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# Gold- and Platinum-Catalyzed Cycloisomerization of Enynyl Esters versus Allenenyl Esters: An Experimental and Theoretical Study

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**Abstract:** Experimental and theoretical studies on Au- and Pt-catalyzed cycloisomerization of a branched dienyne with an acetate group at the propargylic position are presented. The peculiar architecture of the dienyne precursor, which has both a 1,6- and a 1,5-enyne skeleton, leads, in the presence of alkynophilic gold catalysts, to mixtures of bicyclic compounds **3**, **4**, and **5**. Formation of unprecedented bicyclo[3.1.0]hexene **5** is the main focus of this study. The effect of the ancillary ligand on the gold center was examined and found to be crucial for formation of **5**. Further mechanistic studies, involving cyclization of an enantioenriched dienyne precursor, $^{18}O$-labeling experiments, and DFT calculations, allowed an unprecedented reaction pathway to be proposed. We show that bicyclo[3.1.0]hexene **5** is likely formed by a 1,3-OAc shift/allene–ene cyclization/1,2-OAc shift sequence, as calculated by DFT and supported by Au-catalyzed cyclization of isolated allenenyl acetate **7**, which leads to improved selectivity in the formation of **5**. Additionally, the possibility of OAc migration from allenyl acetates was supported by a trapping experiment with styrene that afforded the corresponding cyclopropane derivative. This unprecedented generation of a vinyl metal carbene from an allenyl ester supports a facile enynyl ester/allenenyl ester equilibrium. Further examination of the difference in reactivity between enynyl acetates and their corresponding [3,3]-rearranged allenenyl acetates toward Au- and Pt-catalyzed cycloisomerization is also presented.

**Keywords:** alkynes · allenes · cycloisomerization · density functional calculations · gold

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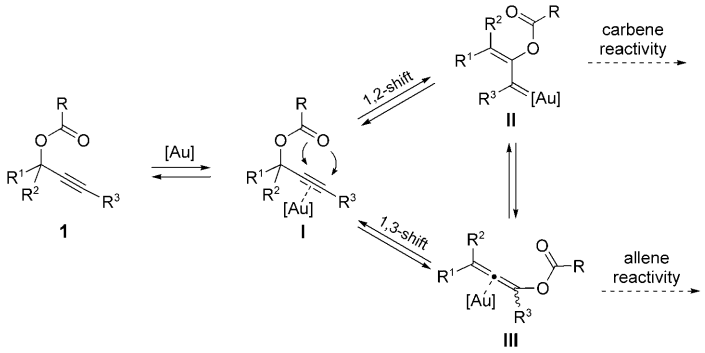
## Introduction

Atom-economic reactions, as defined by Trost,[1] are of primary importance in modern organic chemistry. In this field, polyunsaturated substrates have become ubiquitous and have led to the discovery of a number of unprecedented transformations in the presence of late transition-metal catalysts.[2] Among available atom-economic transformations,[3] the cycloisomerization of enynes remains unique because of the increased molecular complexity achieved in one chemical step.[4] After extensive studies with palladium[5] and platinum,[6] gold(I) and gold(III) salts have emerged lately as powerful catalysts for a myriad of transformations involving enynes.[7,8] In this context, enyne derivatives with an ester group at the propargylic position can be regarded as a special class of substrates due to their atypical reactivity pattern.[9,10] More specifically, an appropriately situated *O*-ester group undergoes an internal 1,2- or 1,3-shift upon electrophilic activation of the C≡C bond (Scheme 1, **I**) to give rearranged products **II** and **III** respectively, which can then further evolve as a function of the remaining pendant groups (Scheme 1).

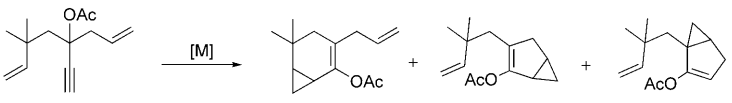



Scheme 1. Reactivity of propargylic acetates in the presence of gold catalysts.

The wide diversity and complexity of accessible structures from readily assembled precursors is probably the most appealing feature of enyne cycloisomerization reactions. However, it can also be seen as a disadvantage, since small changes in the starting compound can lead to unexpected outcomes, so that the reactivity of a specific substrate is often rendered unpredictable. This is why insights into the skeletal rearrangements of enynes catalyzed by gold salts are still needed in order to understand the mechanism of these transformations. Here we present our experimental and theoretical findings on platinum- and gold-catalyzed cycloisomerization of enynes bearing a propargylic acetate group. Driven by theoretical findings, we focused our studies on the reversibility of OAc migration between the propargylic esters and their corresponding [3,3]-rearranged counterparts, namely, the allenyl esters.

## Results and Discussion

Access to extremely elaborate structural motifs, such as fused polycyclic systems from acyclic substrates, is often dependant on subtle modifications in the precursor architecture. In this context, we have reported on the importance of oxo substituents—and of their nature—at the propargylic position in enyne systems.[11] Furthermore, we recently investigated the reactivity of dienyne **2**, which formally exhibits 1,5- and 1,6-enyne scaffolds, and observed different selectivity as a function of the nature of the catalyst employed (Scheme 2).[12]




| | 3 | 4 | 5 |
|---|---|---|---|
| [M] = $PtCl_2$[a] | 88% | 5-10% | -- |
| [(IPr)AuCl]/$AgBF_4$[b] | 30% | 12% | 42% |

Scheme 2. Pt- and Au-catalyzed cycloisomerization of **2**. [a] Reaction conditions: $PtCl_2$ (5 mol%), toluene (0.025 M), 80 °C. [b] Reaction conditions: [(IPr)AuCl]/$AgBF_4$ (2 mol%), $CH_2Cl_2$ (0.1 M), RT.

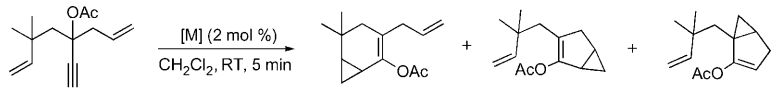
Thus, formation of bicyclo[4.1.0]heptene **3** over bicyclo[3.1.0]hexene **4** was mainly observed when $PtCl_2$ was used,[11a] while various gold catalysts afforded different product ratios. More interestingly, the use of $Au^I$ salts in lieu of $Pt^{II}$ ones led to the formation of unexpected bicyclo[3.1.0]hexene **5**.

We noticed the influence of the ligand on the gold center, a particular set of steric and electronic parameters favoring formation of compound **5**, and the ability of N-heterocyclic carbenes (NHCs)[13,14] to promote this unexpected transformation. Therefore, intrigued by this unprecedented mode of cyclization, we thoroughly examined the reaction parameters that might influence the formation of this type of carbocycle. Moreover, we carried out $^{18}O$-labeling experiments and theoretical calculations to gain further insight into the mechanism of this cyclization. Herein we disclose the results of these studies, which permit a new type of reactivity in the enynyl ester series to be explained. Thus, we have shown that the most likely pathway to **5** involves, after formation of an allenyl ester, carbocyclization of an allenene core followed by "retro-migration" of the ester moiety. The retro-migration process was further studied on an extended set of substrates.

**Influence of reaction conditions**: We began our study on model substrate **2** by evaluating the influence of the ligand using a series of [(NHC)AuCl] complexes[15] leading to the formation of bicyclic product **5** (Table 1).[16] Overall, the combined yields of cycloisomerized products range from good to excellent with a slight decrease of activity for the less encumbered ligands (Table 1, entries 14–16 and 21). Simple "ligandless" gold(I) and gold(III) chloride salts led to the same selectivity,[17] yielded **3** and **4** in similar propor-

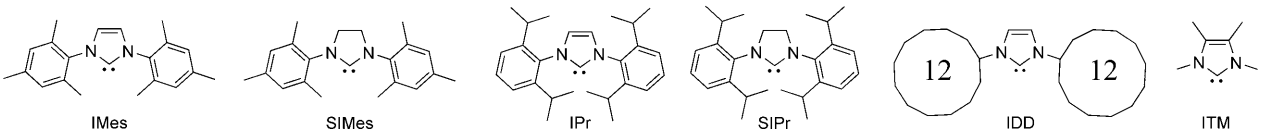
Table 1. Effect of ligands on the cycloisomerization of **2**.

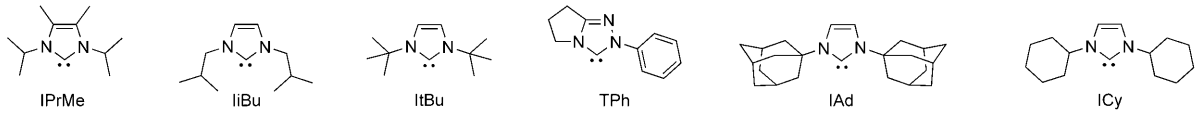


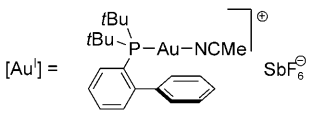

**2** **3** **4** **5**

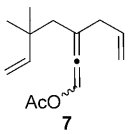
| Entry | [M] | **3**:**4**:**5**[a] | Total yield [%][a] | Entry | [M] | **3**:**4**:**5**[a] | Total yield [%][a] |
|---|---|---|---|---|---|---|---|
| 1[b] | $PtCl_2$ | 1/0.1/0 | 98 | 12 | [(SIPr)AuCl]/$AgBF_4$ | 1/0.3/0.9 | 90 |
| 2[c] | $PtCl_2$/$AgBF_4$ | 1/0.1/0 | 33 | 13 | [(TPh)AuCl]/$AgBF_4$ | 1/0.5/0.4 | 94 |
| 3 | AuCl | 1/0.7/0.2 | 86 | 14[g] | [(ITM)AuCl]/$AgBF_4$ | 1/0.1/0.2 | 62 |
| 4 | AuCl/$AgBF_4$ | 1/0.5/0 | 84 | 15 | [(IiBu)AuCl]/$AgBF_4$ | 1/0.2/0.1 | 70 |
| 5[d] | $AuCl_3$ | 1/0.8/0.2 | 88 | 16[g] | [(IPrMe)AuCl]/$AgBF_4$ | 1/0.2/0.3 | 63 |
| 6[e] | $AuCl_3$/$AgBF_4$ | 1/0.3/0 | 77 | 17 | [(ICy)AuCl]/$AgBF_4$ | 1/0.6/0.4 | 88 |
| 7[f] | [($Me_2S$)AuCl] | 1/0.8/0.1 | 80 | 18 | [(ItBu)AuCl]/$AgBF_4$ | 1/0.1/0.6 | 73 |
| 8[d] | [($Me_2S$)AuCl]/$AgBF_4$ | 1/0.1/0 | 81 | 19 | [(IAd)AuCl]/$AgBF_4$ | 1/0.1/0.7 | 95 |
| 9 | [(IMes)AuCl]/$AgBF_4$ | 1/0.5/1.5 | 78 | 20 | [(IDD)AuCl]/$AgBF_4$ | 1/0.2/0.5 | 76 |
| 10 | [(SIMes)AuCl]/$AgBF_4$ | 1/0.4/1.7 | 72 | 21[g] | [($PPh_3$)AuCl]/$AgBF_4$ | 1/0.1/0.2 | 64 |
| 11 | [(IPr)AuCl]/$AgBF_4$ | 1/0.4/1.4 | 84 | 22 | [$Au^I$] | 1/0.6/0.1 | 54 |

[a] Yields of isolated products, average of two runs, products ratio determined by $^1H$ NMR spectroscopy. [b] Reaction performed with $PtCl_2$ (5 mol%) in toluene at 80°C for 2 h. [c] Reaction performed with $PtCl_2$ (5 mol%)/$AgBF_4$ (10 mol%) in toluene at 80°C for 2 h. 26% of **2** was recovered along with 8% of allenyl ester **7**, and significant amounts of oligomerized byproducts were also formed. [d] Reaction stirred for 2 h. [e] Reaction performed with $AuCl_3$ (2 mol%)/$AgBF_4$ (6 mol%) for 1 h. [f] Reaction stirred for 2 h, 8% of allenyl ester **7** was also formed. [g] No starting material remaining; significant amounts of oligomerized byproducts were formed.




