

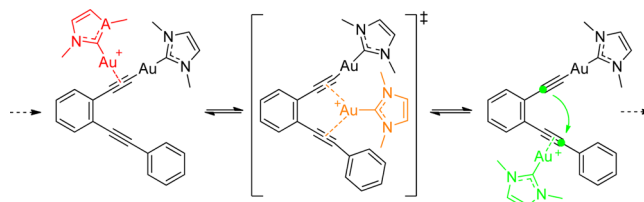
## Dual Gold Catalysis

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### CONSPECTUS



For more than a decade the innovative field of homogeneous catalysis by gold was dominated by the interaction of the substrate molecule with one gold center, in most cases in mononuclear gold complexes. The initial interaction was typically a  $\pi$ -coordination of a carbon–carbon double bond to the gold, an activation of the unsaturated substrate molecule by a  $\pi$ -acidic metal center. Only recently clear evidence for reactions that involve the activation of organic substrates by two gold centers was obtained. In that new class of gold-catalyzed reactions the two gold centers interact with the substrate in a very different way. One gold complex is  $\sigma$ -bonded to a terminal alkynyl group in the substrate, the other one is  $\pi$ -coordinated. Only in a few cases, a combination  $\pi$ -coordination and  $\sigma$ -coordination to the same alkyne, which is the energetically preferred mode of interaction with two gold centers, initiates the reaction. In most of the cases, the reaction proceeds through an intermediate with one alkyne  $\sigma$ -bonded to one gold complex and a different alkyne  $\pi$ -coordinated to the second gold complex.

Experimental and computational results for many new reactions provide a clear picture of the overall sequence of elemental steps of these conversions; some of the steps are unprecedented in organometallic catalysis and chemistry. For example, the reaction of diynes can involve gold vinylidene-like species as very reactive substructures formed by a 5-*exo*-dig cyclization. NBO analysis indicates no gold–carbon double bond character in these “vinylidenes”. In other reactions, a 6-*endo*-dig cyclization is energetically preferred; after that gold aryne complexes are not local minima but transition states of a 1,2-shift of gold. Computational studies showed a good correlation of the cyclization mode with the aromaticity of the intermediate. For both the 5-*exo*-dig and the 6-*endo*-dig cyclization modes, the intermediates are able to react even with unactivated alkyl-C,H bonds, in low yields even in intermolecular reactions. The final step of the catalytic cycles is also remarkable, because the protodeauration has to occur with the next alkyne substrate molecule. Only then the next gold acetylide is formed directly and a loss of selectivity can be avoided. A computational study suggests that two gold complexes are on the substrate throughout the catalytic cycle. The most recent results indicate that analogous intermediates can be accessible by the reaction of other electrophiles with gold acetylides.

With regard to organic synthesis, the overall catalytic conversions open up a universe of new possibilities. Selective C,H-activations now allow to one use usually innocent alkyl side chains for additional annellation reactions by an  $sp^3$ -C,H activation. The C,H activation can even be combined with halogen transfer reactions, directly providing vinyl iodides as versatile building blocks. Short and efficient routes to different carbo- and heterocycles including benzocyclobutenes, fulvenes, and pentalenes demonstrate the synthetic potential not only for total synthesis but also for material science.

### 1. Introduction

After a phase of only sporadic activity<sup>1</sup> and a subsequent “pre-peak” of activity on the catalytic asymmetric aldol reaction by Ito, Sawamura, Hayashi,<sup>2</sup> and Togni<sup>3</sup> between 1986 and 1998,<sup>4</sup> as well as some nucleophilic additions to alkynes by Utimoto<sup>5</sup> and Teles,<sup>6</sup> two publications<sup>7</sup> from 2000 demonstrated the enormous potential of homogeneous

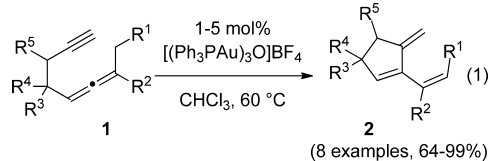
gold catalysis for organic synthesis and initiated a development of the field to a highly active sector in catalysis research.<sup>8</sup> During the first years, the research was dominated by methodology development, but later detailed mechanistic studies were conducted, too.<sup>9</sup> In the last years, an increasing number of applications in synthesis were reported, not only utilizing gold catalysis for the preparation of building blocks

and segments of the target molecules, but also in the last steps.<sup>10</sup>

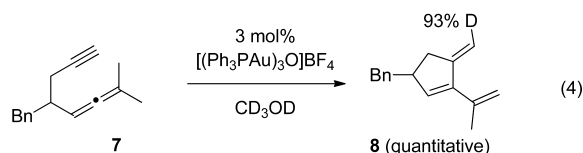
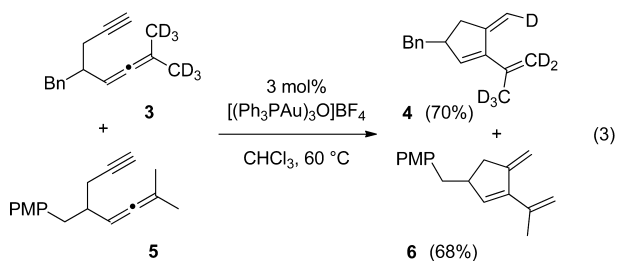
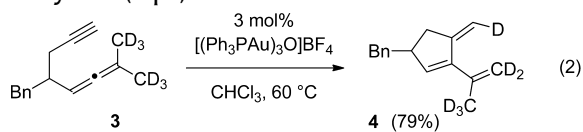
The vast majority of these reactions are based on an activation of the substrate with only *one* gold center. Following early assumptions on a possible simultaneous activation of substrates by *two* gold centers, since early 2012 deep insight was achieved and innovative synthetic perspectives opened up by a series of reports. Herein the basic principles and the current status of this quickly progressing new sector of dual gold catalysis will be discussed.

## 2. First Evidence

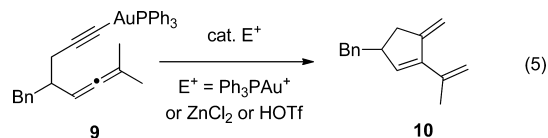
The enyne cycloisomerization has always been a hot topic in homogeneous gold catalysis.<sup>11,12</sup> Based on mechanistic investigation, in 2008 Houk, Toste, and co-workers published a fascinating new reaction mechanism for the cycloisomerization of 1,5-allenynes **1**.<sup>13</sup> With the [(Ph<sub>3</sub>PAu)<sub>3</sub>O]BF<sub>4</sub> catalyst, the interesting cross-conjugated trienes **2** (eq 1) are formed.



Only terminal alkynes delivered **2**, and deuterium labeling studies with **3** revealed a diastereoselective hydrogen transfer (eq 2). A crossover experiment (eq 3) indicated an intramolecular hydrogen transfer. Crucial was the exchange of the hydrogen atom of the terminal alkyne for deuterium if the reaction was run in MeOD, suggesting the presence of gold acetylides (eq 4).



