Rhodium-Catalyzed Oxidative Coupling of Aryl Hydrazones with Internal Alkynes: Efficient Synthesis of Multisubstituted Isoquinolines

Wenting Liu,[a] Xiaohu Hong,[a] Bin Xu*[a,b]

[a] Department of Chemistry, Shanghai University, Shanghai 200444, P. R. of China
Fax +86(21)66134594; E-mail: xubin@shu.edu.cn

[b] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P. R. of China

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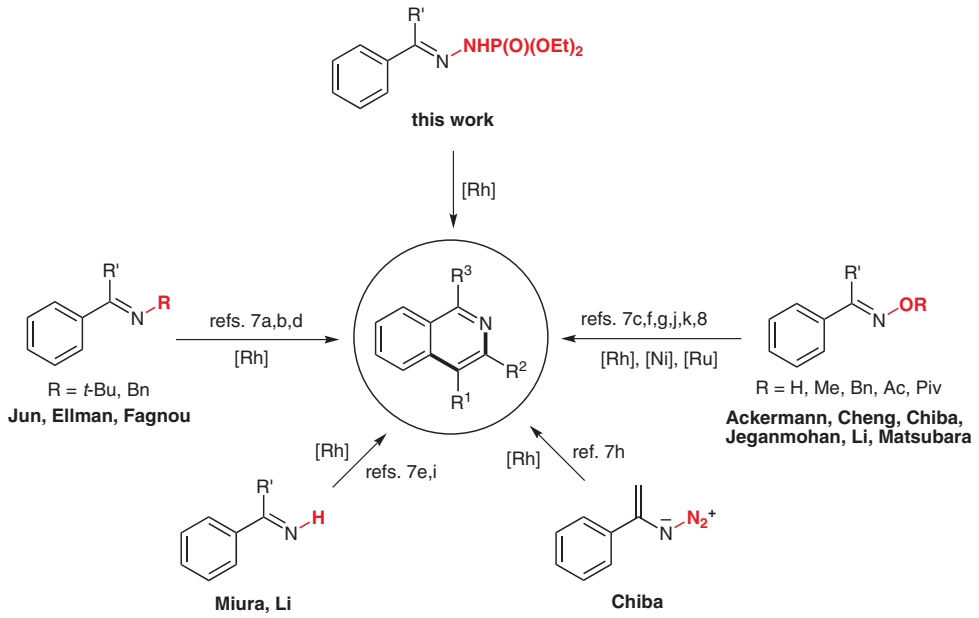
Abstract: An efficient rhodium-catalyzed oxidative coupling reaction has been developed that gives high yields of multisubstituted isoquinolines from easily accessible aryl hydrazones and internal alkynes. Indenone hydrazone can also be synthesized in high yield from the corresponding benzaldehyde hydrazone by using this approach.

Key words: alkynes, cyclization, hydrazones, heterocycles, rhodium, catalysis

With its wide range of biological and pharmacological activities,[1] the isoquinoline skeleton is one of the most interesting frameworks and it has attracted a great deal of attention in the pharmaceutical and agrochemical industries. The prevalence of this physiologically important nucleus in therapeutic agents and natural products[2] has prompted the development of many useful methods for its preparation,[3] In recent decades, metal-catalyzed cyclization reactions have been developed that permit mild and efficient syntheses of isoquinoline frameworks.[4] However, some of these reactions involve harsh conditions or require functionalization of substrates; for example, activated halogen groups may need to be present.[4a–c,f–h] Recently, there has been considerable progress in the development of transition-metal-catalyzed C–H activation reactions directed by many types of functional groups.[5,6] A wide range of metal catalysts based on palladium, platinum, ruthenium, rhodium, and iridium, among others, have been applied with varying degrees of success. In this context, there are several reports of syntheses of isoquinolines by means of metal-catalyzed C–H bond activation of aromatic and alkene imines or oximes, followed by alkenylation with alkynes and subsequent intramolecular annulation (Scheme 1).[7,8]

High yields and high regioselectivities of isoquinolines have been achieved by the use of rhodium,[7a–j,l] ruthenium,[8] or nickel[7k] catalysts in the presence of chelating groups such as aryl vinyl azides,[7h] benzaldimines,[7b,d,e] ketimines,[7a,b,e] or ketoximes.[7c,f,g,j,8] We recently reported a rhodium-catalyzed C–H bond olefination–annulation ap-



Scheme 1 Metal-catalyzed syntheses of isoquinolines from alkynes

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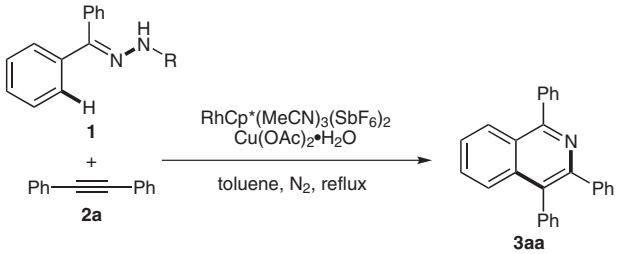
proach that gives 1,2-dihydrophthalazines in good to excellent yields from sulfonylhydrazones and alkenes.[9] In the context of our program aimed at efficient construction of heterocycles through the tandem reaction strategies,[9,10] we describe here a rhodium-catalyzed tandem oxidative cross-coupling process in which sequential C–C/C–N bond formation and N–N bond cleavage reactions of easily accessible substituted aromatic hydrazones with alkynes give multisubstituted isoquinolines in good to excellent yields (Scheme 1). To our knowledge, this reaction represents the first efficient example of a one-pot synthesis of substituted isoquinolines through a tandem C–C/C–N bond-forming process and N–N bond cleavage from aryl hydrazones.

We began our studies by examining the cross-coupling reactions of various *N*-substituted benzophenone-derived hydrazones with diphenylethyne in the presence of tris(acetonitrile)(η^5-pentamethylcyclopentadienyl)rhodium(III) hexafluoroantimonate [RhCp*(MeCN)$_3$(SbF$_6$)$_2$] and copper(II) acetate monohydrate in toluene. However, no satisfactory reaction occurred with benzophenone hydrazone or tosyl hydrazone (Table 1, entries 1–2), and only trace amounts of the isoquinoline **3aa** were obtained (entry 3). When the *N*-benzoyl-substituted benzophenone hydrazone was used as the substrate, **3aa** was isolated in 22% yield (entry 4). Extensive screening of *N*-alkyl or *N*-aryl substituents on the hydrazones (entries 5–8) showed that the use of an electron-rich arene gave better results, and **3aa** was obtained in 63% yield (entry 7). The *N*-diethoxyphosphoryl group turned out to be the best choice of substituent and it gave **3aa** in 82% yield (entry 9) in refluxing toluene, whereas the *N*-diphenoxyphosphoryl group gave a lower yield (entry 10). This shows that the reactivity of the leaving group (as –NHR) is essential for formation of the isoquinoline. From these results, we chose the *N*-diethoxyphosphoryl-substituted hydrazone for further optimization of the reaction.

Having identified the *N*-diethoxyphosphoryl group as the optimal leaving group, we next examined the effects of the reaction temperature, the catalyst source, and the solvent (Table 2). An improved yield was obtained when temperature was decreased to 70 °C (entry 2). In comparison with RhCp*(MeCN)$_3$(SbF$_6$)$_2$, the use of tetrachlorobis(η^5-pentamethylcyclopentadienyl)dirhodium {[RhCp*Cl$_2$]$_2$} as the catalyst gave a much lower yield (entry 3). Switching the solvent from toluene to 2-methylbutan-2-ol, dioxane, 1,2-dichloroethane, tetrahydrofuran, *N*,*N*-dimethylformamide, acetonitrile, or dimethyl sulfoxide also gave decreased yields or only traces of product (entries 4–10).

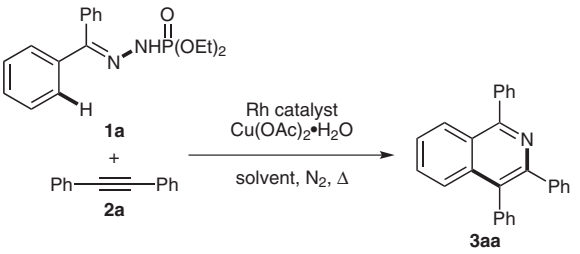
Table 1 Reactions of Hydrazones Bearing Various Leaving Groups



Entry[a]	R	Yield[b] (%)	Entry[a]	R	Yield[b] (%)
1	H	–[c]	6	Ph	54
2	Ts	–[c]	7	4-MeOC$_6$H$_4$	63
3	Ac	<5	8	4-ClC$_6$H$_4$	51
4	Bz	22	**9**	**P(O)(OEt)$_2$**	**82**
5	*t*-Bu	<5	10	P(O)(OPh)$_2$	51

[a] All reactions were performed in a N$_2$-purged flask on 0.3-mmol scale using hydrazone (1.0 equiv), PhC≡CPh (1.2 equiv), RhCp*(MeCN)$_3$(SbF$_6$)$_2$ (3 mol%), and Cu(OAc)$_2$·H$_2$O (2.1 equiv) in toluene (1.5 mL) at 110 °C.
[b] Isolated yield.
[c] No reaction.

