Direct Annulation

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An Approach to Benzophosphole Oxides through Silver- or Manganese-Mediated Dehydrogenative Annulation Involving C–C and C–P Bond Formation**

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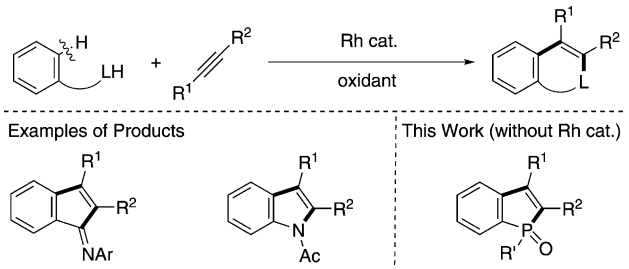
Benzophosphole derivatives have recently attracted much attention in the field of materials chemistry because of their unique optical and electronic properties.[1] However, synthetic approaches to such promising frameworks are so far limited.[2] Most of the currently available methods rely on the cyclization of phenylphosphorus compounds with alkynyl groups preinstalled in the *ortho* position; these precursors are usually prepared through complicated multistep reactions. Moreover, the substituent tolerance is low because the cyclizations are performed under strongly basic conditions. To expand the application of benzophosphole species, the development of new, effective processes for synthesizing them from relatively simple starting materials is much needed.

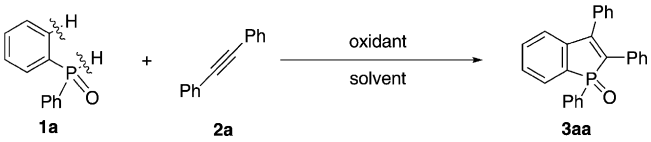
As one promising route from readily available substrates to fused (hetero)aromatic compounds, the rhodium-catalyzed dehydrogenative annulation of monosubstituted benzenes with alkynes through directed C–H bond cleavage has been significantly developed in recent years (Scheme 1).[3,4] For example, both we[5] and Fagnou and co-workers[3c] have reported that indenone imines and indoles can be constructed through the coupling of benzylideneanilines and *N*-acetylanilines, respectively, with internal alkynes through C–H and N–H bond cleavages (–LH = –CH=NAr and –NHAc in Scheme 1).



Scheme 1. Rhodium-catalyzed dehydrogenative annulation. Shown are examples of products from previous reports, and the benzophosphole oxides described in this work.

In light of these results, we undertook to develop a direct method for the construction of benzophospholes by using rhodium catalysis. As an initial attempt, we 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 (–LH = –PH(=O)Ph, $R^1 = R^2 = Ph$ in Scheme 1 and entry 1 in Table 1),[6,7] and succeeded in obtaining the expected benzophosphole derivative **3aa** in a good yield. It was somewhat surprising to observe that the reaction proceeded efficiently even without any rhodium catalyst (see below).

Table 1: Reaction of diphenylphosphine oxide (**1a**) with diphenylacetylene (**2a**).[a]



Entry	Oxidant (mmol)	Solvent	*T* [°C]	Yield of **3aa** [%][b]
1[c]	AgOAc (1)	DMF	100	93
2	AgOAc (1)	DMF	100	96 (96)
3[d]	AgOAc (1)	DMF	100	80
4	AgOAc (0.5)	DMF	100	6
5	$AgNO_3$ (0.05) + $K_2S_2O_8$ (1)	DMF	100	19
6	AgOAc (1)	DMF	80	13
7	AgOAc (1)	AcOH	100	81
8[e]	AgOAc (12)	DMF	100	(82)
9	$Mn(OAc)_3 \cdot 2H_2O$ (1)	DMF	100	50
10	$Mn(OAc)_3 \cdot 2H_2O$ (1)	DMF	RT	70
11	$Mn(OAc)_3 \cdot 2H_2O$ (1)	AcOH	RT	78
12	$Mn(OAc)_3 \cdot 2H_2O$ (1)	CH_2Cl_2	RT	58

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.25 mmol), and oxidant in solvent (3 mL) under N_2 for 4 h. [b] Yield based on the amount of **2a** used as determined by GC. Values in parentheses indicate yield after purification. [c] With $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (0.01 mmol). Cp^* = pentamethylcyclopentadienyl. [d] With **1a** (0.25 mmol). [e] With **1a** (6 mmol) and **2a** (3 mmol) in DMF (36 mL).

