Facile Synthesis of the Dicyanophosphide Anion via Electrochemical Activation of White Phosphorus: An Avenue to Organophosphorus Compounds

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Supporting Information Placeholder

ABSTRACT: Organophosphorus compounds (OPCs) have gained tremendous interest in the past decades due to their wide applications ranging from synthetic chemistry to materials and biological sciences. We describe herein a practical and versatile approach for the transformation of white phosphorus (P₄) into useful OPCs with high P atom economy via a key bridging anion [P(CN)₂]⁻. This anion can be prepared on a gram scale directly from P₄ through an electrochemical process. A variety of OPCs involving phosphinidenes, cyclophosphanes and phospholides have been made readily accessible from P₄ in a two-step manner. Our approach has a significant impact on the future preparation of OPCs in laboratory and industrial settings.

Organophosphorus compounds (OPCs) are widely used as herbicides, flame-retardants, ligands, pharmaceuticals, detergents, and photo-initiators.¹ Currently, their industrial syntheses demand two phosphorus transfer reagents, namely phosphorus trichloride (PCl₃) and phosphine gas (PH₃). PCl₃ is a highly corrosive liquid, which is produced by oxidation of white phosphorus (P₄) with toxic chlorine gas. The preparation of OPCs via PCl₃ involves stepwise displacement of the chloride atoms, and thus inherently has low selectivity and efficiency while concurrently generating chlorinated waste.² Catalytic transformation of PH₃ into OPCs is less preferred as PH₃ is an extremely toxic gas and its synthesis from P₄ requires harsh reaction conditions.³ To bypass PCl₃ and PH₃, tremendous efforts have been devoted into investigating direct functionalization of P₄,⁴ whose industrial production is on a scale of more than 10⁶ tons per year. However, preparation of OPCs directly from P₄ remains extremely challenging; they generally suffer from low selectivity and conversion efficiency or only lead to partial conversion of P₄ into useful OPCs and phosphonium salts via photo-redox catalysis.⁵

Development of phosphorus transfer reagents other than PCl₃ and PH₃ is a promising strategy for the syntheses of OPCs and other value-added phosphorus-containing chemicals. To this end, Cummins and co-workers demonstrated the bis(trichlorosilyl)phosphide anion [P(SiCl₃)₂]⁻ (A) (Figure 1a) derived from phosphates capable of producing OPCs.⁶ The Grützmacher and Goicoechea groups independently synthesized a large array of phosphorus frameworks via the 2-phosphaethylolate anion [PCO]⁻ (B).⁷ More recently, Wolf et. al. reported the synthesis of monophosphines from hydrostannyl phosphines (Bu₃Sn)₂P(Ph)₅(SnBu₃) (x = 1-3) (C) resulting from the direct activation of P₄ with stannyl radicals.⁸ Although chemical reactions for P₄ activation have been explored in depth over the past decades, practical electrochemical activation of P₄ is still in its infancy.⁹ The electrocatalytic C–P bond formation using transition metal catalysts with sacrificial metal electrodes as reducing reagents have been reported.¹⁰

Organophosphorus compounds (OPCs) have derived from phosphates capable of producing OPCs. Known methods to generate [P(CN)₂]⁻ (Figure 1b) include the reduction of P(CN)₃ with NaPO(OEt)₂,¹¹ the ligand exchange of [P(CN)₂]⁶ with NaPO(OEt)₂,¹¹ the ligand exchange of [P(CN)₂]⁶ with K₂[PO(OEt)₂] to generate [P(CN)₂]⁻.¹¹ More recently, Wolf et. al. reported the synthesis of monophosphines from hydrostannyl phosphines (Bu₃Sn)₂P(Ph)₅(SnBu₃) (x = 1-3) (C) resulting from the direct activation of P₄ with stannyl radicals. Although chemical reactions for P₄ activation have been explored in depth over the past decades, practical electrochemical activation of P₄ is still in its infancy.¹⁰ The electrocatalytic C–P bond formation using transition metal catalysts with sacrificial metal electrodes as reducing reagents have been reported.¹⁰