Table 2 Optimization of Reaction Conditions for Isoquinoline Formation



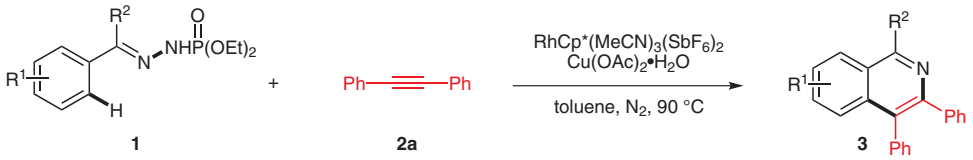
Entry[a]	Rh source[b]	Solvent	Temp (°C)	Time (h)	Yield[c] (%)
1	A	toluene	110	17	82
2	A	toluene	70	23	91
3	B	toluene	70	29	13
4	A	Me$_2$C(Et)OH	70	24	78
5	A	1,4-dioxane	70	26	73
6	A	DCE	70	21	53
7	A	THF	70	28	47
8	A	DMF	70	30	14
9	A	MeCN	70	30	7
10	A	DMSO	70	30	trace
11	**A**	**toluene**	**90**	**18**	**93**
12	–	toluene	90	24	–[d]

[a] All reactions were performed in a N$_2$-purged flask on 0.3-mmol scale using hydrazone (1.0 equiv), PhC≡CPh (1.2 equiv), the Rh catalyst (3 mol%), and Cu(OAc)$_2$•H$_2$O (2.1 equiv) in the appropriate solvent (1.5 mL).
[b] A = RhCp*(MeCN)$_3$(SbF$_6$)$_2$; B = [RhCp*Cl$_2$]$_2$.
[c] Isolated yield.
[d] No reaction.

The yield of the isoquinoline product rose to 93% in the presence of rhodium catalyst A and copper acetate monohydrate at 90 °C in toluene (entry 11). No product was detected in the absence of a rhodium catalyst (entry 12).

Having identified the optimal conditions for catalytic formation of isoquinolines, we extended the reaction to a range of readily available phosphorylhydrazones, as listed in Table 3. In general, the tandem reaction was highly efficient for substrates bearing *para*-, *meta*-, or *ortho*-substituents on the aryl ring (entries 2–8). Substrates with electron-donating groups in either the *para*- or the *meta*-position gave slightly better yields than those containing electron-withdrawing groups at these positions.

Table 3 Hydrazone Scope in the Synthesis of Isoquinolines



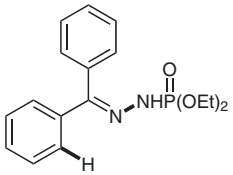
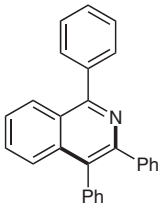
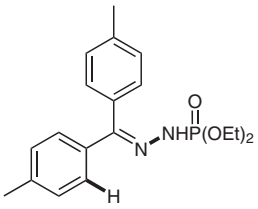
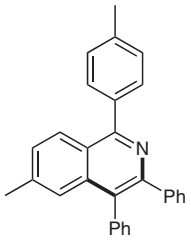
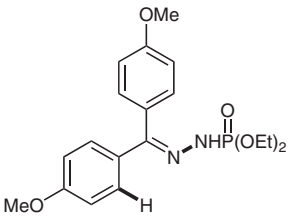
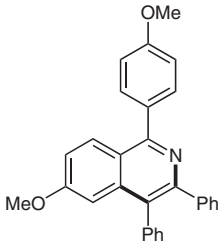
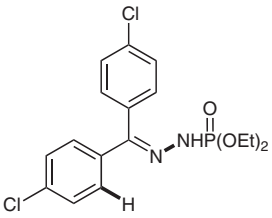
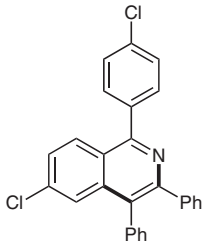
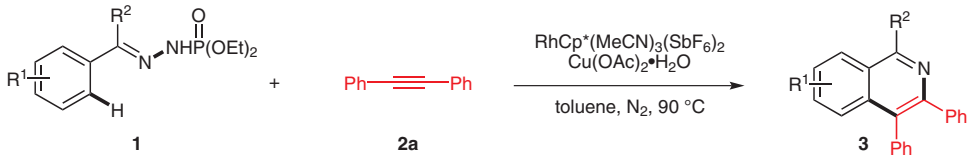
Entry[a]	Hydrazone	Product	Time (h)	Yield[b] (%)
1	 **1a**	 **3aa**	18	93
2	 **1b**	 **3ba**	15	89
3	 **1c**	 **3ca**	14	82
4	 **1d**	 **3da**	28	75

Table 3 Hydrazone Scope in the Synthesis of Isoquinolines (continued)



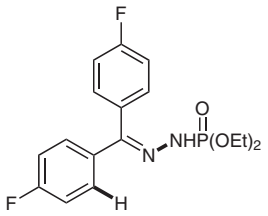
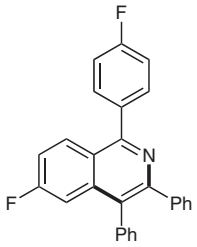
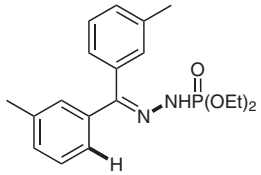
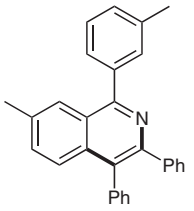
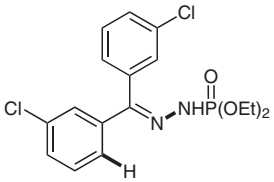
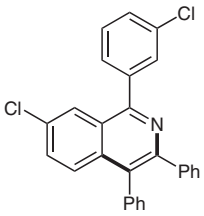
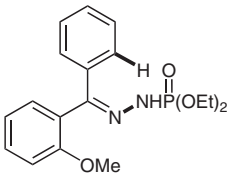
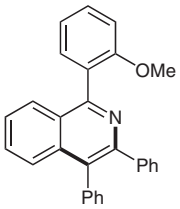
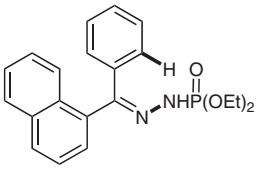
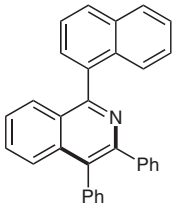
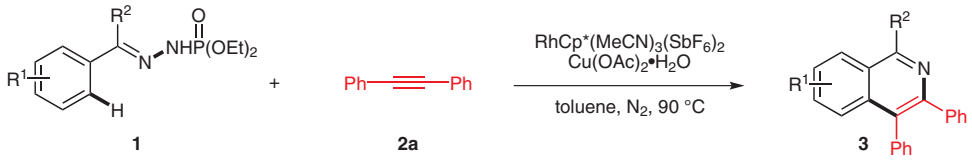
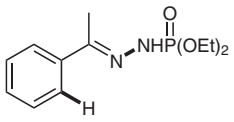
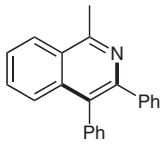
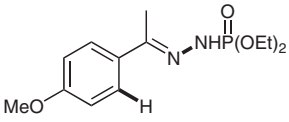
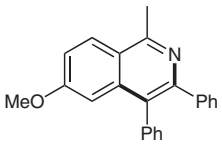
Entry[a]	Hydrazone	Product	Time (h)	Yield[b] (%)
5	 **1e**	 **3ea**	25	80
6	 **1f**	 **3fa**	22	84
7	 **1g**	 **3ga**	27	77
8	 **1h**	 **3ha**	19	81
9	 **1i**	 **3ia**	23	86

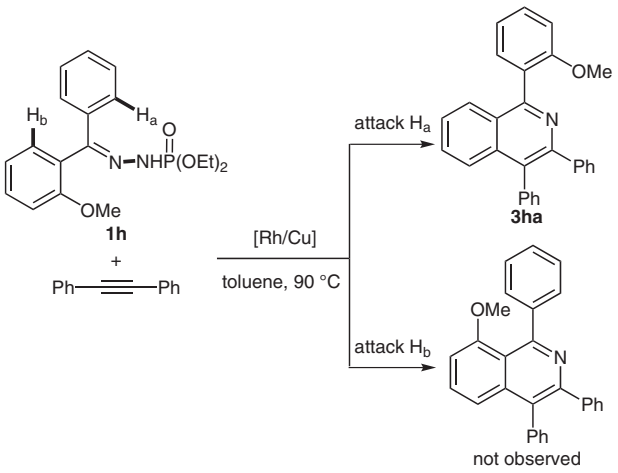
Table 3 Hydrazone Scope in the Synthesis of Isoquinolines (continued)



Entry[a]	Hydrazone	Product	Time (h)	Yield[b] (%)
10	 **1j**	 **3ja**	26	30
11	 **1k**	 **3ka**	23	36

[a] All reactions were performed in a N_2-purged flask on 0.3-mmol scale using hydrazone (1.0 equiv), PhC≡CPh (1.2 equiv), $RhCp^*(MeCN)_3(SbF_6)_2$ (3 mol%), and $Cu(OAc)_2 \cdot H_2O$ (2.1 equiv) in toluene (1.5 mL) at 90 °C.
[b] Isolated yield.

Note that substrate **1h**, which has two potential *ortho* positions available for C–H alkenylation (Scheme 2), gave product **3ha** exclusively in 81% yield and with high regioselectivity (entry 8). The methoxy substituent in the *ortho* position may retard the reaction. The structure of product **3ha** was determined by spectral analysis and confirmed by X-ray crystallography (Figure 1).



Scheme 2 Regioselective C–H alkenylation of **1h**

The reaction was not limited to simple benzene-containing aromatics, as a hydrazone bearing a naphthyl group also gave the desired product **3ia** in 86% yield (entry 9). Furthermore, the method also permitted the construction of the methyl-substituted isoquinolines **3ja** and **3ka** from the acetophenone-derived substrates **1j** and **1k** in 30% and 36% yield, respectively (entries 10–11).

