hindered position selectively to form **3ga** in 89%

Table 2.2. Scope of Substrate[a]



1 2 3



3ba: R = Me, 69%
3ca: R = OMe, 45%
3da: R = F, 47%
3ea: R = Cl, 50%

3fa: 86%

3ga: 89%

3ha: R = OEt, 78%, 87%[b]
3ia: R = *t*-Bu, 30%
3ja: R = OH, 0%
3ka: R = H, 0%

3ab: R = Me, 56%
3ac: R = OMe, 61%
3ad: R = Cl, 79%
3ae: R = CF_3, 58%

3af + **3af'**
66% (93:7)

3ag: 42%

3ah: trace

3ai: trace

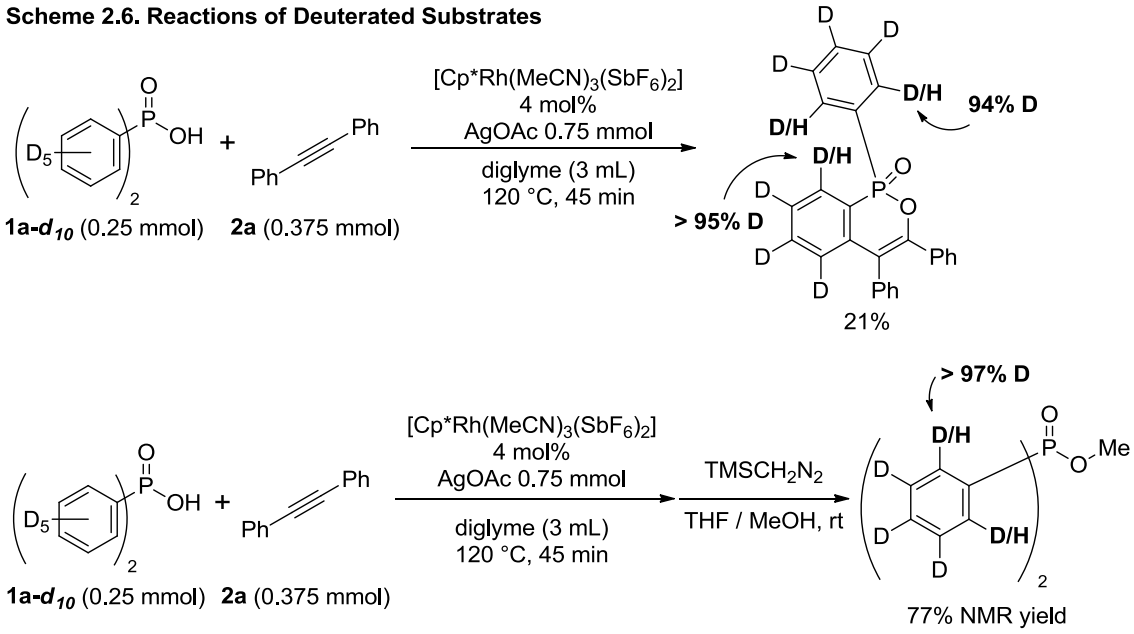
3aj: trace

[a] Reaction conditions: **1** (0.25 mmol), **2** (0.375 mmol), [Cp*Rh(MeCN)$_3$(SbF$_6$)$_2$] (0.01 mmol), AgOAc (0.75 mmol) in diglyme (3 mL) at 120 °C under N_2 for 2 h. [b] 3 mmol scale.

yield. The reaction of phenylphosphonic acid monoethyl ester (**1h**) with **2a** proceeded smoothly to produce **3ha** in 78% yield. In this case, the reaction proceeded efficiently on 3 mmol scale to afford **3ha** in 87%. It should be noted that this compound is an important intermediate and their hydrolysis and alcoholysis with or without ring-opening have been established.[9] Alkylarylphosphinic acid **1i** also reacts with **2a** to

give **3ia** in low yield, while the reaction of phenylphosphonic- and phosphinic acid (**1j**, **1k**) did not gave any coupling product. A variety of *para*-substituted diphenylacetylenes **2b**-**2e** also coupled with **1a** to produce the corresponding phosphaisocoumarins **3ab**-**3ae**. The reaction of unsymmetrical 1-phenyl-1-propyne (**2f**) gave **3af** predominantly, along with minor amounts of an isomer **3af'** and a separable 1:2 coupling product. The dialkylacetylene **2g** coupled with **1a** to afford **3ag** in moderate yield. The reaction of sterically hindered alkynes **2h**, **2i**, and terminal alkyne **2j** did not proceed at all.

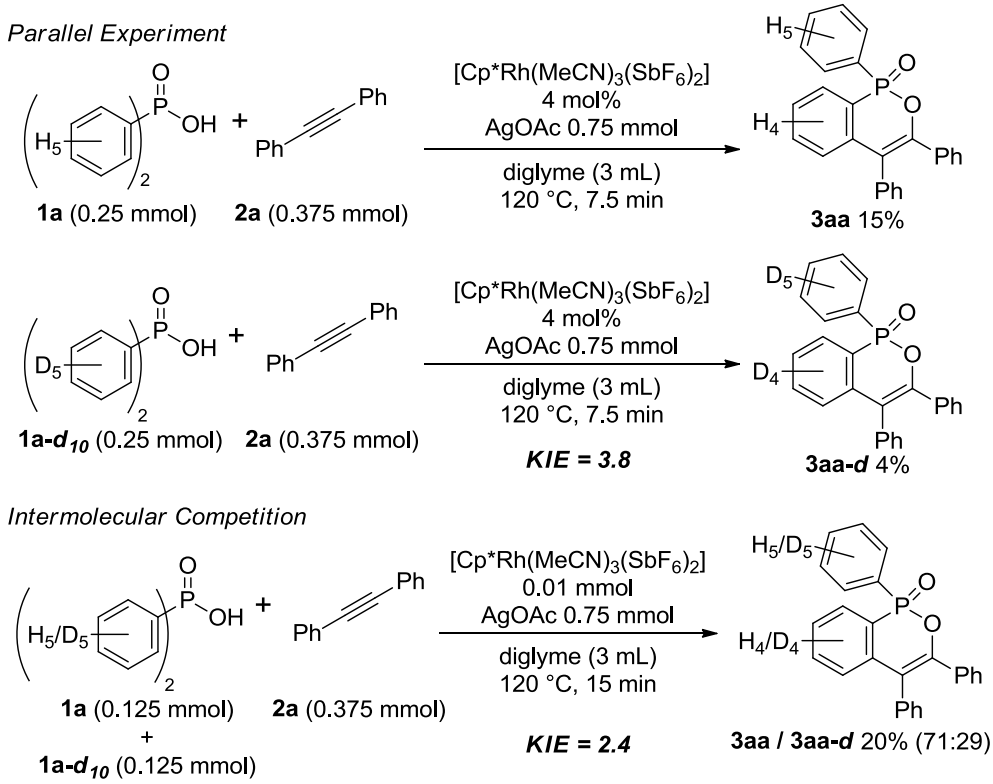
Scheme 2.6. Reactions of Deuterated Substrates



To gain a mechanistic insight, next the author carried out deuterium labeling experiments. The reaction of **1a-*d*$_{10}$** with **2a** under standard conditions for 45 min afforded the coupling product in 21% yield (Scheme 2.6). The starting material was also recovered as methyl ester in 77% yield. In these cases, almost no D/H exchange was observed at *ortho* positions of both **1a-*d*$_{10}$** and annulated product. This result suggests that C-H bond cleavage step seems to be irreversible. In addition, the author carried out

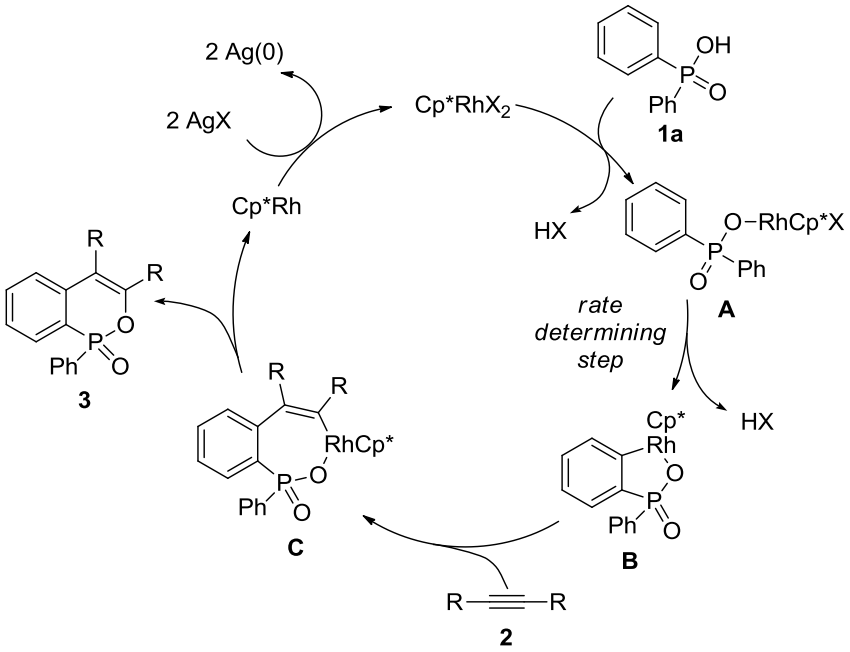
kinetic isotope effect (KIE) measurement (Scheme 2.7). As a result, significant KIE was observed in both parallel experiment (KIE = 3.8) and intermolecular competition (KIE = 2.4). These results imply C-H bond cleavage step seems to be the rate-determining step.

Scheme 2.7. KIE Experiments



Based on the mechanistic studies, a plausible mechanism for the reaction of diphenylphosphinic acid (**1a**) with alkyne **2** is illustrated in Scheme 2.8, in which neutral ligands are omitted. Coordination of **1a** to a Rh^{III} center and subsequent cyclorhodation on one of the phenyl groups of a resulting intermediate **A** take place to form a five-membered rhodacycle intermediate **B**. This step seems to be the rate-determining step. Then, alkyne insertion to form **C** and reductive elimination may occur to release **3**. The Rh^{I} species seems to be oxidized by Ag^{I} to regenerate Rh^{III}.

Scheme 2.8. A Plausible Mechanism



Summary

In Chapter 2, a new straightforward synthesis of phosphaisocoumarins by a rhodium-catalyzed oxidative coupling of phenylphosphinic acids with alkynes is described. A number of substituted phosphaisocoumarins are synthesized in single step from the readily available substrates. This transformation represents an effective example of the annulation depicted in Scheme 2.2 involving C-H bond cleavage directed by phosphinoxy groups.

Experimental Section

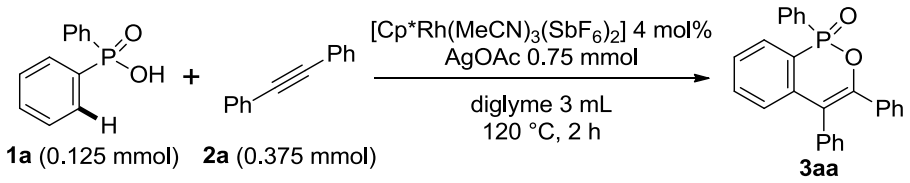
General. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz for $CDCl_3$ solutions. HRMS data were obtained by EI or CI using a double focusing mass spectrometer. GC analysis was carried out using a silicon OV-17 column (i. d. 2.6 mm x 1.5 m). GC-MS analysis was carried out using a CBP-1 capillary column (i. d. 0.25 mm x 25 m). The structures of all products listed below were unambiguously determined by ^{1}H and ^{13}C NMR with the aid of NOE, COSY, HSQC, and HMBC

experiments.

Diarylphosphinic acids **1b-d**,[9] phenylphosphonic acid monoethyl ester **1e**,[10] and diarylacetylenes **2b**,**c**[11] were prepared according to published procedures. Other starting materials were commercially available.

The following experimental procedures may be regarded as typical in methodology and scale.

Representative Procedure for Rh(III)-catalyzed Oxidative Coupling through C-H Bond Cleavage Directed by Phosphinoxy Groups.



1a (0.125 mmol) **2a** (0.375 mmol) **3aa**

Reaction of Diphenylphosphinic Acid (1a) with Diphenylacetylene (2a) (entry 9 in Table 2.1).

To a 20 mL two-necked flask with a reflux condenser, a balloon, and a rubber cap were added diphenylphosphinic acid **1a** (54 mg, 0.25 mmol), diphenylacetylene **2a** (68 mg, 0.38 mmol), $[Cp^*Rh(MeCN)_3(SbF_6)_2]$ (8.3 mg, 0.01 mmol), AgOAc (125 mg, 0.75 mmol), dibenzyl (30~40 mg; as an internal standard), and diglyme (3 mL). The reaction mixture was stirred under N_2 at 120 °C for 2 h. After cooling, the mixture was diluted with 20 mL of ethyl acetate and insoluble solids were filtered off through a short pad of celite. The organic layer was washed with water (20 mL, three times) and dried over Na_2SO_4. Volatiles were removed in vacuo and subsequent purification by column chromatography on silica gel with hexane/ethyl acetate (1:1, v/v) as an eluent gave product **3aa** (94 mg, 95 %).

Characterization Data of Products

1,3,4-Triphenyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3aa): mp 140-142 °C, 94 mg (95%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05 (dd, J = 4.8, 8.0 Hz, 2H), 7.07-7.14 (m, 3H), 7.22-7.62 (m, 12H), 7.94 (dd, J = 7.2, 13.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 119.1 (d, J = 11.0 Hz), 123.2 (d, J = 128.9 Hz), 126.8 (d, J = 9.5 Hz), 127.5, 127.7, 127.8, 128.4 (d, J = 3.1 Hz), 128.6, 128.9, 129.1, 130.1 (d, J = 144.2 Hz), 130.3 (d, J = 12.3 Hz), 131.6, 132.3 (d, J = 10.9 Hz), 132.4 (d, J = 2.5 Hz), 132.9 (d, J = 2.8 Hz), 134.6 (d, J = 5.0 Hz), 136.0, 138.7 (d, J = 5.5 Hz), 146.9 (d, J = 11.1 Hz);

$^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 24.4; HRMS m/z ($M+H^+$) Calcd for $C_{26}H_{20}O_2P$: 395.1195. Found 395.1196.

6-Methyl-1-(4-methylphenyl)-3,4-diphenyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3ba): oil, 73 mg (69%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 3H), 2.42 (s, 3H), 6.84 (d, J = 4.6 Hz, 1H), 7.06-7.16 (m, 4H), 7.21 (dd, J = 1.4, 8.0 Hz, 2H), 7.25-7.33 (m, 4H), 7.35-7.40 (m, 3H), 7.49 (dd, J = 7.6, 13.9 Hz, 1H), 7.81 (dd, J = 8.1, 13.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7, 21.9, 119.0 (d, J = 11.4 Hz), 120.4 (d, J = 131.4 Hz), 127.03 (d, J = 146.8 Hz), 127.03 (d, J = 9.8 Hz), 127.4, 127.7, 128.2, 128.5 (d, J = 15.3 Hz) 128.8, 129.9, 129.2 (d, J = 14.3 Hz), 130.2 (d, J = 12.4 Hz), 131.6, 132.3, (d, J = 11.4 Hz), 134.9, (d, J = 5.7 Hz), 136.2, 138.6 (d, J = 5.0 Hz), 142.8 (d, J = 2.9 Hz), 143.5 (d, J = 2.9 Hz), 146.9 (d, J = 10.5 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 24.3; HRMS m/z (M^+) Calcd for $C_{28}H_{23}O_2P$: 422.1436. Found 422.1440.

6-Methoxy-1-(4-methoxyphenyl)-3,4-diphenyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3ca): oil, 51 mg (45%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.68 (s, 3H), 3.87 (s, 3H), 6.53 (dd, J = 2.4, 4.1 Hz, 1H), 6.87 (td, J = 2.4, 8.5 Hz, 1H), 7.00 (dd, J = 2.9, 8.8 Hz, 2H), 7.07-7.15 (m, 3H), 7.20-7.23 (m, 2H), 7.26-7.28 (m, 2H), 7.32-7.39 (m, 3H), 7.54 (dd, J = 8.4, 13.8 Hz, 1H), 7.85 (dd, J = 8.8, 12.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.2, 55.4, 112.2 (d, J = 10.3 Hz), 113.3 (d, J = 15.3 Hz), 114.1 (d, J = 15.0 Hz), 115.6 (d, J = 135.9 Hz), 118.8 (d, J = 10.5 Hz), 121.8 (d, J = 151.9 Hz), 127.5, 127.8, 128.4, 128.8, 129.1, 131.6, 132.2 (d, J = 13.4 Hz), 134.3 (d, J = 12.4 Hz), 134.9 (d, J = 4.8 Hz), 136.1, 140.9 (d, J = 5.7 Hz), 147.4 (d, J = 10.5 Hz), 162.6 (d, J = 2.9 Hz), 163.2 (d, J = 2.9 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 24.4; HRMS m/z (M^+) Calcd for $C_{28}H_{23}O_4P$: 454.1334. Found 454.1339.

6-Fluoro-1-(4-fluorophenyl)-3,4-diphenyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3da): oil, 50.9 mg (47%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.75 (ddd, J = 2.4, 4.0, 11.2 Hz, 1H), 7.05 (ddt, J = 2.4, 2.4, 8.4 Hz, 1H), 7.09-7.30 (m, 9H), 7.37-7.43 (m, 3H), 7.57 (ddd, J = 6.0, 8.4, 14.4 Hz, 1H), 7.94 (ddd, J = 6.0, 8.4, 14.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.2, 55.4, 112.2 (d, J = 10.3 Hz), 113.3 (d, J = 15.3 Hz), 114.1 (d, J = 15.0 Hz), 115.6 (d, J = 135.9 Hz), 118.8 (d, J = 10.5 Hz), 121.8 (d, J = 151.9 Hz), 127.5, 127.8, 128.4, 128.8, 129.1, 131.6, 132.2 (d, J = 13.4 Hz), 134.3 (d, J = 12.4 Hz), 134.9 (d, J = 4.8 Hz), 136.1, 140.9 (d, J = 5.7 Hz), 147.4 (d, J = 10.5 Hz), 162.6 (d, J = 2.9 Hz), 163.2 (d, J = 2.9 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 22.9; HRMS m/z ($M+H^+$) Calcd for $C_{26}H_{18}F_2O_2P$: 431.1007. Found 431.1009.

6-Chloro-1-(4-chlorophenyl)-3,4-diphenyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3ea): oil, 58.0 mg (50%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.04 (dd, J = 1.9, 4.1 Hz, 1H), 7.10-7.28 (m, 7H), 7.33 (ddd, J = 2.2, 2.2, 8.1 Hz, 1H), 7.38-7.55 (m, 6H), 7.86 (dd, J = 8.5, 13.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 114.3 (d, J = 10.9 Hz), 121.1 (d, J = 136.8 Hz), 126.8 (d, J = 10.1 Hz), 127.7, 128.0 (d, J = 14.8 Hz), 128.1 (d, J = 147.6 Hz), 128.3, 128.9, 129.06, 129.08, 129.2, 131.5, 131.6 (d, J = 13.2 Hz), 133.8 (d, J = 11.9 Hz), 134.2 (d, J = 5.1 Hz), 135.1 139.5 (d, J = 3.4 Hz), 140.1 (d, J = 3.6 Hz), 140.6 (d, J = 6.0 Hz), 148.1 (d, J = 11.1 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 22.7; HRMS m/z ($M+H^+$) Calcd for $C_{26}H_{18}Cl_2O_2P$: 463.0416. Found 463.0418.

8-Methyl-1-(2-methylphenyl)-3,4-diphenyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3fa): mp 53-55 °C, 91 mg (86%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.19 (s, 3H), 2.29 (s, 3H), 6.88 (dd, J = 4.4, 8.1 Hz, 1H), 7.06-7.14 (m, 4H), 7.18-7.21 (m, 2H), 7.22-7.26 (m, 3H), 7.31-7.42 (m, 5H), 7.49 (t, J = 7.4 Hz, 1H), 8.26 (ddd, J = 1.4, 7.8, 14.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.6 (d, J = 4.8 Hz), 21.3 (d, J = 5.8 Hz), 118.8 (d, J = 11.5 Hz), 121.8 (d, J = 127.4 Hz), 125.1 (d, J = 9.6 Hz), 125.8 (d, J = 13.7 Hz), 127.5, 127.7, 128.3, 128.8 (overlapped), 129.0, 130.1 (d, J = 142.8 Hz), 130.2 (d, J = 13.2 Hz), 131.5 (d, J = 12.5 Hz), 131.8, 132.2 (d, J = 1.9 Hz), 132.9 (d, J = 2.6 Hz), 134.5, (d, J = 11.5 Hz), 134.8 (d, J = 4.8 Hz), 139.5 (d, J = 5.8 Hz), 140.5 (d, J = 12.5 Hz), 141.8 (d, J = 10.6 Hz), 146.3 (d, J = 12.5 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 22.2; HRMS m/z (M^+) Calcd for $C_{28}H_{23}O_2P$: 422.1436. Found 422.1425.

7-methyl-3,4-diphenyl-1-(m-tolyl)-*1H*-2,1-benzoxaphosphorin-1-oxide (3ga): gum, 93.9 mg (89%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3H), 2.42 (s, 3H), 6.94 (dd, J = 5.1 Hz, 8.2 Hz, 1H), 7.06-7.15 (m, 3H), 7.21-7.28 (m, 5H), 7.34-7.42 (m, 6H), 7.67-7.72 (m, 1H), 7.80 (d, J = 13.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 21.4, 119.0 (d, J = 10.9 Hz), 123.2 (d, J = 127.8 Hz), 126.8 (d, J = 10.1 Hz), 127.5, 127.8, 128.3, 128.4 (d, J = 14.8 Hz), 128.9, 129.1, 129.5 (d, J = 11.1 Hz), 130.1 (d, J = 143.3 Hz), 130.4 (d, J = 12.2 Hz), 131.6, 132.8 (d, J = 10.8 Hz), 133.4 (d, J = 2.6 Hz), 133.8 (d, J = 2.8 Hz), 134.9 (d, J = 5.0 Hz), 136.1 (d, J = 5.3 Hz), 136.3, 137.8 (d, J = 14.1 Hz), 138.4 (d, J = 13.8 Hz), 146.2 (d, J = 11.0 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 25.0; HRMS m/z ($M+H^+$) Calcd for $C_{28}H_{24}O_2P$: 423.1508. Found 423.1509.

1-Ethoxy-3,4-diphenyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3ha): mp 127-128 °C, 71 mg (78%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32 (t, J = 7.0 Hz, 3H), 4.21-4.31 (m, 2H), 6.96 (t, J = 7.0 Hz, 1H),

7.12-7.26 (m, 7H), 7.35-7.36 (m, 3H), 7.41-7.50 (m, 2H), 7.96 (ddd, J = 1.7, 7.3, 15.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4 (d, J= 5.8 Hz), 63.0 (d, J = 6.7 Hz), 119.8 (d, J = 12.2 Hz), 120.9 (d, J = 180.2 Hz), 127.1 (d, J = 11.9 Hz), 127.62 (d, J = 15.3 Hz), 127.63, 127.9, 128.5, 128.8, 128.9, 129.3 (d, J = 9.3 Hz), 131.5, 132.8 (d, J = 2.9 Hz), 134.5 (d, J = 5.7 Hz), 136.0, 140.2 (d, J = 7.6 Hz), 147.8 (d, J = 10.5 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 11.2; HRMS m/z (M^+) Calcd for $C_{22}H_{19}O_3P$: 362.1072. Found 362.1068.

1-*t*-Butyl-3,4-diphenyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3ia): mp 184-186 °C, 28.4 mg (30%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (d, J = 16.9 Hz, 9H), 6.89-6.93 (m, 1H), 7.11-7.46 (m, 12H), 7.90-95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.8, 35.8 (d, J = 99.7 Hz), 119.3, 119.4 (d, J = 149.5 Hz), 126.7 (d, J = 8.6 Hz), 127.4 (d, J = 12.5 Hz), 127.6 (d, J = 12.5 Hz), 127.6, 127.7, 128.4, 128.8, 128.9 (br), 131.3 (d, J = 9.6 Hz), 131.4 (br), 132.7 (d, J =2.9 Hz), 134.8 (d, J = 5.7 Hz), 136.3, 139.9 (d, J = 6.7 Hz), 148.4 (d, J = 11.5 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 46.3; HRMS m/z ($M+H^+$) Calcd for $C_{24}H_{24}O_2P$: 375.1508. Found 357.1517.

3,4-Bis(4-methylphenyl)-1-phenyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3ab): mp 221-223 °C, 89.2 mg (56%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 3H), 2.40 (s, 3H), 6.92 (d, J = 8.4 Hz, 2H), 7.05 (s, J = 4.7 Hz, 8.0 Hz, 1H), 7.13-7.21 (m, 6H), 7.31 (dt, J = 3.1 Hz, 7.5 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 7.49-7.53 (m, 2H), 7.56-7.62 (m, 2H), 7.93 (ddd, J = 1.4 Hz, 7.2 Hz, 13.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2, 21.3, 118.4 (d, J = 10.5 Hz), 123.1 (d, J = 128.7 Hz), 126.7 (d, J = 9.5 Hz), 127.3 (d, J = 14.3 Hz), 128.3, 128.5 (d, J = 13.4 Hz), 129.0, 129.6 (d, J = 9.5 Hz), 130.2 (d, J = 12.4 Hz), 131.4, 131.5 (d, J = 97.3 Hz), 131.9, 132.3 (d, J = 11.5 Hz), 132.4 (d, J = 2.9 Hz), 132.9 (d, J = 2.4 Hz), 133.1, 137.4, 138.4, 139.0 (d, J = 5.7 Hz), 146.9 (d, J = 2.5 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 24.4; HRMS m/z ($M+H^+$) Calcd for $C_{28}H_{23}O_2P$: 422.1436. Found 422.1438.

3,4-Bis(4-methoxyphenyl)-1-phenyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3ac): mp 49-51 °C, 69 mg (61%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.72 (s, 3H), 3.85 (s, 3H), 6.64 (d, J = 8.5 Hz, 2H), 6.94 (d, J = 8.0 Hz, 2H), 7.07 (dd, J = 4.8, 8.1 Hz, 1H), 7.19 (m, 4H), 7.30 (td, J = 3.1, 7.6 Hz, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.49-7.62 (m, 4H), 7.93 (dd, J = 8.1, 13.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.1, 55.2, 113.0, 114.4, 117.5 (d, J = 11.5 Hz), 122.9 (d, J = 130.3 Hz), 126.6 (d, J = 9.6 Hz), 127.20 (d, J = 14.4 Hz), 127.23 (d, J = 4.8 Hz), 128.4, 128.5 (d, J = 14.4 Hz), 130.19 (d, J = 12.5 Hz), 130.20 (d, J = 145.6 Hz), 130.5, 132.3 (d, J = 11.0 Hz), 132.4 (d, J = 3.4 Hz), 132.7, 132.9 (d, J

= 2.6 Hz), 139.3 (d, J = 4.8 Hz), 146.8 (d, J = 11.5 Hz), 159.1, 159.4; $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 25.0; HRMS m/z (M^+) Calcd for $C_{28}H_{23}O_4P$: 454.1334. Found 454.1336.

3,4-Bis(4-chlorophenyl)-1-phenyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3ad): mp 58-60 °C, 92 mg (79%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.02 (dd, J = 4.8, 8.0 Hz, 1H), 7.12 (d, J = 9.0 Hz, 2H), 7.16 (d, J = 8.8 Hz, 2H), 7.21 (d, J = 8.3 Hz, 2H), 7.34-7.40 (m, 3H), 7.47 (t, J = 7.6 Hz, 1H), 7.51-7.66 (m, 4H), 7.92 (ddd, J = 1.4, 8.4, 13.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 118.5 (d, J = 11.4 Hz), 123.3 (d, J = 128.7 Hz), 126.6 (d, J = 9.5 Hz), 127.97 (d, J = 14.3 Hz), 128.02, 128.6 (d, J = 14.3 Hz), 129.39 (overlapped), 129.44 (d, J = 144.9 Hz), 130.4, 130.5, 132.4 (d, J = 11.4 Hz), 132.6 (d, J = 2.9 Hz), 132.87, 132.93, 133.2 (d, J = 2.9 Hz), 134.2 (d, J = 9.8 Hz), 134.7, 137.9 (d, J = 4.8 Hz), 146.0 (d, J = 10.5 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 25.1; HRMS m/z (M^+) Calcd for $C_{26}H_{17}Cl_2O_2P$: 462.0343. Found 462.0331.

3,4-Bis[4-(trifluoromethyl)phenyl]-1-phenyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3ae): mp 49-51 °C, 75.8 mg (58%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97 (dd, J = 4.8, 8.0 Hz, 1H), 7.33 (d, J = 8.4 Hz, 2H), 7.39-7.45 (m, 5H), 7.50 (t, J = 7.6 Hz, 1H), 7.53-7.66 (m, 4H), 7.69 (d, J = 8.1 Hz, 2H), 7.95 (ddd, J = 1.4, 8.6, 13.6 Hz, 2H); $^{13}C\{^{19}F\}$ NMR (100 MHz, $CDCl_3$): δ 119.5 (d, J = 11.2 Hz), 123.5 (d, J = 128.7 Hz), 123.6, 123.9, 124.8, 126.1 (2C, overlapped), 126.6 (d, J = 9.3 Hz), 128.4 (d, J = 14.6 Hz), 128.7 (d, J = 14.3 Hz), 129.4, 130.2 (d, J = 78.2 Hz), 130.51, 130.52 (d, J = 10.5 Hz), 132.0, 132.5 (d, J = 10.5 Hz), 132.8 (d, J = 2.9 Hz), 133.4 (d, J = 2.9 Hz), 137.4 (d, J = 5.5 Hz), 137.8 (d, J = 5.3 Hz), 139.5, 145.7 (d, J = 10.7 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 25.2; HRMS m/z (M^+) Calcd for $C_{28}H_{17}F_6O_2P$: 530.0870. Found 530.0862.

1,3-Diphenyl-4-methyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3af) + an isomer (3af') [93:7]: oil, 56 mg (66%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.92 (s, 3H), 7.34-7.43 (m, 4H), 7.46-7.52 (m, 3H), 7.56-7.67 (m, 5H), 7.88 (ddd, J = 1.4, 8.3, 13.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.7, 111.0 (d, J = 11.4 Hz), 123.8 (d, J = 129.7 Hz), 124.5 (d, J = 9.5 Hz), 127.4 (d, J = 14.3 Hz), 128.0, 128.2 (d, J = 98.7 Hz), 128.4 (d, J = 13.4 Hz), 129.0, 129.6, 130.1 (d, J = 13.1 Hz), 132.5 (d, J = 11.4 Hz), 132.6 (d, J = 2.9 Hz), 132.9 (d, J = 3.1 Hz), 134.9 (d, J = 4.8 Hz), 138.6 (d, J = 5.7 Hz), 146.3 (d, J = 11.2 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 24.3; HRMS m/z (M^+) Calcd for $C_{21}H_{17}O_2P$: 332.0966. Found 332.0963.

1-Phenyl-3,4-di-*n*-propyl-*1H*-2,1-benzoxaphosphorin-1-oxide (3ag): oil, 34.2 mg (42%); ^{1}H

NMR (400 MHz, $CDCl_3$): δ 0.94 (t, J = 7.3 Hz, 3H), 1.03 (t, J = 7.3 Hz, 3H), 1.55-1.70 (m, 4H), 2.40-2.60 (m, 4H), 7.28 (dt, J = 2.8 Hz, 7.3 Hz, 1H), 7.45-7.50 (m, 4H), 7.55-7.59 (m, 2H), 7.78 (ddd, J = 1.4 Hz, 7.0 Hz, 13.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7, 14.2, 20.2, 22.7, 29.8, 34.1 (d, J = 4.1 Hz), 113.8 (d, J = 11.4 Hz), 123.57 (d, J = 128.7 Hz), 123.60 (d, J = 10.5 Hz), 126.6 (d, J = 14.3 Hz), 128.3 (d, J = 13.4 Hz), 130.3 (d, J = 143.3 Hz), 130.5 (d, J = 12.4 Hz), 132.2 (d, J = 11.4 Hz), 132.5 (d, J = 2.9 Hz), 132.7 (d, J = 2.9 Hz), 137.6 (d, J = 4.8 Hz), 149.8 (d, J = 11.4 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ 23.9; HRMS m/z (M^+) Calcd for $C_{20}H_{23}O_2P$: 326.1436. Found 326.1437.

References and Notes

(1) Li, B.; Zhou, B.; Lu, H.; Ma, L.; Peng, A.-Y. *Eur. J. Med. Chem.* **2010**, *45*, 1955.

(2) (a) Wei, P.; Ding, Y.-X. *Synlett* **2005**, 599. (b) Peng, A.-Y.; Ding, Y.-X. *Org. Lett.* **2004**, *6*, 1119. (c) Peng, A.-Y.; Ding, Y.-X. *J. Am. Chem. Soc.* **2003**, *125*, 15006. (d) Peng, A.-Y.; Hao, F.; Li, B.; Wang, Z.; Du, Y. *J. Org. Chem.* **2008**, *73*, 9012.

(3) Selected recent reviews for C–H functionalization: (a) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814. (b) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788. (c) Mitchell, E. A.; Peschiulli, A.; Lefevre, N.; Meerpoel, L.; Maes, B. U. W. *Chem.—Eur. J.* **2012**, *18*, 10092. (d) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (e) Wencel-Delord, J.; Droge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740. (f) Kuninobu, Y.; Takai, K. *Chem. Rev.* **2011**, *111*, 1938. (g) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780. (h) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. (i) Lapointe, D.; Fagnou, K. *Chem. Lett.* **2010**, *39*, 1118. (j) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (k) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (l) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Commun.* **2010**, *46*, 677. (m) Satoh, T.; Miura, M. *Chem.—Eur. J.* **2010**, *16*, 11212. (n) Satoh, T.; Miura, M. *Synthesis* **2010**, 3395. (o) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (p) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074. (q) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev.* **2009**, *38*, 2447. (r) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335. (s) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013. (t) Ferreira, E. M.; Zhang, H.; Stoltz, B. M. *Tetrahedron* **2008**, *64*, 5987. (u) Park, Y. J.; Park, J.-W.; Jun, C.-H. *Acc. Chem. Res.* **2008**, *41*, 222. (v) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Chem. Rev.* **2007**, *107*, 5318. (w) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (x) Godula, K.; Sames, D. *Science* **2006**, *312*, 67. (y) Kakiuchi, F.; Chatani, N. *Adv. Synth. Catal.* **2003**,

345, 1077. (z) Dyker, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1698.

(4) (a) Ueura, K.; Satoh, T.; Miura, M. *Org. Lett.* **2007**, *9*, 1407. (b) Ueura, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2007**, *72*, 5362.

(5) Selected reports: (a) Unoh, Y.; Hirano, K.; Satoh, T.; Miura, M. *Tetrahedron* **2013**, *69*, 4454. (b) Morimoto, K.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2011**, *76*, 9548. (c) Morimoto, K.; Hirano, K.; Satoh, T.; Miura, M. *Chem. Lett.* **2011**, *40*, 600. (d) Fukutani, T.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2011**, *76*, 2867. (e) Umeda, N.; Hirano, K.; Satoh, T.; Shibata, N.; Sato, H.; Miura, M. *J. Org. Chem.* **2011**, *76*, 13. (f) Mochida, S.; Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *Chem. Lett.* **2010**, *39*, 744. (g) Morimoto, K.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2010**, *12*, 2068. (h) Mochida, S.; Shimizu, M.; Hirano, K.; Satoh, T.; Miura, M. *Chem.—Asian J.* **2010**, *5*, 847. (i) Fukutani, T.; Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *Chem. Commun.* **2009**, 5141. (j) Mochida, S.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 6295. (k) Shimizu, M.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 3478.

(6) Selected examples: (a) Kim, D.-S.; Park, J.-W.; Jun, C.-H. *Chem. Commun.* **2012**, *48*, 11334. (b) He, T.; Too, P. C.; Chen, R.; Chiba, S.; Sun, H. *Chem.—Asian J.* **2012**, *7*, 2090. (c) Li, B.-J.; Wang, H.-Y.; Zhu, Q.-L.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2012**, *51*, 3948. (d) Jayakumar, J.; Parthasawathy, K.; Cheng, C.-H. *Angew. Chem.*, *Int. Ed.* **2012**, *51*, 197. (e) Hyster, T. K.; Rovis, T. *Chem. Commun.* **2011**, *47*, 11846. (f) Wei, X.; Zhao, M.; Du, Z.; Li, X. *Org. Lett.* **2011**, *13*, 4636. (g) Guimond, N.; Gorelsky, S. I.; Fagnou, K. *J. Am. Chem. Soc.* **2011**, *133*, 6449. (h) Patureau, F. W.; Besset, T.; Kuhl, N.; Glorius, F. *J. Am. Chem. Soc.* **2011**, *133*, 2154. (i) Too, P. C.; Wang, Y.-F.; Chiba, S. *Org. Lett.* **2010**, *12*, 5688. (j) Song, G.; Chen, D.; Pan, C.-L.; Crabtree, R. H.; Li, X. *J. Org. Chem.* **2010**, *75*, 7487. (k) Hyster, T. K.; Rovis, T. *J. Am. Chem. Soc.* **2010**, *132*, 10565. (l) Rakshit, S.; Patureau, F. W.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 9585. (m) Li, L.; Brennessel, W. W.; Jones, W. *D. J. Am. Chem. Soc.* **2008**, *130*, 12414. (n) Guimond, N.; Fagnou, K. *J. Am. Chem. Soc.* **2009**, *131*, 12050. (o) Stuart, D. R.; Bertrand-Laperle, M.; Burgess, K. M. N.; Fagnou, K. *J. Am. Chem. Soc.* **2008**, *130*, 16474. (p) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2008**, *130*, 3645. See also reviews: (q) Patureau, F. W.; Wencel-Delord, J.; Glorius, F. *Aldrichim. Acta* **2012**, *45*, 31. (r) Chiba, S. *Chem. Lett.* **2013**, *41*, 1554.

(7) (a) Meng, X.; Kim, S. *Org. Lett.* **2013**, *15*, 1910. (b) Chan, L. Y.; Kim, S.; Ryu, T.; Lee, P. *H. Chem. Commun.* **2013**, *49*, 4682.

(8) Seo, J.; Park, Y.; Jeon, I.; Ryu, T.; Park, S.; Lee, P. H. *Org. Lett.* **2013**, *15*, 3358.

(9) (a) Carpino, L. A.; Xia, J.; Zhang, C.; El-Faham, A. *J. Org. Chem.* **2004**, *69*, 62. (b) Busacca, C. A.; Lorenz, J. C.; Grinberg, N.; Haddad, N.; Hrapchak, M.; Latli, B.; Lee, H.; Sabila, P.; Saha, A.;

Sarvestani, M.; Shen, S.; Varsolona, R.; Wei, X. D.; Senanayake, C. H. *Org. Lett.* **2005**, *7*, 4277.

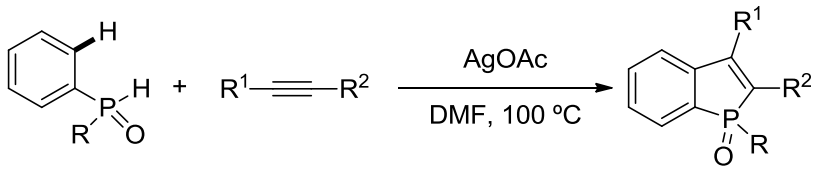
(10) Smith, A. B.; Ducry, L.; Corbett, R. M.; Hirschmann, R. *Org. Lett.* **2000**, *2*, 3887.

(11) Novak, Z.; Nemes, P.; Kotschy, A. *Org. Lett.* **2004**, *6*, 4917.

Chapter 3

Synthesis of Benzo[*b*]phospholes by Ag(I)-promoted Oxidative Annulation of *H*-phosphine Oxides with Internal Alkynes

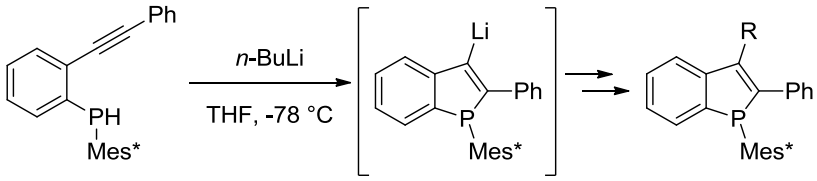
A synthesis of benzo[*b*]phosphole oxides by a Ag(I)-mediated oxidative coupling of *H*-phosphine oxides with internal alkynes is described. A number of substituted benzo[*b*]phosphole derivatives could be synthesized by the simple method from readily available substrates. Several control experiments suggested that radical intermediates involved in the reaction.



Introduction

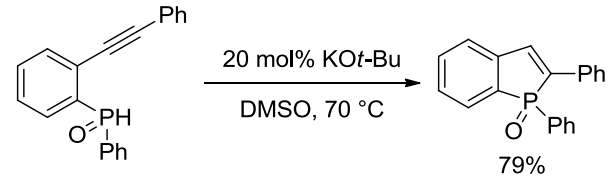
As described in Chapter 1, benzophosphole derivatives have recently attracted much attention in the field of materials chemistry because of their unique optical and electronic properties.[1] However, synthetic approaches to such promising frameworks are so far limited.[2] Most of the currently available methods rely on the cyclization of phenylphosphorus compounds with alkynyl groups preinstalled at the *ortho* position. For recent examples, Nakamura, Tsuji, and co-workers reported the *n*-BuLi promoted cyclization of *ortho*-alkynylarylphosphines (Scheme 3.1).[2a] The formed 3-lithiobenzophosphole species were further employed for the reaction with a number of electrophiles directly or after treating with zinc halides (Negishi couplings).

Scheme 3.1.



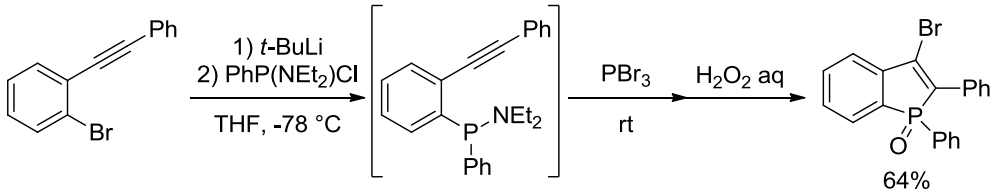
Tanaka, Sanji, and co-workers reported the cyclization of *ortho*-alkynylarylphosphines in the presence of a catalytic amount of KO*t*-Bu (Scheme 3.2).[2b]

Scheme 3.2.



Yamaguchi, Fukazawa, and co-workers reported a benzo[*b*]phosphole synthesis via in situ generated *ortho*-alkynylaryl(amino)phosphines (Scheme 3.3).[2c]

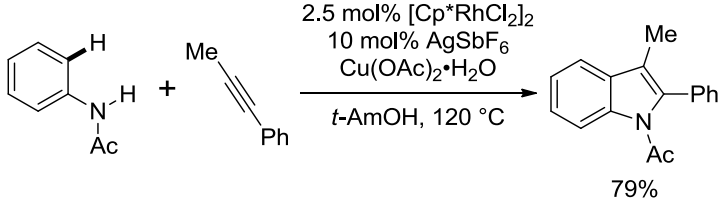
Scheme 3.3.



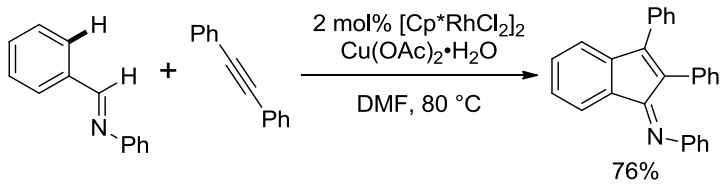
The precursors in the above procedures are usually prepared through complicated multistep reactions. Moreover, the substituent tolerance is low in the cyclizations as they are performed under strongly basic conditions. Thus, development of new, effective processes for synthesizing a broad range of benzophospholes derivatives under mild conditions from relatively simple starting materials is strongly desired.

As the author demonstrated the phosphaisocoumarin synthesis in Chapter 2, the rhodium-catalyzed dehydrogenative annulation of monosubstituted benzenes with alkynes through directed C-H bond cleavage is one of the most promising ways for the straightforward synthesis of phosphorus-containing heterocycles.[3] Not only six-membered ring, but also 5-membered ring construction has been significantly developed in recent years by rhodium catalysis.[4, 5] For example, Fagnou and co-workers reported that indoles can be constructed through the coupling of *N*-acetylanilines with internal alkynes (Scheme 3.4).[4a] Miura, Satoh, and co-workers reported the synthesis of indenone imines synthesis by the oxidative coupling of benzylideneanilines with internal alkynes (Scheme 3.5).[4b]

Scheme 3.4.



Scheme 3.5.



76%

In the light of these results, the author undertook to develop a direct method for the construction of benzophospholes by rhodium catalysis. In the course of this study, the author surprisingly discovered that the direct transformation toward benzophospholes can be achieved by a silver salt without adding any rhodium species. In Chapter 3, the author describes the silver-promoted direct synthesis of benzophospholes by the oxidative annulation reaction of *H*-phosphine oxides with internal alkynes.

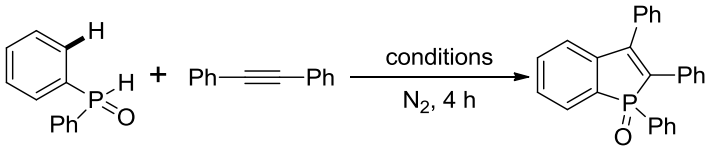
Results and Discussion

As an initial attempt, the author examined the coupling of diphenylphosphine oxide (**1a**) with diphenylacetylene (**2a**) in the presence of a cationic Cp*Rh^{III} complex and AgOAc as catalyst and oxidant, respectively, and succeeded in obtaining the expected benzophosphole derivative **3aa** in a good yield (Table 3.1, entry 1). However, it was somewhat surprising to observe that the reaction proceeded efficiently even without any rhodium catalyst (entry 2). Treatment of **1a** (0.5 mmol) with **2a** (0.25 mmol) in the presence of AgOAc (1 mmol) in DMF (3 mL) at 100 °C for 4 h under N_2 gave the oxidative annulation product 1,2,3-triphenyl-1*H*-phosphindole-1-oxide (**3aa**) in 96 % yield exclusively. Obviously, the mechanism of this reaction seems to be different from that of the annulation reaction in Chapter 2. To obtain additional information about this

mechanism, the author conducted the reaction of **1a** with **2a** in the presence of 0.5 mmol of 2,2,6,6-tetramethylpiperidine-1-oxy (TEMPO) (entry 3) or 2,6-di-*tert*-butyl-α-(3,5-di-*tert*-butyl-4-oxo-2,5-cyclohexadiene-1-ylidene)-*p*-tolyloxy (Galvinoxyl) (entry 4). As a result, these radical inhibitors severely retarded or completely suppressed the reaction. These results suggest that radical species is presumably involved in the course of this reaction.[6,7] While the reaction using the substrates in a 1:1 ratio gave **3aa** in 80 % yield (entry 5), decreasing the amount of AgOAc (0.5 mmol) substantially reduced the product yield (entry 6). At 80 °C, the reaction was sluggish (entry 7). In AcOH, the reaction also proceeded smoothly, but the product yield was somewhat low (entry 8). The combination of $AgNO_3$ (0.05 mmol) and $K_2S_2O_8$ (1 mmol), which has been employed to generate P-centered radicals,[7b,c] was not effective for the present reaction (entry 9). Note that the present reaction could be readily scaled up to a gram scale. Thus, from **1a** (6 mmol) and **2a** (3 mmol), **3aa** was obtained in 82 % yield (0.93 g, entry 10).

It has been reported that P-centered radicals can be formed in the presence of $Mn(OAc)_3$ through homolytic P-H bond cleavage.[8] Therefore, we employed $Mn(OAc)_3 \cdot 2\,H_2O$ (1 mmol) in the place of AgOAc for the reaction of **1a** with **2a**, and **3aa** was formed in 50 % yield (entry 11). Interestingly, the reaction could be conducted even at room temperature (entries 12–14). Comparable results were obtained in DMF and AcOH, whereas the product yield decreased slightly in CH_2Cl_2.

Table 3.1. Reaction of Diphenylphosphine Oxide (1a) with diphenylacetylene (2a)[a]



1a (0.5 mmol) **2a** (0.25 mmol) **3aa**

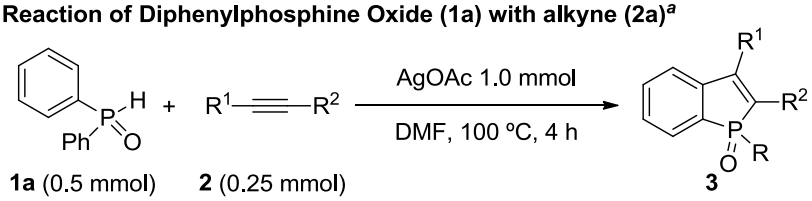
entry	oxidant (mmol)	Temp (ºC)	solvent	yield (%)[b]
1[c]	AgOAc (1)	100	DMF	93
2	***AgOAc (1)***	***100***	***DMF***	***96 (96)***
3[d]	AgOAc (1)	100	DMF	6
4[e]	AgOAc (1)	100	DMF	0
5[f]	AgOAc (1)	100	DMF	80
6	AgOAc (0.5)	100	DMF	6
7	AgOAc (1)	80	DMF	13
8	AgOAc (1)	100	AcOH	81
9	$AgNO_3$ (0.05) + $K_2S_2O_8$ (1)	100	DMF	19
10[g]	AgOAc (12)	100	DMF	6
11	$Mn(OAc)_3•2H_2O$ (1)	100	DMF	50
12	$Mn(OAc)_3•2H_2O$ (1)	RT	DMF	70
13	$Mn(OAc)_3•2H_2O$ (1)	RT	AcOH	78
14	$Mn(OAc)_3•2H_2O$ (1)	RT	CH_2Cl_2	58

[a]Reaction conditions: **1a** (0.5 mmol), **2** (0.25 mmol), and oxidant in solvent (3 mL) under N_2 for 4 h. [b]GC Yield of the product **3aa** based on the amount of **2**. Isolated yield is shown in parentheses. [c]With $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (0.01 mmol). [d]With TEMPO (0.5 mmol). [e]With Galvinoxyl (0.5 mmol). [f]With **1a** (0.25 mmol). [g]With **1a** (6 mmol) and **2a** (3 mmol) in DMF (36 mL).

