ORGANIC CHEMISTRY

Stereospecific nickel-catalyzed [4+2] heteroannulation of alkynes with aminophosphanes

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Enantioenriched phosphorus compounds play crucial roles in many fields ranging from catalyst to materials science to drug development. Despite advances in the construction of phosphacycles, incorporation of a P-chirogenic center into heterocycles remains challenging. Here, we report an effective method for the preparation of phosphacycles through nickel-catalyzed [4+2] heteroannulation of internal alkynes with aminophosphanes derived from *o*-haloanilines. Notably, chiral 2-λ5-phosphaquinolines can be prepared from P-stereogenic substrates via NH/PH tautomeric equilibrium without loss of stereochemical integrity. The strategy is found to exhibit a broad scope in terms of both reaction components, enabling modular construction of libraries of 2-λ5-phosphaquinolines with different steric and electronic properties for fine-tuning photophysical properties, where some of these compounds showed distinct fluorescence with high quantum yields. A series of mechanistic studies further shed light on the pathway of the heteroannulation and reasons for stereospecificity.

INTRODUCTION

Heterocycles are important pharmacophores that are frequently found in drug compounds, as well as agrochemicals and materials (*1*–*4*). Interest in exotic isosteres has flourished over the past few decades, with chemists constantly developing methods to improve the properties of existing drugs and create novel ones in the competitive intellectual property environment of chemical space (*5*–*8*). The azaphosphinine scaffold has been explored as an analog of pyridine for nearly half a century (*9*–*15*). In this context, bioisosteres of quinoline (**I**), 2-λ^5-phosphaquinolines **II** containing nitrogen and phosphorous (V) atoms are challenging to prepare, which have been prepared from 2-ethynylanilines and $P(OPh)_3$ until 2015 (Fig. 1A) (*16*). However, skeletons bearing two OPh motifs are sensitive to moisture and easily form related 2-λ5-phosphaquinolin-2-ones **III** (*17*). In contrast to common heterocycles, phosphacycles confer unique geometric properties (*18*–*24*). Therefore, the development of a reliable method to access stable 2-λ5-phosphaquinolines, especially the preparation of enantiomers, is in high demand (*25*–*30*). Metal-catalyzed carbon–phosphorus coupling has emerged as an effective approach for achieving a diverse collection of phosphorus compounds (*31*–*39*). In 2017, Morandi and coworkers (*40*) reported an important breakthrough for palladium-catalyzed C—P arylation of phosphines through metathesis pathway, enabling the convenient preparation of diverse triarylphosphines and phosphorus heterocycles (Fig. 1B, left). Feringa and coworkers just uncovered an intermolecular stereoselective Pd-catalyzed C—P bond coupling between aryl halides and phosphoramidites to build homochiral stereogenic phosphorus compounds (Fig. 1B, middle) (*41*). Meanwhile, our group also explored a palladium-catalyzed intramolecular C—P cross-coupling involving P-arylation of aminophosphanes with excellent stereoselectivity (Fig. 1B, right) (*42*). These approaches, however, require complicated multistep substrate synthesis and only formation of one chemical bond during reactions. Metal-catalyzed annulation of unsaturated hydrocarbons is a valuable tool to substituted heterocycles and carbocycles by constructing several chemical bonds simultaneously (*43*–*49*). Among them, Larock indole synthesis through palladium-catalyzed reaction of internal alkynes and *o*-haloanilines is particularly important (*50*–*53*), which has been widely applied for the construction of indole skeletons in natural products and pharmaceutically active compounds (Fig. 1C) (*54*–*58*). Inspired by C—P coupling and Larock indole synthesis, we now hypothesize a catalytic [4+2] heteroannulation approach to the modular construction of 2-λ5-phosphaquinoline frameworks in a modular single step.

Here, we report that, using this approach, a nickel-catalyzed intermolecular cyclization between internal alkynes and a class of aminophosphanes derived from *o*-haloanilines can provide single-step access to various 2-λ5-phosphaquinolines (Fig. 1D). In the presence of a base, NH/PH tautomeric equilibrium of aminophosphanes generates secondary iminophosphoranes after deprotonation, which can further undergo cyclization to simultaneously form a C—C and a C—P bond enabled by the nickel catalyst (*59*–*62*). The use of P-stereogenic reactants allow C—P formation step to occur with a high degree of stereospecificity.

RESULTS

Reaction condition optimization

We first explored this concept within the context of a mode reaction between 1,1-di-*tert*-butyl-*N*-(2-iodophenyl)phosphanamine (**1a**) and 1,2-diphenylethyne (**2a**) (Table 1). Conducting the reaction with $Pd_2(dba)_3$ [5 mole percent (mol %)] as a catalyst and Na_2CO_3 as a base in *N*,*N*′-dimethylformamide (DMF) at 130°C under a N_2 atmosphere generated the desired product **3aa** in trace quantities (entry 1). The product was found to be stable to air and moisture, and its structure was further confirmed by nuclear

