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# Synthesis of 1,2,4-azadiphosphole derivatives based on vanadium-catalyzed [2+2+1] cycloaddition reactions of azobenzenes with phosphalkynes†

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A new synthetic method is described to construct 1,2,4-azadiphosphole derivatives based on vanadium-catalyzed [2+2+1] cycloaddition reactions. Reactions of azobenzenes as nitrogen sources with phosphalkynes as phosphorous counterparts in the presence of  $VCl_2(thf)_2$  as a catalyst afford the corresponding 1,2,4-azadiphospholes.

Phosphorus heterocycles have provided important structural motifs to explore materials science and coordination chemistry.<sup>1</sup> To access diverse skeletons, development of new and efficient synthetic methods is quite important. In addition to the conventional synthetic methods typically forming carbon-phosphorous single bonds, the use of phosphalkynes as substrates is beneficial to construct phosphorous-containing  $\pi$ -systems.<sup>2</sup> Stoichiometric reactivity of phosphalkynes with transition metal complexes has been studied extensively,<sup>3</sup> but catalytic reactions of phosphalkynes under transition metal catalysis have been limited to several sporadic examples.<sup>4,5</sup> Recently, our group has reported catalytic [2+2+2] cycloaddition reactions to produce phosphabenzenes and [3+2] cycloaddition reactions to produce 1,3-azaphospholes based on the use of phosphalkynes as substrates.<sup>5</sup> To investigate further utility of phosphalkynes to prepare aromatic compounds containing phosphorus atoms, we have focused on the synthesis of 1,2,4-azadiphospholes as next targets.

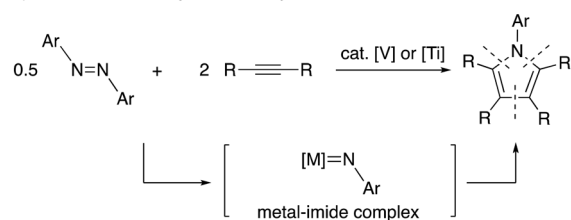
Synthetic examples of 1,2,4-azadiphospholes have been limited to only a few reports.<sup>6,7</sup> To the best of our knowledge, the first synthesis of the 1,2,4-azadiphosphole skeleton was reported in 1991, where a 1,2,4-azadiphosphole derivative was prepared based on a thermal dimerization of an amino-substituted phosphalkyne.<sup>6a</sup> Later, other groups reported stoichiometric reactions of titanium- and vanadium-imide complexes as nitrogen sources with phosphalkynes.<sup>6b-d</sup> Although these stoichiometric reactions provided effective

synthetic methods of 1,2,4-azadiphospholes, transition metal-catalyzed synthesis of 1,2,4-azadiphospholes has never been achieved until now.

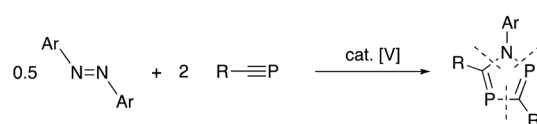
Recently, titanium-catalyzed [2+2+1] cycloaddition reactions have been reported by Tonks and co-workers to prepare pyrroles from reactions of azobenzenes with alkynes (Scheme 1a).<sup>8</sup> In this reaction system, titanium-imide species generated from azobenzenes worked as a key intermediate. More recently, a similar pyrrole synthesis using vanadium-catalyzed reaction system has been reported by Tonks, Mashima, Tsurugi and co-workers.<sup>9</sup>

Based on the research background, we have envisaged metal-catalyzed [2+2+1] cycloaddition reactions of azobenzenes with phosphalkynes to produce 1,2,4-azadiphospholes (Scheme 1b). As a result, we have found that some vanadium complexes worked as effective catalysts toward the formation of 1,2,4-azadiphospholes. Herein, we report experimental results in detail.

a) Previous Works: Synthesis of Pyrroles



b) This Work: Synthesis of 1,2,4-Azadiphospholes



Scheme 1 Catalytic [2+2+1] cycloaddition reactions with azobenzenes as nitrogen sources in heterocycle synthesis.

