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Gold-catalyzed cascade cycloisomerization of 1,7-diyn-3,6-bis(propargyl carbonate)s: stereoselective synthesis of naphtho[*b*]cyclobutenes†

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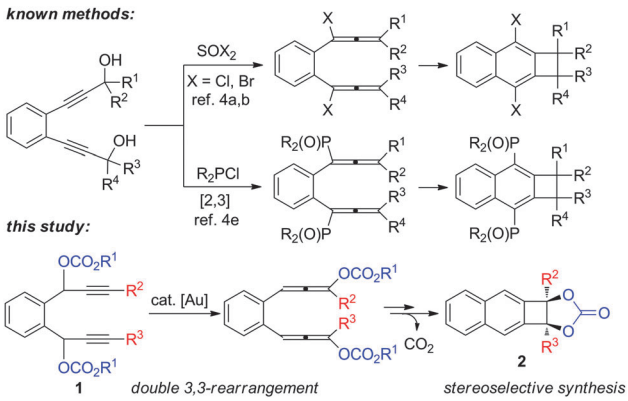
Gold-catalyzed cycloisomerization of 1,7-diyn-3,6-bis(propargyl carbonate)s leads to a highly efficient and diastereoselective synthesis of functionalized naphtho[*b*]cyclobutenes. A cascade sequence involving gold-catalyzed double 3,3-rearrangement, 6π-electrocyclic reaction and a decarbonylative cyclization was proposed for this reaction.

Benzocyclobutenes and naphthocyclobutenes are highly strained aromatic compounds which attracted considerable interest because of their unique structural features[1] and their versatility in organic synthesis.[2] For example, benzocyclobutenes can act as efficient precursors for the generation of *o*-quinodimethane intermediates *via* thermal electrocyclic ring-opening reaction, which have been widely utilized as diene counterparts in Diels–Alder reactions for the construction of polycyclic molecules such as alkaloids, steroids, terpenes, anthracyclines, lignanes and polyacenes, *etc*.[2] Compared with the chemistry of benzocyclobutenes, there are only limited reports on the synthesis and reactivity of naphthocyclobutenes.[3,4] Most of the synthetic routes to naphthocyclobutenes rely on the intramolecular [2+2] cycloaddition of benzene-bridged diallenes which are generated by treatment of various bis(propargyl alcohol)s with $SOCl_2$ (ref. 4a and b) or HX,[4b,c] or through the [2,3]-sigmatropic rearrangement of the *in situ* formed propargyl sulfenates[4d] or phosphinites[4e] (representative reactions are shown in Scheme 1). A Pd(0)/SmI_2 mediated formation of naphthocyclobutenes from *o*-bis(α-acetoxypropargyl)benzene has also been established.[5] Although some progress has been achieved, the reaction involving a stereoselective process is quite rare. On the other hand, in recent years, gold-catalyzed 3,3-rearrangement reactions of propargyl carboxylates have been proved as useful strategies for obtaining rapid access to a wide range of functionalized structural motifs.[6] Recently, we have developed a gold-catalyzed cyclization of



Scheme 1 Synthesis of naphtho[*b*]cyclobutenes.

1,6-diynyl carbonates to benzo[*b*]fluorenes,[7] which is initialized through the formation of an allenyl carbonate *via* 3,3-rearrangement reaction. Our results also suggest that when propargyl carbonates are employed instead of acetates, it is possible to form a more stable oxocarbenium ion intermediate, which can be further attacked by nucleophiles. Inspired by this result, we postulated that the efficient generation of the bisallenic intermediates might be achieved through transition metal-catalyzed reactions of bis(propargyl carbonate)s. Along these lines, we have developed a new route to obtain linear acenes *via* palladium-catalyzed reaction of 1,7-diyn-3,6-bis(propargyl carbonate)s with organoboronic acids in which the bis[(σ-allenyl)palladium(II)] and 2,3-naphthoquinodimethane intermediates might be involved.[8] We next became interested in the potential cyclization reactions of bis(propargyl carbonate)s catalyzed by gold. Herein we report our investigation of the gold-catalyzed cyclization of bis(propargyl carbonate) **1** to synthetically valuable naphtho[*b*]cyclobutene **2** with excellent *cis*-stereoselectivity (Scheme 1). The reaction likely proceeded through the generation of bis(allenyl carbonate) as a key intermediate *via* double 3,3-rearrangement followed by subsequent cyclization. To our knowledge, this type of reaction mode has not been reported in gold-catalyzed transformations.[9]

