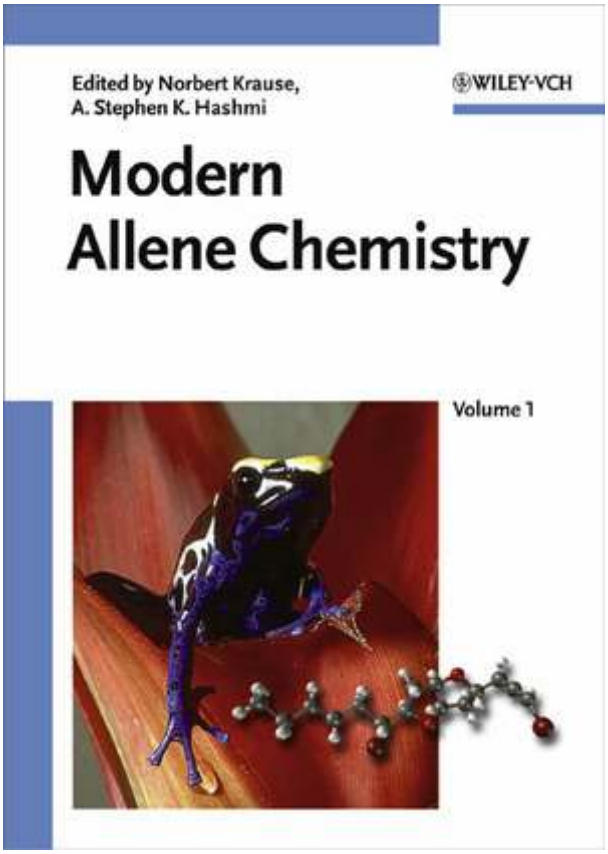
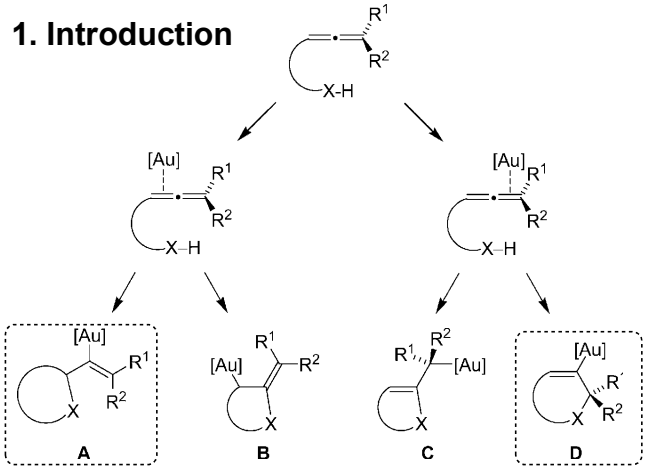
Gold-Catalyzed Nucleophilic Cyclization of Allenes



Norbert Krause graduated from Technical University of Braunschweig in 1984 and received his Ph.D. in 1986. After postdoctoral stays at ETH Zürich and Yale University, he joined Technical University of Darmstadt and obtained his Habilitation in 1993. In 1994, he moved to the University of Bonn as Associate Professor, before being appointed to his present position at Dortmund University of Technology as Full Professor in 1998. He was a Fellow of the Japan Society for the Promotion of Science (2003 and 2009), and Guest Professor at the Universit e Catholique de Louvain, Belgium (2007), at the University of California, Santa Barbara, CA, USA (2009), and at the Ecole Supérieure de Physique et de Chimie Industrielles de la Ville de Paris (ESPCI), France (2009). Since 2006, he is a member of the Editorial Board of the European Journal of Organic Chemistry. His review on "Recent Advances in Catalytic Enantioselective Michael Additions" was the World's Most Cited Chemistry Paper in Nov. 2002. His research focuses on the stereoselective synthesis and transformation of functionalized allenes, taking advantage of coinage metal (copper, silver, and gold) catalysis. In his free time, he enjoys snorkeling and riding his motorbike.

Review: *Chem. Rev*. **2011**, *ASAP*

1. Introduction



Gold-Catalyzed Nucleophilic Cyclization Reactions of Functionalized Allenes

F. Dean Toste

Review: *Chem. Rev*. **2008**, *108*, 3351

Ross A. Widenhoefer

Review: *Eur. J. Org. Chem*. **2006**, 4555.

