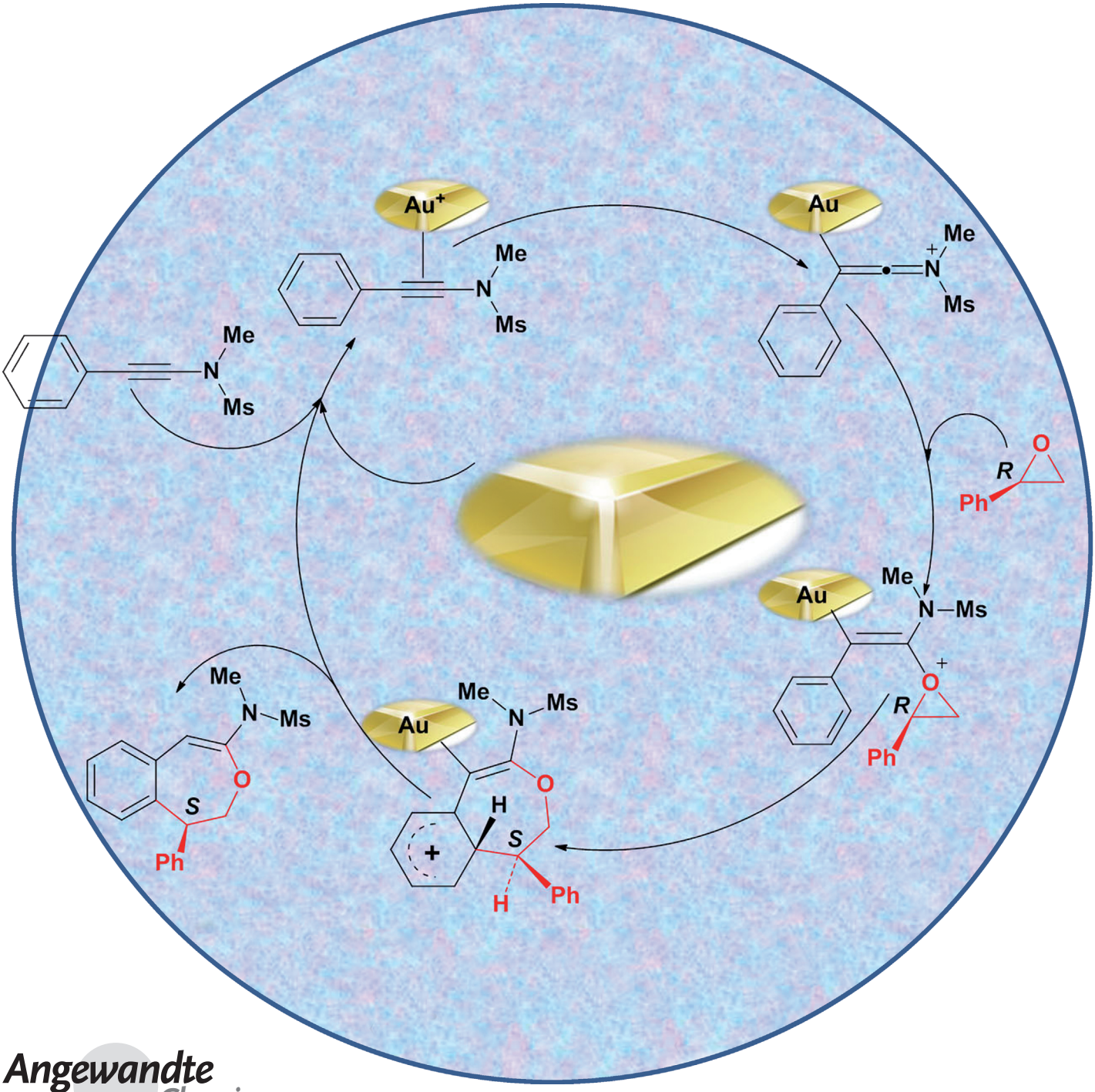
Synthetic Methods

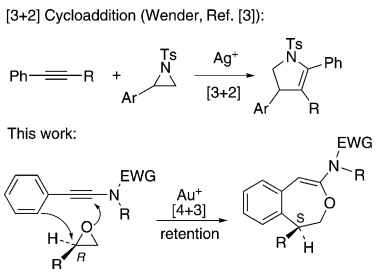
DOI: 10.1002/anie.201203723

Retention of Stereochemistry in Gold-Catalyzed Formal [4+3] Cycloaddition of Epoxides with Arenynamides**