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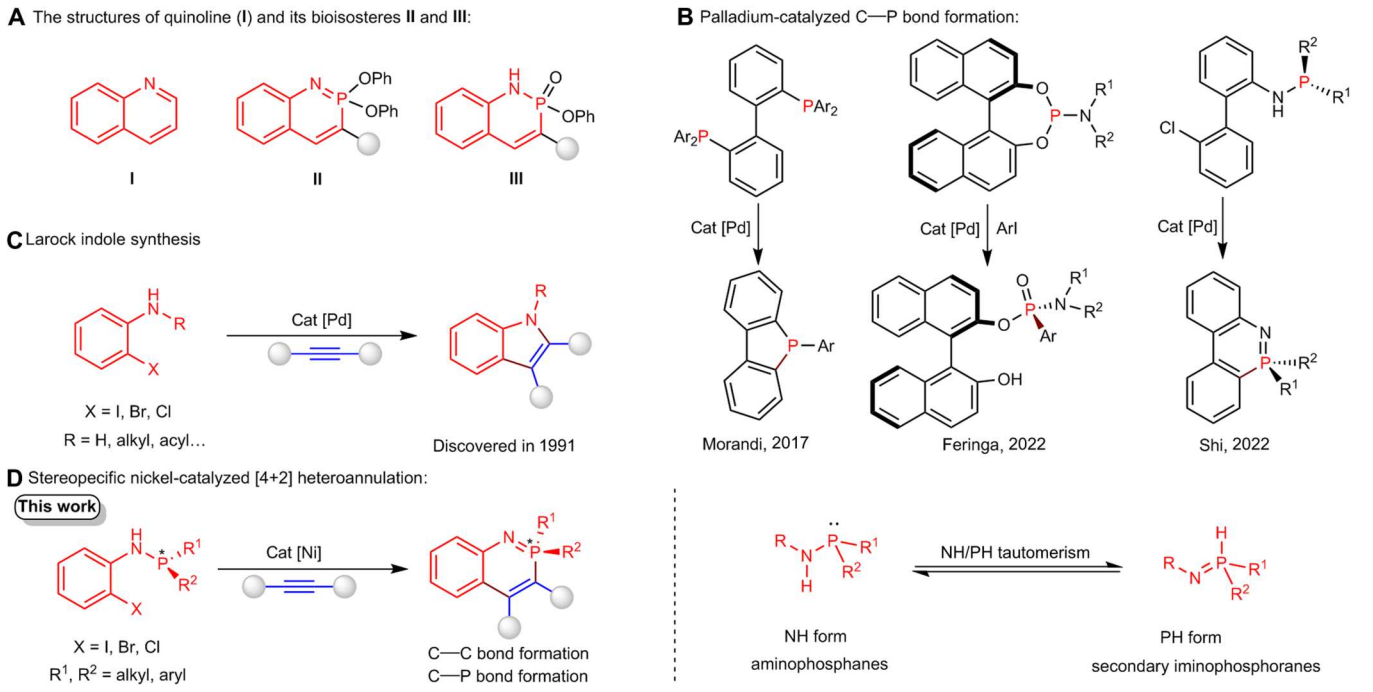


Fig. 1. Development of a nickel-catalyzed platform to synthesize 2-λ5-phosphaquinolines through [4+2] heteroannulation. (**A**) Quinoline and the reported compounds of 2-λ5-phosphaquinolines and 2-λ5-phosphaquinolin-2-ones. (**B**) Recent examples on intermolecular and Intramolecular C—P arylation using palladium catalysts. (**C**) Classical Larock indole synthesis enabled by palladium catalysis. (**D**) Nickel-catalyzed [4+2] heteroannulation of alkynes with aminophosphanes involving tautomerism between aminophosphanes and iminophosphoranes.

magnetic resonance (NMR) spectroscopy and x-ray diffraction analysis. Further metal screening showed that nickel catalysts, such as $NiCl_2$, exhibited the better reactivity (entry 2), where using $Ni(cod)_2$ as a catalyst delivered an improved yield of 19% (entry 3). Replacing Cs_2CO_3 with Na_2CO_3 led to the product **3aa** in 35% yield (entry 4). Prior studies have demonstrated that LiCl can promote the reduction of transition metals, such as Pd and Ni, in cross-coupling reactions (*63*–*65*). The addition of 1.0 equivalent of LiCl to the system had a substantial influence on the reaction outcome, as evidenced by a 67% yield of **3aa** (entry 5). Further optimization of the reaction conditions resulted in an increase in the quantity of base to 3.0 equiv, leading to **3aa** in 87% yield (entry 6). The addition of NaCl instead of LiCl considerably decreased the conversion (entry 7). In addition to DMF, other solvents, such as dimethylamine, N-methylpyrrolidone (NMP), and toluene, also maintained good reactivities (entries 8 to 10). Performing the reaction at a lower temperature (110°C) diminished the yield of **3aa** (entry 11). Decreasing the loading of $Ni(cod)_2$ to 5 mol % slightly reduced the conversion (entry 12). A control experiment showed that the reaction completely failed in the absence of a nickel source (entry 13). On the basis of the optimized reaction conditions, we investigated the use of other types of aryl halides in the reaction. Treating the related aryl bromide **1a′** and chloride **1a″** with alkyne **2a** maintained high reactivity (entries 14 to 15). However, the use of the aryl fluoride **1a″** failed to yield any of the desired products under the current reaction conditions (entry 16).

