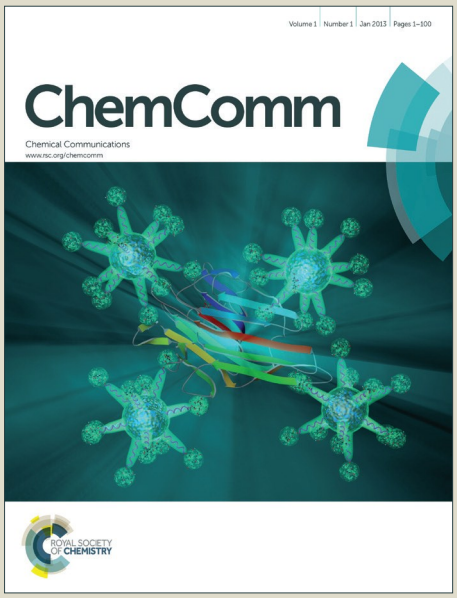
ChemComm

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: J. Gu and C. Cai, *Chem. Commun.*, 2016, DOI: 10.1039/C6CC05509E.



View Article Online
DOI: 10.1039/C6CC05509E

Journal Name

COMMUNICATION

Stereoselective Synthesis of Vinylsilanes via Copper-Catalyzed Silylation of Alkenes with Silanes

Received 00th January 20xx,
Accepted 00th January 20xx

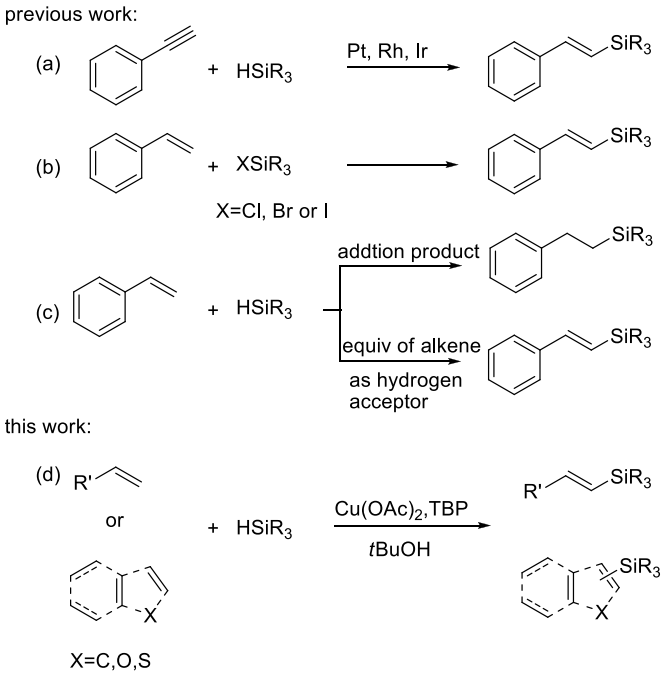
DOI: 10.1039/x0xx00000x

www.rsc.org/

Jian Gu,[a] Chun Cai* [a]

An efficient and stereoselective synthesis of vinylsilanes via copper-catalyzed direct silylation of alkenes with silanes was developed. This study offers a new and expedient strategy for the synthesis of synthetically useful alkenyl organosilicon compounds in satisfactory yields and may provide a low-cost and environmentally benign alternative to currently employed precious metal systems for alkene silylation. Moreover, the transformation is proposed to proceed via a radical process and exhibits a broad substrate scope and good functional group tolerance.