Based on this intriguing observation, we postulated an annulation mechanism with the silver promoter alone as illustrated in Scheme 2. In the presence of the Ag^I salt, a P-centered radical appears to be formed from **1a** through homolytic P–H bond cleavage, as proposed previously.[8] Subsequently, the addition of the radical across the triple

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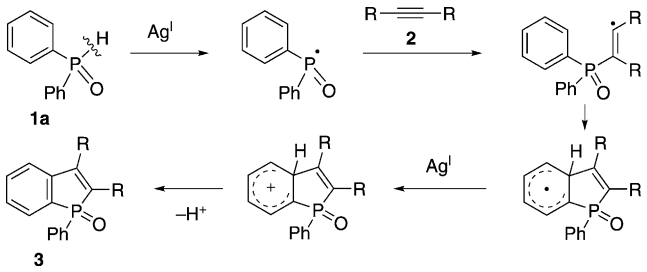


Scheme 2. Proposed mechanism for silver-mediated annulation of **1a** with **2**.

bond of an alkyne **2** followed by cyclization on the phenyl moiety of **1a** may occur to form the benzophosphole oxide **3**. In contrast to well-established reactions involving the addition of P-centered radicals to alkenes, an approach that has been widely employed for synthesizing organophosphorus compounds, intermolecular addition to alkynes has been little explored.[9] In particular, examples of cascade processes involving successive reactions of the resulting alkenyl radicals, aside from simple reduction, are so far limited.[10] Consequently, we investigated the annulation reaction in detail to provide an unprecedented direct route to benzophosphole derivatives. Furthermore, it was found that these radical processes can also be promoted by a Mn^{III} salt[10a,11] as well as Ag^{I}.

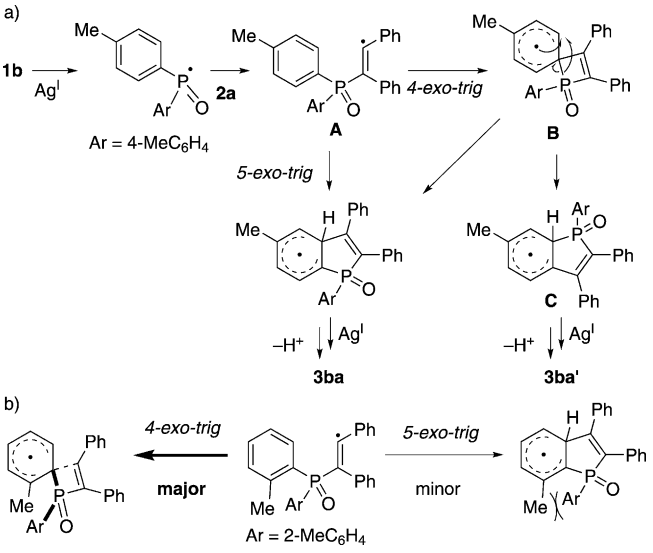
In a typical experiment, diphenylphosphine oxide (**1a**; 0.5 mmol) was treated with diphenylacetylene (**2a**; 0.25 mmol) in the presence of AgOAc (1 mmol) in DMF (3 mL) at 100 °C for 4 h under N_2. The oxidative annulation product 1,2,3-triphenyl-1*H*-phosphindole-1-oxide (**3aa**) was obtained exclusively, in 96 % yield (entry 2 in Table 1). While the reaction using the substrates in a 1:1 ratio gave **3aa** in 80 % yield (entry 3 in Table 1), decreasing the amount of AgOAc (0.5 mmol) substantially reduced the product yield (entry 4). The combination of $AgNO_3$ (0.05 mmol) and $K_2S_2O_8$ (1 mmol), which has been employed to generate P-centered radicals,[8b,c] was not effective for the present reaction (entry 5 in Table 1). At 80 °C, the reaction was sluggish (entry 6 in Table 1). In AcOH, the reaction also proceeded smoothly, but the product yield was somewhat low (entry 7 in Table 1). 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 8 in Table 1).

