Organic LETTERS

Letter

pubs.acs.org/OrgLett

Direct Access to Axially Substituted Subphthalocyanines from Trimethylsilyl-Protected Nucleophiles

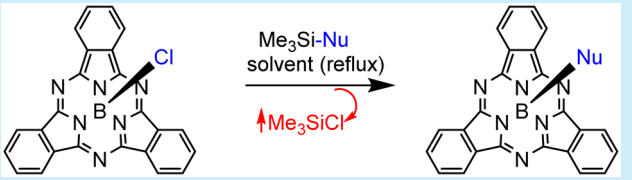
Julia Guilleme,[†] Lara Martínez-Fernández,[‡] Inés Corral,[‡] Manuel Yáñez,[‡] David González-Rodríguez,*[,†] and Tomas Torres*[,†,§]

[†]Departamento de Química Orgánica, and [‡]Departamento de Química, Facultad de Ciencias, Universidad Autónoma de Madrid, E-28049 Madrid, Spain

[§]IMDEA Nanociencia, c/Faraday 9, Campus de Cantoblanco, Madrid, 28049, Spain

Supporting Information

ABSTRACT: A new synthetic one-step approach to perform the axial ligand exchange reaction in subphthalocyanines that employs trimethylsilyl-protected nucleophiles as starting materials is reported. Theoretical calculations indicate that the exchange reaction proceeds through a similar 4-centered σ-bond metathesis transition state as the substitution with phenols. This direct method allowed us to synthesize new axial derivatives of singular importance within the chemistry of subphthalocyanines, for which the reactivity and X-ray crystalline structure were studied.



Subphthalocyanines (SubPcs) are unique nonplanar aromatic macrocycles composed of three diiminoisoindoline *N*-fused units arranged in a cone-shaped structure. These molecules are only known as boron complexes, whose tetrahedral coordination induces the deviation from planarity and thus, their concave nature.[1] Because of their extraordinary spectral and electronic features, SubPcs are considered competent candidates of increasing interest in different applied fields such as organic light-emitting diodes (OLEDs),[2] organic photovoltaic cells (OPVs),[3] or nonlinear optics.[4] For these reasons, the design of simple and general synthetic routes that allow the incorporation of SubPcs into more complex systems still remains an active task.

The reactivity of SubPcs has been addressed by several authors over the last decades,[1,5] and can be classified in three different groups depending on the reactive center:[1] (i) axial reactivity (central boron atom), (ii) peripheral reactivity (functional groups attached to the aromatic carbons), and (iii) ring-opening reaction (imine-type core of the SubPc). Among them, the axial ligand exchange is by far the most common approach employed to functionalize subazamacrocycles without altering the electronic properties of the macrocycle.[1c] Nevertheless, the axial substitution in SubPcs is slower and tougher than the analogous process in subporphyrins, which usually are reported as methoxy-compounds.[1b,6]

Recently, we reported a mechanistic study of the axial ligand exchange reaction between halo-SubPcs and phenols in which we determined a second-order reaction rate law for this process, both dependent on SubPc and phenol concentrations.[7] We proposed that this transformation takes place through a σ-bond metathesis mechanism involving a bimolecular transition state in which the phenol assists in the dissociation of the polar boron−halogen bond by proton coordination, while the new B−O bond is being formed. These observations led us to conclude that in order to perform an axial ligand exchange reaction, a good nucleophile is not strictly required, but rather an agent that has some affinity for the axial halogen and hence can weaken the boron−halogen bond before actual substitution.

