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Pd(II)-Catalyzed *gamma*-C(sp^3)-H Alkynylation of Amides: A selective functionalization of R chain of amides R^{1}C(O)NHR†,‡

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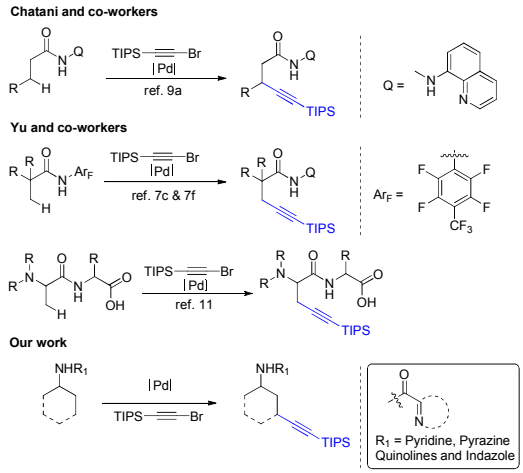
The accomplishment of *gamma* C(sp^3)–H bond alkynylation of R chain of amides R^{1}C(O)NHR, a fundamental class of synthetic substrates, has not been developed to date. Here, the first example of palladium(II)-catalyzed alkynylation of unactivated gamma C(sp^3)-H bond of alkyl amides (cyclic, linear, and amino acids) is reported. The kinetic experiment shows that the rate of the reaction depends on the coupling partner and the amides. Late-stage diversification of alkynylated amides was developed by utilizing amine and alkyne functionalities.

New approaches that selectively incorporate versatile functional group into remote C(sp^3)–H bond is an emerging field of research in contemporary organic synthesis. Alkynes are an essential functional group in organic synthesis and can be used as versatile building blocks in drug discovery, material science, and the chemical industry, employing cross-coupling, metathesis and cycloaddition reactions.[1-2] Pd-catalyzed Sonogashira coupling which couple alkynes with aryl halides is a promising strategy for the incorporation of alkyne into aryl through the sp-sp^2 coupling.[3] The scope of alkynylation is further elaborated by coupling of alkynyl halides (sp) with inert aryl C(sp^2)-H bond, namely "inverse Sonogashira coupling".[4] In addition to Pd-catalyzed alkynylation, other transition metal-catalyzed C-H alkynylation strategy provides a plethora method to selectively functionalize sp^2 and sp^3 C-H bond with high efficiency.[5-8] However, transition metal-catalyzed activation of remote and inert C(sp^3)-H bonds remain extremely rare and underdeveloped.

A few examples are explored for the alkynylation of inert C(sp^3)-H with the aid of directing groups (DG). Noteworthy work by Chatani and co-workers reported a palladium (II)-catalyzed β-alkynylation of secondary C(sp^3)-H bonds of acids derivatives using a bidentate auxiliary.[9a] Yu and co-workers reported a Pd(0)/NHC catalyzed alkynylation of β-methyl C(sp^3)-H bonds of aliphatic amides applying an *N*-arylamide auxiliary.[7c] Recyclable heterogeneous catalytic system is developed using gold supported Pd-nanoparticle for direct ethynylation of secondary C(sp^3)-H aliphatic carboxylic derivatives.[9b] Chen and co-workers developed a diastereoselective β-alkynylation of α-amino acids using Pd(II) *via* aminoquinoline directed primary[10a] and secondary[10b] C(sp^3)-H bond activation. A research group of Chen and Shi have identified the unique directing group, 1,2,3-triazole amine for selective Pd(II)-catalyzed C(sp^3)-H bond activation under silver-free condition followed by alkynylation strategy.[7f] Subsequently, Yu and co-workers introduced Pd(II)/pyridine-based catalytic system for methyl C(sp^3)-H alkynylation of □-quaternary carbon centers of acid derivatives.[7g] Similarly, Pd(II)-catalyzed site-selective C(sp^3)–H alkynylation of oligopeptides was developed using tetrabutylammoniun acetate as a key additive.[11] Nevertheless, this type of C-H bond activations has been mostly achieved for the β-C(sp^3)–H alkynylation of acid derivatives thus accessing R^1 chain of acid derivatives/amides R^{1}C(O)NHR. The accomplishment of C–H alkynylation of alkyl R chain of amides, a fundamental class of synthetic substrates, has not been developed to date



Scheme **1**. Palladium-catalyzed C(sp^3)-H bond activation strategies.

