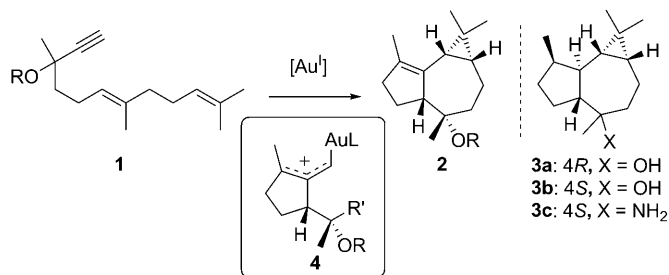


Evolution of Propargyl Ethers into Allylgold Cations in the Cyclization of Enynes**

Eloísa Jiménez-Núñez, Mihai Raducan, Thorsten Lauterbach, Kian Molawi, César R. Solorio, and Antonio M. Echavarren*

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**.

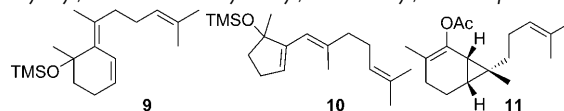
to the sesquiterpenes globulol (**3a**), epiglobulol (**3b**),^[7] and halichonadin F (**3c**).^[8] Significantly, the migration proceeds via allylgold cations **4** by a *syn* addition of the alkyne and the OR group to the alkene. A related 1,6-migration was also found in 1,7-enynes.

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%

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

Entry	1a–g	R	t [min]	Products (yield [%]; ratio)
1	(<i>E</i>)- 1a	H	5	2a + 6a (14; 7:1)
2	(<i>E</i>)- 1b	TMS	10	2b (33) + 6b (5) ^[b,c]
3	(<i>E</i>)- 1c	Me	5	2c (84)
4 ^[d]	(<i>E</i>)- 1d	MOM	10	2d + 6d (57; 50:1)
5	(<i>E</i>)- 1e	Bn	10	2e (64)
6	(<i>E</i>)- 1f	PNBn	15	2f + 6f (74; 16:1)
7	(<i>E</i>)- 1g	Ac	10	2g + 11 (96; 1.4:1)
8	(<i>Z</i>)- 1a	H	5	7a + 8a (52; 11:1)
9 ^[d]	(<i>Z</i>)- 1b	TMS	10	7b + 8b (46; 6:1)
10	(<i>Z</i>)- 1c	Me	5	7c + 8c (81; 9:1)
11 ^[d]	(<i>Z</i>)- 1d	MOM	10	7d + 8d (72; 7:1)
12 ^[d]	(<i>Z</i>)- 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 ¹H NMR methods. [d] 1 mol % **5**. TMS = trimethylsilyl, MOM = methoxymethyl, Bn = benzyl, PNBn = *p*-nitrobenzyl.



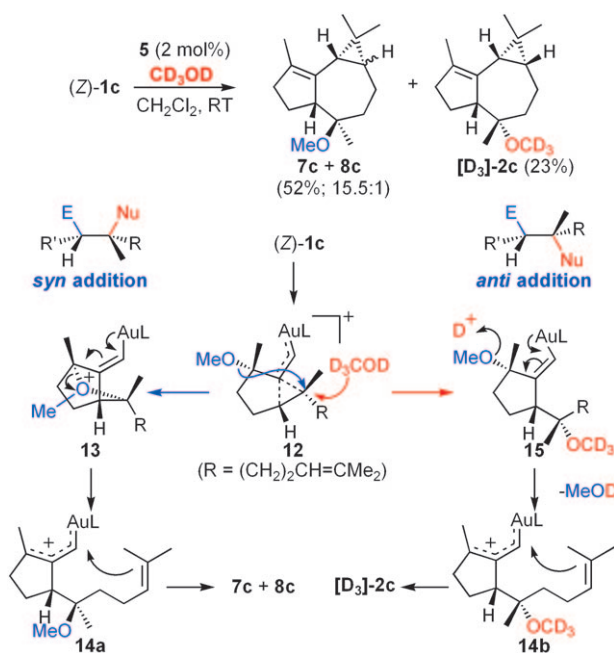
yield (Table 1, entries 2–6). Interestingly, although acetate (*E*)-**1g** had been shown to react exclusively by 1,2-acyl migration to give **11** with AuCl₃ or PtCl₂,^[10] the 1,5-migration derivative **2g** was obtained as the major product using the gold(I) catalyst **5** (Table 1, entry 7). Reactions 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]

