Organic LETTERS
Cite This: Org. Lett. XXXX, XXX, XXX−XXX
Letter
pubs.acs.org/OrgLett

Formal [1 + 2 + 3] Annulation: Domino Access to Carbazoles and Indolocarbazole Alkaloids

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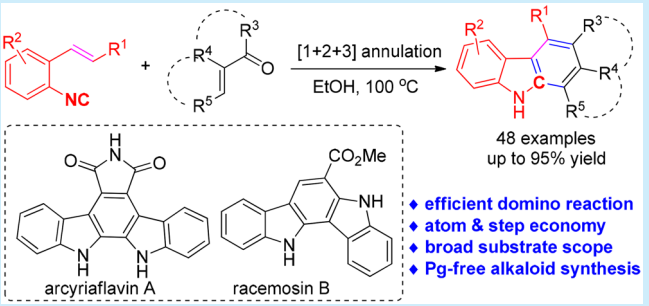
Supporting Information

ABSTRACT: A new formal [1 + 2 + 3] annulation of *o*-alkenyl arylisocyanides with *α*, *β*-unsaturated ketones under metal-, base-, and acid-free conditions is disclosed. This domino reaction provides a general protocol for the efficient and practical synthesis of a wide range of carbazole derivatives from readily available starting materials in a single operation. Furthermore, this methodology was used as the key step in a protecting-group-free synthesis of indolocarbazole alkaloids arcyriaflavin A and racemosin B.



Carbazole and fused carbazole frameworks are prevalent as privileged structural motifs in a large number of biologically active natural products,[1] pharmaceuticals,[2] and functional organic materials.[3] As a consequence, numerous approaches have been developed to access these valuable functionalized heterocycles and their fused derivatives in recent decades.[1,4] Generally, two traditional synthetic strategies are employed to construct these scaffolds: (i) formation of one of the benzenoid rings from substituted indole derivatives through a Diels−Alder reaction,[5] electrocyclization,[6] or benzannulation[7] or (ii) formation of the central pyrrole ring from a substituted biarene or diarylamine by the building of a C−N[8] or C−C[9] bond. To improve the efficiency of carbazole synthesis, a double annulation strategy to form two rings by a tandem reaction has recently emerged as an efficient and promising protocol for their preparation.[10−13] For example, Rh-catalyzed tandem annulation and [5 + 1] cycloaddition of 3-hydroxy-1,4-enyne with CO (Scheme 1a)[10] has been described. So too have Rh-catalyzed inter- and intramolecular alkyne cyclotrimerizations (Scheme 1b),[11] and hexadehydro-Diels−Alder (HDDA) of triynes (Scheme 1c).[12] Despite these great successes, the development of efficient and general methods for the diversity-oriented synthesis of carbazole derivatives under environmentally benign conditions from readily available substrates is still desirable.

Domino reactions have continuously attracted significant attention in chemical synthesis due to the inherent advantages of these processes in terms of synthetic efficiency and sustainability.[14] Because of their versatile reactivities, isocyanides are useful building blocks in domino reactions.[15] Among the various functionalized isocyanides,[16] *o*-alkenyl arylisocyanides, bearing additional alkene functionalities, have proven to be valuable synthons for the construction of indoles[17] and quinolines[18] via 5-*exo* or 6-*endo* cyclizations. Recently, we reported new double annulations of *o*-alkenyl arylisocyanides, where three bonds and two rings were successively created, for the efficient synthesis of pyrrolo[3,4-*b*]indoles[19a] and phenanthridines,[19b] respectively. As a continuation of our studies on isocyanide chemistry[20] and also inspired by Zhu's elegant formal [3 + 2 + 1] cycloaddition of isocyanoacetates with phenylvinyl selenones and water,[21] we herein report a new formal [1 + 2 + 3] annulation of readily available *o*-alkenyl arylisocyanides with *α*,*β*-unsaturated ketones as a general strategy for the expeditious synthesis of polyfunctionalized carbazoles in ethanol under metal-, acid-, and base-free conditions (Scheme 1d). A new reactivity profile of these isocyanides was thus demonstrated by the rapid creation of two rings and three bonds under simple conditions in a single operation. Notably, the synthetic potential of this strategy was demonstrated by the protecting-group-free construction of indolocarbazole alkaloids arcyriaflavin A and racemosin B.

