ChemPubSoc Europe
DOI: 10.1002/chem.201501648
CHEMISTRY A European Journal
Communication

Cyclization

Synthesis and Isolation of Organogold Complexes through a Controlled 1,2-Silyl Migration

Philippe McGee, Gabriel Bellavance, Ilia Korobkov, Anika Tarasewicz, and Louis Barriault*[a]

Abstract: During our efforts toward the synthesis of naturally occurring polyprenylated polycyclic acylphloroglucinol using a Au^{I}-catalyzed 6-*endo* dig carbocyclization, we isolated stable vinyllic gold intermediates. Optimization lead to isolated yields of up to 98%, using 2-(di-*tert*-butylphosphino)biphenyl as the ligand. This transformation is derived from a silyl rearrangement that can be fully controlled according to the nature of the substituent on the ynone. This selective transformation does not require basic conditions to prevent protodeauration. These vinylgold complexes are the first isolated intermediates during a silyl migration with gold(I). More than 16 new organogold complexes were synthesized and characterized by single-crystal X-ray diffraction. Reactivity of these complexes is also presented.

The distinctive reactivity and chemoselectivity of gold complexes have provided a fertile playground for the discovery of unique and innovative transformations in organic chemistry.[1] Notably, phosphinogold(I) complexes have been widely used as catalysts in the formation of complex carbocyclic frameworks.[2] These complexes are soft Lewis acids that selectively coordinate to alkynes, alkenes, and allenes, thus favoring the addition of various nucleophiles.[3] In 2009, our group developed a mild and efficient method using cationic phosphinogold(I) species to generate bicyclo[*m*.*n*.1]alkenones **2** from enol ethers **1** (Scheme 1).[4] This method was successfully applied in the concise total syntheses of biologically active polyprenylated polycyclic acylphloroglucinols (PPAPs) such as hyperforin (**3**), nemorosone (**4**), and papuaforins A (**5**).[5] During these syntheses, we investigated the gold(I)-catalyzed 6-*endo* dig carbocyclization of **6** containing a substituted TBS-alkyne to produce the bridgehead ketone **7**. Based on previous results, we anticipated that alkyne substitution would not affect the cyclization process. However, along with the starting material (>90%), we were able to isolate a very small quantity of an unexpectedly stable vinyllic gold intermediate **8 L^1**, resulting from a 1,2-silyl migration.

Independent research from Fürstner[6] and Gervorgvan[7] reported gold(I/III)-catalyzed cascade cycloisomerizations involving 1,2-migration of halides and silicon groups. It was proposed that the migration proceeds through the formation of gold vinylidene intermediates. Although the alkyne-vinylidene reaction is a common process for W, Ru, Rh, Mo, Ir, Co, Re, and Mn complexes,[8] there are few examples with gold complexes.[9] However, in some specific cases, the migration can proceed via the generation of gold carbenoid species.[10] To the best of our knowledge, the isolation of intermediates during processes involving a silyl rearrangement has yet to be reported.

Intrigued by this result, we further investigated this transformation. As a first step, we performed the reaction using a stoichiometric amount of gold complex [L^{1}AuNCMe][SbF$_6$] in dichloromethane (Scheme 2). After 30 min, enol ether **9** was converted to afford the vinyl gold intermediate **10 L^1** in 32% yield along with a significant amount of hydrolyzed enol ether product **11** (>50%). To prevent the hydrolysis of **9**, the reaction was carried out in the presence of various bases such as K_2CO_3, Et_3N, or proton sponge. In all of the cases, only starting material was recovered. An increase of the loading of **9** from 1 equiv to 3.3 equiv gave **10 L^1** in 84% yield.[11] Interestingly, this transformation does not require basic conditions to prevent protodeauration.[12]

The vinyl gold stability could be attributed to the electron-deficient moiety of the complex, which has also been proposed by Hammond et al.[13] To further understand and optimize the formation of the vinyllic gold species, other ligands were examined. Organogold compounds **10 L^2** and **10 L^3** were isolated in 63% and 70% yields respectively. Migration of the *tert*-butyldimethylsilyl group was observed in each case, unaffected by the type of ligands. The structure was confirmed by single-crystal X-ray diffraction.