As shown in Scheme 2, the present reaction seems to proceed through a radical process promoted by Ag^{I}. To obtain additional support for this mechanism, we conducted the reaction of **1a** with **2a** in the presence of radical inhibitors (see the Supporting Information). As expected, adding 2,2,6,6-tetramethylpiperidine-1-oxy (TEMPO) or 2,6-di-*tert*-butyl-α-(3,5-di-*tert*-butyl-4-oxo-2,5-cyclohexadiene-1-yli-dene)-*p*-tolyloxy (Galvinoxy) severely retarded or completely suppressed the reaction.

It has been reported that P-centered radicals can be formed in the presence of $Mn(OAc)_3$ through homolytic P–H bond cleavage.[10a] Therefore, we employed $Mn(OAc)_3{\cdot}2H_2O$ (1 mmol) in the place of AgOAc for the reaction of **1a** with **2a**, and **3aa** was formed in 50 % yield (entry 9 in Table 1). Interestingly, the reaction could be conducted even at room temperature (entries 10–12 in Table 1). Comparable results were obtained in DMF and AcOH, whereas the product yield decreased slightly in CH_2Cl_2.

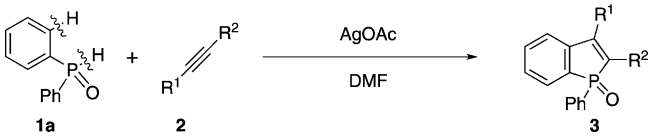
The diarylacetylenes **2b–f** underwent coupling with **1a** when using AgOAc as the oxidant to selectively produce the corresponding 2,3-diaryl-1-phenyl-1*H*-phosphindole-1-ones **3ab–3af** (entries 1–5 in Table 2). 4-Octyne (**2g**) could also be employed in this reaction (entry 6 in Table 2). Interestingly, the asymmetrical phenylacetylenes **2h–p** reacted with **1a** in a regioselective manner to produce the 2-substituted 1,3-diphenyl-1*H*-phosphindole-1-ones **3ah–3ap** in moderate to good yields (entries 7–16 in Table 2). Notably, no other isomers were detected in any of these reactions. One possible reason for the regioselectivity seems to be the facile formation of phenyl-stabilized alkenyl radicals at the addition step (Scheme 2).[9] In the reactions with silylacetylenes **2j** and **2k**, better results were obtained by using $Mn(OAc)_3{\cdot}2H_2O$ as the oxidant at room temperature (entries 10 and 11 in Table 2). Under the standard conditions using AgOAc at 100 °C, small amounts (ca. 10 %) of desilylated coupling products were detected by GC–MS (entry 9 in Table 2). As expected, **1a** reacted with 1,4-di(prop-1-yn-1-yl)benzene (**2q**) in a 2:1 manner to form a bis(benzophosphole-3-yl)benzene framework (entry 17 in Table 2).[2a,12] This type of structure is of interest for application in organic light-emitting diodes and thin-film photovoltaics.[1c,e,g]

Next, the reactions of variously substituted phenylphosphine oxides with **2a** were examined. The reaction of bis(4-methylphenyl)phosphine oxide (**1b**) in the presence of AgOAc gave both the normal coupling product **3ba** and the unexpected isomer **3ba′** as a 1:1 mixture (entry 1 in Table 3). This may imply that an unanticipated pathway in the annulation process intervenes. The formation of **3ba′** may be rationalized by assuming an attack by alkenyl radical **A** on the *ipso*-carbon atom of one of the 4-methylphenyl rings (Scheme 3 a).[10h,13] The resulting spirocyclohexadienyl radical