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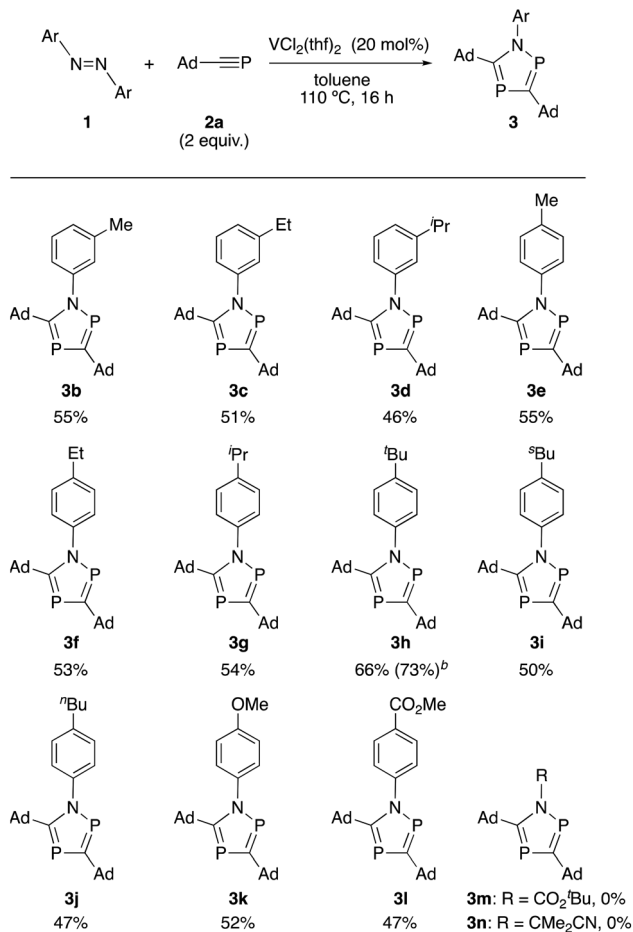
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First, investigation of reaction conditions was carried out with the use of azobenzene (**1a**) and 1-adamantylphosphaethyne (**2a**) as typical substrates. When the reaction of **1a** (1 equiv.) with **2a** (2 equiv.) in the presence of 20 mol% of  $\text{VCl}_3(\text{thf})_3$  was carried out in toluene at 110 °C for 16 hours, the desired 1,2,4-azadiphosphole (**3a**) was obtained in 48% yield (Table 1, entry 1). Replacing  $\text{VCl}_3(\text{thf})_3$  with  $\text{VBr}_3(\text{thf})_3$  and  $\text{VCl}_3(\text{py})_3$  was not effective in the current reaction system (Table 1, entries 2 and 3). Then, we investigated the use of  $\text{VCl}_2(\text{thf})_2$ ,  $\text{VCl}_2(1,4\text{-dioxane})_2$  and  $\text{VI}_2(\text{thf})_4$ . Among these catalysts,  $\text{VCl}_2(\text{thf})_2$  showed the highest reactivity to afford the desired product **3a** in 60% yield (Table 1, entries 4–6). Next, addition of ligands was examined. When bidentate phosphine ligands such as 1,1-bis(diphenylphosphino)methane (dppm) or 1,2-bis(diphenylphosphino)ethane (dppe) was used, only lower yields of the product were obtained (Table 1, entries 7 and 8) while no formation of the desired product was observed when 2,2'-bipyridine was used as a ligand (Table 1, entry 9). Separately, we confirmed no formation of **3a** in the absence of vanadium complexes. Based on these results, we have chosen the use of  $\text{VCl}_2(\text{thf})_2$  as the optimal catalyst.

With the optimized reaction conditions in hand, the use of other substrates was investigated. The use of various functionalized azobenzene derivatives was examined (Scheme 2). When 3-methyl-, 3-ethyl- and 3-isopropyl-substituted azobenzenes were used, the corresponding products (**3b**, **3c** and **3d**) were obtained in 55%, 51% and 46% yield, respectively. Effect of alkyl groups at the 4-position of the benzene rings in azobenzene was also examined. Introduction of methyl, ethyl, isopropyl, *tert*-butyl, *sec*-butyl and *n*-butyl groups afforded the corresponding products (**3e–3j**) in good yields. The reaction system was tolerant toward oxygen functional groups such as 4-methoxyl and 4-methoxycarbonyl groups to give the desired products (**3k** and **3l**) in 52% and 47% yields, respectively. Unfortunately, an



Scheme 2 Reactions of azobenzene with 1-adamantylphosphaethyne **2a**. <sup>a</sup>Reactions of azobenzenes **1** (0.1 mmol) with **2a** (0.2 mmol) in the presence of  $\text{VCl}_2(\text{thf})_2$  (20 mol%) in toluene (2.0 mL) at 110 °C for 16 h. <sup>b</sup><sup>1</sup>H NMR yield with  $\text{C}_6\text{Me}_6$  as an internal standard.