With a value of 1.8–1.9, the primary kinetic isotope effect in this 1,5-H-shift was significantly smaller than that in other 1,5-sigmatropic shifts. Computational chemistry allowed a study of several mechanistic possibilities in detail. Additional experiments included the preparation of the gold(I) acetylide **3**, which is a stable compound, but when catalytic amounts of cationic gold(I) catalysts or Lewis acids like zinc(II) or even triflic acid are present, the product **4** is formed. It is important to note that the corresponding silver acetylides did not show this conversion.

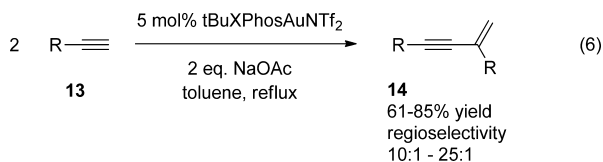


In the introduction of their publication, they announced “...proceeds via a unique mechanism ...”, but in the conclusion, the wording was more careful: “combined experimental and computational evidence reveal that a mechanism involving nucleophilic addition of an allene double bond to a phosphinegold-complexed phosphinegold acetylide is more likely than oxidative cyclization or simple nucleophilic addition to phosphinegold-complexed substrate”.<sup>13</sup> Scheme 1 shows the spectacular catalytic cycle suggested. An important motif for a catalytic cycle for the first time, we see the presence of two gold complexes, one  $\sigma$ -bonded and one  $\pi$ -coordinated (species **A**).

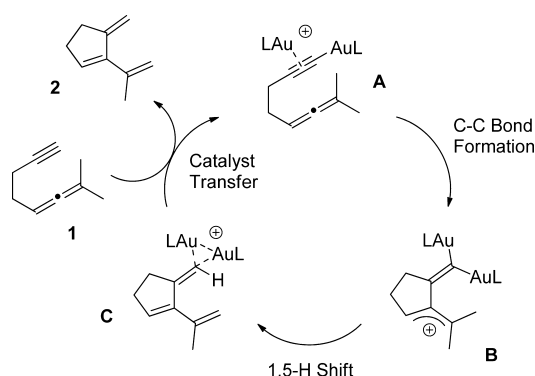
In 2009, Gagosz and co-workers reported the formation of ten-membered medium-sized cycloalkynes **12** from 1,10-diynes **11**.<sup>14</sup> Once more, the ligand on gold is a bulky phosphane ligand. In addition to the mechanism proposed in Scheme 2a, they also considered an alternative mechanism in analogy to the results of Houk and Toste<sup>13</sup> (Scheme 2b). The deuterium isotope labeling experiments did not allow them to distinguish between these two possibilities. The catalyst transfer step suggested by Houk and Toste is not considered by Gagosz, but the potential function of the counterion as a proton acceptor was discussed by Gagosz, an argument later also used by Corma<sup>15</sup> and Widenhofer<sup>16</sup> (see below) for the formation of species related to **A** and **I**.

Gagosz et al. considered all possibilities,<sup>14</sup> and in the Supporting Information the conceivable mechanisms are shown, including two pathways that were not based on dual activation and did not accord with some of the labeling studies. Gagosz for the first time assumes a  $\sigma$ - and a  $\pi$ -bonded gold species at two different alkynyl groups of the substrate (**F**).

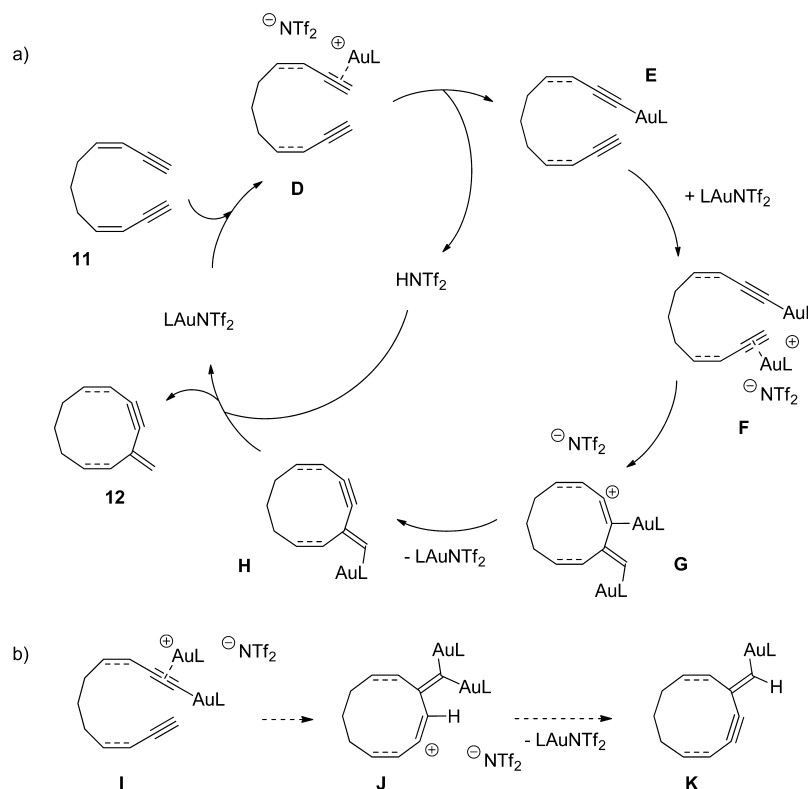
Three years later, in 2012, an intermolecular version of this alkyne homodimerization forming **14** was reported by Zhang, but no new mechanistic insights were provided in this synthetic publication (eq 6).<sup>17</sup> The authors propose an intermolecular reaction of a gold acetylide derived from **13** with a second substrate molecule  $\pi$ -coordinated to another LAu<sup>+</sup> unit, which resembles Gagosz's intermediate **F**.



**SCHEME 1.** Mechanistic Proposal of Houk and Toste



**SCHEME 2.** Mechanistic Proposal of Gagosz



$\sigma,\pi$ -Digold acetylides are a species not uncommon in organometallic chemistry, as recently summarized by Schmidbaur.<sup>18</sup> The suggested reactivity was new; only distorted tetrahedral dimers and larger oligomers had been described for some special alkynes in the solid state, and DOSY measurements indicated that some of them are also dimeric in solution.<sup>19–23</sup> It has been reported that a maximum of four gold centers can coordinate to ethyne.<sup>24</sup> The maximum number of alkynes  $\pi$ -coordinated to one single gold center is three.<sup>25</sup> Also Laguna and co-workers<sup>26</sup> have published  $\sigma,\pi$ -digold acetylides bearing two phosphane ligands at the  $\pi$ -coordinated gold and a very unusual, unsymmetrical coordination of the alkyne with a gold–gold interaction.