Scope of the methodology

To assess the generality of the reaction, a range of aminophosphanes were first investigated with the alkyne **2a**, in which halogen atoms (I, Br, and Cl) in *o*-haloanilines were selected considering cost and convenience (Table 2). Compounds **1b**-**d** with methyl groups at the *ortho*, *meta*, and *para* positions of the aryl motif were converted into the corresponding heterocycles **3ba**-**da** in 69 to 83% yields. Isopropyl (**1e**) and *tert*-butyl (**1f**) were also compatible with this heteroannulation process. The aminophosphane **1g** bearing an electron-donating methoxy group was smoothly converted into the corresponding product **3ga** in 65% yield. The fluorinated substrate **1 h-j**, with single or double substitution patterns, was also amenable to cyclization and was formed in 69 to 81% yields. Using the substrate **1k** with a chlorine atom in the reaction resulted in a good yield. Aminophosphanes incorporating other electron-withdrawing substituents, such as OCF_3 (**1l**), CF_3 (**1m**), CN (**1n**), and Ac (**1o**), were readily tolerated. In addition to the P^tBu_2 substituent, other substituents at the phosphorus center underwent effective annulation: For instance, treatment of aminophosphanes with two isopropyl (**1p**), cyclohexyl (**1q**), and phenyl (**1r**) groups efficiently produced the desired products **3pa-ra** in 78 to 87% yields. Treatment of the aminophosphane **1s** with two different functional groups at the phosphorus atom resulted in smooth conversion into the racemic product **3sa** in good yield. However, the use of diethyl (2-iodophenyl)phosphoramidite did not work (not shown in the table), indicating that the R^1 and R^2 substituents were limited to allyl and aryl groups in this transformation. We next investigated the influence of the substituent in the internal alkynes. A series of symmetrical diarylacetylenes with electron-neutral, electron-donating, and electron-withdrawing groups, including Me (**2b-c**), ^{t}Bu (**2d**), OMe (**2e**), SMe (**2f**), F (**2g**), Cl (**2h-i**), Br (**2j**), CF_3 (**2k**), OCF_3 (**2l**), CF_3 (**2h**), OCF_3 (**2l**), and ^{t}Bu (**2k**), on the aromatic ring did not influence the catalytic activity. Note that a modest

Table 1. Reaction development. Reaction conditions: cat [TM] (5 to 10 mol %), **1a** (0.20 mmol), **2a** (0.20 mmol), base (2.0 to 3.0 equiv), and additive (1.0 equiv) in 2 ml of dry solvent at 130°C for 16 hours under argon.

Entry	X	Cat [TM] (mol %)	Base (equiv)	Additive (equiv)	T (°C)	Solvent	Yield of 3aa (%)*
1	I (**1a**)	$Pd_2(dba)_3$ (5)	Na_2CO_3 (2.0)	–	130	DMF	6
2	I (**1a**)	$NiCl_2$ (10)	Na_2CO_3 (2.0)	–	130	DMF	10
3	I (**1a**)	$Ni(cod)_2$ (10)	Na_2CO_3 (2.0)	–	130	DMF	19
4	I (**1a**)	$Ni(cod)_2$ (10)	Cs_2CO_3 (2.0)	–	130	DMF	35
5	I (**1a**)	$Ni(cod)_2$ (10)	Cs_2CO_3 (2.0)	LiCl (1.0)	130	DMF	67
6	I (**1a**)	**$Ni(cod)_2$ (10)**	**Cs_2CO_3 (3.0)**	**LiCl (1.0)**	130	**DMF**	**87 (81)†**
7	I (**1a**)	$Ni(cod)_2$ (10)	Cs_2CO_3 (3.0)	NaCl (1.0)	130	DMF	40
8	I (**1a**)	$Ni(cod)_2$ (10)	Cs_2CO_3 (3.0)	LiCl (1.0)	130	DMA	82
9	I (**1a**)	$Ni(cod)_2$ (10)	Cs_2CO_3 (3.0)	LiCl (1.0)	130	NMP	86
10	I (**1a**)	$Ni(cod)_2$ (10)	Cs_2CO_3 (3.0)	LiCl (1.0)	130	Toluene	73
11	I (**1a**)	$Ni(cod)_2$ (10)	Cs_2CO_3 (3.0)	LiCl (1.0)	110	DMF	65
12	I (**1a**)	$Ni(cod)_2$ (5)	Cs_2CO_3 (3.0)	LiCl (1.0)	130	DMF	72
13	I (**1a**)	–	Cs_2CO_3 (3.0)	LiCl (1.0)	130	DMF	0
14	Br (**1a′**)	$Ni(cod)_2$ (10)	Cs_2CO_3 (3.0)	LiCl (1.0)	130	DMF	85 (80)†
15	Cl (**1a″**)	$Ni(cod)_2$ (10)	Cs_2CO_3 (3.0)	LiCl (1.0)	130	DMF	73 (69)†
16	F (**1a‴**)	$Ni(cod)_2$ (10)	Cs_2CO_3 (3.0)	LiCl (1.0)	130	DMF	0

*Yields determined by crude ^{1}H NMR using CH_2Br_2 as an internal standard. †Isolated yield.

yield was attained from the heteroannulation of the alkyne **2m**, which contains an amino group. Thiophene (**2n**) and pyridine (**2o**) in the alkynes were also tolerated under the reaction conditions. Unsymmetrical alkynes such as 1-phenyl-propyne (**2p**) and pent-1-yn-1-ylbenzene (**2q**) were further tested. Both alkynes preferred to form a C—P bond at the aryl site. A symmetrical aliphatic alkyne **2r** was also compatible, albeit with a low conversion. Last, we found that the use of terminal alkynes, including phenylacetylene (**2s**) and 1-octyne (**2t**), completely failed under the current reaction conditions (not shown in the table).

We further tested the reaction of a substrate **1t** with two NHP^{t}Bu$_2$ motifs for dual heteroannulation with alkyne **2a**, which effectively formed the product **3ta** in 64% yield (Fig. 2). In addition, other alkynes such as **2e** and **2g** could also be readily tolerated affording the related products **3te** and **3tg** in 84 and 81% yields, respectively.

