ORGANIC LETTERS

2008
Vol. 10, No. 3
521−524

Gold-Catalyzed [4+3]-Annulation of Oxabicyclic Benzenes with 2-Substituted Allylsilanes through Tandem Allylation and Cyclization

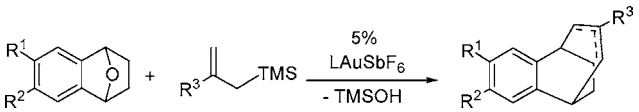
Yu-Chia Hsu, Swarup Datta, Chun-Ming Ting, and Rai-Shung Liu*

Department of Chemistry, National Tsing-Hua University, Hsinchu, Taiwan, ROC

rsliu@mx.nthu.edu.tw

Received December 18, 2007

ABSTRACT



This work reports new gold-catalyzed [4 + 3]-annulations of oxacyclic benzenes with 2-substituted allylsilanes through tandem allylation and cyclization; on the basis of experimental observations, we propose a mechanism involving the opening of the oxacyclic ring by a PPh_3Au^+-assisted S_N2-attack of allylsilanes.

Additions of allylic organometallics to aldehydes, ketones,[1] epoxides,[2] and other oxacyclic electrophiles[3] provide 1,*n*-enols ($n = 4-6$) efficiently, which have served widely as building blocks for complicated bioactive molecules.[1−3] Despite their great utility, these electrophiles react with allylmetal species exclusively through a single-addition pathway as depicted in eqs 1 and 2. We envisage that the values of these reactions would become enhanced significantly if these electrophiles undergo new annulation with allylsilanes as depicted in eq 3. Although gold catalysis has attained a substantial advance in the nucleophilic activations of alkynes and alkenes,[4,5] only limited examples have focused on the activation of oxygen-containing electrophiles.[6,7] Herein, we report an unprecedented gold-catalyzed [4 + 3]-annulation of oxabicyclic benzenes with allylsilanes through a tandem allylation/cyclization route (eq 3). Before this work, activations of oxabicyclic benzenes toward nu-

(1) (a) Chemler, S. R.; Roush, W. R. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 10. (b) Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 11. (c) Ren, H.; Dunet, G.; Mayer, P.; Knochel, P. *J. Am. Chem. Soc*. **2007**, *129*, 5376. (d) Denmark, S. E.; Fu, J. *Chem. Rev*. **2003**, *103*, 2763. (e) Yamamoto, Y.; Asao, N. *Chem. Rev*. **1993**, *93*, 2207. (f) Wadamoto, M.; Ozasa, N.; Yanagisawa, A.; Yamamoto, H. *J. Org. Chem*. **2003**, *68*, 5593. (g) Kruger, J.; Carreira, E. M. *J. Am. Chem. Soc*. **1998**, *120*, 837. (h) Gauthier, D. R., Jr.; Carreira, E. M. *Angew. Chem. Int. Ed*. **1996**, *35*, 2363. (i) Yasuda, M.; Hirata, K.; Nishino, M.; Baba, A. *J. Am. Chem. Soc*. **2002**, *124*, 13442. (j) Zhang, W.-C.; Li, C.-J. *J. Org. Chem*. **1999**, *64*, 3230.

(2) (a) Tanaka, T.; Inoue, T.; Kamei, K.; Murakami, K.; Iwata, C. *J. Chem. Soc., Chem. Commun*. **1990**, 906. (b) Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Springer: Berlin, 1986; pp 218. (c) Tanaka, T.; Hiramatsu, K.; Kobayashi, Y.; Ohno, H. *Tetrahedron* **2005**, *61*, 6726. (d) Overman, L. E.; Renhowe, P. A. *J. Org. Chem*. **1994**, *59*, 4138 and references therein.

(3) (a) Millward, D. B.; Sammis, G.; Waymouth, R. M. *J. Org. Chem*. **2000**, *65*, 3902. (b) Nakamura, M.; Matsuo, K.; Inoue, T.; Nakamura, E. *Org. Lett*. **2003**, *5*, 1373. (c) Lautens, M.; Fagnou, K.; Hiebert, S. *Acc. Chem. Res*. **2003**, *36*. 48. (d) Lautens, M.; Dockendorff, C.; Fagnou, K.; Malicki, A. *Org. Lett*. **2002**, *4*, 1311. (e) Lautens, M.; Ma, S.; Chiu, P. *J. Am. Chem. Soc*. **1997**, *119*, 6478.