It was unclear how a gold acetylide is initially formed. Only in 2011 Corma and co-workers<sup>15,27</sup> as well as Widenhoefer and co-workers studied this in detail.<sup>16</sup> Widenhoefer in his investigation proved that  $\text{NHCAu}^+$ , when generated in situ at low temperatures, forms a  $\pi$ -complex with phenylacetylene. This  $\pi$ -complex converts to  $\sigma,\pi$ -digold acetylides at temperatures above  $-20^\circ\text{C}$ . Corma synthesized a series of  $\sigma,\pi$ -digold acetylides bearing bulky phosphane ligands on gold. These complexes possess very good catalytic activity in the *intermolecular* alkene/alkyne [2 + 2] cycloaddition

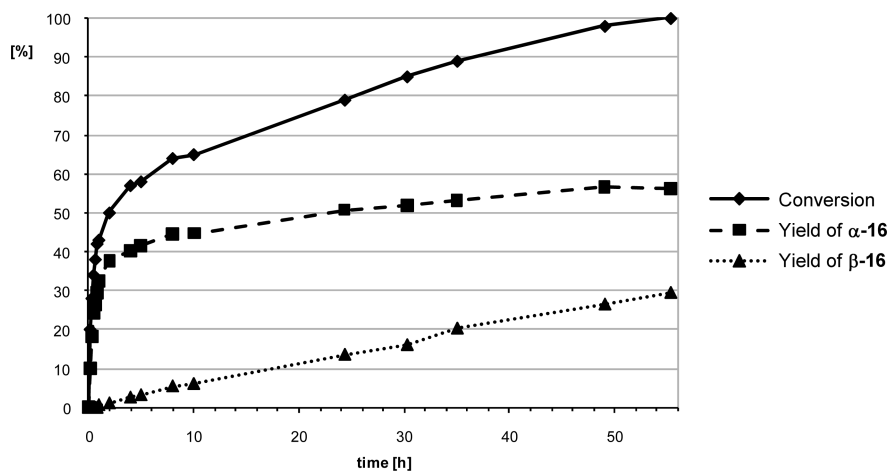
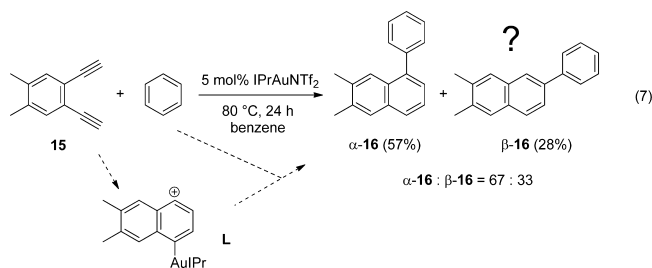


FIGURE 1. The time–conversion graph indicated a switch of mechanism.

developed by Echavarren.<sup>28</sup> For intramolecular enyne cycloisomerizations Fensterbank, Gimbert, and co-workers<sup>29</sup> indeed could detect the dinuclear complexes by electrospray ionization mass spectrometry and could show that the gold-acetylide has a superior affinity for the  $\pi$ -coordination of a  $\text{LAu}^+$  fragment; but their investigation does not indicate that this species is involved in the cycloisomerization reaction.

### 3. An Unexpected Reaction

Then, in 2012, the investigation of diynes of type **15** raised significant questions.<sup>30</sup> Unexpectedly, not only  $\alpha$ -**16** but also a significant amount of  $\beta$ -**16** was isolated. Pure  $\alpha$ -**16** is not converted to  $\beta$ -**16** by a rearrangement induced by the catalyst or by an initial hydroarylation of one of the alkynes followed by an enyne cycloisomerization. The puzzling mechanism for the formation of  $\beta$ -**16** was unknown and thus of significant interest.



A long series of mechanistic experiments followed, the crucial results leading to a first mechanistic hypothesis were as follows: (a) a kinetic analysis revealed that initially mainly  $\alpha$ -**16** is fast, but after less than 50% conversion becomes very slow. At the same time the formation of  $\beta$ -**16** becomes visible (Figure 1). This clearly indicated a switch of mechanism. The gold species might change; a slow formation of the gold(I)–acetylide complex **17** (Figure 2) could be assumed.

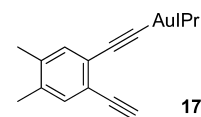
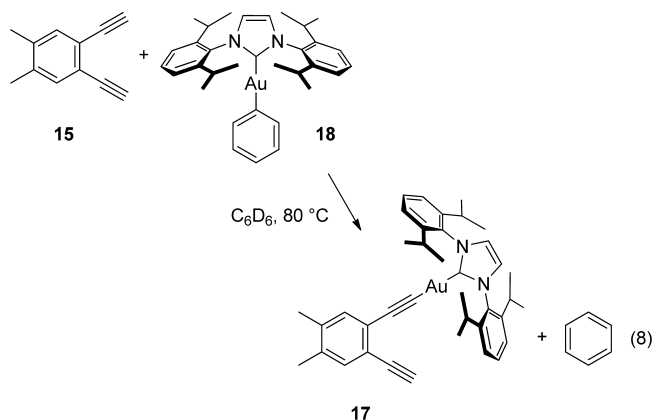


FIGURE 2. Gold(I) acetylide **17** is a stable compound.

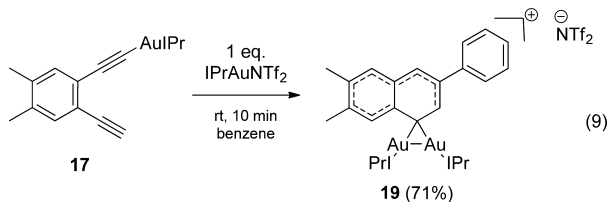
Complex **17** was prepared, but it turned out to be a perfectly stable compound, even at the typical reaction temperature of 80 °C. In general, there exist only a few scattered reports on reaction of gold-acetylides with electrophiles.<sup>31,32</sup> (b) But with a catalytic amount of a gold(I) catalyst and a stoichiometric amount of **17** only  $\beta$ -**16** and no  $\alpha$ -**16** could be detected. Combined, these two pieces of evidence show that two different catalytic cycles compete. Initially, a classical electrophilic activation of **15** by only one gold complex forms  $\alpha$ -**16** in high selectivity. Slowly (seemingly much more slowly than in Fensterbank's<sup>29</sup> experiments with phenylacetylene), some of the gold(I) complex then “leaches” to the gold acetylide, which then is able to form  $\beta$ -**16** with high selectivity. Indeed, in the presence of simple bases like triethylamine or even  $\text{Al}_2\text{O}_3$ , which speeds up the initial formation of **17**, mainly  $\beta$ -**16** (98:2) was observed.

All this explained the initial formation of a gold acetylide and the subsequent selective conversion to  $\beta$ -**16**. Another question concerned the catalyst transfer closing the catalytic cycle. In order to maintain  $\beta$ -selectivity, a final naphthylgold(I) intermediate must directly be protodeaurated by the next alkyne substrate **15**. This would simultaneously go along with the formation of the gold acetylide **17**, a prerequisite for staying  $\beta$ -selective in the next catalytic cycle. If another proton source would be responsible for the protodeauration, **17** would not be generated directly, but free  $\text{LAu}^+$ , which is  $\alpha$ -selective, would be generated. The corresponding control experiment, using **18** as a mimic of the naphthylgold(I)

species in a highly selective protonation with **15** was possible (eq 8).<sup>30</sup> The  $pK_a$  of the free alkyne is only about +25, which should not allow protodeauration; but the combination with the simultaneous formation of the gold acetylide **17** creates a significant thermodynamic driving force, the acidity of the alkyne might be enhanced by coordination to gold(I).