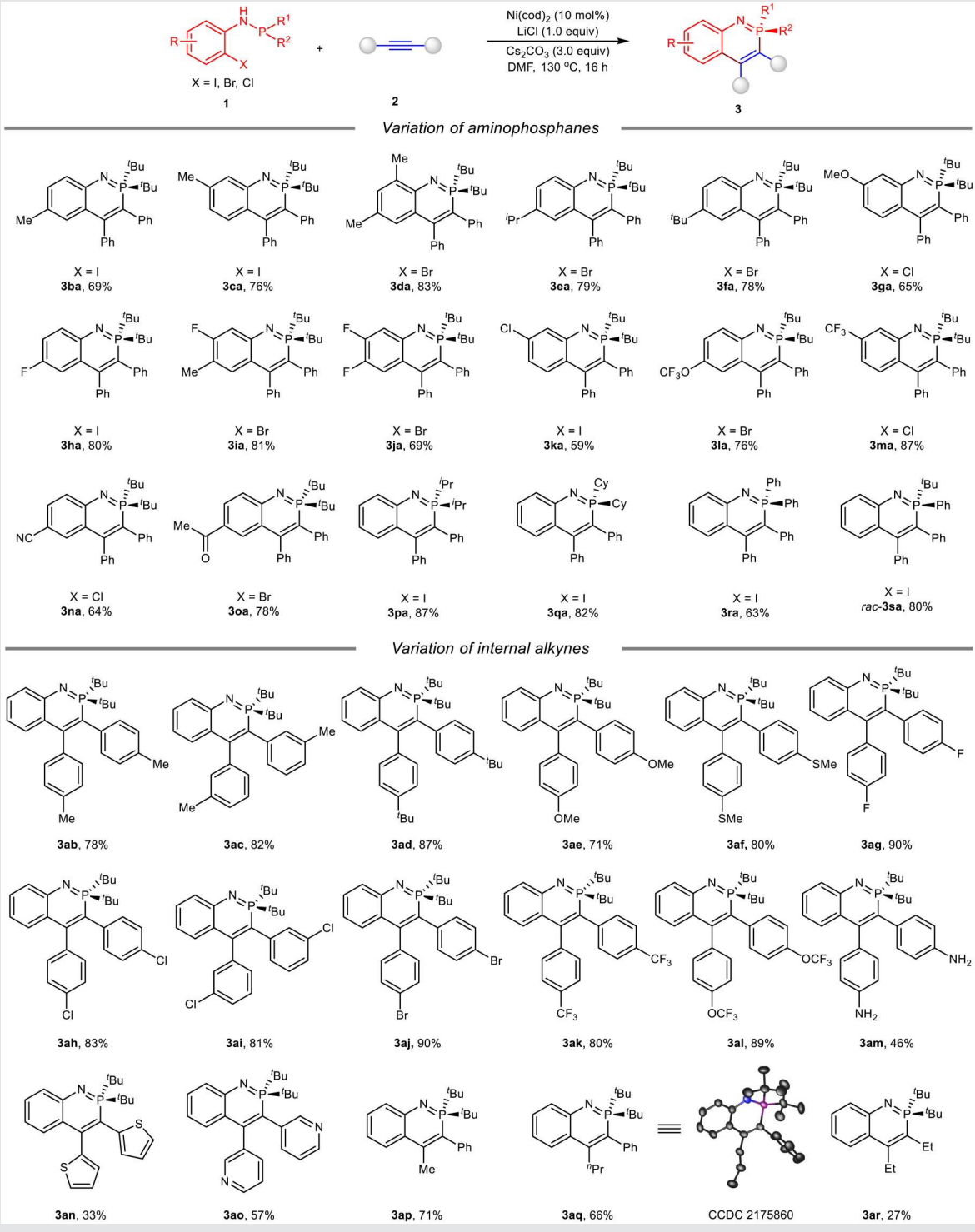
P-stereogenic phosphanamines, in the form of a protected borane complex with BH_3, could be facilely prepared by chiral resolution using high-performance liquid chromatography (HPLC) on a preparative scale (Fig. 3). Under the developed catalytic system, the compounds could undergo deprotection automatically. After the use of a chiral phosphanamine **1u** (>99% ee) with an N-P^{t}BuPh motif, full chirality transfer was observed to afford the heterocycle **3ua**. The reaction of compound **1u** with other alkynes, such as **2g** and **2s**, were also effective, showing excellent stereospecificity.

Treatment of (*R*)-1-*tert*-butyl-*N*-(2-chloro-4-methoxyphenyl)-1-phenylphosphanamine (**1v**) with the alkyne **2a** afforded the product (*S*)-**3va** in 43% yield. Fortunately, the absolute configurations of both the substrate and product were confirmed by x-ray diffraction analysis, demonstrating that the stereochemistry at the phosphorus center was retained during the reaction. Similarly, the enantiomer (*S*)-**1v** reacted with the alkyne **2e** to produce (*R*)-**3ve** in 58% yield.

Photophysical properties

Density functional theory (DFT) calculations at the PBE0-D3BJ/def2TZVP level were performed on **3aa** as a model substrate to determine the molecular orbital distribution of highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) in the ground state (S_0) (Fig. 4A). The HOMO is mainly localized in the phosphaquinoline skeleton, whereas the LUMO is mainly distributed over all the aromatic rings. Thus, substitution modulation at the two phenyl groups will substantially affect the LUMO level, which can be used to tune the photophysical properties in terms of the luminescence. The DFT-optimized geometry is in good agreement with the crystal structure and shows a twisted conformation for the azaphosphinine ring, which is capable of restricting the aggregation-caused quenching effect (*66*). We further tested the photophysical properties of selected products with different substituents on the aryl motifs, including **3aa**, **3ag**, **3ae**, **3ab**, **3ak**, and **3aj** (*67*). It was easily found that the 2-λ5-phosphaquinolines obtained here are photoactive molecules, and their photophysical properties could be tuned by simply modifying the molecular structures, leading to color-tunable emissions in both solution and solid states. The yield of the phosphacycle **3ag** reached up to 90%, indicating that these molecules accessed by the current reaction protocol have great potential for applications as luminescent materials.

