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2-(1-Methylhydrazinyl)pyridine as a Reductively Removable Directing Group in Cobalt-Catalyzed C(sp^2)-H Bond Alkenylation/Annulation Cascade

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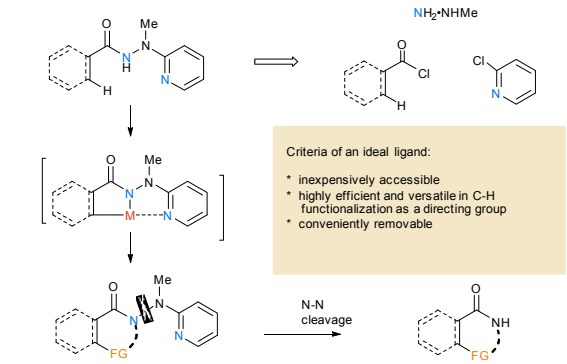
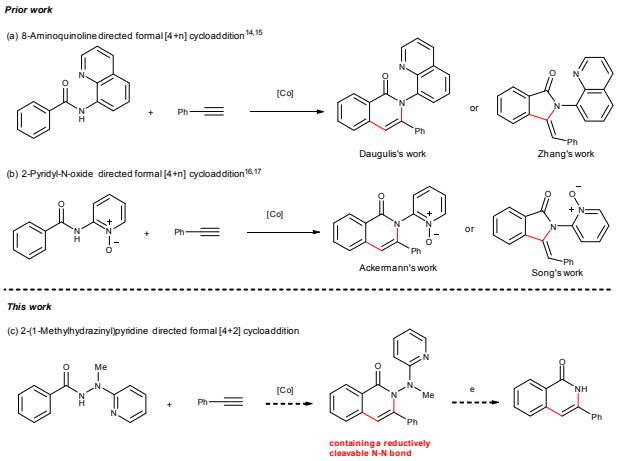
We describe a new application of 2-(1-methylhydrazinyl)pyridine as a bidentate directing group to directing cobalt-catalyzed C(sp^2)-H alkenylation/annulation of the corresponding benzoic hydrazides to form an isoquinoline backbone, via reacting with either a terminal or an internal alkyne followed by annulation. The reaction shows a broad substrate scope with the products obtained in good to excellent yields and high regioselectivity. Moreover, the directing group can be reductively removed in one step under mild conditions.

Research on transition metal-catalyzed C-H functionalization has increased significantly over the past decades[1] and emerged as a powerful strategy for efficient and economic synthesis of complex natural products.[2] Control of the site selectivity is challenging and use of a directing group has proven to be a common, practical, and powerful strategy. In 2005, Daugulis and coworkers reported a groundbreaking palladium-catalyzed C(sp^3)-H arylation using 8-aminoquinoline as a bidentate directing group with excellent regioselectivity.[3] It was believed that bidentate auxiliaries could generate stable metallacycle and promote C-H activation. After their pioneering work, the 8-aminoquinoline was widespreadly studied and proved to be the most successful and promising bidentate directing group,[4] which set a stage for further developing novel approaches to selective C-H functionalization. Various new bidentate auxiliaries have been disclosed over the past a few years,[3,5] but most auxiliaries incorporate a stable C-N linkage that are relatively difficult to remove. Thus, developing novel removable bidentate directing groups remains highly desirable. To the best of our knowledge, the bidentate auxiliaries containing N-X (X = S, N) linkage seem to be rare,[6] although it is well-known that the N-X linkage can be easily cleaved in a traceless fashion compared to the C-N counterpart. Therefore, it is essential to develop new N-hetero bond-containing directing groups that are both easily available and readily removable.



Scheme 1 Novel bidentate directing group-assisted C-H activation



Scheme 2 Cobalt-catalyzed C-H activation

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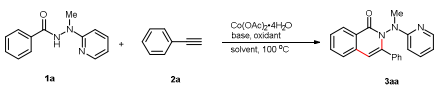
In general, transition metal-catalyzed C-H activation relies mainly on noble metal (such as Ru,[7] Rh,[8] or Pd[9]) catalysts. In spite of their high catalytic activity, these metals are less abundant in nature. So, it would be economically advantageous to achieve catalytic C-H activation using more abundant and lower atomic weight transition metals with comparable efficacy. Recently, cobalt-catalyzed C-H activation has attracted considerable attention in its low valence,[10] cationic,[11] or other forms.[12] Because of its high reactivity, low cost, low toxicity, and abundant availability from the natural sources, cobalt was considered as an attractive catalyst for C-H activation.

