HHS Public Access

Author manuscript

ACS Catal. Author manuscript; available in PMC 2017 February 05.

Published in final edited form as:

ACS Catal. 2016 February 5; 6(2): 551–554. doi:10.1021/acscatal.5b02391.

Cobalt-Catalyzed, Aminoquinoline-Directed Functionalization of Phosphinic Amide sp² C–H Bonds

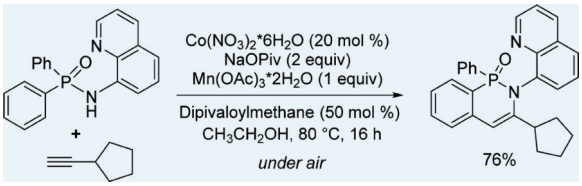
Tung Thanh Nguyen, **Liene Grigorjeva**, and **Olafs Daugulis***

Department of Chemistry, University of Houston, Houston, Texas 77204-5003, United States

Abstract

In this paper, we introduce arylphosphinic acid aminoquinoline amides as competent substrates for cobalt-catalyzed sp^2 C–H bond functionalization. Specifically, the feasibility of their coupling with alkynes, alkenes, and allyl pivalate has been demonstrated. Reactions are catalyzed by simple $Co(NO_3)_2$ hydrate in ethanol or mixed dioxane/*t*BuOH solvent in the presence of $Mn(OAc)_3{\cdot}2H_2O$ additive, sodium pivalate, or acetate base and use oxygen from the air as an oxidant. Directing group removal affords ortho-functionalized *P*,*P*-diarylphosphinic acids.

Graphical abstract



Keywords

cobalt; C–H functionalization; phosphinic amides; alkenes; alkynes

Transition-metal-catalyzed coupling of sp^2 C–H bonds with alkenes and alkynes has been extensively investigated.[1] In most cases, these transformations are promoted by second-row transition-metal complexes.[2] Relatively few papers describe the use of abundant first-row transition metals in these reactions.[3] Among base metals, cobalt catalysis shows perhaps the highest versatility in coupling of sp^2 C–H bonds with alkenes and alkynes and in other C–H bond functionalization reactions.[4–8] An early example showing low-valent cobalt catalysis was reported by Brookhart.[5] Yoshikai has disclosed a series of relevant low-valent cobalt-catalyzed reactions.[6] Cyclopentadienylcobalt(III) complexes were introduced by Kanai as effective catalysts in the coupling of sp^2 C–H bonds with alkynes.[7] We recently reported

***Corresponding Author**. for O.D.: olafs@uh.edu.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.5b02391.

Detailed experimental procedures and characterization data for new compounds (PDF)

The authors declare no competing financial interest.

aminoquinoline- and picolinamide-directed coupling of alkynes, alkenes, and carbon monoxide with sp^2 C–H bonds catalyzed by simple cobalt salts.[8a–c] Dimerization of aminoquinoline benzamides was also described.[8d] Excellent functional group tolerance was observed, the reactions employed oxygen as a terminal oxidant, and silver additives were not required. In these transformations, the aminoquinoline auxiliary is attached to the aryl group via a carbonyl linkage, which allows the removal of the directing group after the functionalization step and increases the synthetic versatility of the methodology.[9] After the directing group was cleaved, a benzoic acid derivative was obtained.

A successful bidentate, monoanionic auxiliary requires a coordinating group and an acidic NH group that can bind to transition metals in a bidentate fashion to form a five-membered-ring chelate (Figure 1).[9c] This requirement is met in aminoquinoline amides (**1**). It is conceivable that the amide functionality in these complexes could be replaced with a phosphinic amide group (**2**). A related 2-pyridylsulfonyl group is efficient in directing the functionalization of amino acid sp^3 C–H bonds.[10] Since phosphorus-containing compounds are important as pesticides, as organocatalysts, and in materials chemistry,[11] we decided to investigate C–H bond functionalization of phosphinamides possessing an aminoquinoline directing group. Relatively few examples of phosphorus-containing directing groups in catalytic sp^2 C–H bond functionalization have been disclosed, and nearly all of these employ second-row transition metals.[12] A rare example of cobalt-catalyzed intramolecular C–H amination with phosphoryl azide has been reported.[13]

We show here that aminoquinoline-containing phosphinic amides are competent substrates in C–H bond functionalization. Cobalt-catalyzed, aminoquinoline-directed couplings of sp^2 C–H bonds with alkynes and ethylene as well as vinyl and allyl pivalates have been reported.