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Amines constitute essential synthetic precursors and are ubiquitous in agrochemical, peptide, pharmaceutical, and functional materials.[12] The representative examples of amine-containing biologically active molecules are shown in Figure 1. In light of our interest and continuation of transition metal-catalyzed alkynylation reactions,[5s-5u,7d] herein we disclose unprecedented palladium(II)-catalyzed alkynylation of *gamma*-C(sp^3)-H bond of amides with the assistance of picolinamide as DG (Scheme 1). The present alkynylation strategy is general method for alkynylation of amine using picolinic acid as a removable auxiliary and has a broad substrate scope. Remarkably, various ring size, α-quaternary, *N*-cyclic, and linear amides were alkynylated under our reaction conditions.

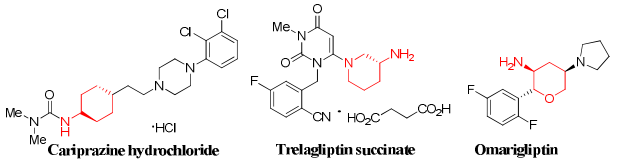
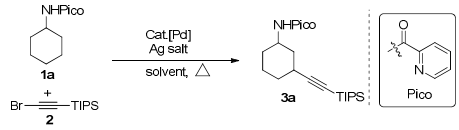


Figure 1. Representative examples of amine containing biologically active molecules

The preliminary investigation on palladium-catalyzed γ-C(sp^3)-H alkynylation of amides is carried out with an evaluation of a range of palladium catalysts, oxidants, bases, solvents, and temperature using *N*-cyclohexylpicolinamide (**1a**), and (triisopropylsilyl)ethynyl bromide **2** as representative coupling partner (Table 1).

Table 1. Optimization of the reaction conditions.[a]

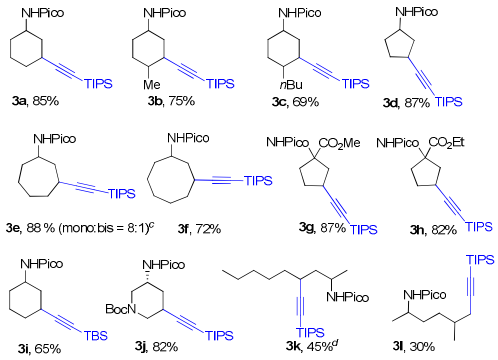


Entry	Reaction conditions	Yield of **3a** (%)[b]	Yield of **1a** (%)[b]
1	$Pd(PPh_3)_2Cl_2$ used as [Pd] source	15	78
2	$Pd(TFA)_2$ used as [Pd] source	n.r.	98
3	standard conditions	85	8
4	$Pd(dba)_3$ used as [Pd] source	20	71
5	$Pd(CH_3CN)_4BF_4$ used as [Pd] source	trace	97
6	$PdCl_2$ used as [Pd] source	trace	98
7	$Pd(acac)_2$ used as [Pd] source	trace	97
8	at 100 °C	75	21
9	without [Pd] cat	n.r.	95
10	without AgOAc	trace	92
11	(bromoethynyl)benzene instead of **2**	n.r.	99
12	3-cyclohexyl-1-propyne instead of **2**	n.r.	96
13	Ag_2CO_3 instead of AgOAc	75	10
14	$PhCO_2Ag$ instead of AgOAc	35	58
15	HFIPused as solvent	trace	98
16	CF_3CH_2OH used as solvent	trace	97

[a]Reaction conditions: **1a** (0.1 mmol), **2** (0.12 mmol), $Pd(OAc)_2$ (0.01 mmol), AgOAc (0.20 mmol) and toluene (1 mL) were heated at 130 °C (bath temperature) for 18 h under argon atm. [b]Isolated yields (yield of **1a** is calculated based on recovery of the starting amide **1a**). n.r.= no reaction.