To test the hypothesis, the substrates of dicarbonates **1a-1** to **1a-3** bearing different protection groups, which were easily

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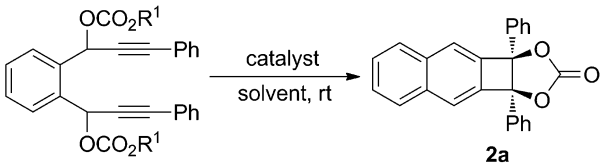
† Electronic supplementary information (ESI) available: Experimental details, NMR spectra of all new products, and X-ray crystallography of compounds **2f** and the *trans*-isomer of **3**. CCDC 943600 (**2f**) and 943601 (the *trans*-isomer of **3**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3cc44757j

prepared from phthalaldehyde as a diastereomeric mixture,[8] were chosen to establish the reaction conditions. The results are shown in Table 1. In light of the superior catalytic activity of [Johnphos(MeCN)Au]SbF_6 (catalyst **A**) in the efficient transformation of mono-propargyl carbonates,[7] we first examined the reaction of bis(propargylic methyl carbonate) **1a-1** using gold(I) complex **A** as the catalyst. However, the starting material remained largely unchanged in toluene at room temperature (Table 1, entry 1). Further optimization indicated that the use of PPh_3AuNTf_2 led to the formation of *cis*-naphtho[*b*]cyclobutene **2a** with a cyclic carbonate structure in 47% yield at room temperature in 4.5 h (entry 2). To our delight, treatment of benzyl carbonate **1a-2** with the more electrophilic PPh_3AuSbF_6 complex in THF improved the yield of **2a** dramatically to 87% with a shorter reaction time (entry 4), perhaps due to the formation of a more stable benzyl cation intermediate during the ring-closure process. It is noted that in this case, the reaction mixture became viscous as the reaction progressed. It was found that partial polymerization of THF solvent occurred under the conditions as evidenced by the NMR spectra of the crude reaction mixture. The reaction could also be performed in toluene or CH_2Cl_2, furnishing **2a** in 76% and 58% yields, respectively (entries 5 and 6). A significant counterion effect on the reactivity was observed, for example, changing the counterion to NTf_2^-, OTf^- or BF_4^- resulted in lower product yields (61–79%) and longer reaction time in THF (entries 7–9). Catalyst **A** was also found to smoothly catalyze the cycloisomerization of **1a-2** into the desired **2a** in toluene (entry 10). Control experiments with PPh_3AuCl or $AgSbF_6$ alone did not give the desired product (entries 11 and 12). The use of Brønsted acid such as TfOH afforded a complex mixture (entry 13).[10] Allyl carbonate **1a-3** was also compatible under the catalysis of PPh_3AuNTf_2 or PPh_3AuSbF_6, leading to the formation of **2a** in 81% and 84% yields, respectively (entries 14 and 15). Notably, the results demonstrated that the cyclization process is highly diastereoselective, as only *cis*-**2a** was obtained in all cases.

Next, we proceeded to investigate the scope of this cyclo isomerization in terms of alkyne substituents. During this process, we found that the scope of allyl carbonates was quite limited, thus we chose benzyl carbonates as substrates to examine the reaction scope. As shown in Scheme 2, a wide variety of diversely substituted aryl alkynes were suitable for this reaction, furnishing the desired naphtho[*b*]cyclobutenes in generally good to high yields as single diastereomers. The electronic nature of the aromatic rings did not have a strong influence on this reaction. Both electron-deficient and electron-rich substituents on the aryl rings were tolerated well during the reaction. For example, *p*-Cl, *p*-Br, *o*-Br, *p*-F, *p*-CF_3 and *p*-CO_2Et substituted aryl alkynes afforded the corresponding

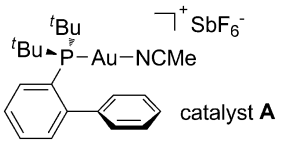
Table 1 Optimization studies for the synthesis of **2a**