*Somnath Narayan Karad, Sabyasachi Bhunia, and Rai-Shung Liu**



Metal-mediated intermolecular cycloadditions are powerful tools to access carbo- and heterocyclic frameworks.[1] Epoxides and aziridines serve as three-atom building units for various metal-mediated [3 + *n*] cycloadditions (*n* = 2,3) with small molecules.[2–7] The cycloadditions of epoxides and aziridines with alkenes or alkynes exclusively proceeded through [3+2] cycloadditions,[3,4] whereas [3+3] cycloadditions occurred for propargylmetal reagents.[5] Catalytic intermolecular [4+3] cycloadditions of epoxides or aziridines have only one precedent.[8] Herein, we report a new synthesis of seven-membered oxacycles through a gold-catalyzed intermolecular [4C+3] cycloaddition[9] of arenynamides with epoxides (Scheme 1). Particularly notable is the observed

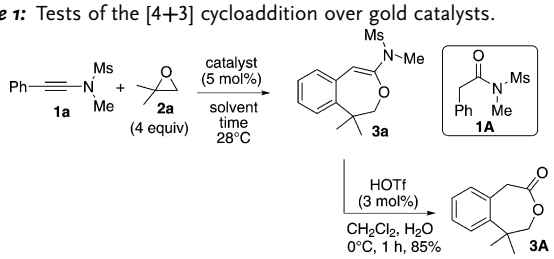


Scheme 1. Cycloadditions of phenylalkynes with epoxides or aziridines. EWG = electron-withdrawing group, Ts = 4-toluenesulfonyl.

retention of stereochemistry in the gold-catalyzed ring opening of epoxides during the attack of external arene nucleophiles (Scheme 1). This process contrasts sharply with a silver-catalyzed [3+2] cycloaddition between 1-phenylalkynes and aziridines, reported by Wender and Strand.[3]

We examined the cycloaddition reactions of arenynamide **1a** with isobutylene oxide **2a** over cationic gold complexes, which are active catalysts for the intermolecular [4+2] cycloadditions of arenynamide **1a** with electron-rich alkenes.[10] The reaction of arenynamide **1a** with epoxide **2a** (4 equiv) using [PPh_3AuCl]/$AgNTf_2$ (5 mol%) in dichloromethane (28 °C, 4 h) gave a mixture of products, from which we isolated [4+3] cycloadduct **3a** in only 4% yield (Table 1, entry 1). To our pleasure, the use of [P(*o*-biphenyl)-(*t*Bu)$_2$AuCl]/$AgNTf_2$ gave cycloadduct **3a** in a significant proportion (62%, entry 2). [IPrAuCl]/$AgNTf_2$ (IPr = 1,3-bis(diisopropylphenyl)imidazol-2-ylidene) improved the yield of desired **3a** to 87% yield (entry 3). Variation of silver salts as in [IPrAuCl]/AgX (X = SbF_6 and OTf, entries 4 and 5) led to compound **3a** in a decreased yield of 71% and 20%, respectively; weakly acidic [IPrAuOTf] appears to be less efficient in this cycloaddition. We found no reactivity for $AgNTf_2$ or $AgSbF_6$ catalysts (entries 6 and 7). HOTf gave

Table 1: Tests of the [4+3] cycloaddition over gold catalysts.



Entry	Catalyst[a]	Solvent	Time [h]	Yield [%]	
				1a	**3a**[b]
1	[PPh_3AuCl]/$AgNTf_2$	CH_2Cl_2	4.0	–	4
2	[LAuCl]/$AgNTf_2$	CH_2Cl_2	4.0	–	62
3	[IPrAuCl]/$AgNTf_2$	CH_2Cl_2	1.8	–	87
4	[IPrAuCl]/[$AgSbF_6$]	CH_2Cl_2	1.7	–	71
5	[IPrAuCl]/AgOTf	CH_2Cl_2	3.0	–	20
6	$AgNTf_2$	CH_2Cl_2	12	85	-
7	[$AgSbF_6$]	CH_2Cl_2	12	80	–
8	HOTf	CH_2Cl_2	4.0	–	–[c]
9	[IPrAuCl]/$AgNTf_2$	$(CH_2Cl)_2$	1.7	20	61
10	[IPrAuCl]/$AgNTf_2$	toluene	12	14	58
11	[IPrAuCl]/$AgNTf_2$	CH_3CN	12	85	–

[a] [**1a**] = 0.20 M. [b] Determined after purification by column chromatography on neutral alumina. [c] Ketone **1A** was isolated in 76% yield. Bn = benzyl, IPr = 1,3-bis(diisopropyl phenyl imidazol-2-ylidene, L = (*o*-biphenyl)(tBu)$_2$P, Ms = methanesulfonyl, Tf = trifluoromethanesulfonyl.

hydration product **1A** in 76% yield (entry 8). For [$IPrAuNTf_2$], the yield of compound **3a** depended on the solvents: dichloroethane (61%), toluene (58%), and acetonitrile (0%); unreacted **1a** was recovered in 14–85% (entries 9–11). Treatment of compound **3a** with HOTf (3 mol%) in wet CH_2Cl_2 (0 °C, 1 h) delivered lactone **3A** in 85% yield.

