ORGANIC CHEMISTRY FRONTIERS

RESEARCH ARTICLE

View Article Online
View Journal | View Issue

Cite this: *Org. Chem. Front.*, 2024, **11**, 3376

Efficient synthesis of benzophosphole oxides *via* Ag-promoted radical cycloisomerization†‡

Liyao Ma, [a] Sonia Mallet-Ladeira,[b] Julien Monot, [a] Blanca Martin-Vaca *[a] and Didier Bourissou *[a]

Received 27th March 2024,
Accepted 16th April 2024

DOI: 10.1039/d4qo00552j

rsc.li/frontiers-organic

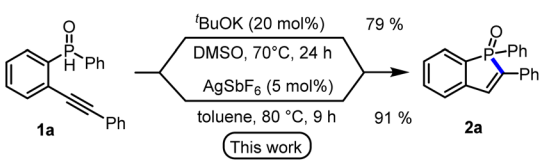
Cycloisomerization reactions involving C–P bond formation have been overlooked for the synthesis of P-heterocycles. In this work, we developed a simple, efficient and versatile route to synthesize benzophosphole oxides by reacting *ortho*-alkynyl secondary phosphine oxides with 5 mol% $AgSbF_6$. Mechanistic investigations revealed a radical-chain mechanism involving phosphinoyl radicals as key intermediates and rare 5-*endo*-*dig* cyclization as a key step, rather than the π-activation of the C≡C triple bond. The transformation is both efficient and versatile. It effectively complements alternative intermolecular approaches. It works with a wide diversity of substitution patterns (alkynyl, benzo and phosphorus moieties) and enables the exquisite control of regioselectivity. Post-functionalization *via* direct C–H vinylation of the C2 position is also substantiated.

Introduction

Cycloisomerization reactions involving intramolecular nucleophilic additions to alkynes and alkenes π-activated by transition metals (TMs) have become a very powerful and versatile tool in synthesis.[1] They enable straightforward and efficient preparation of a wide variety of heterocycles and carbocycles with full atom economy.[2] The as-obtained cyclic motifs are ubiquitous in natural products, synthetic pharmaceuticals and optoelectronic materials. Their preparation is thus a major concern that requires timely resolution. Thus far, most efforts have concentrated on C–O, C–N and C–C bond-forming cycloisomerizations and spectacular progress has been achieved. However, little is known about related C–P bond-forming transformations to give P-heterocycles.

In this regard, benzophosphole oxides (BPOs) are primary targets owing to their application in organic electronics, including light-emitting devices,[3] photovoltaics[4] and cell-imaging dyes.[5] The cycloisomerization route has attracted much attention because of its selectivity and substrate scope, but surprisingly, it has only been much rarely considered thus far and remains largely underdeveloped. Accordingly, the preparation of BPOs through the cyclization of *ortho*-alkynyl secondary phosphine oxides (SPOs) has only been reported once under basic conditions.[6] Typically, heating **1a** at 70 °C for 24 hours in DMSO in the presence of ^{t}BuOK (20 mol%) was found to afford BPO **2a** with 79% yield (Scheme 1). The reaction is simple to operate and does not require a TM-based catalyst, but it is limited in scope. It works only for substrates featuring an internal alkyne substituted by an aryl group.

With the aim to apply and develop a TM-catalyzed cycloisomerization approach for the synthesis of P-heterocycles, such as **2a**, we screened various complexes reported to be efficient in C–O, C–N and C–C bond-forming transformations (mainly Pd and Au complexes).[7] As a result, we discovered that $AgSbF_6$ alone efficiently promotes the cycloisomerization of **1a** into **2a**. This finding prompted us to in-depth investigate Ag^I-promoted cycloisomerization route to benzophosphole oxides and we hereafter discuss this transformation in terms of reac-



Scheme 1 Cycloisomerization of the (2-alkynylphenyl) phosphine oxide **1a** into benzophosphole oxide **2a**: unique precedent under ^{t}BuOK catalysis and the Ag^I-promoted route reported here.

[a]*CNRS/Université Paul Sabatier, Laboratoire Hétérochimie Fondamentale et Appliquée (LHFA, UMR 5069), 118 Route de Narbonne, 31062 Cedex 09 Toulouse, France. E-mail: blanca-maria.martin-vaca@univ-tlse3.fr, didier.bourissou@univ-tlse3.fr*

[b]*Université de Toulouse III Paul Sabatier, Institut de Chimie de Toulouse, ICT, UAR 2599, 118, route de Narbonne, F-31062 Toulouse, France*

† Dedicated to Prof. Denis Curran on the occasion of his 70th birthday.

‡ Electronic supplementary information (ESI) available: Full experimental procedures, characterization data of all new compounds (including ^{1}H and ^{13}C-NMR spectra, ESR spectra and XRD data. CCDC 2332940. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d4qo00552j

tion optimization, mechanistic investigations, scope, comparison with alternative methods and post-functionalization.

Results and discussion

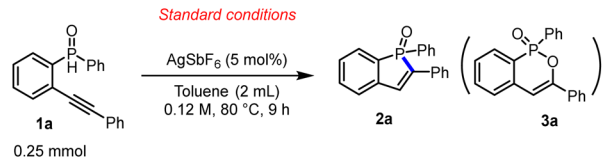
Upon reacting SPO **1a** with 5 mol% $AgSbF_6$ at 120 °C in a toluene solution, complete conversion was achieved within only 2 hours, as indicated by ^{31}P NMR spectroscopy. The doublet signal diagnostic for **1a** (δ 15.8 ppm, $^1J_{PH}$ 498 Hz) disappeared to give a new signal at δ 39.2 ppm, which is attributed to **2a**.[6] The reaction conditions were then varied and optimized (Table 1). Lowering the temperature to 80 °C led to similar results without significantly compromising the reaction time (9 hours). Reducing the loading in $AgSbF_6$ to 2 mol% enabled us to achieve full conversion at 80 °C in 20 hours (increasing the concentration of **1a** from 0.12 to 0.8 M), but side products were formed and the benzophosphole oxide **2a** was obtained in only 80% yield. Other silver salts with more coordinating and/or more basic counter-anions showed lower performance. Longer reaction times were required to achieve high conversion, and more side products were formed. Radical initiators (AIBN, TBHP, and $Mn(OAc)_3$) and oxidizing conditions ($K_2S_2O_7$ or O_2), commonly involved in P–C bond formation, were also tried, but they gave poor results (<30% yield in **2a**, Table S1‡).[7] Of note, in some cases, a side product was detected in the ^1H NMR spectrum of the crude mixture. It was isolated and unambiguously authenticated as the corresponding phosphaisocoumarin **3a**.[7] The formation of **3a** shows that the oxidation of the phosphine oxide/phosphinoyl radical may occur prior to cyclization.