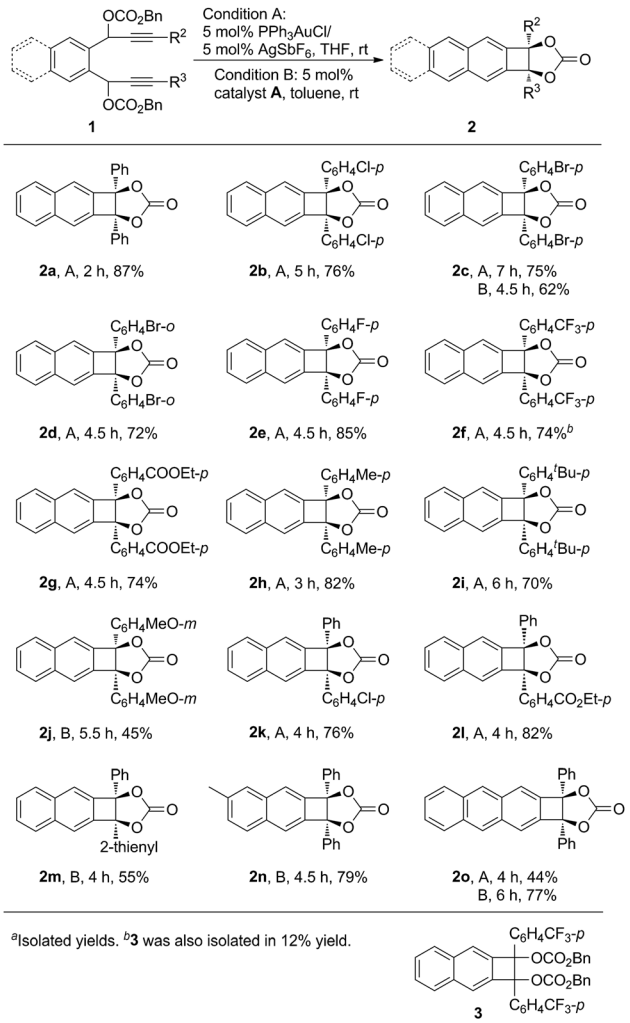


1a-1, R^1 = Me; **1a-2**, R^1 = Bn; **1a-3**, R^1 = allyl

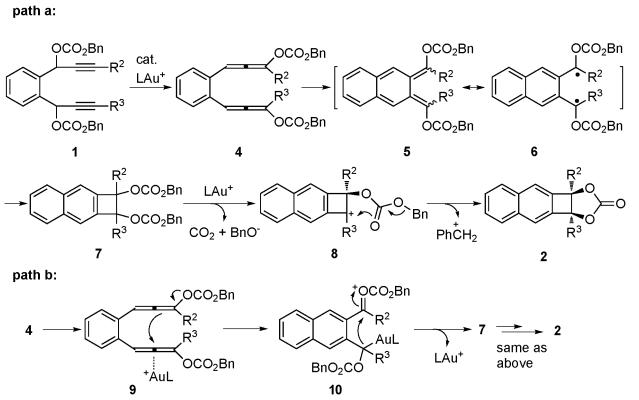
Entry	R^1	Catalyst[a] (5 mol%)	Solvent	Time (h)	Yield[b] (%) of **2a**
1	Me	**A**	Toluene	10	—[c]
2	Me	PPh_3AuNTf_2	THF	4.5	47
3	Me	$PPh_3AuCl/AgSbF_6$	THF	24	18
4	Bn	$PPh_3AuCl/AgSbF_6$	THF	2	87
5	Bn	$PPh_3AuCl/AgSbF_6$	Toluene	3	76
6	Bn	$PPh_3AuCl/AgSbF_6$	CH_2Cl_2	5	58
7	Bn	PPh_3AuNTf_2	THF	17	79
8	Bn	$PPh_3AuCl/AgOTf$	THF	18	61
9	Bn	$PPh_3AuCl/AgBF_4$	THF	17	69
10	Bn	**A**	Toluene	3	86
11	Bn	$AgSbF_6$	THF	14	NR[d]
12	Bn	PPh_3AuCl	THF	14	NR[d]
13	Bn	TfOH	CH_2Cl_2	2	—[e]
14	Allyl	PPh_3AuNTf_2	THF	10	81
15	Allyl	$PPh_3AuCl/ASbF_6$	THF	2	84

[a] [Au] (5 mol%), [Ag] (5 mol%) for entries 3–6, 8, 9 and 15. [b] Isolated yields. [c] 84% of **1a-1** was recovered. [d] NR = no reaction. [e] Complex mixture.