Based on the considerations mentioned above, we envisioned that 2-(1-methylhydrazinyl)pyridine might be a promising bidentate auxiliary candidate,[13] since it can be easily obtained from 2-chloropyridine and methylhydrazine at low cost. Also, the N-N linkage can be much more easily cleaved compared to most other bidentate directing groups (Scheme 1). Cobalt-catalyzed C(sp^2)-H alkenylation/annulation assisted by bidentate directing-group was pioneered by Daugulis and coworkers[14], and later flourished by the groups of Zhang[15], Song,[16] and Ackermann[17] (Schemes 2a, b). Inspired by the previous studies, we initiated our investigations (Scheme 2c) on the reaction of N'-methyl-N'-(pyridin-2-yl)benzohydrazide (**1a**) with phenylacetylene (**2a**), using the catalytic system reported by Daugulis.[14] Gratifyingly, the reaction generated the desired product **3aa** in a moderate yield (Table 1, entry 1), and the structure of **3aa** was determined by an X-ray diffraction analysis.[18] Encouraged by the above results, we then screened some other bases for the reaction and found that Na_2CO_3 and K_2CO_3 were both slightly better than NaOPiv (entries 2 and 3). A significant increase of reaction efficiency was observed when 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) was used as the solvent (entry 4). The yield of **3aa** was further increased by incorporation of tetrabutylammonium iodide (TBAI) as a phase-transfer catalyst into the reaction system (entry 5).[15] In addition, control experiments indicated that the C-H activation step was completely inhibited in the absence of either $Co(OAc)_2{\cdot}4H_2O$ or $Mn(OAc)_3{\cdot}2H_2O$ (entries 6 and 7). Nevertheless, the reaction could still proceed to some extent without a base (entry 8).

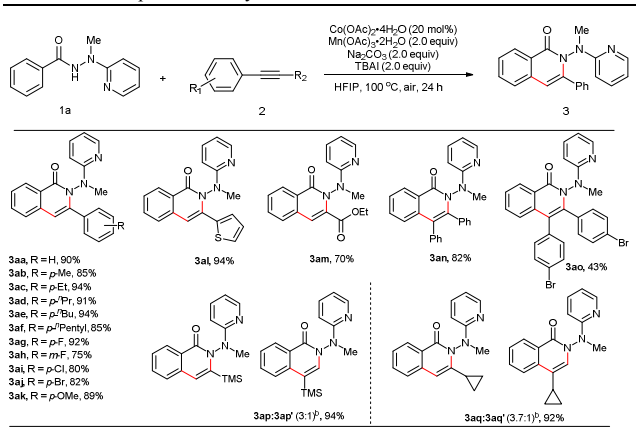
Table 1 Substrate scope studies[a]



Entry	Oxiadnt	Base	Solvent	Yield (%)[b]
1	$Mn(OAc)_3{\cdot}2H_2O$	NaOPiv	TFE	51
2	$Mn(OAc)_3{\cdot}2H_2O$	Na_2CO_3	TFE	61
3	$Mn(OAc)_3{\cdot}2H_2O$	K_2CO_3	TFE	61
4	$Mn(OAc)_3{\cdot}2H_2O$	Na_2CO_3	HFIP	84
5[c]	$Mn(OAc)_3{\cdot}2H_2O$	Na_2CO_3	HFIP	90
6[cd]	$Mn(OAc)_3{\cdot}2H_2O$	Na_2CO_3	HFIP	N.D.
7[c]	/	Na_2CO_3	HFIP	N.D.
8[c]	$Mn(OAc)_3{\cdot}2H_2O$	/	HFIP	44

[a] Reaction conditions: **1a** (0.25 mmol), **2a** (2.0 equiv), $Co(OAc)_2{\cdot}4H_2O$ (20 mol%), air, 100 °C, 24 h. [b] Isolated yield. [c] TBAI (2.0 equiv) was added. [d] No cobalt was added.