Changing toluene for more polar solvents such as 1,2-dichlorobenzene, DCE, DMF or CH_3CN had no benefit, rather the opposite, while similar results were obtained with benzene. Using the optimized reaction conditions ($AgSbF_6$ 5 mol%, toluene, 80 °C), the reaction was then scaled up to 10 mmol of **1a**, operating at 0.8 M to reduce both the time and the quantity of solvent. The transformation was complete in 5 hours, and **2a** was obtained in 90% isolated yield (2.72 g).[7]

Given the state-of-the-art and literature precedent, two mechanistic scenarios can be *a priori* envisioned for the Ag^I-promoted cycloisomerization of **1a**. On the one hand, Ag^I salts are known to activate alkynes *via* π-coordination and to promote the addition of pro-nucleophiles to the C≡C triple bond (Fig. 1a).[8,9] Conversely, Ag^I salts may act as oxidants towards secondary phosphine oxides $R_2P(O)H$ [and phosphonates $(RO)_2P(O)H$] to generate phosphinoyl radicals, which can then undergo radical addition to alkynes (Fig. 1b).[8,10] On the other hand, the Ag^I salt is used in stoichiometric amount or an excess of oxidant is added to regenerate Ag^I *in situ*.[11]

To try to distinguish between these two paths, a series of experiments were performed. First, we assessed the impact of additives that may foster the "π-activation" route (Fig. 2a), *i.e.* weak bases such as $^tBu_2Py$, K_2CO_3 or Et_3N (10 mol%) to activate the pro-nucleophile, PPh_3 to stabilize Ag^I,[12] and hydrogen-bond donors such as $Ph_2P(O)OH$, $C_6H_3(OH)_3$ or HFIP to favor protodemetalation upon H-shuttling.[13] In most cases, the conversion of **1a** was significantly lowered. Complete consumption was only observed with HFIP as an additive, but the benzophosphole oxide **2a** was obtained in low yield (11%). Conversely, the concomitant use of $AgSbF_6$ and TEMPO (5 mol% each) drastically reduced the conversion of **1a** (15%) and the yield in **2a** (10%) (Fig. 2b). Furthermore, the addition of 5 mol% of TEMPO after 4 hours of reaction under standard conditions considerably slowed down further transformation (the conversion of **1a** stopped at 70–80% conversion and the yield in **2a** did not exceed 65–70% after 5 additional hours, Fig. S3‡).[7] These experiments favor the radical pathway over the π-activation route. To further substantiate the formation of the phosphinoyl radical **A** upon oxidation of **1a** with Ag^I, spin

Table 1 Ag-promoted cycloisomerization of **1a** into **2a** and optimization



		Conv[a] (%)	Yield[a] (%)
	Standard conditions	>96	>96 (91)[b]
	Deviation from standard conditions		
Reaction conditions	120 °C, 2 h	>96	93
	20 mol% $AgSbF_6$, 4 h	>96	>96
	2 mol% $AgSbF_6$, 0.8 M, 20 h	95	80
	100 mol% $AgSbF_6$	>96	27 (49)[c]
	NO $AgSbF_6$	9	7
	Under air	87	67 (15)[c]
Silver salt	5 mol% $AgNTf_2$, 9 h	51	49
	5 mol% AgOTf, 9 h	61	60
	5 mol% $AgBF_4$, 9 h	44	44
	5 mol% $AgNO_3$, 9 h	100	20
	5 mol% AgOAc, 72 h	100	20
	5 mol% Ag_2CO_3, 72 h	100	20
Solvent	Benzene, 9 h	>96	>96
	^{t}BuPh, 9 h	85	83
	1,2-Dichlorobenzene, 22 h	>96	84
	CH_3CN, 33 h	>96	86
	DMF, 9 h	61	48
	DCE, 47 h	>96	82

[a] Estimated by ^{31}P NMR spectroscopy. [b] Isolated yield in parentheses. [c] Yield in phosphaisocoumarin **3a** in parentheses.[7]

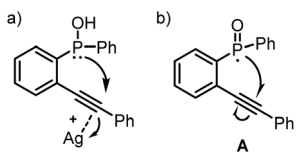


Fig. 1 Key intermediates for the two mechanistic scenarios envisioned to account for the cycloisomerization of **1a** into **2a**: (a) nucleophilic addition of the λ^3-form of the SPO moiety to the alkyne π-activated by Ag^I and (b) formation of the phosphinoyl radical **A** by oxidation of the SPO moiety with Ag^I, followed by radical addition to the alkyne.

