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Gold(I)-Catalyzed Cycloisomerization–Dimerization Cascade of Benzene-Tethered 1,6-Enynes

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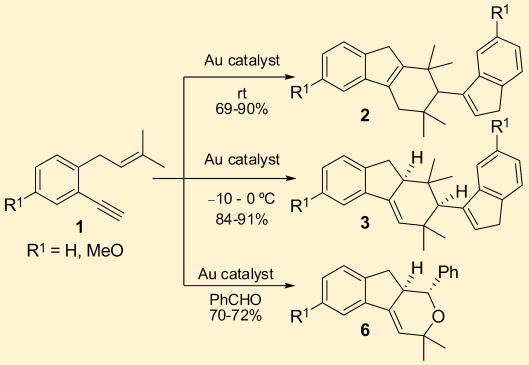
Supporting Information

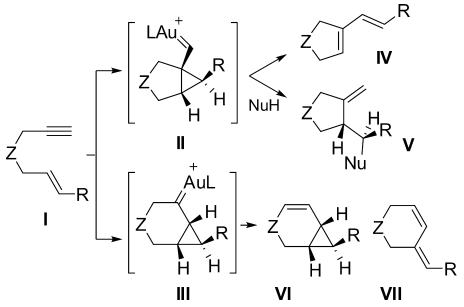
ABSTRACT: An unprecedented stereoselective domino reaction of 1,6-enynes with an aryl ring at C3–C4 in the presence of gold(I) catalysts at low temperature is described. This process involves a novel 5-*exo*-*dig* cycloisomerization–dimerization sequence to afford formal Diels–Alder adducts that undergo a smooth gold-catalyzed double bond migration at room temperature. In addition, the first examples of the gold mesoionic carbene mediated [2+2+2] cycloaddition of these enynes with benzaldehyde are reported.



INTRODUCTION

The highly versatile reactivity of 1,6-enynes in the presence of gold(I) catalysts is well-established.[1] The cycloisomerization of these enynes is particularly useful due to the broad array of products potentially accessible via the different intermediates that are currently accepted depending on the reaction conditions and the gold catalysts used. Thus, 1,6-enynes **I** undergo cycloisomerizations to form cyclopropyl metal carbene intermediates **II** (5-*exo*-*dig*) and/or **III** (6-*endo*-*dig*) (Scheme 1),[2] which evolve through skeletal rearrangements by single cleavage to afford dienes **IV** if external nucleophiles are absent.[3]

Scheme 1. Rationale for Cycloisomerization of 1,6-Enynes



In the presence of nucleophiles, they give rise to substituted exocyclic alkenes **V**.[4] Alternatively, intermediates **III** may lead to fused cyclopropanes **VI** or to methylenecyclohexenes **VII**.[3] Furthermore, gold(I) catalysis encompasses a high potential for the construction of complex target compounds in a domino fashion by trapping intra- or intermolecularly the carbene intermediates with suitable functional groups, producing a rapid increment of molecular complexity in a single operation. In this regard, alkenes can act as partners in cyclopropanations,[5] and carbonyl derivatives may lead to cycloadducts of strikingly different structures depending upon the substitution of the alkene moiety of the enynes.[6] We recently disclosed the straightforward synthesis of gold mesoionic carbenes with a chiral sulfoxide group at C4 and have begun exploring their catalytic activity in the cycloisomerization of 1,6-enynes. These sulfinyl gold carbenes displayed a good catalytic profile in selected examples, producing 1,3-dienes in good yields and with high 5-exo regioselectivity that appears to be related to the steric bulk of the *N*1-substituent of the catalyst.[7] Seeking to broaden the scope of the process, we examined the reactivity of 1,6-enynes with an aromatic tether such as 1-(ethynyl)-2-(3-mehylbut-2-enyl)benzene **1a** that provided a dimeric fluorene-

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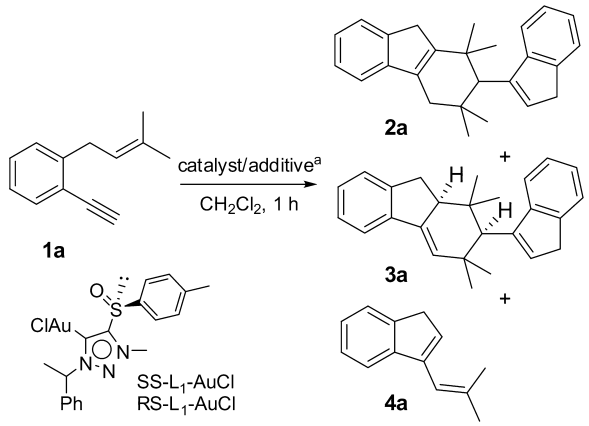
Table 1. Cycloisomerization−Dimerization Cascade of 1-(Ethynyl)-2-(3-methylbut-2-enyl)benzene 1a under Gold(I) Catalysis



			product ratio[b] (yield %)			
entry	substrate	conditions[a]	2a	3a	4a	1a
1	**1a**	3 mol % SS-L_1-AuCl/NaBArF, rt	93 (90)	7		
2	**1a**	3 mol % RS-L_1-AuCl/NaBArF, rt	91 (81)	9		
3	**1a**	3 mol % SS-L_1-AuCl/NaBArF, −10 °C		100 (91)		
4	**3a**	3 mol % RS-L_1-AuCl/NaBArF, rt	100 (93)			
5	**4a**	3 mol % RS-L_1-AuCl/NaBArF, rt	25 (88)[c]	75		
6	**4a**	1 equiv NaBArF, rt[d]		100 (79)		
7	**1a**	3 mol % NaBArF, rt			2	98
8	**1a**	25 mol % NaBArF, rt[e]		14	13	73
9	**1a**	3 mol % SS-L_1-AuCl, rt			6	94
10	**1a**	5 mol % Ph_3PAuCl/NaBArF, rt		20	80	
11	**1a**	5 mol % $Ph_3PAuCl/AgSbF_6$, rt	100 (90)			
12	**1a**	10 mol % $AgSbF_6$, rt	(38)[f]			
13	**1a**	3 mol % $Ph_3PAuCl/AgSbF_6$, 0 °C		86 (84)	14	

[a]In all cases, the additive was employed in an amount to equimolar to that of the gold(I) catalyst. [b]Measured by ^1H NMR of the crude. Unoptimized yields in parentheses. [c]Yield of the combined dimerization. [d]NaBArF was added in 4 portions at 1 h intervals to produce **3a** cleanly; the reaction was allowed to continue for an additional hour (5 h total) to afford pure **3a** in high yield after chromatography. [e]Addition of increasing amounts of NaBArF to this mixture up to 1 equiv led to a 60% yield of **3a** after 2 h. [f]TLC and ^1H NMR analyses showed a complex mixture and substantial decomposition.

like structure assigned as **2a** (Table 1, Figure 1). This unprecedented serendipitous finding along with the presence of fluorene-like skeletons in natural products[8] prompted us to study the process in some depth, and the results are disclosed herein.

RESULTS AND DISCUSSION

Upon examining the reaction of 1-(ethynyl)-2-(3-methylbut-2-enyl)benzene (**1a**) with catalyst SS-L_1-AuCl (Table 1) and NaBArF (3 mol % each) in CH_2Cl_2 at rt (1 h), we obtained an excellent yield (90%) of an unexpected product **2a** (Table 1) that had spectral features (NMR, MS) that were clearly different from those reported for the expected diene **4a**.[9] Careful examination of the data for **2a** suggested a dimeric structure like the one shown in Table 1 and this was then rigorously established by X-ray diffraction analysis (Figure 1).

A more detailed examination of the original experiment revealed minor amounts of a related product **3a** in the crude reaction mixture (Table 1, entry 1). In an effort to clarify the structure of **3a**, the process was tested with diastereomeric catalyst RS-L_1-AuCl that afforded comparable results (Table 1, entry 2). Fortunately, careful control of the reaction temperature (−10 °C) led to very clean crude reaction mixtures with catalyst SS-L_1-AuCl (Table 1, entry 3) that produced **3a** as a single isomer and in excellent yields (91%). At this stage, a detailed spectroscopic study of **3a**, including 2D NMR experiments, strongly supported the proposed structure that may be described as the cycloadduct of a formal Diels−Alder regio- and stereoselective dimerization of 3-indenyl diene **4a**.

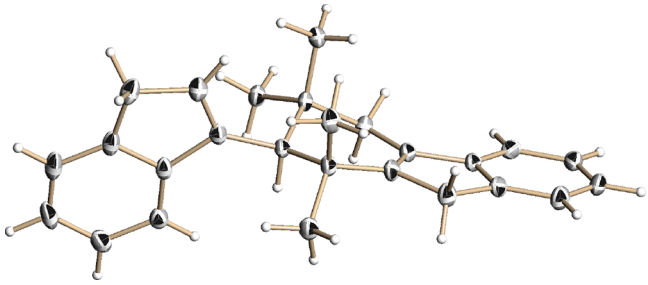


Figure 1. X-ray structure of **2a**.

