OL | Organic Letters

Letter

Cite This: Org. Lett. XXXX, XXX, XXX−XXX

pubs.acs.org/OrgLett

Enantioselective Copper-Catalyzed Electrophilic Dearomative Azidation of β-Naphthols

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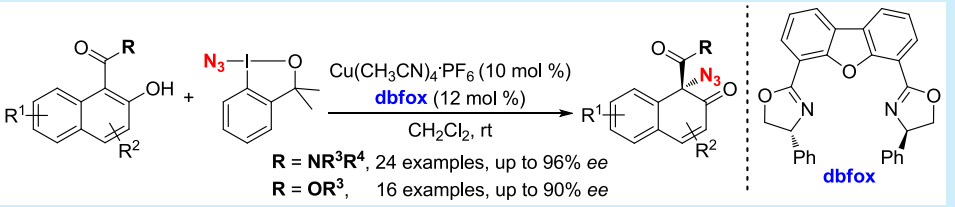
Supporting Information

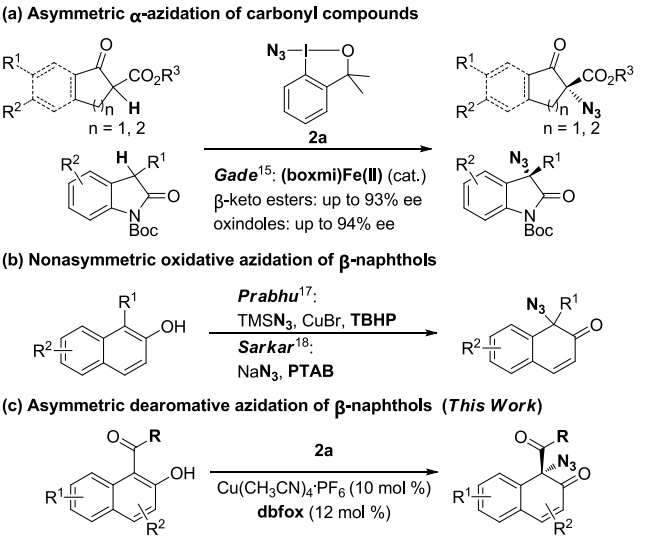


ABSTRACT: The first example of copper-catalyzed enantioselective dearomative azidation of β-naphthols using a readily available N_3-transfer reagent is reported. A series of 2-hydroxy-1-naphthamides bearing a complex *N*-substituent were converted to the corresponding products in high yields with up to 96% ee, and chiral 1-azido-2-hydroxy-1-naphthoates were obtained with up to 90% ee under mild reaction conditions. The azides could be further transformed into the corresponding 1,2,3-triazoles smoothly via "click" reaction.

Organic azides[1] are valuable and versatile molecules. The azide group exists in some clinically approved drugs such as the *anti*-HIV azidonucleoside drug zidovudine AZT.[2] Moreover, organic azides can be easily transformed into a wide range of nitrogen-containing structural motifs via various classic reactions[3] such as the "click" reaction,[4] *aza*-Wittig reaction,[5] Staudinger reduction,[6] and Schmidt rearrangement.[7] They are also currently considered as powerful precursors for reactive species such as nitrenes and nitrenium ions.[8] Therefore, numerous efforts have been devoted to develop the synthetic strategies for organic azides.[9] Among these approaches, the catalytic stereoselective introduction of an azido group into organic compounds is particularly attractive but remains comparatively rare. Up to now, asymmetric direct azidation[10] has mainly focused on asymmetric nucleophilic azido-functionalization of alkenes,[11] allenes,[12] aziridines,[13] and epoxides.[14] However, the corresponding enantioselective electrophilic variant has been rarely reported. In 2013, Gade's group[15] developed the first asymmetric azidations of β-keto esters and oxindoles applying the (boxmi)Fe(II) complex as the catalyst, which provided the desired optically pure azides with high enantioselectivities (Scheme 1a). In view of the importance of chiral azides, developing new methodologies and broadening the substrate scope in this area are still in great demand.