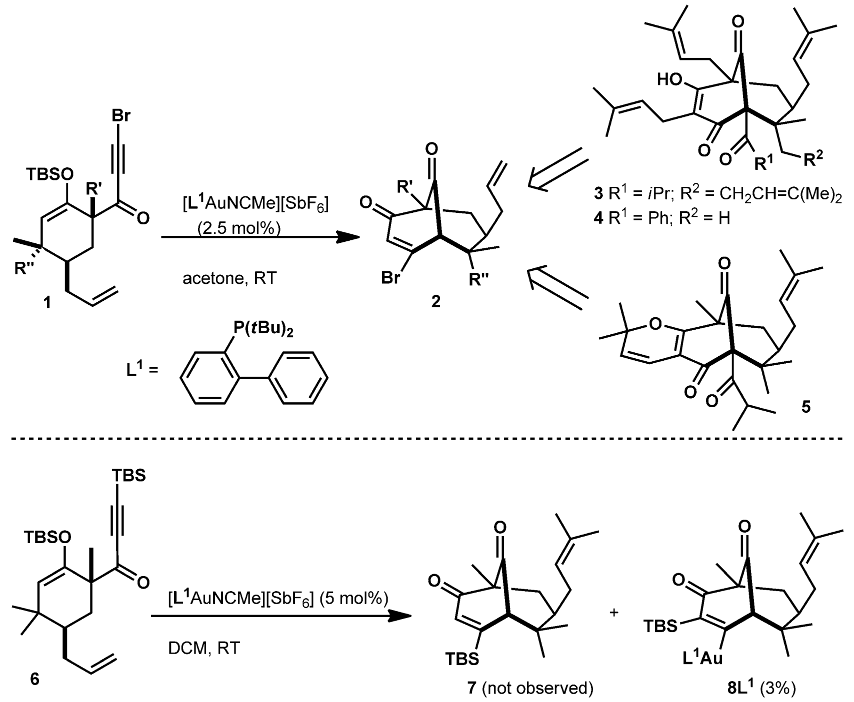
The optimized conditions were then applied to a wider variety of R_3Si-alkynes (Scheme 3). At first glance, we found that the nature of the silyl group controlled the selectivity of the 1,2-shift (Table 1, sections A and B). Noteworthy, a selective 1,2-migration/cyclization proceeded in good yields in a sterically demanding environment. For example, chromatographically stable vinylgold complexes **13 a**, **13 b**, **13 d**, and **13 e** were isolated as the exclusive regioisomers. The replacement of the TBS by a TMS or a TES group on the alkyne had no incidence on the reaction yield; organogold complexes **13 c** and **13 f**

---

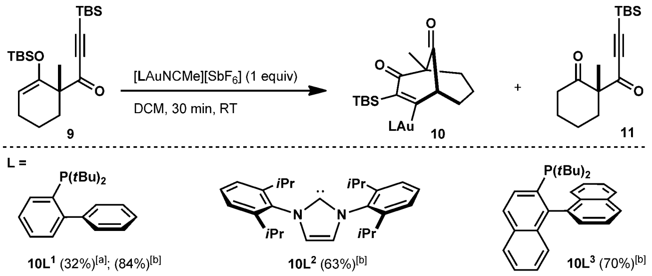
[a] *P. McGee, G. Bellavance, Dr. I. Korobkov,*$^+$ *A. Tarasewicz, Prof. L. Barriault*
Department of Chemistry
Centre for Catalysis, Research and Innovation
University of Ottawa
10 Marie Curie, Ottawa, ON, K1N 6N5 (Canada)
E-mail: lbarriau@uottawa.ca

[+] *Inquiries regarding X-ray diffraction methods should be addressed to this author (korobkov_ilia@yahoo.com).*

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201501648.



Scheme 1. The first organogold complexes isolated during the synthesis of PPAPs natural products.

