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Synthesis of P-Containing Polycyclic Aromatic Hydrocarbons from Alkynyl-phosphonium Salts

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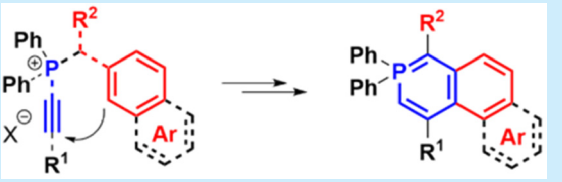
ABSTRACT: This work presents a straightforward method for synthesizing a series of phosphorus-containing polycyclic aromatic hydrocarbons (P-PAHs) featuring an internal ylidic bond. The method involves anion exchange, alkyne annulation, and deprotonation reactions, enabling the efficient production of cyclic phosphonium salts, which serve as pivotal intermediates in the synthesis of P-PAHs. The alkyne annulation reaction exhibits high regioselectivity, ensuring the successful synthesis of λ^5-phosphaphenanthrene isomers. Additionally, the incorporation of electron-withdrawing groups effectively stabilizes the internal ylidic bond of P-PAHs.



Organophosphorus heterocyclic compounds have attracted a significant amount of attention in recent years owing to their diverse bonding capabilities, adaptable coordination modes, and exceptional electronic tunability.[1−6] These compounds have beneficial features such as visual absorbance, luminescence, high electron mobilities, and stability.[7] These attributes make them prime candidates for photoelectric materials in applications such as organic field-effect transistors (OFETs),[8,9] organic light-emitting diodes (OLEDs),[10] and organic photovoltaics (OPVs).[11] The λ^5-phosphinines have emerged as potent components for optoelectronic applications. Specifically, Muller et al. successfully developed an OLED using a blue phosphinine emitter, marking the first instance of its development.[12,13] Despite the extensive research on π-extended six-membered phosphonium salts, the synthesis of neutral phosphorus-containing polycyclic aromatic hydrocarbons (P-PAHs), particularly those featuring λ^5-phosphinine rings, has been less explored due to the limited availability of synthesis methods for these structures. Hayashi and co-workers reported the synthesis of 2,6-dicyano-λ^5-phosphinines, for which the stability of the ylide bond in these molecules is significantly enhanced by the introduction of electron-withdrawing cyano groups (Figure 1a).[14] Beyond the synthesis of phosphinines, π-extended fused phosphinines have been explored. For example, Zefirov and co-workers synthesized a series of benzo-fused phosphinines, known as λ^5-phosphanaphthalenes, by employing phosphonium-iodonium ylides in a nucleophilic addition reaction with alkynes under ultraviolet (UV) light (Figure 1b).[15] Furthermore, the synthesis of λ^5-phosphanaphthalene derivatives has been optimized for high yield through the reaction of *o*-phosphinobenzene with alkynes, as depicted in Figure 1c.[16] More recently, π-conjugated λ^5-phosphaphenanthrene and other innovative P-PAHs have been synthesized efficiently in

