

Synthesis and Photophysical Properties of λ^5 -Phosphinines as a Tunable Fluorophore

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Supporting Information

ABSTRACT: A practical synthesis of a variety of λ^5 -phosphinines, which show distinct fluorescence both in solution and solid state, is described. Both C4-selective electrophilic substitutions and the following conversions realized an easy preparation of a wide range of derivatives having several substituents for electronic modification, which provides the potential for fine-tuning of the photophysical properties.

 \mathbf{F} luorophores attract great interest as functional materials because of wide and general purposes in a variety of fields including fluorescence probes.¹ A variety of aromatic and heterocyclic fluorophores have been created and modified for tuning their properties as desired. Recently, fluorophores including a phosphorus atom come into the spotlight because of their excellent properties.²⁻⁴ Contrary to emerging innovations about 5-membered phospholes,² 6-membered phosphacycles are relatively less investigated as a fluorophore^{3,4} though the series of those compounds are known from 1960s as phosphinines, a heavy analogue of pyridine.^{5–7} Among those phosphacycles, λ^5 -phosphinines having a phosphorus-ylide in the cycle are unique molecules because they are structurally and electronically quite different from pyridine-like λ^3 -phosphinines.^{4,6} Märkl's early extensive works established access to λ^5 phosphinines via pyrylium salts.⁵ Recently, Kostyuk and Matveeva reported several synthetic routes toward λ^5 phosphinines, via sigmatropic rearrangement of phosphonium ylides and cycloaddition of phosphonium-iodonium ylides with alkynes.⁸ In addition, λ^5 -phosphinines have potential as a fluorophore; Dimroth and Müller reported photophysical features of λ^5 -phosphinines including fluorescence.^{4,9} However, limitations due to elaborating synthetic scheme prevented finetuning of their properties; an easy, effective and versatile synthetic method of λ^5 -phosphinine derivatives will open up their application.

We have serendipitously found a formation of a trace amount of an unexpected compound with a distinct fluorescence, during our study about a synthesis of new 3-oxo- λ^5 -phosphole.¹⁰ After the initial discovery of this fluorescent compound, we made considerable efforts to track its formation, and finally found a new synthetic route toward λ^5 -phosphinine 1 (Scheme 1).¹¹ Scheme 1. λ^5 -Phosphinine Formed by the Reaction of Phosphonium Salt 2 and Aldimines 3



Herein, we report a novel and versatile synthesis of fluorescent λ^5 -phosphinines based on our fortuitous discovery. Their photophysical properties tuned by the electronic perturbation with several substituents introduced by the transformations developed here are also described.

We have identified the real substrates necessary for λ^5 -phosphinine formation; one is bis(cyanomethyl)-phosphonium salt **2**, and the other is an aldimine.¹¹ 3,4-Disubstituted 2,6-dicyano- λ^5 -phosphinine **1** (R = *n*Pr) was formed almost quantitatively when phosphonium salt **2** reacted with an excess of aldimine **3** (Scheme 1).

Although a mechanism of this cyclization is not clear, we observed two ylidic intermediates by ³¹P NMR monitoring of the reaction;¹¹ they may be attributed to alkenyl ylide **4A** initially formed via double addition of the ylide to aldimines and dihydrophosphinine **4B** formed by the following electrocyclization similar to the reaction reported by Kostyuk et al.^{8b-d} Further dehydrogenative aromatization⁷ of **4B** gave λ^5 -phosphinine **1**. Unfortunately, λ^5 -phosphinine **1** (R = *n*Pr), having two substituents at the C3 and C4 positions, showed a low quantum yield (Φ_F : 0.02) despite its brilliant visible fluorescence. We anticipated that the use of 1,3-dialdimine instead of two moles of an imine can avoid the incorporation of any substituent at the C3,C4,C5-positions, and can also bypass the oxidation step. Indeed, the reaction of phosphonium salt **2** with 1,3-dialdimine **5** in the presence of DBU gave 2,6-dicyano-

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1,1-diphenyl- λ^5 -phosphinine **6a** as a sole product in fairly good yield (Scheme 2).¹²



The result was seriously affected by the solvent used and amount of the base. Several optimizations of the reaction conditions revealed that use of 2 equiv of DBU in DMSO gave the best results. Two cyano groups are necessary for the effective formation of ylides during the cyclization. Noteworthy is that the multistep transformation proceeded successfully at rt with concurrent formation of two C–C bonds and cleavage of two C–N bonds. It is no doubt that DBU plays essential roles as a base (for deprotonation to form nucleophilic ylides) and an acid (DBU-H⁺ formed by deprotonation will protonate the amine to be eliminated). A plausible mechanism of the reaction is shown in Scheme S5.¹¹

The structure of **6a** was unequivocally determined by an X-ray crystallographic analysis (Figure 1).¹³ The asymmetric unit



Figure 1. Crystal structure of **6a**.¹³ (Left: topview, right: sideview) Only one of three structures in asymmetric unit is shown. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are drawn at the 50% probability level. Selected bond lengths [Å] and angles [°]: P(2)– C(6) 1.747(8), P(2)–C(10) 1.750(9), C(6)–P(2)–C(10) 102.3(4), C(31)–P(2)–C(37) 105.9(4).

