Gold Catalysis

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Evolution of Propargyl Ethers into Allylgold Cations in the Cyclization of Enynes**

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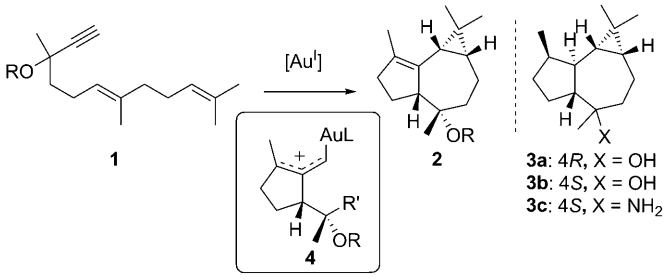
Understanding the mechanisms and stereochemistry by which enynes react with metal catalysts is central for the application of these transformations in synthesis. Recently, the similarities of metal-catalyzed additions of nucleophiles to 1,6-enynes with polyene cyclizations,[1] which proceed with an *anti* stereochemistry,[2-5] have been emphasized. However, substrates with strongly electron-donating groups on the alkene react nonstereospecifically via open carbocations.[6] We have now found that propargyl alcohols, ethers, and silyl ethers **1** react with gold(I) catalysts by a new type of intramolecular 1,5-migration of OR groups (Scheme 1). This reaction leads to the tricyclic compounds **2**, which are related

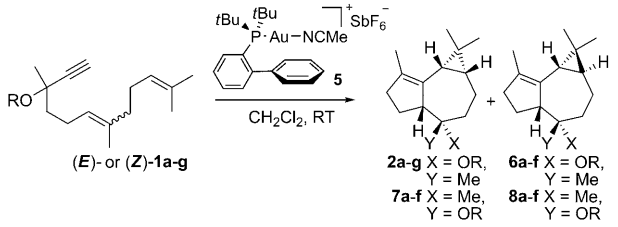


Scheme 1. Gold(I)-catalyzed 1,5-migration of OR groups in dienynes **1**.

to the sesquiterpenes globulol (**3a**), epiglobulol (**3b**),[7] and halichonadin F (**3c**).[8] Significantly, the migration proceeds via allylgold cations **4** by a *syn* addition of the alkyne and the OR group to the alkene. A related 1,6-migration was also found in 1,7-enynes.

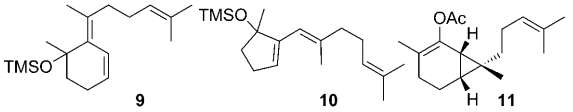
Propargyl alcohol (*E*)-**1a** reacted with the gold(I) catalyst **5** to give a 7:1 mixture of **2a** and **6a** in low yield (Table 1, entry 1). Whereas the TMS-ether (*E*)-**1b** also gave products of skeletal rearrangement,[2,3,9] **9** and **10** (Table 1, entry 2), the reaction of ethers (*E*)-**1c**–**f** gave products **2c**–**f** in 56–84% yield (Table 1, entries 2–6). Interestingly, although acetate (*E*)-**1g** had been shown to react exclusively by 1,2-acyl migration to give **11** with $AuCl_3$ or $PtCl_2$,[10] the 1,5-migration derivative **2g** was obtained as the major product using the gold(I) catalyst **5** (Table 1, entry 7). Reactions of dienynes (*Z*)-**1a**–**f** led to **7a**–**f** in 39–76% yield (Table 1, entries 8–12).[11] The configurations of **2f** and **7f** were confirmed by X-ray diffraction.[12] As minor compounds, products **6a**–**f** and **8a**–**f** having a *trans*-bicyclo[5.1.0]octane skeleton were also obtained.[12] Similar results were obtained with other cationic gold(I) complexes, whereas AuCl or platinum(II) complexes gave poor results.[13]

Table 1: Gold(I)-catalyzed reaction of *E*- or *Z*-dienynes **1a**–**g**.[a]



Entry	**1a–g**	R	*t* [min]	Products (yield [%]; ratio)
1	(*E*)-**1a**	H	5	**2a** + **6a** (14; 7:1)
2	(*E*)-**1b**	TMS	10	**2b** (33) + **6b** (5)[b,c]
3	(*E*)-**1c**	Me	5	**2c** (84)
4[d]	(*E*)-**1d**	MOM	10	**2d** + **6d** (57; 50:1)
5	(*E*)-**1e**	Bn	10	**2e** (64)
6	(*E*)-**1f**	PNBn	15	**2f** + **6f** (74; 16:1)
7	(*E*)-**1g**	Ac	10	**2g** + **11** (96; 1.4:1)
8	(*Z*)-**1a**	H	5	**7a** + **8a** (52; 11:1)
9[d]	(*Z*)-**1b**	TMS	10	**7b** + **8b** (46; 6:1)
10	(*Z*)-**1c**	Me	5	**7c** + **8c** (81; 9:1)
11[d]	(*Z*)-**1d**	MOM	10	**7d** + **8d** (72; 7:1)
12[d]	(*Z*)-**1f**	PNBn	40	**7f** + **8f** (87; 7:1)

[a] 2 mol% **5**. [b] **9** (20% yield) and **10** (14% yield) were obtained. [c] Yield determined by ^{1}H NMR methods. [d] 1 mol% **5**. TMS = trimethylsilyl, MOM = methoxymethyl, Bn = benzyl, PNBn = *p*-nitrobenzyl.