To gain insight into these processes, we examined the stability of **3a** to a hypothetical gold-catalyzed isomerization at rt to afford **2a** and, indeed, submitting pure **3a** to the catalytic reaction conditions at rt gave an excellent yield of **2a** (Table 1, entry 4). This isomerization appears to require gold catalysis because **3a** was stable in the presence of stoichiometric NaBArF (see below entry 6). On the other hand, the treatment of indenyl diene **4a** prepared as described in the literature[10] under

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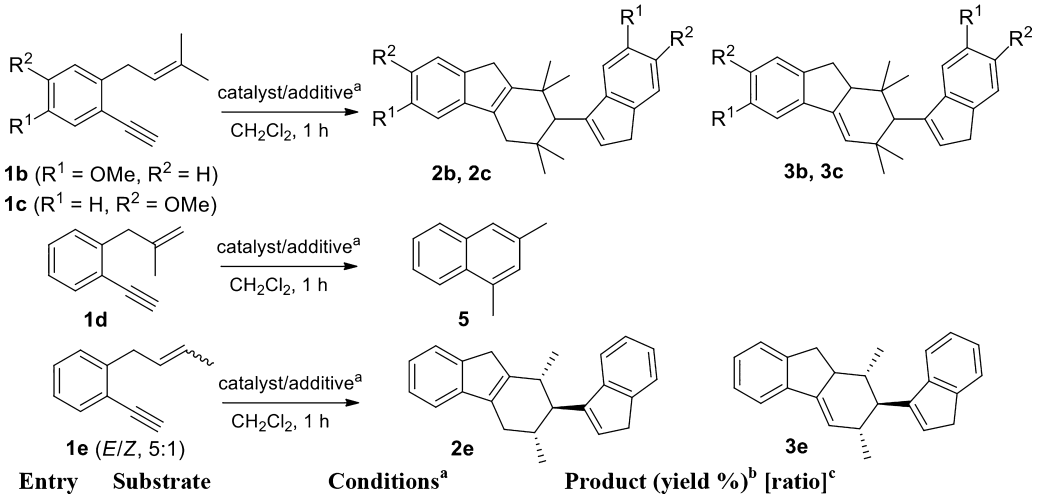
Table 2. Scope of the Cycloisomerization−Dimerization Cascade under Gold(I) Catalysis



entry	substrate	conditions[a]	product (yield %)[b] [ratio][c]
1	**1b**	SS-L_1-AuCl/NaBArF, rt	**2b** (69)
2	**1b**	SS-L_1-AuCl/NaBArF, − 10 °C	**3b** (87)
3	**1c**	SS-L_1-AuCl/NaBArF, − 10 °C	**2c** + **3c** [27:73][c]
4	**2c** + **3c**	SS-L_1-AuCl/NaBArF, rt	**2c** (98)
5	**1d**	$Ph_3PAuCl/AgSbF_6$, rt	**5** (63)
6	**1e**	SS-L_1-AuCl/NaBArF, rt	**2e**/**3e** (74) [50:50][b]
7	**1e**	$Ph_3PAuCl/AgSbF_6$, rt	**2e**/**3e** (73) [72:28][b]
8	**1e**	SS-L_1-AuCl/NaBArF, − 10 °C	**3e** (48)[d]

[a]Three mol % of gold(I) catalyst and additive was used except for entry 5, where 5% of each was employed. The reactions were not optimized. [b]Yields in parentheses. [c]Isomeric ratios in brackets determined by ^{1}H NMR of the crude. [d]Thirteen percent of isomeric 1,5-enyne, (*E*)-1-(ethynyl)-2-(but-1-enyl)benzene, contained in the batch of starting material was recovered unaltered.

the reaction conditions produced a 25:75 mixture of cycloadducts **2a**:**3a** (Table 1, entry 5). To assess the effect of NaBArF on the cycloaddition, diene **4a** was treated with increasing amounts of NaBArF up to stoichiometric and monitored by ^{1}H NMR to yield cycloadduct **3a** (79%, Table 1, entry 6). In view of this unexpected and high-yielding NaBArF catalyzed cycloaddition, we examined the stability of enyne **1a** with 3% NaBArF that afforded mainly starting material and just 2% ratio (^{1}H NMR) of indenyl diene **4a** (Table 1, entry 7). Interestingly, addition of increasing amounts of NaBArF and monitoring by ^{1}H NMR revealed measurable increasing amounts of diene **4a** and cycloadduct **3a** (Table 1, entry 8) that ultimately led to clean conversion to **3a** (60%) upon addition of a full equivalent of NaBArF. Thus, it appears that NaBArF is not just an adequate promoter of the cyclocondensation of diene **4a** to cycloadduct **3a**, but remarkably, it is also possible to trigger the full cycloisomerization−cycloaddition cascade from enyne **1a**. These results are likely to follow a different reaction pathway than upon gold(I) catalysis. As a final control experiment, enyne **1a** was treated with 3 mol % of catalyst SS-L_1-AuCl in the absence of NaBArF to produce a 94:6 mixture of starting material **1a** and diene **4a** (Table 1, entry 9).

At this stage, we decided to examine the behavior of Ph_3PAuCl, a gold(I) complex commonly used in catalysis, in the cycloisomerization−dimerization cascade of enyne **1a**, and the results obtained are summarized in Table 1, entries 10−13. Activation with NaBArF resulted in a 20:80 mixture of dimer **3a** and diene **4a** (Table 1, entry 10). In contrast, activation with $AgSbF_6$ led to a good conversion and yield of isomerized dimer **2a** (Table 1, entry 11). The use of 5 mol % $AgSbF_6$ essentially led to recovery of starting material, and 10 mol % $AgSbF_6$ was required to promote some reaction, affording a complex mixture of side products and a low yield of **2a** (38%, Table 1, entry 12). Finally, reducing the catalyst load in cold CH_2Cl_2 (3%, 0 °C) gave rise to a good yield of dimer **3a** along with some diene **4a** (Table 1, entry 13).

It is worth noting that, from a qualitative standpoint, our carbene catalysts led to slightly faster and cleaner reactions than Ph_3PAuCl. Furthermore, the possibility of having achieved asymmetric induction in the cycloaddition to either **3a** or **2a** with our enantiopure carbene catalysts led us to evaluate the optical purity of these cycloadducts. This was carried out by chiral HPLC and, to our dismay, the cycloadducts resulted to be virtually racemic in all cases (see Supporting Information for details).

At this point, we decided to briefly survey the scope of the process by introducing substituents at the aryl moiety of the 1,6-enynes as well as by varying the substitution of the alkene fragment, and the results obtained are summarized in Table 2. Thus, substrate **1b**, with a MeO group at the *para* position to the allyl residue, gave good yields of cycloadducts **2b** (69%) and **3b** (87%) upon treatment with our carbene catalyst at different temperatures (Table 2, entries 1 and 2). In contrast, regioisomeric substrate **1c** at low temperature afforded a 27:73 mixture of **2c** and **3c**, suggesting a more facile isomerization in this case. Treatment of this mixture with the carbene catalyst at rt gave an excellent yield of **2c** (Table 2, entries 3 and 4).

The effect of a disubstituted terminal alkene was examined next, and substrate **1d**, upon treatment with $Ph_3PAuCl/AgSbF_6$, gave a fair yield of naphthalene derivative **5** (Table 2, entry 5) with spectral data identical to that reported in the

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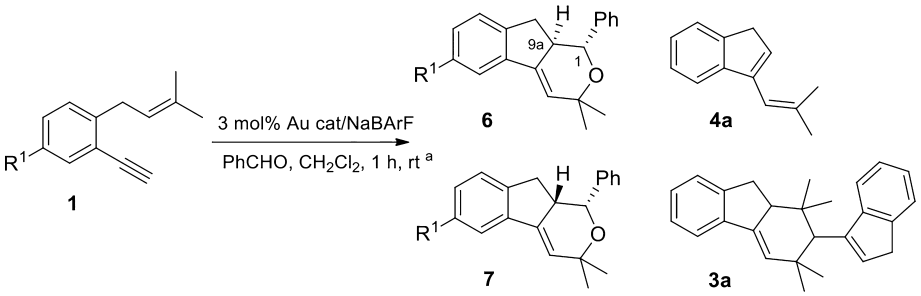
Table 3. Cycloisomerization-Cross-Cycloaddition Cascade of 1,6-Enynes with Benzaldehyde under Gold(I) Catalysis



				product (yield%)[b] [dr][c]			
entry	1	R^1	catalyst	6	7	4a	3a
1	**1a**	H	SS-L_1-AuCl	**6a** (70)			
2	**1a**	H	Ph_3PAuCl	**6a** (21) [60:40]	**7a** (13)	50[d]	8[d]
3	**1b**	MeO	SS-L_1-AuCl	**6b** (72)			

[a]Enyne **1** was added with a syringe pump (1 mL/h). The best yields were accomplished with 5 equiv of PhCHO. In all cases, the additive was employed in an amount equimolar to that of the gold(I) catalyst. [b]Yields in parentheses. [c]Diastereoisomeric ratio as determined by ^{1}H NMR of the crude mixture. [d]An additional 50% conversion to **4a** and 8% conversion to **3a** was shown by the ^{1}H NMR spectrum of the crude.

