ACS Catalysis
Letter
pubs.acs.org/acscatalysis

Highly Efficient and Eco-Friendly Gold-Catalyzed Synthesis of Homoallylic Ketones

Adrián Gómez-Suárez,[†] Danila Gasperini,[†] Sai V. C. Vummaleti,[‡] Albert Poater,[§] Luigi Cavallo,[‡,∥] and Steven P. Nolan*,[†]

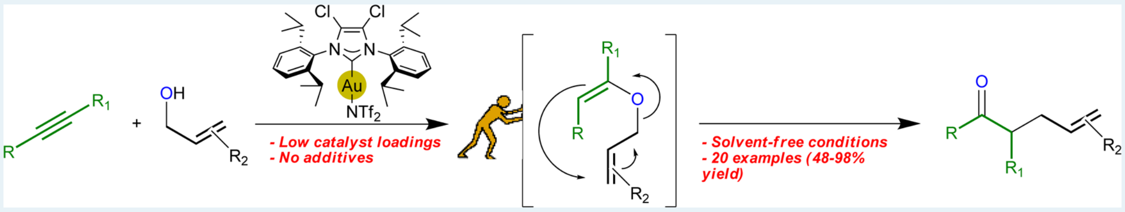
[†]EaStCHEM School of Chemistry, University of St. Andrews, North Haugh, St. Andrews, Fife KY16 9ST, U.K.

[‡]KAUST Catalysis Center, Physical Sciences and Engineering Division, King Abdullah University of Science and Technology, Thuwal 23955-6900, Saudi Arabia

[§]Institut de Química Computacional i Catàlisi, Departament de Química, University of Girona, Campus de Montilivi sn, 17071 Girona, Catalonia, Spain

[∥]Dipartimento di Chimica e Biologia, Universita' di Salerno, Via Papa Paolo Giovanni II, 84084 Fisciano, Italy

Supporting Information



ABSTRACT: We report a new catalytic protocol for the synthesis of γ,δ−unsaturated carbonyl units from simple starting materials, allylic alcohols and alkynes, via a hydroxalkoxylation/Claisen rearrangement sequence. This new process is more efficient (higher TON and TOF) and more eco-friendly (increased mass efficiency) than the previous state-of-the-art technique. In addition, this method tolerates both terminal and internal alkynes. Moreover, computational studies have been carried out in order to shed light on how the Claisen rearrangement is initiated.

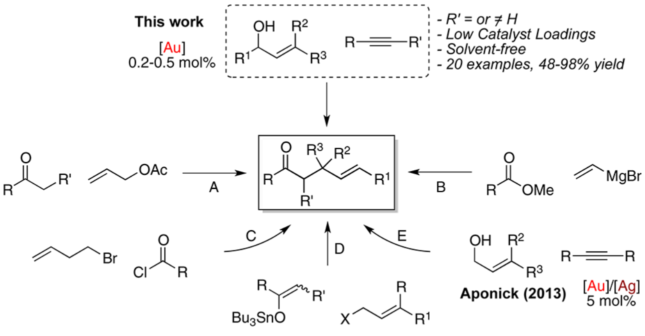
KEYWORDS: *gold, hydroalkoxylation, Claisen rearrangement, homoallylic ketones, solvent-free*

Since the establishment of the 12 principles of Green Chemistry,[1] almost 15 years ago, chemists have been interested in developing more efficient, robust, and environmentally friendly synthetic protocols.[2] One of the outcomes of this quest has been the development of several metrics to assess *how green* is any given chemical process (e.g., atom economy, reaction mass efficiency, E-factor, etc).[3] An additional target of Green Chemistry has been to reduce to a minimum the use of auxiliary substances.[1] In this context, the development of solvent-free reactions has greatly contributed to reduce the environmental impact of chemical processes.[4] In addition, because the use of catalytic reagents is highly desirable in a Green Chemistry context, terms such as turnover number (TON) and turnover frequency (TOF) have shown most informative in describing the efficiency of catalytic reactions.

