JOC Article

Gold-Catalyzed Hydrative Carbocyclization of 1,5- and 1,7-Allenynes Mediated by π-Allene Complex: Mechanistic Evidence Supported by the Chirality Transfer of Allenyne Substrates

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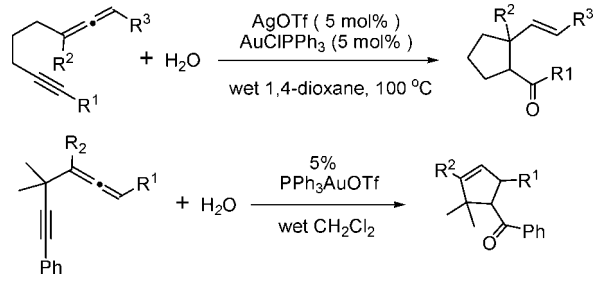

We report $PPh_3AuCl/AgOTf$-catalyzed hydrative carbocyclization of 1,5- and 1,7-allenynes to give cyclized ketones chemoselectively. In this transformation, hydration occurrs regioselectively at the C≡*C*Ph carbon, accompanied by addition of the *C*≡CPh carbon to the two terminal allenyl carbons. This method is effective for the construction of a quaternary carbon center. On the basis of the chirality transfer of allenyne substrates, control experiments, and theoretic calculations, we propose that this hydrative carbocyclization proceeds through an initial π-allene complex with a small energy barrier.

Introduction

The metal-catalyzed carbocyclization of an acyclic molecule with an external nucleophilic addition is useful because new functional groups are thereby introduced onto the cyclized frameworks.[1,2] The cycloisomerization of enynes[3] and allenynes[4] that provides rapid access to carbocyclic compounds is a recent advance in gold and platinum catalysis. These reactions generate reactive carbocations that are trapped with water, alcohols, or electron-rich arenes to give functionalized cyclized products.[5,6] Reported cycloisomerizations[4] and nucleophilic carbocyclizations[6] of allenynes are mediated exclusively by π-alkyne species that form stable allyl cation intermediates through an *exo* or *endo* attack of the central allene carbon at the π-alkyne (eq 1). As a notable exception, Malacria obtained several cyclized products from the π-allene-complexation of hydroxylated 1,5-allenynes.[4i]

We report here gold-catalyzed hydrative carbocyclization of allenynes to give α-ketonyl cyclopentanes or cyclopentenes, which are generated through an attack of the *C*≡CR carbon at the two terminal allenyl carbons[7] (eq 2).The chirality transfer

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(1) For metal-catalyzed cyclizations with addition of water or alcohols, see selected examples: (a) Trost, B. M.; Rudd, M. T. *J. Am. Chem. Soc.* **2003**, *125*, 11516. (b) Trost, B. M.; Brown, R. E.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 5877. (c) Yao, T.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 11164. (d) Chen, Y.; Ho, D. M.; Lee, C. *J. Am. Chem. Soc.* **2005**, *127*, 12184. (e) Odedra, A.; Wu, C.-J.; Pratap, T. B.; Huang, C.-W.; Ran, Y. F.; Liu, R.-S. *J. Am. Chem. Soc.* **2005**, *127*, 3406. (f) Chang, H.-K.; Datta, S.; Das, A.; Odedra, A.; Liu, R.-S. *Angew. Chem., Int. Ed.* **2007**, *46*, 4744.

(2) For metal-catalyzed cyclization with addition of carbon nucleophiles, see selected examples: (a) Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 54. (b) Miura, T.; Shimada, M.; Murakami, M. *J. Am. Chem. Soc.* **2005**, *127*, 1094. (c) Cauble, D. F.; Gipson, J. D.; Krische, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 1110. (d) Lautens, M.; Mancuso, J. *J. Org. Chem.* **2004**, *69*, 3478.

(3) Recent reviews: (a) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410. (b) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395. (c) Jimenez-Nunez, E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333. (d) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271. (e) Hashmi, A. S. H. *Angew. Chem., Int. Ed.* **2005**, *44*, 6990.

(4) Selected examples for cycloisomerization of 1-allen-*n*-ynes: (a) Cadran, N.; Cariou, K.; Hervé, G.; Aubert, C.; Fensterbank, L.; Malacria, M.; Marco-Contelles, J. *J. Am. Chem. Soc.* **2004**, *126*, 3408. (b) Petit, M.; Aubert, C.; Malacria, M. *Tetrahedron* **2006**, *62*, 10582. (c) Petit, M.; Aubert, C.; Malacria, M. *Org. Lett.* **2004**, *6*, 3937. (d) Brummond, K. M.; Painter, T. O.; Probst, D. A.; Mitasev, B. *Org. Lett.* **2007**, *9*, 347. (e) Bayden, A. S.; Brummond, K. M.; Jordan, K. D. *Organometallics* **2006**, *25*, 5204. (f) Matsuda, T.; Kadowaki, S.; Goya, T.; Murakami, M. *Synlett* **2006**, 575. (g) Lee, S. I.; Sim, S. H.; Kim, S. M.; Kim, K.; Chung, Y. K. *J. Org. Chem.* **2006**, *71*, 7120. (h) Lin, G.-Y.; Yang, C.-Y.; Liu, R.-S. *J. Org. Chem.* **2007**, *72*, 6753. (i) Zriba, R.; Gandon, V.; Aubert, C.; Fensterbank, L.; Malacria, M. *Chem. Eur. J.* **2008**, *14*, 1482.

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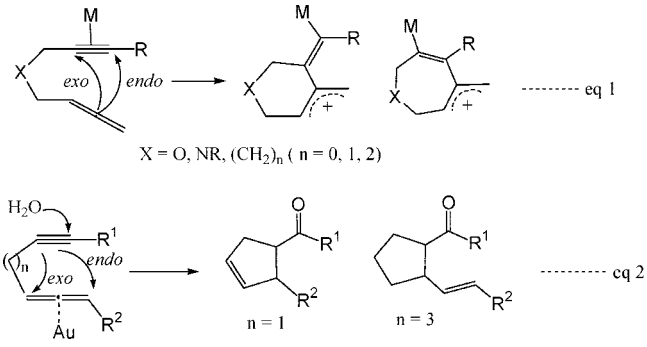
of allenyne substrates to their resulting α-ketonyl cyclopentanes or cyclopentenes provides evidence for a π-allene pathway.