α-Azido β-naphthalenones are attractive targets because they are transformed smoothly into the corresponding naphthalenone derivatives, which are important structural motifs of various biologically active natural products and therapeutic reagents.[16] Surprisingly, only two examples of preparing α-azido-β-naphthalenones via oxidative azidation strategies were reported by Prabhu's group[17] and Sarkar's group,[18] respectively (Scheme 1b). To the best of our knowledge, the direct

Scheme 1. (a) Asymmetric α-Azidation of Carbonyl Compounds and (b, c) Dearomative Azidation of β-Naphthols[a]



[a]TBHP = *tert*-butyl hydroperoxide, PTAB = phenyl trimethyl ammonium tribromide.

Received: July 25, 2019

DOI: 10.1021/acs.orglett.9b02604
Org. Lett. XXXX, XXX, XXX−XXX

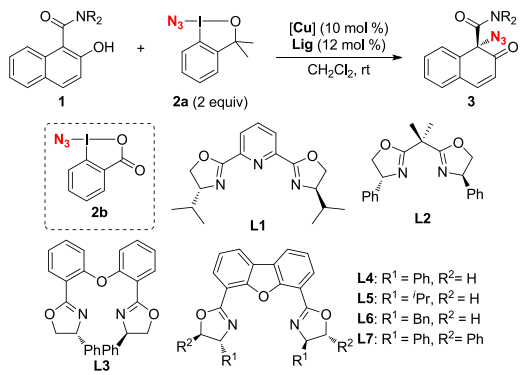
catalytic asymmetric azidation of β-naphthols remains unexplored. In this context, we report herein the first example of copper-catalyzed asymmetric dearomative azidation of β-naphthols for the synthesis of enantioenriched α-azido β-naphthalenones in excellent yields and with moderate to high enantioselectivities (Scheme 1c).

Amide structural motifs are omnipresent in natural products, drugs, and biologically active molecules.[19] However, investigations on dearomatization of arylamides are still rare.[20] Thus, we began by using the reaction of 2-hydroxy-*N*,*N*-diisopropyl-1-naphthamide (**1a**) with T-shaped iodine(III) compound **2a** as a model reaction to investigate different kinds of metal salts combining with various chiral ligands and found copper salts to be the most suitable catalyst precursors (see the Supporting Information). We then chose $Cu(OTf)_2$ as the metal salt to screen a series of chiral bisoxazoline type ligands (Table 1, entries 1−7). Tridentate bisoxazoline (pybox, **L1**) was used as the ligand to generate the desired product **3a** in 37% yield with low enantioselectivity (entry 1). The reaction was promoted efficiently in the presence of bisoxazoline (box) ligand **L2**, but only low enantioselectivity was observed (entry 2). Flexible tridentate bisoxazoline ligand **L3** resulted in slightly higher enantioselectivity (47%, entry 3). The combination of $Cu(OTf)_2$ with dbfox ligands[21] (**L4**−**L7**, dbfox = 4,6-dibenzofurandiyl-2,2′-bisoxazoline) was found to provide very promising results (entries 4−7), and $Cu(OTf)_2$/**L4** enabled the preparation of **3a** in 86% yield with 66% ee (entry 4).

The choice of solvent markedly influenced both the yield and enantioselectivity. Among the solvents evaluated, dichloromethane gave both a higher yield and ee value (see the Supporting Information). To further optimize the catalyst performance in terms of yield and enantioselectivity, various copper salts were tested in the reaction (entries 4 and 8−11). Among these copper salts, $Cu(CH_3CN)_4{\cdot}PF_6$ is the best metal salt and gave the product **3a** in 90% yield with 73% ee (entry 11). Then, it is found that the kind of *N*-substituent is crucial to improve the enantioselectivities (entries 11−14). 2-Hydroxy-*N*,*N*-dibenzyl-1-naphthamide (**1d**) gave the desired product **3d** with excellent enantioselectivity (95% ee, entry 14). In addition, when azido-transfer reagent **2b** was used in place of **2a**, the desired product was obtained in lower yield and decreased enantioselectivity (entry 15). Finally, the molecular sieve or lowering of the reaction temperature to 0 °C did not give better results (entries 16 and 17).

