Organic LETTERS

Letter

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

pubs.acs.org/OrgLett

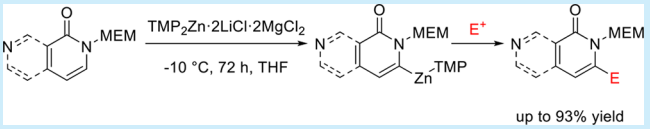
Directed Zincation or Magnesiation of the 2-Pyridone and 2,7-Naphthyridone Scaffold Using TMP Bases

Dorothée S. Ziegler, Robert Greiner, Henning Lumpe, Laura Kqiku, Konstantin Karaghiosoff, and Paul Knochel*

Department of Chemistry, Ludwig-Maximilians-University Munich, Butenandtstr. 5-13, 81377 Munich, Germany

Supporting Information

ABSTRACT: A regioselective zincation of the 2-pyridone and 2,7-naphthyridone scaffolds has been developed. Zincations of the methoxyethoxymethyl (MEM)-protected compounds using $TMP_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ (TMP = 2,2,6,6-tetramethylpiperidyl) followed by trapping with electrophiles provided functionalized 2-pyridones and 2,7-naphthyridones. I/Mg exchange of iodinated 2-pyridone and 2,7-naphthyridone using *i*-PrMgCl·LiCl afforded magnesiated intermediates that reacted with electrophiles. A second magnesiation of the 2-pyridone scaffold was achieved by using TMPMgCl·LiCl. Additionally, we report $CoCl_2$-catalyzed cross-couplings of the 1-chloro-2,7-naphthyridines with arylzinc halides.



The selective functionalization of 2-pyridone (**1**) and 2,7-naphthyridone (**2**) (Figure 1) is an important synthetic goal because of the pharmaceutical relevance of many substituted 2-pyridones and 2,7-naphthyridones.[1] These heterocycles are known to display antibiotic, antifungal, anticancer, and antiviral activity.[2] Typical pharmaceutically and biologically active derivatives are milrinone (**3**),[3] ciclopirox (**4**),[4] pirfenidone (**5**),[5] and lophocladine A (**6**).[6]

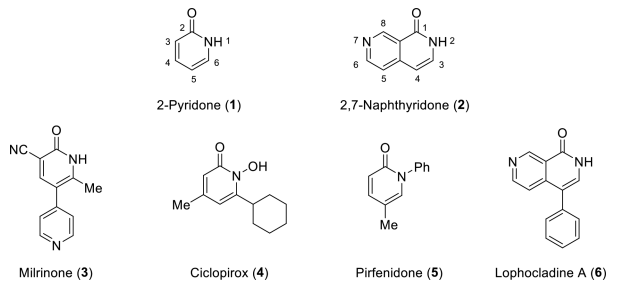


Figure 1. Structures of 2-pyridone and 2,7-naphthyridone derivatives.

Functionalizations of 2-pyridones via lithiation have been reported.[7] Alternatively, a regioselective direct C−H activation allows the functionalization of 2-pyridone at either C(3) or C(6).[8] We recently reported that a broad array of functionalized aromatic and heteroaromatic compounds can be metalated with various TMP-derived Mg and Zn bases (TMP = 2,2,6,6-tetramethylpiperidyl).[9] Preliminary metalation studies showed that TMPLi[10] and TMPMgCl·LiCl (**7**)[11] led to the decomposition of protected 2-pyridones or 2,7-naphthyridones even at low temperatures or produced complex mixtures of products. Therefore, the use of more selective metalating agents was investigated. TMPZnCl·LiCl[12] and $TMP_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ (**8**)[13] have proven to be especially efficient for performing zincations of sensitive (hetero)arenes, as these metalations produce organozinc derivatives that tolerate a range of functional groups.