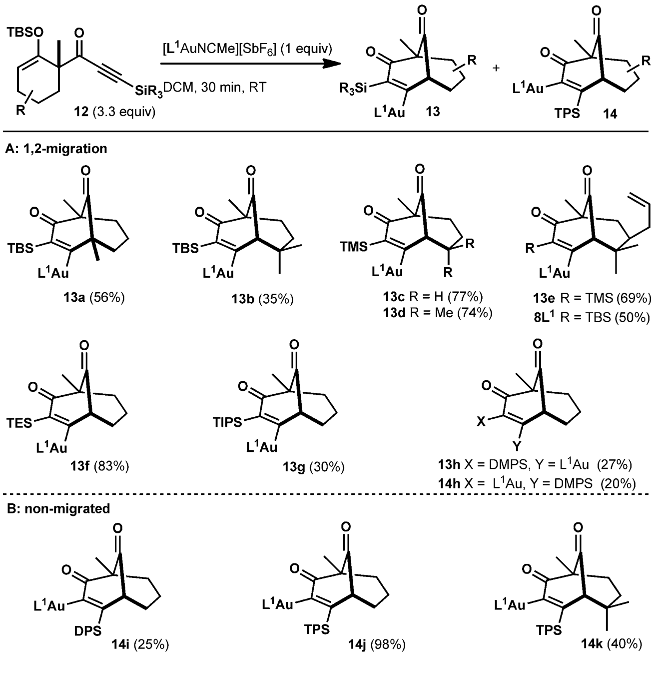


Scheme 2. Ligand optimization in the isolation of vinyl gold species. [a] 1 equiv of **9**. [b] 3.3 equiv of **9**.

were obtained in 77 and 83 % yields, respectively. However, an increase of the R_3Si bulkiness led to a significant decrease in yield, because **13 g** was isolated in 30 % yield. Surprisingly, the treatment of **12 h** afforded a separable mixture of **13 h** (27 %) and **14 h** (20 %). When the silicon group was adorned with two phenyls (DPS), only the non-migrated product **14 i** was isolated in 25 % yield. Moving from DPS to TPS, only the retention products **14 j** and **14 k** were produced, in 98 and 40 % yields, respectively. These results clearly demonstrated that the nature of the silicon group on the alkyne dictates the 1,2-silyl migration. All the structural features of the organogold complexes mentioned above were confirmed by single-crystal X-ray diffraction and NMR analysis.

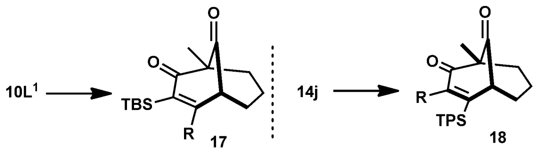
To gain more insight on the cascade 1,2-migration/cyclization, we performed crossover experiments using **9** and **12 d**. Only cyclized products **10 L**^{1} and **13 d** were observed in crude reaction mixture (Scheme 4). In addition, the resubmission of **13 h** did not lead to a mixture of **13 h**/**14 h**, which confirms that both compounds were generated through two specific pathways (path A and path B). In light of these results, one can conclude that the 1,2-silyl migration: 1) occurs mainly with aliphatic silyl groups at the terminal position, 2) proceeds by an intramolecular process, and 3) the cyclization proceeds most likely through the formation of a gold(I) vinylidene intermediate **16**, as depicted in Scheme 4.

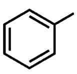
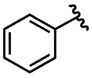
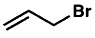
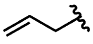
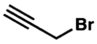
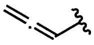
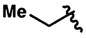
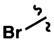
We took advantage of the synthesis of these vinyl gold complexes to further explore their chemical reactivity (Table 1). Recently, it was shown that new C–C bonds can be generated through Pd-catalyzed cross-coupling of vinylgold species with aryl and alkyl halides.[14,15] We identified $Pd(OAc)_2$ (5 mol %) and tricyclohexylphosphine (15 mol %) in $PhCF_3$ at 100 °C to be the optimal conditions for cross-coupling reactions. Under these conditions, the vinylgold **10 L**^{1} was converted to **17 a** in 83 % yield (entry 1). To our surprise, **14 j** proved to be inert under these conditions, and only starting material was recovered. One might suggest that the transmetalation process is thwarted by steric conges-



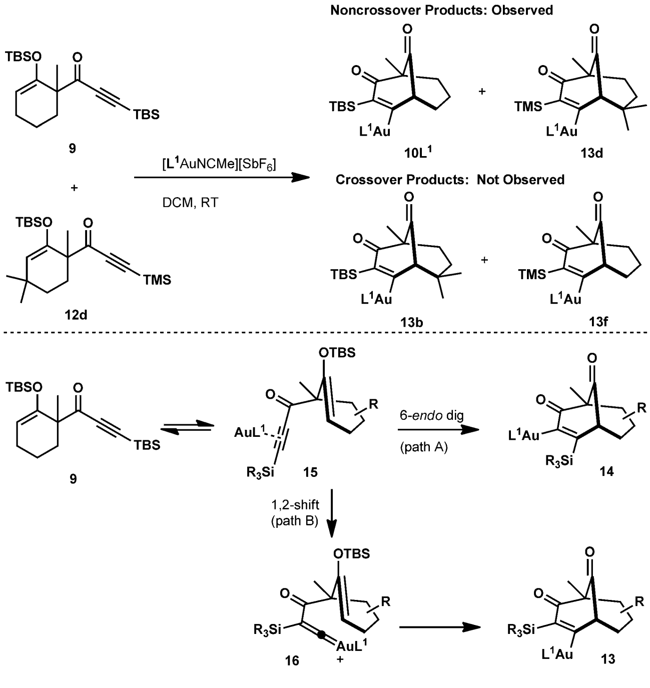
Scheme 3. Scope of the cyclization. TBS = *tert*-butyldimethylsilane, TMS = trimethylsilane, TES = triethylsilane, TIPS = triisopropylsilane, DPS = *tert*-butyldiphenylsilane, DMPS = dimethylphenylsilane, TPS = triphenylsilane.

