Gold(I)-Catalyzed Bis-Cyclization of Allenynes for the Synthesis of Strained and Planar Polycyclic Compounds

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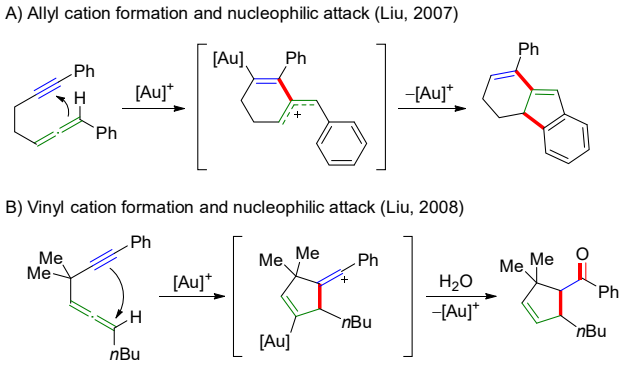
Supporting information: Experimental procedures and characterization data for all new compounds.

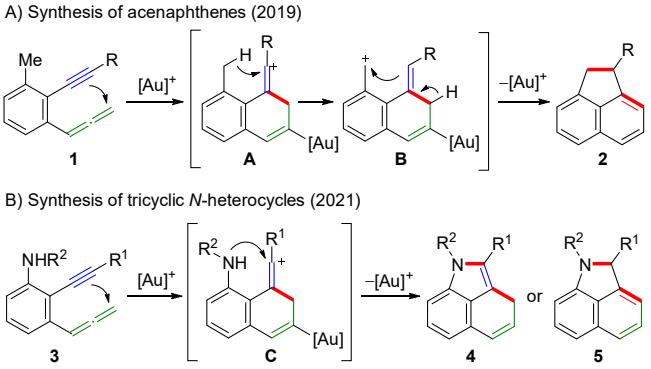
Abstract: A gold-catalyzed cascade cyclization of naphthalene-tethered allenynes gave strained fused phenanthrene derivatives. The reaction proceeds through the nucleophilic reaction of an alkyne with the activated allene to generate a vinyl cation intermediate, followed by arylation with a tethered naphthalene ring to form the 4*H*-cyclopenta[*def*]phenanthrene (CPP) scaffold. When using aryl-substituted substrates on the alkyne terminus, the gold-catalyzed reaction produced dibenzofluorene derivatives along with the CPP derivatives. Selective formation of CPP and dibenzofluorene derivatives depending on the reaction conditions is also presented.

Cationic gold catalysts with high π-acidity activate carbon-carbon multiple bonds to promote various transformations.[1] In contrast to well-investigated reactions using alkynes, allenes, and enynes,[2] the gold-catalyzed reaction of allenynes has not been investigated until recently.[3] When using allenynes in gold-catalyzed reactions, both the allene and the alkyne can function as a nucleophile toward the activated π-bond. For example, Liu and co-workers reported a gold-catalyzed cascade cyclization of 1,5-allenynes, wherein the activation of an alkyne promotes the nucleophilic reaction of an allene to generate an allyl cation intermediate, which undergoes a Nazarov-type cyclization (Scheme 1A).[3b] The same group also demonstrated a gold-catalyzed carbocyclization of 1,4-allenynes proceeding through the nucleophilic attack of an alkyne to the activated allene to promote vinyl cation formation (Scheme 1B).[3c]



Scheme 1. Representative gold-catalyzed cyclization of allenynes.

