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Direct Synthesis of Dibenzophospholes from Biaryls by Double C−P Bond Formation via Phosphenium Dication Equivalents

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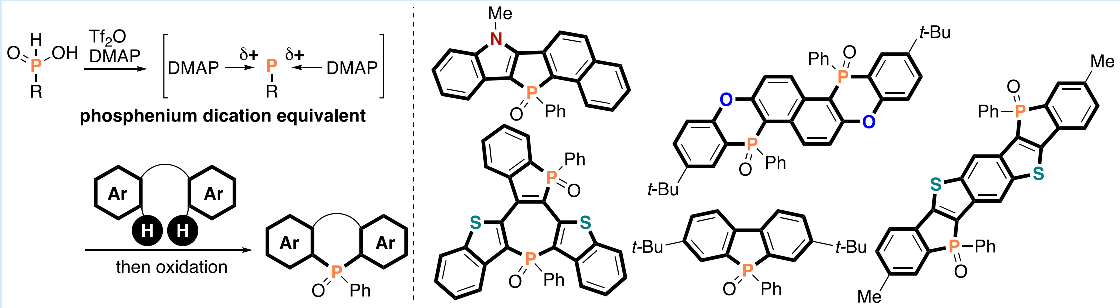
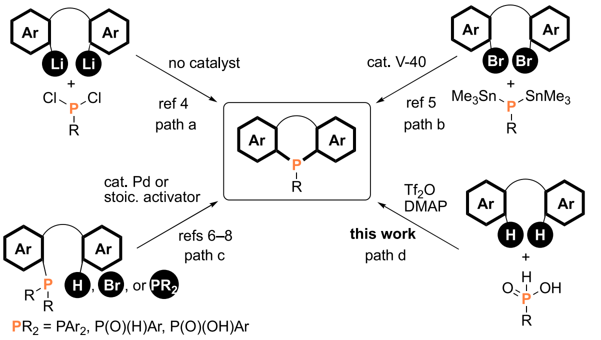


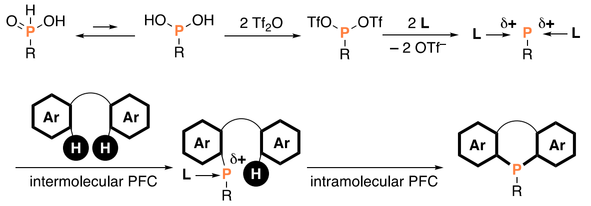
ABSTRACT: We have developed a new strategy for the generation of phosphenium dication equivalents from readily available phosphinic acids and Tf_2O. The in situ-generated dication equivalents can be readily coupled with simple (hetero)biaryls to form the corresponding dibenzophospholes directly. This protocol can also be applied to the concise synthesis of six- and seven-membered phosphacycles as well as the largely π-extended heteroacene derivatives, which are of great interest in the field of organic functional materials.

A dibenzophosphole is a key motif in the design of phosphorus-containing functional organic materials such as light-emitting diodes and photovoltaic devices.[1] Additionally, its six-[2] and seven-membered[3] analogues also show characteristic optoelectronic and physical properties. Accordingly, synthetic chemists have focused considerable attention on the concise construction of the phosphacyclic framework by the development of efficient C−P bond-forming strategies. The most classical and most reliable protocols are the substitution reactions of the dilithiated biaryl compounds with dichlorophosphines $RPCl_2$ (Scheme 1, path a)[4] and radical substitution reactions of dibromobiaryls with the specially designed $RP(SnMe_3)_2$ reagents (path b).[5] Recently, the cyclization of biarylphosphine derivatives via C−H,[6] C−X,[7] or C−P[8] bond cleavage has also been developed as the simpler and relatively functional group-tolerated alternative strategy (path c). However, the procedures mentioned above still suffer from the limited functional group compatibility and somewhat tedious preparation of prefunctionalized starting substrates and/or reagents.