**7**

tion, and only gave small amounts of **5** (Table 1, entries 3 and 5). Interestingly, when these salts were employed in combination with a silver(I) salt, formation of **5** was not observed, and the **3**:**4** ratio increased (Table 1, entries 4 and 6) and approached the selectivity displayed by $PtCl_2$ (Table 1, entry 1). Notably, platinum(II) chloride in conjunction with 2 equiv $AgBF_4$ displayed poorer activity than $PtCl_2$ alone. The last "simple" and commercially available gold salt tested was [($Me_2S$)AuCl] (Table 1, entries 7 and 8). As expected, it could be used without silver salt (Table 1, entry 7) and, under these conditions, behaved as AuCl, supporting decoordination of $Me_2S$ from the gold center prior to catalytic activity.

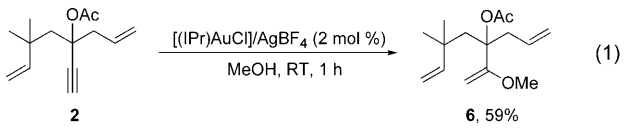
On the other hand, the addition of $AgBF_4$ to [($Me_2S$)AuCl] led to a selectivity comparable with those of AuCl/$AgBF_4$ and $AuCl_3$/$AgBF_4$, whereby formation of **5** was not observed (Table 1, entry 8). This can be interpreted in two ways: either $Me_2S$ as ligand has little influence on the course of the cycloisomerization or the catalytically active species is simply the gold cation, formed upon chloride abstraction and $Me_2S$ decoordination.

If we examine the influence of the ancillary ligand on the gold center by considering the formation of **5** as the main parameter, the ligands employed here can be divided into three classes. Those displaying low steric hindrance furnished only minor amounts of bicycle **5** (Table 1, entries 13–17 and 21; **3**/**5** $1/<0.4$), whereas highly hindered ligands led to slightly higher **3**/**5** ratios (ca. 1/0.6; Table 1, entries 18–20). The third class of ligands can be regarded as intermediate in terms of steric hindrance between the other two classes.[18] It includes the widely used IPr and IMes ligands and their saturated analogues SIPr and SIMes. Only these ligands produced mixtures in which **5** was the major compound (Table 1, entries 9–12). Considering the minor differences in the electronic properties of the NHCs employed here,[18] we believe that formation of unexpected bicyclo[3.1.0]hexene **5** is mainly under steric control and responds favorably to a medium/high steric demand.

Since prolonged reaction time, under strictly similar reaction conditions, led to comparable ratios of cyclopropyl carbocycles, the possibility of chemical equilibrium between the different products is excluded.

Subsequently, we attempted a trapping experiment using methanol as solvent in order to possibly isolate relevant intermediates that would have allowed for a better understanding of the formation of product **5**. Under these conditions, enol ether **6**, which results from addition of methanol to the alkyne moiety, was the only observed product [Eq. (1)].[19]



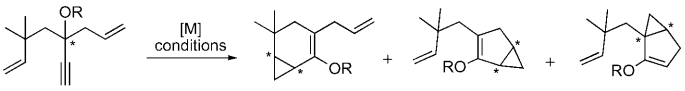

**2** **6**, 59% (1)

**Sequential acetate migration/cyclopropanation**: A key feature of the reactivity of propargylic acetates in the presence of soft π Lewis acidic metals such as gold and platinum lies in the ability of the acetate moiety to act as an internal nucleophile that migrates in a 1,2 or 1,3 fashion onto the C≡C bond. In the context of enyne cycloisomerization, this migrating ability of the acetate group has raised questions about the order of the migration/cyclopropanation sequence.[20,21] In our preliminary study,[12] we proposed a migration *then* cyclopropanation sequence, which appeared more consistent with the formation of bicyclo[3.1.0]hexene **5**. Nevertheless, at the time we did not exclude the possibility that a cyclopropanation *then* migration sequence could be involved in the formation of bicyclic compounds **3** and **4**.

To gain insights into this crucial issue, we synthesized enantioenriched dienyne **2** and subjected it to cycloisomerization conditions. In the case of cyclopropanation followed by migration, some chiral information should be translated into the product, whereas in the case of the opposite sequence, which involves an achiral intermediate of type **II** (see Scheme 1), chirality transfer would be precluded.[22]

Enantioenriched **2**, in the presence of 5 mol% $PtCl_2$, yielded rearranged products **3** and **4** in comparable yields and ratio to those previously observed but with distinct enantioselectivities (Table 2, entries 1 and 2). Cyclohexene derivative **3** was formed with 40% *ee*, while cyclopentene **4** was found to be racemic. Starting from a 66% *ee*-enriched dienyne, this could indicate that in the formation of **3**, the initial cyclopropanation would not be completely stereoselective[22b] or that both sequences are at play with a preference for the scenario of cyclopropanation then migration. On the contrary, the formation of **4** would appear to primarily result from a migration then cyclopropanation sequence, leading to complete loss of chirality transfer. However, in this case, we cannot also exclude a totally nonselective initial cyclopropanation step. Additionally, the nature of the migrating ester group seems to play an important role in the choice of the sequence, since using **2-Piv**, the pivalate analogue of **2**, led to a further decrease of the *ee* of **3-Piv** (Table 2, entry 3 versus entry 1).

Table 2. Au- and Pt-catalyzed cycloisomerization of enantioenriched **2**.




**2** **3** **4** **5**

| Entry | **2** | Conditions | Yield [%] (% *ee*) | | |
|---|---|---|---|---|---|
| | | | **3**[a] | **4**[a] | **5**[a] |
| 1 | R = Ac, 66% *ee* | $PtCl_2$ (5 mol%) toluene, RT→80°C, 2 h | 88 (38) | 8 (*rac*) | – |
| 2 | R = Ac, 66% *ee* | $PtCl_2$ (5 mol%) toluene, RT, 2 h | 83 (42) | 7 (*rac*) | – |
| 3 | R = Piv, 76% *ee* | $PtCl_2$ (5 mol%) toluene, 80°C, 48 h | 78 (20) | 6 (*rac*) | – |
| 4 | R = Ac, 60% *ee* | $AuCl_3$ (2 mol%) $CH_2Cl_2$, RT, 10 min | 46 (8) | 36 (*rac*) | 5 (4) |

[a] Yields of isolated **3**/**4**/**5** mixtures, ratios, and *ee* values determined by chiral GC. *rac* = racemic.

Finally, using gold(III) chloride afforded **3** and **5** with very low *ee* values and **4** as a racemic mixture (Table 2, entry 4), and this suggests that with gold catalysts both sequences are likely to compete in the formation of all cyclopropanated products, with preference given to the migration then cyclopropanation pathway.

At this point of our study, several mechanistic scenarios were still to be considered,[23] including, in addition to the aforementioned two sequential pathways, carbocyclization onto the oxonium intermediate before rupture of the C–O bond to regenerate the ester functionality. This possibility, first proposed by Fehr and Galindo,[22b] implies that the stereochemical information, still present in the oxocarbenium intermediate, is transferred in the cyclization step.

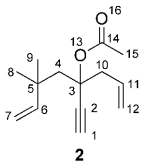
The additional information gathered so far on the cyclization of **2** and the formation of **3**, **4**, and **5** suggests competing pathways, the balance of which can be shifted by means of the ancillary ligand. Greater chirality transfer is observed with platinum(II) chloride compared to gold catalysis.

Nevertheless, a rationale for the formation of the unprecedented cyclopropyl derivative **5** remained elusive, notably because of little precedent in the literature.[12,24] We therefore performed DFT calculations on a full catalytic cycle for the formation of **3**–**5**, focusing on **5**.

**DFT calculations on the formation of 3–5**: For the sake of clarity, we numbered the atoms in dienyne **2** and we labeled structures from the DFT calculations with lowercase bold letters. The only exceptions are starting dienyne **2**, allene **7**, and bicyclic products **3**, **4** and **5**, all of which were characterized experimentally. For these species we use labels such as **2Au**, **4Au**, and so on, to indicate that these substrates are coordinated to Au.

Since N-heterocyclic carbene ligands are necessary in order to obtain satisfactory amounts of unprecedented carbocycle **5**, we performed the calculations with IDM bound to the gold(I) center (IDM = 1,3-dimethylimidazol-2-yli-

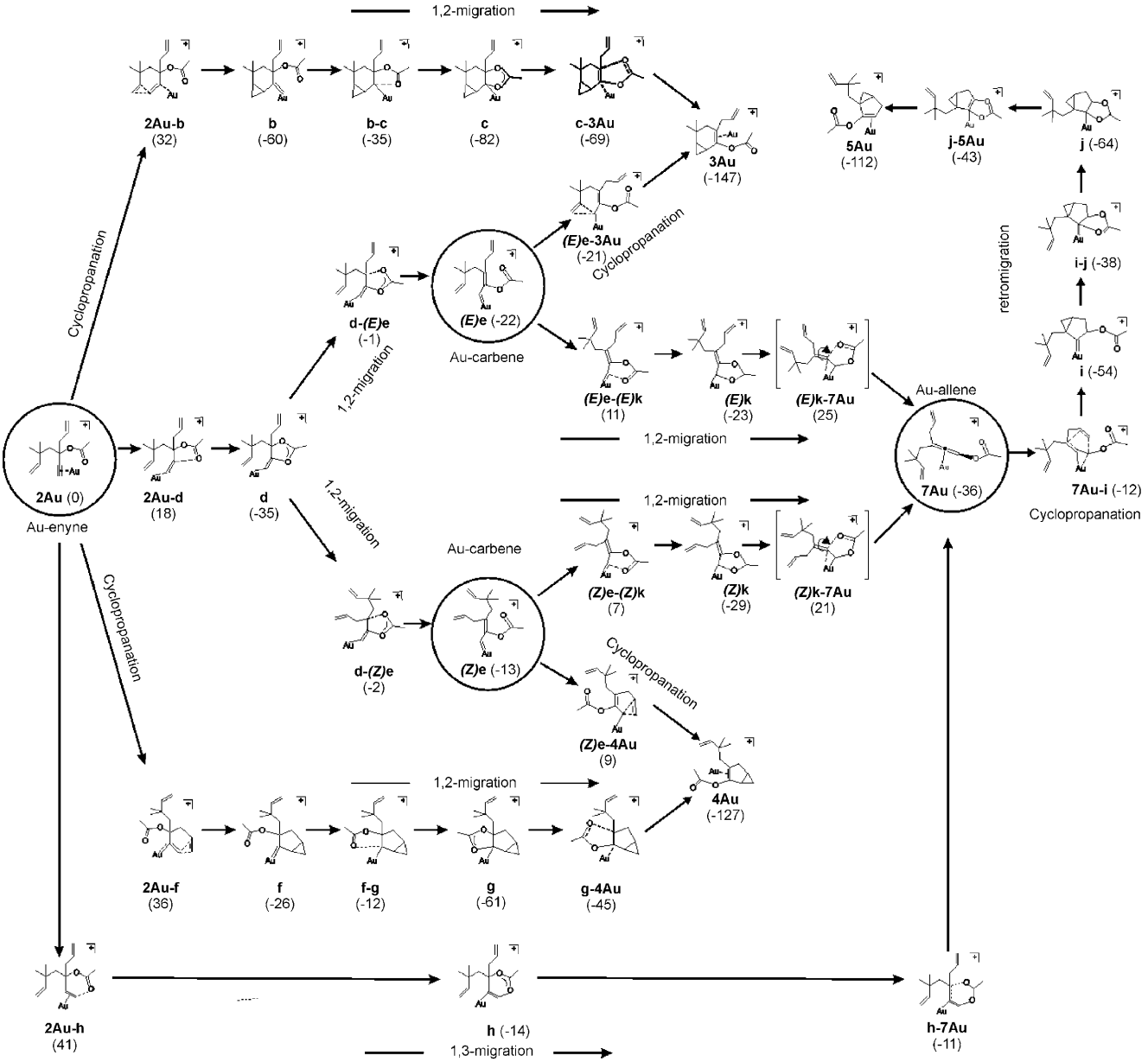


2

IDM

dene); therefore, in all schemes and figures regarding DFT calculations, the label "Au" in fact represents "[(IDM)Au]". For the reader's convenience, the different reaction pathways, which are interconnected, are discussed independently and compared when relevant. Accordingly, a figure depicting the mechanistic pathway and the potential-energy profile for each main path provides the basis for the discussion in a first approach (see Figures S1–S3, Supporting Information). Furthermore, in order to give a general and more realistic picture of the mechanistic processes at play, which are interdependent, we have gathered in one single scheme every pathway considered here.