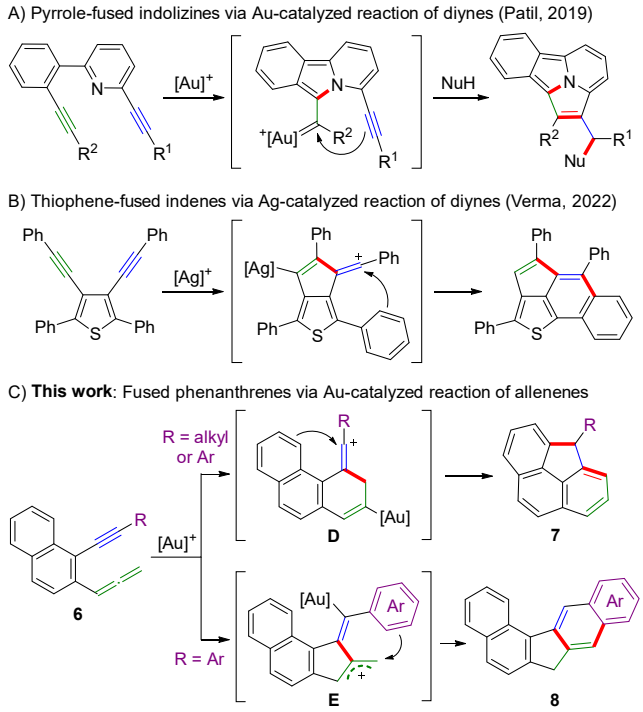
Recently, our group developed gold-catalyzed cyclization reactions using allenynes for the synthesis of tricyclic ring systems. The gold-catalyzed cyclization of allenyne **1** produced acenaphthene **2**; the mechanism can be rationalized as the formation of the vinyl cation intermediate **A**, the subsequent 1,5-hydride shift, and carbocyclization accompanying aromatization (Scheme 2A).[4] We also found that the vinyl cation species can be trapped by a nitrogen nucleophile to produce tricyclic fused indoles **4** and pyrrolonaphthalenes **5** (Scheme 2B).[5] We next envisaged that the intramolecular arylation of vinyl cations might produce highly π-conjugated molecules with a strained structure.



Scheme 2. Our recent works.

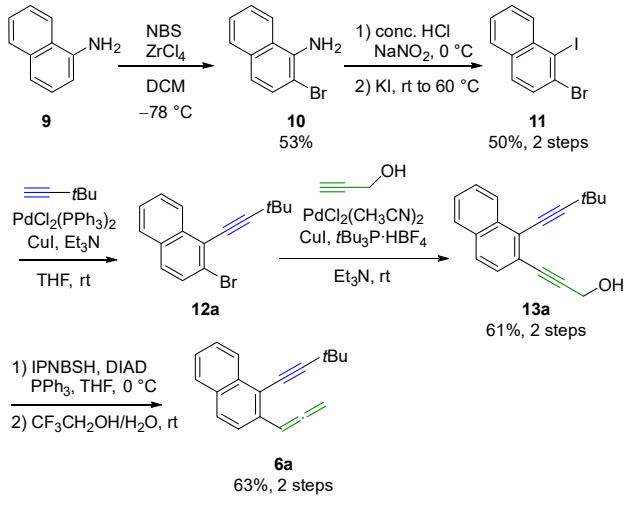
Although the intramolecular trapping of a vinyl cation with arenes is known as a useful strategy for fused arene formation,[6] the reactions involving the construction of highly fused strained molecules have rarely been investigated. In 2019, Patil and co-workers reported that the nucleophilic attack of an alkyne to a gold carbene gave a vinyl gold species, which was then trapped by nucleophiles, including arenes such as indole and azulene (Scheme 3A).[7a] This reaction constructs a strained tetracyclic scaffold during the vinyl cation formation step. Quite recently, Verma and co-workers reported a silver-catalyzed generation of vinyl cation species from diynes, followed by intramolecular arylation to construct a thiophene-fused indenes (Scheme 3B).[7b] This reaction does not require the regioselective formation of a vinyl cation using substrates with a symmetrical structure. In this study, we investigated the gold-catalyzed reaction of a naphthalene-tethered allenynes **6** for the synthesis of 4*H*-cyclopenta[*def*]phenanthrene (CPP)[8] derivatives **7**, with the expectation that regioselective formation of the vinyl cation **D** would facilitate the nucleophilic attack of the naphthalene ring (Scheme 3C). The synthesis of the CPP derivatives **7** and

dibenzofluorenes **8** from aryl-substituted substrates (R = Ar) are also presented.



Scheme 3. Construction of strained ring systems via vinyl cation and this work.

