

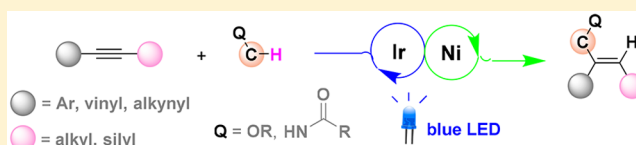
Photoinduced Nickel-Catalyzed Chemo- and Regioselective Hydroalkylation of Internal Alkynes with Ether and Amide α -Hetero C(sp³)–H Bonds

Hong-Ping Deng, Xuan-Zi Fan, Zhi-Hui Chen, Qing-Hua Xu, and Jie Wu*

Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore 117543, Republic of Singapore

Supporting Information

ABSTRACT: A direct hydroalkylation of disubstituted alkynes with unfunctionalized ethers and amides was achieved in an atom-efficient and additive-free manner through the synergistic combination of photoredox and nickel catalysis. The protocol was effective with a wide range of internal alkynes, providing products in a highly selective fashion. Notably, the observed regioselectivity is complementary to conventional radical addition processes. Mechanistic investigations suggest that the photoexcited iridium catalyst facilitated the nickel activation via single-electron transfer.

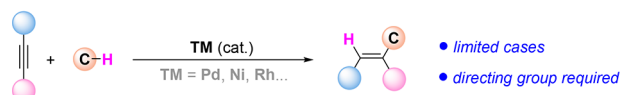


INTRODUCTION

Substituted alkenes are versatile synthetic intermediates in organic synthesis as well as ubiquitous structural motifs in biologically active compounds. Intermolecular C–C bond-forming reactions via hydrofunctionalization of alkynes represent one of the most fundamental reactions to access stereochemically well-defined substituted alkenes. Among these reactions, the direct addition of an unactivated C–H bond across an alkyne's C≡C bond is the most atom- and step-economic strategy. To date, the majority of work in this area has been focused on the activation of C(sp²)–H bonds.^{1,2} Routes for the direct alkenylation of C(sp³)–H bonds are quite limited and suffer from poor selectivity. Furthermore, most reported examples are only effective with substrates equipped with a directing group (Scheme 1a).³ Another approach is the addition of carbon radicals generated from homolytic hydrogen

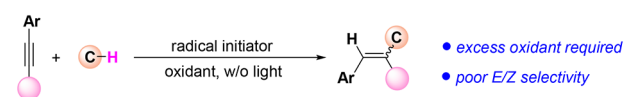
abstraction from C(sp³)–H bonds to alkynes (Scheme 1b). These processes typically require the use of a superstoichiometric amount of an oxidant or a radical initiator, and display low levels of stereoselectivity.⁴

Visible-light-mediated photochemistry has witnessed dramatic developments over the past decade. By activation with visible light, a photocatalyst can function as a single-electron redox mediator or facilitate energy transfer to activate a diverse range of organic substrates, which enables previously inaccessible transformations.⁵ It offers enormous opportunities for C(sp³)–H bond functionalization.⁶ The functionalization of C–H bonds adjacent to a heteroatom is of considerable importance as these heteroatom-containing chemical entities are frequently found in pharmaceutically active agents. As compared to the easy and effective activation of amines,^{6c,d} photoredox activation of ethers and amides is more challenging, as the reduction potentials are significantly higher ($E_{1/2}^{\text{red}} = +1.75$ V vs SCE for tetrahydrofuran (THF),⁷ and $E_{1/2}^{\text{red}} = +2.3$ V vs SCE for *N,N*-dimethylformamide,⁸ as compared to $E_{1/2}^{\text{red}} = +0.7$ V vs SCE for *N,N*-dimethylaniline).⁹ This difficulty can be circumvented by using additional catalyst to enable hydrogen atom abstraction to deliver the desired α -heterocarbon radical.¹⁰ In particular, the Doyle and the Molander groups have described a light-mediated arylation of α -oxy C–H bonds by using a nickel catalyst and an Ir photocatalyst, wherein an in situ generated chlorine radical or triplet–triplet energy transfer was proposed as the C(sp³)–H activation mechanism.¹¹ As part of our continuing efforts in the development of visible-light-mediated green and sustainable chemical processes,¹² we herein report an additive-free visible-light-promoted Ni-catalyzed C(sp³)–H alkenylation of ethers and amides with a range of internal alkynes with excellent selectivity (Scheme 1c).