Au --- [Xe] $4f^{14}5d^{10}6s^{1}$
Au^{I} --- [Xe] $4f^{14}5d^{10}6s^{0}$
Au^{III}--- [Xe] $4f^{14}5d^{8}6s^{0}$

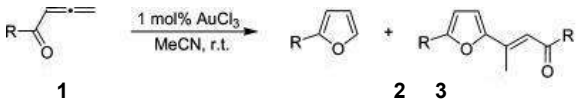
2. Nucleophilic Attack of Heteroatom Nucleophiles

2.1. Oxygen Nucleophiles

2.1.1. Isomerization of Allenyl Ketones : **synthesis of multisubstituted furans**

The first gold-catalyzed addition of a heteroatom nucleophile

Hashmi, A. S. K. *et al. Angew. Chem., Int. Ed.* **2000**, *39*, 2285.



1	2	3
b: R = CH_2-4-(MeO)C_6H_4	60	31
c: R = CH_2-4-(TBDMSO)C_6H_4	35	5
d: R = CH_2CH_2-4-(TBDMSO)C_6H_4	38	6
e: R = 3-(MeO)C_6H_4	34	38
f: R = 4-(O_2N)C_6H_4	88	4
g: R = 2-(O_2N)C_6H_4	72	8
h: R = 3,4-(OCH_2O)C_6H_3	29	24
i: R = 4-(MeS)C_6H_4	48	51
k: R = CH_3	47 [c]	47
m: R = 2,5-$(MeO)_2C_6H_3$	45	36

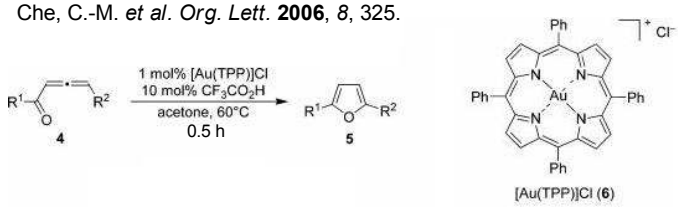
In contrast to other transition metals :

- ♦shorter reaction times — >1 week (silver)
- ♦milder conditions — 1 h (palladium)
- ♦(lower catalyst loadings) — 1 min (gold)

The formation of the undesired dimerization product **3** (which is also generated in the corresponding silver-catalyzed cyclization) is a serious drawback.

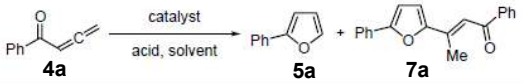
Gold(III) porphyrin-catalyzed cycloisomerization

Che, C.-M. *et al. Org. Lett.* **2006**, *8*, 325.



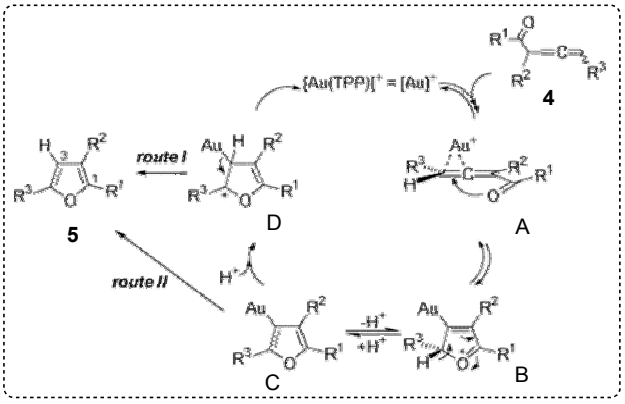
entry	substrate	product	% yield[b]
1		2a, R = H	88
2		2b, R = *p*-Me	84
3		2c, R = *p*-OMe	81
4	1a-i	2d, R = *p*-Br	85
5		2e, R = *m*-Br	87
6		2f, R = *o*-Br	98
7		2g, R = *p*-Cl	86
8[c]		2h, R = *p*-CO_2Me	92
9[c]		2i, R = *p*-NO_2	91
10		2j, R = H	80
11	1j-l	2k, R = Br	85
12[c]		2l, R = CO_2Me	88
13	1m	2m	84
14[c]	1n	2n	73
15		2o, X = O	82
16	1o-p	2p, X = S	78
17		2q, R = Me	89[d]
18	1q-r	2r, R = ^{t}Bu	92
19	1s	2s	90
20	1t	2t	97
21		2u, R = H	95
22[c]	1u-v	2v, R = ^{t}Bu	93
23[c]	1w	2w	90