Initially, the reaction of **1a** and **2** in the presence of $Pd(PPh_3)Cl_2$ (10 mol%), AgOAc (2 equiv.) as oxidant in toluene at 130 °C (bath temperature) for 18 h to yield the expected product **3a** in 15% isolated yield (Table 1, entry 1). Among a variety of palladium salt, $Pd(OAc)_2$ found to be the optimal catalyst to provide the C-H alkynylation product **3a** in 85 % isolated yield with a recovery of **1a** in 8% (Table 1, entries 1-7). The necessity of each of the key reaction components was demonstrated through a series of control experiments (Table 1, entries 9-13). By lowering the temperature from 130 °C to 100 °C, we obtained the product **3a** in 75% yield (Table 1, entry 8), and no reaction was observed in the absence of the palladium catalyst (Table 1, entry 9). Notably, trace (~6%) amounts of C-H alkynylated product **3a** was observed in the absence of an oxidant (Table 1, entry 10). When the reaction was carried out with (bromoethynyl)benzene or 3-cyclohexyl-1-propyne instead of **2**, there is no formation of corresponding desired product (Table 1, entries 11-12). This may be due to a strong coordination of the alkyne moiety with the palladium center and thus may prevent the oxidative addition step.[7c] The effect of solvent was also carried out (Table 1, entries 15-16), and found that the reaction proceeded efficiently in toluene. Other solvents such as DMA, DCE, HFIP, and CF_3CH_2OH were found to be ineffective, and no (or trace) alkynylated product **3a** was observed under optimal conditions.

Scheme 2. Scope of amides.[a,b]



[a]Reaction conditions: amide (0.25 mmol), **2** (0.27 mmol), $Pd(OAc)_2$ (0.025 mmol), AgOAc (0.50 mmol) and toluene (1 mL) were heated at 130 °C for 18 h under argon atm. [b]Isolated yields. [c]The ratios of mono/bis-alkynylation product is based upon the individual isolated yields. [d]Ag_2CO_3 instead of AgOAc.

With an optimized catalytic system in hand, we set out to probe its versatility in the *gamma*-C(sp^3)-alkynylation of various amide substrates using (triisopropylsilyl)ethynyl bromide **2** as coupling partner (Scheme 2). The developed synthetic methodology is general and has a broad substrate scope. As shown in scheme 2, the 4-substituted cyclohexyl amides such as **1b** and **1c** were well tolerated under our optimized conditions and gave the desired products in good yields (**3b** in 75%, **3c** in 69 %). To our delight, carbocyclic amides which containing 5, 7 and 8-membered rings were also successfully alkynylated at the *gamma* position of amides in very good to excellent yields {**3d** (87%), **3e** (78%) and **3f** (72%)}. The present method was also found to be effective for the alkynylation of amino acid substrates containing ⍰-quaternary carbon centers. Thus, compounds **1g** and **1h** gave the corresponding *gamma*-alkynylated amides {**3g** (87%) & **3h** (82%)} in very good yields, which can be used as a linker for the bivalent interaction and for the bio-conjugation process. The alternative alkyne coupling partner (*tert*-butyldimethylsilyl)ethynyl bromide was applied with **1a** under standard conditions to give the alkynylated product **3i** in 65%

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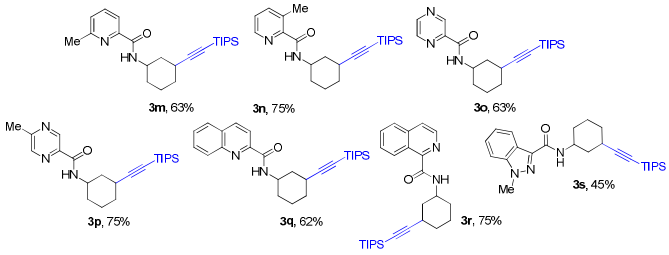
yield. To our delight, the chiral *N*-Boc protected heterocylic amide which is privileged structures in medicinal chemistry was applied for alkynylation reaction under standard conditions to provide **3j** in excellent yield (82%). In addition to that, aliphatic linear amides also proceed smoothly under an optimal condition such as the 2-heptyl amide to give **3k** in 45% yield. The lower in yield in case of aliphatic amides are due to the geometric flexibility of the amides, leading to the complication of a picolinamide-directed cyclometalation. Surprisingly, the alkynylation of alkyl amide **1l** showed the -alkynylated amide **3l** in 30% yield. In all the reactions the unreacted starting material (**1a**) was recovered and there was no formation of bis-alkynylated product (except product **3e**). Gratifyingly, except *gamma*-alkynylation product no different alkynylated product was observed. We have also successfully shown the scalability of this catalytic protocol. In this regard, the present palladium-catalyzed alkynylation was tested for gram-scale synthesis of **3a** (5.0 mmol scale) and it worked excellently with an expected alkynylated product (**3a**) in 82% yield.