Gratifyingly, minor modification of the conditions that were successful for our previous cobalt-catalyzed reactions[8] worked for phosphinic amide functionalization. Reaction optimization with respect to the ligand and control experiments are presented in Table 1. The use of $Co(acac)_2$ catalyst, $Mn(OAc)_3{\cdot}2H_2O$ cocatalyst, and Na pivalate (NaOPiv) base in ethanol at 80 °C gave a respectable 69% yield of **4** (entry 1). If $Co(NO_3)_2{\cdot}6H_2O$ was used instead of $Co(acac)_2$, a 30% yield of product was obtained (entry 2). Addition of dipivaloylmethane ligand to $Co(NO_3)_2{\cdot}6H_2O$ increased the yield to 99% (entry 3). If Co catalyst was omitted, **4** was not formed (entry 4). Omission of $Mn(OAc)_3{\cdot}2H_2O$ reduced the yield to 49% (entry 5). If the reaction was run in degassed solvent under argon, less than 5% of **4** was formed (entry 6). Diketones other than dipivaloylmethane afforded lower yields (entries 7 and 8). Addition of a catalytic amount of $Mn(OAc)_3$ also lowered the conversion (entry 9). Similarly, use of $Co(acac)_2$ with added acetylacetone afforded a lower yield (entry 10).

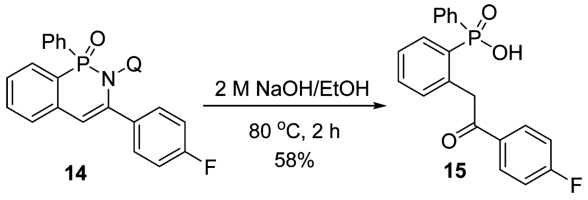
The reaction scope with respect to alkyne coupling partner is presented in Table 2. Nearly all products exist as atropisomer mixtures that likely equilibrate by rotation about the *N*-quinoline bond. Coalescence of their ^1H NMR signals is observed above 85 °C. The coupling reaction is successful for simple, dialkyl-substituted alkynes such as 2-butyne and 3-hexyne, affording products in good yields (entries 1 and 2). Scaling the reaction up from 0.5 to 3 mmol affords the product in nearly the same yield (entry 1). Diphenylacetylene

gives the coupling product in 78% yield (entry 3). An ester functionality is tolerated (entry 4). Arylacetylenes are competent coupling partners (entries 5–8). Steric hindrance in the case of mesitylacetylene lowers the yield of the product to 24% (entry 8). The thiophene functionality is compatible with the reaction conditions (entry 9). Aliphatic terminal alkynes afford products in good yields (entries 10–12). 1-Phenyl-1-propyne gives the coupling product in 72% yield (entry 13). Terminal alkynes and 1-phenyl-1-propyne form regioisomeric mixtures. However, selectivities are reasonably good, ranging from about 9:1 for aryl alkynes (entries 5–7) to >20:1 for 1-hexyne and cyclopentylacetylene (entries 10 and 12).

Substituted diarylphosphinamides are also reactive (Scheme 1). Thus, 2-methyl- and 4-methoxyphenyl derivatives **5** and **7** were reacted with 2-butyne under standard conditions to afford products **6** and **8** in 56 and 75% yields, respectively. Ethoxy-substituted **9** gave **10** in 41% yield.

Reactions with alkenes were also investigated (Scheme 2). Thus, substrate **3** was allylated with allyl pivalate, affording noncyclic **11** in 55% yield. Vinyl pivalate reacted with **3**, giving the product of pivalate elimination **12**. These transformations do not require oxidant; however, omission of $Mn(OAc)_2$ gave products in lower yields. Finally, ethylene was coupled with **3**, affording **13** in 51% yield. Reactions with monosubstituted alkenes were not pursued due to the formation of complicated diastereomer mixtures.