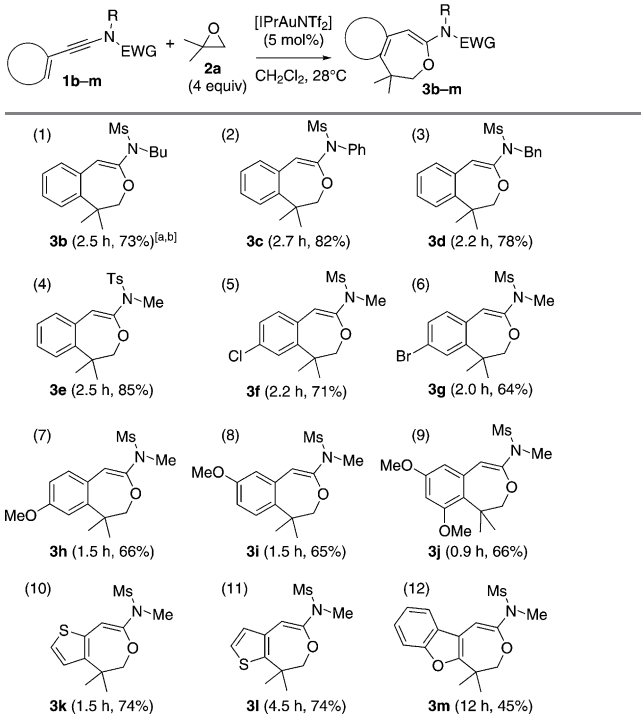
The chemoselectivity for seven-membered oxacycle **3a** is unexpected, because similar reactions typically gave the [3+2] cycloadduct.[3,4] Accordingly, we examined the scope of arenynamides with alterable amides and aryl substituents. Table 2 shows the results for the [4+3] cycloadditions of arenynamides **1b–1m** with epoxide **2a** using [IPrAuCl]/$AgNTf_2$ (5 mol%) in CH_2Cl_2 (28 °C, 0.9–12 h). We obtained only seven-membered oxacycles **3b–3m** after workup; the absence of [3+2] cycloadducts was ascertained by ^{1}H NMR spectroscopy of their crude products. These cycloadditions worked well for substrates **1b–1e**, which bear various amido substituents (EWG = tosyl and mesyl; R = methyl, *n*-butyl, benzyl, and phenyl); the resulting cycloadducts **3b–3e** were obtained in 73–85% yield (entries 1–4). We tested the reactions on arenynes **1f** and **1g**, which bear 4-chloro and 4-bromo substituents, giving desired cycloadducts **3f** and **3g** in 71% and 64% yield, respectively (entries 5 and 6). We studied the reactions on arenynamides **1h–1j**, which bear electron-rich benzenes; their resulting oxacycles **3h–3j** were obtained in 65–66% yield (entries 7–9). The scope of the reactions was further expanded to arenynamides **1k–1m**, which bear 2- and 3-thienyl and 3-benzofuranyl and produced cycloadducts **3k–3m** in 45–74% yield (entries 10–12). A protracted period (12 h) was observed for the formation of benzofuranyl derivative **3m** because of its bulky size, which is unfavorable for an S_N2-type front attack at the epoxide.

[*] S. N. Karad, Dr. S. Bhunia, Prof. Dr. R.-S. Liu
Department of Chemistry, National Tsing Hua University
Hsinchu, 30013 (Taiwan)
E-mail: rsliu@mx.nthu.edu.tw

[**] We thank the National Science Council, Taiwan, for financial support of this work.

