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Iron-Catalyzed [2 + 2 + 2] Cycloaddition Reactions of Diynes with Oxyphosphaethynes To Construct 2-Phosphaphenol Derivatives

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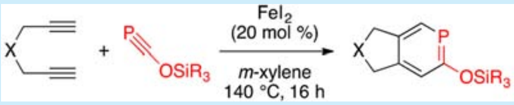
Ⓢ *Supporting Information*

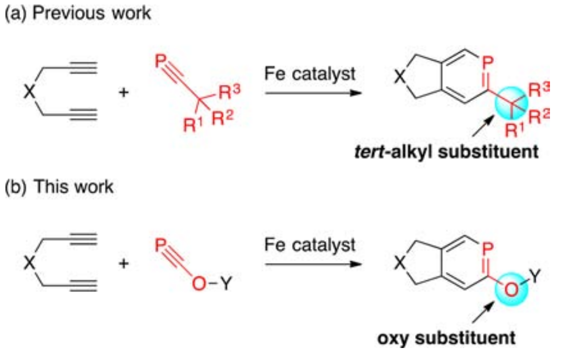
ABSTRACT: Iron-catalyzed [2 + 2 + 2] cycloaddition reactions of diynes with siloxyphosphaethynes have been developed to give 2-phosphaphenol derivatives. The use of electronically neutral siloxyphosphaethynes generated in situ by the reaction of anionic phosphaethynolate with silyl triflates is key to achieving the reactions.



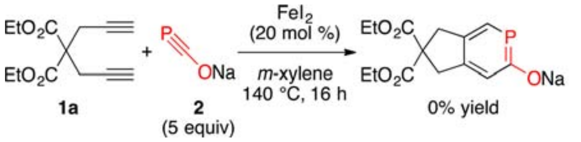
Phosphorus-containing aromatic rings such as phosphabenzene (phosphinine) and its derivatives are quite attractive in materials science.[1] These compounds are also used as ligands of transition-metal complexes utilized in transition-metal-catalyzed transformations.[2] Although a variety of synthetic methods to construct phosphabenzenes have been known to date,[2,3] reactions of pyrylium salts with phosphine equivalents have played a central role since the first synthesis of phosphabenzene derivatives.[4] However, introduction of heteroatom substituents on the phosphabenzene ring by this method is usually difficult. As a result, reliable examples of the synthesis of phosphabenzenes bearing hydroxy or alkoxy substituents (phosphaphenols) have been limited.[5,6] For examples on the synthesis of 2-phosphaphenol derivatives, Diels−Alder-type cycloaddition reactions of phosphaalkynes with α-pyrones[5a,c] and a stepwise transformation of a phosphaalkene−tungsten complex[5b] have been known to date.

Cycloaddition reactions using phosphaalkynes as a building block are also important methods for synthesis of phosphabenzenes.[5c,6b−d,7,8] Recently, our group succeeded in the development of iron-catalyzed [2 + 2 + 2] cycloaddition reactions of diynes with phosphaalkynes as a new method for the synthesis of phosphabenzenes (Scheme 1a).[9] This is the first successful example of the synthesis of phosphabenzenes by transition-metal catalysts. However, in this reaction system, applicable phosphaalkynes have been limited to phosphaethynes bearing a *tert*-alkyl substituent. To expand the scope of phosphaalkynes, we focused our attention on the use of oxyphosphaethyne derivatives (Scheme 1b).[10−12] In fact, we found that siloxyphosphaethynes[11] work as effective substrates to give 2-phosphaphenol derivatives. Herein, we report the synthesis of 2-phosphaphenol derivatives through iron-catalyzed [2 + 2 + 2] cycloaddition reactions of diynes with siloxyphosphaethynes.

Scheme 1. Iron-Catalyzed [2 + 2 + 2] Cycloaddition Reactions of Diynes with Phosphaalkynes To Construct Phosphabenzenes



A phosphaethynolate anion was first synthesized by Becker et al. in 1992,[10a] and its reactivity has been studied extensively since.[10,11] At first, we examined the direct use of sodium phosphaethynolate (**2**) as a substrate (eq 1). In the presence of 20 mol % of iron(II) iodide, the reaction of 4,4-bis(ethoxylcarbonyl)-hepta-1,6-diyne (**1a**) with 5 equiv of **2** in *m*-xylene at 140 °C (bath temperature) for 16 h was carried out. Unfortunately, no formation of desired 2-phosphaphenol derivatives was observed at all.