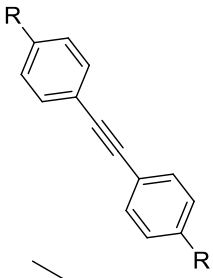
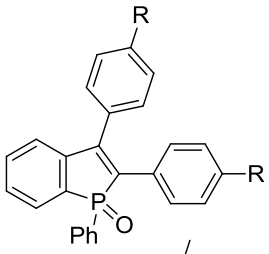
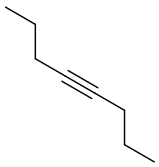
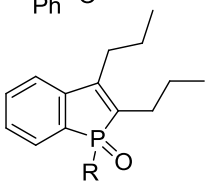
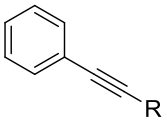
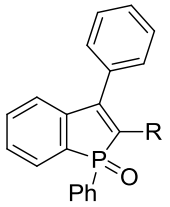
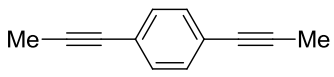
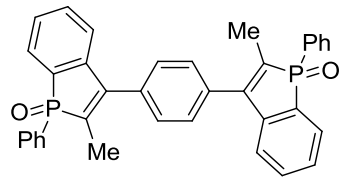
With the optimized conditions (entry 2 in Table 5.1) in hand, the author next explored scope of substrates for the present reaction. The scope of alkynes **2** is summarized in Table 5.2. The diarylacetylenes **2b-g** underwent the coupling with **1a** when using AgOAc as the oxidant to selectively produce the corresponding 2,3-diaryl-1-phenyl-1*H*-phosphindole-1-ones **3ab-3ag**. 4-Octyne (**2h**) could also be employed in this reaction. Interestingly, the unsymmetrical phenylacetylenes **2i-q** reacted with **1 a** in a regioselective manner to produce the 2-substituted 1,3-diphenyl-1*H*-phosphindole-1-ones **3ai-3aq** in moderate to good yields. Notably, no

other isomers were detected in any of these reactions. In the reactions with silylacetylenes **2k** and **2l**, better results were obtained by using $Mn(OAc)_3 \cdot 2\,H_2O$ as the oxidant at room temperature. Under the standard conditions using AgOAc at 100 °C, only small amounts (ca. 10 %) of desilylated coupling products were detected by GC–

Table 3.2. Reaction of Diphenylphosphine Oxide (1a) with alkyne (2a)[a]



1a (0.5 mmol) **2** (0.25 mmol) **3**

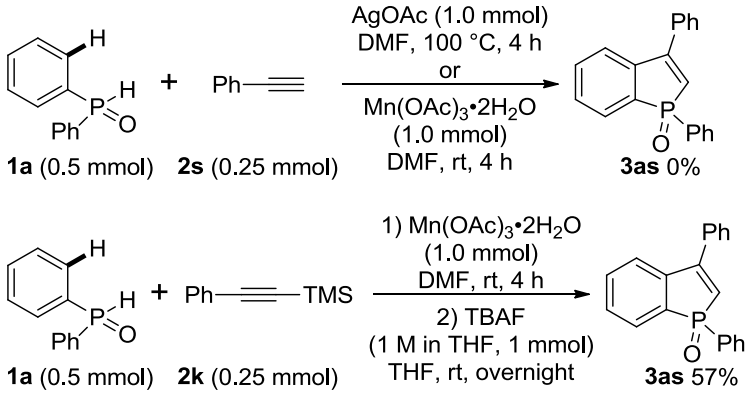
Alkyne **2**	Product **3**, yield (%)[b]
 **2b**: R = Me **2c**: R = OMe **2d**: R = NMe_2 **2e**: R = Cl **2f**: R = Br **2g**: R = Bpin	 **3ab**: R = Me, 80% **3ac**: R = OMe, 77% **3ad**: R = NMe_2, 35% **3ae**: R = Cl, 89% **3af**: R = Br, 60% **3ag**: R = Bpin, 19%
 **2h**	 **3ah**: 63%
 **2i**: R = Me **2j**: R = *n*-Bu **2k**: R = TMS **2l**: R = $SiMe_2Ph$ **2m**: R = CO_2Et **2n**: R =Ac **2o**: R = $C(OH)Me_2$ **2p**: R = CH_2OTBS **2q**: R = $PO(OEt)_2$	 **3ai**: R = Me, 86% **3aj**: R = *n*-Bu, 73% **3ak**: R = TMS, 0%, 54%[c] **3al**: R = $SiMe_2Ph$, 57%[c] **3am**: R = CO_2Et, 57% **3an**: R =Ac, 62% **3ao**: R = $C(OH)Me_2$, 61% **3ap**: R = CH_2OTBS, 58% **3aq**: R = $PO(OEt)_2$, 41%
 **2r**[d]	 **3ar**: 38%[d]

[a]Reaction conditions: **1a** (0.5 mmol), **2** (0.25 mmol), and AgOAc (1.0 mmol) in DMF (3 mL) at 100 °C under N_2 for 4 h. [b]Yield of isolated product based on the amount of **2**. [c]Using $Mn(OAc)_3 \cdot 2H_2O$ (1 mmol) at room temperature in place of AgOAc. [d]Using **1a** (1 mmol) and AgOAc (2 mmol).

MS. As expected, **1a** reacted with 1,4-di(prop-1-yn-1-yl)benzene (**2r**) in a 2:1 manner to form a bis(benzophosphole-3-yl)benzene framework (**3ar**).[2b,9] This type of structure is of interest for application in organic light-emitting diodes and thin-film photovoltaics.[2a,10]

This annulation reaction could not be applied to the terminal alkynes, such as phenylacetylene **2s** (Scheme 3.6). Pleasingly, silylacetylene **2k** could be employed as a terminal alkyne surrogate, the corresponding coupling product **3as** could be synthesized from sequential annulation / desilylation process.

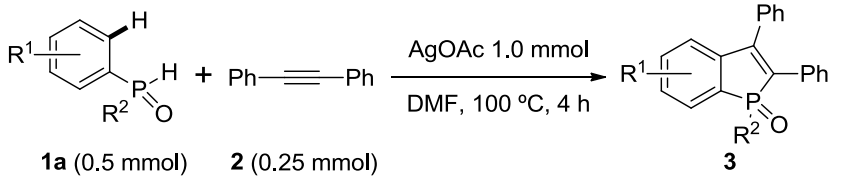
Scheme 3.6. Reaction of 1a with Terminal Alkyne and Its Surrogate



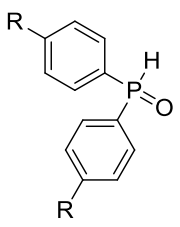
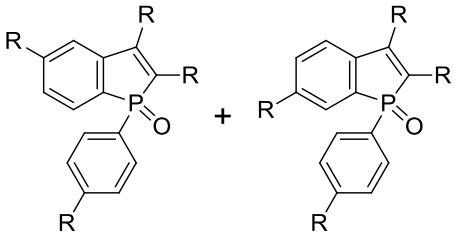
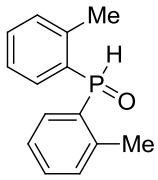
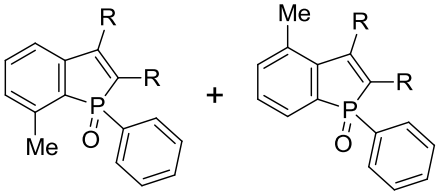
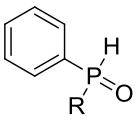
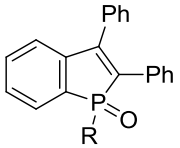
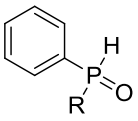
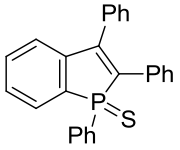
Next, the reactions of variously substituted phenylphosphine oxides with **2a** were examined (Table 3.3). Unexpectedly, the reaction of bis(4-methylphenyl)phosphine oxide (**1b**) in the presence of AgOAc gave both the normal coupling product **3ba** and the isomer **3ba′** as a 1:1 mixture. This may imply that an aryl migration involving C-P bond cleavage and new C-P bond formation process intervenes.[11] The reaction of 4-methoxy-substituted substrate **1c** also gave a 1:1 mixture of **3ca** and **3ca′**. When using $Mn(OAc)_3 \cdot 2\,H_2O$ as the oxidant at room temperature, the relative product ratio of **3ca′** increased. As expected, the reaction of bis(3-methylphenyl)phosphine oxide with **2a**

gave a complex mixture of product isomers (data not shown). By contrast, in the reaction of sterically hindered bis(2-methylphenyl)phosphine oxide (**1d**), **3da′** was formed as the predominant product, along with **3da**. Alkyl(phenyl)phosphine oxides

Table 3.3. Reaction of Arylphosphine Oxide (1) with Diphenylacetylene (2a)[a]



1a (0.5 mmol) **2** (0.25 mmol) **3**

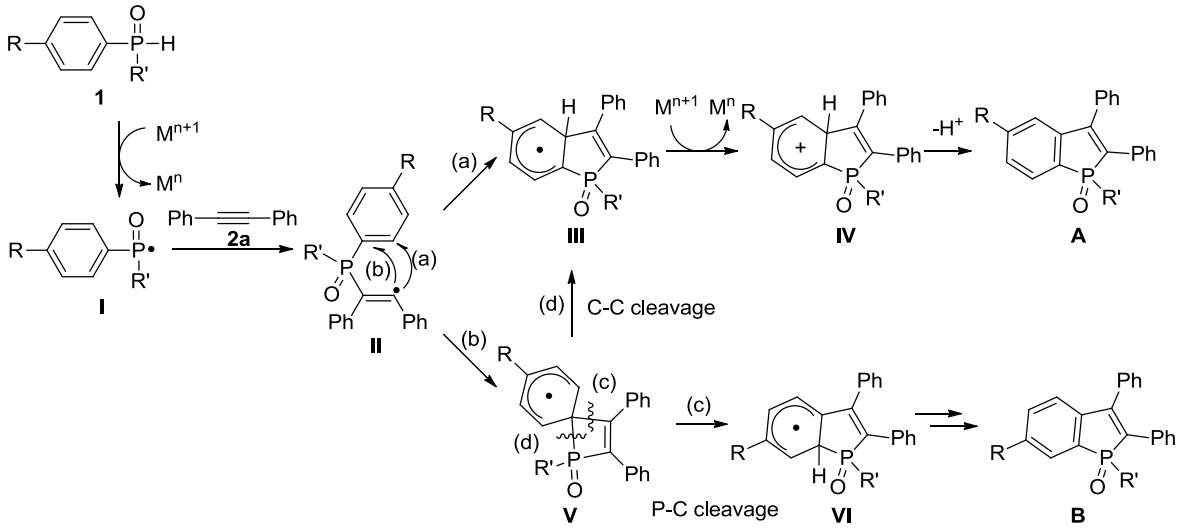
Phosphine oxide **1**	Product(s) **3**, yield (%)[b]
	
1b: R = Me **1c**: R = OMe **1c**: R = OMe[c]	**3ba** + **3ba'**: R = Me, 79% (1:1) **3ca** + **3ca'**: R = OMe, 50% (1:1) **3ca** + **3ca'**: R = OMe, 59% (1:1.9)[c]
	
1d	**3da** + **3da'**: 84% (1:2)
	
1e: R = *n*-Bu **1f**: R = *t*-Bu **1g**: R = OEt	**3ea**: R = *n*-Bu, 59% **3fa**: R = *t*-Bu, 66% **3ga**: R = OEt, 53%
	
1h	**3ha**: 0%, 50%[c]

[a]Reaction conditions: **1a** (0.5 mmol), **2** (0.25 mmol), and AgOAc (1.0 mmol) in DMF (3 mL) at 100 °C under N_2 for 4 h. [b]Yield of isolated product based on the amount of **2**. [c]Using $Mn(OAc)_3 \cdot 2H_2O$ (1 mmol) at room temperature in place of AgOAc.

such as **1e** and **1f** also underwent coupling with **2a** to produce the corresponding *P*-alkylbenzophosphole derivatives **3ea** and **3fa**. As well as phosphine oxides, phenylphosphinate **1g** could also be used in the annulation to **3ga**. The reaction of diphenylphosphine sulfide (**1h**) did not proceed at all under the standard conditions. This is likely due to the thiophilicity of silver. Fortunately, the reaction of **1h** could be carried out by using $Mn(OAc)_3 \cdot 2\ H_2O$ as the oxidant at room temperature to give **3ha** in moderate yield.

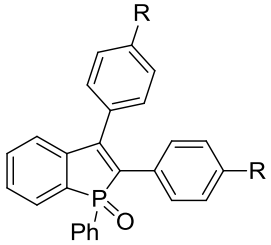
In light of the formation of unexpected isomers in Table 3.3 as well as radical inhibition test in Table 3.1, the author proposed a plausible reaction mechanism for the present system in Scheme 3.7. First, P-centered radical **I** is generated by silver-promoted homolytic P-H bond cleavage of phosphine oxide **1**.[7] Subsequent addition of the resulting radical **I** to the triple bond of alkyne **2a** may occur to form the alkenyl radical intermediate **II**.[12] The regioselectivity in this addition step with unsymmetrical alkynes can be rationalized by the facile formation of benzyl radicals. There are two pathways from this intermediate. In path (a), the alkenyl radical **II** attacks of the phenyl moiety at the *ortho*-position to form the intermediate **III**. Then one-electron oxidation and rearomatization may take place to afford the product **A** via **IV**. On the other hand, in path (b), the radical **II** attacks the *ipso*-carbon of the phenyl ring to form the spirocyclic radical intermediate **V**. Successive ring expansion involving P-C bond cleavage gives the isomer **B** (path (c)). If C-C bond cleavage takes place from **V** (path (d)), the product **A** maybe formed via the intermediate **III**.[11]

Scheme 3.7. Plausible Mechanism



Most of the benzophosphole oxides **3** obtained in this study showed solid-state fluorescence as expected. The optical properties of representative benzophospholes **3aa**, **3ac**, and **3ad** are summarized in Table 3.4. The quantum efficiencies (Φ) of the solid-state fluorescence of **3aa**, **3ac**, and **3ad** were measured as absolute values of 0.54, 0.63, and 0.53, respectively. Notably, **3ad** shows large stokes shift with red-shited fluorescent emission. Recently, the benzophosphole oxides possessing strong electron-donating groups are of interests to be environment-sensitive fluorescent probe.[13]

Table 3.4. Solid-state Fluorescence of 3aa, 3ac, and 3ad



3aa: R = H
3ac: R = OMe
3ad: R = NMe_2

	excitation wavelength (nm)	fluorescence wavelength (nm)[a]	quantum efficiency Φ
3aa	422	451	0.54
3ac	434	496	0.63
3ad	521	595	0.53

[a]Emission maximum in powder.

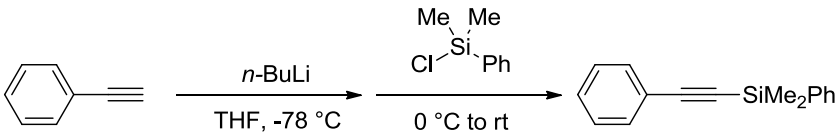
Summary

In chapter 3, the author described synthesis of benzo[*b*]phosphole oxides by a Ag(I)-mediated oxidative coupling of *H*-phosphine oxides with internal alkynes.[14,15] Various benzo[*b*]phospholes bearing functional groups could be synthesized by a simple operation from readily available substrates. Several experiments showed that radical intermediates seemed to be incorporated in the reaction.

Experimental Section

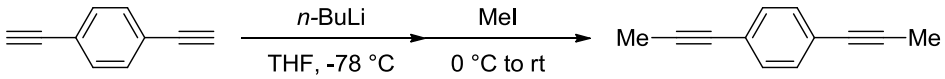
General. ^{1}H NMR spectra were recorded at 400 or 600 MHz, ^{13}C NMR spectra were recorded at 100 or 150 MHz, and ^{31}P NMR spectra were recorded at 162 or 243 MHz for $CDCl_3$ solutions. MS data were obtained by EI or CI. GC analysis was carried out using a silicon OV-17 column (i. d. 2.6 mm x 1.5 m). GC-MS analysis was carried out using a CBP-1 capillary column (i. d. 0.25 mm x 25 m). The structures of all products listed below were unambiguously determined by ^{1}H, ^{13}C, ^{31}P NMR with the aid of COSY, HSQC, and HMBC experiments.

Substituted secondary phosphine oxide **1b-d**[16] and **1e**,**f**,[17] phosphine sulfide **1h**,[18] internal alkynes **2b-c**, **e**,[19] **2d**,[20] **2f**,[21] **2p**,[22] and **2q**[23] were prepared according to published procedures. Substrates **2l** and **2r** were synthesized as following procedures. Other starting materials were commercially available and used as received.



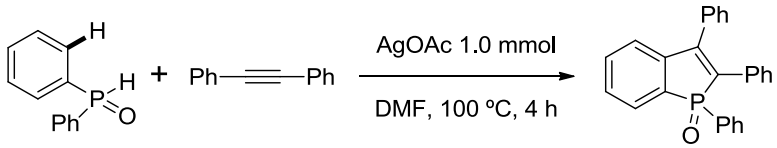
Synthesis of 2l. To a solution of phenylacetylene (30 mmol, 2.2 mL) in dry THF (12 mL) at -78 °C under N_2 atmosphere, *n*-BuLi (1.64 M in hexane, 20 mmol, 12.3 mL) was added. The reaction mixture was stirred for 30 min. To the resulting mixture, dimethylphenylchlorosilane (20 mmol, 3.3 mL) was added, and stirred at 0 °C for 30 min. Then, the reaction mixture was warmed to rt and stirred for additional 1 h. The resulting solution was quenched with sat. NH_4Cl aq and extracted with

diethylether. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. Crude oil was purified by distillation (165-170 °C/1-2 torr) to afford product (4.43 g, 94%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.49 (s, 6H), 7.30-7.41 (m, 6H), 7.48-7.52 (m, 2H), 7.68-7.71 (m, 2H).



Synthesis of 2r. To a solution of 1,4-diethynylbenzene (5 mmol, 771 mg) in dry THF (30 mL) at -78 °C under N_2, *n*-BuLi (1.64 M in hexane, 20 mmol, 12.3 mL) was added. After stirring for 1h, MeI (30 mmol, 1.9 mL) was added slowly at 0 °C. Then, the reaction mixture was warmed to rt and stirred overnight. The reaction was quenched with H_2O and extracted with CH_2Cl_2. Organic layer was dried over Na_2SO_4 and concentrated in vacuo. The crude mixture was recrystallized from toluene to afford pure product (613.9 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.04 (s, 6H), 7.29 (s, 4H).

The following experimental procedures may be regarded as typical in methodology and scale.



Reaction of Diphenylphosphine Oxide (1a) with Diphenylacetylene (2a) (entry 2 in Table 3.1): A mixture of diphenylphosphine oxide (**1a**) (0.5 mmol, 101 mg), diphenylacetylene (**2a**) (0.25 mmol, 45 mg), AgOAc (1.0 mmol, 167 mg), and dibenzyl (ca. 40 mg) as internal standard was stirred in DMF (3.0 mL) under N_2 at 100 °C for 4 h. GC and GC-MS analyses of the mixtures confirmed consumption of **2a**. After cooling, the reaction mixture was diluted with ethyl acetate (40 mL) and insoluble solids were removed on Celite plug. The filtrate was washed with brine (20 mL x 3). The organic layer was dried over Na_2SO_4, and concentrated in vacuo. The desired product **3aa** (90.4 mg, 96%) was isolated by column chromatography on silica gel using dichloromethane-ethyl acetate (1:1 v/v) as eluent.

Characterization Data of Products

1,2,3-Triphenyl-1*H*-phosphindole-1-oxide (3aa): pale yellow solid, mp 70-72 °C, 90.4 mg (96%);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.07-7.09 (m, 3H), 7.20-7.24 (m, 3H), 7.32-7.48 (m, 10H), 7.70 (dd, J = 7.6, 9.4 Hz, 1H), 7.75-7.79 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 120.4 (d, J = 10.3 Hz), 127.8, 128.2, 128.6, 128.8 (d, J = 12.6 Hz), 128.91, 128.96 (br, 2C overlapped), 128.98 (d, J = 10.3 Hz), 129.0 (d, J = 12.6 Hz), 129.9 (d, J = 99.5 Hz), 130.9 (d, J = 10.3 Hz), 132.0 (d, J = 105.3 Hz), 132.1 (d, J = 2.3 Hz), 132.6 (d, J = 10.3 Hz), 132.8 (d, J = 2.3 Hz), 134.17 (d, J = 14.9 Hz), 134.20 (d, J = 95.0 Hz), 143.7 (d, J = 26.3 Hz), 149.9 (d, J = 21.7 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 39.0; HRMS m/z (M^+) Calcd for $C_{26}H_{19}OP$: 378.1174. Found 378.1171.

1-Phenyl-2,3-di-*p*-tolyl-1*H*-phosphindole-1-oxide (3ab): pale yellow solid, mp 79-81 °C, 81.3 mg (80%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.18 (s, 3H), 2.40 (s, 3H), 6.90 (d, J = 7.9 Hz, 2H), 7.15 (d, J = 7.6 Hz, 2H), 7.19-7.24 (m, 5H), 7.33 (td, J = 3.9, 7.3 Hz, 1H), 7.37 (td, J = 2.9, 3.7 Hz, 2H), 7.40-7.46 (m, 2H), 7.68 (dd, J = 7.3, 9.7 Hz, 1H), 7.52-7.79 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.2, 21.4, 123.8(d, J = 11.4 Hz), 128.68 (d, J = 11.4 Hz), 128.76 (d, J = 9.2 Hz), 128.83 (d, J = 6.9 Hz), 128.8 (2C, overlapped), 128.9, 129.6, 129.8 (d, J = 6.9 Hz), 130.1 (d, J = 96.1 Hz), 130.9 (d, J = 10.3 Hz), 131.3 (d, J = 16.0 Hz), 131.97 (d, J = 2.3 Hz), 132.03 (d, J = 105.3 Hz), 132.7 (d, J = 2.3 Hz), 133.63 (d, J = 95.0 Hz), 137.6, 138.4, 144.0 (d, J = 27.5 Hz), 149.3 (d, J = 20.6 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 39.0; HRMS m/z (M^+) Calcd for $C_{28}H_{23}OP$: 406.1487. Found 406.1485.

1-Phenyl-2,3-di-(*p*-methoxyphenyl)-1*H*-phosphindole-1-oxide (3ac): yellowish green solid, mp 85-87 °C, 84.6 mg (77%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.70 (s, 3H), 3.86 (s, 3H), 6.62-6.65 (m, 2H), 6.98 (d, J = 8.7 Hz, 2H), 7.20-7.28 (m, 5H), 7.33 (td, J = 3.8, 7.3 Hz, 1H), 7.37-7.50 (m, 4H), 7.68 (dd, J = 7.3, 9.7 Hz, 1H), 7.74-7.79 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.0, 55.3, 113.8, 114.4, 123.7 (d, J = 11.4 Hz), 125.3 (d, J = 10.3 Hz), 126.6 (d, J = 16.0 Hz), 128.7 (d, J = 10.3 Hz), 128.8 (d, J = 11.4 Hz), 128.9 (d, J = 9.2 Hz), 130.3 (d, J = 98.4 Hz), 130.4 (d, J = 5.7 Hz), 130.5, 130.9 (d, J = 9.5 Hz), 131.98 (d, J = 104.1 Hz), 132.00 (d, J = 2.3 Hz), 132.8 (d, J = 2.3 Hz), 133.1 (d, J = 96.1 Hz), 144.2 (d, J = 27.5 Hz), 148.1 (d, J = 21.7 Hz), 159.0, 159.7; ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 39.0; HRMS m/z (M^+) Calcd for $C_{28}H_{23}O_3P$: 438.1385. Found 438.1389.

1-Phenyl-2,3-di-[*p*-(dimethylamino)phenyl]-1*H*-phosphindole-1-oxide (3ad): orange solid, mp 118-120 °C, 40.6 mg (35%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.85 (s, 6H), 3.02 (s, 6H), 6.44 (d, J = 8.9 Hz, 2H), 6.78 (d, J = 8.9 Hz, 2H), 7.21-7.50 (m, 10H), 7.63 (dd, J = 7.3, 9.7 Hz, 1H), 7.77-7.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.0, 40.3, 111.8, 112.4, 121.1 (d, J = 10.6 Hz), 122.5 (d, J

= 15.9 Hz), 123.3 (d, *J* = 11.0 Hz), 127.9 (d, *J* = 10.6 Hz), 128.5 (d, *J* = 9.6 Hz), 128.7 (d, *J* = 12.2 Hz), 130.1 (d, *J* = 6.5 Hz), 130.2, 131.0 (d, *J* = 10.6 Hz), 131.2 (d, *J* = 85.0 Hz), 131.7 (d, *J* = 2.9 Hz), 132.1 (d, *J* = 92.4 Hz), 132.2 (d, *J* = 91.9 Hz), 132.5 (d, *J* = 1.5 Hz), 145.0 (d, *J* = 27.5 Hz), 146.5 (d, *J* = 21.9 Hz), 149.4, 150.2; $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 39.4; HRMS m/z ($M+H^+$) Calcd for $C_{30}H_{30}N_2OP$: 465.2090. Found 465.2088.

1-Phenyl-2,3-di-(*p*-chlorophenyl)-1*H*-phosphindole-1-oxide (3ae): pale yellow solid, mp 94-96 °C, 99.5 mg (89%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.08-7.10 (m, 2H), 7.16-7.18 (m, 2H), 7.20 (dd, *J* = 2.9, 7.6 Hz, 1H), 7.25-7.27 (m, 2H), 7.38-7.41 (m, 3H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.46-7.50 (m, 2H), 7.70-7.74 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 123.9 (d, *J* = 10.3 Hz), 128.7, 128.9 (d, *J* = 12.6 Hz), 129.2 (d, *J* = 100.7 Hz), 129.3 (d, *J* = 10.3 Hz), 129.43, 129.45 (d, *J* = 8.0 Hz), 130.2 (d, *J* = 5.7 Hz), 130.4, 130.8 (d, *J* = 10.3 Hz), 130.9 (d, *J* = 10.3 Hz), 131.7 (d, *J* = 105.3 Hz), 132.2 (d, *J* = 14.9 Hz), 132.4 (d, *J* = 3.4 Hz), 133.1 (d, *J* = 2.3 Hz), 133.8 (d, *J* = 95.0 Hz), 134.0, 134.9, 143.1 (d, *J* = 26.3 Hz), 149.0 (d, *J* = 20.6 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 38.8; HRMS m/z (M^+) Calcd for $C_{26}H_{17}Cl_2OP$: 446.0394. Found 446.0396.

1-Phenyl-2,3-di-(*p*-bromophenyl)-1*H*-phosphindole-1-oxide (3af): pale yellow solid, mp 99-101 °C, 80.7 mg (60%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.11 (d, *J* = 7.9 Hz, 2H), 7.18-7.28 (m, 5H), 7.38-7.51 (m, 5H), 7.59 (d, *J* = 8.5 Hz, 2H), 7.70-7.73 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 122.4 (d, *J* = 1.1 Hz), 123.1, 123.9 (d, *J* = 10.9 Hz), 129.0 (d, *J* = 12.0 Hz), 129.2 (d, *J* = 100.1 Hz), 129.3 (d, *J* = 9.7 Hz), 129.5 (d, *J* = 10.3 Hz), 130.4 (d, *J* = 5.7 Hz), 130.6, 130.9 (d, *J* = 10.9 Hz), 131.3 (d, *J* = 9.7 Hz), 131.65, 131.74 (d, *J* = 105.8 Hz), 132.40, 132.43 (d, *J* = 2.9 Hz), 132.7 (d, *J* = 14.9 Hz), 133.1 (d, *J* = 1.7 Hz), 133.9 (d, *J* = 95.0 Hz), 143.1 (d, *J* = 26.3 Hz) 149.0 (d, *J* = 21.8 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 38.8; HRMS m/z (M^+) Calcd for $C_{26}H_{17}Br_2OP$: 533.9384. Found 533.9377.

1-Phenyl-2,3-di-[*p*-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)]phenyl-1*H*-phosphindole-1-oxide (3ag): pale yellow solid, mp 310-312 °C, 30.1 mg (19%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.27 (s, 12H), 1.38 (s, 12H), 7.19 (dd, *J* = 2.8 Hz, 7.4 Hz, 1H), 7.24 (dd, *J* = 1.1 Hz, 8.4 Hz, 2H), 7.32 (d, *J* = 7.5 Hz, 2H), 7.34-7.48 (m, 5H), 7.52 (d, *J* = 7.9 Hz, 2H), 7.68-7.77 (m, 3H), 7.85 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.77, 24.85, 24.90, 83.7, 84.0, 124.1 (d, *J* = 10.7 Hz), 128.1, 128.3, 128.8 (d, *J* = 12.3 Hz), 129.12 (d, *J* = 2.2 Hz), 129.13 (d, *J* = 17.6 Hz), 129.7 (d, *J* = 101.1 Hz), 131.9 (d, *J* = 10.5 Hz), 132.07 (d, *J* = 105.1 Hz), 132.14 (d, *J* = 2.7 Hz), 132.9, 134.15 (d, *J* =

94.7 Hz), 134.54, 135.3, 135.4 (d, J = 9.8 Hz), 137.0 (d, J = 14.7 Hz), 143.6 (d, J = 26.5 Hz), 150.4 (d, J = 21.1 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 30.0; HRMS m/z (M^+) Calcd for $C_{38}H_{42}B_2O_5P$: 631.2963. Found 631.2964.

1-Phenyl-2,3-di-*n*-propyl-1*H*-phosphindole-1-oxide (3ah): colorless solid, mp 119-121 °C, 49.0 mg (63%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (t, J = 7.3 Hz, 3H), 1.06 (t, J = 7.4 Hz, 3H), 1.38-1.46 (m, 2H), 1.60-1.68 (m, 2H), 2.00-2.50 (m, 2H), 2.60 (t, J = 8.2 Hz, 2H), 7.27 (dd, J = 4.1, 7.4 Hz, 1H), 7.35-7.50 (m, 5H), 7.54 (dd, J = 7.6, 9.6 Hz, 1H), 7.62-7.68 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.30, 14.37, 21.8 (d, J = 1.9 Hz), 22.3 (d, J = 1.9 Hz), 28.3 (d, J = 10.5 Hz), 28.5 (d, J = 13.4 Hz), 121.3 (d, J = 11.4 Hz), 128.2 (d, J = 10.5 Hz), 128.5 (d, J = 8.6 Hz), 128.6 (d, J = 12.4 Hz), 130.3 (d, J = 94.4 Hz), 130.9 (d, J = 11.4 Hz), 131.8 (d, J = 2.9 Hz), 132.3 (d, J = 104.9 Hz), 132.7 (d, J = 1.9 Hz), 134.7 (d, J = 95.4 Hz), 143.6 (d, J = 29.6 Hz), 150.2 (d, J = 20.0 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 39.5; HRMS m/z (M^+) Calcd for $C_{20}H_{23}OP$: 310.1487. Found 310.1486.

1,3-Diphenyl-2-methyl-1*H*-phosphindole-1-oxide (3ai): colorless gum, 67.7 mg (86%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.91 (d, J = 12.3 Hz, 3H), 7.12 (dd, J = 2.9, 7.6 Hz, 1H), 7.31 (td, J = 3.8, 7.3 Hz, 1H), 7.35 (d, J = 7.3 Hz, 2H), 7.41 (t, J = 7.6 Hz, 1H), 7.43-7.48 (m, 3H), 7.50-7.56 (m, 3H), 7.66 (dd, J = 7.0, 9.4 Hz, 1H), 7.74-7.77 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 10.6 (d, J = 10.3 Hz), 123.1 (d, J = 10.3 Hz), 128.3 (d, J = 10.3 Hz), 128.5, 128.6, 128.7, 128.9 (d, J = 12.6 Hz), 129.0 (d, J = 9.2 Hz), 129.2 (d, J = 97.3 Hz), 130.9 (d, J = 10.3 Hz), 131.4 (d, J = 78.9 Hz), 132.1 (d, J = 70.9 Hz), 132.2 (d, J = 2.3 Hz), 132.8 (d, J = 2.3 Hz), 133.5 (d, J = 16.0 Hz), 144.2 (d, J = 28.6 Hz), 150.0 (d, J = 21.8 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 40.3; HRMS m/z (M^+) Calcd for $C_{21}H_{17}OP$: 316.1017. Found 316.1014.

1,3-Diphenyl-2-*n*-butyl-1*H*-phosphindole-1-oxide (3aj): colorless gum, 65.0 mg (73%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.65 (t, J = 7.3 Hz, 3H), 1.03-1.45 (m, 4H), 2.14-2.50 (m, 2H), 7.02 (dd, J = 2.9, 7.6 Hz, 1H), 7.26-7.35 (m, 3H), 7.39 (dddd, J = 1.4, 1.4, 7.6, 7.6 Hz, 1H), 7.41-7.63 (m, 7H), 7.73-7.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4, 22.6, 26.4 (d, J = 9.9 Hz), 30.8 (d, J = 1.6 Hz), 123.2 (d, J = 10.9 Hz), 128.41, 128.43 (d, J = 8.6 Hz), 128.5, 128.7 (2C overlapped), 128.8 (d, J = 10.1 Hz), 130.1 (d, J = 96.9 Hz), 130.9 (d, J = 10.7 Hz), 131.9 (d, J = 104.3 Hz), 132.0 (d, J = 2.8 Hz), 132.7 (d, J = 1.9 Hz), 133.9 (d, J = 15.7 Hz), 136.9 (d, J = 92.8 Hz), 144.3 (d, J = 27.7 Hz), 150.3 (d, J = 22.0 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 39.8; HRMS m/z ($M+H^+$) Calcd for

$C_{24}H_{24}OP$: 359.1559. Found 359.1570.

1,3-Diphenyl-2-trimethylsilyl-1*H*-phosphindole-1-oxide (3ak): colorless gum, 50.8 mg (54%); ^{1}H NMR (600 MHz, $CDCl_3$): δ -0.14 (s, 9H), 6.93 (dd, J = 2.3, 7.6 Hz, 1H), 7.28-7.53 (m, 10H), 7.62 (dd, J = 7.9, 7.9 Hz, 1H), 7.77 (dd, J = 7.0, 10.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ -0.08 (d, J = 2.3 Hz), 123.7 (d, J = 12.6 Hz), 129.7 (br), 128.3 (br), 128.4 (d, J = 9.2 Hz), 128.6 (d, J = 13.7 Hz), 128.7, 129.3 (d, J = 10.3 Hz), 130.8 (d, J = 96.1 Hz), 130.9, (d, J = 10.3 Hz), 131.8 (d, J = 2.3 Hz), 132.5, 135.1 (d, J = 99.6 Hz), 135.7 (d, J = 57.2 Hz), 136.8 (d, J = 20.6 Hz), 145.1 (d, J = 34.3 Hz), 165.0 (d, J = 9.2 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 243 MHz): δ 47.1; HRMS m/z ($M+H^+$) Calcd for $C_{23}H_{24}OPSi$: 375.1329. Found 375.1329.

2-Dimethyl(phenyl)silyl-1,3-diphenyl-1*H*-phosphindole-1-oxide (3al): colorless gum, 62.3 mg (57%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.09 (s, 3H), 0.17 (s, 3H), 6.92 (m, 1H), 7.03 (d, J = 7.0 Hz, 2H), 7.10-7.14 (m, 4H), 7.20-7.24 (m, 1H), 7.28-7.43 (m, 7H), 7.49-7.53 (m, 1H), 7.60-7.65 (m, 1H), 7.68-7.74 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ -2.10 (d, J = 1.4 Hz), -1.81 (d, J = 1.7 Hz), 123.8 (d, J = 12.4 Hz), 127.4, 128.2 (br, 2C overlapped), 128.4, 128.5 (d, J = 9.4 Hz), 128.6 (d, J = 12.1 Hz), 128.8, 129.5 (d, J = 10.0 Hz), 130.6 (d, J = 96.7 Hz), 131.0 (d, J = 10.3 Hz), 131.7 (d, J = 2.7 Hz), 132.5 (d, J = 1.9 Hz), 133.8, 134.3 (d, J = 58.5 Hz), 135.2 (d, J = 99.8 Hz), 136.3 (d, J = 20.0 Hz), 137.8 (d, J = 2.2 Hz), 145.0 (d, J = 33.6 Hz), 166.0 (d, J = 10.1 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 47.3; HRMS m/z ($M+H^+$) Calcd for $C_{28}H_{26}OPSi$: 437.1485. Found 437.1480.

2-Ethoxycarbonyl-1,3-diphenyl-1*H*-phosphindole-1-oxide (3am): pale yellow solid, mp 119-122 °C, 53.7 mg (57%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (t, J = 7.1 Hz, 3H), 3.99 (qd, J = 7.1, 10.8 Hz, 1H), 4.08 (qd, J = 7.1, 10.8 Hz, 1H), 7.20-7.24 (m, 1H), 7.38-7.58 (m, 10H), 7.71-7.75 (m, 1H), 7.78 (dd, J = 7.0, 12.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 60.8, 126.35 (d, J = 97.7 Hz), 126.36 (d, J = 103.6 Hz), 127.9, 128.2, 128.6 (d, J = 13.0 Hz), 129.1 (d, J = 105.6 Hz), 129.3, 129.5 (d, J = 9.5 Hz), 131.0 (d, J = 10.9 Hz), 131.7 (d, J = 10.6 Hz), 132.3 (d, J = 2.9 Hz), 132.5 (d, J = 96.4 Hz), 133.0 (d, J = 1.9 Hz), 133.1 (d, J = 3.6 Hz), 142.3 (d, J = 24.7 Hz), 162.5 (d, J = 12.1 Hz), 163.8 (d, J = 18.3 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 35.7; HRMS m/z ($M+H^+$) Calcd for $C_{23}H_{20}O_3P$: 375.1145. Found 375.1147.

2-Acetyl-1,3-diphenyl-1*H*-phosphindole-1-oxide (3an): colorless solid, mp 147-149 °C, 53.4 mg (62%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.94 (d, J = 0.4 Hz, 3H), 7.19-7.20 (m, 1H), 7.38-7.58 (m,

10H), 7.70-7.83 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7 (d, J = 2.7 Hz), 126.4 (d, J = 10.7 Hz), 127.9, 128.7 (d, J = 12.7 Hz), 129.0, 129.2 (d, J = 103.4 Hz), 129.4 (d, J = 9.4 Hz), 129.7, 131.0 (d, J = 11.0 Hz), 131.6 (d, J = 10.5 Hz), 132.4 (d, J = 2.9 Hz), 132.6 (d, J = 103.6 Hz), 133.1 (d, J = 1.7 Hz), 133.4 (d, J = 13.7 Hz), 135.3 (d, J = 92.2 Hz), 142.4 (d, J = 25.7 Hz), 159.9 (d, J = 18.8 Hz), 195.7 (d, J = 8.9 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 37.5; HRMS m/z ($M+H^+$) Calcd for $C_{22}H_{18}O_2P$: 345.1039. Found 345.1038.

1,3-Diphenyl-2-(2-hydroxy-2-propyl)-1*H*-phosphindole-1-oxide (3ao): colorless solid, mp 213-215 °C 54.9 mg (61%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.14 (s, 3H), 1.32 (s, 3H), 2.99 (s, 1H), 6.69 (dd, J = 2.6, 7.6 Hz, 1H), 7.24-7.31 (m, 3H), 7.36 (t, 7.3Hz, 1H), 7.43-7.53 (m, 6H), 7.58 (dd, J = 7.3, 7.9 Hz, 1H), 7.79 (dd, J = 7.1, 12.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 30.8 (d, J = 2.3 Hz), 31.8 (d, J = 2.3 Hz), 73.5, (d, J = 6.9 Hz), 123.6 (d, J = 11.4 Hz), 128.2 (d, J = 12.6 Hz), 128.4 (d, J = 9.2 Hz), 128.56 (d, J = 2.3 Hz), 128.64 (d, J = 12.6 Hz), 128.7, 128.9 (d, J = 10.3 Hz), 130.6 (d, J = 97.3 Hz), 130.9 (d, J = 10.3 Hz), 131.3 (d, J = 100.7 Hz), 131.9 (d, J = 2.3 Hz), 132.8 (d, J = 2.3 Hz), 134.7 (d, J = 16.0 Hz), 144.3 (d, J = 91.5 Hz), 145.1 (d, J = 27.5 Hz), 148.6 (d, J = 20.6 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 243 MHz): δ 41.6; HRMS m/z ($M+H^+$) Calcd for $C_{23}H_{22}O_2P$: 361.1343. Found 361.1352.

2-{[(*tert*-Butyldimethylsilyl)oxy]methyl}-1,3-diphenyl-1*H*-phosphindole-1-oxide (3ap): colorless solid, mp 124-126 °C, 68.9 mg (58%); ^{1}H NMR (400 MHz, $CDCl_3$): δ -0.25 (s, 3H), -0.19 (s, 3H), 0.64 (s, 9H), 4.29 (dd, J = 12.2, 19.3 Hz, 1H), 4.60 (dd, J = 7.6, 12.2 Hz, 1H), 7.16 (dd, J = 2.8, 7.5 Hz, 1H), 7.33 (ddt, J = 1.0, 3.8, 7.5 Hz, 1H), 7.38-7.63 (m, 10H), 7.79-7.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.94, -5.86, 18.0, 25.6, 57.4 (d, J = 8.8 Hz), 123.9 (d, J = 10.8 Hz), 128.4 (d, J = 12.5 Hz), 128.58, 128.62, 128.89 (d, J = 9.7 Hz), 128.94, 129.1 (d, J = 10.5 Hz), 130.2 (d, J = 101.0 Hz), 131.2 (d, J = 10.9 Hz), 131.7 (d, J = 2.8 Hz), 132.5 (d, J = 1.9 Hz), 133.06 (d, J = 103.6 Hz), 133.10 (d, J = 14.8 Hz), 134.5 (d, J = 96.6 Hz), 143.1 (d, J = 26.6 Hz), 152.3 (d, J = 21.1 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 38.7; HRMS m/z ($M+H^+$) Calcd for $C_{27}H_{32}O_2PSi$: 447.1904. Found 447.1905.

Diethyl (1-Oxido-1,3-diphenyl-2-benzo[*b*]phospholyl)phosphonate (3aq): colorless solid, mp 120-123 °C, 44.9 mg (41%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.96 (t, J = 4.7 Hz, 3H), 1.09 (t, J = 4.9 Hz, 3H), 3.69 (ddq, J = 4.7, 4.7, 6.6 Hz, 1H), 3.85 (ddq, J = 4.7, 4.7, 6.6 Hz, 1H), 3.89-3.97 (m, 2H),

7.19-7.21 (m, 1H), 7.45-7.56 (m, 10H), 7.67-7.71 (m, 1H), 7.82 (dd, J = 4.7, 8.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 15.87 (d, J = 5.7 Hz), 15.93 (d, J = 6.9 Hz), 61.9 (d, J = 6.9 Hz), 62.2 (d, J = 5.7 Hz), 125.0 (dd, J = 80.1, 187.7 Hz), 125.8 (d, J = 10.3 Hz), 128.1, 128.3 (br), 128.6 (d, J = 12.6 Hz), 128.9 (d, J = 105.3 Hz), 129.5 (d, J = 8.0 Hz), 129.6, 131.1 (d, J = 10.3 Hz), 131.3 (d, J = 10.3 Hz), 132.3 (d, J = 2.3 Hz), 132.9 (d, J = 2.9 Hz), 133.3 (dd, J = 6.9, 14.9 Hz), 133.8 (dd, J = 6.9, 104.1 Hz), 142.3 (dd, J = 20.6, 27.5 Hz), 167.0 (dd, J = 6.9, 167.0 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 11.2 (d, J = 39.5 Hz), 40.8 (d, J = 39.5 Hz); HRMS m/z (M+H$^+$) Calcd for $C_{24}H_{25}O_4P_2$: 439.1223. Found 439.1225.

1,4-Bis(1-oxido-2-methyl-1-phenylbenzo[*b*]phosphole-3-yl)benzene (3ar): pale yellow solid, mp 137-139 °C, 52.6 mg (38%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.99 (dd, J = 2.2, 12.4 Hz, 6H), 7.20 (d, J = 7.5 Hz, 2H), 7.36 (ddd, J = 3.8, 3.8, 7.4 Hz, 2H), 7.46-7.59 (m, 12H), 7.70 (dd, J = 7.2, 9.8 Hz, 2H), 7.77 (dd, J = 6.9, 12.4 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.9 (d, J = 10.6 Hz), 123.1 (d, J = 11.0 Hz), 128.6 (d, J = 10.5 Hz), 129.0 (d, J = 12.1 Hz), 129.1 (d, J = 98.1 Hz), 129.2, 129.3 (d, J = 9.7 Hz), 131.0 (d, J = 10.3 Hz), 131.5 (d, J = 103.7 Hz), 132.4 (d, J = 2.2 Hz), 132.7 (d, J = 127.0 Hz), 133.0 (d, J = 1.4 Hz), 134.0 (d, J = 15.9 Hz), 144.0 (d, J = 27.7 Hz), 149.2 (d, J = 21.9 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 40.3; HRMS m/z (M+H$^+$) Calcd for $C_{36}H_{29}O_2P_2$: 555.1637. Found 555.1631.

1,3-diphenyl-1*H*-phosphindole-1-oxide (3as): colorless gum, 43.1 mg (57%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.37 (d, J = 24.0 Hz, 1H), 7.39-7.83 (m, 14H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 122.9 (d, J = 99.1 Hz), 124.1 (d, J = 11.3 Hz), 127.8, 128.8, 128.9 (d, J = 12.3 Hz), 129.3 (d, J = 9.6 Hz), 129.5 (d, J = 10.5 Hz), 129.589 (d, J = 102.4 Hz), 129.599, 131.0 (d, J = 10.8 Hz), 132.3, (d, J = 2.8 Hz), 132.6 (d, J = 1.9 Hz), 133.9 (d, J = 104.7 Hz), 135.0 (d, J = 16.1 Hz), 141.1 (d, J = 27.2 Hz), 158.1 (d, J = 15.3 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 36.9; HRMS m/z (M+H$^+$) Calcd for $C_{20}H_{16}OP$: 303.0939. Found 303.0933.

5-Methyl-1-*p*-tolyl-2,3-diphenyl-1*H*-phosphindole-1-oxide +
6-Methyl-1-*p*-tolyl-2,3-diphenyl-1*H*-phosphindole-1-oxide (3ba+3ba'); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.32 (s, 3H), 2.33 (s, 3H), 2.34 (s, 3H+3H), 6.99 (s, 1H), 7.07-7.23 (m, 17H), 7.32 (d, J = 6.4 Hz, 2H+2H), 7.39-7.44 (m, 6H), 7.51 (d, J = 10.0 Hz, 1H), 7.58 (dd, J = 7.6, 9.7 Hz, 1H), 7.65 (dd, J = 8.2, 12.3 Hz, 2H), 7.67 (dd, J = 8.2, 12.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 21.6

(2C, overlapped), 21.9, 123.8 (d, J = 11.4 Hz), 124.8 (d, J = 10.3 Hz), 126.6 (d, J = 101.8 Hz), 126.7 (d, J = 101.8 Hz), 127.5, 127.6, 128.1, 128.5 (d, J = 2.3 Hz), 128.85, 128.88, 128.97, 128.98, 129.02 (d, J = 107.6 Hz), 129.03, 129.53, 129.55, 129.58, 129.62, 129.64, 129.66, 129.70, 130.9 (d, J = 10.3 Hz x 2C), 132.1, 132.78, 132.83, 132.85, 132.90, 132.91, 133.15, 133.16, 133.6, 134.38, 134.44, 138.48, 134.53, 135.1, 139.3 (d, J = 10.3 Hz), 141.0 (d, J = 26.3 Hz), 142.52 (d, J = 26.3 Hz), 142.52 (d, J = 10.3 Hz), 142.54 (d, J = 10.3 Hz), 143.4, 144.0 (d, J = 27.5 Hz), 149.7 (d, J = 21.8 Hz), 149.9 (d, J = 21.7 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 243 MHz): δ 39.0, 39.3; HRMS m/z ($M+H^+$) Calcd for $C_{28}H_{24}OP$: 407.1559. Found 407.1558.

5-Methoxy-1-(*p*-methoxyphenyl)-2,3-diphenyl-1*H*-phosphindole-1-oxide (3ca): pale yellow solid, mp 214-217 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.78 (s, 3H), 3.79 (s, 3H), 6.73 (dd, J = 2.2, 2.2 Hz, 1H), 6.84 (ddd, J = 2.8, 2.8, 8.0 Hz, 1H), 6.89 (dd, J = 2.2, 8.8 Hz, 2H), 7.07-7.10 (m, 3H), 7.20-7.22 (m, 2H), 7.28-7.31 (m, 2H), 7.38-7.41 (m, 3H), 7.62 (dd, J = 8.3, 9.2 Hz, 1H), 7.67 (dd, J = 8.8, 11.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 55.5, 111.5 (d, J = 11.8 Hz), 112.8 (d, J = 11.8 Hz), 114.5 (d, J = 13.2 Hz), 121.1 (d, J = 106.5 Hz), 123.2 (d, J = 111.6 Hz), 127.8, 128.2, 128.6, 128.9, 129.0 (d, J = 5.8 Hz), 129.1, 130.5 (d, J = 11.0 Hz), 132.89 (d, J = 12.1 Hz), 132.92 (d, J = 9.2 Hz), 134.3 (d, J = 14.6 Hz), 136.2 (d, J = 94.8 Hz), 146.2 (d, J = 28.4 Hz), 148.8 (d, J = 21.0 Hz), 162.7 (d, J = 2.9 Hz), 163.7 (d, J = 1.9 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 38.1; HRMS m/z ($M+H^+$) Calcd for $C_{28}H_{24}O_3P$: 439.1458. Found 439.1458.

6-Methoxy-1-(*p*-methoxyphenyl)-2,3-diphenyl-1*H*-phosphindole-1-oxide (3ca'): colorless solid, mp 85-87 °C ; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.797 (s, 3H), 3.804 (s, 3H), 6.91 (m, 3H), 7.06-7.09 (m, 3H), 7.11 (dd, J = 3.6, 8.4 Hz, 1H), 7.18-7.21 (m, 2H), 7.25 (dd, J = 2.5, 10.8 Hz, 1H), 7.30-7.32 (m, 2H), 7.38-7.42 (m, 3H), 7.70 (dd, J = 8.9, 11.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 55.7, 114.5 (d, J = 10.6 Hz), 114.6 (d, J = 13.2 Hz), 117.8, 120.6 (d, J = 105.0 Hz), 125.2 (d, J = 12.6 Hz), 127.4, 128.2, 128.5, 128.8, 128.9 (d, J = 5.8 Hz), 129.0, 131.3 (d, J = 100.3 Hz), 132.8 (d, J = 11.9 Hz), 133.0 (d, J = 133.0 Hz), 134.5 (d, J = 104.4 Hz), 134.6 (d, J = 15.2 Hz), 136.0 (d, J = 26.8 Hz), 149.7 (d, J = 21.1 Hz), 160.7 (d, J = 13.3 Hz), 162.8 (d, J = 2.9 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 38.9; HRMS m/z ($M+H^+$) Calcd for $C_{28}H_{24}O_3P$: 439.1458. Found 439.1460.

7-Methyl-2,3-diphenyl-1-(*o*-tolyl)-1*H*-phosphindole-1-oxide (3da): pale yellow solid, mp 168-170 °C ; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.18 (s, 3H), 2.31 (s, 3H), 7.02 (dd, J = 2.9, 7.6 Hz, 1H), 7.03-7.16 (m, 6H), 7.28-7.43 (m, 8H), 8.34 (dd, J = 7.6, 13.2 Hz, 2H); ^{13}C NMR (150 MHz,

$CDCl_3$) δ 19.2 (d, J = 4.6 Hz), 19.9 (d, J = 3.4 Hz), 121.9 (d, J = 10.3 Hz), 126.2 (d, J = 11.4 Hz), 127.5 (d, J = 98.3 Hz), 127.6, 128.1, 128.5, 128.82, 128.83, 128.85, 129.5 (d, J = 103.0 Hz), 130.7 (d, J = 9.2 Hz), 131.4 (d, J = 11.4 Hz), 132.1 (d, J = 3.4 Hz), 132.87, 132.91 (d, J = 12.6 Hz), 133.8 (d, J = 95.0 Hz), 134.6 (d, J = 14.9 Hz), 134.8 (d, J = 8.0 Hz), 140.5 (d, J = 8.0 Hz), 141.0 (d, J = 9.5 Hz), 144.6 (d, J = 27.5 Hz), 150.2 (d, J = 21.7 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3$, 243 MHz): δ 37.3; HRMS m/z ($M+H^+$) Calcd for $C_{28}H_{24}OP$: 407.1559. Found 407.1565.

4-Methyl-2,3-diphenyl-1-(*o*-tolyl)-1*H*-phosphindole-1-oxide (3da'): colorless solid, mp 65-67 °C ; ^1H NMR (600 MHz, $CDCl_3$): δ 1.76 (s, 3H), 2.27 (s, 3H), 7.00-7.04 (m, 3H), 7.08-7.10 (m, 2H), 7.12-7.14 (m, 1H), 7.20 (d, J = 7.6 Hz, 1H), 7.23-7.26 (m, 3H), 7.31 (dd, J = 7.6, 7.6 Hz, 1H), 7.34-7.40 (m, 4H), 7.50 (dd, J = 7.0, 10.6 Hz, 1H), 8.19 (ddd, J = 1.4, 7.6, 13.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2 (d, J = 4.6 Hz), 21.4, 126.0 (d, J = 11.4 Hz), 127.0 (d, J = 9.2 Hz), 127.5, 127.6 (d, J = 96.1 Hz), 128.0, 128.1 (d, J = 13.7 Hz), 128.5 (d, J = 5.7 Hz), 128.8 (d, J = 5.7 Hz), 129.05 (d, J = 11.4 Hz), 129.13, 131.4 (d, J = 11.4 Hz), 132.2 (d, J = 2.3 Hz), 132.6 (d, J = 92.7 Hz), 133.0, 134.3 (d, J = 9.2 Hz), 135.3 (d, J = 91.5 Hz), 135.6 (d, J = 10.3 Hz), 137.3 (d, J = 2.3 Hz), 137.6 (d, J = 14.9 Hz), 140.8 (d, J = 26.3 Hz), 141.1 (d, J = 11.4 Hz), 152.3 (d, J = 21.7 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ 37.1; HRMS m/z ($M+H^+$) Calcd for $C_{28}H_{24}OP$: 407.1559. Found 407.1556.

1-*n*-Butyl-2,3-diphenyl-1*H*-phosphindole-1-oxide (3ea): colorless gum, 52.9 mg (59%); ^1H NMR (400 MHz, $CDCl_3$): δ 0.79 (t, J = 7.3 Hz, 3H), 1.29 (qt, J = 7.4, 7.4Hz Hz, 2H), 1.39-1.51 (m, 2H), 1.84-2.15 (m, 2H), 7.15-7.46 (m, 13H), 7.81-7.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 23.87 (d, J = 17.5 Hz), 23.93, 28.3 (d, J = 66.9 Hz), 123.9 (d, J = 10.2 Hz), 127.9, 128.4, 128.5, 128.6, 128.7 (d, J = 9.8 Hz), 128.9, 129.0 (d, J = 5.3 Hz), 129.1, 130.8 (d, J = 98.9 Hz), 132.6 (d, J = 1.4 Hz), 133.2 (d, J = 9.8 Hz), 133.3 (d, J = 90.0 Hz), 134.3 (d, J = 14.3 Hz), 143.3 (d, J = 25.5 Hz), 148.8 (d, J = 20.0 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ 50.3; HRMS m/z ($M+H^+$) Calcd for $C_{24}H_{24}OP$: 359.1559. Found 359.1563.