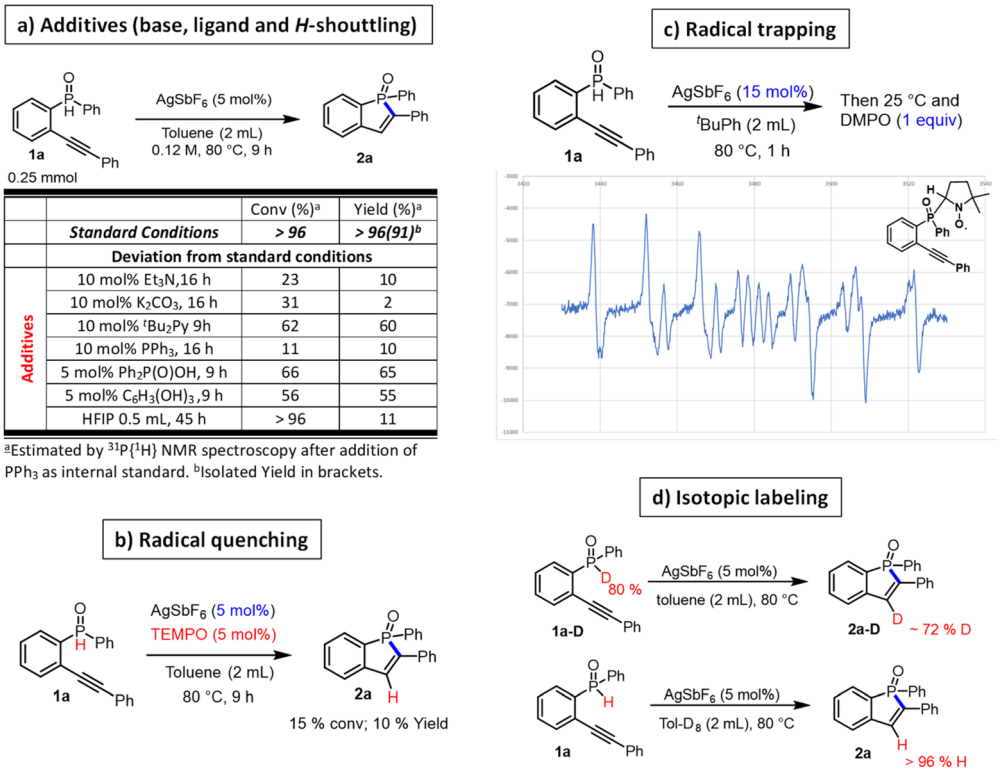


Fig. 2 Experiments performed to discriminate the two mechanistic paths, namely π-activation and radical addition.

trapping with a nitrone (DMPO) was performed (Fig. 2c).[7] The reaction was conducted in ^{t}BuPh with 15 mol% of $AgSbF_6$. The mixture was stirred at 80 °C for 1 hour to initiate the reaction, and then cooled to room temperature (to prevent direct reaction of **1a** with the nitrone)[14] before the addition of DMPO (15 mol%). ESR analysis showed the formation of a nitroxide radical (the pattern is very similar to that reported for the trapping of the phosphinyl radical $Ph_2P(O)^{\bullet}$ by DMPO and to that we obtained ourselves by reacting $Ph_2P(O)H$ instead of **1a** with $AgSbF_6$, Fig. S15‡).[7,15–17] This experiment further supports the radical pathway as the operating mechanism in the Ag^{I}-promoted cycloisomerization of **1a**.

Based on the gathered information, we propose the radical-chain mechanism displayed in Fig. 3 to account for the cycloisomerization of **1a** into **2a** promoted by $AgSbF_6$. The initiation would involve the generation of the phosphinoyl radical **A** upon oxidation of the λ^5-P(O)H/λ^3-P(OH) moiety of **1a**/**1a′** by the Ag^{I} cation. The propagation phase would then involve cyclization of **A** *via* intramolecular 5-*endo-dig* radical addition to the C≡C triple bond, to give the vinyl radical **B**. Finally, hydrogen atom transfer (HAT) would deliver the benzophosphole oxide **2a**. To decipher the H atom source, we resorted to D-labeling experiments using either **1a–D** deuterated at the P atom or toluene-D_8 as the solvent (Fig. 2d).[7] Inspection of the ^{1}H NMR signal for the vinylic =C–*H* of **2a** showed that the SPO substrate indeed acts as a H donor towards **B**, enabling chain propagation. The absence of deuterium incorporation in **2a** when operating in toluene-D_8 indicates that the solvent

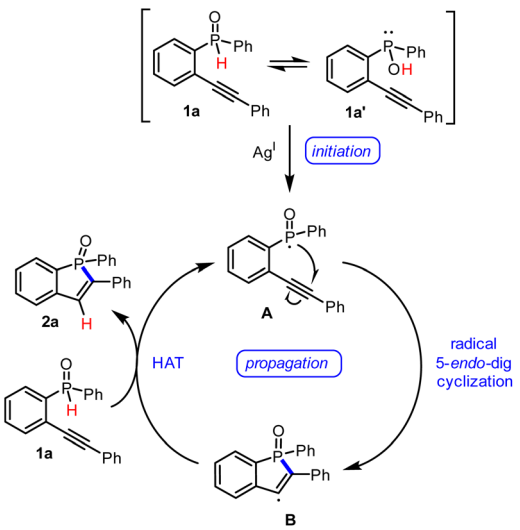


Fig. 3 Proposed radical-chain mechanism to account for the Ag^{I}-promoted cycloisomerization of **1a** into **2a**.

does not take part in the HAT, in line with the similar results observed using toluene or benzene as the solvent.

Of note, radical 5-*endo-dig* cyclization with P(O)-centered radicals has not been previously reported to the best of our knowledge. With other types of radicals, this kind of cyclization is challenging and rare, but not unprecedented. Experimental evidence was first reported with a Si-centered

radical,[18] then with C-centered radicals[19] and more recently with N-[20] and Ge-centered radicals.[21]

Following mechanistic studies, we assessed the scope of the transformation with respect to the substitution pattern of alkynyl, benzo and phosphorus moieties (Fig. 4). The bifunctional substrates were prepared in few steps from *ortho*-bromo, iodo-benzene derivatives upon sequential introduction of alkyne and SPO moieties (by the Sonogashira coupling and ionic coupling with a dichlorophosphine followed by hydrolysis, respectively).[7] Electron-enriched alkynes with a *para*-Me or *para*-OMe phenyl substituent (**1b**,**c**), an alkyl substituent (^{n}Bu, **1d**), and a silyl group ($SiEt_3$, **1e**), were cyclized more rapidly than **1a** and the corresponding benzophosphole oxides were obtained in high yields (in particular **2b–2d**, 81–95%). As for the silyl-substituted BPO **2e**, it was obtained in the mixture with the desilylated benzophosphole oxide **2o** (2/1 ratio) under the standard conditions (5 mol% $AgSbF_6$), but reducing the Ag^I loading to 2 mol% enabled us to increase the isolated yield of **2e** to 72%. Me and MeO substitution of the *ortho* and *meta* positions of the phenyl group (**1f–1h**) resulted in longer reaction times without impacting the yields (92–99%). The introduction of electron-withdrawing groups at the phenyl substituent of the alkyne moiety required longer reaction times than **1a** (15–23 hours) without compromising the efficiency of the cycloisomerization (79–97% yields for **2i–2l**). Compound **2l** was actually characterized by single-crystal X-ray diffraction analysis,[7] unambiguously confirming the benzophosphole oxide structure and the C2-substitution. The cyclization reaction also worked well with substrates bearing π-conjugated alkene or heterocyclic substituents at the alkyne moiety, such as cyclohexene or thiophene, as substantiated by the formation of **2m** and **2n** with 73–74% yield. A longer reaction time was required to cyclize the terminal alkyne **1o** (20 hours), and the corresponding BPO **2o** was obtained in a modest yield (40%) probably due to parasitic reactions between the ≡C–H bond and the silver salt.[22] However, we leveraged on the desilylation process observed with **1e** to develop an alternative route to **2o**. Installing a trimethylsilyl group at the alkyne (substrate **1p**) and using 50 mol% of Ag^I salt, the parent benzophosphole oxide **2o** was formed as very major product within only 1 hour and it could be isolated in 85% yield.[23] Of note, efficient preparation of **2o** is a challenge and only a few precedents exist, as recalled in Scheme 2. Desilylation of **2p** with TBAF affords **2o** in only 50% yield.[24] Better results were obtained by