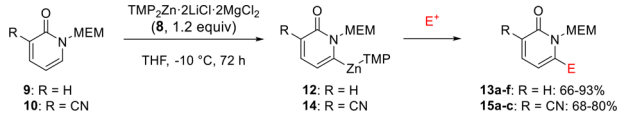
Herein we report the functionalization of 2-methoxyethoxymethyl (MEM)-protected 2-pyridones like **9** and **10** as well as MEM-protected 2,7-naphthyridone **11** using **8** followed by reactions with various electrophiles (E^+). Thus, treatment of the MEM-protected 2-pyridone derivative **9** with zinc amide **8** (1.2 equiv, −10 °C, 72 h) led to the quantitative formation of the corresponding zincated 2-pyridone **12**, which was quenched by various electrophiles to furnish 2-pyridones of type **13** (Table 1). Thus, quenching of **12** with iodine provided 6-iodo-2-pyridone **13a** in 93% yield (Table 1, entry 1). Additionally, Negishi cross-coupling[14] of **12** with various aryl iodides containing electron-withdrawing or -donating substituents in the presence of 4% $Pd(dba)_2$ and 8% tris(*o*-furyl)phosphine[15] afforded a variety of arylated pyridone derivatives (**13b−f**) in 66−92% yield (entries 2−6). This zincation was extended to the MEM-protected 3-cyano-2-pyridone **10**, which was metalated with **8** (1.2 equiv, −10 °C, 72 h) to give C(6)-zincated heterocycle **14**. After iodolysis, the desired product **15a** was isolated in 80% yield (entry 7). Pd-catalyzed cross-coupling of **14** provided arylated 3-cyano-2-pyridone **15b** in 68% yield (entry 8). Moreover, 2-iodothiophene underwent Negishi cross-coupling[14] with zinc species **14** to afford 3-cyano-2-pyridone **15c** in 80% yield (entry 9).

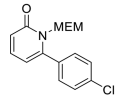
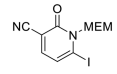
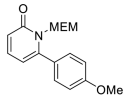
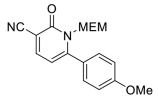
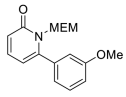
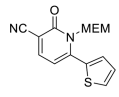
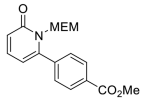
We further explored the scope of this zincation using the zinc base **8** on MEM-protected 2,7-naphthyridone derivative **11**. The MEM protecting group was essential to achieve regioselective zincation of 2,7-naphthyridone **11** at position 3 with **8** (1.2 equiv, −10 °C, 72 h). The resulting zinc reagent **16** was readily functionalized by reaction with various electrophiles to furnish 3-substituted 2,7-naphthyridones of type **17** (Table

Received: August 29, 2017

DOI: 10.1021/acs.orglett.7b02690
Org. Lett. XXXX, XXX, XXX−XXX

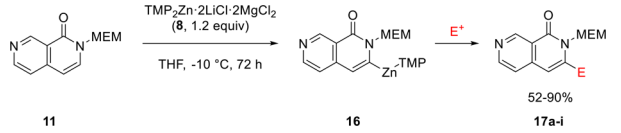
Table 1. Zincation of MEM-Protected 2-Pyridones 9 and 10 and Reactions with Electrophiles

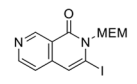
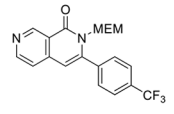
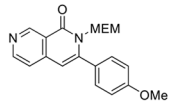
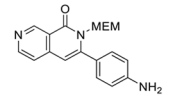
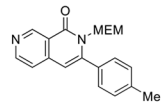
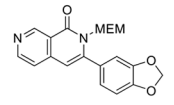
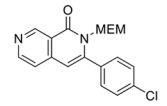
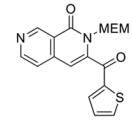
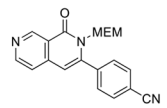


entry	E^+	product/ yield, %[a]	entry	E^+	product/ yield, %[a]
1	I_2	 **13a**, 93	6		 **13f**, 88[b]
2		 **13b**, 92[b]	7	I_2	 **15a**, 80[b]
3		 **13c**, 66[b]	8		 **15b**, 68[b]
4		 **13d**, 80[b]	9		 **15c**, 80[b]
5		 **13e**, 80[b]			