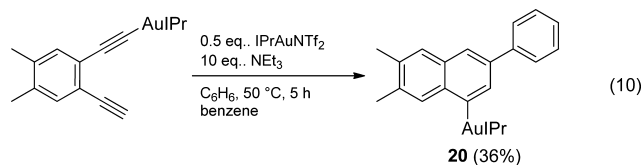


Another important observation was the formation of the *gem*-diaurated species **19** from stoichiometric amounts of **17** and the catalyst (eq 9 and Figure 3).

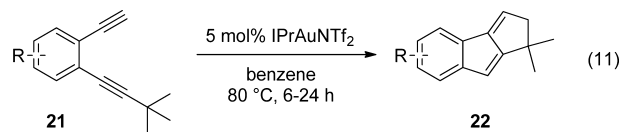


Due to the pioneering work of Schmidbaur,<sup>33</sup> such *gem*-diaurated compounds with an aurophilic interaction are well-known in *stoichiometric organometallic chemistry*. Due to the isolation of such species in the *catalytic intramolecular hydroarylation of allenes by Gagné*,<sup>34</sup> new methods for the preparation of these compounds were developed in the last years.<sup>35,36</sup> In the context of catalysis, there were some speculations about diaurated species being species in the catalytic cycle.<sup>37</sup> Recent work indicated that the substituents influence the delicate equilibrium between the vinyl/arylgold(I) species and the *gem*-diaurated species and delicate balance of stabilization and reactivity needs to be maintained to observe the diaurated species but not to have a catalyst self-poisoning thermodynamic sink, an irreversible equilibrium.<sup>38</sup> The influence of counterions was explored, too.<sup>39</sup> Latest findings indicate that the equilibrium needs to be reversible for an efficient catalysis and that the *gem*-diaurated species is an off-cycle species, less reactive than the corresponding vinyl/arylgold(I) species.<sup>40,41</sup>

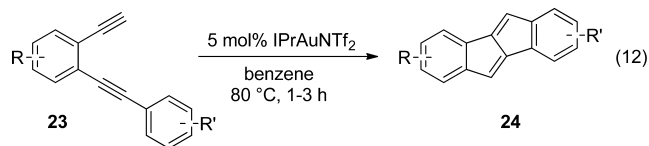
With substoichiometric amounts of catalyst, the naphthylgold(I) intermediate **20**<sup>30</sup> could be isolated by using the simple addition of  $NEt_3$  (eq 10).<sup>42</sup>



(c) But the crucial question of the naphthalene synthesis was still open: *why and how* do **15** and  $LAu^+$  deliver  $\beta$ -**16**. The reaction of the substrate **21**, bearing a *tert*-butyl group at one of the alkynes, did not lead to a naphthalene but to a benzofulvene **22** (eq 11, diaurated species in Figure 3).<sup>43</sup> This suggested the initial formation of a five-membered ring and not a naphthalene system and subsequently the formation of another five-membered ring by a C,H activation of a primary, nonactivated C–H bond of the *tert*-butyl group. In work conducted at the same time, Zhang and co-workers<sup>44</sup> found similar conversions. While we focused on NHC ligands, the Zhang group had very good success with the BrettPhos ligand in the presence of *N*-oxides. In a detailed computational study, Zhang addressed the possible mechanism, which revealed a very interesting bifurcation situation. Two conceivable pathways were considered, the formation of a vinylidene species by an initial 5-*exo*-dig cyclization and the formation of aurated aryl cations as reactive species by an initial 6-*endo*-dig cyclization.

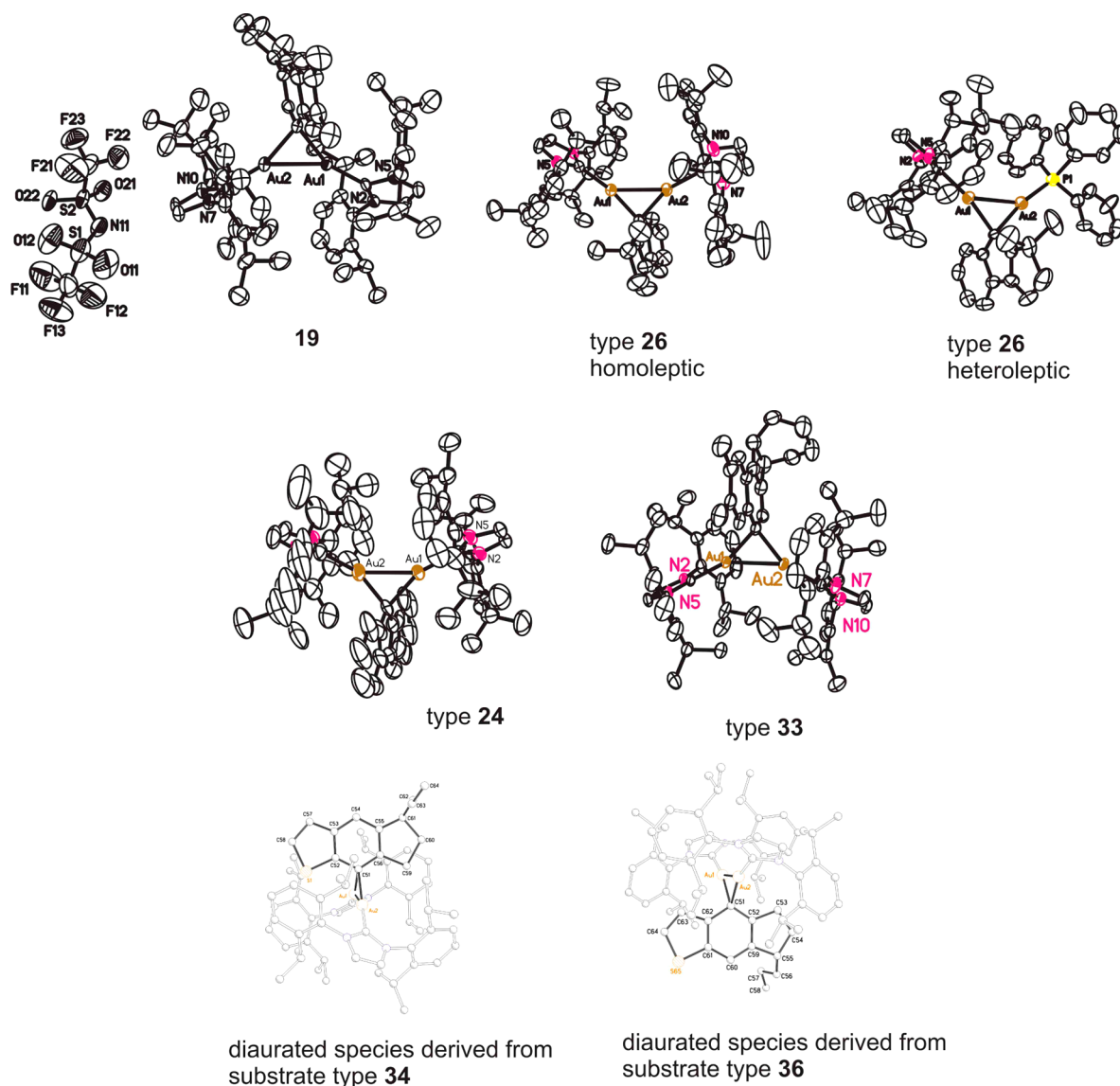


The hypothesis of an initial formation of a five-membered ring rather than a six-membered ring was further supported by another reaction of the substrates **23** bearing an aryl group instead of the *tert*-butyl group. Again two five-membered rings in the dibenzopentalenes **24** were formed (eq 12, diaurated species in Figure 3).<sup>45</sup>