(1)

Based on this result, next, we focused our attention on the use of electronically neutral siloxyphosphaethynes, which were reported by Grützmacher et al.[11] Siloxyphosphaethynes were reported to be unstable for isolation; therefore, we examined the direct use of siloxyphosphaethynes generated in situ. After the generation of *tert*-butyldiphenylsiloxyphosphaethyne (**4a**) in situ by treatment of **2** with *tert*-butyldiphenylsilyl triflate (**3a**) in *m*-xylene at 40 °C for 2 h, the reaction of **1a** with **4a** in the presence of iron(II) iodide was carried out in *m*-xylene at 140 °C (bath temperature) for 16 h (Table 1, entry 1).[13] To our delight, in this case, the desired 5-phospha-6-(*tert*-butyldiphenylsiloxy)-2,2-bis(ethoxycarbonyl)indane (**5a**) was obtained in 47% yield.

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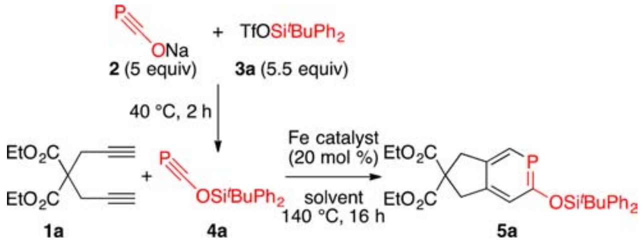
Table 1. Reactions of **1a** with **4a** Generated in Situ from **2** and **3a**[a]



entry	Fe catalyst	solvent	yield of **5a** (%)[b]
1	FeI_2	*m*-xylene	47 (38)[c]
2	$FeBr_2$	*m*-xylene	39
3	$FeCl_2$	*m*-xylene	19
4	FeF_2	*m*-xylene	trace
5	$Fe(OTf)_2$	*m*-xylene	20
6[d]	FeI_2	*m*-xylene	31
7[e]	FeI_2	*m*-xylene	34
8	FeI_2	tetradecane	31
9	FeI_2	DMSO	0
10	FeI_2	DMF	0

[a] After treatment of **2** (0.75 mmol) with **3a** (0.83 mmol) in *m*-xylene (1.5 mL) at 40 °C for 2 h, the resulting mixture was reacted with **1a** (0.15 mmol) in the presence of Fe catalyst (0.030 mmol) at 140 °C (bath temperature) for 16 h. [b] NMR yield. [c] Isolated yield. [d] 30 mol % of FeI_2. [e] At 120 °C.

According to the previous report by Grützmacher et al.,[11] silylation of phosphaethynolate anion produces two possible isomers, siloxyphosphaethyne (O-silylation) and silylphosphaketene (P-silylation). The ratio depends on the reaction conditions. To explore this selectivity under the present reaction conditions, we carried out the reaction of **2** with **3a** in *m*-xylene at 40 °C for 2 h (Scheme 2).[13] The ^{31}P NMR of the reaction mixture of two isomers showed two signals at −300.0 and −346.5 ppm. We identified the resonance at −300.0 ppm as **4a** and at −346.5 ppm as **4a′** by comparison with those of the reported triisopropylsilyl and triphenylsilyl analogues.[11] The measurement revealed that O-silylation product **4a** was generated selectively over P-silylation product **4a′**. Little increase of **4a** was observed after a longer reaction time. Considering the yield of **4a**, roughly 2 equiv of **4a** was generated under the present reaction conditions.

