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Homogeneous Catalysis

Gold-Catalyzed Cyclizations of *cis*-Enediynes: Insights into the Nature of Gold–Aryne Interactions**

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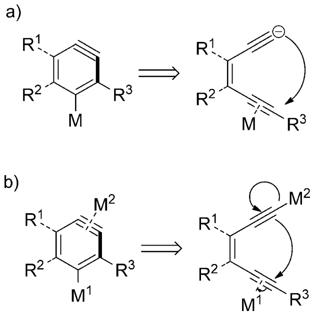
ortho-Benzynes[1] and *ortho*-arynes[2] are reactive and versatile intermediates in organic synthesis.[3] Their diverse chemistry has been further enriched by the formation of metal aryne complexes.[3b,4] They are mostly generated by elimination of two adjacent groups or atoms on the arene ring. The elimination strategy, however, can be synthetically limiting because of difficulties in accessing suitably substituted arenes, demanding reaction conditions, and operational hazards. A notable exception is a de novo aryne formation by intramolecular hexadehydro Diels–Alder reactions.[5]

Considering that the coordination of alkynes to gold complexes often serves as the point of entry into versatile gold catalysis,[6] it is notable that an aryne has seldom served as the substrate for gold catalysis. Although an aryne is highly electrophilic as a result of its low lying LUMO, the HOMO of benzyne was computed to have an energy level similar to that of 2-butyne.[7] Hence, it is not unreasonable to anticipate that the interaction between electrophilic gold complexes and arynes would be plausible. In fact, the study by Zhang and coworkers[8] has invoked a benzyne gold complex, but the interaction between in situ generated benzyne and [Ph_3PAuCl] is not clearly defined and leaves some doubt about its existence. In contrast, another study[9] used in situ generated benzyne to trap a gold intermediate en route to anthracene derivatives, wherein no interaction between gold and benzyne is proposed. We envisioned that gold–aryne interactions, if understood, could serve to advance gold catalysis. Herein, we disclose a study inferring that the interaction between a cationic gold complex and an aryne (i.e., a gold aryne complex) is a transition state and leads to regioisomeric *ortho*-aurophenyl cation intermediates, which could either be trapped by weak nucleophiles or undergo intramolecular C–H insertions by α-carbene gold carbene mesomers.

In our attempt to generate gold aryne complexes, we reasoned that an aryne could be formed upon the addition of a deprotonated terminal alkyne to the other C–C triple bond in a *cis*-enediyne substrate with the assistance of a metal catalyst (Scheme 1 a). Notable in this design is that the strained C–C triple bond in the aryne originates from the terminal alkyne in the substrate and, in contrast to the typical elimination approach, is formally not the bond formed. To implement it, we envisioned that an additional metal could facilitate the pivotal cyclization,[10] as shown in Scheme 1 b, thereby potentially leading to the generation of a metal aryne complex. Moreover, we reasoned that a cationic gold(I) complex could serve as both the metal catalysts M^1 and M^2. It is well established that gold complexes can activate carbon–carbon triple bonds efficiently and, at the meantime, alkynylgold can be readily formed in situ upon reaction with terminal alkynes.[11]



Scheme 1. New approach to the aryne moiety and metal aryne complexes.

We[11] have recently reported the generation of gold vinylidenes (i.e., $\mathbf{A}_{ben}$) from benzene-1,2-dialkynes through a highly regioselective, gold-promoted 5-*endo-dig* cyclization (Scheme 2 a).[12] DFT calculations for the energy surface revealed that $\mathbf{A}_{ben}$ was formed by a bifurcation mechanism in competition with the α-auronaphthyl cation $\mathbf{B}_{ben}$ from a 6-*endo*-dig cyclization[13] (see the Supporting Information of that work). Moreover, $\mathbf{B}_{ben}$ rearranges to its more stable structural isomer $\mathbf{C}_{ben}$ through a low-energy-barrier gold migration. The calculation also predicted the formation of the gold carbene intermediate $\mathbf{E}_{ben}$ from $\mathbf{C}_{ben}$ upon carbene C(sp^3)–H insertion in the next step, thereby indicating the contribution of a mesomeric α-carbene gold carbene (i.e.,