Transition-metal-catalyzed cross-coupling reactions for carbon–silicon bond formation have become one of the most straightforward and powerful ways for the preparation of organosilanes compounds[1], which play an important role in organic synthesis as useful intermediates in a number of synthetic transformations.[2] Among them, vinylsilanes are versatile and valuable starting materials in organic synthesis, such as Hiyama cross-coupling reactions, Hosomi-Sakurai-type allylation, and so on.[3] For these reasons, the development of simple and stereoselective methods to prepare vinylsilanes has become important in organic synthesis. Numerous methods are known for the preparation of vinyl silanes[4]. Among them, besides metathesis between vinylsilanes with olefins[5], transition-metal-catalyzed hydrosilylation of alkyne and dehydrogenative silylation of alkene are particularly noteworthy synthetic methods since the reactions are usually straightforward to perform, fully atom-economical and the reagents are stable, cheap and readily available[6]. However, limitations exist with the above protocols, which often makes the synthesis of unsaturated organosilanes challenging. For example, alkyne hydrosilylation generally is lack of stereoselectivity (a mixture of E/Z products) or a rather expensive catalyst is usually employed (Scheme 1a)[7]. And chemical waste would be produced when transition-metal-catalyzed couplings of alkenes with halide substituted silanes were used to synthesize vinylsilanes (Scheme 1b)[8].



Scheme 1. Strategies for alkenyl silylation.

Recently, Liu reported a free-radical-promoted stereospecific decarboxylative silylation of α, β -unsaturated acids which provided an effective way to synthesis vinylsilanes.[9] In this case, we wondered whether combining silicon-centered radicals with styrenes to get vinylsilanes by a more atom economic way. Alkenes are readily accessed and highly stable building blocks in organic chemistry and using them as starting

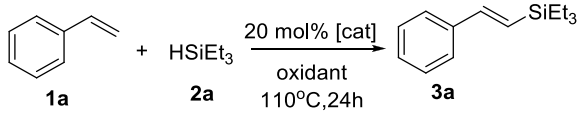
[a] Chemical Engineering College, Nanjing University of Science and Technology, 200 Xiao Ling Wei, Nanjing 210094, People's Republic of China. Email: c.cai@njust.edu.cn.

† Electronic Supplementary Information (ESI) available: Experimental procedures and characterization data for all products. See DOI: 10.1039/x0xx00000x

View Article Online DOI: 10.1039/C6CC05509F

materials would be highly advantageous. Silicon-centered radicals formed by silanes are postulated as key intermediates in various processes in material science, polymer science, and organic chemistry.[10] However, the reactions of olefins with silanes catalyzed by transition metal catalysts, as reported by many chemists, usually give the addition products or an equivalent of alkene is used as a hydrogen acceptor (Scheme 1c).[11] Zhu developed a copper catalyzed direct alkenylation of simple alkanes with styrenes.[12] They used copper and DTBP to produce alkane radical and get the alkenylation products. Inspired by Zhu and Liu's work, we wonder whether vinylsilanes can be synthesized directly from alkenes with silicon-centered radicals in the similar reaction pathway. To our delight, vinylsilanes can indeed be efficiently and stereoselectively synthesized from alkenes and silanes. Moreover, this reaction system can be applied for silylation of some unsaturated heterocycles with silanes in satisfactory yields (Scheme 1d).

Table 1. Optimization of the Reaction Conditions [a]



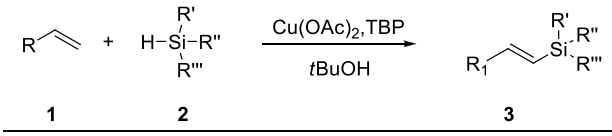
1a 2a 3a

Entry	Cat	Oxidant	Solvent	Yield [b] (%)
1	CuCl	TBHP	*t*BuOH	36
2	CuI	TBHP	*t*BuOH	15
3	$Cu(OTf)_2$	TBHP	*t*BuOH	--
4	CuOAc	TBHP	*t*BuOH	29
5	$Cu(OAc)_2$	TBHP	*t*BuOH	55
6	$CuCl_2$	TBHP	*t*BuOH	--
7	Cu_2O	TBHP	*t*BuOH	10
8	CuI	TBP	*t*BuOH	41
9	$Cu(OAc)_2$	TBP	*t*BuOH	70
10	$Cu(OAc)_2$	H_2O_2	*t*BuOH	--
11	$Cu(OAc)_2$	TBP	toluene	--
12	$Cu(OAc)_2$	TBP	DMF	--
13	$Cu(OAc)_2$	TBP	DMSO	--
14	$Cu(OAc)_2$	TBP	DCE	--
15	$Cu(OAc)_2$	TBP	*t*BuOH	50[c]
16	$Cu(OAc)_2$	TBP	*t*BuOH	55[d]
17	$Cu(OAc)_2$	--	*t*BuOH	--
18	--	TBP	*t*BuOH	--

