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C–C Bond Formation of Benzyl Alcohols and Alkynes using Catalytic Amount of KO^tBu: Unusual Regioselectivity via a Radical Mechanism

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Abstract: We report the C-C bond-forming reaction of benzyl alcohols and alkynes using a catalytic amount of KO^tBu to form α -alkylated ketones in which the C=O group is located on the side derived from the alcohol, a reaction that has not been reported yet in the peer-reviewed literature. The reaction proceeds under thermal condition (125 °C) and produces no waste, making the reaction highly atom-efficient, environmentally benign and sustainable. Based on our mechanistic investigations we propose that the reaction proceeds through radical pathways.

Transition-metal-catalyzed C-C bond formation is one of the most powerful tools for the synthesis of organic compounds.^[1] There has been a tremendous amount of development made in this area offering efficient catalysts for challenging transformations and enriching our mechanistic understanding. Nevertheless, transition-metal catalysts have several limitations such as toxicity, complex handling techniques for many transition-metal catalysts, low abundance and high cost of noble transition-metals. Therefore, the replacement of transition-metal catalysts with transition-metal-free catalysts is of much interest. In fact, significant progress has been made towards the development of C-C bond forming reactions free from transition metals.^[2] Several C-C coupling reactions have also been reported using stoichiometric amounts (or more) of KO^tBu.^[2] Recently Stoltz and Grubbs have reported a transition-metal-free silylation of C-H bonds of aromatic heterocycles catalyzed by KO^tBu.^[3]

Among several C-C bond forming reactions, formation of α -alkylated ketones is important because of their interesting pharmacological and physiological properties.^[4] In particular, dihydrochalcones (a category of α -alkylated ketones) are found in natural products such as Naringin dihydrochalcone and Aspalathin and are used as artificial sweeteners and antioxidants.^[4f, 4g] A conventional route to the synthesis of α -alkylated ketones involves the reaction of an enolate with an alkyl halide in presence of at least a stoichiometric amount of base, thus generating a stoichiometric amount of waste. Dihydrochalcones are also synthesized by the transition-metal catalyzed hydrogenation of chalcones (Scheme 1a).^[5] Much attention has been paid to the C-alkylation of ketones using alcohols as alkylating agents and several catalysts based on transition metals such as iridium, ruthenium, palladium, manganese, cobalt, iron and copper have been reported for this transformation (Scheme 1b).^[6] In most of the cases at least a stoichiometric amount of base is used as additive. Despite significant progress, this reaction is limited to ketones as the

starting materials. For wide synthetic application, it would be attractive to use other substrates instead of ketones for the production of α -alkylated ketones using alcohol as the alkylating agent.

Recently, the C-C bond-forming reaction of alkynes with alcohols using a combination of transition-metal-catalysts and water (or without water) to form α -alkylated ketones has been reported (Scheme 1c).^[7] The reaction proceeds via the Markovnikov hydration of alkynes to form methyl ketones followed by the C-alkylation of methyl ketones using alcohols. The obtained product contains the C=O group on the side derived from the alkyne. Although this reaction is atom-efficient, the development of a catalyst that is free from transition-metals and expensive ligands, and avoids waste generation, would make the overall process simpler, less-expensive, environmentally-benign and sustainable. Herein, we present the C-C bond forming reaction of benzyl alcohols with alkynes using a catalytic amount of an inexpensive and commercially available base - KO^tBu (Scheme 1d). The obtained products, α -alkylated ketones, in particular dihydrochalcones, uniquely contain the C=O group on the side derived from the alcohol; a reaction exhibiting such unusual regioselectivity has not been reported in the peer-reviewed literature.

Scheme 1. (a) Synthesis of dihydrochalcones by the transition-metal-catalyzed hydrogenation of chalcones (b) Transition-metal catalyzed C-alkylation of ketones; (c) transition-metal catalyzed reaction of alcohols and alkynes and (d) the reaction reported in this work.