Table 2 The scope for the alkynes[a]



[a] Reaction conditions: **1** (0.25 mmol), **2n** (2.0 equiv), $Co(OAc)_2{\cdot}4H_2O$ (20 mol%), Na_2CO_3 (2.0 equiv), $Mn(OAc)_3{\cdot}2H_2O$ (2.0 equiv), TBAI (2.0 equiv), HFIP (2 mL), 100 °C, air, 24 h. [b] The reaction performed for 16 h.

The scope for the alkynes was next investigated with the optimal reaction conditions obtained above (see Table 1, entry 5). In general, both electron-rich and electron-deficient alkynes were compatible with the reaction (Table 2, **3aa**-**3ak**). For example, phenylacetylene and 1-ethynyl-4-pentylbenzene produced nearly equivalent yields (**3aa**, **3af**). Phenylacetylenes with a substituent on the benzene ring such as fluoro (**3ag**, **3ah**), chloro (**3ai**), bromo (**3aj**), and methoxy (**3ak**) groups were well tolerated, providing ample opportunities for further derivatization of the products. 2-Ethynylthiophene (**3al**) and ethyl propiolate (**3am**) were also suitable for this reaction. Furthermore, internal alkynes such as diphenylacetylene and its derivatives did not appear to influence the reactions, and gave the products in moderate to good yields (**3an**,[19] **3ao**). In the cases of trimethylsilylacetylene (**3ap**) and cyclopropyl acetylene (**3aq**), the corresponding cyclization products were formed in high yields, yet with relatively low regioselectivities.

Subsequently, a wide range of hydrazides were explored in the cobalt-catalyzed annulation with alkyne **2n** (Table 3). Benzoic hydrazides containing either an electron-donating or electron-withdrawing group (e.g., methyl, methoxy, fluoro, chloro, bromo, or iodo group, in the *para*-position) on the benzene ring (**3bn**-**3gn**) worked well in this reaction. Moreover, the hydrazide with a *para* trifluoromethyl group furnished the product in 72% yield (**3hn**), indicating that the reaction might not be very sensitive to the electronic effect. A single product was generated in an excellent yield of 90% with the *meta*-methyl-substituted benzoic hydrazide **3in** used as the substrate, therefore the current reaction might have a strong steric effect. Indeed, *ortho*-substituted benzoic hydrazides with either an electron-donating or an electron-withdrawing group, gave the corresponding annulation products in only

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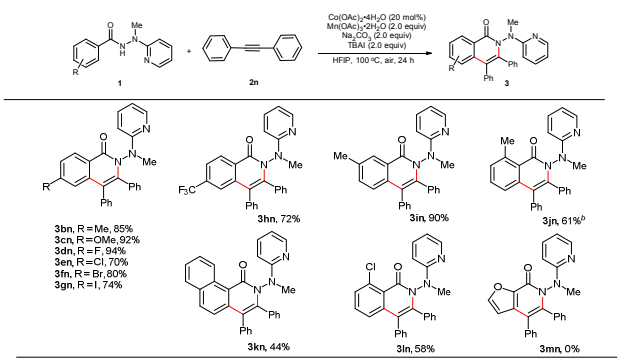
Table 3 The scope for the hydrazides[a]

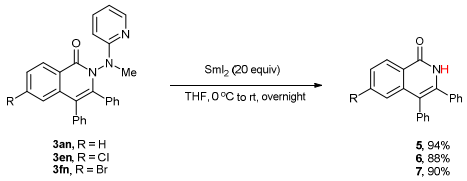


[a] Reaction conditions: **1** (0.25 mmol), **2n** (2.0 equiv), $Co(OAc)_2{\cdot}4H_2O$ (20 mol%), Na_2CO_3 (2.0 equiv), $Mn(OAc)_3{\cdot}2H_2O$ (2.0 equiv), TBAI (2.0 equiv), HFIP (2 mL), 100 °C, air, 24 h. [b] The reaction performed for 16 h.