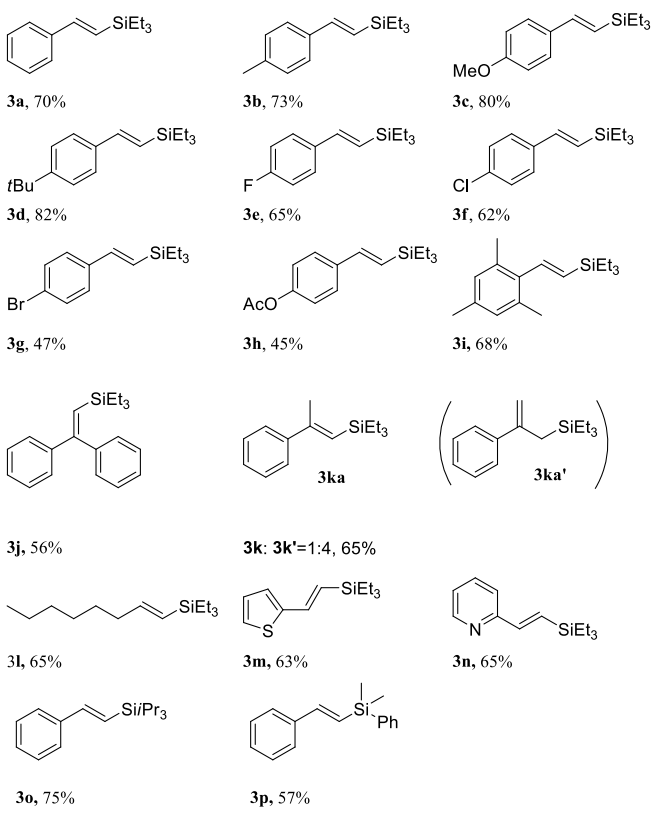
[a] Reaction conditions: catalyst (0.1 mmol), styrene (0.5 mmol), $HSiEt_3$(2.5 mmol), oxidant (1.0 mmol), solvent 3 mL, at 110 °C for 24 h under Ar. [b] Isolated yield. [c]Temperature was 90 °C. [d] 10 mol% $Cu(OAc)_2$ was used.

The reaction of styrene (**1a**) and triethyl silane (**2a**) was chosen as a model reaction to screen the reaction conditions. Firstly, various Cu precursors were screened for the reaction at 110 °C in the presence of tert-butyl hydroperoxide (TBHP) with the finding that $Cu(OAc)_2$ was the optimal choice for the reaction (Table 1, entries 1−7). Note that no product **3a** could be observed in the absence of any catalyst (Table 1, entry 18). Analysis of the ^1H NMR of the final product indicated that the configuration of the double bond was trans, showing the reaction is highly stereoselective. As the next optimization step, we performed an oxidant screening (Table1, entries 8-10). To our delight, switching the oxidant to tert-butyl peroxide (TBP), the yield of **3a** was increased to 70% (Table 1, entry 9). The efficiency of this transformation was dramatically affected by the choice of solvent. When other solvents, such as toluene, DMF, DMSO, DCE, were used instead of *t*BuOH, no desired product was detected (Table 1, entries 11-14). Effects of temperature and the amount of catalyst on the reaction were also investigated, and the optimal yield could be obtained when the reaction was performed in the presence of 20 mol% catalyst at 110 °C (Table 1, entry 9). Finally, control experiment showed that TBP was essential prerequisite for this reaction (Table 1, entry 17).

