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Paving the Way to Novel Phosphorus-Based Architectures: A Noncatalyzed Protocol to Access Six-Membered Heterocycles

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Abstract: *Phosphorus-based heterocycles provide access to materials with properties that are inaccessible from all-carbon architectures. The unique hybridization of phosphorus gives rise to electron-accepting capacities, a large variety of coordination reactions, and the possibility of controlling the electronic properties through phosphorus postfunctionalization. Herein, we describe a new noncatalyzed synthetic protocol to prepare fused six-membered phosphorus heterocycles. In particular, we report the synthesis of novel phosphaphenalenes. These fused systems exhibit the benefits of both five- and six-membered phosphorus heterocycles and enable a series of versatile postfunctionalization reactions. This work thus opens up new horizons in the field of conjugated materials.*

The unique properties of phosphorus heterocycles are a continuous source of scientific breakthroughs. Phosphinines (Figure 1), six-membered phosphorus heterocycles, offer new perspectives in coordination chemistry and catalytic transformations;[1] they exhibit high electron delocalization over the whole ring and special σ-donating and π-accepting properties. In turn, the five-membered analogues, phospholes (Figure 1), are at the center of materials science. The particular nonhybridization of the $\lambda^3\sigma^3$ phosphorus atom and its capacity to reversibly reach the $\lambda^5\sigma^4$ state have led to materials with outstanding optoelectronic properties.[2] Thus, some of us recently developed phosphole-based multifunctional architectures, that is, materials with temperature-dependent luminescence, electrochromism, liquid crystallinity, supramolecular self-assembly, and gel properties.[3] Unraveling the full potential of phosphorus heterocycles requires, however, the development of novel systems. In this context, improved synthetic protocols to access five- and six-membered phosphorus heterocycles have recently emerged. They are largely based on radical[4] and metal-catalyzed reactions with Cu,[5] Al,[6] Ag,[7] and Pd.[8]

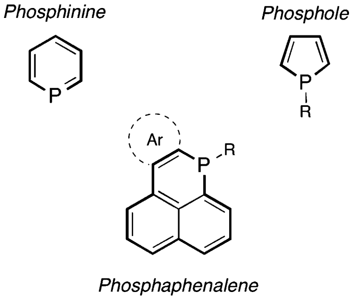

Figure 1. Molecular structures of phosphinines (left), phospholes (right), and designed phosphaphenalene (bottom).

In view of synergistically merging the intriguing properties of five- and six-membered phosphorus heterocycles, we envisaged the development of novel phosphaphenalene derivatives (Figure 1). Particularly, we targeted phosphorus-based architectures exhibiting: 1) high electron delocalization, 2) a reversibly accessible $\lambda^5\sigma^4$ phosphorus center, 3) stability in air, and 4) versatile postfunctionalization reactions.

To prepare the phosphaphenalenes, we investigated conditions suitable for the construction of the phosphorus ring from phenylphosphane-substituted naphthalene derivatives. Our first attempts to isolate the corresponding naphthylchlorophenylphosphane from **A** (Scheme 1) were, however, unsuccessful. Further investigations revealed a new noncatalyzed protocol to access six-membered phosphorus heterocycles. We observed the formation of the phosphorus ring to occur simply when the lithiated naphthalene **A** was treated with an equimolecular amount of dichlorophenylphosphane at 0 °C. To obtain air-stable heterocycles, we subsequently exposed the reaction mixture to H_2O_2, according to established procedures.[9]

Motivated by this finding and in order to explore the synthetic scope of this new synthetic protocol, we expanded our studies to a set of substrates **A** containing different aromatic substituents (Scheme 1). Thus, our methodology was found to be compatible with a variety of both substituted and unsubstituted thiophenes; **1a**,**b** and **2a**,**b** are accessible using our standard conditions. Compound **3**, on the other hand, can only be obtained by increasing the reaction temperature to 50 °C in a modified protocol. Other electron-rich heterocycles such as furan and pyrrole, as well as benzothiophene lead to the fused phosphaphenalenes **4, 5**, and **6**, respectively. To further validate the versatility of the reaction, we also tested aromatic hydrocarbons and obtained the phenyl- and naphthalene-substituted phenalenes **7** and **8**. Accessing the pyridine derivative **9** demonstrated, moreover, the compatibility of our synthetic protocol with electron-deficient heterocycles.