With the optimized reaction conditions in hand, the substrate scope was first examined by varying the substituents on the core of 2-hydroxy-*N*,*N*-dibenzyl-1-naphthamides (Scheme 2). Aryl groups such as Ph, 4-Me-C_6H_4, 4-F-C_6H_4, and 4-CF_3-C_6H_4 on the 6-position or 7-position were well-tolerated, and the corresponding products were all obtained in high yields and enantioselectivities (**3e**−**3i**, 89−99% yields, 92−95% ee). Substrate **1j** with 6-Br, substrate **1k** with 6-Me, and substrate **1l** with 7-MeO could all be successfully

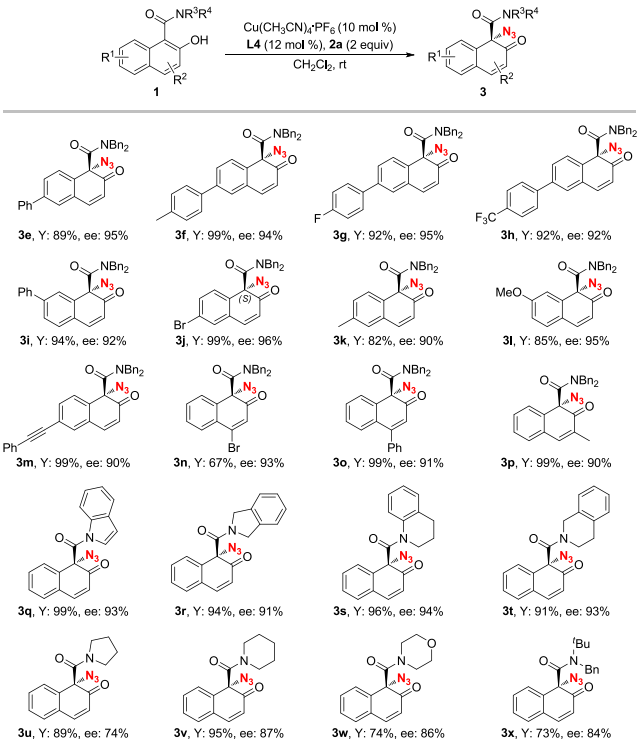
Table 1. Optimization of the Reaction Conditions[a]



entry	**1** (R)	[Cu]	ligand	time (h)	yield[b] (%)	ee[c] (%)
1	**1a** (^{i}Pr)	$Cu(OTf)_2$	**L1**	48	37	9
2	**1a** (^{i}Pr)	$Cu(OTf)_2$	**L2**	24	92	−12
3	**1a** (^{i}Pr)	$Cu(OTf)_2$	**L3**	12	94	47
4	**1a** (^{i}Pr)	$Cu(OTf)_2$	**L4**	20	86	66
5	**1a** (^{i}Pr)	$Cu(OTf)_2$	**L5**	10	80	44
6	**1a** (^{i}Pr)	$Cu(OTf)_2$	**L6**	10	84	42
7	**1a** (^{i}Pr)	$Cu(OTf)_2$	**L7**	12	86	48
8	**1a** (^{i}Pr)	$Cu(OAc)_2{\cdot}H_2O$	**L4**	23	64	27
9	**1a** (^{i}Pr)	(CuOTf)·0.5tol.	**L4**	25	90	65
10	**1a** (^{i}Pr)	$Cu(ClO_4)_2{\cdot}6H_2O$	**L4**	14	91	67
11	**1a** (^{i}Pr)	$Cu(CH_3CN)_4{\cdot}PF_6$	**L4**	13	90	73
12	**1b** (Cy)	$Cu(CH_3CN)_4{\cdot}PF_6$	**L4**	11	75	65
13	**1c** (Ph)	$Cu(CH_3CN)_4{\cdot}PF_6$	**L4**	15	94	76
14	**1d** (Bn)	$Cu(CH_3CN)_4{\cdot}PF_6$	**L4**	19	86	95
15[d]	**1d** (Bn)	$Cu(CH_3CN)_4{\cdot}PF_6$	**L4**	24	45	80
16[e]	**1d** (Bn)	$Cu(CH_3CN)_4{\cdot}PF_6$	**L4**	15	90	92
17[f]	**1d** (Bn)	$Cu(CH_3CN)_4{\cdot}PF_6$	**L4**	45	72	89

[a]Reaction conditions: **1** (0.10 mmol), **2a** (2 equiv), metal salt (10 mol %), ligand (12 mol %), CH_2Cl_2 (1.0 mL), rt (room temperature), argon. [b]The yields of isolated products. [c]Determined by HPLC analysis. [d]**2a** was replaced by **2b**. [e]50 mg of a 4 Å molecular sieve was added. [f]The reaction was carried out under 0 °C.