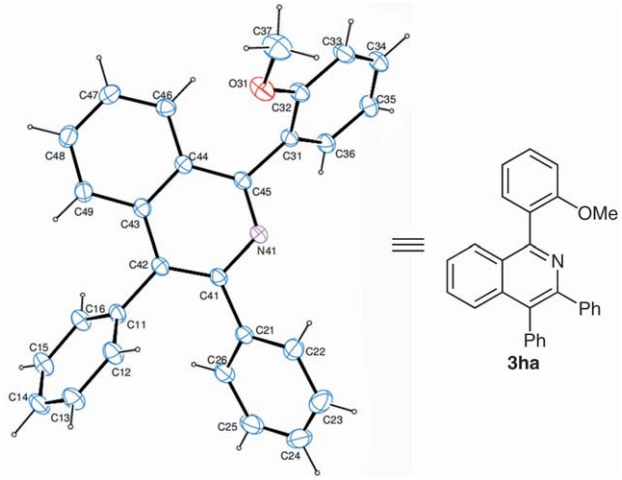
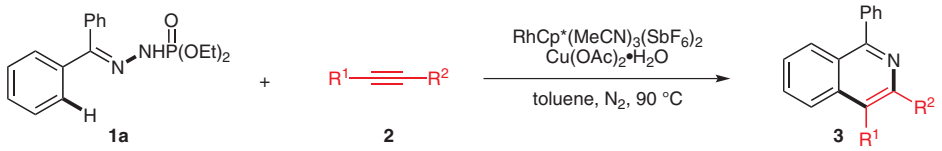
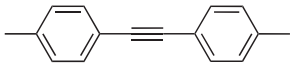
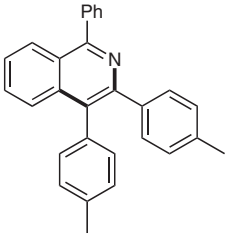
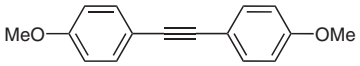
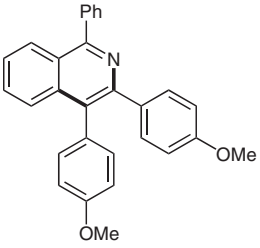
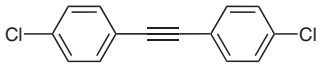
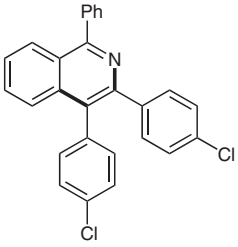
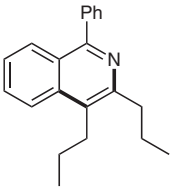
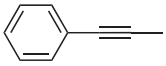
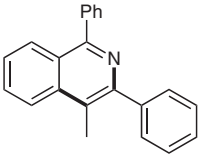


Figure 1 ORTEP drawing of isoquinoline **3ha**

Using our optimized reaction conditions, we examined the scope of the isoquinoline formation with various acetylenes, as shown in Table 4. The reaction tolerated a wide range of substrates containing internal alkyne groups. Symmetrically substituted diarylethynes with electron-donating (entries 1–2) or electron-withdrawing groups (entry 3) reacted well with hydrazone **1a**. The reaction also proceeded smoothly with a dialkyl-substituted alkyne and gave **3ae** in 98% yield (entry 4). An unsymmetrical alkyne also coupled with **1a** and gave isoquinoline **3af**, in which the phenyl group was attached onto the carbon atom next to the nitrogen atom, as the sole product (entry 5).

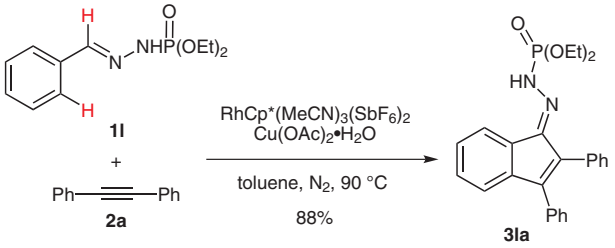
Table 4 Acetylene Scope in the Synthesis of Isoquinolines



Entry[a]	Alkyne	Product	Time (h)	Yield[b] (%)
1	 **2b**	 **3ab**	22	81
2	 **2c**	 **3ac**	18	77
3	 **2d**	 **3ad**	29	73
4	**2e**	 **3ae**	5	98
5	 **2f**	 **3af**	14	62

[a] All reactions were performed in a N_2-purged flask on 0.3-mmol scale, using alkyne **2** (1.2 equiv), hydrazine **1a** (1.0 equiv), $RhCp^*(MeCN)_3(SbF_6)_2$ (3 mol%), and $Cu(OAc)_2•H_2O$ (2.1 equiv) in toluene (1.5 mL) at 90 °C.
[b] Isolated yield.

However, when benzaldehyde hydrazone **1l** was used under similar conditions, the reaction did not give the corresponding isoquinoline product, but instead gave the indenone imine **3la** in 88% yield (Scheme 3). The structure of **3la** was determined by spectral analysis and confirmed by X-ray crystallography (Figure 2).



Scheme 3 Reaction of benzaldehyde hydrazone **1l** with diphenylethyne (**2a**)

A plausible mechanism for the formation of isoquinolines is proposed in Scheme 4; this is based on literature reports,[7d,7f] and neutral ligands are omitted for clarity. The catalytic cycle is probably initiated by *ortho* C–H activation of **1a** with the aid of the hydrazone nitrogen atom to give the five-membered rhodacycle **A**. Insertion of diphenylethyne into the Rh–C bond affords the vinyl rhodium species **B**, which cyclizes by Path A to form the rhodacyclic iminium cation intermediate **C**. A reductive elimination reaction of cation **C** affords rhodium(I) and the isoquinolinium salt **D**, which undergoes an elimination reaction to form isoquinolines **3aa**. The rhodium(III) species is regenerated by oxidation by copper(II) acetate. Currently, we cannot rule out the possibility of the existence of transition state **E** in which the rhodium(III) species retains its valance in the catalytic cycle (Path B).[6d]

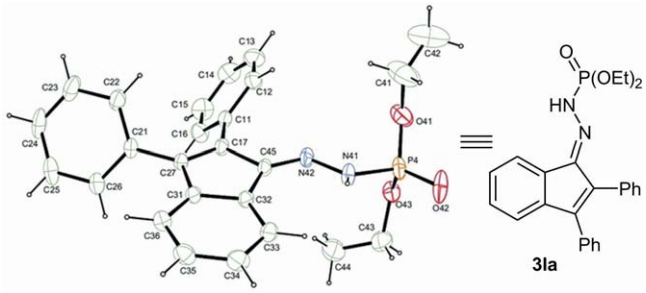
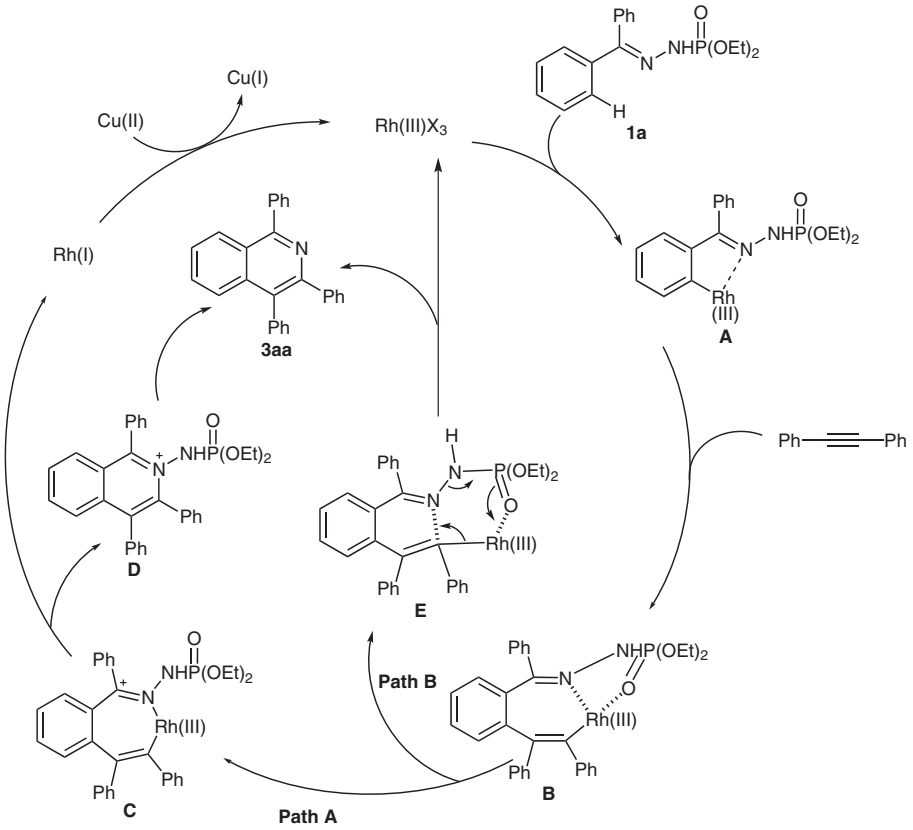


Figure 2 ORTEP drawing of indenone imine **3la**

In summary, we have developed an efficient rhodium-catalyzed oxidative coupling reaction of easily accessible aryl hydrazones and internal alkynes; the reaction proceeds through a tandem C–C/C–N bond-forming process and a N–N bond cleavage. This approach offers a unique strategy and an alternative route for the preparation of multisubstituted isoquinolines in good to excellent yields and high regioselectivities. An indenone hydrazone can



Scheme 4 Plausible mechanism for the formation of **3aa** from **1a**

also be synthesized from the corresponding benzaldehyde hydrazone in high yield by this approach. The mechanism and scope of the reaction and its applications in the synthesis bioactive compounds are under investigation.