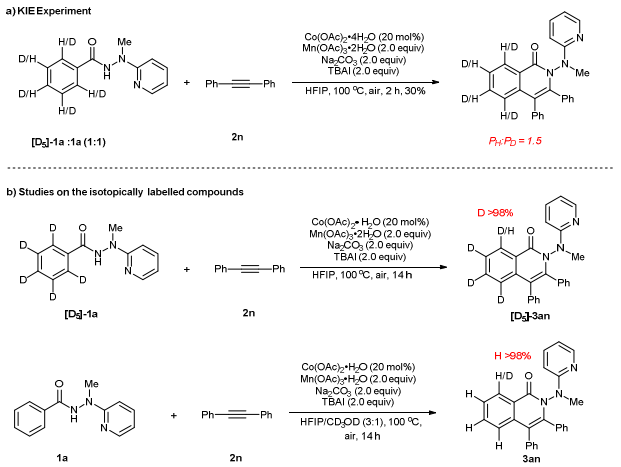
moderate yields (**3jn**, **3kn**, **3ln**). Moreover, for the hydrazide with a heteroaromatic moiety **1m**, no desired product (**3mn**) was formed at all, even at an elevated reaction temperature.

One of the significant merits of the current strategy lies in the reductive removal of the methylaminopyridine moiety (originated from the ligand) under mild conditions. For instance, upon the N-N bond cleavage through treatment with SmI_2 at 0 °C to room temperature overnight, compounds **3an**, **3en**, and **3fn** were transformed smoothly into amides **5**–**7** in 88-94% yields (Scheme 3).[20,21]

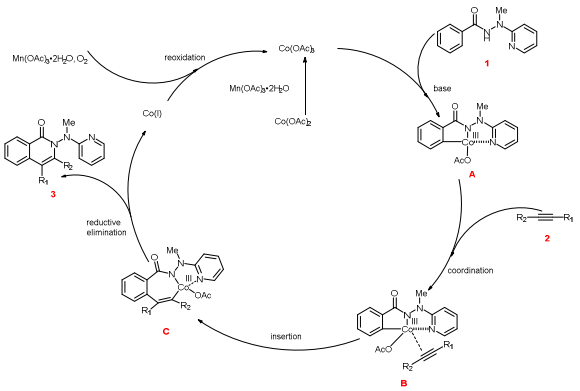
In order to gain further insight into the nature of the present reaction, the following experiments were performed to probethe reaction mechanism (Scheme 4). An intermolecular



Scheme 3 Reductive removal of the directing group



Scheme 4 Preliminary mechanistic studies



Scheme 5 Proposed reaction mechanism

kinetic isotope effect (KIE) experiment was carried out between hydrazide **1a** and isotopically labelled substrate [D_5]-**1a** under standard reaction conditions (Scheme 4a), resulting in a **K** value of approximately 1.5, suggesting that the first step (for the formation of A) in the catalytic cycle was only slightly affected by the H/D isotope**.** Furthermore, no H/D exchange could be detected in both the reaction of isotopically labelled substrate [D_5]-**1a** with **2n**, and that of **1a** with **2n** with CD_3OD added as a co-solvent, indicating presumable irreversibility of the C-H cobaltlation step (Scheme 4b).

Based upon our preliminary mechanistic studies and the relevant literature reports,[17,22] we proposed a mechanism for the cascade reaction sequence (Scheme 5). First, Co(II) is oxidized to Co(III) by $Mn(OAc)_3{\cdot}2H_2O$. Chelation of Co(III) to hydrazide **1** followed by and subsequent C-H activation produces intermediate **A**. Alkyne **2** is then coordinated to the Co(III) center within intermediate **A** to provide intermediate **B**. Coordinative insertion of the carbon-carbon triple bond into the C-Co bond of intermediate **B** results in the seven membered intermediate **C**, reductive elimination of which gives the desired product **3** as well as the low valent Co(I). The active Co(III) species was regenerated through oxidation of Co(I) with $Mn(OAc)_3{\cdot}2H_2O$ and O_2, and the regenerated Co(III) species enters the next catalytic cycle.

In conclusion, we have developed an efficient cobalt-catalyzed C(sp^2)-H bond alkenylation/annulation cascade reaction of benzoic hydrazides with various terminal or internal alkynes via a novel 2-(1-methylhydrazinyl)pyridine-assisted C-H activation, providing a new rapid access to a series of isoquinoline derivatives. Moreover, the methylaminopyridine moiety originated from the ligand can be reductively removed under mild conditions. Further applications of 2-(1-methylhydrazinyl)pyridine as a bidentate directing group in other related types of C-H functionalization and detailed understanding of the mechanisms are currently being investigated in our laboratory.