The isolation of the dicyanophosphide anion salt Na[18-C₆]-[P(CN)₂] (18-C₆ = 18-crown-6) dates back to 1977 by the group of Schmidpeter but its chemistry has been scarcely investigated likely due to the lack of efficient synthetic routes for large scale syntheses (Figure 1b).¹¹ The known procedures include the reduction of P(CN)₃ with NaPO(OEt)₂,¹¹ the ligand exchange of [dppe][BPh₄] with dppe = bis(diphenylphosphino)ethane with cyanides and the disproportionation of P₄ with K[18-C₆]-CN.¹² These are typically associated with low efficiency and poor atom economy. A handful of reports described the displacement of the cyano

Figure 1. (a) Selected examples of phosphorus transfer reagents. (b) Known methods to generate [P(CN)₂]⁻. (c) Electrochemical synthesis of [P(CN)₂]⁻ from P₄.
groups of [P(CN)]2− by carbon- or and phosphorus-based anionic nucleophiles and the halide substitution of 2-chloro imidazolium salts and alkyl iodides.13

We herein present the facile synthesis of [P(CN)]2− via electrochemical activation of P4 at room temperature using hydrogen cyanide (HCN) as the oxidant in an undivided cell (Figure 1c). The electronic structure of [P(CN)]2− is examined by DFT calculations. The utility of [P(CN)]2− towards neutral and anionic carbon-based nucleophiles selectively affords scarcely accessible OPCs, such as cyano-phosphinidenes, cyclophosphines and phospholides. These pave a straightforward path for facile bridging of OPCs from P4.

The nucleophilic disproportionation of P4 by K(18-C-6)CN in boiling MeCN can generate K(18-C-6)[P(CN)]2 but at the cost of losing 15 equivalents of phosphorus (Figure 1b).12b We hypothesized that the controlled oxidation of P4 in the presence of cyanides might selectively afford [P(CN)]2−. Specifically, electrochemical methods may be able to delicately control the oxidation from P(0) to P(+1) with the proper voltage. Hydrogen cyanide (HCN), which is industrially produced, was postulated to work as the electrochemical oxidant and a cyanide source.13 However, to avoid the direct handling of HCN gas the combination of MeSiCN with LiOH as a HCN surrogate was employed. This reaction also generated LiCN and (MeSi)2O (Figure S2) and the former provides another equivalent of cyanide needed for the subsequent electrolysis. Note that MeSiCN (bp 118 °C) is a toxic liquid which releases highly toxic HCN gas upon contact with moisture.

No conversion was observed after stirring the same mixture for 10 h without electrolysis. In the presence of 50% mol LiCN, complete conversion of P4 took a shorter time (10 h) and gave a similar yield. Mechanistically, P4 is formally oxidized to form [P(CN)]2− on the anode and HCN is reduced to dihydrogen on the cathode. Alternatively, cyanide anion is oxidized to form transient cyano radicals or dicyan, which react with P4 under electrolysis to eventually give [P(CN)]2−.6,9 Gas bubbles (i.e. H2) was observed from the Pt electrode during the electrolysis. An analogous reaction using MeCN as solvent gave the same product and the formation of hydrogen was observed by 1H NMR spectroscopy (Figure S4). A similar redox reaction occurred via the combination of P4 with MeSiCN under the same conditions and the byproduct (MeSi)2 was observed by 1H NMR spectroscopy (Figure S5). While we were able to observe the generation of M[P(CN)]2 (M = K, Na) using KOH or NaOH, instead of LiOH, the lack of appropriate electrolyte to maintain the conductivity obviates the isolation of analytically pure M[P(CN)]2.