Table 1. Vinylgold complexes cross-coupling reactions.[a]



Entry	RX	Product	**17** ([%])[a]	**18** ([%])[a]
1			**17 a** (83)[b]	**18 a** (–)[b]
2			**17 b** (75)[c]	**17 b** (65)[c]
3			**17 c** (63)[c]	**18 c** (32)[c]
4	MeI		**17 d** (98)[c]	**18 d** (98)[c]
5	EtI		**17 e** (92)[c]	**18 e** (92)[c]
6	NFSI		**17 f** (33)[d]	**18 f** (–)[d]
7	NBS		**17 g** (98)[d]	**18 g** (98)[d]
8	NIS		**17 h** (98)[d]	**18 h** (98)[d]

[a] Isolated yield. [b] $Pd(OAc)_2$ (5 mol %), PCy_3 (15 mol %). [c] RX, $PhCF_3$, 100 °C, 24 h. [d] Acetone, 35 °C. NIS = *N*-iodosuccinimide, NBS = *N*-bromosuccinimide, NFSI = *N*-fluorodibenzenesulfonimide.



Scheme 4. Crossover experiments and proposed mechanism for the silyl migration and cyclization process.

tion at the C-AuL^1 bond. Initial results showed that vinylgold complex **10 L^1** can also participate in Pd-catalyzed allylic cross-coupling reactions. However, thorough control experiments demonstrated that the allylation reaction proceeded in the absence of Pd catalyst; heating of **10 L^1** and **14 j** in $PhCF_3$ in the presence of allylbromide gave bridgehead ketones **17 b** and **18 b** in 75 % and 65 % yields respectively (entry 2). These results are in contrast with previous findings.[14a–c] Other electrophiles such as propargyl bromide, methyl iodide, and ethyl iodide provided the corresponding ketones **17 c–e** and **18 c–e** in 32–98 % yields (entries 3–5). Treatment of **10 L^1** and **14 j** with electrophilic fluorinating agents proved to be more challenging. Vinylfluoro **17 f** was obtained in 33 % yield, whereas the conversion of **14 j** gave a complex mixture (entry 6).[15] As expected, halogenation using NBS and NIS provided the desired halogenated bridgehead ketones **17 g**, **17 h**, **18 g**, and **18 h** in quantitative yields (entries 7 and 8).

In summary, we reported the isolation of 16 new bicyclo[3.3.1]nonane organogold complexes characterized by X-ray crystallography. Access to these air and chromatographically stable vinylgold complexes was possible through a silyl rearrangement, which was regioselective according to the substituent on the silyl group. Alkyl TBS and TPS groups offer the best yields for the rearranged and not-rearranged products, respectively. Assessment of the chemical properties of these organogold complexes showed that they participated in Pd-catalyzed aryl cross-coupling reactions. It also led to the formation of a C(sp^3)–C(sp^2) bond using electrophilic reagents without the use of Pd catalysts. Adaptation of this transformation into a synergistic dual-catalysis is underway, as is a more detailed mechanistic evaluation and a greater evaluation of the scope.[16]

Acknowledgements

We thank the Natural Sciences and Engineering Research Council (for Accelerator and Discovery grants to L.B.), Fonds de Recherche du Québec - Natures et Technologies (for post-graduate scholarship to P.M.) and the University of Ottawa (for a University Research Chair to L.B.) for support of this research.

Keywords: 1,2-shift · catalysis · cross-coupling · cyclization · gold

[1] For selected reviews, see: a) A. S. K. Hashmi, *Gold Bull.* **2004**, *37*, 51–65; b) A. S. K. Hashmi, G. J. Hutchings, *Angew. Chem. Int. Ed.* **2006**, *45*, 7896–7936; *Angew. Chem.* **2006**, *118*, 8064–8105; c) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211; d) Z. Li, C. Brouwer, C. He, *Chem. Rev.* **2008**, *108*, 3239–3265; e) A. Corma, A. Leyva-Pérez, M. J. Sabater, *Chem. Rev.* **2011**, *111*, 1657–1712; f) N. D. Shapiro, F. D. Toste, *Synlett* **2010**, *2010*, 675–691.