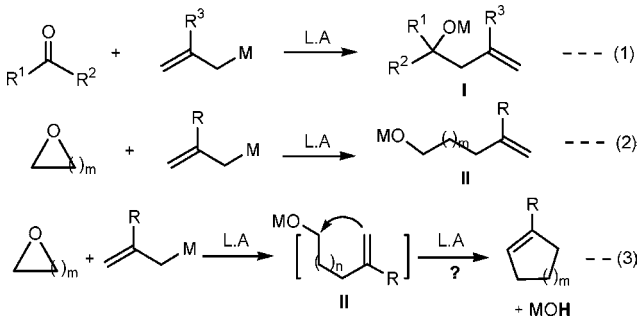
(4) (a) Hashmi, A. S. K. *Chem. Rev*. **2007**, *107*, 3180. (b) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed*. **2007**, *46*, 3410. (c) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395. (d) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun*. **2007**, 333. (e) Kim, S. M.; Park, J. H.; Choi, S. Y.; Chung, Y. K. *Angew. Chem., Int. Ed*. **2007**, *46*, 6172. (f) Li, G.; Zhung, L. *Angew. Chem., Int. Ed*. **2007**, *46*, 5156. (g) Lian, J.-J.; Chen, P.-C.; Lin, Y.-P.; Ting, H.-C.; Liu, R.-S. *J. Am. Chem. Soc*. **2006**, *128*, 11372.

(5) (a) Han, X.; Widenhoefer, R. A. *Angew. Chem., Int. Ed*. **2006**, *45*, 1747. (b) Yao, X.; Li, C.-J. *J. Am. Chem. Soc*. **2004**, *126*, 6884. (c) Zhang, J.; Yang, C.-G.; He, C. *J. Am. Chem. Soc*. **2006**, *128*, 1798. (d) Liu, X.-Y.; Li, C.-H.; Che, C.-M. *Org. Lett*. **2006**, *8*, 2707. (e) Xu, Q.; Imamura, Y.; Fujiwara, M.; Souma, Y. *J. Org. Chem*. **1997**, *62*, 1594.

(6) (a) Schelwies, M.; Dempwolff, A. L.; Rominger, F.; Helmchen, G. *Angew. Chem., Int. Ed*. **2007**, *46*, 5598. (b) Jiménez-Núñez, E.; Claverie, C. K.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem., Int. Ed*. **2006**, *45*, 5452. (c) Lin, C.-C.; Teng, T.-M.; Odedra, A.; Liu, R.-S. *J. Am. Chem. Soc*. **2007**, *129*, 3798. (d) Yao, X.; Li, C.-J. *Org. Lett*. **2006**, *8*, 1953. (e) Kuninobu, Y.; Ishii, E.; Takai, K. *Angew. Chem., Int. Ed*. **2007**, *46*, 3296. (f) Georgy, M.; Boucard, V.; Campagne, J.-M. *J. Am. Chem. Soc*. **2005**, *127*, 14180.

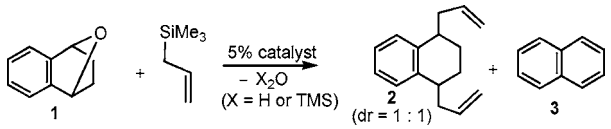
10.1021/ol7030334 CCC: $40.75
Published on Web 01/10/2008

cleophilic attack exclusively proceed through a single addition pathway (eq 2).[8]



Prior to our screening of catalysts, our control experiments revealed that Lewis acids effected catalytic conversions of oxabicyclic benzene **1** to naphthalene **3** slowly.[9] In a typical procedure, the catalyst screening was performed on slow addition of oxacyclic species **1** (ca. 15−20 min) to a mixture of trimethylallylsilane (3 equiv) and acid catalyst (5 mol %) in CH_2Cl_2 (23 °C); the results are shown in Table 1. Hard

