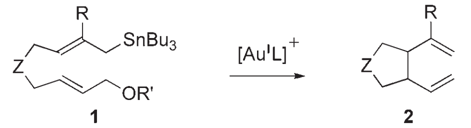
DOI: 10.1002/anie.200704500

Allyl–Allyl Coupling

Gold-Catalyzed Allyl–Allyl Coupling**

*Susana Porcel, Verónica López-Carrillo, Cristina García-Yebra, and Antonio M. Echavarren**

The palladium(0)-catalyzed cyclization of allylstannanes with allyl acetates in substrates of type **1** gives the five- or six-membered rings **2**.[1] This cross-coupling reaction proceeds by oxidative addition of the allyl acetate to Pd^0 followed by transmetalation and an allyl/allyl reductive elimination. After a search for other metal complexes that might promote the cyclization of substrates **1** to give **2** more efficiently and with better stereoselectivity, we found that cationic Au^I complexes outperform all other catalysts for this process (Scheme 1).

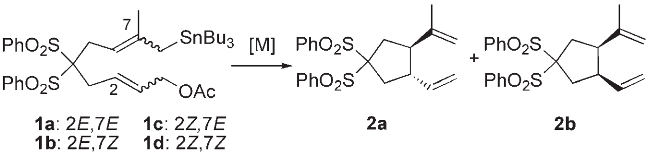


Scheme 1.

Whereas a variety of transformations have been developed based on the selective activation of alkynes, allenes, and alkenes with Au^I catalysts,[2–5] the use of Au^I as a catalyst to couple two allyl fragments is unprecedented. Significantly, although it has been suggested recently that d^{10} Au^I might act similarly to Pd^0 in cross-coupling reactions,[6] there is no definitive mechanistic evidence for this process.

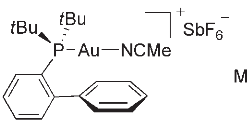
We first assayed Rh^I complexes as catalysts for the cyclization of **1**. Thus, stereoisomers **1a–d** were treated with $[RhCl(PPh_3)_3]$ as catalyst in the presence of five equivalents of LiCl to give **2a**/**b** in 55–73 % yield (Table 1, entries 1–4). A lower yield and stereoselectivity were obtained with **1c** (Table 1, entry 3). Similar results were obtained with $[\{RhCl(CO)_2\}_2]$ and PCy_2(2-biphenyl) in the presence of *i*Pr_2NH (3 equiv).[7] Lower yields were obtained with $[RhCl(CO)(PPh_3)_2]$ as the catalyst, whereas no reaction was observed with $[\{Rh(cod)\}_2]BF_4$ (cod = cyclooctadiene). The Ru^{II} complexes $[CpRu(PPh_3)_2Cl]$ ($Cp = C_5H_5$), $[CpRu(PPh_3)_2Cl]/AgSbF_6$, and $[RuCl_2(CO)_2(PPh_3)_2]$ also proved to be unable to catalyze this cyclization.The cyclization also takes place in the presence of the cationic gold complex **3**[8] in 1,2-dichloroethane (DCE; Table 1, entries 5–9), and the reaction is considerably faster and more stereoselective with substrates **1c** and **1d** (Table 1, entries 7–9). The reaction in the presence of less-electrophilic catalysts formed from complex **4**[8] was not effective (Table 1, entry 10), whereas $AuCl_3$ and the cationic Ag^I complex **5**[4c] gave **2a** in only low yields (Table 1, entries 15 and 16, respectively). Lewis acids,

Table 1: Cyclization of **1a–d** with metal catalysts.[a]