[a]Yields of isolated, analytically pure products. [b]Obtained by Negishi cross-coupling[14] using 4% $Pd(dba)_2$ and 8% P(*o*-furyl)$_3$.[15]

Table 2. Zincation of MEM-Protected 2,7-Naphthyridone 11 and Reactions with Electrophiles



entry	E^+	product/ yield, %[a]	entry	E^+	product/ yield, %[a]
1	I_2	 **17a**, 90	6		 **17f**, 64[b]
2		 **17b**, 81[b]	7		 **17g**, 76[c]
3		 **17c**, 84[b]	8		 **17h**, 80[d]
4		 **17d**, 86[b]	9		 **17i**, 52[e]
5		 **17e**, 74[b]			

[a]Yields of isolated, analytically pure products. [b]Obtained by Negishi cross-coupling[13] using 4% $Pd(dba)_2$ and 8% P(*o*-furyl)$_3$.[15] [c]Obtained by Negishi cross-coupling[14] using 4% $Pd(OAc)_2$ and 8% SPhos.[16] [d]Obtained by Negishi cross-coupling[14] using 4% PEPPSI-*i*Pr.[18] [e]Obtained after transmetalation with CuCN·2LiCl (1.1 equiv).[19]

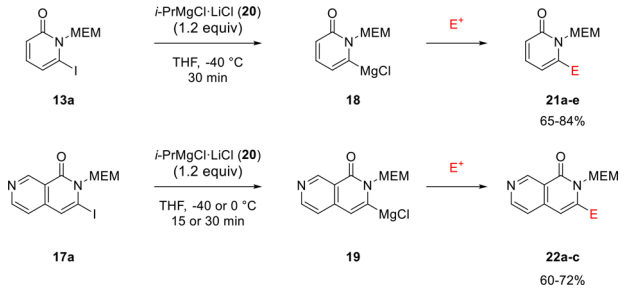
2). After iodolysis, compound **17a** was isolated in 90% yield (Table 2, entry 1). The X-ray structure of compound **17a** confirmed exclusive iodination at position 3 (see the Supporting Information). Furthermore, the zinc reagent **16** underwent smooth Pd-catalyzed Negishi cross-coupling reactions[14] with aryl iodides to afford 3-arylated 2,7-naphthyridones **17b–f** in 64–86% yield (entries 2–6). The cross-coupling with 4-iodoaniline proceeded smoothly using an inverse addition with 4% $Pd(OAc)_2$ and 8% Buchwald's SPhos[16] via syringe pump to afford the desired product **17g** in 76% yield (entry 7).[17] Furthermore, the zinc intermediate **16** reacted with 5-bromo-benzo[*d*][1,3]dioxole in the presence of 4% PEPPSI-*i*Pr[18] to afford the corresponding product **17h** in 80% yield (entry 8). Transmetalation of **16** with CuCN·2LiCl[19] (1.1 equiv, −10 °C, 10 min) and subsequent reaction with 2-thiophenecarbonyl chloride provided 2,7-naphthyridone **17i** in 52% yield (entry 9).

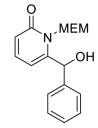
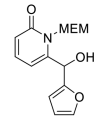
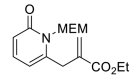
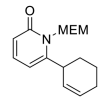
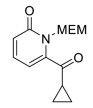
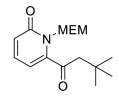
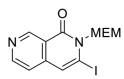
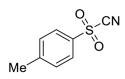
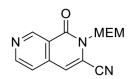
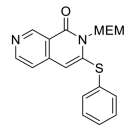
In order to extend the electrophile range, we prepared 6-magnesiated pyridone **18** and magnesiated naphthyridone **19** by treating the corresponding iodoheterocycles **13a** and **17a** with *i*-PrMgCl·LiCl (**20**)[20] at −40 or 0 °C (see Table 3). Magnesium intermediate **18** reacted readily with benzaldehyde and furfural, providing the corresponding alcohols **21a** and **21b** in 80–84% yield (Table 3, entries 1 and 2). After magnesiation of **13a** and transmetalation with CuCN·2LiCl[19] (1.2 equiv, −40 °C, 30 min), copper-mediated allylation with ethyl 2-(bromomethyl)acrylate[21] and 3-bromocyclohex-1-ene led to 6-allylated 2-pyridones **21c** and **21d**, respectively, in 65–76% yield (entries 3 and 4). Copper-mediated acylation with cyclopropanecarbonyl chloride and *tert*-butylacetyl chloride gave 2-pyridone ketones **21e** and **21f**, respectively, in 72–76% yield (entries 5 and 6). Quenching magnesiated 2,7-napthyridone **19** with *p*-toluenesulfonyl cyanide and *S*-phenyl benzenethiosulfonate afforded the desired products **22a** and **22b**, respectively, in 60–72% yield (entries 7 and 8).