Gold has become a powerful tool in organic chemistry, allowing access to important structural motifs.[5] Its use has grown exponentially during the last 10 years, and new reports are published highlighting its catalytic performance at an almost daily rate. However, a search of the literature reveals that the majority of gold-catalyzed transformations require relatively high catalyst loadings (1−10 mol %),[5] affording TON in the range of 10−100. Protocols describing the use of lower catalyst loadings are scarce.[6] Therefore, the design of more efficient catalytic processes involving gold is highly desirable.

γ,δ−Unsaturated carbonyl units are important structural motifs in natural products and also serve as highly versatile building blocks in organic synthesis.[7] Several strategies have been developed for the synthesis of this type of organic molecules (Scheme 1).[8] Aponick and co-workers have recently reported an elegant approach for the synthesis of this

Scheme 1. Strategies toward Homoallylic Ketones



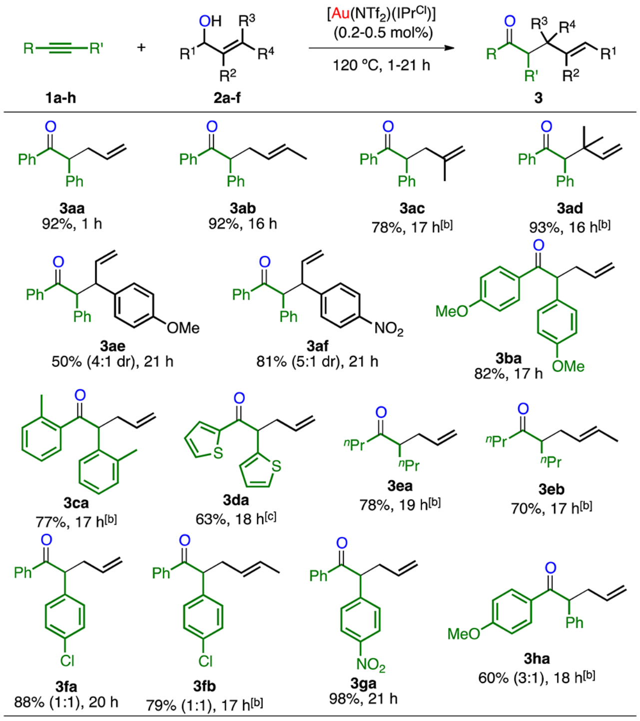
Received: June 11, 2014
Revised: July 10, 2014
Published: July 15, 2014

interesting family of compounds using gold catalysis.[8e] They proposed that homoallylic ketones could be synthesized through a tandem hydroxalkoxylation/Claisen rearrangement process, starting from internal alkynes and allylic alcohols (Scheme 1E).[8e] Although this methodology offers an easy and straightforward approach, it presents several disadvantages, such as the following: (a) the use of high catalyst loadings (5 mol %), thus affording low TON (10−20) and TOF (0.5 to 1 h^{-1}); (b) the need for an expensive silver salt ($AgBF_4$) activator; and (c) a 3:1 alkyne/alcohol ratio, thus affording a reaction mass efficiency of 37.8%.[8e]

We are interested in the development of more efficient, economical, and environmentally friendly processes involving NHC-Au^I catalysts for the synthesis of valuable organic molecules.[9] Therefore, we hypothesized that it should be possible to improve the elegant approach described by Aponick in order to establish a greener and more robust protocol for the synthesis of homoallylic ketones from allylic alcohols and alkynes. In order to achieve this, we reasoned that the following points needed to be addressed: (a) avoid the use of additives to activate the gold catalyst, (b) reduce the environmental impact of the reaction, (c) achieve high TON and TOF, and (d) increase the mass efficiency. We began our investigations focusing on the first two points. In order to avoid the use of silver salts,[10] which are light- and moisture-sensitive as well as costly, we opted to use [Au(NHC)(MeCN)][X][11] (where X = BF_4, SbF_6, or FABA) and $[Au(NHC)NTf_2]$[12] complexes during our optimization studies. Additionally in order to reduce the environmental impact of the reaction, we thought best to remove the need for a reaction solvent and use the allylic alcohol itself as the solvent. Initially, we reacted diphenylacetylene (**1a**) with allylic alcohol (**2a**), in a 1:16 ratio, using 1 mol % of $[Au(IPr)(MeCN)][BF_4]$. After 30 min at 120 °C, 98% conversion to the desired homoallylic ketone **3aa** was observed. It is worth noting that even if a large excess of **2a** was used, no side products due to ketalization of the vinyl ether intermediate were observed.[13] Next, we decided to reduce the alkyne/alcohol ratio to 1:3 and to reduce the catalyst loading to 0.3 mol %. After 30 min, 96% conversion to **3aa** was observed. Further optimization studies were conducted and can be found in the Supporting Information. We concluded that the most effective reaction conditions were 0.2 mol % of $[Au(IPr^{Cl})NTf_2]$, 1:3 alkyne/alcohol ratio, at 120 °C.