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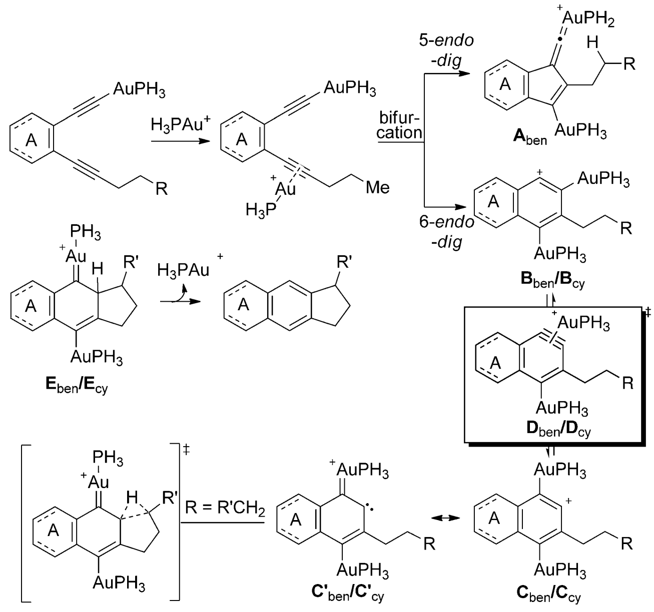
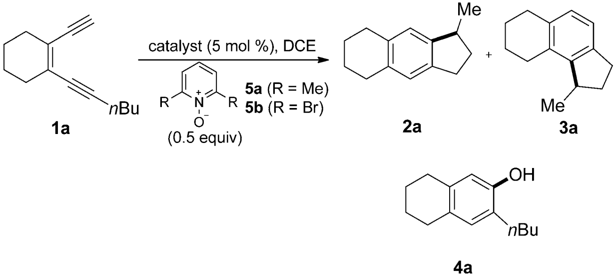


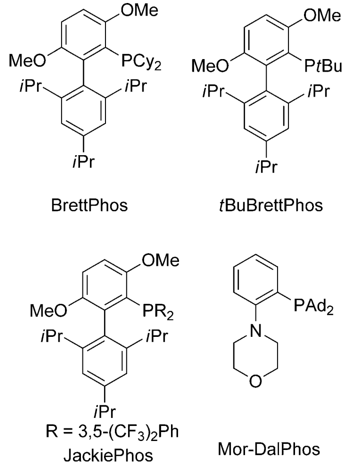
Scheme 2. a) Reaction pathway for ring A = benzene and R = Me as determined from previous DFT calculations. A bifurcation to form two possible intermediates, $\mathbf{A}_{\mathrm{ben}}$ and $\mathbf{B}_{\mathrm{ben}}$, was predicted. The structures are indicated by the subscript ben. b) Reaction pathway for ring A = cyclohexene and R = Et as computed for the formation of **2a**. The structures are indicated by a subscript cy.

Table 1: Initial reaction discovery and optimization.[a]



Entry	Catalyst	Base	T [°C]	t [h]	Yield [%][b]		
					2a	**3a**	**4a**
1	[BrettPhosAu]NTf$_2$	**5a**	RT	17	61	trace	9
2	[BrettPhosAu]NTf$_2$	–	RT	24	24	trace	4
3	[BrettPhosAu]NTf$_2$	**5b**	RT	24	28	trace	4
4	[BrettPhosAu]NTf$_2$	TsNa	RT	24	30	trace	5
5	[BrettPhosAu]NTf$_2$	lutidine	60	24	61	trace	4
6	[*t*BuBrettPhosAu]NTf$_2$	**5a**	60	24	45	trace	10
7	[JackiePhosAu]NTf$_2$	**5b**[c]	RT	20	50	trace	trace
8	Mor-DalPhosAuNTf$_2$	**5a**	60	11	83[d]	trace	trace
9	[Mor-DalPhosAuCl]/ NaBAr$^F_4$	**5a**	60	20	76	trace	trace
10	[Ph$_3$PAu]NTf$_2$	**5a**	60	3.5	8	54	trace

[a] Reaction run in flame-dried vial using dry DCE as solvent. [**1a**] = 0.05 M. [b] Estimated by ^{1}H NMR spectroscopy using diethyl phthalate as the internal reference. [c] 1.1 equiv [d] Yield of isolated product. Tf = trifluoromethanesulfonyl, Ts = 4-toluenesulfonyl.



