

Gold(I)-Catalyzed Tandem Transformation with Diynes: Rapid Access to Linear Cyclopentenone-Fused Polycyclic Molecules**

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Abstract: An efficient and convenient synthesis of useful linear cyclopentenone-fused polycyclic compounds has been achieved through a novel gold(I)-catalyzed transformation of diynes. The method demonstrates high product yields and tolerates a wide variety of important functional groups. Gold-vinylidene formation, methoxy group migration, and Nazarov-type cyclization are proposed to be the key steps in the reaction pathway. The synthetic utility of this method is demonstrated by converting the product to eight-membered-ring-fused compound.

Cyclopentenone and its closely related analogues, in a linearly fused polycyclic molecular skeleton, are frequently observed in natural products (Figure 1)^[1] and advanced

effort, and challenges in controlling the region- and stereochemical outcome, as well as the need to employ harsh reaction conditions further limit its synthetic utility.^[3] Thus, complementary methods for the expedient synthesis of this type of skeleton in a step-economic and flexible fashion are still highly desired.

During the last decade, homogeneous gold-catalyzed cycloisomerization reactions have proven to be exceptionally efficient methods to construct synthetically significant polycyclic molecules. In these reactions, structural complexity can be rapidly built from easily accessible starting materials under mild reaction conditions.^[4] Several elegant examples of cyclopentenone preparation by gold catalysis have also been reported.^[5] Recently, dual gold catalysis using diynes as substrates has been actively studied. Both mechanistic studies and theoretical calculations suggest gold vinylidene as a reaction intermediate.^[6a,b] These highly reactive species were found to undergo facile C(sp³)-H and C(sp²)-H as well as O-H and N-H insertion, thus leading to a range of novel polycyclic products in an atom-economic manner.^[6,7] Inspired by these pioneering works, and encouraged by the rich chemistry from other metal vinylidene complexes such as Ru, W, and Rh,^[8] we were interested in exploring nucleophiles, other than C-H, O-H, or N-H, suitable for gold vinylidenes. Particularly, we envisioned that a properly positioned methoxy group in a diyne molecule would have the potential to serve as a nucleophile.^[9] Its easy installation and chemical stability towards most reaction conditions provide valuable advantages for applications in the late-stage assembly of complex molecules. Herein, we report our findings that the methoxy group can indeed serve as an excellent nucleophile. This novel reactivity toward gold vinylidenes led to the discovery of a new method for the synthesis of complex, linear, cyclopentenone-fused, polycyclic compounds, which are not easily accessible through alternative approaches. We further demonstrate the synthetic potential of this method by converting the product into an eight-membered-ring-fused compound.

Our study began with the (2-ethynylphenyl)alkyne **1a** bearing a tertiary MeO group at the propargylic position (Scheme 1). Previous studies with substrates containing

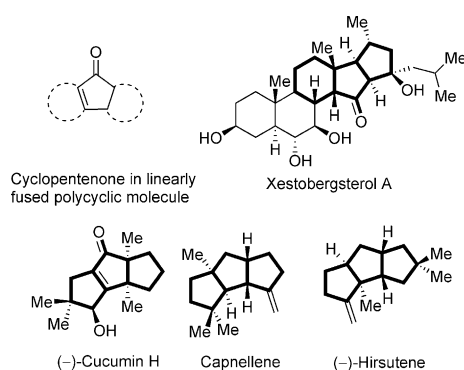


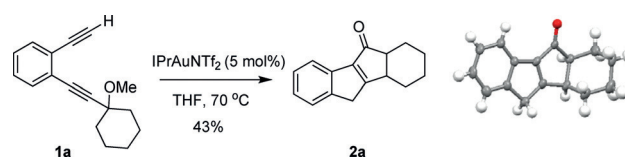
Figure 1. Representative natural products.

intermediates leading to substances of biological or medicinal importance.^[2] Among various approaches to construct such densely functionalized cyclopentenones, the Nazarov reaction is deemed one of the most efficient and reliable. However, for the conventional Nazarov cyclization, pre-installation of a dienone in the starting materials requires extra synthetic

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[**] We are grateful to NSFC-21421091, the "Thousand Plan" Youth program, State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences. We thank Prof. Liming Zhang (University of California, Santa Barbara) for valuable suggestions on this project and Dr. Zhanjie Li (Dow Corning) for help with preparing the manuscript.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.201503599>.