The catalytic cycle starts with displacement of a $BF_4^-$ counterion from $[(IDM)Au^+]BF_4^-$ species **a** by the alkyne group of **2** to furnish intermediate **2Au**.[25] In $CH_2Cl_2$ displacement of the $BF_4^-$ counterion by the substrate is exergonic by 26 kJ mol$^{-1}$. Structure **2Au** is then the branching point for three different reaction paths (Scheme 3). The first consists of nucleophilic attack of the C6–C7 double bond on the C1 atom[26] (see Scheme 3 and Figure S1, Supporting Information). This cyclopropanation step leads to intermediate **b**, which already has the bicyclic skeleton of product **3**. The




Scheme 3. Possible mechanistic pathways based on calculations (energies given in kJ mol$^{-1}$)

Au carbene intermediate **b** is 60 kJ mol$^{-1}$ lower in energy than the starting alkyne-coordinated intermediate **2Au**, and is reached through transition state **2Au-b**, with a rather low energy barrier of 32 kJ mol$^{-1}$ (Scheme 3 and Figure S1, Supporting Information). Formation of **3** from **b** involves a 1,2-shift of the ester group from C3 to C2. After a first step leading to formation of intermediate **c** via transition state **b-c** with a barrier of 25 kJ mol$^{-1}$, the 1,2-shift is then completed via transition state **c-3Au** with a barrier of 13 kJ mol$^{-1}$, and finally affords the coordinated product **3Au**. Both intermediate **c** and **3Au** are lower in energy than intermediate **2Au** (by 82 and 147 kJ mol$^{-1}$, respectively), and thus formation of **3Au** is a substantially downhill path from the starting alkyne-coordinated species **2Au** to the coordinated product species **3Au**. Product release from **3Au** assisted by a coordinating $BF_4^-$ counterion is endergonic by 6 kJ mol$^{-1}$, leads to product **3**, and closes the catalytic cycle by forming the starting [(IDM)Au]$BF_4$ species **a**. However, product **3** can be reached from **2Au** through an alternative reaction pathway. Indeed, as mentioned before, in addition to the cyclopropanation then migration sequence that was just examined, the migration then cyclopropanation sequence must be considered. Thus, starting from alkyne-coordinated species **2Au**, a 1,2-shift of the ester group corresponding to attack of O16 on C2 leads to intermediate **d** through transition state **2Au-d** with an energy barrier of 18 kJ mol$^{-1}$ (Scheme 3). Intermediate **d**, which is 35 kJ mol$^{-1}$ lower in energy than **2Au**, is another branching point in this complex reaction manifold. The branch that leads to **3** involves breaking of the C3–O13 bond to furnish intermediate ***(E)*e**, with a barrier of 34 kJ mol$^{-1}$, and a subsequent cyclopropanation step, corresponding to attack of the C6–C7 double bond on C1 through transition state ***(E)*e-3Au**. A last step with an almost negligible energy barrier of only 1 kJ mol$^{-1}$ leads to coordinated product species **3Au**, from which **3** is released, closing the catalytic cycle. Intermediate ***(E)*e** is 22 kJ mol$^{-1}$ lower in energy than **2Au**.

The actual pathway that is followed to reach **3** is determined by the energy difference between the transition states of highest energy along the two alternative pathways, that is, transition states **2Au-d** and **2Au-b**. According to our calculations, transition state **2Au-d** is lower in energy than **2Au-b** by 14 kJ mol$^{-1}$, which suggests that the main reaction channel leading to **3** involves 1,2-shift of the ester group first and then a cyclopropanation step, although the alternative path corresponding to the cyclopropanation then 1,2-shift sequence is competitive.

Next we focused on the formation of **4**, which can also be reached through two alternative pathways (cyclopropanation then 1,2-shift or the reverse sequence) that are very similar to those described above to rationalize the formation of **3**. The first path again involves nucleophilic attack of a C–C double bond on C1, but in this case it is the C11–C12 double bond that we have to consider (see Scheme 3 and Figure S2, Supporting Information). This cyclopropanation step leads to intermediate **f**, which already has the bicyclic skeleton of product **4**. Gold carbene intermediate **f** is 26 kJ mol$^{-1}$ lower in energy than starting alkyne-coordinated intermediate **2Au**, and is obtained via transition state **2Au-f** with a rather low energy barrier of 36 kJ mol$^{-1}$.

Transition state **2Au-f** is slightly higher in energy than the similar transition state **2Au-b** because of the higher steric strain associated with formation of a more strained five-membered ring in **2Au-f**, compared to formation of a 6-membered ring in **2Au-b**. Formation of **4** from **f** then involves 1,2-shift of the ester group from C3 to C2. The first step of this 1,2-shift is the formation of intermediate **g** through transition state **f-g** with a barrier of 14 kJ mol$^{-1}$. Final formation of coordinated product **4Au** occurs through transition state **g-4Au** with an energy barrier of 16 kJ mol$^{-1}$. Both intermediates **g** and **4Au** are lower in energy than intermediate **2Au** (by 61 and 127 kJ mol$^{-1}$, respectively), and thus formation of **4Au**, similar to that of **3Au**, is a substantially downhill path from the starting alkyne-coordinated reactant **2Au** to the coordinated product **4Au** (Figure S2, Supporting Information). Product release from **4Au** assisted by a coordinating $BF_4^-$ counterion is endergonic by 13 kJ. mol$^{-1}$, leads to product **4**, and closes the catalytic cycle by forming the starting [(IDM)Au][$BF_4$] species **a**.

Like **3**, **4** can be reached from **2Au** through an alternative path that involves initial 1,2-shift of the ester group. As discussed above, the branching point is intermediate **d** (see Scheme 3). In fact, breaking of the C3–O13 bond can alternatively lead to intermediate ***(Z)*e**, with a barrier of 33 kJ mol$^{-1}$, which, upon attack of the C11–C12 double bond on C1, leads to coordinated product species **4Au** via transition state ***(Z)*e-4Au** with an energy barrier of 22 kJ mol$^{-1}$. Bicyclo[3.1.0]hexene **4** is then released from **4Au** by coordination of a $BF_4^-$ anion, and the catalytic cycle closed. Intermediate ***(Z)*e** is 13 kJ mol$^{-1}$ lower in energy than **2Au**, and it is less stable than the ***(E)*e** isomer by 9 kJ mol$^{-1}$. Considering that transition state **2Au-d** is 18 kJ mol$^{-1}$ lower in energy than transition state **2Au-f**, we believe that formation of **4** proceeds to a great extent through a 1,2-shift followed by a cyclopropanation, confirming the results obtained with enantioenriched dienyne **2** (see Table 2).

While the possible mechanistic pathways explaining formation of **3** and **4** from **2Au** were already proposed in the literature,[11a,12,21,22] the formation of **5** from **2Au** had only little mechanistic explanation prior to this study.[12,24,27] We anticipated that **5** could be formed by at least three different reaction paths. In all cases allene-coordinated intermediate **7Au** is the key intermediate for rationalizing formation of **5** (see Scheme 3). The simplest pathway involves a 1,3-shift of the ester group from **2Au** to give intermediate **h** through transition state **2Au-h** with an energy barrier of 41 kJ mol$^{-1}$ (see Scheme 3 and Figure S3, Supporting Information). Intermediate **h**, which is 14 kJ mol$^{-1}$ lower in energy than **2Au**, then evolves, via transition state **h-7Au** with an almost negligible energy barrier of 3 kJ mol$^{-1}$, to allene-coordinated species **7Au**, which is 36 kJ mol$^{-1}$ lower in energy than **2Au**.

Several geometries, each rather similar in energy, can be adopted by **7Au**. For the sake of simplicity, in all reaction

pathways presented, the most stable isomer of **7Au** is discussed. Allene-coordinated species **7Au** can evolve towards coordinated product species **5Au** through simultaneous attack of the C11–C12 double bond on C1 and C3 to form the bicyclo[3.1.0]hexene skeleton of **5** in a single step leading to intermediate **i** through transition state **7Au-i** with an energy barrier of 24 kJ mol$^{-1}$.

Finally, a 1,2-shift of the ester group of **i**, through intermediate **j** and transition states **i-j** and **j-5Au** with energy barriers of 16 kJ mol$^{-1}$ and 21 kJ mol$^{-1}$, respectively, leads to the Au-coordinated product **5Au**. Product release from **5Au** assisted by a coordinating $BF_4^-$ counterion is endergonic by 14 kJ mol$^{-1}$, leads to product **5**, and closes the catalytic cycle by forming the starting [(IDM)Au]$BF_4$ species **a**. The $BF_4^-$ counterion can also displace allene **7** from **7Au**, yielding starting [(IDM)Au][$BF_4$] species **a** and releasing the allene **7** into the reaction medium.

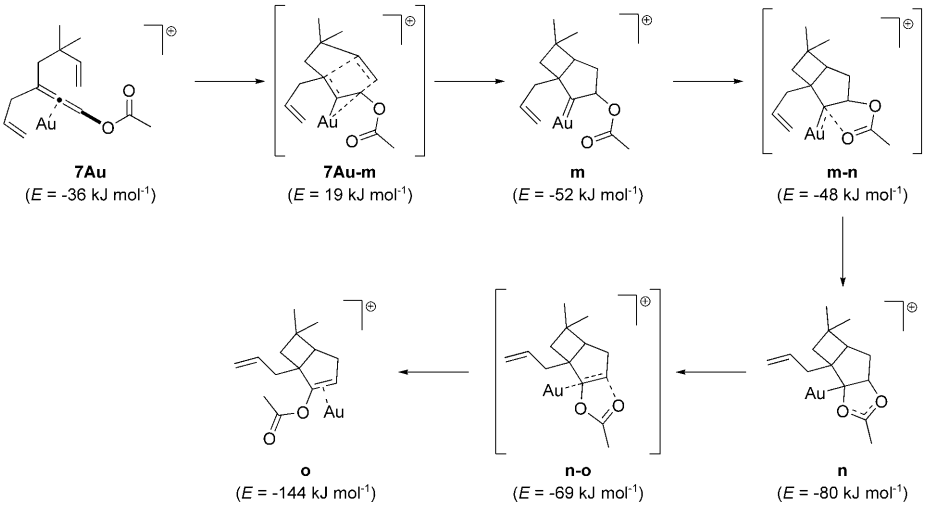
Formation of **5** can be also explained by two other pathways that branch from intermediates **(*E*)e** and **(*Z*)e**, which we already introduced to rationalize formation of **3** and **4**, respectively (Scheme 3). We first discuss branching from intermediate **(*E*)e**. Instead of the cyclopropanation step corresponding to nucleophilic attack of the C6–C7 double bond on C1, **(*E*)e** can undergo a 1,2-shift of the ester group, leading initially to intermediate **(*E*)k** via transition state **(*E*)e-(*E*)k** with an energy barrier of 33 kJ mol$^{-1}$, and then to Au allene species **7Au** through transition state **(*E*)k-7Au** with an energy barrier of 48 kJ mol$^{-1}$. Once intermediate **7Au** has been reached, the reaction can evolve to **5**, as described before (Scheme 3 and Figure S3, Supporting Information). However, this branching is quite unlikely considering that 1,2-shift transition state **(*E*)e-(*E*)k** must compete with cyclopropanation transition state **(*E*)e-3Au**, which is 32 kJ mol$^{-1}$ lower in energy (Scheme 3).