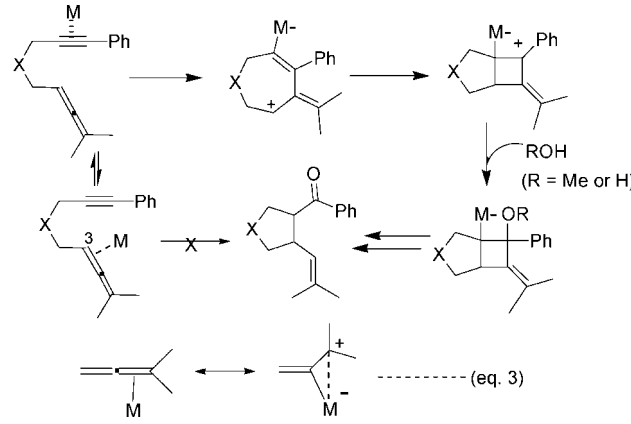


Results/Discussion

Before our work, Murakami reported hydrative cyclization of 1-allen-7-ynes of special types [X = $C(CO_2Me)_2$, NTs, O] using $PtCl_2$ and MeOH solvent;[8] according to a deuterium-labeling experiment. This reaction was proposed to proceed through a π-alkyne complex; the mechanism is depicted in Scheme 1. A disadvantage of this cyclization is the complete loss of product chirality with use of chiral allenynes because an allylic cation is formed as depicted in eq 2. The π-allene moiety[7] is also represented by a zwitter ionic form (eq 1), and a highly substituted allene is generally more active toward nucleophilic attack. As we envisage the connecting unit [X = $C(CO_2Me)_2$, NTs, O] in Murakami's system[8] to be unsuitable to activate the adjacent C(3)-allenyl carbon, we undertook to investigate this cyclization by varying 1-allen-7-yne substrates and catalysts to achieve a π-allene pathway. This approach appears to be more efficient than a π-alkyne pathway in the formation of a new quaternary carbon.

We selected 1-allen-7-yne **1** as the relevant species because its cyclized ketone product **2** bears a quaternary carbon; the methyl group also enhances the allene activity. Table 1 shows the reactions of 1-allen-7-yne **1** over various π-acid catalysts in wet 1,4-dioxane. AuCl, $AuCl_3$, and $AgSbF_6$ caused complete decomposition of starting **1** at 100 °C, whereas $AuClPPh_3$ led exclusively to unreacted **1** under the same conditions. Highly electrophilic $PPh_3AuCl/AgSbF_6$, $PtCl_2/CO$, and $PtCl_4$ preferably

SCHEME 1



gave [4 + 2]-cycloaddition adduct **3**[9] in 43−55% yields. Murakami's catalyst, $PtCl_2$/MeOH, notably led only to a 55% recovery of starting allenyne **1**. AgOTf that showed a distinct chemoselectivity in wet dioxane (100 °C, 6 h) gave a 1:1 diastereomeric mixture of 1-(*E*-styryl)-2-carbonylcyclopentane **2** in a 75% yield. The yield of cyclized ketone **2** improved to 85% with $AuClPPh_3/AgOTf$ catalyst. In dry 1,4-dioxane, $PPh_3AuCl/AgOTf$ catalyst gave ketone **2** (dr = 1.0) in 12% yield besides [4 + 2]-cycloadduct **3** (33%). Compound **3** is formed from a π-alkyne[9] intermediate, which is preferentially mediated by $PtCl_2$ catalyst.

We prepared various 1-allen-7-ynes **4**−**20** to assess the generality of this new hydrative carbocyclization; the results are depicted in Table 2. Similar to compound **2**, the resulting cyclized ketones **21**−**35** bear an *E*-olefin substituent. Entries 1−3 show the variation of the allenyl R^3 substituent; upon comparison of their reaction time and product yields, allenyne **5** bearing a 4-methoxyphenyl substituent appears to be more efficient than its phenyl **4** and *n*-butyl analogues **6** in this carbocyclization. Unreacted allenyne **6** was recovered in a 48% yield (entry 3). Entries 1 and 4−7 show the variation of the alkynyl R^1 substituent of allenyne substrates; this cyclization was less efficient for allenynes **7**−**9** bearing an electron-rich 3-thienyl, 4-methylphenyl, and 4-methoxyphenyl group, and became particularly unsuitable for allenyne **10** bearing an electron-deficient 4-trifluoromethylphenyl group. In these cases, the resulting products **21**−**26** existed preferentially in an *anti*-isomeric form (*anti*/*syn* = 2.6−9.8). This carbocyclization works effectively for allenynes **11**−**19** bearing an alkyl group at the terminal C(3)-allene carbon (R^2 = Me, Et, ^{n}Bu, entries 8−16), which gave satisfactory yields (67−83%) of resulting products **27**−**35** despite generation of a quaternary carbon. Furthermore, these cyclizations were complete within 1−10 h, much less duration than for their unsubstituted analogues **4**−**10** (R^2 = H, 18−72 h). According to these substituent effects, we deduce that a C(3)-substituted 1-allen-7-yne and a phenylalkynyl group are the best combination for allenyne substrates.

Nucleophilic attack on a metal−π-allene occurs regioselectively at two terminal carbons.[7] We prepared 1-allen-5-ynes **36**−**39** to explore the cyclization via attack of the *C*≡CPh carbon at the remote allenyl carbon (Table 3). Treatment of these species with $AuPPh_3OTf$ catalyst (5 mol %) delivered cyclopentenyl ketones **41**−**44** in 65−80% yields, in favor of *syn*-

(5) For cyclization of enynes with nucleophiles, see selected examples: (a) Nieto-Oberhuber, C.; Munoz, M. P.; Lopez, S.; Jimenez-Nunez, E.; Nevado, C; Herrero-Gomez, E.; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677. (b) Nieto-Oberhuber, C.; Munoz, P. M.; Bunuel, E.; Nevado, C.; Cardenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2402. (c) Toullec, P. Y.; Genin, E.; Leseurre, L.; Genet, J.-P.; Michelet, V. *Angew. Chem., Int. Ed.* **2006**, *45*, 7427. (d) Amijis, C. H. M.; Ferre, C.; Echavarren, A. M. *Chem. Commun.* **2007**, 698.