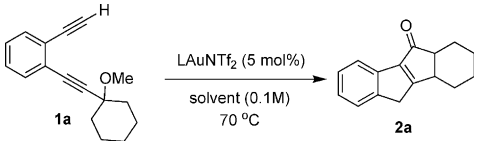


Scheme 1. Formation of **2a**. IPr = 1,3-bis(diisopropylphenyl)imidazol-2-ylidene, Tf = trifluoromethanesulfonyl, THF = tetrahydrofuran.

a similar 1,2-diethynylphenyl motif have led to the proposal of the in situ generated gold vinylidene as the key reactive intermediate. We anticipated that the MeO group in **1a** had the potential to act as nucleophile to attack a gold vinylidene intermediate, therefore leading to intriguing follow-up chemistry. Indeed, heating a solution of **1a** in anhydrous THF at 70 °C in the presence of a catalytic amount of IPrAuNTf₂ gave an unknown compound, **2a**, in 43 % yield upon isolation. Single-crystal X-ray analysis revealed that **2a** contains a unique tetracyclic structure.

Considering the potential utility of this interesting reaction, extensive reaction optimization was carried out, and the results are summarized in Table 1. With IPrAuNTf₂ as the

Table 1: Optimization of the reaction conditions.



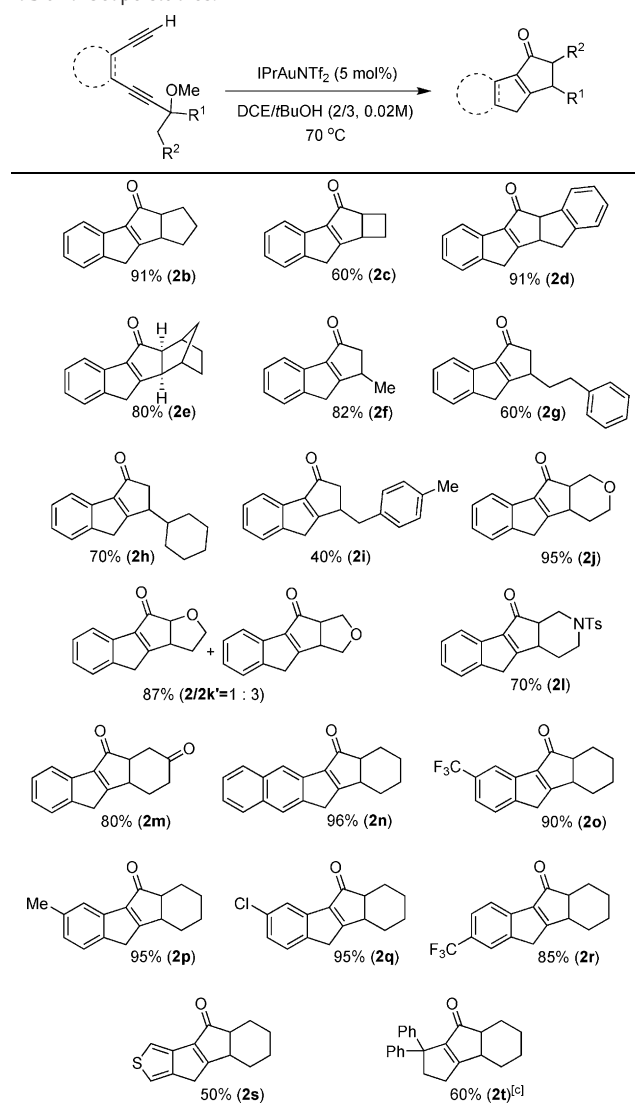
Entry	Catalyst	Solvent	Yield [%] ^[a]
1	IPrAuNTf ₂	THF	43
2	IPrAuNTf ₂	toluene	44
3	IPrAuNTf ₂	DCE	traces
4	PPh ₃ AuNTf ₂	THF	8
5	JohnPhosAuNTf ₂	THF	traces
6	IPrAuNTf ₂	<i>t</i> BuOH	82
7	IPrAuNTf ₂	<i>t</i> BuOH/DCE ^[b]	90
8	IPrAuNTf ₂	<i>t</i> BuOH/DCE ^[c]	91
9	IPrAuNTf ₂	<i>t</i> BuOH/DCE ^[d]	79
10	IPrAuNTf ₂	<i>t</i> BuOH/DCE ^[c,e]	70
11	IPrAuNTf ₂	<i>t</i> BuOH/DCE ^[c,f]	90
12	IPrAuNTf ₂	<i>t</i> BuOH/DCE ^[c,g]	95 (92 ^[h])