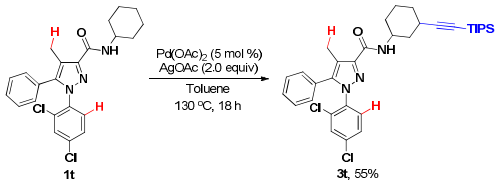
Scheme 3. Influence of different auxiliary groups under the standard conditions.[a,b]



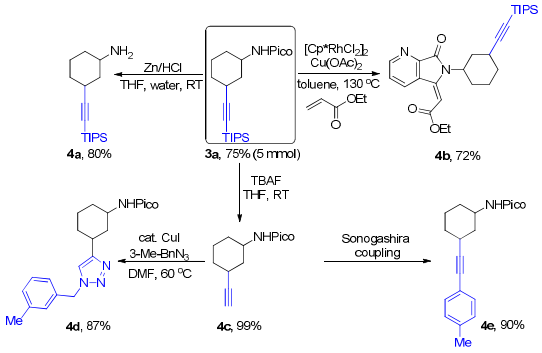
[a]Reaction conditions: amide (0.25 mmol), **2** (0.27 mmol), $Pd(OAc)_2$ (0.025 mmol), AgOAc (0.50 mmol) and toluene (1 mL) were heated at 130 °C for 18 h under argon atm. [b]Isolated yields.

Furthermore, we also evaluated the influence of different protecting groups under the standard conditions, including various picolinic acid-based directing groups and other amide-type directing groups (Scheme 3). The 2- or 3-substituted picolinic acid derived amides underwent the alkynylation reaction with (triisopropylsilyl)ethynyl bromide to afford **3m** (63%) and **3n** (75%) in good yields. Various heterocycles such as pyrazine, quinoline, and isoqiunoline based were also used as DG, the corresponding γ-alkynylated products {**3o** (63%), **3p** (75%), **3q** (62%) and **3r** (75%)} were obtained in good yields. We observed that five-membered heterocyclic indazoline as DG afforded the desired γ-alkynylated product **3s** in 45% isolated yield with a recovery of **1s** in 47%. To highlight the synthetic utility of the DG, the competitive site-selective alkynylation study was carried out in the presence of alkyl amide **1t**, conjugated with pyrazole moiety containing both Ar-$C(sp^3)$–H and Ar-$C(sp^2)$-H bond for chelation (Scheme 4). Significantly, *gamma*-$C(sp^3)$-H bond of amide alkynylation (**3t**) was observed over $C(sp^2)$-H alkynylation under standard reaction conditions in 55% yield with a recovery of **1t** in 37%.

The diversification of alkynylated amide derivatives is shown in Scheme 5. The deprotection of picolinamide was achieved by using Lewis catalyst (Zn/HCl) to obtain terminal *o*-alkynylbenzylamine **4a** in 80% yield. A rhodium(III)-catalyzed cascade oxidative olefination and cyclization of **3a** with ethyl acrylate to enable **4b** in 72% isolated yield. The deprotection of the TIPS group of **3a** was easily achieved by treatment with TBAF under standard reaction conditions to afford **4c** in quantitative yield. The desilylated compound **4c** was applied for the Sonogashira coupling to provide **4e** in 90% isolated yield. The compound **4c** was also successfully employed for the "click" reaction with *m*-methyl benzyl azide to yield **4d** in 87% under standard reaction conditions.