Scheme 1. Synthesis of Substituted Alkenes through Hydroalkylation of Alkynes with C(sp³)–H Bondsa) through transition-metal catalyzed C(sp³)–H activation:

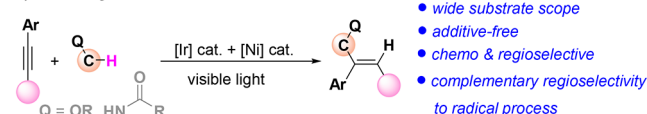
- limited cases
- directing group required

b) through radical addition:



- excess oxidant required
- poor E/Z selectivity

c) this study: new activation mode



- wide substrate scope
- additive-free
- chemo & regioselective
- complementary regioselectivity to radical process

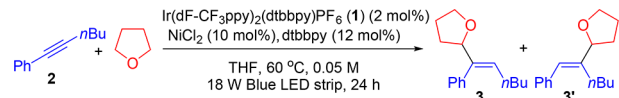
Received: August 2, 2017

Published: September 1, 2017

RESULTS AND DISCUSSION

Reaction Optimization. Our study was commenced by evaluating the visible-light-promoted hydroalkylation of unsymmetric alkyne **2** using THF. After careful investigation of various photocatalysts, Ni catalysts, ligands, and solvents,¹³ we found that the combination of a catalytic amount of Ir(dF-CF₃ppy)₂(dtbbpy)PF₆ **1**, NiCl₂, and 4,4'-di-*tert*-butyl-2,2'-dipyridyl (dtbbpy) ligand in THF at 60 °C under blue LED light irradiation gave the best results. Under these optimized conditions, **3** and **3'** were formed in 81% in a 5:1 regioisomeric ratio, and excellent *E/Z* selectivity was observed for the major isomer **3** (Table 1, entry 1). Remarkably, the major isomer **3**

Table 1. Optimization of the THF Alkenylation



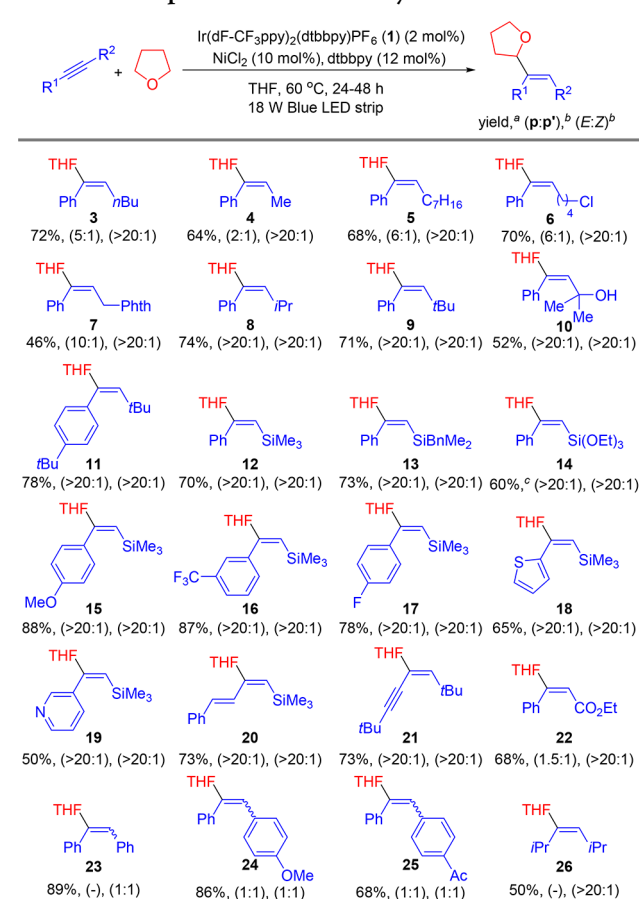
entry	deviation	yield (%) ^a	3:3' ^b	<i>E/Z</i> of 3 ^b
1	none	81	5:1	>20:1
2	NiBr ₂ instead of NiCl ₂	22	2:1	>20:1
3	NiI ₂ or Ni(acac) ₂ instead of NiCl ₂	0	NA	NA
4	NiBr ₂ + LiCl instead of NiCl ₂	40	3:1	>20:1
5	Ni(cod) ₂ instead of NiCl ₂	0	NA	NA
6	Ni(cod) ₂ + LiCl instead of NiCl ₂	0	NA	NA
7	Ru(bpy) ₃ ²⁺ or organocatalysts instead of 1	0	NA	NA
8	adding HCO ₂ H (1 equiv)	12	1:3	>20:1
9	adding Cs ₂ CO ₃ or DBU (2 equiv)	0	NA	NA
10	adding pyridine (2 equiv)	53	5:1	>20:1
11	adding lutidine (2 equiv)	68	5:1	>20:1
12	room temperature instead of 60 °C	21	5:1	>20:1
13	(dtbbpy)NiCl ₂ (10 mol %) instead of NiCl ₂ and dtbbpy	80	5:1	>20:1
14	without NiCl ₂ or 1 or dtbbpy or light	0	NA	NA