We now discuss branching from intermediate **(*Z*)e**. Instead of the cyclopropanation step corresponding to nucleophilic attack of the C11–C12 double bond on C1, **(*Z*)e**, similarly to **(*E*)e**, can undergo a 1,2-shift of the ester group, leading initially to intermediate **(*Z*)k** via transition state **(*Z*)e-(*Z*)k** with an energy barrier of 20 kJ mol$^{-1}$, and then to Au allene species **7Au** through transition state **(*Z*)k-7Au** with an energy barrier of 50 kJ mol$^{-1}$. Once intermediate **7Au** has been reached, the reaction can evolve to **5**, as described before. In this case, 1,2-shift transition state **(*Z*)e-(*Z*)k** must compete with cyclopropanation transition state **(*Z*)e-4Au**, which is only 2 kJ mol$^{-1}$ higher in energy. This implies that branching from **(*Z*)e** along both reaction pathways is a very likely event.

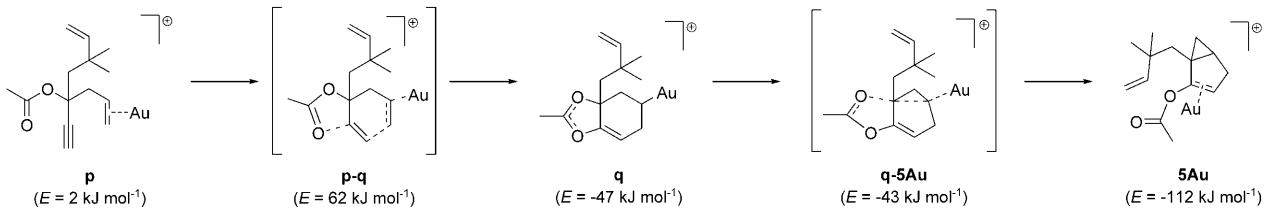
We also explored whether the C1 and C3 atoms of the **7Au** allene species can be attacked by the C6–C7 double bond of the substrate (see Scheme 4). In this case, the bicyclo[3.2.0]heptene skeleton of **m** is formed through transition state **7Au-m** with a barrier of 55 kJ mol$^{-1}$. Transition state **7Au-m** is 31 kJ mol$^{-1}$ higher in energy than transition state **7Au-i**, which is in agreement with the experimental finding that no product having a bicyclo[3.2.0]heptene framework was observed.

For the sake of completeness, we calculated the full catalytic cycle. Thus, intermediate **m** is 52 kJ mol$^{-1}$ lower in energy than **2Au**, and is connected to the product **o** through intermediate **n** at −80 kJ mol$^{-1}$, and transition states **m-n** and **n-o** at −48 kJ mol$^{-1}$ and −69 kJ mol$^{-1}$, respectively. The coordinated product **o** is 144 kJ mol$^{-1}$ lower in energy than **2Au**.

Finally, we also explored formation of **5** according to the pathway shown in Scheme 5, which starts with displacement of the $BF_4^-$ counterion from [(IDM)Au]$BF_4$ species **a** by the




Scheme 4. Alternative cyclization pathway from **7Au**.




Scheme 5. Alternative pathway to form **5**.

C11–C12 double bond of **2**, rather than by the C1–C2 triple bond.[28] Intermediate **p**, in which the C11–C12 double bond is coordinated to the Au atom,[29] is only 2 kJ mol$^{-1}$ higher in energy than **2Au**, which indicates that coordination of the alkyne or of the alkene group of the substrate is scarcely selective. Nucleophilic attack of the C1–C2 triple bond on the coordinated C11–C12 double bond proceeds through transition state **p-q**, which is 62 kJ mol$^{-1}$ higher in energy than **2Au**, so that this reaction path is excluded. In this case too, for the sake of completeness, we calculated the full catalytic cycle. Thus, intermediate **q** is 49 kJ mol$^{-1}$ lower in energy than **p**, and is connected to **5Au** through transition state **q-5Au** with an energy barrier of only 4 kJ mol$^{-1}$.

Our calculations clearly indicate that this catalytic reaction is characterized by numerous highly competitive reaction pathways. We cannot exclude that there are other reaction pathways which we were not able to envisage, and that bulkier NHC ligands could result in somewhat different energetics. However, exploring this complex manifold of reactions with a larger NHC is almost prohibitive. Nevertheless, calculations clearly demonstrate that the high reactivity of the starting structure **2Au** is at the origin of this diversity. As we already indicated, the alkyne-coordinated species can undergo both 1,2 and 1,3-shift of the ester group, leading respectively to Au carbene species **(*E*)e** and **(*Z*)e**, and to Au allene species **7Au**. All these species are connected in a catalytic cycle we dubbed "Golden Carousel". To better illustrate this, the most relevant sections of the numerous reaction pathways are shown in Scheme 6.

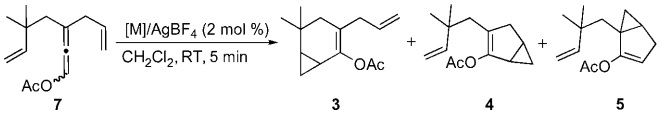
Clearly, alkyne-coordinated species **2Au** is the intermediate of highest energy in the cycle, while the reservoir of active species are intermediate **d** (which is not a way off the cycle) and allene species **7Au**. Intermediate **d** is easily formed from **2Au**. The Au carbene species **(*E*)e** and **(*Z*)e** are ways off the carousel to products **3** and **4**, respectively, while Au-allene species **7Au** is the way off to product **5**. Evolution of **(*E*)e**, **(*Z*)e**, and **7Au** depends on the relative energy of the three transition states (two of them correspond to clockwise and counterclockwise movements on the Golden Carousel, and the third is a way off the carousel) that can be reached from each of these intermediates.

Intermediate **(*E*)e** is an excellent way off the carousel, since the transition state that connects intermediate **(*E*)e** and product **3**, **(*E*)e-3Au**, is quite lower in energy (by 20 kJ mol$^{-1}$ and 32 kJ mol$^{-1}$, respectively) than transition states **d-(*E*)e** and **(*E*)e-(*E*)k**, which are the transition states to be reached by **(*E*)e** in order to move on the carousel. This explains the easy formation of **3**. In contrast, **(*Z*)e** is not a good way off the carousel, since the most likely event is a counterclockwise move on the carousel, to yield the highly stable intermediate **d**. The two other transition states of highest energy accessible from intermediate **(*Z*)e**, namely, **(*Z*)e-4Au** and **(*Z*)k-7Au**, correspond respectively to the way off the carousel leading to **4Au** and to a clockwise move towards allene intermediate **7Au** (Scheme 6). They are 11 and 23 kJ mol$^{-1}$ higher in energy than transition state **d-(*Z*)e**, which explains the small amount of products **4** and **5** formed with NHC ligands of low steric bulk such as ITM (see Table 1).

Finally, **7Au** is another excellent way off the carousel, since the transition state **7Au-i** that connects intermediate **7Au** and product **5** is considerably lower in energy (by 33 and 37 kJ mol$^{-1}$, respectively) than transition states **7Au-(*Z*)k** and **7Au-(*E*)k**, which must be reached by **7Au** to move on the carousel. Thus, the relatively small amount of **5** produced with **2Au** as entry point into the carousel is explained by the relatively high-energy transition state **(*Z*)k-7Au**, which does not allow easy formation of **7Au** from **(*Z*)e**. On the other hand, the direct 1,3-shift pathway from **2Au** to **7Au** is blocked by relatively high energy transition state **2Au-h**. Finally, the golden carousel clearly explains the large amount of **5** that is formed when allene species **7Au** is used as entry point.

Overall, the theoretical results presented allow us to rationalize the formation of unprecedented bicyclo[3.1.0]hexene **5**. According to our calculations, cyclization would occur after formation of the allenyl ester, between the allene and the ene part of the 1,4-allenene core.[30] To verify this hypothesis, we prepared allenyl ester **7** by a simple silver-catalyzed procedure[31] and subjected it to cyclization conditions. In the presence of 2 mol% of [(IPr)AuCl]/$AgBF_4$, cycloisomerization of **7** led to the formation of **5** as major product (Table 3, entry 1). The reaction

Table 3. Cyclization of allenyl ester **7**.




**7** **3** **4** **5**

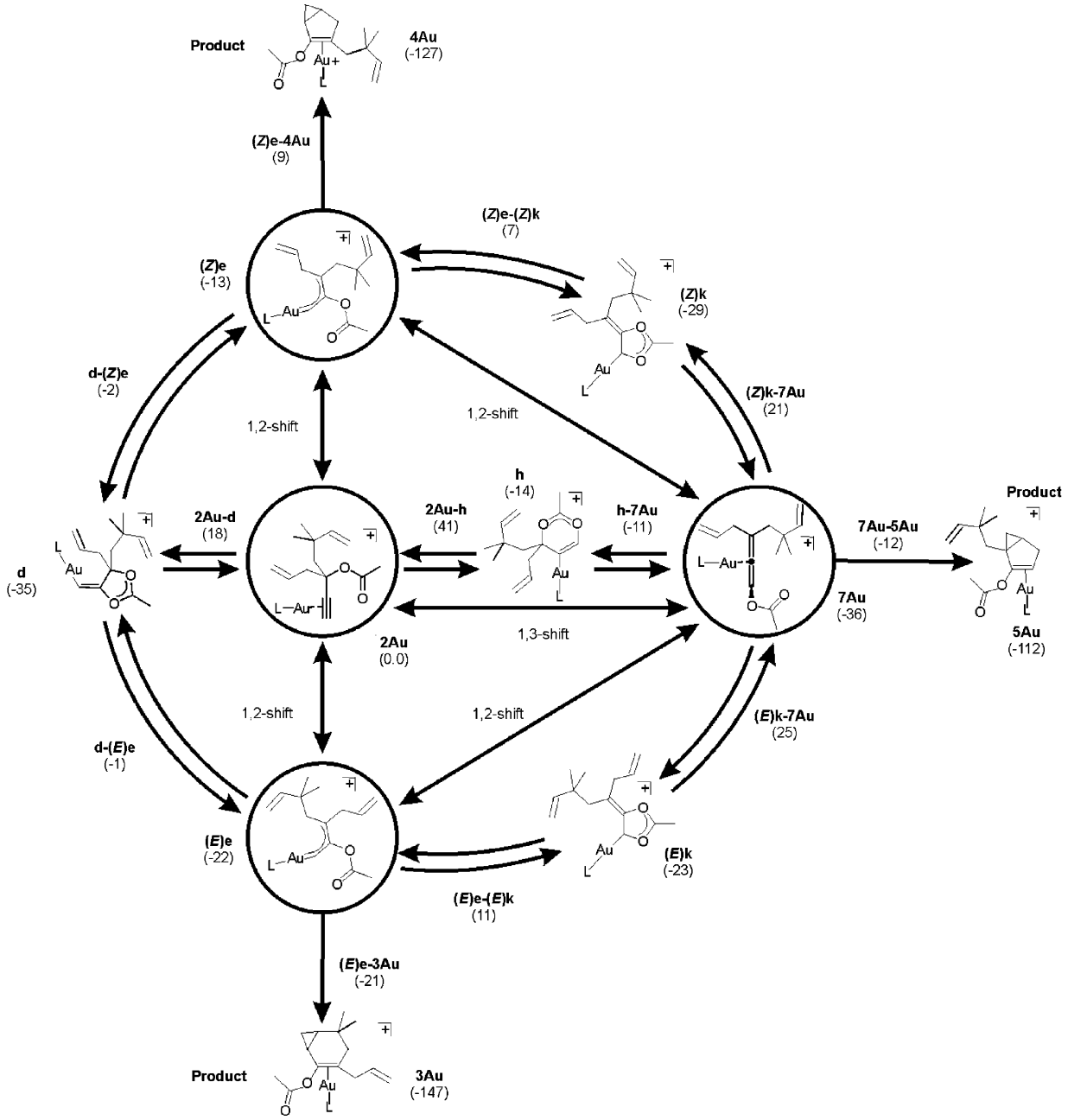
| Entry | [M] | **3**:**4**:**5**[a] | Total yield [%][a] |
|---|---|---|---|
| 1 | [(IPr)AuCl]/$AgBF_4$ | 1/1.4/9.3 | 93 |
| 2[b] | [($PPh_3$)AuCl]/$AgBF_4$ | 1/0.5/0.7 | 51 |
| 3[b] | AuCl | 1/0.8/4.5 | 63 |
| 4[b] | $AuCl_3$ | 1/1.4/1.9 | 50 |