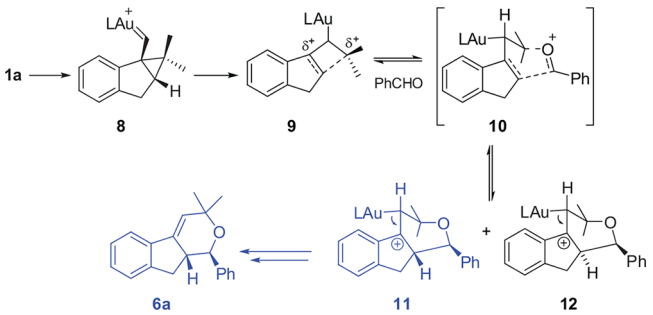
literature.[11] Finally, treatment of crotyl derivative **1e** (5:1, *E*/*Z* mixture) either with our gold carbene or with Ph_3PAuCl/$AgSbF_6$ at rt, produced variable mixtures of cycloadducts **2e**:**3e** depending upon the catalyst/additive used (Table 2, entries 6 and 7). Isomerized adduct **2e** was isolated as a single isomer by careful chromatography of these mixtures. In contrast, our carbene at low temperature gave a fair yield of **3e** as a single isomer after chromatography, along with a less polar fraction that contained unreacted conjugated 1,5-enyne (13%) present in this batch of starting material and a cycloisomerization derived indenyl diene of *Z* geometry, (*Z*)-3-(prop-1-enyl)-1*H*-indene, that appears to be quite unreactive under these conditions.

While 1,6-enynes bearing an aryl ring at C3−C4 are suitable substrates for [2+2+1] annulations with *N*-hydroxyanilines[12] and for [2+2+3] cycloadditions with nitrones,[13] to the best of our knowledge, the related [2+2+2] cycloadditions with aldehydes remain elusive, in sharp contrast with the structurally related 1,7-enynes.[6d] In fact, it has been mentioned that these 1,6-enynes gave only cycloisomerization instead of cycloaddition to benzaldehyde under certain gold-catalyzed conditions.[6d] This prompted us to carry out exploratory experiments on these reactions, and the results obtained are summarized in Table 3.

After some experimentation, we found that slow addition of a solution of enyne **1a** to a solution of our catalyst, NaBArF and 5 equiv of PhCHO, afforded oxacycle **6a** as a single isomer in 70% yield (Table 3, entry 1). In this manner, formation of homocycloaddition derived products (**2a**, **3a**) and diene **4a** was minimized. Switching the gold(I) source to Ph_3PAuCl, (Table 3, entry 2) under identical reaction conditions led to poor yields of a separable 60:40 mixture of **6a** and diastereomer **7a** along with substantial amounts of diene **4a** and a small amount of **3a** (50 and 8% conversion, respectively). Finally, substrate **1b** with a MeO group *para* to the allyl moiety gave rise to oxacycle **6b** as a single isomer in 72% yield under catalysis by our gold carbene (Table 3, entry 3). The structure and relative stereochemistry of compounds **6** were determined by detailed examination of their spectral data including, 2D NMR experiments that indicated a trans relationship for the key proton atoms (H1 and H9a). The optical purity of these products was evaluated by chiral HPLC that indicated that they were also racemic (see Supporting Information).

A rationale to account for the formation and stereochemistry of benzaldehyde cycloadducts **6** is shown in Scheme 2. A gold containing cationic species **9** formed by the accepted Au(I) cyclization of enyne **1a** through intermediate **8** is trapped by the aldehyde to form intermediate Au(I) species **11** and **12**. These species evolve to products **6** (from **11**) and **7** (from **12**) by cationic cyclization and deauration. Because the use of Ph_3PAuCl to promote the cyclization leads to a 60:40 mixture of *syn*-*anti* isomers **6** and **7** in low yield, the complete diastereoselectivity and enhanced yield found with our sulfinyl gold carbene catalyst may be related with the sulfinyl moiety participating in the stabilization of intermediate **11** to produce *syn*-isomer **6**. This hypothesis requires that the cyclization of **9** and the aldehyde through chair-like transition state **10**[6d] has to be reversible (Scheme 2).[14] A similar stabilizing effect of a

Scheme 2. Plausible Reaction Pathway for the Gold(I) Catalyzed Reaction of 1a with PhCHO



cationic species by the sulfoxide moiety of catalyst SS-L_1-AuCl, which determines in those cases the reactivity or inertia of the catalyst, was reported recently by us.[7] At this point, we do not have a full understanding of the nature of this stabilizing interaction.

To clarify the reaction pathway of the cyclodimerization process, a crossover cycloisomerization−dimerization experiment using a 50:50 mixture of **1a** and **1b** as starting material in the presence of SS-L_1-AuCl was carried out (Scheme 3). The

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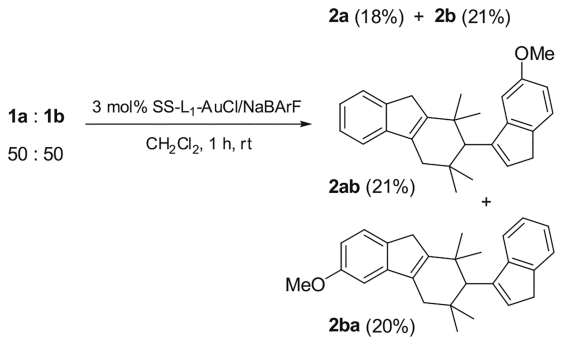
Scheme 3. Crossover in Cycloisomerization−Dimerization of 1a and 1b



resulting reaction mixture contained (^{1}H NMR) an equimolar mixture of the four possible different cycloadducts (**2a**:**2b**:**2ab**:**2ba**) arising from self-condensation of **2a** and **2b** and cross-condensation of **2ab** and **2ba**. It can be concluded that no substrate discrimination occurs during the cyclization process.

In parallel to the mechanism depicted in Scheme 2, cyclization−deauration of intermediate **9** should form 3-indenyl diene **4a** (Scheme 4). Intermediate **9** reacts with diene **4a** to produce a cyclized cation **14** through transition state **13.** The reaction product **3a** is formed from **14** following a pathway analogous to the one depicted for aldehydes in Scheme 2. Allylic isomerization produced the conjugated olefin **2a**. It should be noted that formation of compound **3a** is a formal Diels−Alder reaction of indene **4a** that did not take place in the absence of Au(I) except for stoichiometric amounts of NaBArF (Table 1, entry 8). To rule out a possible Au(I) catalyzed Diels−Alder reaction, highly reactive dienophiles such as methyl 3-methyl-2-butenoate and *N*-phenylmaleimide were added to the reaction mixture. Diels−Alder adducts arising from diene **4a** were not formed, leading instead to variable mixtures of **2a**, **3a**, and **4a.** Other less reactive dienophiles in "normal" (1-hexene, 2-methyl-1-phenyl-1-propene, phenylacetylene, 2,3-dimethyl-1,3-butadiene) or "inverse" Diels−Alder reaction (ethyl vinyl ether) produced analogous results. Therefore, formation of compounds **3** parallels the reaction of species **9** with aldehydes. This species may be formed directly from enyne **1a** or from indene **4a** by Au(I) cycloreversion (Table 1, entry 5). Finally, regarding the NaBArF promoted cycloisomerization−dimerization of enyne **1a** (Table 1, entries 7 and 8), we observed a similar effect in the Nicholas reaction promoted by a Au(I) species.[15] It is tempting to speculate that at least the self-cycloaddition of indenyl diene **4a** is facilitated by some anionic acceleration due to the mildly basic NaBArF,[16] though extensive experimentation is needed to propose a reasonable reaction pathway for these reactions.

CONCLUSION

In summary, an unprecedented and facile gold(I) catalyzed cycloisomerization−dimerization cascade of 1,6-enynes with a benzene tether at C3−C4 was reported. The scope of this serendipitous finding regarding the enyne substrates and the gold catalyst sources was explored briefly, and an interesting NaBArF catalyzed cycloisomerization−dimerization process was unveiled. In addition, these 1,6-enynes appear to be adequate substrates for a gold(I) carbene catalyzed process with benzaldehyde, resulting in a highly diastereoselective [2+2+2] cycloaddition that had not been previously reported in the literature. The presence of the sulfinyl ligand clearly influences the selectivity of the cyclization with benzaldehyde.