^aYields were determined by the crude ¹H NMR spectra using 1,3,5-trimethoxybenzene as an internal standard. ^bSelectivity ratios were determined by the crude ¹H NMR spectra.

possessed a complementary regioselectivity from the direct radical addition process, as **3'** is generally favored in the latter case wherein a transient vinyl radical intermediate is stabilized by the adjacent aryl substituent.⁴ The use of a NiCl₂ catalyst is crucial for achieving an efficient transformation. Replacing NiCl₂ with NiBr₂, NiI₂, or Ni(acac)₂ resulted in a significantly lower yield (entries 2 and 3). Furthermore, the addition of LiCl (20 mol %) to the NiBr₂-based catalytic system enhanced the reactivity (entry 4). To our surprise, a Ni(0) catalyst (e.g., Ni(cod)₂), which is effective in coupling reactions under visible-light promotion,¹¹ showed no reactivity toward alkenylation (entries 5 and 6), suggesting that a Ni(0) species may not be involved in the catalytic cycle. Changing the photocatalyst to Ru(bpy)₃²⁺ or other organic photocatalysts resulted in no product formation (Table S1). The reactivity was almost killed in the presence of a strong acid or base (entries 8 and 9). However, the relatively milder organic bases, pyridine and lutidine, were tolerated (entries 10 and 11). Conducting the reaction at room temperature instead of 60 °C resulted in a significantly lower conversion (entry 12). Utilizing a preformed (dtbbpy)NiCl₂ catalyst afforded a similar result (entry 13). Finally, no product formation was detected in the absence of

either **1**, the Ni catalyst, ligand, or light, demonstrating the need for these components (entry 14).

Scope Evaluation. Adopting the optimized condition, the generality of the hydroalkylation was determined by evaluating a variety of alkynes. As shown in Scheme 2, 1-alkyl-2-

Scheme 2. Scope of Substituted Alkynes^a

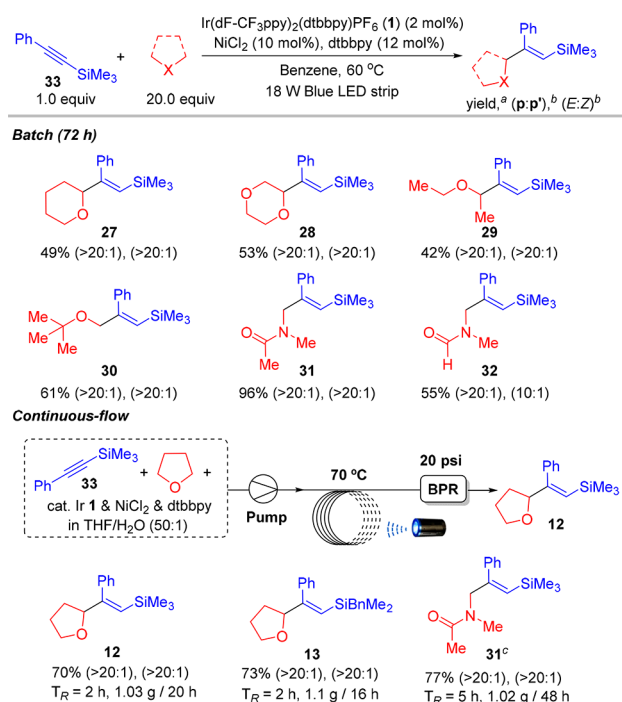
^a(a) Isolated yields. (b) Regioselectivity and *E/Z* ratios of major products determined by the crude ¹H NMR spectra. (c) Yields based on the crude ¹H NMR spectrum using trimethoxybenzene as an internal standard. Phth = phthalimide.