1-*tert*-Butyl-2,3-diphenyl-1*H*-phosphindole-1-oxide (3fa): colorless solid, mp 219-220 °C, 59.1 mg (66%); ^1H NMR (400 MHz, $CDCl_3$): δ 1.08 (d, J = 15.2 Hz, 9H), 7.12-7.45 (m, 13H), 7.79-7.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.3, 32.9 (d, J = 67.8 Hz), 123.9 (d, J = 9.9 Hz), 127.7, 128.3, 128.4, 128.5, 128.8 (br), 129.1 (br), 129.2 (d, J = 4.9 Hz), 129.6 (d, J = 93.6 Hz), 129.7 (d, J = 8.6 Hz), 132.2 (d, J = 84.3 Hz), 132.5 (d, J = 1.7 Hz), 134.2 (d, J = 13.6 Hz), 134.6 (d, J = 9.4 Hz),

144.1 (d, J = 23.8 Hz), 150.3 (d, J = 18.7 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 59.2; HRMS m/z ($M+H^+$) Calcd for $C_{24}H_{24}OP$: 359.1559. Found 359.1563.

1-Ethoxy-2,3-diphenyl-1*H*-phosphindole-1-oxide (3ga): colorless gum, 45.6 mg (53%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (t, J = 7.0 Hz, 3H), 4.00-4.16 (m, 2H), 7.10-7.13 (m, 1H), 7.18-7.27 (m, 5H), 7.37-7.44 (m, 7H), 7.73-7.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5 (d, J = 6.2 Hz), 62.1 (d, J = 6.2 Hz), 123.9 (d, J = 13.3 Hz), 127.2 (d, J = 133.1 Hz), 127.6 (d, J = 8.7 Hz), 127.9, 128.3, 128.6, 128.909 (d, J = 5.4 Hz), 128.912, 128.95 (d, J = 10.8 Hz), 129.00, 130.5 (d, J = 94.0 Hz), 132.5 (d, J = 9.1 Hz), 133.0 (d, J = 2.1 Hz), 133.9 (d, J = 17.9 Hz), 141.9 (d, J = 34.2 Hz), 148.6 (d, J = 27.1 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 45.8; HRMS m/z ($M+H^+$) Calcd for $C_{22}H_{20}O_2P$: 347.1195. Found 347.1206.

1,2,3-Triphenyl-1*H*-phosphindole-1-sulfide (3ha): colorless solid, mp 65-67 °C, 49.6 mg (50%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05-7.13 (m, 3H), 7.17-7.19 (m, 2H), 7.30 (dd, J = 3.1, 7.6 Hz, 1H), 7.32-7.50 (m, 10H), 7.70 (dd, J = 7.1, 10.6 Hz, 1H), 7.86 (dd, J = 7.0, 14.1 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 124.4 (d, J = 9.8 Hz), 127.9, 128.0, 128.6 (d, J = 8.9 Hz), 128.806 (d, J = 12.8 Hz), 128.814 (2C, overlapped), 129.33 (d, J = 11.1 Hz), 129.34, 129.4 (d, J = 77.3 Hz), 129.5 (d, J = 5.6 Hz), 131.9 (d, J = 11.6 Hz), 132.0 (d, J = 3.0 Hz), 132.3 (d, J = 1.8 Hz), 132.4 (d, J = 10.8 Hz), 134.2 (d, J = 14.3 Hz), 136.0 (d, J = 89.4 Hz), 136.4 (d, J = 77.9 Hz), 143.7 (d, J = 23.4 Hz), 149.2 (d, J = 18.6 Hz); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 162 MHz): δ 48.1; HRMS m/z ($M+H^+$) Calcd for $C_{26}H_{20}PS$: 395.1018. Found 395.1024.

References and Notes

(1) Reviews for phospholes: (a) Mathey, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1578. (b) Baumgartner, T.; Reau, R. *Chem. Rev.* **2006**, *106*, 4681. (c) Matano, Y.; Imahori, H. *Org. Biomol. Chem.* **2009**, *7*, 1258.

(2) (a) Tsuji, H.; Sato, K.; Ilies, L.; Itoh, Y.; Sato, Y.; Nakamura, E. *Org. Lett.* **2008**, *10*, 2263. (b) Sanji, T.; Shiraishi, K.; Kashiwabara, T.; Tanaka, M. *Org. Lett.* **2008**, *10*, 2689. (c) Fukazawa, A.; Ichihashi, Y.; Kosaka, Y.; Yamaguchi, S. *Chem.—Asian J.* **2009**, *4*, 1729. See also General introduction section.

(3) (a) Unoh, Y.; Hashimoto, Y.; Takeda, D.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2013**, *15*, 3258. (b) Seo, J.; Park, Y.; Jeon, I.; Ryu, T.; Park, S.; Lee, P. H. *Org. Lett.* **2013**, *15*, 3358. (c) Zhao,

D.; Nimphius, C.; Lindale, M.; Glorius, F. *Org. Lett.* **2013**, *15*, 4504. (d) Park, Y.; Seo, J.; Park, S.; Yoo, E. J.; Lee, P. H. *Chem.—Eur. J.* **2013**, *19*, 16461. (e) Sun, Y.; Cramer, N. *Angew. Chem., Int. Ed.* **2017**, *56*, 364.

(4) (a) Stuart, D. R.; Bertrand-Laperle, M.; Burgess, K. M. N.; Fagnou, K. *J. Am. Chem. Soc.* **2008**, *130*, 16474. (b) Fukutani, T.; Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *Chem. Commun.* **2009**, 5141. (c) Rakshit, S.; Patureau, F. W.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 9585.

(5) Selected reviews for transition-metal-catalyzed C–H functionalization: (a) Godula, K.; Sames, D. *Science* **2006**, *312*, 67. (b) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (c) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Chem. Rev.* **2007**, 107, 5318. (d) Park, Y. J.; Park, J.-W.; Jun, C.-H. *Acc. Chem. Res.* **2008**, *41*, 222. (e) Ferreira, E. M.; Zhang, H.; Stoltz, B. M. *Tetrahedron* **2008**, *64*, 5987. (f) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013. (g) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335. (h) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev.* **2009**, *38*, 2447. (i) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074. (j) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (k) Satoh, T.; Miura, M. *Synthesis* **2010**, 3395. (l) Satoh, T.; Miura, M. *Chem.—Eur. J.* **2010**, *16*, 11212. (m) Sun, C.-L.; Li, B.-J.; Shi, Z.- J. *Chem. Commun.* **2010**, *46*, 677. (n) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (o) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (p) Lapointe, D.; Fagnou, K. *Chem. Lett.* **2010**, *39*, 1118. (q) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. (r) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780. (s) Kuninobu, Y.; Takai, K. *Chem. Rev.* **2011**, 111, 1938. (t) Wencel-Delord, J.; Droge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740. (u) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (v) Mitchell, E. A.; Peschiulli, A.; Lefevre, N.; Meerpoel, L.; Maes, B. U. W. *Chem.—Eur. J.* **2012**, *18*, 10092. (w) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788. (x) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814.

(6) For reviews of P-centered radicals: (a) Leca, D.; Fensterbank, L.; Lacote, E.; Malacria, M. *Chem. Soc. Rev.* **2005**, *34*, 858. (b) Pan, X.-Q.; Zou, J.-P.; Yi, W.-B.; Zhang, W. *Tetrahedron* **2015**, *71*, 7481.

(7) For examples of Ag-promoted generation of P-centered radical species: (a) Effenberger, F.; Kottmann, H. *Tetrahedron* **1985**, *41*, 4171. (b) Xiang, C.-B.; Bian, Y.-J.; Mao, X.-R.; Huang, Z.-Z. *J. Org. Chem.* **2012**, *77*, 7706. (c) Mao, X.; Ma, X.; Zhang, S.; Hu, H.; Zhu, C.; Cheng, Y. *Eur. J. Org. Chem.* **2013**, 4245. (d) Sun, M.; Wang, H.-L.; Ting, Q.-P.; Yang, S.-D. *Angew. Chem., Int. Ed.* **2013**, *52*, 3972. Review: (e) Zheng, Q.-Z.; Jiao, N. *Chem. Soc. Rev.* **2016**, *45*, 4590. For related Ag-mediated C–H/C–H dehydrogenative coupling, see: (f) He, C.; Guo, S.; Ke, J.; Hao, J.; Xu, H.;

Chen, H.; Lei, A. *J. Am. Chem. Soc.* **2012**, *134*, 5766.

(8) For selected examples on the use of manganese salt in radical reactions, see: (a) Snider, B. B. *Chem. Rev.* **1996**, *96*, 339. (b) Tayama, O.; Nakano, A.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **2004**, *69*, 5494. (c) Beaufils, F.; Denes, F.; Renaud, P. *Angew. Chem., Int. Ed.* **2005**, *44*, 5273. (d) Kagayama, T.; Nakano, A.; Sakaguchi, S.; Ishii, Y. *Org. Lett.* **2006**, *8*, 407. (e) Mu, X.-J.; Zou, J.-P.; Qian, Q.-F.; Zhang, W. *Org. Lett.* **2006**, *8*, 5291. (f) Zhou, J.; Zhang, Z.-G.; Zou, J.-P.; Zhang, W. *Eur. J. Org. Chem.* **2011**, 3412. (g) Tobisu, M.; Koh, K.; Furukawa, T.; Chatani, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 11363. (h) Liu, K.; Jia, F.; Xi, H.; Li, Y.; Zheng, X.; Guo, Q.; Shen, B.; Li, Z. *Org. Lett.* **2013**, *15*, 2026.

(9) Compound **3ar** seems to be formed as a mixture of diastereomers. However, the ratio could not be determined owing to overlap in the NMR chemical shifts.

(10) (a) Tsuji, H.; Sato, K.; Sato, Y.; Nakamura, E. *J. Mater. Chem.* **2009**, *19*, 3364. (b) Tsuji, H.; Sato, K.; Sato, Y.; Nakamura, E. *Chem.—Asian J.* **2010**, *5*, 1294.

(11) For selected examples of radical aryl migration reactions, see: (a) Clive, D. L. J.; Kang, S. *Tetrahedron Lett.* **2000**, *41*, 1315. (b) Benati, L.; Calestani, G.; Leardini, R.; Minozzi, M.; Nanni, D.; Spagnolo, P.; Strazzari, S.; Zanardi, G. *J. Org. Chem.* **2003**, *68*, 3454. (c) Roman, D. S.; Takahashi, Y.; Charette, A. B. *Org. Lett.* **2011**, *13*, 3242. (d) Bhakuni, B. S.; Kumar, A.; Balkrishna, S. J.; Sheikh, J. A.; Konar, S.; Kumar, S. *Org. Lett.* **2012**, *14*, 2838. For reviews, see: (e) Studer, A.; Bossart, M. *Tetrahedron* **2001**, *57*, 9649. (f) Bowman, W. R.; Storey, J. M. D. *Chem. Soc. Rev.* **2007**, *36*, 1803.

(12) For selected examples for the related processes, see: (a) Brumwell, J. E.; Simpkins, N. S. *Tetrahedron* **1994**, *50*, 13533. (b) Sato, A.; Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 1694. Review: (c) Wille, U. *Chem. Rev.* **2013**, *113*, 813.

(13) (a) Yamaguchi, E.; Fukazawa, A.; Kosaka, Y.; Yokogawa, D.; Irle, S.; Yamaguchi, S. *Bull. Chem. Soc. Jpn.* **2015**, *88*, 1545. (b) Yamaguchi, E.; Wang, C. G.; Fukazawa, A.; Taki, M.; Sato, Y.; Sasaki, T.; Ueda, M.; Sasaki, N.; Higashiyama, T.; Yamaguchi, S. *Angew. Chem., Int. Ed.* **2015**, *54*, 4539. (c) Wang, C.; Fukazawa, A.; Taki, M.; Sato, Y.; Higashiyama, T.; Yamaguchi, S. *Angew. Chem., Int. Ed.* **2015**, *54*, 15213.

(14) After the author reported the results in Chapter 3 (11 October 2013), Duan and co-workers independently reported a similar benzophosphole synthesis: Chen, Y.-R.; Duan, W.-L. *J. Am. Chem. Soc.* **2013**, *135*, 16754 (28 October 2013).

(15) After this report, similar Ag-promoted radical phosphinylation reactions are reported: (a) Zhang, B.; Daniliuc, C. G.; Studer, A. *Org. Lett.* **2014**, *16*, 250. (b) Zheng, J.; Zhang, Y.; Wang, D.;

Cui, S. *Org. Lett.* **2016**, *18*, 1768. (c) Gao, Y.; Lu, G.; Zhang, P.; Zhang, L.; Tang, G.; Zhao, Y. *Org. Lett.* **2016**, *18*, 1242.

(16) Busacca, C. A.; Lorenz, J. C.; Grinberg, N.; Haddad, N.; Hrapchak, M.; Latli, B.; Lee, H.; Sabila, P.; Saha, A.; Sarvestani, M.; Shen, S.; Varsolona, R.; Wei, X. D.; Senanayake, C. H. *Org. Lett.* **2005**, *7*, 4277.

(17) Xu, Q.; Zhao, C.-Q.; Han, L.-B. *J. Am. Chem. Soc.* **2008**, *130*, 12648.

(18) Semezin, D.; Emetad-Moghadam, G.; Albouy, D.; Diallo, O.; Koenig, M. *J. Org. Chem.* **1997**, *62*, 2414.

(19) Novak, Z.; Nemes, P.; Kotschy, A. *Org. Lett.* **2004**, *6*, 4917.

(20) Finke, A. D.; Dumele, O.; Zalibera, M.; Confortin, D.; Cias, P.; Jayamurugan, G.; Gisselbrecht, J.-P.; Boudon, C.; Schweizer, W. B.; Gescheidt, G.; Diederich, F. *J. Am. Chem. Soc.* **2012**, *134*, 18139.

(21) Mio, M. J.; Kopel, L. C.; Braun, J. B.; Gadzikwa, T. L.; Hull, K. L.; Brisbois, R. G.; Markworth, C. J.; Grieco, P. A. *Org. Lett.* **2002**, *4*, 3199.

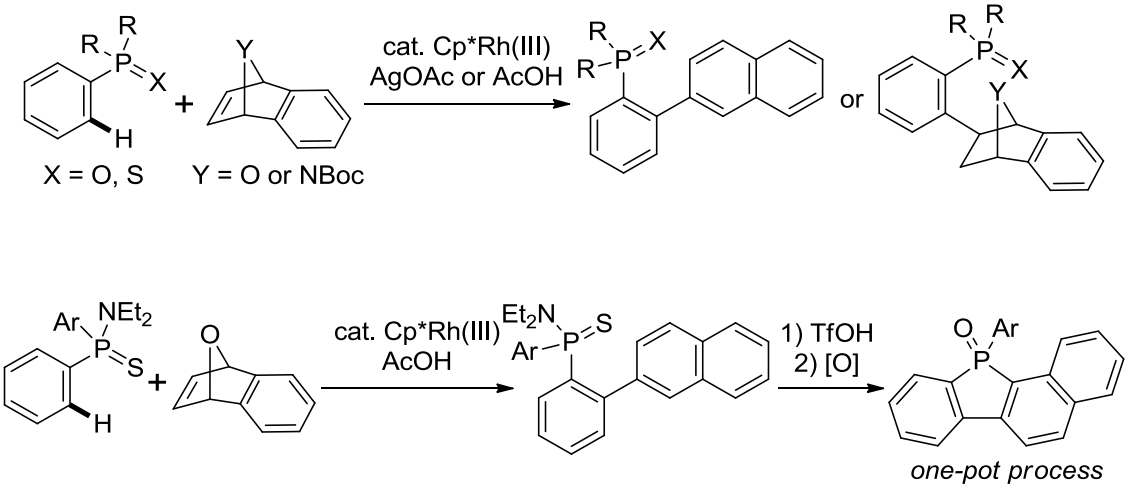
(22) Wang, C.; Rakshit, S.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 14006.

(23) Lecerclé, D.; Sawicki, M.; Taran, F. *Org. Lett.* **2006**, *8*, 4283.

Chapter 4

Rhodium(III)-Catalyzed Direct Coupling of Arylphosphine Derivatives with Heterobicyclic Alkenes

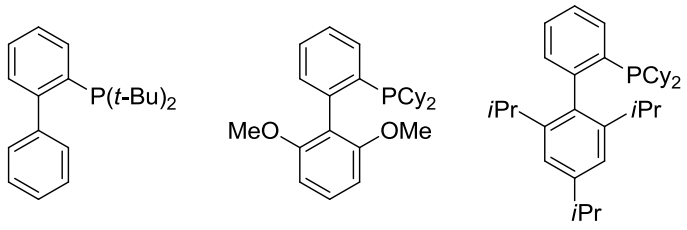
The redox-neutral direct coupling of arylphosphine oxides with heterobicyclic alkenes proceeds smoothly under rhodium(III) catalysis involving hydroarylation of the alkenes followed by dehydrative aromatization to form biarylphosphine oxides. Related phenylphosphinic- and phenylphosphonic esters as well as phenylphosphine sulfides also undergo the *ortho*-arylative coupling. Furthermore, phenylphosphinothioic amides can be transformed to fused dibenzophosphole derivatives through the rhodium-catalyzed coupling with heterobicyclic alkenes and successive intramolecular phospha-Friedel-Crafts reaction in a one-pot manner.



Introduction

The biarylphosphines are important scaffolds in organic synthesis. Various *P*,*P*-dialkylbiarylphosphines are known as Buchwald-type ligands (Figure 4.1), which are effective ligands for transition-metal catalyzed C-C and C-X bond forming cross-coupling reactions.[1]

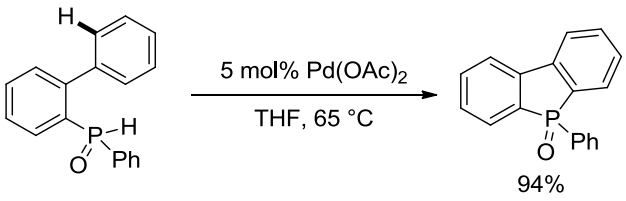
Figure 4.1. Buchwald-type Ligands



JohnPhos SPhos XPhos

In addition, biarylphosphine derivatives are useful synthetic intermediates for the synthesis of fused phosphorus-containing heterocycles.[2] For example, Takai, Kuninobu, and co-workers reported the palladium-catalyzed intramolecular dehydrogenative coupling of secondary biarylphosphine oxides to give dibenzo[*b*]phosphole oxide derivatives (Scheme 4.1).[2a]

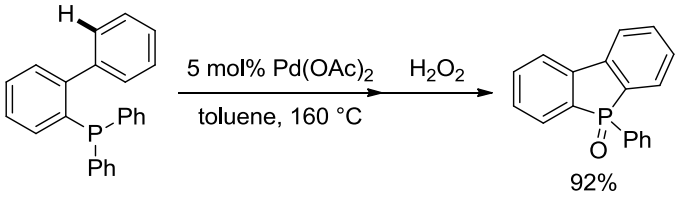
Scheme 4.1.



94%

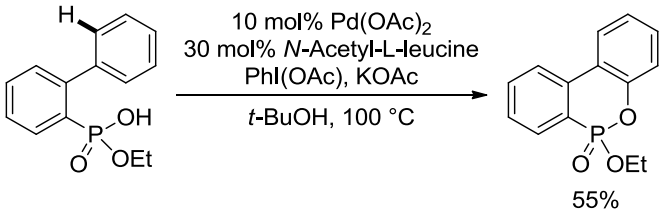
Chatani, Tobisu, and co-workers disclosed the palladium-catalyzed intramolecular cyclization of biarylphosphines involving C-H and C-P bond cleavages to afford dibenzo[*b*]phosphole derivatives (Scheme 4.2).[2b]

Scheme 4.2.



Lee and co-workers reported the palladium-catalyzed intramolecular oxidative coupling reaction of biarylphosphinic acid derivatives to synthesize the fused phospha-lactones (Scheme 4.3).[2c]

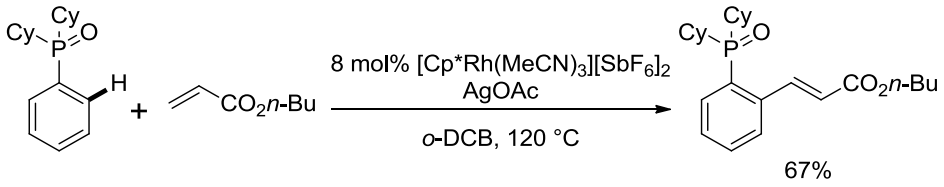
Scheme 4.3.



The above biarylphoshine scaffolds are usually synthesized by multi-step transformations including the Suzuki coupling. Therefore, convenient methods for the preparation of biarylphosphines and their synthetic intermediates including biarylphosphine oxides and sulfides continuously remain to be developed.

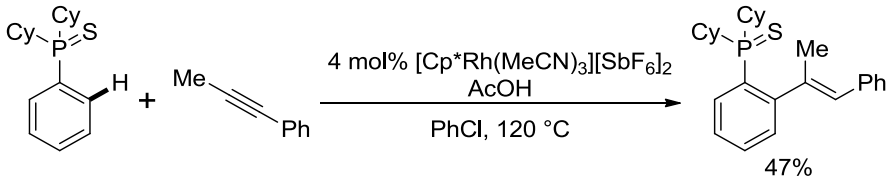
Meanwhile, transition metal-catalyzed direct C–H bond functionalization reactions with the assistance of a coordinating-functional group (directing group) are now regarded as atom- and step-economical synthetic tools, because they allow the regioselective direct modification of given substrates without prefunctionalization.[3,4] The authors[5] and others[6-9] have recently reported that the P=O and P=S groups in arylphosphine oxides and sulfides act as good directing groups in catalytic direct functionalization reactions. The author and co-workers previously disclosed the Cp*Rh(III)-catalyzed oxidative *ortho* direct alkenylation of arylphosphine oxides with acrylates (Scheme 4.4).

Scheme 4.4.



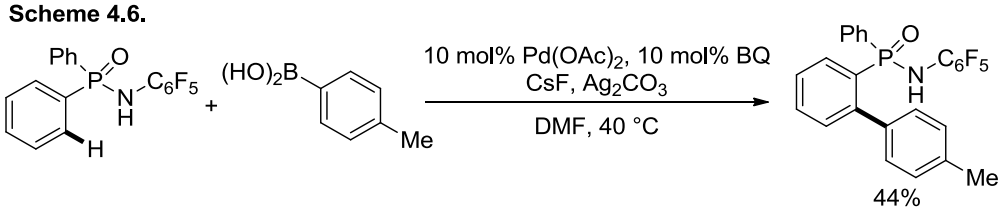
Additionally, the same group showed the direct coupling reaction of arylphosphine sulfides with alkynes (Scheme 4.5).

Scheme 4.5.



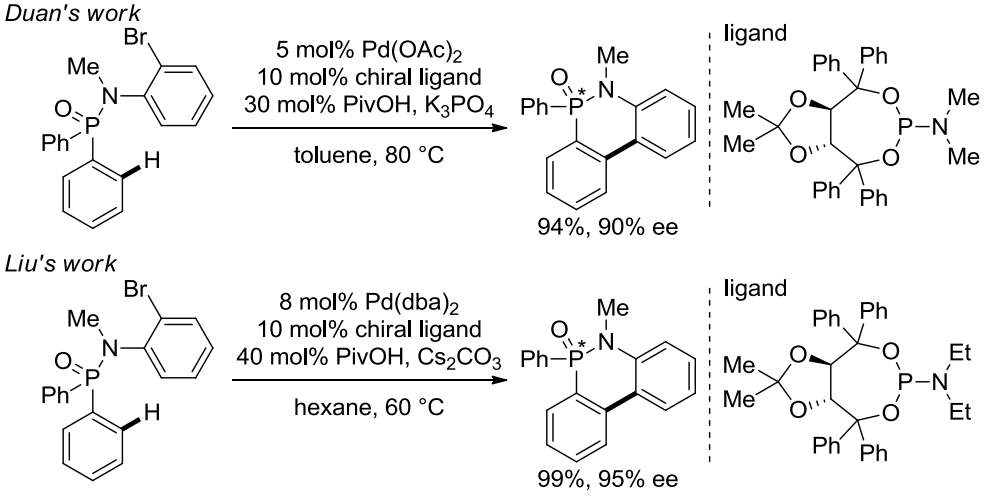
Compared to such *ortho*-alkenylations, the *ortho*-arylation of arylphosphine derivatives has been less explored.[6m,6o,6t-v,7c] As a recent example, Han and co-workers reported the palladium-catalyzed *ortho*-arylation of diarylphosphinamides with arylboronic acids (Scheme 4.6).[6o, 6q]

Scheme 4.6.



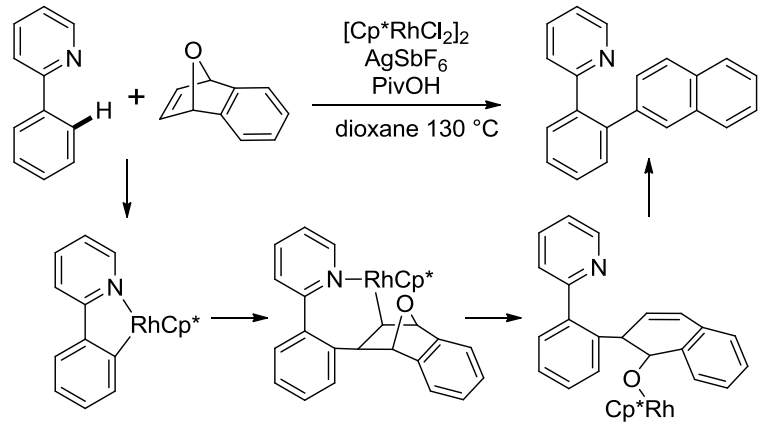
Duan and Liu independently reported the palladium catalyzed C-H arylation of arylphosphinamides (Scheme 4.7).[6t, 6u] However, these arylation reactions are limited to the case with special phosphinamides or the intramolecular reaction. Therefore, development of the direct arylation on more general arylphosphine derivatives is desired.

Scheme 4.7.



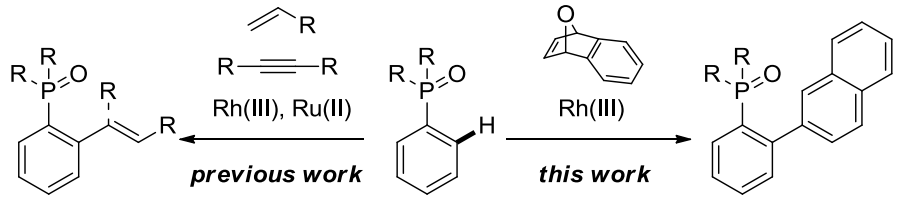
In 2013, Li and co-workers reported the rhodium-catalyzed direct coupling reaction of 2-phenylpyridines with oxabicycloalkenes (Scheme 4.8).[10a] They proposed that the reaction proceeds through the alkene insertion to the 5-membered rhodacycle, ring opening via *β*–oxygen elimination, and dehydrative aromatization to form the naphthylated product.

Scheme 4.8.



Inspired by the above work, the author succeeded in finding that arylphosphine oxides also undergo the direct coupling with 1,4-epoxydihydronaphthalenes under rhodium catalysis to produce biarylphosphine oxides (Scheme 4.9, right).

Scheme 4.9. Transition-Metal-Catalyzed Direct Functionalization of Arylphosphine Oxides



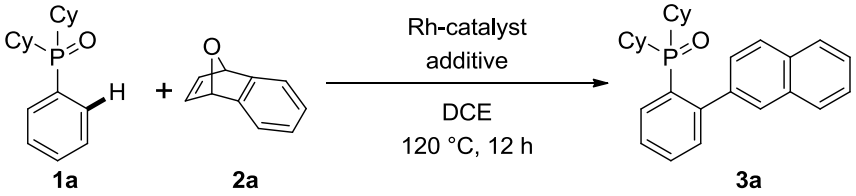
It has been confirmed that thus obtained biarylphosphine oxides can be readily reduced to the corresponding biarylphosphines. Furthermore, a one-pot synthesis of dibenzophosphole derivatives has also been achieved by the direct coupling of phenylphosphinothioic amides with 1,4-epoxydihydronaphthalenes and successive TfOH-mediated phospha-Friedel-Crafts reaction. These new findings are described in this Chapter.

Results and Discussion

First, the author carried out optimization studies using dicyclohexylphenylphosphine oxide (**1a**) and 1,4-epoxydihydronaphthalene (**2a**) as model substrates (Table 4.1). Thus, **1a** (0.25 mmol) was treated with **2a** (0.25 mmol) in the presence of $[Cp^*Rh(MeCN)_3(SbF_6)_2]$ (0.01 mmol, 4 mol %) and AgOAc (0.05 mmol, 20 mol %) in DCE at 120 °C under N_2 for 12 h. As a result, the desired *ortho*-arylated product **3a** was formed in 60% GC yield (entry 1). As additive, $Cu(OAc)_2•H_2O$ and Ag_2CO_3 in place of AgOAc were not suitable (entries 2 and 3). A neutral rhodium complex, $[Cp^*RhCl_2]_2$, did not show any catalytic activity (entry 4). A combination of $[Cp^*RhCl_2]_2$ and $AgSbF_6$, which appears to form a cationic rhodium species in situ, was less effective than $[Cp^*Rh(MeCN)_3(SbF_6)_2]$ (entry 5). Increasing the amount of **2a** (1.5 equiv) improved the product yield up to 69% (entry 6). Addition of 3 equiv of acetic acid or pivalic acid

in place of AgOAc was found to be comparably effective (entries 7 and 8). Finally, **3a** was obtained in 78% isolated yield by using 1.2 equiv of **2a** at 130 °C (entry 9).

Table 4.1. Optimization Studies for the Rh-Catalyzed Direct Naphthylation of Dicyclohexylphenylphosphine Oxide (1a)[a]



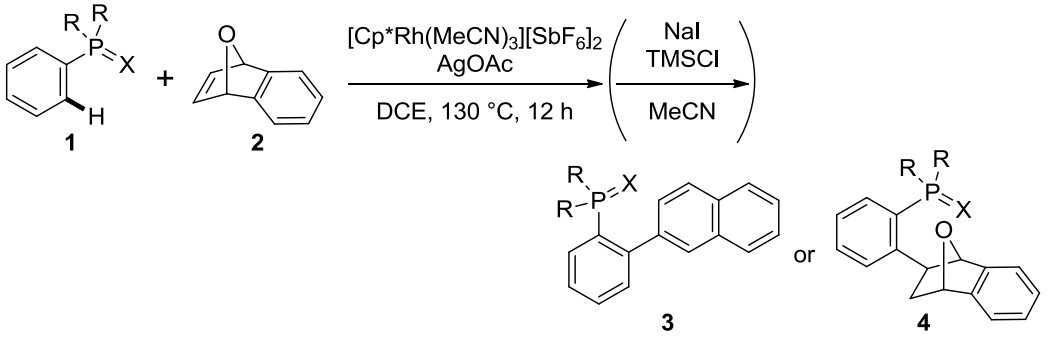
1a **2a** **3a**

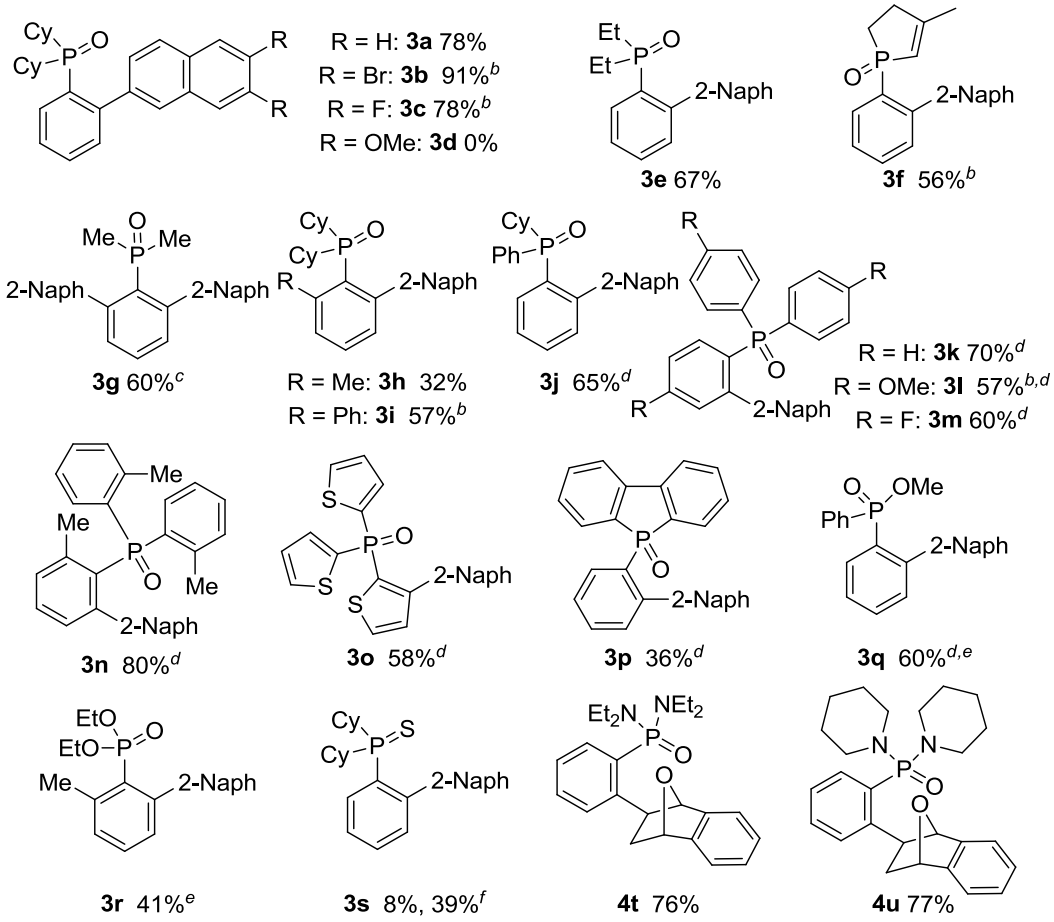
entry	Rh-catalyst (mol %)	**2a** (equiv)	additive (mol %)	yield (%)[b]
1	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	1.0	AgOAc (20)	60
2	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	1.0	$Cu(OAc)_2 \cdot H_2O$ (20)	trace
3	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	1.0	Ag_2CO_3 (10)	trace
4	$[Cp^*RhCl_2]_2$ (2)	1.0	AgOAc (20)	0
5	$[Cp^*RhCl_2]_2$ (2)	1.0	AgOAc (20) $AgSbF_6$ (8)	38
6	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	1.5	AgOAc (20)	69
7	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	1.5	AcOH (300)	68
8	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	1.5	PivOH (300)	67
9[c]	$[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4)	1.2	AgOAc (20)	80 (78)

[a] Reaction conditions: **1a** (0.25 mmol) in DCE (2 mL) under N_2 for 12 h.
[b] GC yield. Yield after purification is given in parentheses. [c] At 130 °C.

With the optimized conditions in hand (entry 9 in Table 4.1), the author investigated the substrate scope of this reaction (Table 4.2). Halogen-substituted alkenes **2b** and **2c** smoothly coupled with **1a** to give **3b** and **3c** in good yields. In these cases, as well as in some other reactions described below, mixtures of naphthylated **3** and oxabicycle-retained **4** were formed. Therefore, the crude products were treated with trimethylsilyl chloride/NaI in MeCN to convert partially formed **4** to **3**. In contrast, methoxy-substituted **2d** underwent the fast ring-opening isomerization to fail to form expected **3d** in any amount. While diethylphenylphosphine oxide (**1e**) and 2,3-dihydro-4-methyl-1-phenyl-1*H*-phosphole oxide (**1f**) reacted with **2a** in a similar manner to give **3e** and **3f**, the sterically less hindered dimethylphenylphosphine oxide (**1g**) underwent

Table 4.2. Reaction of Arylphosphine Derivatives 1 with 1,4-Epoxydihydronaphthalene 2a



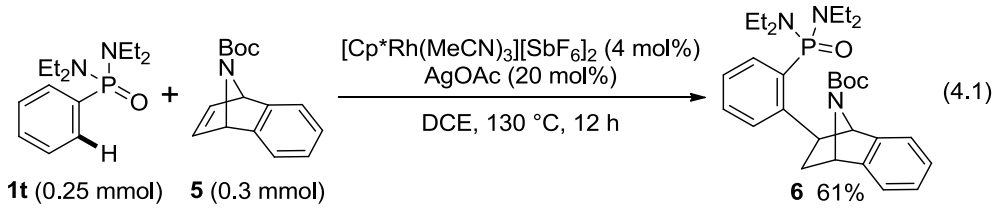


[a] Reaction conditions: **1** (0.25 mmol), **2** (0.3 mmol), $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (0.01 mmol), AgOAc (0.05 mmol), in DCE (2 mL) at 130 °C under N_2 for 12 h. Isolated yields are shown. [b] The resulting crude mixture was treated with TMSCl (0.5 mmol) and NaI (0.5 mmol) in MeCN (3 mL) at 80 °C for 12 h. [c] **2** (0.6 mmol) was used. [d] **1** (0.5 mmol) and **2** (0.25 mmol) were used. [e] AgOAc (0.5 mmol) was used. [f] AcOH (0.75 mmol) was used in place of AgOAc.

1:2 coupling under conditions with 2.4 equiv of **2a** to produce **3g** in 60% yield. The reactions of *ortho*-methyl- and *ortho*-phenyl-substituted dicyclohexylphenylphophine oxides **1h** and **1i** were somewhat sluggish, probably due to steric reasons. In the latter case, 6-arylated product **3i** was exclusively obtained, no 2'-arylation being observed. It

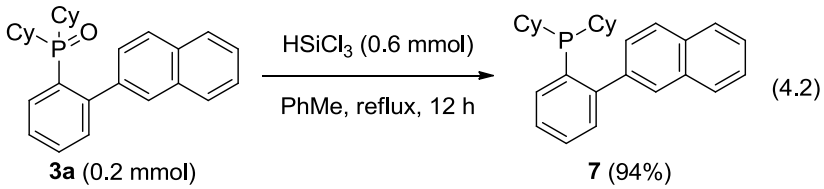
should be noted that the direct arylation of the same substrate **1i** is known to take place at the 2'-position under palladium catalysis.[6m] The reactions of di- and triarylphosphine oxides with **2a** were carried out using them in a 2:1 ratio to suppress the formation of multi-arylated products. Thus, cyclohexyldiphenylphosphine oxide (**1j**), *para*- (**1k-m**) and *ortho*- (**1n**) substituted triphenylphosphine oxides, and tris(2-thienyl)phosphine oxide (**1o**) underwent the monoarylation to afford the corresponding products **3j-o** selectively. The arylation of 5-phenyl-5*H*-dibenzophosphole oxide (**1p**) occurred not on the dibenzophosphole ring but on the phenyl moiety, probably because of favorable geometry of the phenyl C–H bond toward the metal center. In addition to phosphine oxides, methyl diphenylphosphinate (**1q**) and diethyl *o*-tolylphosphonate (**1r**) also underwent the arylation. However, these substrates were less reactive and required the addition of a stoichiometric amount of AgOAc. Dicyclohexylphenylphosphine sulfide (**1s**) coupled with **2a** under the standard conditions to give the arylated product **3s** in only 8% yield. The use of 3 equiv of AcOH in place of AgOAc improved the yield of **3s** to 39%. The silver salt additive seems to be not suitable for the reaction because of its strong thiophilicity.[5c] Interestingly, the reactions of phenylphosphonamides **1t** and **1u** with **2a** gave the bicyclic scaffold-retained products **4t** and **4u** selectively in good yields.

Phenylphosphonamide **1t** also reacted with *N*-Boc-bridged alkene **5** to produce the azabicycle-retained compound **6** in 61% yield (eq 4.1).



(4.1)

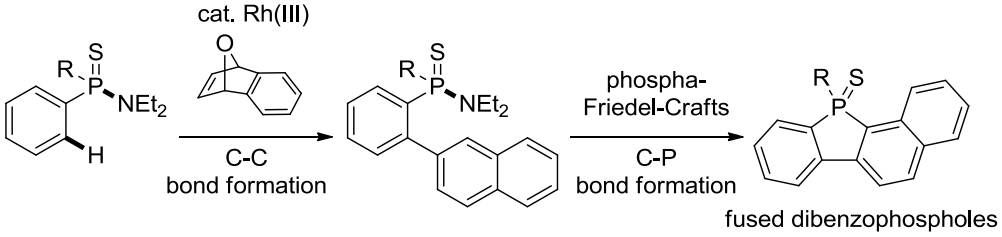
Next, the author examined the reduction of product **3a** to deliver the corresponding biarylphosphine. Thus, **3a** was treated with $HSiCl_3$ in refluxing toluene to afford the Buchwald-type dialkylbiarylphosphine **7** (eq 4.2). This sequence is effective for the synthesis of biarylphoshine derivatives from simple arylphosphine oxides.



3a (0.2 mmol) **7** (94%) (4.2)

To demonstrate further utility of this Rh catalysis, the author next attempted to combine the present arylation of **3** with a phospha-Friedel-Crafts (PFC) type cyclization to produce dibenzophosphole derivatives. It is worth noting that benzo-fused phospholes have recently attracted much attention in the field of organic materials because of their unique optoelectronic properties, and the straightforward synthesis of these molecules has become an important challenge.[11,12] It is known that phosphinothioic amides undergo Friedel-Crafts type P-arylation with simple arenes in the presence of an appropriate Lewis acid.[13] Therefore, the author envisaged that if phenylphosphinothioic amides couple with **2** to form *ortho*-naphthylated products, they may undergo the Friedel-Crafts type cyclization (Scheme 4.10).

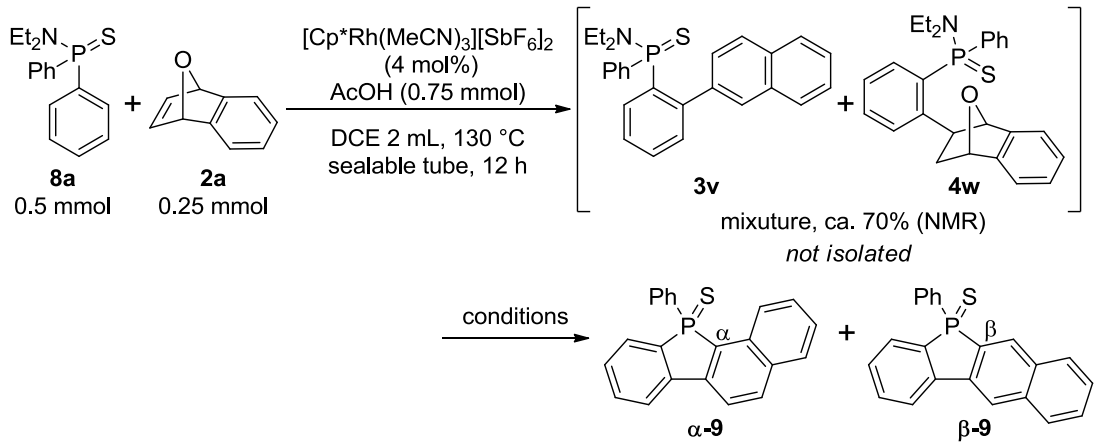
Scheme 4.10. Synthetic Application: Phospha-Friedel-Crafts Reaction



To establish PFC cyclization conditions, the optimization studies were carried out (Table 4.3). Treatment of *N*,*N*-diethyldiphenylphosphinothionic amide (**8a**) (0.5 mmol) with alkene **2a** (0.25 mmol) under the conditions used for the reaction of phosphine

sulfide **3s** in Table 4.2 gave a mixture of **3v** and **4w** in ca.70% total yield. To simplify the experimental procedure, the crude mixture was used for the next step without purification. When this crude mixture was treated with 10 equiv. of $AlCl_3$ in *ortho*-dichlorobenzene at 150 °C for 24 h, the PFC reaction proceeded to afford a mixture of **α-9** and **β-9** in 63% combined yield (entry 2). Further screening showed Brønsted acids promoted the regioselective cyclization at relatively mild temperature. The reaction with an excess amount of *p*-TsOH at 100 °C gave **α-9** in 30% yield selectively (entry 5). The structure of **α-9** was confirmed by X-ray crystal structure

Table 4.3. Optimization Studies for Phospha-Friedel-Crafts Reaction

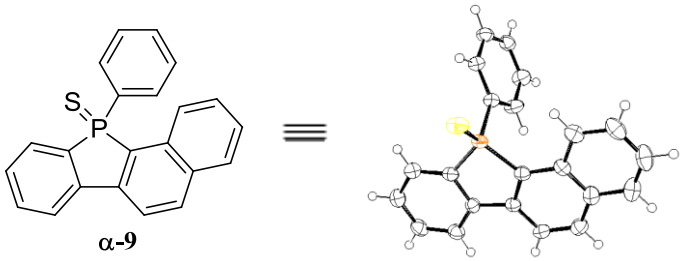


entry	conditions	^{1}H NMR yield[a]	product (α/β)
1	w*orkup, then* $AlCl_3$ (2 mmol), toluene, 100 °C, 14 h	No Reaction	-
2	w*orkup, then* $AlCl_3$ (2.5 mmol), *o*-DCB, 150 °C, 24 h	76% (63%)	α/β (3:1)
3	w*orkup, then* $AlCl_3$ (2.5 mmol), $PhCF_3$, 150 °C, 24 h	No Reaction	-
4	w*orkup, then* TMSCl (2 mmol), NaI (2 mmol), MeCN, 80 °C, 12 h	complex mixture	-
5	w*orkup, then p*-TsOH (2.5 mmol), toluene, 100 °C, 12 h	- (30%)	α
6	w*orkup, then p*-TsOH (1.25 mmol), *o*-DCB, 130 °C, 24 h	41%	α
7	w*orkup, then* TfOH (0.5 mL), DCE, 80 °C, 12 h	45%	α
8	w*orkup, then* TfOH (0.5 mL), $MeNO_2$, 80 °C, 12 h	decomposition	-
9	w*orkup, then* $AlCl_3$ (2.5 mmol), TfOH (0.5 mL), DCE, 80 °C, 12 h	46%	α
10	w*orkup, then* HCl in dioxane (2.0 mL), 80 °C, 12 h	0%	-
11	o*ne pot,* TfOH (0.5 mL), 80 °C, 12 h	56% (57%)	α
12	o*ne pot,* TfOH (0.5 mL), 60 °C, 12 h	40%	α
13	***one pot, TfOH (0.5 mL), 100 °C, 12 h***	***55%[b]***	*α*

[a] Yield of product was determined by ^{1}H NMR using CH_2Br_2 as an internal standard. Isolated yield are shown in parentheses. [b] Corresponding phosphole oxide **10a** (11%) was also formed.

analysis (Figure 4.2). Finally, it was disclosed that simple one-pot conditions using TfOH gave the best result (entry 13). After the rhodium-catalyzed coupling reaction, an excess amount of TfOH was added to the resultant solution and heated at 100 °C for 12 h, resulting in the formation of **α-9** in 55% NMR yield. In this case, a minor amount of the corresponding phosphole oxide **10a** was formed, therefore, this mixture was additionally treated with mCPBA for oxygenation on the phosphorus atom of **α-9** to provide 11-phenyldibenzo[*b*,*g*]phosphindole 11-oxide (**10a**) in 62% yield (Table 4.4)

Figure 4.2. X-ray analysis of α-9



α-9

The same one-pot procedure could be applied to the reactions using a number of phosphinothioic amides and alkenes to produce a series of dibenzophosphole oxides **10b-f** (Table 4.4). A related diphenylphosphinamide (**1x**) also underwent the phaspha-Friedel-Crafts reaction, albeit with a poor yield (eq 4.3). In all cases, the C-P bond formation proceeded at α-position of the naphthalene exclusively. In the recently reported naphthalene-fused benzophosphole synthesis by means of the Pd-catalyzed direct coupling,[2a,b] the α/β-selectivity has been found to be sterically controlled in favor of the β-isomer. Thus, this new methodology is complimentary to the previous report.

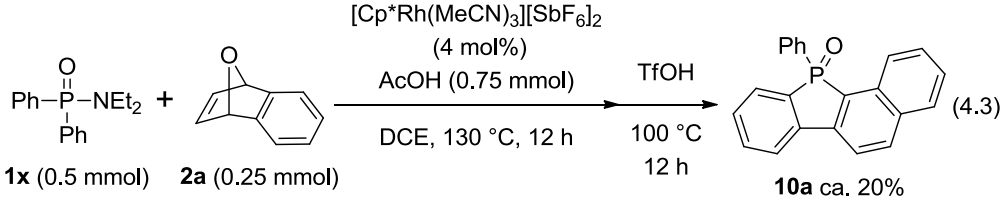
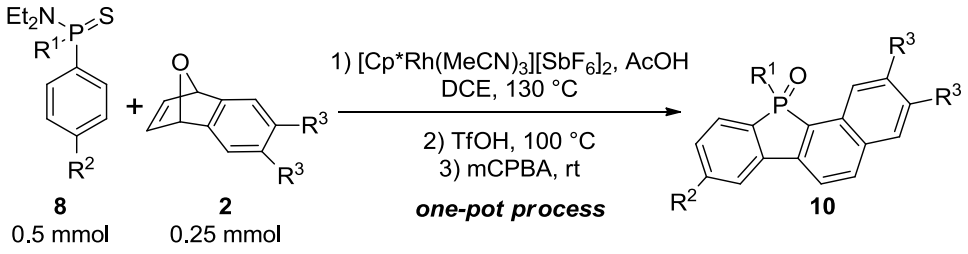
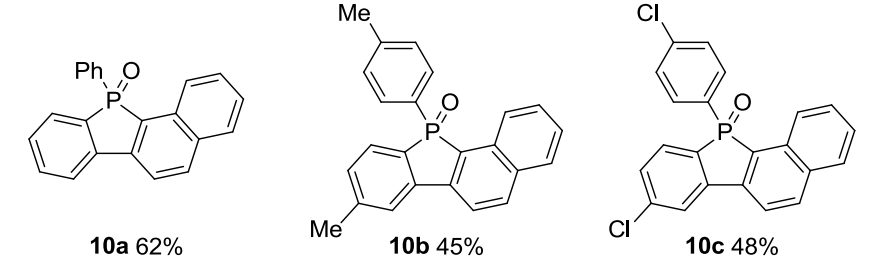


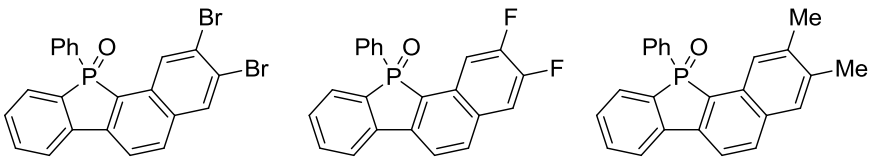
Table 4.4. One-pot Synthesis of Dibenzophophole oxides 9 by Rh(III)-catalyzed Direct Naphthylation-Intramoleculer Phospha-Friedel-Crafts Reaction of Arylphosphinothioic Amide 8[a]



8 0.5 mmol **2** 0.25 mmol **10**



10a 62% **10b** 45% **10c** 48%

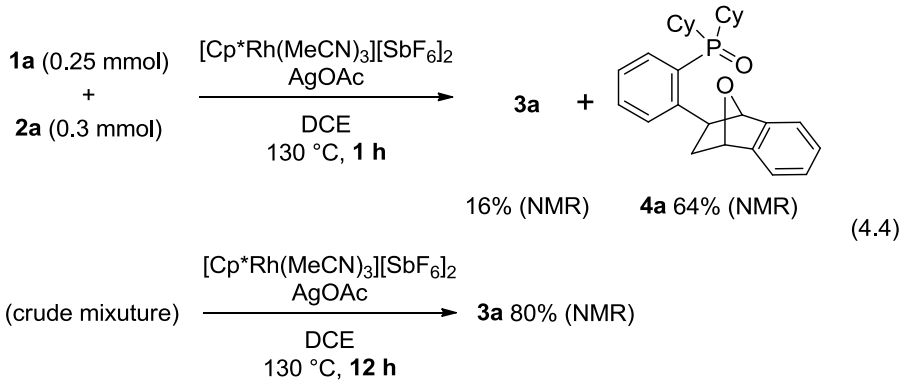


10d 64% **10e** 65% **10f** 59%

[a] Reaction conditions: 1) **8** (0.5 mmol), **2** (0.25 mmol), $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (0.01 mmol), AcOH (0.75 mmol), in DCE (2 mL) at 130 °C under N_2 for 12 h; 2) TfOH (0.5 mL) at 100 °C under N_2 for 12 h; 3) mCPBA, rt. Isolated yields are shown.