EXPERIMENTAL SECTION

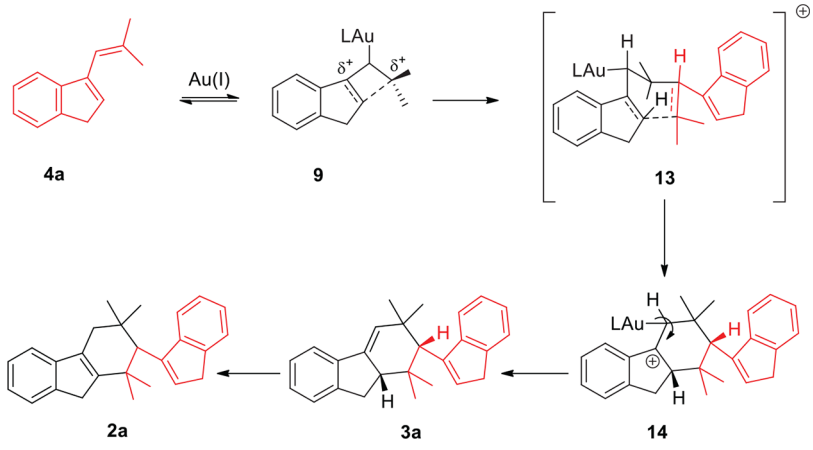
General Synthetic Methods. Reagents and solvents were handled using standard syringe techniques. Anhydrous solvents were purified by filtration on a solvent purification system (SPS). Crude products were purified by flash chromatography on 230−400 mesh silica gel with distilled solvents. ^{1}H and ^{13}C NMR spectra were recorded at 300, 400, or 500 MHz (^{1}H NMR) and at 100 or 126 MHz (^{13}C NMR) using $CDCl_3$ and d_3-MeCN at 298 K, unless otherwise stated. Chemical shifts are given in ppm. Only the characteristic peaks in the infrared spectra (ν max) are quoted. Optical rotations were measured with a 100 mm path cell, at 20 °C and using a sodium lamp. High resolution mass spectra (HRMS) were recorded using an accurate mass QTOF spectrometer. HRMS MALDI/TOF spectra were recorded in a MALDI TOF/TOF spectrometer in positive mode of detection using dithranol as matrix.

Analytical chiral HPLC was performed with detection at 254 nm using a Chiralcel OD-H column.

Enynes **1**[13] and catalysts SS-L_1-AuCl and RS-L_1-AuCl[7] were synthesized as previously described. **4a**[8] and **5**[11] have been previously reported, and only their ^{1}H NMR is given.

General Procedure for the [2+2+2] Cycloisomerization−dimerization Cascades. A mixture of the gold(I) catalyst and the activating agent (3−5% mol of each one) in 1 mL anhydrous CH_2Cl_2 was prepared in a 2-necked round-bottom flask under argon. A solution of the enyne (1 equiv, 0.10−0.17 mmol) in 1 mL of

Scheme 4. Plausible Reaction Pathway for the Gold(I) Catalyzed Cycloisomerization−Dimerization of 1a



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anhydrous CH_2Cl_2 was then added in one portion at rt (for **2**) or at −10 °C (for **3**). The reaction was monitored by TLC to assess the consumption of starting material and diene and by ^1H NMR to assess the **2**:**3** ratio. The reaction was filtered through a short pad of Celite with hexane or pentane and purified by flash chromatography on silica gel after removal of solvents.

*2-(1H-Inden-3-yl)-1,1,3,3-tetramethyl-2,3,4,9-tetrahydro-1H-fluorene (**2a**).* Following the general protocol, enyne **1a** (19.3 mg, 0.113 mmol), SS-L_1-AuCl (1.90 mg, 3.4 μmol, 3 mol %), and NaBArF (3.01 mg, 3.4 μmol, 3 mol %) were mixed in 2 mL of CH_2Cl_2 under argon. After purification, 17.4 mg of **2a** (0.051 mmol, 90%) was obtained (Table 1, entry 1). Alternatively, reaction of RS-L_1-AuCl (2.80 mg, 5.0 μmol, 3 mol %), NaBArF (4.40 mg, 5.0 μmol, 3 mol %) and enyne **1a** (28.4 mg, 0.167 mmol) in 2 mL of CH_2Cl_2 gave 23.0 mg of **2a** (0.068 mmol, 81%) after purification (Table 1, entry 2). Starting from **3a** (32.6 mg, 0.096 mmol), SS-L_1-AuCl (1.60 mg, 2.9 μmol, 3 mol %), and NaBArF (2.55 mg, 2.9 μmol, 3 mol %) in 2 mL CH_2Cl_2, 30.3 mg of **2a** (0.089 mmol, 93%) was obtained (Table 1, entry 4). Using Ph_3PAuCl (3.2 mg, 6.4 μmol, 5 mol %), $AgSbF_6$ (2.2 mg, 6.4 μmol, 5 mol %), and enyne **1a** (28.4 mg, 0.167 mmol) in 2 mL of CH_2Cl_2, 19.7 mg of **2a** (0.057 mmol, 90%) was isolated (Table 1, entry 11).

Data for **2a**: crystalline solid. Mp 108−110 °C. R_f 0.18 (Hex). ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (m, 3H), 7.15 (m, 5H), 6.34 (s, 1H), 3.38 (s, 2H), 3.32 (s, 2H), 3.02 (s, 1H), 2.37 (br s, 2H), 1.23 (s, 3H), 1.09 (s, 3H), 1.01 (s, 3H), 0.84 (s, 3H). $^{13}C\{^1H\}$NMR, HSQC, HMBC (100 MHz, $CDCl_3$) δ 148.9, 148.6, 146.4, 143.3, 143.2, 143.1, 133.4 (C), 130.4, 126.3, 126.1, 124.5, 124.1, 123.7, 123.6, 119.2, 118.1, 51.7 (CH), 39.1, 38.5 (CH_2), 37.5 (C), 36.5 (CH_2), 35.1 (C), 32.4, 31.2, 25.2, 24.1 (CH_3). IR (KBr): 3042, 2960, 2888, 1629, 1605, 1470, 1458, 1393, 1380, 1362, 1260, 1210, 1019, 972, 778, 756, 719 cm^{-1}. HRMS (ESI) *m*/*z* calcd for $C_{26}H_{28}$ $[M]^+$: 340.2186; found 340.2185. Elemental analysis calcd for $C_{26}H_{28}$: C, 91.71; H, 8.29; found: 91.65; H, 8.52. $[\alpha]_D^{25} \sim 0$ (*c* = 1.0, $CHCl_3$).

*6-Methoxy-2-(5-methoxy-1H-inden-3-yl)-1,1,3,3-tetramethyl-2,3,4,9-tetrahydro-1H-fluorene (**2b**).* Following the general protocol, SS-L_1-AuCl (1.73 mg, 3.1 μmol, 3 mol %), NaBArF (2.75 mg, 3.1 μmol, 3 mol %), and enyne **1b** (20.7 mg, 0.103 mmol) were mixed in 2 mL of CH_2Cl_2 to give 14.4 mg of **2b** (0.036 mmol, 69%) after purification (Hex:CH_2Cl_2) (Table 2, entry 1).

Data for **2b**: crystalline solid. Mp 113−115 °C. R_f 0.18 (Hex:CH_2Cl_2, 1:1). ^1H NMR, COSY, NOESY (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.1 Hz, 1H, H7′), 7.24 (d, *J* = 8.1 Hz, 1H, H8), 6.89 (d, *J* = 2.0 Hz, 1H, H4′), 6.76 (d, *J* = 2.2 Hz, 1H, H5), 6.70 (dd, *J* = 8.1, 2.0 Hz, 1H, H6′), 6.65 (dd, *J* = 8.1, 2.2 Hz, 1H, H7), 6.38 (s, 1H, H2′), 3.79 (s, 3H, OMe), 3.77 (s, 3H, OMe), 3.34 (s, 2H, H1′), 3.29 (s, 2H, H9), 2.95 (s, 1H, H2), 2.35 (s, 2H, H4), 1.23 (s, 3H), 1.10 (s, 3H), 1.04 (s, 3H), 0.86 (s, 3H). $^{13}C\{^1H\}$NMR, HSQC, HMBC (100 MHz, $CDCl_3$) δ 159.2, 159.0, 150.5, 150.2, 147.9, 143.0, 135.5, 135.3, 133.3 (C), 131.9 (C2′), 123.93, 123.89, 109.7 (2), 105.7, 104.2 (CH), 55.7 (2 CH_3), 51.8 (CH, C2), 39.1 (C4), 37.8 (CH_2, C1′), 37.6 (C), 35.8 (CH_2, C9), 35.1 (C), 32.5, 31.2, 25.2, 24.1 (CH_3). IR (KBr): 2958, 2885, 1618, 1607, 1475, 1362, 1286, 1214, 1160, 1032, 798 cm^{-1}. HRMS (ESI) *m*/*z* calcd for $C_{28}H_{33}O_2$ $[M + H]^+$ 401.2475; found 401.2493.