[a] Yields of isolated products, average of two runs, products ratio determined by $^1$H NMR spectroscopy. [b] No starting material remained; significant amounts of oligomerized by-products were formed.

was more selective in favor of **5** than the cyclization of **2** (**3**/**4**/**5**, 1/1.4/9.3 vs. 1/0.4/1.4), which strongly supports allenyl ester **7** as intermediate in the transformation **2**→**5**. Importantly, this is the first reaction producing **3** as the minor product.

Further examination of the reactivity of **7** in the presence of [($PPh_3$)AuCl] revealed the importance of the ligand on the gold center (Table 3, entry 2). The phosphine-containing catalyst notably produced significant amounts of oligomerized products, as previously observed in the cyclization of dienyne **2**, and afforded a more contrasting ratio of cyclopropanated bicycles. Keeping in mind that products **3** and **4** are likely produced via direct cyclopropanation of enyne **2** and/or intermediate **I**, both arising from "retro-migration" of the

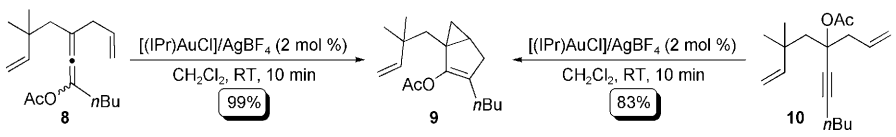
  




Scheme 6. Golden Carousel linking **2**, **3**, **4**, **5**, and **7**.

OAc group in **7**, it appears that the competition between acetate and alkene as internal nucleophiles in **7** is strongly influenced by the ligand on gold. More precisely, allenyl acetate **7** seems to be less prone to isomerization back to **I** and **2** when activated by the cationic $[(NHC)Au]^+$ species than with the phosphine gold catalyst.[32] Finally, the absence of rearranged product from the 1,5-allenene framework seems to indicate a strong preference for the 1,4-allenene scaffold in the present catalytic system, as was predicted in our theoretical studies (see Scheme 4).[33,34]

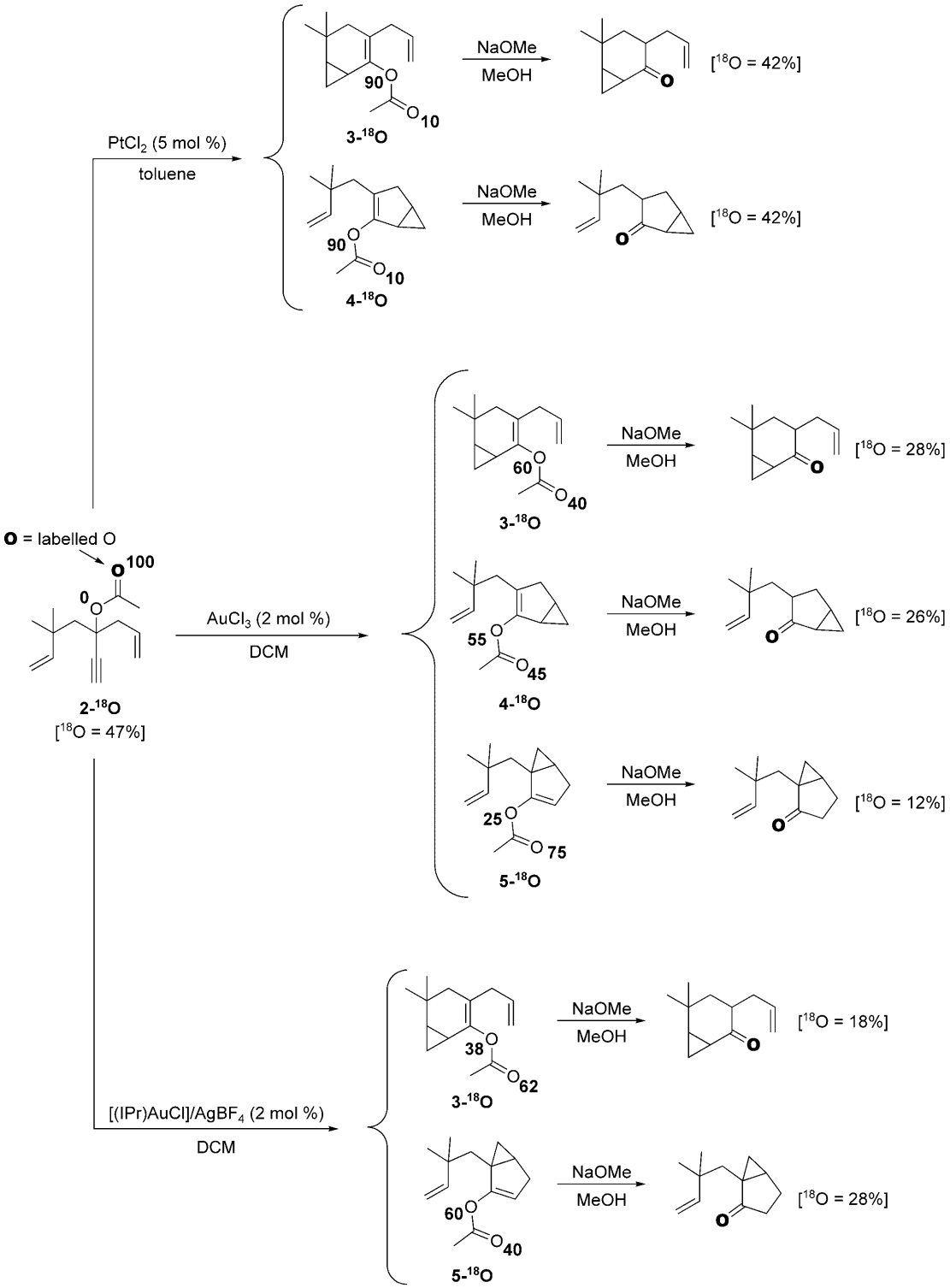
We also carried out the cycloisomerization of allenene **8**, which afforded a quantitative yield of novel cyclopropyl compound **9** [Eq. (2)]. In this case, excellent selectivity was already obtained when starting from the corresponding propargylic acetate **10**, but the yield of **9** was clearly improved. While this total selectivity in favor of the new type of product was unexpected at the time of our preliminary



(2)

communication,[12] it can now be easily rationalized. Formation of allenyl acetate **8** from **10** is favored by the alkyl substituents of the alkyne, and therefore leads straightforwardly to cyclized product **9**.

**1,2- versus 1,3-OAc migration: $^{18}$O-labeling experiments**: Upon π activation, propargylic esters can lead to allenyl esters that are further activated by the metal center, giving rise to a wide variety of products.[9] Even though it is also observed in the presence of platinum,[35] this reactivity is mostly triggered by gold catalysts.[36] We have established




Scheme 7. $^{18}$O-labeling experiments in the cycloisomerization of **2**.

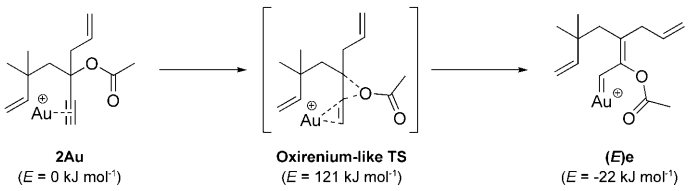
  

that allenyl ester **7** is very likely a key intermediate in the pathway leading to carbocycle **5**. This crucial insight was provided by our theoretical calculations. Additionally, the computed values for the double 1,2-OAc migration were found to be slightly higher than those for the direct 1,3-OAc migration (i.e., 50 vs. 41 kJ mol$^{-1}$), which, taking into consideration the possible experimental error, renders both pathways competitive. Therefore, in an effort to try to understand every aspect of the cyclization studied here, and willing to consider thoroughly any possibility, we carried out labeling experiments with **2-$^{18}$O**, our model substrate with a carbonyl oxygen atom 47% enriched in $^{18}$O, to address this issue.[37]

We then analyzed, by high-resolution mass spectrometry, the isotopic distribution of different mixtures of products from reactions performed in the presence of $PtCl_2$, $AuCl_3$,and [(IPr)AuCl]/$AgBF_4$ (Scheme 7). Both products of the Pt-catalyzed cycloisomerization showed nearly quantitative transfer of the $^{18}$O content at the vinylic position (Scheme 7, top bracket), consistent with a net 1,2-migration of the acetate group. On the contrary, the reactions conducted in the presence of gold revealed a more complex behavior (middle and bottom brackets). The three produced carbocycles **3-$^{18}$O**, **4-$^{18}$O**, and **5-$^{18}$O** displayed scrambled isotopic contents carbonyl/enol ranging from 75/25 to 40/60. These results indicate that gold catalysts, both $AuCl_3$ and the cationic $[(IPr)Au]^+$ fragment, isomerize propargylic acetates to allenyl acetates by both double 1,2-migration (Scheme 1, **I**→**II**→**III**) and direct 1,3-migration (**I**→**III**) randomly. Notably, under the present conditions, isomerization between the alkyne and the allene presumably occurs several times before the cyclization step is achieved.[38,39]

We also envisaged, as a possible alternative, that migration of the acetate group could occur via an oxirenium intermediate, as proposed by Gevorgyan et al. for the isomerization of propargylic acetates and phosphates,[40] and by Hotha and Kashyap for the activation of propargyl glycosides.[41,42] This possibility was ruled out by DFT calculations, since the oxirenium-like transition state, connecting in a single step the alkyne-coordinated species **2Au** and the Au carbene intermediate **(*E*)e**, lies 121 kJ mol$^{-1}$ above **2Au** (see Scheme 8), which is much higher in energy than other transition states that can be reached from **2Au**.