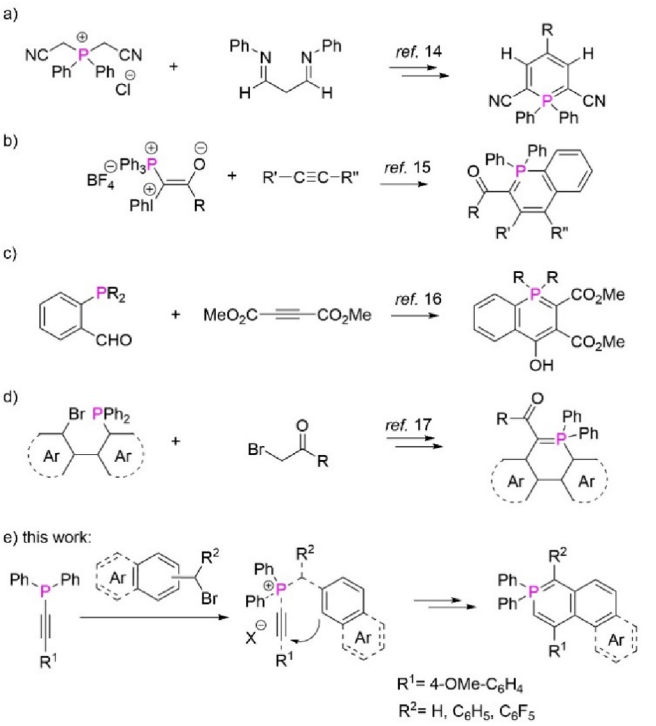


Figure 1. Synthesis of λ^5-phosphinine derivatives and six-membered π-extended λ^5-P-containing PAHs.

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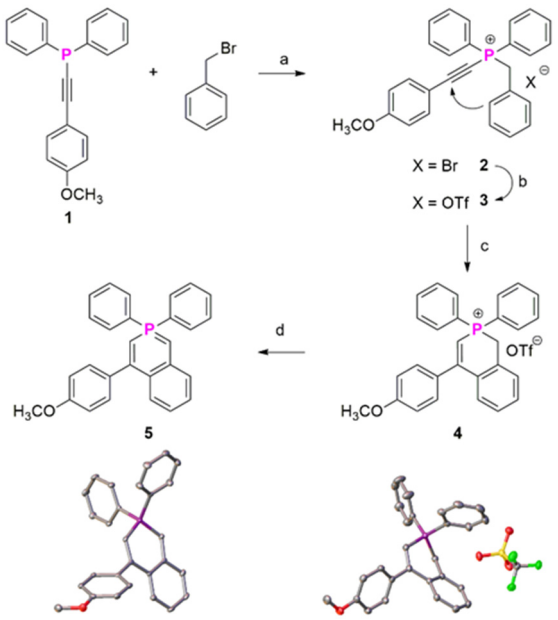
a one-pot process through the intramolecular cyclization of carbonyl-stabilized phosphonium ylide (Figure 1d).[17]

The presence of cyano or carbonyl groups on the ylide's carbon atom is instrumental in these synthesis methods, as these groups effectively stabilize the ylidic bond by reducing the electron density at the ylide center, thereby mitigating reactivity and enhancing the stability of the compounds. Consequently, the development of new synthetic strategies that enable the formation of phosphine rings is a valuable goal in organophosphorus chemistry. Such methods would not only broaden the synthetic capabilities of chemists but also potentially lead to the discovery of new materials with unique properties and applications.

Alkyne annulation reactions are widely employed for the synthesis of carbon-rich compounds.[18−20] Our previous work has demonstrated that polycyclic aromatic hydrocarbons (PAHs) and graphene nanoribbons can be synthesized through multiple alkyne benzannulation reactions, facilitated by Brønsted or Lewis acids.[19−22] Building on this foundation, we present a modular strategy for preparing P-PAHs, which involves a sequence of anion exchange, alkyne annulation, and deprotonation reactions (Figure 1e). The synthesis of P-PAHs hinges on the creation of cyclic phosphonium salts. These salts are produced in high yield through alkyne annulation reactions, promoted by triflic acid (TfOH). The stability of the resulting internal phosphorus ylides in P-PAHs can be enhanced by incorporating an electron-withdrawing substituent. This efficient protocol allows for the facile synthesis of P-PAHs.

A modular synthetic approach was initially contemplated for the synthesis of the cyclic phosphonium salts, serving as pivotal precursors for the subsequent construction of neutral P-PAHs. As depicted in Scheme 1, tertiary alkynylphosphine **1** was reacted with benzyl bromide in acetonitrile, forming phosphonium salt **2**.