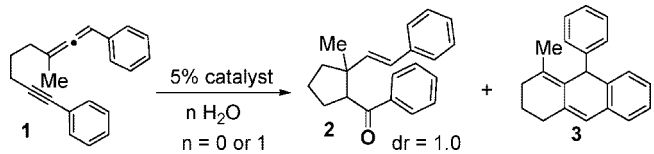
(6) For cyclization of allenynes with nucleophiles, see: Lemiére, G.; Gandon, V.; Agenet, N.; Goddard, J.; de.Kozak, A.; Aubert, C.; Fensterbank, L.; Malacria, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 7596.

(7) Nucleophilic attack on π-allenes exclusively occurs at the two terminal carbons except for a few cases reported by Widenhoefer,[7d] and see selected examples: (a) Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, D. F. *Science* **2007**, *317*, 496. (b) 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. (c) Nishina, N.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 3314. (d) Zhang, Z.; Liu, C.; Kinder, R. E.; Han, X.; Qian, H.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2006**, *128*, 9066. (e) Liu, Z.; Wasmuth, A. S.; Nelson, S. G. *J. Am. Chem. Soc.* **2006**, *128*, 10352. (f) Gockel, B.; Krause, N. *Org. Lett.* **2006**, *8*, 4485. (g) Wang, S.; Zhang, L. *Org. Lett.* **2006**, *8*, 4585. (h) Zhang, G.; Catalano, V. J.; Zhang, L. *J. Am. Chem. Soc.* **2007**, *129*, 11359. (i) Hashmi, A. S. K.; Blanco, M. C.; Fischer, D.; Bats, J. W. *Eur. J. Org. Chem.* **2006**, 1387. (j) Hashmi, A. S. K.; Schwartz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 2285.

(8) Matsuda, T.; Kadowaki, S.; Murakami, M. *Helv. Chim. Acta* **2006**, *89*, 1672.

(9) For mechanistic formation of [4 + 2]-cycloadducts **3**, see: Nieto-Oberhuber, C.; Lopez, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178.

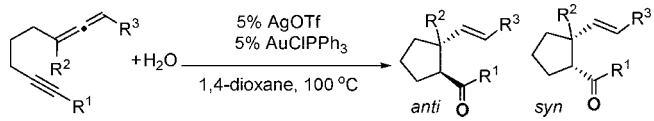
TABLE 1. Catalytic Cyclization over Various Catalysts



		yield[c] (%)		
catalyst[a]	solvent (conditions)	**1**	**2**	**3**
(1) AuCl[b]	1,4-dioxane (100 °C, 24 h)			
(2) $AuCl_3$[b]	1,4-dioxane (100 °C, 24 h)			
(3) $AgSbF_6$[b]	1,4-dioxane (100 °C, 24 h)			
(4) $AuClPPh_3$[b]	1,4-dioxane (100 °C, 24 h)	85		
(5) $AuClPPh_3/AgSbF_6$	CH_2Cl_2 (23 °C, 30 min)			45
(6) $PtCl_2/CO$[b]	1,4-dioxane (100 °C, 4 h)			55
(7) $PtCl_4$[b]	1,4-dioxane (100 °C, 24 h)			43
(8) $PtCl_2$[b] (10%)	MeOH (70 °C, 48 h)	55		
(9) AgOTf[b]	1,4-dioxane (100 °C, 6 h)		75	
(10) $AuClPPh_3/AgOTf$[b]	1,4-dioxane (100 °C, 4 h)		85	
(11) $AuClPPh_3/AgOTf$[b]	dry 1,4-dioxane (100 °C, 24 h)		12	33

[a] 5 mol % catalyst, [allenyne] = 0.20 M. [b] At 23 °C for 12 h, starting species **1** was recovered exclusively for entries 1−3 and 5−7. [c] Products were separated on a silica column.

TABLE 2. Gold-Catalyzed Hydrative Carbocyclizations of 1,7-Allenynes



entry	allenynes[a]	R^1	R^2	R^3	time (h)	products[b] (yields, *anti*/*syn*)
1	**4**	Ph	H	Ph	36	21 (73%, 5.1)
2	**5**	Ph	H	4-$MeOC_6H_4$	18	22 (82%, 2.6)
3	**6**	Ph	H	*n*-Bu	48	23 (35%, 11.4)[c]
4	**7**	3-thienyl	H	Ph	28	24 (55%, 9.1)
5	**8**	4-MeC_6H_4	H	Ph	30	25 (46%, 7.1)
6	**9**	4-$MeOC_6H_4$	H	Ph	72	26 (16%, 9.8)
7	**10**	4-$CF_3C_6H_4$	H	Ph	72	
8	**11**	Ph	ethyl	Ph	10	27 (78%, 1.2)
9	**12**	Ph	*n*-butyl	Ph	8	28 (75%, 1.0)
10	**13**	Ph	methyl	methyl	6	29 (70%, 1.4)
11	**14**	3-thienyl	methyl	Ph	6	30 (67%, 1.2)
12	**15**	Ph	methyl	*n*-butyl	8	31 (75%, 1.7)
13	**16**	Ph	methyl	2-thienyl	8	32 (74%, 1.7)
14	**17**	Ph	methyl	4-$MeOC_6H_4$	1	33 (83%, 1.3)
15	**18**	Ph	methyl	4-$CF_3C_6H_4$	10	34 (75%, 1.2)
16	**19**	Ph	ethyl	*n*-butyl	8	35 (75%, 1.2)
17	**20**	*n*-propyl	methyl	Ph	12	20 (65%)

[a] 1,7-allenyne **1** (1 equiv, 0.20 M), $PPh_3AuCl/AgOTf$ (5 mol %), 1,4-dioxane (100 °C). [b] Product yields are given after separation from a silica column. [c] Starting allenyne **6** was recovered in a 48% yield.

isomers (*syn*/*anti* = 1.5−6.7),[10] But the cyclization of 1-allen-6-ynes **40** led to its recovery (56%) in wet 1,4-dioxane (100 °C, 12 h); we isolated no side product from an alkyne hydration of species **40**.