Scheme 1. Approaches to Dibenzophosphole Derivatives via C−P Bond Formation



Scheme 2. Working Hypothesis (L = neutral Lewis base)



Meanwhile, our research group recently focused on the synthetic potential of highly electrophilic and coordinately unsaturated phosphenium cations[9] and developed a metal-free,

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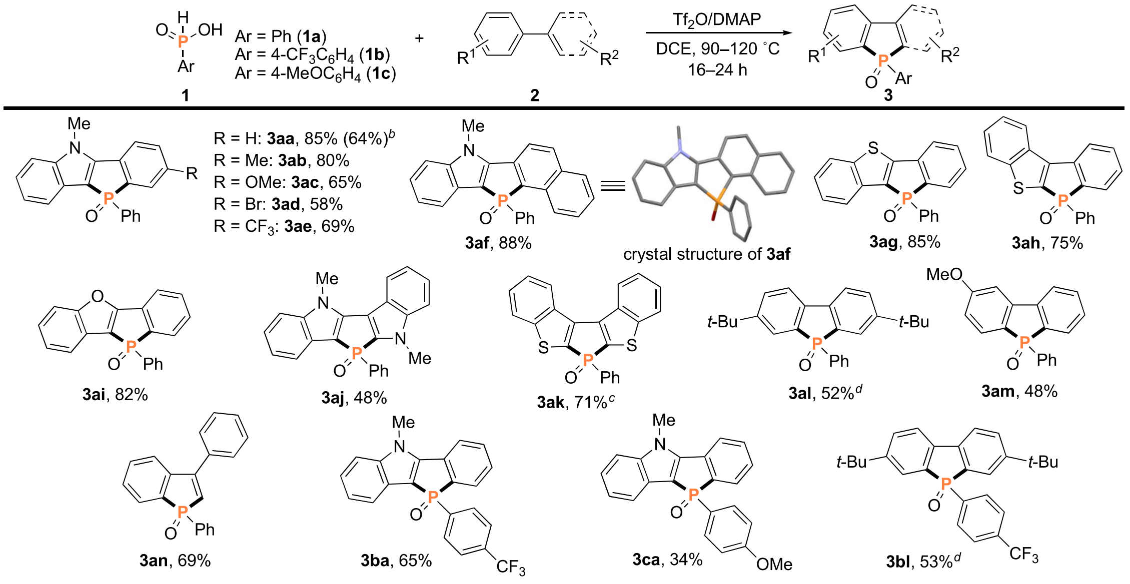
Scheme 3. Direct Synthesis of Dibenzophospholes 3 by Double C−P Bond Formation of Biaryls 2 with Phosphinic Acids 1[a]



[a] Reaction conditions: **1** (2.0 equiv), **2** (0.10 mmol), Tf_2O (4.8 equiv), DMAP (4.8 equiv), DCE (1.5−3.0 mL), N_2. See the Supporting Information for detailed conditions for each substrate. Isolated yields are shown. The formed C−P bonds are illustrated with a bold line. [b] On a 1.0 mmol scale for 168 h. [c] At 70 °C for 168 h. [d] With **1a** (10 equiv) and Tf_2O/DMAP (24 equiv).