#### 4. An Initial Mechanistic Hypothesis

Parallel work of the Zhang group (in analogy to eq 11, including a deuterium labeling experiment and extensive calculations on the mechanism) as well as a series of

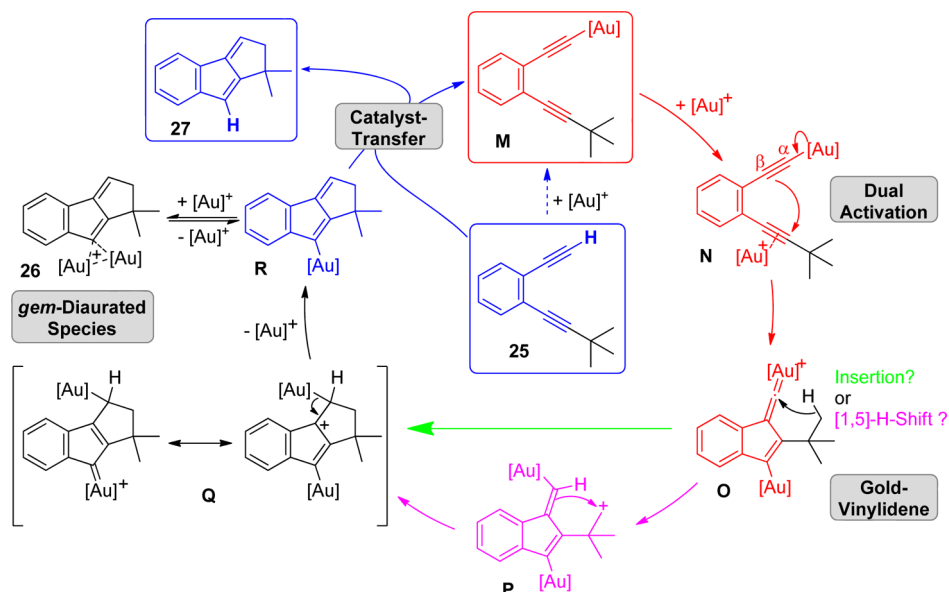


**FIGURE 3.** *gem*-Diaurated organic compounds isolated in the context of dual activation studies.

additional deuterium isotope labeling experiments in my group (labeled substrates and incorporation of deuterium) are in full agreement with the following mechanistic cycle (Scheme 3).

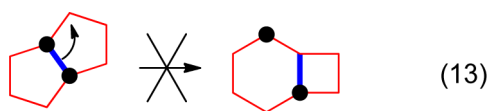
The generation of the gold(I) acetylide **M** is essential.  $\pi$ -Coordination of a second  $[\text{Au}]^+$  unit (dual activation) to the other triple bond activates the system for an electrophilic attack in  $\beta$ -position of the gold acetylide (species **N**). One difficulty with that step is the fact that a  $\pi$ -coordination of the cationic gold catalyst at the gold acetylide (analogous to Houk and Toste's species **A**) is clearly preferred.<sup>29,46</sup> One has to assume an equilibrium, with the reactive species **N**; then a gold(I) vinylidene-like species **O** is formed. Vinylidenegold(I) complexes are unknown, thus we synthesized the corresponding allenylidenes. There is no significant  $\text{Au}=\text{C}$  double

bond character (see section 5).<sup>47</sup> These reagents represent highly electrophilic carbenoids. The subsequent step is an insertion into the C–H bond of the *tert*-butyl group. Looking at other results discussed herein, for example, a diastereospecific reaction with olefins, we propose that this should proceed in a concerted way. A stepwise sequence comprising a hydride abstraction followed by a subsequent electrophilic attack<sup>48</sup> of the carbenium ion at the vinylgold unit should show competing Wagner–Meerwein rearrangements at the stage of the primary carbocationic intermediate **P**. An elimination of  $[\text{Au}]^+$  from **Q** should deliver the vinylgold(I) species **R**. Readdition of  $[\text{Au}]^+$  at the *ipso*-position of gold establishes the side equilibrium with the *gem*-diaurated species **26**. In this and all other related reactions discussed, such digold species could be isolated and

**SCHEME 3.** First Suggestion for the Catalytic Cycle for the Formation of Benzofulvenes by Gold-Catalyzed Dual Activation and C,H-Activation of the Alkyl Side Chain

characterized by X-ray crystal structure analyses. Restarting the catalysis by adding the substrate to the isolated and purified digold species proves the reversibility of this side equilibrium. The final step of the catalytic cycle is the catalyst transfer, a protodeauration by the terminal alkyne of the next substrate molecule **25** delivering the product **27** (in analogy to eq 8).

Probably, for the formation of the two annellated six-membered rings of the naphthalene core, after the initial formation of a new five-membered ring, the catalytic cycle also comprises a ring expansion. Due to the second five-membered ring from the *intramolecular* reaction of the vinylidene intermediate, in the reaction leading to **26**, no ring expansion to a six-membered ring is possible, because the other five-membered ring would suffer a ring-contraction to a four-membered ring, which overall is thermodynamically not feasible (eq 13).