Reaction of dienyne (*Z*)-**1c** in a 30:1 mixture of CH_2Cl_2 and MeOH gave the ether **2c** in addition to **7c** and **8c**. The ether **2c** was the product of the reaction of dienyne (*E*)-**1c** (Table 1, entry 3). When this reaction was performed with CD_3OD, **7c** and **8c** showed no deuterium incorporation, whereas the methoxy group of **2c** was deuterated (Scheme 2). This experiment confirms that the 1,5-migration is an intra-

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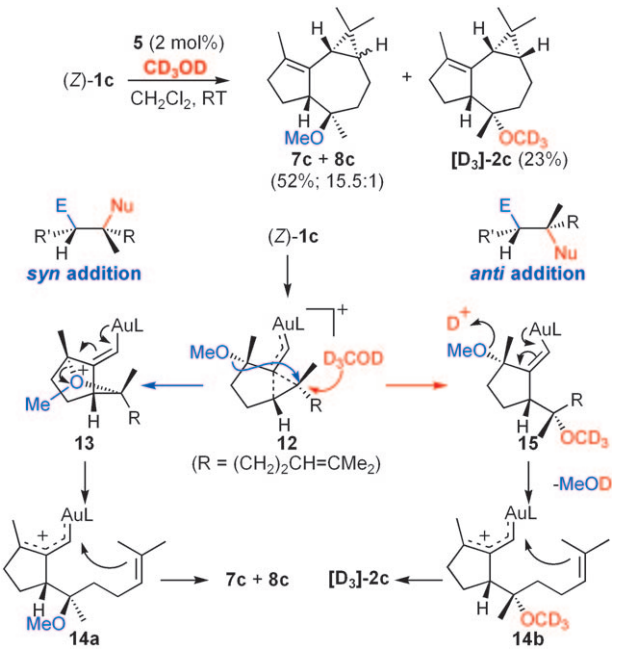
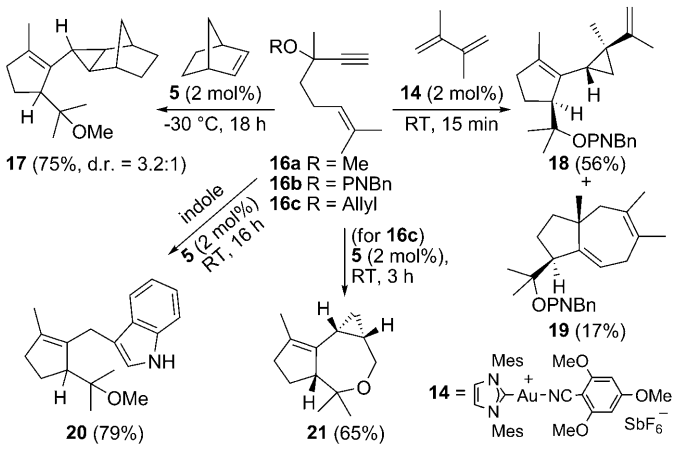
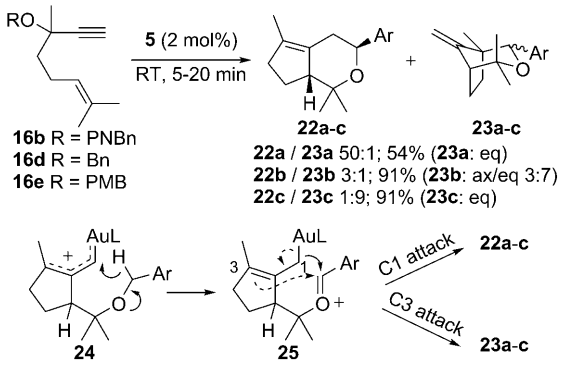


Scheme 2. 1,5-Migration of OR groups via allylgold cations **12**.



Scheme 3. Reactions of 1,6-enynes **16a–c** in CH_2Cl_2 by 1,5-migration of the OR group.



Scheme 4. 1,5-Migration in 3-benzyloxy-1,6-enynes and subsequent formal C–H insertion.