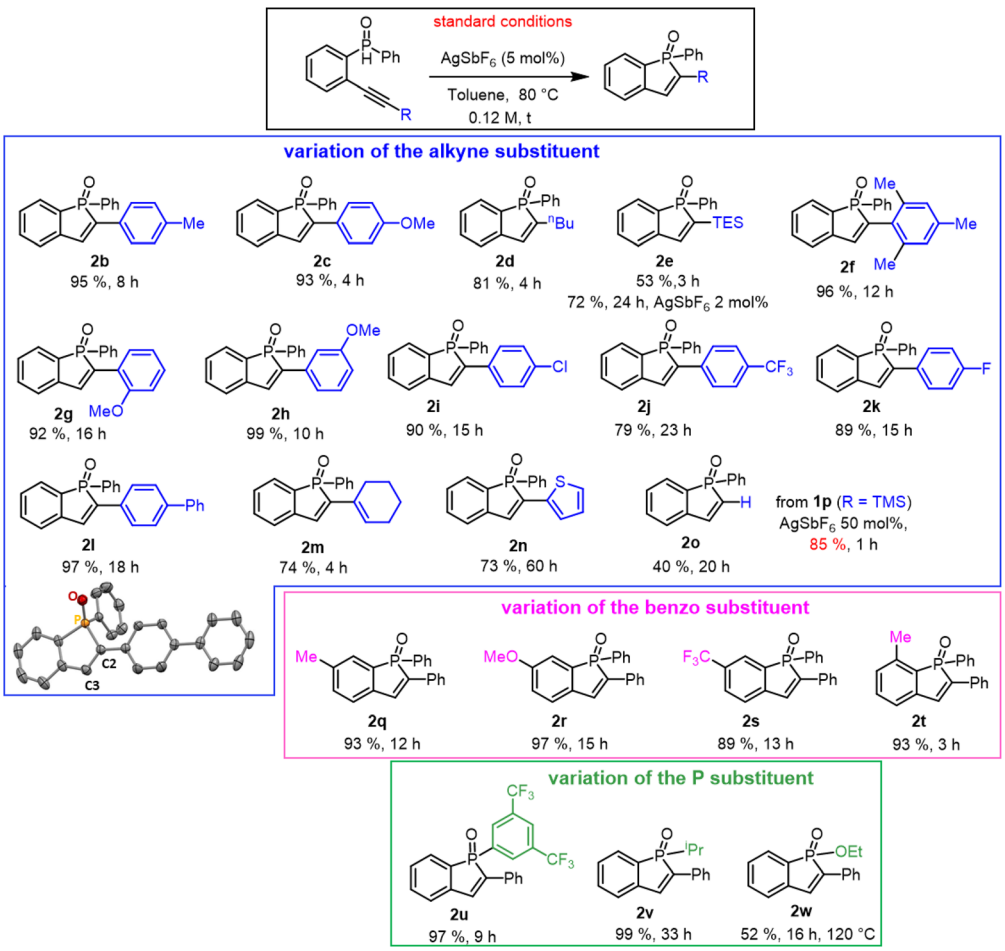
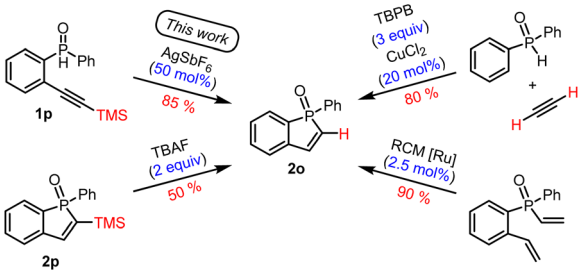


Fig. 4 Synthesis of benzophosphole oxides *via* Ag^I-promoted cycloisomerization and substrate scope.



Scheme 2 Alternative syntheses of the unsubstituted benzophosphole oxide **2o**.

ring-closing metathesis of a divinyl precursor with an Hoveyda–Grubbs second-generation catalyst[25a] or by direct cyclization of $Ph_2P(O)H$ with acetylene promoted by $CuCl_2$ in the presence of an excess of *tert*-butyl peroxobenzoate (TBPB) as an oxidant.[25b]

Substitution of the phenyl ring linking the SPO and alkynyl moieties was then investigated (substrates **1q–t**). In all cases, the corresponding benzophosphole oxides were obtained in high yields (89–97%). Here, the cycloisomerization approach inherently provides precise control of the BPO structure. The reaction proceeds at the phenyl ring bearing the alkynyl moiety and gives a single regioisomer, in contrast to the intermolecular variant involving $Ar_2P(O)H$ secondary phosphine oxides and alkynes (see below). No significant electronic bias was observed between electron-donating and -withdrawing substituents, the reaction times to obtain **2q** (Me), **2r** (OMe) and **2s** (CF_3) (13 hours) being essentially identical (12–15 hours). Interestingly, Me substitution of the position *ortho* to P proved more impactful. The formation of **2t** proceeded faster (3 hours), which may be due to some buttressing effects favoring the 5-*endo-dig* cyclization. Finally, variation of the P substituent was explored. Introducing the electron-withdrawing group 3,5-$(CF_3)_2$Ph (**1u**) made no noticeable difference with the reference substrate **1a** in terms of reaction time and yield of the obtained BPO (9 hours, 97%). Comparatively, electron-enriched substrates proved more difficult to cyclize. For the ^{i}Pr-substituted substrate **1v**, 33 hours were required to achieve full conversion, but the yield of **2v** was not compromised (96%). Phosphinates $(RO)_2P(O)H$ are more challenging substrates than SPO in oxidative radical couplings.[16] Consistently, harsher conditions were required to cyclize the ethoxy-substituted substrate **1w** (120 °C, 16 h), but the corresponding BPO **2w** was nonetheless obtained in 52% isolated yield.[26]