of **6a** contains three independent molecules with similar metrical data. The 6-membered ring is distorted around the phosphorus but is almost flat.¹⁴ The phosphorus atom is approximately proper tetrahedral orientation; therefore two phenyl groups are extended over the phosphinine plane. Essentially equal two P–C bond lengths (P2–C6:1.747 Å and P2–C10 1.750 Å) show no existence of bond alternation inside the phosphinine ring. These characteristics are nearly identical to the previously reported λ^5 -phosphinines except small differences of P–C bond lengths.^{8a,b,e}

DFT calculation of **6a** at B3LYP/6-31+G(d,p) level showed that both HOMO and LUMO are delocalized over the phosphinine ring and cyano groups. It is noteworthy that the HOMO shows a significant orbital contribution at the C4 position, whereas no contribution of the C4 to the LUMO is estimated, as illustrated in Figure 2. Thus, an electronic modulation at the C4 position will mostly modulate the HOMO level, but it will affect essentially little to the LUMO. This is favorable to tune the photophysical properties of the λ^5 -phosphinines by substitution at the C4 position.

The C4 should be the most nucleophilic because of an ylidic nature of P=C bond and resonance structure of the phosphinine ring; electrophilic substitution would be effective



Figure 2. Frontier molecular orbitals of **6a** calculated at the B3LYP/6-31+G(d, p) level; left: HOMO, right: LUMO.

for incorporation of several substituents at the C4 position for tuning the properties. Indeed, the reaction of **6a** under the Vilsmeier–Haack conditions gave 4-formyl derivative **6b** in good yield (Scheme 3a). 4-Bromophosphinine **6c** was obtained

Scheme 3. Several Conversions of 6a to 4-Substituted λ^5 -Phosphinines^{*a*}



^a(a) POCl₃ (1.2 equiv), DMF, 60 °C, 3 h (84%); (b) Py·HBr₃ (1.0 equiv), CH₂Cl₂, rt, 1 h (88%); (c) Ph₃P=CHPh (1.1 equiv), THF, rt, 12 h (56%); (d) Phenylacetylene (1.2 equiv), 5 mol % PdCl₂(dppf), 10 mol % CuI, DBU (1.5 equiv), DMF, 80 °C, 12 h (69%); (e) PhB(OH)₂ (1.7 equiv), 4 mol % PdCl₂(PPh₃)₂, 2 M Na₂CO₃ aq. (8 equiv), toluene-H₂O-EtOH, reflux, 24 h (76%).

by electrophilic bromination with pyridinium bromide perbromide (Scheme 3b). Smooth progress of these electrophilic substitutions indicates that sufficient nucleophilicity at the C4 is preserved despite two electron-withdrawing cyano groups at the C2- and C6-positions. Further conversions of these two fundamental compounds, 6b and 6c, allow us to prepare 4-alkenyl, 4-alkynyl and 4-aryl derivatives. 4-Formylphosphinine 6b could be converted into 4-alkenylphosphinine derivatives by the Wittig olefination. The reaction of benzylidenephosphorane with 6b at rt for 12 h gave the desired 4- β -styrylphosphinine 6d in 56% yield (Scheme 3c).¹⁵ 4-Bromo derivative 6c was subjected to the Sonogashira and the Suzuki-Miyaura cross-coupling reactions to give the 4alkynyl and the 4-aryl derivatives, respectively (Scheme 3d,e). The reaction of 6c with phenylacetylene in the presence of Pd and Cu catalysts and DBU in DMF gave 4-(2-phenylethynyl)phosphinine 6e in 69% yield. DPPF was the best ligand in this coupling reaction. The reaction of **6c** with phenylboronic acid in the presence of Pd catalyst and aqueous base successfully afforded 4-phenylphosphinine 6f in 76% yield. The success of these fundamental conversions indicated that fine electronic tunings at the C4-position would be available based on these schemes by using more electronically modified substrates in these well-established reactions.

The photophysical properties of the λ^5 -phosphinines **6a-6f** were examined (Figure 3, Table 1). All prepared λ^5 -



Figure 3. (a) Ambient and fluorescence images of λ^5 -phosphinines (**6b**, **6a**, **6c**, **6f**, **6e**, **6d**: left to right); (upper) in CHCl₃ irradiated at 352 nm; (middle) solid under ambient light; (bottom) solid irradiated at 352 nm. (b) Normalized emission spectra of **6a**–**6f**.