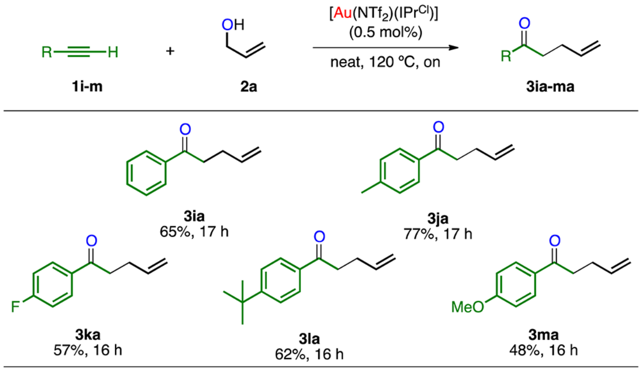
Having established the optimized reaction conditions, we next explored the scope and limitations of our methodology (Scheme 2). Once more challenging substrates were tested, it became obvious that longer reaction times were required. Therefore, for practical reasons, we carried out reactions between 16−21 h. In addition, when significant amounts of ketone side products were observed, due to hydration of the alkyne,[6a,b,f,h,14] reactions were carried out under an argon atmosphere in the presence of molecular sieves (4 Å). We began our studies by reacting several allylic alcohols (**2b**−**f**) with diphenylacetylene (**1a**). We were pleased to observe that the use of the secondary allylic alcohol **2b** afforded the corresponding homoallylic ketone **3ab** in excellent yields (92%). However, if the steric hindrance about the reactive centers is increased, the reaction does not proceed. The use of α-vinylbenzyl alcohol only afforded traces of the addition product (>5%) and no homoallylic ketone was observed after 24 h. Adding substituents to the α-position of the allylic alcohol did not affect the reaction and it proceeded smoothly, affording the desired product **3ac** in good yields (78%). Varying the substituent in the β−position of the allylic alcohol (**2d**−**f**), afforded compounds **3ad**−**f** in moderate to excellent yields (50−93%). In addition, the observed diasteroselectivities were in agreement with those reported by Aponick.[8e] Once the substituents on the alcohol were evaluated, we next examined the effect of modifying the alkyne. Changing **1a** for a more electron-rich alkyne, **1b**, still afforded good yields (82%). We were pleased to observe that even the use of a sterically hindered alkyne (**1c**) was well tolerated and **3ca** was obtained in good yields (77%). Heteroaromatic substituted alkynes, such as **1d**, were also well tolerated by our methodology and afforded the corresponding homoallylic ketone **3da** in good yields (63%). The reaction using dialkyl-substituted alkynes proceeded smoothly with both primary and secondary allylic alcohols, affording **3ea** and **3eb** in good yields (78 and 70%, respectively). In order to assess the regioselectivity of the reaction, three unsymmetrically substituted internal alkynes were also tested, **1f**−**h**. The use of 1-chloro-4-(phenylethynyl)benzene (**1f**) had no preferential effect on the regioselectivity and a 1:1 ratio between the two possible isomers was observed with both **2a** and **2b**. However, the reaction of 1-nitro-4-(phenylethynyl)benzene (**1g**) and allyl alcohol **2a** afforded only one product **3ga** in excellent yields, 98%. Finally, 1-methoxy-4-(phenylethynyl)benzene (**1h**) was also tested. The reaction of **1h** with **2a** afforded a 3:1 ratio between both possible regioisomers.