Overall, the cycloisomerization methodology reported here allows for the efficient preparation of a wide structural variety of benzophosphole oxides with electron-donating/electron-withdrawing substituents at C2, the benzo ring and/or the P atom (17 examples, 88% average yield). This transformation is versatile and complementary to the alternative intermolecular routes developed over the last decade (Fig. 5 and S7‡).[7] The most studied route involves the dehydrogenative coupling of diaryl SPO and internal alkynes (Fig. 5a).[17,27–29] It requires an

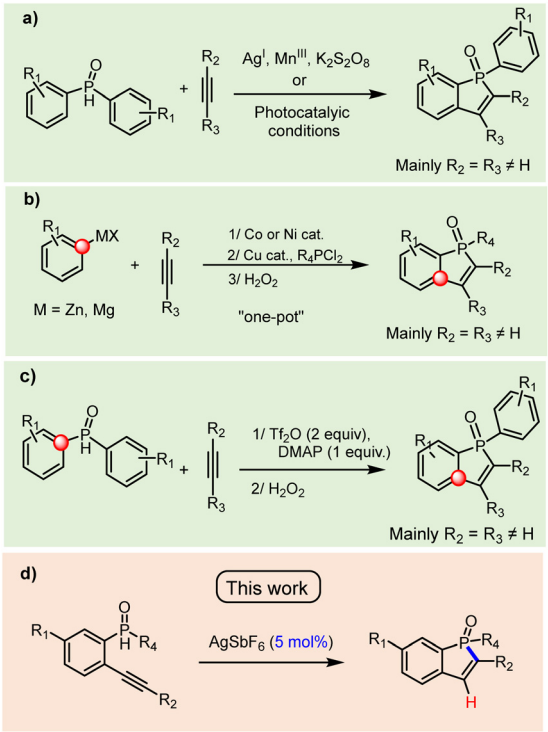
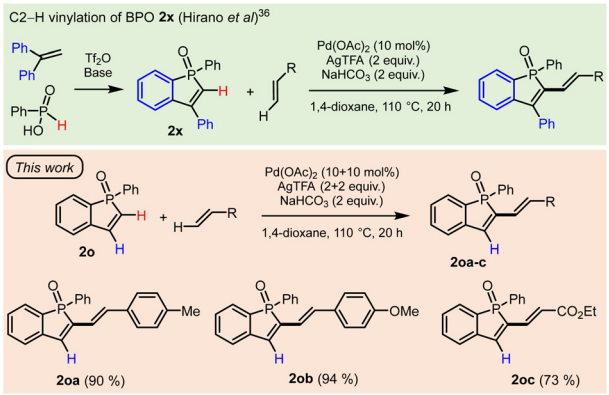


Fig. 5 Comparison of the main synthetic routes developed to access benzophosphole oxides: known intermolecular strategies (a–c) *versus* the cycloisomerization approach reported here (d).

oxidant (typically Ag^I, Mn^{III} or $K_2S_2O_8$) in stoichiometric amount or excess. Greener variants have been uncovered recently using an organic photocatalyst and a pyridinium salt as an oxidant,[17] or even simply dioxygen.[30] Another strategy relies on a one-pot multicomponent reaction involving Co/Ni-catalyzed migratory carbometallation of alkynes, Cu-catalyzed C–P coupling and phosphorus oxidation (Fig. 5b).[31] A third method is based on the electrophilic annulation of SPO with internal alkynes in the presence of an excess of Tf_2O and a base (Fig. 5c).[32] All these routes use internal alkynes and thus give C2/C3-disubstituted benzophosphole oxides. Moreover, symmetric internal alkynes are largely preferred to prevent the formation of regioisomeric mixtures. The same limitation applies to the diaryl SPO substrates used in the first and third strategies, and symmetric SPOs are used routinely to prevent selectivity issues in the cyclization step. It is worth noting that the cycloisomerization approach reported here requires the preparation of alkynyl-SPO substrate **1**, but it inherently proceeds with complete selectivity and it circumvents the formation of BPO mixtures. This is nicely illustrated by the selective formation of compounds **2q–t**, where related intermolecular transformations suffered from the randomization of the regiochemistry of the "benzo" fragment (Fig. S8‡).[7,17,27,29,32,33]

As mentioned above, another attractive feature of the Ag^I-promoted cycloisomerization route is to provide efficient access to the parent benzophosphole oxide **2o**. Given the



Scheme 3 C2–H vinylation of benzophosphole oxides.

recent progress achieved in the post-functionalization of BPO[26,34–37] we wondered about the possibility to derivatize **2o** by C–H activation. In particular, we became interested in the installation of vinyl groups at C2 since it is challenging by other means. One option is to achieve Pd-catalyzed Mizoroki–Heck or Stille cross-coupling from the BPO bearing a bromine atom at C2 (Fig. S9‡).[7,34]

More attractive synthetically is the Pd-catalyzed and Ag-assisted C–H vinylation reported recently by Hirano *et al.* from the BPO **2x** (obtained by electrophilic coupling of 1,1-diphenylethylene and phenylphosphinic acid) (Scheme 3).[35,36] It was observed that under similar conditions, the parent BPO **2o** was fully consumed but a complicated mixture of products was obtained. Intrigued by the influence of the Ph group at C3 on this transformation, we tested the functionalization of **2o** under the same conditions (10 mol% $Pd(OAc)_2$, 2 equiv. AgTFA, 2 equiv. $NaHCO_3$, dioxane, 110 °C) using *para*-methyl styrene as the partner. ^{31}P NMR monitoring indeed showed consumption of **2o** but the reaction leveled off at 40% conversion after 7 hours. To drive complete conversion, more Pd $(OAc)_2$ (10 mol%) and AgTFA (2 equivalents) were added and gratifyingly, the C2-vinylated BPO **2oa** was thereby obtained in 90% isolated yield.[7] These forcing reaction conditions were then applied to *para*-methoxy styrene and ethyl acrylate, affording the corresponding C2-functionalized BPO **2ob** and **2oc** in good yields (94 and 73%, respectively).