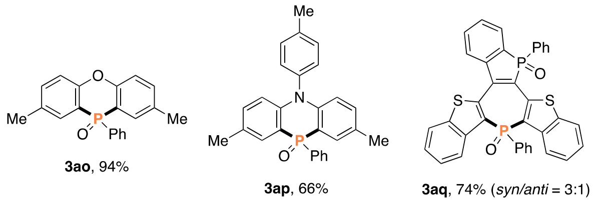


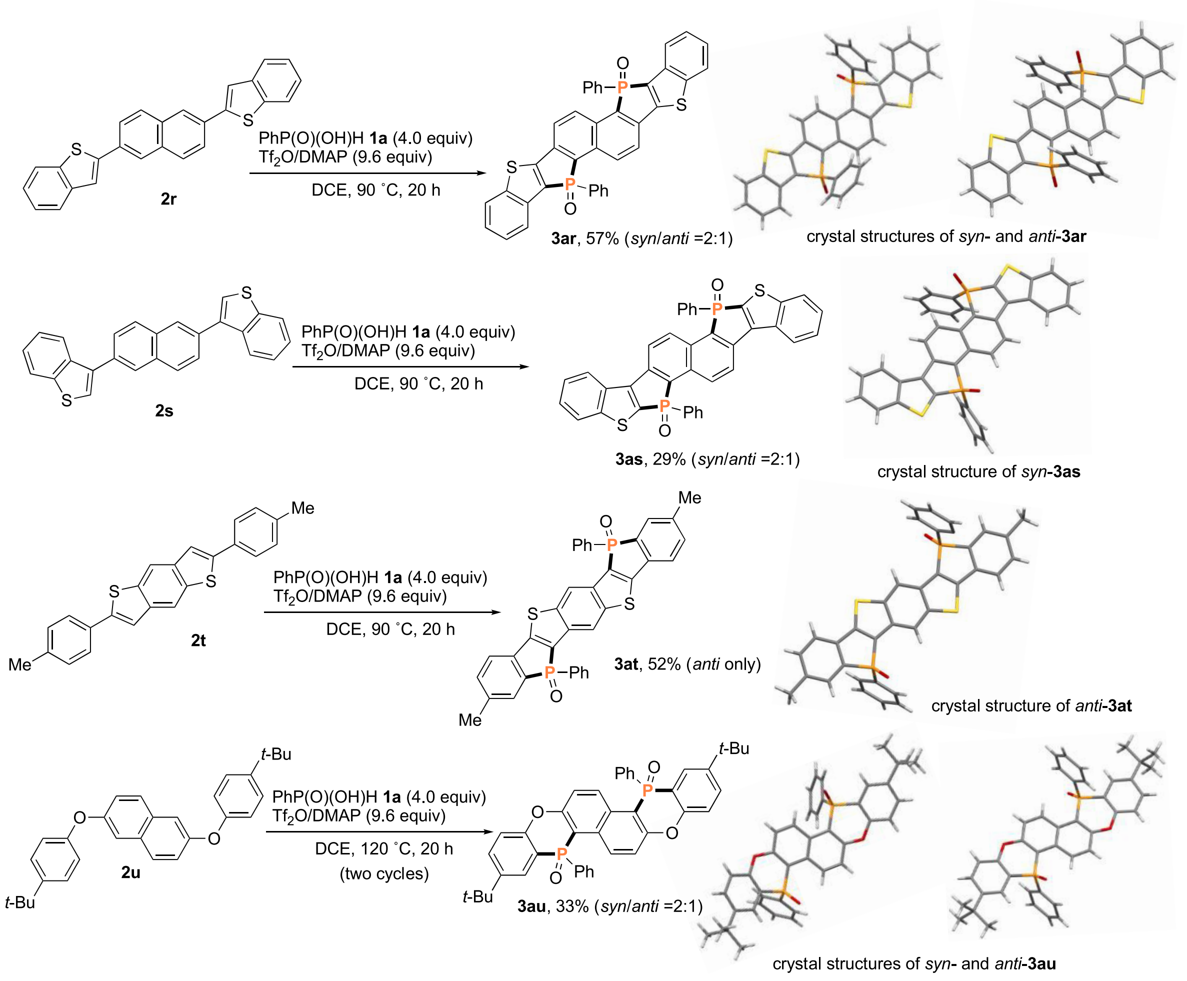
Figure 1. Six- and seven-membered phosphacycles prepared by double C−P bond formation.

Tf_2O-mediated C−P bond formation of alkynes with the readily available secondary phosphine oxides $R_2P(O)H$ to form the corresponding phosphinative cyclization products and benzophospholes.[10] This strategy can also be applied to the cyclization of biarylphosphine oxides, delivering the corresponding dibenzophospholes.[6f] Because of the continuing interest in this chemistry, we envisioned that, if the more coordinately unsaturated phosphenium dications can be generated, the double C−P bond-forming reaction of simple biaryls can form the corresponding dibenzophospholes directly, which is highly attractive because the starting simple biaryls are readily available through the well-established biaryl cross-coupling chemistry. Herein, we report a Tf_2O-promoted inter- and intramolecular C−P bond formation sequence of simple (hetero)biaryls with the easily accessible and stable phosphinic acids RP(O)(OH)H (path d). This newly developed protocol allows the rapid synthesis of not only dibenzophospholes but also six- and seven-membered phosphacycles and largely *π*-extended P-containing heteroacene derivatives. A related reaction of more reactive 1,3-dienes with dichlorophosphines $RPCl_2$ to provide the monocyclic phospholes is known as the McCormack reaction,[11] but the extension to the biaryl system remains largely elusive.[12]

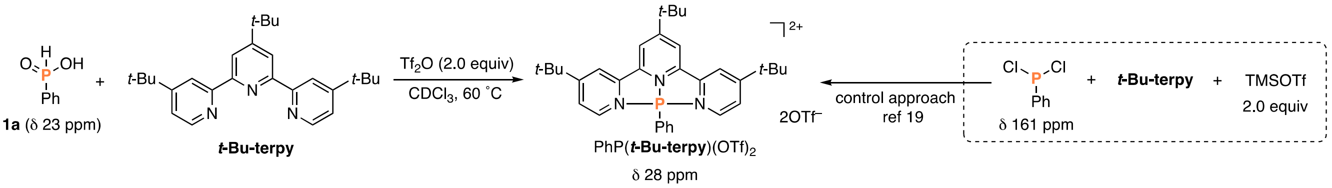
Our initial working hypothesis is shown in Scheme 2. The phosphinic acid RP(O)(OH)H undergoes tautomerization to the corresponding dihydroxylphosphine $RP(OH)_2$.[13] If the two OH groups could be activated with 2 equiv of Tf_2O, the corresponding $RP(OTf)_2$ would form. Two OTf ligands are then kicked out by the external neutral Lewis base (**L**) to generate highly electrophilic, coordinately more unsaturated phosphenium P(III) dication equivalent. Subsequent inter- and intramolecular phospha-Friedel−Crafts (PFC)-type reactions[2a,b,14] with the biaryl successfully deliver the targeted dibenzophosphole derivative.