*7-Methoxy-2-(6-methoxy-1H-inden-3-yl)-1,1,3,3-tetramethyl-2,3,4,9-tetrahydro-1H-fluorene (**2c**).* Following the general protocol, SS-L_1-AuCl (1.86 mg, 3.3 μmol, 3 mol %) was dissolved in CH_2Cl_2 under argon at −10 °C. NaBArF (2.96 mg, 3.3 μmol, 3 mol %) and **1c** (22.3 mg, 0.111 mmol) in 1 mL CH_2Cl_2 were subsequently added. After 1 h, the reaction was filtered through Celite using hexane and analyzed by ^1H NMR, which indicated a **2c**:**3c** 27:73 ratio (Table 2, entry 3). This mixture was redissolved in 1 mL of CH_2Cl_2 and added onto a mixture of SS-L_1-AuCl (1.86 mg, 3.3 μmol, 3 mol %) and NaBArF (2.96 mg, 3.3 μmol, 3 mol %) in 1 mL of CH_2Cl_2 at rt. After 1 h, filtration through Celite (hexane) and flash chromatography (Hex:CH_2Cl_2), 22.2 mg of **2c** (0.055 mmol, 98%) were obtained (Table 2, entry 4).

Data for **2c**: crystalline solid. Mp 162−164 °C. R_f 0.17 (Hex:CH_2Cl_2, 3:2). ^1H NMR, COSY, NOESY (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.3 Hz, 1H, H4′), 7.07 (d, *J* = 8.3 Hz, 1H, H5), 7.03 (d, *J* = 1.8 Hz, 1H, H7′), 7.00 (d, *J* = 2.3 Hz, 1H, H8), 6.80 (d, *J* = 8.3 Hz, 2H, H6+H5′), 6.21 (s, 1H, H2′), 3.78 (s, 6H, 2OMe), 3.37 (s, 2H, H1′), 3.32 (s, 2H, H9), 2.96 (s, 1H, H2), 2.34 (s, 2H, H4), 1.23 (s, 3H), 1.10 (s, 3H), 1.02 (s, 3H), 0.86 (s, 3H). $^{13}C\{^1H\}$NMR, HSQC, HMBC (100 MHz, $CDCl_3$) δ 157.8, 157.6, 146.3, 145.04, 145.01, 142.7, 142.3, 139.7, 132.8 (C), 128.1 (C2′), 119.5, 118.2, 111.6, 111.5, 110.8, 110.2 (CH), 55.9, 55.7 (CH_3), 51.9 (CH, C2), 39.2 (CH_2, C4), 38.4 (CH_2, C1′), 37.4 (C), 36.5 (CH_2, C9), 35.1 (C), 32.4, 31.2, 25.1, 24.1 (CH_3). IR (KBr): 2960, 2925, 2875, 1608, 1595, 1482, 1467, 1381, 1283, 1240, 1225, 1121, 1027, 853, 815, 803 cm^{-1}. HRMS (ESI) *m*/*z* calcd for $C_{28}H_{33}O_2$ $[M + H]^+$ 401.2475; found 401.2475. Elemental analysis calcd for $C_{28}H_{32}O_2$: C, 83.96; H, 8.05; found: 83.64; H, 8.35.

*(1RS,2SR,3RS)-2-(1H-Inden-3-yl)-1,3-dimethyl-2,3,4,9-tetrahydro-1H-fluorene (**2e**).* Following the general protocol, SS-L_1-AuCl (2.29 mg, 4.1 μmol, 3 mol %), NaBArF (3.64 mg, 4.1 μmol, 3 mol %), and enyne **1e** (21.4 mg, 0.137 mmol) in 2 mL of CH_2Cl_2 were mixed at rt. After 1 h and filtration through Celite, ^1H NMR indicated a 50:50 mixture of **2e**:**3e** (Table 2, entry 6). Purification (hexane) gave 16.0 mg of the mixture of products (0.051 mmol, 74%). Alternatively, Ph_3PAuCl (2.24 mg, 4.4 μmol, 3 mol %), $AgSbF_6$ (1.5 mg, 4.4 μmol, 3 mol %), and enyne **1e** (21.0 mg, 0.134 mmol) were mixed in 2 mL of CH_2Cl_2 and protected from light. Analysis by ^1H NMR after 1 h and filtration through Celite indicated a 72:28 mixture of **2e**:**3e** (Table 2, entry 7). Purification (hexane) gave 15.3 mg of combined products (0.049 mmol, 73%). After a second careful chromatography, pure **2e** (5 mg) was isolated for characterization.

Data for **2e**: colorless oil. R_f 0.17 (Hex). ^1H NMR, COSY (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.3 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 7.3 Hz, 1H), 7.24−7.32 (m, 3H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.15 (t, *J* = 7.3 Hz, 1H), 6.30 (t, *J* = 1.9 Hz, 1H, H2′), 3.46−3.38 (m, 3H, H1′ + H9α), 3.25 (d, *J* = 22.1 Hz, 1H, H9β), 3.00 (br s, 1H, H1), 2.73 (d, *J* = 15.7 Hz, 1H, H4α), 2.39 (t, *J* = 10.2 Hz, 1H, H2), 2.28−2.42 (br s, 1H, H3), 2.18 (m, 1H, H4β), 1.07 (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 6.0 Hz, 3H). ^1H homodecoupling (500 MHz, 318 K): J_{H1-H2} = 8.4, J_{H2-H3} = 10.8 Hz. NOESY 2D (400 MHz, 328 K): correlation peaks between H2-Me1, H2-Me3, H1-H3, H2′-H3. $^{13}C\{^1H\}$NMR, HSQC, HMBC (100 MHz, $CDCl_3$, 328 K) δ 147.4 (br), 146.0, 145.4, 145.2, 143.4, 135.7 (C), 129.6 (br, C2′), 126.4, 126.0, 124.7, 124.1, 124.1, 123.6, 120.2, 118.1, 50.9 (br, CH, C2), 38.7 (C9), 37.9 (CH_2, C1′), 37.1 (br, C1), 33.8 (br, CH, C3), 32.0 (CH_2, C4), 20.7, 19.6 (CH_3). IR (film): 3019, 2955, 2924, 2854, 1742, 1683, 1457, 1377, 1261, 1154, 968, 769, 719 cm^{-1}. HRMS (MALDI/TOF) *m*/*z* calcd for $C_{24}H_{23}$ $[M + H]^+$ 311.1799; found 311.1785.

*(2SR,9aSR)-2-(1H-Inden-3-yl)-1,1,3,3-tetramethyl-2,3,9,9a-tetrahydro-1H-fluorene (**3a**).* Following the general protocol at −10 °C, SS-L_1-AuCl (1.95 mg, 3.5 μmol, 3 mol %), NaBArF (3.09 mg, 3.5 μmol, 3 mol %), and **1a** (19.8 mg, 0.116 mmol) in 2 mL of CH_2Cl_2 yielded after purification (Hex) 18.0 mg of **3a** (0.053 mmol, 91%) (Table 1, entry 3). Alternatively, reaction of **4a** (10.2 mg, 0.060 mmol) with NaBArF (53 mg, 0.060 mmol, 1 equiv) in 1 mL anhydrous CH_2Cl_2 afforded 8.17 mg (0.024 mmol, 79%) of **3a** (Table 1, entry 6). Also, reaction of **1a** (22.3 mg, 0.131 mmol) with NaBArF (116 mg, 0.060 mmol, 1 equiv) in 2 mL of CH_2Cl_2 afforded after 2 h 13.4 mg (0.039 mmol, 60%) of **3a** (Table 1, entries 7 and 8).

Data for **3a**: crystalline solid. Mp 133−135 °C. R_f 0.17 (Hex). ^1H NMR, COSY, NOESY (500 MHz, $CDCl_3$) δ 7.52−7.42 (m, 3H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.29−7.26 (m, 1H), 7.24−7.16 (m, 3H), 6.49 (t, *J* = 2.0 Hz, 1H, H2′), 5.96 (d, *J* = 2.5 Hz, 1H, H4), 3.48 (dd, *J* = 4.1, 1.9 Hz, 2H, H1′), 3.08 (s, 1H, H2), 3.02−2.91 (m, 2H, H9a + H9α), 2.83 (dd, *J* = 14.4, 7.3 Hz, 1H, H9β), 1.20 (s, 3H), 1.08 (s, 3H), 1.00 (s, 3H), 0.81 (s, 3H). ^1H NMR, COSY, NOESY (500 MHz, d_3-MeCN) δ 7.53−7.48 (m, 2H), 7.48−7.43 (m, 1H), 7.33−7.24 (m, 2H), 7.23−7.15 (m, 3H), 6.54 (t, *J* = 2.3 Hz, 1H, H2′), 6.01 (d, *J* = 2.9 Hz, 1H, H4), 3.48 (s, 2H, H1′), 3.14 (s, 1H, H2), 3.02 (td, *J* = 8.6, 2.9 Hz, 1H, H9a), 2.95 (dd, *J* = 15.8, 8.9 Hz, 1H, H9α), 2.80 (dd, *J* = 15.8, 8.5 Hz, 1H, H9β), 1.20 (s, 3H), 1.06 (s, 3H), 0.95 (s, 3H), 0.78 (s, 3H). NOESY 2D (500 MHz, d_3-MeCN): correlation peaks between H2-H9a, H2-Me (0.78), H9a-Me (0.78). $^{13}C\{^1H\}$NMR, HSQC, HMBC (126 MHz, $CDCl_3$) δ 149.0, 144.7, 143.3, 142.6, 141.2, 139.1 (C),