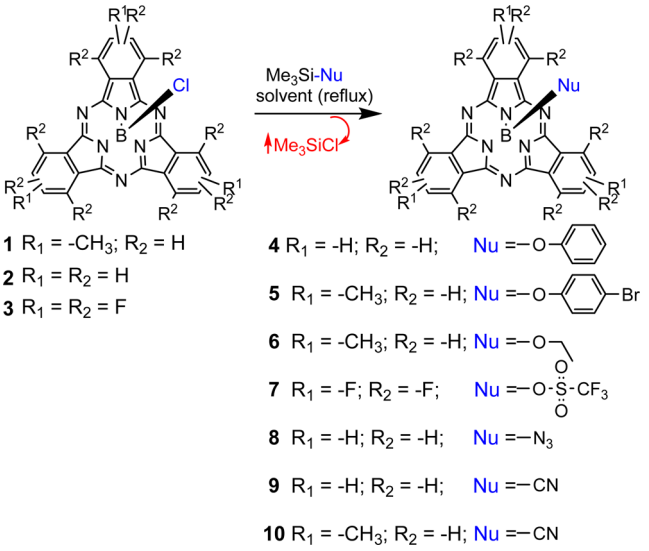
Encouraged by these results, we thought that using alcohols or other nucleophiles that are "protected" with a trialkylsilyl group (R_3Si−Nu) may lead to a similar transition state, since silanes are well-known halophilic electrophiles.[8] The initial chlorine atom of the SubPc would be now coordinated to the halophilic Si center in the transition state promoting the weakening of the B−Cl bond. Our assumption would be supported by previous work from Kato et al., who reported in 2006 the synthesis of a boron SubPc cation as a salt with a weakly coordinated carborane anion by reaction between $Et_3Si(CHB_{11}Me_5Br_6)$ and the corresponding chloro-SubPc.[8c] Moreover, the use of trimethylsilyl-protected reagents presents several advantages. For instance, the byproduct (Me_3SiX) that would be generated in this axial ligand exchange would be volatile in the reaction media, which should shift the equilibrium toward the products and simplify the purification step. In addition, their lower nucleophilicity in comparison with the deprotected nucleophile analogues (Nu-H) should generate lower amounts of SubPc decomposition products. In this work, we report on the theoretical and experimental study of a new synthetic route to axially substituted SubPcs by direct reaction of chloro-SubPcs and trimethylsilyl (TMS)-protected nucleophiles (Scheme 1). We also evaluate the scope of this novel

Received: July 30, 2015

DOI: 10.1021/acs.orglett.5b02213
Org. Lett. XXXX, XXX, XXX−XXX

synthetic methodology and its potential to prepare novel SubPc derivatives that are otherwise not accessible by other methods.

Scheme 1. Synthesis of Axially Substituted SubPcs by Direct Reaction between Chloro-SubPcs and TMS-Nucleophiles



We initiated our studies with a classical, well-known reaction in SubPc chemistry: the axial ligand exchange with phenol derivatives. This reaction, as mentioned before, has been thoroughly studied in our laboratories, both from the experimental and theoretical perspective.[7] As a proof of concept and to make a direct comparison with our mechanistic study, we reacted chloro-SubPc **2** with O-TMS-phenol or phenol in exactly the same conditions in refluxing toluene. The desired phenoxy-SubPc **4** was obtained in 89% (entry 1, Table 1) using PhOTMS or 85% employing PhOH. This transformation took place in a few hours using an excess of the TMS derivative, and no decomposition products were observed by TLC. The reaction with PhOH progressed initially faster but it took longer to reach completion. We attribute this effect to the presence of remaining HCl in the reaction media at high conversion, which can shift the equilibrium toward the starting chloro-SubPc reagent. As expected, other substituted TMS-phenols were reactive as well. For instance, the axial ligand exchange with the (4-bromophenol)trimethylsilane also proceeded successfully yielding SubPc **5** (entry 2, Table 1).

To investigate the reaction mechanism at a molecular level for trialkylsilyl protected nucleophiles we have mapped the ground state potential energy surface for SubPcCl **2** and the nucleophile *O*-TMS-phenol by locating the corresponding stationary points along the axial substitution reaction coordinate. Figure 1 depicts the potential energy profile as predicted by density functional theory (DFT) calculations. Further computational details can be found in the Supporting Information. Similarly to what was found for unprotected phenol nucleophiles,[7] the axial ligand exchange reaction is facilitated by the interaction of the two reagents (prereaction complex $Reac_2$ in Figure 1) and proceeds via a bimolecular transition state to a postreaction complex ($Prod_2$ in Figure 1), where the leaving Me_3SiCl group and the phenoxy-SubPc are still interacting.