Table 2. Substrate Scope for Silylation of Alkenes[a]



1 2 3

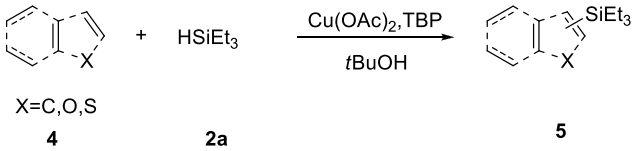


[a] Reaction conditions: $Cu(OAc)_2$ (0.1 mmol), alkenes (0.5 mmol), silanes (2.5 mmol), TBP (1.0 mmol), *t*BuOH 3 mL, at 110 °C for 24 h under Ar. Isolated yield.

With the above optimized conditions in hand, the scope of substituted styrenes and silanes was tested and the results were listed in Table 2. Styrene derivatives in reaction with **2a** were examined first. In general, the electron-donating substituted styrenes showed superior reaction efficiency to that of the electron-withdrawing ones. Styrene bearing electron donating groups and weak electron withdrawing groups reacted smoothly under the optimized conditions to form the corresponding vinylsilanes in satisfactory yields (**3a-**

3h). In addition to alkyl and alkoxy groups, halo- substituted alkenyls were compatible with the standard conditions (**3e-3g**). The halo- substituted vinylsilanes were beneficial for further functionalization. Sterically hindered 2,4,6-trimethylstyrene, α-phenylstyrene, and α-methylstyrene were also suitable for this transformation (**3i-3k**). However, a 1 : 4 olefin isomerization mixture was obtained when α- methylstyrene was used. Moreover, the protocol was effective on aliphatic olefins, when 1- octylene was used in the catalytic system, we also can get the corresponding product (**3l**). The arene ring is not limited to benzene rings. Heteroaromatic alkenyls could also be used as suitable substrates, thus providing the corresponding desired products in 63–65% yield (**3m, 3n**). Only trace bis-silylation product was detected by GC-MS when 2-vinylthiophene was employed. This silylation of styrene with silanes could also be extended to the corresponding vinylsilanes when we used other silanes as the substrates. The desired alkenyl silanes were isolated in moderate to good yields when using both aliphatic silanes and arylsilanes (**3o–3p**).

Table 3. Substrate Scope for Silylation of Heteroaromatics and Cycloolefin [a]

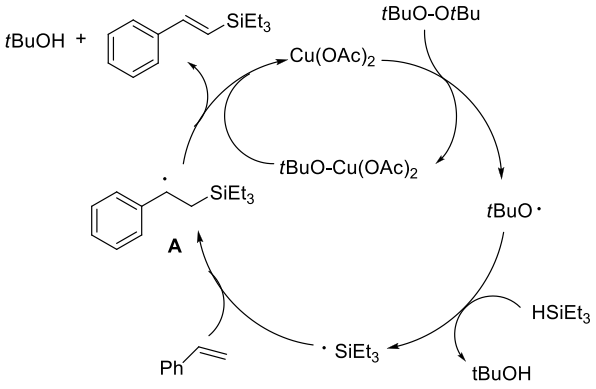


4 **2a** **5**

Entry	Substrate (4)	Product (5)	Yield (%)[b]
1	**4a**	**5a**	35
2	**4b**	**5b**	63
3	**4c**	**5c**	55
4	**4d**	**5d**	51
5	**4e**	**5e**	60
6	**4f**	**5f**	65
7	**4g**	**5g**	73

[a] Reaction conditions: $Cu(OAc)_2$ (0.1 mmol), heteroaromatics or cycloolefin (0.5 mmol), silanes (2.5 mmol), TBP (1.0 mmol), *t*BuOH 3 mL, at 110 °C for 24 h under Ar. [b]Isolated yield.