Conclusions

In summary, reacting *ortho*-alkynyl secondary phosphine oxides with 5 mol% of $AgSbF_6$ turned to be a very efficient and general route to synthesize benzophosphole oxides. Compared with intermolecular approaches, such cycloisomerization inherently proceeds with complete selectivity.

Besides the specific preparation of BPO, these results point out the synthetic potential of C–P bond-forming cycloisomerization reactions to access P-heterocycles. This strategy is illustrated here in a radical transformation, but ionic as well as TM-catalyzed variants can certainly be conceived and are worth investigating. This work also highlights the synthetic potential of silver salts. Long neglected compared to other TM, Ag^I species have found increasing applications as π-activators, halide abstractors[38] as well as oxidants.[39] In this work, $AgSbF_6$ was used as a radical initiator, in catalytic amounts and without any external oxidant.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This work was supported financially by the Agence Nationale de la Recherche (ANR CE6-MLC-Photophos). L. M. thanks the Chinese Scholarship Council (CSC) for a Ph.D. Fellowship. Baptiste Martin (LCC toulouse) is acknowledged for the radical trapping experiments.

References

1 (*a*) X. Zeng, Recent Advances in Catalytic Sequential Reactions Involving Hydroelement Addition to Carbon–Carbon Multiple Bonds, *Chem. Rev.*, 2013, **113**, 6864–6900; (*b*) C. Praveen, Cycloisomerization of π-Coupled Heteroatom Nucleophiles by Gold Catalysis: En Route to Regiochemically Defined Heterocycles, *Chem. Rec.*, 2021, **21**, 1697–1737; (*c*) N. T. Patil and Y. Yamamoto, Coinage Metal-Assisted Synthesis of Heterocycles, *Chem. Rev.*, 2008, **108**, 3395–3442.

2 F. Alonso, I. P. Beletskaya and M. Yus, Transition-Metal-Catalyzed Addition of Heteroatom–Hydrogen Bonds to Alkynes, *Chem. Rev.*, 2004, **104**, 3079–3160.

3 (*a*) O. Fadhel, M. Gras, N. Lemaitre, V. Deborde, M. Hissler, B. Geffroy and R. Réau, Tunable Organophosphorus Dopants for Bright White Organic Light-Emitting Diodes with Simple Structures, *Adv. Mater.*, 2009, **21**, 1261–1265; (*b*) Y. Zhou, S. Yang, J. Li, G. He, Z. Duan and F. Mathey, Phosphorus and silicon-bridged stilbenes: synthesis and optoelectronic properties, *Dalton Trans.*, 2016, **45**, 18308–18312.

4 (*a*) Y. Matano, H. Ohkubo, T. Miyata, Y. Watanabe, Y. Hayashi, T. Umeyama and H. Imahori, Phosphole- and Benzodithiophene-Based Copolymers: Synthesis and Application in Organic Photovoltaics, *Eur. J. Inorg. Chem.*, 2014, **2014**, 1620–1624; (*b*) K. H. Park, Y. J. Kim, G. B. Lee, T. K. An, C. E. Park, S.-K. Kwon and Y.-H. Kim, Recently Advanced Polymer Materials Containing Dithieno[3,2-*b*:2′,3′-*d*]phosphole Oxide for Efficient Charge Transfer in High-Performance Solar Cells, *Adv. Funct. Mater.*, 2015, **25**, 3991–3997.

5 (*a*) C. Wang, A. Fukazawa, M. Taki, Y. Sato, T. Higashiyama and S. Yamaguchi, A Phosphole Oxide Based Fluorescent Dye with Exceptional Resistance to Photobleaching: A

Practical Tool for Continuous Imaging in STED Microscopy, *Angew. Chem., Int. Ed.*, 2015, **54**, 15213–15217; (*b*) C. Wang, M. Taki, Y. Sato, A. Fukazawa, T. Higashiyama and S. Yamaguchi, Super-Photostable Phosphole-Based Dye for Multiple-Acquisition Stimulated Emission Depletion Imaging, *J. Am. Chem. Soc.*, 2017, **139**, 10374–10381.

6 T. Sanji, K. Shiraishi, T. Kashiwabara and M. Tanaka, Base-Mediated Cyclization Reaction of 2-Alkynylphenylphosphine Oxides: Synthesis and Photophysical Properties of Benzo[*b*]phosphole Oxides, *Org. Lett.*, 2008, **10**, 2689–2692.

7 See the ESI‡ for details.

8 G. Fang and X. Bi, Silver-catalysed reactions of alkynes: recent advances, *Chem. Soc. Rev.*, 2015, **44**, 8124–8173.

9 (*a*) M. Neetha, T. Aneeja, C. M. A. Afsina and G. Anilkumar, An Overview of Ag-catalyzed Synthesis of Six-membered Heterocycles, *ChemCatChem*, 2020, **12**, 5330–5358; (*b*) J.-M. Weibel, A. Blanc and P. Pale, Ag-Mediated Reactions: Coupling and Heterocyclization Reactions, *Chem. Rev.*, 2008, **108**, 3149–3173.

10 (*a*) Z.-Y. Wang, Q. Guo, K.-K. Wang and S. Xu, H-phosphinates, H-phosphonates and secondary phosphine oxides in radical reactions and strategy analysis, *Tetrahedron Lett.*, 2021, **81**, 153352; (*b*) S. Hore and R. P. Singh, Phosphorylation of arenes, heteroarenes, alkenes, carbonyls and imines by dehydrogenative cross-coupling of P(O)–H and P(R)–H, *Org. Biomol. Chem.*, 2022, **20**, 498–537.

11 (*a*) L.-J. Wang, A.-Q. Wang, Y. Xia, X.-X. Wu, X.-Y. Liu and Y.-M. Liang, Silver-catalyzed carbon–phosphorus functionalization of *N*-(*p*-methoxyaryl)propiolamides coupled with dearomatization: access to phosphorylated aza-decenones, *Chem. Commun.*, 2014, **50**, 13998–14001; (*b*) H.-L. Hua, B.-S. Zhang, Y.-T. He, Y.-F. Qiu, X.-X. Wu, P.-F. Xu and Y.-M. Liang, Silver-Catalyzed Oxidative Cyclization of Propargylamide-Substituted Indoles: Synthesis of Phosphorated Indoloazepinones Derivatives, *Org. Lett.*, 2016, **18**, 216–219.

