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PAPER

Gold(I)-catalyzed Claisen rearrangement of allenyl vinyl ethers; synthesis of substituted 1,3-dienes†

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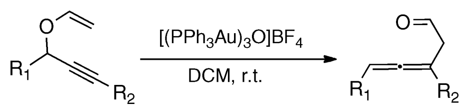
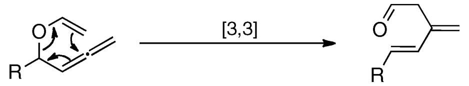
Synthesis of substituted 1,3-dienes was achieved *via* gold(I)-catalyzed Claisen rearrangement of allenyl vinyl ethers. The N-heterocyclic carbene gold chloride catalyst (IPrAuCl) was superior in terms of activity and selectivity and afforded the 3,3-product in excellent yields. A proposed cation-π inter-action played a significant role in affecting the reaction rate.

Conjugated dienes are structural motifs found in a wide variety of natural products of biological and pharmacological importance.[1] They are also common intermediates for several important organic transformations such as the Diels–Alder reaction and the Ziegler–Natta polymerization reaction.[2] Additionally, aryl substituted dienes and polyenes are widely used in non-linear optical materials and liquid crystals.[3] As a consequence of their ubiquitous nature, the development of efficient and practical methods for the synthesis of substituted dienes is an important area of research in organic chemistry.[4] Recently homogeneous gold catalysis has become an area of significant interest due to its synthetic utility in a wide range of organic transformations, particularly in the rearrangement and synthesis of various unsaturated systems.[5] Toste *et al.*, reported a gold(I)-catalyzed Claisen-type rearrangement of propargylic vinyl ethers to the corresponding homoallenic aldehydes (eqn (1)).[6]



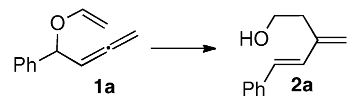
(1)



(2)

We envisioned that a Claisen-type rearrangement of allenyl vinyl ethers would give 1,3-dienes with different substitution patterns (eqn (2)).[7–10] Allenyl vinyl ether **1a** was chosen as a model substrate for catalyst screening and optimization of reaction conditions. After screening a number of transition metal catalysts we found that use of the N-heterocyclic carbene gold catalyst (IPrAuCl) with silver hexafluoroantimonate ($AgSbF_6$) gave the best results in terms of regioselectivity and yield, and the 3,3-product was isolated as a single regioisomer in 65% yield (Table 1, entry 9). Further modification of the reaction conditions, by reducing the catalyst loading, afforded the 3,3-product **2a** in 86% yield after *in situ* reduction of the labile aldehyde to the alcohol (Table 2, entry 1).

Table 1 Catalyst screening and optimization



1a **2a**

Entry	Catalyst[b]	Result[d]	Product [3,3]/[1,3]
1[a]	—	60% in 1.5 h	1
2	BF_3.OEt$_2$	Hydrolysis	—
3	$PdCl_2$	Conv. < 10% after 16 h	—
4	$NiCl_2(PPh_3)_2$	Conv. < 10% after 16 h	—
5	$PtCl_2$	Conv. < 10% after 16 h	—
6[c]	$AgSbF_6$	35% after 15 min	1/—
7[c]	$AuClPPh_3/AgSbF_6$	30% after 15 min	2/1
8	$[(Ph_3PAu)_3O]BF_4$	conv.< 40% after 5 h	3/1
9[c]	$IPrAuCl/AgSbF_6$	65% after 15 min	1/—

[a] Refluxing toluene, [b] 5 mol% of catalyst, CH_2Cl_2(0.05 M), [c] Isolated yield. [d] Workup by addition of $NaBH_4$ afforded alcohol **2a**.