Scheme 2. Scope of the Reaction Using Internal Alkynes. [a] Reaction Conditions: 1 (1 equiv), 2 (3 equiv), [Au] (0.2 mol %), 120 °C. Isolated Yields, Average of Two Runs. [b] [Au] (0.5 mol %). [c] [Au] (0.6 mol %)



Encouraged by these results, we expanded the intermolecular hydroxalkoxylation/Claisen rearrangement strategy to the use of terminal alkynes (Scheme 3). This transformation proved to be more challenging than the reaction using internal alkynes. Therefore, the catalyst loading was increased to 0.5 mol %. Gratifyingly, the reaction of allyl alcohol **2a** with several phenylacetylene derivatives, **1i**−**m**, afforded the desired

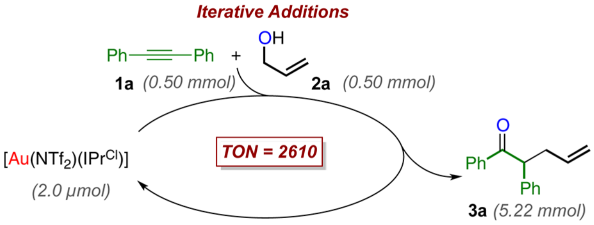
Scheme 3. Reaction between Allylic Alcohols and Terminal Alkynes. [a] **Reaction Conditions: 1 (1 equiv), 2 (3 equiv), [Au] (0.5 mol %), 120 °C. Isolated Yields, Average of Two Runs**



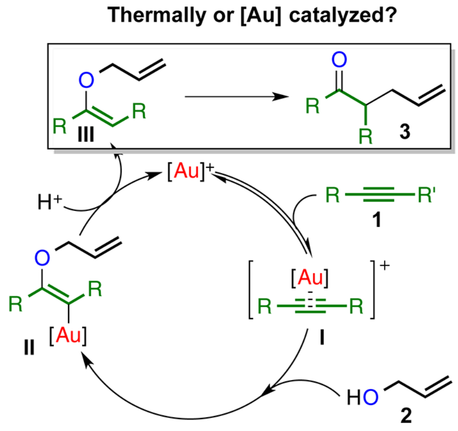
γ,δ−unsaturated ketones **3ia**−**3ma** in moderate to good yields (48−77%).

Both internal and terminal alkynes were tolerated by our methodology, and the corresponding homoallylic ketones were isolated in moderate to excellent yields. Once the scope of the reaction was examined, TON and TOF were evaluated. The new catalytic process afforded TON from 96 to 465 and TOF ranging from 6 to 1396 h^{-1}. To relate this to the previous state-of-the-art method, the Aponick procedure afforded TONs from 10 to 20 and TOFs from 0.5 to 1 h^{-1}.[8e] We were also interested in assessing the mass efficiency of our methodology.[3] By changing the molar ratio between the alkyne and the allyl alcohol to 1:3, instead of the 3:1 from the previous procedure, we were able to increase the mass efficiency from 37.8 to 61.7%.[15] In addition, we also assessed the recyclability of our catalyst. Once the reaction involving **1a** and **2a** in the presence of 0.2 mol % of [Au(IPr^{Cl})(NTf$_2$)] was complete, iterative additions of both substrates (0.5 mmol of each) were conducted. As a result, 5.22 mmol of **2a** were converted over 14 h by using 2 μmol of [Au(IPr^{Cl})(NTf$_2$)], affording a TON of 2610 and a TOF of 186 h^{-1} (Scheme 4).