All reagents and metal catalysts were obtained from commercial sources and used without further purification. Commercially available solvents were purified before use. All new compounds were fully characterized. All melting points were determined on a Tsingtao Unicom-Optics WRS-1A or WRS-1B digital melting-point apparatus without correction. IR spectra were recorded by using a Thermo Nicolet Avatar 370 FTIR spectrometer. ^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectra were recorded on a Bruker AV-500 spectrometer operated at 500, 125, 470, or 202 MHz respectively; chemical shifts are reported in ppm relative to $CHCl_3$ (δ = 7.26 ppm), DMSO (δ = 2.50 ppm), or TMS (δ = 0.00 ppm) for ^{1}H NMR, to $CHCl_3$ (δ = 77.16 ppm) or DMSO (δ = 39.52 ppm) for ^{13}C NMR, to C_6F_6 (δ = –164.9 ppm) for ^{19}F NMR, and to H_3PO_4 (δ = 0.00 ppm) for ^{31}P NMR. Mass spectra and high-resolution mass spectra were recorded with an Agilent 5975N in the EI or ESI mode. Elemental analyses were carried out on an Elementar Vario EL elemental analyzer. Silica gel plates GF254 were used for TLC, and silica gel H or 300–400 mesh was used for flash column chromatography. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise indicated.

1-(Diethoxyphosphoryl)-2-(diphenylmethylidene)hydrazine[11] (1a); Typical Procedure

A suspension of Ph_2CO (0.91 g, 5.0 mmol) and $H_2NNHP(O)(OEt)_2$ (1.26 g, 7.5 mmol) in EtOH was treated with four drops of concd aq HCl, and the mixture was refluxed for 2 h until the reaction was complete (TLC). The mixture was then cooled to r.t. and evaporated to dryness under reduced pressure. The crude product was purified by column chromatography [silica gel, PE–EtOAc (4:1)] to give a colorless solid; yield: 1.55 g (93%); mp 96–97 °C.

IR (KBr): 3333, 2990, 2976, 2903, 1580, 1444, 1408, 1255, 1023, 975, 892, 782, 702 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.56–7.48 (m, 5 H), 7.34–7.28 (m, 3 H), 7.23 (dd, *J* = 8.0, 1.5 Hz, 2 H), 6.59 (d, $^{2}J_{P-H}$ = 29.0 Hz, 1 H), 4.26–4.14 (m, 4 H), 1.39 (td, *J* = 7.0, 0.5 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 151.6 (d, $^{3}J_{P-C}$ = 17.5 Hz), 137.2, 131.6, 129.9, 129.7, 129.1, 128.5, 128.2, 127.1, 63.5 (d, $^{2}J_{P-C}$ = 6.3 Hz), 16.2 (d, $^{3}J_{P-C}$ = 7.5 Hz).

^{31}P NMR (202 MHz, $CDCl_3$): δ = 1.3.

LC/MS (ESI): *m/z* 333 $[M + H]^+$.

1-[Bis(4-tolyl)methylidene]-2-(diethoxyphosphoryl)hydrazine (1b)

This was prepared from $(4\text{-Tol})_2CO$ (1.05 g, 5.0 mmol) and $H_2NNHP(O)(OEt)_2$ (1.26 g, 7.5 mmol). The crude product was purified by column chromatography [silica gel, PE–EtOAc (4:1)] to give a colorless solid; yield: 1.65 g (92%); mp 107–109 °C.

IR (KBr): 3335, 2986, 1927, 1612, 1409, 1392, 1253, 1165, 1073, 1025, 892 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 8.0 Hz, 2 H), 7.33 (d, *J* = 8.0 Hz, 2 H), 7.10 (d, *J* = 8.0 Hz, 4 H), 6.56 (d, $^{2}J_{P-H}$ = 29.0 Hz, 1 H), 4.25−4.13 (m, 4 H), 2.43 (s, 3 H), 2.34 (s, 3 H), 1.38 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 151.9 (d, $^{3}J_{P-C}$ = 17.5 Hz), 139.7, 139.1, 134.8, 130.5, 128.9, 128.7, 128.4, 127.1, 63.4 (d, $^{2}J_{P-C}$ = 6.3 Hz), 21.4, 21.3, 16.2 (d, $^{3}J_{P-C}$ = 7.5 Hz).

MS (EI): *m/z*: 360 (87) $[M^+]$, 359 (43), 223 (100), 179 (63).

HRMS (EI): *m/z* $[M^+]$ calcd for $C_{19}H_{25}N_2O_3P$: 360.1603; found: 360.1607.

1-[Bis(4-methoxyphenyl)methylidene]-2-(diethoxyphosphoryl)hydrazine (1c)

This was prepared from $(4\text{-MeOC}_6H_4)_2CO$ (1.21 g, 5.0 mmol) and $H_2NNHP(O)(OEt)_2$ (1.26 g, 7.5 mmol). The crude product was purified by column chromatography [silica gel, PE–EtOAc (1:1)] to give a colorless solid; yield: 1.71 g (87%); mp 51–54 °C.

IR (KBr): 3233, 2988, 2940, 1608, 1510, 1469, 1415, 1289, 1249, 1177, 1164, 1030 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 8.5 Hz, 2 H), 7.14 (d, *J* = 8.5 Hz, 2 H), 7.03 (d, *J* = 8.5 Hz, 2 H), 6.81 (d, *J* = 8.5 Hz, 2 H), 6.54 (d, $^{2}J_{P-H}$ = 29.0 Hz, 1 H), 4.24–4.12 (m, 4 H), 3.86 (s, 3 H), 3.78 (s, 3 H), 1.36 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.4, 151.4 (d, $^{3}J_{P-C}$ = 17.5 Hz), 130.5, 130.0, 128.6, 123.6, 115.2, 113.5, 63.4, 63.3, 55.4 (d, $^{2}J_{P-C}$ = 6.3 Hz), 16.2 (d, $^{3}J_{P-C}$ = 6.3 Hz).

LC/MS (ESI): *m/z* 393 $[M + H]^+$.

HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{19}H_{26}N_2O_5P$: 393.1574; found: 393.1587.

1-[Bis(4-Chlorophenyl)methylidene]-2-(diethoxyphosphoryl)hydrazine (1d)

This was prepared from $(4\text{-ClC}_6H_4)_2CO$ (1.26 g, 5.0 mmol) and $H_2NNHP(O)(OEt)_2$ (1.26 g, 7.5 mmol). The crude product was purified by column chromatography [silica gel, PE–EtOAc (6:1)] to give a white solid; yield: 1.81 g (90%); mp 105–107 °C.

IR (KBr): 3100, 2930, 1560, 1490, 1421, 1398, 1249, 1168, 1090, 1037, 1014 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 8.0 Hz, 2 H), 7.40 (d, *J* = 8.0 Hz, 2 H), 7.26 (d, *J* = 8.0 Hz, 2 H), 7.17 (d, *J* = 8.0 Hz, 2 H), 6.53 (d, $^{2}J_{P-H}$ = 29.0 Hz, 1 H), 4.24–4.12 (m, 4 H), 1.37 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.3 (d, $^{3}J_{P-C}$ = 17.5 Hz), 136.2, 135.4, 135.3, 130.4, 130.0, 129.4, 128.5, 128.2, 63.6 (d, $^{2}J_{P-C}$ = 5.0 Hz), 16.2 (d, $^{3}J_{P-C}$ = 6.3 Hz).

LC/MS (ESI): *m/z* 405 $[M + H\ (^{37}Cl)]^+$, 403 $[M + H\ (^{37}Cl, ^{35}Cl)]^+$, 401 $[M + H\ (^{35}Cl)]^+$.

HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{17}H_{20}Cl_2N_2O_3P$: 401.0583; found: 401.0592.

1-[Bis(4-Fluorophenyl)methylidene]-2-(diethoxyphosphoryl)hydrazine (1e)

This was prepared from $(4\text{-FC}_6H_4)_2CO$ (1.09 g, 5.0 mmol) and $H_2NNHP(O)(OEt)_2$ (1.26 g, 7.5 mmol). The crude product was purified by column chromatography [silica gel, PE–EtOAc (6:1)] to give a white solid; yield: 1.34 g (73%); mp 108–110 °C.

IR (KBr): 3134, 2983, 1610, 1507, 1414, 1254, 1225, 1153, 1057, 1034, 974 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50–7.46 (m, 2 H), 7.29–7.23 (m, 4 H), 7.03–6.99 (m, 2 H), 6.53 (d, $^{2}J_{P-H}$ = 28.5 Hz, 1 H), 4.28–4.15 (m, 4 H), 1.40 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.4 (d, $^{1}J_{F-C}$ = 248 Hz), 163.3 (d, $^{1}J_{F-C}$ = 250 Hz), 149.6 (d, $^{3}J_{P-C}$ = 17.5 Hz), 133.4 ($^{4}J_{F-C}$ = 3.8 Hz), 130.7 ($^{3}J_{F-C}$ = 8.8 Hz), 128.8 ($^{3}J_{F-C}$ = 8.8 Hz), 127.2 ($^{4}J_{F-C}$ = 3.8 Hz), 117.2 ($^{2}J_{F-C}$ = 21.3 Hz), 115.2 ($^{2}J_{F-C}$ = 21.3 Hz), 63.6 (d, $^{2}J_{P-C}$ = 5.0 Hz), 16.2 (d, $^{3}J_{P-C}$ = 6.3 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –109.9 (m, Ar-F), –111.9 (m, Ar-F).

MS (EI): *m/z* (%) 368 (70) $[M^+]$, 367 (35), 244 (36), 231 (85), 216 (23), 202 (59), 201 (100).

HRMS (EI): *m/z* $[M^+]$ calcd for $C_{17}H_{19}F_2N_2O_3P$: 368.1101; found: 368.1099.

1-[Bis(3-tolyl)methylidene]-2-(diethoxyphosphoryl)hydrazine (1f)

This was prepared from $(3\text{-Tol})_2CO$ (1.05 g, 5.0 mmol) and $H_2NNHP(O)(OEt)_2$ (1.26 g, 7.5 mmol). The crude product was purified by column chromatography [silica gel, PE–EtOAc (4:1)] to give a yellow oil; yield: 1.62 g (90%).