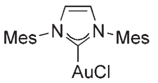


Entry	1	[M] (mol %)	*T* [°C]	*t* [h]	Yield [%] (**2a**/**2b**)
1	**1a**	$[RhCl(PPh_3)_3]$ (10)	80	14	63 (73:27)
2	**1b**	$[RhCl(PPh_3)_3]$ (10)	80	14	62 (81:19)
3	**1c**	$[RhCl(PPh_3)_3]$ (10)	80	14	55 (58:42)
4	**1d**	$[RhCl(PPh_3)_3]$ (10)	80	14	73 (87:13)
5	**1a**	**3** (3)	80	19	40 (56:44)[b]
6	**1b**	**3** (3)	80	19	47 (56:44)[b]
7	**1c**	**3** (3)	50	1.25	92 (100:0)
8	**1d**	**3** (3)	50	0.25	95 (100:0)
9	**1d**	**3** (3)	23	14	88 (100:0)
10	**1c**	**4**/$AgSbF_6$ (5)	80	22	–[c]
11	**1d**	$[AuCl(PPh_3)]/AgSbF_6$ (10)	50	0.6	92 (100:0)
12	**1c**	AuCl (20)	50	5	11 (100:0)
13	**1c**	[AuClCO] (17)	50	5	< 5
14	**1c**	$[AuCl(SMe_2)]$ (18)	50	5	–[c]
15	**1c**	$AuCl_3$ (18)	50	1	36 (100:0)[d]
16	**1d**	**5** (10)	50	7.5	44 (100:0)

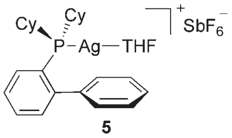
[a] The reactions with Rh^I were performed in DMF containing 5 equivalents of LiCl and those with Au^I or Ag^I in DCE. [b] The destannylated products were isolated in 17–18 % yield. [c] The starting material was recovered. [d] The destannylated product was isolated in 43 % yield.



3



4



5

---

[*] S. Porcel, V. López-Carrillo, Dr. C. García-Yebra, Prof. Dr. A. M. Echavarren
Institute of Chemical Research of Catalonia (ICIQ)
Av. Països Catalans 16, 43007 Tarragona (Spain)
and
Departamento de Química Orgánica
Universidad Autónoma de Madrid (UAM)
Cantoblanco, 28049 Madrid (Spain)
Fax: (+34) 97-792-0225
E-mail: aechavarren@iciq.es
Homepage: http://www.iciq.es/english/research/grups_eng/echavarren/entrada.htm

[**] We thank the MEC (projects CTQ2007-60745/BQU, Consolider Ingenio 2010 Grant CSD2006-0003, and a predoctoral fellowship to V.L.-C.), the UAM (predoctoral fellowship to S.P.), the CAM (postdoctoral fellowship to C.G.-Y.), the AGAUR (2005 SGR 00993), and the ICIQ Foundation. Dr. C. García-Yebra is a recipient of a Ramón y Cajal contract at the Departamento de Química Inorgánica, Universidad de Zaragoza.

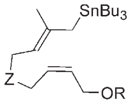
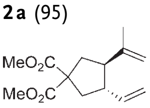
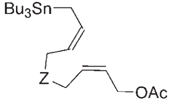
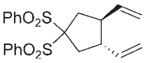
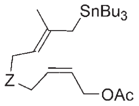
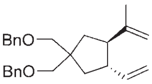
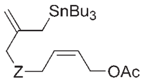
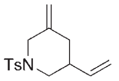
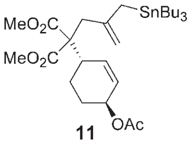
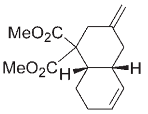
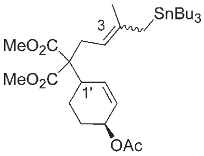
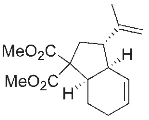
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

such as $AlCl_3$ or $SnCl_4$, failed to cyclize **1a** or **1c** (DCE, 80 °C, 12 h) and gave only mixtures of destannylated products. Similar negative results were obtained with $AgSbF_6$ or $IrCl_3$.

In comparison with the gold-catalyzed reaction, the Pd-catalyzed cyclization of **1c** under the optimum conditions requires larger catalyst loadings and harsher conditions (10 mol % at 80 °C in DMF/H_2O for 17 h) and proceeds less stereoselectively to give a 2/1 mixture of **2a** and **2b**.[1a]