[2] a) R. Dorel, A. M. Echavarren *Chem. Rev.* **2015**, DOI: 10.1021/cr500691k; b) M. Rudolph, A. S. K. Hashmi, *Chem. Soc. Rev.* **2012**, *41*, 2448–2462; c) A. Arcadi, *Chem. Rev.* **2008**, *108*, 3266–3325; d) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*, 3351–3378.

[3] D. J. Gorin, F. D. Toste, *Nature* **2007**, *446*, 395–403.

[4] a) F. Barabé, G. Bétournay, G. Bellavance, L. Barriault, *Org. Lett.* **2009**, *11*, 4236–4238; b) B. Sow, G. Bellavance, F. Barabé, L. Barriault, *Beilstein J. Org. Chem.* **2011**, *7*, 1007–1013.

[5] G. Bellavance, L. Barriault, *Angew. Chem. Int. Ed.* **2014**, *53*, 6701–6704; *Angew. Chem.* **2014**, *126*, 6819–6822.

[6] V. Mamane, P. Hannen, A. Furstner, *Cent. Eur. J. Chem.* **2004**, *10*, 4556–4575.

[7] I. V. Seregin, V. Gevorgyan, *J. Am. Chem. Soc.* **2006**, *128*, 12050–12051.

[8] For selected reviews, see: a) M. I. Bruce, *Chem. Rev.* **1991**, *91*, 197–257; b) C. Bruneau, P. H. Dixneuf, *Angew. Chem. Int. Ed.* **2006**, *45*, 2176–2203; *Angew. Chem.* **2006**, *118*, 2232–2260.

[9] a) E. Soriano, J. Marco-Contelles, *Organometallics* **2006**, *25*, 4542–4553; b) V. Lavallo, G. D. Frey, S. Kousar, B. Donnadieu, G. Bertrand, *Proc. Natl. Acad. Sci. USA* **2007**, *104*, 13569–13573; c) I. D. Jurberg, Y. Odabachian, F. Gagosz, *J. Am. Chem. Soc.* **2010**, *132*, 3543–3552; d) P. Morán-Poladura, S. Suárez-Pantiga, M. Piedrafita, E. Rubio, J. M. González, *J. Organomet. Chem.* **2011**, *696*, 12–15; e) A. S. K. Hashmi, M. Wieteck, I. Braun, P. Nösel, L. Jongbloed, M. Rudolph, F. Rominger, *Adv. Synth. Catal.* **2012**, *354*, 555–562; f) A. S. K. Hashmi, M. Wieteck, I. Braun, M. Rudolph, F. Rominger, *Angew. Chem. Int. Ed.* **2012**, *51*, 10633–10637; *Angew. Chem.* **2012**, *124*, 10785–10789; g) L. Ye, Y. Wang, D. H. Aue, L. Zhang, *J. Am. Chem. Soc.* **2012**, *134*, 31–34; h) M. M. Hansmann, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2013**, *52*, 2593–2598; *Angew. Chem.* **2013**, *125*, 2653–2659; i) P. Morán-Poladura, E. Rubio, J. M. González, *Beilstein J. Org. Chem.* **2013**, *9*, 2120–2128; j) P. Morán-Poladura, E. Rubio, J. M. González, *Angew. Chem. Int. Ed.* **2015**, *54*, 3052–3055; *Angew. Chem.* **2015**, *127*, 3095–3098.

[10] a) Y. Xia, A. S. Dudnik, Y. Li, V. Gevorgyan, *Org. Lett.* **2010**, *12*, 5538–5541; b) A. S. Dudnik, Y. Xia, Y. Li, V. Gevorgyan, *J. Am. Chem. Soc.* **2010**, *132*, 7645–7655.

[11] It was found that a prolonged stirring leads to decomposition of the desired vinyl gold complex, see optimization table in the Supporting Information.