IR (KBr): 3147, 2982, 1602, 1585, 1571, 1483, 1399, 1257, 1166, 1143, 1029, 973 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.42 (t, *J* = 8.0 Hz, 1 H), 7.35 (s, 1 H), 7.28 (t, *J* = 8.5, 1 H), 7.19 (t, *J* = 7.5 Hz, 1 H), 7.13 (d, *J* = 7.0 Hz, 1 H), 7.01 (s, 2 H), 6.57 (d, $^2J_{P-H}$ = 29.0 Hz, 1 H), 4.26–4.14 (m, 4 H), 2.41 (s, 3 H), 2.31 (s, 3 H), 1.39 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.1 (d, $^3J_{P-C}$ = 17.5 Hz), 139.7, 137.8, 137.3, 131.8, 130.4, 129.9, 129.7, 128.8, 128.1, 127.5, 125.4, 124.4, 63.4 (d, $^2J_{P-C}$ = 6.3 Hz), 21.5, 21.4, 16.2 (d, $^3J_{P-C}$ = 6.3 Hz).

LC/MS (ESI): *m/z* 361 $[M + H]^+$.

HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{19}H_{26}N_2O_3P$: 361.1676; found: 361.1683.

1-[Bis(3-chlorophenyl)methylidene]-2-(diethoxyphosphoryl)hydrazine (1g)

This was prepared from $(3\text{-}ClC_6H_4)_2CO$ (1.26 g, 5.0 mmol) and $H_2NNHP(O)(OEt)_2$ (1.26 g, 7.5 mmol). The crude product was purified by column chromatography [silica gel, PE–EtOAc (6:1)] to give a white solid; yield: 1.22 g (61%); mp 56–59 °C.

IR (KBr): 3121, 2986, 1580, 1438, 1245, 1180, 1030 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.52 (d, *J* = 5.0 Hz, 2 H), 7.50 (t, *J* = 1.5 Hz, 1 H), 7.31 (d, *J* = 7.5 Hz, 2 H), 7.25–7.21 (m, 2 H), 7.12 (t, *J* = 4.0 Hz, 1 H), 6.56 (d, $^2J_{P-H}$ = 29.0 Hz, 1 H), 4.27–4.14 (m, 4 H), 1.39 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.5 (d, $^3J_{P-C}$ = 17.5 Hz), 138.6, 136.2, 134.5, 132.8, 131.4, 130.3, 129.6, 129.3, 128.5, 126.7, 126.6, 125.2, 63.7 (d, $^2J_{P-C}$ = 6.3 Hz), 16.2 (d, $^3J_{P-C}$ = 6.3 Hz).

MS (EI): *m/z* (%) 404 (8) [M^+ (^{37}Cl)], 402 (33) [M^+ (^{37}Cl, ^{35}Cl)], 400 (60) [M^+ (^{35}Cl)], 276 (58), 263 (58), 199 (100).

HRMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{17}H_{20}Cl_2N_2O_3P$: 401.0583; found: 401.0507.

1-(Diethoxyphosphoryl)-2-[(2-methoxyphenyl)(phenyl)methylidene]hydrazine (1h)

This was prepared from $2\text{-}MeOC_6H_4COPh$ (1.06 g, 5.0 mmol) and $H_2NNHP(O)(OEt)_2$ (1.26 g, 7.5 mmol). The crude product was purified by column chromatography [silica gel, PE–EtOAc (2:1)] to give a colorless solid; yield: 1.01 g (56%); mp 100–101 °C.

IR (KBr): 3146, 2980, 2836, 1602, 1491, 1416, 1253, 1166, 1058, 1023, 898, 801, 762, 698, 512 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 2.0 Hz, 1 H), 7.51 (d, *J* = 4.0 Hz, 1 H), 7.49–7.46 (m, 1 H), 7.30 (d, *J* = 2.0 Hz, 2 H), 7.29 (d, *J* = 1.0 Hz, 1 H), 7.11–7.07 (m, 2 H), 7.05 (d, *J* = 8.5 Hz, 1 H), 6.48 (d, $^2J_{P-H}$ = 29.0 Hz, 1 H), 4.26–4.14 (m, 4 H), 3.75 (s, 3 H), 1.38 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.7, 149.1 (d, $^3J_{P-C}$ = 17.5 Hz), 137.2, 131.5, 130.1, 128.9, 128.2, 126.7, 121.7, 119.9, 111.8, 63.4 (d, $^2J_{P-C}$ = 5.0 Hz), 55.5, 16.2 (d, $^3J_{P-C}$ = 7.5 Hz).

MS (EI): *m/z* (%) 362 (40) [M^+], 195 (100), 167 (47).

HRMS (EI) *m/z* $[M^+]$ calcd for $C_{18}H_{23}N_2O_4P$: 362.1395; found: 362.1392.

1-(Diethoxyphosphoryl)-2-[(1-naphthyl)(phenyl)methylidene]hydrazine (1i)

This was prepared from 1-naphthyl(phenyl)methanone (1.16 g, 5.0 mmol) and $H_2NNHP(O)(OEt)_2$ (1.26 g, 7.5 mmol). The crude product was purified by column chromatography [silica gel, PE–EtOAc (4:1)] to give a colorless solid; yield: 1.64 g (86%); mp 122–123 °C.

IR (KBr): 3124, 1587, 1506, 1429, 1249, 1162, 1027, 895 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.5 Hz, 1 H), 7.96 (d, *J* = 8.0 Hz, 1 H), 7.61 (t, *J* = 7.5 Hz, 1 H), 7.56–7.52 (m, 4 H), 7.43 (t, *J* = 7.5 Hz, 1 H), 7.36 (d, *J* = 7.0 Hz, 1 H), 7.33–7.27 (m, 3 H), 6.34 (d, $^2J_{P-H}$ = 29.5 Hz, 1 H), 4.23–4.08 (m, 4 H), 1.42–1.37 (m, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.6 (d, $^3J_{P-C}$ = 18.8 Hz), 137.3, 134.0, 130.2, 129.5, 129.2, 128.9, 128.3, 127.4, 127.1, 127.0, 126.8, 125.9, 124.7, 63.5 (d, $^2J_{P-C}$ = 6.3 Hz), 63.3 (d, $^2J_{P-C}$ = 5.0 Hz), 16.3 (d, $^3J_{P-C}$ = 6.3 Hz).

MS (EI): *m/z* (%) 382 (3) [M^+], 231 (20), 230 (100), 229 (41).

HRMS (EI): *m/z* $[M^+]$ calcd for $C_{21}H_{23}N_2O_3P$: 382.1446; found: 382.1444.

1-(Diethoxyphosphoryl)-2-(1-phenylethylidene)hydrazine (1j)[12]

This was prepared from PhCOMe (0.60 g, 5.0 mmol) and $H_2NNHP(O)(OEt)_2$ (0.84 g, 5.0 mmol), but without using HCl as a catalyst. The crude product was purified by column chromatography [silica gel, PE–EtOAc (8:1)] to give a colorless solid; yield: 1.32 g (98%); mp 49–52 °C.

IR (KBr): 3160, 2984, 1610, 1446, 1257, 1037, 976, 764, 694 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.69 (dd, *J* = 8.0, 1.5 Hz, 2 H), 7.37–7.30 (m, 3 H), 7.11 (d, $^2J_{P-H}$ = 27.0 Hz, 1 H), 4.26–4.13 (m, 4 H), 2.19 (s, 3 H), 1.35 (td, *J* = 7.0 Hz, 0.5 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.2 (d, $^3J_{P-C}$ = 17.5 Hz), 138.4, 128.7, 128.3, 125.9, 63.5 (d, $^2J_{P-C}$ = 6.3 Hz), 16.2 (d, $^3J_{P-C}$ = 6.3 Hz), 12.2.

LC/MS (ESI): *m/z* 271 $[M + H]^+$.

1-(Diethoxyphosphoryl)-2-[1-(4-methoxyphenyl)ethylidene]hydrazine (1k)[13]

This was prepared from $4\text{-}MeOC_6H_4COMe$ (0.60 g, 5.0 mmol) and $H_2NNHP(O)(OEt)_2$ (1.01 g, 6.0 mmol), but without using HCl as a catalyst. The crude product was purified by column chromatography [silica gel, PE–EtOAc (2:1)] to give a colorless solid; yield: 1.43 g (95%); mp 104–105 °C.

IR (KBr): 3173, 2981, 1609, 1513, 1454, 1441, 1311, 1253, 1185, 1099, 1027, 983 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 9.0 Hz, 2 H), 6.86 (d, *J* = 9.0 Hz, 2 H), 7.1–7.3 (br s, 1 H, NH), 4.25–4.12 (m, 4 H), 3.80 (s, 3 H), 2.16 (s, 3 H), 1.34 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.1, 148.1 (d, $^3J_{P-C}$ = 18.8 Hz), 127.3, 115.0, 113.6, 63.4 (d, $^2J_{P-C}$ = 5.0 Hz), 55.3, 16.2 (d, $^3J_{P-C}$ = 6.3 Hz), 12.3.

LC/MS (ESI): *m/z* 300 $[M + H]^+$.

1-(Diethoxyphosphoryl)-2-(phenylmethylidene)hydrazine (1l)[12]

This was prepared from PhCHO (0.53 g, 5.0 mmol) and $H_2NNHP(O)(OEt)_2$ (0.84 g, 5.0 mmol), but without using HCl as a catalyst. The crude product was purified by column chromatography [silica gel, PE–EtOAc (8:1)] to give a colorless solid; yield: 1.16 g (91%); mp 81–84 °C.

IR (KBr): 3169, 2981, 1605, 1474, 1446, 1239, 1166, 1099, 1054, 1027, 978 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.39–8.25 (br s, 1 H), 7.85 (s, 1 H), 7.61 (dd, *J* = 8.0 Hz, 1.5 Hz, 2 H), 7.37–7.31 (m, 3 H), 4.27–4.14 (m, 4 H), 1.37 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.8 (d, $^3J_{P-C}$ = 18.8 Hz), 134.5, 129.4, 128.6, 126.7, 63.5 (d, $^2J_{P-C}$ = 6.3 Hz), 16.2 (d, $^2J_{P-C}$ = 7.5 Hz).