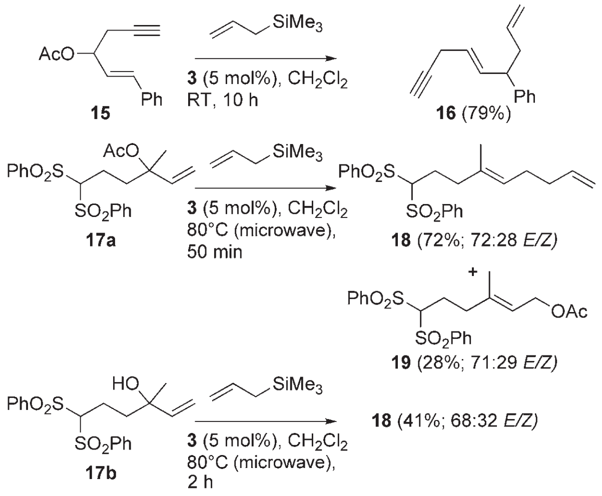
The reaction with other substrates proceeded satisfactorily with catalyst **3** in DCE (Table 2). Allyl alcohol **1e** and carbonates **1f** and **1g** also provided **2a** (Table 2, entries 1–3, respectively). Acetate **1h** and methyl ether **1i** afforded **2c** (Table 2, entries 4 and 5, respectively), whereas the TBS-protected analogue was recovered unchanged. The cyclization of **11** to give *cis*-decalin **12** took place with total stereoselectivity and good yield (Table 2, entry 9), and excellent yields and stereoselectivities were also obtained for the cyclization of **13a–c**, which afforded *cis*-hydrindane **14** exclusively (Table 2, entries 10–12, respectively).

Table 2: Gold-catalyzed intramolecular allyl–allyl coupling.[a]

Entry	Substrate	*T* [°C]	*t* [h]	Product (yield [%])
1	 **1e**: Z= C(SO_2Ph), R = H	50	1	**2a** (63)[b]
2	**1f**: Z=C(SO_2Ph)$_2$, R=CO_2Et	50	8	**2a** (88)
3	**1g**: Z=C(SO_2Ph)$_2$, R=TROC[c]	50	1	**2a** (95)
4	**1h**: Z=C(CO_2Me)$_2$, R=Ac	80	0.5	 **6** (98; 90:10)
5	**1i**: Z=C(CO_2Me)$_2$, R=Me	80	3.5	**6** (62; 88:12)[d]
6	 **1j**: Z= C(SO_2Ph)$_2$	80	1	 **7** (86; 87:13)
7	 **1k**: Z= C(CH_2OBn)$_2$	50	0.5	 **8** (96)
8	 **9**: Z= NTs[e]	80	1	 **10** (41)[f]
9[g]	 **11**	80	0.5	 **12** (90)
10	 **13a**: 1',4'-*cis*, 3*Z*	50	0.5	 **14** (99)
11	**13b**: 1′,4′-*trans*, 3*Z*	50	0.5	**14** (94)
12	**13c**: 1′,4′-*trans*, 3*E*	50	0.5	**14** (94)

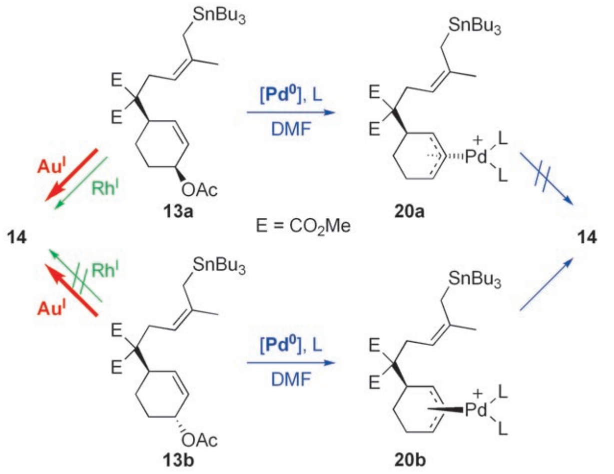
[a] 3 mol % of **3** in DCE. [b] Along with 27 % of the destannylated product. [c] TROC = 2,2,2-trichloroethoxycarbonyl. [d] Along with 15 % of the destannylated product. [e] Ts = *p*-Toluenesulfonyl. [f] Along with 59 % of the destannylated product. [g] 5 mol % of **3**.