Reaction of diyne (*Z*)-**1c** in a 30:1 mixture of CH₂Cl₂ and MeOH gave the ether **2c** in addition to **7c** and **8c**. The ether **2c** was the product of the reaction of diyne (*E*)-**1c** (Table 1, entry 3). When this reaction was performed with CD₃OD, **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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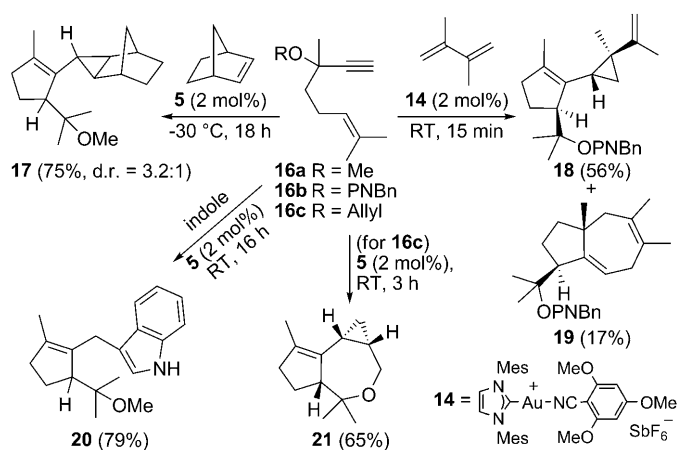


Scheme 2. 1,5-Migration of OR groups via allylgold cations **12**.

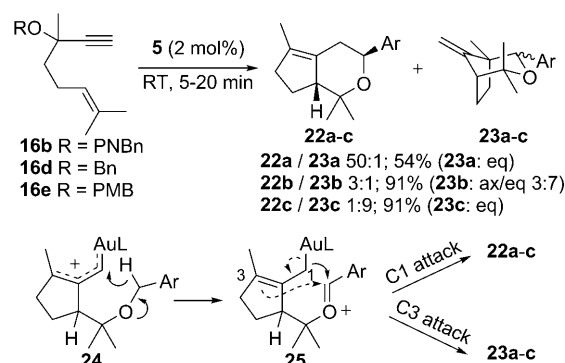
molecular transformation.^[14] Accordingly, upon activation of the alkyne with gold(I), an intermediate such as **12** is probably formed, which is not an open carbocation since the original configuration at the alkene is preserved. The OR group migrates to form **13**, which then opens to give allylgold 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 alkoxy-cyclizations 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 dienyne 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]



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

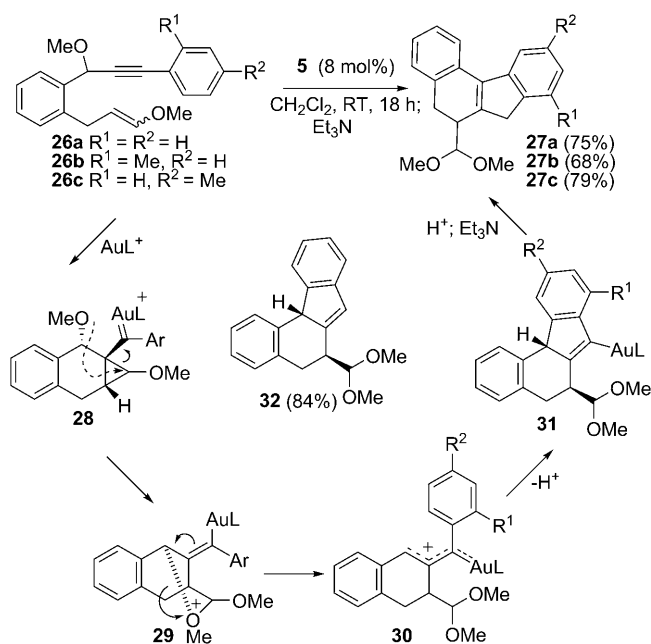


Scheme 4. 1,5-Migration in 3-benzyloxy-1,6-enynes and subsequent formal C–H insertion.

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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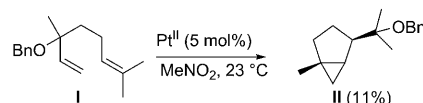
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