Table 1 Investigation of reaction conditions<sup>a</sup>

Entry	[V] catalyst	Ligand	Yield (%)
1	$\text{VCl}_3(\text{thf})_3$	—	48
2	$\text{VBr}_3(\text{thf})_3$	—	42
3	$\text{VCl}_3(\text{py})_3$	—	0
4	$\text{VCl}_2(\text{thf})_2$	—	60
5	$\text{VCl}_2(1,4\text{-dioxane})_2$	—	47
6	$\text{VI}_2(\text{thf})_4$	—	27
7	$\text{VCl}_2(\text{thf})_2$	dppm	27
8	$\text{VCl}_2(\text{thf})_2$	dppe	20
9	$\text{VCl}_2(\text{thf})_2$	2,2'-Bipyridine	0

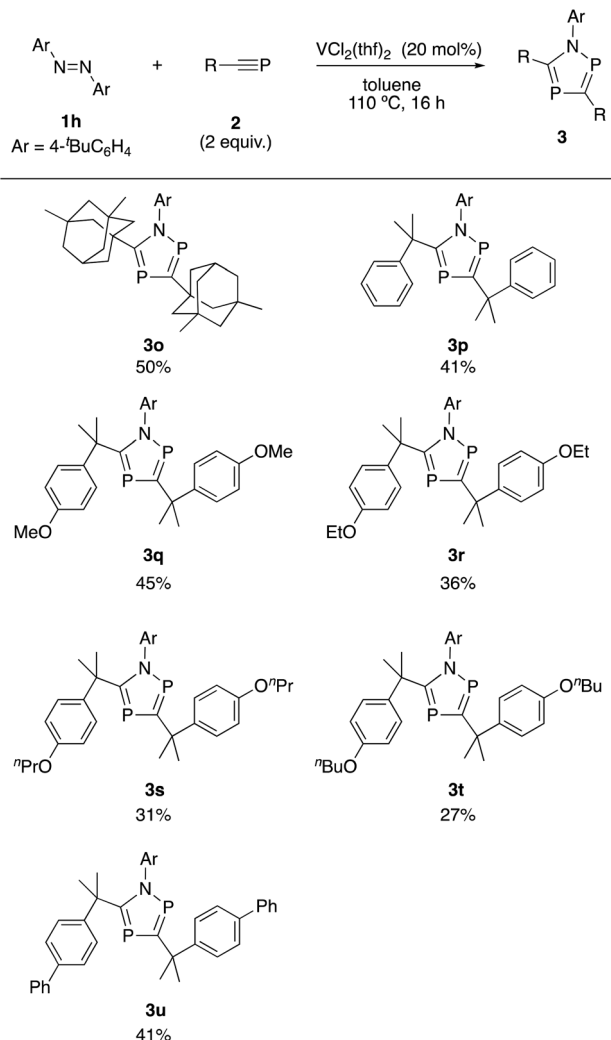
<sup>a</sup> Reactions of **1a** (0.10 mmol) with **2a** (0.20 mmol) in the presence of a catalyst (20 mol%) and a ligand (20 mol%) in toluene (2.0 mL) at 110 °C for 16 h.

azodicarboxylate ester was not applicable in this reaction system resulting in no formation of the corresponding product (**3m**). We also examined 2,2'-azobis(isobutyronitrile) as an aliphatic azo compound, but the corresponding product (**3n**) was not obtained at all.

Next, the use of various phosphalkynes was investigated (Scheme 3). A phosphalkyne bearing 3,5-dimethyl-1-adamantyl moiety was successfully transformed into the corresponding product (**3o**) in 50% yield. The use of phosphalkyne bearing a benzene ring was also successful to afford the corresponding product (**3p**) in 41% yield. Introduction of various alkoxyphenyl moieties into the phenyl ring was also investigated and the corresponding products were obtained in moderate yields (**3q–3t**). When the biphenyl substituent was introduced in phosphalkyne, the corresponding product (**3u**) was obtained in 41% yield.