[a] Measured by ¹H NMR analysis using diethyl phthalate as an internal standard. [b] *t*BuOH/DCE = 2:1. [c] *t*BuOH/DCE = 1.5:1. [d] *t*BuOH/DCE = 1:1. [e] 0.2 M. [f] 0.05 M. [g] 0.02 M. [h] Yield of isolated product. DCE = 1,2-dichloroethane, JohnPhos = 2-(di-*tert*-butylphosphino)bi-phenyl.

catalyst, **2a** was obtained in 44 % yield when using toluene as the solvent (entry 2), whereas only trace amounts of **2a** were observed in DCE (entry 3). Representative phosphine gold complexes, PPh₃AuNTf₂ and JohnPhosAuNTf₂, were not effective for this reaction (entries 4 and 5). At this stage, we realized that the formation of **2a** likely involves steps such as protodeauration and hydrolysis, which generally require a proton-transfer process. Therefore, a couple of protic solvents were tested. Gratefully, a dramatic yield increase was observed when *tert*-butanol was used as the solvent, and **2a** was formed in 82 % yield (entry 6). Interestingly, doping of *tert*-butanol with a certain amount of DCE further improved the yield of **2a** to 90 % (entry 7). Adjustments of the ratio of DCE to *tert*-butanol and concentration eventually led to the following optimal conditions: IPrAuNTf₂ (5 mol %), DCE/*t*-butanol (1:1.5), 0.02 M, 70 °C (entries 8–12). Under these reaction conditions **2a** was obtained in 92 % yield upon isolation (entry 12).

With the optimal reaction conditions in hand, the investigation of the substrate scope was performed, and the results

Table 2: Scope studies.^[a,b]



[a] All reactions were performed in DCE/*t*BuOH (1:1.5, 0.02 M) at 70 °C. [b] Yield of isolated product. [c] Another 5 mol % IPrAuNTf₂ added after 3 h.

are summarized in Table 2. Besides the cyclohexyl group, substrates bearing other cyclic moieties such as cyclobutyl and cyclopentyl groups reacted well to produce the corresponding tetracyclic products, having differently sized terminal rings, in moderate to high yields (**2b** and **2c**). The substrate derived from 3-indenone gave the pentacyclic product **2d** in 91 % yield. A rather complex product, **2e**, having a bicyclo-[2.2.1]heptane substructure was generated in 80 % yield as a single diastereomer. Substrates derived from acyclic aliphatic ketones, including acetone, 4-phenylbutan-2-one, 1-cyclohexylethanone, and 1-(*p*-tolyl) propan-2-one, also participated in this reaction. Notably, the major products with these substrates were the trisubstituted cyclopentenone isomers (**2f–i**), and the tetrasubstituted cyclopentenone isomers were isolated as a *cis/trans* mixture in very small amounts.^[10] Synthetically valuable heterocycles including tetrahydrofuran, tetrahydropyran, and Ts-protected piperi-

dine were all compatible with the reaction conditions, and the corresponding products **2j–l** were obtained in high yields. A substrate containing a ketone functionality also worked very well to produce the diketone **2m** in 80 % yield.