Scheme 2 Gold-catalyzed cyclization of bis(propargyl carbonate)s to naphtho[*b*]cyclobutenes.[a]



Scheme 3 Possible reaction mechanism.

products **2b–2g** in 72–85% yields. In the case of **2f** ($R^2 = R^3 = p\text{-}CF_3C_6H_4$), dicarbonate **3** was also obtained in 12% yield as a mixture of diastereomers. The structures of **2f** and the *trans*-isomer of **3** were unambiguously determined by X-ray crystallography.[11] *p*-Me or *p*-^{t}Bu substituted aryl alkynes provided **2h** and **2i** in good yields of 82% and 70%, respectively. However, a *m*-MeO substituted one gave the desired **2j** only in moderate yield of 45%. The reaction also proceeded well with unsymmetrically substituted dicarbonates **1k–1m** to afford **2k–2m** in 55–82% yields. The parent phenyl rings modified by introducing a methyl group or a fused benzene ring were also compatible in this cyclization, leading to the formation of **2n** and **2o** in 79% and 77% yields, respectively. In the latter case, catalyst **A** afforded better results than PPh_3AuSbF_6. When substrates **1** bearing two alkyl groups, or one alkyl, one aryl group on the alkyne terminus were employed, the desired naphtho[*b*]cyclobutenes could not be obtained.

Based on the above results, a possible reaction mechanism is depicted in Scheme 3. First, double 3,3-rearrangement reaction occurs through the nucleophilic attack of the benzyloxycarbonyl group on the gold(I)-activated alkyne moiety leading to the formation of the bis(allenyl carbonate) **4**. This is followed by 6π-electrocyclic reaction to deliver a 2,3-naphthoquinodimethane species **5**, which can also be represented by the resonance structure **6**, a highly stabilized biradical.[12] **5**/**6** undergoes cyclization spontaneously to provide dicarbonate **7**. Then, a gold-assisted C–O bond cleavage takes place to give a benzylic cation intermediate **8**.[7] Subsequent ring-closure proceeded by attack of the benzyloxycarbonyl group from the top side furnishes exclusively *cis*-**2** (path a). The attack from the bottom side would require considerable ring strain. The released benzyl cation might induce a polymerization process of THF.[13] It might also be trapped by a small amount of water since BnOH could be detected in 23% isolated yield in gold-catalyzed cyclization of **1a**-**2**. We also tried to trap the 2,3-naphthoquinodimethane intermediate by addition of dienophiles such as maleic anhydride or 1-phenyl-1*H*-pyrrole-2,5-dione, however, the desired Diels–Alder product was not observed. We assumed that the steric bulk of the substituents on the 1,3-diene moiety might inhibit the intermolecular [4+2] reaction. Alternatively, intramolecular nucleophilic attack of the allenic moiety on the gold-activated allene affords oxocarbenium ion intermediate **10**. Subsequent nucleophilic attack of the Au–C(sp^3) bond on the carbonyl moiety of the oxocarbenium ion gives the same dicarbonate **7** (path b), which is similar to that of the [2+2] cycloaddition sequence involved in gold-catalyzed cyclization of 1,7-enyne benzoates.[14]

In summary, we have discovered a novel gold-catalyzed cascade cyclization of 1,7-diyn-3,6-bis(propargyl carbonate)s, which allows the facile synthesis of functionalized naphtho[*b*]-cyclobutenes with high stereoselectivity. The reaction likely proceeds through the generation of bisallenes *via* gold-catalyzed double 3,3-rearrangement, followed by cascade cyclization reactions including a decarbonylative cyclization. Bisallenes are well known to serve as powerful π-components in metal-catalyzed cyclization reactions.[15] The present protocol might be potentially applied for the efficient generation of bisallenes from non-benzene-fused propargyl carbonate systems. We are now exploiting new cascade reactions toward this goal.

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