The directing group can be cleaved under basic conditions, giving *ortho*-functionalized phosphinic acids (eq 1). The *p*-fluorophenyl derivative **14** was treated with NaOH in ethanol to afford **15** in 58% yield.



(1)

In conclusion, a method for cobalt-catalyzed, aminoquinoline-directed functionalization of phosphinic acid amide sp^2 C–H bonds has been developed. Specifically, the feasibility of their coupling with alkynes, alkenes, and allyl pivalate has been demonstrated. Reactions proceed in ethanol or mixed dioxane/*t*BuOH solvent in the presence of $Mn(OAc)_3$ additive, sodium pivalate, or acetate base and use oxygen from air as an oxidant. Good to excellent regioselectivities are observed for unsymmetrical and terminal alkynes. Directing group removal gives ortho-functionalized arylphosphinic acids.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank the Welch Foundation (Chair E-0044), NIGMS (Grant No. R01GM077635), and the University of Houston for supporting this research.

REFERENCES

1. Reviews: Ritleng V, Sirlin C, Pfeffer M. Chem. Rev. 2002; 102:1731–1769. [PubMed: 11996548] Colby DA, Bergman RG, Ellman JA. Chem. Rev. 2010; 110:624–655. [PubMed: 19438203] Messaoudi S, Brion J-D, Alami M. Eur. J. Org. Chem. 2010:6495–6516. Ye B, Cramer N. Acc. Chem. Res. 2015; 48:1308–1318. [PubMed: 25884306] Engle KM, Mei T-S, Wasa M, Yu J-Q. Acc. Chem. Res. 2012; 45:788–802. [PubMed: 22166158]
2. Selected examples: Kakiuchi F, Yamamoto Y, Chatani N, Murai S. Chem. Lett. 1995:681–682. Dong C-G, Yeung P, Hu Q-S. Org. Lett. 2007; 9:363–366. [PubMed: 17217305] Tunge JA, Foresee LN. Organometallics. 2005; 24:6440–6444. Jia C, Piao D, Oyamada J, Lu W, Kitamura T, Fujiwara Y. Science. 2000; 287:1992–1995. [PubMed: 10720319] Chernyak N, Tilly D, Li Z, Gevorgyan V. Chem. Commun. 2010; 46:150–152. Ackermann L, Lygin AV, Hofmann N. Angew. Chem., Int. Ed. 2011; 50:6379–6382. Yi CS, Yun SY. J. Am. Chem. Soc. 2005; 127:17000–17006. [PubMed: 16316246] Guimond N, Gouliaras C, Fagnou K. J. Am. Chem. Soc. 2010; 132:6908–6909. [PubMed: 20433170] Ueura K, Satoh T, Miura M. J. Org. Chem. 2007; 72:5362–5367. [PubMed: 17550295] Zhang YJ, Skucas E, Krische MJ. Org. Lett. 2009; 11:4248–4250. [PubMed: 19739691] Colby DA, Bergman RG, Ellman JA. J. Am. Chem. Soc. 2008; 130:3645–3651. [PubMed: 18302381] Hong P, Cho B-R, Yamazaki H. Chem. Lett. 1979:339–342. Wang H, Grohmann C, Nimphius C, Glorius F. J. Am. Chem. Soc. 2012; 134:19592–19595. [PubMed: 23146122] Lu Y, Wang D-H, Engle KM, Yu J-Q. J. Am. Chem. Soc. 2010; 132:5916–5921. [PubMed: 20359184] Miura M, Tsuda T, Satoh T, Pivsa-Art S, Nomura M. J. Org. Chem. 1998; 63:5211–5215. Tani M, Sakaguchi S, Ishii Y. J. Org. Chem. 2004; 69:1221–1226. [PubMed: 14961674]
3. (a) Nakao Y, Kashihara N, Kanyiva KS, Hiyama T. J. Am. Chem. Soc. 2008; 130:16170–16171. [PubMed: 18998690] (b) Shiota H, Ano Y, Aihara Y, Fukumoto Y, Chatani N. J. Am. Chem. Soc. 2011; 133:14952–14955. [PubMed: 21875095] (c) Liu W, Zell D, John M, Ackermann L. Angew. Chem., Int. Ed. 2015; 54:4092–4096.(d) Zhou B, Chen H, Wang C. J. Am. Chem. Soc. 2013; 135:1264–1267. [PubMed: 23286776]
4. (a) Gandeepan P, Cheng C-H. Acc. Chem. Res. 2015; 48:1194–1206. [PubMed: 25854540] (b) Gao K, Yoshikai N. Acc. Chem. Res. 2014; 47:1208–1219. [PubMed: 24576170] (c) Hyster TK. Catal. Lett. 2015; 145:458–467.(d) Wang A, Sun H, Li X. Organometallics. 2008; 27:5434–5437.(e) Hummel JR, Ellman JA. J. Am. Chem. Soc. 2015; 137:490–498. [PubMed: 25494296] (f) Ackermann L. J. Org. Chem. 2014; 79:8948–8954. [PubMed: 25102352] (g) Li J, Ackermann L. Angew. Chem., Int. Ed. 2015; 54:8551–8554.(h) Zhao D, Kim JH, Stegemann L, Strassert CA, Glorius F. Angew. Chem., Int. Ed. 2015; 54:4508–4511.(i) Zhang L-B, Hao X-Q, Zhang S-K, Liu Z-J, Zheng X-X, Gong J-F, Niu J-L, Song M-P. Angew. Chem., Int. Ed. 2015; 54:272–275.(j) Fallon BJ, Derat E, Amatore M, Aubert C, Chemla F, Ferreira F, Perez-Luna A, Petit M. J. Am. Chem. Soc. 2015; 137:2448–2451. [PubMed: 25625542] (k) Schaefer BA, Margulieux GW, Small BL, Chirik PJ. Organometallics. 2015; 34:1307–1320.(l) Pawar AB, Chang S. Org. Lett. 2015; 17:660–663. [PubMed: 25602639]
5. Lenges CP, White PS, Brookhart M. J. Am. Chem. Soc. 1998; 120:6965–6979.
6. (a) Lee PS, Fujita T, Yoshikai N. J. Am. Chem. Soc. 2011; 133:17283–17295. [PubMed: 21954903] (b) Ding Z, Yoshikai N. Angew. Chem., Int. Ed. 2012; 51:4698–4701.(c) Gao K, Lee P-S, Fujita T, Yoshikai N. J. Am. Chem. Soc. 2010; 132:12249–12251. [PubMed: 20712366] (d) Yamakawa T, Yoshikai N. Org. Lett. 2013; 15:196–199. [PubMed: 23259673]
7. (a) Yoshino T, Ikemoto H, Matsunaga S, Kanai M. Chem. - Eur. J. 2013; 19:9142–9146. [PubMed: 23729365] (b) Ikemoto H, Yoshino T, Sakata K, Matsunaga S, Kanai M. J. Am. Chem. Soc. 2014; 136:5424–5431. [PubMed: 24650237]
8. (a) Grigorjeva L, Daugulis O. Angew. Chem., Int. Ed. 2014; 53:10209–10212.(b) Grigorjeva L, Daugulis O. Org. Lett. 2014; 16:4684–4687. [PubMed: 25146300] (c) Grigorjeva L, Daugulis O. Org. Lett. 2014; 16:4688–4690. [PubMed: 25146415] (d) Grigorjeva L, Daugulis O. Org. Lett. 2015; 17:1204–1207. [PubMed: 25689275]