Scheme 1. Synthesis of λ^5-Isophosphanaphthalene Derivative 5[a]



[a]Reagents and conditions: (a) acetonitrile, 60 °C, 6 h; (b) NaOTf, CH_2Cl_2, H_2O, rt, 10 min; (c) TfOH, CH_2Cl_2, 0 °C, 10 min; (d) *t*-BuOK, THF, −78 °C to rt, 30 min.

However, subsequent attempts to achieve the desired cyclization through a series of alkyne annulation reactions, utilizing various Lewis and Brønsted acids, such as $InCl_3$, $PtCl_2$, AuCl, TfOH, and TFA, were unsuccessful. This was likely due to the inhibitory effect of the bromide anion. To address this issue, the bromide salt was converted into the corresponding triflate salt **3** via a highly efficient anion exchange reaction. The addition of TfOH to a CH_2Cl_2 solution of **3** led to the formation of cyclized phosphonium salt **4**, but complete conversion was not achieved even with prolonged reaction times. A breakthrough was achieved by introducing an excess of TfOH (3 equiv), which rapidly and cleanly facilitated the 6-endo alkyne cyclization, affording the product in a high yield of 90%. Further deprotonation of **4** with 1 equiv of *t*-BuOK resulted in the isolation of neutral λ^5-isophosphanaphthalene **5** as a red solid in 91.1% yield. The 6-endo-dig cyclization was unambiguously confirmed by single-crystal X-ray analysis of compounds **4** and **5** (Scheme 1). In conclusion, the optimal reaction pathway involves a sequence of anion exchange, alkyne annulation, and deprotonation reactions.

Our previous research has shown that the regioselectivity of the alkyne benzannulation could be manipulated by altering the positions of the substituents.[21,22] Following this approach, we have successfully synthesized two isomers of λ^5-phosphaphenanthrene, **10** and **11** (Scheme 2).

Naphthalene-based phosphonium triflate salts **8** and **9** were synthesized individually. Subsequent treatment with 3 equiv of TfOH led to the formation of expected cyclized phosphonium salts **8** and **9**, respectively. The regioselectivity of the alkyne annulation was unambiguously confirmed by the X-ray crystal structures of compounds **8** and **9** (Scheme 2).[21,23,24] Ultimately, neutral λ^5-phosphaphenanthrene isomers **10** and **11** were obtained in good yields by deprotonating **8** and **9**, respectively. Compound **11** was more soluble in hexanes than was **10**, possibly due to its twisted backbone resulting from steric hindrance within the bay region. The distortion of the P ring disrupts the normal planar arrangement of **11**, which, in turn, reduces the effectiveness of orbital interactions. This change in molecular structure leads to less efficient stacking and, as a result, an increase in the solubility of **11** in hexane.

Compounds **5**, **10**, and **11** were found to be unstable in the presence of air and moisture, a condition primarily attributed to their internal ylidic bonds. To address this issue, we investigated the addition of substituent groups to improve their stability. It is well-established that the incorporation of electron-withdrawing groups (EWGs) on the ylidic carbon can significantly enhance the stability of phosphorus ylides. Therefore, by introducing a pentafluorophenyl group, we have successfully obtained air-stable red solid compound **14** (Scheme 3), demonstrating the crucial role of EWGs in stabilizing the buildup of negative charge on the phosphorus ylide. Concurrently, we have investigated the potential of steric hindrance to stabilize ylides, as exemplified by the introduction of the 2,4,6-trimethylphenyl substituent (Scheme 3). However, the resulting compound has proven to be sensitive to air. Intriguingly, X-ray crystal structure analysis of **16** reveals that the 2,4,6-trimethylphenyl group, rather than the phenyl group, is engaged in the alkyne annulation reaction. Moreover, a methyl group migration was observed during the cyclization process, resulting in the formation of compound **16**.[21]

The UV−visible (UV−vis) absorption of compounds **5**, **10**, **11**, **14**, and **17** was measured in a toluene solution (Figure 2). These compounds demonstrated significant bathochromic