MS (EI): *m/z* (%) 256 (15) [M^+], 153 (27), 126 (100), 109 (21), 98 (93), 81 (47).

1,3,4-Triphenylisoquinoline (3aa);[7e] Typical Procedure
A 15-mL, oven-dried, N_2-purged flask was charged with RhCp*$(MeCN)_3(SbF_6)_2$ (2.5 mg, 0.009 mmol) and $Cu(OAc)_2·H_2O$ (125.7 mg, 0.63 mmol) then a soln of hydrazone **1a** (99.7 mg, 0.3 mmol) and PhC≡CPh (64.2 mg, 0.36 mmol) in toluene (1.5 mL) was added. The mixture was stirred at 90 °C for 18 h, cooled to r.t., and diluted with EtOAc (10 mL) and H_2O (30 mL). The aqueous layer was separated and extracted with EtOAc (3 × 10 mL). The organic phases were combined, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by column chromatography [silica gel, PE–EtOAc (30:1)] to give a colorless solid; yield: 99.7 mg (93%); mp 195–197 °C.

IR (KBr): 3054, 1610, 1540, 1386, 1336, 1073, 1030, 981, 1073, 1030, 981 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 8.5 Hz, 1 H), 7.83 (d, *J* = 7.0 Hz, 2 H), 7.73 (d, *J* = 8.5 Hz, 1 H), 7.62 (t, *J* = 7.0 Hz, 1 H), 7.58–7.51 (m, 4 H), 7.44–7.37 (m, 5 H), 7.30 (d, *J* = 6.5 Hz, 2 H), 7.21–7.16 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.8, 149.6, 140.8, 139.7, 137.5, 137.1, 131.4, 130.5, 130.3, 130.1, 129.9, 128.7, 128.4, 128.4, 127.6, 127.4, 127.1, 126.7, 126.1, 125.5.

LC/MS (ESI): *m/z* 358 $[M + H]^+$.

6-Methyl-3,4-diphenyl-1-(4-tolyl)isoquinoline (3ba)
This was prepared from hydrazone **1b** (108.1 mg, 0.3 mmol), RhCp*$(MeCN)_3(SbF_6)_2$ (2.5 mg, 0.009 mmol), PhC≡CPh (64.2 mg, 0.36 mmol), and $Cu(OAc)_2·H_2O$ (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 15 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (30:1)] gave a colorless solid; yield: 102.8 mg (89%); mp 167–169 °C.

IR (KBr): 3050, 2920, 1915, 1770, 1615, 1541, 1492, 1444, 1377, 1328, 983, 706 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.5 Hz, 1 H), 7.76 (d, *J* = 8.0 Hz, 2 H), 7.51 (s, 1 H), 7.46–7.36 (m, 8 H), 7.33–7.31 (m, 2 H), 7.23–7.17 (m, 3 H), 2.50 (s, 3 H), 2.46 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.5, 149.7, 141.0, 140.4, 138.4, 137.8, 137.3, 137.0, 131.5, 130.5, 130.2, 129.2, 129.0, 128.8, 128.3, 127.6, 127.5, 127.2, 127.0, 124.9, 123.9, 22.2, 21.4.

MS (EI): *m/z* (%) 385 (69) $[M^+]$, 384 (100).

HRMS (EI) *m/z* $[M^+]$ calcd for $C_{29}H_{23}N$: 385.1830; found: 385.1834.

6-Methoxy-1-(4-methoxyphenyl)-3,4-diphenylisoquinoline (3ca)
This was prepared from hydrazone **1c** (117.7 mg, 0.3 mmol), RhCp*$(MeCN)_3(SbF_6)_2$ (2.5 mg, 0.009 mmol), PhC≡CPh (64.2 mg, 0.36 mmol), and $Cu(OAc)_2·H_2O$ (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 14 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (10:1)] gave a colorless solid; yield: 102.7 mg (82%); mp 168–172 °C.

IR (KBr): 3053, 2837, 2048, 1958, 1609, 1514, 1407, 1251, 1219, 1178, 1032, 840, 706 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 9.0 Hz, 1 H), 7.78 (d, *J* = 8.5 Hz, 2 H), 7.43–7.41 (m, 2 H), 7.39 (d, *J* = 7.0 Hz, 2 H), 7.36 (d, *J* = 7.0 Hz, 1 H), 7.34–7.30 (m, 2 H), 7.21–7.14 (m, 4 H), 7.09 (d, *J* = 8.5 Hz, 2 H), 6.98 (d, *J* = 2.0 Hz, 1 H), 3.91 (s, 3 H), 3.74 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.6, 160.1, 158.8, 150.1, 139.2, 137.9, 131.6, 131.3, 130.5, 129.6, 128.8, 128.4, 127.5, 127.3, 127.0, 121.2, 118.8, 113.8, 104.3, 55.5, 55.3.

MS (EI): *m/z* (%) 417 (73) $[M^+]$, 416 (100).

Anal. Calcd for $C_{29}H_{23}NO_2$: C, 83.43; H, 5.55; N, 3.35. Found: C, 83.56; H, 5.54; N, 3.42.

6-Chloro-1-(4-chlorophenyl)-3,4-diphenylisoquinoline (3da)
This was prepared from hydrazone **1d** (120.4 mg, 0.3 mmol), RhCp*$(MeCN)_3(SbF_6)_2$ (2.5 mg, 0.009 mmol), PhC≡CPh (64.2 mg, 0.36 mmol), and $Cu(OAc)_2·H_2O$ (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 28 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (30:1)] gave a colorless solid; yield: 95.9 mg (75%); mp 179–180 °C.

IR (KBr): 3056, 3027, 1946, 1602, 1538, 1493, 1443, 1403, 1381, 1328, 1090, 981, 839 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 9.0 Hz, 1 H), 7.75 (d, *J* = 8.0 Hz, 2 H), 7.70 (d, *J* = 2.0 Hz, 1 H), 7.54 (d, *J* = 8.5 Hz, 2 H), 7.32 (dd, *J* = 9.0 Hz, 2.0 Hz, 1 H), 7.43–7.38 (m, 5 H), 7.28 (d, *J* = 2.0 Hz, 1 H), 7.26 (s, 1 H), 7.21–7.19 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.5, 150.9, 140.3, 138.1, 137.8, 136.7, 136.7, 135.1, 131.6, 131.2, 130.4, 129.3, 129.0, 128.7, 128.7,, 127.8, 127.8, 127.7, 127.4, 125.1, 123.6.

MS (EI): *m/z* (%) 429 (8) $[M^+ (^{37}Cl)]$, 428 (20), 427 (42) $[M^+ (^{37}Cl, ^{35}Cl)]$, 426 (79), 425 (61) $[M^+ (^{35}Cl)]$, 424 (100).

Anal. Calcd for $C_{27}H_{17}Cl_2N$: C, 76.06; H, 4.02; N, 3.29. Found: C, 75.79; H, 4.03; N, 3.04.

6-Fluoro-1-(4-fluorophenyl)-3,4-diphenylisoquinoline (3ea)
This was prepared hydrazone **1e** (110.5 mg, 0.3 mmol), RhCp*$(MeCN)_3(SbF_6)_2$ (2.5 mg, 0.009 mmol), PhC≡CPh (64.2 mg, 0.36 mmol), and $Cu(OAc)_2·H_2O$ (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 25 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (30:1)] gave a colorless solid; yield: 94.4 mg (80%); mp 171–174 °C.

IR (KBr): 3070, 1899, 1622, 1601, 1501, 1383, 1332, 1256, 1221, 1180, 1158, 1111, 987, 846 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 8.20 (dd, *J* = 9.0, 6.0 Hz, 1 H), 7.87–7.83 (m, 2 H), 7.60 (td, *J* = 9.0, 2.5 Hz, 1 H), 7.48–7.41 (m, 5 H), 7.40–7.37 (m, 2 H), 7.33–7.31 (m, 2 H), 7.25–7.21 (m, 3 H), 7.17 (dd, *J* = 11.0, 2.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.3 (d, $^1J_{F–C}$ = 248 Hz), 163.2 ($^1J_{F–C}$ = 252 Hz), 158.6, 150.6, 140.5, 139.1 ($^3J_{F–C}$ = 10.0 Hz), 137.0, 135.6, 132.1, 132.0, 131.2, 130.5 ($^3J_{F–C}$ = 10.0 Hz), 130.4, 129.7 ($^4J_{F–C}$ = 5.0 Hz), 128.7, 127.7, 127.4, 122.7, 117.1 ($^2J_{F–C}$ = 25.0 Hz), 115.5 ($^2J_{F–C}$ = 21.3 Hz), 109.8 ($^2J_{F–C}$ = 21.3 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –106.9 (s, Ar-F), –112.7 (s, Ar-F).

MS (EI): *m/z* (%) 393 (69) $[M^+]$, 392 (100).

HRMS (EI) *m/z* $[M^+]$ calcd for $C_{27}H_{17}F_2N$: 393.1329; found: 393.1330.

7-Methyl-3,4-diphenyl-1-(3-tolyl)isoquinoline (3fa)
This was prepared from **1f** (108.1 mg, 0.3 mmol), RhCp*$(MeCN)_3(SbF_6)_2$ (2.5 mg, 0.009 mmol), PhC≡CPh (64.2 mg, 0.36 mmol), and $Cu(OAc)_2·H_2O$ (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 22 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (30:1)] gave a colorless solid; yield: 97.1 mg (84%); mp 161–162 °C.

IR (KBr): 3054, 2917, 1960, 1542, 1504, 1382, 1320, 832 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 7.86 (s, 1 H), 7.59 (dd, J_1 = 8.5 Hz, J_2 = 1.5 Hz, 1 H), 7.56 (s, 1 H), 7.53–7.47 (m, 3 H), 7.45–7.34 (m, 6 H), 7.31 (d, *J* = 1.5 Hz, 1 H), 7.29 (t, *J* = 1.5 Hz, 1 H), 7.22–7.19 (m, 3 H), 2.46 (s, 3 H), 2.45 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.1, 137.7, 136.6, 135.3, 132.3, 131.4, 130.8, 130.5, 129.7, 129.3, 128.3, 128.1, 127.5, 127.4, 127.3, 126.9, 126.4, 125.9, 125.7, 21.9, 21.6.