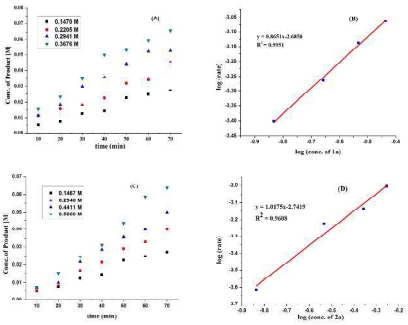
Scheme-4. Site-selective alkynylation strategy.



Scheme 5. Diversification of γ-alkynylated amide **3a**.

The kinetic studies were carried out to determine the order of reaction on palladium catalyzed γ-alkynylation of amide **1a** with **2** by using the initial rate approximation (Figure 2). The data shows that the increasing the concentration of **1a** enhance the rate of reaction with a slope of 0.86 obtained from the plot of log(rate) *vs* log(conc. of **1a**), indicating a fractional order alkynylation reaction. Similarly, with increasing the concentration of **2**, the rate of reaction increased, and a

Figure 2. Kinetics Study.



(**A**) The graph of product concentration *vs* time with increasing concentration of **1a**. (**B**) graph of log(rate) *vs* log(conc of **1a**). (**C**) Graph of product concentration *vs* time with increasing concentration of **2**. (**D**) Graph of log(rate) *vs* log(conc of **2**).

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slope of 1.01 was obtained from the plot of log(rate) vs log(conc. of **2**). Thus, the rate of reaction depends on both the substrates.

Conclusions

In summary, we have developed the first example of γ-alkynylation of various alkyl amides, particularly selective γ-alkynylation of R chain of amides $R^1C(O)NHR$. Easily removable picolinamide and its derivatives were identified as suitable auxiliaries for enabling Pd-catalyzed γ-alkynylation process. The substrate scope was successfully expanded applying carbocyclic and acyclic alkyl amides. Interestingly, the present protocol showed site-selective γ-alkynylation C(sp^3)-H bond in the presence of accessible Ar-C(sp^3)–H and Ar-C(sp^2)-H bonds.

Conflicts of interest

"There are no conflicts to declare".