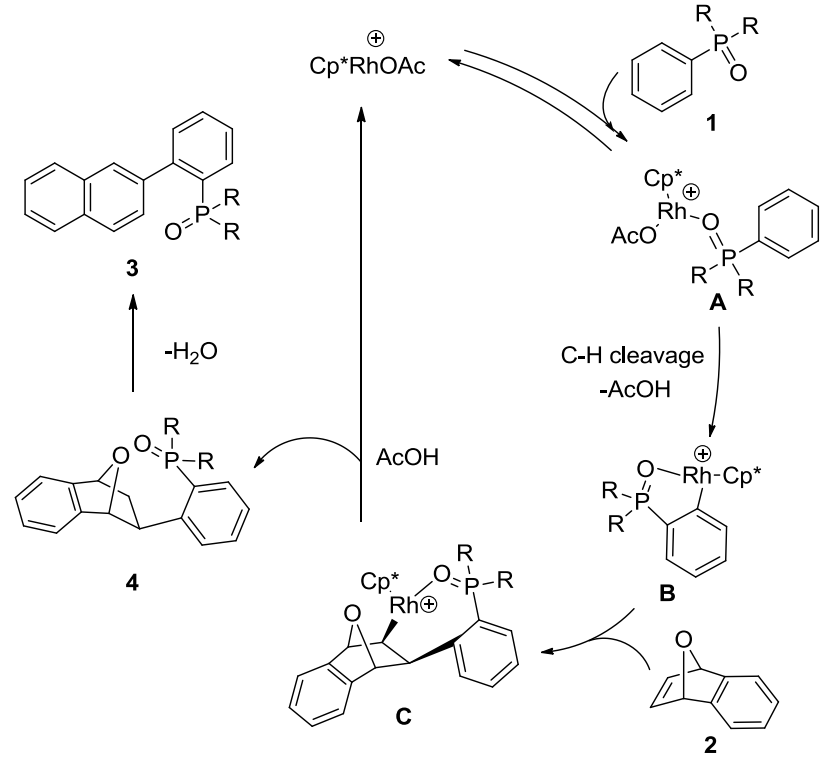
To obtain mechanistic insight, additional experiments were performed. At an early stage (1 h) of the reaction of **1a** with **2a** under standard conditions, a significant amount of **4a** (64%) was formed together with **3a** (16%) (eq 4.4). Further treatment of the mixture led to the complete disappearance of once formed **4a** and selective formation of **3a**. Thus, **4a** is considered to be the initial principal product. A plausible mechanism for the formation of **4** from phenylphosphine oxide **1** with oxabicyclic alkene **2** is illustrated in Scheme 4.11. Coordination of the P=O directing group of **1** to the metal center of catalyst forms a cationic Rh(III) intermediate **A**, and C-H bond cleavage at the *ortho*-position of **A** takes place to yield a five-membered rhodacycle intermediate **B**.

Then, the alkene insertion and subsequent protonolysis of a resulting intermediate **C** may occur to produce the oxabicycle-retained product **4**. Further heating may induce the dehydrative aromatization to afford the biarylphosphine oxide **3**. *β*-Oxygen elimination in the intermediate **C** leading to the ring-opening product (Scheme 4.8) could occur, but, only to a minor extent.[10a]

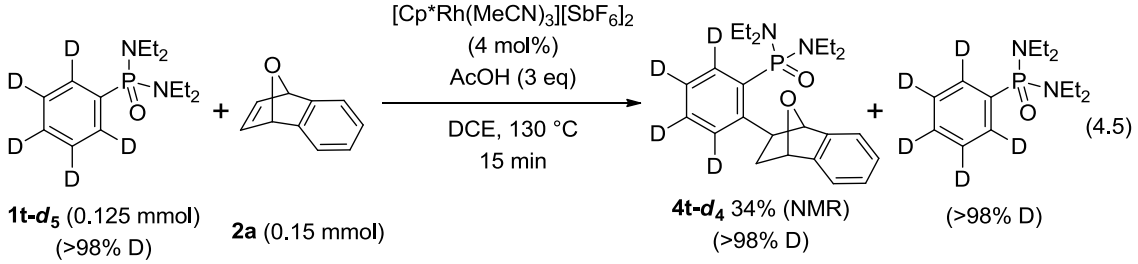


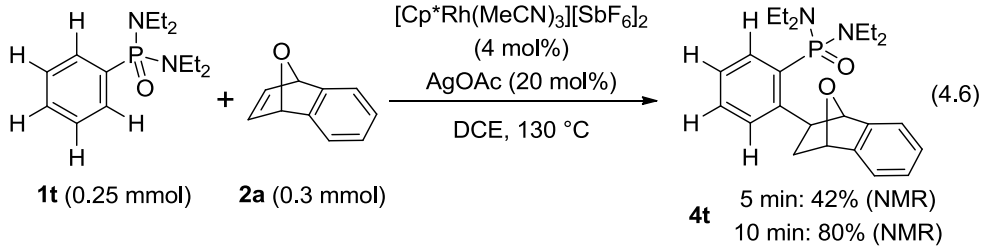
(4.4)

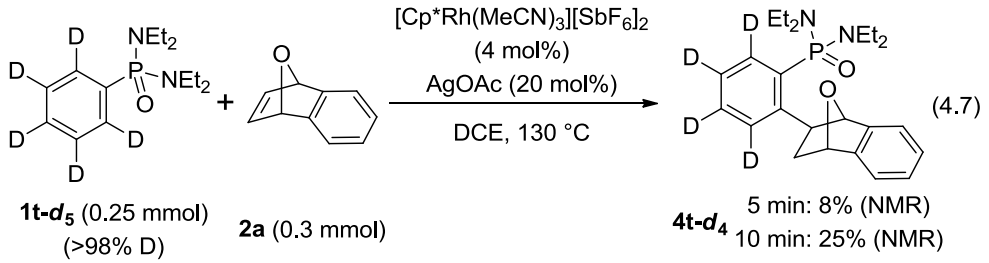
Scheme 4.11. Plausible Reaction Mechanism

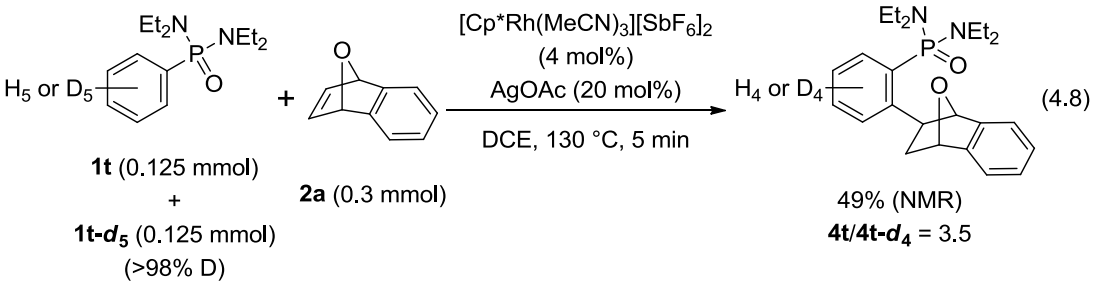


Next, some deuterium labeling studies were also conducted. As shown in eq 4.4, the reaction of **1a** with **2a** gave a mixture of **3a** and **4a** at an early stage (15 min). Therefore, the author chose **1t** as a model substrate for simplification, because the reaction of **1t** with **2a** gave only **4t** (Table 4.2). When **1t-*d*$_5$** was treated in the presence of 3 equiv of acetic acid for 15 min, no D/H scrambling was observed in recovered **1t-*d*$_5$** as well as formed **4t-*d*$_4$** (eq 4.5). Furthermore, significant kinetic isotope effects (KIE) were observed in parallel and competitive reactions of **1t** and **1t-*d*$_5$** (eqs 4.6/7 and 4.8). These results suggest the C–H bond cleavage step is most likely irreversible and rate-limiting.

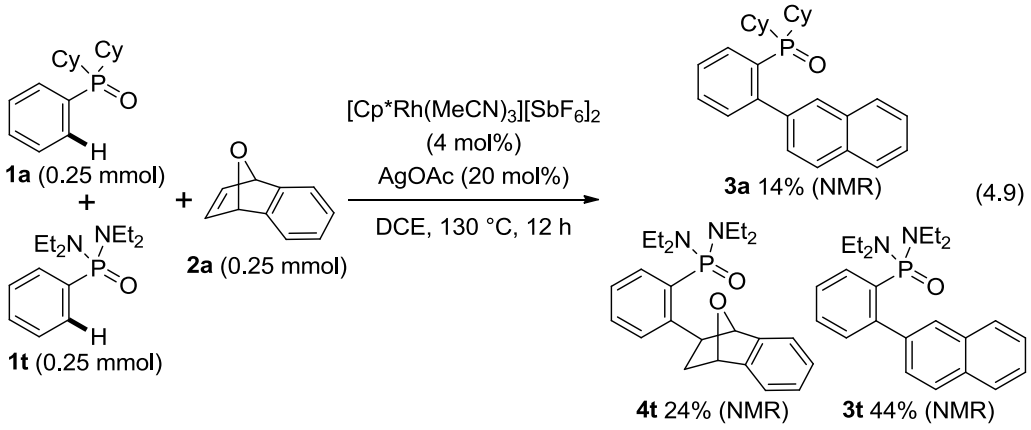




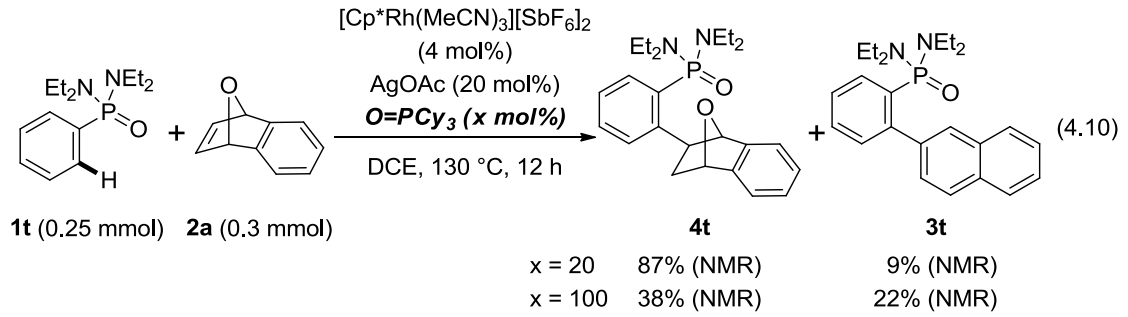




In addition, the author investigated relative reactivity between phosphine oxide **1a** and phosphinamide **1t** (eq 4.9). In a competitive experiment with **2a**, **1t** reacted more smoothly than **1a**. Furthermore, a significant amount of aromatized **3t** was also formed, in contrast to the independent reaction in which only a trace amount of **3t** was observed as described above.



Based on the result of eq 4.9, the author examined the effect of a phosphine oxide additive. When 20 mol% of $O{=}PCy_3$ was added to the reaction of **1t** with **2a** under standard conditions, **4t** and **3t** were formed in 87% and 9% yields, respectively (eq 10). Increasing the amount of $O{=}PCy_3$ to 1 equiv enhanced the yield of **3t** to 22%, while the total yield of **3t** and **4t** was somewhat lower. Although the exact role of the added phosphine oxide is unclear at this stage, these results indicate that a phosphine oxide can promote the dehydrative aromatization of **4t**.



(4.10)

Summary

In Chapter 4, the author has demonstrated the rhodium-catalyzed redox-neutral direct *ortho*-arylation of arylphosphine derivatives with heterobicyclic alkenes. A number of biaryl phosphine derivatives could be obtained from simple aryl phosphine oxides. Furthermore, the combination of rhodium-catalyzed *ortho*-arylation and acid-mediated intramolecular phospha-Friedel-Crafts reaction enables the concise synthesis of dibenzophosphole derivatives from readily available diarylphosphinothionic amides in a one-pot manner.

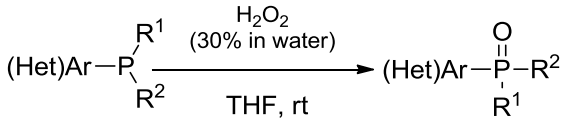
Experimental Section

General. ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded at 400, 100, 376 and 162 MHz for $CDCl_3$ solutions. HRMS data were obtained by APCI using a TOF mass spectrometer, unless noted. GC analysis was carried out using a silicon OV-17 column (i. d. 2.6 mm x 1.5 m). GC-MS analysis was carried out using a CBP-1 capillary column (i. d. 0.25 mm x 25 m). The structures of all products listed below were unambiguously determined by ^{1}H and ^{13}C NMR with the aid of NOE, COSY, HSQC, and HMBC experiments and X-ray crystal structure analysis.

Arylphosphine oxides **1** were prepared by oxidation of the corresponding commercially available phosphines with H_2O_2 as described below. Diarylthiophosphinamides **8b** and **8c** were prepared from Cl_2PNEt_2 as described below. Dibenzophosphole oxide **1p**,[2b] methyl diphenylphosphinate **1q**,[14] phosphine sulfide **1s**,[15] phosphinamide **1t** and **1u**,[16] oxabicyclic alkene **2b**-**2d**,[17] azabicyclic alkene **5**,[18] and diphenylthiophosphinamide **8a**[19] were prepared according to published procedures. DCE was freshly distillated from CaH_2 before use. Other starting materials were commercially available

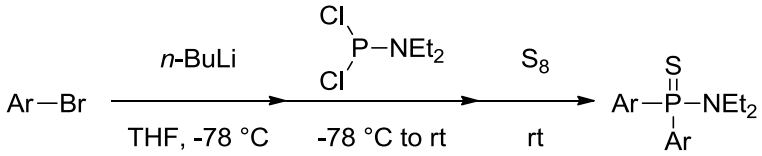
and used as received. The following experimental procedures may be regarded as typical in methodology and scale.

Preparation of Arylphosphine Oxides 1



To a solution of an arylphosphine in THF (4~5 M), H_2O_2 (30% in water, 3~5 eq) was dropped slowly and stirred at room temperature. The exothermic reaction terminated within a few minutes. The resulting mixture was continued to stir for 15 minutes. After checking the complete conversion of the phosphine by TLC, the reaction mixture was quenched by sat. $NaHCO_3$ solution and sat. $Na_2S_2O_3$ solution and stirred for a few minutes additionally. The reaction mixture was separated, and the water layer was extracted with DCM. The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. The corresponding phosphine oxide was obtained quantitatively and used without further purification.

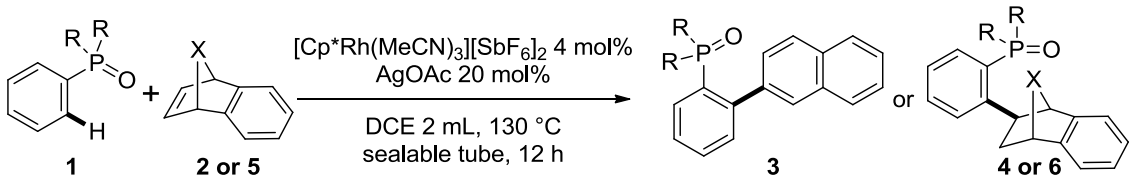
Preparation of Diarylthiophoshinamides 8



To a solution of an aryl bromide (10 mmol) in dry THF (20 mL) at -78 °C under N_2 atmosphere, *n*-BuLi (1.55 M in hexane, 10 mmol, 6.45 mL) was slowly added. The reaction mixture was stirred for 30 min at this temperature. To the resulting mixture, Cl_2PNEt_2 (5 mmol, 870 mg) in THF (5 mL) was then added by a syringe. Then, the reaction mixture was slowly warmed to rt with an additional 3 h stirring. To this mixture, S_8 (7.5 mmol, 240 mg) was added and stirred for overnight. The resulting solution was quenched with water, extracted with ethyl acetate, and the organic layer was dried over Na_2SO_4 and concentrated in vacuo. The crude mixture was purified by column chromatography on silica gel with hexane/ethyl acetate to afford product. Further purification was performed by recrystallization if necessary.

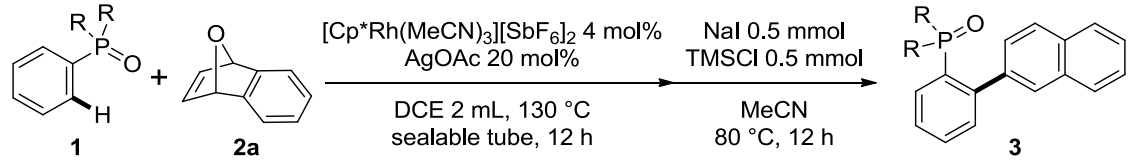
General Procedures for Rh(III)-Catalyzed Coupling of Phosphine Derivatives with Heterobicyclic Alkenes.

Condition A



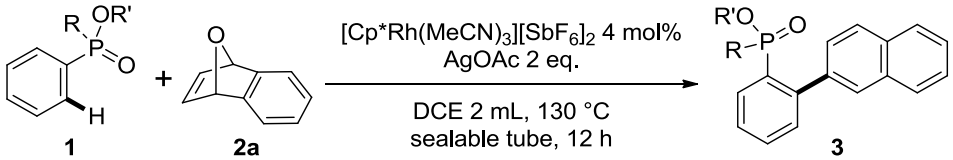
In a 10 mL sealable tube, the indicated amounts of **1** and **2** or **5** in Table 2, $[Cp^*Rh(MeCN)_3(SbF_6)_2]$ (8.3 mg, 0.01 mmol), and AgOAc (8.4 mg, 0.05 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, DCE (2 mL) was added by a syringe. The reaction mixture was heated at 130 °C in an oil bath for 12 h. After cooling, the reaction was quenched with 10 mL of water and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. Purification of the residue by column chromatography on silica gel gave product.

Condition B



In a 10 mL sealable tube, the indicated amounts of **1** and **2a** in Table 2, $[Cp^*Rh(MeCN)_3(SbF_6)_2]$ (8.3 mg, 0.01 mmol), and AgOAc (8.4 mg, 0.05 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, DCE (2 mL) was added by a syringe. The reaction mixture was heated at 130 °C in an oil bath for 12 h. After cooling, the reaction was quenched with 10 mL of water and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. The resulting mixture and NaI (74.9 mg, 0.5 mmol) were placed in a flask with a magnetic stir bar. To this, MeCN (3 mL) and TMSCl (54.3 mg, 0.5 mmol) were added by a syringe. The reaction mixture was stirred at 80 °C under N_2 atmosphere for overnight. After cooling, the reaction was quenched with sat. $NaHCO_3$ and sat. $Na_2S_2O_3$ and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. The crude mixture was purified by column chromatography on silica gel to give product.

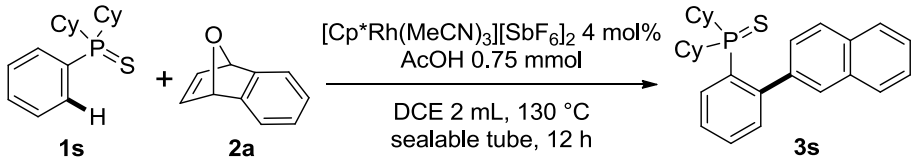
Condition C



In a 10 mL sealable tube, the indicated amounts of **1** and **2a** in Table 1, $[Cp^*Rh(MeCN)_3(SbF_6)_2]$

(8.3 mg, 0.01 mmol), and AgOAc (83.5 mg, 0.5 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, DCE (2 mL) was added by a syringe. The reaction mixture was heated at 130 °C in an oil bath for 12 h. After cooling, the reaction was quenched with 10 mL of water and diluted with 10 mL DCM. Then, insoluble solids were filtered off through a short pad of Celite. The resulting mixture was extracted three times with DCM (20 mL x 3) and the combined organic layer was dried over Na_2SO_4. Volatiles were removed in vacuo and subsequent purification by column chromatography on silica gel gave product.

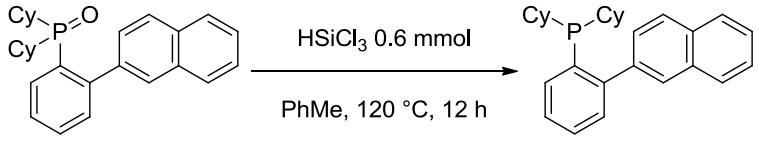
Condition D



1s **2a** **3s**

In a 10 mL sealable tube, **1s** (0.25 mmol), **2a** (0.3 mmol), and $[Cp^*Rh(MeCN)_3(SbF_6)_2]$ (8.3 mg, 0.01 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, DCE (2 mL) and AcOH (43 μl, 0.75 mmol) were added by a syringe. The reaction mixture was heated at 130 °C in an oil bath for 12 h. After cooling, the reaction was quenched with 10 mL of water and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. Purification of the residue by column chromatography on silica gel gave product.

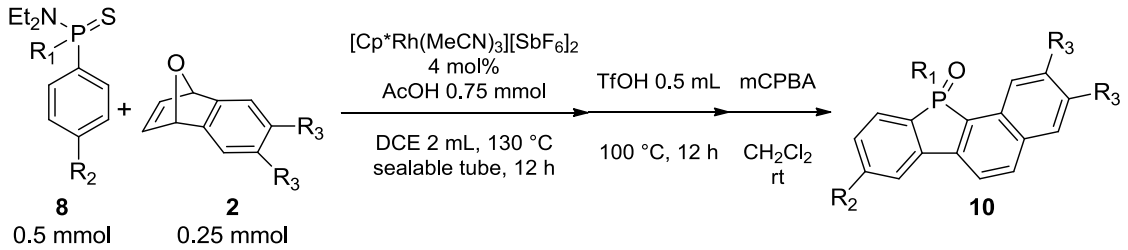
Reduction of 3a (eq 4.2)



3a (0.2 mmol) **7**

In a 10 mL sealable tube, **3a** (83.2 mg, 0.2 mmol) was placed with a magnetic stir bar under N_2 atmosphere. Then, toluene 1 mL and $HSiCl_3$ (61 μL, 0.6 mmol) were added by a syringe. The reaction mixture was heated at 120 °C in an oil bath for 12 h. After cooling, 1 mL of 10% aq. NaOH was added and stirred for 5 min. The resulting mixture was diluted with water and extracted three times with ethyl acetate (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. Purification of the residue by column chromatography on silica gel using hexane/ethyl acetate (10:1, v/v) gave product **7** (75.6 mg, 94%)

Synthesis of Dibenzo[*b*]phosphole Derivatives by One-Pot Rh-Catalyzed Coupling and Phospha-Friedel-Crafts Reactions.

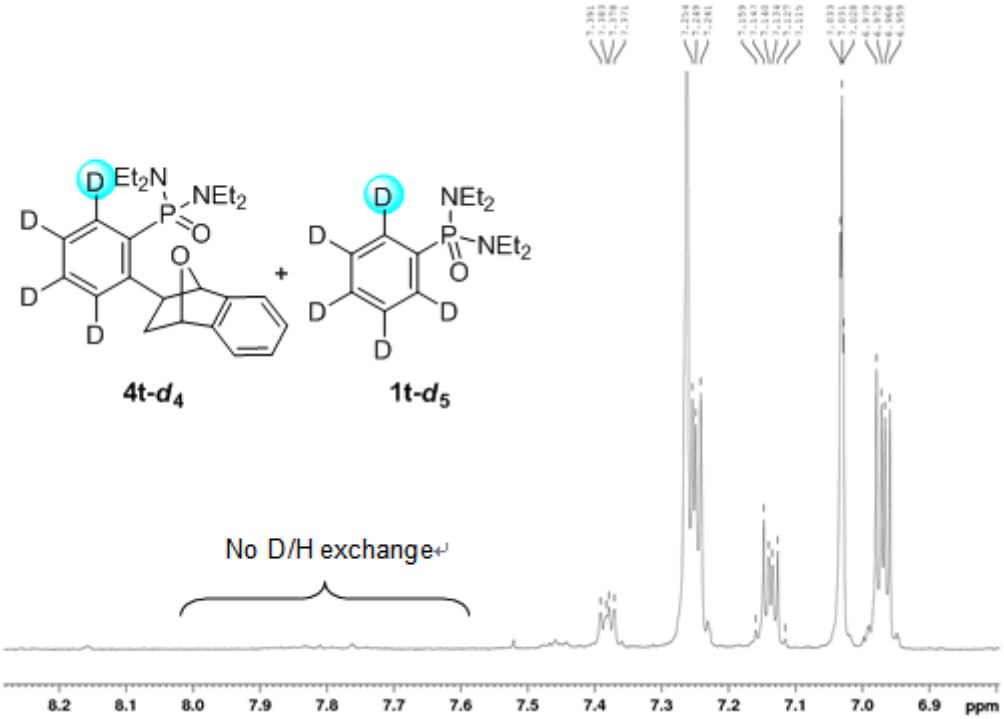


In a 10 mL sealable tube, **8** (0.5 mmol), **2** (0.25 mmol), and $[Cp^*Rh(MeCN)_3(SbF_6)_2]$ (8.3 mg, 0.01 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, DCE (2 mL) and AcOH (43 μl, 0.75 mmol) were added by a syringe. The reaction mixture was heated at 130 °C in an oil bath for 12 h. After cooling, TfOH (0.5 mL) was added by a syringe. The resulting mixture was heated up again to 100 °C for 12 h. After cooling, the reaction mixture was poured into sat. $NaHCO_3$ aq, and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed under reduced pressure. The obtained mixture was dissolved in DCM (5 mL) again, and mCPBA (~70 wt%, 130 mg, ~0.5 mmol) was slowly added and stirred for a few minutes. After checking the full conversion of phosphole sulfide **9** on TLC, the reaction was quenched by sat. $NaHCO_3$ and sat. $Na_2S_2O_3$. Subsequently the crude material was extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed under reduced pressure. The desired product was obtained after purification by column chromatography on silica gel.

Deuterium Labeling Studies.

D/H exchange (eq 4.5 in the text):

In a 10 mL sealable tube, **1t-*d*$_5$** (34.2 mg, 0.125 mmol), **2a** (21.7 mg, 0.15 mmol), and $[Cp^*Rh(MeCN)_3(SbF_6)_2]$ (4.2 mg, 0.005 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, DCE (2 mL) and AcOH (21 μl, 0.375 mmol) were added by a syringe. The reaction mixture was heated at 130 °C in an oil bath for 15 min. After cooling, the reaction was quenched with 10 mL of water and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. The obtained crude mixture was analyzed by ^1H NMR in $CDCl_3$ using CH_2Br_2 as an internal standard.

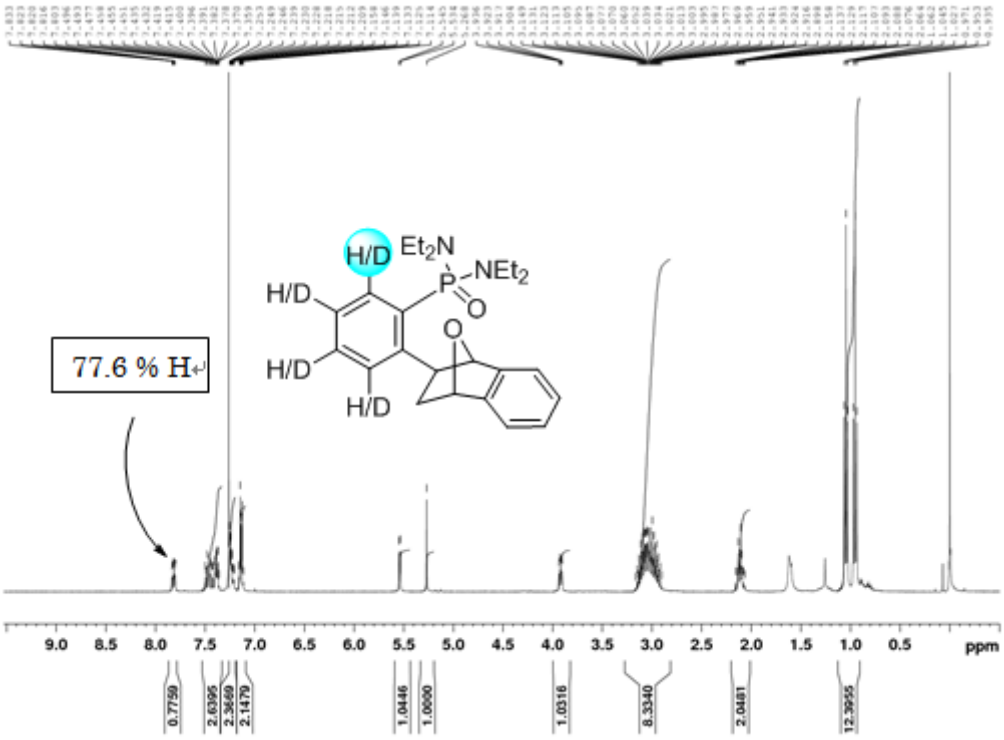


KIE Measurement (parallel) (eqs 4.6 and 4.7 in the text):

Under condition A, **1t** and **1t-*d*$_5$** were independently treated with **2a**. The yield of **4t** was traced by crude ^{1}H NMR using CH_2Br_2 as an internal standard.

KIE Measurement (competitive) (eq 4.8 in the text):

In a 10 mL sealable tube, **1t** (33.5 mg, 0.125 mmol), **1t-*d*$_5$** (34.2 mg, 0.125 mmol), **2a** (43.3 mg, 0.3 mmol), [Cp*Rh(MeCN)$_3$(SbF$_6$)$_2$] (8.3 mg, 0.01 mmol), and AgOAc (8.4 mg, 0.05 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, DCE (2 mL) was added by a syringe. The reaction mixture was heated at 130 °C in an oil bath for 5 min. After cooling, the reaction was quenched with 10 mL of water and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. Purification of the residue by column chromatography on silica gel gave mixture of **4t** and **4t-*d*$_4$**. The ratio of **4t** and **4t-*d*$_4$** were determined by ^{1}H NMR. Thus, **4t**:**4t-*d*$_4$** = 77.6:22.4 and k_H / k_D = 3.5.



Characterization Data of Products

Dicyclohexyl(2-(naphthalen-2-yl)phenyl)phosphine oxide (3a): Condition A, colorless solid, mp 190-192 °C, 80.9 mg (78%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87-1.80 (m, 22H), 7.26-7.29 (m, 1H), 7.37 (dd, J = 8.4, 1.7 Hz, 1H), 7.51-7.59 (m, 4H), 7.67 (s, 1H), 7.82-7.84 (m, 1H), 7.90 (d, J = 8.5 Hz, 1H), 7.91-7.94 (m, 1H), 8.13-8.18 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.7, 26.352 (d, J = 16.6 Hz), 26.371 (d, J = 16.6 Hz), 26.393 (d, J = 12.2 Hz), 26.525 (d, J = 14.2 Hz), 38.3 (d, J = 65.6 Hz), 126.4, 126.8, 127.32, 127.37 (d, J = 9.5 Hz), 127.38, 127.6, 127.86, 127.91, 130.47 (d, J = 2.6 Hz), 130.51 (d, J = 79.5 Hz), 131.2 (d, J = 9.5 Hz), 132.5, 132.6, 134.0 (d, J = 6.3 Hz), 139.5, 143.7 (d, J = 8.8 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 48.0; HRMS m/z (M+H^{+}) Calcd for $C_{28}H_{34}OP$: 417.2342. Found 417.2343.

Dicyclohexyl(2-(6,7-dibromonaphthalen-2-yl)phenyl)phosphine oxide (3b): Condition B, pale brown solid, mp 154-156 °C, 130.5 mg (91%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.94-1.92 (m, 22H), 7.24-7.30 (m, 1H), 7.44 (dd, J = 8.4, 1.7 Hz, 1H), 7.50-7.57 (m, 2H), 7.57 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.91-7.99 (m, 1H), 8.12 (s, 1H), 8.21 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.6, 25.9 (d, J = 3.5 Hz), 26.2 (d, J = 3.0 Hz), 26.4 (d, J = 12.2 Hz), 26.6 (d, J = 12.8 Hz), 37.9 (d, J = 65.8 Hz), 122.4, 122.8, 125.8, 126.5, 127.5 (d, J = 10.0 Hz), 129.2, 129.7 (d, J = 79.3 Hz), 130.6 (d, J = 2.3 Hz), 131.6 (d, J = 9.1 Hz), 132.1, 132.2 (3C), 133.1 (d, J = 7.4 Hz), 141.0 (d, J = 2.3 Hz), 144.4 (d, J = 7.3 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 47.6; HRMS m/z (M+H^{+}) Calcd for $C_{28}H_{32}Br_2OP$: 573.0552.

Found 573.0553.

Dicyclohexyl(2-(6,7-difluoronaphthalen-2-yl)phenyl)phosphine oxide (3c): Condition B, pale brown solid, mp 184-186 °C, 107.8 mg (95%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.94-2.08 (m, 22H), 7.25-7.30 (m, 1H), 7.39 (d, J = 8.4 Hz, 1H), 7.51-7.58 (m, 3H), 7.61 (s, 1H), 7.64 (dd, J = 10.8, 8.0 Hz, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.96-8.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.6, 26.0 (d, J = 3.6 Hz), 26.3 (d, J = 2.9 Hz), 26.4 (d, J = 12.4 Hz), 26.6 (d, J = 12.9 Hz), 38.0 (d, J = 65.9 Hz), 113.5 (d, J = 4.3 Hz), 113.7 (d, J = 4.5 Hz), 126.3 (d, J = 3.5 Hz), 126.9 (d, J = 3.5 Hz), 127.5 (d, J = 9.9 Hz), 127.9 (d, J = 2.1 Hz), 129.27, 129.35. 129.9 (d, J = 79.5 Hz), 130.6 (d, J = 2.2 Hz), 131.5 (d, J = 9.3 Hz), 133.3 (d, J = 7.1 Hz), 140.0, 144.2 (d, J = 7.9 Hz), 150.3 (dd, J = 247.1, 13.3 Hz), 150.5 (dd, J = 255.9, 22.3 Hz); ^{19}F{^{1}H} NMR (376 MHz): δ -136.3 (d, J = 20.5 Hz), -136.0 (d, J = 20.5 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 47.9; HRMS m/z (M+H$^+$) Calcd for $C_{28}H_{32}F_2OP$: 453.2153. Found 453.2150.

Diethyl(2-(naphthalen-2-yl)phenyl)phosphine oxide (3e): Condition A, colorless solid, mp 104-105 °C, 52.0 mg (67%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.00 (dt, J = 17.1, 7.6 Hz, 6H), 1.40 (ddt, J = 24.0, 7.8, 7.8 Hz, 2H), 1.60 (ddt, J = 28.2, 7.6, 7.6 Hz, 2H), 7.30-7.33 (m, 1H), 7.42 (dd, J = 8.4, 1.8 Hz, 1H), 7.54-7.59 (m, 4H), 7.74 (s, 1H), 7.83-7.93 (m, 3H), 8.21-8.29 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.7 (d, J = 5.2 Hz), 22.9 (d, J = 68.6 Hz), 126.6, 126.9, 127.2, 127.5 (d, J = 9.9 Hz), 127.7, 127.87, 127.95 128.0, 129.9 (d, J = 85.7 Hz), 131.1 (d, J = 2.6 Hz), 131.2 (d, J = 9.9 Hz), 132.5, 132.7, 134.3 (d, J = 6.5 Hz), 138.9, 144.2 (d, J = 9.9 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 45.1; HRMS m/z (M+H$^+$) Calcd for $C_{20}H_{22}OP$: 309.1403. Found 309.1398.

4-Methyl-1-(2-(naphthalen-2-yl)phenyl)-2,3-dihydro-1*H*-phosphole 1-oxide (3f): Condition B, pale brown solid, mp 161-163 °C, 44.8 mg (56%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.48-2.00 (m, 6H), 2.25-2.37 (m, 1H), 5.76 (dd, J = 24.9, 1.3 Hz, 1H), 7.36-7.42 (m, 1H), 7.50-7.60 (m, 5H), 7.84-7.91 (m, 4H), 8.16 (ddd, J = 12.4, 7.2, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.7 (d, J = 17.3 Hz), 27.7 (d, J = 70.1 Hz), 33.6 (d, J = 8.8 Hz), 121.3 (d, J = 101.3 Hz), 126.5, 126.6, 127.3 (d, J = 10.9 Hz), 127.5, 127.7 (2C), 128.2, 128.8, 131.17 (d, J = 2.4 Hz), 132.23 (d, J = 4.5 Hz), 132.6 (d, J = 12.5 Hz), 132.7 (2C), 133.2 (d, J = 92.6 Hz), 138.4 (d, J = 3.6 Hz), 144.8 (d, J = 9.8 Hz), 163.6 (d, J = 26.6 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 62.1; HRMS m/z (M+H$^+$) Calcd for $C_{21}H_{20}OP$: 319.1246. Found 319.1241.

(2,6-Di(naphthalen-2-yl)phenyl)dimethylphosphine oxide (3g): Condition A, colorless solid, mp 246-248 °C, 60.4 mg (60%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.82 (d, J = 12.4 Hz, 6H), 7.48-7.63 (m, 7H), 7.82 (d, J = 8.2 Hz, 2H), 7.89-7.92 (m, 2H), 7.97 (d, J = 7.6 Hz, 2H), 7.98-8.00 (m, 2H), 8.22 (s,

2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1 (d, J = 73.0 Hz), 126.59, 126.64, 127.8, 128.2 (4C), 128.6, 129.4, 130.3, 131.1 (d, J = 9.3 Hz), 132.6 (d, J = 94.3 Hz), 132.9, 133.0, 140.0 (d, J = 3.8 Hz), 147.6 (d, J = 8.8 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 36.4; HRMS m/z ($M+H^+$) Calcd for $C_{28}H_{24}OP$: 407.1559. Found 407.1563.

Dicyclohexyl(2-methyl-6-(naphthalen-2-yl)phenyl)phosphine oxide (3h): Condition A, pale yellow solid, mp 95-97 °C, 34.3 mg (32%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.80-1.90 (m, 22H), 2.85 (s, 3H), 7.04 (ddd, J = 7.4, 3.4, 1.0 Hz, 1H), 7.25-7.29 (m, 1H), 7.32 (ddd, J = 7.5, 7.5, 2.8 Hz, 1H), 7.38 (dd, J = 8.4, 1.8 Hz, 1H), 7.53-7.59 (m, 2H), 7.62 (s, 1H), 7.78-7.84 (m, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.90-7.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.1 (d, J = 2.1 Hz), 25.7 (d, J = 16.1 Hz), 26.2, 26.3, 26.4, 26.5, 26.8, 27.0, 39.3 (d, J = 64.7 Hz), 40.5 (d, J = 63.9 Hz), 126.3, 126.8, 127.3, 127.4, 127.5, 127.9 (2C), 128.9 (d, J = 77.0 Hz), 129.5 (d, J = 2.3 Hz), 129.9 (d, J = 9.6 Hz), 132.2 (d, J = 9.3 Hz), 132.4 (2C), 140.9 (d, J = 2.9 Hz), 144.6 (br), 145.9 (br) (observed complexity is due to C-P coupling); ^{31}P{^{1}H} NMR (162 MHz): δ 53.9; HRMS m/z ($M+H^+$) Calcd for $C_{29}H_{36}OP$: 431.2498. Found 431.2504.

Dicyclohexyl(3-(naphthalen-2-yl)-[1,1'-biphenyl]-2-yl)phosphine oxide (3i): Condition B, pale brown solid, mp 103-105 °C, 70.6 mg (57%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.80-1.86 (m, 22H), 7.19-7.24 (m, 2H), 7.28-7.33 (m, 2H), 7.35-7.55 (m, 7H), 7.68 (d, J = 0.7 Hz, 1H), 7.81-7.91 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.6, 26.3, 26.4, 26.5, 26.6, 26.7, 39.7 (br, d, J = 68.1 Hz), 125.8, 126.3 (d, J = 1.7 Hz), 127.0, 127.1 (2C), 127.2, 127.9 (d, J = 1.7 Hz), 128.1, 128.7, 128.8, 128.9, 129.1 (d, J = 74.8 Hz), 131.8 (d, J = 9.1 Hz), 132.0 (d, J = 9.2 Hz), 132.4, 132.5, 141.2 (d, J = 2.5 Hz), 143.5 (d, J = 2.7 Hz), 146.8 (d, J = 7.9 Hz), 147.1 (d, J = 7.6 Hz) (observed complexity is due to C-P coupling); ^{31}P{^{1}H} NMR (162 MHz): δ 50.4; HRMS m/z ($M+H^+$) Calcd for $C_{34}H_{38}OP$: 493.2655. Found 493.2657.

Cyclohexyl(2-(naphthalen-2-yl)phenyl)(phenyl)phosphine oxide (3j): Condition A, pale brown solid, mp 84-86 °C, 66.9 mg (65%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90-2.00 (m, 11H), 7.10-7.21 (m, 5H), 7.23-7.36 (m, 3H), 7.47-7.65 (m, 5H), 7.68 (d, J = 8.4 Hz, 1H), 7.82-7.88 (m, 1H), 8.17-8.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.1 (d, J = 2.7 Hz), 25.78, 25.82, 26.3 (d, J = 17.3 Hz), 26.4 (d, J = 13.7 Hz), 36.0 (d, J = 72.4 Hz), 126.3 (d, J = 8.1 Hz), 127.1, 127.2 (d, J = 9.8 Hz), 127.4, 127.6, 127.8, 127.9, 128.2, 128.8, 130.8 (d, J = 2.7 Hz), 132.11 (d, J = 91.7 Hz), 131.14 (d, J = 2.3 Hz), 131.23 (d, J = 8.7 Hz), 131.5 (d, J = 9.4 Hz), 132.0 (d, J = 70.4 Hz), 132.3, 132.5, 133.2 (d, J = 7.8 Hz), 138.2 (d, J = 3.1 Hz), 145.6 (d, J = 8.9 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 35.9; HRMS m/z ($M+H^+$) Calcd for $C_{28}H_{28}OP$: 411.1872. Found 411.1870.

(2-(Naphthalen-2-yl)phenyl)diphenylphosphine oxide (3k): Condition A, pale orange gum, 70.3 mg (70%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16-7.33 (m, 7H), 7.36-7.46 (m, 4H), 7.47-7.71 (m, 9H), 7.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.8, 125.9, 126.7 (d, J = 12.3 Hz), 126.8, 127.2, 127.8, 127.9 (d, J = 12.1 Hz), 128.3, 129.7, 131.0 (d, J = 2.7 Hz), 131.5 (d, J = 9.3 Hz), 131.7 (d, J = 2.4 Hz), 132.0 (d, J = 9.9 Hz), 132.1 (d, J = 101.8 Hz), 132.20, 132.23, 133.0 (d, J = 90.0 Hz), 134.1 (d, J = 11.9 Hz), 137.6 (d, J = 4.2 Hz), 147.5 (d, J = 8.6 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 27.6; HRMS m/z (M+H$^+$) Calcd for $C_{28}H_{22}OP$: 405.1403. Found 405.1405.

(4-Methoxy-2-(naphthalen-2-yl)phenyl)bis(4-methoxyphenyl)phosphine oxide (3l): Condition B, pale yellow solid, mp 133-135 °C, 70.5 mg (57%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.69 (s, 6H), 3.86 (s, 3H), 6.64-6.70 (m, 4H), 6.86-6.91 (m, 2H), 7.28 (dd, J = 8.4, 1.8 Hz, 1H), 7.37-7.55 (m, 8H), 7.59 (s, 1H), 7.60-7.64 (m, 1H), 7.69-7.73 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.2, 55.4, 112.0 (d, J = 13.2 Hz), 113.4 (d, J = 13.0 Hz), 117.4 (d, J = 10.8 Hz), 124.6 (d, J = 107.8 Hz), 125.0 (d, J = 110.8 Hz), 125.7, 125.8, 126.6, 127.3, 127.8, 128.2, 129.2, 132.26, 132.32, 133.3 (d, J = 10.6 Hz), 136.0 (d, J = 12.9 Hz), 137.9 (d, J = 4.0 Hz), 149.3 (d, J = 9.9 Hz), 161.6 (d, J = 2.9 Hz), 161.7 (d, J = 2.6 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 26.7; HRMS m/z (M+H$^+$) Calcd for $C_{31}H_{28}O_4P$: 495.1720. Found 495.1718.

(4-Fluoro-2-(naphthalen-2-yl)phenyl)bis(4-fluorophenyl)phosphine oxide (3m): Condition A, pale brown solid, mp 110-112 °C, 68.6 mg (60%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.85-6.93 (m, 4H), 7.07-7.14 (m, 1H), 7.17 (ddd, J = 9.4, 2.8, 2.8 Hz, 1H), 7.20 (dd, J = 8.4, 1.8 Hz, 1H), 7.43-7.54 (m, 7H), 7.54 (d, J = 8.4 Hz, 1H), 7.65-7.75 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 114.0 (dd, J = 20.5, 13.6 Hz), 115.0 (dd, J = 21.3, 13.2 Hz), 119.3 (dd, J = 21.2, 11.0 Hz), 126.3, 126.5, 127.1, 127.2, 127.4, 128.0 (dd, J = 105.6, 3.5 Hz), 128.2, 128.5 (dd, J = 108.2, 3.5 Hz), 129.7, 132.1, 132.4, 133.8 (dd, J = 10.8, 8.8 Hz), 136.2 (dd, J = 3.4, 1.2 Hz), 136.5 (dd, J = 13.5, 9.0 Hz), 150.0 (dd, J = 10.1, 8.7 Hz), 163.3 (d, J = 9.0, 3.4 Hz), 165.8 (dd, J = 6.8, 3.1 Hz); ^{19}F NMR (376 MHz) δ -107.4, -106.5; ^{31}P{^{1}H} NMR (162 MHz): δ 25.3; HRMS m/z (M+H$^+$) Calcd for $C_{28}H_{19}F_3OP$: 459.1120. Found 459.1128.

(2-Methyl-6-(naphthalen-2-yl)phenyl)bis(2-methylphenyl)phosphine oxide (3n): Condition A, pale yellow solid, mp 139-141 °C, 89.5 mg (80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 6H), 2.67 (s, 3H), 6.60-7.70 (br, m, 12H), 6.98 (dd, J = 8.4, 1.8 Hz, 2H), 7.11 (ddd, J = 7.4, 3.9, 0.7 Hz, 2H), 7.47 (ddd, J = 7.6, 7.6 Hz, 1.6, 1H), 7.57 (d, J = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.0 (br), 24.3 (d, J = 3.8 Hz), 124.5 (br), 125.7 (d, J = 9.5 Hz), 126.8 (br), 127.1, 127.7, 127.9 (br), 129.94 (d, J = 97.1 Hz), 130.00 (d, J = 9.6 Hz), 130.5 (d, J = 2.3 Hz), 131.3, 131.5 (br), 131.7, 131.8, 132.0, 132.4, 132.8 (br), 139.4 (d, J = 4.1 Hz), 143.2 (br), 145.5 (d, J = 8.6 Hz), 146.6 (d, J = 10.3

Hz) (observed complexity is due to C-P coupling and the presence of equilibrium of rotamer); $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 37.4; HRMS m/z ($M+H^+$) Calcd for $C_{31}H_{28}OP$: 447.1872. Found 447.1876.

(3-(Naphthalen-2-yl)thiophen-2-yl)di(thiophen-2-yl)phosphine oxide (3o): Condition A, pale brown solid, mp 131-133 °C, 61.3 mg (58%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97-7.01 (m, 2H), 7.35 (dd, J = 4.8, 2.5 Hz, 1H), 7.41-7.44 (m, 2H), 7.48 (ddd, J = 7.9, 3.6, 1.0 Hz, 2H), 7.56-7.60 (m, 3H), 7.68 (d, J = 8.8 Hz, 1H), 7.71 (d, J = 4.9 Hz, 1H), 7.72-7.77 (m, 2H), 8.04 (d, J = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 126.1 (d, J = 11.7 Hz), 127.0, 127.4, 127.5, 127.8, 128.0, 128.4, 129.0, 130.1 (d, J = 124.0 Hz), 132.3 (d, J = 7.1 Hz), 132.4 (d, J = 13.3 Hz), 132.6, 132.7 (d, J = 2.7 Hz), 132.8, 133.9 (d, J = 5.7 Hz), 134.5 (d, J = 130.0 Hz), 136.8 (d, J = 11.0 Hz), 151.7 (d, J = 9.5 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 5.4; HRMS m/z ($M+H^+$) Calcd for $C_{22}H_{16}OPS_3$: 423.0095. Found 423.0099.

5-(2-(Naphthalen-2-yl)phenyl)-5*H*-benzo[*b*]phosphindole 5-oxide (3p): Condition A, pale yellow solid, mp 194-196 °C, 36.2 mg (36%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.45 (dd, J = 8.3, 1.7 Hz, 1H), 6.68 (s, 1H), 6.82-6.87 (m, 2H), 7.08-7.18 (m, 3H), 7.19-7.29 (m, 4H), 7.31 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.40 (ddd, J = 8.1, 6.8, 1.3 Hz, 1H), 7.52-7.63 (m, 4H), 7.68 (dddd, J = 7.6, 7.6, 1.8, 1.4 Hz, 1H), 8.78 (dddd, J = 13.0, 7.7, 1.5, 0.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 120.8 (d, J = 10.2 Hz), 125.5, 126.0, 126.3, 126.6, 127.1, 127.6 (d, J = 11.2 Hz), 127.9 (d, J = 99.1 Hz), 128.1, 128.5, 128.7 (d, J = 11.4 Hz), 129.1 (d, J = 10.0 Hz), 131.0 (d, J = 10.3 Hz), 131.86, 131.89 (d, J = 2.8 Hz), 132.0, 131.7 (d, J = 1.9 Hz), 133.5 (d, J = 107.5 Hz), 134.9 (d, J = 8.0 Hz), 136.1 (d, J = 3.9 Hz), 141.9 (d, J = 22.0 Hz), 145.7 (d, J = 11.6 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 30.6; HRMS m/z ($M+H^+$) Calcd for $C_{28}H_{20}OP$: 403.1246. Found 403.1245.

Methyl (2-(naphthalen-2-yl)phenyl)(phenyl)phosphinate (3q): Condition C, pale brown gum, 46.0 mg (51%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.56 (d, J = 11.1 Hz, 3H), 7.00-7.08 (m, 2H), 7.16-7.35 (m, 5H), 7.43-7.62 (m, 5H), 7.52 (s, 1H), 7.53 (s, 1H), 7.78-7.83 (m, 1H), 8.17 (ddd, J = 12.6, 7.7, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.0 (d, J = 5.8 Hz), 126.0, 126.8, 126.9 (d, J = 11.3 Hz), 127.47, 127.55, 127.7, 127.8, 128.2, 128.9, 130.2 (d, J = 116.8 Hz), 131.38 (d, J = 6.6 Hz), 131.45, 131.55, 131.57 (d, J = 116.8 Hz), 131.9 (d, J = 2.7 Hz), 132.38, 132.41, 133.1 (d, J = 8.5 Hz), 137.9 (d, J = 4.3 Hz), 146.3 (d, J = 11.6 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 32.8; HRMS m/z ($M+H^+$) Calcd for $C_{23}H_{20}O_2P$: 359.1195. Found 359.1197.

Diethyl (2-methyl-6-(naphthalen-2-yl)phenyl)phosphonate (3r): Condition C, pale yellow oil, 36.3 mg (41%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90-1.05 (m, 6H), 2.78 (d, J = 1.8 Hz, 3H),

3.50-3.93 (m, 4H), 7.15-7.20 (m, 1H), 7.28-7.33 (m, 1H), 7.41 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 7.45-7.52 (m, 3H), 7.77-7.88 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9 (d, J = 6.9 Hz), 23.3 (d, J = 3.4 Hz), 61.3 (d, J = 6.2 Hz), 125.8, 126.0 (d, J = 184.0 Hz), 126.1, 126.6, 127.3, 127.6, 127.9, 128.0, 129.7 (d, J = 13.9 Hz), 130.8 (d, J = 11.5 Hz), 130.9, 132.3, 132.8, 141.0 (d, J = 2.6 Hz), 143.7 (d, J = 10.9 Hz), 147.1 (d, J = 9.7 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 18.0; HRMS m/z (M+H$^+$) Calcd for $C_{21}H_{24}O_3P$: 355.1458. Found 355.1452.

Dicyclohexyl(2-(naphthalen-2-yl)phenyl)phosphine sulfide (3s): Condition D, colorless solid, mp 188-190 °C, 42.4 mg (39%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88-1.76 (m, 22H), 7.20-7.23 (m, 1H), 7.38 (dd, J = 8.4, 1.7 Hz, 1H), 7.48-7.64 (m, 4H), 7.69 (s, 1H), 7.84-7.86 (m, 1H), 7.94-7.98 (m, 2H), 8.72 (ddd, J = 15.2, 7.4, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.5, 26.2 (d, J = 13.7 Hz), 26.5 (br), 26.9 (br), 27.7 (br), 28.3 (br), 38.9 (d, J = 48.1 Hz), 39.8 (d, J = 48.1 Hz), 126.7, 127.14, 127.15, 127.6 (d, J = 10.8 Hz), 127.7, 127.8, 127.90, 127.93, 128.1 (d, J = 61.9 Hz), 130.4 (d, J = 2.7 Hz), 131.4 (d, J = 9.2 Hz), 132.4, 132.7, 136.8 (d, J = 10.9 Hz), 139.4, 143.1 (d, J = 7.3 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 69.1; HRMS m/z (M+H$^+$) Calcd for $C_{28}H_{34}PS$: 433.2113. Found 433.2117.