[12] a) D. Weber, M. A. Tarselli, M. R. Gagné, *Angew. Chem. Int. Ed.* **2009**, *48*, 5733–5736; *Angew. Chem.* **2009**, *121*, 5843–5846; b) A. S. K. Hashmi, A. M. Schuster, F. Rominger, *Angew. Chem. Int. Ed.* **2009**, *48*, 8247–8249; *Angew. Chem.* **2009**, *121*, 8396–8398; c) A. S. K. Hashmi, T. D. Ramamurthi, F. Rominger, *Adv. Synth. Catal.* **2010**, *352*, 971–975; d) X. Zeng, R. Kinjo, B. Donnadieu, G. Bertrand, *Angew. Chem. Int. Ed.* **2010**, *49*, 942–945; *Angew. Chem.* **2010**, *122*, 954–957; e) I. I. F. Boogaerts, S. P. Nolan, *J. Am. Chem. Soc.* **2010**, *132*, 8858–8859; f) Y. Chen, D. Wang, J. L. Petersen, N. G. Akhmedov, X. Shi, *Chem. Commun.* **2010**, *46*, 6147–6153; g) M. Melchionna, M. Nieger, J. Helaja, *Chem. Eur. J.* **2010**, *16*, 8262–8267; h) A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2010**, *49*, 5232–5241; *Angew. Chem.* **2010**, *122*, 5360–5369; i) A. S. K. Hashmi, A. M. Schuster, S. Gaillard, L. Cavallo, A. Poater, S. P. Nolan, *Organometallics* **2011**, *30*, 6328–6337; j) A. S. K. Hashmi, I. Braun, P. Nösel, J. Schädlich, M. Wieteck, M. Rudolph, F. Rominger, *Angew. Chem. Int. Ed.* **2012**, *51*, 4456–4460; *Angew. Chem.* **2012**, *124*, 4532–4536; k) T. P. Cornell, Y. Shi, S. A. Blum, *Organometallics* **2012**, *31*, 5990–5993; l) A. Johnson, A. Laguna, M. Concepción Gimeno, *J. Am. Chem. Soc.* **2014**, *136*, 12812–12815.

[13] a) L.-P. Liu, B. Xu, M. S. Mashuta, G. B. Hammond, *J. Am. Chem. Soc.* **2008**, *130*, 17642–17643; b) W. Wang, G. B. Hammond, B. Xu, *J. Am. Chem. Soc.* **2012**, *134*, 5697–5705; c) L.-P. Liu, G. B. Hammond, *Chem. Rev. Soc.* **2012**, *41*, 3129–3139.

[14] a) Y. Shi, K. E. Roth, S. D. Ramgren, S. A. Blum, *J. Am. Chem. Soc.* **2009**, *131*, 18022–18023; b) A. S. K. Hashmi, C. Lothschütz, R. Döpp, M. Rudolph, T. D. Ramamurthi, F. Rominger, *Angew. Chem. Int. Ed.* **2009**, *48*, 8243–8246; *Angew. Chem.* **2009**, *121*, 8392–8395; c) Y. Shi, S. D. Ramgren, S. A. Blum, *Organometallics* **2009**, *28*, 1275–1277; d) A. S. K. Hashmi, R. Döpp, C. Lothschütz, M. Rudolph, D. Riedel, F. Rominger, *Adv. Synth. Catal.* **2010**, *352*, 1307–1314; e) K. E. Roth, S. A. Blum, *Organometallics* **2011**, *30*, 4811–4813; f) J. J. Hirner, Y. Shi, S. A. Blum, *Acc. Chem. Res.* **2011**, *44*, 603–613; g) J. J. Hirner, K. E. Roth, Y. Shi, S. A. Blum, *Organometallics* **2012**, *31*, 6843–6850; h) M. Al-Amin, K. E. Roth, S. A. Blum, *ACS Catal.* **2014**, *4*, 622–629; i) M. Al-Amin, J. S. Johnson, S. A. Blum, *Organometallics* **2014**, *33*, 5448–5456.

[15] A. S. K. Hashmi, T. D. Ramamurthi, F. Rominger, *J. Organomet. Chem.* **2009**, *694*, 592–597.

[16] Experimental procedures and analytical data for all new compounds can be found in the Supporting Information. CCDC 1055125 (**8L^1**), 1055126 (**10L^1**), 1055127 (**10L^2**), 1055128 (**10L^3**), 1055129, (**13a**), 1055130 (**13b**), 1055131 (**13c**), 1055132 (**13d**), 1055133 (**13e**), 1055134 (**13f**), 1055135 (**13g**), 1055136 (**13h**), 1055137 (**14i**), 1055138 (**14j**), 1055139 (**14k**) and 1055140 (**18b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif..

Received: April 28, 2015