Heteroaromatic compounds containing carbon–silicon bonds which have very useful physicochemical properties are of great interest in organic electronics and photonics, drug discovery, nuclear medicine and complex molecule synthesis[13]. Therefore, in order to show the generality of the transformation, this protocol is also applied for a range of cyclic olefin and heterocyclic aromatics. A variety of cyclic olefin and heteroaromatics including cyclooctane, indenes, furans, thiophenes and coumarins underwent silylation in satisfactory yields. (**5a-5g**). It is noteworthy that our Cu catalyzed oxidative coupling process furnishing synthetically useful C2-silylated heteroaromatics in satisfactory yields and with up to 10:1 regioselectivity. The wide scope of both the alkenyls and heteroaromatics illustrates the good functional group tolerance and potential applications of this method.



Scheme 2. Proposed reaction mechanism.

To gain some insight into the mechanism for the Cu-catalyzed cross-coupling of alkenyls with silanes, control experiments under the standard reaction conditions were carried out. No target product was observed by the addition of TEMPO or BHT as a radical inhibitor, indicating that a radial pathway might be involved in the process. Although the mechanistic details of this transformation are not clear at the moment, on the basis of the above results and previous reports,[9] a plausible mechanism for the present process is proposed and shown in Scheme 2. First, tBuO· and Cu(III) species are generated from $Cu(OAc)_2$ and TBP through a single electron transfer process. Subsequently, tBuO· abstracts a hydrogen atom from silane to generate the silyl radical which adds to alkene gives the benzylic radical A. Finally, direct oxidation of radical A by deprotonation affords the final product, and the $Cu(OAc)_2$ was regenerated to reinitiate the reaction cycle.

In summary, a novel and stereospecific protocol for the synthesis of vinylsilanes is developed. This process exhibits a broad substrate scope and excellent functional-group tolerance, and offers a low-cost and environmentally benign alternative to currently employed precious metal systems for alkene silylation. Further studies on detailed mechanistic aspects and application to other substrates are on the way in our lab.

We gratefully acknowledge Nature Science Foundation of Jiangsu Province (BK 20131346, BK 20140776) for financial support. This work was also supported by National Natural Science Foundation of China (21476116, 21402093) and Chinese Postdoctoral Science Foundation (2015M571761, 2016T90465) for financial support.

Notes and references

* Chemical Engineering College, Nanjing University of Science & Technology, Nanjing, Jiangsu 210094, P. R. China
E-mail: c.cai@mail.njust.edu.cn.

Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/c000000x/

[1] For selected reviews and references on the transition-metal-catalyzed carbon−silicon bond formation, see: a) Marciniec. B, *Chem. Rev.* 2005, **249**, 2374 – 2390; b) Cheng. C, Hartwig. J. F, *Chem. Rev.* 2015, **115**, 8946 – 8975; c) Tondreau. A. M, Atienza. C. H, Weller. K. J, Nye. S. A, Lewis. K. M, J. Delis. G. P, Chirik. P. J, *Science*. 2012, **335**, 567 – 570; d) Peng. D, Zhang. Y, Du. X, Lei. X, Leng. X, Walter. M. D, Huang. Z, *J. Am. Chem. Soc.* 2013, **135**, 19154 – 19166; e) Muchnij. J. A, Kwaramba. F. B, Rahaim. R. J, *Org. Lett.* 2014, **16**, 1330 – 1333; f) Mo. Z, Xiao. J, Gao. Y, Deng. L, *J. Am. Chem. Soc.* 2014, **136**, 17414 – 17417; g) Dierick. S, Cercruysse. E, Berthon-Gelloz. G, Marký. I. E, *Chem. Eur. J.* 2015, **21**, 17073 – 17078; h) Chen. C, Hecht. M. B, Kavara. A, Brennessel. W. W, Mercado. B. Q, Weix. D. J, Holland. P. L, *J. Am. Chem. Soc.* 2015, **137**, 13244 – 13247; i) Buslov. I, Becouse. J, Mazza. S, Montandon-Clerc. M, Hu. X, *Angew. Chem. Int. Ed.* 2015, **54**, 14523-14526; j) Terao. J, Torii. K, Saito. K, Kambe. N, Baba. A, Sonoda. A, *Angew. Chem. Int. Ed.* 1998, **37**, 2653 – 2656; k) McAtee. J. R, Martin. S. E, Ahneman. D. T, Johnson. K. A, Watson. D. A, *Angew. Chem. Int. Ed.* 2012, **51**, 3663 – 3667; l) Martin. S. E. S, Watson. D. A, *J. Am. Chem. Soc.* 2013, **135**, 13330 – 13333; m) McAtee. J. R, Yap. G. P. A, Watson. D. A, *J. Am. Chem. Soc.* 2014, **136**, 10166 –10172.