We commenced the study with *o*-alkenyl arylisocyanide **1a** and benzyliden-1,3-diketone **2a** as the model substrates and systematically screened the reaction conditions (Table 1). Fortunately, when a mixture of **1a** (0.45 mmol) and **2a** (0.3 mmol) was heated at 60 °C in ethanol (1 mL) for 24 h, the desired product, carbazole **3a** (CCDC 1826091), was obtained in 10% yield (Table 1, entry 1). To our delight, the yield of **3a**

Received: July 19, 2018

DOI: 10.1021/acs.orglett.8b02266
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Scheme 1. Double Annulation for Carbazole Assembly

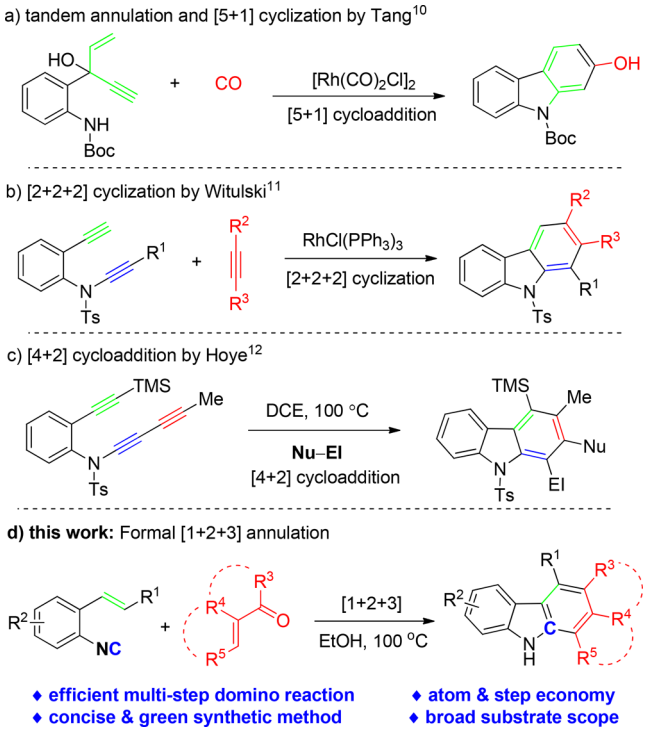
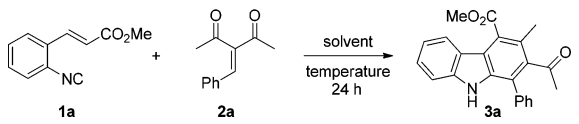


Table 1. Optimization of Reaction Conditions[a]



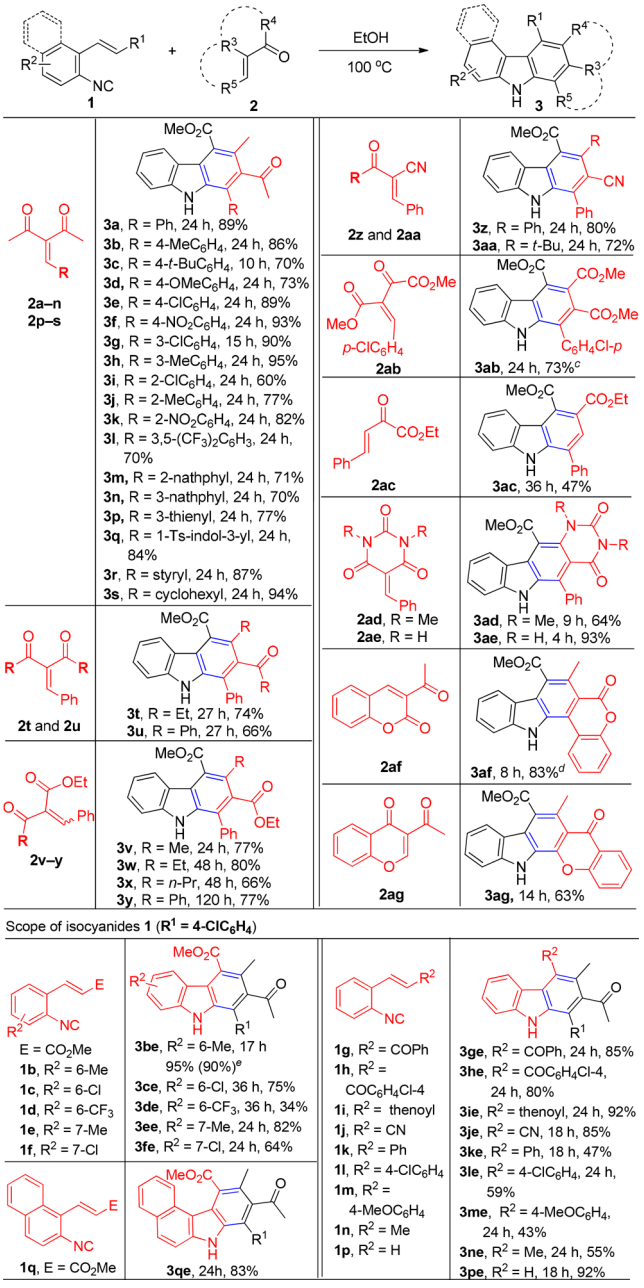
entry	solvent	temp (°C)	yield of **3a** (%)[b]
1	EtOH	60	10[c]
2	EtOH	80	85
3	EtOH	100	89
4	EtOH	120	57