Table 1. Photophysical Data for λ^5 -Phosphinines

Compd	$\lambda_{\rm abs,max}/{\rm nm} \ (\log \varepsilon)^{a,c}$	$rac{\lambda_{ m em,max}/nm}{\left(\Phi_{ m F}/\% ight)^{a,d}}$	$\lambda_{ m em,max}/ m nm \ (\Phi_{ m F}/\%)^{b,d}$
6a	458 (4.22)	491 (92)	561 (14)
6b	434 (4.09)	463 (72)	514 (42)
6c	482 (4.22)	519 (52)	554 (5)
6d	506 (4.05)	581 (13)	616 (5)
6e	489 (4.17)	538 (61)	572 (11)
6f	480 (4.14)	525 (75)	557 (17)

 a In CHCl₃. b In solid state. c Only the longest absorption maxima is shown. d Emission maxima upon excitation at the absorption maximum wavelength.

phosphinines 6a-6f showed distinct fluorescence. Substituent at the C4-position significantly influenced both the absorption and the emission, both in solution and solid phase. The images of fluorescence both in solution and in the solid state, and the normalized emission spectra of 6a-6f are shown in Figure 3.

The parent phosphinine 6a shows absorption maxima at 458 nm with ε of 10^4 level. Emission maxima of **6a** appeared at 491 nm with excellent quantum yield ($\Phi_{\rm F} = 0.92$) in CHCl₃ solution. Noteworthy is that most of the symmetrical λ^5 phosphinines showed distinct fluorescence with high quantum yields. As anticipated by the DFT calculations (vide supra), an electron-withdrawing substituent caused hypsochromic shifts both in absorption and emission (formyl, 6b; 24 nm/28 nm). 4-Bromo derivative 6c showed bathochromic shifts (24 nm/28 nm), due to efficient electron-donation over the electronegativity of the bromine atom. 4-Alkenyl, 4-alkynyl and 4-aryl derivatives 6d-6f also showed bathochromic shifts, at emission maxima range from 525 to 581 nm. Except for 6d, symmetrical 2,6-dicyano- λ^5 -phosphinines showed high quantum yields ($\Phi_{\rm F}$: 0.92-0.52). Two cyano groups appeared to be essential for high quantum yields; quantum yields of similar λ^5 -phosphinines with two heteroaryls instead of cyano groups are reported as 0.05-0.20 (Table S2),9 where the symmetrical derivative also showed better quantum yield.^{4b} A relatively weak fluorescence of 4-alkenyl derivative ($\Phi_{\rm F}$: 0.13) is attributed to nonemissive transition by its stilbene-like structure. Those compounds are also emissive in the solid state, probably because the tetrahedral orientation of the phosphorus should effectively avoid strong $\pi - \pi$ interaction, which will cause quenching of the emission in the solid state. Solid state fluorescence showed substantial red shifts with relatively high quantum yields.

As described, the most important feature of these series of λ^5 phosphinines is the presence of two cyano groups at C2- and C6-positions. DFT calculations revealed that two cyano groups electronically impact to both HOMO and LUMO.¹ For example, HOMO of 6a (-5.82 eV) lies about 1 eV higher than that of λ^5 -phosphinine 7 without cyano groups (Figure S4), and LUMO of 6a (-2.23 eV) lies about 1 eV lower than that of 7. The LUMO levels of 6a–6f are substantially the same ($\Delta E <$ 0.2 eV) whereas the HOMO levels are varied at a range of 0.94 eV, as anticipated (vide supra). Small HOMO-LUMO gaps of 6a-6f resulted in absorption and emission of visible light of which wavelength is mainly affected by its HOMO. The lowlying LUMO characterized this core as an electron-accepting part. On the other hand, two cyano groups did not affect aromaticity of the phosphinine; this type of phosphinine naturally shows low aromaticity (NICS(0) of 7 is -2.53, NICS(0) of 6a is -2.46). However, two cyano groups play a crucial role to stabilize the vlidic structure of the phosphinine; 7 was reported as highly reactive and air-sensitive molecule,⁵ but the phosphinines reported here are thermally and chemically quite stable and remain intact for a long time even in the air in the solid state.^{16,17}

In conclusion, we have synthesized a series of novel fluorescent 2,6-dicyano- λ^5 -phosphinines via newly developed one-pot, multistep ring formation. Regioselective functionalization and further conversions enabled preparation of λ^5 -phosphinines with several substituents at the C4-position, which were suitable for tuning their photophysical properties. More detailed study for this new fluorophore is now under investigation.

ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b13018.

Structural analysis, mechanistic investigations and full experimental and computational details (PDF) NMR data (ZIP)

X-ray crystallographic data for **6a** (CIF) X-ray crystallographic data for **6d** (CIF)

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The authors declare no competing financial interest.

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(9) Comparison of measured/calculated data is described in SI.¹¹

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(11) See Supporting Information for details.

(12) Although 1,3-dialdimine 5 exists as a conjugate imine-enamine form, it was depicted as a dialdimine form for an analogy to Scheme 1.

(13) Results of crystallographic analyses were submitted as CIF file.
(14) Deviations of each atom location from the mean plane of phosphinine ring are less than 0.023 Å.

(15) The structure of **6d** was confirmed by an X-ray crystallographic analysis; see: Supporting Information.

(16) Decomposition was observed when a chloroform solution of 6a and 6c left in the air with exposure to the light. No decomposition was observed with shade.

(17) 2,4,6-Triaryl derivatives are also reported as air and moisture stable solid. $^{4\mathrm{b}}$