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Notes and references

1 For selected reviews on C-H activation, see: (a) K. M. Engle, T.-S. Mei, M. Wasa and J.-Q. Yu, *Acc. Chem. Res.,* **2012***, 45,* 788-802. (b) B. Su, Z.-C. Cao and Z.-j. Shi, *Acc. Chem. Res.,* **2015***, 48,* 886-896. (c) V. Ritleng, C. Sirlin and M. Pfeffer, *Chem. Rev*., **2002**, *102*, 1731-1769. (d) I. Mkhalid, J. Barnard, T. Marder, J. Murphy and J. Hartwig, *Chem. Rev*., **2010**, *110*, 890-931. For selected examples on C-H activation, see: (a) C.-Z. Luo, P. Gandeepan, Y.-C. Wu, C.-H. Tsai and C.-H. Cheng, *ACS Catal*., **2015**, *5*, 4837-4841. (b) W. Liu and L. Ackermann, *ACS Catal.,* **2016***, 6,* 3743-3752. (c) L.-C. Liang, P.-S. Chien and Y.-L. Huang, *J. Am. Chem. Soc.,* **2016**, *128*, 15562-15563. (d) J. Norinder, A. Matsumoto, N. Yoshikai and E. Nakamura, *J. Am. Chem. Soc.,* **2008**, *130*, 5858-5859. (e) J. Park, J. Lee and S. Chang, *Angew. Chem. Int. Ed*., **2017**, *56*, 4256-4260.

2 For selected examples, see: (a) J. Johnson, N. Li and D. Sames, *J. Am. Chem. Soc.,* **2002**, *124*, 6900-6903. (b) S. O'Malley, K. Tan, A. Watzke, R. Bergman and J. Ellman, *J. Am. Chem. Soc.,* **2005**, *127*, 13496-13497. (c) H. Davies, X. Dai and M. Long, *J. Am. Chem. Soc.,* **2006**, *128*, 2485-2490. (d) W. Gutekunst and P. Baran, *J. Am. Chem. Soc.,* **2011**, *133*, 19076-19079. (e) D.-H. Wang and J.-Q. Yu, *J. Am. Chem. Soc.,* **2011**, *133*, 5767-5769. (f) B. Wang, Y. Liu, R. Jiao, Y. Feng, Q. Li, C. Chen, L. Liu, G. He and G. Chen, *J. Am. Chem. Soc.,* **2016**, *138*, 3926-3932.

3 V. Zaitsev, D. Shabashov and O. Daugulis, *J. Am. Chem. Soc.,* **2005**, *127*, 13154-13155.

4 For selected examples, see: (a) Z. Liu, Y. Wang, Z. Wang, T. Zeng, P. Liu and K. M. Engle, *J. Am. Chem. Soc.,* **2017**, *139*, 11261-11270. (b) H. M. Omer and P. Liu, *J. Am. Chem. Soc.,* **2017**, *139*, 9909-9920. (c) K. Shibata, S. Natsui and N. Chatani, *Org. Lett.,* **2017**, *19*, 2234-2237. (d) L. Ilies, Y. Itabashi, R. Shang and E. Nakamura, *ACS. Catal*., **2017**, *7*, 89-92. (e) B. Wang, C. Lu, S.-Y. Zhang, G. He, W. A. Nack and G. Chen, *Org. Lett.,* **2014**, *16*, 6260-6263. (f) K. Takamatsu, K. Hirano and M. Miura, *Angew. Chem. Int. Ed*., **2017**, *56*, 5353-5357. (g) N. THrimurtulu, A. Dey, D. Maiti and C. M. R. Volla, *Angew. Chem. Int. Ed*., **2016**, *55*, 12361-12365.