To get further insight into the extension of the cyclization, we targeted the preparation of five- and seven-membered phosphorus rings (Scheme 2). Reaction of **10** under our

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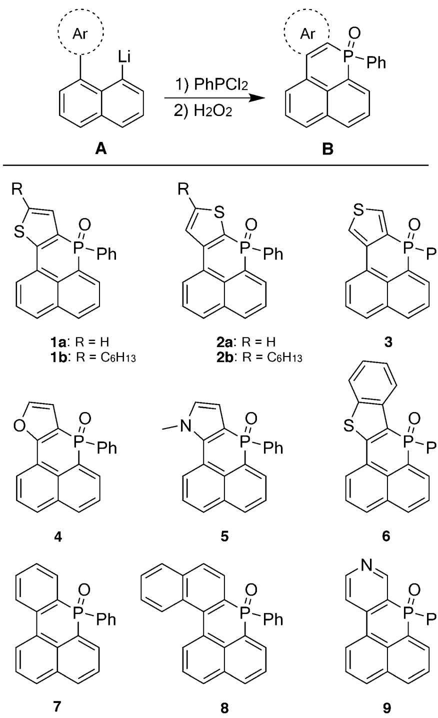
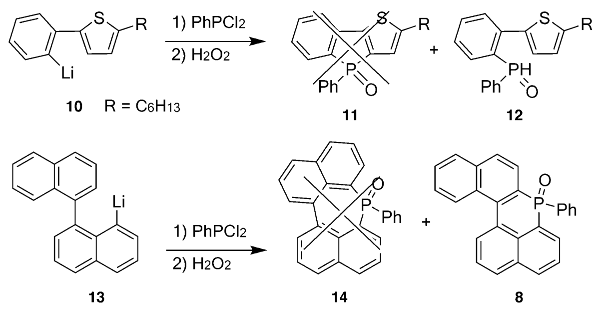


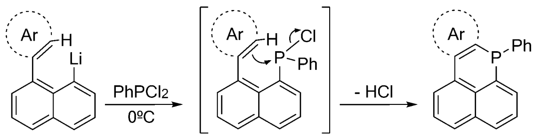
Scheme 1. Noncatalyzed reaction to access fused phosphaphenalene derivatives **1**–**9**.



Scheme 2. Attempts to access five- and seven-membered phosphorus heterocycles.

standard and modified conditions led exclusively to the formation of **12**. In turn, when we exposed **13** to our synthetic conditions, we were also unable to detect the formation of derivative **14**. The latter results are in consonance with the reaction enthalpies obtained from DFT calculations (see the Supporting Information). Whereas the formation of six-membered heterocycles appears exothermic, the annulations of five- and seven-membered rings correlate with endothermic processes. Thus, our methodology is found to be highly selective for the synthesis of six-membered phosphorus heterocycles.

A plausible mechanism for the cyclization reaction is shown in Scheme 3. Phosphorus atoms can act as either nucleophiles or electrophiles.[2f,10] We therefore propose a nucleophilic attack of the Ar peripheral ring on the phosphorus center followed by the elimination of HCl, according to a classical electrophilic aromatic substitution mechanism. Major difficulties in isolating the chlorophosphane intermediate prevented us from direct experiments to elucidate the reaction mechanism in greater detail. To circumvent this bottleneck, we turned to low-temperature $^{31}P\{^1H\}$ NMR measurements (Figure 2). The results are consistent with our hypothesis. In situ monitoring of the reaction to obtain **5** at −80 °C allowed us to detect the formation of the chlorophosphane intermediate with a singlet at $\delta = +86.2$ ppm.[11] Surprisingly, several experiments indicated the formation of the cyclized product already at low temperature; that is, appearance of a singlet at $\delta = -46.4$ ppm. When we increased the temperature stepwise, the signal at $\delta = +86.2$ ppm progressively faded away giving rise to the fully cyclized product between −30 and −20 °C. Finally, treatment with H_2O_2 afforded a singlet at $\delta = +8.6$ ppm, which is characteristic of the oxidized phosphaphenalenes **5** (see the Supporting Information). To sum up, we were able to detect the progressive formation of the cyclized phosphorus ring from its chlorophenylphosphane precursor, without the mediation of any catalyst. All fused phosphaphenalenes were characterized by standard analytical techniques (see the Supporting Information).[12] $^{31}P\{^1H\}$ NMR spectra of **1**–**9** are characterized by a singlet whose chemical shift varies from $\delta = 6.0$ to 10.1 ppm.