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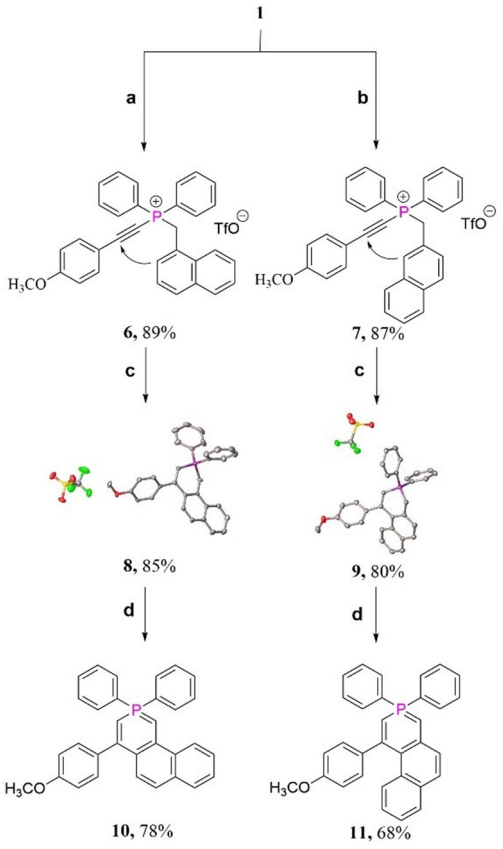
Scheme 2. Synthesis of λ^5-Phosphaphenanthrenes 10 and 11[a]

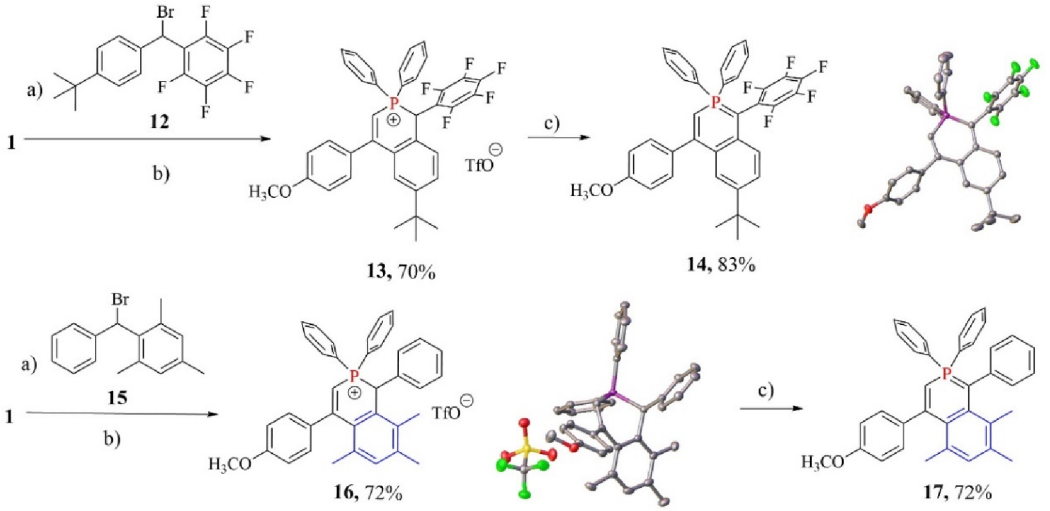


[a]Reagents and conditions: (a) 1-bromomethylnaphthalene, acetonitrile, 60 °C, 6 h; NaOTf, CH_2Cl_2, H_2O, rt, 10 min; (b) 2-bromomethylnaphthalene, acetonitrile, 60 °C, 6 h; NaOTf, CH_2Cl_2, H_2O, rt, 10 min; (c) TfOH, CH_2Cl_2, 0 °C, 10 min; (d) *t*-BuOK, THF, −78 °C to rt, 30 min.