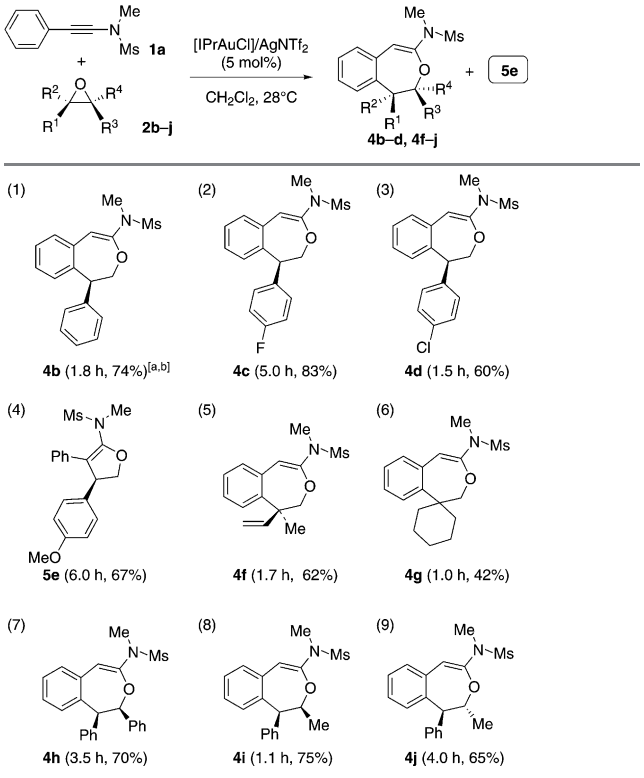
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201203723.

Table 2: [4+3] Cycloadditions on various arenynes.



[a] [arenynamides] = 0.20 M, [IPrAuCl]/$AgNTf_2$ (5 mol%), CH_2Cl_2. 28 °C. [b] Determined after purification by column chromatography on neutral alumina.

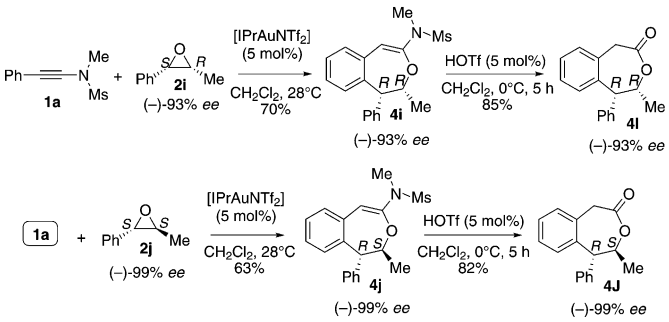
Table 3: Cycloaddition reactions on various epoxides.



[a] [arenynamides] = 0.20 M. [b] Determined after purification by column chromatography on neutral alumina.

Various epoxides **2b**–**2j** were subjected to gold-catalyzed cycloadditions on arenynamide **1a** (Table 3); except 4-methoxyphenyloxirane **2e** (entry 4), all these substrates produced [4+3] cycloadducts. With styrene oxide **2b** and its 4-fluoro- and 4-chlorophenyl derivatives **2c** and **2d**, respectively, the corresponding [4+3] cycloadducts **4b**–**4d** were produced in 60–83% yield (entries 1–3). Notably, electron-rich 4-methoxyphenyloxirane **2e** gave [3+2] cycloadduct **5e** in 67% yield, however, the reaction took longer (6 h), thus reflecting a significant electronic effect to alter reaction chemoselectivity (entry 4). This [4+3] cycloaddition is extensible to 1,1-disubstituted epoxides **2f** and **2g**, which gave desired products **4f** and **4g** in 62% and 42% yield, respectively (entries 5 and 6). We tested *cis*- or *trans*-1,2-disubstituted epoxides **2h**–**2j** to study the stereochemical course of this [4+3] cycloaddition (entries 7–9). In the reactions of *cis*-stilbene oxide **2h** ($R^1 = R^3 = Ph$, $R^2 = R^4 = H$), the resulting cycloadduct **4h** was obtained in 70% yield. X-ray diffraction study on compound **4h** showed a *cis*-configuration for its two phenyl substituents,[11] indicative of the retention of stereochemistry. For *cis*-2-methylstyrene oxide **2i** ($R^1 = Ph$, $R^3 = Me$, $R^2 = R^4 = H$) and its *trans* analogue **2j** ($R^1 = Ph$, $R^4 = Me$, $R^2 = R^3 = H$), their corresponding products **4i** and **4j** were produced stereoselectively with 75% and 65% yield, respectively (entries 8 and 9); we did not obtain the other diastereomer. The *cis* configuration of cycloadduct **4i** was likewise determined by X-ray diffraction,[11] again showing the retention of stereochemistry.

This cycloaddition is applicable to the synthesis of enantiopure oxacycle **4i** (93% *ee*) using (*2R*,*3S*)-(−)-2-methyl-3-phenyloxirane **2i** (93% *ee*, Scheme 2). X-ray diffraction of **4i** confirmed the retention of stereochemistry.[11]

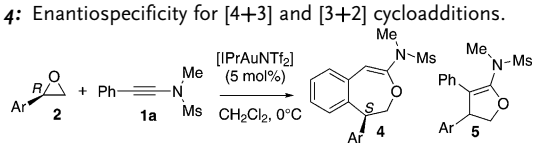


Scheme 2. Synthesis of enantiopure seven-membered lactones.