Scheme 3. Proposed mechanism.

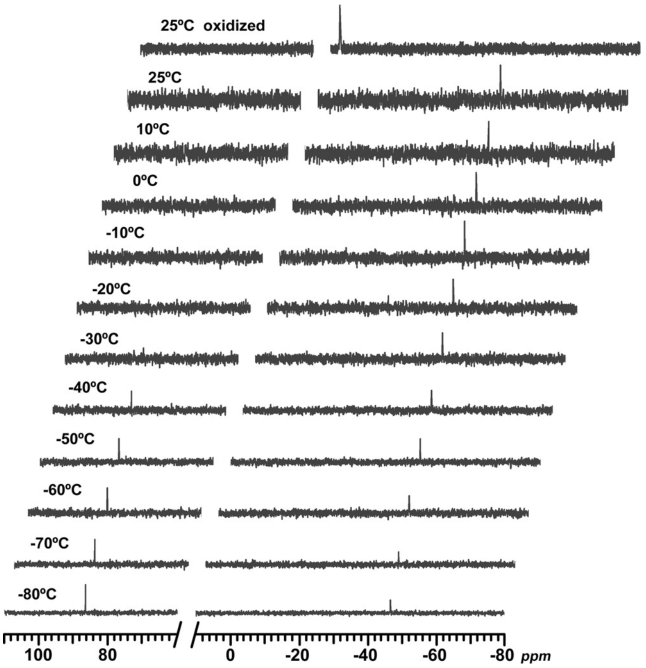


Figure 2. In situ $^{31}P\{^1H\}$ NMR spectra of the synthesis of **5** at increasing temperatures from −80 °C to 25 °C.

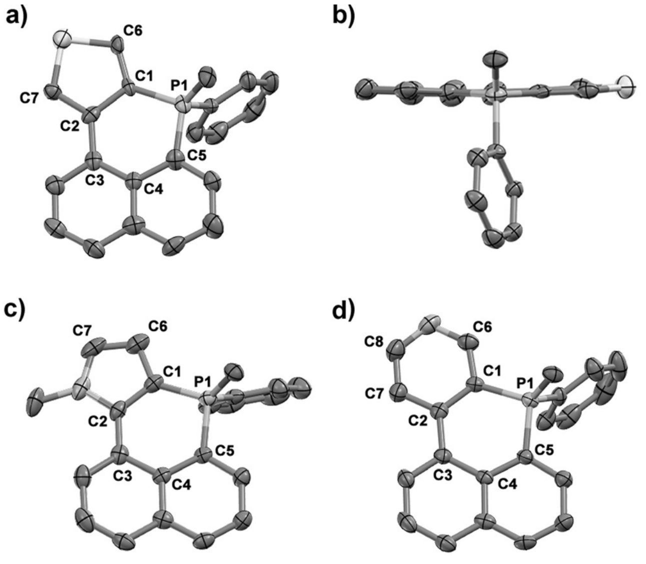
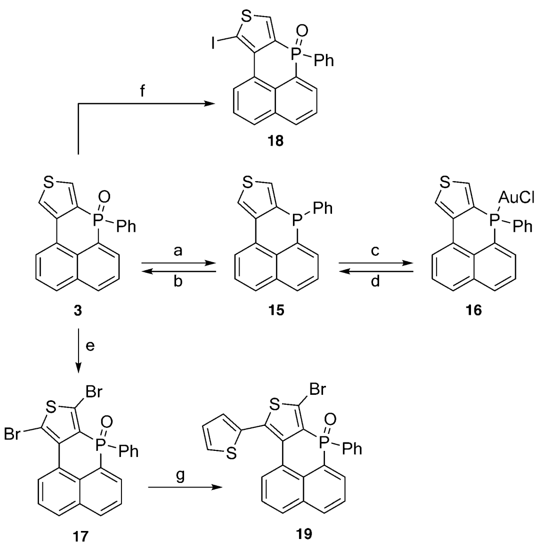