[a]Reaction conditions: **1a** (0.45 mmol), **2a** (0.3 mmol), solvent (1 mL). [b]Isolated yields. [c]**1a** and **2a** were recovered.

was improved to 89% when the reaction temperature was elevated to 100 °C (Table 1, entries 2 and 3). Increasing the temperature to 120 °C led to a decreased yield of **3a** (Table 1, entry 4). Some selected solvents, such as methanol, 2,2,2-trifluoroethanol, isopropanol, *tert*-butanol, DMF, acetonitrile, and THF, were also examined (Supporting Information, Table S1), and all the tested reactions gave **3a** in lower yields.

With the optimal conditions identified, the scope of both the isocyanides **1** and ketones **2** were examined, and the results are summarized in Scheme 2. The double annulation generally tolerates a wide range of ketones **2**, and a series of polysubstituted (**3a**–**n** and **3p**–**z**, **3aa** and **3ab**), cyclo[*b*]fused (**3ac** and **3ad**), and cyclo[*a*]fused (**3ae** and **3af**) carbazoles were obtained in good to high yields. Various 3-methylene-pentane-2,4-diones **2** bearing different R^5 groups at the *β*-position such as phenyl (**2a**), electron-rich aryls (**2b**–**d**, **2h** and **2j**) or electron-poor aryls (**2e**–**g**, **2i**, **2k**, and **2l**), *α*- and *β*-naphthyl (**2m** and **2n**), heteroaryls (**2p** and **2q**), a vinyl group (**2r**), and an alkyl group (**2s**) were all effective three-carbon-atom components, respectively. The annulation tolerates ketones **2** with various R^3 groups such as acetyl (**2a**–**n** and

Scheme 2. Substrate Scope for the Formal [1 + 2 + 3] Annulation[a,b]



[a]Reaction conditions: **1** (0.45 mmol), **2a** (0.3 mmol) in EtOH (1 mL) at 100 °C. [b]Isolated yields. [c]130 °C. [d]4 h; DBU (0.2 equiv) was added for another 4 h. [e]1.642 g of **3be** was obtained.

2p–**s**), propionyl (**2t**), benzoyl (**2u**), esters (**2v**–**y** and **2ab**), and cyano groups (**2z** and **2aa**), and with an R^4 group including methyl (**2a**–**n**, **2p**–**s** and **2v**), ethyl (**2t** and **2w**), propyl (**2x**), *tert*-butyl (**2aa**), phenyl (**2u**, **2y**, and **2z**), and ester groups (**2ab** and **2ac**). Furthermore, cyclo[*a*]- and -[*b*]-fused carbazoles such as pyrimido[5,4-*b*]- (**3ad** and **3ae**), chromeno-[4,3-*a*]- (**3af**), and chromeno[2,3-*a*]carbazole (**3ag**) were conveniently synthesized.