Hydrolysis of this cycloadduct afforded chiral lactone **4l** in 93% *ee*. The use of enantiopure (*2S*,*3S*)-(−)-2-methyl-3-phenyloxirane **2j** (99% *ee*) efficiently delivered the corresponding cycloadduct **4j** (99% *ee*), and subsequently lactone **4J** (99% *ee*).

We examined the enantiospecificity of the [4+3] and [3+2] cycloadditions using enantiopure aryl-substituted oxiranes (Table 4); this information may enable us to understand

Table 4: Enantiospecificity for [4+3] and [3+2] cycloadditions.

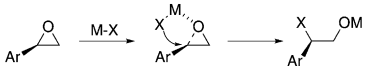


Entry	Epoxide[a] 2 (Ar)	*ee* [%]	Products 4/5 (*ee* [%])[b]	Yield [%][c]
1	**2b** (C_6H_5)	99 (+)	(+)-**4b** (81)	73
2	**2c** (4-FC_6H_4)	99 (+)	(+)-**4c** (70)	68
3	**2d** (4-ClC_6H_4)	99 (+)	(+)-**4d** (75)	55
4	**2k** (4-MeC_6H_4)	99 (−)	(−)-**4k** (39), *rac*-**5k** (0)	65 (**4k**/**5k**=1:4)
5	**2e** (4-$MeOC_6H_4$)	99 (−)	*rac*-**5e** (0)	61

[a] [**1a**] = 0.20 M, 4 h for entries 1–3, 10 h for entries 4 and 5. [b] *ee* values were determined by HPLC analysis on a chiral stationary phase (chiralpak AD-H). [c] Determined after separation by column chromatography on neutral alumina.

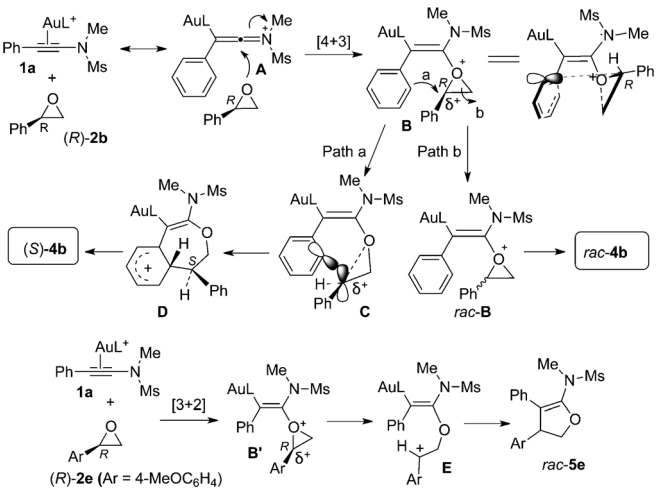
the reaction chemoselectivity. For (*R*)-styrene oxide **2b** (99% *ee*), its gold-catalyzed cycloaddition with arenyne **1a** afforded [4+3] cycloadduct **4b** with (+)-81% *ee* (entry 1). Its absolute configuration was determined to be *S* by X-ray diffraction,[11] again indicating a retention of stereochemistry. For (*R*)-4-fluoro- and (*R*)-4-chlorophenyl oxirane **2c** and **2d** (99% *ee*), their corresponding [4+3] cycloadducts (*S*)-**4c** and (*S*)-**4d** was obtained with 70% and 75% *ee*, respectively (entries 2 and 3). (*R*)-4-Methylphenyl oxirane **2k** (99% *ee*) gave an inseparable mixture of two the cycloadducts **4k**/**5k** = 1:4 (entry 4); seven-membered oxacycle **4k** was obtained with 39% *ee*, whereas five-membered species **5k** was completely racemic. For (*R*)-4-methoxyphenyl oxirane **2e**, we obtained only the racemic form of [3+2] cycloadduct **5e** in 61% yield. Our results show that formation of seven-membered oxacycle **4** occurs at the early stage of oxirane cleavage to achieve an S_N2-type retention, whereas five-membered oxacycles **5** are produced on a free benzylic cation after a complete oxirane cleavage.

S_N2-type retention of stereochemistry was documented for few stoichiometric reactions between epoxides and AlX_3 (X = Cl, Me),[12] in which a coordinated ligand X attacks at the reacting carbon center from the front side (Scheme 3).