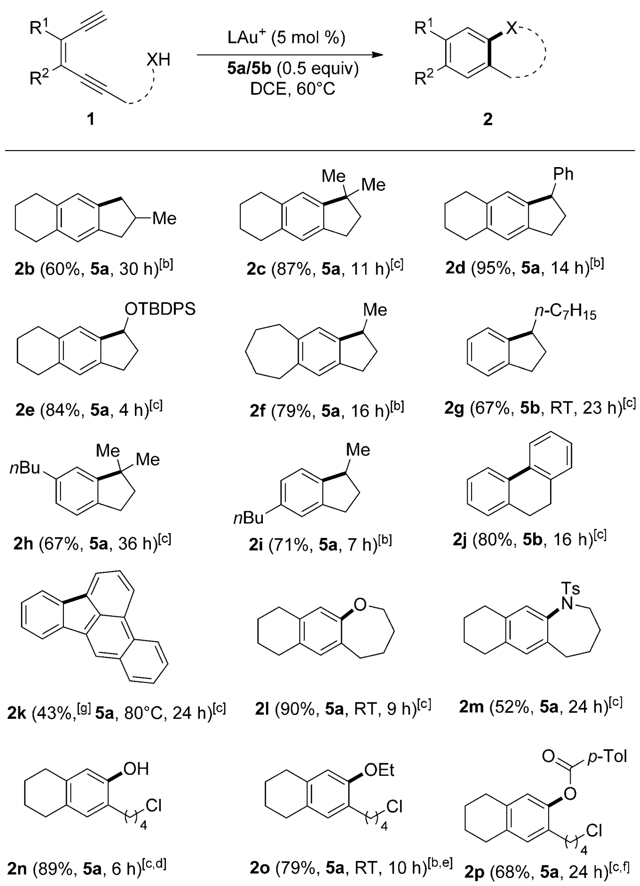
$\mathbf{C'}_{\mathrm{ben}}$). Although the naphthalene-type products were not detected, likely due to the fact that the bulky BrettPhos[14] was used in place of PH$_3$ as the ligand in our experiments, we were nevertheless intrigued by the 6-*endo*-dig reaction path.

The isomerization from $\mathbf{B}_{\mathrm{ben}}$ to $\mathbf{C}_{\mathrm{ben}}$ was calculated to proceed via a transition state in the form of an aryne-coordinated gold complex (i.e., $\mathbf{D}_{\mathrm{ben}}$). The phenyl cationic structures $\mathbf{B}_{\mathrm{ben}}$ and $\mathbf{C}_{\mathrm{ben}}$ can be viewed as resulting from a shift of the gold atom to the ends of the coordinating triple bond in $\mathbf{D}_{\mathrm{ben}}$. As a result, $\mathbf{B}_{\mathrm{ben}}$ and $\mathbf{C}_{\mathrm{ben}}$ appear to be the appropriate structures from the interaction between a cationic gold(I) and an aryne. It is most likely that they are more electrophilic than typical arynes because of their aryl cation nature, which would be consistent with known silver catalysis[15] where in situ generated benzyne in the presence of Ag$^+$ reacts with significantly enhanced electrophilicity.

After having no success with benzene-1,2-dialkyne substrates in achieving the desired 6-*endo-dig* cyclization, we switched to the *cis*-enediyne **1a**, and the reaction discovery and optimizations are shown in Table 1. Much to our delight, the C–H insertion product **2a** was indeed formed when the substrate was treated with [BrettPhosAu]NTf$_2$ (5 mol %) and 2,6-lutidine *N*-oxide (**5a**, 0.5 equiv) in 1,2-dichloroethane (DCE; entry 1). The formation of **2a** can be readily rationalized by invoking the mechanism shown in Scheme 2 b, and is additionally supported by DFT calculations (see the Supporting Information). The additive **5a**, in line with our previous study, acted as a mild base to facilitate the formation of the alkynylgold species in Scheme 2. This mechanism can also explain the formation of the phenol **4a**, which is attributed to the regioselective addition of adventitious H$_2$O to the *ortho*-aurophenyl cation $\mathbf{C}_{\mathrm{ben}}$. The side-product **3a**, though present in trace amounts, is likely formed by a mechanism similar to that reported by Liu and co-workers for the use of PtCl$_2$ as the catalyst.[16]

Other base additives and gold complexes were then examined to improve the intended chemistry. In the absence of a base, only 24 % of **2a** was obtained (Table 1, entry 2). Other bases such as 2,6-dibromopyridine *N*-oxide (**5b**; entry 3) and TsNa (conjugate acid pK_a = 1.99;[17] entry 4) could not improve the reaction, either. With the more basic lutidine (entry 5), the reaction was slower but resulted in an identical yield to that of entry 1. With regard to the gold catalyst, [*t*BuBrettPhosAu]NTf$_2$ (entry 6), a bulkier catalyst than [BrettPhosAu]NTf$_2$, and [JackiePhosAu]NTf$_2$ (entry 7), a more Lewis-acidic catalyst, were less efficient. However, Mor-DalPhos[18] turned out to be the most efficient ligand, thus affording **2a** in 83 % yield (entry 8). The use of the less coordinating $BAr^F{}_4{}^-$,[19] however, did not lead to additional improvement (entry 9). In all the cases discussed above, **3a** was formed in trace amounts, but much to our surprise the Gagosz catalyst, $[Ph_3PAu]NTf_2$,[20] promoted the formation of **3a** at the expense of **2a** (entry 10). It appears that the smaller steric size of Ph_3P is the cause for the switch of selectivity.[21]