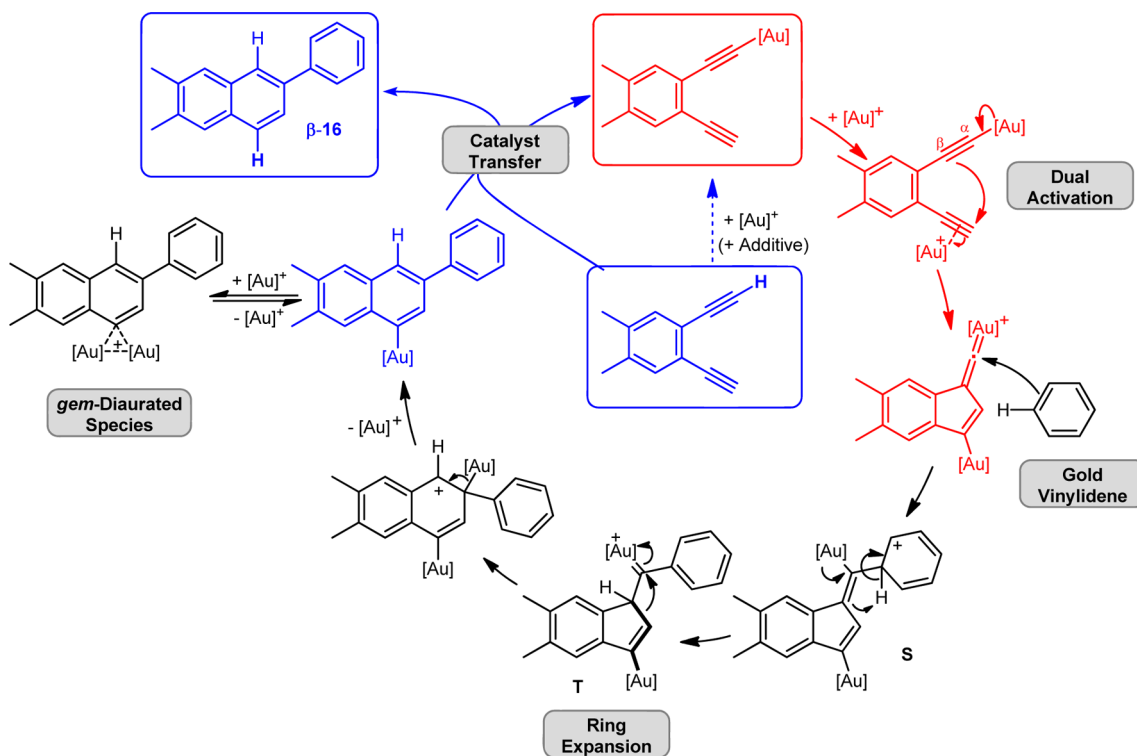


If this is correct, when the reactions involving C,H activation are conducted in an *intermolecular* manner, naphthalenes should be formed. Experimentally, symmetrical hydrocarbons had to be used in order to avoid regioselectivity problems, and the hydrocarbons had to be used as solvents. Still the yields were low in these first examples of intermolecular gold-catalyzed C,H activations. But indeed,

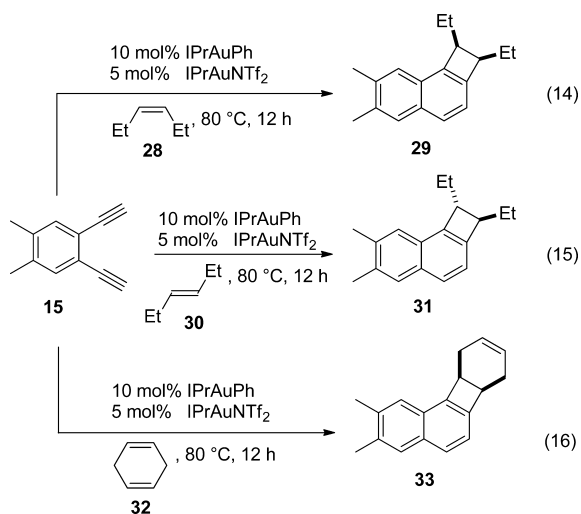
naphthalenes were formed, as also proven by an X-ray crystal structure analysis.<sup>49</sup>

Now it was possible to suggest a mechanistic scheme for the naphthalene synthesis, too (Scheme 4). Deuterium isotope labeling and crossover experiments prove the intramolecular H-shift in the step from **S** to **T**. The carbenoid species **T** then would allow the ring expansion by an 1,2-shift of the benzylic C–C bond to the carbenoid carbon. It must be stressed that in this case the situation is different from the  $\alpha$ -/ $\beta$ -selectivity in electrophilic substitution reactions at naphthalenes. The catalytic cycle depicted in Scheme 4 is not *selective* but *specific* for the formation of the  $\beta$ -substituted naphthalene.

Another intermolecular reaction that could be developed on the basis of these insights is the formation of benzocyclobutenes from diynes **15** and alkenes (diaurated species in Figure 3).<sup>49</sup> Two important insights could be gained from this new reaction: (a) The reactions are diastereoselective; the (*Z*)-olefin **28** would lead to the *cis*-product **29** (eq 14), and the (*E*)-olefin **30** yields the *trans*-product **31** (eq 15). This stereoselectivity indicates a concerted pathway, which also was the reason for presuming a direct C,H-insertion rather than a stepwise process for the formation of the benzofulvenes in Scheme 3 (**Q** directly being formed from **O** and not via **P**). (b) In all these substrates with ene-diyne substructures, one could speculate on the participation of Bergman cyclization-like pathways involving radical intermediates. This is ruled out by the reaction with the typical interceptor for such

SCHEME 4. Suggestion for the Mechanistic Cycle Leading to the  $\beta$ -Substituted Naphthalenes by Gold-Catalyzed Dual Activation

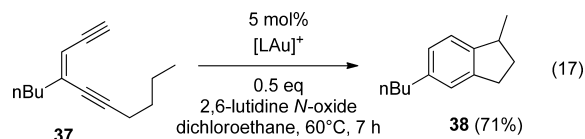
radicals, the hydrogen atom donor 1,4-cyclohexadiene (**32**) provided the benzocyclobutene **33**. Hydrogen addition could not be detected (eq 16).



## 5. Further Insights from Other Substrates

The computational results on the benzofulvene synthesis of Zhang and co-workers<sup>44</sup> had shown an alternative pathway that should be preferred and deliver a new six-membered ring (a naphthalene-type product), but a new five-membered ring is observed experimentally. We investigated a thiophene (**34**) instead of a benzene backbone, and now isolated

