Photocatalytic Cycloaddition Reaction of Triarylphosphines with Alkynes Forming Cyclic Phosphonium Salts

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Herein reported is a photocatalytic cycloaddition reaction of triarylphosphines with alkynes. Phosphonium salts of unique bicyclic structures are synthesized through a radical pathway under mild reaction conditions. The phosphonium salts are subjected to the Wittig olefination reaction to afford structurally interesting phosphine oxides.

Keywords: Phosphonium salt • Alkyne • Photoredox catalyst

Phosphonium salts belong to an important class of compounds that are utilized as synthetic reagents,[1] organo-catalysts,[2] and ionic liquid,[3] among others.[4] The most conventional method for the synthesis of quaternary phosphonium salts is given by a nucleophilic substitution reaction of alkyl halides with tertiary phosphines.[5] An alternative preparative approach to phosphonium salts via a radical pathway recently appeared.[6] However, the phosphonium salts that are accessible by these methods are limited to those of acyclic structures. It presents a challenge to develop a facile method to synthesize phosphonium salts of cyclic structures from readily available starting substances. Herein reported is a photocatalytic cycloaddition reaction of triarylphosphines with alkynes. The phosphonium salts of unique bicyclic structures were synthesized from those readily available starting materials.

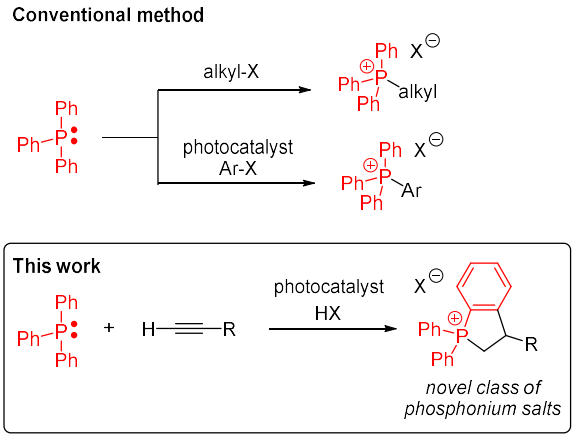
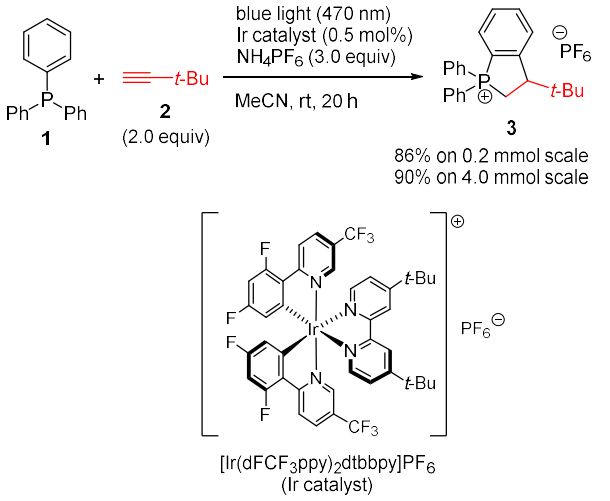


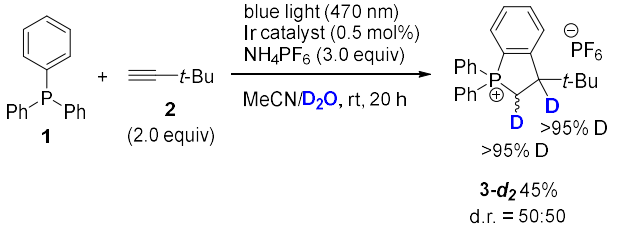
Figure 1. Syntheses of phosphonium salts.

We recently reported a three component coupling reaction of triarylphosphines, alkenes, and water.[7] It was marked by dramatic skeletal changes involving C–P bond formation and dearomatization of the phenyl ring. We next examined an analogous reaction using an alkyne instead of an alkene; a mixture of triphenylphosphine (**1**), alkyne **2** (2.0 equiv), ammonium hexafluorophosphate (NH_4PF_6, 3.0 equiv), and an iridium photocatalyst ($[Ir(dFCF_3ppy)_2dtbbpy]PF_6$, 0.5 mol%) in acetonitrile was irradiated with blue light (470 nm) for 20 h, and the reaction mixture was subjected to chromatographic purification on silica gel. To our surprise, the phosphonium salt having a bicyclic structure **3** was obtained in 86% isolated yield (Scheme 1). The structure of **3** was confirmed by an X-ray crystallographic analysis (CCDC 2084056). In a formal sense, [3 + 2]-type cycloaddition took place to construct the five-membered ring. Light, NH_4PF_6, and the iridium catalyst were all indispensable for the production of **3**.[8] When the reaction was scaled up to a 4.0 mmol scale, the product **3** could be isolated by recrystallization in place of chromatography, and its yield improved to 90%.