With the optimized reaction conditions in hand, we then studied the scope of the reaction featuring C–H insertions, and the results are shown Scheme 3. In these reactions, 4 Å molecular sieves were added to minimize the formation of phenol derivatives. Various types of aliphatic C–H bonds, including a primary C–H (**2b**), a tertiary C–H (**2c**), a benzylic C–H (**2d**), and a C–H α to a silyoxy group (for **2e**) were readily inserted, thus leading to indane derivatives in mostly excellent yields. Changing the cyclohexane ring in the enediyne substrates discussed so far revealed that a smaller cyclopentene ring hindered the reaction as the corresponding substrate mostly remained unchanged. However, a bigger cycloheptene ring was inconsequential, and the indane **2f** was isolated in 79% yield. Moreover, the ring could be completely removed (**2g**) or replaced with an *n*-butyl group at either end of the C–C double bond (**2h** and **2i**) without significantly impacting the reaction yield. Notably, in several cases the reaction conditions deviated from the optimized reaction conditions (Table 1, entry 8) by the use of a different catalyst (e.g., $BrettPhosAuNTf_2$ for **2c**,**e**,**g**,**h**) and base (e.g., **5b** for **2g**).

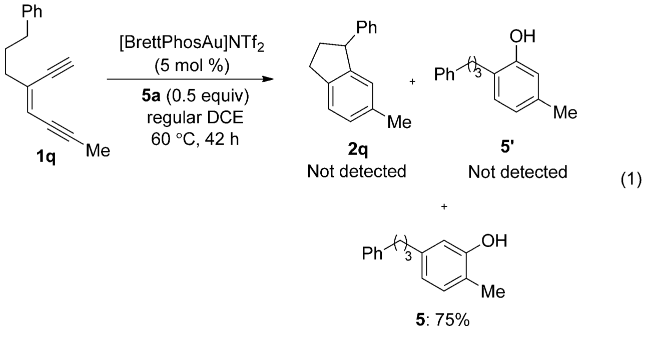


Scheme 3. Reaction scope of aryne gold chemistry.[a] [a] [**1**] = 0.05 M. Reactions were run in flame-dried vials in the presence of 4 Å M.S. except entry 13. Yield of isolated product reported. [b] [MorDalPhosAu]NTf_2 was used. [c] [BrettPhosAu]NTf_2 was used. [d] Wet DCE as solvent. [e] 10 equiv of ethanol was used. [f] 5 equiv of *p*-toluic acid was used. [g] 6% of starting material recovered. TBDPS = *tert*-butyldiphenylsilyl.

Besides the C–H insertions by the carbene-type reactivity from the mesomer $\mathbf{C'_{cy}}$ (Scheme 2b), the phenyl cation character of the isomeric $\mathbf{C_{cy}}$ could also be exploited. For example, a tethered phenyl group served as the reacting nucleophile partner, and the reaction led to the formation of 9,10-dihydrophenanthrene (**2j**; Scheme 3) in 80% yield. When phenanthrene was the tethered nucleophile, the reaction resulted in a direct transformation of an enediyne into pentacyclic benzo[*e*]acephenanthrylene in a serviceable yield (**2k**). We were pleased to find out that a tethered HO group worked well as the nucleophile, and the tetrahydrooxepin **2l** was formed in 90% yield. This highly efficient formation of a seven-membered O-heterocycle and the lack of competing C–H insertion are particularly noteworthy, thus suggesting that $\mathbf{C_{cy}}/\mathbf{C'_{cy}}$ prefers to react as a phenyl cation (i.e., in the form of $\mathbf{C_{cy}}$). This observation is consistent with cationic gold complexes as strong soft Lewis acids[6] but weak π-back donors.[22] Similarly, a tethered sulfonamide was able to trap the cationic intermediate to deliver the seven-membered N-heterocycle **2m** in a moderate yield. Again, no competing intramolecular C–H insertion was detected.