Cyclization of the trimethylsilyl analogue of **1e** gave only traces of **2a** even under forcing conditions, whereas the intermolecular reaction of 1,5-enyne **15** with allyltrimethylsilane afforded dienyne **16** in a rare reaction in which an allyl acetate reacts with Au^I in the presence of an alkyne (Scheme 2). Indeed, 1,5-enynes similar to **15** have been shown to act as nucleophiles and to react with water or alcohols by 5-*endo* hydroxy- and alkoxycyclization in the presence of Au^I to give selective activation of the alkyne.[9] The reaction of **17a** with allyltrimethylsilane and catalyst **3** proceeds under microwave irradiation to give **18** and rearranged acetates **19**.[3a] None of the product allylated at C-3 was observed. The same reaction catalyzed by $Sc(OTf)_3$ (5 mol %) gave a 1:1 mixture of **18** and the C-3 allylated isomer. Alcohol **17b** also gave **18**, although the yield was lower.[10] Interestingly, when substrate **17a** was heated at 80 °C (microwave irradiation, 50 min) with catalyst **3** (5 mol %) in MeOH, the rearranged acetates **19** (75:25 *E*/*Z*) were obtained quantitatively.



Scheme 2.

Significantly, in contrast to Au^I, the Pd^0-catalyzed reaction of substrate **13a** (10 mol % Pd^0) did not provide any cyclization product and a 1:1 mixture of destannylated products was obtained quantitatively. Substrate **13b** gave **14** in only 38 % yield along with products of destannylation (1:1 mixture, 61 %). The result obtained in the Pd^0-catalyzed reaction of **13** is consistent with the known mechanism for this reaction,[1] since the (η^3-allyl)palladium complex **20a**, which is obtained upon oxidative addition of Pd^0 to **13a**, cannot undergo intramolecular transmetalation with the allylstannane (Scheme 3). Complex **20b**, however, which is derived from **13b**, has the correct relative configuration to give **14**. The reaction of **13a** with $[RhCl(PPh_3)_3]$ (20 mol %, 80 °C, 20 h) in the presence of iPr_2NH (3 equiv) and LiCl (5 equiv), on the



Scheme 3.

other hand, gave **14** (48 %) and destannylation products (1:1 mixture, 46 %), whereas **13b** gave only a 1:1 mixture of destannylated products (92 %).[11] These results show that the processes catalyzed by Au^I, Pd^0, and Rh^I are mechanistically distinct.

Additional reactions were performed to determine the role played by the cationic Au^I complex in this cyclization. Thus, the reaction of **13b** in the presence of $AuCl_3$ (5 mol %, DCE, 80 °C, 15 h) gave a 2:1 mixture of destannylated products quantitatively.[12] Similarly, the reaction of this substrate in the presence of $Yb(OTf)_3$ (5 mol %, DCE, 80 °C, 15 h) gave a 67 % yield of destannylated product. None of the cyclized product **14** was detected in these experiments.

We also considered the possible formation of an allylgold(I) species by a transmetalation-type process.[13,14] ^{1}H and ^{31}P NMR spectroscopic monitoring of the reaction between complex **3** and allyltriphenylstannane or allyltributylstannane in CD_2Cl_2 shows that complexation of Au^I to the alkene occurs at low temperature (−78 to −20 °C)[15] and that propene is formed at about 0 °C. Similar results were obtained with crotyl- and cinnamyltributylstannane, which gave 1-butene and allylbenzene, respectively. The reaction between **3** and allyltrimethylsilane also led to the formation of propene at around −40 °C. Complex **3** gave the aquo complex $[Au\{(o\text{-}PhC_6H_4)P\mathit{t}Bu_2\}H_2O]SbF_6$ in the presence of a stoichiometric amount of water,[16] and formation of propene from allyltributylstannane or allyltrimethylsilane was observed at the same temperatures.

Although cleavage of the allylsilane and allylstannanes was observed in these experiments, direct evidence for the formation of allylgold(I) species could not be obtained. In addition, we were unable to observe oxidative addition of the allyl acetate to Au^I in a series of experiments carried out with **17a** and complex **3** in CD_2Cl_2.[17] The fact that, in contrast to Pd^0 and Rh^I, the cationic catalyst **3** leads to similar high yields of **14** from **13a** and **13b** (Table 2, entries 10 and 11) suggests that Au^I acts as a mild and selective Lewis acid that promotes formation of an allyl cation from the allyl acetate, which then reacts with the allylstannane or allylsilane.[18]

In summary, we have found that cationic Au^I complexes are the most efficient catalysts for the intramolecular coupling of allyl acetates with allylstannanes. This process is mechanistically very different from that catalyzed by Pd^0 or Rh^I. Additional synthetic applications and mechanistic studies of this new coupling reaction are underway.