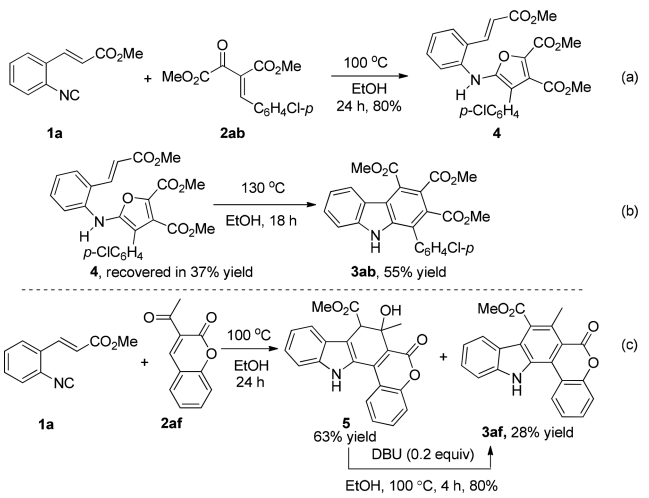
Subsequently, the scope of this [1 + 2 + 3] annulation was evaluated with respect to isocyanides **1**; the results are summarized at the bottom of Scheme 2. The reaction is tolerant of isocyanides **1** bearing various R^2 groups on the

DOI: 10.1021/acs.orglett.8b02266
Org. Lett. XXXX, XXX, XXX–XXX

benzene ring. Isocyanides **1b** and **1e** bearing an electron-donating methyl group at both the 6- and 7-position give higher yields of the carbazoles **3be** and **3ee**. Contrastingly, isocyanides **1c**, **1d**, and **1f** bearing electron-withdrawing groups at both the 6- and 7-positions gave lower yields of the carbazoles **3ce**, **3de**, and **3fe**. When the R^1 groups of the isocyanide **1** are electron-withdrawing groups such as an ester (**1a**), carbonyl (**1g–i**), and cyano group (**1j**), the reactions afford the carbazole products (**3ge–je**) in high to excellent yields. When the R^1 groups of the isocyanide **1** are aryl (**1k–m**) and alkyl groups (**1n**), the reaction affords the carbazoles (**3ke–ne**) in moderate yields. In contrast, 2-isocyanostyrene **1p** gives the carbazole **3pe** in 92% yield probably due to less steric hindrance. Benzo[*c*]carbazole **3qe** was obtained in 83% yield when 3-(2-isocyanonaphthalen-1-yl)acrylate **2q** was employed. In addition, the practicability of the present [1 + 2 + 3] annulation was demonstrated by gram-scale synthesis of **3be**.

To shed light on the reaction mechanism of this domino reaction, control experiments were performed. When isocyanide **1a** was treated with ketoester **2ab** under the standard conditions, the aminofuran **4** was obtained in 80% yield (Scheme 3a). However, when **4** was heated to 130 °C for 18 h,