Scheme 2. Evaluation of the Substrate Scope of 2-Hydroxy-1-naphthamides[a]



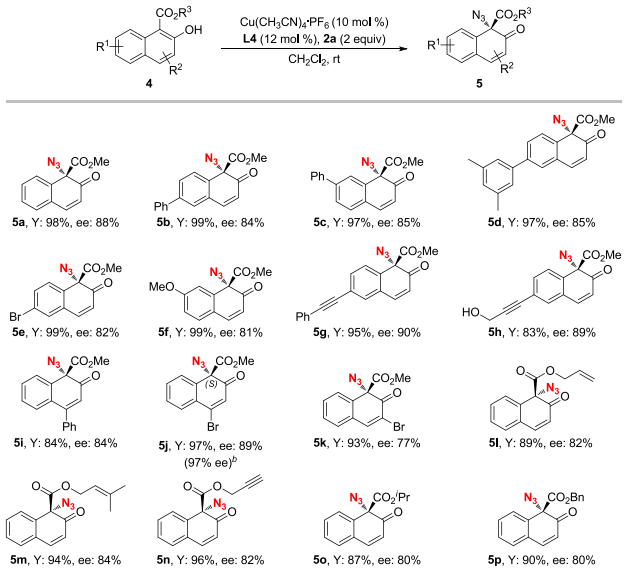
[a]Isolated yields of reactions performed on a 0.10 mmol scale; ee values were determined by HPLC.

DOI: 10.1021/acs.orglett.9b02604
Org. Lett. XXXX, XXX, XXX−XXX

converted to their corresponding products in high yields and enantioselectivities (**3j**–**3l**, 82–99% yields, 90–96% ee). To our delight, 6-phenylethynyl-substituted substrate **1m** was compatible with the reaction conditions, and no "click" reaction of the triple bond with azide occurred, giving the dearomatization product **3m** in 99% yield and 90% ee. Furthermore, installation of substituents to the 4- and 3-positions did not influence the reaction efficiency, and the substrates **1n** with 4-Br, **1o** with 4-Ph, and **1p** with 3-Me could accomplish the asymmetric azidation with the outcomes of 67–99% yields and 90–93% ee (**3n**–**3p**). Notably, 2-hydroxy-1-naphthamides bearing the complex *N*-substituent were also well-tolerated. The substrates tethering indole (**1q**), isoindoline (**1r**), tetrahydroquinoline (**1s**), and tetrahydroisoquinoline (**1t**) motifs achieved the corresponding products **3q**–**3t** in high yields with excellent enantioselectivities (91–99% yields, 91–94% ee); the substrates attaching pyrrolidine (**1u**), piperidine (**1v**), morpholine (**1w**), and *N*-benzyl-*N*-(*tert*-butyl) (**1x**) groups also were converted to the desired products **3u**–**3x** in moderate to high ee values (74–87% ee).

Encouraged by the above results, we also broadened the substrate scope to 2-hydroxy-1-naphthoates (Scheme 3).[22]

Scheme 3. Evaluation of the Substrate Scope of 2-Hydroxy-1-naphthoates[a]



[a]Isolated yields of reactions performed on the 0.10 mmol scale; ee values were determined by HPLC. [b]ee value of product after recrystallization.

When methyl 2-hydroxy-1-naphthoate (**4a**) was utilized, the desired product **5a** was obtained in 98% yield and 88% ee. The derivatives with aryl groups on the 6- or 7-position (**4b**–**4d**) also performed well and provided the corresponding products **5b**–**5d** in excellent yields and good enantioselectivities (97–99% yields, 84–85% ee). Substrate **4e** with 6-Br and substrate **4f** with 7-MeO could all be successfully converted to their corresponding products in excellent yields and good enantioselectivities (**5e**–**5f**). It is noteworthy that substrate **4g** with a phenylethynyl group as well as substrate **4h** with both a triple bond and a hydroxyl group were also well-tolerated, and the corresponding products **5g** and **5h** were obtained in 95% yield and 90% ee, and 83% yield and 89% ee, respectively. Additionally, the substrates bearing substituents on the 4-position of naphthols, such as **4i** with 4-Ph and **4j** with 4-Br, could be successfully converted to their corresponding products **5i** (84% yield, 84% ee) and **5j** (97% yield, 89% ee), respectively. However, the substituents on the 3-position obviously interfere with the enantiocontrol of the reaction. The ee value was only moderate for product **5k** with 3-Br (77% ee).