During the scope study of C–H insertion reactions, we found that a 4-chlorobutyl group at the alkyne terminus did not participate in the C–H insertion. While this result again suggests that the carbene reactivity of $\mathbf{C'_{cy}}$ might be limited, the chloride substrate was used to examine intermolecular trapping of $\mathbf{C_{cy}}$. With wet DCE as the solvent, the phenol **2n** was indeed formed in a very good yield (Scheme 3). Similarly, ethanol and *p*-toluic acid, also used in excess, were suitable trapping nucleophiles, and the phenyl ether **2o** and the phenyl ester **2p** were isolated in 79% and 68% yields, respectively. Importantly, these intermolecular trapping reactions were highly regioselective as the isomer anticipated from trapping of the phenyl cation of type $\mathbf{B_{cy}}$ (Scheme 2b) was not detected in each case.

Attempts to switch the regioselectivity were unsuccessful. For example, subjecting the enediyne **1q** to the typical reaction conditions in DCE led to the formation of the phenol **5** in 75% yield in 42 hours [Eq. (1)]. Neither the regioiso-



(1)

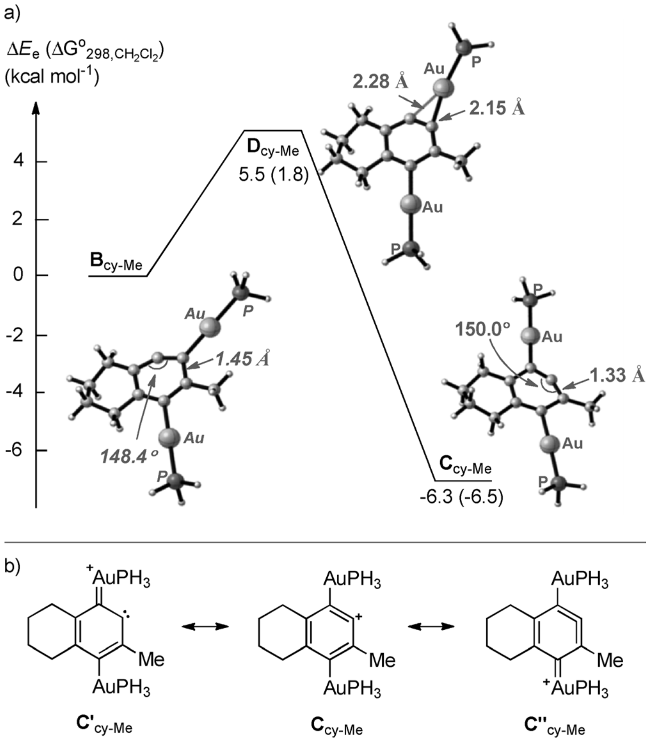
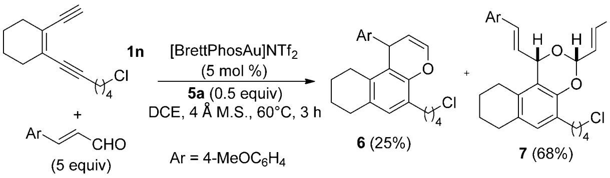


Figure 1. a) The rearrangement of $\mathbf{B}_{cy\text{-}Me}$ into $\mathbf{C}_{cy\text{-}Me}$. The energy diagram shows the electronic energies and free energies (see value within parentheses) in methylene chloride, as well as the structures optimized at the M06/6-31+G(d,p)/SDD(Au) level of theory. b) The resonance structures of $\mathbf{C}_{cy\text{-}Me}$.

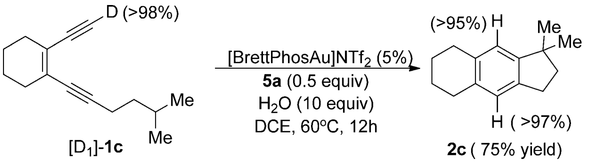
meric phenol **5′** nor the C–H insertion product **2q** by an α-carbene gold carbene mesomeric to **B** was detected. This is consistent with the DFT calculations (Figure 1 a), where $\mathbf{B}_{cy\text{-}Me}$ has a very low barrier to rearrangement to $\mathbf{C}_{cy\text{-}Me}$ and is 6.5 kcal mol^{-1} less stable. It is expected that $\mathbf{B}_{cy\text{-}Me}$ cannot be trapped because of its predicted, very short lifetime in solution. The reason for the enhanced stability of $\mathbf{C}_{cy\text{-}Me}$ could be attributed to the contribution of its mesomeric bent allene form, $\mathbf{C}''_{cy\text{-}Me}$ (Figure 1 b),[23] which is in accordance with the DFT-optimized structure in which the bond length of C2-C3 is 1.33 Å, and is significantly shorter than 1.40 Å in benzene. In contrast, the corresponding bond length for $\mathbf{B}_{cy\text{-}Me}$ is 1.45 Å.