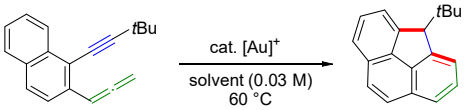
The naphthalene-tethered allenyne **6a** was synthesized in a straightforward manner as shown in Scheme 4. Commercially available 1-aminonaphthalene (**9**) was converted to 1-iodo-2-bromonaphthalene (**11**) via regioselective bromination and the Sandmeyer reaction, according to the reported procedure.[9] Sequential Sonogashira coupling reactions of **11** with 3,3-dimethylbut-1-yne and propargyl alcohol, and subsequent allene formation by Movassaghi deoxygenation,[10] afforded the allenyne **6a**. Other allenynes were also prepared in a similar manner (see the Supporting information).



Scheme 4. Synthesis of allenyne **6a**. DCM=1,2-dichloromethane, IPNBSH = *N*-isopropylidene-*N*'-2-nitrobenzenesulfonyl hydrazine.

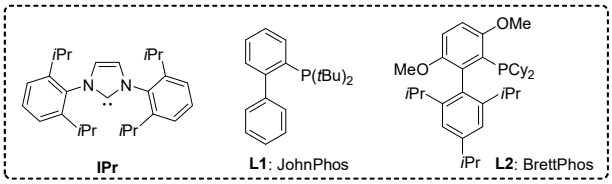
Then we investigated the gold-catalyzed reaction of allenyne **6a**. Treatment of **6a** with $PPh_3AuCl/AgNTf_2$ (5 mol %) in 1,2-dichloroethane (DCE) at 60 °C at 0.03 M gave the desired CPP derivative **7a** in 18% yield (Table 1, entry 1). Optimization of the gold catalysts (entries 1–5) has proven that $BrettPhosAuNTf_2$ (5 mol %) showed good performance to give **7a** in 58% yield (entry 5). Unfortunately, the reaction in THF, toluene, MeCN, or *i*PrOH produced only trace amounts, if any, of **7a** (entries 6–9). From these results, we identified the conditions shown in entry 5 as optimal for further investigations.

Table 1. Optimization of the reaction conditions using **6a**.



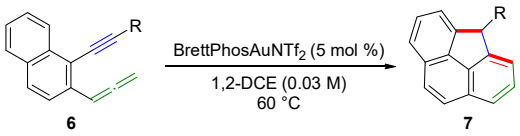
Entry	Catalysts [5 mol %]	Solvent[a]	Time [h]	Yield [%]	Recov. [%]
1	$PPh_3AuCl/AgNTf_2$	DCE	17	18	0
2	$IPrAuCl/AgNTf_2$	DCE	18	37[b]	17[b]
3	**L1**$AuNTf_2$	DCE	18	27[b]	45[b]
4	**L2**$AuCl/AgNTf_2$	DCE	15	37[b]	24[b]
5	**L2**$AuNTf_2$	**DCE**	**17**	**58**	**0**
6	**L2**$AuNTf_2$	THF	19	<5[b]	45[b]
7	**L2**$AuNTf_2$	toluene	21	0	81
8	**L2**$AuNTf_2$	MeCN	18	0	91
9	**L2**$AuNTf_2$	*i*PrOH	20	0	13

[a] 1,2-DCE = 1,2-dichloroethane. [b] Combined isolated yields.

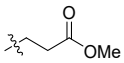
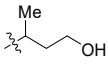


The substituent effect at the alkyne terminus was then examined (Table 2). When the *n*Bu-substituted allenyne **6b** was used, the reaction became sluggish, and only 9% yield of **7b** was obtained (entry 2). In contrast, the reactions using **6c** (R = *i*Pr) or **6d** (R = 3-cyclopentenyl) bearing a branched alkyl group gave **7** in moderate yields (39–45%, entries 3 and 4), suggesting that the bulkiness of the alkyne terminus has an important role in the reaction. This sensitivity to steric effects can be attributed to the preferential activation of the allene over the alkyne by the gold catalyst to generate the vinyl cation intermediate. The functionalized products **7e** and **7f** bearing a methoxycarbonyl or hydroxy group were also obtained by the reaction, although their yields were low to moderate (5–39%, entries 5 and 6).

Table 2. Reaction scope (1).