Table 2. Substrate scope of alkynes and aminophosphanes. Reaction conditions: $Ni(cod)_2$ (10 mol %), **1** (0.20 mmol), **2** (0.20 mmol), LiCl (0.20 mmol), and Cs_2CO_3 (0.60 mmol) in 2 ml of dry DMF at 130°C for 16 hours under argon, isolated yields.



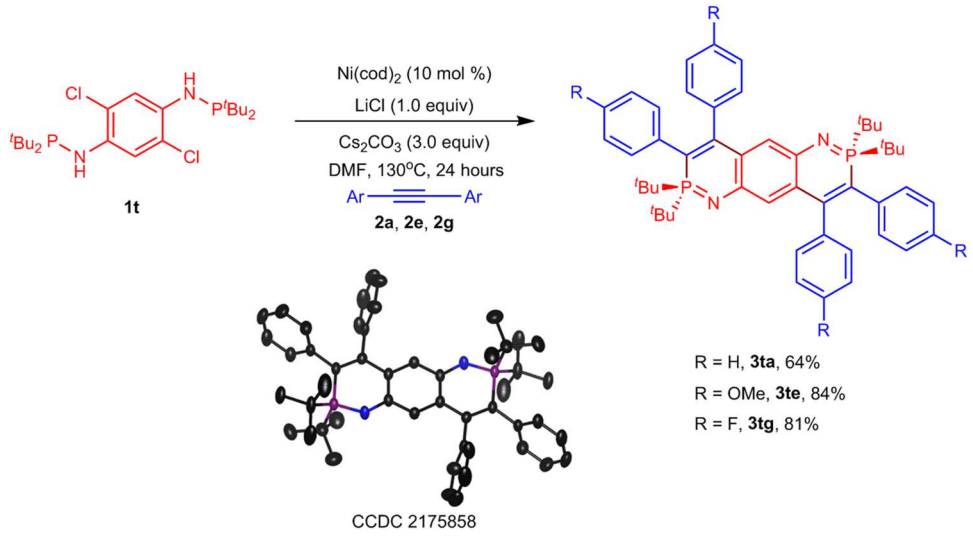


Fig. 2. Nickel-catalyzed dual heteroannulation of internal alkynes with an aminophosphane 1t. Reaction conditions: $Ni(cod)_2$ (10 mol %), **1t** (0.20 mmol), **2** (0.40 mmol), LiCl (0.20 mmol), and Cs_2CO_3 (0.60 mmol) in 2 ml of dry DMF at 130°C for 24 hours under argon, isolated yields.

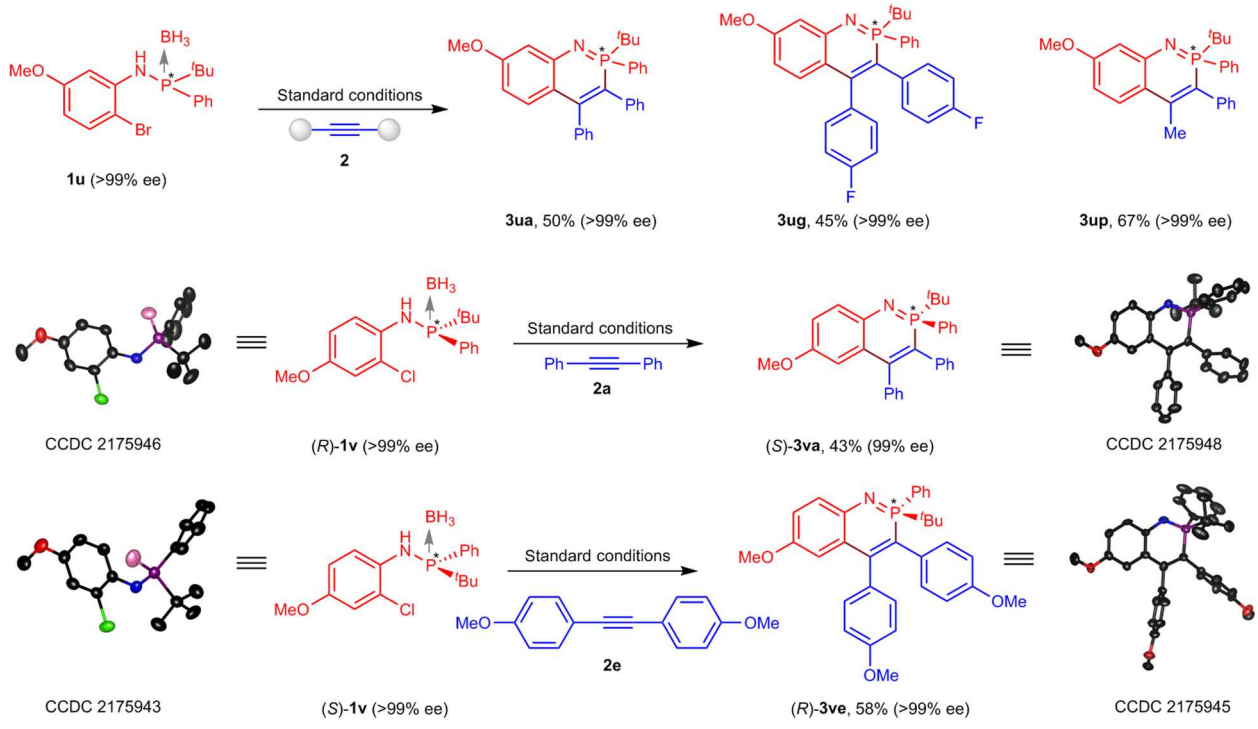
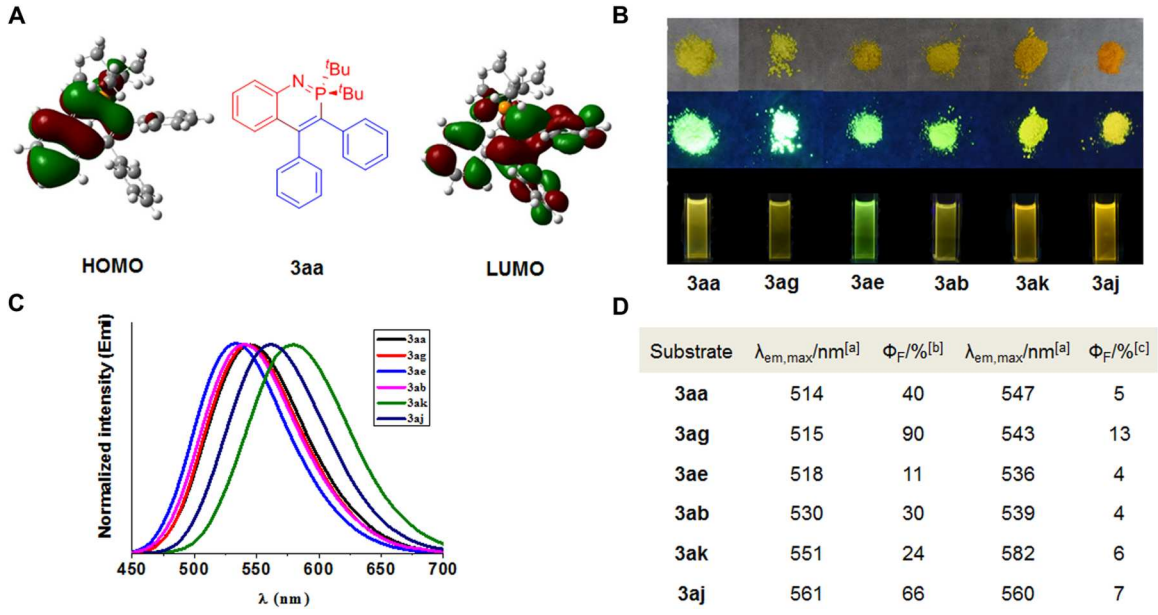