The substituent effect of the ester group (R^3) was then investigated (Scheme 3). The ester groups bearing an unsaturated double bond or triple bond, like allyl, isoprenyl, and propargyl, were tolerated, and the corresponding products were obtained (**5l**–**5n**, 89–96% yields, 82–84% ee). The bulkier groups, such as isopropyl and benzyl, could not improve the enantioselectivity, and the corresponding dearomatized products **5o**–**5p** were obtained with good enantioselectivities.

Notably, the absolute configurations of the enantiopure **3j** (96% ee) and **5j** (97% ee) were both established to be *S* by single-crystal X-ray structure analysis (Figure 1). The stereochemical assignment of all other products was also made by analogy.

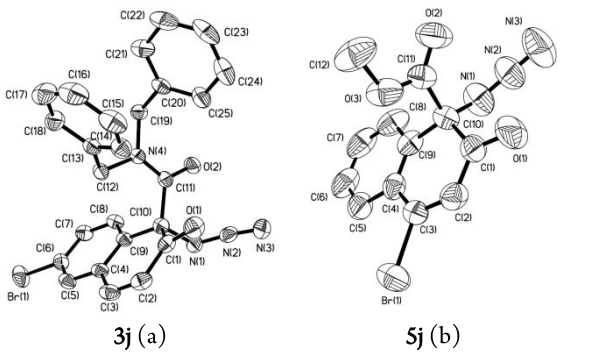
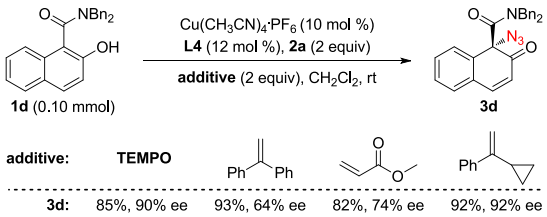


Figure 1. X-ray structures of product **3j** (a) and **5j** (b).

When the radical inhibitors such as 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), 1,1-diphenylethene, methyl acrylate, and even (1-cyclopropylvinyl)benzene were added to the reaction mixture, the reaction could still be carried out to provide the corresponding product **3d** smoothly (Scheme 4). These results indicated that the reaction pathway probably does not involve a radical process.

Scheme 4. Control Experiments for Mechanistic Investigations



On the basis of these data as shown above and in previous related reports,[23] we proposed a model for the key intermediate to explain the stereochemistry of the reaction (Figure 2). In this model, the catalyst functions as a chiral Lewis acid, and the copper center coordinates with the substrate by two-point binding, thus providing a rigid chiral environment around the reaction site. The *Re* face of the substrate is blocked by the phenyl group in the oxazolinyl unit,

DOI: 10.1021/acs.orglett.9b02604
Org. Lett. XXXX, XXX, XXX–XXX

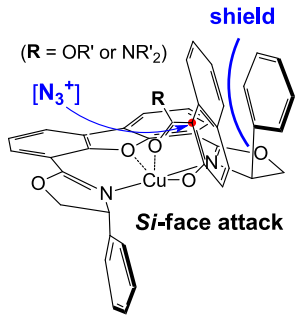
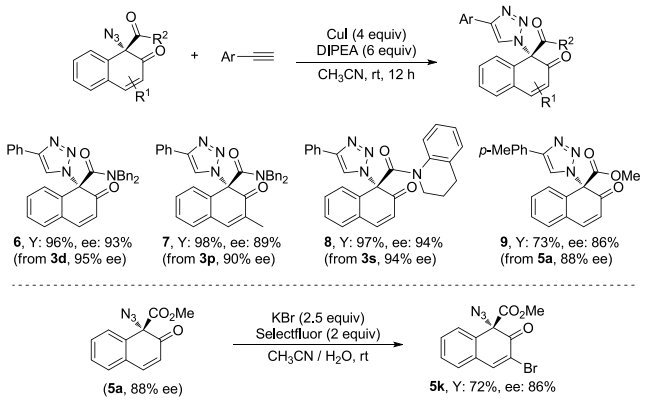


Figure 2. Proposed spatial model for the key intermediate.

and the azido species therefore preferentially approaches from the *Si* face of the substrate, which is consistent with the absolute configuration of products **3j** and **5j**.