arylacetylenes participated well in the targeted hydroalkylation. Excellent regioselectivity was observed with bulkier alkyl substituents (**3–11**). Changing the alkyl group to a silyl substituent also resulted in excellent regioselectivity (**12–19**). Notably, the incorporation of a Si(OEt)₃ moiety furnished a highly selective product **14**, rendering this synthetic route important to material science,¹⁴ as well as providing an additional handle for further derivatization.¹⁵ The reactions proceeded smoothly with heterocyclic alkynes (e.g., thiophene **18** and pyridine **19**). Replacing the aryl substituents of the alkyne with vinyl (**20**) or alkynyl groups (**21**) resulted in equally good reactivity and regioselectivity, indicating a highly selective alkenylation with a broad internal alkyne substrate scope. However, an alkynyl ester afforded product **22** in good yield but poor selectivity. With diaryl-substituted alkynes (**23–25**), the alkenylation was unselective regardless of the electronic parameters of the substituents on the alkyne terminus, resulting in a mixture of regio- and *E/Z* isomers. Control experiments showed that the diaryl-substituted alkene product underwent isomerization under the photoalkenylation

reaction conditions,^{13,16} which accounts for the poor *E/Z* selectivity of this type of substrates. The hydroalkylation protocol was also effective for dialkyl-substituted alkynes (26). However, terminal alkynes were not suitable substrates due to the competing [2+2+2] cycloaddition.

We next surveyed the reactivity patterns of ether and amide C(sp³)–H bonds undergoing this hydroalkylation (Scheme 3).

Scheme 3. Scope of Ether and Amide C(sp³)–H Partners in the Hydroalkylation Using Batch and Continuous-Flow Reactors^a



^a(a) Isolated yields. (b) Regioselectivity and *E/Z* ratios were determined by the crude ¹H NMR spectra. (c) Using benzene as the solvent.

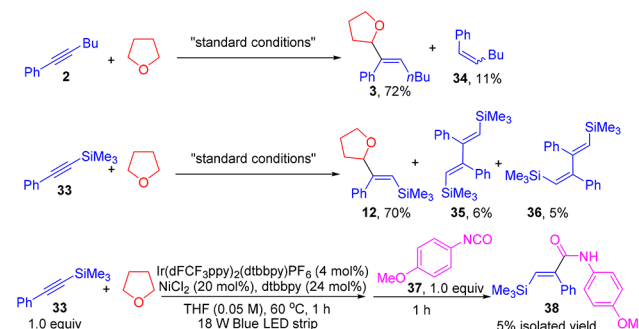
Employing benzene as the solvent, various ether substrates, including tetrahydropyran (27), dioxane (28), diethyl ether (29), and *tert*-butyl methyl ether (30), participated in the alkenylation with excellent selectivity but lower efficiency as compared to the reaction with THF. The lower reactivity could be due to the higher C–H bond dissociation energies of these ether substrates.^{11c} The reactions were also efficient with α -amino C(sp³)–H bonds in amides (31, 32). To further demonstrate the synthetic utility of this methodology, the hydroalkylations were shown to be amenable to scale up to the gram scale utilizing a continuous-flow reactor (12, 1.03 g/20 h; 13, 1.1 g/16 h; 31, 1.02 g/48 h).¹⁷

Control Experiments To Elucidate the Reaction Pathway. Although the catalytic system applied for this hydroalkylation is similar to that for the aryl coupling reported by Doyle and Molander,¹¹ we suspect a mechanistically distinct pathway for the alkenylation due to the following observations: (i) only a catalytic amount of chloride was present in the reaction mixture; (ii) Ni(0) is an ineffective precatalyst and no catalytically active species can be generated from this precursor; and (iii) the obtained regioselectivity is different from the direct radical addition with alkynes, but similar to the hydro-

functionalization of alkynes involving a catalytic Ni-hydride intermediate.¹⁸

Thus, control experiments were performed to gain further insights into the nature of this C–H alkenylation. First, careful examination of the product mixtures revealed that reduced alkenes (34) and dienes (35, 36) were the major side products (Scheme 4), indicating the presence of a hydride reducing

Scheme 4. Control Experiments Supporting the Formation of a Ni–H Species^a

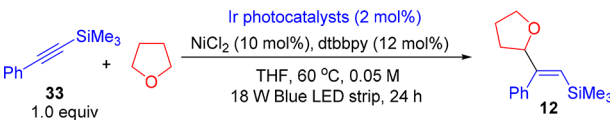


^aStandard conditions: Ir(dFCF₃ppy)₂(dtbbpy)PF₆ (2 mol %), (dtbbpy)NiCl₂ (10 mol %), THF (0.05 M), 60 °C, 24 h, 18 W blue LED strip.

species. More importantly, when isocyanate 37, which has been reported to intercept an in situ generated alkenyl nickel species,^{18a} was added to the hydroalkylation reaction mixture, the alkyne hydroamidation product 38 was isolated in 5% yield, strongly supporting the generation of an alkenyl nickel intermediate, most likely accessed through Ni–H hydro-nickelation of the internal alkyne starting substrate.