It is well known that arynes can undergo [4+2] cycloaddition with furan,[3] however, our attempts to perform the reaction with the enediyne substrates in the presence of gold catalysts led to no desired product. In contrast, the reaction of **1n** with *trans-p*-methoxycinnamaldehyde did lead to the formation of the [4+2] adduct **6** [Eq. (2), M.S. = molecular sieves]. The formation of the [2+2+2] adduct **7** as the major product suggests that **6** is most likely generated by a stepwise process involving an *ortho*-aurophenyl cation of type $\mathbf{C}_{cy}$.

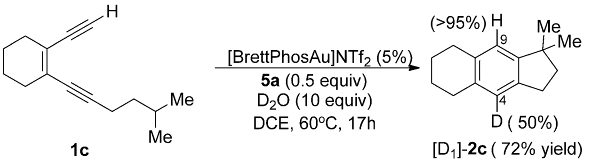


(2)

Deuterium-labeling studies were performed to gain additional experimental support for the reaction mechanism. First, the alkyne terminus of **1c** was labeled by a deuterium. With 10 equivalents of H_2O added, the reaction resulted in nearly complete loss of the isotope [Eq. (3)]. In contrast, with the same amount of D_2O as the additive, the nonlabeled **1c** proceeded to give [D$_2$]-**2c** with a significant amount of deuterium at C4, but very little at C9 [Eq. (4)]. These two experiments confirm that the alkyne terminal hydrogen is removed as a proton during the reaction and the C4 hydrogen atom is installed by protonation. The origin of the C9 hydrogen atom was revealed experimentally by deuterium-labeling the side chain in a related substrate [Eq. (5)]. All the isotope-labeling results are consistent with the mechanism shown in Scheme 2 b.



(3)



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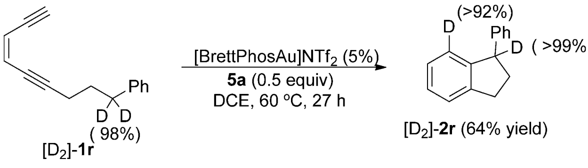

(5)

The remaining question with this chemistry is how the lack of the fused benzene ring in the substrates led to a complete switch of the initial cyclization from 5-*endo-dig*[11] to 6-*endo-dig* (Scheme 2). It can be explained by considering the difference in gained aromatic stabilization: when ring A is a benzene ring, the additional resonance energy gained upon the 6-*endo-dig* cyclization is 28 kcal mol^{-1} (64 kcal mol^{-1} for naphthalene and 36 kcal mol^{-1} for benzene). However, when ring A is neither benzene nor nonexistent, the aromaticity gained by the newly formed benzene ring would be 8 kcal mol^{-1} greater (36 kcal mol^{-1}). Our DFT calculations in methylene chloride solution at 298 K confirm this idea. We find that the free energies for the formation of **A** and **B** favor **B** by 12.0 kcal mol^{-1} when the fused ring is cyclohexene, and by 15.6 kcal mol^{-1} when benzene is the fused ring. These values are much larger than the 2.2 kcal mol^{-1} difference observed for the fused ring as a benzene, where the 5-*endo*-dig product is favored.[11] It is not unreasonable to imagine in the bifurcation mechanism that making the 6-*endo-dig* product much more stable relative to the 5-*endo-dig* product could skew the energy surface in a fashion such that the 6-*endo-dig* path is favored.

In summary, we have disclosed a dual gold-catalyzed cyclization[24] of *cis*-enediynes, which offers a new approach to various substituted indanes, heterocycle-fused benzenes, and phenol derivatives. This chemistry represents a dramatic switch from the initial cyclization of the previously observed 5-*endo*-dig[11] to the 6-*endo*-dig path in the bifurcation mechanism. Besides its synthetic utility, this chemistry offers, for the first time, insights on the interaction between cationic gold(I) and arynes. This interaction can be viewed as leading to a gold aryne transition state which results in the formation of two regioisomeric *ortho*-auroaryl cation intermediates, and can be considered to be the result of a shift of the metal along the highly strained C–C triple bond. The more stable of these aryl cation forms reacts regiospecifically with a range of nucleophiles in a manner similar to arynes, though the cation should be more electrophilic. While cycloaddition reactions observed with arynes could not be realized, new reactivities with the polarized forms, such as facile intramolecular insertions into C(sp^3)–H bonds through mesomeric α-carbene gold carbenes are realized.

