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Noninnocent Counterion Effect on the Rearrangements of Cationic Intermediates in a Gold(I)-Catalyzed Alkenylsilylation Reaction

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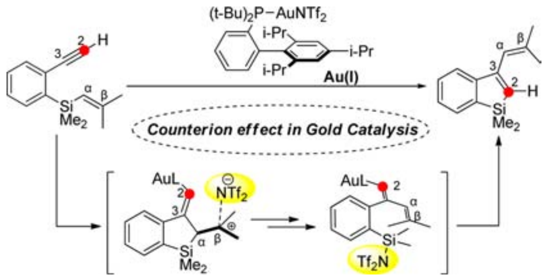
ABSTRACT



A mechanistic DFT study of the gold(I)-catalyzed alkenylsilylation reaction of a silyl-tethered 1,6-enyne system is reported. A novel pathway involving bistriflimide counterion-assisted rearrangements of carbocation and silyl cation intermediates corroborates the experimental observations. The results suggest the important role of the counterion in modulating the reactivity of cationic intermediates in gold catalysis.

Homogeneous gold catalysis has received considerable attention during the past decade.[1] Among the gold complexes, gold(I) species LAuX (L = neutral ligand; X = counterion) is the most common precatalyst, which is typically prepared from LAuCl and silver salt AgX.[2] While the resulting cationic $[\mathrm{LAu}]^+$ is assumed to be an active catalyst,[3] the counterion also has a profound influence on the efficiency and selectivity of many reactions.[4] Recent theoretical studies disclosed the important effect of counterions in catalyzing proton transfer and in forming hydrogen bonds.[5] However, other possible roles for the counterion in gold(I)-catalyzed reactions are yet to be discovered.

Gold catalysis has been widely employed for the facile constructions of various hetero- and carbocycles.[1] In this context, recent studies by Murakami et al. showed that 1-silaindene derivative **B** could be obtained from the gold(I)-catalyzed intramolecular alkenylsilylation reaction of

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(3) For recent examples, see: (a) Hansmann, M. M.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2013**, *52*, 2593. (b) Lu, B.; Li, Y.; Wang, Y.; Aue, D.; Luo, H. Y.; Zhang, L. *J. Am. Chem. Soc.* **2013**, *135*, 8512. (c) Rao, W.; Koh, M. J.; Li, D.; Hirao, H.; Chan, P. W. H. *J. Am. Chem. Soc.* **2013**, *135*, 7926. (d) Ghebreghiorgis, T.; Biannic, B.; Kirk, B. H.; Ess, D. H.; Aponick, A. *J. Am. Chem. Soc.* **2012**, *134*, 16307. (e) Felix, R. J.; Weber, D.; Gutierrez, O.; Tantillo, D. J.; Gagné, M. R. *Nature Chem.* **2012**, *4*, 405. (f) Hashmi, A. S. K.; Yang, W.; Yu, Y.; Hansmann, M. M.; Rudolph, M.; Rominger, F. *Angew. Chem., Int. Ed.* **2013**, *52*, 1329.

(4) For selected examples, see: (a) Yu, Y.; Yang, W.; Rominger, F.; Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2013**, *52*, 7586. (b) Li, W.; Li, Y.; Zhang, J. *Chem.—Eur. J.* **2010**, *16*, 6447. (c) Zuccaccia, D.; Belpassi, L.; Tarantelli, F.; Macchioni, A. *J. Am. Chem. Soc.* **2009**, *131*, 3170. (d) Davies, P. W.; Martin, N. *Org. Lett.* **2009**, *11*, 2293. (e) LaLonde, R. L.; Sherry, B. D.; Kang, E. J.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 2452. (f) Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science* **2007**, *317*, 496.