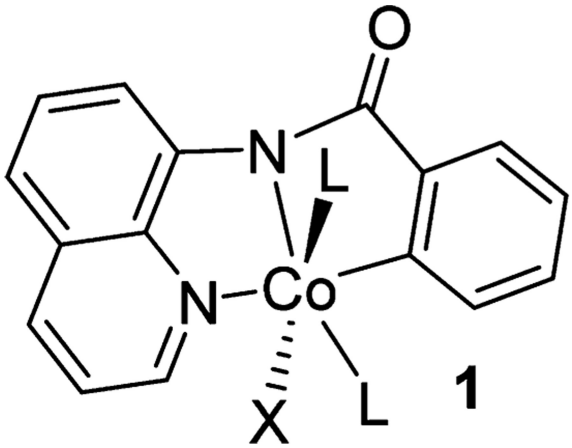
9. (a) Zaitsev VG, Shabashov D, Daugulis O. J. Am. Chem. Soc. 2005; 127:13154–13155. [PubMed: 16173737] (b) Shabashov D, Daugulis O. J. Am. Chem. Soc. 2010; 132:3965–3972. [PubMed: 20175511] (c) Daugulis O, Roane J, Tran LD. Acc. Chem. Res. 2015; 48:1053–1064. [PubMed: 25756616]