A second metalation of 6-substituted 2-pyridones **13a** and **13b** occurred at position 3 using TMPMgCl·LiCl (**7**).[11] Thus, treatment of 6-iodinated 2-pyridone **13a** with magnesium amide **7** (1.2 equiv, −40 °C, 2 h) led to the quantitative formation of 3-magnesiated pyridone **23a** (Scheme 1). The magnesium reagent **23a** reacted with iodine, benzaldehyde, and *p*-toluenesulfonyl cyanide to provide the corresponding 3,6-disubstituted 2-pyridones **24a–c** in 40–80% yield (Scheme 1). Furthermore, 6-arylated 2-pyridone **13b** was metalated at position 3 with **7** (1.2 equiv, −40 °C, 2 h), and this

DOI: 10.1021/acs.orglett.7b02690
Org. Lett. XXXX, XXX, XXX–XXX

Table 3. Iodine/Magnesium Exchange of Iodinated 2-Pyridone 12a and Iodinated 2,7-Naphthyridone 17a and Reactions with Electrophiles



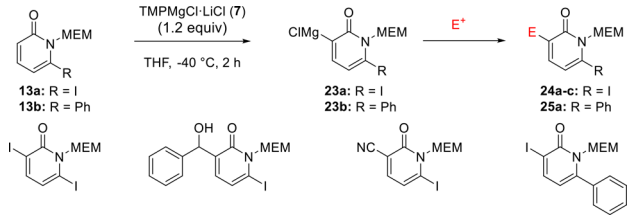
entry	educt	E^+	product/ yield, %[a]
1	 **13a**		 **21a**, 80
2	**13a**		 **21b**, 84
3	**13a**		 **21c**, 65[b]
4	**13a**		 **21d**, 76[b]
5	**13a**		 **21e**, 76
6	**13a**		 **21f**, 72[b]
7	 **17a**		 **22a**, 60
8	**17a**	$PhSSO_2Ph$	 **22b**, 72

[a]Yields of isolated, analytically pure products. [b]Obtained after transmetalation with CuCN·2LiCl (1.2 equiv).[19]

magnesiated species was then iodinated to provide iodo derivative **25a** in 70% yield (Scheme 1).

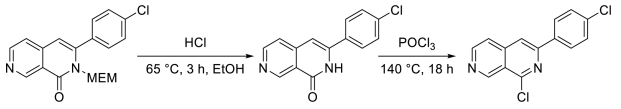
As an application of this method, we converted functionalized MEM-protected 2,7-naphthyridone **17d** into bioactive

Scheme 1. 3,6-Disubstituted Pyridones of Types 24 and 25 Obtained by Regioselective Magnesiation of 2-Pyridone Derivatives of Type 13 Using TMPMgCl·LiCl (7)[11] and Quenching with Electrophiles