(2-(Naphthalen-2-yl)phenyl)phosphonic acid bis(diethylamide) (3t): colorless oil, 44.8 mg (45%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (t, J = 7.1 Hz, 12H), 2.83-3.01 (m, 8H), 7.38-7.49 (m, 4H), 7.52 (tdd, J = 6.8, 1.5, 1.5 Hz, 1H), 7.69 (m, 1H), 7.55 (dd, J = 8.5, 1.8 Hz, 1H), 7.82 (d, J = 8.6 Hz, 1H), 7.82-7.90 (m, 2H), 8.15 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9 (d, J = 2.2 Hz), 39.1 (d, J = 4.8 Hz), 125.7, 125.8, 126.4, 126.6 (d, J = 13.0 Hz), 127.5, 128.4, 129.0, 129.2, 130.8 (d, J = 2.5 Hz), 130.9 (d, J = 153.2 Hz), 132.5, 132.7, 132.91 (d, J = 22.1 Hz), 132.92, 139.2 (d, J = 3.7 Hz), 147.2 (d, J = 9.3 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 29.4; HRMS m/z (M+H$^+$) Calcd for $C_{24}H_{32}N_2OP$: 395.2247. Found 395.2249.

***exo*-(2-(1,2,3,4-Tetrahydro-1,4-epoxynaphthalen-2-yl)phenyl)phosphonic acid bis(diethylamide) (4t)**: Condition A, pale yellow oil, 78.7 mg (76%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.95 (t, J = 7.0 Hz, 6H), 1.04 (t, J = 7.1 Hz, 6H), 2.06-2.16 (m, 2H), 2.90-3.17 (m, 8H), 3.92 (dd, J = 7.5, 5.2 Hz, 1H), 5.27 (s, 1H), 5.44 (d, J = 4.0 Hz, 1H), 7.11-7.16 (m, 2H), 7.20-7.24 (m, 2H), 7.35-7.52 (m, 3H), 7.82 (ddd, J = 8.7, 5.0, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9 (d, J = 2.0 Hz), 14.1 (d, J = 1.9 Hz), 39.13, 39.18 (d, J = 6.3 Hz), 39.23 (d, J = 6.3 Hz), 42.1 (d, J = 4.5 Hz), 79.2, 85.7, 118.9, 119.4, 125.5 (d, J = 13.3 Hz), 126.46, 126.50, 128.5 (d, J = 11.4 Hz), 130.9 (d, J = 153.1 Hz), 131.7 (d, J = 10.4 Hz), 131.8 (d, J = 2.4 Hz), 145.9, 146.0, 150.5 (d, J = 9.4 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 30.8; HRMS m/z (M+H$^+$) Calcd for $C_{24}H_{34}N_2O_2P$: 413.2352. Found 413.2353.

***exo*-(2-(1,2,3,4-Tetrahydro-1,4-epoxynaphthalen-2-yl)phenyl]phosphonic acid bis(dipiperidinylamide) (4u)**: Condition A, pale yellow oil, 83.5 mg (77%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33-1.66 (m, 12H), 2.09 (ddd, J = 11.8, 4.7, 4.7 Hz, 1H), 2.16 (dd, J = 11.9, 8.5 Hz, 1H), 2.94-3.16 (m, 8H), 4.00 (dd, J = 8.3, 4.7 Hz, 1H), 5.27 (s, 1H), 5.54 (d, J = 4.7 Hz, 1H), 7.13-7.30 (m, 4H), 7.35-7.53 (m, 3H), 7.84 (dd, J = 7.8, 5.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.7, 24.8, 26.29 (d, J = 4.4 Hz), 23.31 (d, J = 4.7 Hz), 39.1, 42.3 (d, J = 4.1 Hz), 45.4 (d, J = 2.3 Hz), 45.5 (d, J = 2.1 Hz), 79.2, 85.7, 119.0, 119.4, 125.5 (d, J = 13.4 Hz), 126.48, 126.50, 128.6 (d, J = 11.7 Hz), 130.1 (d, J = 153.0 Hz), 131.80 (d, J = 14.3 Hz), 131.83 (d, J = 1.3 Hz), 146.12, 146.14, 150.5 (d, J = 9.3 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 27.6; HRMS m/z (M+H^{+}) Calcd for $C_{26}H_{34}N_2O_2P$: 437.2352. Found 437.2358.

***exo-tert*-Butyl 2-(2-(bis(diethylamino)phospholyl)phenyl)-1,2,3,4-tetrahydro-1,4-epiminonaphthalene-9-carboxylate (6)**: Condition A, pale yellow oil, 78.3 mg (61%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.80-1.20 (m, 12H), 1.33 (s, 9H), 1.80-2.25 (m, 2H), 2.80-3.20 (m, 8H), 3.76-3.86 (m, 1H), 5.00-5.45 (m, 2H), 7.07-7.13 (m, 2H), 7.20-7.30 (m, 2H), 7.33-7.50 (m, 3H), 7.81 (br, s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (br), 28.3, 38.3 (br), 39.2 (br), 42.8 (br), 60.8 (br), 67.7 (br), 80.0, 119.8 (br), 120.1, 125.6 (d, J = 13.4 Hz), 126.3 (2C), 127.9 (d, J = 11.5 Hz), 131.8, 131.9, 145.8 (br), 149.9 (br) (some peaks were not detected due to broadening caused by fast NBoc stereoinversion as well as C-P coupling); ^{31}P{^{1}H} NMR (162 MHz): δ 30.7; HRMS m/z (M+H^{+}) Calcd for $C_{29}H_{43}N_3O_3P$: 512.3037. Found 512.3036.

Dicyclohexyl(2-(naphthalen-2-yl)phenyl)phosphine (7): colorless solid, mp 122-124 °C, 75.6 mg (94%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.00-1.29 (m, 10H), 1.56-1.73 (m, 10H), 1.80-1.90 (m, 2H), 7.33-7.42 (m, 3H), 7.44-7.50 (m, 3H), 7.60-7.66 (m, 1H), 7.70 (s, 1H), 7.80-7.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.4, 27.2, 27.3 (d, J = 4.4 Hz), 29.3 (d, J = 8.8 Hz), 30.4 (d, J = 16.9 Hz), 34.7 (d, J = 14.2 Hz), 125.6, 125.9, 126.5, 126.6, 127.8, 128.0, 128.3, 128.9 (d, J = 2.9 Hz), 129.6 (d, J = 5.4 Hz), 130.5 (d, J = 5.5 Hz), 132.3, 132.95 (d, J = 3.1 Hz), 132.98, 134.2 (d, J = 21.1 Hz), 140.7 (d, J = 6.1 Hz), 150.5 (d, J = 28.4 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ -13.3; HRMS m/z (M+H^{+}) Calcd for $C_{28}H_{34}P$: 401.2393. Found 401.2391.

11-Phenyl-11*H*-dibenzo[*b*,*g*]phosphindole 11-sulfide (α-9): colorless solid, mp 178-180 °C, 48.8 mg (57%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.53 (m, 6H), 7.61 (dd, J = 7.5, 7.5 Hz, 1H), 7.74 (dd, J = 7.3, 3.2 Hz, 1H), 7.76-7.85 (m, 2H), 7.86-7.91 (m, 1H), 7.93 (dd, J = 7.7, 2.9 Hz, 1H), 7.99 (dd, J = 8.5, 2.6 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 8.24-8.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 118.9 (d, J = 10.8 Hz), 121.6 (d, J = 9.6 Hz), 125.5 (d, J = 6.3 Hz), 126.8, 128.3, 128.7 (d, J = 12.7

Hz), 129.0, 129.2 (d, J = 11.5 Hz), 129.8 (d, J = 11.8 Hz), 129.9 (d, J = 88.2 Hz), 130.4 (d, J = 79.6 Hz), 131.1 (d, J = 12.1 Hz), 131.9 (d, J = 8.6 Hz), 132.0 (d, J = 2.9 Hz), 132.7 (d, J = 2.1 Hz), 134.1 (d, J = 7.6 Hz), 134.2 (d, J = 1.8 Hz), 137.2 (d, J = 91.2 Hz), 140.9 (d, J = 17.8 Hz), 141.4 (d, J = 19.6 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 39.9; HRMS m/z ($M+H^+$) Calcd for $C_{22}H_{16}SP$: 343.0705. Found 343.0707.

11-Phenyl-11*H*-dibenzo[*b*,*g*]phosphindole 11-oxide (10a)[2b]: colorless solid, mp 224-226 °C, 50.2 mg (62%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.44 (m, 3H), 7.44-7.52 (m, 3H), 7.60 (dd, J = 7.6, 7.6 Hz, 1H), 7.70-7.77 (m, 3H), 7.85-7.92 (m, 2H), 7.95 (dd, J = 8.5, 2.6 Hz, 1H), 8.07-8.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 118.7 (d, J = 11.4 Hz), 121.3 (d, J = 10.3 Hz), 125.9 (d, J = 5.2 Hz), 126.8, 128.3 (d, J = 102.3 Hz), 128.5, 128.81, 128.82 (d, J = 12.5 Hz), 129.5 (d, J = 11.1 Hz), 129.8 (d, J = 9.9 Hz), 130.9 (d, J = 101.6 Hz), 131.0 (d, J = 10.9 Hz), 132.1 (d, J = 2.9 Hz), 132.4 (d, J = 9.1 Hz), 133.3 (d, J = 2.0 Hz), 133.84 (d, J = 8.5 Hz), 133.85 (d, J = 110.7 Hz), 134.5 (d, J = 2.1 Hz), 141.5 (d, J = 20.8 Hz), 141.8 (d, J = 22.8 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 34.3; HRMS m/z ($M+H^+$) Calcd for $C_{22}H_{16}OP$: 327.0933. Found 327.0938.

8-Methyl-11-(4-methylphenyl)-11*H*-dibenzo[*b*,*g*]phosphindole 11-oxide (10b): colorless solid, mp 221-223 °C, 40.0 mg (45%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3H), 2.48 (s, 3H), 7.15-7.21 (m, 3H), 7.46 (dtd, J = 9.6, 6.9, 2.0 Hz, 2H), 7.57-7.65 (m, 3H), 7.70 (s, 1H), 7.84-7.87 (m, 1H), 7.93 (dd, J = 8.4, 2.6 Hz, 1H), 8.06-8.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6 (d, J = 1.1 Hz), 22.0, 118.6 (d, J = 11.2 Hz), 122.1 (d, J = 10.5 Hz), 125.9 (d, J = 5.2 Hz), 126.7, 127.7 (d, J = 104.0 Hz), 128.4, 128.8, 129.6 (d, J = 105.7 Hz), 129.58 (d, J = 12.9 Hz), 129.64 (d, J = 10.3 Hz), 130.2 (d, J = 11.4 Hz), 130.9 (d, J = 109.4 Hz), 131.0 (d, J = 11.4 Hz), 132.4 (d, J = 8.8 Hz), 133.8 (d, J = 8.4 Hz), 134.2 (d, J = 2.3 Hz), 141.4 (d, J = 20.5 Hz), 142.0 (d, J = 23.2 Hz), 142.6 (d, J = 2.9 Hz), 143.8 (d, J = 1.9 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 34.3; HRMS m/z ($M+H^+$) Calcd for $C_{24}H_{20}OP$: 355.1246. Found 355.1250.

8-Chloro-11-(4-chlorophenyl)-11*H*-dibenzo[*b*,*g*]phosphindole 11-oxide (10c): colorless solid, mp 244-246 °C, 47.8 mg (48%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.40 (m, 3H), 7.49-7.55 (m, 2H), 7.59-7.67 (m, 3H), 7.86-7.92 (m, 3H), 8.03-8.07 (m, 1H), 8.13 (d, J = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 118.6 (d, J = 11.4 Hz), 122.1 (d, J = 10.9 Hz), 125.7 (d, J = 5.3 Hz), 127.4, 128.6 (d, J = 105.6 Hz), 128.90, 128.93 (d, J = 101.5 Hz), 129.0 (d, J = 1.0 Hz), 129.4 (d, J = 13.17 Hz), 129.5 (d, J = 11.7 Hz), 130.8 (d, J = 10.7 Hz), 131.6 (d, J = 109.0 Hz), 132.3 (d, J = 9.0 Hz), 132.4 (d, J = 11.8 Hz), 134.1 (d, J = 8.8 Hz), 135.0 (d, J = 2.2 Hz), 139.0 (d, J = 3.5 Hz), 140.1 (d, J = 20.3 Hz), 140.2 (d, J = 2.8 Hz), 143.7 (d, J = 24.4 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 32.3; HRMS m/z ($M+H^+$) Calcd for $C_{22}H_{14}Cl_2OP$: 395.0154. Found 395.0158.

2,3-Dibromo-11-phenyl-11*H*-dibenzo[*b*,*g*]phosphindole 11-oxide (10d): colorless solid, mp 253-255 °C, 77.6 mg (64%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.52 (m, 4H), 7.58-7.64 (m, 1H), 7.68 (dd, J = 12.4, 7.6 Hz, 2H), 7.75 (dd, J = 8.6, 8.6 Hz, 1H), 7.83-7.97 (m, 3H), 8.11-8.18 (m, 1H), 8.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 120.0 (d, J = 11.0 Hz), 121.6 (d, J = 10.2 Hz), 123.4, 125.3, 127.7 (d, J = 103.2 Hz), 129.0 (d, J = 12.6 Hz), 129.9 (d, J = 10.0 Hz), 130.0, 130.2 (d, J = 102.2 Hz), 130.5 (d, J = 11.1 Hz), 130.9 (d, J = 11.0 Hz), 131.8 (d, J = 8.5 Hz), 132.5 (d, J = 2.8 Hz), 133.0, 133.2 (d, J = 28.1 Hz), 133.3, 133.5 (d, J = 1.9 Hz), 133.7 (d, J = 77.7 Hz), 141.1 (d, J = 22.2 Hz), 142.5 (d, J = 20.2 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 33.7; HRMS m/z (M+H^{+}) Calcd for $C_{22}H_{14}Br_2OP$: 482.9144. Found 482.9147.

2,3-Difluoro-11-phenyl-11*H*-dibenzo[*b*,*g*]phosphindole 11-oxide (10e): colorless solid, mp 234-236 °C, 58.5 mg (65%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.45 (m, 3H), 7.48-7.54 (m, 1H), 7.57-7.64 (m, 2H), 7.67-7.76 (m, 3H), 7.84 (dd, J = 10.8, 7.8 Hz, 1H), 7.88 (dd, J = 7.7, 2.9 Hz, 1H), 7.93 (dd, J = 8.5, 2.3 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 112.0 (dd, J = 17.5, 5.1 Hz), 114.8 (d, J = 16.8 Hz), 119.1 (dd, J = 11.0, 2.0 Hz), 121.5 (d, J = 10.3 Hz), 128.2 (ddd, J = 104.0, 5.6, 1.7 Hz), 129.0 (d, J = 12.6 Hz), 129.4 (dd, J = 8.7, 8.7 Hz), 129.8 (d, J = 8.7 Hz), 129.9 (d, J = 7.5 Hz), 130.2 (d, J = 102.1 Hz), 130.8 (d, J = 7.2 Hz), 131.96 (d, J = 10.9 Hz), 132.5 (d, J = 2.8 Hz), 133.4 (d, J = 107.6 Hz), 133.51, 133.55 (d, J = 4.7 Hz), 141.3 (d, J = 22.4 Hz), 141.7 (dd, J = 20.4, 2.8 Hz), 149.6 (dd, J = 91.1, 15.8 Hz), 151.1 (dd, J = 92.8, 15.7 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 33.9; ^{19}F{^{1}H} NMR (376 MHz): δ -134.7 (d, J = 20.5 Hz), -131.7 (d, J = 20.6 Hz); HRMS m/z (M+H^{+}) Calcd for $C_{22}H_{14}F_2OP$: 363.0745. Found 363.0740.

2,3-Dimethyl-11-phenyl-11*H*-dibenzo[*b*,*g*]phosphindole 11-oxide (10f): pale brown solid, mp 184-186 °C, 52.0 mg (59%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34 (s, 3H), 2.38 (s, 3H), 7.32-7.40 (m, 3H), 7.46 (dd, J = 7.4, 7.4 Hz, 1H), 7.57 (dd, J = 7.5, 7.5 Hz, 1H), 7.61 (s, 1H), 7.67-7.77 (m, 3H), 7.81-7.86 (m, 3H), 7.97 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.2, 20.4, 117.8 (d, J = 10.7 Hz), 121.1 (d, J = 9.3 Hz), 125.2, 127.0 (d, J = 104.7 Hz), 128.3, 128.8 (d, J = 11.8 Hz), 129.1 (d, J = 10.2 Hz), 129.7 (d, J = 8.9 Hz), 131.0 (d, J = 10.0 Hz), 131.1 (d, J = 106.7 Hz), 131.4 (d, J = 7.4 Hz), 132.0, 132.9 (d, J = 7.6 Hz), 133.2, 133.5, 133.8 (d, J = 106.1 Hz), 136.9, 138.8, 140.7 (d, J = 20.8 Hz), 142.1 (d, J = 22.6 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 34.5; HRMS m/z (M+H^{+}) Calcd for $C_{24}H_{20}OP$: 355.1246. Found 355.1242.

References and Notes

(1) (a) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461. (b) Surry, D. S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 6338. (c) Surry, D. S.; Buchwald, S. L. *Chem. Sci.* **2011**, *2*, 27.

(d) Hoshiya, N.; Buchwald, S. L. *Adv. Synth. Catal.* **2012**, *354*, 2031.

(2) (a) Kuninobu, Y.; Yoshida, T.; Takai, K. *J. Org. Chem.* **2011**, *76*, 7370, (b) Baba, K.; Tobisu, M.; Chatani, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 11892, (c) Shin, S.; Kang, D.; Jeon, W. H.; Lee, P. *H. Beilstein J. Org. Chem.* **2014**, *10*, 1220.

(3) For pioneering work, see: Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529.

(4) Selected recent reviews for C−H functionalization: (a) Dyker, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1698. (b) Kakiuchi, F.; Chatani, N. *Adv. Synth. Catal.* **2003**, *345*, 1077. (c) Godula, K.; Sames, D. *Science* **2006**, *312*, 67. (d) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (e) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Chem. Rev.* **2007**, 107, 5318. (f) Park, Y. J.; Park, J.-W.; Jun, C.-H. *Acc. Chem. Res.* **2008**, *41*, 222. (g) Ferreira, E. M.; Zhang, H.; Stoltz, B. M. *Tetrahedron* **2008**, *64*, 5987. (h) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013. (i) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335. (j) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev.* **2009**, *38*, 2447. (k) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074. (l) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (m) Satoh, T.; Miura, M. *Synthesis* **2010**, 3395. (n) Satoh, T.; Miura, M. *Chem.—Eur. J.* **2010**, *16*, 11212. (o) Sun, C.-L.; Li, B.-J.; Shi, Z.- J. *Chem. Commun.* **2010**, *46*, 677. (p) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (q) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (r) Lapointe, D.; Fagnou, K. *Chem. Lett.* **2010**, *39*, 1118. (s) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. (t) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780. (u) Kuninobu, Y.; Takai, K. *Chem. Rev.* **2011**, 111, 1938. (v) Wencel-Delord, J.; Droge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740. (w) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (x) Mitchell, E. A.; Peschiulli, A.; Lefevre, N.; Meerpoel, L.; Maes, B. U. W. *Chem.—Eur. J.* **2012**, *18*, 10092. (y) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788. (z) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814. (aa) Patureau, F. W.; Wencel-Delord, J.; Glorius, F. *Aldrichimica Acta* **2012**, *45*, 31. (ab) Chiba, S. *Chem. Lett.* **2013**, *41*, 1554. (ac) Wencel-Delord, J.; Glorius, F. *Nat. Chem.* **2013**, *5*, 369. (ad) Engle, K. M.; Yu, J.-Q. *J. Org. Chem.* **2013**, *78*, 8927. (ae) Miura, M.; Satoh, T.; Hirano, K. *Bull. Chem. Soc. Japan.* **2014**, *87*, 751. (af) De Sarkar, S.; Liu, W.; Kozhushkov, S. I.; Ackermann, L. *Adv. Synth. Catal.* **2014**, *356*, 1461. (ag) Kuhl, N.; Schröder, N.; Glorius, F. *Adv. Synth. Catal.* **2014**, *356*, 1443. (ah) Song, G.; Li, X. *Acc. Chem. Res*. **2015**, *48*, 1007. (ai) Chen, Z.; Wang, B.; Zhang, J.; Yu, W.; Liu, Z.; Zhang, Y.; *Org. Chem. Front.,* **2015**, *2*, 1107.

(5) (a) Unoh, Y.; Hashimoto, Y.; Takeda, D.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2013**, *15*, 3258. (b) Itoh, M.; Hashimoto, Y.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2013**, *78*, 8098. (c) Yokoyama, Y.; Unoh, Y.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2014**, *79*, 7649.

(6) Pd catalysis: (a) Meng, X.; Kim, S. *Org. Lett.* **2013**, *15*, 1910. (b) Chan, L. Y.; Kim, S.; Ryu, T.;

Lee, P. H. *Chem. Commun.* **2013**, *49*, 4682. (c) Chan, L. Y.; Cheong, L.; Kim, S. *Org. Lett.* **2013**, *15*, 2186. (d) Chan, L. Y.; Meng, X.; Kim, S. *J. Org. Chem.* **2013**, *78*, 8826. (e) Meng, X.; Kim, S. *J. Org. Chem.* **2013**, *78*, 11247. (f) Chary, B. C.; Kim, S.; Park, Y.; Kim, J.; Lee, P. H. *Org. Lett.* **2013**, *15*, 2692. (g) Wang, H.-L.; Hu, R.-B.; Zhang, H.; Zhou, A.-X.; Yang, S.-D. *Org. Lett.* **2013**, *15*, 5302. (h) Zhang, H.-Y.; Yi, H.-M.; Wang, G.-W.; Yang, B.; Yang, S.-D. *Org. Lett.* **2013**, *15*, 6186. (i) Jeon, W. H.; Lee, T. S.; Kim, E. J.; Moon, B.; Kang, J. *Tetrahedron* **2013**, *69*, 5152. (j) Eom, D.; Jeong, Y.; Kim, Y. R.; Lee, E.; Choi, W.; Lee, P. H. *Org. Lett.* **2013**, *15*, 5210. (k) Wang, H.-L.; Hu, R.-B.; Zhang, H.; Zhou, A.-X.; Yang, S.-D. *Org. Lett.* **2013**, *15*, 5302. (l) Shin, S.; Jeong, Y.; Jeon, W. H.; Lee, P. H. *Org. Lett.* **2014**, *16*, 2930. (m) Hu, R.-B.; Zhang, H.; Zhang, X.-Y.; Yang, S.-D. *Chem. Commun.* **2014**, *50*, 2193. (n) Zhang, H.; Hu, R.-B.; Zhang, X.-Y.; Li, S.-X.; Yang, S.-D. *Chem. Commun.* **2014**, *50*, 4686. (o) Guan, J.; Wu, G.-J.; Han, F. S. *Chem.—Eur. J.* **2014**, *20*, 3301. (p) Shin, S.; Kang, D.; Jeon, W. H.; Lee, P. H. *Beilstein J. Org. Chem.* **2014**, *10*, 1220. (q) Du, Z.-J.; Guan, J.; Wu, G. J.; Xu, P.; Gao, L. X.; Han, F. S. *J. Am. Chem. Soc.* **2015**, *137*, 632. (r) Jeon, W. H.; Son, J.-Y.; Kim, S.-E.; Lee, P. H. *Adv. Synth. Catal.* **2015**, *357*, 811. (s) Ma, Y.-N.; Zhang, H.-Y.; Yang, S.-D. *Org. Lett.* **2015**, *17*, 2034. (t) Lin, Z.-Q.; Wang, W.-Z.; Yan, S.-B.; Duan, W.-L. *Angew. Chem., Int. Ed.* **2015**, *54*, 6265, (u) Liu, L.; Zhang, A.-A.; Wang, Y.; Zhang, F.; Zuo, Z.; Zhao, W.-X.; Feng, C.-L.; Ma, W. *Org. Lett.* **2015**, *17*, 2046, (v) Xu, G.; Li, M.; Wang, S.; Tang, W. *Org. Chem. Front.* **2015**, *2*, 1342.

(7) Rh catalysis: (a) Seo, J.; Park, Y.; Jeon, I.; Ryu, T.; Park, S.; Lee, P. H. *Org. Lett.* **2013**, *15*, 3358. (b) Ryu, T.; Kim, J.; Park, Y.; Kim, S.; Lee, P. H. *Org. Lett.* **2013**, *15*, 3986. (c) Zhao, D.; Nimphius, C.; Lindale, M.; Glorius, F. *Org. Lett.* **2013**, *15*, 4504. (d) Park, Y.; Seo, J.; Park, S.; Yoo, E. J.; Lee, P. H. *Chem.—Eur. J.* **2013**, *19*, 16461. (e) Park, S.; Seo, B.; Shin, S.; Son, J.-Y.; Lee, P. H. *Chem. Commun.* **2013**, *49*, 8671. (f) Mo, J.; Lim, S.; Ryu, T.; Kim, S.; Lee, P. H. *RSC Adv.* **2013**, *3*, 18296. (g) Chary, B. C.; Kim, S. *Org. Biomol. Chem.* **2013**, *11*, 6879. (h) Liu, L.; Wu, Y.; Wang, T.; Gao, X.; Zhu, J.; Zhao, S. *J. Org. Chem.* **2014**, *79*, 5074. (i) Gu, L.-J.; Jin, C.; Wang, R.; Ding, H.-Y. *ChemCatChem* **2014**, *6*, 1225.

(8) Ru catalysis: Park, Y.; Jeon, I.; Shin, S.; Min, J.; Lee, P. H. *J. Org. Chem.* **2013**, *78*, 10209.

(9) Ir catalysis: Gwon, D.; Lee, D.; Kim, J.; Park, S.; Chang, S. *Chem.—Eur. J.* **2014**, *20*, 12421.

(10) (a) Qi, Z.; Li, X. *Angew. Chem., Int. Ed.* **2013**, *52*, 8995. Relevant catalytic C-H functionalization reactions with bicyclic alkenes, see: (b) Yang, T.; Zhang, T.; Yang, S.; Chen, S.; Li, X. *Org. Biomol. Chem.* **2014**, *12*, 4290. (c) Dong, W.; Parthasarathy, K.; Cheng, Y.; Pan, F.; Bolm, C. *Chem.—Eur. J.* **2014**, *20*, 15732. (d) Cheng, H.; Dong, W.; Dannenberg, C. A.; Dong, S.; Guo, Q.; Bolm, C. *ACS Catal.*, **2015**, *5*, 2770.

(11) (a) Unoh, Y.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 12975. See also: (b) Chen, Y.; Duan, W. *J. Am. Chem. Soc.* **2013**, *135*, 16754. (c) Ma, W.; Ackermann, L. *Synthesis* **2014**, *46*, 2297.

(12) (a) Matano, Y.; Imahori, H. *Org. Biomol. Chem.* **2009**, *7*, 1258. (b) Fukazawa, A.; Hara, M.; Okamoto, T.; Son, E.-C.; Xu, C.; Tamao, K.; Yamaguchi, S. *Org. Lett.* **2008**, *10*, 913. (c) Fukawa, N.; Osaka, T.; Noguchi, K.; Tanaka, K. *Org. Lett.* **2010**, *12*, 1324. (d) Matano, Y.; Saito, A.; Fukushima, T.; Yokudome, Y.; Suzuki, F.; Sakamaki, D.; Kaji, H.; Ito, A.; Tanaka, K.; Imahori, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 8016. (e) Bruch, A.; Fukazawa, A.; Yamaguchi, E.; Yamaguchi, S.; Studer, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 12094. (f) Cui, Y.; Fu, L.; Cao, J.; Deng, Y.; Jiang, J. *Adv. Synth. Catal.* **2014**, *356,* 1217. (g) Furukawa, S.; Haga, S.; Kobayashi, J.; Kawashima, T. *Org. Lett.* **2014**, *16,* 3228. (h) Baba, K.; Tobisu, M.; Chatani, N. *Org. Lett.*, **2015**, 17, 70.

(13) (a) Olah, G. A.; Hehemann, D. *J. Org. Chem.* **1977**, *42*, 2190. (b) Wang, Z.-W.; Wang, L.-S. *Green Chem.* **2003**, *5*, 737. (c) Diaz, A. A.; Young, J. D.; Khan, M. A.; Wehmschulte, R. J. *Inorg. Chem.* **2006**, *45*, 5568. (d) Diaz, A. A.; Buster, B.; Schomich, D.; Khan, M. A.; Baum, J. C.; Wehmschulte, R. J. *Inorg. Chem.* **2008**, *47*, 2858. (e) Hatakeyama, T.; Hashimoto, S.; Nakamura, M. *Org. Lett.* **2011**, *13*, 2130. (f) Hashimoto, S.; Nakatsuka, S.; Nakamura, M.; Hatakeyama, T. *Angew. Chem., Int. Ed.* **2014**, *53*, 14074.

(14) Berlin, K. D.; Austin, T. H.; Nagabhushanam, M. *J. Org. Chem.* **1965**, *30*, 1267.

(15) Saito, M.; Nishibayashi, Y.; Uemura, S. *Organometallics* **2004**, *23*, 4012.

(16) Stankevič, M.; Włodarczyk, A.; Nieckarz, D. *Eur. J. Org. Chem*., **2013**, 4351.

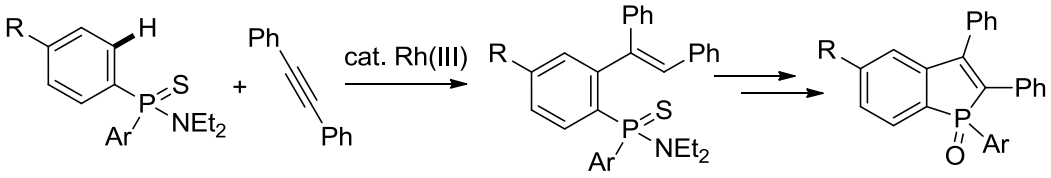
(17) Davoust, M.; Kitching, J. A.; Fleming, M. J.; Lautens, M. *Chem.—Eur. J.* **2010**, *16*, 50.

(18) Otani, Y.; Nagae, O.; Naruse, Y.; Inagaki, S.; Ohno, M.; Yamaguchi, K.; Yamamoto, G.; Uchiyama, M.; Ohwada, T. *J. Am. Chem. Soc.* **2003**, *125*, 15191.

Chapter 5

Regioselective Synthesis of Benzo[*b*]phospholes via Direct Alkenylation and Cyclization of Arylthiophosphinamides

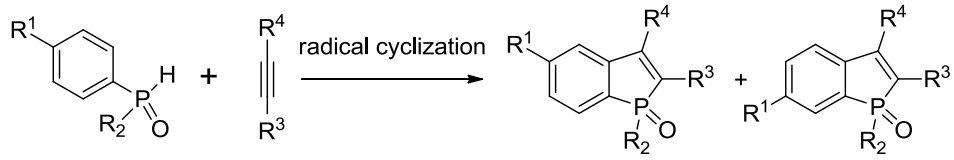
A new regioselective synthetic methodology for benzo[*b*]phosphole derivatives has been developed. Thus, a range of functionalized benzo[*b*]phosphole oxides could be synthesized via Rh(III)-catalyzed C-H alkenylation of arylthiophosphinamides with alkynes followed by formal phospha-Friedel-Crafts cyclization.



Introduction

As described in Chapter 1 and Chapter 3, the benzo[*b*]phospholes are unique and attractive building blocks among a series of benzoheterole scaffolds, which show intriguing electronic and optical properties caused by distinctive orbital interaction between butadiene π^* and σ*(P-R).[1] While they have attracted considerable interest in the area of materials chemistry, their synthetic methods have been still less explored than those of the isosteric indoles.[2] Conventionally, benzo[*b*]phosphole scaffolds have been constructed through the cyclization of *ortho*-alkynylarylphosphines,[3a-c] *H*-phosphine oxides,[3d] and aminophosphines.[3e,f] These methods often require tedious multi-step preparations of the corresponding cyclization precursors, involving air- and moisture-sensitive intermediates. In 2013, the author[4a] and Duan group[4b] independently reported the Ag(I)- or Mn(III)-mediated synthesis of benzo[*b*]phosphole derivatives via the direct annulation reaction of secondary phosphine oxides with internal alkynes (Scheme 5.1a-c).[4] While this protocol provides a short access to benzo[*b*]phosphole derivatives, the regioselectivity problem arises when substituted phenylphosphine oxides are employed due to the radical intermediate involving the rearrangement of phosphorus moiety. After these reports, several improved methods based on a similar radical mechanism under metal-catalyzed (Scheme 5.1d),[5a] photo-catalyzed,[5b] and metal-free conditions (Scheme 5.1e,f)[5c,d] have also been disclosed. However, the regioselectivity issue has not been overcome.

Scheme 5.1. Synthesis of Benzo[*b*]phosphole Derivatives by Radical Cyclization



(a) *The author (Chapter3)* 2013
conditions:
stoic. AgOAc
DMF, 100 °C
or
stoic. $Mn(OAc)_3•2H_2O$
DMF, rt

(b) *Duan* 2013
conditions:
stoic. Ag_2O
or
cat. Ag_2O
$Zn(NO_3)_2•6H_2O$
DMF, 100 °C

(c) *Ackermann* 2014
conditions:
stoic. AgOAc
DMSO, 120 °C

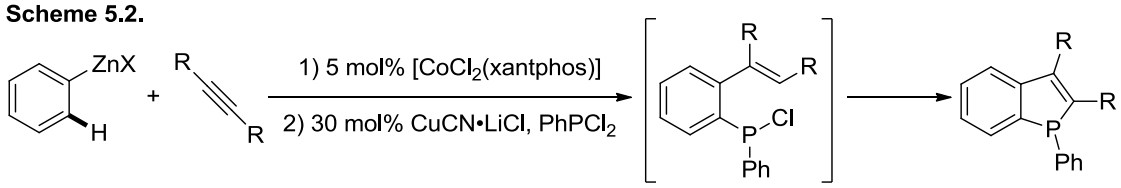
(d) *Zhao* 2016
conditions:
cat. $CuSO_4•5H_2O$
TBHP, $NH_3•H_2O$
MeCN, 60 °C

(e) *Zhao* 2016
conditions:
$K_2S_2O_8$
MeCN, 90 °C

(f) *Lakhdar* 2016
conditions:
cat. eosin Y
N-ethoxy-2-methylpyridinium
$NaHCO_3$
Green LED
DMF, 35 °C

Recently, Yoshikai and co-workers reported an elegant multi-component coupling for the synthesis of benzo[*b*]phosphole derivatives via carbometallation of alkynes with arylzinc and magnesium reagents (Scheme 5.2).[6] Yet, development of more efficient synthetic routes to benzo[*b*]phospholes is desired.

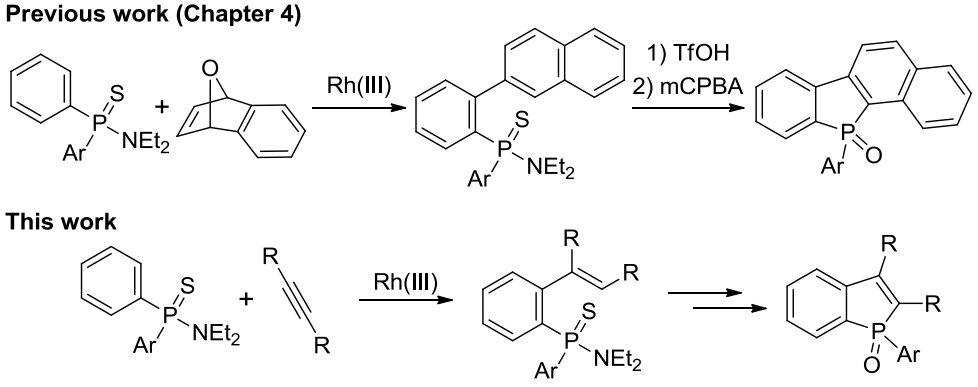
Scheme 5.2.



Meanwhile, transition-metal-catalyzed directed C-H bond functionalization reactions have been regarded as powerful synthetic tools from the atom and step economical points of view.[7,8] In the context of the studies on the C-H bond functionalization of aromatic phosphorus compounds,[9,10] the author recently developed the Cp*Rh(III)-catalyzed *ortho*-naphthylation reaction of arylthiophosphinamides with oxabicyclic alkenes (Scheme 5.3 and Chapter 4).[9d] The naphthylated products were readily converted to fused dibenzo[*b*]phosphole derivatives by intramolecular phospha-Friedel-Crafts reaction[11] in a one-pot procedure. Subsequently, the author envisioned that a regioselective synthesis of benzo[*b*]phospholes could be achieved

through the *ortho*-alkenylation of arylthiophosphinamides and subsequent intramolecular phospha-Friedel-Crafts reaction. Herein, the author reports a new method for constructing benzo[*b*]phosphole oxides by the C-H alkenylation/cyclization protocol.

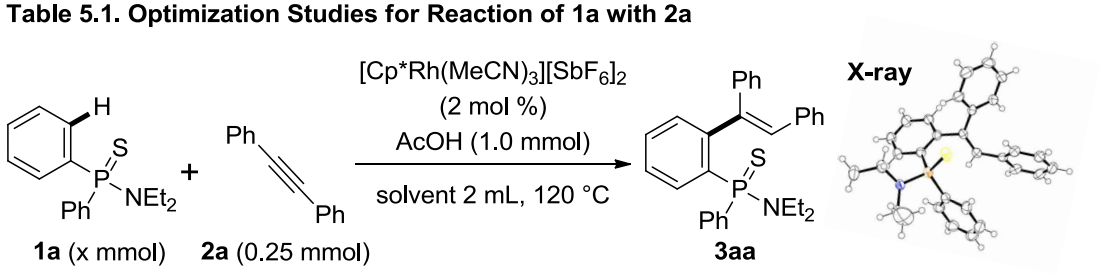
Scheme 5.3. Rh (III)-Catalyzed C-H Bond Functionalization Approaches to Benzo[*b*]phosphole Scaffolds



Results and discussion

First, the author carried out optimization studies on the C-H alkenylation using *N*,*N*-diethyl-*P*,*P*-diphenylthiophosphinamide (**1a**) and diphenylacetylene (**2a**) as model substrates (Table 5.1). Treatment of **1a** (0.25 mmol) with **2a** (0.25 mmol) in the presence of 2 mol% of $[Cp^*Rh(MeCN)_3][SbF_6]_2$ and AcOH(1.0 mmol) in diglyme at 120 °C for 5 h gave **3aa** in 22% yield (entry 1). Solvent screening showed PhCl was the best choice (entries 2-6). Increasing the amount of **1a** (0.5 mmol) to prevent multi coupling reaction enhanced the product yield (entry 7). Finally, **3aa** was obtained in 90% isolated yield by using 4 mol% of Rh catalyst with longer reaction time (entry 8). The geometry of the alkenyl moiety was determined to be *E* by X-ray crystal structure analysis.

Table 5.1. Optimization Studies for Reaction of 1a with 2a



1a (x mmol) **2a** (0.25 mmol) **3aa**

entry	x (mmol)	solvent	time (h)	yield of **3aa** (%)[a]
1	0.25	diglyme	5	22
2	0.25	DMF	5	trace
3	0.25	dioxane	5	14
4	0.25	THF	5	21
5	0.25	DCE	5	30
6	0.25	PhCl	5	50
7	0.5	PhCl	12	83[b]
8[c]	0.5	PhCl	12	91[b](90)

[a] GC yield based on the amount of **2a**. Isolated yield is shown in parentheses. [b] ^{1}H NMR yield using CH_2Br_2 as an internal standard. [c] $[Cp^*Rh(MeCN)_3][SbF_6]_2$ 4 mol %.

The author next examined the second step, i.e. cyclization. In Chapter 4, it was disclosed that TfOH efficiently promoted the intramolecular phospha-Friedel-Crafts reaction of biarylthiophosphinamides.[9d] Thus, the crude product formed by the Rh-catalyzed alkenylation (entry 8 in Table 5.1) was treated with TfOH under similar conditions (Scheme 5.4). Unfortunately, the desired benzo[*b*]phosphole **4aa-S** was observed only in a trace amount, and instead, phosphonium salt **5** was formed in 73% yield as a diastereomeric mixture. Obviously, **5** seems to be formed via protonation of the alkenyl moiety of **3aa** with TfOH and electrophilic attack of a resulting carbocation to the P=S bond. The author also examined other activating reagents including HCl, $AlCl_3$, BF_3•OEt_2, AgOTf and Me_3OBF_4, but all attempts were unsuccessful (Table 5.2).

Scheme 5.4. Attempt of Phospha-Friedel-Crafts Reaction via Intermediate 3aa

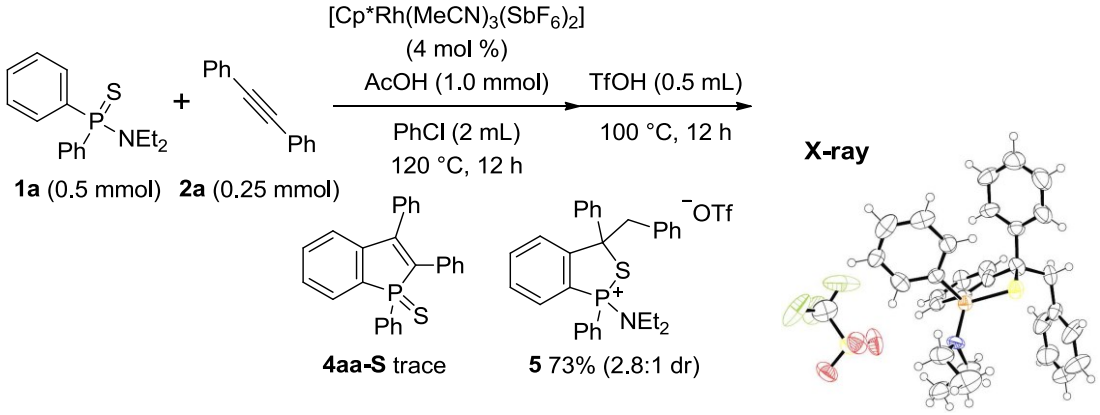
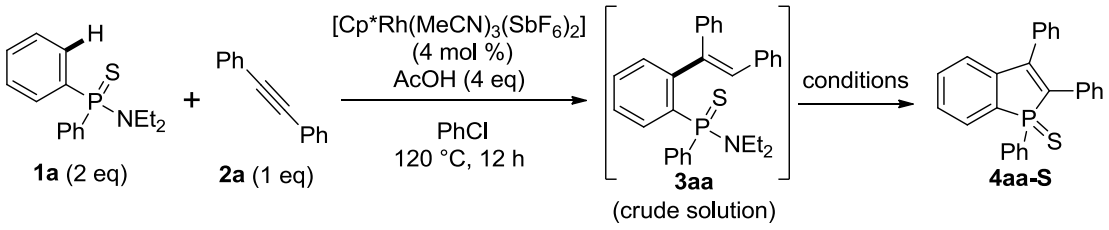


Table 5.2. Optimization Studies for Cyclization via 3aa



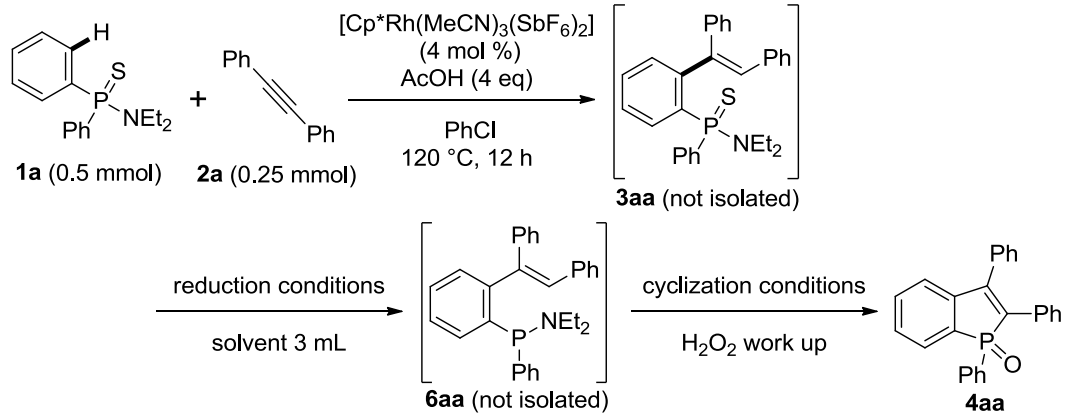
entry	conditions	NMR yield [a]
1	TfOH (ca. 20 eq), 100 °C, 12 h	trace / nd
2	Tf_2O (10 eq), 100 °C, 12 h	trace / nd
3	BF_3•OEt_2 (10 eq), 100 °C, 12 h	trace / nd
4	Me_3OBF_4 (10 eq), 100 °C, 12 h	trace / nd
5	4M HCl in dioxane (20 eq), 100 °C, 12 h	trace / nd
6	Me_3OBF_4 (10 eq), 100 °C, 12 h	trace / nd
7	$AlCl_3$ (10 eq), 80 °C, 12 h	trace / nd
8	$Cu(OTf)_2$ (10 eq), 80 °C, 12 h	decomp.
9	$Bi(OTf)_3$ (10 eq), 80 °C, 12 h	trace / nd
10	$POCl_3$ (10 eq), 100 °C, 12 h	trace / nd
11	TMSOTf (10 eq), 100 °C, 12 h	trace / nd
12	PCl_5 (10 eq), 100 °C, 12 h	trace / nd
13	AgOTf (2 eq), 80 °C, 12 h	trace / nd
14	$Al(OTf)_3$ (10 eq), 80 °C, 12 h	trace / nd
15	$Al(OTf)_3$ (10 eq), 2,6-lutidine (12 eq), 80 °C, 12 h	trace / nd

[a] Yield was estimated by ^{31}P NMR.

Taking these results, the author examined another cyclization route via P(III) intermediate. Thus, **3aa** was reduced to aminophosphine **6aa** before cyclization. Screening of the conditions for reduction and cyclization are summarized in Table 5.3. As a result, the desired **4aa** was obtained in 72% yield by 1) desulfurization of crude

3aa with MeOTf/$P(NMe_2)_3$,[12] 2) cyclization with TfOH at room temperature, 3) workup with H_2O_2 (entry 3). Employing other acids for the cyclization step slightly reduced the yield (entries 4-7). The desulfurization by radical conditions ($(Me_3Si)_3SiH$ / AIBN) was inefficient (entry 9).

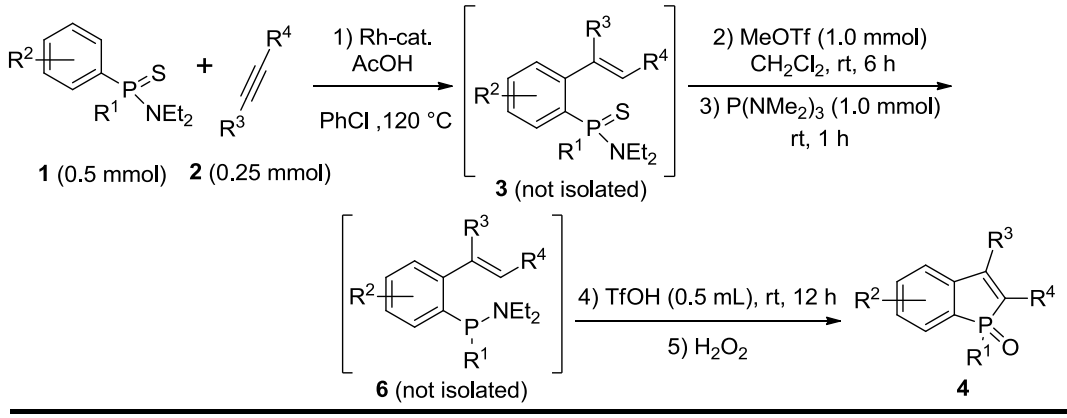
Table 5.3. Optimization Studies for Reduction/Cyclization via 3aa

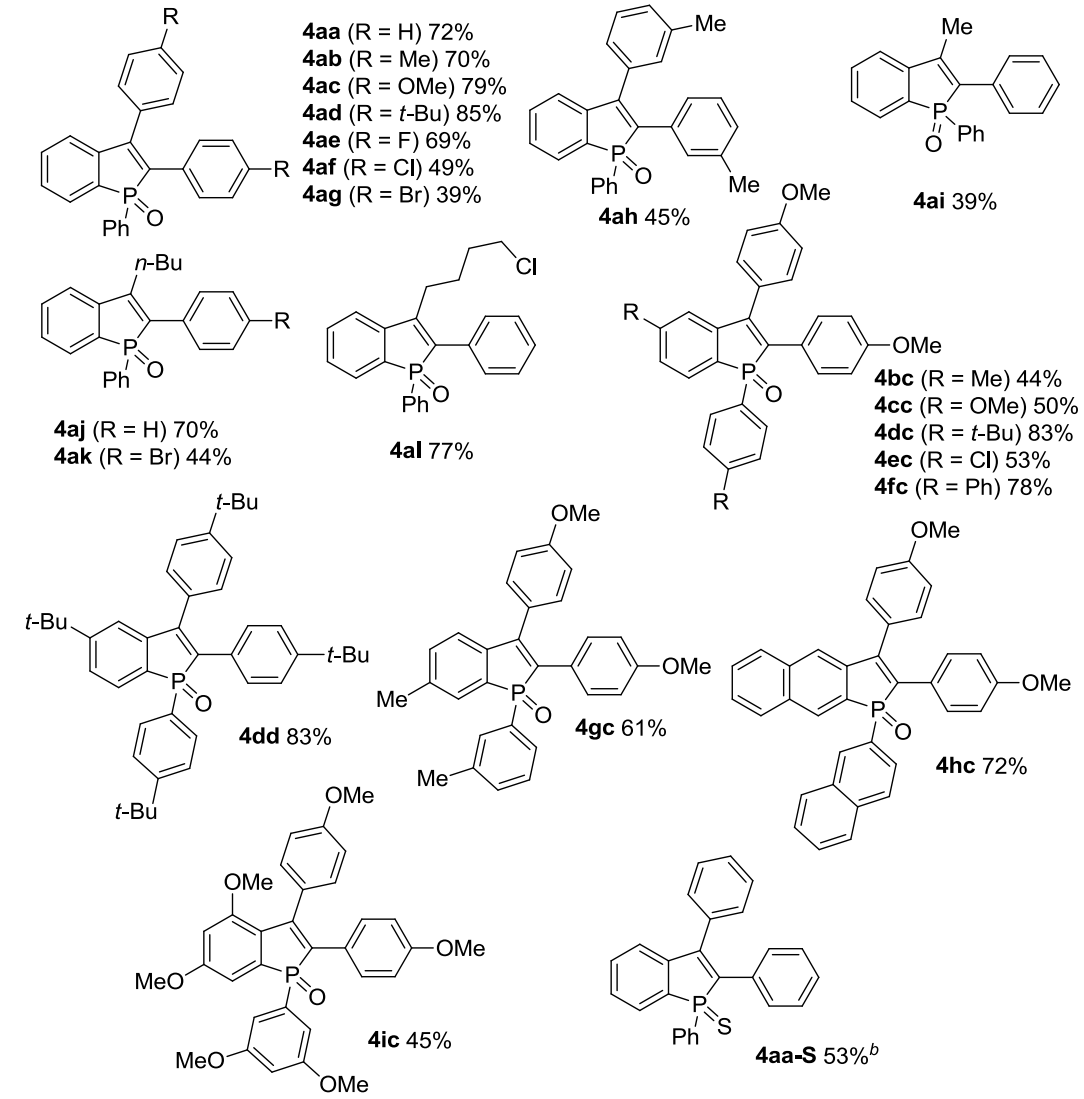


entry	reduction conditions	cyclization conditions	solvent	yield of **4a**(%)[a]
1	MeOTf 1.0 mmol, rt, 12 h then $P(NMe_2)_3$ 1.0 mmol, rt, 1 h	TfOH (0.5 mL), 100 °C, 12 h	DCE	53
2	MeOTf 1.0 mmol, rt, 12 h then $P(NMe_2)_3$ 1.0 mmol, rt, 1 h	TfOH (0.5 mL), 60 °C, 12 h	CH_2Cl_2	57
3	***MeOTf 1.0 mmol, rt, 6 h then $P(NMe_2)_3$ 1.0 mmol, rt, 1 h***	***TfOH (0.5 mL), rt, 12 h***	***CH_2Cl_2***	***72***
4	MeOTf 1.0 mmol, rt, 6 h then $P(NMe_2)_3$ 1.0 mmol, rt, 1 h	HCl (4M in dioxane, 1.4 mL) 60 °C, 12 h	CH_2Cl_2	61
5	MeOTf 1.0 mmol, rt, 6 h then $P(NMe_2)_3$ 1.0 mmol, rt, 1 h	$MeSO_3H$ (0.37 mL), 60 °C, 12 h	CH_2Cl_2	ca. 70
6	MeOTf 1.0 mmol, rt, 6 h then $P(NMe_2)_3$ 1.0 mmol, rt, 1 h	HCl (4M in dioxane, 1.4 mL) rt, 12 h	CH_2Cl_2	53
7	MeOTf 1.0 mmol, rt, 6 h then $P(NMe_2)_3$ 1.0 mmol, rt, 1 h	$MeSO_3H$ (0.37 mL), rt, 12 h	CH_2Cl_2	71
8	MeOTf 1.0 mmol, rt, 6 h then $P(NMe_2)_3$ 1.0 mmol, rt, 1 h	TfOH (0.1 mL), rt, 12 h	CH_2Cl_2	69
9	$(Me_3Si)_3SiH$ 0.5 mmol, AIBN 0.1 mmol, 80 °C, 12 h	-	toluene	-[b]

[a] Isolated yield based on the amount of alkyne **2a**. [b] Desulfulization reaction was not efficient.