10. Poveda A, Alonso I, Fernández-Ibáñez MA. Chem. Sci. 2014; 5:3873–3882.

11. (a) Marinetti A, Voituriez A. Synlett. 2010:174–194.(b) Baumgartner T. Acc. Chem. Res. 2014; 47:1613–1622. [PubMed: 24802764] (c) Eto M. Biosci., Biotechnol., Biochem. 1997; 61:1–11.

12. (a) Du Z-J, Guan J, Wu G-J, Xu P, Gao L-X, Han F-S. J. Am. Chem. Soc. 2015; 137:632–635. [PubMed: 25569141] (b) Park S, Seo B, Shin S, Son J-Y, Lee PH. Chem. Commun. 2013; 49:8671–8673.(c) Ma W, Ackermann L. Synthesis. 2014; 46:2297–2304.(d) Unoh Y, Hashimoto Y, Takeda D, Hirano K, Satoh T, Miura M. Org. Lett. 2013; 15:3258–3261. [PubMed: 23772867] (e) Gwon D, Lee D, Kim J, Park S, Chang S. Chem. - Eur. J. 2014; 20:12421–12425. [PubMed: 25145858] (f) Lin Z-Q, Wang W-Z, Yan S-B, Duan W-L. Angew. Chem., Int. Ed. 2015; 54:6265–6269.(g) Park Y, Jeon I, Shin S, Min J, Lee PH. J. Org. Chem. 2013; 78:10209–10220. [PubMed: 24028218] (h) Zhao D, Nimphius C, Lindale M, Glorius F. Org. Lett. 2013; 15:4504–4507. [PubMed: 23971502] (i) Itoh M, Hashimoto Y, Hirano K, Satoh T, Miura M. J. Org. Chem. 2013; 78:8098–8104. [PubMed: 23883373]