The variations on the diyne aromatic backbone were also briefly investigated (Table 2). The pentacyclic product **2n**, containing a naphthalene motif, was formed in 96 % yield. Substituents such as Me, Cl, and CF₃ on the benzene ring at the *para* position of the internal alkyne were well tolerated, and the corresponding tetracyclic products **2o–q** were isolated in 90–95 % yields. Compared with **2o**, its isomer **2r**, having CF₃ at the *meta*-position, was obtained in a slightly lower yield (85 %). The thiophene-fused product **2s** was formed in moderate yield (50 %).^[11] Moreover, the tricyclic product **2t**, containing *gem*-diphenyl subunit, was isolated in 60 % yield.

Limitations of this method were also defined during our substrate scope studies (Figure 2), and the information deduced from these observations is summarized as the

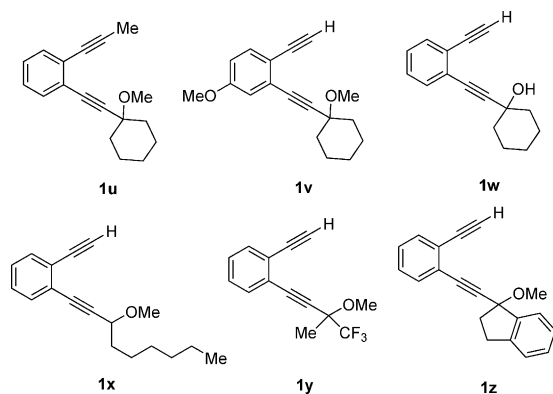
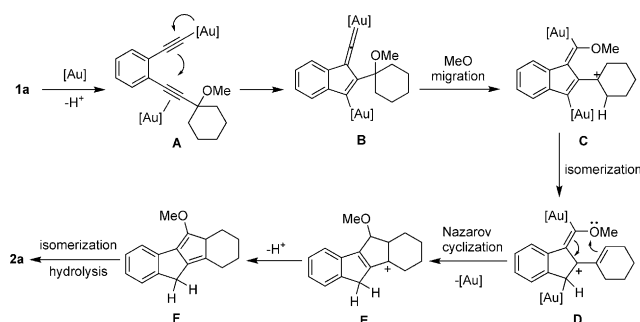


Figure 2. Substrates which failed to give desired products.

following: 1) A terminal alkyne with proper C≡C–H acidity is essential to the success of this gold-catalyzed tandem cyclization process. Both substitution of C≡C–H with a Me group (**1u**) or the addition of an electron-donating (MeO) group on the phenyl (**1v**) shut down the reaction and the starting materials were recovered. It implies that the formation of the alkynyl gold might be the first step of this tandem cyclization process. 2) A free –OH group was not compatible with the reaction. Most of **1w** was recovered with partial decomposition, and was consistent with a related study.^[12] 3) Substituents at the propargylic position have profound impact on the reactivity of the substrates. Both the secondary ether **1x** and tertiary ether **1y** were fully recovered, whereas the tertiary ether **1z** gave a complex mixture.^[13]

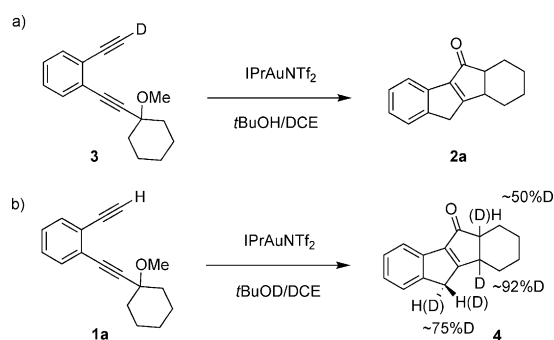
In accordance with reported studies and our experimental results,^[6] a preliminary mechanism for the formation of **2a** is proposed. As shown in Scheme 2, activation of **1a** by dual gold catalysis leads to the formation of the gold vinylidene **B**. The oxygen atom of MeO readily attacks the vinylidene carbon atom in **B**, with subsequent migration of MeO to form the tertiary carbon cation **C**. Presumably, the stability of **C** plays a critical role in the whole transformation, as both **1x**, with weaker ability to stabilize the corresponding cation, and



Scheme 2. Proposed reaction mechanism.