To demonstrate the synthetic utility of this method, we undertook further transformations of the resulting azides (Scheme 5). The Cu-catalyzed azide−alkyne cycloaddition was

Scheme 5. Further Transformations of the Azide Products



used to transform azide products into the corresponding 1,2,3-triazoles **6**−**9** in good yields and enantioselectivities.[24] When **5a** was subjected to oxidative bromination conditions,[25] the brominated product **5k** could be achieved in 72% yield with 86% ee, serving as a complementary route to access **5k** with a higher ee value.

In conclusion, by employing the dbfox/Ph as a stereo-directing ligand, we have developed the first copper-catalyzed asymmetric dearomative azidation of *β*-naphthols. A wide range of chiral naphthalenones with a N_3-containing all-substituted carbon stereocenter were obtained in high yields and with moderate to excellent enantioselectivities under mild reaction conditions. The method exhibits a good tolerance of diverse functional groups. A further extension of the scope of the methodology and mechanistic investigations are underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b02604.

Experimental procedures, characterization data, copies of NMR spectra for all new products, and HPLC data for chiral compounds (PDF)

Accession Codes

CCDC 1813765 and 1845678 contain 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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Author Contributions

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from the Program of the Professor of Special Appointment (Eastern Scholar) at Shanghai Institutions of Higher Learning, Shanghai Engineering Research Center of Green Energy Chemical Engineering (18DZ2254200), the National Natural Science Foundation of China (21402119, 21772122), and Shanghai Rising-Star Program (16QA1403100) is greatly appreciated.

■ REFERENCES

(1) For selected reviews on the application of azides, see: (a) Hu, B.; DiMagno, S. G. *Org. Biomol. Chem.* **2015**, *13*, 3844. (b) Yang, M.; Li, J.; Chen, P. R. *Chem. Soc. Rev.* **2014**, *43*, 6511. (c) Intrieri, D.; Zardi, P.; Caselli, A.; Gallo, E. *Chem. Commun.* **2014**, *50*, 11440. (d) Ramil, C. P.; Lin, Q. *Chem. Commun.* **2013**, *49*, 11007. (e) Schilling, C. I.; Jung, N.; Biskup, M.; Schepers, U.; Brase, S. *Chem. Soc. Rev.* **2011**, *40*, 4840. (f) Nimmo, C. M.; Shoichet, M. S. *Bioconjugate Chem.* **2011**, *22*, 2199. (g) Lallana, E.; Riguera, R.; Fernandez-Megia, E. *Angew. Chem., Int. Ed.* **2011**, *50*, 8794. (h) Chu, C.; Liu, R. *Chem. Soc. Rev.* **2011**, *40*, 2177. (i) Amblard, F.; Cho, J. H.; Schinazi, R. F. *Chem. Rev.* **2009**, *109*, 4207.

(2) (a) Gnad, F.; Reiser, O. *Chem. Rev.* **2003**, *103*, 1603. (b) Huryn, D. M.; Okabe, M. *Chem. Rev.* **1992**, *92*, 1745. (c) Piantadosi, C.; Marasco, C. J.; Morris-Natschke, S. L.; Meyer, K. L.; Gumus, F.; Surles, J. R.; Ishaq, K. S.; Kucera, L. S.; Iyer, N. *J. Med. Chem.* **1991**, *34*, 1408.

(3) Kurti, L., Czako, B., Eds. *Strategic Applications of Named Reactions in Organic Synthesis*; Academic Press, 2005.

(4) (a) Tiwari, V. K.; Mishra, B. B.; Mishra, K. B.; Mishra, N.; Singh, A. S.; Chen, X. *Chem. Rev.* **2016**, *116*, 3086. (b) Kacprzak, K.; Skiera, I.; Piasecka, M.; Paryzek, Z. *Chem. Rev.* **2016**, *116*, 5689. (c) Thirumurugan, P.; Matosiuk, D.; Jozwiak, K. *Chem. Rev.* **2013**, *113*, 4905. (d) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004.