In order to test the scope of our rearrangement, allenyl vinyl ethers **1b–g** were prepared and subjected to the optimal reaction conditions (Table 2). *In situ* reduction of the aldehyde motif in the 1,3-diene product afforded the corresponding alcohols **2b–g**. Under the optimized reaction conditions (3 mol% of IprAuCl/$AgSbF_6$), allenyl vinyl ethers **1a–c** rearranged successfully to the corresponding 1,3 dienes **2a–c** in 25 min at room temperature (entries 1–3). However, under the same conditions allenyl vinyl ether **1d**, with an alkyl substituent at C-4, gave a mixture of 1,3 and 3,3-products, with full conversion achieved in less than 15 min suggesting higher reactivity with aliphatic substrates. Lowering the catalyst loading to 2 mol% greatly enhanced the regioselectiviy (>20 : 1) in favor of the 3,3-product, with **2d** isolated in 65% yield after 30 min (entry 4). With the lower catalyst loading allenyl vinyl ethers **1e–g** with different cyclic and acyclic substituents rearranged successfully to the corresponding 1,3-dienes **2e–g** (entries 5–7). These results indicated that the

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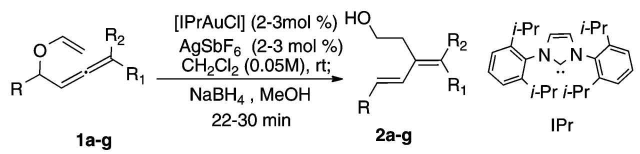
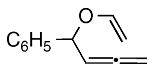
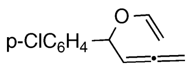
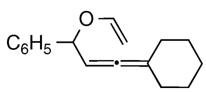
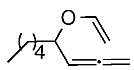
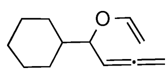
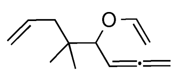
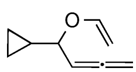
† Electronic supplementary information (ESI) available: Experimental procedures, characterization of compounds and copies of proton and carbon spectra. See DOI: 10.1039/c1ob06297b

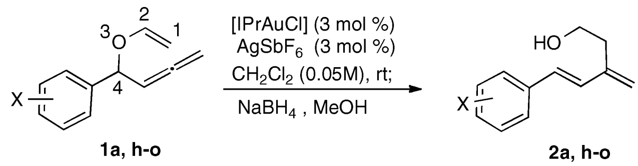
Table 2 Reaction scope



Entry		Allenyl vinyl ether	Product	Yield (%)[c]
1[a]	**1a**		**2a**	86
2[a]	**1b**		**2b**	80
3[a]	**1c**		**2c**	65
4[b]	**1d**		**2d**	65
5[b]	**1e**		**2e**	75
6[b]	**1f**		**2f**	60
7[b]	**1g**		**2g**	77

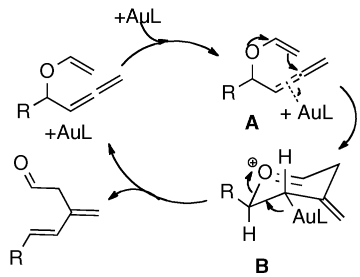
[a] 3 mol%. [b] 2 mol%. [c] isolated yield (average of three runs).

Table 3 Rearrangement of vinyl ethers with aromatic substituents at C-4



Entry		Allenyl Vinyl Ether	Time	Product	Yield[b]
1	**1a**	X = H	22–25 min	**2a**	86%
2[a]	**1h**	X = 4-CN	9 h	**2h**	93%
3	**1i**	X = 4-F	30 min	**2i**	75%
4	**1j**	X = 2-Me	10–12 min	**2j**	84%
5	**1k**	X = 2-Et	10–12 min	**2k**	79%
6	**1l**	X = 4-Me	10–12 min	**2l**	70%
7	**1m**	X = 2,6-dimethyl	15–18 min	**2m**	82%
8	**1n**	X = 2,4,6-trimethyl	15–18 min	**2n**	70%
9	**1o**	X = 4-MeO	5 h	**2o**	<40%

[a] Refluxing CH_2Cl_2, [b] Isolated yield (average of 3 runs).



Scheme 1 Proposed reaction mechanism.

nature of the substituent at C-4 (aromatic or aliphatic) had a significant impact on the reaction rate.

The main difference between aliphatic and aromatic groups is electronic, with the latter being more electron rich. In order to ascertain whether the electronic nature of the substituent at C-4 had an impact on the reaction rate, vinyl ethers **1h–o** with different electron rich and electron poor aromatic substituents at C-4 were prepared and subjected to the reaction conditions (Table 3). Allenyl vinyl ethers with electron withdrawing aromatic substituents (entries 2 and 3) were less reactive than **1a** (entry 1) and rearranged at a slower rate with allenyl vinyl ether **1h** being particularly slow. On the other hand, those with electron rich aromatic substituents **1j–n** (entries 4–8) were more reactive and rearranged at a faster rate than **1a**. Surprisingly, the rearrangement of **1o**, with a *p*-methoxy group on the benzene ring (entry 9), was very slow (less than 40% conversion after 5 h). Careful examination of these results indicated that the electronic nature of substituents at C-4 indeed had a significant impact on the reaction rate; however some of the results were puzzling.