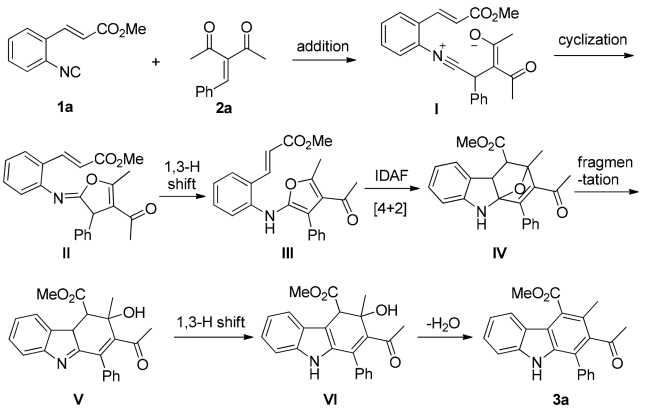
Scheme 3. Control Experiments



carbazole **3ab** was obtained in 55% yield along with recovery of **4** in 37% yield (Scheme 3b). This result indicated that aminofuran **4** is most likely an intermediate, formed by an isocyanide-based [1 + 4] annulation.[22] In addition, the reaction of **1a** and **2af** gave chromeno[4,3-*a*]carbazole **3af** in 28% yield along with the hydroxyl carbazole **5** in 63% yield (Scheme 3c). Transformation of **5** to **3af** was achieved by the treatment with DBU (0.2 equiv) in ethanol at 100 °C for 4 h. These results demonstrate that **5** is also the possible intermediate, produced by a domino aminofuran-based Diels–Alder reaction and fragmentation sequence.[23] It was well established that [1 + 4] annulation of isocyanides with α,β-unsaturated ketones produces 2-aminofuran derivatives.[22] Meanwhile, 2-aminofurans are reactive dienes in Padwa's aniline and indole syntheses.[24] However, only a few examples employing an isocyanide-based [1 + 4] annulation and intermolecular [4 + 2] cycloaddition cascade for the synthesis of anilines and 4-aminoxanthones have recently been reported by Marcos and co-workers.[25]

On the basis of the present results, and the literature precedent,[22−25] a possible mechanistic pathway is proposed (Scheme 4, taking the reaction of isocyanide **1a** with ketone **2a**

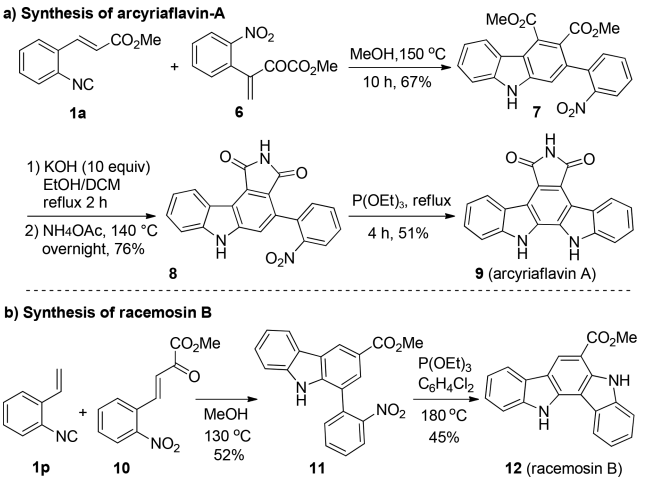
Scheme 4. Proposed Mechanism



as an example). First, nucleophilic attack of isocyanide **1a** onto the β-carbon of the enone **2a** generates the zwitterionic intermediate **I**. Then cyclization of **I** gives intermediate **II**, which undergoes a 1,3-proton shift to afford the formal [1 + 4] product aminofuran **III**.[22] Next, a furan-based intramolecular Diels–Alder reaction occurs to produce the bridged intermediate **IV**, which is followed by subsequent C–O scission, 1.3-proton shift, and elimination of water to give the final carbazole **3a**.[23,24]

The synthetic potential of this domino reaction was illustrated by the protecting-group-free synthesis of indolocarbazole alkaloids (Scheme 5). Arcyriaflavin A is an

Scheme 5. Synthesis of Arcyriaflavin A and Racemosin B



indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole alkaloid[2627] that serves as a human cytomegalovirus replication inhibitor.[27] As depicted in Scheme 5a, arcyriaflavin A **9** was prepared from isocyanide **1a** and the known compound 3-(2-nitrophenyl)-2-oxobut-3-enoate **6**[28] in three steps. Moreover, racemosin B possesses an interesting pentacyclic indolo[3,2-*a*]carbazole framework[29] and exhibits moderate neuroprotective activity with a 5.5% increase in cell viability (10 μM).[30] By using this domino annulation as a key transformation, racemosin B **12**

DOI: 10.1021/acs.orglett.8b02266
Org. Lett. XXXX, XXX, XXX–XXX

was readily prepared from 2-isocyanostyrene **1p** and unsaturated ketoester **10**[31] in two steps (Scheme 5b).

In summary, an unprecedented environmentally benign formal [1 + 2 + 3] annulation of *o*-alkenyl arylisocyanides with *α,β*-unsaturated ketones has been developed as a general strategy for the efficient synthesis of polyfunctionalized carbazoles. This strategy features operational simplicity; metal-, acid-, and base-free conditions; high chemical efficiency; readily available starting materials; a wide substrate scope; amenability to gram-scale synthesis, and atom and step economy. Furthermore, the protecting-group-free synthesis of alkaloids arcyriaflavin A and racemosin B was also accomplished via this [1 + 2 + 3] annulation as a key step.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b02266.