Notably, without THF (using benzene with or without water as solvent) only the starting alkyne was recovered (Scheme 5a), suggesting that THF was essential for the formation of the hydride species. Deuterium labeling experiments were performed to elucidate the hydride source (Scheme 5b). When using a 1:1 ratio of THF and *d*₈-THF as the ether reaction partner, both THF (12) and *d*₈-THF (39) incorporated products were detected, with a 12:39 ratio of approximately 2:1. To our surprise, no vinyl-*D* product was observed. With solely *d*₈-THF as the coupling partner, only 33% deuterium incorporation of the vinyl proton was detected in the alkene product. We thus suspect that the hydride source may preferentially arise from trace water in the reaction mixtures. This hypothesis was further supported by adding H₂O or D₂O as an additive in the deuterium labeling study. On the basis of these experimental results, we conclude that the hydride source originated from the ether C(sp³)–H bonds, but exchanged with water present in the reaction system. Although the generation of a Ni–H intermediate from C(sp²)–H bonds is well documented,¹⁹ this study represents a rare example of Ni–H generation using C(sp³)–H bonds as the hydride source.²⁰

When the reaction was performed in the presence of the radical scavenger (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO), a THF-TEMPO adduct was detected (Scheme 6a), indicating the formation of THF radicals. Interestingly, THF radicals generated by an excess amount of a di-*tert*-butyl peroxide (DTBP) oxidant²¹ did not form any desired product 12 with alkyne 33, even in the presence of the Ni catalyst under photoconditions (Scheme 6b).

Table 2. Evaluation of Ir Photocatalysts with Different Energy States²³


Ir photocatalysts	yield (%) ^a	E _T (kcal/mol) ²³	E _{1/2} (M [•] /M [−]) ²³	E _{1/2} (M [•] /M ⁺) ²³
Ir(ppy) ₃	0	55.2	+0.55	−1.97
Ir(dFppy) ₂ (dtbbpy)PF ₆	12	55.4	+1.14	−0.93
Ir(4-Fppy) ₃	0	58.6	+0.73	−1.86
Ir(dFCF ₃ ppy) ₂ (dtbbpy)PF ₆	70	60.1	+1.21	−0.89
Ir(2,4-dFppy) ₃	0	60.1	+0.39	−1.23
Ir(dFCF ₃ ppy) ₂ (phen)PF ₆	34	60.2	+1.39	−0.83
Ir(dFCF ₃ ppy) ₂ (bpy)PF ₆	34	60.4	+0.97	−0.97

^aIsolated yields.

Scheme 7. Further Control Experiments

a) UV light experiment:

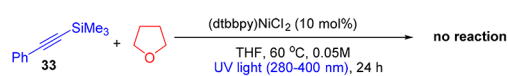
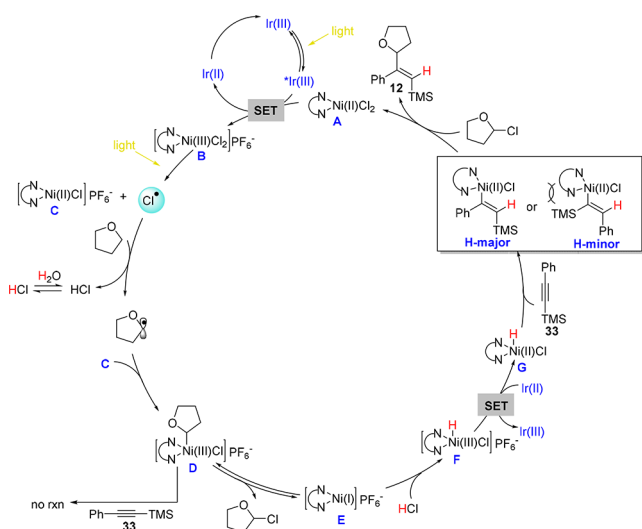
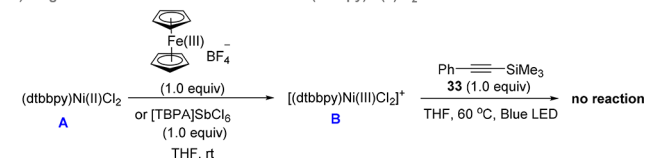
b) Single electron oxidation of stoichiometric (dtbbpy)Ni(II)Cl₂:

Figure 2. Tentatively proposed mechanism.