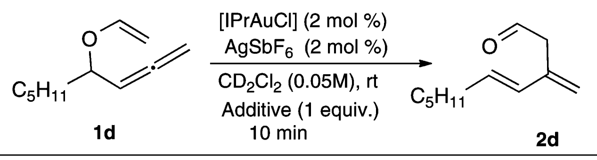
In order to explain the results above, a mechanism similar to that proposed for the gold(I)-catalyzed propargyl Claisen rearrangement is proposed (Scheme 1).[6] Coordination of gold to the allene increases its electrophilicity and activates it toward nucleophilic addition of the vinyl ether. A six-membered cyclic intermediate is formed which upon elimination of gold gives the corresponding [3,3]-rearrangement product. A rate acceleration results from development of a partial positive charge at the carbinol carbon C-4 in the transition state and the presence of electron donating substituents at C-4 that would stabilize such a transition state.

Based on this mechanism, substrates with electron releasing aromatic substituents **1j–o** were expected to rearrange at a faster rate than **1a** whereas those with electron poor aromatic substituents **1h–i** were expected to rearrange at a slower rate. With the exception of the rearrangement of allene **1o**, our expectations were met. Substrates **1j–n** (entries 4–8) rearranged as expected at a faster rate than **1a**, however the rearrangement of allenes **1m** and **1n** was slower than that of **1j–l**, although they were expected to be faster because they are more electron rich. Similarly, the rearrangement of **1o** was the slowest among all tested substrates, although it was anticipated it would be the fastest. The rearrangement of substrates with electron poor aromatic substituents **1h** and **1i** (entries 2 and 3) was slow as expected, but the rearrangement of **1h** was very slow and complete conversion was only observed after 9 h in refluxing CH_2Cl_2 (entry 2). We envisioned that coordination between the gold catalyst and the lone pair of the cyano group, which is well known as a deactivating ligand,[11] reduces the fraction of gold catalyst that is available for activating the allenyl vinyl ether to rearrange. In addition, allenyl vinyl ether **1a** with a phenyl substituent at C-4 was expected to rearrange at a faster rate than **1d** with a n-pentyl group (Table 2, entry 4), since a phenyl group is a better cation stabilizing donor group than the pentyl group, however the result was completely opposite and **1d** was more reactive and required a reduction in the catalyst concentration from 3 mol% to 2 mol%. These results strongly suggested there was another factor affecting the reaction rate other than just the stabilization of the developing positive charge at C-4.

Since we attributed the reduction in the reaction rate in case of vinyl ether **1h**, with a *p*-cyano aromatic group at C-4, to the coordination of the gold catalyst to the lone pair of the CN group reducing the amount of catalyst available for reaction, we envisioned that an interaction between the π-system of the aromatic ring and the gold catalyst could be responsible for the observed anomaly in the reaction rate by also reducing the amount of available catalyst.[12,13] As a result of this interaction, the amount of gold complex available for catalysis decreases in the presence of electron rich aromatic rings thus explaining why allenyl vinyl ether **1d** with an aliphatic group at C-4, rearranged at a faster rate than allenyl vinyl ether **1a** with an aromatic ring at C-4. With increased electron density of the aromatic ring π-complexation became a significant competitor for the catalyst and a decrease in the reaction rate was observed as illustrated in entries 7–9, Table 3.