Notes and references

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1 Acetylene Chemistry; F., Diederich, P. J. Stang and R. R. Tykwinski, Eds.; Wiley-VCH: Weinheim, Germany, 2005.
2 (a) H. C. Kolb, M. G. Finn and K. B. Sharpless, *Angew. Chem. Int. Ed.* 2001, **40**, 2004-2021; (b) A. Fürstner and P. W. Davies, *Chem. Commun.* 2005, 2307-2320; (c) W. Zhang andJ. S. Moore, *Adv. Synth. Catal.* 2007, **349**, 93-120; (d) S. Toyota, *Chem. Rev.* 2010, **110**, 5398-5424.
3 (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.*1975, **16**, 4467-4470; (b) Sonogashira, K. *J. Organomet. Chem.*2002, **653**, 46-49.
4 Reviews for inverse Sonogashira coupling, see: (a) A. S. Dudnik andV. Gevorgyan, *Angew. Chem. Int. Ed*. 2010, **49**, 2096-2098; (b) S. Messaoudi, J.-D. Brion and M. Alami, *Eur. J. Org. Chem*. 2010, 6495-6516.
5 (a) I. V. Seregin, V. Ryabova and V. Gevorgyan, *J. Am. Chem. Soc.* 2007, **129**, 7742-7743; (b) B. A. Trofimov, L. N. Sobenina, Z. V. Stepanova, T. I. Vakul'skaya, O. N. Kazheva, G. G. Aleksandrov, O. A. Dyachenko and A. I. Mikhaleva, *Tetrahedron* 2008, **64**, 5541-5544; (c) Y. Gu and X.-m. Wang, *Tetrahedron Lett.* 2009, **50**, 763-766; (d) N. Matsuyama, K. Hirano, T. Satoh and M. Miura, *Org. Lett.* 2009, **11**, 4156-4159; (e) J. P. Brand, J. Charpentier and J. Waser, *Angew. Chem., Int. Ed.* 2009, **48**, 9346-9349; (f) F. Besselièver and S. Piguel, *Angew. Chem. Int. Ed.* 2009, **48**, 9553-9556; (g) T. Kawano, N. Matsuyama, K. Hirano, T. Satoh and M. Miura, *J. Org. Chem.* 2010, **75**, 1764-1766; (h) S. H. Kim and S. Chang, *Org. Lett.* 2010, **12**, 1868-1871; (i) J. P. Brand and J. Waser, *Angew. Chem., Int. Ed.* 2010, **49**, 7304-7307; (j) Y. Ano, Y. M. Tobisu and N. Chatani, *Org. Lett.* 2012, **14**, 354-357; (k) F. Xie, Z. Qi, S. Yu and X. Li, *J. Am. Chem. Soc.* 2014, **136**, 4780-4787; (l) K. D. Collins, F. Lied and F. Glorius, *Chem. Commun.* 2014, **50**, 4459-4461; (m) T.-P. Loh and C. Feng, *Angew. Chem. Int. Ed.* 2014, **53**, 2722-2726; (n) M. Guan, C. Chen, J. Zhang, R. Zeng and Y. Zhao, *Chem. Commun.* 2015, **51**, 12103-12106; (o) Z.-Z. Zhang, B. Liu, C.-Y. Wang and B. F. Shi, *Org. Lett.* 2015, **17**, 4094-4097; (p)Y.-J. Liu, Y.-H. Liu, S.-Y. Yan and B.-F. Shi, *Chem. Commun.* 2015, **51**, 6388-6391; (q) N. Sauermann, M. J. González and L. Ackermann, *Org. Lett.* **2015**, *17*, 5316-5319; (r) Z. Ruan, S. Lackner and L. Ackermann, *ACS Catal.*2016, **6**, 4690-4693; (s) V. G. Landge, G. Jaiswal and E. Balaraman, *Org. Lett.* 2016, **18**, 812-815; (t) V. G. Landge, S. P. Midya, J. Rana, D. R. Shinde and E. Balaraman, *Org. Lett.* 2016, **18**, 5252-5255; (u) V. G. Landge, C. H. Shewale, G. Jaiswal, M. K. Sahoo, S. P. Midya and E. Balaraman, *Catal. Sci. Technol.* 2016, **6**, 1946-1951; (v) P. Wang, G. -C. Li, P. Jain, M. E. Farmer, J. He, P.-X. Shen and J.-Q. Yu, *J. Am. Chem. Soc.* 2016, **138**, 14092-14099; (w) Z. Ruan, N. Sauermann, E. Manoni and L. Ackermann, *Angew. Chem. Int. Ed.* 2017, **56**, 3172-3176; (x) R. Mei, S.-K. Zhang and L. Ackermann, *Org. Lett.* 2017, **19**, 3171-3174; (y) E. Tan, A. I. Konovalov, G. A. Fernández, R. Dorel and A. M. Echavarren, *Org. Lett.* 2017, **19**, 5561-5564; (z) C. Chen, P. Liu, J. Tang, G. Deng and X. Zeng, *Org. Lett.* 2017, **19**, 2474-2477; (aa) X. Li, G. Wu, X. Liu, Z. Zhu, Y. Huo and H. Jiang, *J. Org. Chem.* 2017, **82**, 13003-13011; (ab) G. Jiang, W. Hu, J. Li, C. Zhu, W. Wu and H. Jiang, *Chem. Commun.* 2018, **54**, 1746-1749; (ac) E. Tan, O. Quinonero, M. E. de Orbe, A. M. Echavarren, *ACS Catal.* 2018, **8**, 2166-2172.