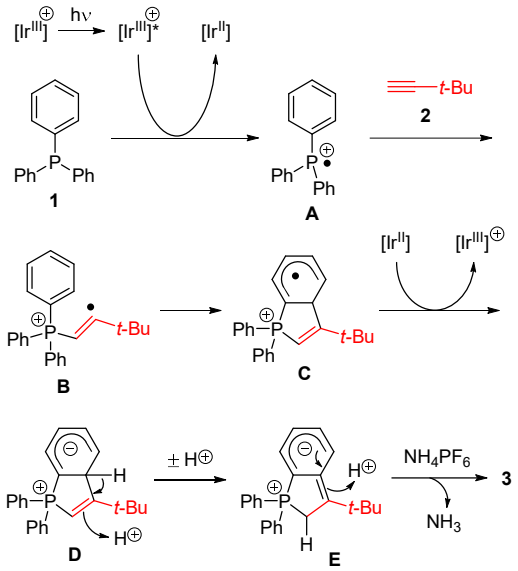
Scheme 1. Photocatalyzed cyclization of triphenylphosphine (**1**) and alkyne **2**.

Next, the reaction was conducted in the presence of D_2O (1 mL). Two deuterium atoms were incorporated on the two ring carbons, each α and β to phosphorus (Scheme 2).



Scheme 2. Reaction in the presence of D_2O.

We propose a reaction pathway shown in Scheme 3 to explain the formation of **3** from **1** and **2**. Initially, the iridium(III) catalyst absorbs light to get excited. Triphenylphosphine (**1**) ($E_{1/2}^{red}$ = +0.98 V vs SCE in CH_3CN)[9] transfers a single electron to the excited iridium(III) catalyst ($E_{1/2}^{red}$[Ir(III)*/Ir(II)] = +1.21 V vs SCE in CH_3CN),[10] generating radical cation **A** and an iridium(II) species. The phosphine radical cation **A** adds across the C–C triple bond of **2** to generate substituted alkenyl radical **B**, which adds onto the phenyl ring to form the five-membered ring. The resulting cyclohexadienyl radical **C** accepts a single electron from the iridium(II) species to become the cyclohexadienyl anion **D**, the anionic charge of which is delocalized onto the attached cationic phosphorus, thereby regenerating the iridium(III) catalyst. The following 1,3-prototropic shift extends delocalization even further, giving rise to the conjugated alkene **E**. Finally, aromaticity is regained upon protonation at the carbon β to the phosphorus atom to furnish the bicyclic phosphonium salt **3**.

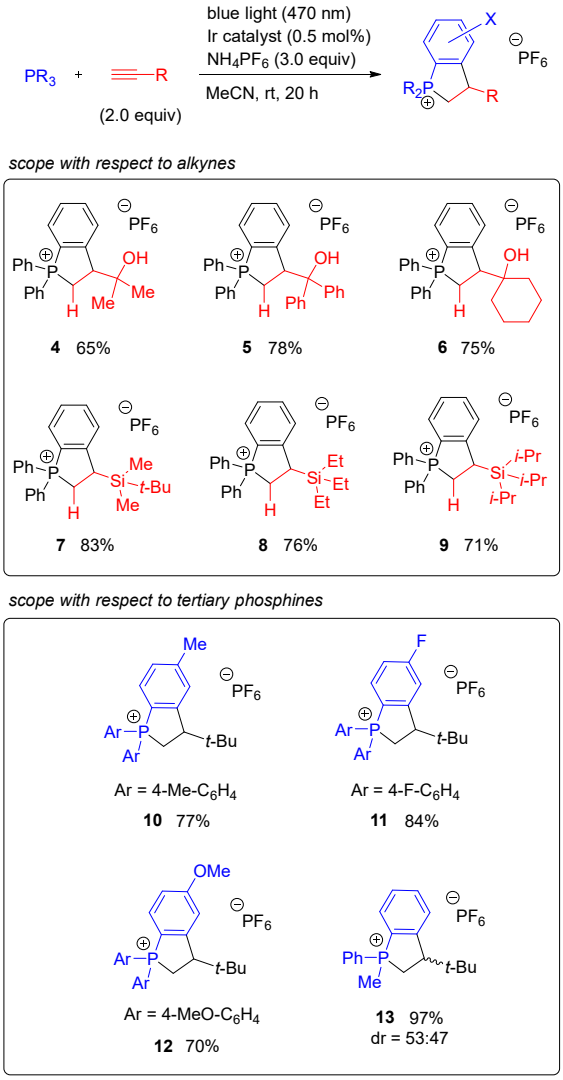


Scheme 3. A proposed reaction pathway.

Various terminal alkynes were reacted with triphenylphosphine (**1**). Propargylic alcohols afforded the corresponding phosphonium salts **4-6** in good yields, suggesting the tolerance of a hydroxy functionality. The silylated phosphonium salts **7-9** were produced from silyl-substituted alkynes in yields ranging from 49% to 83%. Although internal alkynes such as 3-hexyne also participated in the reaction, we failed to isolate the corresponding phosphonium salts in a pure form because some byproducts were inseparable.