5 For selected examples, see: (a) D. Shabashov and O. Daugulis, *J. Am. Chem. Soc.,* **2010**, *132*, 3965-3972. (b) N. Hasegawa, V. Charra, S. Inoue, Y. Fukumoto and N. Chatani, *J. Am. Chem. Soc.,* **2011**, *133*, 8070-8073. (c) M. Fan and D. Ma, *Angew. Chem. Int. Ed*., **2013**, *52*, 12152-12155. (d) F.-J. Chen, S. Zhao, F. Hu, K. Chen, Q. Zhang, S.-Q. Zhang and B.-F. Shi, *Chem. Sci.,* **2013**, *4*, 4187-4192. (e) Q. Gu, H. H. Al Mamari, K. Graczyk, E. Diers and L. Ackermann, *Angew. Chem. Int. Ed.,* **2014**, *53*, 3868-3871. (f) M. Shang, S.-Z. Sun, H.-X. Dai and J.-Q. Yu, *J. Am. Chem. Soc.,* **2014**, *136*, 3354-3357. (g) Y.-F. Zhang, H.-W. Zhao, H. Wang, J.-B. Wei and Z.-J. Shi, *Angew. Chem. Int. Ed.,* **2015**, *54*, 13686-13690. (h) L.-B. Zhang, X.-Q. Hao, S.-K. Zhang, Z.-J. Liu, X.-X. Zheng, J.-F. Gong, J.-L. Niu and M.-P. Song, *Angew. Chem. Int. Ed.,* **2015**, *54*, 272-275. (i) H. M.-F. Viart, A. Bachmann, W. Kayitare and R. Sarpong, *J. Am. Chem. Soc.,* **2017**, *139*, 1325-1329. (j) T. Liu, J. X. Qiao, M. A. Poss and J.-Q. Yu, *Angew. Chem. Int. Ed.,* **2017**, *56*, 10924-10927. (k) R.-Y. Zhu, L.-Y. Liu and J.-Q. Yu, *J. Am. Chem. Soc.,* **2017**, *139*, 12394-12397.

6 (a) N. Rodríguez, J. Romero-Revilla, M. Fernández-Ibáñez and J. Carretero, *Chem. Sci.,* **2013**, *4*, 175-179. (b) R. Rit, R. Yadav and A. Sahoo, *Org. Lett.,* **2012**, *14*, 3724-3727.

7 (a) L. Ackermann, *Acc. Chem. Res.,* **2014***, 47,* 281-295. (b) P. Arockiam, C. Bruneau and P. Dixneuf, *Chem. Rev*., **2012**, *112*, 5879-5918. (c) S. Ko, H. Han and S. Chang, *Org. Lett.,* **2003**, *5*, 2687-2690. (d) K. Muralirajan, K. Parthasarathy and C.-H. Cheng, *Org. Lett.,* **2012**, *14*, 4262-4265.

8 For selected reviews on Rh-catalyzed C-H activations, see: (a) G. Song and X. Li, *Acc. Chem. Res.,* **2015***, 48,* 1007-1020. (b) B. Ye and N. Cramer, *Acc. Chem. Res.,* **2015***, 48,* 1308-1318. (c) D. Colby, A. Tsai, R. Bergman and J. Ellman, *Acc. Chem. Res.,* **2012***, 45,* 814-825. (d) J. Lewis, R. Bergman and J. Ellman, *Acc. Chem. Res.,* **2008***, 41,* 1013-1025. (e) G. Song, F. Wang and X. Li, *Chem. Soc. Rev*., **2012**, *41*, 3651-3678. (f) D. Colby, R. Bergman and J. Ellman, *Chem. Rev*., **2010**, *110*, 624-655.

9 For selected reviews, see: (a) Y. Minami and T. Hiyama, *Acc. Chem. Res.,* **2016***, 49,* 67-77. (b) N. Ca', M. Fontana, E. Motti and M. Catellani, *Acc. Chem. Res.,* **2016***, 49,* 1389-1400. (c) O. Baudoin, *Acc. Chem. Res.,* **2017***, 50,* 1114-1123. (d) O. Daugulis, H.-Q. Do and D. Shabashov, *Acc. Chem. Res.,* **2009***, 42,* 1074-1086.

10 (a) K. Gao and N. Yoshikai, *Acc. Chem. Res.,* **2014***, 47,* 1208-1219. (b) P. Gandeepan and C.-H. Cheng, *Acc. Chem. Res.,* **2015***, 48,* 1194-1206. (c) W. Song and L. Ackermann, *Angew. Chem. Int. Ed*., **2012**, *51*, 8251-8254. (d) X. Cong, S. Zhai and X. Zeng, *Org. Chem. Front*., **2016**, *3*, 673-677.