From the geometric viewpoint, the formation of the prereaction complex $Reac_2$ assists the nucleophilic attack by

Table 1. TMS Derivatives Employed for the Axial Ligand Exchange Reaction

entry	SubPc	TMS-Nu	yield/%[a]	product
1	**2**	TMS–O–	89[c]	**4**
2	**1**	TMS–O–Br	66[c]	**5**
3	**1**	TMS–O–	-	**6**[b]
4	**1**	TMS–O–	-	-
5	**3**	TMS–O–S(=O)(=O)–CF3	62	**7**
6	**2**	TMS–N3	79[c]	**8**
7	**2**	TMS–C≡C–	-	-
8	**2**	TMS–	-	-
9	**2**	TMS–(2,3,5,6-tetrafluorophenyl)	-	-
10	**2**	TMS–CN	-[c]	-
11	**2**	TMS–CN	52[d]	**9**
12	**1**	TMS–CN	54[d]	**10**

[a]Yields calculated with respect to the starting SubPc. [b]Traces of the product were detected. [c]In toluene. [d]In nitrobenzene.

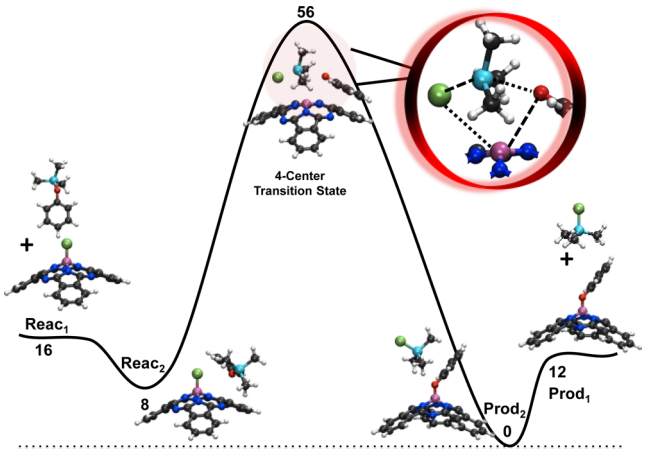


Figure 1. Reaction profile for the axial ligand substitution reaction as predicted by DFT calculations. Energies in kcal/mol.

activating the B–Cl bond, which slightly stretches (0.01 Å), and by simultaneously approaching the O atom of the phenol nucleophile to the B reaction center. A further respective reinforcement and weakening of the B–O and B–Cl bonds is observed at the TS structure, concomitant to the imminent rupture and formation of the Si–O and Cl–Si bonds, before the new B–O bond consolidates in the postreaction complex, where the phenoxySubPc is formed. Interestingly, the computed barrier is 17 kcal/mol larger than for the reaction with the unprotected nucleophile. This can be attributed, among other reasons, to the large size of the silane moiety that

DOI: 10.1021/acs.orglett.5b02213
Org. Lett. XXXX, XXX, XXX–XXX

hinders the preparation of nucleophilic attack in the prereaction complex and the arrangement of the incoming and leaving nucleophile at the 4-center transition state. This increase in the energy barrier is consistent with the slower reaction rates observed for the TMS-protected phenol in comparison with the unprotected phenol (see above).

To get further insight into the reactivity of SubPc with protected nucleophiles, we next examined and compared the same reaction with aliphatic alcohols. In the case of the reaction with chloro-SubPcs, aliphatic alcohols are known to produce lower yields than aromatic alcohols mainly because of SubPc decomposition, presumably via ring-opening, after prolonged heating times. However, under the simple standard conditions employed in this work (see Supporting Information), that involve the use of only a small excess of the nucleophile, the reaction did not afford the corresponding axially substituted SubPcs after 1 day of reaction, either using the TMS-protected or the unprotected alcohol. More drastic conditions and additional solvents (refluxing nitrobenzene or benzonitrile) were also tested but, unfortunately, only traces of SubPc product were detected in the reaction media. The formation of the corresponding alkoxy-SubPc **6** could be favored in the presence of a much larger excess of nucleophile, but we did not analyze this situation because it is not practical from the synthetic point of view. On the other hand, the silyl enol ether (entry 4, Table 1), which can be viewed as a masked ketone, rapidly provoked the decomposition of the macrocycle.

We then selected different TMS derivatives other than alcohol nucleophiles, such as the triflate (Me_3SiOTf) or azide (Me_3SiN_3). We published a procedure in the past with which the generation of triflate-SubPcs was carried out successfully.[9] These interesting derivatives, however, were only produced *in situ* as transient activated intermediates for the axial substitution with other nucleophiles,[9] but could not be isolated because of their rapid hydrolysis. A decrease in reactivity could be achieved by using electron-withdrawing macrocycles, such as **3**. The resulting perfluorinated-triflate-SubPc was much more inert and could be isolated by standard column chromatography in 62% yield. In the case of Me_3SiN_3, the axial ligand exchange took place efficiently under the standard conditions (i.e., toluene at 110 °C), and the product, the first example of a SubPc with an axial B−N_3 bond, was perfectly stable.