1y, with a destabilizing effect, failed to give the cyclization product.^[14] Isomerization of **C** leads to the formation of the more stable tertiary pentadienyl cation **D** by a deprotonation and protonation. Subsequent Nazarov-type cyclization of **D** and hydrolysis delivers the observed product **2a**. It needs to be noted that we have not excluded alternative reaction pathways at this stage, as more in-depth investigations are being carried out in our laboratory.^[15]

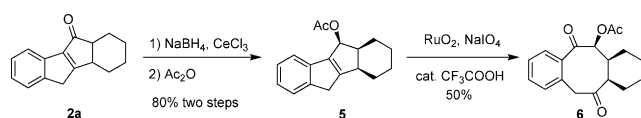
Results from deuterium-labeling experiments provide additional information regarding the proposed mechanism. When the deuterated substrate **3** was subjected to the standard reaction conditions, complete loss of deuterium labelling was observed in **2a** (Scheme 3a). When deuterated



Scheme 3. Deuterium-labeling experiments.

tert-butanol (*t*BuOD) was used as a cosolvent, the deuterium incorporation was observed (Scheme 3b). There is approximately 92 % deuterium incorporation at the allylic tertiary carbon atom and about 50 % deuterium incorporation at the carbon atom α to the carbonyl group, and it can be attributed to the final isomerization and hydrolysis processes.^[16]

The cyclopentenone-fused, polycyclic products reported here can be further elaborated into other useful compounds. For example, oxidative cleavage of the tetrasubstituted double bond in these products can lead to the formation of eight-membered-ring-fused compounds, which are widely observed in natural products and advanced materials.^[17] As shown in Scheme 4, a three-step procedure, including Luche reduction, esterification, and oxidative cleavage of **2a** gave eight-membered-ring-fused tricyclic product **6** in good yield. The two carbonyl functionalities of **6** also allow a high degree of freedom for additional transformations if needed.



Scheme 4. Approach for the synthesis of eight-membered ring-fused product.

In summary, an efficient method has been developed to prepare linearly fused polycyclic products, containing a cyclopentenone motif, from readily available diynes through gold catalysis. The key features of this method include the mild reaction conditions, broad substrate scope, and elegant product structures. A novel reaction cascade involving gold vinylidene formation, methoxy group migration, and Nazarov-type cyclization, is postulated. The synthetic potential of this chemistry is demonstrated by converting one of the products (**2a**) into an eight-membered-ring-fused compound. Future work will focus on elucidation of the reaction mechanism and applying this method to complex-molecule synthesis.

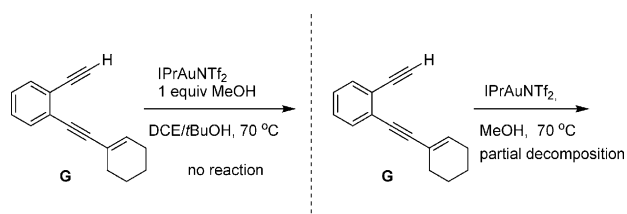
Keywords: alkynes · cyclizations · gold · polycycles · synthetic methods

How to cite: *Angew. Chem. Int. Ed.* **2015**, *54*, 10903–10907
Angew. Chem. **2015**, *127*, 11053–11057