Scheme 4. Iterative Additions of 1a and 2a to the Catalytic Reaction



Scheme 5. Proposed Reaction Mechanism



Once the scope and limitations of our methodology were established we began to probe the reaction mechanism. A typical hydroxalkoxylation mechanism was hypothesized for the initial step of the tandem process (Scheme 5). First, coordination of the gold catalyst to the alkyne (**1**) to form a π−gold−alkyne complex (**I**), thus activating it toward nucleophilic attack from the allyl alcohol (**3**) in *anti*-fashion. This would afford a vinyl gold intermediate (**II**). Finally, protodeauration of **II** would afford the vinyl ether species **III**. Then, rearrangement of the latter would afford the desired homoallylic ketone **3**. Aponick and co-workers have attempted to determine whether this last step was thermally or gold-catalyzed.[8e] After isolation of the corresponding vinyl ether intermediate, the Claisen rearrangement in the presence and absence of gold catalyst under the same reaction conditions (THF, 65 °C, 18 h) was tested.[8e] Unfortunately, both reactions afforded very similar conversions (40 and 30%, respectively).[8e] As the experimental results reported by Aponick were quite similar,[8e] we turned to computational analysis for support.

COMPUTATIONAL STUDIES

We considered the thermodynamics and energy barrier for the last step of the hydroalkoxylation/Claisen rearrangement process shown in Scheme 5, to understand whether the Claisen process is thermally or gold catalyzed. On the basis of previous mechanistic studies,[16] three different scenarios were envisioned: (a) thermal rearrangement from compound **III**; (b) gold mediated rearrangement from vinyl gold intermediate **II**; (c) gold-catalyzed rearrangement from compound **III** via a Au−O interaction (**IV**) or π-coordination of the Au to the vinylic olefin (**V**). In order to best mimic the experimental conditions, the substrates chosen for the in silico work were diphenylacetylene (**1a**) and allyl alcohol (**2a**). Geometries were optimized with the BP86 functional in connection with the SVP basis set for main group atoms and the SDD ECP, together with the associated triple-ζ valence basis set for Au. The reported reaction free energies (ΔG in kcal/mol) were built through single point energy calculations on the BP86/SVP geometries using the M06 functional and the triple-ζ TZVP basis set on main group atoms. Solvent effects were included with the PCM model using THF as the solvent. To these M06/TZVP electronic energies in solvent, zero point energy and thermal corrections were included from the gas-phase frequency calculations at the BP86/SVP level.

Figure 1 shows the thermodynamics and energy barrier for the Claisen step with and without gold for the above-mentioned scenarios, and Figure 2 presents the corresponding transition state (TS) structures. Focusing on energy, the calculated ΔG of the reaction shows that it is clearly exergonic in all the three cases. Moving to the energy barrier for the transformation, ΔG‡, it is lower in the presence of the gold catalyst, with a ΔG‡ of 21.2 and 24.5 kcal/mol from **IV** and **II**, whereas in the absence of gold, the ΔG‡, 26.0 kcal/mol, is clearly higher.

This strongly suggests that there is a significant preference for the isomerization step in the presence of gold, especially for **IV**. Attempts to locate a transition state for the rearrangement

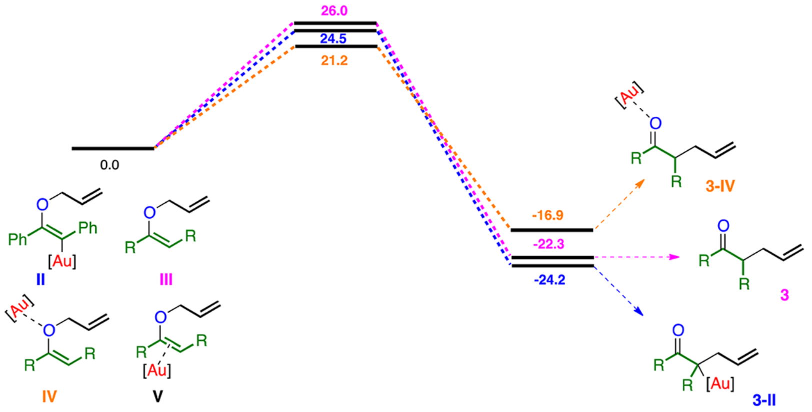


Figure 1. Thermodynamics of the hydroalkoxylation step from intermediates **II** (blue lines), **III** (pink lines), and **IV** (orange lines). Free energies, ΔG, are given in kcal/mol.