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[1] C. Wentrup, *Aust. J. Chem.* **2010**, *63*, 979–986.

[2] H. H. Wenk, M. Winkler, W. Sander, *Angew. Chem.* **2003**, *115*, 518–546; *Angew. Chem. Int. Ed.* **2003**, *42*, 502–528.

[3] For selected reviews on arynes, see: a) S. V. Kessar in *Comprehensive organic synthesis: selectivity, strategy, and efficiency in modern organic chemistry*, *Vol. 4*, 1st ed. (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, **1991**, pp. 483–515; b) H. Pellissier, M. Santelli, *Tetrahedron* **2003**, *59*, 701–730; c) R. Sanz, *Org. Prep. Proced. Int.* **2008**, *40*, 215–291; d) T. Kitamura, *Aust. J. Chem.* **2010**, *63*, 987–1001; e) C. M. Gampe, E. M. Carreira, *Angew. Chem.* **2012**, *124*, 3829–3842; *Angew. Chem. Int. Ed.* **2012**, *51*, 3766–3778; f) P. M. Tadross, B. M. Stoltz, *Chem. Rev.* **2012**, *112*, 3550–3577.

[4] For examples of metal aryne chemistry, see: a) E. W. Gowling, S. F. A. Kettle, G. M. Sharples, *J. Chem. Soc. Chem. Commun.* **1968**, 21–22; b) S. L. Buchwald, R. B. Nielsen, *Chem. Rev.* **1988**, *88*, 1047–1058; c) R. Broene, S. Buchwald, *Science* **1993**, *261*, 1696–1701; d) J. H. Tidwell, S. L. Buchwald, *J. Am. Chem. Soc.* **1994**, *116*, 11797–11810; e) K. L. Houseknecht, K. E. Stockman, M. Sabat, M. G. Finn, R. N. Grimes, *J. Am. Chem. Soc.* **1995**, *117*, 1163–1164; f) W. M. Jones, J. Klosin, *Adv. Organomet. Chem.* **1998**, *42*, 147–221.

[5] a) T. R. Hoye, B. Baire, D. Niu, P. H. Willoughby, B. P. Woods, *Nature* **2012**, *490*, 208–212; b) A. Z. Bradley, R. P. Johnson, *J. Am. Chem. Soc.* **1997**, *119*, 9917–9918; c) K. Miyawaki, R. Suzuki, T. Kawano, I. Ueda, *Tetrahedron Lett.* **1997**, *38*, 3943–3946; d) R. Karmakar, P. Mamidipalli, S. Y. Yun, D. Lee, *Org. Lett.* **2013**, *15*, 1938–1941.

[6] For selected reviews, see: a) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211; b) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*, 3351–3378; c) L. Zhang, J. Sun, S. A. Kozmin, *Adv. Synth. Catal.* **2006**, *348*, 2271–2296; d) E. S. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326–3350; e) Z. Li, C. Brouwer, C. He, *Chem. Rev.* **2008**, *108*, 3239–3265; f) N. T. Patil, Y. Yamamoto, *Chem. Rev.* **2008**, *108*, 3395–3442; g) S. M. Abu Sohel, R.-S. Liu, *Chem. Soc. Rev.* **2009**, *38*, 2269–2281; h) M. N. Hopkinson, A. D. Gee, V. Gouverneur, *Isr. J. Chem.* **2010**, *50*, 675–690; i) A. Fürstner, P. W. Davies, *Angew. Chem.* **2007**, *119*, 3478–3519; *Angew. Chem. Int. Ed.* **2007**, *46*, 3410–3449; j) S. Sengupta, X. Shi, *ChemCatChem* **2010**, *2*, 609–619; k) F. López, J. L. Mascarenas, *Beilstein J. Org. Chem.* **2011**, *7*, 1075–1094; l) A. Corma, A. Leyva-Perez, M. J. Sabater, *Chem. Rev.* **2011**, *111*, 1657–1712; m) B. Biannic, A. Aponick, *Eur. J. Org. Chem.* **2011**, 6605–6617.

[7] N. G. Rondan, L. N. Domelsmith, K. N. Houk, A. T. Bowne, R. H. Levin, *Tetrahedron Lett.* **1979**, *20*, 3237–3240.

[8] C. Xie, Y. Zhang, Y. Yang, *Chem. Commun.* **2008**, 4810–4812.

[9] N. Asao, K. Sato, *Org. Lett.* **2006**, *8*, 5361–5363.