The electronic structure of the [P(CN)]2− anion was probed by density functional theory (DFT) calculations (M06-2X/def2-SVP) (Figure 3). While the C−N bond lengths (1.173 Å) and C−P−C bond angle (97.4°) in the optimized structure of [P(CN)]2− are comparable to the solid-state structure of K(18-C-6)[P(CN)]2 (1.140 Å av.; 95.22°),12c the computed P−C bond lengths (1.779 Å) are longer than those in the solid-state structure (1.692 Å and 1.666 Å) (Figure S101), probably due to the crystal packing effects. The HOMO−1 (−4.72 eV) and HOMO (−1.73 eV) are predominantly the in-plane and out-of-plane P lone pairs, respectively, while the LUMO exhibits features of π* orbitals over the anion with the major contribution of P. The natural population analysis (NPA) (M06-2X/def2-TZVP) reveals that the anionic charges are considerably located at two N atoms (−0.47 a.u.) whereas the P atom bears almost no net charge (−0.01 a.u.). The Wiberg bond indices (WBIs) of P−C and C−N bonds are 1.1 and 2.8, respectively. Collectively, these results demonstrate the amphiphilic nature of P.
We then investigated the synthetic potential of \([P(CN)]^2^-\) for OPCs using carbon-based nucleophiles. Albeit the \([P(CN)]^2^-\) has an overall anionic nature, treatment of 1 with various neutral carbon nucleophiles [i.e. N-heterocyclic carbene (NHC) and cyclic(alkyl)(amino)carbene (CAAC)] gave base-stabilized phosphinidenes 2-4 (Figure 4), concurrent with the elimination of LiCN. The \(^{31}P\) NMR spectra of 2, 3 and 4 consist of a singlet at –133.7, –153.8 and –55.8 ppm in C6D6, respectively. Further confirmation of structures of 2-4 was carried out with single crystal X-ray diffraction (Figures 5a, S16 and S17). A close related compound of 2 with methyl substituents on the N-heterocycle was reported by Schmidpeter.\(^{13a}\) The formation of 2-4 indicates the facile replacement of LiCN with nucleophilic carbene, reminiscent of examples of ligand exchange reactions at a phosphinidine described by Bertrand et al.\(^{16}\) Notably, while the chemistry of base-stabilized phosphinidenes is quite rich, their syntheses usually require multiple steps and relatively harsh conditions.\(^{17}\) Our synthetic route represents a two-step procedure accessing rare examples of cyano-substituted phosphinidenes from PhLi.

Figure 4. Synthesis of phosphinidenes from \([P(CN)]^2^-\) and the reduction of 4. \(^{90}\text{NHC} = \text{N}^-,\text{N}^\text{2}-\text{diisopropyl-4,5-dimethyl-2-ylidene}; \(^{90}\text{NHC}^{10} = \text{N}^-,\text{N}^\text{2}-\text{diisopropylbenzimidazolylidene}; \(^{5}\text{CAAC} = 2,6\text{-diisopropylphenyl-4,4-diethyl-2,2-dimethyl-pyridolinyl-5-ylidene.}\)

In addition, reduction of 4 with excess KC\(_6\) at ambient temperature in THF for 2 h followed by addition of 18-C-6 afforded species 5 (Figure 4), which was after workup isolated as an orange solid. The \(^{31}P\) NMR resonance of 5 (230.2 ppm) is high-frequency shifted relative to those observed for \[^{35}\text{CAAC=PLi}\] (179.3 ppm)\(^{18}\) and \(^{5}\text{CAAC=PK}\) (206.9 ppm).\(^{19}\) In contrast to the dimeric structures of \[^{35}\text{CAAC=PLi}\] and \(^{5}\text{CAAC=PK}\), 5 represents a rare example of a monomeric carbene-stabilized P' anion (Figure 5b). The conversion of \([P(CN)]^2^-\) to \(^{35}\text{CAAC=PLi}\) can be viewed as a formal “P” anion delivery to carbenes, and thus showcases huge potential of \([P(CN)]^2^-\) for P atom transfer reactions. Nonetheless, the formation of 5 is unique as the analogous reaction of 2 or 3 with KC\(_6\) is apparently inert.