Scheme 2. Reaction of **2** with **3a**

	4a	4a'
2 h:	42%	3%
4 h:	49%	4%
8 h:	46%	10%

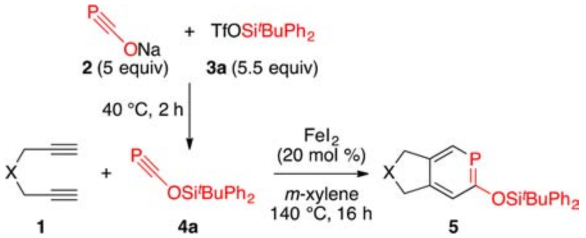
Next, we investigated other reaction conditions (Table 1). Other iron catalysts such as iron(II) bromide, chloride, fluoride, and triflate were not effective to give **5a** in only lower yields (Table 1, entries 2−5). The use of a larger amount of iron(II) iodide (30 mol %) did not improve the yield (Table 1, entry 6). Decreasing the reaction temperature to 120 °C was not effective (Table 1, entry 7). The reaction proceeded in tetradecane (Table 1, entry 8), but the use of DMSO and DMF as solvents did not give **5a** at all (Table 1, entries 9 and 10).

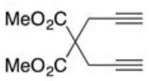
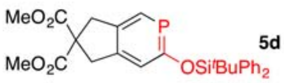
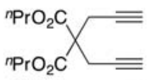
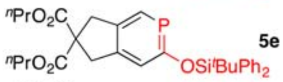
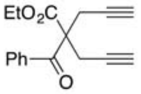
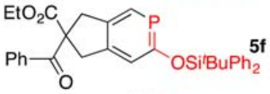
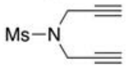
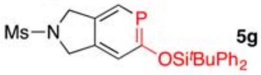
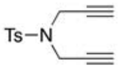
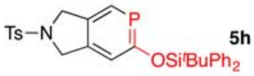
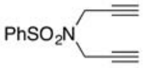
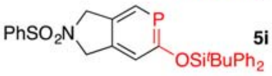
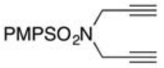
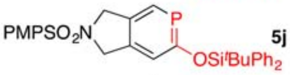
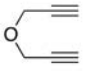
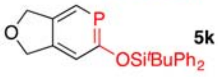
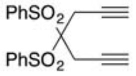
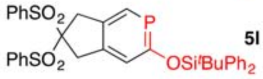
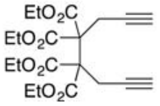
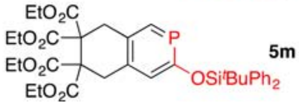
To examine the nature of the silyl group, we used other silyl triflates (Scheme 3). When triisopropylsilyl triflate (**3b**) was used

Scheme 3. Effect of Silyl Triflates (**3**) in the Reactions of **1a**

$SiR_3 = Si^tBuPh_2$ (**5a**): 47%
$SiR_3 = Si^iPr_3$ (**5b**): 33%
$SiR_3 = SiMe_3$ (**5c**): 0%

Table 2. Reactions of Diynes **1** with **4a** Generated in Situ from **2** and **3a**[a]



entry	diyne (**1**)		2-phosphaphenol (**5**)		yield (%)[b]
1		**1b**		**5d**	66 (42)
2		**1c**		**5e**	53
3		**1d**		**5f**	53
4		**1e**		**5g**	61
5		**1f**		**5h**	70
6		**1g**		**5i**	71 (52)
7[c]		**1h**		**5j**	55
8[d]		**1i**		**5k**	57
9		**1j**		**5l**	57 (39)
10		**1k**		**5m**	trace

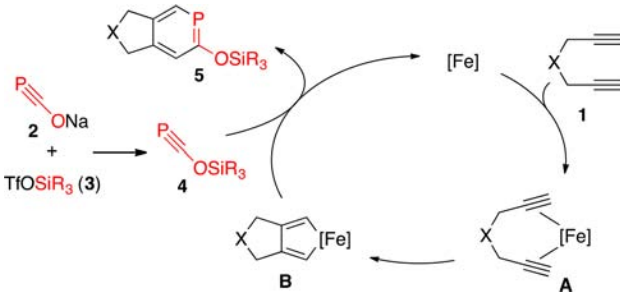
[a] After treatment of **2** (0.75 mmol) with **3a** (0.83 mmol) in *m*-xylene (1.5 mL) at 40 °C for 2 h, the resulting mixture was reacted with **1** (0.15 mmol) in the presence of Fe catalyst (0.030 mmol) at 140 °C (bath temperature) for 16 h. [b] NMR yield; isolated yield in parentheses. [c] PMP = *p*-C_6H_4OMe. [d] At 80 °C in toluene.

instead of **3a**, the corresponding 2-phosphaphenol derivative (**5b**) was obtained in 33% yield. Trimethylsilyl triflate (**3c**) was not effective, and the corresponding product (**5c**) was not observed. These results indicate that the use of a bulky silyl group is important in this reaction system.