We prepared chiral allenynes **45** and **47**[11] to elucidated the reaction mechanism (Scheme 2). We propose the absolute configurations of resulting ketones **46** and **48** on the basis of our reaction model depicted in Scheme 3. Treatment of (*S*)-1-allen-7-yne **45** (ee >98%) with 5 mol % $AgOTf/AuClPPh_3$ in wet 1,4-dioxane at 90 °C for 2 h produced chiral α-ketonyl cyclopentene product **46** (80% yield) in *syn*/*anti* = 2:1 ratio. The *syn*-diastereomer of **46** was obtained in 55% ee, whereas the *anti*-diastereomer was obtained in 67% ee. Some loss of the enantiopurity of products **46** is likely caused by gold-catalyzed epimerization[12] of allenynes in hot 1,4-dioxane. In the case of (*R*)-1-allen-5-yne **47** (59% ee), the mild conditions (25 °C) effected complete chirality transfer to resulting products **48**-*syn* (58% ee) and **48**-*anti* (58% ee). The chirality transfer of substrates tentatively excludes a π-alkyne mechanism proposed by Murakami, which is expected to show a complete loss of product chirality. To assess the role of allenyl ketone **49** in this $AgOTf/AuClPPh_3$ system, Scheme 2 shows a control experiment, which gave only unreacted **49** in the absence or presence of Et_3N; this observation eliminates the intermediacy

(10) We have treated cyclopentenyl ketone **42** (*syn*/*anti* = 5.1) with PPh_3AuOTf (5 mol %) in hot 1,4-dioxane (100 °C, 3 h); we recovered ketone **42** present in a 1:1 mixture of *syn*/*anti* isomers. This information reveals that PPh_3AuOTf promotes the *syn*/*anti* isomerization of ketone **42** in hot 1,4-dioxane.

(11) Preparation of chiral allenes and determination of the ee values of products are provided in the Supporting Information.

(12) (a) Zhang, Z.; Bender, C. F.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2007**, *129*, 14148. (b) Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *126*, 15978.

SCHEME 2

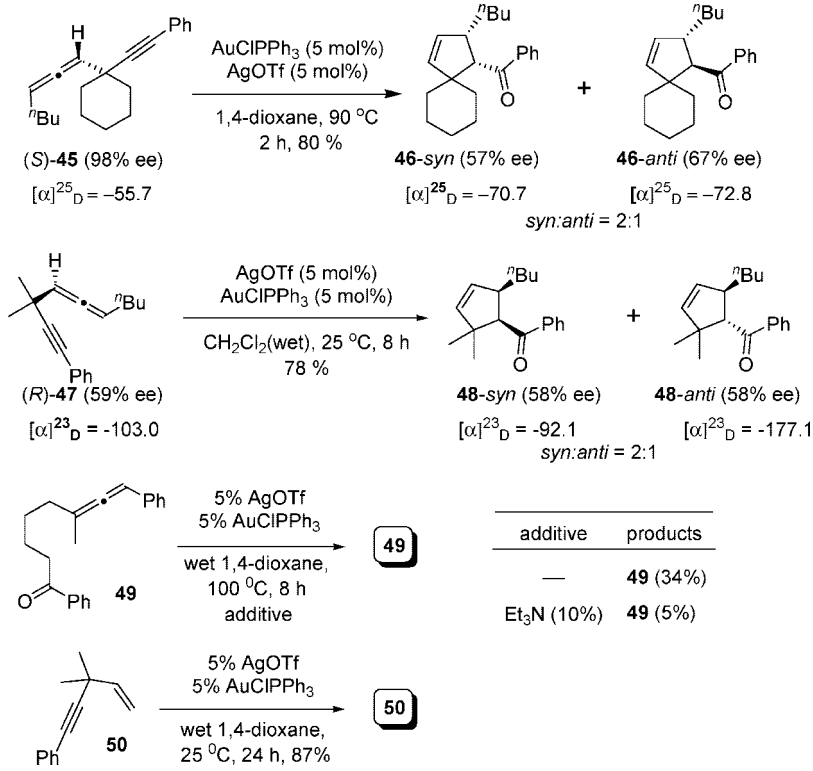
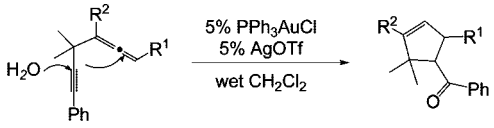
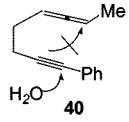


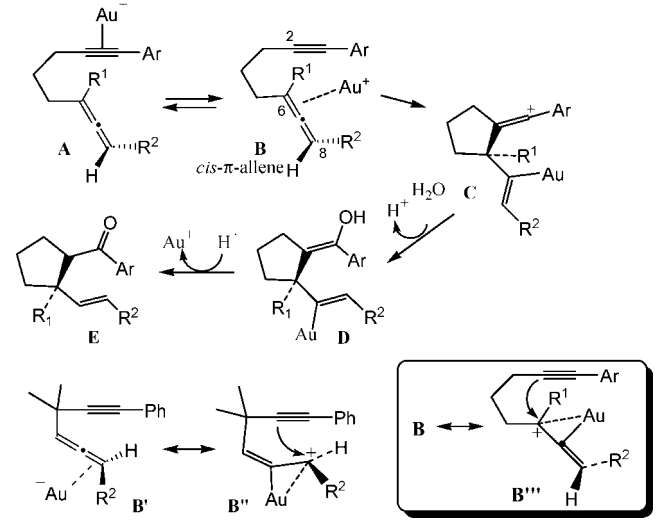
TABLE 3. Catalytic Cyclization of 1,5- and 1,6- Allenyenes