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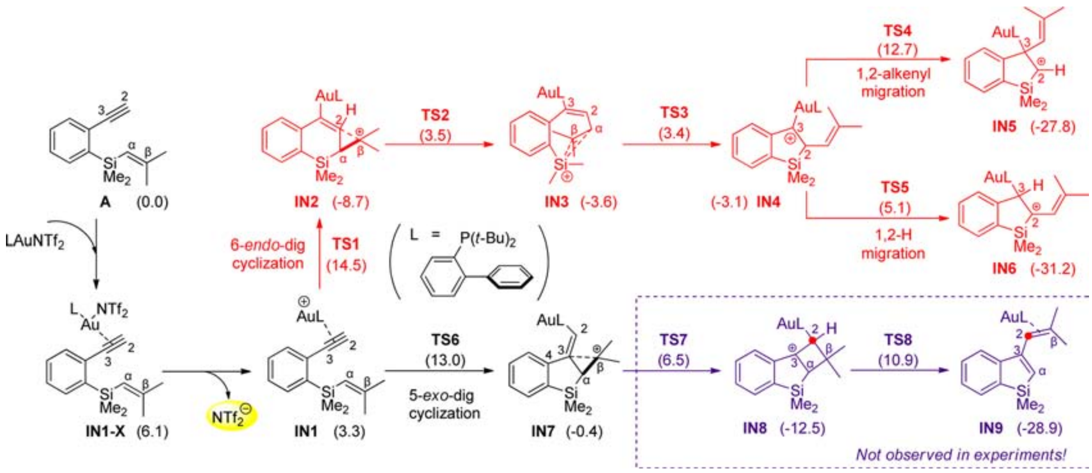
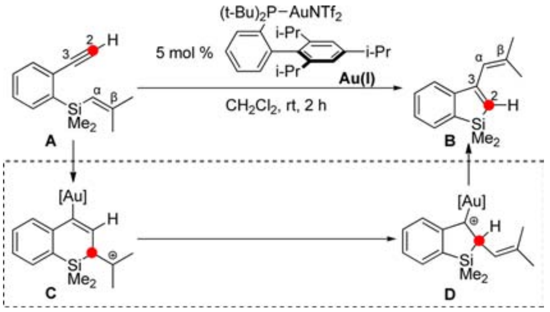


Figure 1. Energetic profiles for the possible 6-*endo*-dig and 5-*exo*-dig pathways (values in parentheses are ΔG_{sol} in kcal/mol).

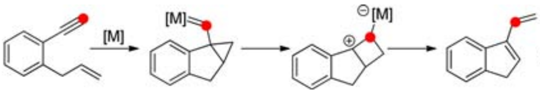
Scheme 1. Gold(I)-Catalyzed Alkenylsilylation of **A**



1,6-enyne **A** (Scheme 1) under very mild conditions,[6a] and the corresponding aryl- and allylsilylation reactions were also developed with a similar strategy.[6]

To probe the possible reaction mechanism, a deuterium-labeling experiment was carried out. The labeling pattern clearly indicates that the C_2 atom bearing the deuterium label is connected to the silicon (Scheme 1).[6a] Accordingly, the authors proposed that the alkenylsilylation reaction of **A** could be initiated by the gold-triggered 6-*endo*-dig cyclization to generate intermediate **C**, which evolves to carbenoid **D** via an intramolecular bond reorganization. Finally, a more favorable alkenyl migration over the hydrogen migration was proposed to selectively deliver the observed product containing an alkenyl group at C_3.

Thus, the reaction of the silicon-containing substrate is mechanistically different from that of the all-carbon analog (eq 1).[7] The latter reaction is believed to proceed via the well-established mechanism of enyne cycloisomerization involving a complete cleavage of the carbon−carbon double bond, generating a 3-alkenyl-1*H*-indene derivative.[8,9] However, the origin of the above divergence has not been clarified.[6,7]



(1)

In the current report we studied the mechanism of the gold(I)-catalyzed alkenylsilylation reaction described in Scheme 1 by DFT calculations at the M06/6-31G*/LanL2DZ level of theory[10] using the Gaussion 09 software package.[11] All energies reported (ΔG_{sol}) are relative free energies including single-point solvation correction calculations with the PCM model for CH_2Cl_2.[12] A new mechanism involving the bistriflimide counterion-assisted rearrangements of carbocation and silyl cation intermediates was proposed to account for the experimental observations by Murakami et al.[6]

At the outset of this study, the feasibility of the originally proposed mechanism was evaluated. Calculations show the direct dissociation of $LAuNTf_2$, in which L is a slightly simplified phosphine ligand (shown in Figure 1),[13] into charged species (LAu^+ and NTf^-) is endergonic by 21.9 kcal/mol. Alternatively, the formation of cationic reaction complex **IN1** could be realized by dissociation of the counterion from alkyne π-complex **IN1-X** of **A** and $LAuNTf_2$ (Figure 1), as the former is 2.8 kcal/mol lower in energy. The 6-*endo*-dig cyclization via **TS1** requires an activation barrier of 11.2 kcal/mol, leading to a nonclassical carbocation intermediate **IN2**, which is −8.7 kcal/mol

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(8) For reviews, see: (a) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271. (b) Diver, S. T.; Giessert, A. J. *Chem. Rev.* **2004**, *104*, 1317. (c) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 200. (d) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (e) Obradors, C.; Echavarren, A. M. *Acc. Chem. Res.* Article ASAP, DOI: 10.1021/ar400174p.