shifts in their absorption spectra when compared to that of a previously reported λ^5-phosphaphenanthrene derivative (λ_{max} = 419 nm).[17] Notably, compound **17** stood out with the most significant red-shift, exhibiting a λ_{max} of 527 nm. The observed red-shift in the UV−vis spectra could be ascribed to the increased planarity of the P cycle, which leads to improved orbital overlap. For compound **17**, the $\sigma-\pi$ conjugation with the methyl group allows more expanded molecular orbitals, leading to a more pronounced red-shift in its absorption spectrum. Upon comparison of compounds **5** (λ_{max} = 490 nm) and **14** (λ_{max} = 499 nm), it was observed that the EWGs had no significant effect on the UV−vis absorption spectra of these compounds. Furthermore, compound **10** (λ_{max} = 500 nm) displayed a slight bathochromic shift compared to **11** (λ_{max} = 479 nm), which is likely due to its planar backbone resulting from the repositioning of the phosphorus atom. All compounds exhibited very weak fluorescence in solution, with compounds **11** and **17** displaying negligible fluorescence, as depicted in Figure S1. The fluorescence quantum yields of compounds **5**, **10**, and **14** are <1% (Table S1).

At the LC-BLYP/6-311G* theoretical level, time-dependent (TD) density functional theory calculations were performed to explain the red-shifted absorption of **17**. The energy gaps between the highest occupied molecular orbital (HOMO) energy level and the lowest unoccupied molecular orbital (LUMO) energy level are similar for **5**, **11**, and **14**, as shown in Figure 2b. Compound **17** shows a smaller energy gap between its HOMO and LUMO due to the relatively highest HOMO energy level. Cyclic voltammetry experiments also confirmed that adjusting the planarity of the P cycle by changing the substituents can increase the HOMO level (Figure S3). The increase in the HOMO level of **17** can be attributed to the $\sigma-\pi$ conjugation between the σ (C−C) orbital and the π (C−C) orbital. Figure 2b illustrates that the HOMO of **17** exhibits more delocalization across the molecule due to the $\sigma-\pi$ conjugation between the carbon atom and the phenyl group. In contrast, the HOMO of **14** is concentrated on one side of the phenyl group, which may be attributable to the limited involvement of $\sigma-\pi$ conjugation. Compounds **5**, **10**, **11**, **14**, and **17** were assessed for their aromaticity using nucleus-independent chemical shift (NICS) calculations at the B3LYP/

Scheme 3. Synthesis of λ^5-P-Containing PAHs 14 and 17[a]



[a]Reagents and conditions: (a) acetonitrile, 60 °C, 6 h; NaOTf, CH_2Cl_2, H_2O, rt, 10 min; (b) TfOH, CH_2Cl_2, 0 °C, 10 min; (c) *t*-BuOK, THF, −78 °C to rt, 30 min.