Scheme 5.5. Synthesis of Benzo[*b*]phosphole Oxides 4 by Semi-One-Pot Protocol[a]

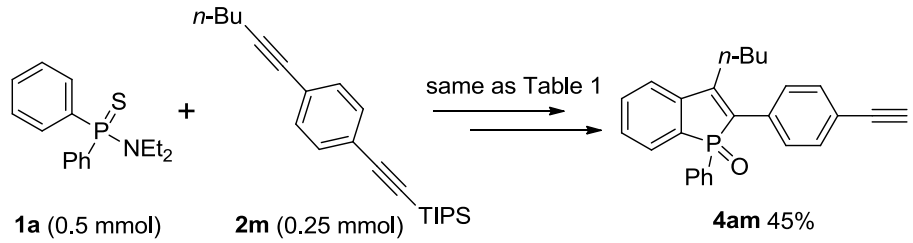




[a]Reaction conditions: 1) **1** (0.5 mmol), **2** (0.25 mmol), $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (0.01 mmol), AcOH (1.0 mmol) in PhCl (2 mL) at 120 °C under N_2 for 12 h; 2) MeOTf (1.0 mmol) in CH_2Cl_2 (3 mL), rt, 6 h; 3) $P(NMe_2)_3$ (1.0 mmol), rt, 1 h; 4) TfOH (0.5 mL), rt, 12 h; 5) H_2O_2 work up. See the Supporting Information for details. Isolated yields are shown based on the amount of **2**. [b] Work up was carried out using S_8 powder instead of H_2O_2.

The results for the synthesis of a series of benzo[*b*]phosphole oxides by the semi-one-pot protocol are summarized in Scheme 5.5. A variety of diarylacetylenes **2a**-**2h** smoothly coupled with **1a** to afford the corresponding benzo[*b*]phosphole oxides **4aa**-**4ah** in moderate to good yields. The reaction of a more electron-deficient alkyne, bis(4-ethoxycarbonylphenyl)acetylene, did not give any expected product at all. In the cases with unsymmetrical alkylarylacetylenes, the Rh-catalyzed hydroarylation reaction proceeded regioselectively to lead to 2-aryl-3-alkylbenzo[*b*]phosphole derivatives **4ai**-**4aj** exclusively. It is worth noting that this regioselectivity is complementary to that of the Ag(I)- or Mn(III)-mediated annulation reaction reported previously.[4,5] A dialkylacetylene, 4-octyne, did not couple with **1a** at all. Next, the reactions of substituted diarylthiophosphinamides were carried out. The *para*-substituted **1b**-**1f** reacted with **2c** or **2d** regioselectively to give **4bc**-**4fc** and **4dd** in good yields. 3-Methylphenyl and 2-naphtylthiophosphinamides, **1g** and **1h**, coupled with **2c** at the less hindered positions to form **4gc** and **4hc**. By post-treatment using sulfur powder in place of H_2O_2 in the reaction of **1a** with **2a**, benzo[*b*]phosphole sulfide **4aa-S** was selectively obtained in 53% yield.

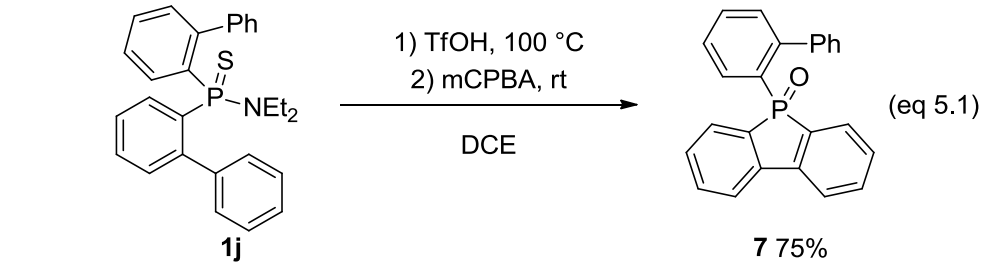
Scheme 5.6. Chemoselective Coupling Reaction of 1a with Diyne 2m

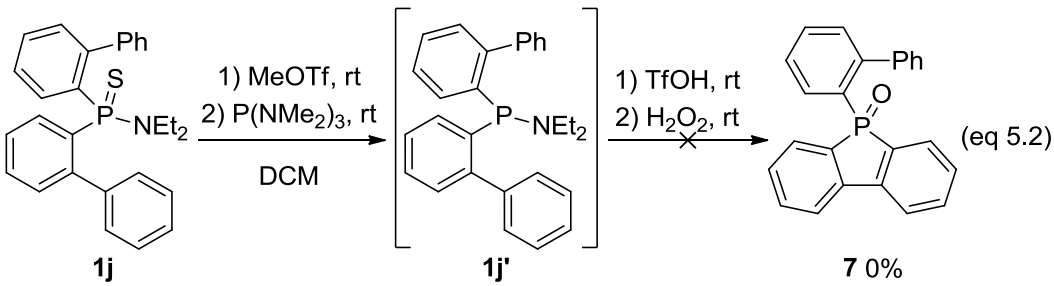


Under this new process, silyl acetylenes did not undergo the Rh-catalyzed hydroarylation with **1**. Utilizing the different reactivity of alkynes, the author attempted the chemoselective coupling reaction of **1a** with diyne **2m** (Scheme 5.6). Under standard conditions, the alkyl acetylene unit of **2m** over the silyl acetylene moiety selectively coupled with **1a** to form **4am** in 45% yield. The TIPS group was removed upon treatment with TfOH.

To gain some mechanistic information about the C-P bond-forming ring-closure step,

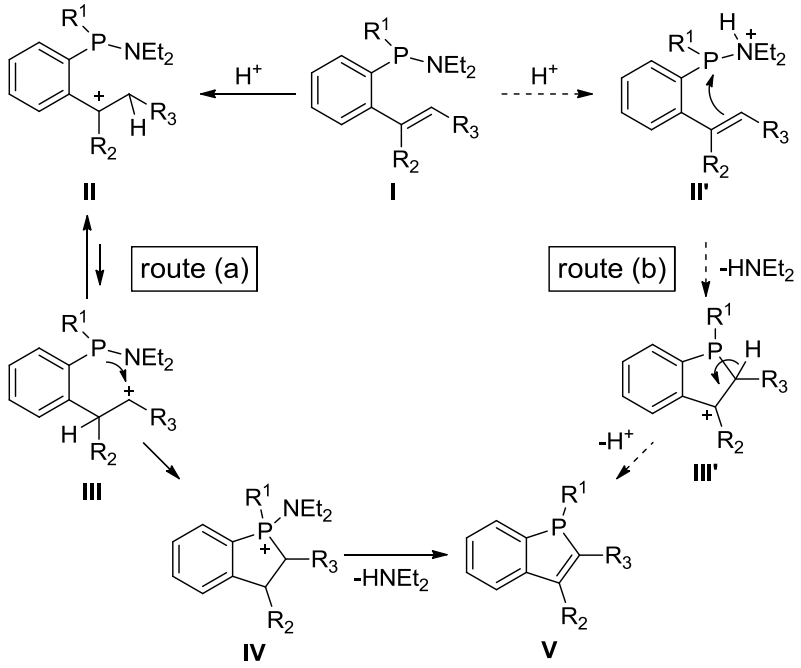
the author investigated the difference of reactivities between P(III) and P(V) intermediates using an aryl model substrate **1j**. Under previous conditions in Chapter 4 (TfOH, 100 °C),[9d] **1j** was smoothly converted to dibenzophosphole **7** in 75% yield (eq 5.1). In sharp contrast, the present ring-closing procedure involving P(III) species did not give **7** at all (eq 5.2). These results indicate that phospha-Friedel-Crafts type aromatic electrophilic substitution in P(III) intermediate **1j'** does not occur on its benzene ring under the present conditions. The lack of such a reactivity was also observed in related Lewis acid-promoted phospha-Friedel-Crafts reactions.[11a,c,e]





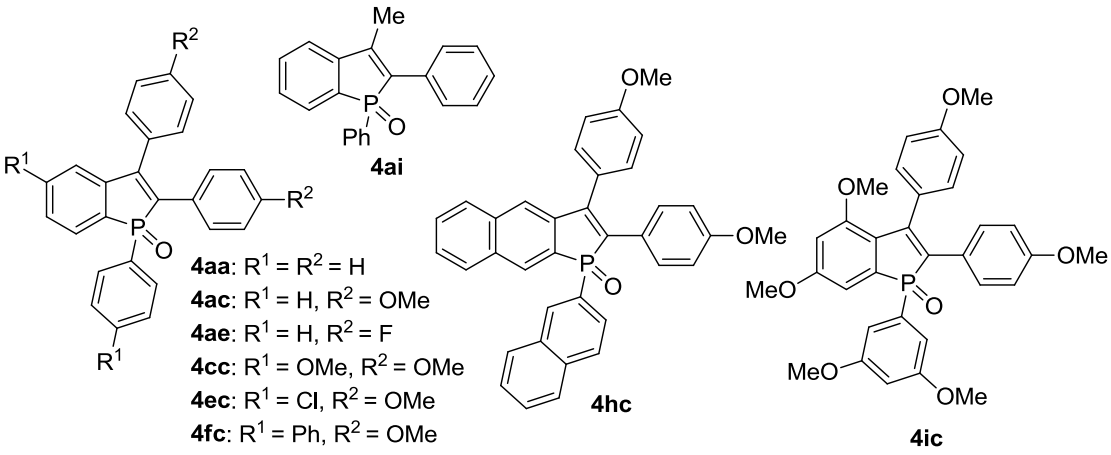
Based on the experimental results, plausible reaction pathways are depicted in Scheme 5.7. In route (a), TfOH protonates the alkenyl moiety of amino phosphine **I** (= **6**) to generate carbocations **II** and **III** which may exist in equilibrium with the major contribution of tertiary carbocation **II**. The phosphonium salt **5** in Scheme 5.4 may be generated from **3aa** via a similar tertiary carbocation. In the case of aminophosphine **I**, five-membered phosphonium salt **IV** selectively formed from the secondary carbocation **III** with "nucleophilic P center", after which diethylamine is eliminated to generate benzo[*b*]phosphole **V**.[3e] Although the other general phospha-Friedel-Crafts route from "electrophilic P center" in route (b)[6] cannot be completely excluded at this stage, route (a) seems to be the major route based on the control experiment shown in eq 5.2.

Scheme 5.7. Plausible Reaction Mechanism of C-P Bond-Forming Step



As expected, most of benzo[*b*]phosphole oxides obtained in this study showed remarkable fluorescence in their solid state.[13] Optical properties including absolute fluorescent quantum yields determined by using an integrating sphere system are summarized in Table 5.4 and Figure 5.1. 2,3-Diaryl products **4aa-4ie** exhibit relatively strong fluorescence in a range of 446 to 519 nm. Remarkably, 3-methyl **4ai** showed a blue-shifted emission in a high quantum yield (420 nm, $\Phi_F = 0.9$)

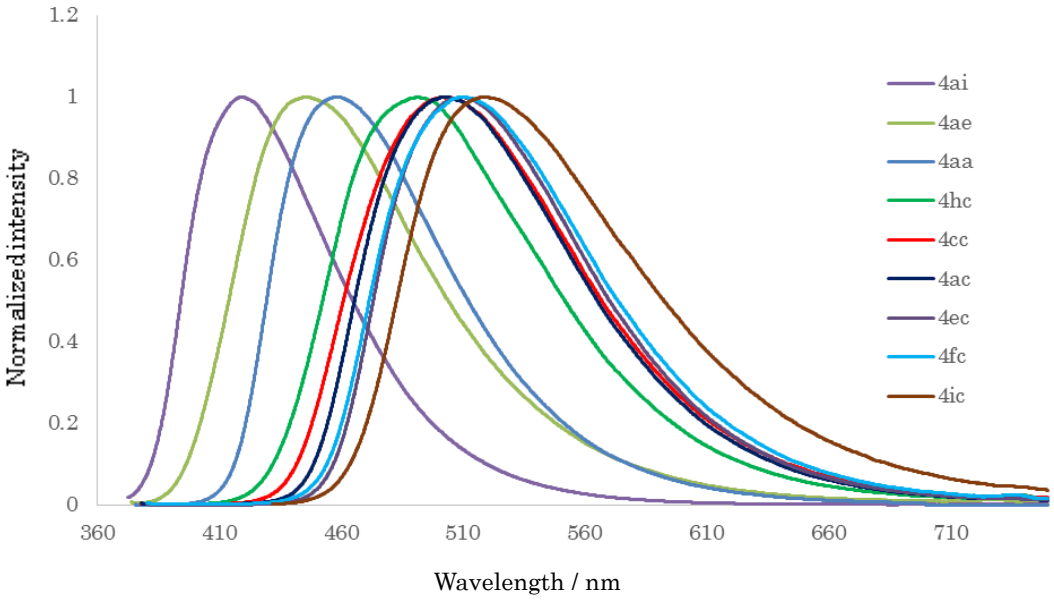
Table 5.4. Optical Properties of Benzo[*b*]phosphole Oxides 4



entry	compound	λ_{abs} [nm][b]	λ_{em} [nm][c]	Φ_F [%][d]
1	**4aa**	364	458	63
2	**4ac**	367	502	62
3	**4ae**	364	446	32
4	**4cc**	367	502	24
5	**4ec**	369	509	54
6	**4fc**	368	511	46
7	**4ai**	362	420	90
8	**4hc**	370	492	38
9	**4ic**	369	519	39

[a] In solid state. [b] UV/Vis absorption maxima are shown. [c] Excited at wave length of each absorption maximum. [d] Fluorescence quantum yields determined by a calibrated integrating sphere system.

Figure 5.1. Normalized Solid State Fluorescent Spectra of 4.



Summary

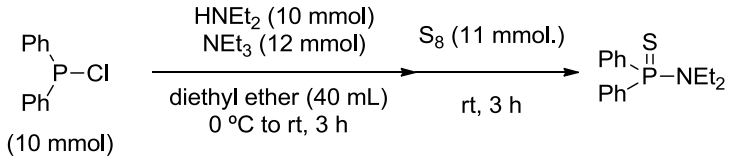
In chapter 5, the author has developed a new regioselective synthetic sequence leading to benzo[*b*]phosphole derivatives via rhodium(III)-catalyzed C-H alkenylation followed by intramolecular cyclization in a semi-one-pot manner. Thus, a range of functionalized benzo[*b*]phosphole oxides can be synthesized from readily available arylthiophosphinamides. This new methodology may contribute to expand the utility of benzophospholes in materials chemistry.

Experimental Section

General. ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded at 400, 100, 376 and 162 MHz for $CDCl_3$ solutions. HRMS data were obtained by APCI using a TOF mass spectrometer, unless noted. GC analysis was carried out using a silicon OV-17 column (i. d. 2.6 mm x 1.5 m). GC-MS analysis was carried out using a CBP-1 capillary column (i. d. 0.25 mm x 25 m). The structures of all products listed below were unambiguously determined by ^{1}H and ^{13}C NMR with the aid of NOE, COSY, HSQC, and HMBC experiments and X-ray crystal structure analysis.

Diarylthiophosphinamides **1a-1j** were prepared by the procedures described below. Alkynes **2b**-**2f**,[14] **2h**,[14] **2k,**[15] **2l,**[16] **2m**[17] were prepared according to published procedures. PhCl and DCE were distilled from CaH_2 and stored over MS4A. CH_2Cl_2 was dried over MS4A. Other starting materials were commercially available and used as received. The following experimental procedures may be regarded as typical in methodology and scale.

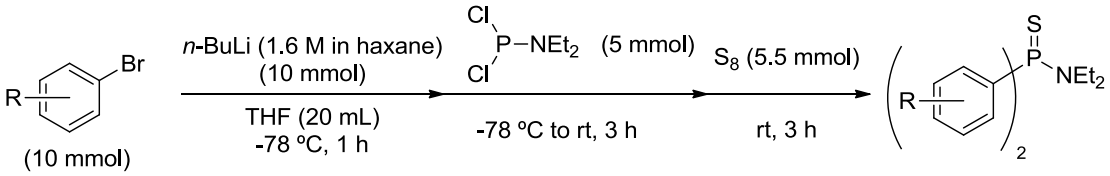
Preparation of Diphenylthiophosphinamide 1a



To a solution of chlorodiphenylphosphine (10 mmol, 2.21 g) in dry ether (40 mL) at 0 °C under N_2 atmosphere, triethylamine (12 mmol, 1.67 mL), and diethylamine (10 mmol, 1.03 mL) were

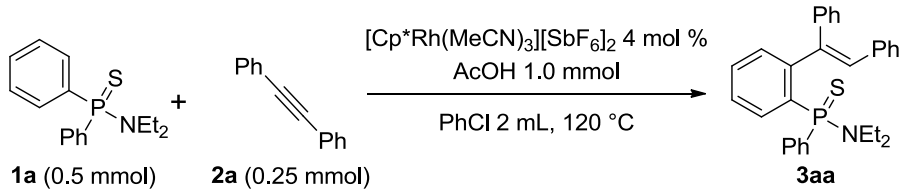
slowly added. The reaction mixture was warmed to room temperature and stirred for 3 h. To this mixture, S_8 (11 mmol, 353 mg) was added and vigorously stirred for 3 h. Then, insoluble solids were filtered off using Celite pad and the resulting solution was washed with brine. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The crude mixture was purified by column chromatography on silica gel with hexane/ethyl acetate (10:1, v/v) to afford the desired product as a colorless solid (2.77 g, 96%).

Preparation of Diarylthiophosphinamides 1b-1j



To a solution of an aryl bromide (10 mmol) in dry THF (20 mL) at -78 °C under N_2 atmosphere, *n*-BuLi (1.6 M in hexane, 10 mmol, 6.25 mL) was slowly added. The reaction mixture was stirred for 30 min at this temperature. To the resulting mixture, Cl_2PNEt_2 (5 mmol, 870 mg) was then added by a syringe. Then, the reaction mixture was slowly warmed to room temperature with an additional 3 h stirring. To this mixture, S_8 (7.5 mmol, 240 mg) was added and stirred for 3 h. The resulting solution was quenched with water, extracted with ethyl acetate, and the organic layer was dried over Na_2SO_4 and concentrated in vacuo. The crude mixture was purified by column chromatography on silica gel with hexane/ethyl acetate to afford product. Further purification was performed by recrystallization if necessary.

Rh(III)-Catalyzed Direct Alkenylation of 1a with 2a (entry 8 in Table 5.1).

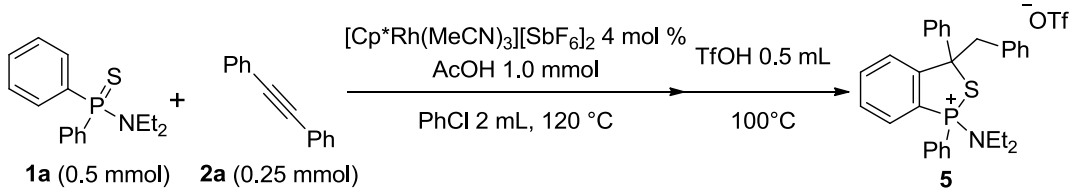


1a (0.5 mmol) **2a** (0.25 mmol) **3aa**

In a 10 mL sealable tube, **1a** (149.7 mg, 0.5 mmol), **2a** (44.6 mg, 0.25 mmol), and $[Cp^*Rh(MeCN)_3(SbF_6)_2]$ (8.3 mg, 0.01 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, PhCl (2 mL) and AcOH (57 μL, 1.0 mmol) were added by a syringe. The reaction mixture was heated at 120 °C in an oil bath for 12 h. After cooling, the reaction was quenched with 10 mL of sat. $NaHCO_3$ and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. Purification of the residue by

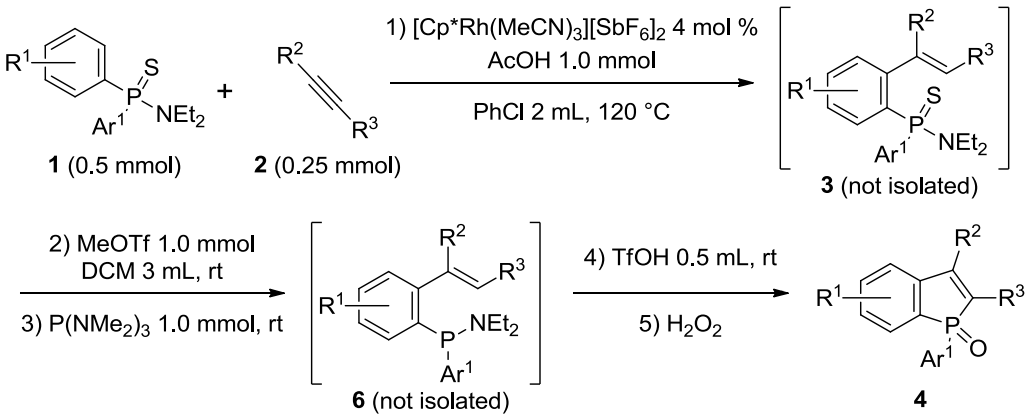
column chromatography on silica gel gave **3aa** (106 mg, 90%). The single crystal for X-ray analysis was obtained from DCM by slow evaporation crystal growth technique.

Formation of Phosphonium Salt 5 (Scheme 5.4).



In a 10 mL sealable tube, **1a** (149.7 mg, 0.5 mmol), **2a** (44.6 mg, 0.25 mmol), and $[Cp^*Rh(MeCN)_3(SbF_6)_2]$ (8.3 mg, 0.01 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, PhCl (2 mL) and AcOH (57 μL, 1.0 mmol) were added by a syringe. The reaction mixture was heated at 120 °C in an oil bath for 12 h. After cooling, TfOH (0.5 mL) was added by a syringe and heated at 100 °C again for 12 h. Then, the reaction was quenched with 10 mL of sat. $NaHCO_3$ and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. The resulting crude mixture was purified by preparative GPC to give product **5** (diastereomeric mixture, 113 mg, 73%). Recrystallization from DCM/hexane afforded the major diastereomer ($2S_P$*,5*R**).

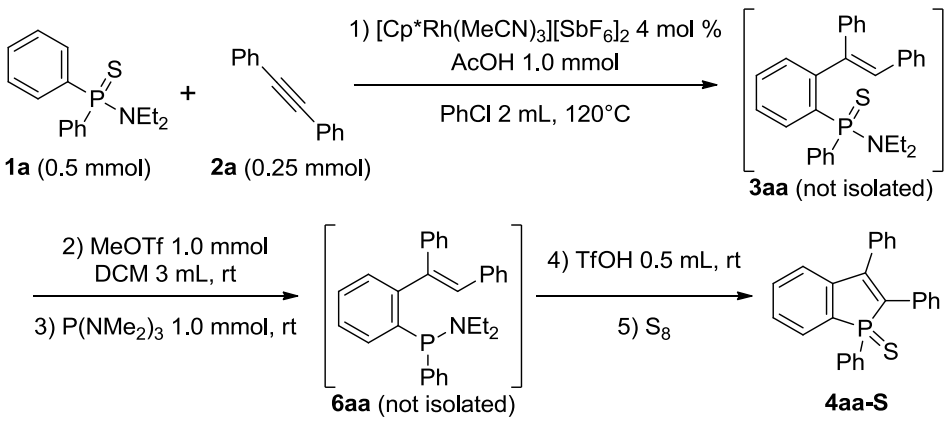
Synthesis of Benzo[*b*]phosphole Derivatives by Semi-One-Pot Rh-Catalyzed Coupling and Formal Phospha-Friedel-Crafts Reactions (Schemes 5.5).



In a 10 mL sealable tube, **1** (0.5 mmol), **2** (0.25 mmol), and $[Cp^*Rh(MeCN)_3(SbF_6)_2]$ (8.3 mg, 0.01 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, PhCl (2 mL) and AcOH (57 μL, 1.0 mmol) were added by a syringe. The reaction mixture was heated at 120 °C in an oil bath for 12 h. After cooling, the reaction was quenched with 10 mL of sat. $NaHCO_3$ and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and

volatiles were removed in vacuo. The residue was dissolved to dry DCM (3 mL) and transferred in 20 mL two-necked flask with magnetic stir bar under N_2 atmosphere. MeOTf (1.0 mmol, 0.11 mL) was added by a syringe and stirred at room temperature for 6 h. Then, $P(NMe_2)_3$ (1.0 mmol, 0.18 mL) was added by a syringe (exothermic reaction was observed). After additional stirring for 1 h at room temperature, TfOH (0.5 mL) was added by a syringe and reacted for 12 h at this temperature. After that, the resulting mixture was neutralized by sat. $NaHCO_3$. To this mixture, H_2O_2 (30% aqueous solution, ca. 0.5 mL) was added and stirred for 15 min. The reaction mixture was quenched by sat. $Na_2S_2O_3$, and extracted by DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. Purification of the residue by column chromatography on silica gel gave product.

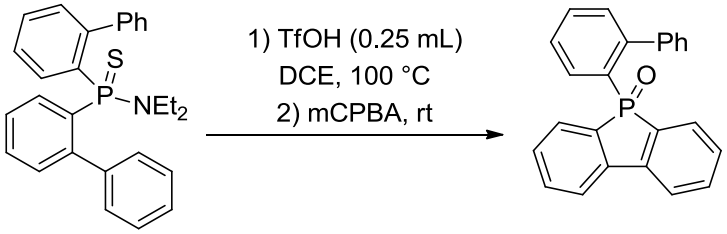
Synthesis of Benzo[*b*]phosphole Sulfide 4aa-S (Schemes 5.5).



In a 10 mL sealable tube, **1a** (149.7 mg, 0.5 mmol), **2a** (44.6 mg, 0.25 mmol), and $[Cp^*Rh(MeCN)_3(SbF_6)_2]$ (8.3 mg, 0.01 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, PhCl (2 mL) and AcOH (57 μL, 1.0 mmol) were added by a syringe. The reaction mixture was heated at 120 °C in an oil bath for 12 h. After cooling, the reaction was quenched with 10 mL of sat. $NaHCO_3$ and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. The residue was dissolved to dry DCM (3 mL) and transferred in 20 mL two-necked flask with magnetic stir bar under N_2 atmosphere. MeOTf (1.0 mmol, 0.11 mL) was added by a syringe and stirred at room temperature for 6 h. Then, $P(NMe_2)_3$ (1.0 mmol, 0.18 mL) was added by a syringe (exothermic reaction was observed). After additional stirring for 1 h at room temperature, TfOH (0.5 mL) was added by a syringe and reacted for 12 h at this temperature. After that, the resulting mixture was neutralized by sat. $NaHCO_3$. To this mixture, S_8 powder (32 mg, 1.0 mmol) was added and stirred for 1 h. The reaction mixture was extracted by DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles

were removed in vacuo. Purification of the residue by column chromatography on silica gel and preparative GPC gave product **4aa-S** (52.1 mg, 53%).

Synthesis of Dibenzo[*b*]phosphole Oxide 7 (eq 5.1).



1j (0.25 mmol) **7**

In a 10 mL sealable tube, **1j** (110.4 mg, 0.25 mmol) was placed with a magnetic stir bar under N_2 atmosphere. Then, DCE (2 mL) and TfOH (0.25 mL) were added by a syringe. The reaction mixture was heated at 100 °C in an oil bath for 12 h. After cooling, the reaction was quenched with sat. $NaHCO_3$ and diluted with DCM (ca. 5 mL). Then, mCPBA (ca. 70wt%, 130 mg, ca. 0.5 mmol) was added and resulting biphasic solution was vigorously stirred for 15 min. After checking the full conversion of phosphole sulfide on TLC, the reaction mixture was quenched with sat. $Na_2S_2O_3$ and extracted with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed in vacuo. The residue was purified by column chromatography on silica gel gave product.

Characterization Data of Products

(*E*)-*P*-(2-(1,2-diphenylvinyl)phenyl)-*N*,*N*-diethyl-*P*-phenylthiophosphinamide (3aa): colorless solid, mp: 104-106 °C, 106 mg (90%); column chromatography eluent: hexane-ethyl acetate (10:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (t, J = 7.1 Hz, 6H), 3.00-3.23 (m, 4H), 6.19 (s, 1H), 6.84-6.90 (m, 2H), 7.05-7.41 (m, 14H), 7.76 (dd, J = 13.4, 7.2 Hz, 2H), 7.98-8.05 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8 (d, J = 4.2 Hz), 40.9 (d, J = 3.3 Hz), 126.4 (d, J = 11.5 Hz), 126.6, 127.1, 127.6, 127.7, 128.0 (d, J = 12.8 Hz), 129.5, 130.6 (d, J = 2.6 Hz), 130.7 (d, J = 2.8 Hz), 131.2, 131.7 (d, J = 10.7 Hz), 132.5, 132.9 (d, J = 2.1 Hz), 133.0, 133.3 (d, J = 101.1 Hz), 135.1 (d, J = 99.7 Hz), 137.2, 140.3, 140.4 (d, J = 3.6 Hz), 149.3 (d, J = 11.9 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 67.5; HRMS *m/z* calcd for $C_{30}H_{31}NPS$ ($M+H^+$) 468.1909, found 468.1911.

1,2,3-Triphenyl-1*H*-phosphindole 1-oxide (4aa)[4a]: colorless form, 68 mg (72%); column chromatography eluent: hexane-ethyl acetate (1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07-7.11 (m, 3H), 7.19-7.25 (m, 3H), 7.31-7.51 (m, 10H), 7.68-7.81 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 124.0 (d, J = 10.9 Hz), 127.8, 128.2, 128.7 (d, J = 12.4 Hz), 128.8-129.2 (m, 6C, overlapped), 130.0 (d, J = 99.1 Hz), 131.0 (d, J = 10.7 Hz), 132.1 (d, J = 105.1 Hz), 132.2 (d, J = 2.9 Hz), 132.7 (d, J = 10.1 Hz), 132.9 (d, J = 1.4 Hz), 134.27 (d, J = 14.7 Hz), 134.30 (d, J = 95.1 Hz), 143.8 (d, J = 26.8 Hz), 150.0 (d, J = 21.1 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 39.0; HRMS *m/z* calcd for $C_{26}H_{20}PO$ ($M+H^+$) 379.1246, found 379.1245.

2,3-Bis(4-methylphenyl)-1-phenyl-1*H*-phosphindole 1-oxide (4ab) [4a]: colorless solid, 71 mg (70%); column chromatography eluent: hexane-ethyl acetate (1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 3H), 2.41 (s, 3H), 6.90 (d, J = 2.4 Hz, 2H), 7.15 (d, J = 7.4 Hz, 2H), 7.18-7.25 (m, 5H), 7.30-7.51 (m, 5H), 7.68 (dd, J = 9.7, 6.6 Hz, 1H), 7.72-7.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 21.5, 123.9 (d, J = 10.7 Hz), 128.82 (d, J = 12.3 Hz), 128.84 (d, J = 9.0 Hz), 128.92 (d, J = 5.9 Hz), 128.95, 128.97, 129.02, 129.7, 129.8 (d, J = 8.1 Hz), 130.3 (d, J = 80.7 Hz), 131.0 (d, J = 10.7 Hz), 131.4 (d, J = 15.2 Hz), 132.0 (d, J = 2.7 Hz), 132.1 (d, J = 104.9 Hz), 132.8 (d, J = 1.5 Hz), 133.7 (d, J = 95.3 Hz), 137.7, 138.5, 144.1 (d, J = 27.0 Hz), 149.4 (d, J = 21.5 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 39.1; HRMS *m/z* calcd for $C_{28}H_{24}PO$ ($M+H^+$) 407.1559, found 407.1558.

2,3-Bis(4-methoxyphenyl)-1-phenyl-1*H*-phosphindole 1-oxide (4ac)[4a]: pale yellow solid, 86 mg (79%); column chromatography eluent: dichloromethane-ethyl acetate (2:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (s, 3H), 3.86 (s, 3H), 6.60-6.69 (m, 2H), 6.97 (d, J = 8.8 Hz, 2H), 7.18-7.30 (m, 5H), 7.31-7.51 (m, 5H), 7.68 (dd, J = 9.0, 7.2, Hz, 1H), 7.72-7.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.1, 55.3, 113.8, 114.5, 123.7 (d, J = 10.9 Hz), 125.3 (d, J = 10.2 Hz), 126.6 (d, J = 15.4 Hz), 128.7 (d, J = 10.1 Hz), 128.8 (d, J = 11.9 Hz), 128.9 (d, J = 8.9 Hz), 130.3 (d, J = 98.6 Hz), 130.4 (d, J = 5.9 Hz), 130.5, 131.0 (d, J = 10.5 Hz), 132.0 (d, J = 104.9 Hz), 132.4 (d, J = 2.8 Hz), 137.8 (d, J = 1.4 Hz), 133.1 (d, J = 95.9 Hz), 144.2 (d, J = 26.9 Hz), 148.1 (d, J = 21.8 Hz), 159.1, 159.8; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 39.1; HRMS *m/z* calcd for $C_{28}H_{24}PO_3$ ($M+H^+$) 439.1458, found 439.1458.

2,3-Bis(4-(tert-butyl)phenyl)-1-phenyl-1*H*-phosphindole 1-oxide (4ad)[5c]: colorless solid, 104 mg (85%); column chromatography eluent: hexane-ethyl acetate (1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 9H), 1.38 (s, 9H), 7.08 (d, J = 6.6 Hz, 2H), 7.11-7.23 (m, 3H), 7.26-7.54 (m, 9H), 7.67 (dd,

J = 9.0, 7.2 Hz, 1H), 7.75-7.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1, 31.4, 34.5, 34.8, 124.0 (d, J = 10.9 Hz), 125.2, 125.9, 128.67, 128.68, 128.70 (d, J = 8.1 Hz), 128.8 (d, J = 10.2 Hz), 128.9 (d, J = 12.3 Hz), 129.7 (d, J = 10.1 Hz), 130.6 (d, J = 98.1 Hz), 131.0 (d, J = 10.5 Hz), 131.6 (d, J = 15.4 Hz), 132.0 (d, J = 2.6 Hz), 132.2 (d, J = 105.4 Hz), 132.7 (d, J = 7.2 Hz), 133.5 (d, J = 95.5 Hz), 144.2 (d, J = 27.2 Hz), 149.3 (d, J = 21.4 Hz), 150.7, 151.7; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 39.2; HRMS *m/z* calcd for $C_{34}H_{36}PO$ ($M+H^+$) 491.2498, found 491.2498.

2,3-Bis(4-fluorophenyl)-1-phenyl-1*H*-phosphindole 1-oxide (4ae)[5c] colorless solid, 72 mg (64%); column chromatography eluent: hexane-ethyl acetate (1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77-6.86 (m, 2H), 7.10-7.18 (m, 2H), 7.18-7.24 (m, 3H), 7.27-7.35 (m, 2H), 7.36-7.44 (m, 3H), 7.44-7.54 (m, 2H), 7.67-7.78 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.6 (d, J = 21.4 Hz), 116.3 (d, J = 21.5 Hz), 123.9 (d, J = 10.7 Hz), 128.6 (dd, J = 10.6, 3.0 Hz), 129.0 (d, J = 12.2 Hz), 129.3 (dd, J = 10.4, 8.1 Hz), 129.5 (d, J = 99.7 Hz), 129.8 (d, J = 15.1, 3.5 Hz), 130.8 (dd, J = 8.2, 5.6 Hz), 130.92 (d, J = 10.4 Hz), 130.98 (d, J = 8.0 Hz), 130.99 (d, J = 7.9 Hz), 131.8 (d, J = 105.2 Hz), 132.4 (d, J = 2.8 Hz), 133.1 (d, J = 1.9 Hz), 133.9 (d, J = 95.4 Hz), 143.5 (d, J = 26.7 Hz), 148.8 (d, J = 22.0 Hz), 162.3 (dd, J = 247.1, 1.2 Hz), 162.8 (d, J = 247.5 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 38.8; HRMS *m/z* calcd for $C_{26}H_{18}F_2OP$ ($M+H^+$) 415.1058, found 415.1059.

2,3-Bis(4-chlorophenyl)-1-phenyl-1*H*-phosphindole 1-oxide (4af)[4a]: colorless solid, 55 mg (49%); column chromatography eluent: hexane-ethyl acetate (1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06-7.14 (m, 2H), 7.14-7.22 (m, 3H), 7.23-7.31 (m, 2H), 7.37-7.54 (m, 7H), 7.66-7.78 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 123.9 (d, J = 10.8 Hz), 128.8, 128.9 (d, J = 99.8 Hz), 129.0 (d, J = 12.4 Hz), 129.4 (d, J = 9.6 Hz), 129.49, 129.51 (d, J = 10.5 Hz), 130.2 (d, J = 5.7 Hz), 130.4, 130.91 (d, J = 10.6 Hz), 130.94 (d, J = 10.2 Hz), 131.7 (d, J = 92.3 Hz), 132.4 (d, J = 1.5 Hz), 132.5 (d, J = 2.8 Hz), 133.1 (d, J = 1.7 Hz), 134.0 (d, J = 94.8 Hz), 134.1, 135.0, 143.2 (d, J = 26.3 Hz), 149.0 (d, J = 21.5 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 38.8; HRMS *m/z* calcd for $C_{26}H_{18}Cl_2OP$ ($M+H^+$) 447.0467, found 447.0469.

2,3-Bis(4-bromophenyl)-1-phenyl-1*H*-phosphindole 1-oxide (4ag)[4a]: colorless solid, 48 mg (36%); column chromatography eluent: hexane-ethyl acetate (1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (dd, J = 8.6, 1.0 Hz, 2H), 7.12-7.29 (m, 5H), 7.37-7.54 (m, 5H), 7.59 (d, J = 8.5 Hz, 2H), 7.65-7.78 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 122.4 (d, J = 1.3 Hz), 123.2, 123.9 (d, J = 10.8 Hz), 129.0, (d, J = 12.3 Hz), 129.2 (d, J = 99.8 Hz), 129.4 (d, J = 9.6 Hz), 129.5 (d, J = 10.5 Hz),

130.5 (d, J = 5.4 Hz), 130.7, 130.9 (d, J = 10.8 Hz), 131.3 (d, J = 4.7 Hz), 131.7, 131.9 (d, J = 90.7 Hz), 132.4, 132.5 (d, J = 3.1 Hz), 132.7 (d, J = 14.8 Hz), 133.1 (d, J = 1.5 Hz), 134.0 (d, J = 94.9 Hz), 143.1 (d, J = 26.3 Hz), 149.1 (d, J = 21.7 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$) δ 38.8; HRMS *m/z* calcd for $C_{26}H_{18}Br_2OP$ ($M+H^+$) 534.9457, found 534.9432.

2,3-Bis(3-methylphenyl)-1-phenyl-1*H*-phosphindole 1-oxide (4ah)[5a]: colorless solid, 45 mg (45%); column chromatography eluent: hexane-ethyl acetate (1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.12 (s, 3H), 2.36 (m, 3H), 6.88-7.03 (m, 3H), 7.07-7.17 (m, 3H), 7.17-7.24 (m, 2H), 7.28-7.52 (m, 6H), 7.69 (dd, J = 9.0, 7.2, Hz, 1H), 7.73-7.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 21.5, 124.0 (d, J = 10.9 Hz), 126.1, 126.2 (d, J = 5.9 Hz), 128.0, 128.6, 128.8, 128.87 (d, J = 8.8 Hz), 128.88, 129.0 (d, J = 2.6 Hz), 129.3, 129.4, 129.6 (d, J = 5.5 Hz), 130.2 (d, J = 98.9 Hz), 131.0 (d, J = 10.7 Hz), 132.06 (d, J = 2.7 Hz), 132.12 (d, J = 105.4 Hz), 132.6 (d, J = 8.9 Hz), 132.8 (d, J = 1.8 Hz), 137.7, 138.6, 134.0 (d, J = 94.6 Hz), 134.5 (d, J = 5.9 Hz), 144.0 (d, J = 27.0 Hz), 150.0 (d, J = 21.3 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$) δ 39.1; HRMS *m/z* calcd for $C_{28}H_{24}OP$ ($M+H^+$) 407.1559, found 407.1549.

3-Methyl-1,2-diphenyl-1*H*-phosphindole 1-oxide (4ai): colorless solid, mp: 199-200 °C, 35 mg (39%); column chromatography eluent: DCM-ethyl acetate (1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.32 (d, J = 2.4 Hz, 3H), 7.24-7.51 (m, 10H), 7.57 (dddd, J = 7.6, 7.6, 1.3, 1.3 Hz, 1H), 7.62-7.68 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6 (d, J = 13.0 Hz), 122.0 (d, J = 11.0 Hz), 127.9 (d, J = 1.0 Hz), 128.6, 128.67 (d, J = 9.3 Hz), 128.70 (d, J = 12.1 Hz), 128.9 (d, J = 5.0 Hz), 129.0 (d, J = 10.6 Hz), 129.9 (d, J = 99.1 Hz), 131.1 (d, J = 10.7 Hz), 131.99 (d, J = 104.9 Hz), 132.01 (d, J = 2.8 Hz), 133.0 (d, J = 1.2 Hz), 133.2 (d, J = 11.0 Hz), 134.4 (d, J = 98.2 Hz), 144.0 (d, J = 27.8 Hz), 147.0 (d, J = 21.0 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 38.1; HRMS *m/z* calcd for $C_{21}H_{18}OP$ ($M+H^+$) 317.1090, found 317.1090.

3-Butyl-1,2-diphenyl-1*H*-phosphindole 1-oxide (4aj): colorless gum, 63 mg (70%); column chromatography eluent: DCM-ethyl acetate (4:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (t, J = 7.3 Hz, 3H), 1.34-1.50 (m, 2H), 1.57-1.75 (m, 2H), 2.65-2.71 (m, 2H), 7.24-7.40 (m, 8H), 7.43-7.51 (m, 2H), 7.56 (dddd, J = 7.6, 7.6, 1.4, 1.4 Hz, 1H), 7.60-7.68 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 22.9, 26.9 (d, J = 1.2 Hz), 31.0 (d, J = 1.2 Hz), 122.3 (d, J = 11.1 Hz), 127.8, 128.60, 128.61, 128.71 (d, J = 8.8 Hz), 128.908, 129.13 (d, J = 19.6 Hz), 129.8 (d, J = 98.9 Hz), 131.0 (d, J = 10.7 Hz), 132.0 (d, J = 2.8 Hz), 132.4 (d, J = 104.4 Hz), 132.9, 133.2 (d, J = 9.7 Hz), 134.2 (d, J = 96.8

Hz), 143.2 (d, J = 28.2 Hz), 151.6 (d, J = 19.6 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 38.3; HRMS *m/z* calcd for $C_{24}H_{24}OP$ ($M+H^+$) 359.1559, found 359.1556.

2-(4-Bromophenyl)-3-butyl-1-phenyl-1*H*-phosphindole 1-oxide (4ak): colorless gum, 49 mg (44%); column chromatography eluent: hexane-ethyl acetate (1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, J = 7.3 Hz, 3H), 1.32-1.74 (m, 4H), 2.60-2.72 (m, 2H), 7.18-7.22 (m, 2H), 7.33-7.52 (m, 7H), 7.54-7.68 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 22.9, 27.0 (d, J = 11.8 Hz), 31.0, 122.1 (d, J = 1.5 Hz), 122.5 (d, J = 11.2 Hz), 128.8 (d, J = 12.2 Hz), 129.0 (d, J = 9.6 Hz), 129.1 (d, J = 10.7 Hz), 129.4 (d, J = 99.2 Hz), 130.2 (d, J = 4.6 Hz), 131.0 (d, J = 10.7 Hz), 131.6, 132.14 (d, J = 3.1 Hz), 132.18 (d, J = 9.3 Hz), 132.21 (d, J = 105.3 Hz), 133.0 (d, J = 1.5 Hz), 133.2 (d, J = 97.5 Hz), 143.0 (d, J = 27.7 Hz), 152.1 (d, J = 19.4 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 38.1; HRMS *m/z* calcd for $C_{24}H_{23}BrOP$ ($M+H^+$) 437.0664, found 437.0661.

3-(4-Chlorobutyl)-1,2-diphenyl-1*H*-phosphindole 1-oxide (4al): colorless gum, 76 mg (77%); column chromatography eluent: DCM-ethyl acetate (2:1 to 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.78-1.91 (m, 4H), 2.68-2.75 (m, 2H), 3.46-3.53 (m, 2H), 7.26-7.42 (m, 8H), 7.44-7.53 (m, 2H), 7.55-7.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.7 (d, J = 1.8 Hz), 26.1 (d, J = 12.3 Hz), 32.1, 44.2, 122.3 (d, J = 11.0 Hz), 128.0, 128.6 (d, J = 4.5 Hz), 128.732, 128.735 (d, J = 12.3 Hz), 129.070 (d, J = 19.7 Hz), 129.074, 129.6 (d, J = 99.0 Hz), 131.0 (d, J = 10.2 Hz), 132.1 (d, J = 2.7 Hz), 132.3 (d, J = 104.6 Hz), 132.99 (d, J = 7.8 Hz), 133.04, 135.2 (d, J = 96.1 Hz), 142.9 (d, J = 27.8 Hz), 150.6 (d, J = 19.8 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 38.1; HRMS *m/z* calcd for $C_{24}H_{23}ClOP$ ($M+H^+$) 393.1170, found 393.1166.

2,3-Bis(4-methoxyphenyl)-5-methyl-1-(4-methylphenyl)-1*H*-phosphindole 1-oxide (4bc): pale yellow solid, 51 mg (44%); column chromatography eluent: hexane-ethyl acetate (1:1 to 1:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.327 (s, 3H), 2.331 (s, 3H), 3.69 (s, 3H), 3.87 (s, 3H), 6.60-6.67 (m, 2H), 6.94-7.03 (m, 3H), 7.10-7.29 (m, 7H), 7.55 (dd, J = 9.5, 7.4 Hz, 1H), 7.63 (dd, J = 12.3, 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 21.9, 55.1, 55.3, 113.7, 114.5, 124.5 (d, J = 11.1 Hz), 125.6 (d, J = 10.1 Hz), 126.8 (d, J = 15.4 Hz), 127.2 (d, J = 101.2 Hz), 128.8 (d, J = 9.7 Hz), 129.0 (d, J = 106.1 Hz), 129.2 (d, J = 10.9 Hz), 129.6 (d, J = 12.6 Hz), 130.4 (d, J = 5.9 Hz), 130.5, 131.0 (d, J = 10.8 Hz), 133.7 (d, J = 95.7 Hz), 142.4 (d, J = 2.8 Hz), 143.3 (d, J = 1.7 Hz), 144.5 (d, J = 27.1 Hz), 147.9 (d, J = 21.7 Hz), 159.0, 159.6; $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 39.0; HRMS *m/z* calcd for $C_{30}H_{28}O_3P$ ($M+H^+$) 467.1771, found 467.1770.

5-Methoxy-1,2,3-tris(4-methoxyphenyl)-1H-phosphindole 1-oxide (4cc): yellow solid, 62 mg (50%); column chromatography eluent: hexane-ethyl acetate (2:1 to 1:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (s, 3H), 3.78 (s, 3H), 3.79 (s, 3H), 3.85 (s, 3H), 6.63 (d, J = 8.8 Hz, 2H), 6.74 (dd, J = 2.3, 2.3 Hz, 1H), 6.81 (ddd, J = 8.0, 2.7, 2.7 Hz, 1H), 6.89 (dd, J = 8.7, 2.1 Hz, 2H), 6.95 (d, J = 8.7 Hz, 2H), 7.20 (dd, J = 8.8, 0.8 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 7.59 (dd, J = 9.0, 8.3 Hz, 1H), 7.66 (dd, J = 11.8, 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.1, 55.2, 55.3, 55.5, 111.1 (d, J = 11.8 Hz), 112.4 (d, J = 11.6 Hz), 113.7, 114.41 (d, J = 13.2 Hz), 114.45, 121.5 (d, J = 105.9 Hz), 123.2 (d, J = 111.3 Hz), 125.6 (d, J = 10.1 Hz), 126.6 (d, J = 15.2 Hz), 130.3 (d, J = 9.5 Hz), 130.4 (d, J = 5.8 Hz), 130.5, 132.8 (d, J = 11.8 Hz), 135.0, (d, J = 95.6 Hz), 146.7 (d, J = 28.6 Hz), 147.0 (d, J = 21.2 Hz), 159.0, 159.7, 162.6 (d, J = 2.9 Hz), 163.6 (d, J = 2.6 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 38.0; HRMS *m/z* calcd for $C_{30}H_{28}O_5P$ ($M+H^+$) 499.1669, found 499.1663.

5-(tert-Butyl)-1-(4-(tert-butyl)phenyl)-2,3-bis(4-methoxyphenyl)-1*H*-phosphindole 1-oxide (4dc): pale yellow solid, 114 mg (83%); column chromatography eluent: hexane-ethyl acetate (2:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (s, 9H), 1.27 (s, 9H), 3.70 (s, 3H), 3.87 (s, 3H), 6.65 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 7.18-7.28 (m, 5H), 7.35 (ddd, J = 9.3, 3.6, 1.6 Hz, 1H), 7.39 (dd, J = 8.4, 2.6 Hz, 2H), 7.61 (dd, J = 9.3, 7.8 Hz, 1H), 7.68 (dd, J = 12.1, 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.09, 31.13, 35.0, 35.2, 55.1, 55.3, 113.7, 114.4, 120.9 (d, J = 11.0 Hz), 125.5 (d, J = 10.7 Hz), 125.79 (d, J = 8.6 Hz), 125.81 (d, J = 11.9 Hz), 126.8 (d, J = 11.9 Hz), 127.2 (d, J = 104.7 Hz), 128.6 (d, J = 9.6 Hz), 129.1 (d, J = 109.1 Hz), 130.49 (d, J = 8.4 Hz), 130.51, 130.81 (d, J = 10.8 Hz), 133.4 (d, J = 96.0 Hz), 144.1 (d, J = 27.1 Hz), 148.4 (d, J = 21.7 Hz), 155.3 (d, J = 2.7 Hz), 156.4 (d, J = 1.5 Hz), 158.9, 159.6; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 38.8; HRMS *m/z* calcd for $C_{36}H_{40}O_3P$ ($M+H^+$) 551.2710, found 551.2714.

5-Chloro-1-(4-chlorophenyl)-2,3-bis(4-methoxyphenyl)-1*H*-phosphindole 1-oxide (4ec): yellow solid, 67 mg (53%); column chromatography eluent: hexane-ethyl acetate (1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 (s, 3H), 3.88 (s, 3H), 6.65 (d, J = 8.7 Hz, 2H), 7.00 (d, J = 8.8 Hz, 2H), 7.17-7.28 (m, 5H), 7.33 (ddd, J = 7.8, 3.2, 1.8 Hz, 1H), 7.35-7.39 (m, 2H), 7.58 (dd, J = 9.4, 7.7 Hz, 1H), 7.67 (dd, J = 12.0, 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.1, 55.3, 114.0, 114.8, 124.2 (d, J = 11.7 Hz), 124.7 (d, J = 10.2 Hz), 125.7 (d, J = 15.4 Hz), 128.3 (d, J = 100.6 Hz), 128.6 (d, J = 11.3 Hz), 129.4, (d, J = 12.7 Hz), 129.7 (d, J = 106.8 Hz), 129.9 (d, J = 10.4 Hz), 130.3, 130.4 (d, J = 6.1 Hz), 132.3 (d, J = 11.3 Hz), 134.4 (d, J = 96.0 Hz), 139.0 (d, J = 3.5 Hz), 139.7 (d, J = 2.4 Hz),

146.2 (d, J = 28.5 Hz), 147.0 (d, J = 21.1 Hz), 159.4, 160.0; $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 36.9; HRMS *m/z* calcd for $C_{28}H_{22}Cl_2O_3P$ ($M+H^+$) 507.0678, found 507.0682.