Entry	Allenynes	Conditions[a]	Products (yields, *syn*/*anti*)[b]
1	R^1 = Me, R^2 = H (**36**)	25 °C, 12 h	**41** (65%, 5.1[c])
2	R^1= *n*-Bu, R^2 = H (**37**)	25 °C, 8 h	**42** (78%, 1.5)
3	R^1= Me, R^2 = Me (**38**)	25 °C, 6 h	**43** (80%, 5.1)
4	R^1= *n*-Bu, R^2 = Me (**39**)	25 °C, 6 h	**44** (75%, 6.7)
5		5% PPh_3AuCl, 5% AgOTf, wet 1,4-dioxane, 100 °C, 12 h	**40** (56%)

[a] 1,7-Allenyne (1 equiv, 0.20 M). [b] Product yields are given after separation from a sillica column. [c] *syn*/*anti* ratios.

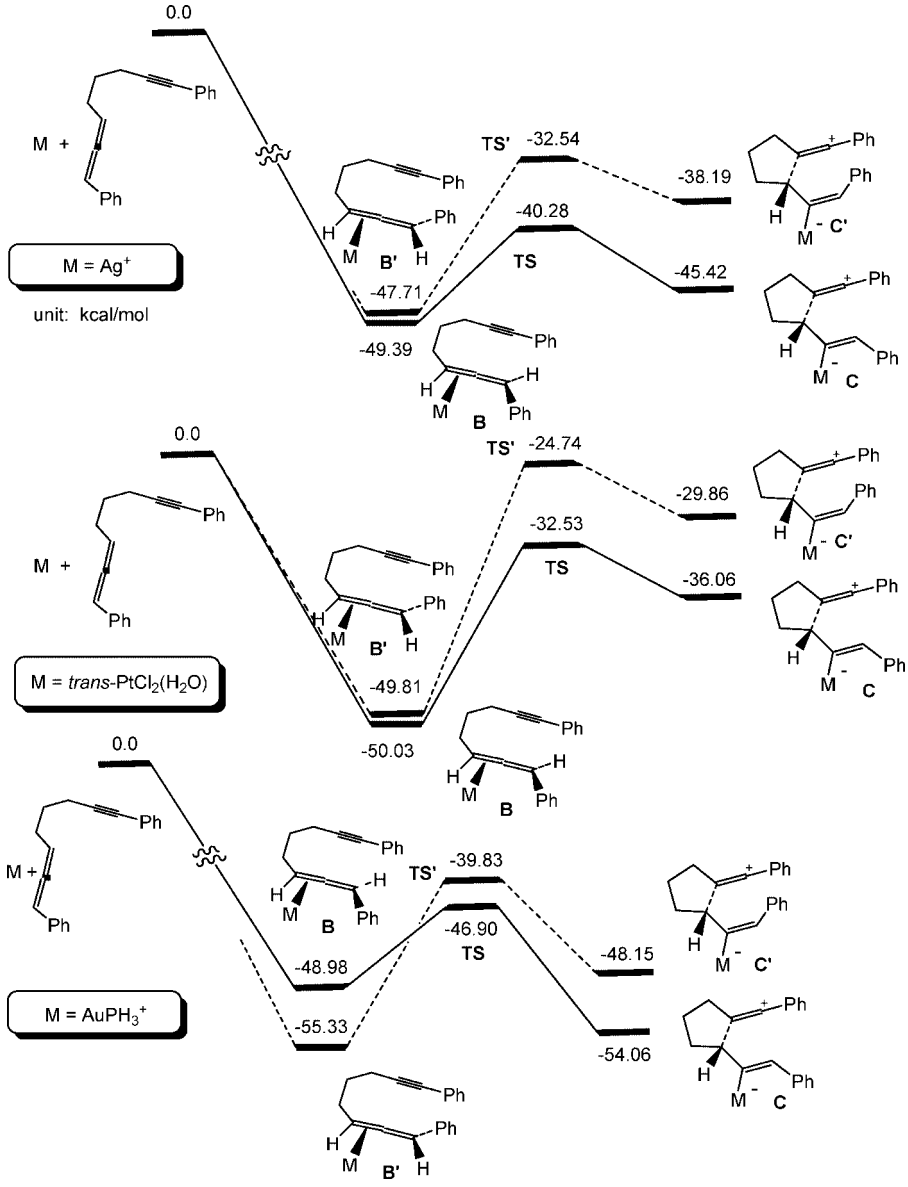
SCHEME 3



of ketone **49**. As shown in Table 3 (entry 5), we obtained no hydration product from allenyne **49** in wet 1,4-dioxane under catalytic conditions (25−100 °C, 12 h). To understand the role of alkyne hydration for substrates **36**−**39** (entry 1−4) which were readily converted to cyclized ketoens **41**−**44** at 25 °C, we prepared alkyne **50**, but we observed no alkyne hydration only its exclusive recovery under similar conditions. *This information indicates that the allene functionality of allenynes* **36**−**39** *facilitates their alkyne hydration.*

The carbocyclization proceeds through a regioselective hydration at the C≡*C*Ph carbon, accompanied by attack of the *C*≡CPh carbon at the two terminal allenyl carbons. Furthermore, the use of chiral substrates **45** and **47** led to chirality transfer to their products **46** and **48**. These observations show the electrophilic behavior of π-allene, due to gold complexation. Scheme 3 shows a plausible mechanism to rationalize the accelerating effect of the allene groups of allenynes **36**−**39** on the alkyne hydration. This mechanistic pathway is proposed with reference to a paper by Widenhoefer.[7d] Among π-alkyne **A**[9] or π-allene **B** intermediates, PPh_3AuCl/AgOTf preferably triggers the π-allene pathway via 5-*exo*-attack of the *C*≡CPh at the proximate allenyl terminal carbon to form species **C**, of which the adjacent phenyl group stabilizes the vinyl cation. To rationalize the observed *E*-styryl geometry of cyclized ketones **E**, we envisage that species **B** adopts a *cis*-conformation with its R^2 substituent opposite the entering alkyne group to minimize the steric hindrance because the C(2)−C(6) bond is formed parallel to the C(8)−H bond. In the case of 1-allen-5-ynes **36**−**37**, we propose that PPh_3Au^+ polarizes the π-allene **B′**