- [1] a) N. Shoji, A. Umeyama, K. Shin, K. Takeda, S. Arihara, *J. Org. Chem.* **1992**, *57*, 2996–2997; b) A. Srikrishna, D. H. Dethe, *Org. Lett.* **2003**, *5*, 2295–2298; c) S. J. Shen, W. Z. Li, *J. Org. Chem.* **2013**, *78*, 7112–7120.
- [2] a) S. Arseniyadis, D. V. Yashunsky, M. Dorado, B. Alves, E. Toromanoff, L. Toupet, P. Potier, *Tetrahedron Lett.* **1993**, *34*, 4927–4930; b) S. Arseniyadis, D. V. Yashunsky, M. Munoz Dorado, R. Brondi Alves, Q. Wang, P. Potier, L. Toupet, *Tetrahedron* **1996**, *52*, 6215–6232.
- [3] a) K. L. Habermas, S. E. Denmark, T. K. Jones, *Org. React.* **1994**, *45*, 1–158; b) M. A. Tius, *Eur. J. Org. Chem.* **2005**, 2193–2206; c) H. Pellissier, *Tetrahedron* **2005**, *61*, 6479–6517; d) T. N. Grant, C. J. Rieder, F. G. West, *Chem. Commun.* **2009**, 5676–5688; e) N. Shimada, C. Stewart, M. A. Tius, *Tetrahedron* **2011**, *67*, 5851–5870; f) T. Vaidya, R. Eisenberg, A. J. Frontier, *ChemCatChem* **2011**, *3*, 1531–1548; g) W. T. Spencer III, T. Vaidya, A. J. Frontier, *Eur. J. Org. Chem.* **2013**, 3621–3633; h) M. A. Tius, *Chem. Soc. Rev.* **2014**, *43*, 2979–3002; i) M. J. Di Grandi, *Org. Biomol. Chem.* **2014**, *12*, 5331–5345; j) A. Jolit, P. M. Wallester, G. P. A. Yap, M. A. Tius, *Angew. Chem. Int. Ed.* **2014**, *53*, 6180–6183; *Angew. Chem.* **2014**, *126*, 6294–6297; k) D. R. Wenz, J. Read de Alaniz, *Eur. J. Org. Chem.* **2015**, 23–37.
- [4] a) A. Fürstner, P. W. Davies, *Angew. Chem. Int. Ed.* **2007**, *46*, 3410–3449; *Angew. Chem.* **2007**, *119*, 3478–3519; b) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211; c) Z. Li, C. Brouwer, C. He, *Chem. Rev.* **2008**, *108*, 3239–3265; d) A. Arcadi, *Chem. Rev.* **2008**, *108*, 3266–3325; e) E. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326–3350; f) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*, 3351–3378; g) A. S. K. Hashmi, M. Rudolph, *Chem. Soc. Rev.* **2008**, *37*, 1766–1775; h) V. Michelet, P. Y. Touillec, J. P. Genêt, *Angew. Chem. Int. Ed.* **2008**, *47*, 4268–4315; *Angew. Chem.* **2008**, *120*, 4338–4386; i) A. Fürstner, *Chem. Soc. Rev.* **2009**, *38*, 3208–3221; j) F. Gagosz, *Tetrahedron* **2009**, *65*, 1757–1757; k) A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2010**, *49*, 5232–5241; *Angew. Chem.* **2010**, *122*, 5360–5369; l) B. Alcaide, P. Almendros, J. M. Alonso, *Org. Biomol. Chem.* **2011**, *9*, 4405–4416; m) B. Alcaide, P. Almendros, J. M. Alonso, *Molecules* **2011**, *16*, 7815–7843; n) C. Aubert, L. Fensterbank, P. Garcia, M. Malacria, A. Simonneau, *Chem. Rev.* **2011**, *111*, 1954–1993; o) N. Krause, C. Winter, *Chem. Rev.* **2011**, *111*, 1994–2009; p) S. P. Nolan, *Acc. Chem. Res.* **2011**, *44*, 91–100; q) M. Rudolph, A. S. K. Hashmi, *Chem. Soc. Rev.* **2012**, *41*, 2448–2462; r) B. L. Lu, L. Dai, M. Shi, *Chem. Soc. Rev.* **2012**, *41*, 3318–3339; s) C. Obradors, A. M. Echavarren, *Acc. Chem. Res.* **2014**, *47*, 902–912; t) Y.-M. Wang, A. D. Lackner, F. D. Toste, *Acc. Chem. Res.* **2014**, *47*, 889–901.
- [5] a) X. Shi, D. J. Gorin, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 5802–5803; b) L. Zhang, S. Wang, *J. Am. Chem. Soc.* **2006**, *128*, 1442–1443; c) T. Jin, Y. Yamamoto, *Org. Lett.* **2008**, *10*, 3137–3139; d) W. Zi, H. Wu, F. D. Toste, *J. Am. Chem. Soc.* **2015**, *137*, 3225–3228.