Fig. 3. Stereospecific nickel-catalyzed heteroannulation of internal alkynes with enantioenriched aminophosphanes. Reaction conditions: $Ni(cod)_2$ (10 mol%), **1** (0.20 mmol), **2** (0.40 mmol), LiCl (0.20 mmol), and Cs_2CO_3 (0.60 mmol) in 2 ml of dry DMF at 130°C for 16 hours under argon, isolated yields.

DISCUSSION

To probe the reaction pathways, several mechanistic experiments were carried out in Fig. 5. When we added 1,2-bis(4-fluorophenyl)ethyne (**2g**) with stoichiometric amounts of $Ni(cod)_2$, LiCl, and Cs_2CO_3 in d7-DMF at 25°C, the appearance of a new ^{19}F NMR peak at $\delta = -117.8$ parts per million indicated the existence of a nickel(0)-alkyne complex in the system (Fig. 5A) (*68*). To learn about the electronic effects of two reaction components in the catalytic cycle, we further conducted a series of competition experiments (Fig. 5B). A competition experiment between a large excess of aminophosphanes **1g** and **1m** (10.0 equiv for each) was carried out, forming a >20:1 ratio of products **3ga** and **3ma**. The electron-rich aryl halides react faster than the electron-deficient ones, suggesting that carbon-halogen oxidative addition appears not to be a rate-determining step. Furthermore, the reaction of aminophosphane **1a** with 5.0 equiv of electron-rich (*p*-methoxy, **2e**) and



Substrate	$\lambda_{em,max}$/nm[a]	Φ_F/%[b]	$\lambda_{em,max}$/nm[a]	Φ_F/%[c]
3aa	514	40	547	5
3ag	515	90	543	13
3ae	518	11	536	4
3ab	530	30	539	4
3ak	551	24	582	6
3aj	561	66	560	7

Fig. 4. Characterization of 2-λ5-phosphaquinolines. (**A**) Frontier molecular orbitals of 3aa. (**B**) Ambient and fluorescence images of selected products: solid under ambient light (top); solid irradiated at 365 nm (middle); and in DCM irradiated at 365 nm (bottom). (**C**) Normalized emission spectra of phosphacycles (1×10^{-5} in DCM). (**D**) Photophysical data for phosphacycles. [a]Emission maxima upon excitation at the absorption maximum wavelength. [b]In the solid state. [c]In DCM.