Experimental procedures and characterization data for all compounds (PDF)

Accession Codes

CCDC 1826091 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support provided by the NSFC (21672034) is gratefully acknowledged.

■ REFERENCES

(1) (a) Schmidt, A. W.; Reddy, K. R.; Knölker, H.-J. *Chem. Rev.* **2012**, *112*, 3193. (b) Bauer, I.; Knölker, H.-J. *Top. Curr. Chem.* **2011**, *309*, 203. (c) Knölker, H.-J.; Reddy, K. R. *Chem. Rev.* **2002**, *102*, 4303.

(2) Cheng, J.; Kamiya, K.; Kodama, I. *Cardiovasc. Drug Rev.* **2001**, *19*, 152.

(3) (a) Li, J.; Grimsdale, A. C. *Chem. Soc. Rev.* **2010**, *39*, 2399. (b) Jiang, H.; Sun, J.; Zhang, J. *Curr. Org. Chem.* **2012**, *16*, 2014. (c) Liu, X.; Xu, Y.; Jiang, D. *J. Am. Chem. Soc.* **2012**, *134*, 8738. (d) Tsvelikhovsky, D.; Buchwald, S. L. *J. Am. Chem. Soc.* **2011**, *133*, 14228.

(4) For recent reviews, see: (a) Yoshikai, N.; Wei, Y. *Asian J. Org. Chem.* **2013**, *2*, 466. (b) Bauer, I.; Knölker, H.-J. *Alkaloid Synthesis*; Springer, 2012; p 203. (c) Roy, J.; Jana, A. K.; Mal, D. *Tetrahedron* **2012**, *68*, 6099.

(5) (a) Krishna, N. H.; Saraswati, A. P.; Sathish, M.; Shankaraiah, N.; Kamal, A. *Chem. Commun.* **2016**, *52*, 4581. (b) Reddy, C. R.; Valleti, R. R.; Dilipkumar, U. *Chem. - Eur. J.* **2016**, *22*, 2501.

(6) (a) Banerjee, A.; Sahu, S.; Maji, M. S. *Adv. Synth. Catal.* **2017**, *359*, 1860. (b) Laha, J. K.; Dayal, N. *Org. Lett.* **2015**, *17*, 4742.

(7) Recent examples: (a) Zhou, J.; Qiu, Y.; Li, J.; Fu, C.; Zhang, X.; Ma, S. *Chem. Commun.* **2017**, *53*, 4722. (b) Huang, Y.-W.; Li, X.-Y.; Fu, L.-N.; Guo, Q.-X. *Org. Lett.* **2016**, *18*, 6200. (c) Zhao, J.; Li, P.; Xia, C.; Li, F. *Chem. - Eur. J.* **2015**, *21*, 16383. (d) Zheng, X.; Lv, L.; Lu, S.; Wang, W.; Li, Z. *Org. Lett.* **2014**, *16*, 5156. (e) Qiu, Y.; Zhou, J.; Fu, C.; Ma, S. *Chem. - Eur. J.* **2014**, *20*, 14589. (f) Zhang, Z.; Tang, X.; Xu, Q.; Shi, M. *Chem. - Eur. J.* **2013**, *19*, 10625.

(8) (a) Gao, H.; Xu, Q.-L.; Yousufuddin, M.; Ess, D. l. H.; Kürti, L. *Angew. Chem., Int. Ed.* **2014**, *53*, 2701. (b) Cho, S. H.; Yoon, J.; Chang, S. *J. Am. Chem. Soc.* **2011**, *133*, 5996. (c) Wang, M.; Fan, Q.; Jiang, X. *Org. Lett.* **2018**, *20*, 216.

(9) (a) Budén, M. E.; Vaillard, V. A.; Martin, S. E.; Rossi, R. A. *J. Org. Chem.* **2009**, *74*, 4490. (b) Schuster, C.; Rönnefahrt, M.; Julich-Gruner, K. K.; Jäger, A.; Schmidt, A. W.; Knölker, H.-J. *Synthesis* **2015**, *48*, 150.