[10] For examples of this type of bond formation, see: a) Y. Odabachian, X. F. Le Goff, F. Gagosz, *Chem. Eur. J.* **2009**, *15*, 8966–8970; b) S. Sun, J. Kroll, Y. Luo, L. Zhang, *Synlett* **2012**, 54.

[11] L. Ye, Y. Wang, D. H. Aue, L. Zhang, *J. Am. Chem. Soc.* **2012**, *134*, 31–34.

[12] a) A. S. K. Hashmi, M. Wieteck, I. Braun, P. Nösel, L. Jongbloed, M. Rudolph, F. Rominger, *Adv. Synth. Catal.* **2012**, *354*, 555–562; b) A. S. K. Hashmi, I. Braun, M. Rudolph, F. Rominger, *Organometallics* **2012**, *31*, 644–661; c) A. S. K. Hashmi, M. Wieteck, I. Braun, M. Rudolph, F. Rominger, *Angew. Chem.* **2012**, *124*, 10785–10789; *Angew. Chem. Int. Ed.* **2012**, *51*, 10633–10637; d) A. S. K. Hashmi, I. Braun, P. Nösel, J. Schädlich, M. Wieteck, M. Rudolph, F. Rominger, *Angew. Chem.* **2012**, *124*, 4532–4536; *Angew. Chem. Int. Ed.* **2012**, *51*, 4456–4460.

[13] For a study involving 6-*endo*-dig cyclization, see: a) S. Naoe, Y. Suzuki, K. Hirano, Y. Inaba, S. Oishi, N. Fujii, H. Ohno, *J. Org. Chem.* **2012**, *77*, 4907–4916; for a closely related work, which was published after our work was submitted, see: b) M. M. Hansmann, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem.* **2013**, *125*, 2653–2659; *Angew. Chem. Int. Ed.* **2013**, *52*, 2593–2598.

[14] a) B. P. Fors, D. A. Watson, M. R. Biscoe, S. L. Buchwald, *J. Am. Chem. Soc.* **2008**, *130*, 13552–13554; b) L. Ye, W. He, L. Zhang, *Angew. Chem.* **2011**, *123*, 3294–3297; *Angew. Chem. Int. Ed.* **2011**, *50*, 3236–3239.

[15] a) L. Friedman, *J. Am. Chem. Soc.* **1967**, *89*, 3071–3073; b) E. Vedejs, R. A. Shepherd, *Tetrahedron Lett.* **1970**, *11*, 1863–1864; c) L. A. Paquette, *J. Chem. Soc. Chem. Commun.* **1971**, 1076–1077.

[16] B. P. Taduri, Y.-F. Ran, C.-W. Huang, R.-S. Liu, *Org. Lett.* **2006**, *8*, 883–886.

[17] R. K. Burkhard, D. E. Sellers, F. DeCou, J. L. Lambert, *J. Org. Chem.* **1959**, *24*, 767–769.

[18] a) K. D. Hesp, M. Stradiotto, *J. Am. Chem. Soc.* **2010**, *132*, 18026–18029; b) R. J. Lundgren, B. D. Peters, P. G. Alsabeh, M. Stradiotto, *Angew. Chem.* **2010**, *122*, 4165–4168; *Angew. Chem. Int. Ed.* **2010**, *49*, 4071–4074; c) Y. Luo, K. Ji, Y. Li, L. Zhang, *J. Am. Chem. Soc.* **2012**, *134*, 17412–17415.

[19] H. Nishida, N. Takada, M. Yoshimura, T. Sonoda, H. Kobayashi, *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2600–2604.

[20] N. Mézailles, L. Ricard, F. Gagosz, *Org. Lett.* **2005**, *7*, 4133–4136.

[21] Detailed studies of this switch of regioselectivity will be disclosed soon.

[22] G. Seidel, R. Mynott, A. Fürstner, *Angew. Chem.* **2009**, *121*, 2548–2551; *Angew. Chem. Int. Ed.* **2009**, *48*, 2510–2513.

[23] For bent allenes, see: a) M. M. Hänninen, A. Peuronen, H. M. Tuononen, *Chem. Eur. J.* **2009**, *15*, 7287–7291; b) M. T. Reetz, K. Sommer, *Eur. J. Org. Chem.* **2003**, 3485–3496; c) A related structure was mentioned in Hashmi's work in Ref. [13b].

[24] A. Gómez-Suárez, S. P. Nolan, *Angew. Chem.* **2012**, *124*, 8278–8281; *Angew. Chem. Int. Ed.* **2012**, *51*, 8156–8159.