Next, we prepared allene **7-$^{18}$O** from **2-$^{18}$O** and subjected it to cyclization conditions. Interestingly, we observed complete loss of $^{18}$O [Eq. (3)], in strong support of 1,2-migration of the acetate group through its carbonyl oxygen atom, from




Scheme 8. 1,2-OAc migration via an oxirenium intermediate.

**7-$^{18}$O** to **5-$^{18}$O**. The absence of scrambling in this case could appear surprising and points to the faster rate of nucleophilic attack by the alkene than by the carbonyl group. We believe that the improved selectivity observed in the formation of **5** when allene **7** was used as cyclization precursor in place of **2** and the absence of $^{18}$O scrambling from **7-$^{18}$O** both support this reactivity pattern.[43,44]

Interestingly, these findings correlate well with the results of the cycloisomerization of the enantioenriched precursor **2**. Better chirality transfer was observed with platinum(II) catalysis, while gold catalysis, which shows significant $^{18}$O scrambling, also furnished nearly racemic products.

**Reversibility of acetate migration**: One of the main findings of the experimental and theoretical studies described above on the model dienyne **2** is that an apparent 1,2-OAc migration in the final cyclized product can in fact result from a 1,3-shift followed by a "retro" 1,2-migration of the acetate group. This "retro-migration" process has only been observed adventitiously previously[45] and has not been the subject of further investigations. We now provide additional data supporting this reactivity.

**Intermolecular cyclopropanation**: Intermolecular cyclopropanation of propargylic esters with alkene was first reported by Ohe and Uemura using ruthenium(II) catalysts[46] and subsequently studied by Toste et al. with gold catalysts.[21] Our goal was to use allenyl acetates in this reaction and prove "retro-migration" of the ester by intermolecular trapping of the gold carbenoid by an olefin.

We carried out the reaction of allenyl acetate **11** with 3 equivalents of styrene in the presence of platinum(II), gold(I), and gold(III) catalysts (Table 4). Thus, under typical "platinum conditions" (toluene, 80°C), we observed formation of cyclopropane derivative **12** in moderate yield (Table 4, entry 1). Gold(III) chloride led to decomposition (Table 4, entry 2), while gold(I) catalysts showed comparable activity to $PtCl_2$ and had the advantage of being active

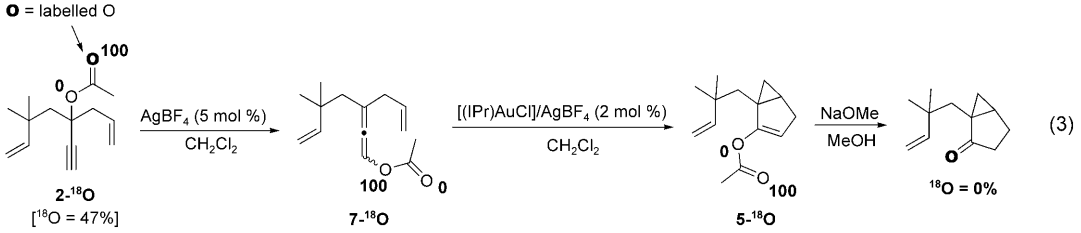



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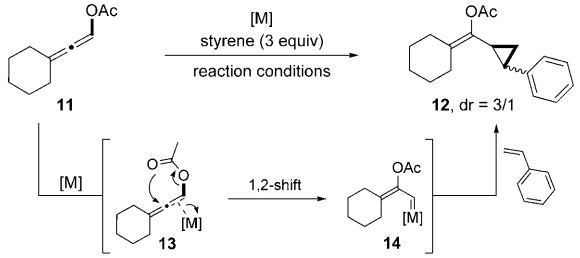
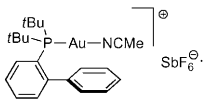
Table 4. Intermolecular cyclopropanation of allenyl ester **11**.




| Entry | [M] | Reaction conditions | Yield of **12** [%][a] |
|---|---|---|---|
| 1 | $PtCl_2$ (5 mol%) | toluene, 80°C, 15 min | 55 |
| 2[b] | $AuCl_3$ (2 mol%) | $CH_2Cl_2$, RT, 2 h | – |
| 3 | $[(PPh_3)AuCl]/AgBF_4$ (2 mol%) | $CH_2Cl_2$, RT, 20 min | 46 |
| 4 | $[(IPr)AuCl]/AgBF_4$ (2 mol%) | $CH_2Cl_2$, RT, 4 h | 51 |
| 5 | $[Au^I]$[c] (2 mol%) | $CH_2Cl_2$, RT, 2 h | 62 |

[a] Yields of isolated products, d.r. determined by $^1H$ NMR spectroscopy. [b] Decomposition of **11** was mainly observed. [c] $[Au^I]$ =




at room temperature (Table 4, entries 3 and 4). This set of experiments validates the aforementioned possibility of forming transition metal vinyl carbenoid intermediates on activation of an allenyl ester moiety, which, to the best of our knowledge, is unprecedented.[47] In the present case, **12** is likely formed through the intermediacy of carbene species **14**, resulting from a 1,2-OAc shift in **13**.[48] Encouraged by these results, we decided to further examine the behavior of allenyl esters in the presence of soft π-acid catalysts and especially the possible dichotomy between allenenyl esters and their corresponding enynyl esters.

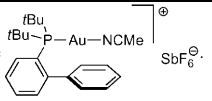
**Cyclization of propargylic acetates versus allenyl acetates: scope and limitations**: Acetate **15** having a 1,6-allenene core was subjected to typical cyclization conditions in the presence of gold and platinum catalysts (Table 5).

Formation of tricyclic compound **16** was observed in all cases, whereby $PtCl_2$ and $[(PPh_3)AuCl]/AgSbF_6$ were the most efficient catalytic systems (Table 5, entries 1, 2, and 4). The gold(I) catalyst bearing a bulky *ortho*-biphenylphosphine ligand was less effective in this

Table 5. Cycloisomerization of allenyl acetate **15**.

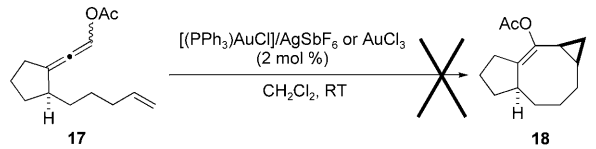

| Entry | [M] (mol%) | Reaction conditions | Yield of **16** [%][a] |
|---|---|---|---|
| 1 | $PtCl_2$ (5 mol%) | toluene, 80°C, 4 h | 49 |
| 2 | $PtCl_2$ (5 mol%) | neat, 80°C, 2 h | 61 |
| 3 | $AuCl_3$ (2 mol%) | $CH_2Cl_2$, reflux, 2 h | 24 |
| 4 | $[(PPh_3)AuCl]/AgSbF_6$ (2 mol%) | $CH_2Cl_2$, reflux, 2 h | 51 |
| 5[b] | $[Au^I]$ (2 mol%) | $CH_2Cl_2$, reflux, 8 h | 20 |

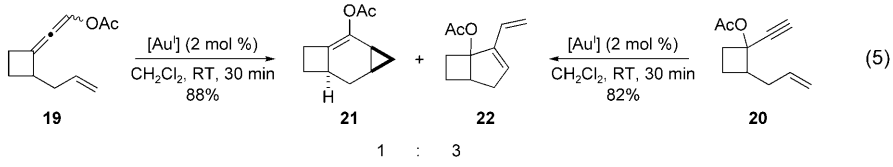
[a] Yields of isolated products. [b] $[Au^I]$ =

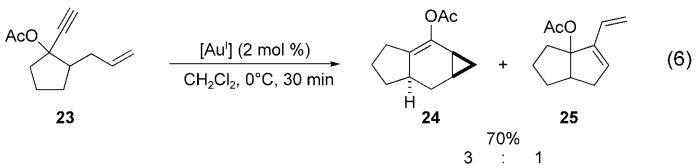


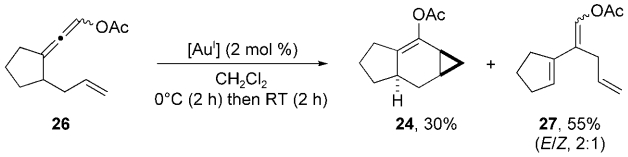

transformation than its triphenylphosphine counterpart (Table 5, entry 5 versus entry 4). The results presented here show the viability of ester migration onto the allene moiety in the context of intramolecular cyclization. As observed previously in the cyclization of the corresponding propargylic acetate,[49] the reaction produced only one diastereomer.

In an attempt to extend the scope of this reaction, formation of tricyclic derivative **18** was envisioned. Unexpectedly, we only recovered the unchanged allene **17**, even after prolonged reaction in the presence of $Au^I$ and $Au^{III}$ catalysts [Eq. (4)].



Even though a thorough explanation of this observation is lacking at the moment, it appears that, as in the case of enyne, minute changes in the architecture of the allenene precursor can be detrimental to the cycloisomerization process.

Turning our attention to other substrates, we examined the reactivity of different unsaturated cyclization precursors. Interestingly, 1,5-allenene **19** and its 1,6-enyne counterpart **20** afforded similar yields and product ratio of **21** and **22** [Eq. (5)], whereby the cyclization from the allene was slightly more efficient than from the alkyne.[50] The formation of cyclized product **22**, which is formally an enyne ring-closing metathesis product,[51] from allene **19** implies in situ formation of alkyne **20** via 1,3-shift of the acetate moiety.

In light of the difference in reactivity observed between **15** and **17**, we decided to examine close analogues of **19** and **20**, namely, **23** and **26**. In the presence of gold(I) catalyst, alkyne **23** afforded a mixture of cyclopropane and diene derivatives **24** and **25** [Eq. (6)].[52] In contrast to the cyclobutyl derivatives, in this series the cyclopropanated product **24** is favored and formed in a 3/1 ratio over the metathesis product, diquinane **25**.

Starting from the corresponding allenyl acetate **26** revealed a different behavior of the gold(I) catalyst employed here. In this case, tricyclic acetate **24** was only formed as the minor product along with triene **27** as major compound [Eq. (7)]. Additionally, no formal metathesis product **25** could be observed. The formation of **27** results presumably from a [3,3] rearrangement catalyzed by the cationic gold(I) center. A thermal [3,3] sigmatropic rearrangement is presumably ruled out since the reaction occurs at room temperature.[53]

## Conclusion

A thorough study of the reactivity pattern of a peculiar branched dienyne in the presence of gold and platinum catalysts has been presented. We examined the effect of the ancillary ligand bound to the gold center and found that bulky N-heterocyclic carbenes are a key parameter for obtaining significant ratios of bicyclo[3.1.0]hexene **5** over compounds **3** and **4**. Further experimental and theoretical mechanistic studies allowed the formation of all cyclized products to be accounted for. Notably, a reaction pathway leading to cyclized compound **5** has been proposed. The cycloisomerization reaction leading from **2** to **5** would occur by a 1,3-OAc shift/allene–ene cyclization/1,2-OAc shift sequence. Supporting this hypothesis, which translates the apparent 1,2-OAc shift from **2** to **5** in a 1,3-OAc migration followed by a 1,2-OAc "retro-migration", cyclization of allenenyl acetate **7** afforded a greater proportion of **5** over **3** and **4**. Additionally, theoretical calculations suggested that the selectivity towards the three cyclopropyl derivatives **3**, **4**, and **5** is dictated by the following equilibrium: [gold propargyl acetates **I**⇄gold carbenoid vinyl acetates **II**⇄gold allenyl acetates **III**]. Finally, examination of the differences in reactivity of various enynyl acetates with their corresponding allenenyl acetates showed that the latter substrates could lead to formation of alternative products.