electron-withdrawing (*p*-trifluoromethyl, **2k**) tolanes afforded a mixture of products **3ae** and **3ak** in a 1:3.4 ratio, suggesting that more electron-deficient alkynes were favored in the insertion event. The stereoselective NH/PH tautomeric equilibrium between aminophosphanes and secondary iminophosphoranes can be illustrated by the calculated frontier molecular orbitals (Fig. 5C). Using a P-stereogenic aminophosphane (*R*)-**1s** as a model molecule, treatment of Cs_2CO_3 as the base is effective for deprotonation through transition **TS1** with an activation energy barrier of only 0.3 kcal·mol^{-1}, giving the deprotonated intermediate (*R*)-**1s′**. The analysis of the frontier molecular orbitals suggests that the lone electron pair on P atom is more prone to coordinate with Ni center. The detailed calculated reaction pathway was also shown in Fig. 5D, where nickel(0)-alkyne complex **INT1A** was chosen as the relative zero in the Gibbs free energy profile (*69*, *70*). Intermediate (*R*)-**1s′** initially exchanges with the cod (1,5-cyclooctadiene) ligand of **INT1A**, leading to the P-coordinated six-membered species **INT2A**. The oxidative addition of the C—I bond into Ni(0) center through transition state **TS3A** with an energy barrier of 5.6 kcal·mol^{-1} gives Ni(II) complex **INT3A**, which then release iodine anion to form **INT4A**. Subsequently, an extra diphenylacetylene **2a** coordinates with Ni(II) center of **INT4A**, and the insertion of the carbon-carbon triple bond to the aryl-Ni bond affords a complex **INT5A** through transition state **TS5A** with an energy barrier of 9.8 kcal·mol^{-1}. The result indicates that this process is the rate-determining step in the catalytic cycle, which is in agreement with the competition experiments shown in Fig. 5B. Notably, the energy barrier of transition state **TS5B** for the direct carbon-carbon triple bond insertion is 27.2 kcal·mol^{-1}, which is much higher than the insertion process via **TS5A**. Isomerization of η^2-coordinated **INT5A** to seven-membered vinyl-Ni(II) complex **INT6A** is thermodynamically favorable with an exothermic energy of 18.3 kcal·mol^{-1}. Last, C—P reductive elimination and ligand exchange occur to form the chiral 2-λ5-phosphaquinoline (*S*)-**3sa** and regenerate the metal catalyst **INT1A** to complete the catalytic cycle. In the whole energy profile, each step is considered to occur with a high degree of stereospecificity, where the stereochemistry at the phosphorus center does not change during cyclization.

In summary, we have developed nickel-catalyzed [4+2] heteroannulation of internal alkynes with aminophosphanes enabled to provide a series of 2-λ5-phosphaquinolines. The reaction exhibits good functional group compatibility, showing excellent site selectivity for alkyne insertion. Furthermore, utilization of P-stereogenic aminophosphanes as substrates allows the stereospecific formation of chiral phosphacycles. Some of the phosphacycles exhibit distinct fluorescence with high quantum yields. With the help of a series of experimental and computational results, the reaction mechanism for the stereospecific heteroannulation was also demonstrated. We anticipate that the discovery can facilitate the synthesis of chiral phosphacycles through incorporation of the P-chirogenic center.

MATERIALS AND METHODS

General information

Unless otherwise noted, all reactions were performed under an argon atmosphere using flame-dried glassware. Anhydrous DMF were purchased from J&K Chemical and were used as received. All new compounds were fully characterized. NMR spectra were recorded on an ARX-400 MHz or an ARX-500 Associated. ^{1}H NMR spectra data were reported as δ values in parts per million relative to chloroform (δ 7.26) or methanol (δ 3.31) if collected in $CDCl_3$ or CD_3OD. ^{13}C NMR spectra data were reported as δ values in parts per million relative to chloroform (δ 77.00) or methanol (δ 48.80) if collected in $CDCl_3$ or CD_3OD (the carbon attached to B was not observed). ^{1}H NMR coupling constants were reported in hertz,