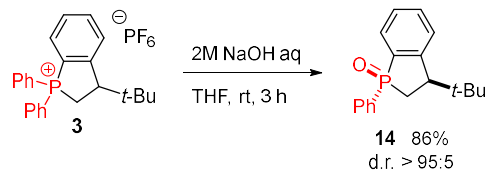
Other triarylphosphines than **1** were also examined. Functional groups such as fluoro (**11**) and methoxy (**12**) groups were tolerated on the aromatic ring of triarylphosphines. Not only triarylphosphines but also methyldiphenylphosphine participated in the cycloaddition reaction with alkyne. The cyclic phosphonium salt **13** was produced in 97% yield as a mixture of diastereomers.

Table 1. Substrate scope.[a]



[a] Reaction conditions: tertiary phosphine (0.20 mmol), alkene (0.40 mmol, 2.0 equiv), NH_4PF_6 (0.60 mmol, 3.0 equiv), Ir catalyst (0.001 mmol, 0.5 mol%), MeCN (3 mL), blue LEDs (470 nm), rt, 20 h. Isolated yield.

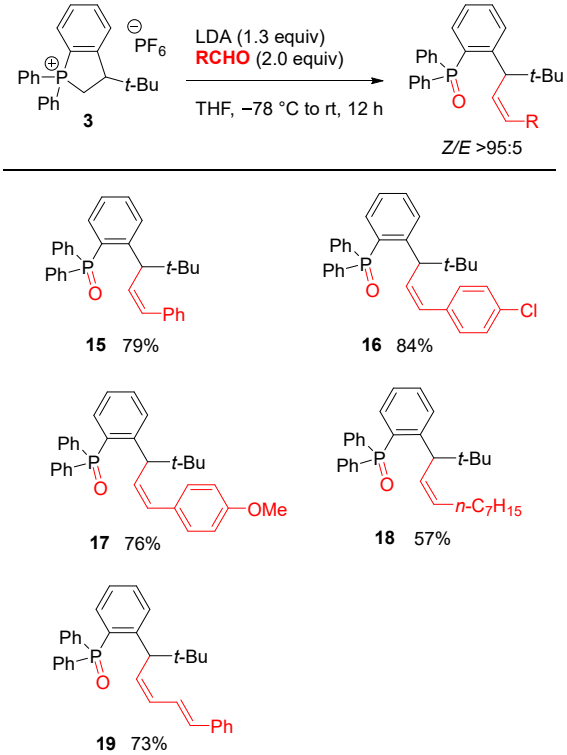
It was possible to convert the produced phosphonium salts to the corresponding phosphine oxides according to a literature procedure;[11] the phosphonium salt **3** was treated with NaOH in THF/water at room temperature for 3 h. $P(III)^+$ was oxidized to P(V)=O and the phenyl substituent on it was protonated to afford benzophospholane oxide **14** in 86% yield as a single diastereomer.



Scheme 4. Derivatization of the produced phosphonium salts.

The phosphonium salts were used in the Wittig olefination reaction (Table 2). After a solution of the phosphonium salt **3** in tetrahydrofuran (THF) was treated with lithium diisopropylamide (LDA, 1.3 equiv) at –78 °C for 1 h, benzaldehyde (2.0 equiv) was added to the generated ylide, and the reaction mixture was stirred at room temperature for 12 h. The corresponding alkenylated phosphine oxide **15** was obtained in 79% yield. A high *Z*-selectivity (*Z*/*E* > 95/5) was observed, as is often the case with the Wittig reaction of unstable ylides.[12] Not only benzaldehyde but also octanal served as an aldehyde to furnish the alkene **18** in 57% yield. Cinnamyl aldehyde produced 1,3-diene **19** in 73% yield. Of note is that the phosphine oxide moiety remaining in the product is amenable to further transformation.[13]

Table 2. Wittig-type coupling of phosphonium salt **3** with aldehydes.[a]



[a] Reaction conditions: **3** (0.20 mmol), LDA (1.0 M in THF/hexane, 0.26 mmol, 1.3 equiv), THF (3 mL), –78 °C, 1 h; then aldehyde (0.40 mmol, 2.0 equiv), rt, 12 h. Isolated yield.

In conclusion, the present study discloses a new synthetic approach to the phosphonium salts of unique cyclic structures starting from tertiary phosphines and alkynes, which are both readily available. The produced phosphonium salts are engaged in the Wittig olefination reaction to afford the corresponding phosphine oxides of interesting structures.

This work was supported by JSPS KAKENHI Grant Numbers 19K15562 and 21K14626 (Y.M.).

Supporting Information is available on http://dx.doi.org/10.1246/cl.******.

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Graphical Abstract

Textual Information

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Title(required)	Photocatalytic Cycloaddition Reaction of Triarylphosphines with Alkynes Forming Cyclic Phosphonium Salts
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