Next, we examined reactions of various diynes **1** with **4a** (Table 2). The use of diynes bearing ester moieties (**1b**−**d**) gave the corresponding 2-phosphaphenol derivatives (**5d**−**f**) in good yields (Table 2, entries 1−3). We found the use of diynes tethered by mesyl (Ms), tosyl (Ts), benzenesulfonyl, and *para*-methoxybenzenesulfonyl amide moieties (**1e**−**h**) gave the corresponding products (**5g**−**j**) in higher yields (Table 2, entries 4−7). Reactions of diynes bearing ether and sulfonyl moieties (**1i**,**j**) were also successful to give **5k** and **5l** in good yields (Table 2, entries 8 and 9). We tried to construct a six-membered ring-fused skeleton by using **1k** as a substrate. Unfortunately, no desired product (**5m**) was obtained at all (Table 2, entry 10).[14]

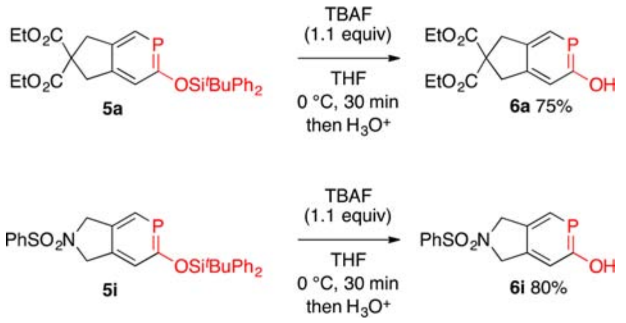
A plausible reaction pathway is shown in Scheme 4, which is similar to our previous work.[9] At first, coordination of a diyne (**1**) to an iron center occurs, and subsequent oxidative cyclization gives the ferracyclopentadiene intermediate (**B**).[15] Then, the reaction of the ferracyclopentadiene with a siloxyphosphaalkye (**4**) generated in situ from the phosphaethynolate anion (**2**) and a silyl triflate (**3**) produces the corresponding 2-phosphaphenol derivative (**5**). At present, however, we cannot exclude other reaction pathways such as via a 3-phospha-1-ferracyclopentadiene species.[16]

Scheme 4. Plausible Reaction Pathway



Finally, desilylation of the obtained 2-siloxyphosphabenzenes (**5**) was demonstrated (Scheme 5). Treatment of **5a** and **5i** with 1.1 equiv of TBAF in THF at 0 °C for 30 min and subsequent aqueous workup afforded the corresponding 2-hydroxyphosphabenzenes (**6a**,**i**) in high yields.

Scheme 5. Desilylation Reactions of 5a and 5i



In summary, we have succeeded in the iron-catalyzed [2 + 2 + 2]cycloaddition reactions to give 2-phosphaphenol derivatives. The use of electronically neutral siloxyphosphaethynes as substrates is key to achieving the reactions. Desilylation of the obtained products was successful under common desilylation conditions to give 2-hydroxyphosphabenzenes. Further transformations and utilization of the obtained 2-phosphaphenol derivatives are now in progress.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b02462.

Experimental details, spectroscopic data (PDF)

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Notes

The authors declare no competing financial interest.

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(13) See Supporting Information for experimental details.

(14) We also examined a reaction of a diyne bearing an internal alkyne moiety (4,4-bis(methoxycarbonyl)octa-1,6-diyne). The corresponding product was obtained in low yield as a mixture of isomers (16% NMR yield with ca. 1:1 isomeric ratio).

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