carbo-nickelation with alkynes under the optimal photo condition (Scheme 6b),²⁶ a reductive elimination delivers the Ni(I) intermediate E,²⁷ which subsequently forms the key nickel-hydride species F through oxidative addition to HCl.²⁸ The observed side-products 34, 35, and 36 (Scheme 4) strongly supported the presence of a hydride reducing species. The proposed D → F also explains the experimental observation that the hydride source originated from THF, but can exchange with trace water presented in the reaction mixture as illustrated in the deuterium labeling experiments (Scheme 5).²⁹ The acid/base additive studies also support this proposed process. As a strong base will quench HCl, while an acid may consume Ni-hydride, both strong base and acid additives are

detrimental to the reaction (Table 1, entries 8 and 9).³⁰ A SET reduction of highly reactive Ni(III)–H intermediate F by the reducing Ir(II) species ($E_{1/2} = -1.37$ V vs SCE in MeCN) gives Ni(II)-hydride G. The control experiment in Scheme 7b also suggests that the Ni(III) intermediate may undergo reduction before it can react with the internal alkyne substrate.³¹ Subsequent hydronickelation of the alkyne,^{19a,31} in which the regioselectivity is determined, results in the less sterically hindered vinyl nickel intermediate H-major, which corresponds to the observed major isomer product. The generation of alkyne hydroamidation product 38 using isocyanate 37 under this reaction condition strongly supports the formation of an alkenyl nickel intermediate. The final nucleophilic substitution with the in situ generated THF chloride produces the observed major alkene product while regenerating the Ni(II) catalyst A.

CONCLUSION

Overall, an unprecedented photoinduced hydroalkylation of alkynes with ether and amide C(sp³)–H bonds was achieved in an atom- and redox-efficient manner through the combination of photoredox and nickel catalysis. A variety of internal alkynes were excellent substrates for this transformation, delivering alkene products with high regioselectivity, which is complementary to the direct radical addition process. Mechanistic experiments indicated a rare example of nickel-hydride generation with C(sp³)–H bonds as the hydride source. The presented C(sp³)–H activation protocol through a unique nickel-hydride formation pathway promises more applications for C(sp³)–H functionalization with other unsaturated systems.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b08158.

Experimental procedures and spectral data (PDF)

AUTHOR INFORMATION

Corresponding Author

*chmjie@nus.edu.sg

ORCID

Jie Wu: 0000-0002-9865-180X

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for the financial support provided by the National University of Singapore (R-143-000-645-112, R-143-000-665-114) and GSK-EDB (R-143-000-687-592). We thank Prof. Frank Glorius, Miss Lena Pitzer (Universität Münster), Assistant Prof. Rowan Young (NUS), Dr. Sarah Tasker (UIUC), and Dr. Yang Yang (UC-Berkeley) for helpful discussions.