Scheme 3. Metal-assisted ligand migration in S_N2-type retention.

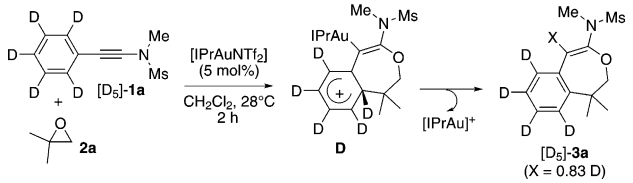
This 1,4 ligand migration is in disagreement with the mechanism of the retention chemistry in our system. Scheme 4 shows a plausible mechanism for the [4+3] cycloaddition, Au-π-ynamide **1a** is highly electrophilic, and also represented by its ketenimine resonance structure **A**.[13,14] An attack of (*R*)-epoxide **2b** at the C=NMeMs carbon center of species **A** gives an oxonium species **B**, which still retains an oxiranyl ring. Attack of the neighboring benzene at the epoxide in an S_N2-type inversion is unlikely because of its front orientation. Instead, we envisage that species **B** has a ground-state conformation that involves a parallel orientation between the benzene and oxiranyl rings. This conformation facilitates a front attack of benzene at the reacting oxiranyl carbon atom because of their proximity. Formation of the C–C bond and C–O bond cleavage might be concerted, as shown in structure **C** (path a), subsequently forming a cyclohexadienyl cation **D**, which bears an *S*-configuration. This pathway is expected to give oxacyclic product (*S*)-**4b**. We envisage that the oxiranyl PhC–O bond of species **B** is rather weak to allow a C–C bond rotation. Accordingly, a small portion of intermediate **B** undergoes an epimerization of oxirane to form *rac*-**B**; this process rationalizes a small loss of chirality for resulting cycloadduct **4b**. The high stereospecificity for 1,2-disubstituted epoxides **2i** and **2j** is attributed to their rigid conformation **B**, which has a barrier to rotate the C–O bond between the oxiranyl and alkenylgold moieties.



Scheme 4. Plausible mechanisms for [4+3] and [3+2] cycloadditions.

This postulated model also rationalizes the non-stereospecific [3+2] cycloaddition of (*R*)-4-methoxyphenyloxirane **2e** and arenynamide **1a** (Table 4, entry 5). In this instance, the corresponding benzylic cation **E** is readily attained because of the stabilization effect of 4-methoxyphenyl. This benzylic cation moves freely toward gold alkenyl to deliver a [3+2] oxacycle **5e** with a complete loss of chirality.

We prepared [D_5]-**1a** to confirm the intermediacy of species **D** (Scheme 5); its resulting cycloadduct [D_5]-**3a** has a high deuterium content (X = 0.83 D) at its alkenyl position.



Scheme 5. Deuterium labeling experiment.

This result indicates the occurrence of a deauration process at this alkenyl carbon atom.

Thus far, epoxides participated almost exclusively in metal-catalyzed [3+2][3,4] or [3+3] cycloaddition[5] reactions. We have now developed a gold-catalyzed [4+3] cycloaddition of epoxides with arenynamides with a broad substrate scope.

Of particular interest is the retention of stereochemistry[15,16] for an intermolecular aryl attack at the epoxide. We used various enantiopure aryl-substituted oxiranes to study the chirality transfer in the [4+3] and [3+2] cycloadditions; their mechanisms are thus elucidated. We postulate an S_N2-type front-side attack of phenyl at the oxiranyl ring for [4+3] cycloadducts, whereas an attack at a free benzylic cation leads to [3+2] products that contain benzoxepine frameworks (represented by cycloadducts **3**), which can be found in several naturally occurring compounds;[17] their enantioselective synthesis is under current investigations.

Received: May 14, 2012
Revised: June 26, 2012
Published online: July 23, 2012

Keywords: [4+3] cycloaddition · arenynamide · epoxide · gold catalysis · retention

[1] For metal-catalyzed cycloaddition reactions, see selected reviews: a) P. A. Wender, V. A. Verma, T. H. Paxton, *Acc. Chem. Res.* **2008**, *41*, 40 – 49; b) M. Lautens, W. Klute, W. Tam, *Chem. Rev.* **1996**, *96*, 49 – 92; c) P. A. Inglesby, P. A. Evans, *Chem. Soc. Rev.* **2010**, *39*, 2791 – 2805; d) S. M. A. Sohel, R.-S. Liu, *Chem. Soc. Rev.* **2009**, *38*, 2269 – 2281.