This combined experimental and theoretical study permitted the details of a novel cycloisomerization mode to be uncovered and more generally to gain insight into mechanistic aspects of the intricate cyclization mode of enynes bearing a propargylic ester group. Further studies taking advantage of this experimental/theoretical approach to complex synthetic issues are ongoing.

## Experimental Section

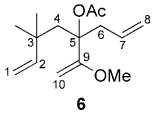
**General information**: All reagents were used as purchased. Dry THF and dry dichloromethane were purified by passing through a purification column from Innovative Technology Inc. (SPS-400-6). Silver salts were stored in a desiccator wrapped in aluminum foil. TLC analysis of reaction mixtures was performed on EMD Chemicals silica gel 60 $F_{254}$ plates and visualized by UV. Flash chromatography was performed on silica gel 60 (230–400 mesh, Silicycle). $^1$H and $^{13}$C NMR spectra were recorded on a Varian 300, Varian 400, or Bruker 300 MHz spectrometer at ambient temperature in $CDCl_3$ containing TMS. Chemical shifts were referenced to the peak of TMS (0.0 ppm). Assignments of some $^1$H and $^{13}$C NMR signals rely on COSY and/or HMBC experiments. Chiral GC analyses were performed under isothermal conditions (110 °C) on a chiral column CP-Chirasil-DEX CB (25 m). [(NHC)AuCl][15] complexes and [Au$^I$][54] were synthesized according to literature procedures. Compounds **2**,[11a] **7**,[12] **10**,[12] **15**,[49] **17**,[49] **19**,[49] **20**,[49] and **23**[49] were synthesized according to literature procedures, and their spectroscopic data found to be in good agreement with previously reported characteristic data. Characterization of cyclized compounds **3**,[11a] **4**,[12] **5**,[12] **9**,[12] **16**,[49] **21**,[49] and **24**[49] was based on previous reports, and their spectroscopic data were in good agreement with previously reported characteristic data.

**Synthesis of [(IDD)AuCl]**: [(IDD)AgCl][55] (200 mg, 0.37 mmol, 1 equiv) and dimethyl sulfide gold(I) chloride (130 mg, 0.44 mmol, 1.1 equiv) were dissolved in a minimal amount of $CH_2Cl_2$ and stirred overnight at room temperature. Charcoal was added and the reaction mixture stirred for a further 3 h. After filtration over Celite, a clear greenish solution was obtained. The volume of $CH_2Cl_2$ was reduced, and the desired complex precipitated and was washed with pentane to yield 180 mg (77% yield) of a white powder. $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 6.94$ (s, 2H, $CH^{Im}$), 4.91 (pent, $J = 6.6$ Hz, 2H, $CH^{Cyclododecyl}$), 2.06–1.96 (m, 4H), 1.69–1.60 (m, 8H), 1.56–1.5 (m, 2H), 1.46–1.28 ppm (m, 30H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 169.8$ (C, CAu), 117.6 (CH, $CH^{Im}$), 58.0 (CH, $CH^{Cyclododecyl}$), 31.2 ($CH_2$), 23.7 ($CH_2$), 23.5 ($CH_2$), 23.4 ($CH_2$), 23.2 ($CH_2$), 21.6 ppm ($CH_2$); HRMS calcd for $C_{29}H_{52}AuN_3$ $[M-Cl+MeCN]^+$: 639.3821; found: 639.3825. CCDC 679915 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif..

**Typical procedure for cycloisomerization of (2)**: To a solution of gold [platinum] catalyst (2 mol% [5 mol%]) in $CH_2Cl_2$ [toluene] (5 mL) in a scintillation vial equipped with a stir bar, $AgBF_4$ (if required) was added. The solution instantly became cloudy. A solution of dienyne **2** (44 mg, 0.2 mmol) in $CH_2Cl_2$ [toluene] (3 mL) was then added. After consumption of the starting material, the solvent was removed. The resulting mixture was dissolved in pentane, filtered through Celite, and the filtrate concentrated in vacuo. Yields refer to mixtures of isolated products; ratios are based on $^1$H NMR integration.

**Trapping experiment in methanol**: **formation of 4-acetyl-6,6-dimethylocta-1,7-dien-4-yl acetate (6)**: Following the typical procedure for the cycloisomerization of **2** (1 mmol) in methanol, the crude product was purified by flash chromatography (pentane/*tert*-butyl methyl ether 8/2), which afforded 149 mg (59% yield) of **6**. $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 5.83$

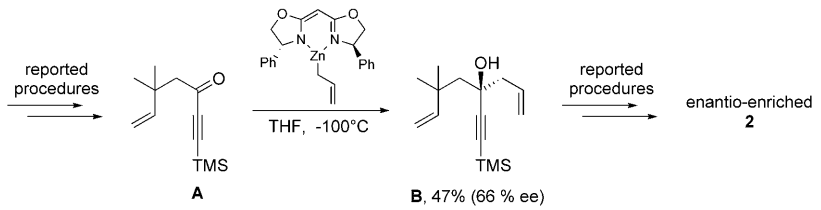
  



**6**

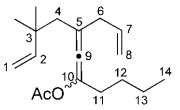
(dd, $J=17.6$, 10.8 Hz, 1H, $H^2$), 5.62–5.51 (m, 1H, $H^7$), 5.01–4.96 (m, 2H, $H^8$), 4.84–4.77 (m, 2H, $H^1$), 4.38 (d, $J=2.0$ Hz, 1H, $1H^{10}$), 4.04 (d, $J=2.0$ Hz, 1H, $1H^{10}$), 3.50 (s, 3H, OMe), 3.07 (dd, $J=14.4$, 8.8 Hz, 1H, $1H^6$), 2.54–2.47 (m, 2H, $1H^6 + 1H^4$), 1.97 (s, 3H, OAc), 1.87 (d, $J=15.2$ Hz, 1H, $1H^4$), 1.01 ppm (s, 6H, $2\times CH_3$); $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta=169.6$ (C, O*C*(O)Me), 161.3 (C, *C*OMe), 148.4 (CH, $C^2$), 132.8 (CH, $C^7$), 117.9 ($CH_2$, $C^8$), 109.1 ($CH_2$, $C^1$), 85.3 (C, $C^5$), 82.2 ($CH_2$, $C^{10}$), 54.4 ($CH_3$, OMe), 44.8 ($CH_2$, $C^4$), 40.8 ($CH_2$, $C^6$), 37.0 (C, $C^3$), 27.8 ($CH_3$, Me), 27.4 ($CH_3$, Me), 22.7 ppm ($CH_3$, OAc); elemental analysis (%) calcd for $C_{15}H_{24}O_3$ ($M=252.35$): C 71.39, H 9.09, found: C 71.18, H 9.15.

**Preparation of enantioenriched dienyne acetate (2)**:[56] A 2.2 M solution of *n*BuLi in hexanes was added to a solution of bis-oxazoline (322 mg, 1.05 mmol, 1.05 equiv) and 2,2′-bipyridine (0.2 mg) in THF (1.8 mL) at 0 °C till the solution turned red. After completion of addition, the reaction mixture became a red-brown suspension. The reaction mixture was warmed to room temperature and stirred for 15 min. A solution of allylzinc bromide (1.5 M, 0.7 mL, 1 mmol, 1 equiv) was added to the solution of lithiated bis-oxazoline. After 30 min, ketone **A**[11a] (187 mg, 0.9 mmol, 0.9 equiv) in THF (1.3 mL) was added at −100 °C. When the reaction was complete, the mixture was quenched with MeOH/$H_2O$ (0.04 mL, 1/1). The solvent was removed under vacuum and the crude product purified by flash chromatography on silica gel (pentane/dichloromethane 7/3) to afford **B** (105 mg, 47%). All spectroscopic data were in agreement with a racemic sample. The enantiomeric excess was determined by chiral gas chromatography (isotherm 110 °C): enantiomer 1 (rt1 = 32.4 min) and enantiomer 2 (rt2 = 33.2 min), 66% *ee*. $[\alpha]_D^{20}=+7.5°$ (c = 0.3, $CHCl_3$). Desilylation and acylation of enantioenriched alcohol **B** according to reported procedures[11a] led to formation of enantioenriched **2**; $[\alpha]_D^{20}=+3.2°$ (c = 0.99, $CHCl_3$).




**Computational details**: All DFT calculations were performed with the Gaussian 03 package.[57] The BP86 GGA functional of Becke and Perdew was used.[58] The TZVP triple-ζ basis set with one polarization function was used for main group atoms,[59] while the relativistic SDD effective core potential in combination with a triple-ζ basis set was used for the Au atom.[60] All geometries were verified by frequency calculations that resulted in 0 and 1 imaginary frequency for intermediates and transition states, respectively. The reported energies include the vibrational gas-phase zero-point energy term, and a solvation term that was obtained through single-point calculations on the gas-phase optimized geometries. The polarizable continuous solvation model IEF-PCM as implemented in the Gaussian 03 package was used.[59] $CH_2Cl_2$ was chosen as model solvent, with a dielectric constant of $\varepsilon=8.93$. Standard nonelectrostatic terms were also included.

**Typical procedure for synthesis of allenyl acetates**: A solution of propargylic acetate (1 mmol) in $CH_2Cl_2$ (5 mL) was added to a suspension of $AgBF_4$ (5 mg, 0.05 mmol, 5 mol%) in $CH_2Cl_2$ (10 mL) in a scintillation vial equipped with a stir bar in the absence of light. When TLC analysis showed total consumption of the starting material, the solvent was removed. The resulting mixture was dissolved in pentane, filtered through Celite, and evaporated. The crude oil was purified, when necessary, by flash chromatography on silica gel.



**8**

*7-Allyl-9,9-dimethylundeca-5,6,10-trien-5-yl acetate (**8**)*: The general procedure using propargylic acetate **10**[12] (442 mg, 1.6 mmol) yielded 420 mg (95%) of **8**. $^1$H NMR (400 MHz, $CDCl_3$): $\delta=5.83$ (dd, $J=17.4$, 10.7 Hz, 1H, $H^2$), 5.86–5.75 (m, 1H, $H^7$), 5.05–5.00 (m, 2H, $2H^8$), 4.91 (dd, $J=17.5$, 1.4 Hz, 1H, $1H^1$), 4.89 (dd, $J=11.4$, 1.4 Hz, 1H, $1H^1$), 2.87–2.73 (m, 2H, $2H^6$), 2.25–2.13 (m, 2H, $2H^{11}$), 2.08 (s, 3H, OAc), 1.43–1.32 (m, 4H, $2H^{12} + 2H^{13}$), 1.04 (s, 3H, Me), 1.03 (s, 3H, Me), 0.89 ppm (t, $J=7.1$ Hz, 3H, $3H^{14}$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta=193.9$ (C, $C^9$), 168.6 (C, C=O), 148.0 (CH, $C^7$), 135.6 (CH, $C^2$), 123.6 (C, $C^{10}$), 116.0 ($CH_2$, $C^8$), 111.7 ($CH_2$, $C^1$), 110.3 (C, $C^5$), 46.1 ($CH_2$, $C^6$), 40.3 ($CH_2$, $C^4$), 37.4 (C, $C^3$), 31.5 ($CH_2$, $C^{11}$), 28.5 ($CH_2$), 27.0 ($CH_3$), 26.8 ($CH_3$), 22.1 ($CH_2$), 21.0 ($CH_3$, OAc), 13.8 ppm ($CH_3$, $C^{14}$); HRMS (ES+): *m/z* calcd for $C_{18}H_{28}O_2Na$ $[M+Na]^+$: 299.1982; found: 299.1990.