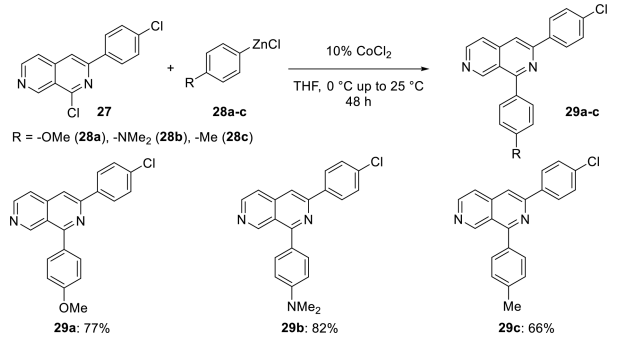
deprotected 2,7-naphthyridone **26**, which acts as an inhibitor of tankyrase.[6a] The MEM group was selectively removed by treatment with HCl at 65 °C, which furnished the unprotected 2,7-naphthyridone **26** in 84% yield (Scheme 2). Further

Scheme 2. Preparation of a Functionalized Halonaphthyridine from Naphthyridone 17d



functionalization at position 1 of the 2,7-naphthyridone scaffold in **26** was achieved by chlorination with $POCl_3$, leading to naphthyridine **27** in 82% yield (Scheme 2).[22] Finally, treatment of 1-chloro-2,7-naphthyridine **27** with arylzinc chlorides **28a–c**[23b] in the presence of 10% $CoCl_2$[23] in THF (0 °C up to 25 °C, 48 h) gave the cross-coupling products **29a–c** in 66–82% yield (Scheme 3).

Scheme 3. Cobalt-Catalyzed Negishi Cross-Couplings[14] of Chlorinated 2,7-Naphthyridine 27



In conclusion, we have developed a new general method for the regioselective metalation of MEM-protected 2-pyridones **9** and **10** as well as MEM-protected 2,7-naphthyridone **11** using $TMP_2Zn·2MgCl_2·2LiCl$ (**8**), leading to a variety of new functionalized 2-pyridones and 2,7-naphthyridones. Furthermore, I/Mg exchange of iodinated 2-pyridone **13a** and 2,7-naphthyridone **17a** using *i*-PrMgCl·LiCl (**20**) afforded magnesiated intermediates that reacted with a broad range of electrophiles. A second metalation of the 2-pyridone scaffold was achieved using TMPMgCl·LiCl (**7**). Additionally, cobalt(II) chloride-catalyzed cross-couplings of 1-chloro-2,7-naphthyridine **27** with arylzinc halides led to the desired naphthyridines in satisfying yields.

DOI: 10.1021/acs.orglett.7b02690
Org. Lett. XXXX, XXX, XXX–XXX

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.7b02690.

Full experimental details, crystallographic data for **17a**, GC data, melting points, mass spectra, infrared spectra, and ^{1}H and ^{13}C NMR spectra (PDF)
Crystallographic data for **17a** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*paul.knochel@cup.uni-muenchen.de

ORCID

Paul Knochel: 0000-0001-7913-4332

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Ludwig-Maximilians-University Munich for financial support. We thank Albemarle Corporation for the generous gift of chemicals and the DIP (German-Israeli Project Cooperation) for financial support.

■ REFERENCES

(1) (a) Ukita, T.; Nakamura, Y.; Kubo, A.; Yamamoto, Y.; Moritani, Y.; Saruta, K.; Higashijima, T.; Kotera, J.; Fujishige, K.; Takagi, M.; Kikkawa, K.; Omori, K. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2341. (b) Jessen, H. J.; Gademann, K. *Nat. Prod. Rep.* **2010**, *27*, 1168. (c) Yu, G.; Rao, P. N. P.; Chowdhury, M. A.; Abdellatif, K. R. A.; Dong, Y.; Das, D.; Velázquez, C. A.; Suresh, M. R.; Knaus, E. E. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 2168. (d) Hamama, W. S.; Waly, M.; El-Hawary, I.; Zoorob, H. H. *Synth. Commun.* **2014**, *44*, 1730.

(2) (a) Desai, N. C.; Rajpara, K. M.; Joshi, V. V. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 2714. (b) Lv, Z.; Zhang, Y.; Zhang, M.; Chen, H.; Sun, Z.; Geng, D.; Niu, C.; Li, K. *Eur. J. Med. Chem.* **2013**, *67*, 447. (c) Jia, H.; Song, Y.; Yu, J.; Zhan, P.; Rai, D.; Liang, X.; Ma, C.; Liu, X. *Eur. J. Med. Chem.* **2017**, *136*, 144. (d) Singh, S.; Goo, J.-I.; Noh, H.; Lee, S. J.; Kim, M. W.; Park, H.; Jalani, H. B.; Lee, K.; Kim, C.; Kim, W.-K.; Ju, C.; Choi, Y. *Bioorg. Med. Chem.* **2017**, *25*, 1394.