12 (*a*) R. Nolla-Saltiel, E. Robles-Marín and S. Porcel, Silver(I) and gold(I)-promoted synthesis of alkylidene lactones and 2H-chromenes from salicylic and anthranilic acid derivatives, *Tetrahedron Lett.*, 2014, **55**, 4484–4488; (*b*) U. A. Carrillo-Arcos, J. Rojas-Ocampo and S. Porcel, Oxidative cyclization of alkenoic acids promoted by AgOAc, *Dalton Trans.*, 2016, **45**, 479–483.

13 (*a*) T. Chen, C. Q. Zhao and L. B. Han, Hydrophosphorylation of Alkynes Catalyzed by Palladium: Generality and Mechanism, *J. Am. Chem. Soc.*, 2018, **140**, 3139–3155; (*b*) C. Yu, J. Sanjosé-Orduna, F. W. Patureau and M. H. Pérez-Temprano, Emerging unconventional organic solvents for C–H bond and related functionalization reactions, *Chem. Soc. Rev.*, 2020, **49**, 1643–1652; (*c*) J. Monot, P. Brunel, C. E. Kefalidis, N. A. Espinosa-Jalapa, L. Maron, B. Martin-Vaca and D. Bourissou, A case study of proton shuttling in palladium catalysis, *Chem. Sci.*, 2016, **7**, 2179–2187.

14 SPO were reported to react with DMPO at 90 °C to give α-hydroxyamino phosphine oxides: P. Zhao, P. Li, J. Xiao, Y. Wang, X. Hao, A. Meng and C. Liu, Synthesis and antitumor activities of α-hydroxyamino phosphine oxides by catalyst-free hydrophosphinylation of nitrones, *Chem. Commun.*, 2023, **59**, 2624–2627.

15 P. Peng, Q. Lu, L. Peng, C. Liu, G. Wang and A. Lei, Dioxygen-induced oxidative activation of a P–H bond: radical oxyphosphorylation of alkenes and alkynes toward β-oxy phosphonates, *Chem. Commun.*, 2016, **52**, 12338–12341.

16 H. Wang, Y. Li, Z. Tang, S. Wang, H. Zhang, H. Cong and A. Lei, Z-Selective Addition of Diaryl Phosphine Oxides to Alkynes via Photoredox Catalysis, *ACS Catal.*, 2018, **8**, 10599–10605.

17 V. Quint, F. Morlet-Savary, J.-F. Lohier, J. Lalevée, A.-C. Gaumont and S. Lakhdar, Metal-Free, Visible Light-Photocatalyzed Synthesis of Benzo[*b*]phosphole Oxides: Synthetic and Mechanistic Investigations, *J. Am. Chem. Soc.*, 2016, **138**, 7436–7441.

18 (*a*) S. Amrein and A. Studer, Intramolecular radical hydrosilylation—the first radical 5-endo-dig cyclisation, *Chem. Commun.*, 2002, 1592–1593; (*b*) C. H. Schiesser, H. Matsubara, I. Ritsner and U. Wille, Unexpected dual orbital effects in radical addition reactions involving acyl, silyl and related radicals, *Chem. Commun.*, 2006, 1067–1069.

19 (*a*) I. V. Alabugin and M. Manoharan, 5-*Endo-Dig* Radical Cyclizations: "The Poor Cousins" of the Radical Cyclizations Family, *J. Am. Chem. Soc.*, 2005, **127**, 9534–9545; (*b*) I. V. Alabugin, V. I. Timokhin, J. N. Abrams, M. Manoharan, R. Abrams and I. Ghiviriga, In Search of Efficient 5-*Endo-dig* Cyclization of a Carbon-Centered Radical: 40 Years from a Prediction to Another Success for the Baldwin Rules, *J. Am. Chem. Soc.*, 2008, **130**, 10984–10995; (*c*) S. K. Pagire, P. Kreitmeier and O. Reiser, Visible-Light-Promoted Generation of α-Ketoradicals from Vinylbromides and Molecular Oxygen: Synthesis of Indenones and Dihydroindeno[1,2-c]chromenes, *Angew. Chem., Int. Ed.*, 2017, **56**, 10928–10932.

20 (*a*) I. V. Alabugin and C. Hu, New heterocycles via an intriguing visible-light-promoted 5-*endo-dig* cyclization, *Chem Catal.*, 2021, **1**, 976–977; (*b*) T.-D. Tan, T.-Y. Zhai, B.-Y. Liu, L. Li, P.-C. Qian, Q. Sun, J.-M. Zhou and L.-W. Ye, Controllable synthesis of benzoxazinones and 2-hydroxy-3-indolinones by visible-light-promoted 5-*endo-dig* N-radical cyclization cascade, *Cell Rep. Phys. Sci.*, 2021, **2**, 100577.

21 S. Kassamba, A. Perez-Luna, F. Ferreira and M. Durandetti, Modular access to substituted germoles by intramolecular germylzincation, *Chem. Commun.*, 2022, **58**, 3901–3904.

22 U. Halbes-Letinois, J.-M. Weibel and P. Pale, The organic chemistry of silver acetylides, *Chem. Soc. Rev.*, 2007, **36**, 759–769.

23 Using lower amounts of $AgSbF_6$ led to mixtures of **2j** and **2k**, from which it was not possible to achieve high-yield desilylation.

24 A. Decken, F. Bottomley, B. E. Wilkins and E. D. Gill, Organometallic Complexes of Benzannelated Phospholyls: Synthesis and Characterization of Benzophospholyl and the First *iso*-Benzophospholyl Metal Complexes, *Organometallics*, 2004, **23**, 3683–3693.