(10) (a) Li, X.; Song, W.; Tang, W. *J. Am. Chem. Soc.* **2013**, *135*, 16797. (b) Song, W.; Li, X.; Yang, K.; Zhao, X.-l.; Glazier, D. A.; Xi, B.-M.; Tang, W. *J. Org. Chem.* **2016**, *81*, 2930.

(11) (a) Witulski, B.; Alayrac, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 3281. (b) Alayrac, C.; Schollmeyer, D.; Witulski, B. *Chem. Commun.* **2009**, *45*, 1464.

(12) Wang, T.; Hoye, T. R. *J. Am. Chem. Soc.* **2016**, *138*, 13870.

(13) (a) Choi, S.; Srinivasulu, V.; Ha, S.; Park, C.-M. *Chem. Commun.* **2017**, *53*, 3481. (b) Fan, X.; Yu, L.-Z.; Wei, Y.; Shi, M. *Org. Lett.* **2017**, *19*, 4476. (c) Krishna, N. H.; Saraswati, A. P.; Sathish, M.; Shankaraiah, N.; Kamal, A. *Chem. Commun.* **2016**, *52*, 4581. (d) Poudel, T. N.; Lee, Y. R. *Chem. Sci.* **2015**, *6*, 7028.

(14) For reviews on tandem reactions, see: (a) Tietze, L. F.; Bell, H. P.; Brasche, G. *Domino Reactions in Organic Synthesis*; Wiley-VCH: Weinheim, 2006. (b) Enders, D.; Grondal, C.; Hüttl, M. R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1570. (c) Padwa, A.; Bur, S. K. *Tetrahedron* **2007**, *63*, 5341.

(15) (a) Dömling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3168. (b) Lygin, A. V.; de Meijere, A. *Angew. Chem., Int. Ed.* **2010**, *49*, 9094. (c) *Isocyanide Chemistry Applications in Synthesis and Materials Science*; Nenajdenko, V., Ed.; Wiley-VCH: Weinheim, 2012.

(16) Giustiniano, M.; Basso, A.; Mercalli, V.; Massarotti, A.; Novellino, E.; Tron, G. C.; Zhu, J. *Chem. Soc. Rev.* **2017**, *46*, 1295.

(17) For a review, see: (a) Tokuyama, H.; Fukuyama, T. *Chem. Rec.* **2002**, *2*, 37. (b) Mitamura, T.; Tsuboi, Y.; Iwata, K.; Tsuchii, K.; Nomoto, A.; Sonoda, M.; Ogawa, A. *Tetrahedron Lett.* **2007**, *48*, 5953. (c) Zhang, B.; Studer, A. *Org. Lett.* **2014**, *16*, 1216. (d) Tobisu, M.; Fujihara, H.; Koh, K.; Chatani, N. *J. Org. Chem.* **2010**, *75*, 4841.

(18) (a) Onitsuka, K.; Suzuki, S.; Takahashi, S. *Tetrahedron Lett.* **2002**, *43*, 6197. (b) Kobayashi, K.; Takagoshi, K.; Kondo, S.; Morikawa, O.; Konishi, H. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 553. (c) Ichikawa, J.; Wada, Y.; Miyazaki, H.; Mori, T.; Kuroki, H. *Org. Lett.* **2003**, *5*, 1455.

(19) (a) Hu, Z.; Yuan, H.; Men, Y.; Liu, Q.; Zhang, J.; Xu, X. *Angew. Chem., Int. Ed.* **2016**, *55*, 7077. (b) Hu, Z.; Dong, J.; Men, Y.; Li, Y.; Xu, X. *Chem. Commun.* **2017**, *53*, 1739.