■ REFERENCES

- (1) (a) Boyarskiy, V. P.; Ryabukhin, D. S.; Bokach, N. A.; Vasilyev, A. *V. Chem. Rev.* **2016**, *116*, 5894. (b) Ackermann, L. *Acc. Chem. Res.* **2014**, *47*, 281. (c) Gao, K.; Yoshikai, N. *Acc. Chem. Res.* **2014**, *47*, 1208.
- (2) For selected works, see: (a) Zhou, B.; Chen, H.; Wang, C. *J. Am. Chem. Soc.* **2013**, *135*, 1264. (b) Wang, C.; Sun, H.; Fang, Y.; Huang, Y. *Angew. Chem., Int. Ed.* **2013**, *52*, 5795. (c) Kwak, J.; Ohk, Y.; Jung, Y.; Chang, S. *J. Am. Chem. Soc.* **2012**, *134*, 17778. (d) Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992.
- (3) For selected examples, see: (a) Xu, Y.; Young, M. C.; Dong, G.-B. *J. Am. Chem. Soc.* **2017**, *139*, 5716. (b) Xu, J.-W.; Zhang, Z.-Z.; Rao, W.-H.; Shi, B.-F. *J. Am. Chem. Soc.* **2016**, *138*, 10750. (c) Sen, M.; Emayavaramban, B.; Barsu, N.; Premkumar, J. R.; Sundararaju, B. *ACS Catal.* **2016**, *6*, 2792. (d) Maity, S.; Agasti, S.; Earsad, A. M.; Hazra, A.; Maiti, D. *Chem. - Eur. J.* **2015**, *21*, 11320. (e) Liu, B.; Zhou, T.; Li, B.; Xu, S.; Song, H.; Wang, B. *Angew. Chem., Int. Ed.* **2014**, *53*, 4191.
- (4) (a) Zhang, M.; Zhao, Y.; Chen, W.-Z. *Synthesis* **2017**, *49*, 1342. (b) Feng, S.-B.; Xie, X.-G.; Zhang, W.; Liu, L.; Zhong, Z.; Xu, D.; She, X.-G. *Org. Lett.* **2016**, *18*, 3846. (c) Li, J.; Zhang, J.; Tan, H.; Wang, D. *Z. Org. Lett.* **2015**, *17*, 2522. (d) Huang, L.-H.; Cheng, K.; Yao, B.-B.; Zhao, J.-L.; Zhang, Y.-H. *Synthesis* **2009**, *20*, 3504. (e) Doohan, R. A.; Geraghty, N. W. A. *Green Chem.* **2005**, *7*, 91.
- (5) For selected reviews, see: (a) Romero, N. A.; Nicewicz, D. A. *Chem. Rev.* **2016**, *116*, 10075. (b) Ravelli, D.; Protti, S.; Fagnoni, M. *Chem. Rev.* **2016**, *116*, 9850. (c) Skubi, K. L.; Blum, T. R.; Yoon, T. P. *Chem. Rev.* **2016**, *116*, 10035. (d) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322. (e) Xuan, J.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2012**, *51*, 6828. (f) Narayanam, J. M. R.; Stephenson, C. R. *Chem. Soc. Rev.* **2011**, *40*, 102.
- (6) For selected recent reviews, see: (a) Qin, Q.; Jiang, H.; Hu, Z.-T.; Ren, D.-A.; Yu, S.-Y. *Chem. Rev.* **2017**, *17*, 754. (b) Ravelli, D.; Protti, S.; Fagnoni, M. *Acc. Chem. Res.* **2016**, *49*, 2232. (c) Nakajima, K.; Miyake, Y.; Nishibayashi, Y. *Acc. Chem. Res.* **2016**, *49*, 1946. (d) Shi, L.; Xia, W.-J. *Chem. Soc. Rev.* **2012**, *41*, 7687.
- (7) Esswein, A. J.; Nocera, D. G. *Chem. Rev.* **2007**, *107*, 4022–4047.
- (8) Hall, L. R.; Iwamoto, R. T.; Hanzlik, R. P. *J. Org. Chem.* **1989**, *54*, 2446.
- (9) Seo, E. T.; Nelson, R. F.; Fritsch, J. M.; Marcoux, L. S.; Leedy, D. W.; Adams, R. N. *J. Am. Chem. Soc.* **1966**, *88*, 3498.
- (10) For selected recent examples, see: (a) Shaw, M. H.; Shurtleff, V. W.; Terrett, J. A.; Cuthbertson, J. D.; MacMillan, D. W. C. *Science* **2016**, *352*, 1304. (b) Jin, J.; MacMillan, D. W. C. *Angew. Chem., Int. Ed.* **2015**, *54*, 1565. (c) Qvortrup, K.; Rankic, D. A.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2014**, *136*, 626. (d) Dai, C.; Meschini, F.; Narayanam, J. M. R.; Stephenson, C. R. *J. Org. Chem.* **2012**, *77*, 4425.
- (11) (a) Nielsen, M. K.; Shields, B. J.; Liu, J.; Williams, M. J.; Zacuto, M. J.; Doyle, A. G. *Angew. Chem., Int. Ed.* **2017**, *56*, 7191. (b) Shields, B. J.; Doyle, A. G. *J. Am. Chem. Soc.* **2016**, *138*, 12719. (c) Heitz, D. R.; Tellis, J. C.; Molander, G. A. *J. Am. Chem. Soc.* **2016**, *138*, 12715.
- (12) (a) Zhou, R.; Liu, H.-W.; Tao, H.-R.; Yu, X.-J.; Wu, J. *Chem. Sci.* **2017**, *8*, 4654. (b) Xue, F.; Deng, H.-P.; Xue, C.-W.; Mohamed, D. K. B.; Tang, K. Y.; Wu, J. *Chem. Sci.* **2017**, *8*, 3623.
- (13) See the [Supporting Information](#) for more details of reaction optimization and control experiments.
- (14) Witucki, G. L. *J. Coat. Technol.* **1993**, *65*, 57.
- (15) (a) Cornelissen, L.; Lefrancq, M.; Riant, O. *Org. Lett.* **2014**, *16*, 3024. (b) Koike, T.; Du, X.; Sanada, T.; Danda, Y.; Mori, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 89.