1-([1,1'-Biphenyl]-4-yl)-2,3-bis(4-methoxyphenyl)-5-phenyl-1*H*-phosphindole 1-oxide (4fc): yellow solid, 116 mg (78%); column chromatography eluent: hexane-ethyl acetate (1:1 to 1:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (s, 3H), 3.86 (s, 3H), 6.68 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 7.27 (d, J = 9.0 Hz, 2H), 7.30-7.39 (m, 4H), 7.39-7.46 (m, 5H), 7.48-7.59 (m, 5H), 7.62 (dd, J = 8.4, 2.6 Hz, 2H), 7.77 (dd, J = 9.4, 7.6 Hz 1H), 7.87 (d, J = 12.1, 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.1, 55.3, 113.9, 114.6, 122.6 (d, J = 11.1 Hz), 125.4 (d, J = 10.2 Hz), 126.5 (d, J = 15.4 Hz), 127.2, 127.3, 127.5, 127.6 (d, J = 10.6 Hz), 127.7, 128.1 (d, J = 10.2 Hz), 128.91 (2C, overlapped), 128.94 (d, J = 100.4 Hz), 129.3 (d, J = 9.7 Hz), 130.5 (d, J = 9.0 Hz), 130.55, 130.58 (d, J = 106.3 Hz), 131.5 (d, J = 10.7 Hz), 133.8 (d, J = 96.0 Hz), 140.0, 140.2, 144.9 (d, J = 3.0 Hz), 145.0 (d, J = 27.5 Hz), 146.0 (d, J = 1.6 Hz), 148.0 (d, J = 21.5 Hz), 159.2, 159.8; $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$) δ 38.6; HRMS *m/z* calcd for $C_{40}H_{32}O_3P$ ($M+H^+$) 591.2084, found 591.2085.

5-(tert-Butyl)-1,2,3-tris(4-(tert-butyl)phenyl)-1*H*-phosphindole 1-oxide (4dd): colorless solid, mp: 202-204 °C, 125 mg (83%); column chromatography eluent: hexane-ethyl acetate (3:1 to 2:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 9H), 1.25 (s, 9H), 1.30 (s, 9H), 1.39 (s, 9H), 7.04-7.14 (m, 4H), 7.20 (dd, J = 2.0, 2.0 Hz, 1H), 7.24-7.29 (m, 2H), 7.35 (dd, J = 7.7, 3.6, 1.6 Hz, 1H), 7.40-7.47 (m, 4H), 7.60 (dd, J = 9.3, 7.9 Hz, 1H), 7.73 (dd, J = 12.1, 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1 (3C overlapped), 31.3, 34.5, 34.8, 35.0, 35.2, 121.2 (d, J = 10.9 Hz), 125.1, 125.66 (d, J = 13.8 Hz), 125.74, 125.9 (d, J = 12.4 Hz), 127.6 (d, J = 100.7 Hz), 128.5 (d, J = 9.7 Hz), 128.76, 128.79 (d, J = 5.4 Hz), 130.1 (d, J = 9.7 Hz), 130.4 (d, J = 93.9 Hz), 130.9 (d, J = 10.8 Hz), 131.7 (d, J = 15.2 Hz), 133.9 (d, J = 95.5 Hz), 144.1 (d, J = 27.1 Hz), 149.5 (d, J = 21.4 Hz), 150.4, 151.6, 155.2 (d, J = 2.8 Hz), 156.4 (d, J = 2.0 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$) δ 38.8; HRMS *m/z* calcd for $C_{42}H_{52}OP$ ($M+H^+$) 603.3750, found 603.3748.

2,3-Bis(4-methoxyphenyl)-6-methyl-1-(3-methylphenyl)phosphindole 1-oxide (4gc): yellow gum, 71 mg (61%); column chromatography eluent: hexane-ethyl acetate (1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24 (s, 6H, overlapped), 3.69 (s, 3H), 3.86 (s, 3H), 6.63 (d, J = 8.6 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 7.10 (dd, J = 7.8, 3.2 Hz, 1H), 7.17-7.31 (m, 7H), 7.476 (d, J = 9.1 Hz, 1H), 7.477 (dd, J = 9.1, 5.7 Hz, 1H), 7.68 (d, J = 12.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 21.5, 55.1, 55.3, 113.7, 114.4, 123.5 (d, J = 11.4 Hz), 125.6 (d, J = 10.2 Hz), 126.8 (d, J = 15.5 Hz), 127.7 (d, J = 11.2

Hz), 128.7 (d, J = 13.0 Hz), 129.6 (d, J = 9.5 Hz), 130.2 (d, J = 98.2 Hz), 130.4 (d, J = 6.0 Hz), 130.5, 131.7 (d, J = 10.0 Hz), 132.1 (d, J = 96.2 Hz), 132.3 (d, J = 103.8 Hz), 132.9 (d, J = 3.0 Hz), 133.2 (d, J = 1.6 Hz), 138.7 (d, J = 11.9 Hz), 138.9 (d, J = 10.3 Hz), 141.5 (d, J = 26.9 Hz), 148.3 (d, J = 21.8 Hz), 158.9, 159.7,; $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$) δ 39.3; HRMS *m/z* calcd for $C_{30}H_{28}O_3P$ ($M+H^+$) 467.1771, found 467.1762.

2,3-Bis(4-methoxyphenyl)-1-(Naphthalen-2-yl)-1*H*-benzo[*f*]phosphindole 1-oxide (4hc): yellow solid, 97 mg (72%); column chromatography eluent: hexane-ethyl acetate (1:1 to 1:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65 (s, 3H), 3.89 (s, 3H), 6.62 (ddd, J = 8.8, 0.7, 0.4 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 7.21-7.30 (m, 2H), 7.39 (d, J = 8.4 Hz, 2H), 7.42-7.59 (m, 5H), 7.62 (d, J = 3.0 Hz, 1H), 7.69-7.85 (m, 4H), 7.87-7.96 (m, 1H), 8.16 (d, J = 11.3 Hz, 1H), 8.67 (d, J = 14.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.1, 55.3, 113.8, 114.6, 123.1 (d, J = 10.2 Hz), 125.4 (d, J = 12.9 Hz), 125.5 (d, J = 9.8 Hz), 126.7, 126.8 (d, J = 14.6 Hz), 127.1, 127.8, 127.9 (d, J = 101.1 Hz), 128.1, 128.4, 128.7 (d, J = 12.5 Hz), 128.81, 128.83, 129.1, 130.2 (d, J = 105.8 Hz), 130.5 (d, J = 6.0 Hz), 130.6, 130.9 (d, J = 9.3 Hz), 132.9 (d, J = 13.1 Hz), 133.1 (d, J = 11.7 Hz), 134.0 (d, J = 8.7 Hz), 134.3 (d, J = 96.0 Hz), 134.9 (d, J = 2.2 Hz), 135.6, 140.4 (d, J = 27.3 Hz), 149.4 (d, J = 20.4 Hz), 159.1, 159.9; $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$) δ 37.3; HRMS *m/z* calcd for $C_{36}H_{28}O_3P$ ($M+H^+$) 539.1771, found 539.1776.

1-(3,5-Dimethoxyphenyl)-4,6-dimethoxy-2,3-bis(4-methoxyphenyl)-1*H*-phosphindole 1-oxide (4ic): yellow form, 63 mg (45%); column chromatography eluent: DCM-ethyl acetate (2:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.47 (s, 3H), 3.68 (s, 3H), 3.76 (s, 6H), 3.80 (s, 3H), 3.83 (s, 3H), 6.47 (d, J = 2.2 Hz, 1H), 6.53 (dd, J = 2.4, 2.4 Hz, 1H), 6.58-6.62 (m, 2H), 6.81-6.89 (m, 3H), 6.92 (dd, J = 13.6, 2.3 Hz, 2H), 7.04-7.07 (m, 2H), 7.17 (d, J = 7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.0, 55.2, 55.5, 55.6, 55.8, 104.1, 104.3 (d, J = 2.1 Hz), 106.0 (d, J = 10.8 Hz), 108.3 (d, J = 12.7 Hz), 113.1, 113.6, 123.4 (d, J = 28.1 Hz), 129.8 (d, J = 10.2 Hz), 129.6 (d, J = 16.2 Hz), 130.0, 130.476 (d, J = 96.5 Hz), 130.483 (d, J = 5.9 Hz), 132.7 (d, J = 97.6 Hz), 135.8 (d, J = 102.7 Hz), 149.2 (d, J = 21.9 Hz), 157.0 (d, J = 17.4 Hz), 158.5, 158.9, 161.0 (d, J = 17.9 Hz), 162.2 (d, J = 15.9 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 39.2; HRMS *m/z* calcd for $C_{32}H_{32}O_7P$ ($M+H^+$) 559.1880, found 559.1876.

3-Butyl-2-(4-ethynylphenyl)-1-phenyl-1*H*-phosphindole 1-oxide (4am): colorless gum, 43 mg (45%); column chromatography eluent: hexane-ethyl acetate (1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$)

δ 0.91 (t, J = 7.3 Hz, 3H), 1.35-1.47 (m, 2H), 1.55-1.75 (m, 2H), 2.61-2.73 (m, 2H), 3.09 (s, 1H), 7.28-7.52 (m, 2H), 7.33-7.41 (m, 3H), 7.43-7.52 (m, 4H), 7.54-7.69 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 22.9, 27.0 (d, J = 11.9 Hz), 31.0 (d, J = 1.3 Hz), 77.9, 83.4, 121.5, 122.5 (d, J = 11.1 Hz), 128.6 (d, J = 4.7 Hz), 128.8 (d, J = 12.2 Hz), 129.0 (d, J = 9.6 Hz), 129.1 (d, J = 10.2 Hz), 130.5 (d, J = 96.5 Hz), 130.9 (d, J = 10.6 Hz), 132.1 (d, J = 2.8 Hz), 132.2 (d, J = 105.0 Hz), 132.4, 133.0, 133.6 (d, J = 96.8 Hz), 133.9 (d, J = 10.1 Hz), 143.0 (d, J = 27.8 Hz), 152.1 (d, J = 19.3 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 38.3; HRMS *m/z* calcd for $C_{26}H_{24}OP$ ($M+H^+$) 383.1559, found 383.1556.

1,2,3-Triphenyl-1*H*-phosphindole 1-sulfide (4aa-S)[4a]: colorless form, 52 mg (53%) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00-7.14 (m, 3H), 7.16-7.21 (m, 2H), 7.30 (dd, J = 7.6, 3.1 Hz, 1H), 7.32-7.50 (m, 10H), 7.70 (ddd, J = 10.5, 7.3, 0.8 Hz, 1H), 7.81-7.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 124.4 (d, J = 5.8 Hz), 127.9 (d, J = 1.1 Hz), 128.0, 128.6, 128.76 (d, J = 11.0 Hz), 128.09 (d, J = 12.6 Hz), 128.81, 129.33 (d, J = 11.2 Hz), 129.34, 129.39 (d, J = 77.4 Hz), 129.6 (d, J = 5.4 Hz), 130.9 (d, J = 11.6 Hz), 132.0 (d, J = 3.0 Hz), 132.3 (d, J = 1.9 Hz), 132.4 (d, J = 10.9 Hz), 134.2 (d, J = 14.3 Hz), 135.8 (d, J = 89.3 Hz), 136.4 (d, J = 77.8 Hz), 143.7 (d, J = 23.5 Hz), 149.3 (d, J = 18.7 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 48.1; HRMS *m/z* calcd for $C_{26}H_{20}PS$ ($M+H^+$) 395.1018, found 395.1019.

3-Benzyl-1-(diethylamino)-1,3-diphenyl-1,3-dihydrobenzo[*c*][1,2]thiaphosphol-1-ium Trifluoromethanesulfonate (5) (diastereo mixture, (2S_P*,5R*):(2Sp*,5S*) = 2.8:1): colorless solid, mp (major): 121-123 °C, 113 mg (73%); ^{1}H NMR (400 MHz, $CDCl_3$) for a major product δ 0.93 (t, J = 6.2 Hz, 6H), 2.22-2.38 (m, 2H), 2.50-2.67 (m, 2H), 4.05 (dd, J = 14.1, 1.4 Hz, 1H), 4.12 (d, J = 14.2 Hz, 1H), 6.91-6.96 (m, 2H), 7.03-7.09 (m, 2H), 7.15-7.78 (m, 10H), 7.86-7.92 (m, 2H), 8.02-8.12 (m, 2H), 8.25-8.42 (m, 1H); for a minor product δ 1.03 (t, J = 6.2 Hz, 6H), 2.92-3.05 (m, 4H), 3.86 (d, J = 14.1 Hz, 1H), 3.98 (d, J = 14.2 Hz, 1H), 6.46-6.51 (m, 2H), 6.73-6.82 (m, 3H), 7.15-7.78 (m, 11H), 7.92-8.00 (m, 2H), 8.25-8.42 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) for a major product δ 13.4 (d, J = 15.1 Hz), 40.7 (d, J = 2.2 Hz), 47.1, 121.1 (q, J = 319.1 Hz), 121.9 (d, J = 111.5 Hz), 125.6 (d, J = 108.3 Hz), 126.7, 127.7, 128.4, 128.5 (d, J = 15.9 Hz), 128.9, 129.1, 130.4 (d, J = 8.5 Hz), 130.7 (d, J = 14.2 Hz), 131.8 (d, J = 12.2 Hz), 132.1, 132.9 (d, J = 11.6 Hz), 134.4, 135.5 (d, J = 2.5 Hz), 135.7 (d, J = 3.2 Hz), 143.4 (d, J = 1.3 Hz), 148.9 (d, J = 24.1 Hz); for a minor product δ 13.3 (d, J = 3.8 Hz), 41.6, 48.2, 119.5, 121.2, 126.9, 127.9, 128.0, 129.2, 129.4, 130.9, 132.3 (d, J = 12.3 Hz), 133.8, 134.9 (all observed signals are shown); ^{31}P{^{1}H} NMR (162 MHz,

$CDCl_3$) δ 79.2 (major), 78.2 (minor); HRMS *m/z* calcd for $C_{30}H_{31}NPS$ ($[M\text{-}OTf]^+$) 468.1909, found 468.1920.

5-([1,1'-Biphenyl]-2-yl)-5*H*-benzo[*b*]phosphindole 5-oxide (7): colorless solid, 67 mg (75%); column chromatography eluent: hexane-ethyl acetate (1:1 to 1:4, v/v); ^1H NMR (400 MHz, $CDCl_3$) δ 6.29-6.31 (m, 2H), 6.64-6.68 (m, 2H), 6.68-6.93 (m, 1H), 7.05-7.08 (m, 1H), 7.25-7.30 (m, 2H), 7.34 (dd, J = 7.5, 2.9 Hz, 2H), 7.38-7.42 (m, 2H), 7.51 (dd, J = 10.0, 7.4 Hz, 2H), 7.53-7.65 (m, 2H), 8.69 (ddd, J = 13.0, 7.6, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 121.2 (d, J = 10.3 Hz), 126.4, 126.9, 127.4 (d, J = 11.2 Hz), 127.8 (d, J = 98.8 Hz), 128.7, 128.8 (d, J = 11.2 Hz), 129.3 (d, J = 10.0 Hz), 131.1 (d, J = 10.3 Hz), 131.8 (d, J = 2.7 Hz), 132.7 (d, J = 2.0 Hz), 133.5 (d, J = 107.6 Hz), 134.8 (d, J = 8.3 Hz), 138.9 (d, J = 4.1 Hz), 142.1 (d, J = 22.2 Hz), 146.0 (d, J = 11.5 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 31.0; HRMS *m/z* calcd for $C_{24}H_{18}OP$ ($M+H^+$) 353.1090, found 353.1087.

Referneces and Notes

(1) (a) Mathey, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1578. (b) Baumgartner, T.; Reau, R. *Chem. Rev.* **2006**, *106*, 4681. (c) Matano, Y.; Imahori, H. *Org. Biomol. Chem.* **2009**, *7*, 1258. (d) Stolar, M.; Baumgartner, T. *Chem.—Asian J.* **2014**, *9*, 1212. (e) Fourmy, K.; Nguyen, D. H.; Dechy-Cabaret, O.; Gouygou, M. *Catal. Sci. Technol.* **2015**, *5*, 4289. (f) Duffy, M. P.; Delaunay, W.; Bouit, P.-A.; Hissler, M. *Chem. Soc. Rev.* **2016**, *45*, 5296. (g) Shameem, M. A.; Orthaber, A. *Chem.—Eur. J.* **2016**, *22*, 10718.

(2) (a) Rausch, M. D.; Klemann, L. P. *J. Am. Chem. Soc.* **1967**, *89*, 5732. (b) Kurita, J.; Ishii, M.; Yasuike, S.; Tsuchiya, T. *J. Chem. Soc., Chem. Commun.* **1993**, 1309. (c) Cordaro, J. G.; Stein, D.; Grützmacher, H. *J. Am. Chem. Soc.* **2006**, *128*, 14962. (d) Ogasawara, M.; Arae, S.; Watanabe, S.; Subbarayan, V.; Sato, H.; Takahashi, T. *Organometallics* **2013**, *32*, 4997. (e) Matano, Y.; Motegi, Y.; Kawatsu, S.; Kimura, Y. *J. Org. Chem.* **2015**, *80*, 5944. (f) Yamaguchi, E.; Wang, C. G.; Fukazawa, A.; Taki, M.; Sato, Y.; Sasaki, T.; Ueda, M.; Sasaki, N.; Higashiyama, T.; Yamaguchi, S. *Angew. Chem., Int. Ed.* **2015**, *54*, 4539. (g) Wei, X.; Lu, Z.; Zhao, X.; Duan, Z.; Mathey, F. *Angew. Chem., Int. Ed.* **2015**, *54*, 1583. (h) Hong, E. Y.-H.; Poon, C.-T.; Yam, V. W.-W. *J. Am. Chem. Soc.* **2016**, *138*, 6368. (i) Wu, B.; Yoshikai, N. *Org. Biomol. Chem.* **2016**, *14*, 5402.

(3) (a) Tsuji, H.; Sato, K.; Ilies, L.; Itoh, Y.; Sato, Y.; Nakamura, E. *Org. Lett.* **2008**, *10*, 2263. (b) Xu, Y.-Z.; Wang, Z.-H.; Gan, Z.-J.; Xi, Q.-Z.; Duan, Z.; Mathey, F. *Org. Lett.* **2015**, *17*, 1732. (c) Zhou, Y.; Gan, Z.; Su, B.; Li, J.; Duan, Z.; Mathey, F. *Org. Lett.* **2015**, *17*, 5722. (d) Sanji, T.; Shiraishi, K.; Kashiwabara, T.; Tanaka, M. *Org. Lett.* **2008**, *10*, 2689. (e) Fukazawa, A.; Hara, M.; Okamoto, T.; Son, E.-C.; Xu, C.; Tamao, K.; Yamaguchi, S. *Org. Lett.* **2008**, *10*, 913. (f) Fukazawa, A.; Ichihashi, Y.; Kosaka, Y.; Yamaguchi, S. *Chem.—Asian J.* **2009**, *4*, 1729.

(4) (a) Unoh, Y.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 12975. (b) Chen, Y.-R.; Duan, W.-L. *J. Am. Chem. Soc.* **2013**, *135*, 16754. See also, (c) Ma, W.; Ackermann, L. *Synthesis* **2014**, *46*, 2297.

(5) (a) Zhang, P.; Gao, Y.; Zhang, L.; Li, Z.; Liu, Y.; Tang, G.; Zhao, Y. *Adv. Synth. Catal.* **2016**, *358*, 138. (b) Quint, V.; Morlet-Savary, F.; Lohier, J.-F.; Lalevée, J.; Gaumont, A.-C.; Lakhdar, S. *J. Am. Chem. Soc.* **2016**, *138*, 7436. (c) Ma, D.; Chen, W.; Hu, G.; Zhang, Y.; Gao, Y.; Yina, Y.; Zhao, Y. *Green Chem.* **2016**, *18*, 3522. (d) Zhang, Y.; Hu, G.; Ma, D.; Xu, P.; Gao, Y.; Zhao, Y. *Chem. Commun.* **2016**, *52*, 2815. (e) Hu, G.; Zhang, Y.; Su, J.; Li, Z.; Gao, Y.; Zhao, Y. *Org. Biomol. Chem.* **2015**, *13*, 8221.

(6) (a) Wu, B.; Santra, M.; Yoshikai, N. *Angew. Chem., Int. Ed.* **2014**, *53*, 7543. (b) Wu, B.; Chopra, R.; Yoshikai, N. *Org. Lett.* **2015**, *17*, 5666.

(7) Selected recent reviews for C−H functionalization: (a) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013. (b) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335. (c) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev.* **2009**, *38*, 2447. (d) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074. (e) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (f) Satoh, T.; Miura, M. *Synthesis* **2010**, 3395. (g) Satoh, T.; Miura, M. *Chem.—Eur. J.* **2010**, *16*, 11212. (h) Sun, C.-L.; Li, B.-J.; Shi, Z.- J. *Chem. Commun.* **2010**, *46*, 677. (i) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (j) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (k) Lapointe, D.; Fagnou, K. *Chem. Lett.* **2010**, *39*, 1118. (l) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. (m) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780. (n) Kuninobu, Y.; Takai, K. *Chem. Rev.* **2011**, 111, 1938. (o) Wencel-Delord, J.; Droge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740. (p) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (q) Mitchell, E. A.; Peschiulli, A.; Lefevre, N.; Meerpoel, L.; Maes, B. U. W. *Chem.—Eur. J.* **2012**, *18*, 10092. (r) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788. (s) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814. (t) Patureau, F. W.; Wencel-Delord, J.; Glorius, F. *Aldrichimica Acta* **2012**, *45*, 31. (u) Chiba, S. *Chem. Lett.* **2013**, *41*, 1554. (v) Miura, M.; Satoh, T.; Hirano, K. *Bull. Chem. Soc. Jpn.* **2014**, *87*, 751. (w) Chen, Z.; Wang,

B.; Zhang, J.; Yu, W.; Liu, Z.; Zhang, Y. *Org. Chem. Front.* **2015**, *2*, 1107. (x) Boyarskiy, V. P.; Ryabukhin, D. S.; Bokach, N. A.; Vasilyev, A. V. *Chem. Rev.* **2016**, *116*, 5894. (y) Gulías, M.; Mascareñas, J. L. *Angew. Chem., Int. Ed.* **2016**, *55*, 11000.

(8) For pioneering work, see: Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529.

(9) (a) Unoh, Y.; Hashimoto, Y.; Takeda, D.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2013**, *15*, 3258. (b) Itoh, M.; Hashimoto, Y.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2013**, *78*, 8098. (c) Yokoyama, Y.; Unoh, Y.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2014**, *79*, 7649. (d) Y. Unoh, T. Satoh, K. Hirano, M. Miura *ACS. Catal.* **2015**, *5*, 6634.

(10) For relevant Rh-catalyzed C-H functionalization directed by phosphorus containing directing group: (a) Seo, J.; Park, Y.; Jeon, I.; Ryu, T.; Park, S.; Lee, P. H. *Org. Lett.* **2013**, *15*, 3358. (b) Ryu, T.; Kim, J.; Park, Y.; Kim, S.; Lee, P. H. *Org. Lett.* **2013**, *15*, 3986. (c) Zhao, D.; Nimphius, C.; Lindale, M.; Glorius, F. *Org. Lett.* **2013**, *15*, 4504. (d) Park, Y.; Seo, J.; Park, S.; Yoo, E. J.; Lee, P. H. *Chem.—Eur. J.* **2013**, *19*, 16461. (e) Park, S.; Seo, B.; Shin, S.; Son, J.-Y.; Lee, P. H. *Chem. Commun.* **2013**, *49*, 8671. (f) Mo, J.; Lim, S.; Ryu, T.; Kim, S.; Lee, P. H. *RSC Adv.* **2013**, *3*, 18296. (g) Chary, B. C.; Kim, S. *Org. Biomol. Chem.* **2013**, *11*, 6879. (h) Liu, L.; Wu, Y.; Wang, T.; Gao, X.; Zhu, J.; Zhao, S. *J. Org. Chem.* **2014**, *79*, 5074. (i) Gu, L.-J.; Jin, C.; Wang, R.; Ding, H.-Y. *ChemCatChem* **2014**, *6*, 1225. (k) Hu, X.-H.; Yang, X. F.; Loh, T.-P. *Angew. Chem., Int. Ed.* **2015**, *54*, 15535. (j) Sun, Y.; Cramer, N.; *Angew. Chem., Int. Ed*. **2017**, *56*, 364.

(11) (a) Olah, G. A.; Hehemann, D. *J. Org. Chem.* **1977**, *42*, 2190. (b) Wang, Z.-W.; Wang, L.-S. *Green Chem.* **2003**, *5*, 737. (c) Diaz, A. A.; Young, J. D.; Khan, M. A.; Wehmschulte, R. J. *Inorg. Chem.* **2006**, *45*, 5568. (d) Diaz, A. A.; Buster, B.; Schomich, D.; Khan, M. A.; Baum, J. C.; Wehmschulte, R. J. *Inorg. Chem.* **2008**, *47*, 2858. (e) Hatakeyama, T.; Hashimoto, S.; Nakamura, M. *Org. Lett.* **2011**, *13*, 2130. (f) Hashimoto, S.; Nakatsuka, S.; Nakamura, M.; Hatakeyama, T. *Angew. Chem., Int. Ed.* **2014**, *53*, 14074. (g) Romero-Nieto, C.; López-Andarias, A.; Egler-Lucas, C.; Gebert, F.; Neus, J.-P.; Pilgram, O. *Angew. Chem., Int. Ed.* **2015**, *54*, 15872. (h) Jayaraman, A.; Sterenberg, B. T. *Organometallics* **2016**, *35*, 2367.

(12) (a) Omelańczuk, J.; Mikołgajczyk, M. *Tetrahedron Lett.* **1984**, *25*, 2493. (b) Hajjouji, H. e.; Belmonte, E.; García-López, J.; Fernández, I.; Iglesias, M. J.; Roces, L.; García-Granda, S.; Laghdach, A. E.; Ortiz, F. L. *Org. Biomol. Chem.* **2012**, *10*, 5647.

(13) For a discussion about aggregation induced emission: Bu, F.; Wang, E.; Peng, Q.; Hu, R.; Qin, A.; Zhao, Z; Tang, B. Z. *Chem.—Eur. J.* **2015**, *21*, 4440.

(14) Novak, Z.; Nemes, P.; Kotschy, A. *Org. Lett.* **2004**, *6*, 4917.

(15) Semba, K.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem.—Eur. J.* **2012**, *18*, 4179.

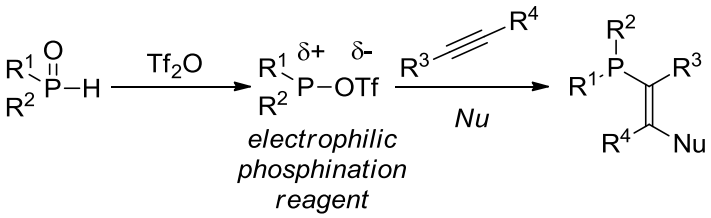
(16) Börjesson, M.; Moragas, T.; Martin, R. *J. Am. Chem. Soc.* **2016**, *138*, 7504.

(17) Hundertmark, T.; Littke, A. F.; Buchwald, S. L.; Fu, G. C. *Org. Lett.* **2000**, *2*, 1729.

Chapter 6

Metal-free Electrophilic Phosphination of Alkynes

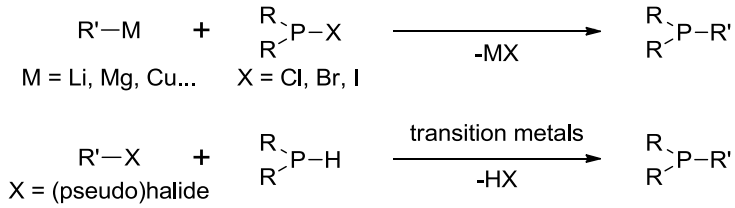
A new metal-free electrophilic phosphination reaction of alkynes has been developed. The electrophilic phosphenium species generated *in situ* from secondary phosphine oxides with Tf_2O smoothly coupled with a variety of alkynes to afford a range of phosphine derivatives. The mechanistic studies to observe the reactive intermediates have also been carried out.



Introduction

As described in Chapter 1, a variety of organophosphorus compounds are now broadly utilized not only as building blocks for preparing bioactive molecules and functional materials, but also as ligands for transition metals.[1] The C(sp^2)-P bond formation is one of the most important and fundamental reactions for the synthesis of aromatic phosphorus compounds. The classical synthetic approaches to form a C(sp^2)-P bond are the reaction of halophosphine electrophiles with organometallic carbon nucleophiles such as organolithium and Grignard reagents[1a,b] and the transition-metal catalyzed cross-coupling reactions of phosphines with C(sp^2)-(pseudo)halides (Scheme 6.1).[2] These methodologies, however, often suffer from low functional group compatibility and long step preparation of the coupling precursors. The C-H/P-H type catalytic direct coupling reactions have recently been reported,[3] while still they are rare. In addition, simple phosphines are substantially not compatible for these oxidative coupling conditions since they are easily oxidized.

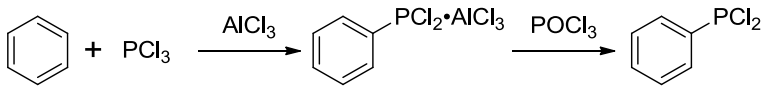
Scheme 6.1. Classical Synthetic Approaches for C(sp^2)-P Bond Formation



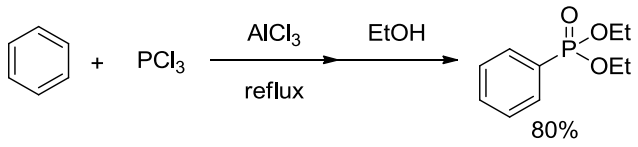
An alternative way for the formation of the C(sp^2)-P bond is the Friedel-Crafts-type electrophilic phosphination reaction.[4] This process was already known in 1870's as exemplified by the reaction of benzene with PCl_3 in the presence of $AlCl_3$ (Scheme 6.2).[4a] As described in Chapter 1, the electrophilic C(sp^2)-P bond forming reaction has

sometimes been studied to date (as an earlier example, Scheme 6.3).[4b]

Scheme 6.2.



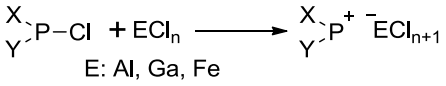
Scheme 6.3.



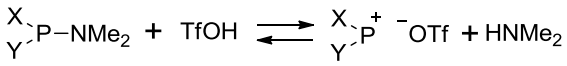
These transformations are usually conducted under harsh conditions in the presence of a stoichiometric amount of Lewis acid such as $AlCl_3$. Generation of phosphenium cations,[5] which is considered as an active species in the electrophilic phosphination reaction, mostly relies on the halogen abstraction from halophosphines using a Lewis acid (Scheme 6.4 A). Other methodologies (Scheme 6.4 B-D) are also known; however, these are limited in the special cases and not utilized in common organic synthesis.

Scheme 6.4. Generation of Phosphenium Species

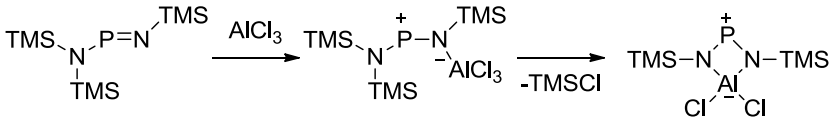
A. Phosphorus-Halogen Bond Heterolysis



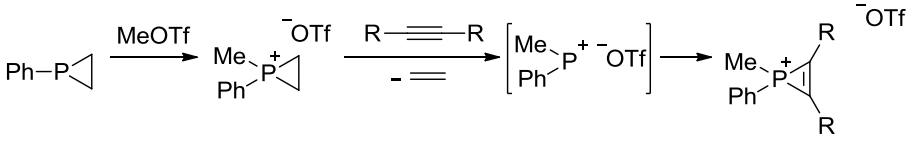
B. Protonation of Phosphorus-Nitrogen Bonds



C. Electrophilic Activation of Element-Phosphorus Double Bonds



D. Retro-cycloaddition from Phosphiranium Salt



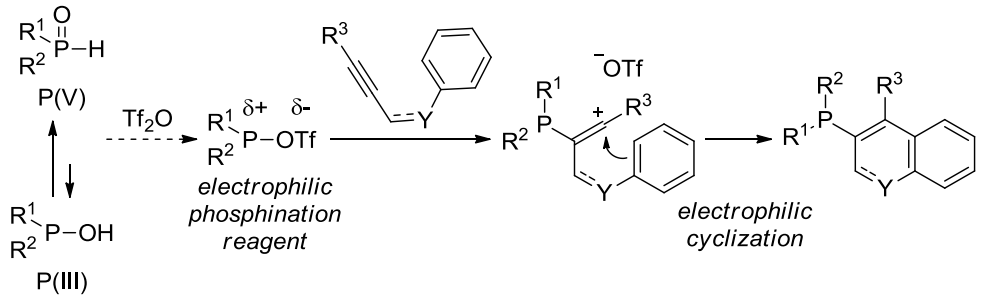
Recently, metal-free electrophilic C-heteroatom bond forming reactions have attracted attention as environmentally-friendly processes.[6] The metal-free C-B,[7] C-N,[8]

C-Si[9], and C-S[10] bond formations have recently been achieved. In contrast, to the best of my knowledge, there is no report on the metal-free intermolecular electrophilic C-P bond forming reaction. In Chapter 6, the author describes development of the metal-free electrophilic phosphination (phospha-Friedel-Crafts: PFC) reaction of alkynes.

Results and discussion

Secondary phosphine oxides, which are employed as the substrates in Chapter 3, are basically stable and readily available phosphorus(V) compounds. It is known that they exist in equilibrium between P(V) and P(III) (hydroxyphosphine) in a solution (Scheme 6.5, left).[1a,11] The author envisioned that if this hydroxyl group could be replaced by a leaving group, an electrophilic phosphorus species would be generated and utilized for PFC reactions under metal-free conditions. To verify this concept, the author designed an electrophilic cyclization of aromatic ring-tethered alkynes (Scheme 6.5 right). Thus, the formed phosphorus electrophile may activate such an alkyne to promote subsequent intramolecular cyclization with the pendant aromatic π system.

Scheme 6.5. Concept of This Study



Under this hypothesis, the author commenced exploring the electrophilic phosphinative cyclization using diphenylphosphine oxide (**1a**) and the alkyne (**2a**) as

model substrates (Table 6.1). In an initial attempt, **1a** (0.5 mmol) and **2a** (0.25 mmol) were treated with Tf_2O (0.6 mmol) and 2,6-lutidine (1.0 mmol) in DCM (2 mL) at 60 °C for 3 h in a schlenk tube. As expected, desired phosphinylated **3a** was obtained in 63% yield after oxidative workup using H_2O_2 (entry 1). The reaction did not proceed at all at room temperature (entry 2). In DCE solvent, the efficiency was slightly decreased (entry 3). Increasing the amount of Tf_2O improved the product yield to 83% (entry 4). Use of more nucleophilic DMAP or sterically hindered 2,6-di(tert-buthyl)pyridine were comparable to 2,6-lutidine (entries 5, 6). At 80 °C in DCE, the yield was decreased (entry 7). Finally, **3a** was obtained in a nearly quantitative yield by decreasing the amounts of both Tf_2O and 2,6-lutidine (0.5 mmol for each) (entry 8). The reaction without base led to decomposition of the product (entry 9). Further decreasing the amount of **1a**, Tf_2O, and 2,6-lutidine resulted in a slightly lower yield (entry 10). In the present process, the initial coupling product is phosphine **4a**, which was actually confirmed by NMR analysis of the crude material (Scheme 6.6). In addition, the coupling product was also isolated as phosphine sulfide **3b** in 84% yield after workup treatment with elemental sulfur.

Scheme 6.6.

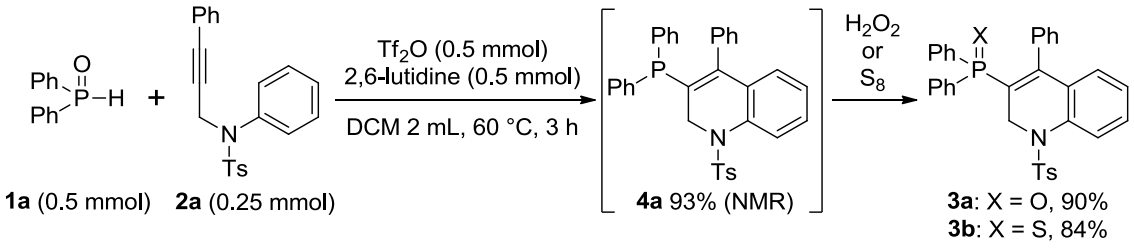
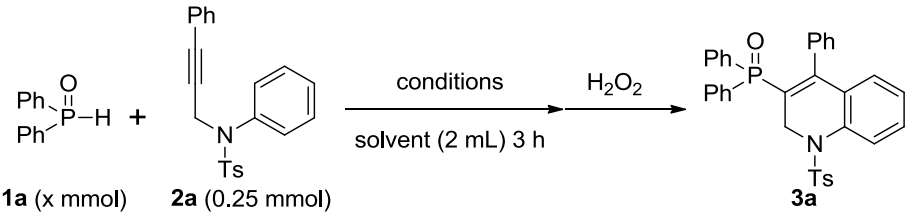


Table 6.1. Reaction of 1a with 2a



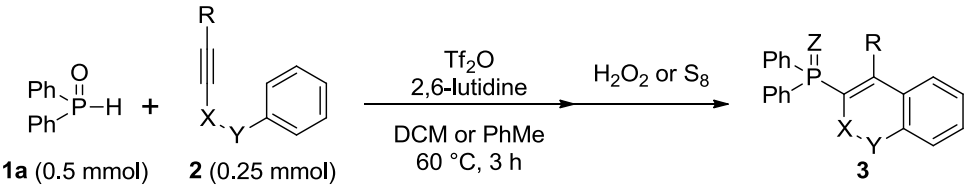
1a (x mmol) **2a** (0.25 mmol) **3a**

entry	x (mmol)	activator (mmol)	base (mmol)	solvent	temp (°C)	NMR yield[a]
1	0.5	Tf_2O (0.6)	2,6-lutidine (1.0)	DCM	60	(63%)
2	0.5	Tf_2O (0.6)	2,6-lutidine (1.0)	DCM	rt	trace
3	0.5	Tf_2O (0.6)	2,6-lutidine (1.0)	DCE	60	59%
4	0.5	Tf_2O (1.0)	2,6-lutidine (1.0)	DCM	60	82% (83%)
5	0.5	Tf_2O (1.0)	DMAP (1.0)	DCM	60	85%
6	0.5	Tf_2O (1.0)	2,6-di*t*-Bupyridine (1.0)	DCM	60	79%
7	0.5	Tf_2O (1.0)	2,6-lutidine (1.0)	DCE	80	54%
8	0.5	Tf_2O (0.5)	2,6-lutidine (0.5)	DCM	60	96% (90%)
9	0.5	Tf_2O (0.5)	-	DCM	60	trace
10	0.375	Tf_2O (0.375)	2,6-lutidine (0.375)	DCM	60	74%

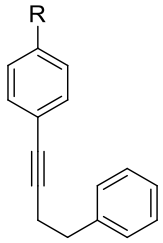
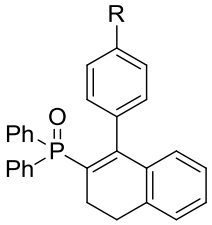
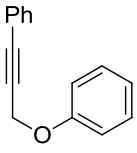
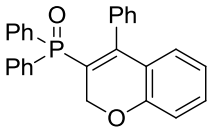
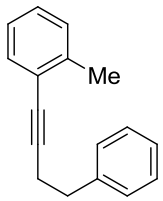
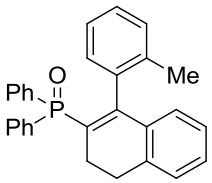
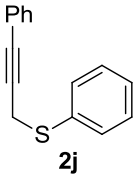
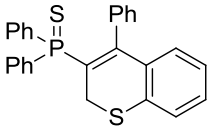
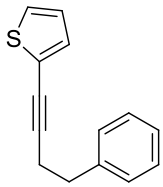
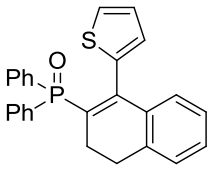
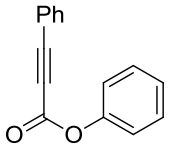
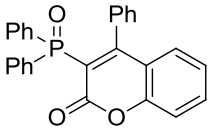
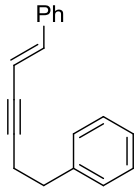
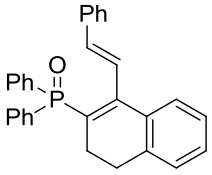
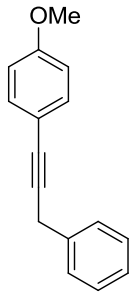
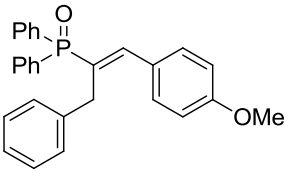
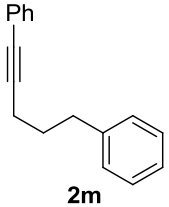
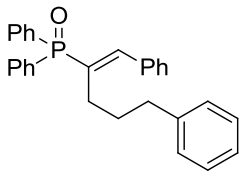
[a] ^{1}H NMR yield based on the amount of **2a** using dibromomethane as an internal standard. Isolated yield is shown in parentheses.

With the optimum conditions (entry 8 in Table 6.1) in hand, the author next examined the scope of substrates (Table 6.2). It was found that toluene is also a suitable solvent in some cases, therefore, better results of the reaction in DCM or toluene are shown in Table 6.2. A variety of arylalkynes possessing both electron-donating and withdrawing-groups (**2c**-**2f**), thiophene (**2g**), and conjugated alkene (**2h**) could be employed in the reaction. In addition, ether (**2i**), thioether (**2j**), and ester (**2k**) could also be involved as the linker. It should be noted that when the alkynes have a shorter or longer linker (**2l**, **2n**), the cyclization did not occur and corresponding hydrophosphinylated product **5l** and **5m** were obtained in high yield. 4,4'-Disubstituted diphenylphosphine oxides **1n** and **1o** reacted with **2a** in toluene to afford the corresponding coupling products **3n**, and **3o** respectively (Scheme 6.7). In the case of electron-rich **1n**, a longer reaction time (12 h) was required for completion.

Table 6.2. Scope of Substrates[a]

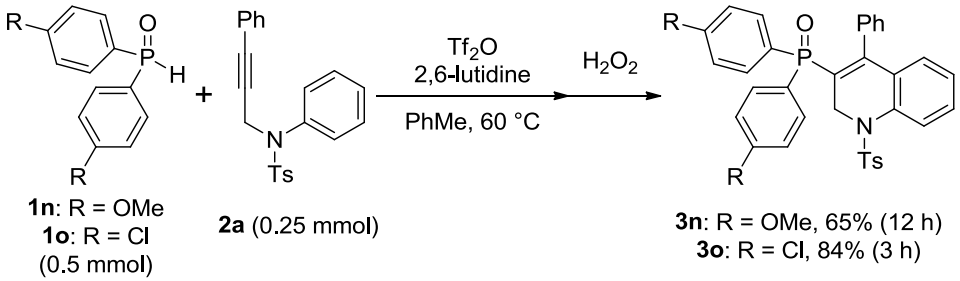


1a (0.5 mmol) **2** (0.25 mmol) **3**

alkyne **2**	product **3**, yield(%)[b]	alkyne **2**	product **3**, yield(%)[b]
 **2c**: R = OMe **2d**: R = CN **2e**: R = CF_3	 **3c**: R = OMe, 78% (DCM) **3d**: R = CN, 81% (PhMe) **3e**: R = CF_3, 85% (PhMe)	 **2i**	 **3i**: 71% (DCM)
 **2f**	 **3f**: 89% (DCM)	 **2j**	 **3j**: 66% (DCM)
 **2g**	 **3g**: 77% (PhMe)	 **2k**	 **3k**: 55% (DCM)
 **2h**	 **3h**: 57% (PhMe)	 **2l**	 **5l** 83%(DCM)
		 **2m**	 **5m** 92%(DCM)

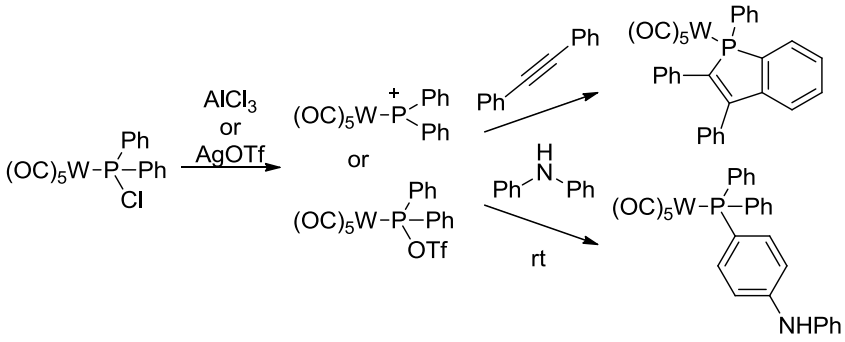
[a] Reaction conditions: 1) **1** (0.5 mmol), **2** (0.25 mmol), Tf_2O (0.5 mmol), 2,6-lutidine (0.5 mmol) in DCM or PhMe (2 mL) at 60 °C under N_2 for 3 h; 2) H_2O_2 or S_8 work up. [b] Isolated yields are shown based on the amount of **2**.

Scheme 6.7.



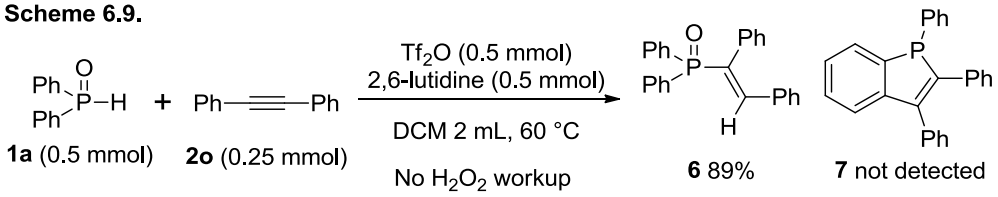
Recently, Sterenberg and co-workers reported the electrophilic phosphination reaction on tungsten complexes under mild conditions (Scheme 6.8).[12] In their report, the diphenylphosphenium triflate complex smoothly underwent the coupling reaction with diphenylacetylene to form a benzophophole skelton.[12b]

Scheme 6.8. Electophilic Phosphination on Tungsten Complexes by Sterenberg *et al.*



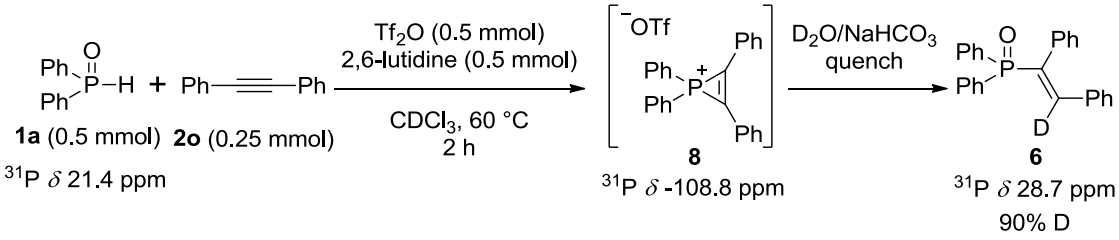
To examine whether the similar transformation is executable in the present system or not, the author attempted the reaction of **1a** with diphenylacetylene (**2o)** (Scheme 6.9). Unfortunately, the expected benzophosphole **7** did not formed at all. Instead, hydrophosphinylated product **6** was obtained in a high yield. Interestingly, the product was entirely formed as the phosphine oxide **6** without any oxidative workup. To obtain some mechanistic information of present reaction system, the author carried out *in situ* $^{31}P\{^{1}H\}$ NMR studies for the reaction in Scheme 6.9 as a model reaction.

Scheme 6.9.



First, **1a** and **2o** were treated in $CDCl_3$ under the standard conditions and the resulting reaction mixture was monitored by $^{31}P\{^1H\}$ NMR (Scheme 6.10). Phosphine oxide **1a** has a singlet signal at δ 21.4 ppm. After addition of Tf_2O and 2,6-lutidine, this signal immediately disappeared and several new signals appeared. After 10 min at room temperature, it showed two singlet signals (δ -108.9 and 42.2), one AB system (δ -18.5 and -18.4, $^1J_{pp}$ = 363 Hz), and one AX system (δ 13.0 and 15.3, $^1J_{pp}$ = 350 Hz) (Scheme 6.11). In this case, signals assignable to free phosphenium species (generally δ > 260)[5,13] were not observed. This solution was further heated at 60 °C for 2 h. Consequently, the intensity of these AX and AB systems apparently decreased, and the two singlet signals became major peaks (Scheme 6.10). Finally, the reaction mixture was quenched by D_2O and $NaHCO_3$ at room temperature. In the crude solution after general workup, **6** and the starting material **1** were mainly observed. Furthermore, ^1H and ^2D NMR analyses showed the 90% deuterium incorporation at the β-positon of **6**. Breslow and co-workers previously reported that Ph_2PCl underwent [2+1] cycloaddition with diphenylacetylene **2o** in the presence of $AlCl_3$ to form a tetraphenylphosphirenium cation, which is immediately hydrolyzed upon treatment with H_2O to form the same hydrophosphinylated product **6** (Scheme 6.12).[14]

Scheme 6.10. ***In Situ*** **$^{31}P\{^{1}H\}$ NMR Study of The Reaction of 1a with 2o**



1a (0.5 mmol) **2o** (0.25 mmol)

^{31}P δ 21.4 ppm

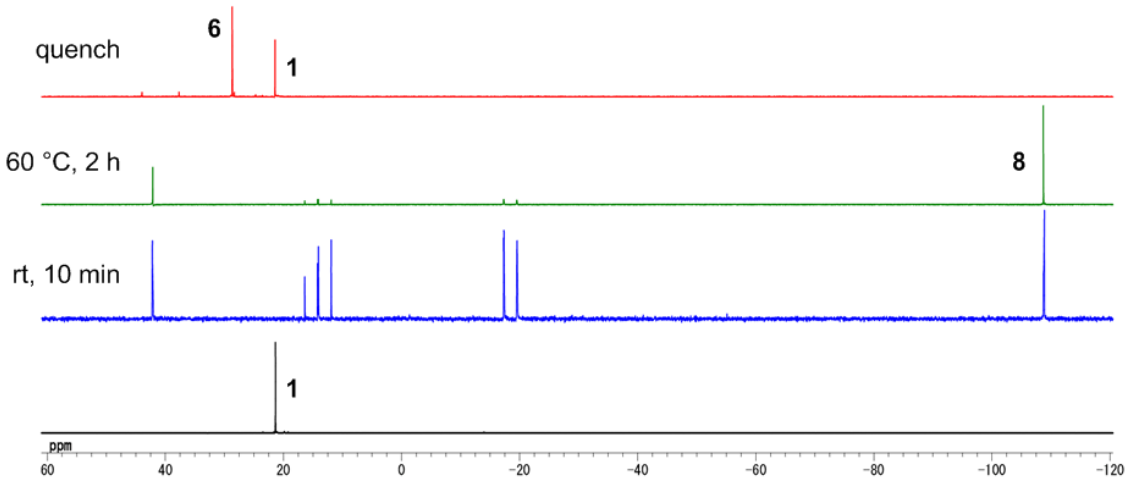
8

^{31}P δ -108.8 ppm

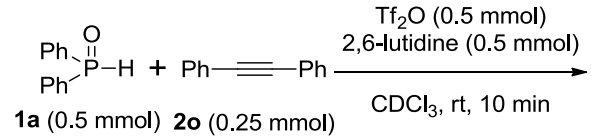
6

^{31}P δ 28.7 ppm

90% D

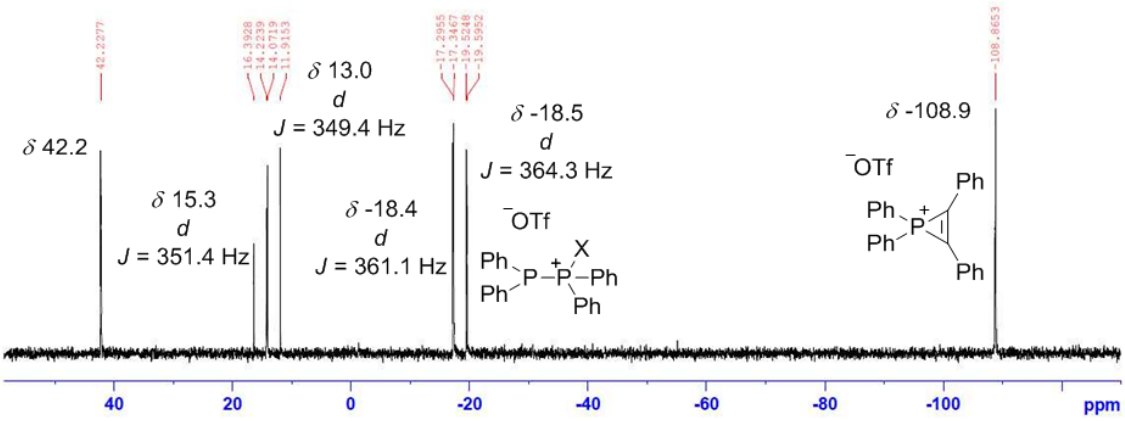


Scheme 6.11. Observation of Electrophilic Phosphorus Species

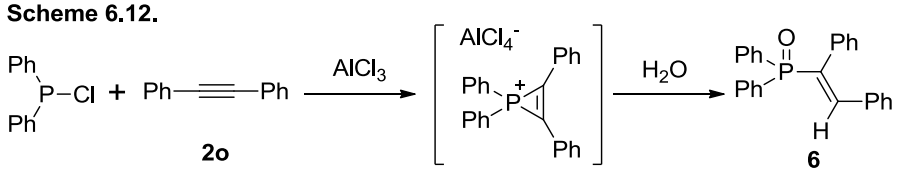


1a (0.5 mmol) **2o** (0.25 mmol)

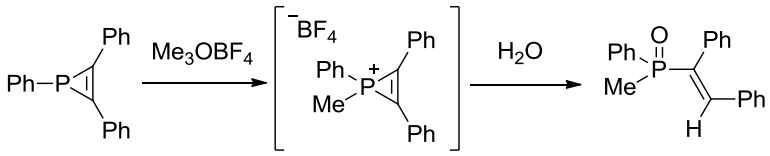
^{31}P δ 21.4 ppm



Scheme 6.12.