MS (EI): *m/z* (%) 385 (67) $[M^+]$, 384 (100).

Anal. Calcd for $C_{29}H_{23}N$: C, 90.35; H, 6.01; N, 3.63. Found: C, 90.36; H, 5.86; N, 3.49.

7-Chloro-1-(3-chlorophenyl)-3,4-diphenylisoquinoline (3ga)
This was prepared from hydrazone **1g** (120.4 mg, 0.3 mmol), RhCp*(MeCN)$_3$(SbF$_6$)$_2$ (2.5 mg, 0.009 mmol), PhC≡CPh (64.2 mg, 0.36 mmol), and Cu(OAc)$_2$·H$_2$O (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 14 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (30:1)] gave a colorless solid; yield: 98.5 mg (77%); mp 181–183 °C.

IR (KBr): 3056, 1955, 1598, 1564, 1541, 1496, 1378, 1078, 882, 838 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.08 (d, *J* = 2.0 Hz, 1 H), 7.81 (d, *J* = 1.0 Hz, 1 H), 7.69 (d, *J* = 9.0 Hz, 1 H), 7.67–7.65 (m, 1 H), 7.54 (dd, *J* = 9.0, 2.0 Hz, 1 H), 7.51 (d, *J* = 1.0 Hz, 1 H), 7.50 (d, *J* = 1.0 Hz, 1 H), 7.42–7.37 (m, 5 H), 7.28 (d, *J* = 2.0 Hz, 1 H), 7.28 (d, *J* = 2.0 Hz, 1 H), 7.22–7.19 (m, 3 H).

^{13}C NMR (125 MHz, CDCl$_3$): δ = 157.4, 150.1, 140.9, 140.2, 136.8, 135.5, 134.7, 132.9, 131.2, 131.1, 130.4, 130.2, 130.2, 129.7, 129.0, 128.5, 128.3, 128.2, 127.7, 127.4, 126.0, 125.7.

MS (EI): *m/z* (%) 429 (8) [M$^+$ (^{37}Cl)], 428 (18), 427 (42) [M$^+$ (^{37}Cl, ^{35}Cl)], 426 (73), 425 (64) [M$^+$ (^{35}Cl)], 424 (100).

HRMS (EI): *m/z* [M – H]$^+$ calcd for $C_{27}H_{16}Cl_2N$: 424.0660; found: 424.0659.

1-(2-Methoxyphenyl)-3,4-diphenylisoquinoline (3ha)
This was prepared from hydrazone **1h** (108.7 mg, 0.3 mmol), RhCp*(MeCN)$_3$(SbF$_6$)$_2$ (2.5 mg, 0.009 mmol), PhC≡CPh (64.2 mg, 0.36 mmol), and Cu(OAc)$_2$·H$_2$O (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 19 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (15:1)] gave a colorless solid; yield: 94.2 mg (81%); mp 191–193 °C.

IR (KBr): 3057, 2835, 1961, 1720, 1542, 1433, 1380, 1331, 1246, 1048, 1020, 981, 966, 702, 569 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.81 (d, *J* = 8.0 Hz, 1 H), 7.70 (d, *J* = 8.5 Hz, 1 H), 7.59–7.54 (m, 2 H), 7.51–7.46 (m, 2 H), 7.42–7.37 (m, 6 H), 7.25 (s, 1 H), 7.19–7.14 (m, 4 H), 7.09 (d, *J* = 8.0 Hz, 1 H), 3.78 (s, 3 H).

^{13}C NMR (125 MHz, CDCl$_3$): δ = 158.2, 157.4, 149.8, 140.9, 137.6, 136.3, 131.8, 131.4, 130.6, 130.1, 129.9, 129.0, 128.3, 128.2, 128.0, 127.6, 127.3, 126.9, 126.4, 126.4, 125.8, 121.0, 111.2, 55.6.

MS (EI): *m/z* (%) 387 (100) [M$^+$], 386 (98), 370 (63), 70 (83), 61 (87).

HRMS (EI) *m/z* [M$^+$] calcd for $C_{28}H_{21}NO$: 387.1623; found: 387.1625.

Crystallographic data:[14] $C_{28}H_{21}NO$, M = 387.462, monoclinic, $P2_1/c$ (No. 14), *a* = 10.398(3) Å, *b* = 11.246 (2) Å, *c* = 18.179 (4) Å, β = 100.392 (18)°, V = 2090.9 (8) Å^3, Z = 4; Crystal size: 0.25 × 0.21 × 0.19 mm, T = 295 K, ρ_{calcd} = 1.231 g·cm^{-3}, *R*1 = 0.0430 [I > 4σ(I)], *wR*2 = 0.1195 (all data), GOF = 1.045, reflections collected/unique: 4635/3027 (R_{int} = 0.0182), Data: 3027, restraints: 0, parameters: 272.

1-(1-Naphthyl)-3,4-diphenylisoquinoline (3ia)
This was prepared from hydrazone **1i** (114.7 mg, 0.3 mmol), RhCp*(MeCN)$_3$(SbF$_6$)$_2$ (2.5 mg, 0.009 mmol), PhC≡CPh (64.2 mg, 0.36 mmol), and Cu(OAc)$_2$·H$_2$O (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 23 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (30:1)] gave a colorless solid; yield: 105.1 mg (86%); mp 191–193 °C.

IR (KBr): 3047, 1609, 1543, 1498, 1368, 1326, 969, 799, 770 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.01 (d, *J* = 8.0 Hz, 1 H), 7.97 (d, *J* = 8.0 Hz, 1 H), 7.77 (d, *J* = 8.5 Hz, 1 H), 7.73 (dd, *J* = 7.0, 1.0 Hz, 1 H), 7.70 (d, *J* = 8.5 Hz, 1 H), 7.65 (t, *J* = 7.5 Hz, 2 H), 7.60 (td, *J* = 7.5, 1.0 Hz, 1 H), 7.51 (td, *J* = 7.5, 1.0 Hz, 1 H), 7.44–7.36 (m, 9 H), 7.20–7.13 (m, 3 H).

^{13}C NMR (125 MHz, CDCl$_3$): δ = 159.6, 149.9, 140.7, 137.5, 137.2, 136.6, 133.8, 132.6, 131.5, 131.4, 130.6, 130.3, 128.9, 128.5, 128.4, 128.3, 128.1, 127.9, 127.7, 127.4, 127.1, 127.1, 126.7, 126.3, 126.0, 126.0, 125.3.

MS (EI): *m/z* (%) 407 (63) [M$^+$], 406 (100).

HRMS (EI): *m/z* [M – H]$^+$ calcd for $C_{31}H_{20}N$: 406.1596; found: 406.1601.

1-Methyl-3,4-diphenylisoquinoline (3ja)[7c]
This was prepared from hydrazone **1j** (81.1 mg, 0.3 mmol), RhCp*(MeCN)$_3$(SbF$_6$)$_2$ (2.5 mg, 0.009 mmol), PhC≡CPh (64.2 mg, 0.36 mmol), and Cu(OAc)$_2$·H$_2$O (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 26 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (30:1)] gave a colorless solid; yield: 26.6 mg (30%); mp 149–153 °C.

IR (KBr): 3055, 1610, 1552, 1432, 1390, 1334, 1026, 767 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.23–8.19 (m, 1 H), 7.69–7.65 (m, 1 H), 7.62–7.58 (m, 2 H), 7.38–7.31 (m, 5 H), 7.24–7.17 (m, 5 H), 3.09 (s, 3 H).

^{13}C NMR (125 MHz, CDCl$_3$): δ = 157.9, 149.6, 141.2, 137.7, 136.1, 131.6, 130.4, 130.1, 129.3, 128.3, 127.8, 127.3, 127.1, 126.7, 126.4, 126.3, 125.7, 22.9.

LC/MS (ESI): *m/z* 296 [M + H]$^+$.

6-Methoxy-1-methyl-3,4-diphenylisoquinoline (3ka)[7f]
This was prepared from hydrazone **1k** (90.1 mg, 0.3 mmol), RhCp*(MeCN)$_3$(SbF$_6$)$_2$ (2.5 mg, 0.009 mmol), PhC≡CPh (64.2 mg, 0.36 mmol), and Cu(OAc)$_2$·H$_2$O (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 23 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (10:1)] gave a colorless solid; yield: 35.1 mg (36%); mp 172–183 °C.

IR (KBr): 3081, 1619, 1575, 1501, 1443, 1411, 1280, 1231, 1207, 1071, 1027, 854 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.13 (d, *J* = 9.0 Hz, 1 H), 7.36–7.31 (m, 5 H), 7.25–7.17 (m, 6 H), 6.92 (d, *J* = 2.5 Hz, 1 H), 3.74 (s, 3 H), 3.07 (s, 3 H).

^{13}C NMR (125 MHz, CDCl$_3$): δ = 160.9, 157.0, 150.8, 141.9, 138.4, 136.7, 131.3, 130.3, 128.9, 128.3, 127.6, 127.5, 127.2, 127.2, 121.9, 119.0, 104.6, 55.3, 22.6.

LC/MS (ESI): *m/z* 326 [M + H]$^+$.

1-Phenyl-3,4-bis(4-tolyl)isoquinoline (3ab)[7e]
This was prepared from hydrazone **1a** (99.7 mg, 0.3 mmol), RhCp*(MeCN)$_3$(SbF$_6$)$_2$ (2.5 mg, 0.009 mmol), bis(4-tolyl)ethyne (74.3 mg, 0.36 mmol), and Cu(OAc)$_2$·H$_2$O (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 22 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (30:1)] gave a colorless solid; yield: 93.7 mg (81%); mp 169–172 °C.