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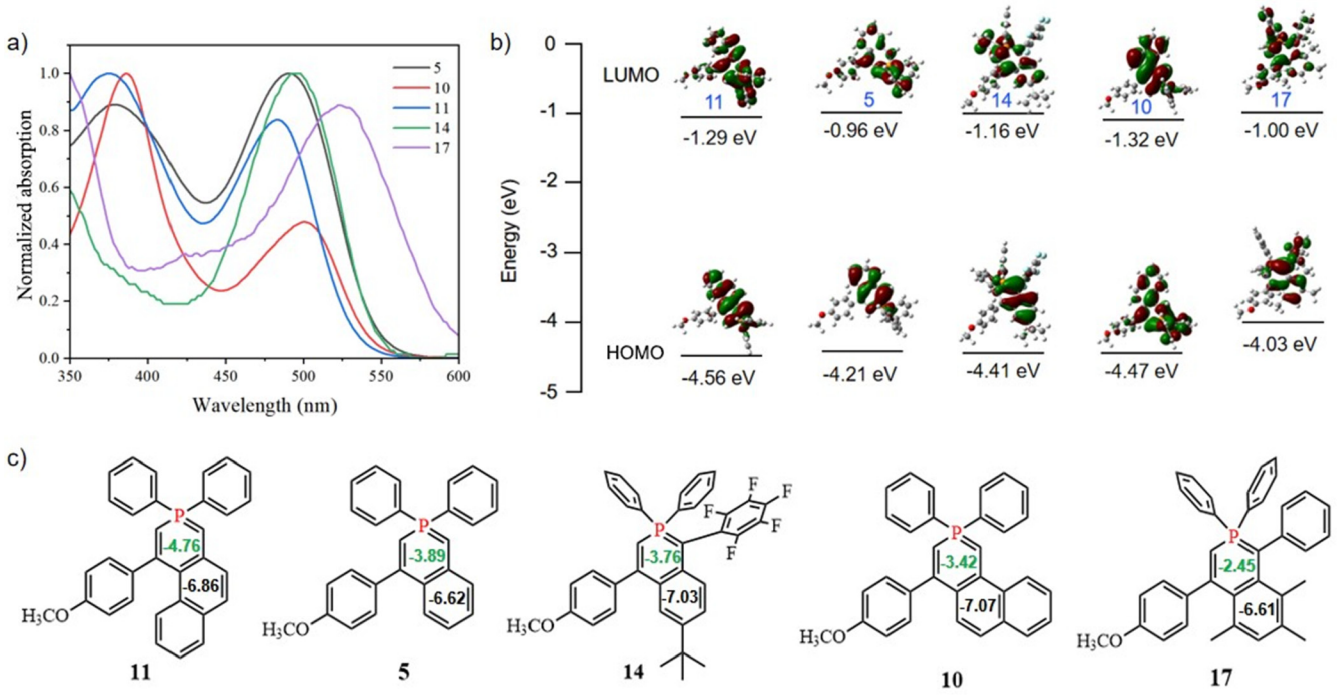

Figure 2. UV−vis absorption of **5**, **10**, **11**, **14**, and **17** in toluene at 298 K. (b) Molecular orbital diagrams of the LUMO and HOMO of **5**, **10**, **11**, **14**, and **17**. (c) Calculated NICS(1) values (in parts per million) of **5**, **10**, **11**, **14**, and **17**.

6-311G(d,p) level. Figure 2c demonstrates that all of the P cycles are slightly aromatic. As the structure changes, the aromaticity goes from 4.76 ppm of **11** to 3.89 ppm of **5**, 3.76 ppm of **14**, 3.42 ppm of **10**, and 2.45 ppm of **17**. The increase in the number of delocalized π electrons caused by conjugation expansion explains this. Alterations to electron delocalization cause a decrease in the NICS(1) value because of the strong relationship between the electron density and the magnetic shielding tensor.

In conclusion, we have presented a stepwise route for synthesizing P-containing PAHs. This optimized procedure involves a sequence of anion exchange, alkyne annulation, and deprotonation reactions. The efficient alkyne annulation process enables the synthesis of λ^5-phosphaphenanthrene isomers. X-ray crystallographic analysis of the resulting cyclized phosphonium salts unambiguously confirmed the regioselectivity of the alkyne annulation. Additionally, the stability of the ylidic bonds within these structures can be enhanced by incorporating EWGs. The synthetic strategy described herein holds significant potential for precisely synthesizing more phosphorus-containing PAHs with enhanced π conjugation.

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.4c01579.

Detailed information, including additional experimental details, materials, methods, and NMR spectra (PDF)

Accession Codes

CCDC 2240366, 2240368, 2240377−2240379, 2240383, 2337135, and 2337137 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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Author Contributions

[▽]Y.W. and G.S. contributed equally to this work.

Notes

The authors declare no competing financial interest.

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■ ABBREVIATIONS

CCR2, CC chemokine receptor 2; CCL2, CC chemokine ligand 2; CCR5, CC chemokine receptor 5; TLC, thin layer chromatography

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