(3) (a) Santhosh, K. T.; Elkhateeb, O.; Nolette, N.; Outbih, O.; Halayko, A. J.; Dakshinamurti, S. Dakshinamurti. *Br. J. Pharmacol.* **2011**, *163*, 1223. (b) Ravinder, M.; Mahendar, B.; Mattapally, S.; Hamsini, K. V.; Reddy, T. N.; Rohit, C.; Srinivas, K.; Banerjee, S. K.; Rao, V. J. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 6010.

(4) Monti, D.; Saccomani, L.; Chetoni, P.; Burgalassi, S.; Tampucci, S.; Mailland, F. *Br. J. Dermatol.* **2011**, *165*, 99.

(5) (a) Takakura, K.; Mizukami, K.; Mitori, H.; Noto, T.; Tomura, Y. *Eur. J. Pharmacol.* **2014**, *737*, 106. (b) Kim, E. S.; Keating, G. M. *Drugs* **2015**, *75*, 219.

(6) (a) Kumpan, K.; Nathubhai, A.; Zhang, C.; Wood, P. J.; Lloyd, M. D.; Thompson; Haikarainen, T.; Lehtiö, L.; Threadgill, M. D. *Bioorg. Med. Chem.* **2015**, *23*, 3013. (b) Theeramunkong, S.; Vajragupta, O.; Mudjupa, C. *Med. Chem. Res.* **2016**, *25*, 2959.

(7) (a) Meghani, P.; Joule, J. A. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1. (b) Effenberger, F.; Daub, W. *Chem. Ber.* **1991**, *124*, 2119. (c) Mongin, F.; Quéguiner, G. *Tetrahedron* **2001**, *57*, 4059.

(8) (a) Nakao, Y.; Idei, H.; Kanyiva, K. S.; Hiyama, T. *J. Am. Chem. Soc.* **2009**, *131*, 15996. (b) Nakatani, A.; Hirano, K.; Satoh, T.; Miura, M. *Chem. - Eur. J.* **2013**, *19*, 7691. (c) Modak, A.; Rana, S.; Maiti, D. *J. Org. Chem.* **2015**, *80*, 296.

(9) (a) Haas, D.; Sustac-Roman, D.; Schwarz, S.; Knochel, P. *Org. Lett.* **2016**, *18*, 6380. (b) Nafe, J.; Knochel, P. *Synthesis* **2016**, *48*, 103. (c) Klier, L.; Ziegler, D. S.; Rahimoff, R.; Mosrin, M.; Knochel, P. *Org. Process Res. Dev.* **2017**, *21*, 660. (d) Castello-Mico, A.; Nafe, J.; Higashida, K.; Karaghiosoff, K.; Gingras, M.; Knochel, P. *Org. Lett.* **2017**, *19*, 360. (e) For a review of metallic TMP bases, see: Haag, B.; Mosrin, M.; Ila, H.; Malakhov, V.; Knochel, P. *Angew. Chem., Int. Ed.* **2011**, *50*, 9794.

(10) (a) Kissel, C. L.; Rickborn, B. *J. Org. Chem.* **1972**, *37*, 2060. (b) Olofson, R. A.; Dougherty, C. M. *J. Am. Chem. Soc.* **1973**, *95*, 581. (c) Uzelac, M.; Kennedy, A. R.; Hevia, E.; Mulvey, R. E. *Angew. Chem., Int. Ed.* **2016**, *55*, 13147.