11 (a) J. Hummel and J. Ellman, *J. Am. Chem. Soc.,* **2015**, *137*, 490-498. (b) Y. Suzuki, B. Sun, K. Sakata, T. Yoshino, S. Matsunaga and M. Kanai, *Angew. Chem. Int. Ed*., **2015**, *54*, 9944-9947. (c) R. Mei, J. Loup and L. Ackermann, *ACS. Catal.,* **2016**, *6*, 793-797. (d) Q. Lu, S. Vásquez-Céspedes, T. Gensch and F. Glorius, *ACS. Catal.,* **2016**, *6*, 2352-2356.

12 For selected examples, see: (a) P. Gandeepan, P. Rajamalli and C.-H. Cheng, *Angew. Chem. Int. Ed*., **2016**, *55*, 4308-4311. (b) W. Ma and L. Ackermann, *ACS. Catal.,* **2015**, *5*, 2822-2825. (c) D. Kalsi and B. Sundararaju, *Org. Lett.,* **2015**, *17*, 6118-6121. (d) O. Planas, C. Whiteoak, A. Company and X. Ribas, *Adv. Synth. Catal.,* **2015**, *357*, 4003-4012.

13 For 2-hydrazinylpyridine applied to direct C-H activation in hydrazones, see: (a) S. Zhou, M. Wang, L. Wang, K. Chen, J. Wang, C. Song and J. Zhu, *Org. Lett.,* **2016**, *18*, 5632-5635. (b) Y. Xu, M. Young and G. Dong, *J. Am. Chem. Soc.,* **2017**, *139*, 5716-5719.

14 (a) L. Grigorjeva and O. Daugulis, *Angew. Chem. Int. Ed*., **2014**, *53*, 10209-10212. (b) T. Nguyen, L. Grigorjeva and O. Daugulis, *ACS. Catal*., **2016**, *6*, 551-554.

15 J. Zhang, H. Chen, C. Lin, Z. Liu, C. Wang and Y. Zhang, *J. Am. Chem. Soc.,* **2015**, *137*, 12990-12996.

16 L.-B. Zhang, X.-Q. Hao, Z.-J. Liu, X.-X. Zheng, S.-K. Zhang, J.-L. Niu and M.-P. Song, *Angew. Chem. Int. Ed*., **2015**, *54*, 10012-10015.

17 R. Mei, H. Wang, S. Warratz, S. Macgregor and L. Ackermann, *Chem. Eur. J.,* **2016**, *22*, 6759-6763.

18 The structure of compound **3aa** was confirmed by X-ray crystallography. The CCDC number is: 1547832. Data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

19 The structure of compound **3an** was confirmed by X-ray crystallography. The CCDC number is: 1548078. Data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

20 C.-Q. Wang, L. Ye, C. Feng and T.-P. Loh, *J. Am. Chem. Soc.,* **2017**, *139*, 1762-1765.

21 Application of a lower amount of SmI_2 resulted in much lower yield of the product although the unreacted starting material could be recovered.

22 (a) N. Thrimurtulu, A. Dey, D. Maiti and C. Volla, *Angew. Chem. Int. Ed*., **2016**, *55*, 12361-12365. (b) W. Ma and L. Ackermann, *ACS. Catal.,* **2015**, *5*, 2822-2825. (c) C. Kuai, L. Wang, B. Li, Z. Yang and X. Cui, *Org. Lett.,* **2017**, *19*, 2102-2105.

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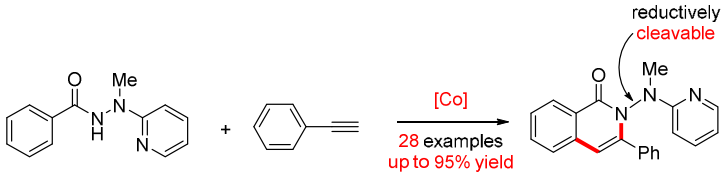

A new application of 2-(1-methylhydrazinyl)pyridine as a reductively bidentate directing group to directing cobalt-catalyzed C(sp^2)-H alkenylation/annulation to form isoquinoline backbones.