On the basis of the aforementioned scenario, we began optimization studies with phenylphosphinic acid (**1a**; 0.20 mmol) and *N*-methyl-2-phenylindole (**2a**; 0.10 mmol) as the phosphenium dication precursor and model (hetero)biaryl substrate, respectively (Scheme 3). After extensive screening of various reaction parameters, we pleasingly found that the desired reaction proceeded in the presence of Tf_2O and *N*,*N*-dimethyl-4-aminopyridine (DMAP) in 1,2-dichloroethane (DCE) solvent at 120 °C to form the corresponding indolobenzophosphole oxide **3aa** in 85% isolated yield. Some observations should be noted. The effect of the base was critical, and almost no reaction occurred without any bases (<5%). The other potential P dication precursors such as $PhPCl_2$ and $PhP(O)(OH)_2$ resulted in no formation of the dibenzophosphole structure.[15] The initially formed P(III) benzophosphole product was spontaneously oxidized with residual Tf_2O and/or its derivatives, and oxide form **3aa** was detected exclusively even without special oxidative workup, which is similar to our previous observation.[6f,10] Additionally, the reaction was also conducted on a 1.0 mmol scale. We then examined the scope of double C−P bond-forming reaction. The phenyl ring of model **2a** could be replaced with several electron-donating and -withdrawing aryl groups, and the corresponding indolobenzophospholes **3ab**−**3ae** were obtained in good yields. The 2-naphthalene-substituted **2f** furnished **3af** as the single isomer through C−P bond formation at the more congested C1 position of naphthalene [unambiguously confirmed by X-ray analysis (CCDC 1987698)], which is reflected by the electronically controlled

Scheme 4. Direct Synthesis of S,P- (3ar–3at) and O,P-Acenes (3au) via Four-Fold C–P Bond Formation



Scheme 5. $^{31}P\{^1H\}$ NMR Studies



PFC-type reaction mechanism: the more electron-rich C1 position selectively reacted with **1a** over the C3 position. In addition to the indoles, benzothiophenes **2g** and **2h** and benzofuran **2i** could be converted to benzothienobenzophospholes **3ag** and **3ah** and benzofuranobenzophosphole **3ai**, respectively. Notably, in the case of benzothiophene substrates, both ladder-type (**3ag**) and bent-type (**3ah**) products were readily obtained. Bis(heteroaryl)s such as bisindole **2j** and bisbenzothiophene **2k** also underwent the double PFC reaction to afford N,P- and S,P-acenes **3aj** and **3ak**, respectively, in acceptable yields. Particularly notable is the successful application to simple biaryls: 4,4′-di(*tert*-butyl)-biphenyl (**2l**) and 3-methoxybiphenyl (**2m**) reacted with the phosphinic acid **1a** to regioselectively produce dibenzophospholes **3al** and **3am**, respectively, in synthetically useful yields. In the case of **3al**, the steric bulkiness of *tert*-Bu groups is an important key for controlling the regioselectivity. Actually, less hindered 4,4′-dimethylbiphenyl provided a complicated mixture (data not shown). Also in the reaction of **1l**, a small amount of simply *ortho*-phosphinated byproducts was detected but not fully identified. The simple 1,1-diphenylethylene (**2n**) instead of the biaryl was also viable, and 3-phenylbenzophosphole **3an** was isolated in 69% yield, in which the free C2–H can be easily modified via a halogenation and metal-catalyzed cross-coupling.[16] We also investigated the substitution effect on phosphinic acid **1**. The electron-deficient CF_3-substituted **1b** showed an efficiency similar to that of parent **1a**, whereas the electron-rich MeO-substituted **1c** decreased the yield of the product (**3ba**, **3ca**, and **3bl**).[17]

This strategy was also extended to six- and seven-membered phosphacycle synthesis (Figure 1). The diaryl ether and triarylamine were directly converted to the corresponding six-membered phenoxaphosphine **3ao** and phenophosphazine **3ap** in one shot. The doubly benzothiophene-fused seven-membered phosphepine **3aq** was also readily constructed. These results demonstrate the high potential of this phosphenium dication protocol for the synthesis of configurationally flexible medium-sized phospha macrocycles.