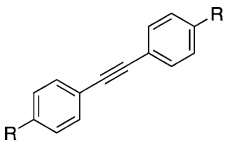
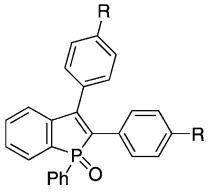
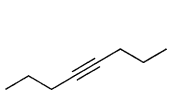
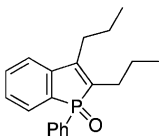
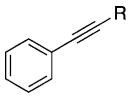
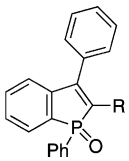
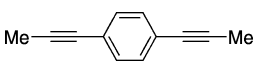
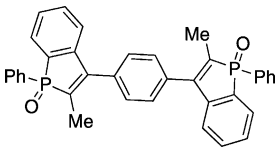


Scheme 3. Possible pathways to **3ba** and **3ba′**.

Table 2: Reaction of diphenylphosphine oxide (**1a**) with alkynes **2**.[a]

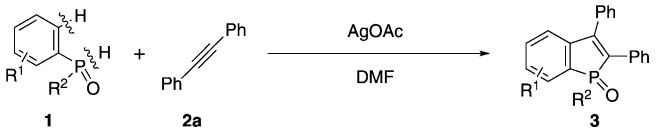


1a **2** **3**

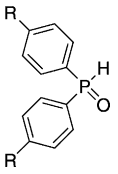
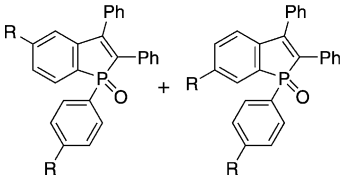
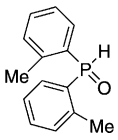
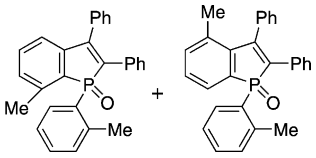
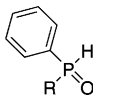
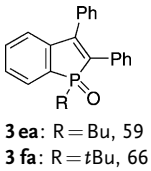
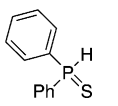
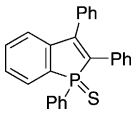
Entry	2	Product, yield [%][b]
		
1	**2b**: R = Me	**3ab**: R = Me, 80
2	**2c**: R = OMe	**3ac**: R = OMe, 77
3	**2d**: R = NMe_2	**3ad**: R = NMe_2, 35
4	**2e**: R = Cl	**3ae**: R = Cl, 89
5	**2f**: R = Br	**3af**: R = Br, 60
		
6	**2g**	**3ag**, 63
		
7	**2h**: R = Me	**3ah**: R = Me, 86
8	**2i**: R = Bu	**3ai**: R = Bu, 73
9	**2j**: R = TMS	**3aj**: R = TMS, 0
10[c]	**2j**: R = TMS	**3aj**: R = TMS, 54
11[c]	**2k**: R = $SiMe_2Ph$	**3ak**: R = $SiMe_2Ph$, 57
12	**2l**: R = CO_2Et	**3al**: R = CO_2Et, 57
13	**2m**: R = Ac	**3am**: R = Ac, 62
14	**2n**: R = $C(OH)Me_2$	**3an**: R = $C(OH)Me_2$, 61
15	**2o**: R = CH_2OTBS	**3ao**: R = CH_2OTBS, 58
16	**2p**: R = $PO(OEt)_2$	**3ap**: R = $PO(OEt)_2$, 41
		
17[d]	**2q**	**3aq**, 38

[a] Reaction conditions: **1a** (0.5 mmol), **2** (0.25 mmol), and AgOAc (1 mmol) in DMF (3 mL) at 100 °C under N_2 for 4 h. TMS = trimethylsilyl, TBS = *tert*-butyldimethylsilyl. [b] Yield of isolated product. [c] Using $Mn(OAc)_3{\cdot}2H_2O$ (1 mmol) at RT in place of AgOAc. [d] Using **1a** (1 mmol) and AgOAc (2 mmol).