(5) Palacios, F.; Alonso, C.; Aparicio, D.; Rubiales, G.; delos Santos, J. M. *Tetrahedron* **2007**, *63*, 523.

(6) (a) van Berkel, S. S.; van Eldijk, M. B.; van Hest, J. C. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 8806. (b) Kohn, M.; Breinbauer, R. *Angew. Chem., Int. Ed.* **2004**, *43*, 3106.

(7) Wrobleski, A.; Coombs, T. C.; Huh, C. W.; Li, S.-W.; Aube, J. *Org. React.* **2012**, *78*, 1.

(8) (a) Uchida, T.; Katsuki, T. *Chem. Rec.* **2014**, *14*, 117. (b) Intrieri, D.; Zardi, P.; Caselli, A.; Gallo, E. *Chem. Commun.* **2014**, *50*, 11440. (c) Driver, T. G. *Org. Biomol. Chem.* **2010**, *8*, 3831.

(9) For the monographs and reviews on organic azides, see: (a) Goswami, M.; de Bruin, B. *Eur. J. Org. Chem.* **2017**, 1152. (b) Wu,

DOI: 10.1021/acs.orglett.9b02604
Org. Lett. XXXX, XXX, XXX−XXX

K.; Liang, Y.; Jiao, N. *Molecules* **2016**, *21*, 352. (c) Bräse, S.; Banert, K. *Organic Azides: Syntheses and Applications*; Wiley: Chichester, 2009. (d) Scriven, E. F. V. *Azides and Nitrenes: Reactivity and Utility*; Academic Press: Orlando, 1984. (e) Bräse, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem., Int. Ed.* **2005**, *44*, 5188. (f) Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 297.

(10) Ding, P.-G.; Hu, X.-S.; Zhou, F.; Zhou, J. *Org. Chem. Front.* **2018**, *5*, 1542.

(11) (a) Zhou, P.; Liu, X.; Wu, W.; Xu, C.; Feng, X. *Org. Lett.* **2019**, *21*, 1170. (b) Liang, Y.; Zhao, X. *ACS Catal.* **2019**, *9*, 6896. (c) Zhang, Y.; Liao, Y.; Liu, X.; Xu, X.; Lin, L.; Feng, X. *Chem. Sci.* **2017**, *8*, 6645. (d) Zhou, P.; Lin, L.; Chen, L.; Zhong, X.; Liu, X.; Feng, X. *J. Am. Chem. Soc.* **2017**, *139*, 13414. (e) Meyer, D.; Renaud, P. *Angew. Chem., Int. Ed.* **2017**, *56*, 10858. (f) Nielsen, M.; Zhuang, W.; Jorgensen, K. A. *Tetrahedron* **2007**, *63*, 5849. (g) Taylor, M. S.; Zalatan, D. N.; Lerchner, A. M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2005**, *127*, 1313. (h) Guerin, D. J.; Miller, S. J. *J. Am. Chem. Soc.* **2002**, *124*, 2134. (i) Horstmann, T. E.; Guerin, D. J.; Miller, S. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 3635. (j) Myers, J. K.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1999**, *121*, 8959.

(12) Khrakovsky, D. A.; Tao, C.; Johnson, M. W.; Thornbury, R. T.; Shevick, S. L.; Toste, F. D. *Angew. Chem., Int. Ed.* **2016**, *55*, 6079.

(13) (a) Wu, B.; Gallucci, J. C.; Parquette, J. R.; Rajanbabu, T. V. *Angew. Chem., Int. Ed.* **2009**, *48*, 1126. (b) Rowland, E. B.; Rowland, G. B.; Rivera-Otero, E.; Antilla, J. C. *J. Am. Chem. Soc.* **2007**, *129*, 12084. (c) Fukuta, Y.; Mita, T.; Fukuda, N.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 6312.

(14) (a) Martinez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5897. (b) Nugent, W. A. *J. Am. Chem. Soc.* **1992**, *114*, 2768.

(15) Deng, Q.-H.; Bleith, T.; Wadepohl, H.; Gade, L. H. *J. Am. Chem. Soc.* **2013**, *135*, 5356.