SCHEME 4

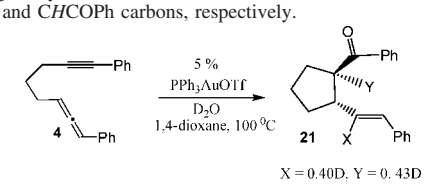


to form an angular geometry as represented by **B″**, which facilitates the 5-*endo*-cyclization.[13]

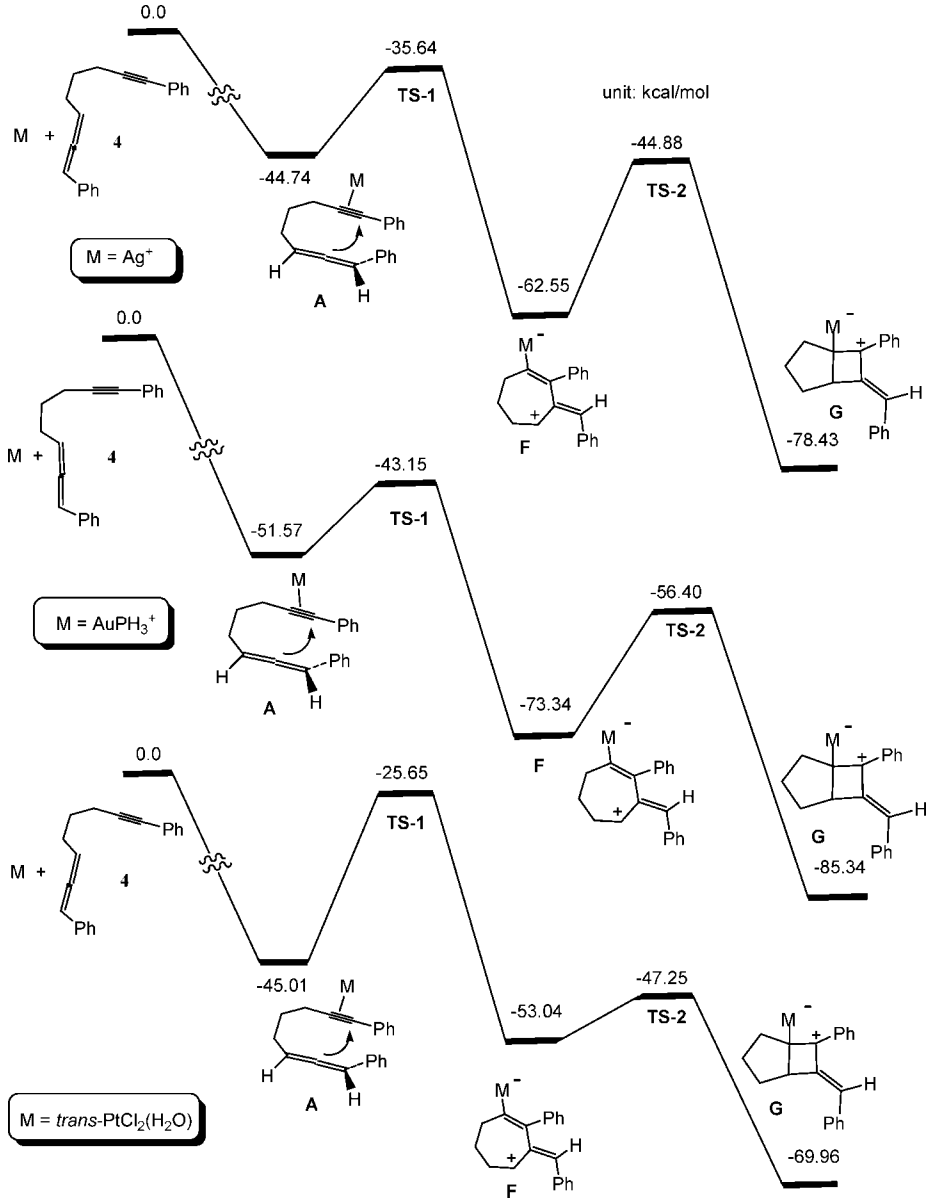
The proposed mechanism rationalizes also our observed activity−structure relationship as shown in Table 2. Consistent with our observations (entries 8−17 versus entries 1−7), π-allene intermediate **B** bearing a R^1 = alkyl substituent is expected to be more active than its unsubstituted analogue (R^1 = H) in this catalysis because the former tends to form a more polarized structure **B‴** stabilized by the tertiary cation. To account for the effects of the arylalkynes of 1-allen-7-ynes, we envisage that, for production of products **E**, substrates **8**−**9** bearing an electron-rich aryl group are less efficient than their phenyl analogue **4** because the former greatly favors π-alkyne complex **A** in the alkyne/allene equilibrium. In contrast, the electron-deficient arylalkyne as in allenyne **10** (Table 2, entry 7) is incapable of stabilizing the vinyl cation **C** to give desired product **E**.

To assess our proposed mechanism, Scheme 4 shows the results of theoretical calculations[14] (B3LYP/LANL2DZ). Two possible π-allene conformers are **B** and **B′**. We take the sum of energies of the free substrate and metal as the energy zero. In the case of Ag^+ and *trans*-$PtCl_2(H_2O)$, *cis*-π-allenes **B** are likely to be the active intermediates because their corresponding transition structures **TS** have lower energies [**TS**: −40.28 kcal/mol for Ag^+, −32.53 kcal/mol for *trans*-$PtCl_2(H_2O)$] than those of *trans*-π-allene complex **B′** [**TS′**: −32.54 kcal/mol for Ag^+, −24.74 kcal/mol for *trans*-$PtCl_2(H_2O)$]. The preference for *cis*-π-allene intermediates **B** is also shown by their resulting vinyl cations **C**, which are more exothermic (ca. 6.2−7.3 kcal/mol) than species **C′** generated from *trans*-π-allene **B′**. For M = $AuPH_3^+$, although the *trans*-π-allene **B′** is more stable than the

(13) The proposed mechanism is also supported by deuterium labeling experiments. Hydrative carbocyclization with allenyne **4** in the presence of D_2O (1.0 equiv) gave cyclized ketone **21** with 40% and 43% deuterium content at its C*H*=CHPh and C*H*COPh carbons, respectively.