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130.8 (C2′), 127.9 (C4), 127.7, 126.6, 126.1, 125.4, 124.4, 123.6, 120.3, 119.2, 53.7 (C9a), 52.8 (CH, C2), 38.6 (CH_2, C1′), 37.33, 37.25 (C), 33.0 (CH_3), 32.2 (CH_2, C9), 28.1, 26.7, 17.6 (CH_3). $^{13}C\{^1H\}$NMR, HSQC, HMBC (126 MHz, d_3-MeCN) δ 149.9, 145.6, 144.3, 143.1, 141.9 140.2 (C), 132.3 (C2′), 128.7, 128.4 (C4), 127.5, 126.9, 126.3, 125.3, 124.6, 121.0, 120.0, 54.1 (C9a), 53.2 (CH, C2), 39.1 (CH_2, C1′), 37.9, 37.8 (C), 32.9 (CH_3), 32.6 (CH_2, C9), 28.1, 27.0, 17.8 (CH_3). IR (KBr): 2952, 2877, 1604, 1461, 1362, 1166, 975, 860, 755 cm^{-1}. HRMS (ESI) m/z calcd for $C_{26}H_{29}$ $[M + H]^+$ 341.2264; found 341.2269. Elemental analysis calcd for $C_{26}H_{28}$: C, 91.71; H, 8.29; found: 91.81; H, 8.60. $[\alpha]_D^{25} \sim 0$ (c = 0.64, $CHCl_3$).

*(2SR,9aSR)-6-Methoxy-2-(5-methoxy-1H-inden-3-yl)-1,1,3,3-tetramethyl-2,3,9,9a-tetrahydro-1H-fluorene (**3b**).* Following the general protocol, SS-L_1-AuCl (1.85 mg, 3.3 μmol, 3 mol %), NaBArF (2.93 mg, 3.3 μmol, 3 mol %) and enyne **1b** (22.1 mg, 0.110 mmol) were mixed in 2 mL of CH_2Cl_2 under argon at −10 °C. After purification (Hex:CH_2Cl_2), 19.3 mg of **3b** (0.048 mmol, 87%) was isolated (Table 2, entry 2).

Data for **3b**: crystalline solid. Mp 152−154 °C. R_f 0.23 (Hex:CH_2Cl_2, 3:2). ^1H NMR, COSY, NOESY (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.1 Hz, 1H, H7′), 7.09 (d, J = 8.2 Hz, 1H, H8), 6.92 (s, 2H, H5 + H4′), 6.71 (m, 2H, H7 + H6′), 6.44 (s, 1H, H2′), 5.86 (d, J = 2.8 Hz, 1H, H4), 3.77 (s, 6H, 2OMe), 3.35 (s, 2H, H1′), 2.96−2.88 (m, 2H, H9a + H2), 2.81 (dd, J = 15.4, 8.7 Hz, 1H, H9α), 2.68 (dd, J = 15.3, 8.3 Hz, 1H, H9β), 1.12 (s, 3H), 1.00 (s, 3H), 0.94 (s, 3H), 0.74 (s, 3H). $^{13}C\{^1H\}$NMR, HSQC, HMBC (126 MHz, $CDCl_3$) δ 159.1, 159.0, 150.7, 142.5, 142.4, 139.4, 136.9, 135.5 (C), 132.4 (C2′), 127.9 (C4), 126.0, 123.9, 115.0, 109.6, 105.7, 104.5 (CH), 55.7, 55.6 (CH_3), 54.3 (C9a), 53.0 (CH, C2), 37.9 (CH_2, C1′), 37.4, 37.3 (C), 33.0 (CH_3), 31.4 (CH_2, C9), 28.1, 26.8, 17.5 (CH_3). IR (KBr): 2954, 2832, 1607, 1487, 1475, 1362, 1288, 1217, 1158, 1034, 841 cm^{-1}. HRMS (ESI) m/z calcd for $C_{28}H_{33}O_2$ $[M + H]^+$ 401.2475; found 401.2493. Elemental analysis calcd for $C_{28}H_{32}O_2$: C, 83.96; H, 8.05; found: 83.82; H, 8.08.

*(2SR,9aSR)-7-Methoxy-2-(6-methoxy-1H-inden-3-yl)-1,1,3,3-tetramethyl-2,3,9,9a-tetrahydro-1H-fluorene (**3c**).* Following the general protocol, SS-L_1-AuCl (1.86 mg, 3.3 μmol, 3 mol %), NaBArF (2.96 mg, 3.3 μmol, 3 mol %), and enyne **1c** (22.3 mg, 0.111 mmol) reacted in 2 mL of CH_2Cl_2 at −10 °C. Purification (Hex:CH_2Cl_2) gave 6.9 mg of **3c** (0.017 mmol, 30%), which readily isomerized to a 27:73 mixture of **2c**:**3c** (Table 2, entry 3).

Partial data for **3c** from a 27:73 **2c**:**3c** mixture: R_f 0.18 (Hex:CH_2Cl_2, 3:2). ^1H NMR, COSY, NOESY (400 MHz, $CDCl_3$) δ 7.30 (d, J = 8.3 Hz, 1H, H4′ or H5), 7.23 (d, J = 8.3 Hz, 1H, H5 or H4′), 7.02 (d, J = 2.3 Hz, 1H, H7′ or H8), 6.79 (dd, J = 8.3, 2.3 Hz, 1H, H5′ or H6), 6.74 (s, 1H, H8 or H7′), 6.71 (dd, J = 8.4, 2.1 Hz, 1H, H6 or H5′), 6.25 (s, 1H, H2′), 5.73 (d, J = 2.8 Hz, 1H, H4), 3.77 (s, 3H, OMe), 3.75 (s, 3H, OMe), 3.37 (s, 2H, H1′), 2.92 (s, 1H, H2), 2.92−2.68 (m, 3H, H9a + H9α+ H9β), 1.10 (s, 3H), 0.99 (s, 3H), 0.91 (s, 3H), 0.73 (s, 3H). $^{13}C\{^1H\}$NMR, HSQC, HMBC (100 MHz, $CDCl_3$) δ 159.9, 157.8, 146.3, 145.0, 142.4, 142.2, 138.5, 134.2 (C), 128.5 (C2′), 125.9 (C4), 121.1, 119.5, 113.2, 111.6, 110.3, 110.2 (CH), 55.7, 55.6 (CH_3), 54.1 (C9a), 53.0 (CH, C2), 38.5 (CH_2, C1′), 37.4, 37.2 (C), 33.1 (CH_3), 32.4 (CH_2, C9), 28.2, 26.9, 17.5 (CH_3). IR (film): 2926, 2855, 1741, 1683, 1482, 1466, 1381, 1289, 1244, 1226, 1141, 1111, 1033, 840, 805 cm^{-1}. HRMS (ESI) m/z calcd for $C_{28}H_{33}O_2$ $[M + H]^+$ 401.2475; found 401.2475.

*(1SR,2SR,3RS,9aSR)-2-(1H-Inden-3-yl)-1,3-dimethyl-2,3,9,9a-tetrahydro-1H-fluorene (**3e**).* Following the general protocol, SS-L_1-AuCl (2.31 mg, 4.1 μmol, 3 mol %), NaBArF (3.67 mg, 4.1 μmol, 3 mol %), and enyne **1e** (24.8 mg, 87% purity, 0.138 mmol) in 2 mL of CH_2Cl_2 were mixed at −10 °C. Filtration through Celite and purification (hexane) gave 8.90 mg of **3e** (0.029 mmol, 48%) and 2.81 mg of unaltered 1,5 enyne (*E*)-1-(ethynyl)-2-(but-1-enyl)benzene (0.018 mmol, 13%) (Table 2, entry 8).