IR (KBr): 3051, 1610, 1542, 1512, 1441, 1385, 1333, 1183, 1024, 981, 830 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.21 (AA′ of AA′BB′, *J* = 8.0 Hz, 1 H), 8.87 (AA′ of AA′BB′, *J* = 8.0 Hz, 2 H), 7.77 (BB′ of AA′BB′, *J* = 8.0 Hz, 1 H), 7.62–7.50 (m, 5 H), 7.41 (BB′ of AA′BB′, *J* = 8.0 Hz, 2 H), 7.25–7.24 (m, 4 H), 7.05 (d, *J* = 8.0 Hz, 2 H), 2.46 (s, 3 H), 2.32 (s, 3 H).

^{13}C NMR (125 MHz, CDCl$_3$): δ = 159.6, 149.6, 139.9, 138.1, 137.3, 136.9, 136.7, 134.7, 131.2, 130.4, 130.4, 129.9, 129.6, 129.2, 128.6, 128.4, 128.3, 127.5, 126.5, 126.1, 125.4, 21.4, 21.3.

MS (EI): *m/z* (%) 385 (94) [M$^+$], 384 (100).

3,4-Bis(4-methoxyphenyl)-1-phenylisoquinoline (3ac)[7e]
This was prepared from hydrazone **1a** (99.7 mg, 0.3 mmol), RhCp*(MeCN)$_3$(SbF$_6$)$_2$ (2.5 mg, 0.009 mmol), 1,2-bis(4-methoxyphenyl)ethyne (85.8 mg, 0.36 mmol), and Cu(OAc)$_2$·H$_2$O (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 18 h at 90 °C. Purification

by column chromatography [silica gel, PE–EtOAc (10:1)] gave a colorless solid; yield: 96.7 mg (77%); mp 176–179 °C.

IR (KBr): 3055, 1894, 1607, 1573, 1511, 1462, 1440, 1387, 1364, 1331, 1290, 1247, 1179, 1107, 1031, 981, 829 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 8.0 Hz, 1 H), 7.85 (t, *J* = 7.0 Hz, 2 H), 7.77 (t, *J* = 8.5 Hz, 1 H), 7.61–7.49 (m, 5 H), 7.44 (t, *J* = 8.5 Hz, 2 H), 7.24 (d, *J* = 5.5 Hz, 2 H), 6.98 (d, *J* = 8.5 Hz, 2 H), 6.78 (d, *J* = 9.0 Hz, 2 H), 3.88 (s, 3 H), 3.78 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.5, 158.8, 158.7, 149.4, 139.9, 137.5, 133.5, 132.5, 131.8, 130.3, 129.9, 129.0, 128.6, 128.3, 127.5, 126.4, 126.0, 125.3, 114.0, 113.2, 55.3, 55.2.

LC/MS (ESI): *m/z* 418 $[M + H]^+$.

3,4-Bis(4-chlorophenyl)-1-phenylisoquinoline (3ad)[7e]
This was prepared from hydrazone **1a** (99.7 mg, 0.3 mmol), $RhCp^*(MeCN)_3(SbF_6)_2$ (2.5 mg, 0.009 mmol), 1,2-bis(4-chlorophenyl)ethyne (89.0 mg, 0.36 mmol), and $Cu(OAc)_2·H_2O$ (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 29 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (30:1)] gave a colorless solid; yield: 93.4 mg (73%); mp 192–195 °C.

IR (KBr): 3062, 1906, 1609, 1558, 1540, 1491, 1338, 1178, 1150, 1094, 1013, 980 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 8.0 Hz, 1 H), 7.82–7.81 (m, 2 H), 7.69 (d, *J* = 8.5 Hz, 1 H), 7.64 (d, *J* = 8.0 Hz, 1 H), 7.59–7.52 (m, 4 H), 7.41 (d, *J* = 7.5 Hz, 2 H), 7.38–7.36 (m, 2 H), 7.24 (AA′ of AA′BB′, *J* = 8.0 Hz, 2 H), 7.20 (BB′ of AA′BB′, *J* = 8.0 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.4, 148.5, 139.5, 139.1, 136.8, 135.8, 133.7, 133.4, 132.6, 131.8, 130.4, 130.2, 128.9, 128.8, 128.7, 128.4, 128.0, 127.8, 127.0, 125.7, 125.6.

MS (EI): *m/z* (%) 429 (6) [M^+ (^{37}Cl)], 428 (19), 427 (40) [M^+ (^{37}Cl, ^{35}Cl)], 426 (74), 425 (58) [M^+ (^{35}Cl)], 424 (100).

1-Phenyl-3,4-dipropylisoquinoline (3ae)[7e]
This was prepared from hydrazone **1a** (99.7 mg, 0.3 mmol), $RhCp^*(MeCN)_3(SbF_6)_2$ (2.5 mg, 0.009 mmol), 1,2-bis(4-propylphenyl)ethyne (52.8 μL, 0.36 mmol), and $Cu(OAc)_2·H_2O$ (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 5 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (30:1)] gave a colorless solid; yield: 85.1 mg (98%); mp 55–57 °C.

IR (KBr): 2959, 1615, 1555, 1445, 1387, 1334, 1087, 1030, 954, 774 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.05 (dd, *J* = 13.0, 8.0 Hz, 2 H), 7.71–7.66 (m, 3 H), 7.55–7.47 (m, 3 H), 7.43 (t, *J* = 8.0 Hz, 1 H), 3.12–3.06 (m, 4 H), 1.91–1.84 (m, 2 H), 1.79–1.75 (m, 2 H), 1.19–1.14 (m, 3 H), 1.12–1.05 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.1, 152.2, 140.1, 136.2, 130.1, 129.6, 128.3, 128.3, 128.1, 127.3, 125.4, 125.3, 123.4, 37.4, 30.0, 24.2, 23.7, 14.7, 14.4.

LC/MS (ESI): *m/z* 290 $[M + H]^+$.

4-Methyl-1,3-diphenylisoquinoline (3af)[7e]
This was prepared from hydrazone **1a** (99.7 mg, 0.3 mmol), $RhCp^*(MeCN)_3(SbF_6)_2$ (2.5 mg, 0.009 mmol), PhC≡CEt (44.7 μL, 0.36 mmol), and $Cu(OAc)_2·H_2O$ (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 14 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (30:1)] gave a colorless solid; yield: 55.3 mg (62%); mp 112–115 °C.

IR (KBr): 3048, 1664, 1610, 1549, 1443, 1387, 1335, 1270, 1156, 1072, 1027, 1004, 948 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.5 Hz, 2 H), 7.77 (t, *J* = 7.5 Hz, 1 H), 7.73 (d, *J* = 8.0 Hz, 2 H), 7.65 (d, *J* = 7.5 Hz, 2 H), 7.57–7.46 (m, 6 H), 7.40 (t, *J* = 8.0 Hz, 1 H), 2.71 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.2, 137.2, 130.3, 130.2, 129.2, 128.9, 128.7, 128.6, 128.4, 128.3, 128.1, 127.7, 127.2, 126.6, 125.4, 124.8, 124.0, 15.7.

LC/MS (ESI): *m/z* 296 $[M + H]^+$.

Diethyl *N′*-(2,3-Diphenyl-1*H*-inden-1-ylidene)phosphorohydrazidate (3la)
This was prepared by following the same procedure as used for **2a** from hydrazone **3a** (76.9 mg, 0.3 mmol), $RhCp^*(MeCN)_3(SbF_6)_2$ (2.5 mg, 0.009 mmol), PhC≡CPh (64.2 mg, 0.36 mmol), and $Cu(OAc)_2·H_2O$ (125.7 mg, 0.63 mmol) in toluene (1.5 mL) for 3 h at 90 °C. Purification by column chromatography [silica gel, PE–EtOAc (1:1)] gave a yellow solid; yield: 114.3 mg (88%); mp 198–205 °C.

IR (KBr): 3178, 1945, 1585, 1461, 1406, 1247, 1166, 1129, 1022, 966, 911, 698 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 9.59 (d, *J* = 24 Hz, 1 H), 8.26 (d, *J* = 7.5 Hz, 1 H), 7.42–7.33 (m, 5 H), 7.27–7.21 (m, 6 H), 7.19–7.18 (m, 2 H), 4.09–3.98 (m, 4 H), 1.16 (t, *J* = 7.0 Hz, 6 H).

^{31}P NMR (202 MHz, DMSO-d_6): δ = 0.9.

^{13}C NMR (125 MHz, DMSO-d_6): δ = 150.7 (d, $^3J_{P–C}$ = 18.8 Hz), 143.4, 142.0, 137.0, 134.0, 133.6, 131.3, 130.4, 129.5, 129.0, 128.3, 127.8, 127.4, 126.3, 126.1, 120.6, 63.7 (d, $^2J_{P–C}$ = 6.3 Hz), 16.4 (d, $^3J_{P–C}$ = 6.3 Hz).

MS (EI): *m/z* (%) 432 (5) [M^+], 281 (23), 280 (84), 279 (100), 265 (26).

Anal. Calcd For $C_{25}H_{25}N_2O_3P$: C, 69.43; H, 5.83; N, 6.48. Found: C, 69.41; H, 5.81; N, 6.49.

Crystallographic data:[14] $C_{25}H_{25}N_2O_3P$, M = 432.44, monoclinic, $P2_1/c$ (No. 14), *a* = 15.842(3) Å, *b* = 7.741(2) Å, *c* = 19.083(4) Å, β = 101.363(3)°, V = 2294.1 (8) $Å^3$, Z = 4; Crystal size: 0.28 × 0.15 × 0.14 mm, T = 295 K, ρ_{calcd} = 1.252 $g·cm^{-3}$, *R*1 = 0.0360 [I > 4σ(I)], *wR*2 = 0.1016 (all data), GOF = 1.033, reflections collected/unique: 5241/3099 (R_{int} = 0.0362), Data: 3099, restraints: 0, parameters: 284.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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