SCHEME 5

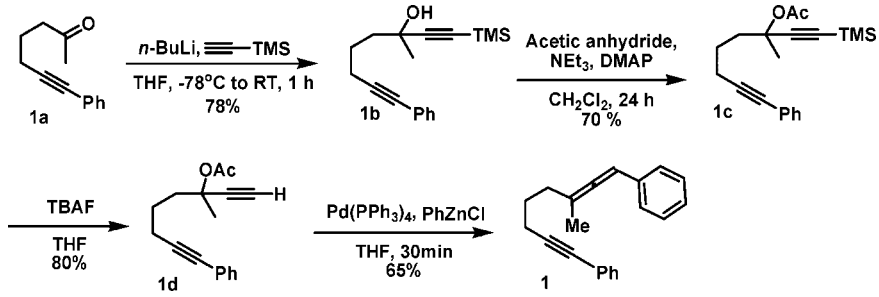


cis-complex **B** by 6.35 kcal/mol, the barrier height for **B** → **C** (+2.08 kcal/mol) is still much smaller than that for **B′**→ **C′** (+15.50 kcal/mol). Here, vinyl cation **C** has an energy of 5.1 kcal/mol less than that of complex **C′**. On the basis of the energy profiles in Scheme 4, we envisage that Ag^+ and$AuPH_3^+$ are more efficient than *trans*-$PtCl_2(H_2O)$ in activating *cis*-π-allene because the platinum system has a large barrier of +17.5 kcal/mol for the transformation **B** → **C**.

Our calculations support the preference for allenyne substrates bearing an arylalkyne group. For allenyne **20** bearing a propylalkyne group, with $AuPH_3^+$ catalyst, we found a high energy of the corresponding vinyl cation **C** (−45.2 kcal/mol) with a large activation barrier (+5.12 kcal/mol) in the **B** → **C** conversion (see the Supporting Information).

We performed calculations on π-alkyne pathways, proposed by Murakami, to assess their possible participation. The activation energies to form allylic cation **F** are +9.11, +19.36, and +8.42 kcal/mol for M = Ag^+, *trans*-$PtCl_2(H_2O)$, and $AuPH_3^+$, respectively. These barrier heights are larger than those for the π-allene pathways that we propose. The role of $PtCl_2$ in a π-alkyne mechanism is excluded because its transition state **TS-1** has an extraordinary large energy (−25.65 kcal/mol). For Ag^+ and $AuPH_3^+$, the activation energies for transformation **F** → **G** are up to 17.66 and 17.50 kcal/mol, respectively. This information indicates that the π-alkyne mechanism is less likely to occur here. Furthermore, *cis*-π-allene intermediate **B** is more exothermic than π-alkyne species **A** in the complexation of allenyne with metal species. The energy differences are 4.64, 5.02, and 3.76 kcal/mol for Ag^+, *trans*-$PtCl_2(H_2O)$, and $AuPH_3^+$,respectively, in favor of *cis*-π-allene **B**. The thermodynamic perference for *cis*-π-allenes **B** and the small energy barrier in the formation of vinyl cations **C** imply that the hydrative cyclization of allenynes are performed better by $AuPH_3^+$ and Ag^+ through *cis*-π-allene **B** (Scheme 5).

In summary, we report a new hydrative carbocyclization of 1,5- and 1,7-allenynes catalyzed by $PPh_3AuCl/AgOTf$, giving cyclized ketones chemoselectively. In such cyclizations, water attacks regioselectively at the C≡*C*Ph carbon, accompanied by attack of the tethered *C*≡CPh carbon at the two terminal allenyl carbons. The use of chiral allenynes provides desired ketones



with small loss of chirality. In our control experiments, the allene group of substrates facilitates the hydration of their tethered alkynes. On the basis of theoretic calculations, we conclude that the hydrative cyclization is likely mediated by π-allene intermediates with a low energy barrier. This new method is efficient to provide cyclized ketones bearing a new quaternary carbon; the reaction is usefully complementary to Murakami's work.[8] The application of this method to the synthesis of bioactive molecules is under current investigation.

Experimental Section

I. Procedures for Theoretic Calculations. All geometries (reactants, intermediates, transition states, and products) had been fully optimized by using the B3LYP method[14,15] with the LANL2DZ basis set[16] (B3LYP/LANL2DZ). Density Functional Theory (DFT) is recognized as a valuable tool for the study of transition sates and reaction intermediates. The vibrational frequencies, at the same level of theory, were computed to characterize the stationary points as true minima or saddle points on the potential energy hypersurfaces. All of the calculations were performed with the GAUSSIAN 03 package.[17] The unscaled zero-point vibrational energies (ZPE) are included in the reported energies.

II. Experimental Procedures for Synthesis of the Substrates.

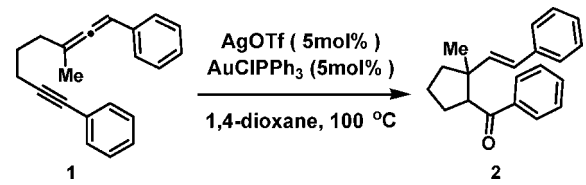
Synthesis of 3-Methyl-1,8-diphenylocta-1,2-dien-7-yne (1). (a) Synthesis of 3-Methyl-1-(trimethylsilyl)-8-phenylocta-1,7-diyn-3-ol (1b). To a mixture of trimethylsilylacetylene (0.80 g, 8.2 mmol) and THF (20 mL) was added *n*-BuLi (2.5 M in hexanes, 2.1 mL, 5.3 mmol) dropwise at −78 °C, and the solution was stirred for 30 min before addition of compound **1a** (762 mg, 4.1 mmol). The solution was stirred for 1 h before treatment with an aqueous NH_4Cl solution, then extracted with ethyl acetate, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to afford compound **1b** (908 mg, 3.2 mmol, 78%) as a yellow oil.