We discovered that refluxing a toluene solution of benzyl alcohol (0.5 mmol) and phenyl acetylene (0.5 mmol) at 125 °C for 24 h in the presence of KO^tBu (5 mol%) results in the formation of 1,3-diphenylpropan-1-one (**1**) in 80% yield. The reaction also proceeds, although with relatively lower yields, with other potassium bases such as KH, KOH and KHMDS (Table 1, entries 2-4). However, no product formation was observed when the weaker base K₂CO₃ was used. Poor yield of the product was obtained when NaO^tBu and NaOH (entries 6-7) were used, suggesting that potassium ion is important for the catalysis. Lowering the reaction temperature to 55 °C completely thwarted the reaction, whereas increasing the temperature to 135 °C slightly lowered the yield (entries 8-9). We also observed that use of non-polar solvents such as toluene or methyl cyclohexane resulted in better product yield compared to polar solvents such as THF, 1,4-dioxane or acetonitrile (entries 10-13). Using DMF as a solvent also resulted in lower yield of **1** (entry 14); styryl ether (**1**, *vide infra*, 55% yield) was observed as the major product. DMF

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in presence of KO^tBu can be deprotonated to form CONMe₂ anion that can be involved in the electron transfer reactions.^[8] Finally, no conversion of reactants was observed when the reaction was performed in the absence of base (entry 15).

Table 1: Optimization of the reaction of benzyl alcohol and phenyl acetylene.^a

Entry	base	solvent	temperature	product yield
1	KO ^t Bu	toluene	125 °C	80%
2	KH	toluene	125 °C	66%
3	KOH	toluene	125 °C	61%
4	KHMDS	toluene	125 °C	59%
5	K ₂ CO ₃	toluene	125 °C	0%
6	NaO ^t Bu	toluene	125 °C	25%
7	NaOH	toluene	125 °C	30%
8	KO ^t Bu	toluene	55 °C	0%
9	KO ^t Bu	toluene	135 °C	78%
10	KO ^t Bu	methyl cyclohexane	125 °C	79%
11	KO ^t Bu	THF	125 °C	40%
12	KO ^t Bu	1,4-dioxane	125 °C	50%
13	KO ^t Bu	CH ₃ CN	125 °C	15%
14	KO ^t Bu	DMF	125 °C	10%
15	no base	toluene	125 °C	0%

^aConditions: KO^tBu (0.025 mmol), benzyl alcohol (0.5 mmol), phenyl acetylene (0.5 mmol), solvent (1 mL), 24 h (reaction time), temperature: 125°C. The yield of the product (**1**) was determined by ¹H NMR spectroscopy using mesitylene as an internal standard.

Table 2: Substrate scope for the formation of α-alkylated ketones.^a

^aConditions: KO^tBu (0.05 mmol), alcohol (1 mmol), alkyne (1 mmol), toluene (2 mL), 24 h, 125°C. ^bKOtBu (0.2 mmol). ^cKO^tBu (0.05 mmol), benzyl alcohol (1 mmol), 1,4-diethynylbenzene (0.5 mmol). Products were confirmed by GC-MS. The yields of the products were determined by ¹H NMR spectroscopy using mesitylene as an internal standard. Numbers in parentheses represent the isolated yields.

We next explored the substrate scope of this reaction. As shown in Table 2, the reaction works well with various substituted benzyl alcohols and substituted phenyl acetylenes. Electron-donating substituents on the benzyl alcohol such as methoxy and ^t-Bu groups (**3** and **4**) gave better yields relative to the electron

withdrawing substituents fluoride and CF₃ (**8** and **9**). Product **2** was also isolated on a gram scale (1.45 g, 65% yield). The structure of product **4** was confirmed by single crystal X-ray diffraction, proving that the carbonyl group is on the side derived from the alcohol (SI, Figure S11). It is worth noting that the only transformation with the regioselectivity of this type was reported in a recent patent^[9] using an iridium catalyst, and to the best of our knowledge it is unknown in the peer-reviewed literature. Only 20% of the ketone product (**16**) was observed when 1-octyne was used; dimerization of 1-octyne was detected as the major product by GC-MS. Heterocyclic alcohols and alkynes such as 3-pyridinemethanol and furfuryl alcohol also resulted in poor yield of the corresponding ketone (< 20%, see Table S2 in SI). Using an internal alkyne, diphenyl acetylene in place of phenyl acetylene, also did not result in any product formation, benzyl alcohol and diphenyl acetylene were recovered after the reaction (see Table S2, in SI).

Reaction of 1-hexanol (1 mmol) with phenyl acetylene (1 mmol) using 10 mol% KO^tBu in toluene for 24 h at 125°C did not result in the formation of the expected ketone product; instead, addition of the alkoxide to phenyl acetylene took place forming a mixture of two geometrical isomers of 2-(hexyloxy)vinyl benzene in 1:3 ratio (65% overall isolated yield, Scheme 2). This is similar to that reported by Kondo for alkyne functionalization using a phosphazane base P₄-t-Bu as a catalyst.^[10]

Scheme 2. Reaction of hexanol with phenyl acetylene catalyzed by KO^tBu.