In order to further support our hypothesis invoking a gold-arene-π interaction, we studied the rearrangement of allene **1d**, bearing an aliphatic substituent at C-4, in the presence of different electron rich and electron poor aromatic compounds as additives. In this case, the stabilizing effect of the substituent at C-4 is minimal and the change in the reaction rate will be only due to the metal-π interaction changing the amount of catalyst available for reaction. Rearrangement of **1d** was carried out using 2 mol% of the catalytic system (IPrAuCl/$AgSbF_6$) in deuterated dichloromethane (CD_2Cl_2) in the presence of different electron rich and electron poor aromatic additives. The reaction was monitored by ^{1}H NMR spectroscopy and the percent conversion was determined from the spectral data at t = 10 min. (Each reaction proceeded to completion within 30 min except for the example in entry 6.) Table 4 summarizes the results we obtained for the rearrangement of **1d** in the presence of different additives. The rate of conversion of **1d** in the absence of additives (entry 1) was considered as the reference for all the other experiments. As expected, in the presence of 1 equiv. of benzene (entry 2), the reaction rate was slower and the relative conversion was found to be 0.9 with respect to the control experiment (entry 1). In the presence of toluene which is more electron rich (entry 3), the conversion rate was even slower (0.81). The rate reduction in case of *tert*-butyl benzene (0.85, entry 4) was less than that in toluene because of the increased steric hindrance that decreased the metal-π interaction. In the case of the more electron rich aromatic additive "anisole" the rate was even slower (0.71, entry 5). In the presence of aniline (entry 6) the reaction didn't proceed as expected and numerous unknown side products were obtained. The electron poor nitrobenzene additive (0.91, entry 7) still exhibited a modest effect on the reaction rate, suggesting an interaction between the nitro group and the gold catalyst was responsible for this slight reduction in the reaction rate. In the presence of cyanobenzene, a significant reduction in the reaction rate was observed (0.31, entry 8). An interaction between the gold catalyst and the cyano group lone pair can be used to explain this large decrease in the reaction rate. The electron poor chlorobenzene additive (entry 9) didn't affect the reaction rate, as expected, and the relative conversion was about 0.98. Thus, the overall rates of rearrangement represent a balance between a rate increase due to a substituent effect and a rate decrease from π-complexation.

Table 4 Rearrangement of allene enol ether **1d** in the presence of additives



Entry	Additive	Relative conv.	Entry	Additive	Relative conv.
1	None	1	6	Aniline	—
2	Benzene	0.9	7	Nitrobenzene	0.91
3	Toluene	0.81	8	Benzonitrile	0.31
4	t-Bu-benzene	0.85	9	Chlorobenzene	0.98
5	Anisole	0.71			

In conclusion we have developed an efficient method for the synthesis of 1,3-dienes through a gold(I)-catalyzed Claisen rearrangement of allenyl vinyl ethers. A study using aromatic additives demonstrated the impact of a metal-π interaction on the reaction rate. A more detailed mechanistic study of the reaction is currently underway and results will be reported in due course.

Experimental

General procedure for synthesis of allenyl vinyl ethers

Vinyl ethers were prepared according to the method of Yamamoto,[14] the allenyl alcohol was dissolved in ethyl vinyl ether (0.1 M) and then mercuric acetate (0.66 equiv.) was added. The reaction mixture was stirred at room temperature overnight. Potassium carbonate was added to the reaction mixture and the product was extracted with diethyl ether, the organic layer was dried over sodium sulfate and then the product was purified using column chromatography with hexane as an eluent.

Synthesis of (1-(vinyloxy)buta-2,3-dien-1-yl)benzene (1a). (1-(Vinyloxy)buta-2,3-dien-1-yl)benzene was prepared according to the same procedure used for the synthesis of allenyl vinyl ethers. The crude mixture was purified by flash chromatography using an alumina column and hexane as an eluent and afforded the allenyl vinyl ether in 66% yield as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 6.44 (dd, J = 14.2, 6.7 Hz, 1H), 5.38 (ddd, J = 7.8, 6.5, 6.5 Hz, 1H), 5.32 (ddd J = 7.8, 1.55, 1.45 Hz, 1H), 4.93 (υ_{obs}) (ABdd, J_{AB} = 11 Hz, J = 6.5, 1.55 Hz, $\Delta\upsilon$ = +23.5 Hz, 1H; ABdd, J_{AB} = 11 Hz, J = 6.5, 1.45 Hz, $\Delta\upsilon$ = -23.5 Hz, 1H), 4.39 (dd, J = 14.2, 1.8 Hz, 1H), 4.11 (dd, J = 6.7, 1.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.7, 150.1, 140.1, 128.6, 128.1, 126.5, 92.5, 90.1, 79.5, 77.3; IR (cm^{-1}) 1617.64, 1636.78, 1956.06, 2894.81, 3031.30, 3064.35; HRMS (EI$^+$) calc'd for $[C_{12}H_{12}O]^+$: *m/z* 172.08882, found 172.08888.