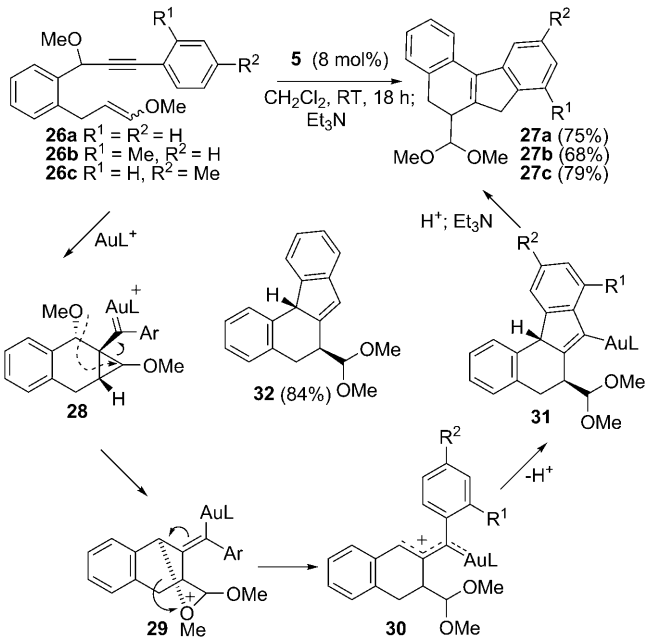
molecular transformation.[14] Accordingly, upon activation of the alkyne with gold(I), an intermediate such as **12** is probably formed, which is not an open carbocation since the original configuration at the alkene is preserved. The OR group migrates to form **13**, which then opens to give allylgold cation **14a**.[15] An intramolecular cyclopropanation with the alkene on the side chain then gives tricyclic compounds **7c** and **8c**.[16] In the presence of CD_3OD, an alternative intermolecular addition to **12** gives **15**, which then forms **2c** via allylic carbocation **14b**. The relative configuration of **14b** is that obtained in the hydroxy- and alkoxycyclizations of 1,6-enynes (an *anti* addition),[2–4,5b] whereas that of **14a** corresponds to a *syn* addition. Remarkably, migration of the OR group is faster than the interception of the first intermediate of type **12** by the pendant alkene, which have been previously shown to be a fast process in dienynes leading to biscyclopropanation.[16]

To confirm the involvement of allylgold cations in these migrations, we examined the reactions of enynes **16a–e** bearing different OR groups at the propargyl position. Thus, the gold-catalyzed reaction of **16a** in the presence of norbornene gave cyclopropane **17** (Scheme 3).[16d] An intermolecular cyclopropanation also occurred in the reaction of **16b** with 2,3-dimethyl-1,3-butadiene using catalyst **14**. In this case, a 3.3:1 mixture of **18** and **19**[17] was obtained. Hexahydroazulene **19** presumably arises by a Cope rearrangement[18] of a *cis*-divinylcyclopropane diastereoisomer of **18**.[19] Trapping of the migration intermediate from **16a** using indole[3e] led to adduct **20**. Enyne **16c** with an allyloxy group gave **21** as a single stereoisomer as a result of an 1,5-migration and subsequent intramolecular cyclopropanation.[16a,b]

Enyne **16b** reacted with catalyst **5** to give **22a** as a single stereoisomer, whose structure was confirmed by X-ray diffraction (Scheme 4). The bicyclic derivative is the product of a migration and a subsequent formal C–H insertion.[20] Benzyl ether **16d** gave **22b** and **23b** in a 3:1 ratio, whereas **16e** led to **23c** as the major product. These results are consistent with a mechanism in which the intermediate allyl cation in **24** abstracts a hydride from the $ArCH_2O$ group to form a η^1-allyl–gold(I) **25**,[21] which reacts at C1 or C3 with the oxonium cation to give **22a–c** or **23a–c**, respectively.[20c]

A related 1,6-shift of a methoxy group was found in the gold-catalyzed cyclization of 1,7-enynes **26a–c** (Scheme 5). This reaction led to dehydro-5*H*-benzo[*c*]fluorenes **27a–c** or **32** by a new cascade transformation that presumably occurs by OMe migration in **28** to give **29**, which opens to form benzylic/allylic cation **30**. A Nazarov-type electrocyclization[22] then gives **27a–c** via **31**. Notably, the 1,6-shift of MeO is faster than the opening of the cyclopropane of **28** by the aryl, which would have formed a tetracene derivative by a [4+2] cycloaddition.[3b,d]

In summary, propargylic OR groups in 1,*n*-enynes undergo gold(I)-catalyzed intramolecular 1,(*n*−1)-migration via allylgold cations. This results in a rare *syn*-electrophilic addition to alkenes that, although nonconcerted, are nevertheless stereospecific. This migration is faster than the intramolecular cyclopropanation and arylation and competes with the 1,2-acyl migration of a propargyl acetate. The



Scheme 5. 1,6-Shift of MeO group and subsequent Nazarov-type cyclization.

intermediate allylgold cations react at α- or γ-position with alkenes, aryl groups, or by formal C–H insertion reactions, which opens new opportunities for the synthesis of new carbon skeletons in a highly concise manner.

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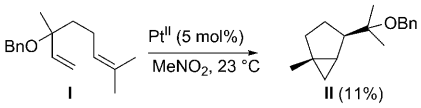

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