13. Lu H, Tao J, Jones JE, Wojtas L, Zhang XP. Org. Lett. 2010; 12:1248–1251. [PubMed: 20184343]



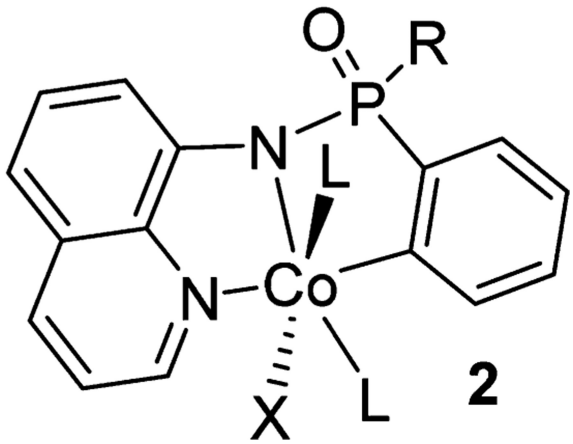
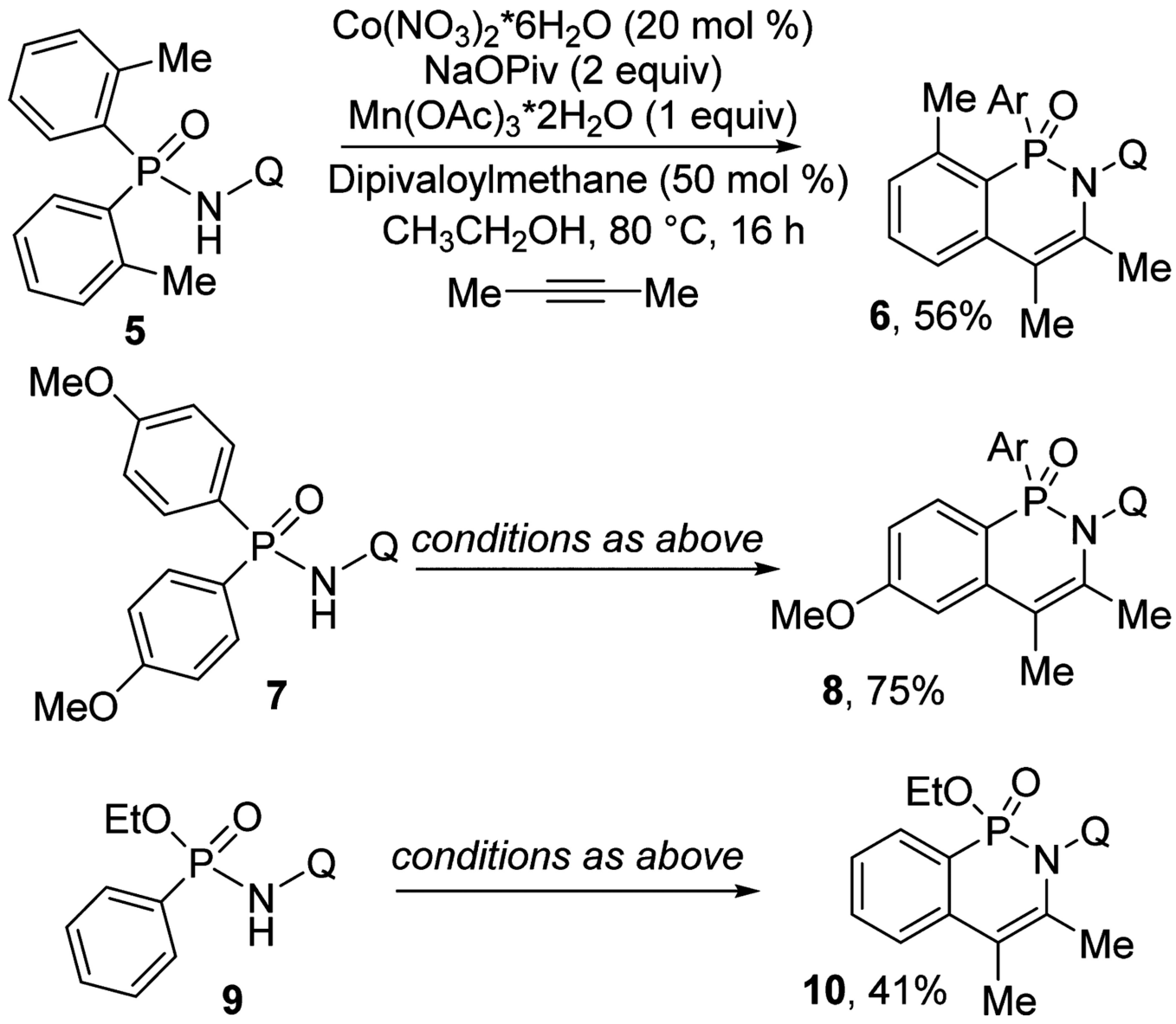
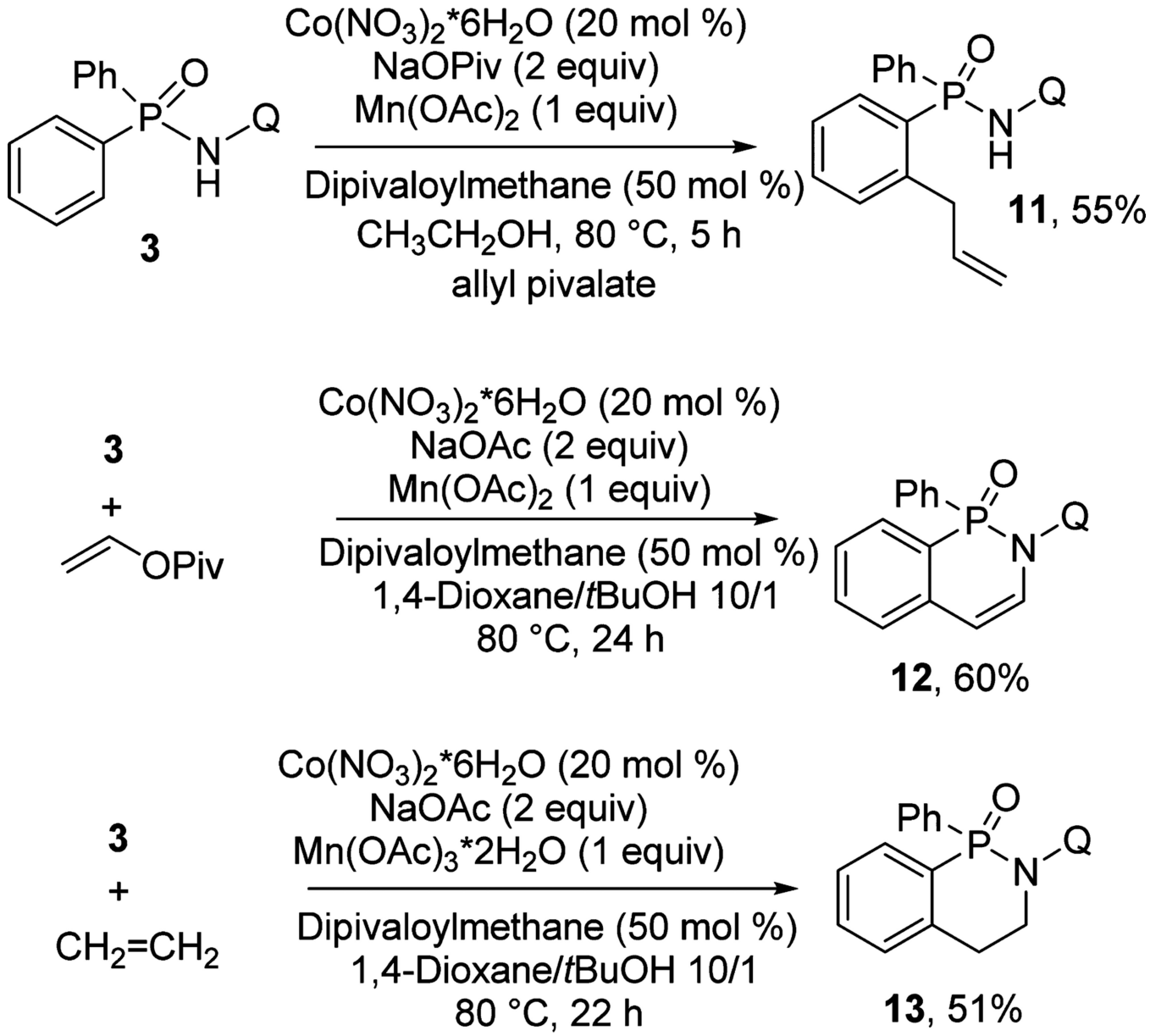