[2] For selected reviews and references on the application of organosilanes compounds in synthetic transformations, see:a) Michl. J, *Chem. Rev.* 1995, **95**, 1135 – 1673; b) Jones. G. R, Landais. Y, *Tetrahedron* 1996, **52**, 7599 – 7662; c) Fleming. I, Barbero. A, Walter. D, *Chem. Rev.* 1997, **97**, 2063 – 2192; d) Curtis-Long. M. J, Aye. Y, *Chem. Eur. J.* 2009, **15**, 5402 – 5416; e) Bracegirdle. S, Anderson. E. A, *Chem. Soc. Rev*. 2010, **39**, 4114 – 4129; f) Xu. L. W, Li. L, Lai. G. Q, Jiang. J. X, *Chem. Soc. Rev.* 2011, **40**, 1777 – 1790; g) Nakao. Y, Hiyama. T, *Chem. Soc. Rev.* 2011, **40**, 4893 – 4901.

[3] a) Fleming. I, Barbero. A, Walter. D, *Chem. Rev*. 1997, **97**, 2063 – 2192; b) Nakao. Y, Hiyama. T, *Chem. Soc. Rev.* 2011, **40**, 4893 – 4901; c) Denmark. S. E, Liu. J. H, *Angew. Chem.* 2010, **122**, 3040 – 3049; d) Hosomi. A, Endo. M, Sakurai. H, *Chem. Lett.* 1976, 941 – 942; e) Masse. C. E, Panek. J. S, *Chem. Rev*. 1995, **95**, 1293 – 1316; f) Denmark. S. E, Fu. J, *Chem. Rev.* 2003, **103**, 2763 – 2793; (g) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* 1997, **97**, 2063−2192.

[4] a) Trost. B. M, Ball. Z. T, *J. Am. Chem. Soc.* 2005, **127**, 17644 – 17655; b) Ohmiya. H, Yorimitsu. H, Oshima. K, *Org. Lett*. 2006, **8**, 3093 – 3096; c) Hayashi. S, Hirano. K, Yorimitsu. H, Oshima. K, *J. Am. Chem. Soc.* 2007, **129**, 12650 – 12651; d) Berthon-Gelloz. G, Schumers. J.-M, De Bo. G, Mark. I. E, *J. Org. Chem.* 2008, **73**, 4190 – 4197; e) Nakamura. S, Yonehara. M, Uchiyama. M, *Chem. Eur. J.* 2008, **14**, 1068 – 1078; f) Murakami. K, Yorimitsu. H, Oshima. K, *J. Org. Chem.* 2009, **74**, 1415 – 1417; g) Rooke. D. A, Ferreira. E. M, *J. Am. Chem. Soc.* 2010, **132**, 11926 – 11928; h) Lim. D. S. W, Anderson. E. A, *Org. Lett.* 2011, **13**, 4806 – 4809.

[5] Nakamura. S, Yonehara. M, Uchiyama. M, *Chem. Eur. J.* 2008, **14**, 1068 – 1078

[6] a) Nishiyama, H.; Furuta, A. *Chem. Commun.* 2007, **43**, 760-762; b) Tsutsumi, H.; Sunada, Y.; Nagashima, H. *Chem. Commun.*2011, **47**, 6581-6583.