As the catalytic reaction of benzyl alcohols and alkynes using KO^tBu was unprecedented, we endeavored to understand the mechanism of this reaction. The influence of light or trace transition metals was ruled out by control experiments and ICP-MS analysis (see SI). As demonstrated earlier, potassium ion is important for catalysis as lower yields are obtained using the corresponding sodium bases (Table 1). Moreover, addition of 18-Crown-6 (10 mol%) to the catalytic mixture decreased the product yield to 40%, confirming the important role of the potassium ion in the catalysis, as also previously observed by Stoltz and Houk, and Wilden.^[3c, 11]

A possible mechanism for this transformation could proceed via a hydrogenation/dehydrogenation pathway; dehydrogenation of the alcohol to aldehyde followed by its coupling with the alkyne and then hydrogenation and rearrangement. However, formation of hydrogen during the reaction was not detected by GC or ¹H NMR spectroscopy. We also did not observe the formation of any aldehyde or styrene that might be formed via the transfer hydrogenation mechanism. Additionally, reaction of benzaldehyde with either styrene or phenyl acetylene in presence of 10 mol% KO^tBu (125 °C, 24 h) resulted in the formation of benzyl benzoate as the major product, most likely through the Tischenko mechanism,^[12] while styrene or phenyl acetylene were found to be mostly unreacted. This suggests that the reaction does not proceed through hydrogenation/dehydrogenation pathways.

We also ruled out the possibility of a mechanism where the coupling of alcohol and alkyne proceeds via the Markovnikov addition of water to the alkyne since the presence of molecular sieves in the reaction mixture did not affect the product yield. Also, the reaction proceeding via the Markovnikov addition of water to alkyne would result in a product where the C=O group is located on the side of the alkyne derivative as previously reported.^[7] However in this case, as confirmed by the X-ray diffraction, the product contains the C=O group on the side of alcohol (SI, Figure S11).

Another pathway we considered involves reaction of benzyl alcohol and phenyl acetylene to give styryl ether **I** that undergoes a 1,2-Wittig type rearrangement^[13] to give an allylic

alcohol (**II**) which can isomerize to the ketone product **1** (Scheme 3). However, this possibility was ruled out since no conversion of the styryl ether (**I**) was obtained when refluxed in toluene in presence of 10 mol% KO^tBu.

Scheme 3. Ruling out of the mechanism involving styryl ether intermediate.

Furthermore, we explored the possibility of a radical mechanism. Interestingly, addition of one equivalent of the radical scavengers TEMPO or galvinoxyl to the reaction mixture under the conditions of Table 1, entry 1, decreased the yield of the product to 40% and 0%, respectively. Unfortunately, attempts to characterize any trapped radical were not successful. Interestingly, an EPR spectrum taken after 5 minutes of heating (125 °C) of benzyl alcohol and phenyl acetylene in the presence of KO^tBu (10 mol%) showed a signal suggesting a carbon-based radical (Figure 1). No EPR signal was detected by heating a toluene solution of benzyl alcohol and phenyl acetylene in the absence of KO^tBu or by reacting benzyl alcohol, phenyl acetylene and KO^tBu (10 mol% in toluene) at room temperature. Control EPR experiments performed by reacting KO^tBu (10 mol%) and benzyl alcohol or KO^tBu (10 mol%) and phenyl acetylene in toluene (125 °C) also did not show the presence of any radical. This suggests that perhaps the role of KO^tBu is to deprotonate the alcohol and that the radical is generated by interaction of the alkoxide with the alkyne. This is consistent with the observation of product formation, albeit in lower yields, with bases such as KOH and KH that are not known for exhibiting electron transfer reactivity under the catalytic conditions used here. Mechanisms where KO^tBu or KH are not the radical source itself but assist in the generation of a radical source by reacting with an additive or substrate were proposed before.^[2b, 14]

Figure 1. EPR spectrum upon heating a toluene solution of benzyl alcohol, phenyl acetylene and KO^tBu.