To explore the limits of this new synthetic route for axial ligand exchange in SubPcs, the reaction was next carried out with different TMS-carbon nucleophiles. We thought it would be highly interesting to test Csp^2 (phenyl-) and Csp (alkynyl- or nitrile-) trimethylsilanes (entries 7−9, Table 1), which would generate novel SubPcs with B−C bonds. However, these reagents exhibited an evident lack of reactivity and only decomposition products were observed after days in refluxing toluene or nitrobenzene. The only exception was the Me_3SiCN reagent, whose nucleophilicity seems to be the actual limit of this reaction for practical purposes. However, the reaction had to be carried out in the more polar nitrobenzene solvent in order to increase the reaction rate (see our previous work)[7] and at temperatures close to its boiling point. In this way, the valuable cyano-SubPcs **9** and **10** could be obtained in moderate yields.

On the other hand, the effect of the electronic nature of the macrocycle was also analyzed. Both SubPcs functionalized with peripheral electron donating- (entries 2 and 12, Table 1) or electron-withdrawing groups (entry 5, Table 1) react with these TMS-nucleophiles. Their reactivity follows the same order as in any other axial-ligand exchange reaction: electron-rich SubPcs react faster than electron-poor SubPcs. All new products were characterized by ^1H NMR, ^{13}C NMR, UV−vis, Fourier transform infrared spectroscopy, mass spectroscopy, and high-resolution mass spectroscopy. Suitable crystals for X-ray diffraction analysis were obtained for **7**, **8**, and **9**, and their resolved structure is shown in Figure 2.

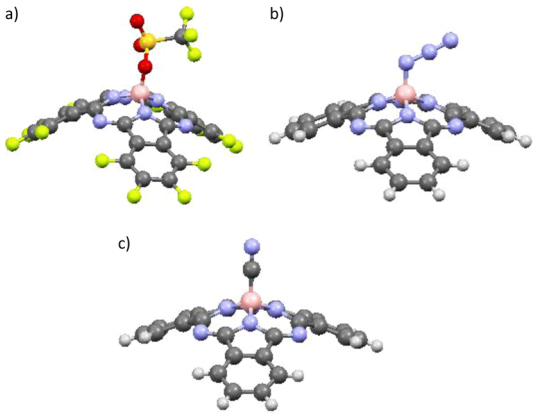


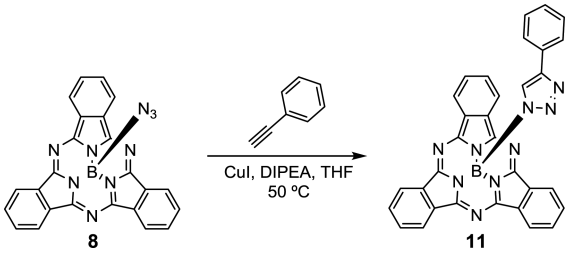
Figure 2. Molecular structure of SubPcs **7** (a), **8** (b), and **9** (c) in the crystal as determined from X-ray diffraction analysis.

The new SubPcs **7**, **8**, **9**, and **10** could be regarded as useful organic synthons to prepare a wide variety of other axially substituted products. Subsequently, we set out to investigate the behavior of these common organic functional groups when attached to the SubPc macrocycle. Triflate-SubPcs (**7**) have already demonstrated to be extraordinary activated intermediates to efficiently substitute the halogen atom with diverse nucleophiles.[9] On the other hand, we tested a set of common chemical transformations of nitriles (nucleophilic addition, hydrolysis, and reduction reactions) or azides (reductions or 1,3-dipolar cycloadditions). These reactions were considered as highly valuable, since they could lead to a new family of "exotic" SubPcs bearing formyl, ketone, or amine functional groups, among others, at the axial position of SubPcs. However, and despite all our efforts, which are summarized in the Supporting Information, these nitrile and azido groups displayed a rather unusual reactivity, and none of these reactions worked in our hands. Either the axial functional group did not react under classical mild conditions or the SubPc macrocycle decomposed when using harsher conditions. All these premises denote that these new SubPcs do not present the expected reactivity related with these common functional groups, probably as a consequence of the electronic and/or steric effect exerted by the boron macrocycle.