Data for **3e**: colorless oil. R_f 0.19 (Hex). ^1H NMR, COSY, NOESY (500 MHz, $CDCl_3$) δ 7.49 (dd, J = 7.1, 3.8 Hz, 2H), 7.44 (d, J = 7.6 Hz, 1H), 7.34 (t, J = 7.4 Hz, 1H), 7.25−7.10 (m, 3H), 6.17−6.12 (m, 1H, H2′), 6.13 (t, J = 3.3 Hz, 1H, H4), 3.35−3.30 (m, 2H, H1′), 3.02−2.92 (m, 1H, H9a), 2.86 (s, 1H, H2), 2.82−2.77 (m, 2H, H9), 2.77−2.70 (m, 1H, H3), 2.38−2.30 (m, 1H, H1), 1.29 (d, J = 7.6 Hz, 3H), 1.09 (d, J = 7.2 Hz, 3H). NOESY 2D (500 MHz, $CDCl_3$): correlation peaks between H2′-H3, H3−H4. $^{13}C\{^1H\}$NMR, HSQC, HMBC (126 MHz, $CDCl_3$) δ 149.3, 145.3, 145.2, 144.8, 141.2, 140.2 (C), 128.1 (C2′), 127.6, 126.5, 126.1, 125.4, 124.6, 124.1, 121.0 (C4), 120.2, 119.1, 45.8 (C2), 39.7 (CH, C9a), 37.9 (CH_2, C1′), 34.3 (CH, C3), 33.2 (CH_2, C9), 31.6 (CH, C1), 23.8, 16.7 (CH_3). IR (film): 3018, 2957, 2926, 2872, 1742, 1668, 1605, 1462, 1377, 1255, 1153, 1021, 969, 771, 754, 724 cm^{-1}. HRMS (MALDI/TOF) m/z calcd for $C_{24}H_{23}$ $[M + H]^+$ 311.1799; found 311.1784.

*3-(2-Methylprop-1-en-1-yl)-1H-indene (**4a**).*[8] ^1H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, J = 7.3 Hz, 1H), 7.40 (d, J = 7.4 Hz, 1H), 7.31 (t, J = 7.4 Hz, 1H), 7.21 (td, J = 7.3, 1.3 Hz, 1H), 6.34 (s, 1H), 6.19 (m, 1H), 3.46 (s, 2H), 1.97 (s, 3H), 1.91 (s, 3H). HRMS (ESI) m/z calcd for $C_{13}H_{15}$ $[M + H]^+$ 171.1168; found 171.1170.

*1,3-Dimethylnaphthalene (**5**).*[11] Following the general protocol, $AgSbF_6$ (5.73 mg, 16.7 μmol, 5 mol %), Ph_3PAuCl (8.25 mg, 16.7 μmol, 5 mol %) and enyne **1d** (52.1 mg, 0.334 mmol) were mixed in 5.2 mL of CH_2Cl_2 and protected from light. After filtration through Celite and purification (Hex), 33.0 mg of **5** (0.212 mmol, 63%) were obtained. ^1H NMR (300 MHz, $CDCl_3$) δ 7.99−7.90 (m, 1H), 7.80−7.72 (m, 1H), 7.51−7.39 (m, 3H), 7.18 (s, 1H), 2.67 (s, 3H), 2.48 (s, 3H). MS (EI) m/z 156 (M^+, 100), 141 (92), 128 (14), 115 (18).

*Procedure for the Cross-Cascade between **1a** and **1b**.* Following the general protocol, to a mixture of SS-L_1-AuCl (3.11 mg, 5.6 μmol, 3 mol %) and NaBArF (4.94 mg, 5.6 μmol, 3 mol %) in 1.7 mL of CH_2Cl_2 was added a solution of **1a** (16.3 mg, 96 μmol, 0.53 equiv) and **1b** (18.3 mg, 91 μmol, 0.50 equiv) in 1.7 mL of CH_2Cl_2. After 1 h, analysis by ^1H NMR of the reaction crude indicated an equimolar mixture of **2a**:**2b**:**2ab**:**2ba**. Purification (Hex:CH_2Cl_2) gave 5.7 mg of **2a** (0.017 mmol, 18%), 7.2 mg of **2ab** (0.019 mmol, 21%), 6.7 mg of **2ba** (0.018 mmol, 20%), and 7.4 mg of **2b** (0.019 mmol, 21%).

*Data for 2-(5-Methoxy-1H-inden-3-yl)-1,1,3,3-tetramethyl-2,3,4,9-tetrahydro-1H-fluorene (**2ab**).* Colorless oil. R_f 0.39 (Hex:CH_2Cl_2, 2:1). ^1H NMR, COSY (500 MHz, $CDCl_3$) δ 7.44 (d, J = 7.3 Hz, 1H), 7.37 (d, J = 8.1 Hz, 1H, H7′), 7.30 (t, J = 7.3 Hz, 1H), 7.25 (d, J = 6.1 Hz, 1H), 7.17 (td, J = 7.3, 1.2 Hz, 1H), 6.96 (d, J = 2.3 Hz, 1H, H4′), 6.77 (dd, J = 8.1, 2.3 Hz, 1H, H6′), 6.45 (t, J = 1.8 Hz, 1H, H2′), 3.84 (s, 3H, OMe), 3.41 (s, 4H, H9+H1′), 3.02 (s, 1H, H2), 2.47 (dt, J = 16.6, 2.1 Hz, 1H, H4), 2.41 (dt, J = 16.6, 3.3 Hz, 1H, H4), 1.30 (s, 3H), 1.16 (s, 3H), 1.11 (s, 3H), 0.93 (s, 3H). $^{13}C\{^1H\}$NMR, HSQC, HMBC (126 MHz, $CDCl_3$) δ 158.9, 150.53, 148.6, 146.4, 143.2, 143.0, 135.5, 133.4 (C), 131.94 (C2′), 126.3, 124.1, 123.9 (C7′), 123.6, 118.1, 109.7 (C6′), 105.6 (CH, C4′), 55.7 (CH_3), 51.8 (C2), 39.1 (CH_2), 37.8 (CH_2), 37.5 (C), 36.5 (CH_2), 35.1 (C), 32.5, 31.2, 25.2, 24.1 (CH_3). IR (film): 3046, 2961, 2888, 2833, 1618, 1607, 1573, 1472, 1396, 1381, 1363, 1289, 1265, 1217, 1180, 1166, 1147, 1052, 1033, 798, 759, 739, 722, 705 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{31}O$ $[M + H]^+$: 371.2369; found 371.2363.

*Data for 2-(1H-Inden-3-yl)-6-methoxy-1,1,3,3-tetramethyl-2,3,4,9-tetrahydro-1H-fluorene (**2ba**).* Colorless oil. R_f 0.35 (Hex:CH_2Cl_2, 2:1). ^1H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, J = 7.3 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.31 (d, J = 7.7 Hz, 2H), 7.21 (t, J = 7.1 Hz, 1H), 6.82 (d, J = 2.4 Hz, 1H, H5), 6.72 (dd, J = 8.0, 2.4 Hz, 1H, H7), 6.42 (t, J = 2.0 Hz, 1H, H2′), 3.86 (s, 3H, OMe), 3.46 (s, 2H, H1′), 3.35 (t, J = 2.4 Hz, 2H, H9), 3.09 (s, 1H, H2), 2.41 (s, 2H, H4), 1.30 (s, 3H), 1.16 (s, 3H), 1.09 (s, 3H), 0.91 (s, 3H). $^{13}C\{^1H\}$NMR, HSQC, HMBC (126 MHz, $CDCl_3$) δ 159.2, 150.2, 148.9, 147.9, 143.3, 143.2, 135.3, 133.3 (C), 130.4 (C2′), 126.1, 124.5, 123.9, 123.7, 119.2, 109.7 (C7), 104.2 (C5), 55.7 (CH_3), 51.7 (CH, C2), 39.1 (CH_2, C1′), 38.6 (CH_2), 37.6 (C), 35.8 (CH_2), 35.1 (C), 32.4, 31.2, 25.2, 24.1 (CH_3). IR (film): 2962, 2887, 2833, 1618, 1607, 1574, 1475, 1381, 1287, 1265, 1214, 1163, 1033, 910, 858, 782, 760, 738, 722, 705 cm^{-1}. HRMS (ESI) m/z calcd for $C_{27}H_{31}O$ $[M + H]^+$: 371.2369; found 371.2381.

General Procedure for the [2+2+2] Cycloisomerization-Cross-Cyclization Cascades. A mixture of the gold(I) catalyst (3% mol), the activating agent (3% mol), and benzaldehyde (5 equiv) in 1 mL of anhydrous CH_2Cl_2 was prepared in a 2-necked round-bottom flask under argon at rt. A 0.08−0.12 M solution of the enyne

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in anhydrous CH_2Cl_2 (1 equiv, 0.12 mmol) was slowly added (1 mL/h) by a syringe pump. After completion of the addition, the crude was filtered through a short pad of Celite and purified by flash chromatography on silica gel.

*(1SR,9aSR)-3,3-Dimethyl-1-phenyl-1,3,9,9a-tetrahydroindeno-[2,1-c]pyran (**6a**).* Following the general protocol, **1a** (19.2 mg, 0.113 mmol) in 1 mL of CH_2Cl_2 was slowly added (1 mL/h) to a mixture of SS-L_1-AuCl (1.89 mg, 3.4 μmol, 3 mol %), NaBArF (3.00 mg, 3.4 μmol, 3 mol %), and benzaldehyde (57.4 μL, 0.56 mmol, 5 equiv) in CH_2Cl_2. Purification (Hex:CH_2Cl_2) afforded 21.9 mg of **6a** (0.079 mmol, 70%) and 3.1 mg **3a** (0.009 mmol, 16%) (Table 3, entry 1).