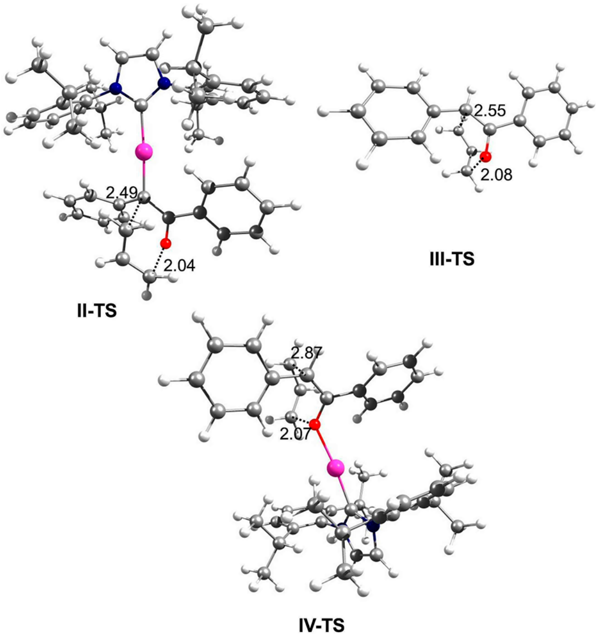


Figure 2. Transition state structures along with the important bond lengths in Å.

of π-complex **V** failed, suggesting that this route is not viable. The geometry of the transition states connecting **II**, **III**, and **IV** to the products are shown in Figure 2.

In summary, we have developed a new catalytic protocol for the synthesis of homoallylic ketones from alkynes and allylic alcohols via a hydroalkoxylation/Claisen rearrangement sequence. This new procedure provides several advantages over the existing state-of-the-art, such as (a) higher TONs and TOFs, (b) higher mass efficiency, and (c) the absence of additives to activate the gold catalyst. In addition, by removing the need for auxiliary solvents, a more eco-friendly synthetic protocol has been developed. Moreover, computational studies revealed that the Claisen rearrangement step is, most likely, aided by the presence of the gold catalyst. Ongoing studies are aimed at exploring further this intriguing transformation in conjunction with other tandem processes.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Optimization studies, characterization data for all the compounds, computational details, and Cartesian coordinates. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: snolan@st-andrews.ac.uk.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The ERC (Advanced Investigator Award-FUNCAT), EPSRC and Syngenta are gratefully acknowledged for support. Umicore AG is acknowledged for their generous gift of materials. The EPSRC National Mass Spectrometry Service Centre (NMSSC) is gratefully acknowledged for HRMS analyses. S.P.N. is a Royal Society Wolfson Research Merit Award holder. S.P.N. and L.C. thank King Abdullah University of Science and Technology (CCF project) for support. L.C. thanks the HPC team of Enea for using the ENEA-GRID and the HPC facilities CRESCO in Portici (Italy) for access to remarkable computational resources. A.P. thanks the Spanish MINECO for a Ramón y Cajal contract (RYC-2009-05226) and European Commission for a Career Integration Grant (CIG09-GA-2011-293900).

■ ABBREVIATIONS

NHC, *N*-heterocylic carbene; FABA, tetrakis(pentafluorophenyl)borate; IPr, 1,3-bis(2,6-di*iso*propylphenyl)imidazol-2-ylidene; IPr^{Cl}, 4,5-dichloro-1,3-bis(2,6-diisopropylphenyl)-1*H*-imidazol-2-ylidene

■ REFERENCES

(1) Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, U.K., 1998.

(2) (a) Irina, P. B.; Leonid, M. K. *Russ. Chem. Rev.* **2010**, *79*, 441. (b) Lipshutz, B.; Abela, A.; Bošković, Ž.; Nishikata, T.; Duplais, C.; Krasovskiy, A. *Top. Catal.* **2010**, *53*, 985−990. (c) Parmeggiani, C.; Cardona, F. *Green Chem.* **2012**, *14*, 547−564. (d) Jessop, P. G.; Mercer, S. M.; Heldebrant, D. J. *Energy Environ. Sci.* **2012**, *5*, 7240−7253. (e) Boisvert, L.; Goldberg, K. I. *Acc. Chem. Res.* **2012**, *45*, 899−910. (f) Ciriminna, R.; Pagliaro, M. *Org. Process Res. Dev.* **2013**, *17*, 1479−1484.