The only exception was the 1,3-dipolar cycloaddition reaction to azide-SubPc **8** (Scheme 2). It is known that the chemistry and reactivity of boryl azides is rare, and so is their role as 1,3-dipoles in cycloaddition reactions.[10] To the best of our knowledge only a few examples have been reported in which electron-rich boryl azides are able to thermally react with electron-poor alkynes, alkenes, and nitriles to afford the corresponding cycloaddition adducts.[10] SubPc **8** was subjected to a copper(I)-catalyzed cycloaddition (CuAAC) with phenylacetylene in THF and the corresponding triazole-SubPc **10** was obtained in a reasonable 30% yield, despite the absence of electron-withdrawing groups attached to the acetylene moiety. The cycloadduct was obtained as a single 1,4-regioisomer due

DOI: 10.1021/acs.orglett.5b02213
Org. Lett. XXXX, XXX, XXX−XXX

Scheme 2. Cycloaddition Reaction between SubPc 8 and Ethynylbenzene



to obvious steric hindrance. Although these conditions are far from the typical "click" reactions, which usually proceed quantitatively in the presence of catalytic amounts of Cu^{+}, this "click" approach may still be regarded as a convenient procedure to attach these functional macrocycles to more complex systems, such as electroactive multicomponent systems or polymers.

In conclusion, we have described a new synthetic route to carry out the axial ligand exchange reaction in SubPcs in one step that employs TMS-protected nucleophiles as starting materials. Theoretical calculations indicate that the ligand exchange reaction proceeds through a similar 4-centered σ-bond metathesis transition state as the substitution with phenols, in which the TMS group concomitantly coordinates to the leaving chlorine atom and initiates the nucleophilic attack at the boron atom. Although this procedure cannot be established as a general and practical methodology, it can be considered as a good alternative to performing the axial exchange with aromatic alcohols, because the new reactants are not nucleophiles and a lower amount of decomposition side-products are detected. This clean method led us to synthesize three new "exotic" derivatives of singular importance within the chemistry of SubPcs, the structure of which has been unambiguously determined by X-ray diffraction.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02213.

Synthesis, characterization of products and computational details (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: tomas.torres@uam.es. Tel: +34 91 497 4151. Fax: +34 91 497 3966.

*E-mail: david.gonzalez.rodriguez@uam.es. Tel: +34 91 497 2778. Fax: +34 91 497 3966.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from the MINECO, Spain (CTQ-2014-52869-P, T.T.; CTQ2014-57729-P, D.G.-R.), and the Comunidad de Madrid (S2013/MIT-2841 FOTOCARBON, T.T.) is acknowledged. The work of J.G. and L.M.F. was funded by MECD (FPU fellowship). L.M.F., I.C., and M.Y. thank the MICINN (Spain) for the Project No.CTQ2012-35513-C02-01. The Centro de Computación Científica of the Universidad Autónoma de Madrid is gratefully acknowledged for generous allocation of computational time.

■ REFERENCES

(1) (a) Claessens, C. G.; González-Rodríguez, D.; Torres, T. *Chem. Rev.* **2002**, *102*, 835. (b) Torres, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 2834. (c) Claessens, C. G.; González-Rodríguez, D.; Rodríguez-Morgade, M. S.; Medina, A.; Torres, T. *Chem. Rev.* **2014**, *114*, 2192. (d) Samdal, S.; Volden, H. V.; Ferro, V. R.; García de la Vega, J. M.; González-Rodríguez, D.; Torres, T. *J. Phys. Chem. A* **2007**, *111*, 4542−4550. (e) Claessens, C. G.; González-Rodríguez, D.; Iglesias, R. S.; Torres, T. *C. R. Chim.* **2006**, *9*, 1094−1099.

(2) (a) Morse, G. E.; Helander, M. G.; Maka, J. F.; Lu, Z.-H.; Bender, T. P. *ACS Appl. Mater. Interfaces* **2010**, *2*, 1934−1944. (b) Morse, G. E.; Castrucci, J. S.; Helander, M. G.; Lu, Z.-H.; Bender, T. P. *ACS Appl. Mater. Interfaces* **2011**, *3*, 3538−3544.