(20) (a) Tan, J.; Xu, X.; Zhang, L.; Li, Y.; Liu, Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 2868. (b) Li, Y.; Xu, X.; Tan, J.; Xia, C.; Zhang, D.; Liu, Q. *J. Am. Chem. Soc.* **2011**, *133*, 1775. (c) Xu, X.; Zhang, L.; Liu, X.; Pan, L.; Liu, Q. *Angew. Chem., Int. Ed.* **2013**, *52*, 9271. (d) Hu, Z.; Dong, J.; Men, Y.; Lin, Z.; Cai, J.; Xu, X. *Angew. Chem., Int. Ed.* **2017**, *56*, 1805. (e) Zhang, X.; Wang, X.; Gao, Y.; Xu, X. *Chem. Commun.* **2017**, *53*, 2427. (f) Gao, Y.; Hu, Z.; Dong, J.; Liu, J.; Xu, X. *Org. Lett.* **2017**, *19*, 5292. (g) Lin, Z.; Hu, Z.; Zhang, X.; Dong, J.; Liu, J.-B.; Chen, D.-Z.; Xu, X. *Org. Lett.* **2017**, *19*, 5284. (h) Dong, J.; Bao, L.; Hu, Z.; Ma, S.; Zhou, X.; Hao, M.; Li, N.; Xu, X. *Org. Lett.* **2018**, *20*, 1244. (i) Bao, L.; Liu, J.; Xu, L.; Hu, Z.; Xu, X. *Adv. Synth. Catal.* **2018**, *360*, 1870. (j) Zhang, L.; Li, J.; Hu, Z.; Dong, J.; Zhang, X.-M.; Xu, X. *Adv. Synth. Catal.* **2018**, *360*, 1938.

(21) Buyck, T.; Wang, Q.; Zhu, J. *J. Am. Chem. Soc.* **2014**, *136*, 11524.

DOI: 10.1021/acs.orglett.8b02266
Org. Lett. XXXX, XXX, XXX−XXX

(22) (a) Chen, J.-R.; Hu, X.-Q.; Lu, L.-Q.; Xiao, W.-J. *Chem. Rev.* **2015**, *115*, 5301. (b) Kaur, T.; Wadhwa, P.; Bagchi, S.; Sharma, A. *Chem. Commun.* **2016**, *52*, 6958. (c) Kruithof, A.; Ruijter, E.; Orru, R. V. A. *Chem. - Asian J.* **2015**, *10*, 508.
(23) Bornadiego, A.; Díaz, J.; Marcos, C. F. *J. Org. Chem.* **2015**, *80*, 6165.
(24) (a) Kappe, C. O.; Murphree, S. S.; Padwa, A. *Tetrahedron* **1997**, *53*, 14179. (b) LaPorte, M.; Hong, K. B.; Xu, J.; Wipf, P. *J. Org. Chem.* **2013**, *78*, 167. (c) Li, G.; Padwa, A. *Org. Lett.* **2011**, *13*, 3767.
(25) (a) Neo, A. G.; Bornadiego, A.; Díaz, J.; Marcaccini, S.; Marcos, C. F. *Org. Biomol. Chem.* **2013**, *11*, 6546. (b) Bornadiego, A.; Díaz, J.; Marcos, C. F. *Adv. Synth. Catal.* **2014**, *356*, 718.
(26) (a) Lee, S.; Kim, K.-H.; Cheon, C.-H. *Org. Lett.* **2017**, *19*, 2785. (b) Alonso, D.; Caballero, E.; Medarde, M.; Tomé, F. *Tetrahedron Lett.* **2005**, *46*, 4839.
(27) Slater, M. J.; Cockerill, S.; Baxter, R.; Bonser, R. W.; Gohil, K.; Gowrie, C.; Robinson, J. E.; Littler, E.; Parry, N.; Randall, R.; Snowden, W. *Bioorg. Med. Chem.* **1999**, *7*, 1067.
(28) Nicolaou, K. C.; Lee, S. H.; Estrada, A. A.; Zak, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 3736.
(29) (a) Janosik, T.; Wahlströmb, N.; Bergman, J. *Tetrahedron* **2008**, *64*, 9159. (b) Liang, L.-n.; Fan, T.-y.; Huang, T.; Yan, C.; Xu, M.; Liu, S. *Tetrahedron Lett.* **2015**, *56*, 434.
(30) Liu, D.-Q.; Mao, S.-C.; Zhang, H.-Y.; Yu, X.-Q.; Feng, M.-T.; Wang, B.; Feng, L.-H.; Guo, Y.-W. *Fitoterapia* **2013**, *91*, 15.
(31) Feng, J.; Fu, X.; Chen, Z.; Lin, L.; Liu, X.; Feng, X. *Org. Lett.* **2013**, *15*, 2640.

DOI: 10.1021/acs.orglett.8b02266
Org. Lett. XXXX, XXX, XXX−XXX