The most salient advantage of this strategy is the direct use of relatively simple aromatic substrates in the synthesis of largely π-extended dibenzophosphole derivatives (Scheme 4). 2,6-Bis(2-benzothienyl)naphthalene **2r**, which can be readily prepared by the Suzuki−Miyaura coupling, was transformed via 4-fold C−P bond formation to the highly condensed ladder-type S,P-acenes **3ar** in 57% yield. Its bent-type isomer **3as** was also accessible under the same conditions from 2,6-bis(3-benzothienyl)naphthalene **2s**. Moreover, the organic semiconductor scaffold **2t** was easily modified with the two phosphole rings (**3at**). Furthermore, this double cyclization could be directly applied to the construction of highly fused O,P-acene **3au** based on the six-membered ring system. Similar to the case of **3af**, the regioselectivity was perfectly controlled in all cases, which was unambiguously confirmed by X-ray crystallographic analysis (CCDC 1987699, 1987700, 1987701, 1989209, 1989210, and 1989211).

Although we initially hypothesized the formation of the highly coordinately unsaturated phosphenium P(III) dication (Scheme 2), an alternative process via phosphonium P(V) or phosphenium P(III) monocations is also plausible. To gain mechanistic insight, we finally performed $^{31}P\{^1H\}$ NMR studies in $CDCl_3$ solutions. Upon treatment of PhP(O)(OH)H (**1a**, δ 23 ppm) with 2.0 equiv of Tf_2O at 60 °C, some unidentified signals were observed (Figure S14). However, the addition of 2.0 equiv of DMAP formed two new signals at δ 185 ppm and δ 110 ppm, which are assigned to $PhP(OTf)_2$ and $PhP(DMAP)_2(OTf)_2$, respectively (Figure S15). Actually, the almost same signal (δ 180 ppm) appeared by simple mixing of $PhPCl_2$ (δ 161 ppm) and 2.0 equiv of AgOTf (Figure S16), thus suggesting that the former is $PhP(OTf)_2$. However, the reported $^{31}P\{^1H\}$ chemical shift of the latter $PhP(DMAP)_2(OTf)_2$ in CD_2Cl_2 is δ 121 ppm,[18] which is not fully consistent with the observed value. Given the labile and reversible coordinating nature of monodentate DMAP under Tf_2O-mediated conditions, we then tested the more rigidly coordinating tridentate terpyridine derivative ***t*-Bu-terpy** instead of DMAP (Scheme 5). Gratifyingly, we observed the distinct signal at δ 28 ppm, which is typical to the tetracoordinated P(III) center (Figure S17). The control experiment of $PhPCl_2$ and 2.0 equiv of TMSOTf in the presence of ***t*-Bu-terpy** also provided the same signal at δ 28 ppm (Figure S18), which can support the formation of tetracoordinated phosphenium dication PhP(***t*-Bu-terpy**)$(OTf)_2$.[19] The outcomes described above indicate the intermediacy of the phosphenium dication, rather than P(V) phosphonium and P(III) phosphenium monocations, in the present double C−P bond formation with the phosphinic acids and Tf_2O.[20] However, the details of the C−P bond-forming step (stepwise or concerted) remain unclear, and further studies are essential.

In conclusion, we have developed a new protocol for the generation of highly coordinately unsaturated phosphenium dication equivalents from the readily available phosphinic acids and Tf_2O and succeeded in the inter- and intramolecular phospha-Friedel−Crafts reaction sequence under metal-free conditions. This strategy allows the relatively simple (hetero)-biaryls to undergo double C−P bond formation to form the corresponding dibenzophospholes in one shot. Moreover, the more configurationally flexible six- and seven-membered phosphacycles as well as highly π-extended phosphorus-containing planar acenes can also be easily constructed. Thus, the phosphenium dication-based strategy will find wide applications in the design and synthesis of new functional organic materials based on the phosphole molecules.[21] Further development of related C−P bond-forming reactions with coordinately unsaturated and highly reactive P(III) species and applications of this concept to other heteroatom species are currently underway and will be reported in due course.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c00944.

^1H, $^{13}C\{^1H\}$, and $^{19}F\{^1H\}$ NMR spectra, ORTEP drawing, and detailed optimization studies (PDF)

Accession Codes

CCDC 1987698−1987701 and 1989209−1989211 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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(20) See the Supporting Information for more details.

(21) See the Supporting Information for preliminary investigations of photochemical properties of **3ar**−**3au**.