- [6] a) L. Ye, Y. Wang, D. H. Aue, L. Zhang, *J. Am. Chem. Soc.* **2012**, *134*, 31–34; b) A. S. K. Hashmi, I. Braun, M. Rudolph, F. Rominger, *Organometallics* **2012**, *31*, 644–661; c) A. S. K. Hashmi, M. Wietek, I. Braun, P. Noël, L. Jongbloed, M. Rudolph, F. Rominger, *Adv. Synth. Catal.* **2012**, *354*, 555–562; d) A. S. K. Hashmi, I. Braun, P. Noël, J. Schlich, M. Wietek, M. Rudolph, F. Rominger, *Angew. Chem. Int. Ed.* **2012**, *51*, 4456–4460; *Angew. Chem.* **2012**, *124*, 4532–4536; e) A. Gómez-Suárez, S. P. Nolan, *Angew. Chem. Int. Ed.* **2012**, *51*, 8156–8159; *Angew. Chem.* **2012**, *124*, 8278–8281; f) A. S. K. Hashmi, M. Wietek, I. Braun, M. Rudolph, F. Rominger, *Angew. Chem. Int. Ed.* **2012**, *51*, 10633–10637; *Angew. Chem.* **2012**, *124*, 10785–10789; g) 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; h) P. Noël, T. Lauterbach, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Chem. Eur. J.* **2013**, *19*, 8634–8641; i) D. D. Vachhani, M. Galli, J. Jacobs, L. Van Meerelt, E. V. Van der Eycken, *Chem. Commun.* **2013**, *49*, 7171–7173; j) Y. Wang, A. Yepremyan, S. Ghorai, R. Todd, D. H. Aue, L. Zhang, *Angew. Chem. Int. Ed.* **2013**, *52*, 7795–7799; *Angew. Chem.* **2013**, *125*, 7949–7953; k) I. Braun, A. M. Asiri, A. S. K. Hashmi, *ACS Catal.* **2013**, *3*, 1902–1907; l) M. H. Vilhelmsen, A. S. K. Hashmi, *Chem. Eur. J.* **2014**, *20*, 1901–1908; m) M. Wietek, Y. Tokimizu, M. Rudolph, F. Rominger, H. Ohno, N. Fujii, A. S. K. Hashmi, *Chem. Eur. J.* **2014**, *20*, 16331–16336; n) A. S. K. Hashmi, *Acc. Chem. Res.* **2014**, *47*, 864–876; o) J. Bucher, T. Stöber, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2015**, *54*, 1666–1670; *Angew. Chem.* **2015**, *127*, 1686–1690; p) R. J. Harris, R. A. Widenhoefer, *Angew. Chem. Int. Ed.* **2015**, *54*, 6867–6869; *Angew. Chem.* **2015**, *127*, 6971–6973.
- [7] For alternative approaches to access gold-vinylidene species, see: a) V. Mamane, D. C. P. Hannen, A. Fürstner, *Chem. Eur. J.* **2004**, *10*, 4556–4575; b) P. Morán-Poladura, S. Suárez-Pantiga, M. Piedrafita, E. Rubio, J. M. González, *J. Organomet. Chem.* **2011**, *696*, 12–15; c) P. Morán-Poladura, E. Rubio, J. M. González, *Beilstein J. Org. Chem.* **2013**, *9*, 2120–2128; d) P. Morán-Poladura, E. Rubio, J. M. González, *Angew. Chem. Int. Ed.* **2015**, *54*, 3052–3055; *Angew. Chem.* **2015**, *127*, 3095–3098.
- [8] a) M. I. Bruce, *Chem. Rev.* **1991**, *91*, 197; b) F. E. McDonald, *Chem. Eur. J.* **1999**, *5*, 3103; c) C. Bruneau, P. H. Dixneuf, *Acc. Chem. Res.* **1999**, *32*, 311; d) C. Bruneau, *Top. Organomet. Chem.* **2004**, *11*, 125; e) C. Bruneau, P. H. Dixneuf, *Angew. Chem. Int. Ed.* **2006**, *45*, 2176–2203; *Angew. Chem.* **2006**, *118*, 2232–2260; f) J. A. Varela, C. Saá, *Chem. Eur. J.* **2006**, *12*, 6450; g) *Metal Vinylidenes and Allenylidenes in Catalysis: From Reactivity to Applications in Synthesis* (Eds.: C. Bruneau, P. H. Dixneuf), Wiley-VCH: Weinheim, Germany, **2008**; h) B. M. Trost, A. McClory, *Chem. Asian J.* **2008**, *3*, 164; i) J. M. Lynam, *Chem. Eur. J.* **2010**, *16*, 8238; j) P. H. Dixneuf, *Catal. Lett.* **2015**, *145*, 360–372.
- [9] For literature precedence of methoxide addition to metal carbene and vinylidene, see: a) M. I. Bruce, M. G. Humphrey,