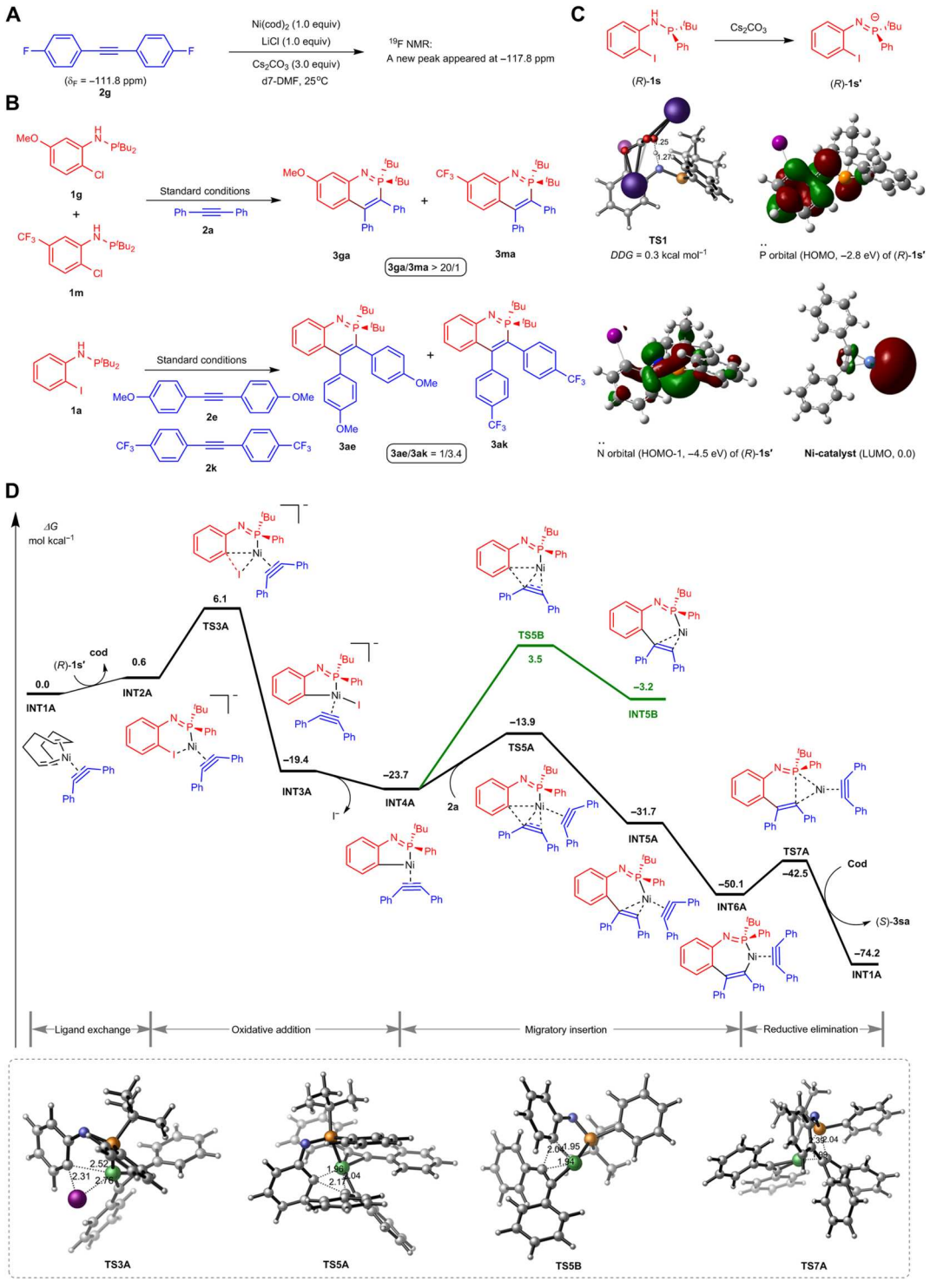


Fig. 5. Mechanistic studies. (**A**) Detecting the coordination of alkyne **2g** with $Ni(cod)_2$ by ^{19}F NMR experiment. (**B**) Competition experiments. (**C**) The deprotonation of model substrate (*R*)-**1w** and the analysis of the frontier molecular orbitals. (**D**) The whole energy profile of the Ni-catalyzed stereospecific heteroannulation of alkyne **2a** with aminophosphane (*R*)-**1s**. DFT calculations were performed at the M06-D3/6–311 + G(d,p)-SDD (Ni and I)/SMD(DMF)//B3LYP-D3/6-31G(d)-SDD(Ni and I) level of theory.

and multiplicity was indicated as follows: s (singlet); d (doublet); t (triplet); q (quartet); quint (quintet); m (multiplet); dd (doublet of doublets); ddd (doublet of doublet of doublets); dt (doublet of triplets); td (triplet of doublets); ddt (doublet of doublet of triplets); dq (doubletof quartets); and br (broad). High-resolution mass spectra were obtained by using the Ultra High Definition (UHD) accurate mass quadrupole orthogonal acceleration–time-of-flight. Infrared spectra were recorded on a Fourier transform infrared spectrometer. Fluorescence spectral measurements were carried out by using a Hitachi F-4600 fluorescence spectrophotometer. The absolute photoluminescence quantum yields (absolute photoluminescence quantum yield (PLQY) measured via an integrating sphere) of the compounds were measured with HORIBA Fluorolog-3 fluorescence spectrometer. Optical rotations were measured on an automatic polarimeter with $[\alpha]_D^{25}$ values reported in degrees; concentration (*c*) is in gram/100 ml. Chiral HPLC analyses were performed on UltiMate 3000 or Agilent 1260 liquid chromatography. All reactions were carried out in flame-dried 10-ml Schlenk tubes with Teflon screw caps under argon. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Acetylenes were synthesized according to literature methods.

General procedures for synthesis of 3

To an oven-dried 10-ml Schlenk tube, **1** (1.0 equiv, 0.20 mmol), **2** (1.0 equiv, 0.20 mmol), $Ni(cod)_2$ (10 mol %, 5.5 mg, 0.02 mmol), Cs_2CO_3 (195.5 mg, 0.60 mmol,) and LiCl (8.5 mg, 0.20 mmol) were dissolved in dry DMF (2.0 ml). The mixture was stirred at 130°C under argon for 16 hours. Upon the completion of the reaction, the solvent was removed. The crude mixture was directly subjected to column chromatography on Al_2O_3 using petroleum-ether/ethyl acetate as eluent to give the desired products **3**.

Supplementary Materials

This PDF file includes:
Sections S1 to S7
Figs. S1 to S21
Table S1

Other Supplementary Material for this manuscript includes the following:
Data S1 to S7

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Acknowledgments: We are grateful to the High-Performance Computing Center of Nanjing University for performing the numerical calculations in this paper on its blade cluster system. **Funding:** We would like to thank the National Key R&D Program of China (2022YFA1503202), National Natural Science Foundation of China (grants 22025104, 21972064, and 21901111), and the Fundamental Research Funds for the Central Universities (grant 020514380254) for financial support. The project is also supported by Open Research Fund of School of Chemistry and Chemical Engineering, Henan Normal University. **Author contributions:** Z.S. and H.Y. conceived and designed the study and wrote the paper. R.H., H.D., and J.X. performed the experiments and mechanistic studies and analyzed the data. M.W. performed the DFT calculations. Y.Z. performed the crystallographic studies. **Competing interests:** The authors declare that they have no competing interests. **Data and materials availability:** All data needed to evaluate the conclusions in the paper are present in the paper and/or the Supplementary Materials.

Submitted 13 September 2022
Accepted 9 December 2022
Published 13 January 2023
10.1126/sciadv.ade8638