General procedure for the gold(I)-catalyzed Claisen rearrangement of allenyl vinyl ethers

To a solution of $AgSbF_6$ in CH_2Cl_2 (0.01 M) was added a solution of IPrAuCl in CH_2Cl_2 (0.01 M). After stirring for 5 min at rt, the mixture was filtered through a cotton plug and added to a mixture of the allenyl vinyl ether in CH_2Cl_2 (0.05 M). The reaction mixture was stirred at rt until complete consumption of the starting material was observed by TLC. The reaction mixture was then diluted with MeOH (2x CH_2Cl_2) and $NaBH_4$ (1 equiv.) was added.

The resulting mixture was stirred for 30 min, concentrated and the product was purified using column chromatography.

Synthesis of (*E*)-3-methylene-5-phenylpent-4-en-1-ol (2a). (*E*)-3-Methylene-5-phenylpent-4-en-1-ol was prepared according to the general procedure for the gold-catalyzed Claisen rearrangement of allenyl vinyl ethers. The crude mixture was purified by flash chromatography (5 : 1 Hexane:EtOAc) and afforded the alcohol in 86% yield as a white solid (m.p = 39 °C): ^{1}H NMR (500 MHz, C_6D_6) δ 7.31–7.25 (m, 2H), 7.22–7.05 (m, 3H), 6.76 (d, J = 16.3 Hz, 1H), 6.58 (d, J = 16.3 Hz, 1H), 5.12 (s, 1H), 5.05 (s, 1H), 3.66 (t, J = 6.5 Hz, 2H), 2.48 (t, J = 6.5 Hz, 2H); ^{13}C NMR (126 MHz, C_6D_6) δ 143.1, 137.6, 130.9, 128.8, 128.8, 127.8, 126.9, 117.9, 61.3, 35.7; IR (cm^{-1}) 1602.95, 2345.91, 2368.8, 2883.25, 2947.87, 3026.55, 3081.97, 3343.85; HRMS (EI$^+$) calc'd for $[C_{12}H_{14}O]^+$: m/z 174.10447, found 174.10423.

Acknowledgements

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Notes and references

1 E. Negishi, Z. Huang, G. Wang, S. Mohan, C. Wang and S. Hattori, *Acc. Chem. Res.*, 2008, **41**, 1474 and references cited therein; J. S. Glasby, *Encyclopaedia of the Terpenoids*; Wiley, Chichester, UK, 1982; T. K. Devon, A. I. Scott, *Handbook of Naturally Occurring Compounds*, Academic, New York, NY, 1972, Vol. II; M. DellaGreca, C. D Marino, A. Zarrelli and B. D'Abrosca, *J. Nat. Prod.*, 2004, **67**, 1492.

2 K. C. Nicolaou, S. S. Snyder, T. Montagnon and G. Vassilikogiannakis, *Angew. Chem., Int. Ed.*, 2002, **41**, 1668; L. Friebe, O. Nuyken and W. Obrecht, *Adv. Polym. Sci.*, **204**, 1; A. A. Fischbach and R. Anwander, *Adv. Polym. Sci.*, **204**, 155; A. Deagostino, C. Prandi, C. Zavattaro and P. Venturello, *Eur. J. Org. Chem.*, 2006, 2463; W. Oppolzer, In *Comprehensive Organic Chemistry*, B. M. Trost, I. Fleming, ed.; Pergamon Press, Oxford, 1991; Vol. 5, Chapter 4.1, pp 315–400.

3 Braatz, S. Hecht, S. Seifert, S. Helm, J. Bendig and W. Rettig, *J. Photochem. Photobiol., A*, 1999, **123**, 99 and references cited therein.