(9) For selected examples of mechanistic study on cycloisomerization of 1,6-enyne systems, see: (a) Zhuo, L.-G.; Zhang, J.-J.; Yu, Z.-X. *J. Org. Chem.* **2012**, *77*, 8527. (b) Escribano-Cuesta, A.; Pérez-Galán, P.; Herrero-Gómez, E.; Sekine, M.; Braga, A. A. C.; Maseras, F.; Echavarren, A. M. *Org. Biomol. Chem.* **2012**, *10*, 6105. (c) Nieto-Oberhuber, C.; López, S.; Jiménez-Núñez, E.; Echavarren, A. M. *Chem.—Eur. J.* **2006**, *12*, 5916. (d) Soriano, E.; Ballesteros, P.; Marco-Contelles, J. *Organometallics* **2005**, *24*, 3172. (e) Soriano, E.; Ballesteros, P.; Marco-Contelles, J. *Organometallics* **2005**, *24*, 3182.

(10) (a) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215. (b) Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* **2008**, *41*, 157.

below the starting materials. Prior to the formation of the carbenoid intermediate **IN4**, **IN2** should be first transformed into **IN3** via **TS2**. The silyl cation **IN3** stabilized by the $C_\alpha-C_\beta$ double bond, the original alkenyl moiety in precursor **A**, is ~5.0 kcal/mol higher in energy than **IN2**. From **IN3**, the electrophilic attack of Si to C_2 is realized via **TS3** with a barrier of 7.0 kcal/mol, forming carbenoid **IN4** reversibly. In the following step, a 1,2-group migration from C_2 to C_3 is highly chemoselective, as the 1,2-H migration via **TS5** is 7.6 kcal/mol lower in energy than the 1,2-alkenyl migration via **TS4**. Thus, the formation of σ-complex **IN6** is more favorable both kinetically and thermodynamically, from which the formation of the final product 2-alkenyl-1- silaindene is predicted. These theoretical results contradict the experimental observations, and thus the rearrangement mechanism involving a carbenoid intermediate in the 6-*endo*-dig pathway is discarded.

To gain a more realistic picture of the reaction profile of **A**, a 5-*exo*-dig cyclization from complex **IN1** was also calculated. The cyclization via **TS6** requires an activation barrier of 9.7 kcal/mol, which is 1.5 kcal/mol lower than that of the cyclization via **TS1** (Figure 1).[14] Thus, the generation of nonclassical carbocation **IN7** is kinetically more favorable than **IN2**. Notably, the relative energies for the transition states of the following steps from **IN7** are lower than that of **TS6**, suggesting the 5-*exo*-dig cyclization would be irreversible. From **IN7**, the formation of the 3-alkenyl-1-silaindene product is possible via a typical metathesis mechanism.[8,9] The process to form a new bond between C_β and C_2 through **TS7** requires a barrier of only 6.9 kcal/mol and forms tricyclic intermediate **IN8** exergonically. In the following step, the ring-opening reaction of **IN8** via **TS8**, with a higher barrier of 23.4 kcal/mol, produces product complex **IN9**. The formation of the 3-alkenyl-1-silaindene product from this pathway, however, is constitutionally different from the reported structure assigned on the basis of the experimentally observed deuterium-labeling pattern.[6a]

As the above results indicate that the 5-*exo*-dig cyclization is more favorable than the 6-*endo*-dig cyclization, we assumed that the reaction pathway should be bifurcated after the formation of nonclassical carbocation **IN7**, in which the positive charge on the C_β is delocalized over the $C_2-C_3-C_4$ plane, as evidenced by its geometric structure.[12] Similar to the facile transformation between **IN2** and **IN3**, the flipping of the C_β moiety via **TS9** requires a small barrier of 5.1 kcal/mol (Figure 2), which is 1.8 kcal/mol lower than that of the ring closure via **TS7**. **TS9** then leads to intermediate **IN10**, which is an olefin-stabilized silyl cation with the $Si-C_\alpha$, $Si-C_\beta$, and $C_\alpha-C_\beta$ distances being 2.107, 2.550, and 1.391 Å, respectively.[15] To form the C_2-Si bond in the product, the shifting of the Si moiety toward the alkenylgold moiety could be achieved via **TS10** with a barrier of about 20 kcal/mol, which generates product complex **IN9′** directly.