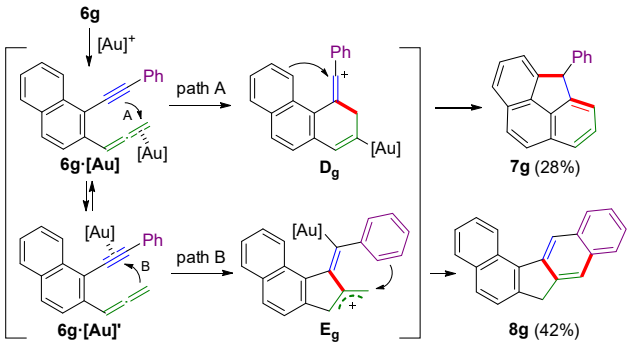


6 7

Entry	Allenyne	R	Yield [%]
1	**6a**	*t*Bu	58
2	**6b**	*n*Bu	9[a]
3	**6c**	*i*Pr	45
4	**6d**		39
5	**6e**		5–8%[b]
6[c]	**6f**		<39%[b]

[a] The reaction was conducted at 80 °C. [b] Obtained as a crude material. [c] Using silylated substrate and CSA treatment after completion.

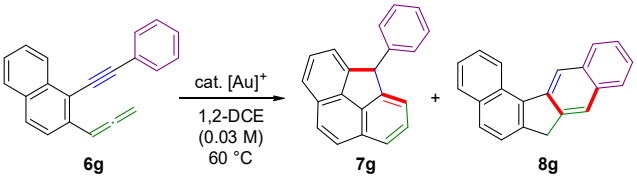
We then proceeded to the reaction of phenyl-substituted allenyne **6g** (Scheme 5). Interestingly, the reaction gave two isomeric products: the CPP derivative **7g** (28%) and the dibenzofluorene **8g**[11] (42%). As initially expected, the CPP derivative **7g** would be formed via activation of the allene as depicted in **6g·[Au]**, nucleophilic attack of the alkyne (path A), and arylation of the resulting vinyl cation $\mathbf{D_g}$. In contrast, the formation of the dibenzofluorene **8g** can be rationalized by activation of the alkyne (**6g·[Au]'**), nucleophilic attack of the allene (path B), and arylation of the allyl cation intermediate $\mathbf{E_g}$ by the terminal phenyl group.



Scheme 5. The rationale for formation of **7g** and **8g**.

Expecting that the selective activation of the allene or alkyne in the substrates might lead to the selective formation of **7** or **8**, we then evaluated several gold complexes for the reaction of **6g** (Table 3).[1d] Compared to BrettPhos (**L2**, 27–29%, entries 1–3), the use of *t*BuBrettPhos (**L3**, entries 4 and 5) and Me$_4$*t*BuXPhos (**L4**, entries 6 and 7) increased the yield **7g** (33–50%), presumably through a preferential activation of the sterically less hindered allene by the bulky gold complexes. In contrast, the use of BisPhePhos (**L5**) and IPr improved the selectivity for **8g** (entries 8 and 9).[12] Using BrettPhosAgNTf$_2$ in hexafluoroisopropanol (HFIP), the yield of **8g** was increased to 64% (entry 10), which is in striking contrast to the reaction in 1,2-DCE (entry 1). Although the reasons for the change in selectivity are unclear, the observed selectivity can be partly attributed to accelerated protodeauration of the intermediate $\mathbf{E_g}$. That is, if the formation of $\mathbf{D_g}$ and $\mathbf{E_g}$ is reversible, sterically congested intermediate $\mathbf{E_g}$ would be easily converted to $\mathbf{D_g}$. In contrast, protonation of $\mathbf{E_g}$ over intermediate $\mathbf{D_g}$ would produce the corresponding deaurated intermediate, which would facilitate formation of **8g**. From these results, entry 6 (**cat. A**) and entry 8 (**cat. B**) were selected as the optimal conditions for the synthesis of **7** and **8**, respectively.