Scheme 6.13.

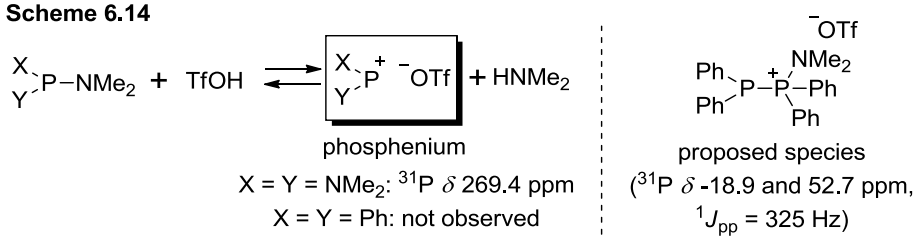


^{31}P δ -109.9 ppm
in CD_2Cl_2

Mathey and co-worker also previously described that the phosphirenium cation generated by the *P*-alkylation of a phosphirene showed a signal at δ -109.9 in CD_2Cl_2 and underwent a similar ring opening reaction with water (Scheme 6.13).[15] According to the literature, a similar phosphirenium **8** seems to be generated in the present system. As mentioned above, the free phosphenium cations were not observed during the ^{31}P NMR experiments. Generally, they are considered to be unstable unless they are stabilized sterically or electronically.[5] Actually, Dahl and co-workers previously described the effect of the substituents on the phosphorus atom in the reaction of various amino phosphine and TfOH (Scheme 6.14).[16] In their report, diphenylphosphenium triflate was not observed by ^{31}P NMR in the reaction of dimethylaminodiphenylphosphine, when electronically stabilizing amino groups were absent on the phosphorus atom. Instead, they noted the formation of other species that showed AB system (δ -18.9 and 52.7, $^{1}J_{pp}$ = 325 Hz) in ^{31}P NMR. They concluded its structure to be the Lewis acid/base adduct dimer (Scheme 6.14, right). The observed two doublet pairs in the present system, which also have large coupling constants, seem to be the relevant phosphine-phosphenium species. This species is presumably intermediate or "resting

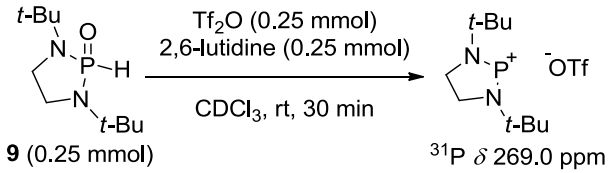
state" of the unstable diphenylphosphenium cation. On the other hand, the signal at δ 42.2 is unidentified at present.

Scheme 6.14



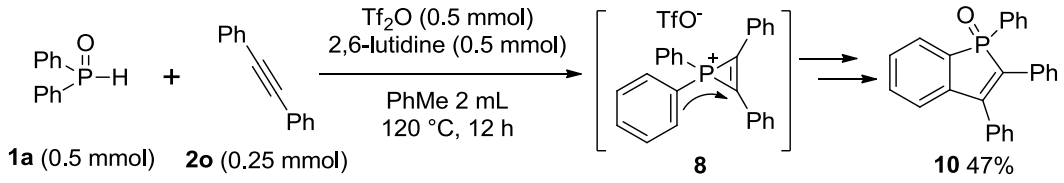
To obtain a further evidence the fact that the present Tf_2O/2,6-lutidine system can generate the phosphenium species, the author conducted the reaction of 1,3-di-*t*-butyl-1,3,2-diazaphospholidine 2-oxide (**9**) (Scheme 6.15). As expected, the corresponding free phosphenium species was observed as highly downshifted singlet signal by $^{31}P\{^{1}H\}$ NMR.

Scheme 6.15.



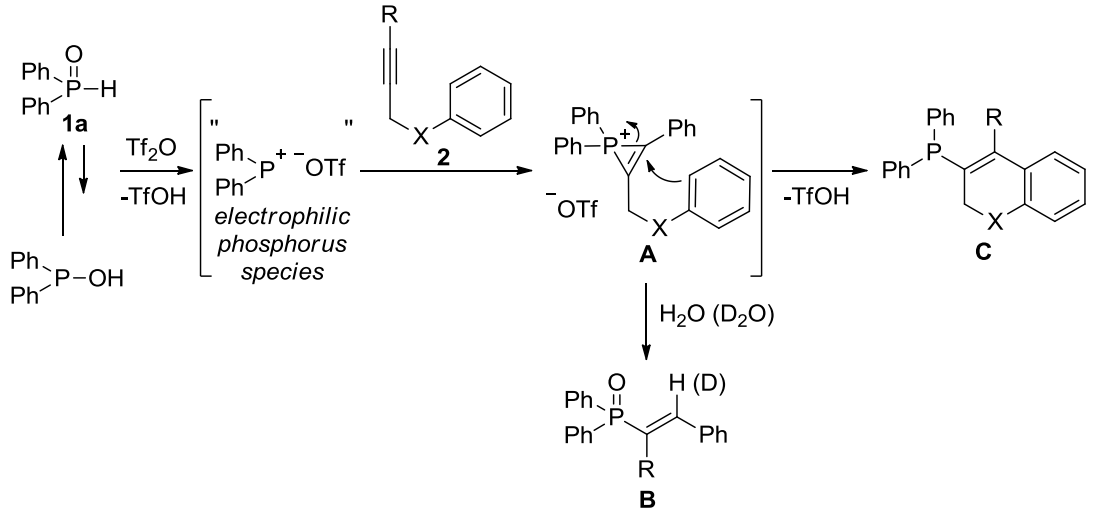
On the basis of the ^{31}P NMR spectra in Scheme 6.10, the formed phosphenium species **8** is concluded to be stable under the present conditions (60 °C, 3 h in DCM, Scheme 6.8) before quench. Hence, the author subjected this reaction system to more harsh conditions. Thus, a mixture of **1a** and **2o** was treated with Tf_2O and 2,6-lutidine in toluene at 120 °C for 12 h (Scheme 6.16). In consequence, benzophosphole oxide **10** was formed in 47% yield. This may occur via ring opening / intramolecular Friedel-Crafts reaction of the phosphirenium intermediate **8** as seen in Scheme 6.8.

Scheme 6.16.



Based on the mechanistic studies, the author proposed a tentative reaction mechanism for the present phosphinative ring-closure reaction in Scheme 6.17. The electrophilic phosphorus species generated from **1a** and Tf_2O undergo the [2+1] cycloaddition with alkyne **2** to form the phosphirenium cation **A**. The phosphirenium **A** may immediately undergo the ring opening hydrolysis to form the corresponding hydrophosphinylated product **B** in the presence of water. If the alkyne **2** has a pendant aryl moiety as a nucleophilic moiety at the appropriate position, the arylative ring opening of the phosphirenium may occur to form the phosphinative cyclization product **C**.

Scheme 6.17. Proposed Mechanism



Summary

In Chapter 6, the author described development of the metal-free electrophilic phosphination reaction of alkynes. The electrophilic phosphiation reagent generated *in*

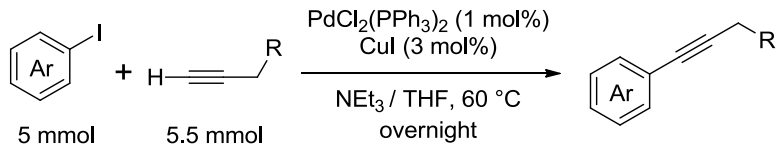
situ from secondary diarylphosphine oxides with the Tf_2O / 2,6-lutidine system smoothly undergoes the coupling reaction with alkynes to form various phosphine derivatives. The ^{31}P NMR mechanistic studies confirmed conceivable reactive species and intermediates in the reaction medium.

Experimental Section

General. ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded at 400, 100, 376 and 162 MHz for $CDCl_3$ solutions. HRMS data were obtained by APCI using a TOF mass spectrometer, unless noted. GC analysis was carried out using a silicon OV-17 column (i. d. 2.6 mm x 1.5 m). GC-MS analysis was carried out using a CBP-1 capillary column (i. d. 0.25 mm x 25 m). The structures of all products listed below were unambiguously determined by ^{1}H and ^{13}C NMR with the aid of NOE, COSY, HSQC, and HMBC experiments.

Substituted secondary phosphine oxide **1n** and **1o**,[17] alkynes **2a**, **2d**, **2f**, **2h**, and **2i**,[7d] **2c** and **2l**,[18] **2k**[19] were prepared according to published procedures. Substrates **2e**, **2g**, **2j**, **2m** and **2r** were synthesized by Sonogashira coupling as following procedures. Other starting materials were commercially available and used as received

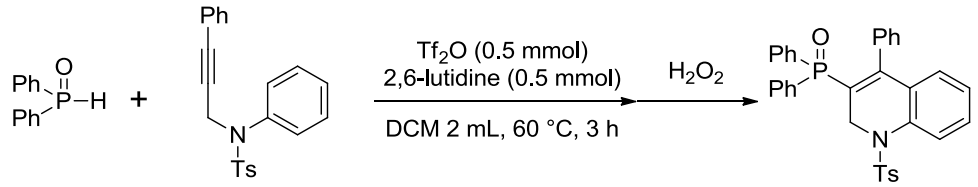
Synthesis of Alkynes 2e, 2g, 2j, 2m, and 2r.



In 50 mL two-necked flask, (hetro)aryl iodide (5 mmol), terminal alkyne (5.5 mmol), $PdCl_2(PPh_3)_2$ (35 mg, 1 mol%), and CuI (29 mg, 3 mol%) were placed with a magnetic stir bar under N_2 atmosphere. Then, THF (5 mL) and NEt_3 (5mL) were added by a syringe. The resulting mixture was stirred at 60 °C in an oil bath overnight. After cooling, the reaction mixture was diluted with ether (30 mL) and washed with brine (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed under reduced pressure. The desired product was obtained after

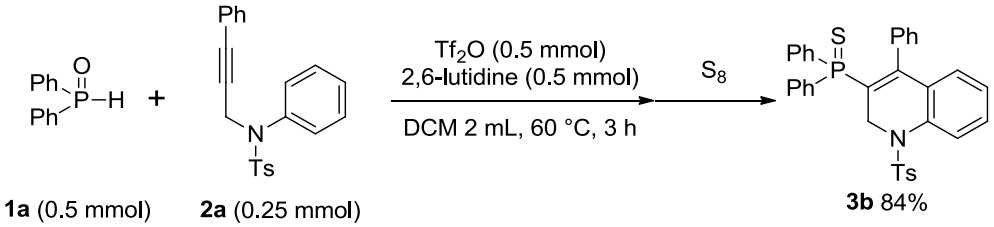
purification by column chromatography on silica gel.

Representative Procedures for Electrophilic Phosphination/Cyclization of Secondary Phosphines 1 with Alkynes 2 (H_2O_2 workup).



In a schlenk tube, **1a** (0.5 mmol), and **2a** (0.25 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, DCM (2 mL) and 2,6-lutidine (58 μl, 0.5 mmol) were added by a syringe. The resulting mixture was stirred until it became homogeneous solution. Then, Tf_2O (82 μl, 0.5 mmol) was added by syringe. The reaction mixture was heated at 60 °C in an oil bath for 3 h. After cooling, the reaction mixture was poured into sat. $NaHCO_3$ aq, and oxidized with H_2O_2 (30% aq, ca.0.5mL) for 15 min under open air. The resulting mixture was quenched by sat. $Na_2S_2O_3$ aq and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed under reduced pressure. The desired product was obtained after purification by column chromatography on silica gel.

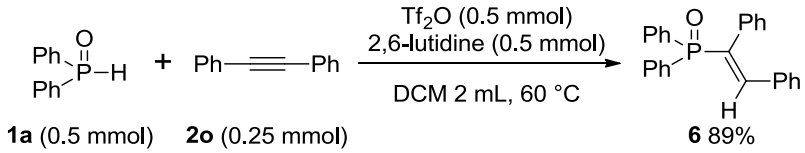
Representative Procedures for Electrophilic Phosphination/Cyclization of Secondary Phosphines 1 with Alkynes 2 (S_8 workup).



In a schlenk tube, **1a** (0.5 mmol), and **2a** (0.25 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, DCM (2 mL) and 2,6-lutidine (58 μl, 0.5 mmol) were added by a syringe. The resulting mixture was stirred until it became homogeneous solution. Then, Tf_2O (82 μl, 0.5 mmol) was added by syringe. The reaction mixture was heated at 60 °C in an oil bath for 3 h. After cooling, S_8 powder (32 mg, 1.0 mmol) was added and stirred for 1 h. The resulting reaction mixture was quenched with sat. $NaHCO_3$ aq, and extracted three times with DCM (20 mL x 3). The

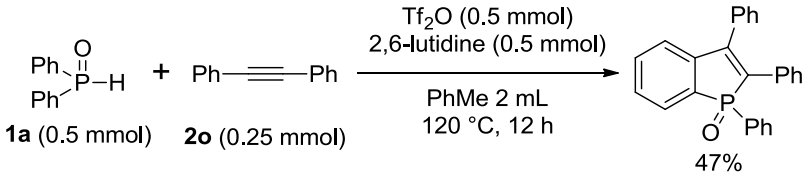
combined organic layer was dried over Na_2SO_4 and volatiles were removed under reduced pressure. The desired product was obtained after purification by column chromatography on silica gel.

Synthesis of 6 (Scheme 6.9).



In a schlenk tube, **1a** (0.5 mmol), and **2o** (0.25 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, DCM (2 mL) and 2,6-lutidine (58 µl, 0.5 mmol) were added by a syringe. The resulting mixture was stirred until it became homogeneous solution. Then, Tf_2O (82 µl, 0.5 mmol) was added by syringe. The reaction mixture was heated at 60 °C in an oil bath for 3 h. After cooling, the reaction mixture was poured into sat. $NaHCO_3$ aq, and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed under reduced pressure. The desired product was obtained after purification by column chromatography on silica gel.

Synthesis of 10 (Scheme 6.16).



In a schlenk tube, **1a** (0.5 mmol), and **2o** (0.25 mmol) were placed with a magnetic stir bar under N_2 atmosphere. Then, toluene (2 mL) and 2,6-lutidine (58 µl, 0.5 mmol) were added by a syringe. The resulting mixture was stirred until it became homogeneous solution. Then, Tf_2O (82 µl, 0.5 mmol) was added by syringe. The reaction mixture was heated at 120 °C in an oil bath for 12 h. After cooling, the reaction mixture was poured into sat. $NaHCO_3$ aq, and extracted three times with DCM (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and volatiles were removed under reduced pressure. The desired product was obtained after purification by column chromatography on silica gel.

Characterization Data of Products

Diphenyl(4-phenyl-1-tosyl-1,2-dihydroquinolin-3-yl)phosphine oxide (3a): pale yellow solid, mp

128-130 °C, 126.3 mg (90%); column chromatography eluent: hexane-ethyl acetate (1:0 to 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H), 4.65 (d, J = 6.6 Hz, 2H), 6.40 (d, J = 7.8 Hz, 2H), 6.62 (d, J = 7.8 Hz, 1H), 6.88 (dd, J = 7.5, 7.5 Hz, 2H), 7.00 (dd, J = 8.6, 8.6 Hz, 1H), 7.06 (dd, J = 8.4, 8.4 Hz, 1H), 7.23 (d, J = 8.1 Hz, 2H), 7.27-7.51 (m, 13H), 7.78 (dd, J = 8.1, 1.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 46.8 (d, J = 16.1 Hz), 125.8 (d, J = 94.1 Hz), 126.1, 126.3, 127.4, 127.76 (d, J = 12.2 Hz), 127.79, 128.3 (d, J = 12.3 Hz), 129.5, 129.8, 130.1, 131.3 (d, J = 11.6 Hz), 131.5 (d, J = 9.9 Hz), 131.6 (2C, overlapped), 132.1 (d, J = 108.1 Hz), 134.8 (d, J = 6.2 Hz), 135.8 (d, J = 1.5 Hz), 136.4, 143.6, 148.5 (d, J = 6.6 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 23.6; HRMS m/z ($M+H^+$) Calcd for $C_{34}H_{29}O_3PS$: 562.1600. Found 562.1608.

Diphenyl(4-phenyl-1-tosyl-1,2-dihydroquinolin-3-yl)phosphine sulfide (3b): colorless solid, mp 208-210 °C, 121.4 mg (84%); column chromatography eluent: hexane-ethyl acetate (1:0 to 5:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.44 (s, 3H), 4.71 (d, J = 7.7 Hz, 2H), 6.30-6.33 (m, 2H), 6.56 (d, J = 7.8 Hz, 1H), 6.80 (dd, J = 7.9, 7.9 Hz, 2H), 6.91-6.96 (m, 1H), 7.02 (ddd, J = 7.8, 7.8, 1.2 Hz, 1H), 7.21-7.39 (m, 9H), 7.56-7.67 (m, 6H), 7.80 (dd, J = 8.1, 1.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 47.4 (d, J = 18.3 Hz), 125.2 (d, J = 76.6 Hz), 125.9, 126.2, 127.4, 127.6, 127.7, 128.0, 128.2 (d, J = 12.7 Hz), 129.4, 129.86, 129.91, 131.2 (d, J = 2.9 Hz), 131.6 (d, J = 85.4 Hz), 131.7 (d, J = 11.3 Hz), 132.9 (d, J = 10.8 Hz), 134.3 (d, J = 6.3 Hz), 135.5 (d, J = 1.6 Hz), 135.9, 143.6, 146.5 (d, J = 5.7 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 39.1; HRMS m/z ($M+H^+$) Calcd for $C_{34}H_{29}O_2PS_2$: 578.1372. Found 578.1374.

(1-(4-Methoxyphenyl)-3,4-dihydronaphthalen-2-yl)diphenylphosphine oxide (3c): pale yellow gum, 84.6 mg (78%); column chromatography eluent: DCM-ethyl acetate (1:0 to 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.58-2.64 (m, 2H), 2.87-2.91 (m, 2H), 3.72 (s, 3H), 6.48 (d, J = 8.5 Hz, 2H), 6.70 (d, J = 7.8 Hz, 1H), 6.87 (d, J = 8.4 Hz, 2H), 7.03-7.07 (m, 1H), 7.17-7.40 (m, 8H), 7.59 (dd, J = 11.8, 7.0 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.2 (d, J = 10.8 Hz), 28.1 (d, J = 6.4 Hz), 55.1, 113.0, 126.5, 127.3, 127.8, 128.1 (d, J = 12.0 Hz), 129.0, 129.1, 129.4 (d, J = 6.9 Hz), 130.8 (d, J = 2.7 Hz), 131.4 (d, J = 9.4 Hz), 131.5, 134.0 (d, J = 102.7 Hz), 136.0 (d, J = 13.7 Hz), 137.0 (d, J = 2.3 Hz), 150.7 (d, J = 8.3 Hz), 158.7; ^{31}P{^{1}H} NMR (162 MHz): δ 28.9; HRMS m/z ($M+H^+$) Calcd for $C_{29}H_{26}O_2P$: 437.1665. Found 437.1666.

4-(2-(Diphenylphosphoryl)-3,4-dihydronaphthalen-1-yl)benzonitrile (3d): pale yellow gum, 87.0 mg (81%); column chromatography eluent: DCM-ethyl acetate (1:0 to 1:1, v/v); ^{1}H NMR (400 MHz,

$CDCl_3$): δ 2.54 (td, J = 7.8, 5.8 Hz, 2H), 2.89 (d, J = 7.3 Hz, 2H), 6.53 (d, J = 7.8 Hz, 1H), 7.06 (ddd, J = 7.8, 7.8 Hz, 1H), 7.13-7.25 (m, 4H), 7.34-7.40 (m, 6H), 7.43-7.49 (m, 2H), 7.56-7.63 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.5 (d, J = 10.5 Hz), 27.8 (d, J = 6.5 Hz), 111.3, 118.8, 126.8, 127.2, 127.6, 128.5 (d, J = 11.9 Hz), 129.5, 129.8 (d, J = 96.6 Hz), 131.0, 131.3 (d, J = 12.5 Hz), 131.4, 131.5 (d, J = 2.7 Hz), 133.1 (d, J = 103.0 Hz), 134.8 (d, J = 12.9 Hz), 136.6 (d, J = 2.1 Hz), 142.5 (d, J = 6.8 Hz), 149.5 (d, J = 7.0 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 28.2; HRMS m/z ($M+H^+$) Calcd for $C_{29}H_{23}NOP$: 432.1512. Found 432.1517.

Diphenyl(1-(4-(trifluoromethyl)phenyl)-3,4-dihydronaphthalen-2-yl)phosphine oxide (3e): pale yellow gum, 100.6 mg (85%); column chromatography eluent: hexane-ethyl acetate (1:0 to 0:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.60-2.68 (m, 2H), 2.87-2.96 (m, 2H), 6.54 (d, J = 7.8 Hz, 1H), 7.01-7.13 (m, 3H), 7.19-7.27 (m, 4H), 7.28-7.35 (m, 4H), 7.40 (ddq, J = 6.8, 6.8, 1.4 Hz, 2H), 7.53-7.62 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.3 (d, J = 10.2 Hz), 27.9 (d, J = 6.4 Hz), 124.0 (q, J = 270.6 Hz), 124.4 (q, J = 3.8 Hz), 126.7, 127.4, 127.5, 128.3 (d, J = 12.1 Hz), 129.36 (q, J = 31.8 Hz), 129.37, 129.7 (d, J = 99.4 Hz), 130.6, 131.3, 131.4 (d, J = 9.6 Hz), 132.3 (d, J = 102.9 Hz), 135.1 (d, J = 13.3 Hz), 136.8 (d, J = 2.2 Hz), 140.9 (d, J = 6.2 Hz), 149.4 (d, J = 7.8 Hz); ^{19}F{^{1}H} NMR (376 MHz): δ -62.8; ^{31}P{^{1}H} NMR (162 MHz): δ 28.5; HRMS m/z ($M+H^+$) Calcd for $C_{29}H_{23}F_3OP$: 475.1433. Found 475.1435.

Diphenyl(1-(2-methylphenyl)-3,4-dihydronaphthalen-2-yl)phosphine oxide (3f): colorless solid, mp 152-154 °C, 93.2 mg (89%); column chromatography eluent: DCM-ethyl acetate (1:0 to 2:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.87 (s, 3H), 2.51-2.62 (m, 1H), 2.77-3.02 (m, 3H), 6.51 (d, J = 7.8 Hz, 1H), 6.73-6.78 (m, 1H), 6.87-7.50 (m, 4H), 7.18-7.25 (m, 4H), 7.31-7.52 (m, 6H), 7.63-7.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.8, 26.0 (d, J = 10.4 Hz), 28.1 (d, J = 6.2 Hz), 125.1, 126.7 (d, J = 1.0 Hz), 126.8, 127.4, 127.9 (d, J = 11.9 Hz), 128.0, 128.2 (d, J = 11.9 Hz), 129.0, 129.7, 130.3 (d, J = 1.3 Hz), 130.8 (d, J = 2.6 Hz), 131.2 (d, J = 2.8 Hz), 131.4 (d, J = 9.8 Hz), 132.8 (d, J = 1.8 Hz), 133.8, 135.0 (d, J = 13.9 Hz), 136.2, 136.7 (d, J = 6.5 Hz), 136.9 (d, J = 2.2 Hz), 149.9 (d, J = 8.3 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 28.9; HRMS m/z ($M+H^+$) Calcd for $C_{29}H_{26}OP$: 421.1716. Found 421.1716.

Diphenyl(1-(thiophen-2-yl)-3,4-dihydronaphthalen-2-yl)phosphine oxide (3g): pale yellow gum, 79.2 mg (77%); column chromatography eluent: DCM-ethyl acetate (1:0 to 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.60-2.66 (m, 2H), 2.86-2.90 (m, 2H), 6.62 (dd, J = 5.1, 3.5 Hz, 1H), 6.83 (dd, J =

3.5, 1.2 Hz, 1H), 6.88 (d, J = 7.8 Hz, 1H), 7.05 (dd, J = 5.1, 1.2 Hz, 1H), 7.10 (ddd, J = 7.7, 7.7, 1.3 Hz, 1H), 7.18 (d, J = 7.4 Hz, 1H), 7.23 (ddd, J = 7.3, 7.3, 1.1 Hz, 1H), 7.30-7.44 (m, 6H), 7.60-7.67 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.5 (d, J = 10.1 Hz), 27.8 (d, J = 6.4 Hz), 126.3, 126.6, 127.0, 127.2, 127.5, 128.2 (d, J = 11.9 Hz), 129.3, 130.8, 131.1 (d, J = 2.6 Hz), 131.4 (d, J = 9.7 Hz), 132.3 (d, J = 98.1 Hz), 133.4 (d, J = 103.7 Hz), 135.8 (d, J = 12.8 Hz), 136.8 (d, J = 2.1 Hz), 137.6 (d, J = 2.1 Hz), 143.9 (d, J = 7.0 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 29.2; HRMS m/z (M+H$^+$) Calcd for $C_{26}H_{21}OPS$: 413.1129. Found 413.1119.

(*E*)-Diphenyl(1-styryl-3,4-dihydronaphthalen-2-yl)phosphine oxide (3h): pale yellow gum, 62.0 mg (57%); column chromatography eluent: hexane-ethyl acetate (1:0 to 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (dt, J = 7.8, 7.1 Hz, 2H), 2.73 (t, J = 7.2 Hz, 2H), 6.68 (d, J = 16.4 Hz, 11H), 7.17-7.31 (m, 8H), 7.39-7.50 (m, 6H), 7.56 (d, J = 8.7 Hz, 1H), 7.69 (dm, J = 16.4 Hz, 1H), 7.73-7.81 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.0 (d, J = 11.4 Hz), 28.3 (d, J = 6.5 Hz), 125.7 (d, J = 8.5 Hz), 126.3, 126.9, 127.0 (d, J = 99.3 Hz), 127.5, 127.6, 127.9, 128.4, 128.6 (d, J = 11.9 Hz), 128.9, 131.5, 131.6 (d, J = 9.6 Hz), 133.5 (d, J = 102.9 Hz), 134.1 (d, J = 3.2 Hz), 135.6, 136.8, 138.2 (d, J = 2.4 Hz), 149.2 (d, J = 6.4 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 30.6; HRMS m/z (M+H$^+$) Calcd for $C_{30}H_{26}OP$: 433.1716. Found 433.1717.

Diphenyl(4-phenyl-2*H*-chromen-3-yl)phosphine oxide (3i)[20]: pale yellow solid, mp 173-175 °C, 72.1 mg (71%); column chromatography eluent: hexane-ethyl acetate (1:0 to 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.88 (d, J = 6.7 Hz, 2H), 6.64 (dd, J = 7.8, 1.3 Hz, 1H), 6.81 (dd, J = 7.6, 7.6 Hz, 1H), 6.91-7.10 (m, 6H), 7.21-7.43 (m, 7H), 7.55-7.66 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 66.3 (d, J = 17.0 Hz), 116.2, 121.0 (d, J = 100.3 Hz), 121.6, 125.1 (d, J = 11.7 Hz), 127.6, 128.0, 128.2, 128.4 (d, J = 12.3 Hz), 129.9, 131.40, 131.41 (d, J = 10.0 Hz), 131.6, 132.8 (d, J = 104.6 Hz), 135.1 (d, J = 6.2 Hz), 149.4 (d, J = 6.4 Hz), 155.4; ^{31}P{^{1}H} NMR (162 MHz): δ 25.1; HRMS m/z (M+H$^+$) Calcd for $C_{27}H_{22}O_2P$: 409.1352. Found 409.1353.

Diphenyl(4-phenyl-2*H*-thiochromen-3-yl)phosphine sulfide (3j): colorless solid, mp 144-146 °C, 72.6 mg (66%); column chromatography eluent: hexane-ethyl acetate (1:0 to 10:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.63 (d, J = 11.0 Hz, 2H), 6.61 (d, J = 8.0 Hz, 1H), 6.87-7.00 (m, 4H), 7.03-7.09 (m, 2H), 7.16 (ddd, J = 7.5, 7.5, 1.4 Hz, 1H), 7.19-7.32 (m, 6H), 7.39 (dd, J = 7.8, 1.0 Hz, 1H), 7.88-7.95 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.3 (d, J = 15.7 Hz), 122.5 (d, J = 78.9 Hz), 125.2, 127.4 (d, J = 11.0 Hz), 127.6, 128.0 (d, J = 12.5 Hz), 128.1, 129.0, 130.6, 130.8 (d, J =

2.9 Hz), 131.1 (d, J = 1.1 Hz), 131.8 (d, J = 10.8 Hz), 132.8 (d, J = 83.7 Hz), 135.6 (d, J = 2.3 Hz), 136.1 (d, J = 12.2 Hz), 137.3 (d, J = 6.5 Hz), 149.9 (d, J = 7.7 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 44.8; HRMS m/z ($M+H^+$) Calcd for $C_{27}H_{22}PS_2$: 441.0895. Found 441.0897.

3-(Diphenylphosphoryl)-4-phenyl-2*H*-chromen-2-one (3k)[20]: colorless form, 57.7 mg (55%); column chromatography eluent: DCM-ethyl acetate (1:0 to 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 (dd, J = 8.1, 1.7 Hz, 1H), 7.18 (ddd, J = 8.2, 7.1, 1.1 Hz, 1H), 7.21-7.26 (m, 2H), 7.35 (dd, J = 7.5, 0.8 Hz, 1H), 7.37-7.52 (m, 9H), 7.58 (ddd, J = 8.6, 7.2, 1.7 Hz, 1H), 7.73-7.80 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.8, 118.5 (d, J = 100.5 Hz), 120.9 (d, J = 9.4 Hz), 124.4, 127.8, 128.2 (d, J = 12.6 Hz), 128.3, 128.8, 129.0, 131.56, 131.61 (d, J = 10.3 Hz), 133.1 (d, J = 109.9 Hz), 133.6 (d, J = 5.7 Hz), 133.7, 154.4, 159.6 (d, J = 13.4 Hz), 165.9 (d, J = 5.1 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 24.3; HRMS m/z ($M+H^+$) Calcd for $C_{27}H_{20}O_3P$: 423.1145. Found 423.1147.

(*E*)-(1-(4-Methoxyphenyl)-3-phenylprop-1-en-2-yl)diphenylphosphine oxide (5l): pale brown solid, mp 128-130 °C, 87.9 mg (83%); column chromatography eluent: DCM-ethyl acetate (1:0 to 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.78 (s, 3H), 3.96 (d, J = 18.0 Hz, 2H), 6.80-6.85 (m, 2H), 6.95-7.07 (m, 5H), 7.31-7.48 (m, 8H), 7.59 (d, J = 21.8 Hz, 1H), 7.64-7.71 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 34.2 (d, J = 11.1 Hz), 55.3, 114.0, 125.9, 127.9 (d, J = 18.8 Hz), 128.1, 128.2, 128.3 (d, J = 11.8 Hz), 129.1 (d, J = 95.2 Hz), 131.2, 131.68 (d, J = 2.6 Hz), 131.70 (d, J = 104.4 Hz), 132.2 (d, J = 9.5 Hz), 137.5 (d, J = 1.7 Hz), 144.9 (d, J = 10.6 Hz), 160.1; $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 32.7; HRMS m/z ($M+H^+$) Calcd for $C_{28}H_{26}O_2P$: 425.1665. Found 425.1666.

(*E*)-(1,5-Diphenylpent-1-en-2-yl)diphenylphosphine oxide (5m): colorless gum, 97.1 mg (92%); column chromatography eluent: DCM-ethyl acetate (1:0 to 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.61-1.72 (m, 2H), 2.47 (t, J = 7.3 Hz, 2H), 2.51-2.63 (m, 2H), 6.96-7.00 (m, 2H), 7.06 (d, J = 22.7 Hz, 1H), 7.12-7.27 (m, 8H), 7.45-7.59 (m, 6H), 7.70-7.78 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.1 (d, J = 10.1 Hz), 30.3 (d, J = 1.1 Hz), 35.8, 125.8, 128.2, 128.4 128.53 (2C), 128.54 (d, J = 11.7 Hz), 129.1, 131.88 (d, J = 2.7 Hz), 131.93 (d, J = 100.8 Hz), 132.1 (d, J = 9.6 Hz), 135.2 (d, J = 93.9 Hz), 135.5 (d, J = 19.2 Hz), 141.4, 142.9 (d, J = 11.7 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 33.7; HRMS m/z ($M+H^+$) Calcd for $C_{29}H_{28}OP$: 423.1878. Found 423.1873.

Bis(4-methoxyphenyl)(4-phenyl-1-tosyl-1,2-dihydroquinolin-3-yl)phosphine oxide (3n): colorless form, 100.6 mg (65%); column chromatography eluent: DCM-ethyl acetate (1:0 to 1:1,

v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H), 3.81 (s, 6H), 4.68 (d, J = 6.6 Hz, 2H), 6.36 (d, J = 7.5 Hz, 2H), 6.58 (d, J = 7.8 Hz, 1H), 6.80 (dd, J = 8.7, 2.0 Hz, 4H), 6.92 (dd, J = 7.7 Hz, 2H), 6.98-7.08 (m, 2H), 7.21 (d, J = 8.1 Hz, 2H), 7.31-7.39 (m, 5H), 7.45 (d, J = 8.2 Hz, 2H), 7.78 (dd, J = 8.1, 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 46.8 (d, J = 16.0 Hz), 55.3, 113.9 (d, J = 13.2 Hz), 123.5 (d, J = 111.1 Hz), 126.1, 126.2, 126.6 (d, J = 92.8 Hz), 127.4, 127.5, 127.7, 127.8, 129.5, 129.7, 129.9, 131.5 (d, J = 11.5 Hz), 133.3 (d, J = 11.2 Hz), 135.1 (d, J = 6.2 Hz), 135.7, 136.4, 143.5, 147.6, 162.1 (d, J = 2.5 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 23.6; HRMS m/z ($M+H^+$) Calcd for $C_{36}H_{33}NO_5PS$: 622.1812. Found 322.1809.

Bis(4-chlorophenyl)(4-phenyl-1-tosyl-1,2-dihydroquinolin-3-yl)phosphine oxide (3o): colorless form, 131.9 mg (84%); column chromatography eluent: hexane-ethyl acetate (1:0 to 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 3H), 4.61 (d, J = 6.8 Hz, 2H), 6.44 (dd, J = 8.3, 1.3 Hz, 2H), 6.64 (dd, J = 7.9, 1.3 Hz, 1H), 6.93 (dd, J = 7.9, 7.9 Hz, 2H), 7.03-7.7.12 (m, 2H), 7.22-7.30 (m, 7H), 7.33-7.42 (m, 5H), 7.50-7.53 (m, 2H), 7.74 (dd, J = 8.1, 1.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 46.5 (d, J = 16.3 Hz), 124.9 (d, J = 97.7 Hz), 125.9, 126.3, 127.6, 127.8, 127.9, 128.0, 128.7 (d, J = 12.7 Hz), 129.6, 129.8, 130.3 (d, J = 99.1 Hz), 130.4, 130.9 (d, J = 11.7 Hz), 132.7 (d, J = 10.7 Hz), 134.7 (d, J = 6.4 Hz), 135.9 (d, J = 1.8 Hz), 136.3, 138.3 (d, J = 3.7 Hz), 143.9, 149.3 (d, J = 7.0 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ 22.5; HRMS m/z ($M+H^+$) Calcd for $C_{34}H_{27}Cl_2NO_3PS$: 630.0826. Found 630.0830.

(*E*)-(1,2-diphenylvinyl)diphenylphosphine oxide (6)[21]: colorless solid, mp 153-155 °C, 84.3 mg (89%); column chromatography eluent: hexane-ethyl acetate (1:0 to 1:2, v/v);^{1}H NMR (400 MHz, $CDCl_3$): δ 6.90-6.95 (m, 2H), 7.02-7.06 (m, 2H), 7.10-7.25 (m, 6H), 7.38-7.44 (m, 4H), 7.51 (ddd, J = 6.8, 2.7, 1.3 Hz, 2H), 7.59 (d, J = 20.9 Hz, 1H), 7.64-7.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 127.7 (d, J = 2.1 Hz), 128.2, 128.3, 128.7, 128.9, 130.0 (d, J = 4.3 Hz), 130.3, 131.7 (d, J = 102.8 Hz), 131.8 (d, J = 2.6 Hz), 132.4 (d, J = 9.3 Hz), 135.0 (d, J = 3.8 Hz), 135.4 (d, J = 107.0Hz), 135.6 (d, J = 8.9 Hz), 143.1 (d, J = 9.6 Hz); ^{31}P{^{1}H} NMR (162 MHz): δ28.6; HRMS m/z ($M+H^+$) Calcd for $C_{26}H_{22}OP$: 381.1403. Found 381.1405.

1,2,3-Triphenyl-1*H*-phosphindole 1-oxide (10)[22]: colorless gum, 44.1 mg (47%); column chromatography eluent: hexane-ethyl acetate (1:0 to 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07-7.11 (m, 3H), 7.19-7.25 (m, 3H), 7.31-7.51 (m, 10H), 7.68-7.81 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 124.1 (d, J = 10.8 Hz), 127.8, 128.3, 128.7 (d, J = 12.4 Hz), 128.9 -129.2 (m, 6C,

overlapped), 130.0 (d, J = 99.1 Hz), 131.0 (d, J = 10.7 Hz), 132.1 (d, J = 105.1 Hz), 132.2 (d, J = 2.8 Hz), 132.7 (d, J = 9.5 Hz), 132.9 (d, J = 2.0 Hz), 134.29 (d, J = 15.1 Hz), 134.33 (d, J = 95.7 Hz), 143.8 (d, J = 27.0 Hz), 150.0 (d, J = 21.3 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz): δ 39.1; HRMS m/z ($M+H^{+}$) Calcd for $C_{26}H_{20}OP$: 379.1246. Found 379.1243.

References and Notes

(1) (a) Quin, L. D. *A Guide to Organophosphorus Chemistry*; Wiley Interscience: New York, **2000**. (b) *Organophosphorus Reagents*; Murphy, P. J., Ed.; Oxford University Press: Oxford, U.K., **2004**. (c) van Leeuwen, P. W. N. M.; Kamer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem. Rev.* **2000**, *100*, 2741. (d) Baumgartner, T.; Réau, R. *Chem. Rev.* **2006**, *106*, 4681. (e) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461. (f) Demmer, C. S.; Krogsgaard-Larsen, N.; Bunch, L. *Chem. Rev.* **2011**, *111*, 7981. (g) Queffelec, C.; Petit, M.; Janvier, P.; Knight, D. A.; Bujoli, B. *Chem. Rev.* **2012**, *112*, 3777.

(2) Reviews: (a) Beletskaya, I. P.; Kazankova, M. A. *Russ. J. Org. Chem.* **2002,** *38,* 1391. (b) Schwan, A. L. *Chem. Soc. Rev.* **2004,** *33,* 218. (c) Belabassi, Y.; Alzghari, S.; Montchamp, J.-L. *J. Organomet. Chem.* **2008**, *693*, 3171. (d) Tappe, F. M. J.; Trepohl, V. T.; Oestreich, M. *Synthesis* **2010**, 3037. (e) Wauters, I.; Debrouwer, W.; Stevens, C. V. *Beilstein J. Org. Chem.* **2014**, *10*, 1064. (f) Montchamp, J.-L. *Acc. Chem. Res.* **2014**, *47*, 77. For an earlier example, see: (g) Hirao, T.; Masunaga, T.; Ohshiro, Y.; Agawa, T. *Tetrahedron Lett.* **1980**, *21*, 3595.

(3) (a) Feng, C. G.; Ye, M.; Xiao, K. J.; Li, S.; Yu, J. Q. *J. Am. Chem. Soc.* **2013**, *135*, 9322. (b) Li, C.; Yano, T.; Ishida, N.; Murakami, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 9801. (c) Hong, G.; Mao, D.; Wu, S.; Wang, L. *J. Org. Chem.* **2014**, *79*, 10629. (d) Min, M.; Kang, D.; Jung, S.; Hong, S. *Adv. Synth. Catal.*, **2016**, *358*, 1296.

(4) (a) Michaelis, M. *Ber.* **1879**, *12*, 1009. (b) Kosolapoff, G. M.; Huber, W. F. *J. Am. Chem. Soc.* **1947**, *69*, 2020. (c) Miles, J. A.; Beeny, M. T.; Ratts, K. W. *J. Org. Chem.* **1975**, *40*, 343. (d) Olah, G. A.; Hehemann, D. *J. Org. Chem.* **1977**, *42*, 2190. (e) Diaz, A. A.; Young, J. D.; Khan, M. A.; Wehmschulte, R. J. *Inorg. Chem.* **2006**, *45*, 5568. (b) Hashimoto, S.; Nakatsuka, S.; Nakamura, M.; Hatakeyama, T. *Angew. Chem., Int. Ed.* **2014**, *53*, 14074.

(5) For reviews on phosphenium species, see: (a) Cowley, A. H.; Kemp, R. A. *Chem. Rev.* **1985**, *85*, 367. (b) Gudat, D. *Coord. Chem. Rev.* **1997**, *163*, 71. (c) Gudat, D. *Acc. Chem. Res.* **2010**, *43*, 1307.

(6) Sun, C.-L.; Shi, Z.-J. *Chem. Rev.* **2014**, *114*, 9219.

(7) (a) Ingleson, M. J. *Synlett* **2012**, *23*, 1411. (b) De Vries, T. S.; Prokofjevs, A.; Vedejs, E. *Chem.*

Rev. **2012**, *112*, 4246. (c) Bagutski, V.; Del Grosso, A.; Ayuso Carrillo, J.; Cade, I. A.; Helm, M. D.; Lawson, J. R.; Singleton, P. J.; Solomon, S. A.; Marcelli, T.; Ingleson, M. J. *J. Am. Chem. Soc.* **2013**, *135*, 474. (d) Warner, A. J.; Lawson, J. R.; Fasano, V.; Ingleson, M. J. *Angew. Chem., Int. Ed.* **2015**, *54*, 11245. (e) Faizi, D. J.; Issaian, A.; Davis, A. J.; Blum, S. A. *J. Am. Chem. Soc.* **2016**, *138*, 2126.

(8) (a) Cho, S. H.; Yoon, J.; Chang, S. *J. Am. Chem. Soc.* **2011**, *133*, 5996. (b) Antonchick, A. P.; Samanta, R.; Kulikov, K.; Lategahn, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 8605. (c) Kim, H. J.; Kim, J.; Cho, S. H.; Chang, S. *J. Am. Chem. Soc.* **2011**, *133*, 16382. (d) Kantak, A. A.; Potavathri, S.; Barham, R. A.; Romano, K. M.; DeBoef, B. *J. Am. Chem. Soc.* **2011**, *133*, 19960.

(9) (a) Furukawa, S.; Kobayashi, J.; Kawashima, T. *J. Am. Chem. Soc.* **2009**, *131*, 14192. (b) Oestreich, M.; Hermeke, J.; Mohr, J. *Chem. Soc. Rev.* **2015**, *44*, 2202. (c) Ma, Y.; Wang, B.; Zhang, L.; Hou, Z. *J. Am. Chem. Soc.* **2016**, *138*, 3663. (d) Chen, Q.-A.; Klare, H. F. T.; Oestreich, M. *J. Am. Chem. Soc.* **2016**, *138*, 7868. (e) Bähr, S.; Oestreich, M. *Angew. Chem., Int. Ed.* **2017**, *56*, 62.

(10) (a) Wu, Q.; Zhao, D.; Qin, X.; Lan, J.; You, J. *Chem. Commun.* **2011**, *47*, 9188. (b) Fernández-Salas, J. A.; Pulis A. P.; Procter, D. J. *Chem. Commun.*, **2016**, *52*, 12364.

(11) Christiansen, A.; Li, C.; Garland, M.; Selent, D.; Ludwig, R.; Spannenberg, A.; Baumann, W.; Franke, R.; Börner, A. *Eur. J. Org. Chem.* **2010**, 2733.

(12) (a) Jayaraman, A.; Jacob, T. V.; Bisskey, J.; Sterenberg, B. T. *Dalton Trans.* **2015**, *44*, 8788. (b) Jayaraman, A.; Sterenberg, B. T. *Organometallics* **2016**, *35*, 2367.

(13) Kühl, O. *Phosphorus-31 NMR Spectroscopy: A Concise Introduction for the Synthetic Organic and Organometallic Chemist*; Springer Science & Business Media: Heidelberg, Germany, **2008**.

(14) Breslow, R.; Deuring, L. *Tetrahedron Lett*. **1984**, *25*, 1345.

(15) Marinetti, A.; Mathey, F. *J. Am. Chem. Soc.* **1985**, *107*, 4700.

(16) Dahl, O. *Tetrahedron Lett.* **1982**, *23*, 1493.

(17) Busacca, C. A.; Lorenz, J. C.; Grinberg, N.; Haddad, N.; Hrapchak, M.; Latli, B.; Lee, H.; Sabila, P.; Saha, A.; Sarvestani, M.; Shen, S.; Varsolona, R.; Wei, X. D.; Senanayake, C. H. *Org. Lett.* **2005**, *7*, 4277.

(18) Walkinshaw, A. J.; Xu, W.; Suero, M. G.; Gaunt, M. J. *J. Am. Chem. Soc.* **2013**, *135*, 12532.

(19) Gao, W.-C.; Liu, T.; Zhang, B.; Li, X.; Wei, W.-L.; Liu, Q.; Tian, J.; Chang, H.-H. *J. Org. Chem.* **2016**, *81*, 11297.

(20) Li, D. P.; Pan, X. Q.; An, L. T.; Zou, J. P.; Zhang, W. *J. Org. Chem.* **2014**, *79*, 1850.

(21) Takaki, K.; Komeyama, K.; Takehira, K. *Tetrahedron* **2003**, *59*, 10381.

(22) Unoh, Y.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 12975.

Conclusions

The research described in this thesis is study on the synthesis of phosphorus-containing heterocycles by using C-H bond functionalization strategy. A variety of phospholes and other phosphorus heterocycles are now easily accessible from readily available simple substrates by newly developed straightforward methods. Since these phosphorus-containing heterocycles have recently been attracted much attentions as unique building blocks but the traditional synthetic ways are limited and not effective, the results obtained in this thesis have significant advantage in the synthetic chemistry area.

The author focused on characteristic reactivities and behaviors of each organophosphorus compound and designed new reactions to utilize their features to achieve the straightforward transformation. Regarding to the Lewis basic behaviors of P=O and P=S (V) compounds, the new catalytic direct C-C bond forming reactions have been developed by using the phosphorus moieties as directing group (Chapters 2, 4, and 5). With a unique reactivity of phosphorus-centered radical species, the new benzo[*b*]phosphole synthesis by oxidative radical cyclization has been achieved (Chapter 3). Furthermore, by utilizing the synthetically valuable thiophosphinamide group as a directing group, the regioselective synthesis of the benzo[*b*]phospholes and the dibenzo[*b*]phospholes has been realized (Chapters 4 and 5). Finally, a new type of metal-free electrophilic phosphination/cyclization reaction has been accomplished by focusing on the tautomerization of secondary phosphine oxide and the high π-philicity of phosphenium cations (Chapter 6).

Although organophosphorus chemistry has a long history, still there is undiscovered unique transformation. The author believes that the new findings presented in this thesis would contribute to further advances in the synthesis and application of unique phosphorus molecules and create a new aspect of organophosphorus chemistry.

List of Publication

1. Rhodium(III)-Catalyzed Oxidative Coupling through C-H Bond Cleavage Directed by Phosphinoxy Groups
Yuto Unoh, Yuto Hashimoto, Daisuke Takeda, Koji Hirano, Tetsuya Satoh, Masahiro Miura
Org. Lett. **2013***, 15,* 3258.

2. An Approach to Benzophosphole Oxides through Silver- or Manganese-Mediated Dehydrogenative Annulation Involving C-C and C-P Bond Formation
Yuto Unoh, Koji Hirano, Tetsuya Satoh, Masahiro Miura
Angew. Chem. Int. Ed. **2013***, 52*, 12975.

3. Rhodium(III)-Catalyzed Direct Coupling of Arylphosphine Derivatives with Heterobicyclic Alkenes: A Concise Route to Biarylphosphines and Dibenzophosphole Derivatives
Yuto Unoh, Tetsuya Satoh, Koji Hirano, Masahiro Miura
ACS Catal., **2015**, *5*, 6634.

4. Regioselective Synthesis of Benzo[*b*]phosphole Derivatives via Rhodium(III)-Catalyzed *ortho*-Alkenylation and Cyclization of Arylthiophosphinamides
Yuto Unoh, Yuki Yokoyama, Tetsuya Satoh, Koji Hirano, Masahiro Miura
Org. Lett. **2016***, 18,* 5436.

5. Tf_2O-Mediated Metal Free Electrophilic Phosphination of Alkynes
Yuto Unoh, Koji Hirano, Masahiro Miura
Manuscript in preparation

Supplementary list of publication

1. Synthesis of Highly Substituted Isocoumarins by Rhodium-Catalyzed Annulation of Readily Available Benzoic Acids
Yuto Unoh, Koji Hirano, Tetsuya Satoh, Masahiro Miura
Tetrahedron. **2013**, *69*, 4454.

2. Palladium-Catalyzed Decarboxylative Arylation of Benzoylacrylic Acids toward the Synthesis of Chalcones
Yuto Unoh, Koji Hirano, Tetsuya Satoh, Masahiro Miura
J. Org. Chem. **2013**, *78*, 5096.

3. Rhodium(III)-Catalyzed Regioselective C-H Alkenylation of Phenylphosphine Sulfides
Yuki Yokoyama, Yuto Unoh, Koji Hirano, Tetsuya Satoh, Masahiro Miura
J. Org. Chem. **2014***, 79,* 7649.

4. Rhodium-Catalyzed Intramolecular Dehydrogenative Aryl-Aryl Coupling Using Air as Terminal Oxidant
Hannah Baars, Yuto Unoh, Takeshi Okada, Koji Hirano, Tetsuya Satoh, Ken Tanaka, Carsten Bolm, Masahiro Miura
Chem. Lett. **2014***, 43,* 1782.

5. Rhodium(III)-Catalyzed Oxidative Alkenylation of 1,3-Dithiane-Protected Arenecarbaldehydes via Regioselective C-H Bond Cleavage
Yuto Unoh, Koji Hirano, Tetsuya Satoh, Masahiro Miura
Org. Lett. **2015***, 17,* 704.

6. Rhodium-Catalyzed Direct Coupling of Benzothioamides with Alkenes and Alkynes through Directed C-H Bond Cleavage
Yuki Yokoyama, Yuto Unoh, Rebekka Anna Bohmann, Tetsuya Satoh, Koji Hirano, Carsten Bolm, Masahiro Miura
Chem. Lett. **2015**, *44*, 1104.

7. Rhodium(III)-Catalyzed Intramolecular Ar-H/Ar-H Coupling Directed by Carboxylic Group to Produce Dibenzofuran Carboxylic Acids
Takeshi Okada, Yuto Unoh, Tetsuya Satoh, Masahiro Miura
Chem. Lett. **2015**, *44*, 1598.

8. Synthesis of Benzo[*c*]thiophenes by Rhodium(III)-Catalyzed Dehydrogenative Annulation
Keita Fukuzumi, Yuto Unoh, Yuji Nishii, Tetsuya Satoh, Koji Hirano, Masahiro Miura
J. Org. Chem. **2016***, 81*, 2474.

9. 1,2-Thiazines: One-Pot Syntheses Utilizing Mono- and Diaza-Analogs of Sulfones
Rebekka Anna Bohmann, Yuto Unoh, Masahiro Miura, Carsten Bolm
Chem.—Eur. J. **2016**, *22*, 6783.