Received: September 30, 2007
Revised: November 11, 2007
Published online: January 29, 2008

Keywords: cross-coupling · cyclization · gold · palladium · rhodium

---

[1] a) M. Méndez, J. M. Cuerva, E. Gómez-Bengoa, D. J. Cárdenas, A. M. Echavarren, *Chem. Eur. J.* **2002**, *8*, 3620–3628; b) M. Méndez, A. M. Echavarren, *Eur. J. Org. Chem.* **2002**, 15–28.

[2] a) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211; b) A. Fürstner, P. W. Davies, *Angew. Chem.* **2007**, *119*, 3478–3519; *Angew. Chem. Int. Ed.* **2007**, *46*, 3410–3449; c) D. J. Gorin, F. D. Toste, *Nature* **2007**, *446*, 395–403; d) E. Jiménez-Núñez, A. M. Echavarren, *Chem. Commun.* **2006**, 333–346.

[3] a) N. Marion, R. Gealageas, S. P. Nolan, *Org. Lett.* **2007**, *9*, 2653–2656, and references therein. For a discussion of the role of Au^I in the activation of alkenes, see: b) Z. Li, J. Zhang, C. Brouwer, C.-G. Yang, N. W. Reich, C. He, *Org. Lett.* **2006**, *8*, 4175–4178; c) D. C. Rosenfeld, S. Shekhar, A. Takemiya, M. Utsunomiya, J. F. Hartwig, *Org. Lett.* **2006**, *8*, 4179–4182.

[4] For the reaction of allylsilanes or allylstannanes with alkynes in the presence of electrophilic metal catalysts to form hetero- or carbocycles, see: a) C. Fernández-Rivas, M. Méndez, A. M. Echavarren, *J. Am. Chem. Soc.* **2000**, *122*, 1221–1222; b) C. Fernández-Rivas, M. Méndez, C. Nieto-Oberhuber, A. M. Echavarren, *J. Org. Chem.* **2002**, *67*, 5197–5201; c) S. Porcel, A. M. Echavarren, *Angew. Chem.* **2007**, *119*, 2726–2730; *Angew. Chem. Int. Ed.* **2007**, *46*, 2672–2676.

[5] Allylstannanes also react with alkynes in the presence of Pd^0 in a process that involves an oxidative addition of the allylstannane to Pd^0: a) B. Martín-Matute, E. Buñuel, D. J. Cárdenas, M. Méndez, C. Nieto-Oberhuber, A. M. Echavarren, *J. Organomet. Chem.* **2003**, *687*, 410–419; b) S. Shin, T. V. RajanBabu, *J. Am. Chem. Soc.* **2001**, *123*, 8416–8417.

[6] a) C. González-Arellano, A. Corma, M. Iglesias, F. Sánchez, *J. Catal.* **2006**, *238*, 497–501; b) C. González-Arellano, A. Abad, A. Corma, H. García, M. Iglesias, F. Sánchez, *Angew. Chem.* **2007**, *119*, 1558–1560; *Angew. Chem. Int. Ed.* **2007**, *46*, 1536–1538.

[7] See the Supporting Information for additional results.

[8] C. Nieto-Oberhuber, S. López, A. M. Echavarren, *J. Am. Chem. Soc.* **2005**, *127*, 6178–6179.

[9] a) A. Buzas, F. M. Istrate, F. Gagosz, *Angew. Chem.* **2007**, *119*, 1159–1162; *Angew. Chem. Int. Ed.* **2007**, *46*, 1141–1144. For the selective activation of the alkyne moiety of 1-phenylprop-2-ynyl acetate with gold(I) and Lewis acids, such as $Sc(OTf)_3$, see: C. H. M. Amijs, V. López-Carrillo, A. M. Echavarren, *Org. Lett.* **2007**, *9*, 4021–4024.