6 W. Wu andH. Jiang, Haloalkynes: *Acc. Chem. Res.*2014, **47**, 2483-2504.
7 (a) Z. Li and C.-J. Li, *J. Am. Chem. Soc.* 2004, **126**, 11810-11811; (b) Z. Li, P. D. MacLeod and C.-J. Li, *Tetrahedron: Asymmetry* 2006, **17**, 590-597; (c) J. He, M. Wasa, L. S. L. Chan and J.-Q. Yu, *J. Am. Chem. Soc.* 2013, **135**, 3387-3390; (d) V. G. Landge, M. K. Sahoo, S. P. Midya, G. Jaiswal and E. Balaraman, *Dalton Trans.* 2015, **44**, 15382-15386; (e) J. Kim, M. Sim, N. Kim and S. Hong, *Chem. Sci*., 2015, **6**, 3611-3616. (f) X. Ye, C. Xu, L. Wojtas, N. G. Akhmedov, H. Chem and X. Shi, *Org. Lett.* 2016, **18**, 2970-2973; (g) H. Fu, P.-X. Shen, J. He, F. Zhang, S. Li, P. Wang, T. Liu and J.-Q. Yu, *Angew. Chem. Int. Ed.* 2017, **56**, 1873-1876.
8 For selected review on C-H bond activation: (a) Y. Segawa, T. Maekawa and K. Itami, *Angew. Chem., Int. Ed.* 2015, **54**, 66-81; (b) L. Ackermann, *Org. Process Res. Dev.*2015, **19**, 260-269; (c) L. Ackermann and J. Li, *Nat. Chem.* 2015, **7**, 686-687; (d) K. Shin, H. Kim and S. Chang, *Acc. Chem. Res.* 2015, **48**, 1040-1052; (e) O. Daugulis, J. Roane and L. D. Tran, *Acc. Chem. Res.* 2015, **48**, 1053-1064; (f) G. Song and X. Li, *Acc. Chem. Res.* 2015, **48**, 1007-1020; (g) C. Liu, J. Yuan, M. Gao, S. Tang, W. Li, R. Shi and A. Lei, *Chem. Rev.* 2015, **115**, 12138-12204; (h) P. Gandeepan and C.-H. Cheng, *Chem.-Asian J.* 2015, **10**, 824-838; (i) T. Iwai and M. Sawamura, *ACS Catal.* 2015, **5**, 5031-5040; (j) L. Yang and H. Huang, *Chem. Rev.* 2015, **115**, 3468-3517; (k) T. Cernak, K. D. Dykstra, S. Tyagarajan, P. Vachal and S. W. Krska, *Chem. Soc. Rev.* 2016, **45**, 546-576; (l) T. Gensch, M. N. Hopkinson and F. Glorius and J. Wencel-Delord, *Chem. Soc. Rev.* 2016, **45**, 2900-2936; (m) M. Moselage, J. Li and L. Ackermann, *ACS Catal.* 2016, **6**, 498-525; (n) W. Liu and L. Ackermann, *ACS Catal.* 2016, **6**, 3743-3752; (o) J. He, M. Wasa, K. S. L. Chen, Q. Shao and J.-Q. Yu, *Chem. Rev.* 2017, **117**, 8754-8786; (p) R. Cano, K. Mackey and G. P. McGlacken, *Catal. Sci. Technol.* 2018, **8**, 1251-1266.
9 (a) Y. Ano, M. Tobisu and N. Chatani, *J. Am. Chem. Soc.*2011, **133**, 12984-12986; (b) M. Al-Amin, M. Arisawa, S. Shuto, Y. Ano, M. Tobisu and N. Chatani, *Adv. Synth. Catal.* 2014, **356**, 1631-1637.
10 (a) B. Wang, C. Lu, S. -Y. Zhang, G. He, W. A. Nack and G. Chen, *Org. Lett.* 2014, **16**, 6260-6263; (b) B. Wang, G. He and G. Chen, *Sci. China Chem.* 2015, **58**, 1345-1348.
11 T. Liu, J. X. Qiao, M. A. Poss and J.-Q. Yu, *Angew. Chem. Int. Ed.* 2017, **56**, 10924-10927.
12 (a) J. M. Gajbhiye, N. A. More, M. D. Patil, R. Ummanni, S. S. Kotapalli, P. Yogeeswari, D. Sriram and V. H. Masand, *Med. Chem. Res.* 2015, **24**, 2960-2971; (b) Y. Huang, X. He, T. Wu and F. Zhang, *Molecules* 2016, **21**, 1041.