4 B. M. Trost and A. B. Pinkerton, *J. Am. Chem. Soc.*, 1999, **121**, 4068; A. Kinoshita, N. Sakakibara and M. Mori, *J. Am. Chem. Soc.*, 1997, **119**, 12388; E.-I. Negishi, Z. Huang, G. Wang, S. Mohan, C. Wang and H. Hattori, *Acc. Chem. Res.*, 2008, **41**, 1474 and references cited therein; K. C. Nicolaou, P. G. Bulger and D. Sarlah, *Angew. Chem., Int. Ed.*, 2005, **44**, 4442; S. T. Diver and A. J. Giessert, *Chem. Rev.*, 2004, **104**, 1317; E. S. Hansen and D. Lee, *Acc. Chem. Res.*, 2006, **39**, 509; R. P. Murelli and M. L. Snapper, *Org. Lett.*, 2007, **9**, 1749.

5 For leading reviews, see: A. S. K. Hashmi and G. J Hutchings, *Angew. Chem., Int. Ed.*, 2006, **45**, 7896; A. Fürstner and P. W. Davies, *Angew. Chem., Int. Ed.*, 2007, **46**, 3410; A. S. K. Hashmi, *Chem. Rev.*, 2007, **107**, 3180; Z. Li, C. Brouwer and C. He, *Chem. Rev.*, 2008, **108**, 3239; A. Arcadi, *Chem. Rev.*, 2008, **108**, 3266.

6 B. D. Sherry and F. D. Toste, *J. Am. Chem. Soc.*, 2004, **126**, 15978.

7 During the preparation of this manuscript an example of a gold-catalyzed Claisen rearrangement of electron deficient allenyl vinyl ethers was reported. H. Wei, Y. Wang, B. Yue and P.-F. Xu, *Adv. Synth. Catal.*, 2010, **352**, 2450.

8 For an example of a thermal Claisen rearrangement of allenyl vinyl ethers see, E. Egert, H. Beck, D. Schmidt, C. Gonschorrek and D. Hoppe, *Tetrahedron Lett.*, 1987, **28**, 789.

9 Allyl allenyl ethers undergo thermal rearrangement to the corresponding α,β-unsaturated aldehydes. P. J. Parsons, P. Thomson, A. Taylor and T. Sparks, *Org. Lett.*, 2000, **2**, 571 Using the conditions described herein, electron deficient allenyl vinyl ethers do not undergo Claisen rearrangement.

10 Allenic esters undergo gold catalyzed rearrangement to 1,3-butadien-2-ol esters. A. K. Buzas, F. M. Istrate and F. Gagosz, *Org. Lett.*, 2007, **9**, 985.

11 P. De Fremont, N. Marion and S. P. Nolan, *J. Organomet. Chem.*, 2009, **694**, 551.

12 Gold-Arene complexes: H. Schmidbaur and A. Schier, *Organometallics*, 2010, **29**, 2; F.-B. Xu, Q.-S. Li, L.-Z. Wu, X.-B. Leng, Z.-C. Li, X.-S. Zeng, Y. L. Chow and Z.-Z Zhang, *Organometallics*, 2003, **22**, 633; D. Schroder, J. Hrusak, R. H. Hertwig, W. Koch, P. Schwerdtfeger and H. Schwarz, *Organometallics*, 1995, **14**, 312; E. Herrero-Gomez, C. Nieto-Oberhuber, S. Lopez, J. BenetBuchholz and A. M. Echevarren, *Angew. Chem., Int. Ed.*, 2006, **45**, 5455; V. Lavallo, G. D. Frey, S. Kousar, B. Donnadieu and G. Bertrand, *Proc. Natl. Acad. Sci. U. S. A.*, 2007, **104**, 13569; X. Zeng, G. Frey, S. Kousar and G. Bertrand, *Chem.–Eur. J.*, 2009, **15**, 3056; G. D. Frey, R. D. Dewhurst, S. Kousar, B. Donnadieu and G. Bertrand, *J. Organomet. Chem.*, 2008, **693**, 1674; V. Lavallo, G. D. Frey, B. Donnadieu, M. Soleilhavoup and G. Bertrand, *Angew. Chem., Int. Ed.*, 2008, **47**, 5224.

13 For an example of an unexpected regioselectivity with an aryl substituent in a Au catalyzed cyclopropene rearrangement, see: M. S. Hadfield, J. T. Bauer, P. E. Glen and A.-L. Lee, *Org. Biomol. Chem.*, 2010, **8**, 4090.

14 K. Nonoshita, H. Banno, K. Maruoka and H. Yamamoto, *J. Am. Chem. Soc.*, 1990, **112**, 316.