M. J. Liddell, *J. Organomet. Chem.* **1987**, 321, 91–102; b) C. F. Bernasconi, L. Garcia-Rio, *J. Am. Chem. Soc.* **2000**, 122, 3821–3829.

- [10] For **2g** and **2i**, small amounts of regioisomers were isolated as a *cis/trans* mixture, contaminated with inseparable and unidentified side products. For **2h**, no regioisomer was detected.
- [11] Unidentified side products were observed.
- [12] M. M. Hansmann, S. Tšupova, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Chem. Eur. J.* **2014**, 20, 2215–2223.
- [13] Possibly, with extra stabilization, the benzylic cation is less prone to undergoing isomerization, the key step leading to the precursor for Nazarov-type cyclization.
- [14] For thermodynamic data of secondary and tertiary cations, see: D. H. Aue, M. T. Bowers in *Gas Phase Ion Chemistry*, Vol. 2 (Ed.: M. T. Bowers), Academic Press, New York, **1979**, pp. 1.
- [15] An alternative reaction pathway involves gold-catalyzed addition of methanol across the enediyne, which is generated upon elimination of **1a**. For related examples, see: a) J. H. Teles, S. Brode, M. Chabanas, *Angew. Chem. Int. Ed.* **1998**, 37, 1415–1418; *Angew. Chem.* **1998**, 110, 1475–1478; b) A. Corma, V. R. Ruiz, A. Leyva-Pérez, M. J. Sabater, *Adv. Synth. Catal.* **2010**, 352, 1701–1710; c) J. M. Ketcham, B. Biannic, A. Aponick, *Chem. Commun.* **2013**, 49, 4157; d) R. M. P. Veenboer, S. Dupuy, S. P. Nolan, *ACS Catal.* **2015**, 5, 1330–1334; As a result, we prepared the proposed intermediate **G**. However, **G** remained intact under the standard reaction conditions in the presence of 1 equivalent of methanol. If pure methanol was used as solvent, only partial decomposition was observed.



- [16] Only about 75 % of deuterium incorporation at the benzylic carbon atom with about 25 % of hydrogen incorporation implies that the proposed cation isomerization(**C** to **D**, Scheme 2) involves an intramolecular proton-transfer process.
- [17] a) P. Joseph-Nathan, M. R. Hernández-Medel, E. Martínez, M. Rojas-Gardida, C. M. Cerda, *J. Nat. Prod.* **1988**, 51, 675–689; b) R. S. Ward, *Tetrahedron* **1990**, 46, 5029–5041; c) N. A. Petasis, M. A. Patane, *Tetrahedron* **1992**, 48, 5757–5821; d) S. M. Sieburth, N. T. Cunard, *Tetrahedron* **1996**, 52, 6251–6282; e) G. Mehta, V. Singh, *Chem. Rev.* **1999**, 99, 881–930; f) L. Yet, *Chem. Rev.* **2000**, 100, 2963–3008; g) C. Ferrer, C. H. M. Amijs, A. M. Echavarren, *Chem. Eur. J.* **2007**, 13, 1358–1373.

Received: April 20, 2015

Revised: May 22, 2015

Published online: July 16, 2015