25 (*a*) D. J. Carr, J. S. Kudavalli, K. S. Dunne, H. Müller-Bunz and D. G. Gilheany, Synthesis of 2,3-Dihydro-1-phenylbenzo[*b*]phosphole (1-Phenylphosphindane) and Its Use as a Mechanistic Test in the Asymmetric Appel Reaction: Decisive Evidence against Involvement of Pseudorotation in the Stereoselecting Step, *J. Org. Chem.*, 2013, **78**, 10500–10505; (*b*) Z. Jianping, T. Zekun, L. Shuaishuai, L. Chengkun and L. Jianan, Phosphindole Derivative, Benzophosphindole Derivative and Preparation Method Therefor, WO2020/073210, 2020.

26 For functionalization of BPO by nucleophilic substitution of the ethoxy group at P, see: T. Yamagishi, F. Natori, T. Ohtani, K. Nakahara, M. Kato and K. Kaneda, Divergent synthesis of benzo[*b*]phosphole oxide derivatives focusing on substituents on phosphorus atom, *Tetrahedron*, 2023, **143**, 133562.

27 Y. Unoh, K. Hirano, T. Satoh and M. Miura, An Approach to Benzophosphole Oxides through Silver- or Manganese-Mediated Dehydrogenative Annulation Involving C–C and C–P Bond Formation, *Angew. Chem., Int. Ed.*, 2013, **52**, 12975–12979.

28 (*a*) Y. R. Chen and W. L. Duan, Silver-Mediated Oxidative C–H/P–H Functionalization: An Efficient Route for the Synthesis of Benzo[*b*]phosphole Oxides, *J. Am. Chem. Soc.*, 2013, **135**, 16754–16757; (*b*) W. Ma and L. Ackermann, Silver-Mediated Alkyne Annulations by C–H/P–H Functionalizations: Step-Economical Access to Benzophospholes, *Synthesis*, 2014, **46**, 2297–2304; (*c*) D. Ma, W. Chen, G. Hu, Y. Zhang, Y. Gao, Y. Yin and Y. Zhao, K_2S_2O8-mediated metal-free direct P–H/C–H functionalization: a convenient route to benzo[*b*]phosphole oxides from unactivated alkynes, *Green Chem.*, 2016, **18**, 3522–3526.

29 W. Q. Liu, T. Lei, S. Zhou, X. L. Yang, J. Li, B. Chen, J. Sivaguru, C. H. Tung and L. Z. Wu, Cobaloxime Catalysis: Selective Synthesis of Alkenylphosphine Oxides under Visible Light, *J. Am. Chem. Soc.*, 2019, **141**, 13941–13947.

30 During the final preparation of this manuscript, H. Huang, Q. Xiao *et al.* reported direct air-induced dehydrogenative coupling of SPO and internal alkynes: M. Huang, H. Huang, M. You, X. Zhang, L. Sun, C. Chen, Z. Mei, R. Yang and Q. Xiao, Direct air-induced arylphosphinoyl radicals for the synthesis of benzo[*b*]phosphole oxides, *Green Chem.*, 2024, **26**, 295–299.

31 (*a*) B. Wu, M. Santra and N. Yoshikai, A Highly Modular One-Pot Multicomponent Approach to Functionalized Benzo[*b*]phosphole Derivatives, *Angew. Chem., Int. Ed.*, 2014, **53**, 7543–7546; (*b*) B. Wu, R. Chopra and N. Yoshikai, One-Pot Benzo[*b*]phosphole Synthesis through Sequential Alkyne Arylmagnesiation, Electrophilic Trapping, and Intramolecular Phospha-Friedel–Crafts Cyclization, *Org. Lett.*, 2015, **17**, 5666–5669.

32 K. Nishimura, Y. Unoh, K. Hirano and M. Miura, Phosphenium-Cation-Mediated Formal Cycloaddition Approach to Benzophospholes, *Chem. – Eur. J.*, 2018, **24**, 13089–13092.

33 W. Huang, J. Byun, I. Rörich, C. Ramanan, P. W. M. Blom, H. Lu, Di Wang, L. Da Caire Silva, R. Li, L. Wang, K. Landfester and K. A. I. Zhang, Asymmetric Covalent Triazine Framework for Enhanced Visible-Light Photoredox Catalysis via Energy Transfer Cascade, *Angew. Chem., Int. Ed.*, 2018, **57**, 8316–8320.

34 Y. Matano, Y. Hayashi, K. Suda, Y. Kimura and H. Imahori, Synthesis of 2-Alkenyl- and 2-Alkynyl-benzo[*b*]phospholes by Using Palladium-Catalyzed Cross-Coupling Reactions, *Org. Lett.*, 2013, **15**, 4458–4461.

35 S. Xu, K. Nishimura, K. Saito, K. Hirano and M. Miura, Palladium-catalysed C–H arylation of benzophospholes with aryl halides, *Chem. Sci.*, 2022, **13**, 10950–10960.

36 Y. Tokura, S. Xu, Y. Kojima, M. Miura and K. Hirano, Pd-catalysed, Ag-assisted C2–H alkenylation of benzophospholes, *Chem. Commun.*, 2022, **58**, 12208–12211.

37 (*a*) Y. Hayashi, Y. Matano, K. Suda, Y. Kimura, Y. Nakao and H. Imahori, Synthesis and Structure–Property Relationships of 2,2′-Bis(benzo[*b*]phosphole) and 2,2′-Benzo[*b*]phosphole–Benzo[*b*]heterole Hybrid π Systems, *Chem. – Eur. J.*, 2012, **18**, 15972–15983; (*b*) A. Wakatsuki, M. Yukimoto, M. Minoura, K. Fujii, Y. Kimura and Y. Matano, Regioselective functionalization at the 7-position of 1,2,3-triphenylbenzo[*b*]phosphole oxide via P=O-directed lithiation, *Dalton Trans.*, 2018, **47**, 7123–7127; (*c*) Y. Tokura, S. Xu, K. Yasui, Y. Nishii and K. Hirano, Pd-catalysed C–H alkynylation of benzophospholes, *Chem. Commun.*, 2024, **60**, 2792–2795.

38 For a recent example, see: B. R. Brutiu, G. Iannelli, M. Riomet, D. Kaiser and N. Maulide, Stereodivergent 1,3-difunctionalization of alkenes by charge relocation, *Nature*, 2024, **626**, 92–97.

39 Q.-Z. Zheng and N. Jiao, Ag-catalyzed C–H/C–C bond functionalization, *Chem. Soc. Rev.*, 2016, **45**, 4590–4627.