Data for **6a**: crystalline solid. Mp 64−66 °C. R_f 0.23 (Hex:CH_2Cl_2,10:1). ^{1}H NMR, COSY, NOESY (500 MHz, $CDCl_3$) δ 7.48−7.41 (m, 3H), 7.39 (t, J = 7.5 Hz, 2H), 7.32 (t, J = 7.3 Hz, 1H), 7.24−7.16 (m, 3H), 5.96 (d, J = 2.8 Hz, 1H, H4), 4.48 (d, J = 9.5 Hz, 1H, H1), 3.09 (dddd, J = 9.5, 8.7, 8.6, 2.8 Hz, 1H, H9a), 2.78 (dd, J = 15.7, 8.6 Hz, 1H, H9α), 2.64 (dd, J = 15.7, 8.7 Hz, 1H, H9β), 1.48 (s, 3H), 1.41 (s, 3H). NOESY 2D (400 MHz): correlation peaks between H9a-H9, H1-H-9, H1-Me, H1-ArH. ^{13}C{^{1}H}NMR, HSQC, HMBC (126 MHz, $CDCl_3$) δ 144.5, 141.7, 140.9, 140.4 (C), 128.7 (Ph-2C_{meta}), 128.3, 128.0, 127.1 (Ph-2C_{ortho}), 126.9, 125.3, 124.3 (C4), 120.7, 77.6 (CH, C1), 74.6 (C), 46.7 (CH, C9a), 33.9 (CH_2, C9), 29.9, 27.2 (CH_3). IR (KBr): 3034, 2970, 2923, 1604, 1462, 1358, 1230, 1157, 1039, 750, 701 cm^{-1}. HRMS (ESI) m/z calcd for $C_{20}H_{21}O$ $[M + H]^+$ 277.1587; found 277.1594. $[\alpha]_D^{25} \sim 0$ (c = 1.0, $CHCl_3$).

*(1SR,9aRS)-3,3-Dimethyl-1-phenyl-1,3,9,9a-tetrahydroindeno-[2,1-c]pyran (**7a**).* Following the general protocol enyne **1a** (20.7 mg, 0.122 mmol), Ph_3PAuCl (1.80 mg, 3.7 μmol, 3 mol %), NaBArF (3.24 mg, 3.7 μmol, 3 mol %), and benzaldehyde (18.6 μL, 0.183 mmol, 1.5 equiv) in 2 mL of CH_2Cl_2 gave after purification (Hex:EtOAc, 99:1) 7.1 mg of **6a** (0.026 mmol, 21%) and 4.4 mg of **7a** (0.016 mmol, 13%) (Table 3, entry 2). **4a** (50%) and **3a** (8%) were also identified in the reaction mixture by ^{1}H NMR.

Data for **7a**: crystalline solid. Mp 75−77 °C. R_f 0.09 (Hex:EtOAc, 99:1). ^{1}H NMR, COSY, NOESY (500 MHz, $CDCl_3$) δ 7.49 (d, J = 6.8 Hz, 1H), 7.28 (dd, J = 7.8, 1.9 Hz, 2H, Ph-H_{ortho}), 7.25−7.16 (m, 6H), 6.12 (d, J = 3.3 Hz, 1H, H4), 5.37 (d, J = 7.3 Hz, 1H, H1), 3.50 (dddd, J = 9.3, 8.2, 7.3, 3.3 Hz, 1H, H9a), 2.92 (dd, J = 16.2, 9.3 Hz, 1H, H9α), 2.62 (dd, J = 16.2, 8.2 Hz, 1H, H9β), 1.41 (s, 3H), 1.08 (s, 3H). NOESY 2D (400 MHz): correlation peaks between H9a-H9, H1-H-9a, H1-Me, H1-ArH. ^{13}C{^{1}H}NMR, HSQC, HMBC (126 MHz, $CDCl_3$) δ 144.5, 140.8, 140.1, 139.8 (C), 128.9 (Ph-2C_{ortho}), 128.5, 128.2 (Ph-2C_{meta}), 127.5, 125.7, 124.4, 124.3 (C4), 120.7, 75.8 (CH, C1), 72.5 (C), 41.2 (CH, C9a), 34.4 (CH_2, C9), 29.5, 29.2 (CH_3). IR (KBr): 3018, 2961, 1602, 1461, 1356, 1269, 1155, 1032, 754, 700 cm^{-1}. MS (EI) m/z 276 (M^+, 6), 261 (75), 170 (100), 155 (81).

*(1SR,9aSR)-6-Methoxy-3,3-dimethyl-1-phenyl-1,3,9,9a-tetrahydroindeno[2,1-c]pyran (**6b**).* Following the general protocol enyne **1b** (22.7 mg, 0.113 mmol), SS-L_1-AuCl (1.90 mg, 3.4 μmol, 3 mol %), NaBArF (3.01 mg, 3.4 μmol, 3 mol %) and benzaldehyde (57.7 μL, 0.57 mmol, 5 equiv) in 2 mL of CH_2Cl_2 gave after purification (Hex:CH_2Cl_2) 24.8 mg of **6b** (0.081 mmol, 72%) and 3.3 mg **3b** (0.008 mmol, 14%) (Table 3, entry 3).

Data for **6b**: colorless oil. R_f 0.18 (Hex: CH_2Cl_2, 1:1). ^{1}H NMR, COSY, NOESY (500 MHz, $CDCl_3$) δ 7.45 (d, J = 7.3 Hz, 2H, H_{ortho}), 7.38 (t, J = 7.3 Hz, 2H, H_{meta}), 7.30 (t, J = 7.3 Hz, 1H, H_{para}), 7.09 (d, J = 8.2 Hz, 1H, H8), 6.95 (d, J = 2.5 Hz, 1H, H5), 6.76 (dd, J = 8.2, 2.5 Hz, 1H, H7), 5.94 (d, J = 2.9 Hz, 1H, H4), 4.47 (d, J = 9.5 Hz, 1H, H1), 3.82 (s, 3H), 3.10 (dddd, J = 9.5, 8.6, 8.5, 2.9 Hz, 1H, H9a), 2.71 (dd, J = 15.3, 8.6 Hz, 1H, H9α), 2.57 (dd, J = 15.3, 8.5 Hz, 1H, H9β), 1.48 (s, 3H), 1.40 (s, 3H). NOESY 2D (400 MHz): correlation peaks between H9a-H9, H1-H-9, H1-Me, H1-ArH. ^{13}C{^{1}H}NMR, HSQC, HMBC (126 MHz, $CDCl_3$) δ 159.2, 141.7 (2C), 141.1, 136.7 (C), 128.7 (Ph−C_{meta}), 128.0 (Ph-2C_{para}), 127.1 (Ph-2C_{ortho}), 125.9 (C8), 124.3 (C4), 115.2 (C7), 105.1 (C5), 77.5 (CH, C1), 74.6 (C), 55.7 (CH_3), 47.4 (CH, C9a), 33.1 (CH_2, C9), 29.9, 27.2 (CH_3). IR (film): 2969, 2932, 2855, 1679, 1610, 1487, 1466, 1454, 1358, 1328, 1285, 1238, 1176, 1147, 1032, 840, 745, 700 cm^{-1}. HRMS (ESI) m/z calcd for $C_{21}H_{23}O_2$ $[M + H]^+$ 307.1698; found 307.1750.

Crystal Data. Data were collected at low temperature using oil-coated shock-cooled crystals on a Bruker-AXS APEX II diffractometer with Mo Kα radiation (λ = 0.71073 Å). The structure was solved by direct methods,[17] and all nonhydrogen atoms were refined anisotropically using the least-squares method on F^2.[18]

Crystal data for **2a**: Crystals were obtained by slow evaporation of a concentrated solution of compound **2a** in hexanes. $C_{26}H_{28}$, M_r = 340.48, crystal dimensions 0.4 × 0.3 × 0.3 mm^3, monoclinic, $P2_1/c$, a = 8.125(1) Å, b = 21.014(2) Å, c = 11.266(2) Å, β = 99.032(3)°, cell volume = 1899.6(3) Å^3, Z = 4, ρ_{calcd} = 1.191 Mg/m^3, μ = 0.067 mm^{-1}, T = 100(2) K, $2\theta_{max}$ = 52.7°, 31344 reflections collected, 3861 independent, R_{int} = 0.1211, $R1$ = 0.0496 and $wR2$ = 0.1002 for $I > 2\sigma(I)$, $R1$ = 0.0961 and $wR2$ = 0.1174 for all data, residual electron density = 0.244 eA^{-3}.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01273.

Copies of 1D and 2D NMR spectra of compounds **2**, **3**, **6** and **7** and ^{1}H NMR of **4a** and **5** and HPLC profiles for **3a** and **6a** (PDF)

Crystal structure of **2a** (CIF)

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Notes

The authors declare no competing financial interest.

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