(3) (a) Gommans, H.; Aernouts, T.; Verreet, B.; Heremans, P.; Medina, A.; Claessens, C. G.; Torres, T. *Adv. Funct. Mater.* **2009**, *19*, 3435. (b) Beaumont, N.; Cho, S. W.; Sullivan, P.; Newby, D.; Smith, K. E.; Jones, T. S. *Adv. Funct. Mater.* **2012**, *22*, 561. (c) Verreet, B.; Cnops, K.; Cheyns, D.; Heremans, P.; Stesmans, A.; Zango, G.; Claessens, C. G.; Torres, T.; Rand, B. P. *Adv. Energy Mater.* **2014**, *4*, 1301413. (d) Cnops, K.; Rand, B. P.; Cheyns, D.; Verreet, B.; Empl, M. A.; Heremans, P. *Nat. Commun.* **2014**, *5*, No. 3406, DOI: 10.1038/ncomms4406.

(4) (a) Sastre, A.; Torres, T.; Díaz-García, M. A.; Agulló-López, F.; Dhenaut, C.; Brasselet, S.; Ledoux, I.; Zyss, J. *J. Am. Chem. Soc.* **1996**, *118*, 2746. (b) Martínez-Díaz, M. V.; del Rey, B.; Torres, T.; Agricole, B.; Mingotaud, C.; Cuvillier, N.; Rojo, G.; Agulló-López, F. *J. Mater. Chem.* **1999**, *9*, 1521. (c) de la Torre, G.; Vázquez, P.; Agulló-López, F.; Torres, T. *Chem. Rev.* **2004**, *104*, 3723.

(5) (a) Geyer, M.; Plenzig, F.; Rauschnabel, J.; Hanack, M.; del Rey, B.; Sastre, A.; Torres, T. *Synthesis* **1996**, *1996*, 1139. (b) Potz, R.; Göldner, M.; Hückstädt, H.; Cornelissen, U.; Tutaβ, A.; Homborg, H. *Z. Anorg. Allg. Chem.* **2000**, *626*, 588. (c) González-Rodríguez, D.; Torres, T. *Eur. J. Org. Chem.* **2009**, *2009*, 1871. (d) Caballero, E.; Fernández-Ariza, J.; Lynch, V. M.; Romero-Nieto, C.; Rodríguez-Morgade, M. S.; Sessler, J. L.; Guldi, D. M.; Torres, T. *Angew. Chem., Int. Ed.* **2012**, *50*, 11337. (e) Morse, G. E.; Bender, T. P. *Inorg. Chem.* **2012**, *51*, 6460.

(6) (a) Tsurumaki, E.; Hayashi, S.; Tham, F. S.; Reed, C. A.; Osuka, A. *J. Am. Chem. Soc.* **2011**, *133*, 11956−11959. (b) Tsurumaki, E.; Sung, J.; Kim, D.; Osuka, A. *J. Am. Chem. Soc.* **2015**, *137*, 1056−1059.

(7) Guilleme, J.; Martínez-Fernández, L.; González-Rodríguez, D.; Corral, I.; Yáñez, M.; Torres, T. *J. Am. Chem. Soc.* **2014**, *136*, 14289−14298.

(8) (a) Xie, Z.; Manning, J.; Reed, R. W.; Mathur, R.; Boyd, P. D. W.; Benesi, A.; Reed, C. A. *J. Am. Chem. Soc.* **1996**, *118*, 2922. (b) Reed, C. A. *Acc. Chem. Res.* **1998**, *31*, 325. (c) Kato, T.; Tham, F. S.; Boyd, P. D. W.; Reed, C. A. *Heteroat. Chem.* **2006**, *17*, 209.

(9) Guilleme, J.; González-Rodríguez, D.; Torres, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 3506.

(10) (a) Merling, E.; Lamm, V.; Geib, S. J.; Lacôte, E.; Curran, D. P. *Org. Lett.* **2012**, *14*, 2690. (b) Melen, R. L.; Stephan, D. W. *Dalton Trans.* **2013**, *42*, 4795. (c) Müller, M.; Maichle-Mössmer, C.; Bettinger, H. F. *J. Org. Chem.* **2014**, *79*, 5478.

DOI: 10.1021/acs.orglett.5b02213
Org. Lett. XXXX, XXX, XXX−XXX