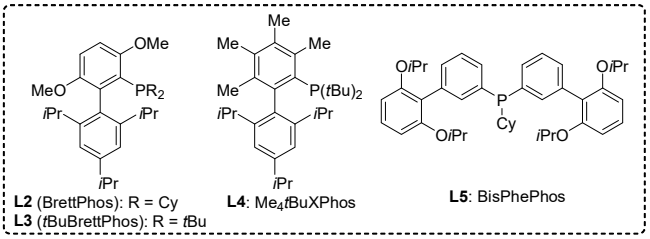
Table 3. Optimization of reaction conditions using **6g**.



6g 7g 8g

Entry	Catalysts [mol %]	Time [h]	**7g** [% yield][a]	**8g** [% yield][a]
1	**L2**AuNTf$_2$ [5]	12	28	56
2	**L2**AuCl/AgNTf$_2$ [5/5]	17	29	62
3	**L2**AuCl/AgSbF$_6$ [5/5]	2	27	43
4	**L3**AuCl/AgNTf$_2$ [5/5]	9	33	29
5	**L3**AuCl/AgSbF$_6$ [5/5]	1	41	31
6	**L4AuCl/AgSbF$_6$ [5/5] (cat. A)**	**7**	**50**	**21**
7	**L4**Au(MeCN)SbF$_6$ [5]	6	50	20
8	**L5AuCl/AgNTf$_2$ [5/5] (cat. B)**	**1**	**0**	**77**
9	IPrAuCl/AgNTf$_2$ [5/5]	12	<5	40
10[b]	**L2**AuNTf$_2$ [5]	24	<5	64

[a] NMR yields using 1,3,5-trimethoxybenzene as an internal standard. [b] The reaction was conducted in HFIP (0.03 M).

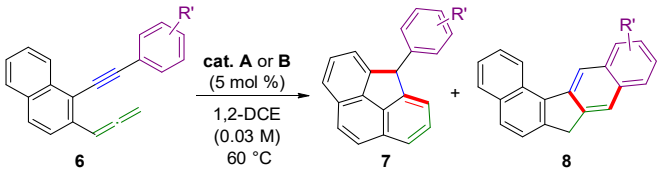


L2 (BrettPhos): R = Cy
L3 (*t*BuBrettPhos): R = *t*Bu
L4: Me$_4$*t*BuXPhos
L5: BisPhePhos

Next, the reaction scope using various substrates bearing different aryl groups at the alkyne terminus was investigated (Table 4). Using Me$_4$*t*BuXPhosAuCl/AgSbF$_6$ (**cat. A**), the CPP derivative **7** was preferentially obtained (entries 1–10), although the yields and selectivities were low in some cases (entries 3 and 5). As expected, the reaction using BisPhePhosAuCl/AgNTf$_2$ (**cat. B**) gave the dibenzofluorene derivatives **8** with moderate to good selectivity (entries 11–18). The selectivity was affected not only by the catalyst, but also by the electronic and steric effects of the

substituent. Thus, the formation of the CPP derivatives **7** was favored when using substrates with an electron-donating substituent (**6h**, entry 2) or sterically hindered *o*-substituted substrates (**6l**, **m**, **o**, and **p**; entries 6, 7, 9, and 10). The structure of **7o** was confirmed by X-ray crystallography.[13] For the reaction using **cat. B**, sufficient yields (>75%) and selectivities (>95:5) were observed for the formation of **8g** (R = H), **8i** (R = *p*-Me), and **8n** (R = *m*-Me) (entries 11, 13, and 18).

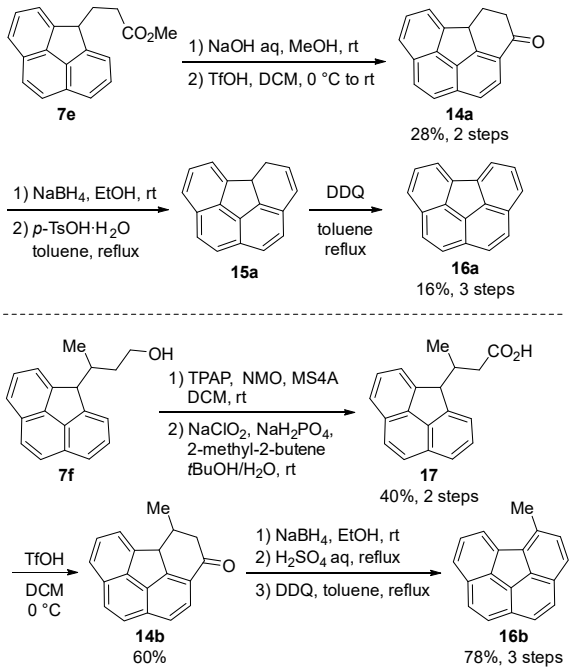
Table 4. Reaction scope (2).