[2] For selected reviews for epoxides and aziridines, see: a) A. K. Yudin in *Aziridines and Epoxides in Organic Synthesis*, Wiley-VCH, Weinheim, **2006**; b) K. V. Gothelf, K. A. Jørgensen, *Chem. Rev.* **1998**, *98*, 863 – 910; c) W. Carruthers in *Cycloaddition in Organic Synthesis*, Pergamon, Oxford, **1990**, p. 1.

[3] P. A. Wender, D. Strand, *J. Am. Chem. Soc.* **2009**, *131*, 7528 – 7529.

[4] a) I. Ungureanu, P. Klotz, A. Mann, *Angew. Chem.* **2000**, *112*, 4790 – 4792; *Angew. Chem. Int. Ed.* **2000**, *39*, 4615 – 4617; b) J. Sisko, S. M. Weinreb, *J. Org. Chem.* **1991**, *56*, 3210 – 3211; c) R. J. Madhushaw, C.-C. Hu, R.-S. Liu, *Org. Lett.* **2002**, *4*, 4151 – 4153; d) S. C. Bergmeier, S. L. Fundy, P. P. Seth, *Tetrahedron* **1999**, *55*, 8025 – 8038; e) Y. Sugita, Y. Kimura, I. Yokoe, *Tetrahedron Lett.* **1999**, *40*, 5877 – 5880; f) M. Nakagawa, M. Kawahara, *Org. Lett.* **2000**, *2*, 953 – 955; g) J.-G. Shim, Y. Yamamoto, *J. Org. Chem.* **1998**, *63*, 3067 – 3071; h) J. S. Yadav, B. V. S. Reddy, S. K. Pandey, P. P. Srihari, I. Prathap, *Tetrahedron Lett.* **2001**, *42*, 9089 – 9092; i) J. Fan, L. Gao, Z. Wang, *Chem. Commun.* **2009**, 5021 – 5023.

[5] a) R. J. Madhushaw, C.-L. Li, J.-C. Hu, R.-S. Liu, *J. Am. Chem. Soc.* **2001**, *123*, 7427 – 7428; b) K.-H. Shen, S.-F. Lush, T.-L. Chen, R.-S. Liu, *J. Org. Chem.* **2001**, *66*, 8106 – 8111; c) S. Hedley, W. J. Moran, D. A. Price, J. P. A. Harrity, *J. Org. Chem.* **2003**, *68*, 4286 – 4292.

[6] a) K. Yamaguchi, K. Ebitani, T. Yoshida, H. Yoshida, K. Kaneda, *J. Am. Chem. Soc.* **1999**, *121*, 4526 – 4527; b) C. M. Miralda, E. E. Macias, M. Zhu, P. Ratnasamy, M. A. Carreon, *ACS Catal.* **2012**, *2*, 180 – 183.

[7] a) B. M. Trost, A. R. Sudhakar, *J. Am. Chem. Soc.* **1987**, *109*, 3792 – 3794; b) B. M. Trost, A. R. Sudhakar, *J. Am. Chem. Soc.* **1988**, *110*, 7933 – 7935; c) C. Larksarp, H. Alper, *J. Am. Chem. Soc.* **1997**, *119*, 3709 – 3715; d) G. Bez, C.-G. Zhao, *Org. Lett.* **2003**, *5*, 4991 – 4993.

[8] A BF_3-mediated [4+3] cycloaddition was recently reported for epoxides and aromatic unsaturated ketones, but no stereochemistry was involved. See: Y.-Q. Zhou, N.-X. Wang, S.-B. Zhou, Z. Huang, L. Cao, *J. Org. Chem.* **2011**, *76*, 669 – 672.

[9] For gold-catalyzed [4+3] cycloadditions, reported examples were performed exclusively in an intramolecular fashions. See a) F. López, J. L. Mascareñas, *Beilstein*, *Beilstein J. Org. Chem.* **2011**, *7*, 1075 – 1094; b) M. Gulías, F. López, J. L. Mascareñas, *Pure Appl. Chem.* **2011**, *83*, 495 – 506; c) P. Mauleón, R. M. Zeldin, A. Z. González, F. D. Toste, *J. Am. Chem. Soc.* **2009**, *131*, 6348 – 6349; d) B. Trillo, F. López, S. Montserrat, G. Ujaque, L. Castedo, A. Lledós, J. L. Mascareñas, *Chem. Eur. J.* **2009**, *15*, 3336 – 3339; e) I. Alonso, H. Faustino, F. López, J. L. Mascareñas, *Angew. Chem.* **2011**, *123*, 11698 – 11702; *Angew. Chem. Int. Ed.* **2011**, *50*, 11496 – 11500; f) I. Alonso, B. Trillo, F. López, S. Montserrat, G. Ujaque, L. Castedo, A. Lledós, J. L. Mascareñas, *J. Am. Chem. Soc.* **2009**, *131*, 13020 – 13030.