While the silyl cation rearrangement mechanism seems to be the only possible channel that leads to the experimentally observed product, it should be noted that the relative free energy of the transition state, **TS10**, lies at a relatively high value of 16.3 kcal/mol. Actually, this energy is significantly higher than any of the transition states in Figure 1; thus, the rearrangement via **TS10** should not be a favorable pathway. We reasoned that the relatively high barrier of this step could be attributed to the fused geometry of **TS10** (Figure 2), in which the migrating Si atom has strong interactions with both C_α and C_3 ($Si-C_\alpha$ = 2.469 and $Si-C_3$ = 2.270 Å). We further assumed that if the silyl cation is stabilized by a possible nucleophile in the system, such as the bistriflimide counterion released from complex **IN1-X**, the transition state would be more flexible and the rearrangement could be facilitated. In fact, calculations with a counterion found that even though the N$-$Si bond was first fixed at a long distance of 3.5 Å, the NTf_2 anion would bound to the Si atom of **IN10** simultaneously to form **IN10-X** with an exergonicity of 7.3 kcal/mol (Figure 2), implying the stronger ability of the counterion to stabilize the positive charges than π electrons.[15] Upon the nucleophilic addition of the NTf_2 anion to the silyl cation, a gold-containing 1,3-diene moiety is formed in **IN10-X**. Finally, the C_2-Si bond required for the silaindene product could be formed by an S_N1-type reaction via **TS10-X** (C_2-Si = 2.372 and $Si-N$ = 2.232 Å).[16] This process requires a barrier of 7.1 kcal/mol and leads directly to cationic product complex **IN11**.[17] Thus, the counterion-involved silyl cation rearrangement mechanism in Figure 2 represents a more favorable pathway and correlates well with the experimental results.

Theoretically, the counterion may also be involved in other steps of the reaction. Hence, the possible effects of the bistriflimide on the whole reaction were evaluated in detail. When the counterion is involved, the activation energies for the 6-*endo*-dig and 5-*exo*-dig cyclizations are 18.3 and 18.1 kcal/mol, respectively.[12] These are ~4.0 kcal/mol higher than those via **TS1** and **TS6**, indicating the initial cyclization favors the cationic form. Following the cationic 5-*exo*-dig cyclization, carbocation **IN7** will be generated accordingly (Figure 1). While the direct rearrangement of **IN7** to

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(11) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, revision A.01; Gaussian, Inc.: Wallingford, CT, 2009.

(12) See the Supporting Information for details.

(13) Calculations of key steps with the bulky phosphine ligand in Scheme 1 indicated that such a simplification did not affect the conclusions reached herein.[12]

(14) **TS6** would be 2.6 kcal/mol more favorable than **TS1** when calculated with the bulky phosphine ligand in Scheme 1.[12]

(15) Ariafard, A.; Asadollah, E.; Ostadebrahim, M.; Rajabi, N. A.; Yates, B. F. *J. Am. Chem. Soc.* **2012**, *134*, 16882.

(16) Asao, N.; Shimada, T.; Shimada, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2001**, *123*, 10899.

(17) The counterion-contained product complex is 6.8 kcal/mol higher in energy than **IN11**.

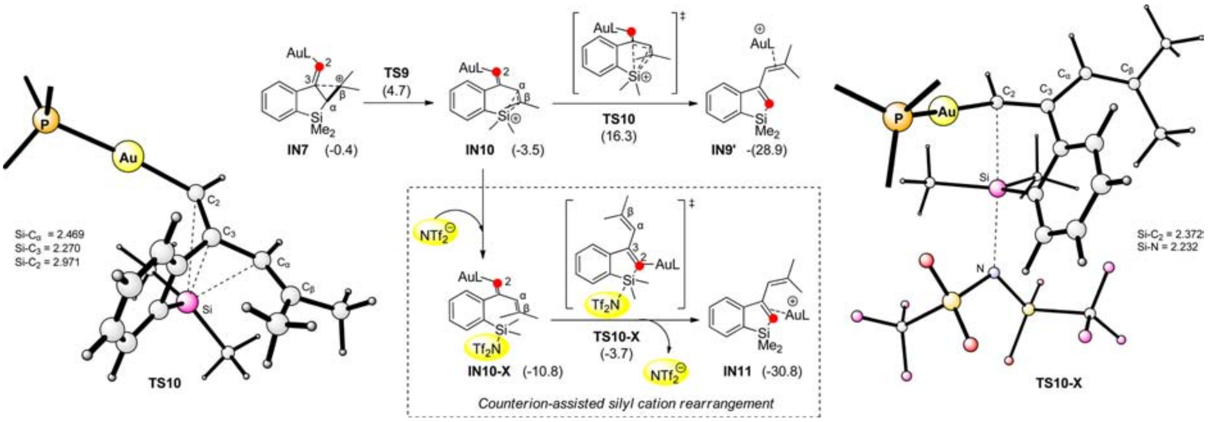
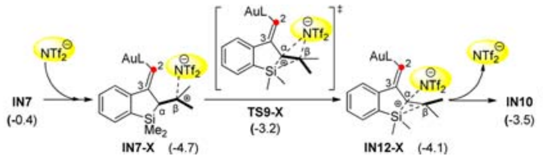