Entry	Substrate	R	Cat.[a]	**7** [% yield][b]	**8** [% yield][b]
1	**6g**	H	**A**	50	18
2	**6h**	*p*-OMe	**A**	40	10
3	**6i**	*p*-Me	**A**	37	32
4	**6j**	*p*-Cl	**A**	29	12
5[c]	**6k**	*p*-CO_2Me	**A**	<5	<5
6	**6l**	*o*-Me	**A**	78	8
7[c]	**6m**	*o*-Cl	**A**	38	<5
8	**6n**	*m*-Me	**A**	64	24[d]
9	**6o**	2,6-Me_2	**A**	58	0
10	**6p**	2,6-Cl_2	**A**	47	0
11	**6g**	H	**B**	0	75
12	**6h**	*p*-OMe	**B**	<5	26
13	**6i**	*p*-Me	**B**	<5	88
14	**6j**	*p*-Cl	**B**	<5	19
15	**6k**	*p*-CO_2Me	**B**	0	59
16	**6l**	*o*-Me	**B**	25	55
17	**6m**	*o*-Cl	**B**	0	49
18	**6n**	*m*-Me	**B**	<5	90[d]

[a] **cat A**: Me$_4$*t*BuXPhosAuCl/AgSbF$_6$; **cat B**: BisPhePhosAuCl/AgNTf$_2$. [b] Isolated yields. [c] The reaction was conducted at 80 °C. [d] Regioisomeric mixture (2:1) was formed.

Finally, the construction of a highly fused polycyclic scaffold using the cyclization products was investigated (Scheme 6). Hydrolysis of the methyl ester **7e** and intramolecular Friedel–Crafts acylation of the resulting acid with TfOH gave the ketone **14a** with a pentacyclic scaffold. Subsequent reduction of the ketone with $NaBH_4$, acid-mediated dehydration, and oxidation with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) afforded benzo[*ghi*]fluoranthene (**16a**)[14] in low yield. In contrast, the methylated acid **17**, obtained from **7f** by two-step oxidation in 40% yield, produced the corresponding ketone **14b** in 60% yield via intramolecular Friedel–Crafts acylation. The three-step sequence including reduction, dehydration, and oxidation afforded 5-methylbenzo[*ghi*]fluoranthene (**16b**) in 78% yield in 3 steps. This methyl group can be potentially used for further elaboration, *e.g.*, for corannulene synthesis.



Scheme 6. Synthesis of polycyclic aromatic hydrocarbons. DDQ = 2,3-dichloro-5,6-dicyano-*p*-benzoquinone, TPAP = tetrapropylammonium perruthenate.

In conclusion, we have developed a gold-catalyzed reaction of allenynes for the construction of a fused phenanthrene scaffold. Using two different catalysts in the reaction of aryl-substituted allenynes, CPP and dibenzofluorene derivatives can be preferentially produced in moderate to good selectivity. The cyclization products were converted to highly fused benzo[*ghi*]fluoranthene derivatives via intramolecular Friedel–Crafts acylation.

Acknowledgements

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Keywords: gold catalysis • allenes • domino reaction • polycycles • vinyl cation • CPP

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A gold-catalyzed cascade cyclization of naphthalene-tethered allenynes gave 4*H*-cyclopenta[*def*]phenanthrene (CPP) derivatives. The reaction proceeds through the nucleophilic reaction of an alkyne with the activated allene to generate a vinyl cation intermediate followed by arylation. Selective formation of CPP and dibenzofluorene derivatives using aryl-substituted substrates, depending on the reaction conditions, is also presented.