(b) Synthesis of 3-Methyl-1-(trimethylsilyl)-8-phenylocta-1,7-diyn-3-yl Acetate (1c). To a dichloromethane solution of **1b** (0.50 g, 1.76 mmol) was added DMAP (12 mg, 0.1 mmol), acetic anhydride (0.61 mg, 6.0 mmol), and triethylamine (0.92 g, 9.0 mmol) at 28 °C; the resulting solution was stirred for 12 h before being quenched with a saturated $NaHCO_3$ solution. The solution was extracted with dichloromethane, washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The residues were purified by filtration on a short silica pad to afford compound **1c** (401 mg, 1.23 mmol, 70%) as a yellow oil.

(c) Synthesis of 3-Methyl-1-(trimethylsilyl)-8-phenylocta-1,7-diyn-3-yl Acetate (1d). To a THF solution (20.0 mL) of compound **1c** (1.12 g, 3.43 mmol) was added Bu_4NF (1.0 M, 3.5 mL, THF) at 25 °C. The resulting mixture was stirred for 30 min, the solvent was removed in vacuo, and a saturated NH_4Cl solution was added. The organic layer was extracted with ethyl acetate, washed with water, dried over $MgSO_4$, and concentrated in vacuo. The residues were chromatographed on a silica column (hexane:ethyl acetate 1:9, R_f 0.5) to afford compound **1d** (697 mg, 2.74 mmol, 80%) as a colorless oil.

(d) Synthesis of 3-Methyl-1,8-diphenylocta-1,2-dien-7-yne (1). To a THF solution of phenylmagnesium bromide (181 mg, 1.0 mmol) was added $ZnCl_2$ (1 M in THF, 1.0 mL, 1.0 mmol) dropwise at 0 °C; the mixture was stirred for 1.0 h before adding $Pd(PPh_3)_4$ (4.6 mg, 0.004 mmol) and compound **1d** (203 mg, 0.8 mmol). The resulting mixture was stirred for 1.0 h before warming near 23 °C; the solvent was removed in vacuo before treatment with a saturated $NaHCO_3$ solution. The organic layer was extracted with diethyl ether, washed with a saturated NaCl solution, and dried over anhydrous $MgSO_4$. The residues were chromatographed through a silica gel column (hexane) to afford compound **1** (141 mg, 0.52 mmol, 65%) as a yellow oil. IR (neat, cm^{-1}): 3080 (m), 2210 (w), 1961 (s), 1598 (m), 1495 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.35 (m, 2 H), 7.28−7.24 (m, 7 H), 7.17−7.14 (m, 1 H), 6.08 (q, J = 2.8 Hz, 1 H), 2.44 (t, J =7.2 Hz, 2 H), 2.27−2.21 (m, 2 H), 1.83 (d, J = 2.8 Hz, 3 H), 1.78 (td, J = 7.4, 2.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 135.7, 131.5, 128.5, 128.1, 127.4, 126.5, 126.4, 123.9, 103.0, 94.3, 89.8, 80.9, 33.0, 26.5, 19.0, 18.9; HRMS calcd for $C_{21}H_{20}$ 272.1565, found 272.1568.

III. A Typical Procedure for Catalytic Cyclization of 3-Methyl-1,8-diphenylocta-1,2-dien-7-yne (1).



Synthesis of (*E*)-(2-Methyl-2-styrylcyclopentyl)(phenyl)methanone (2). A solution of PPh_3AuOTf (5 mol %) was prepared by mixing PPh_3AuCl (9.1 mg, 0.018 mmol) and AgOTf (4.6 mg, 0.018 mmol) in 1,4-dioxane (1.9 mL). To this solution was added compound **1** (100 mg, 0.37 mmol) at 100 °C, then the mixture was stirred for 4 h. The resulting solution was filtered through a celite bed and eluted through a silica gel column (ethyl acetate/hexane 1/15) to give compound **2** (91 mg, 0.28 mmol, 85%) as a yellow oil. IR (neat, cm^{-1}) 3050 (m), 2945 (s), 1708 (s), 1513 (s); ^1H NMR (400 MHz, $CDCl_3$) (*anti*/*syn* = 1.0) δ 7.90 (d, J = 7.2 Hz, 2 H), 7.85 (d, J = 8.8 Hz, 2 H), 7.51−7.45 (m, J = 8.0 Hz, 2 H), 7.44−7.36 (m, 4 H), 7.30−7.24 (m, 4 H), 7.22−7.13 (m, 4 H), 7.08 (d, J = 8.0 Hz, 2 H), 6.29, 6.22 (AB quartet, J = 16.0 Hz, 2 H), 6.20, 6.13 (AB quartet, J = 16.0 Hz, 2 H), 3.82 (t, J = 7.6 Hz, 1 H), 3.76 (t, J = 7.2 Hz, 1 H), 2.40−2.29 (m, 2 H), 2.05−1.62 (m, 10 H), 1.08 (s, 3 H), 1.37 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.9, 202.2, 139.3, 138.7, 138.3, 137.6, 137.4, 136.1, 132.5, 132.3, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 126.9, 126.7, 126.6, 126.2, 125.9, 125.9, 56.5, 54.9, 48.9, 48.4, 41.3, 39.6, 28.2, 27.8, 26.3, 23.0, 22.8, 20.9; HRMS calcd for $C_{21}H_{22}O$ 290.1671, found 290.1673.

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Supporting Information Available: Experimental procedures including synthesis of allenyne **45**, spectra data for compounds **1**−**49**, and copies of ^{1}H and ^{13}C NMR spectra for compounds **1**−**49**. This material is available free of charge via the Internet at http://pubs.acs.org.

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