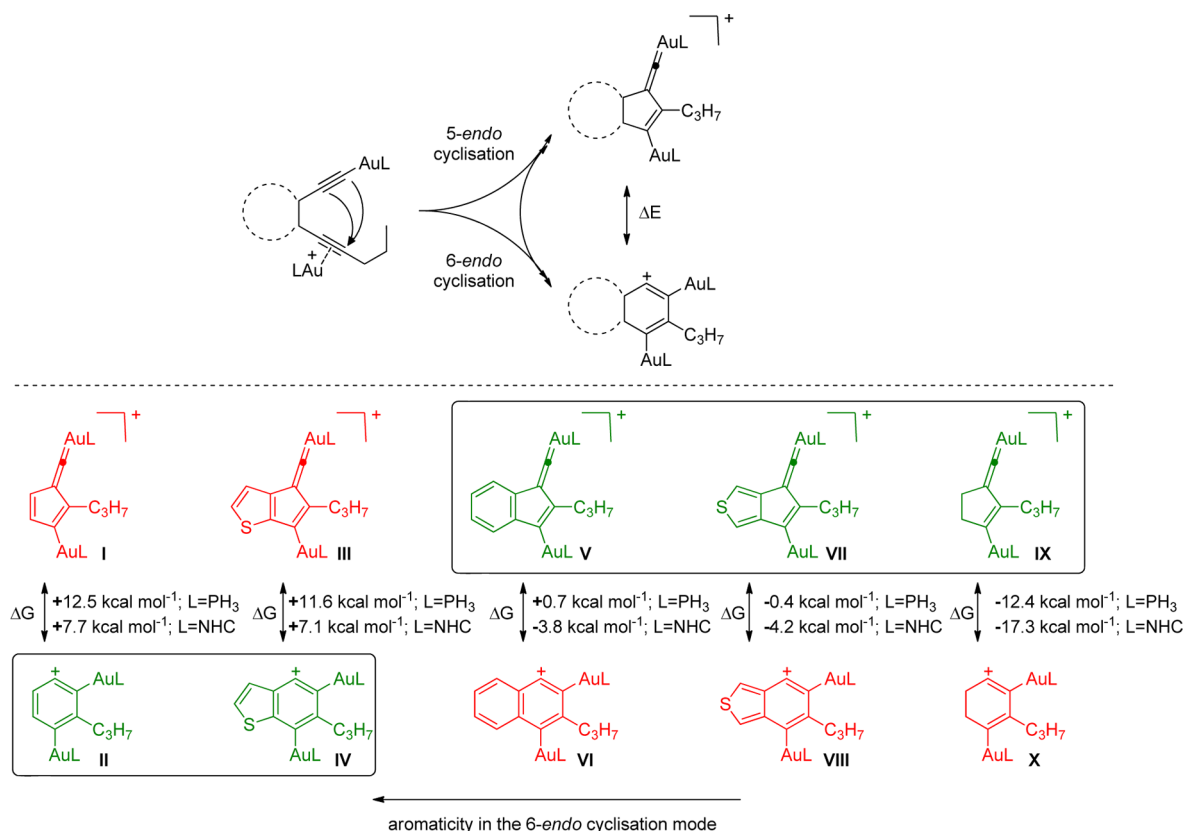
**35** with a new six-membered ring (Scheme 5).<sup>50</sup> We were delighted to see once more a positionally selective C,H activation of an alkyl side chain. For this system, our calculations indicated a bifurcation pathway; the *direct* ring closure to a six-membered ring is preferred (**U**, not the vinylidene **V**). The transition state of the 1,2-gold shift to form **W/X** is a aryne–gold(I)  $\pi$ -complex. In parallel work Liming Zhang and co-workers<sup>51</sup> found a similar transition state for the reaction of ene-diyne substrates (eq 17). Our species **W/X** possesses carbene character and can form the new C–C bond by C,H insertion. Species **V** is not formed because in the case of the thiophene backbone an annelation to another five-membered is energetically less feasible. With substrates like **34**, bearing the alkyl side chain on the alkyne on 2-position of the thiophene, significantly higher yields than with substrates **36** (Scheme 5) were isolated (diaurated species in Figure 3). This might originate from an additional interaction of the catalyst with the thiophene sulfur atom when reacting with **34**.



This option of generating a species **W/X** directly and not via the vinylidene-gold(I) complex raised the question



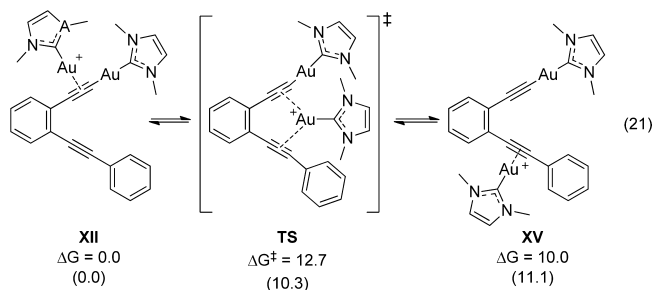




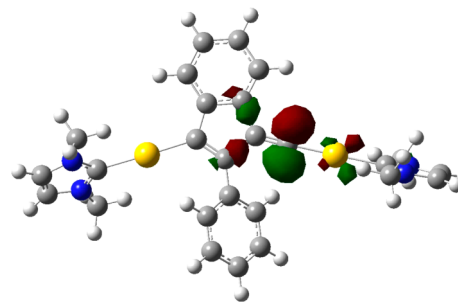
**FIGURE 4.** The selectivity seems to switch with increasing aromaticity of the intermediate of the 6-*endo* cyclization mode.

sink for the  $[LAu]^+$  species; both prefer to be on the same substrate molecule.

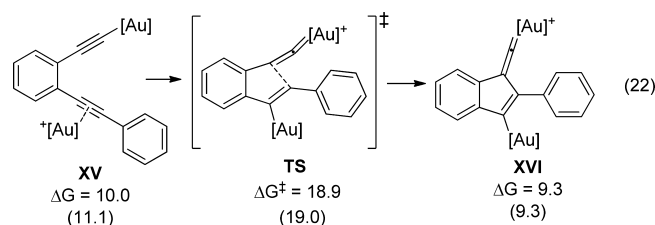
(b) There is an equilibrium with a low barrier to form the reactive species **XV**, bearing the  $\pi$ -coordinated  $[LAu]^+$  at the other triple bond (eq 21). We could locate the transition state; the gold is almost in plane with the two alkynes.



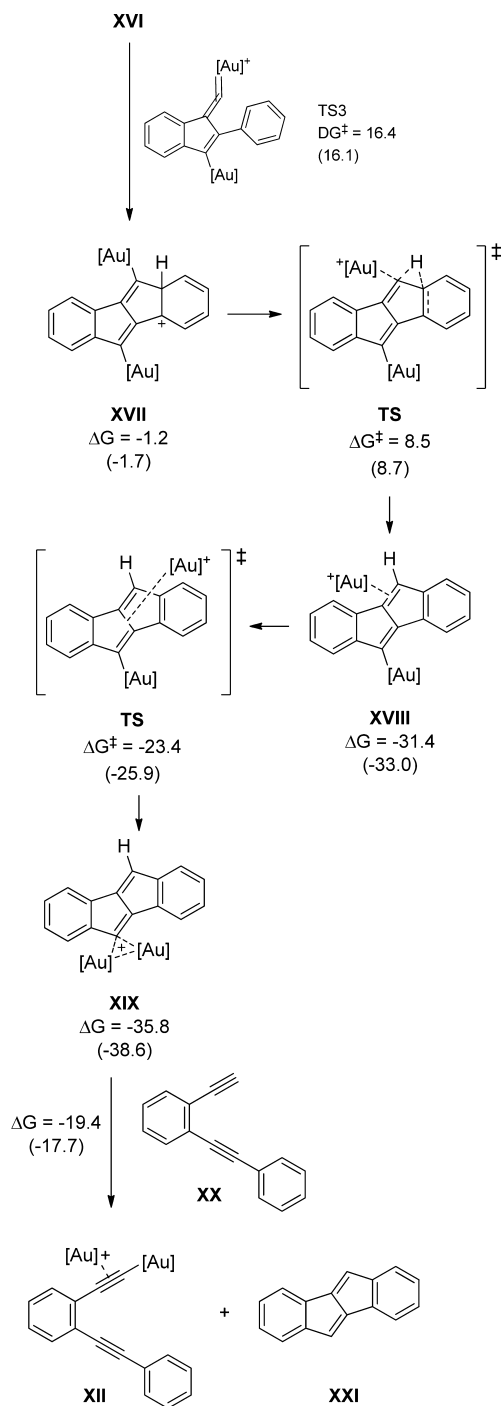
(c) The reactive species **XV** exists in low concentration and cyclizes to the gold(II) vinylidene intermediate **XVI** (eq 22). NBO analysis shows that there is barely any gold–carbon double bond character in **XVI**. Rather than vinylidene, the species should be called “vinyldienoid”; it resembles a vinylation with a linear coordination to gold and an empty p-orbital (in plane with the five-membered ring) at the central carbon of the LUMO of this electrophilic and highly reactive intermediate (Figure 5).