*2-(2-Allylcyclopentylidene)vinyl acetate (**26**)*: The general procedure using propargylic acetate **23** (44 mg, 0.2 mmol) yielded 23 mg (51%) of the title compound as a mixture of two diastereomers (1/1). $^1$H NMR ($CDCl_3$, 400 MHz): $\delta=7.44$ (m, 1H, one dia), 7.35 (m, 1H, one dia), 5.87–5.73 (m, 1H), 5.07–4.98 (m, 2H), 2.67–2.61 (m, 1H), 2.59–2.43 (m, 2H), 2.41–2.32 (m, 1H), 2.14 (s, 3H, one dia), 2.13 (s, 3H, one dia), 2.11–1.99 (m, 1H), 1.97–1.89 (m, 1H), 1.84–1.75 (m, 1H), 1.70–1.59 (m, 1H), 1.45–1.31 ppm (m, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta=190.4$ (2C), 169.1 (2C), 137.3, 137.2, 124.9 (2C), 116.4, 116.3, 112.6, 112.1, 45.0, 44.2, 38.8, 38.4, 32.9, 32.8, 32.7, 32.6, 25.4, 25.3, 21.4, 21.3 ppm; IR (neat): $\tilde{\nu}=$ 3066, 2957, 1976, 1753, 1640, 1434 $cm^{-1}$; HRMS (ES+): *m/z* calcd for $C_{12}H_{16}O_2Na$ $[M+Na]^+$: 215.1042; found: 215.1042.

**Procedure for isotopic labeling**: $^{18}$O-labeled water (95% $^{18}$O, 0.84 mL, 41.6 mmol) was added to a solution of acetyl chloride (2.96 mL, 41.6 mmol) in dry dichloromethane (20 mL) at room temperature with vigorous stirring. After 2 h, 5.5 mL of this solution (corresponding to 9.85 mmol of acetic acid) was added to a solution of thionyl chloride (0.790 mL, 10.83 mmol) in dry dichloromethane (2 mL), and the solution was stirred at room temperature for 12 h. The resulting reaction mixture was transferred to a solution of dienyne **2** (350 mg, 1.97 mmol) in dry dichloromethane (2 mL) with triethylamine (4.15 mL, 30 mmol) and 4-dimethylaminopyridine (120 mg, 0.98 mmol). The reaction was stirred at room temperature for 50 h, and the resulting brown solution was diluted with diethyl ether (100 mL) and washed successively with a saturated aqueous solution of $NH_4Cl$ ($2\times50$ mL), a saturated aqueous solution of $NaHCO_3$ ($2\times30$ mL), and brine (50 mL). The organic phase was dried over anhydrous magnesium sulfate and the solvent was removed by evaporation under vacuum. The crude mixture was purified by flash chromatography on silica gel with pentane/diethyl ether (98/2). The $^{18}$O-labeled acetate was obtained as a colorless oil (312 mg, 71%). The spectroscopic data were in agreement with those of the corresponding $^{16}$O acetate except for the carbonyl signal, which appeared as two peaks in the $^{13}$C spectrum: 169.2 ppm for C=$^{16}$O and 169.3 ppm for C=$^{18}$O. The HRMS spectrum confirmed the labeling of the acetate group: $^{16}$O-**2**: HRMS (ES+): *m/z* calcd for $C_{14}H_{20}O_2Li$ $[M+Li]^+$: 227.1618; found: 227.1620; $^{18}$O-**2**: HRMS (ES+): *m/z* calcd for $C_{14}H_{20}O^{18}OLi$ $[M+Li]^+$: 229.1660; found: 229.1661. Integration of mass peaks gave an isotopic abundance of 47%. All the isotopic labeling was localized on the oxygen atom of the carbonyl group, which is in agreement with the preparation procedure.

**Determination of isotopic distribution**: Due to experimental constraints, the isotopic distribution was not determined directly on the enol acetates obtained after the cycloisomerization reaction. The three products were separated and immediately subjected to methanolysis conditions (MeONa/MeOH solution). Neutralization was done by addition of solid $NH_4Cl$ to avoid addition of water and hydration of the corresponding car-

bonyl derivatives. MS analysis allowed for the $^{18}O$ isotopic abundance (the ratio between $C_{12}H_{18}OLi$ and $C_{12}H_{18}O^{18}Li$ peaks) to be determined on the carbonyl derivatives, and comparison with the starting material afforded the structural isotopic distribution (MS spectra for each experiment are provided in the Supporting Information).

**Carbene trapping experiment**: **formation of cyclopropyl derivative 12**: $AgSbF_6$ (16.5 mg, 0.048 mmol) was added to a solution of [$(PPh_3)$AuCl] (24 mg, 0.048 mmol) in dry dichloromethane (10 mL). The solution became cloudy. A solution of allenyl ester **11** (400 mg, 2.41 mmol) and styrene (1.38 mL, 12.05 mmol) in dry dichloromethane (2 mL) was added after 5 min and the mixture stirred under the conditions (time and temperature) indicated in Table 4. When TLC analysis indicated total consumption of the starting material, the crude product was immediately purified by flash chromatography (pentane/diethyl ether 95/5) to afford cyclopropane derivatives **12**[45] (300 mg, 46%) as a 3/1 mixture of *cis*/*trans* diastereomers. Application of the same procedure to $AuCl_3$ catalysis without silver salt and to [(IPr)AuCl]/$AgBF_4$ afforded respectively less than 10 and 51% of cyclopropane derivatives **12** with similar diastereomeric ratio. Platinum ($PtCl_2$, 5 mol%) catalysis was carried out in toluene at 80°C and the same products were isolated in 55% yield. All the spectroscopic data were in agreement with those already reported.[45] The *cis* diastereomer was isolated as an analytical sample: $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta = 7.26$–$7.19$ (m, 2H), 7.18–7.14 (m, 1H), 7.06 (d, $J = 8.4$ Hz, 2H), 2.38–2.25 (m, 2H), 2.23–2.10 (m, 4H), 2.08–1.92 (m, 2H), 1.84–1.75 (m, 1H), 1.50–1.38 (m, 1H), 1.37–1.23 (m, 4H), 1.13–1.01 (m, 2H), 0.51–0.39 ppm (m, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta = 169.5$ (C), 139.4 (C), 135.2 (C), 130.6 (C), 127.6 (CH), 127.4 (CH), 125.6 (CH), 28.7 ($CH_2$), 27.6 ($CH_2$), 26.6 ($CH_2$), 26.5 ($CH_2$), 26.2 (C), 24.6 (CH), 21.6 (CH), 20.7 ($CH_3$), 11.6 ppm ($CH_2$).

**Cycloisomerization of propargylic acetates versus allenyl acetates**: Applying the general cycloisomerization procedure to **19** or **20** with [$Au^I$] catalyst gave **21** and **22** in 1/3 ratio and in 88% yield from **19** and 82% from **20**. Dienyl derivative **22**: $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta = 6.33$ (dd, $J =$ 11.1, 18.0 Hz, 1H), 5.99 (brs, 1H), 5.29 (d, $J = 18.0$ Hz, 1H), 5.03 (d, $J =$ 11.1 Hz, 1H), 3.12–3.06 (m, 1H), 2.90–2.84 (m, 1H), 2.56–2.45 (m, 1H), 2.43–2.33 (m, 1H), 2.19–2.07 (m, 2H), 1.98 (s, 3H), 1.36–1.28 ppm (m, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta = 169.4$, 140.9, 136.0, 129.7, 115.0, 90.0, 43.5, 38.8, 31.9, 22.8, 21.6 ppm: IR (neat): $\tilde{\nu} = 2934$, 2855, 1741, 1636, 1586, 1432 $cm^{-1}$; HRMS (ES+): *m/z* calcd for $C_{11}H_{14}O_2Na$ $[M+Na]^+$, 201.0886; found, 201.0887.

Applying the general cycloisomerization procedure to **23** with [$Au^I$] catalyst gave **24** and formal metathesis product **25** in 70% yield as a 3/1 mixture. Diquinane derivative **25**: $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta = 6.32$ (dd, $J = 11.1$, 18.0 Hz, 1H), 5.81 (m, 1H), 5.34 (dd, $J = 1.0$, 18.0 Hz, 1H), 5.05 (dd, $J = 1.0$, 11.1 Hz, 1H), 2.97–2.90 (m, 1H), 2.88–2.82 (m, 1H), 2.13–1.93 (m, 3H), 1.97 (s, 3H), 1.76–1.66 (m, 1H), 1.56–1.44 (m, 1H), 1.27–1.25 ppm (m, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta = 170.1$, 141.6, 134.6, 130.5, 114.4, 102.1, 47.3, 38.8, 38.3, 34.9, 25.0, 21.9 ppm: IR (neat): $\tilde{\nu} =$ 2999, 2951, 2856, 1752, 1711, 1643, 1451 $cm^{-1}$; HRMS (ES+): *m/z* calcd for $C_{12}H_{16}O_2Na$ $[M+Na]^+$: 215.1042; found: 215.1043.

Applying the general cycloisomerization procedure to **26** with [$Au^I$] catalyst gave **24** and triene **27** in 85% yield as a 35/65 mixture. Triene **27** was isolated as a 2/1 (*E*/*Z*) isomer mixture: $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta =$ 7.23 (s, $1H^M$), 6.99 (s, $1H^m$), 5.87–5.77 (m, 2H), 5.10–4.97 (m, 2H), 3.12 (d, $J = 6.3$ Hz, 2 $H^M$), 2.92 (dd, $J = 6.6$, 1.6 Hz, $2H^m$), 2.72–2.67 (m, $2H^m$), 2.46–2.35 (m, $4H^M + 2H^m$), 2.17 (s, 3 $H^M$), 2.14 (s, $3H^m$), 1.95–1.86 ppm (m, 2 $H^M + 2H^m$); $^{13}C$ NMR ($CDCl_3$, 100 MHz): major diastereomer: $\delta = 168.0$, 139.9, 136.2, 133.3, 128.2, 121.1, 115.2, 33.0, 32.2, 31.1, 23.2, 21.0 ppm; minor diastereomer: $\delta = 168.0$, 139.4, 136.8, 131.6, 130.4, 119.2, 116.2, 36.3, 34.9, 32.3, 23.6, 21.0 ppm; IR (neat): $\tilde{\nu} = 3320$, 3080, 2960, 2860, 1750, 1640, 1610 $cm^{-1}$; HRMS (ES+): m/z calcd for $C_{12}H_{16}O_2Na$ $[M+Na]^+$, 215.1042; found, 215.1043.

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[39] A referee evoked the possibility of ionization of the propargylic carboxylate leading to scrambling. We cannot, at the present time, unequivocally exclude such a possibility. However, the following points are indicative of the absence of ionization of the propargylic acetate: 1) There is no solvolysis of the acetate group in MeOH under gold catalysis [see Eq. (1)]. 2) Gevorgyan et al. did not observe ionization with gold catalysts.[37] 3) Under platinum catalysis, the *ee* of enantioenriched starting material **2-Ac** at half-conversion showed no racemization of the substrate. This precludes ionization of the starting propargyl carboxylate under these reaction conditions. We thank this referee for this insightful remark.

[40] Note that the architecture of the substrates of Gevorgyan et al. differs greatly from ours. The presence of a hydrogen atom at the propargylic position, available for 1,3-H shift, and the particular structural features of conjugated ynones allow for mechanistic pathways distinct from those proposed here.[37]

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[43] Nevertheless, a clear explanation accounting for the great differences in selectivity between pre-isolated allene and allene formed in situ is still needed. We believe that, during the isomerization process from the alkyne to the allene, the gold center is ideally bound to the allene moiety to catalyze another migration of the acetate group. On the other hand, with a preformed allene, coordination of the gold center might be slightly different, and lead preferentially to cyclization with the alkene. Further studies clarifying the coordination behavior of gold toward allenes, and more specifically allenyl esters, are needed. See ref. [44].

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