(11) (a) Krasovskiy, A.; Krasovskaya, V.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 2958. (b) Lin, W.; Baron, O.; Knochel, P. *Org. Lett.* **2006**, *8*, 5673. (c) Mulvey, R. E. *Organometallics* **2006**, *25*, 1060. (d) Mulvey, R. E.; Mongin, F.; Uchiyama, M.; Kondo, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 3802. (e) Mosrin, M.; Knochel, P. *Org. Lett.* **2008**, *10*, 2497. (f) Garcia-Alvarez, P.; Graham, D. V.; Hevia, E.; Kennedy, A. R.; Klett, J.; Mulvey, R. E.; O'Hara, C. T.; Weatherstone, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 8079.

(12) (a) Mosrin, M.; Bresser, T.; Knochel, P. *Org. Lett.* **2009**, *11*, 3406. (b) Bresser, T.; Knochel, P. *Angew. Chem., Int. Ed.* **2011**, *50*, 1914. (c) Duez, S.; Steib, A. K.; Manolikakes, S. M.; Knochel, P. *Angew. Chem., Int. Ed.* **2011**, *50*, 7686. (d) Unsinn, A.; Ford, M. J.; Knochel, P. *Org. Lett.* **2013**, *15*, 1128. (e) Haas, D.; Mosrin, M.; Knochel, P. *Org. Lett.* **2013**, *15*, 6162. (f) Shen, J.; Wong, B.; Gu, C.; Zhang, H. *Org. Lett.* **2015**, *17*, 4678.

(13) (a) Wunderlich, S.; Knochel, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 7685. (b) Mosrin, M.; Knochel, P. *Chem. - Eur. J.* **2009**, *15*, 1468. (c) Klier, L.; Bresser, T.; Nigst, T. A.; Karaghiosoff, K.; Knochel, P. *J. Am. Chem. Soc.* **2012**, *134*, 13584. (d) Hammann, J. M.; Haas, D.; Knochel, P. *Angew. Chem., Int. Ed.* **2015**, *54*, 4478. (e) Tichý, M.; Smoleň, S.; Tloušťová, E.; Pohl, R.; Ožd'ian, T.; Hejtmánková, K.; Lišková, B.; Gurská, S.; Džubák, P.; Hajdúch, M.; Hocek, M. *J. Med. Chem.* **2017**, *60*, 2411.

(14) (a) Negishi, E.; Valente, L. F.; Kobayashi, M. *J. Am. Chem. Soc.* **1980**, *102*, 3298. (b) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340.

(15) (a) Farina, V.; Baker, S. R.; Benigni, D. A.; Sapino, C., Jr. *Tetrahedron Lett.* **1988**, *29*, 5739. (b) Farina, V.; Baker, S. R.; Benigni, D. A.; Hauck, S. I.; Sapino, C., Jr. *J. Org. Chem.* **1990**, *55*, 5833.

(16) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461.

(17) (a) Manolikakes, G.; Schade, M. A.; Muñoz Hernandez, C.; Mayr, H.; Knochel, P. *Org. Lett.* **2008**, *10*, 2765. (b) Manolikakes, G.; Muñoz Hernandez, C.; Schade, M. A.; Metzger, A.; Knochel, P. *J. Org. Chem.* **2008**, *73*, 8422.

(18) Valente, C.; Belowich, M. E.; Hadei, N.; Organ, M. G. *Eur. J. Org. Chem.* **2010**, *2010*, 4343.

(19) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390.

(20) (a) Krasovskiy, A.; Straub, B. F.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 159. (b) *i*-PrMgCl·LiCl in THF is available from Albemarle (Germany).

(21) Villieras, J.; Rambaud, M. *Org. Synth.* **1988**, *66*, 220.

(22) PyBroP-mediated Suzuki couplings of 2,7-naphthyridone **26** and 2-pyridone **1** with phenylboronic acid were unsuccessful (see the Supporting Information).

(23) (a) Cahiez, G.; Moyeux, A. *Chem. Rev.* **2010**, *110*, 1435. (b) Haas, D.; Hammann, J. M.; Lutter, F. H.; Knochel, P. *Angew. Chem., Int. Ed.* **2016**, *55*, 3809.

DOI: 10.1021/acs.orglett.7b02690
Org. Lett. XXXX, XXX, XXX−XXX