[10] However, alcohols are more reactive than acetates with allylsilanes in the presence of $InCl_3/Me_3SiBr$: T. Saito, Y. Nishimoto, M. Yasuda, A. Baba, *J. Org. Chem.* **2006**, *71*, 8516–8522.

[11] The rhodium(I)-catalyzed reaction probably starts with a transmetalation of the allylstannane by Rh^I: a) E. W. Abel, S. Moorhouse, *Angew. Chem.* **1971**, *83*, 360–361; *Angew. Chem.*

Int. Ed. Engl. **1971**, *10*, 339 – 340; b) E. W. Abel, S. Moorhouse, *J. Chem. Soc. Dalton Trans.* **1973**, 1706 – 1711; c) S. Oi, M. Moro, H. Ito, Y. Honma, S. Miyano, Y. Inoue, *Tetrahedron* **2002**, *58*, 91 – 97. d) For a transmetalation from boron to Rh^I, see: P. Zhao, C. D. Incarvito, J. F. Hartwig, *J. Am. Chem. Soc.* **2007**, *129*, 1876 – 1877.

[12] The substitution of benzylic-propargylic alcohols by allylsilane is more efficiently catalyzed by Au^{III}: M. Georgy, V. Boucard, J.-M. Campagne, *J. Am. Chem. Soc.* **2005**, *127*, 14180 – 14181.

[13] Allylgold(I) complexes are not known, although a few allylgold(III) complexes have been shown to react as nucleophiles with carbonyl compounds at the γ carbon: T. Sone, S. Ozaki, N. C. Kasuga, A. Fukuoka, S. Komiya, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1523 – 1533.

[14] Transmetalation of allyltrimethylstannane has been observed with pincer Pd^{II} complexes and the resulting allylpalldium(II) intermediate undergoes protonolysis to form propene: a) N. Solin, J. Kjellgren, K. Szabó, *Angew. Chem.* **2003**, *115*, 3784 – 3786; *Angew. Chem. Int. Ed.* **2003**, *42*, 3656 – 3658; b) N. Solin, J. Kjellgren, K. Szabó, *J. Am. Chem. Soc.* **2004**, *126*, 7026 – 7033.

[15] The ^1H NMR spectrum (CD_2Cl_2, $-80\,^{\circ}C$) of a 1:1 mixture of **3** and allyltriphenylstannane shows an upfield shift of the $=CH_2$ signals. A well-characterized ethylene–gold(I) complex shows the ethylene hydrogen atoms at $\delta = 3.56$ ppm (a shift of -1.70 ppm with respect to free ethylene): H. V. Rasika Dias, J. Wu, *Angew. Chem.* **2007**, *119*, 7960 – 7962; *Angew. Chem. Int. Ed.* **2007**, *46*, 7814 – 7816. A styrene–gold(I) complex shows upfield shifts of the CH and CH_2 resonances: M. A. Cinellu, G. Minghetti, S. Stoccoro, A. Zucca, M. Manassero, *Chem. Commun.* **2004**, 1618 – 1619.

[16] E. Herrero-Gómez, C. Nieto-Oberhuber, S. López, J. Benet Buchholz, A. M. Echavarren, *Angew. Chem.* **2006**, *118*, 5581 – 5585; *Angew. Chem. Int. Ed.* **2006**, *45*, 5455 – 5459.

[17] a) A. Tamaki, J. K. Kochi, *J. Organomet. Chem.* **1972**, *40*, C81 – C84; b) A. Tamaki, J. K. Kochi, *J. Chem. Soc. Dalton Trans.* **1973**, 2620 – 2626; c) A. Tamaki, J. K. Kochi, *J. Organomet. Chem.* **1973**, *64*, 411 – 425; d) A. Tamaki, S. A. Magennis, J. K. Kochi, *J. Am. Chem. Soc.* **1974**, *96*, 6140 – 6148.

[18] For the reaction of allylsilanes with allyl cations formed in a gold-catalyzed reaction, see: C.-C. Lin, T.-M. Teng, A. Odedra, R.-S. Liu, *J. Am. Chem. Soc.* **2007**, *129*, 3798 – 3799.