Table 1. Addition of Trimethylallylsilane to Oxabicyclic Benzene **1**



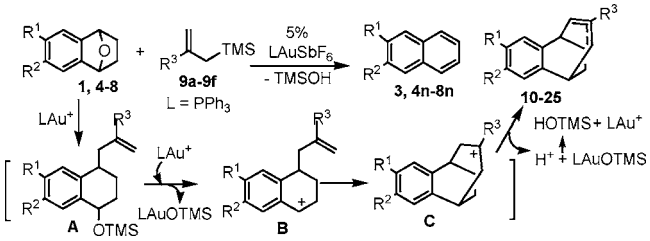
entry	catalyst	time[a] (h)	product (yield, %)[b]
1	$BF_3{\cdot}Et_2O$	30	**1** (58), **2** (28), **3** (13)
2	TMSOTf	2	**1** (15), **2** (14), **3** (60)
3	HOTf	24	**1** (90)
4	$Zn(OTf)_2$	24	**1** (83), **3** (12)
5	AuCl	24	**1** (96)
6	$AuCl_3$	24	**1** (96)
7	$PtCl_2$	24	**1** (96)
8	$AuClPPh_3/AgSbF_6$[c]	0.5	**2** (92)

[a] Conditions: 23 °C, [substrates] = 0.15 M in CH_2Cl_2. [b] Product yields were reported after separation from a silica column. [c] This mixture was prepared from 5 mol % of $AuClPPh_3$ and 5 mol % of $AgSbF_6$.

acids including $BF_3{\cdot}Et_2O$ and TMSOTf gave 1,4-addition product **2** (dr = 1 : 1) in low yields (14−28%), whereas unreacted **1** and naphthalene **3** were the major species in the reactions (entries 1 and 2). The use of Brönsted acid HOTf led to exclusive recovery of starting oxacyclic species **1** because of its incompatibility with allylsilane. $Zn(OTf)_2$, AuCl, $AuCl_3$, and $PtCl_2$ were too weakly acidic to effect the allylation reaction. The use of PPh_3AuSbF_6 in CH_2Cl_2 (23 °C, 0.5 h) exclusively gave the doubly allylated product **2** with a yield up to 92%.

The double-allylation of oxacyclic benzene **1**, depicted in Table 1, implies the feasibility of a new [4 + 3]-annulation if a 2-substituted allylsilane is used. Table 2 shows a working

Table 2. Gold-Catalyzed [4 + 3]-Annulation of Oxacyclic Benzenes with 2-Substituted Allylsilanes



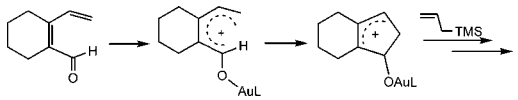
entry	substrate[a]	silane	time (h)	products (yield, %)[b]
1	$R^1 = R^2 =$ H (**1**)	R^3 = Ph (**9a**)	3.0	**10** (43), **3** (2)
2	R^1 = H, R^2 = Me (**4**)	R^3 = Ph (**9a**)	3.0	**11** (52),[c] **4n** (16)
3	**4**	R^3 = 4-^{t}BuPh (**9b**)	3.0	**12** (50),[c] **4n** (16)
4	$R^1 = R^2 =$ Me (**5**)	R^3 = Ph (**9a**)	3.0	**13** (73), **5n** (2)
5	R^1 = H, R^2 = OMe (**6**)	R^3 = Ph (**9a**)	3.0	**14** (60),[c] **6n** (14)
6	**6**	R^3 = 4-^{t}BuPh (**9b**)	3.0	**15** (62),[c] **6n** (14)
7	$R^1 = R^2 =$ OMe (**7**)	R^3 = *n*-Bu (**9c**)	0.5	**16** (45), **7n** (19)
8	**7**	R^3 = Ph (**9a**)	3.0	**17** (85), **7n** (5)
9	**7**	R^3 = 4-MePh (**9d**)	1.0	**18** (75), **7n** (12)
10	**7**	R^3 = 4-MeOPh (**9e**)	0.5	**19** (75), **7n** (12)
11	**7**	R^3 = 4-^{t}BuPh (**9b**)	2.0	**20** (82), **7n** (12)
12	**7**	R^3 = Me (**9f**)	1.0	**21** (65), **7n** (25)
13	$R^1, R^2 =$ OCH_2O (**8**)	R^3 = Ph (**9a**)	3.0	**22** (70), **8n** (10)
14	**8**	R^3 = 4-^{t}BuPh (**9b**)	3.0	**23** (75), **8n** (11)
15	**8**	R^3 = 4-MePh (**9d**)	1.5	**24** (51), **8n** (25)
16	**8**	R^3 = 4-MeOPh (**9e**)	0.5	**25** (62), **8n** (6%