Table S1. Optimization of Reaction Conditions[a]



entry	acid	catalyst	solvent	time (h)	yield (%)[b, c]
1	TFA	[Au(TPP)]Cl[d]	acetone	0.5	88[e]
2	TFA	[Au(F_{20}-TPP)]Cl[f]	acetone	0.25	78
3	TFA	[Au(TPP)]Cl	EtOH	0.5	87
4	TFA	[Au(TPP)]Cl	1,2-dichloroethane	1	79
5	TFA	[Au(TPP)]Cl	DMF	0.5	78
6	TFA	[Au(TPP)]Cl	DMSO	0.5	81
7	TFA	[Au(TPP)]Cl	CH_3CN	1	82
8	TFA	[Au(TPP)]Cl	C_6H_6	2	28
9	TFA	[Au(TPP)]Cl	EtOAc	2	17
10[g]	TFA	[Au(TPP)]Cl	acetone	2	28[h]
11	TsOH	[Au(TPP)]Cl	acetone	0.5	87
12	CH_3CO_2H	[Au(TPP)]Cl	acetone	1	29
13	-	[Au(TPP)]Cl	acetone	2	-[i]
14	-	[Au(TPP)]OTf	acetone	2	-[i]
15	TFA	$AuCl_3$	acetone	0.5	49[j]
16	TFA	$AuPPh_3Cl$	acetone	0.5	48[k]
17	TFA	[Au(salen)]Cl[l]	acetone	0.5	38[m]
18[n]	TFA	$AgNO_3$	acetone	0.5	10[o]

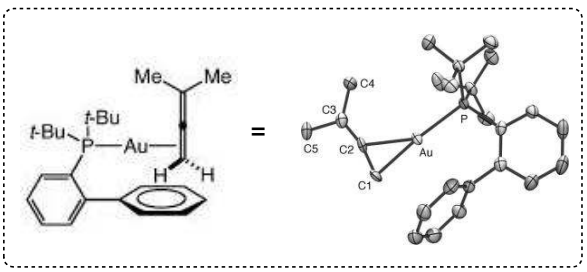
[a]Reactions were performed with 1 mol% catalyst at 60°C. [b]^{1}H NMR yield. [c]All substrate conversions were quantitative based on ^{1}H NMR analysis. [d]H_2(TPP) = *meso*-tetraphenylporphyrin. [e]Isolated yield. [f]H_2(F_{20}-TPP) = *meso*-tetrakis(pentafluorophenyl)porphyrin. [g]Reaction conducted at room temperature. [h]31% substrate conversion as determined by ^{1}H NMR analysis. [i]No reaction. [j]The dimer **7a** was also isolated in 16% yield. [k]58% substrate conversion based on ^{1}H NMR analysis. [l]H_2(salen) = *N,N*'-bis(salicylidene)ethylenediamine. [m]47% substrate conversion based on ^{1}H NMR analysis. [n]Conducted with 2 mol% $AgNO_3$ catalyst. [o]21% substrate conversion based on ^{1}H NMR analysis. The dimer **7a** was also isolated in 2% yield.



- ♦The Au(III) catalyst **6** is highly reactive and can be recovered and reused in up to nine consecutive runs with no appreciable loss of reactivity or decrease of yield.
- ♦The employment of CF_3CO_2H and a temperature of 60°C for the cycloisomerization reaction is essential.
- ♦a rapid irreversible demetalation step resulting from unfavorable steric interactions between the porphyrin ring and the newly formed furyl moiety.
- ♦The active gold species is coordinated to the "distal" double bond of the allene

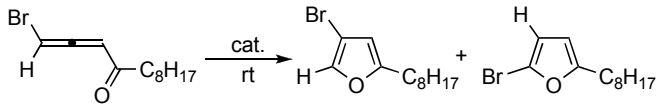
Gold π-allene complex

Widenhoefer, R. A. *et al.Organometallics* **2010**, *29*, 4207.