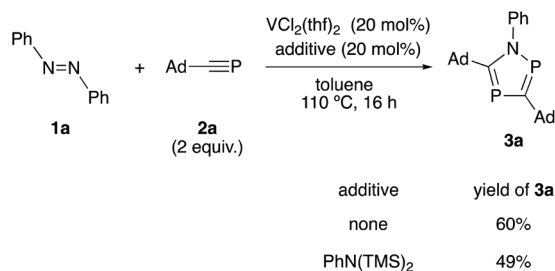
As mentioned above, recently vanadium-catalyzed [2+2+1] cycloaddition reactions of azobenzenes with alkynes to afford the pyrroles were reported.<sup>9</sup> In this reaction system, bis-(trimethylsilyl)aniline was used as an additive along with  $\text{VCl}_3(\text{thf})_3$  catalyst, and a vanadium-bis(imide) complex was proposed to be a catalytically active species. Bis(trimethylsilyl)aniline



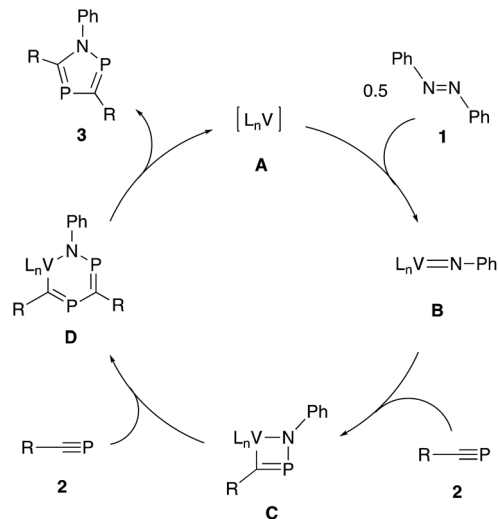


**Scheme 3** Reactions of 1,2-di(4-*tert*-butyl)diazene **1h** with phosphalkynes **2**. <sup>a</sup>Reactions of **1h** (0.1 mmol) with phosphalkynes **2** (0.2 mmol) in the presence of VCl<sub>2</sub>(thf)<sub>2</sub> (20 mol%) in toluene (2.0 mL) at 110 °C for 16 h.

supplies an imide moiety on the vanadium center through a redox neutral ligand exchange process and the second imide moiety comes from azobenzene substrates through an oxidative process, where the generated vanadium-bis(imide) complex is supposed to undergo further reactions to give the pyrroles.



**Scheme 4** Effect of bis(trimethylsilyl)aniline as additive.



**Scheme 5** Plausible reaction pathway.

According to the experimental result, we investigated the effect of bis(trimethylsilyl)aniline as an additive in the current reaction system (Scheme 4). When bis(trimethylsilyl)aniline (20 mol%) was added along with VCl<sub>2</sub>(thf)<sub>2</sub> catalyst in the reaction of **1a** with **2a**, the yield of **3a** did not improve. This result suggests that the introduction of imide moiety from bis(trimethylsilyl)aniline was not effective in this reaction system. Previously, vanadium-mono(imide) complexes were reported to react stoichiometrically with phosphalkynes to give the corresponding 1,2,4-azadiphospholes.<sup>5b,c</sup> Based on the experimental result, we consider that a vanadium-mono(imide) species may work as a catalytically active species in the current reaction system.

Based on these observations, a plausible reaction pathway is shown in Scheme 5. First, vanadium complex **A** reacts with an azobenzene **1** to give vanadium-imide complex **B**. Then, [2+2] cycloaddition reaction occurs between **B** and a phosphalkyne **2** to afford a four-membered ring intermediate **C**. Subsequent insertion of the second phosphalkyne **2** forms a six-membered ring intermediate **D**. Finally, reductive elimination affords the desired 1,2,4-azadiphosphole **3** accompanied by the regeneration of the initial vanadium complex **A**.

In summary, we have succeeded in the development of the first vanadium-catalyzed [2+2+1] cycloaddition reactions of azobenzenes with phosphalkynes to synthesize a variety of 1,2,4-azadiphospholes. We believe the present study has opened a new aspect of synthetic application for the utilization of phosphalkynes as building blocks in the construction of phosphorous-containing heterocyclic skeletons.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

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