- (16) Metternich, J. B.; Gilmour, R. *Synlett* **2016**, *27*, 2541.
- (17) Cambié, D.; Bottecchia, C.; Straathof, N. J. W.; Hessel, V.; Noël, T. *Chem. Rev.* **2016**, *116*, 10276.
- (18) (a) Wang, X.; Nakajima, M.; Serrano, E.; Martin, R. *J. Am. Chem. Soc.* **2016**, *138*, 15531. (b) Wang, X.; Nakajima, M.; Martin, R. *J. Am. Chem. Soc.* **2015**, *137*, 8924.
- (19) For reviews on Ni-hydride formation and application, see: (a) Eberhardt, N. A.; Guan, H.-R. *Chem. Rev.* **2016**, *116*, 8373. (b) Cai, X.-H.; Xie, B. *ARKIVOC* **2015**, *1*, 184.
- (20) To the best of our knowledge, only one report has documented Ni-hydride generation from C(sp³)-H bonds. However, there is not strong experimental data to support the proposed mechanism: Gartia, Y.; Ramidi, P.; Jones, D. E.; Pulla, S.; Ghosh, A. *Catal. Lett.* **2014**, *114*, 507.
- (21) Zhou, L.-L.; Tang, S.; Qi, X.-T.; Lin, C.-T.; Liu, K.; Liu, C.; Lan, Y.; Lei, A.-W. *Org. Lett.* **2014**, *16*, 3404.
- (22) For selected recent examples of energy transfer-mediated catalytic photochemical transformations, see: (a) Welin, E. R.; Le, C.; Arias-Rotondo, D. M.; McCusker, J. K.; MacMillan, D. W. C. *Science* **2017**, *355*, 380. (b) Blum, T. R.; Miller, Z. D.; Bates, D. M.; Guzei, I. A.; Yoon, T. P. *Science* **2016**, *354*, 1391. (c) Singh, A.; Fennell, C. J.; Weaver, J. D. *Chem. Sci.* **2016**, *7*, 6796. (d) Arceo, E.; Montroni, E.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2014**, *53*, 12064.
- (23) Singh, A.; Teegardin, K.; Kelly, M.; Prasad, K. S.; Krishnan, S.; Weaver, J. D. *J. Organomet. Chem.* **2015**, *776*, 51.
- (24) Peng, B.; Yu, G.-N.; Liu, X.-F.; Liu, B.; Liang, X.; Deng, L.-J.; Sum, T. C.; Loh, K. P. *2D Mater.* **2016**, *3*, 025020.
- (25) We thank a reviewer for pointing out the possibility of the transient THF radical reacting at a different nickel center A other than C. The Weix group has shown a radical-chain process in Ni-catalysis where an alkyl radical is formed at one nickel center, and then reacts with a second nickel center, see: (a) Everson, D. A.; Weix, D. J. *J. Org. Chem.* **2014**, *79*, 4793. (b) Biswas, S.; Weix, D. J. *J. Am. Chem. Soc.* **2013**, *135*, 16192.
- (26) The regioselectivity of products does not support the process of a Ni-THF species *syn* insertion to an alkyne as well.
- (27) All attempts to detect the 2-Cl-THF intermediate failed probably due to the instability of this compound. For the instability of 2-Cl-THF, see: Lee, S.; Kaib, P. S. J.; List, B. *J. Am. Chem. Soc.* **2017**, *139*, 2156. However, we were able to trap the 2-Cl-THF intermediate by using a silyl enol ether. For discussion of the control experiments, see the [Supporting Information](#).
- (28) For selected examples of Ni-hydride formation via oxidative addition with HCl, see: (a) Lin, S.; Day, M. W.; Agapie, T. *J. Am. Chem. Soc.* **2011**, *133*, 3828. (b) James, T. L.; Cai, L.-S.; Muetterties, M. C.; Holm, R. H. *Inorg. Chem.* **1996**, *35*, 4148.
- (29) Another possibility for the generation of Ni-hydride species from intermediate D is through a β -hydride elimination process. However, the deuterium labeling experiments do not support this process.
- (30) However, the relatively milder organic bases, such as pyridine and lutidine, are tolerated (Table 1, entries 10 and 11). We suspect that the protonated pyridine (pK_a \approx 5.25) still can deliver HCl for the oxidative addition. However, protonated DBU (pK_a \approx 13.5) and Cs₂CO₃ are not acidic enough to deliver HCl, which cease the reaction. DBU may also reduce the excited Ir ¹* to stop the catalytic cycle.
- (31) For examples of Ni(II)-hydride *syn* insertion to alkynes, see: (a) Nakao, Y.; Kashiwara, N.; Kanyiva, K. S.; Hiyama, T. *J. Am. Chem. Soc.* **2008**, *130*, 16170. (b) Nakao, Y.; Kanyiva, K. S.; Oda, S.; Hiyama, T. *J. Am. Chem. Soc.* **2006**, *128*, 8146. On the other hand, existing reports on transformations involving Ni(III)-hydride and vinyl-Ni(III) are rare.