Additionally, cyclic voltammetry experiments (SI, Figures S3-S4) exhibited a high potential gap $\Delta E = 1.83$ V between the first oxidation peak potential of a mixture of PhCH₂OH/KO^tBu (+0.58 V) and the first reduction peak potential of phenyl acetylene (-1.25 V) excluding a fast outer sphere electron transfer, as also suggested by Jutand and Lei for the electron transfer between KO^tBu and 1,10-phenanthroline.^[15]

Based on these experiments we propose the following mechanism for the C-C bond forming reaction of benzyl alcohols and alkynes (Scheme 4).

Initiation: We suggest that the first step is the deprotonation of benzyl alcohol by KO^tBu to form PhCH₂OK. The catalytic reaction can get initiated by a Hydrogen Atom Transfer (HAT) from PhCH₂O⁻ to phenyl acetylene resulting in the formation of the radicals **A** and **A'**.^[16] The transfer of a hydrogen radical from the benzylic position of the corresponding alkoxides has previously been proposed.^[16a, 17] The transfer of a hydrogen radical to phenyl acetylene was also documented before.^[16b] Additionally, based on our DFT calculations at the M062X/6-31+G(d,p) level, ΔG for the HAT from PhCH₂O⁻ to phenyl acetylene was found to be 8.3 kcal mol⁻¹ suggesting that the process might be feasible under the reaction conditions used here. We suggest that the radical **A'** generated in the initiation process gets consumed by its reaction

with phenyl acetylene as the conversion of alkynes are greater than the conversion of benzyl alcohols (Table S1, SI). Additionally, ESI-MS experiment of the reaction mixture showed signals with a mass difference of 102 in the region of *m/z* 491 to 799 indicative of the formation of poly(phenyl acetylene), presumably from the reaction of **A'** with phenyl acetylene (see SI, Figure S10). Although all the reactions have been performed under nitrogen atmosphere using deoxygenated solvents, radical initiation via reaction of KO^tBu with adventitious molecular oxygen is a possibility, and has been suggested by Houk and Stoltz based on DFT calculations.^[3c] To explore this possibility, we carried out a catalytic experiment in presence of 200 or 2000 ppm of oxygen gas using the reaction conditions as described in Table 1, entry 1. After completion of the reaction, similar conversion of reactants and the similar product yield was observed as that observed without adding any external oxygen gas (see SI). However, when a reaction was performed using 1 bar of oxygen, no formation of **1** and almost no conversion of benzyl alcohol was observed. Based on these experimental evidences, it seems unlikely that molecular oxygen is involved in the reaction, and more detailed mechanistic investigation will be pursued in future communications.

Scheme 4. Proposed mechanism for the reaction of benzyl alcohols and phenyl acetylene using a catalytic amount of base.

Radical chain catalytic cycle: The alkoxide radical **A** can insert into phenyl acetylene to form the radical intermediate **B**, ΔG for which was found to be 10.8 kcal mol⁻¹. **B** can undergo a 1,2-hydrogen shift to form the intermediate **C** ($\Delta G = 6.8$ kcal mol⁻¹). Intermediates **B** and **C** can convert to intermediate **D** via 1,3 and 1,2-hydrogen shifts, respectively, which is related to the radical **E** via resonance (ΔG , **B** to **D** = -57.7 kcal mol⁻¹ & ΔG , **C** to **D** = -64.5 kcal mol⁻¹). **E** can then be protonated by PhCH₂OH to form the radical **F** and PhCH₂O⁻ anion ($\Delta G = 38.6$ kcal mol⁻¹). PhCH₂O⁻ anion can transfer a hydrogen radical (HAT) to **F** to form the intermediate **G** and regenerate the intermediate **A** ($\Delta G = -22.7$ kcal mol⁻¹). Upon tautomerization, **G** transforms to product **1** ($\Delta G = -5.5$ kcal mol⁻¹). It is very likely that the reaction is driven by the highly favorable thermodynamics of the product formation as the ΔG of the overall reaction was found to be -36.5 kcal mol⁻¹. It is worth noting that the values of ΔG presented here are only for the purpose of comparing the relative energy of the intermediates as potassium is excluded from the calculation for the sake of simplicity. We believe that the stability of radical intermediates such as **A** and **B** is critical for the catalysis since the reaction scope is limited to benzylic alcohols where the radicals are stabilized by resonance with the phenyl ring. Similarly, higher yields are obtained with phenyl acetylene compared to aliphatic alkynes where self-coupling of the alkyne is observed as the major product (**18**, Table 2, also see Table S1 in SI).