(3) Constable, D. J. C.; Curzons, A. D.; Cunningham, V. L. *Green Chem.* **2002**, *4*, 521–527.

(4) (a) Singh, M. S.; Chowdhury, S. *RSC Adv.* **2012**, *2*, 4547–4592. (b) Gawande, M. B.; Bonifacio, V. D.; Luque, R.; Branco, P. S.; Varma, R. S. *ChemSusChem* **2013**, *7*, 24–44.

(5) (a) Hashmi, A. S. K. *Gold Bull.* **2004**, *37*, 51–65. (b) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896–7936. (c) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180–3211. (d) Hashmi, A. S. K.; Rudolph, M. *Chem. Soc. Rev.* **2008**, *37*, 1766–1775. (e) Marion, N.; Nolan, S. P. *Chem. Soc. Rev.* **2008**, *37*, 1776–1782. (f) Liu, L.; Xu, B.; Hammond, G. B. *Beilstein J. Org. Chem.* **2011**, *7*, 606–614. (g) Krause, N.; Winter, C. *Chem. Rev.* **2011**, *111*, 1994–2009. (h) Corma, A.; Leyva-Perez, A.; Sabater, M. J. *Chem. Rev.* **2011**, *111*, 1657–1712. (i) Boorman, T. C.; Larrosa, I. *Chem. Soc. Rev.* **2011**, *40*, 1910–1925.

(6) (a) Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1415–1418. (b) Mizushima, E.; Sato, K.; Hayashi, T.; Tanaka, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 4563–4565. (c) Comotti, M.; Della Pina, C.; Matarrese, R.; Rossi, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 5812–5815. (d) Hashmi, A. S. K.; Weyrauch, J. P.; Rudolph, M.; Kurpejović, E. *Angew. Chem., Int. Ed.* **2004**, *43*, 6545–6547. (e) Zhou, C.-Y.; Chan, P. W. H.; Che, C.-M. *Org. Lett.* **2005**, *8*, 325–328. (f) Marion, N.; Ramón, R. S.; Nolan, S. P. *J. Am. Chem. Soc.* **2008**, *131*, 448–449. (g) Nun, P.; Egbert, J. D.; Oliva-Madrid, M.-J.; Nolan, S. P. *Chem.—Eur. J.* **2011**, *18*, 1064–1067. (h) Nun, P.; Ramón, R. S.; Gaillard, S.; Nolan, S. P. *J. Organomet. Chem.* **2011**, *696*, 7–11. (i) Bouhrara, M.; Jeanneau, E.; Veyre, L.; Coperet, C.; Thieuleux, C. *Dalton Trans.* **2011**, *40*, 2995–2999. (j) Hashmi, A. S. K.; Loos, A.; Doherty, S.; Knight, J. G.; Robson, K. J.; Rominger, F. *Adv. Synth. Catal.* **2011**, *353*, 749–759. (k) Oliver-Meseguer, J.; Cabrero-Antonino, J. R.; Domínguez, I.; Leyva-Pérez, A.; Corma, A. *Science* **2012**, *338*, 1452–1455. (l) Xi, Y.; Wang, D.; Ye, X.; Akhmedov, N. G.; Petersen, J. L.; Shi, X. *Org. Lett.* **2013**, *16*, 306–309. (m) Blanco Jaimes, M. C.; Böhling, C. R. N.; Serrano-Becerra, J. M.; Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2013**, *52*, 7963–7966. (n) Canseco-Gonzalez, D.; Petronilho, A.; Mueller-Bunz, H.; Ohmatsu, K.; Ooi, T.; Albrecht, M. *J. Am. Chem. Soc.* **2013**, *135*, 13193–13203. (o) Gómez-Suárez, A.; Oonishi, Y.; Meiries, S.; Nolan, S. P. *Organometallics* **2013**, *32*, 1106–1111. (p) Wang, Y.; Wang, Z.; Li, Y.; Wu, G.; Cao, Z.; Zhang, L. *Nat. Commun.* **2014**, *5*, 3470. (q) Blanco Jaimes, M. C.; Rominger, F.; Pereira, M. M.; Carrilho, R. M. B.; Carabineiro, S. A. C.; Hashmi, A. S. K. *Chem. Commun.* **2014**, *50*, 4937–4940.