Figure 2. Energies and structures of key transition states for the silyl cation rearrangement pathways (groups attached to the P atom of the phosphine ligand are omitted for clarity; distances in Å).

the silyl cation **IN10** is very facile, the inclusion of the counterion makes this rearrangement an almost barrierless scenario (eq 2).[18] In this process, the combination of **IN7** with the NTf_2 anion is exergonic by 4.3 kcal/mol upon the formation of ion pair **IN7-X**, which contains an open carbocation at C_β that is stabilized by both Si and N atoms ($N-C_\beta = 2.926$ and $Si-C_\beta = 2.617$ Å). Then, only a very small barrier of 1.5 kcal/mol is required to transform this ion pair into intermediate **IN12-X** via **TS9-X**. In intermediate **IN12-X** the Si atom is connected to C_β while the positively charged C_α atom has interactions with both Si and N atoms ($Si-C_\alpha = 2.528$ and $N-C_\alpha = 2.893$ Å). In the next step, the dissociation of the NTf_2 anion from **IN12-X** to generate the silyl cation **IN10** is endergonic by only 0.6 kcal/mol, which will be followed by the NTf_2-assisted rearrangement shown in Figure 2.[18]



(2)

Accordingly, the lowest energy pathway for the Au(I)-catalyzed alkenylsilylation of **A** could be depicted as in Figure 3. The 5-*exo*-dig cyclization (**TS6**) from the cationic complex **IN1** is more kinetically favorable. This step also represents the rate-determing step of the whole reaction, and the small activation barrier of 13 kcal/mol correlates well with the very mild experimental conditions.[19] The generated nonclassical carbocation **IN7** undergoes rearrangement facilely with the incorporation of the NTf_2 counterion, which generates an olefin-stabilized silyl cation **IN10**. Finally, the counterion-assisted silyl cation rearrangement was disclosed as the key step to form the 1-silaindene product that is regiochemically different from the reaction of the all carbon analog.[7−9]

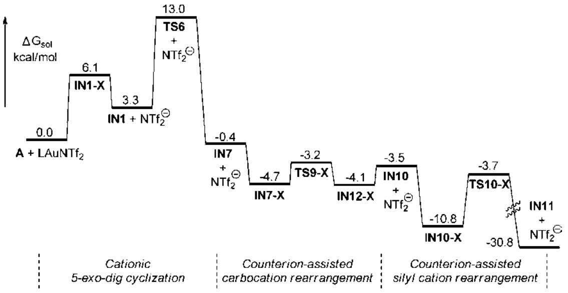


Figure 3. Energy profile for the overall catalytic cycle.

In summary, the mechanism of the gold(I)-catalyzed alkenylsilylation reaction of a silyl-tethered enyne system was better understood by DFT calculations. The results highlight an overlooked effect of the counterion on the reactivity and selectivity in gold catalysis and should have an important implication in the mechanistic understanding of related reactions.[15,16,20]

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Supporting Information Available. Computational details and results. This material is available free of charge via the Internet at http://pubs.acs.org.

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[18] On the other hand, the relative energy for the transition state of ring closure between C_2 and C_β will be 8.2 kcal/mol when the counterion is involved, suggesting the metathesis mechanism is even more unfavorable.[12]

[19] Geometry optimizations in CH_2Cl_2 solution with the experimentally used bulky phosphine ligand (Scheme 1) show the activation free energy of this step is 15.0 kcal/mol.

[20] (a) Li, J.; Liu, X.; Lee, D. *Org. Lett.* **2012**, *14*, 410. (b) Park, S.; Lee, D. *J. Am. Chem. Soc.* **2006**, *128*, 10664. (c) Horino, Y.; Luzung, M. R.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 11364.

The authors declare no competing financial interest.