To lend support for the hydrogen shifts as proposed in the mechanism, we performed experiments with deuterated substrates. Indeed, the reaction of PhCCD with PhCH₂OH, or PhCCH with the PhCH₂OD under the conditions described in Table 2 resulted in deuterium scrambling at the α and β carbons of the product **1** as detected by the ¹H and ²H NMR spectroscopy and GC-MS (Scheme 5). The deuterium scrambling also suggests the possibility of proton exchange between benzyl alcohol and phenyl acetylene, possibly via an alkoxide intermediate.

Scheme 5. Catalytic reaction of PhCCD/H and PhCH₂OD/H.

In conclusion, we report a transition-metal free C-C bond-forming reaction of benzyl alcohols and alkynes to form α -alkylated ketones using a catalytic amount of KO^tBu. The reaction proceeds at 125 °C and shows unusual regioselectivity. Additionally, the reaction does not produce any waste. Overall, this is a highly atom-efficient, environmentally benign and sustainable reaction. Based on our mechanistic investigations, especially the detection of a radical species from the EPR spectroscopy, we propose that the reaction proceeds through radical pathways as outlined in Scheme 4.

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Keywords: Potassium tert-butoxide • α -alkylated ketone • radical • dihydrochalcone • benzyl alcohol • alkyne •