[10] R. B. Dateer, B. S. Shaibu, R.-S. Liu, *Angew. Chem.* **2012**, *124*, 117 – 121; *Angew. Chem. Int. Ed.* **2012**, *51*, 113 – 117.

[11] X-ray crystallographic data of [4+3] cycloadducts **4h**, **4i**, and (*S*)-**4b** are provided in the Supporting Information.

[12] a) J. H. Brewster, *J. Am. Chem. Soc.* **1956**, *78*, 4061 – 4064; b) M. Inoue, T. Sugita, Y. Kiso, K. Ichikawa, *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1063 – 1071; c) T. Nakajima, S. Suga, T. Sugita, K. Ichikawa, *Tetrahedron* **1969**, *25*, 1807 – 1916.

[13] For chemistry of ynamides, see: a) K. A. DeKorver, H. Li, A. G. Lohse, R. Hayashi, Z. Lu, Y. Zhang, R. P. Hsung, *Chem. Rev.* **2010**, *110*, 5064 – 5106; b) G. Evano, A. Coste, K. Jouvin, *Angew. Chem.* **2010**, *122*, 2902 – 2921; *Angew. Chem. Int. Ed.* **2010**, *49*, 2840 – 2859; c) A. S. K. Hashmi, M. Rudolph, J. Huck, W. Frey, J. W. Bats, M. Hamzić, *Angew. Chem.* **2009**, *121*, 5962 – 5966; *Angew. Chem. Int. Ed.* **2009**, *48*, 5848 – 5852.

[14] For gold-catalyzed electrophilic activation of ynamides, see reference [13] and selected examples: a) C.-W. Li, K. Pati, G.-Y. Lin, S. M. A. Sohel, H.-H. Hung, R.-S. Liu, *Angew. Chem.* **2010**, *122*, 10087 – 10090; *Angew. Chem. Int. Ed.* **2010**, *49*, 9891 – 9894; b) P. W. Davies, A. Cremonesi, N. Martin, *Chem. Commun.* **2011**, *47*, 379 – 381; c) C. Li, L. Zhang, *Org. Lett.* **2011**, *13*, 1738 – 1741; d) D. Vasu, H. H. Hung, S. Bhunia, S. A. Gawade, A. Das, R.-S. Liu, *Angew. Chem.* **2011**, *123*, 7043 – 7046; *Angew. Chem. Int. Ed.* **2011**, *50*, 6911 – 6914; e) S. Kramer, Y. Odabachian, J. Overgaard, M. Rottländer, F. Gagosz, T. Skrydstrup, *Angew. Chem.* **2011**, *123*, 5196 – 5200; *Angew. Chem. Int. Ed.* **2011**, *50*, 5090 – 5094; f) A. S. K. Hashmi, M. Bührle, M. Wölfle, M. Rudolph, M. Wieteck, F. Rominger, W. Frey, *Chem. Eur. J.* **2010**, *16*, 9846 – 9854; g) P. W. Davies, A. Cremonesi, L. Dumitrescu, *Angew. Chem.* **2011**, *123*, 9093 – 9097; *Angew. Chem. Int. Ed.* **2011**, *50*, 8931 – 8935; h) P. Garcia, Y. Harrak, L. Diab, P. Cordier, C. Ollivier, V. Gandon, M. Malacria, L. Fensterbank, C. Aubert, *Org. Lett.* **2011**, *13*, 2952.

[15] Complete retention of stereochemistry has been reported for the reactions of epoxides or aziridines with CO[16] and CO_2[6a] using low-valent metals; their mechanisms are distinct from those reactions that use Lewis acid to implement nucleophilic attack at epoxides.

[16] a) J.-T. Lee, P. J. Thomas, H. Alper, *J. Org. Chem.* **2001**, *66*, 5424 – 5426; b) S. Calet, F. Urso, H. Alper, *J. Am. Chem. Soc.* **1989**, *111*, 931 – 934.

[17] a) J.-H. Liu, A. Steigel, E. Reininger, R. Bauer, *J. Nat. Prod.* **2000**, *63*, 403 – 405; b) F. Meriçli, A. H. Mericli, H. Becker, A. Ulubelen, *Phytochemistry* **1996**, *42*, 1257 – 1258; c) A. Ulubelen, E. Tuzlaci, N. Atilan, *Phytochemistry* **1989**, *28*, 649 – 650.