Figure 1.
Aminoquinoline directing group.



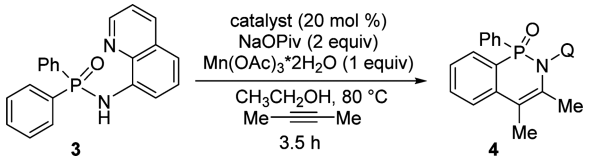
Scheme 1.
Substituted Phosphinamides



Scheme 2.
Reaction with Alkenes

Table 1

Optimization of Reaction Conditions and Control Experiments[a]



entry	catalyst	cooxidant	yield of 4, %
1	$Co(acac)_2$	$Mn(OAc)_3{\cdot}2H_2O$	69
2	$Co(NO_3)_2{\cdot}6H_2O$	$Mn(OAc)_3{\cdot}2H_2O$	30
3[b]	$Co(NO_3)_2{\cdot}6H_2O$	$Mn(OAc)_3{\cdot}2H_2O$	>99
4[b]	none	$Mn(OAc)_3{\cdot}2H_2O$	0
5[b]	$Co(NO_3)_2{\cdot}6H_2O$	none	49
6[b,c]	$Co(NO_3)_2{\cdot}6H_2O$	$Mn(OAc)_3{\cdot}2H_2O$	<5
7[d]	$Co(NO_3)_2{\cdot}6H_2O$	$Mn(OAc)_3{\cdot}2H_2O$	74
8[e]	$Co(NO_3)_2{\cdot}6H_2O$	$Mn(OAc)_3{\cdot}2H_2O$	53
9[b,f]	$Co(NO_3)_2{\cdot}6H_2O$	$Mn(OAc)_3{\cdot}2H_2O$	82
10[g]	$Co(acac)_2$	$Mn(OAc)_3{\cdot}2H_2O$	76

[a] Conditions unless specified otherwise: amide (0.1 mmol), alkyne (0.12 mmol), catalyst (0.02 mmol), Na pivalate (0.2 mmol), CH_3CH_2OH (1 mL), air. Yields were determined by NMR of reaction mixtures, with triphenylmethane internal standard.