- [1] (a) A. Behr, *Organometallic Compounds and Homogeneous Catalysis*, Wiley-VCH: Weinheim, **2002**; (b) F. Diederich, Stang, P. J., *Metal-Catalyzed Cross-Coupling Reactions*, Wiley-VCH: Weinheim, **1998**; (c) G. Dyker, Ed, *Handbook of C-H Transformations: Applications in Organic Synthesis*, Wiley-VCH: Weinheim, **2005**; (d) R. Jana, T. P. Pathak, M. S. Sigman, *Chem. Rev.* **2011**, *111*, 1417-1492.
- [2] (a) C.-L. Sun, Z.-J. Shi, *Chem. Rev.* **2014**, *114*, 9219-9280; (b) J. P. Barham, G. Coulthard, K. J. Emery, E. Doni, F. Cumine, G. Nocera, M. P. John, L. E. A. Berlouis, T. McGuire, T. Tuttle, J. A. Murphy, *J. Am. Chem. Soc.* **2016**, *138*, 7402-7410.
- [3] (a) A. A. Toutov, W.-B. Liu, K. N. Betz, A. Fedorov, B. M. Stoltz, R. H. Grubbs, *Nature* **2015**, *518*, 80; (b) S. Banerjee, Y.-F. Yang, I. D. Jenkins, Y. Liang, A. A. Toutov, W.-B. Liu, D. P. Schuman, R. H. Grubbs, B. M. Stoltz, E. H. Krenske, K. N. Houk, R. N. Zare, *J. Am. Chem. Soc.* **2017**, *139*, 6880-6887; (c) W.-B. Liu, D. P. Schuman, Y.-F. Yang, A. A. Toutov, Y. Liang, H. F. T. Klare, N. Nesnas, M. Oestreich, D. G. Blackmond, S. C. Virgil, S. Banerjee, R. N. Zare, R. H. Grubbs, K. N. Houk, B. M. Stoltz, *J. Am. Chem. Soc.* **2017**, *139*, 6867-6879.
- [4] (a) D. L. Boger, H. Miyauchi, W. Du, C. Hardouin, R. A. Fecik, H. Cheng, I. Hwang, M. P. Hedrick, D. Leung, O. Acevedo, C. R. W. Guimarães, W. L. Jorgensen, B. F. Cravatt, *J. Med. Chem.* **2005**, *48*, 1849-1856; (b) J. Y. Hwang, L. A. Arnold, F. Zhu, A. Kosinski, T. J. Mangano, V. Setola, B. L. Roth, R. K. Guy, *J. Med. Chem.* **2009**, *52*, 3892-3901; (c) K. Biswas, T. A. N. Peterkin, M. C. Bryan, L. Arik, S. G. Lehto, H. Sun, F.-Y. Hsieh, C. Xu, R. T. Freneau, J. R. Allen, *J. Med. Chem.* **2011**, *54*, 7232-7246; (d) R. Perrone, F. Berardi, N. A. Colabufo, E. Lacivita, M. Leopoldo, V. Tortorella, *J. Med. Chem.* **2003**, *46*, 646-649; (e) C. Baskakis, V. Magrioti, N. Cotton, D. Stephens, V. Constantinou-Kokotou, E. A. Dennis, G. Kokotos, *J. Med. Chem.* **2008**, *51*, 8027-8037; (f) G. H. Robertson, J. P. Clark, R. Lundin, *Ind. Eng. Chem. Prod. Res. Develop.* **1974**, *13*, 125-129; (g) M. J. Matos, S. Vazquez-Rodriguez, E. Uriarte, L. Santana, *Expert Opin. Ther. Pat.* **2015**, *25*, 351-366.
- [5] (a) L. Krbecek, G. E. Inglett, M. Holik, B. Dowling, R. Wagner, R. Riter, *J. Agric. Food Chem.* **1968**, *16*, 108-112; (b) H. A. B. Linde, D. E. Eveleigh, in *Z. Naturforsch. B*, **1975**, *30*, 606.
- [6] (a) F. Huang, Z. Liu, Z. Yu, *Angew. Chem. Int. Ed.* **2016**, *55*, 862-875; (b) M. Pena-Lopez, P. Piehl, S. Elangovan, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2016**, *55*, 14967-14971; (c) S. Elangovan, J.-B. Sortias, M. Beller, C. Darcel, *Angew. Chem. Int. Ed.* **2015**, *54*, 14483-14486; (d) G. Zhang, J. Wu, H. Zeng, S. Zhang, Z. Yin, S. Zheng, *Org. Lett.* **2017**, *19*, 1080-1083; (e) S. Liao, K. Yu, Q. Li, H. Tian, Z. Zhang, X. Yu, Q. Xu, *Org. Biomol. Chem.* **2012**, *10*, 2973-2978.
- [7] (a) J. Ma, N. Wang, F. Li, *Asian J. Org. Chem.* **2014**, *3*, 940-947; (b) J. Umasish, B. Srijit, M. Sukhendu, *Eur. J. Org. Chem.* **2008**, *2008*, 5798-5804; (c) L. R. Jefferies, S. P. Cook, *Tetrahedron* **2014**, *70*, 4204-4207.
- [8] (a) C. J. Evoniuk, G. dos Passos Gomes, S. P. Hill, S. Fujita, K. Hanson, I. V. Alabugin, *J. Am. Chem. Soc.* **2017**, *139*, 16210-16221; (b) M. Pichette Drapeau, I. Fabre, L. Grimaud, I. Ciofini, T. Ollevier, M. Taillefer, *Angew. Chem., Int. Ed.* **2015**, *54*, 10587-10591.
- [9] X. Li, H. Li, C. Xu, X. Hao, Z. Xiao, **2016**, CN103242372A.
- [10] T. Imahori, C. Hori, Y. Kondo *Adv. Synth. Catal.* **2004**, *346*, 1090-1092.
- [11] J. Cuthbertson, J. D. Wilden, *Tetrahedron* **2015**, *71*, 4385-4392.
- [12] (a) S. Tsunetake, N. Tetsuo, O. Makoto, *Chem. Lett.* **2006**, *35*, 824-829; (b) M. K. Barman, A. Baishya, S. Nembenna, *J. Organomet. Chem.* **2015**, *785*, 52-60.
- [13] F. Kurosawa, T. Nakano, T. Soeta, K. Endo, Y. Ukaji, *J. Org. Chem.* **2015**, *80*, 5696-5703.
- [14] J. P. Barham, S. E. Dalton, M. Allison, G. Nocera, A. Young, M. P. John, T. McGuire, S. Campos, T. Tuttle, J. A. Murphy, *J. Am. Chem. Soc.* **2018**, *140*, 11510-11518.
- [15] H. Yi, A. Jutand, A. Lei, *Chem. Commun.* **2015**, *51*, 545-548.
- [16] (a) B. Suchand, G. Satyanarayana, *Eur. J. Org. Chem.* **2017**, *2017*, 3886-3895; (b) D. P. Estes, J. R. Norton, S. Jockusch, W. Sattler, *J. Am. Chem. Soc.* **2012**, *134*, 15512-15518.
- [17] (a) H.-X. Zheng, Z.-F. Xiao, C.-Z. Yao, Q.-Q. Li, X.-S. Ning, Y.-B. Kang, Y. Tang, *Org. Lett.* **2015**, *17*, 6102-6105; (b) S. Furukawa, Y. Ohno, T. Shishido, K. Teramura, T. Tanaka, *ChemPhysChem* **2011**, *12*, 2823-2830.

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