Figure 3. X-ray structures of a) **3**, top view, b) **3**, front view, c) **5**, and d) **9**. Thermal ellipsoids at the 50% probability level; hydrogen atoms omitted for clarity. Selected bond lengths [Å] for **3**: C1–C2 1.441(8), C2–C3 1.465(9), C3–C4 1.439(9), C4–C5 1.434(8), C1–C6 1.364 (8), C2–C7 1.385(8); for **5**: C1–C2 1.392(5), C2–C3 1.459(5), C3–C4 1.446(5), C4–C5 1.440(5), C1–C6 1.419(6), C6–C7 1.346(6); for **9**: C1–C2 1.399(5), C2–C3 1.485(5), C3–C4 1.442 (5), C4–C5 1.425 (5), C1–C6 1.398 (5), C2–C7 1.400(5), C7–C8 1.371(6).



Scheme 4. Postfunctionalization reactions of **3**: a) $HSiCl_3$, 100 °C; b) H_2O_2, 0 °C; c) Au(tht)Cl; d) $P(NMe_2)_3$; e) NBS/AcOH; f) NIS/AcOH; g) 2-(tributylstannyl)thiophene, $Pd(PPh_3)_4$, 120 °C. NBS = *N*-bromosuccinimide, NIS = *N*-iodosuccinimide, tht = tetrahydrothiophene.

The most interesting structural features were available from X-ray diffraction analyses. Figure 3 shows the molecular structures of **3**, **5**, and **9** in the solid state.[13] All three structures are essentially planar (Figure 3 b and Figures S2 and S3 in the Supporting Information); **5** exhibits a slight twist of 12.2° due to the repulsion between the methyl group of the pyrrole and the naphthalene moiety (Figure S2). Particularly in **3**, the six-membered phosphorus heterocycle does not exhibit any bond alternation; the bond lengths are in the range of 1.43–1.46 Å. A similar scenario is known for phosphinines.[1a] Compounds **5** and **9** exhibit shorter C1-C2 distances (Figure 3). The fused heterocycles, pyrrole and pyridine, appear nevertheless distorted; that is, they feature irregular bond length distribution. The latter is consistent with a high degree of π-conjugation. DFT calculations provide further information on the electronic distribution (see the Supporting Information). The frontier orbitals of **3**, **5**, and **8** are fully delocalized over the entire fused systems, with a large contribution of the phosphorus center in both HOMO and LUMO. Finally, the X-ray crystallographic data reveal different angles between the exocyclic phenyl ring and the main framework. The latter angles strongly differ as a function of the fused aromatic ring: from 114.9° for **3** to 123.3° and 124.5° for **5** and **9**, respectively. This phenomenon was already observed in extended phosphole derivatives; it is attributed to different electronic densities at the phosphorus center.[14]

The evaluation of the postfunctionalization reactions is commonly employed to ascertain the potential of phosphorus heterocycles as promising building blocks.[15] To prove the versatility of our phosphaphenalene derivatives, we representatively targeted the postfunctionalization reactions of **3** on both the phosphorus atom and the main framework (Scheme 4). Whereas $\lambda^5\sigma^4$ phosphorus centers provide air and moisture stability, $\lambda^3\sigma^3$ centers have attracted particular attention as they enable a wide array of reversible reactions with Lewis acids and transition metals.[9b,c,13,14] Thus, we focused on establishing suitable conditions to reversibly convert the $\lambda^5\sigma^4$ center into its $\lambda^3\sigma^3$ relative. As a result, we found that treatment of **3** with $HSiCl_3$ at 100 °C quantitatively reduces its $\lambda^5\sigma^4$ phosphorus atom into the $\lambda^3\sigma^3$ center of **15** (Scheme 4). The latter compound was found to be very versatile. Treatment of **15** with Au(tht)Cl leads to the gold derivative **16**; this complexation is quantitatively reversed by the reaction with $P(NMe_2)_3$. In turn, the oxidation of **15** with H_2O_2 at 0 °C regenerates the pentavalent state of the phosphorus atom. Moreover, compound **3** can be regioselectively halogenated at the α positions of the sulfur atom by treatment with *N*-bromosuccinimide, providing derivative **17**. Asymmetric functionalization is particularly appealing for materials development. In this context, **3** can be monohalogenated to obtain **18** by simple treatment with *N*-iodosuccinimide. Finally, **17** can also be converted by selective Stille cross-coupling into the monosubstituted **18**. This derivative presents great potential as a building block for obtaining further extended systems.