[a] Conditions: 23 °C, allylsilane (1.5 equiv), 5% $AuClPPh_3$/5% $AgSbF_6$, [substrates] = 0.15 M in CH_2Cl_2. [b] Product yields are reported after separation from a silica column. [c] dr = 1 : 1.

mechanism comprising a tandem allylation and cyclization. We envisage that the initial gold-catalyzed allylation of oxacyclic substrates leads to single addition products **A** bearing a siloxy group because of the lower oxaphilicity of PPh_3Au^+.[10] In contrast with conventional hard acids, this cationic gold catalyst retains acidity to effect the ionization of species **A** to generate benzylic cations **B**, which ultimately produce [4 + 3]-annulated products via intermediates **C**.

We prepared various oxacyclic species **1** and **4**−**8** to test this hypothesis. To our delight, treatment of oxacyclic species

(7) We recently reported allylic addition of *cis*-dienals[6c] through an initial Au(I)-catalyzed Nazarov cyclization of dienal substrate to generate an allyl cation intermediate, which is subject to nucleophilic attack. This mechanism is completely distinct from those described for oxacyclic benzenes in this work.



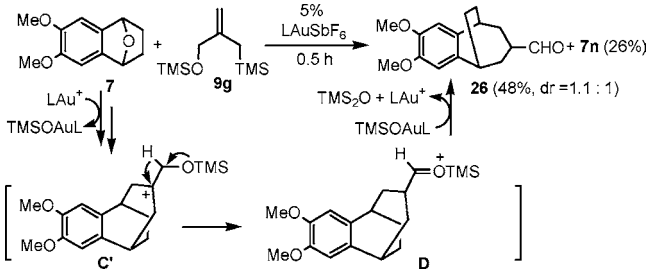
(8) (a) Chen, C.-L.; Martin, S. F. *J. Org. Chem.* **2006**, *71*, 4810. (b) Zhang, W.; Wang, L.-X.; Shi, W.-J.; Zhou, Q.-L. *J. Org. Chem.* **2005**, *70*, 3734. (c) Wu, M.-S.; Jeganmohan, M.; Cheng, C.-H. *J. Org. Chem.* **2005**, *70*, 9545. (d) Li, M.; Yan, X.-X.; Hong, W.; Zhu, X.-Z.; Cao, B.-X.; Sun, J.; Hou, X.-L. *Org. Lett.* **2004**, *6*, 2833. (e) Cabrera, S.; Arrayás, R. G.; Alonso, I.; Carretero, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 17938. (f) Lautens, M.; Hiebert, S. *J. Am. Chem. Soc.* **2004**, *126*, 1437. (g) Lautens, M.; Fagnou, K.; Yang, D. *J. Am. Chem. Soc.* **2003**, *125*, 14884.

(9) Treatment of oxacyclic benzene **1** with $PPh_3AuCl/AgSbF_6$ (5 mol %) in CH_2Cl_2 (23 °C, 20 min) gave naphthalene **3** in 48% yield in addition to unreacted **1** (50%).

1 and **4** with trimethyl(2-arylallyl)silanes (aryl = phenyl **9a**, 4-*tert*-butylphenyl **9b**, 1.5 equiv) gave the annulated products **10**−**12** in 43−52% yields (entries 1−3); the cyclization efficiencies were affected by acid-catalyzed polymerization of oxacyclic benzenes.[11] The yields of this [4 + 3]-annulation became further improved for substrates **5**−**8** bearing electron-rich phenyl groups; the desired products **13**−**15** and **17**−**22** were obtained in good yields (>60%) using various 2-substituted allylsilanes as the nucleophiles. As we expected, 2-butylallylsilane (entry 7) was less effective than 2-arylallylsilanes because of its inefficient stabilization of carbocation intermediates **C**. Notable mechanistic information is the brief period (0.5 h) of reaction in the annulation of species **7** and **8** with electron-rich silanes such as 2-butylallylsilane **9c** and 4-methoxyphenylallylsilane **9e** (entries 7, 10 and 16).