(7) (a) Yamamoto, I.; Tanaka, S.; Fujimoto, T.; Ohta, K. *J. Org. Chem.* **1989**, *54*, 747–750. (b) Yoshida, J.-i.; Nakatani, S.; Isoe, S. *Tetrahedron Lett.* **1990**, *31*, 2425–2428. (c) Chen, F.; Mudryk, B.; Cohen, T. *Tetrahedron* **1994**, *50*, 12793–12810. (d) Hutton, T. K.; Muir, K.; Procter, D. J. *Org. Lett.* **2002**, *4*, 2345–2347. (e) Agatsuma, T.; Ogawa, H.; Akasaka, K.; Asai, A.; Yamashita, Y.; Mizukami, T.; Akinaga, S.; Saitoh, Y. *Bioorg. Med. Chem.* **2002**, *10*, 3445–3454.

(8) (a) Yasuda, M.; Tsuji, S.; Shigeyoshi, Y.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 7440–7447. (b) Hansford, K. A.; Dettwiler, J. E.; Lubell, W. D. *Org. Lett.* **2003**, *5*, 4887–4890. (c) Yan, X.-X.; Liang, C.-G.; Zhang, Y.; Hong, W.; Cao, B.-X.; Dai, L.-X.; Hou, X.-L. *Angew. Chem., Int. Ed.* **2005**, *44*, 6544–6546. (d) Gribkov, D. V.; Hultzsch, K. C.; Hampel, F. *J. Am. Chem. Soc.* **2006**, *128*, 3748–3759. (e) Ketcham, J. M.; Biannic, B.; Aponick, A. *Chem. Commun.* **2013**, *49*, 4157.

(9) (a) Nolan, S. P. *Acc. Chem. Res.* **2011**, *44*, 91–100. (b) Gaillard, S.; Cazin, C. S. J.; Nolan, S. P. *Acc. Chem. Res.* **2012**, *45*, 778–787.

(10) Schmidbaur, H.; Schier, A. *Z. Naturforsch.* **2011**, *66b*, 329–350.

(11) de Frémont, P.; Stevens, E. D.; Fructos, M. R.; Mar Diaz-Requejo, M.; Perez, P. J.; Nolan, S. P. *Chem. Commun.* **2006**, 2045–2047.

(12) (a) Ricard, L.; Gagosz, F. *Organometallics* **2007**, *26*, 4704–4707. (b) Patrick, S. R.; Gómez-Suárez, A.; Slawin, A. M. Z.; Nolan, S. P. *Organometallics* **2013**, *33*, 421–424.

(13) Corma, A.; Ruiz, V. R.; Leyva-Pérez, A.; Sabater, M. J. *Adv. Synth. Catal.* **2010**, *352*, 1701–1710.

(14) Leyva, A.; Corma, A. *J. Org. Chem.* **2009**, *74*, 2067–2074.

(15) Calculations based on isolated yields of **3aa**: 92% for our methodology, 95% for Aponick.

(16) (a) Ganem, B. *Angew. Chem., Int. Ed.* **1996**, *35*, 936–945. (b) Gourlaouen, C.; Marion, N.; Nolan, S. P.; Maseras, F. *Org. Lett.* **2009**, *11*, 81–84. (c) Vidhani, D. V.; Cran, J. W.; Krafft, M. E.; Manoharan, M.; Alabugin, I. V. *J. Org. Chem.* **2012**, *78*, 2059–2073. (d) Vidhani, D. V.; Cran, J. W.; Krafft, M. E.; Alabugin, I. V. *Org. Biomol. Chem.* **2013**, *11*, 1624–1630. (e) Rehbein, J.; Hiersemann, M. *Synthesis* **2013**, *45*, 1121–1159.