Next, attempts to efficiently synthesize cyclophosphanes were undertaken (Figure 6). These species with a small P\(_6\) (n = 2-5) ring are usually prepared via reduction reactions of mono-substituted phosphorus dichlorides with undesirable reagents (e.g. alkaline-earth reductants), which typically suffer from low chemoselectivity and operational complexity for purification.\(^{20}\) Dropwise addition of B\(_3\)Li to a THF solution of 1 at –35 °C forms an intermediate 6 (\(^{31}P\) NMR: –90.0 ppm) that upon warming up to room temperature smoothly converted into two products (B\(_3\)P)\(_7\), 7 (\(^{31}P\) NMR: –70.5 and –109.5 ppm) and (B\(_3\)P)\(_8\) (\(^{31}P\) NMR: –57.5 ppm) in a molar ratio of 1:1.\(^{21}\) Heating the reaction mixture at 70 °C for 24 h resulted in complete conversion into 8. As early work by Schmidpeter and co-workers described the reaction of K[P(CN)] with PhLi leading to an equilibrium of M[PhPCN] (M = Li or K) and the pentaphenyl pentaphosphonaphosphate (Ph\(_5\)P)\(_8\),\(^{18}\) the cyanide anion in the reaction mixture is proposed to promote the transformation of 7 to 8. As Baudler et al. reported in 1984, in the absence of cyanide the thermal arrangement of 7 to 8 requires much higher temperatures (i.e. 200 °C).\(^{22}\) In a similar vein, we reacted ArLi (Ar = 1,1'-biphenyl-2-yl) (9) with 1 at room temperature to give (ArP)\(_7\) in 82% yield (Figures 5c and 6b). In this case, no cyclotriphosphane (ArP)\(_3\) was observed.
Phospholides featuring an anionic unsaturated five-membered P,C,C ring have received tremendous interest in the past decades due to the fundamental significance of the structural and electronic properties as well as their applications in synthetic chemistry. We envisioned the likelihood that the simple reaction of P(CN)_{2}^- with organo-dilithium reagents would furnish phospholides, which are versatile precursors for synthesis of phosphole-based materials. Gratifyingly, addition of 1 to the respective dilithium reagents gave rise to the corresponding phospholides 13-15 as a single P-containing product (Figure 7). 13-15 were isolated in moderate to good yield (56%-94%). Although X-ray quality single crystals of the lithium salts have not been obtained, the connectivity of the phospholides was further authenticated by X-ray diffraction with the analogous sodium salts 13'-15' derived from Na(18-C-6)[P(CN)_{2}^-] (Figures 5d-S21 and S22). The synthetic method presented herein provides access to phospholides from P_4 in a two-step fashion via [P(CN)_{2}^-] as a bridge. It is important to note that the current protocols for phospholides generation require multistep synthesis, involving the use of phosphorus trihalides. Zhang et al. reported the direct facile synthesis of phospholides from P_4 but with low P atom economy (theoretically loss of 75% P atoms).

Figure 6. Synthesis of cyclophosphanes from [P(CN)_{2}^-].

To conclude, we have showcased a practical versatile approach for the conversion of P_4 into useful OPCs with high P atom economy via [P(CN)_{2}^-]: exemplified by the effective synthesis of base-stabilized cyano-phosphinidenes 2-4, cyclophosphanes 8 and 10, and phospholides 13-15. Importantly, this anion is readily available from an electrochemical activation of P_4 on a gram scale. The practical simplicity of our strategy may spur considerable interest in development of [P(CN)_{2}^-] that has been relatively dormant for many years. The utility of this approach directly from P_4 to construct other useful OPCs as well as unusual inorganic/organic phosphorus skeletons are the subject of ongoing work.

Supporting Information

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

Synthesis procedures for the compounds, NMR spectroscopic and X-ray characterization of the compounds, and computational details (PDF)

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Notes

The authors declare no competing financial interests.

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High P atom economy.
Two-step synthesis of OPCs from P₄.