Table 3: Reaction of arylphosphine oxides **1** with **2a**.[a]



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

Entry	1	Product(s), yield [%][b]
		
1	**1b**: R = Me	**3ba** + **3ba′**: R = Me, 79 (1:1)
2	**1c**: R = OMe	**3ca** + **3ca′**: R = OMe, 50 (1:1)
3[c]	**1c**: R = OMe	**3ca** + **3ca′**: R = OMe, 56 (1.9:1)
		
4	**1d**	**3da** + **3da′**, 84 (1:2)
		
5	**1e**: R = Bu	**3ea**: R = Bu, 59
6	**1f**: R = *t*Bu	**3fa**: R = *t*Bu, 66
7	**1g**: R = OEt	**3ga**: R = OEt, 53
		
8	**1h**	**3ha**, 0
9[c]	**1h**	**3ha**, 50

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

B may then undergo ring expansion to form **C**, thus leading to **3ba′**.

The reaction of 4-methoxy-substituted substrate **1c** also gave a 1:1 mixture of **3ca** and **3ca′** (entry 2 in Table 3). When using $Mn(OAc)_3{\cdot}2H_2O$ as the oxidant at room temperature, the relative product ratio of **3ca** increased (entry 3 in Table 3). As expected, the reaction of bis(3-methylphenyl)-phosphine oxide with **2a** gave a complex mixture of product isomers. By contrast, in the reaction of sterically hindered bis(2-methylphenyl)phosphine oxide (**1d**), **3da′** was formed as the predominant product, along with **3da** (entry 4 in Table 3). It is possible that the 5-*exo-trig* cyclization is retarded by steric repulsion between the methyl group and the aryl moiety on the phosphorus atom (Scheme 3b).[14]

Alkyl(phenyl)phosphine oxides such as **1e** and **1f** also underwent coupling with **2a** to produce the corresponding *P*-alkylbenzophosphole derivatives **3ea** and **3fa** (entries 5 and 6 in Table 3). As well as phosphine oxides, phenylphosphinate **1g** could also be used in the annulation (entry 7 in Table 3). The reaction of diphenylphosphine sulfide (**1h**) did not proceed at all under the standard conditions (entry 8 in Table 3). This is likely due to the thiophilicity of silver. Fortunately, the reaction of **1h** could be carried out by using

$Mn(OAc)_3 \cdot 2H_2O$ as the oxidant at room temperature to give **3ha** (entry 9 in Table 3).

Most of the benzophosphole oxides **3** obtained showed solid-state fluorescence as expected. 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 (see the Supporting Information).

In summary, we have demonstrated that the silver- or manganese-mediated dehydrogenative coupling of phenylphosphine oxides with alkynes proceeds efficiently to produce benzophosphole oxide derivatives. Given that a wide range of substrates can be utilized for annulative coupling, this simple protocol may provide a general, one step approach to benzophosphole oxide frameworks of importance in materials chemistry.

Experimental Section

General procedure for the reaction of phenylphosphine oxides **1** with alkynes **2**: A mixture of phenylphosphine oxide (**1**, 0.5 mmol), alkyne (**2**, 0.25 mmol), AgOAc (1.0 mmol, 167 mg), and dibenzyl (ca. 40 mg) as an 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 **2**. After cooling, the reaction mixture was diluted with ethyl acetate (40 mL) and insoluble solids were removed on a Celite plug. The filtrate was washed with brine (20 mL × 3). The organic layer was then dried over Na_2SO_4 and concentrated in vacuo. The desired product **3** was isolated by column chromatography on silica gel using dichloromethane/ethyl acetate (1:1 *v*/*v*) as eluent. Characterization data of the products are summarized in the Supporting Information.

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Keywords: annulation · C–C coupling · dehydrogenation · phosphorus heterocycles · radical reactions

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