To conclude, we have discovered a new non-catalyzed synthetic protocol to access fused six-membered phosphorus heterocycles. The versatility of this reaction enables preparing fused phosphaphenalenes with a wide variety of heterocycles as well as with aromatic hydrocarbons. The new phosphaphenalene derivatives synergistically converge properties from the five- and six-membered phosphorus heterocycles; that is, a) high electron delocalization, b) reversible λ^5 σ^4 center and c) versatile postfunctionalization reactions. Altogether, both this new synthetic protocol and the phosphaphenalene structures introduce new opportunities to develop superior phosphorus-based architectures. Detailed spectroscopic investigations to further corroborate the potential of the new phosphaphenalenes as building blocks for functional materials are currently underway.

Acknowledgements

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Keywords: cyclization · phosphaphenalene · phosphorus heterocycles · postfunctionalization

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[12] It is important to highlight that all derivatives showed a strong capacity to adsorb small molecules. Further investigations on this particularity are currently in progress.

[13] Crystal data for **3**: ($C_{20}H_{13}OPS$): $M_r = 332.33$, $T = 200(2)$ K, monoclinic, space group $C2/c$, $a = 29.618(4)$, $b = 14.9711(18)$, $c = 16.587(2)$ Å, $V = 6372.9(13)$ Å^3, $Z = 16$, $\rho_{calcd} = 1.38$ g cm^{-3}, $\mu = 0.30$ mm^{-1}, $\lambda = 0.71073$ Å, $\theta_{max} = 22.7$, 16395 measured reflections, 4269 [R(int) = 0.1263] independent reflections, GOF on $F^2 = 1.04$, $R_1 = 0.068$, $wR_2 = 0.136$ ($I > 2\sigma(I)$), largest difference peak and hole 0.45 and −0.42 e Å^{-3}; Crystal data for **5**: ($C_{21}H_{18}NO_2P$): $M_r = 347.33$, $T = 200(2)$ K, monoclinic, space group $P2_1/c$, $a = 12.233(5)$, $b = 7.464(3)$, $c = 18.839(8)$ Å, $V = 1690.8(12)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.36$ g cm^{-3}, $\mu = 0.18$ mm^{-1}, $\lambda = 0.71073$ Å, $\theta_{max} = 23.1$, 11497 measured reflections, 2357 [R(int) = 0.0686] independent reflections, GOF on $F^2 = 1.14$, $R_1 = 0.068$, $wR_2 = 0.128$ ($I > 2\sigma(I)$), largest difference peak and hole 0.39 and −0.29 e Å^{-3}; Crystal data for **9**: ($C_{21}H_{14}NOP$): $M_r = 327.30$, $T = 200(2)$ K, orthorhombic, space group $Pbca$, $a = 8.9283(12)$, $b = 15.903(2)$, $c = 22.236(3)$ Å, $V = 3157.1(7)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.38$ g cm^{-3}, $\mu = 0.18$ mm^{-1}, $\lambda = 0.71073$ Å, $\theta_{max} = 25.0$, 18872 measured reflections, 2799 [R(int) = 0.1115] independent reflections, GOF on $F^2 = 1.01$, $R_1 = 0.056$, $wR_2 = 0.125$ ($I > 2\sigma(I)$), largest difference peak and hole 0.24 and −0.34 e Å^{-3}. X-ray crystal structure analyses were measured on Bruker Smart CCD or Bruker Smart APEX instrument using $Mo_{K\alpha}$ radiation. Diffraction intensities were corrected for Lorentz and polarization effects. An empirical absorption correction was applied using SADABSS3 based on the Laue symmetry of reciprocal space. Hydrogen atoms were either isotropically refined or calculated. The structures were solved and refined using the SHELXTLS4 software package. CCDC 1418419, 1418420, and 1418421 (for compounds **3**, **5**, and **9**, respectively) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

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