The utility of this reaction is further manifested by its applicability to oxygen-containing silane **9g**, as illustrated in Scheme 1, which afforded annulated product **26** in 48%

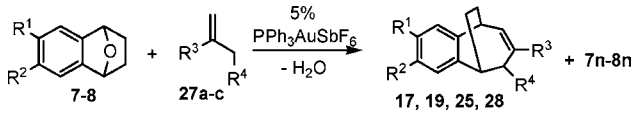
Scheme 1. [4 + 3]-Annulation Using Oxygen-Containing Allylsilane



yield (dr = 1.1:1). This transformation likely proceeds through formation of tertiary carbocation **C′**, which undergoes Pinacol-type rearrangement[12] to give oxonium species **D**, ultimately giving the desired aldehyde **26**.

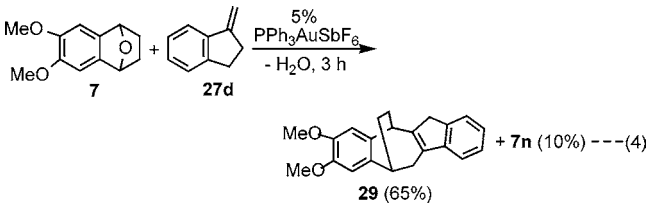
The value of this annulation is further enhanced by the expanded scope of substrates including alkene-based nucleophiles **27a**−**c**; the examples are shown in Table 3. Formation of [4 + 3]-annulated products **17**, **19**, **25**, **28** is accompanied by generation of one H_2O through this annulation. Electron-rich alkene **27b** is more efficient than its unsubstituted analogue **27a** upon comparison of the yields of products **19** (68%), **25** (51%), and **17** (20%). This cycloaddition was extendible to bicyclic alkene **27d**, which gave desired compound **29** in a 65% yield (eq 4) in addition to naphthalene **7n** (10%).

Table 3. Annulation of Oxacyclic Species **7**−**8** with Alkenes



entry	substrate[a]	alkene	time (h)	product (yield, %)[b]
1	$R^1 = R^2 = OCH_3$ (**7**)	R^3 = Ph, R^4 = H (**27a**)	3	**17** (20), **7n** (25)
2	**7**	R^3 = 4-MeOPh, R^4 = H (**27b**)	3	**19** (68)
3	**7**	R^3 = 4-MeOPh, R^4 = Me (**27c**)	3	**28** (42, dr = 2:1), **7n** (23)
4	R^1, $R^2 = OCH_2O$ (**8**)	**27b**	3	**25** (51), **8n** (6)

[a] Conditions: 23 °C, alkene (3 equiv), 5% $AuClPPh_3$/5% $AgSbF_6$, [substrates] = 0.15 M in CH_2Cl_2. [b] Product yields are reported after separation from a silica column.



Although few gold−allyl species can undergo allylation with aldehydes,[13] these species are unlikely to be involved in the annulation mechanism. Treatment of 2-phenylallylsilane (**9a**) with PPh_3AuSbF_6 (1.0 equiv) in $CDCl_3$ only showed the ^1H and ^{13}P NMR signals of unreacted **9a** (66%), cationic gold species, and 2-phenylpropene (24%). This information indicates no generation of allylgold(I) species through transmetalation. This hypothesis is also supported by a report on Au(I)-catalyzed Sila-Cope rearrangement, which revealed that PPh_3AuPF_6 did not react with allylsilane to give Au(I)−allyl species.[14] Hence, we propose that the ring opening of the oxacyclic substrates is initiated on coordination with PPh_3Au^+ to facilitate a S_N2-attack of allylsilane, as represented by state **E** in path a, giving species **F** and ultimately species **A** via a TMS exchange (Scheme 2). The evidence for this process is based on our observation that the rates of reaction are enhanced with electron-rich silanes (Table 2, entries 7, 9, and 10). Notably, $AuPPh_3SbF_6$ alone catalyzed slowly the transformation of oxacyclic