[b] Dipivaloylmethane (50 mol %) added.

[c] Degassed ethanol, under an Ar atmosphere.

[d] $PhCOCH_2CO$*t*Bu (50 mol %) added.

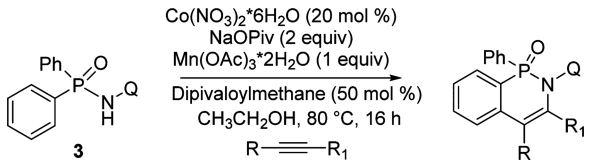
[e] $PhCOCH_2COPh$ (50 mol %) added.

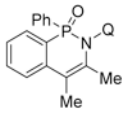
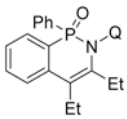
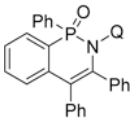
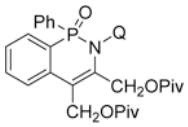
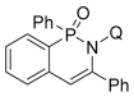
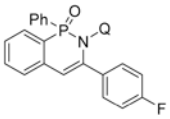
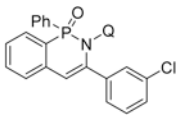
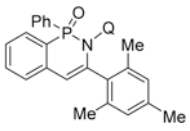
[f] $Mn(OAc)_3{\cdot}2H_2O$ (50 mol %).

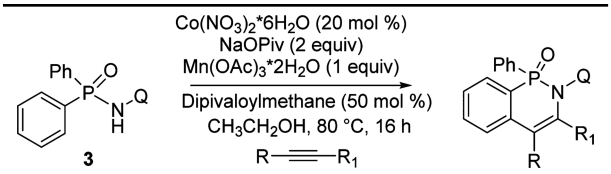
[g] Acetylacetone (10 mol %) added. Q = 8-quinolinyl.

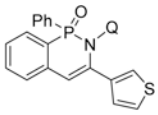
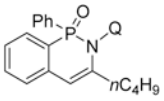
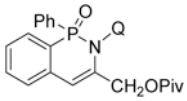
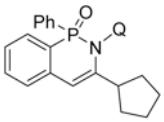
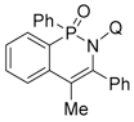
Table 2

Reaction Scope with Respect to Alkynes[a]



entry	alkyne	product	yield, %
1	2-butyne		78 79[b]
2	3-hexyne		87
3	diphenylacetylene		78
4	butyne-1,4-dioldipivalate		61
5[c]	phenylacetylene		81
6[c]	4-F-phenylacetylene		80
7[c]	3-Cl-phenylacetylene		81
8[d]	mesitylacetylene		24



entry	alkyne	product	yield, %
9[e]	3-ethynylthiophene		80
10[f]	1-hexyne		74
11[g]	prop-2-ynylpivalate		65
12[f]	cyclopentylacetylene		76
13[h]	1-phenyl-1-propyne		72

[a]Conditions: phosphinic amide (0.5 mmol), alkyne (0.6 mmol), $Co(NO_3)_2 \cdot 6H_2O$ (0.1 mmol), Na pivalate (1 mmol), $Mn(OAc)_3 \cdot 2H_2O$ (0.5 mmol), dipivaloylmethane (0.25 mmol), ethanol (5 mL), air. Yields are isolated yields. Please see the Supporting Information for details.

[b]Scale: 3 mmol, 24 h.

[c]Isolated as a 9:1 regioisomer mixture.

[d]Isolated as a 14:1 regioisomer mixture, 1 mmol scale.

[e]Isolated as a 10:1 regioisomer mixture.

[f]Regioisomer ratio: >20:1.

[g]Isolated as a 14:1 regioisomer mixture.

[h]Isolated as a 20:1 regioisomer mixture.

Piv = pivalate.