(16) (a) Randolph, J. T.; Flentge, C. A.; Huang, P. P.; Hutchinson, D. K.; Klein, L. L.; Lim, H. B.; Mondal, R.; Reisch, T.; Montgomery, D. A.; Jiang, W. W.; Masse, S. V.; Hernandez, L. E.; Henry, R. F.; Liu, Y.; Koev, G.; Kati, W. M.; Stewart, K. D.; Beno, D. W. A.; Molla, A.; Kempf, D. J. *J. Med. Chem.* **2009**, *52*, 3174. (b) Bevalot, F.; Leboeuf, M.; Bouquet, A.; Cave, A. *Ann. Pharm. Fr.* **1977**, *35*, 65. (c) Harris, W. M.; Geissman, T. A. *J. Org. Chem.* **1965**, *30*, 432.

(17) Dhineshkumar, J.; Samaddar, P.; Prabhu, K. R. *Chem. Commun.* **2016**, *52*, 11084.

(18) Sarkar, D.; Ghosh, M. K.; Rout, N.; Kuila, P. *New J. Chem.* **2017**, *41*, 3715.

(19) For selected monographs and reviews on applications of amides, see: (a) Lundberg, H.; Tinnis, F.; Selander, N.; Adolfsson, H. *Chem. Soc. Rev.* **2014**, *43*, 2714. (b) Castanho, M., Santos, N., Eds. *Peptide Drug Discovery and Development*; Wiley: Weinheim, Germany, 2011. (c) Greenberg, A., Breneman, C. M., Liebman, J. F., Eds. *The Amide Linkage: Structural Significance in Chemistry, Biochemistry, and Materials Science*; Wiley-Interscience: New York, 2000. (d) Humphrey, J. M.; Chamberlin, A. R. *Chem. Rev.* **1997**, *97*, 2243.

(20) (a) Zhang, D.-Y.; Xu, L.; Wu, H.; Gong, L.-Z. *Chem. - Eur. J.* **2015**, *21*, 10314. (b) Rousseau, G.; Robert, F.; Landais, Y. *Chem. - Eur. J.* **2009**, *15*, 11160. (c) Sakamoto, M.; Unosawa, A.; Kobaru, S.; Saito, A.; Mino, T.; Fujita, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 5523. (d) Ohno, H.; Iwasaki, H.; Eguchi, T.; Tanaka, T. *Chem. Commun.* **2004**, 2228.

(21) The latest selected reviews and examples on dbfox ligand, see: (a) Itoh, K.; Sibi, M. P. *Org. Biomol. Chem.* **2018**, *16*, 5551−5565. (b) Shen, X.; Li, Y.; Wen, Z.; Cao, S.; Hou, X.; Gong, L. *Chem. Sci.* **2018**, *9*, 4562. (c) Yang, X.; Cheng, F.; Kou, Y. D.; Pang, S.; Shen, Y. C.; Huang, Y. Y.; Shibata, N. *Angew. Chem., Int. Ed.* **2017**, *56*, 1510. (d) Qiu, J.-S.; Wang, Y.-F.; Qi, G.-R.; Karmaker, P. G.; Yin, H.-Q.; Chen, F.-X. *Chem. - Eur. J.* **2017**, *23*, 1775.

(22) For details for screening reaction conditions, see the Supporting Information.

(23) (a) Deng, Q.-H.; Rettenmeier, C.; Wadepohl, H.; Gade, L. H. *Chem. - Eur. J.* **2014**, *20*, 93. (b) Deng, Q.-H.; Wadepohl, H.; Gade, L. H. *J. Am. Chem. Soc.* **2012**, *134*, 2946. (c) Shibata, N.; Kohno, J.; Takai, K.; Ishimaru, T.; Nakamura, S.; Toru, T.; Kanemasa, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 4204.

(24) Zhu, L.; Yu, H.; Xu, Z.; Jiang, X.; Lin, L.; Wang, R. *Org. Lett.* **2014**, *16*, 1562.

(25) Yin, Q.; Wang, S.-G.; Liang, X.-W.; Gao, D.-W.; Zheng, J.; You, S.-L. *Chem. Sci.* **2015**, *6*, 4179.

DOI: 10.1021/acs.orglett.9b02604
Org. Lett. XXXX, XXX, XXX−XXX