(10) Recent examples using $AuPPh_3SbF_6$ as an π-alkyne activator: (a) Shapiro, N. D.; Toste, F. D. *J. Am. Chem. Soc*. **2007**, *129*, 4160. (b) Witham, C. A.; Mauleón, P.; Shapiro, N. D.; Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc*. **2007**, *129*, 5838. (c) Staben, S. T.; Kennedy-Smith, J. J.; Huang, D.; Corkey, B. K.; LaLonde, R. L.; Toste, F. D. *Angew. Chem., Int. Ed*. **2006**, *45*, 5991. (d) Lemière, G.; Gandon, V.; Agenet, N.; Goddard, J.-P.; de Kozak, A.; Aubert, C.; Fensterbank, L.; Malacria, M. *Angew. Chem., Int. Ed*. **2006**, *45*, 7596. (e) Genin, E.; Toullec, P. Y.; Antoniotti, S.; Brancour, C.; Genêt, J.-P.; Michelet, V. *J. Am. Chem. Soc*. **2006**, *128*, 3112. (f) Wang, S.; Zhang, L. *J. Am. Chem. Soc*. **2006**, *128*, 14274. (g) Mézailles, N.; Ricard, L.; Gagosz, F. *Org. Lett*. **2005**, *7*, 4133. (h) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed*. **2004**, *43*, 2402. (i) Lian, J.-J.; Chen, P.-C.; Lin, Y.-P.; Ting, H.-C.; Liu, R.-S. *J. Am. Chem. Soc*. **2006**, *128*, 11372.

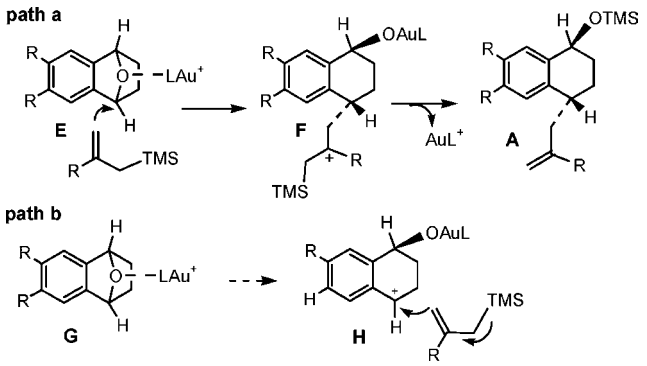
(11) (a) Toneri, T.; Sanda, F.; Endo, T. *Macromolecules* **2001**, *34*, 1518. (b) Yasuda, T.; Aida, T.; Inoue, S. *Bull. Chem. Soc. Jpn*. **1986**, *59*, 3931.

(12) (a) Overman, L. E.; Pennington, L. D. *J. Org. Chem*. **2003**, *68*, 7143. (b) Hanaki, N.; Link, J. T.; MacMillan, D. W. C.; Overman, L. E.; Trankle, W. G.; Wurster, J. A. *Org. Lett*. **2000**, *2*, 223. (c) Kirsch, S. F.; Binder, J. T.; Crone, B.; Duschek, A.; Haug, T. T.; Liébert, C.; Menz, H. *Angew. Chem., Int. Ed*. **2007**, *46*, 2310. (d) Huang, X.; Zhang, L. *J. Am. Chem. Soc*. **2007**, *129*, 6398.

(13) Allylgold(I) still remains unknown, although several allylgold(III) complexes undergo allylation with organic carbonyl compounds; see: Sone, T.; Ozaki, S.; Kasuga, N. C.; Furuoka, A.; Komiya, S. *Bull. Chem. Soc. Jpn*. **1995**, *68*, 1523.

(14) Horino, Y.; Luzung, M. R.; Toste, F. D. *J. Am. Chem. Soc*. **2006**, *128*, 11364.

Scheme 2. Proposed Mechanisms for Ring-Opening and Allylation



species into naphthalenes, and a S_N1 process (path b) is also likely involved in the initial allylation particularly for electron-rich benzenes.

This work reports unprecedented [4 + 3]-annulations of oxacyclic benzenes with 2-substituted allylsilanes through tandem allylation and cyclization; PPh_3AuSbF_6 is better than common Lewis acids in this annulation because of its less oxaphilicity and reasonable electrophilicity. The synthetic value of this catalytic reaction is enhanced by its compatibility with oxygen-containing silane **9g** and electron-rich alkenes. The use of this method for the synthesis of bioactive molecules is currently under study.

Acknowledgment. We thank the National Science Council, Taiwan, for supporting this work.

Supporting Information Available: Experimental procedures for the synthesis of starting substrates and catalytic operations, NMR spectra, and spectral data of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL7030334