[7] a) Denmark, S. E.; Wang, Z. *Org. Lett.* 2001, **3**, 1073−1076; b) Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* 2005, **127**, 17644−17655; c) Roy, A. K. *Adv. Organomet. Chem.* 2008, **55**, 1-59; d) Buisine, O.; Berthon-Gelloz, G.; Briere, J.- F.; Sterin, S.; Mignani, G.; Branlard, P.; Tinant, B.; Declercq, J.-P.; Marko, I. E. *Chem. Commun.* 2005, **41**, 3856-3858; e) Belger, C.; Plietker, B. *Chem. Commun.* 2012, **48**, 5419-5421; f) Konno, T.; Taku, K.; Yamada, S.; Moriyasu, K.;Ishihara, T. *Org. Biomol. Chem.* 2009, **7**, 1167-1170; g) W. Wu, C.-J. Li, *Chem. Commun.* 2003, **39**, 1668 –1669;

[8] a) Yamashita. H, Hayashi. T, Kobayashi. T, Tanaka. M, Goto. M, *J. Am. Chem. Soc.* 1988, **110**, 4417 – 4418; b) Yamashita. H, Tanaka. M, Goto. M, *Organometallics.* 1997, **16**, 4696 – 4704; c) Stçhr. F, Sturmayr. D, Kickelbick. G, Schubert. U, *Eur. J. Inorg. Chem.* 2002, 2305 – 2311; d) Gatard. S, Chen. C.H, Foxman. B, Ozerov. O, *Organometallics* 2008, **27**, 6257 – 6263.

[9] Zhang. L, Hang. Z, Liu. Z.Q. *Angew. Chem. Int. Ed.* 2016, **55**, 236 –239.

[10] a) Chatgilialoglu. C, *Acc. Chem. Res.* 1992, **25**, 188 – 194; b) Chatgilialoglu. C, *Chem. Rev.* 1995, **95**, 1229 – 1251; c) Chatgilialoglu. C, Timokhin. V. I, *Adv. Organomet. Chem.* 2008, **57**, 117 – 181; d) Baguley. P. A, Walton. J. C, *Angew. Chem. Int. Ed.* 1998, **37**, 3072; e) Chatgilialoglu. C, *Chem. Eur. J.* 2008, **14**, 2310 – 2320; f) Fedorov. A, Toutov. A. A, Swisher. N. A, Grubbs. R. H, *Chem. Sci.* 2013, **4**, 1640 – 1645; g) Wang. L, Zhu. H, Guo. S, Cheng. J, Yu. J. T, *Chem. Commun*. 2014, **50**, 10864 – 10867.

[11] a) Troegel, D.; Stohrer, J. Coord. *Chem. Rev.* 2011, **255**, 1440-1459; b) Speier, J. L.; Webster, J. A.; Barnes, G. H. *J. Am. Chem. Soc.* 1957, **79**, 974-979; c) Speier. J. L, *Adv. Organomet. Chem.* 1979, **17**,407-447; d) Nakajima. Y, Shimada. S, *RSC Adv.* 2015, **5**, 20603-20616. e) Lipschutz. M. I, Tilley. T. D, *Chem. Commun*. 2012, **48**, 7146-7148; f) Jia. X, Zhang. L, Qin. C, Leng. X, Huang. Z, *Chem. Commun.* 2014, **50**, 11056-11059. g) Sakaki. S.; Sumimoto. M.; Fukuhara. M,; Sugimoto. M.; Matsuzaki. H, *Organometallics*. 2002, **21**, 3788-3820. h) Marciniec. B, *Chem. Rev.* 2005, **249**, 2374 – 2390

[12] Zhu. Y, Wei. Y, *Chem. Sci.* 2014, **5**, 2379-2382.

[13] a) Zhang. F, Wu. D, Xu. Y, Feng. X, *J. Mater. Chem.* 2011, **21**, 17590–17600; b) Ball. L. T, Lloyd-Jones. G. C, Russell. C. A, *Science*. 2012, **337**, 1644–1648; c) Franz. A. K, Wilson. S. O, *J. Med. Chem.* 2013, **56**, 388–405.