**FIGURE 5.** LUMO of intermediate **XVI**.



(d) Based on the calculations, it is conceivable that in the course of the whole reaction the two gold centers stay on the same molecule all the time (Figure 6). This would mean that the diaurated species are in cycle and not off cycle and may apply to all reactions in that sector of gold catalysis. We are currently investigating this point.

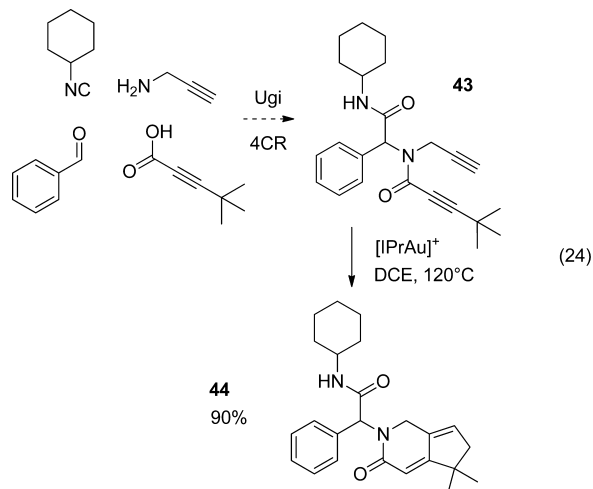


**FIGURE 6.** The lowest energy pathway could be composed of digold species only.

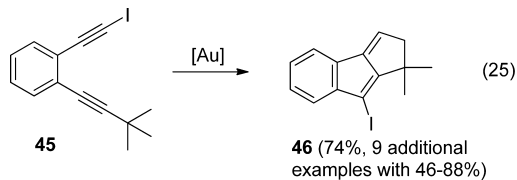
With regard to mechanistic details, the Ohno group assumed the participation of gold acetylides in the addition of nucleophiles to diynes, which would have been in contradiction to our results.<sup>54</sup> Now it could be proven that the gold-acetylides are responsible for the dual activation pathways and not for the addition of nucleophiles.<sup>55</sup> In the meantime researchers have started to specifically run experiments in

order to exclude dual activation mechanisms for some of the reactions they investigate.<sup>56,57</sup> Asensio and Ramírez de Arellano now have in detail studied the competing pathways for an intramolecular hydroamination reaction.<sup>58</sup>

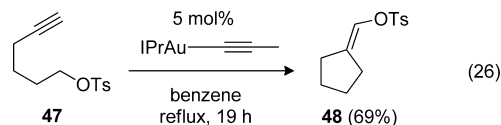
With regards to applications, van der Eycken<sup>59</sup> has used an Ugi four component reaction to construct functionalized (free NH group!) diyne substrates like **43** and then successfully applied in the vinylidene-type conversions, including the synthesis of spiro compounds.



We achieved a catalyst transfer step for iodoalkynes like **45**; the overall reaction then combined alkyl C,H activation and halogenation for the formation of **46** (eq 25).<sup>60</sup>



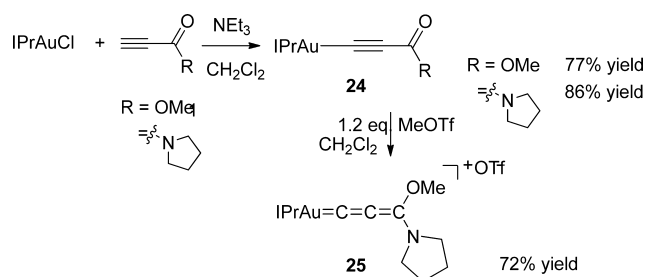
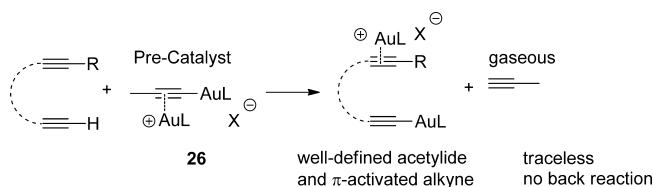
The most exciting recent extension is the observation of gold vinylidene-derived products when intramolecular electrophiles are directed to the  $\beta$ -position of a gold acetylide (eq 26).<sup>61</sup>



## 6. Gold Allenylidenes

Since gold vinylidenes are not stable, we tried to synthesize allenylidene complexes of gold(I). In an alkylation reaction, **24** indeed delivered **25** as a stable compound (Scheme 6).<sup>47</sup> Detailed structure investigations by both experimental and by computational methods revealed that the main stabilization of the carbenium ion came from the lone pair of the

## SCHEME 6. Generation of "Gold(I) Allenyldenes"

SCHEME 7. Activation via Dual Activation Catalysts **26**

strongly donating heteroatom (O or N) and not from gold. There is no significant Au–C double bond character. Recently, Che has extended this to gold(III).<sup>62</sup>

## 7. Dual Activation Catalysts

The ideal ratio of gold acetylide to  $\text{LAu}^+$  is 1:1. This is crucial but is difficult to achieve by mixing different types of pre-catalysts or one pre-catalyst and base. In an insufficient amount of base, the excess of  $\text{LAu}^+$  would, for example, ruin the  $\beta$ -selectivity in the naphthalene synthesis (Figure 1). An excess of base would "bury" most of the gold as inactive gold acetylide. Isolated diaurated species like **19** or **26** would solve that problem, but the organic moiety in **19** or **26** will lead to 1 equiv (with regard to the catalyst) of a product-related impurity (unless a specific pre-catalyst derived from the substrate will be used, but then each reaction would need a specific pre-catalyst). The catalysts **26** (dual activation catalysts = DACs, Scheme 7) are easily accessible, can be stored, and proved to be active in a number of reactions proceeding by a dual activation mechanism.<sup>63</sup> These are superior to the digold hydroxides.<sup>64–66</sup>

## 8. Summary and Future Outlook

The concept of dual activation by gold opens up new and innovative possibilities, both with regard to the synthetic potential (alkyl C,H-activation, even in combination with halogenation) and with regard to new mechanisms in organometallic chemistry (reactivities of different digoldorganyls). This will inspire chemists in the field of gold catalysis, and maybe some of the new principles can even be transferred

to other metals. The progress in this sector will continue to depend on the combined input of experimental and computational mechanistic studies.

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## FOOTNOTES

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