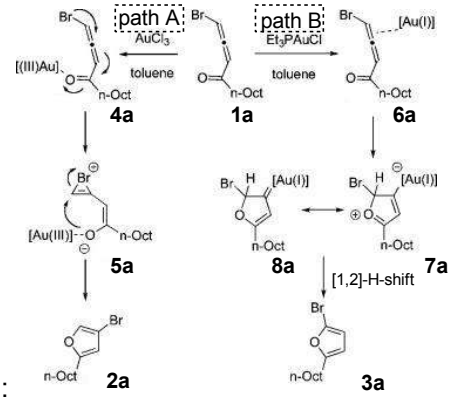
Cyclization of haloallenyl ketone

Gevorgyan, V. *et al. J. Am. Chem. Soc.* **2005**, *127*, 10500.
J. Am. Chem. Soc. **2008**, *130*, 6940.



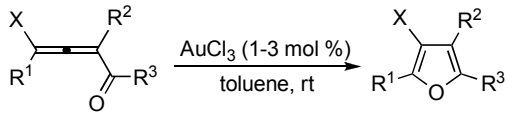
1a **2a** **3a**

entry	cat.(mol %)	solvent	time	GC yield, %(**2a**:**3a**)
1	CuCl (10)	toluene	1 day	29 (**2a** only)
2	$AuCl_3$ (1)	toluene	5 min	86 (95:5)
3	$AuCl_3$ (1)	THF	5 min	78 (5:95)
4	$Au(PPh_3)Cl$ (1)	toluene	9 h	ND (16:85)
5	$Au(PEt_3)Cl$ (1)	toluene	9 h	ND (<1:99)

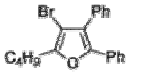
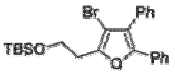
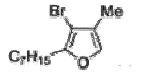
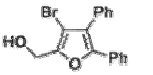
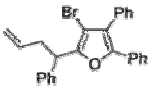
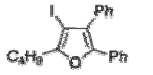
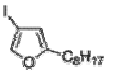
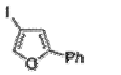
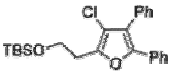


path A :
- ♦more oxophilic Au(III) chloride: coordinates to oxygen.
- ♦intramolecular Michael addition of Br to the enone moiety lead to bromoirenium ion **5a**.

path B :
- ♦more π–philic Au(I) species: coordinates to the distal double bond of allene.



1 **2**

#	R^1	R^2	R^3	X	Time	Product	Yield, %[a]
1	C_4H_9	Ph	Ph	Br	1 day		75%
2	$(CH_2)_2OTBS$	Ph	Ph	Br	1 day		73%
3	C_7H_{15}	Me	H	Br	1 hr		73%
4	CH_2OH	Ph	Ph	Br	1 day		61%
5		Ph	Ph	Br	0.5 hr		88%
6	C_4H_9	Ph	Ph	I	3 days		73%
7	H	H	C_8H_{17}	I	5 min		97%
8[b]	H	H	Ph	I	1 hr		71%
9	$(CH_2)_2OTBS$	Ph	Ph	Cl	3 days		48%

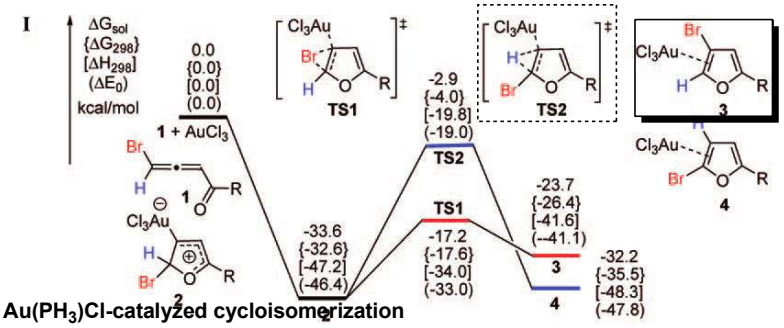
- ♦Chlorinated and iodinated allenes show a similar behavior and can be converted to the corresponding halogenated furans.
- ♦Moreover,silyl-, thio-, or selenofurans can be obtained from the corresponding allenes by a 1,2-Si, 1,2-S, or 1,2-Se shift.

Potential energy surfaces for $AuCl_3$- and $Au(PR'_3)Cl$-catalyzed cycloisomerizations

Li, Y. *et al. J. Am. Chem. Soc.* **2008**, *130*, 6940.

- ♦computational studies confirmed possible formation of the originally proposed Au(III)-coordination complex **4a**; however, neither cyclization transition state nor halirenium intermediate **5a** were located.

$AuCl_3$ -catalyzed cycloisomerization

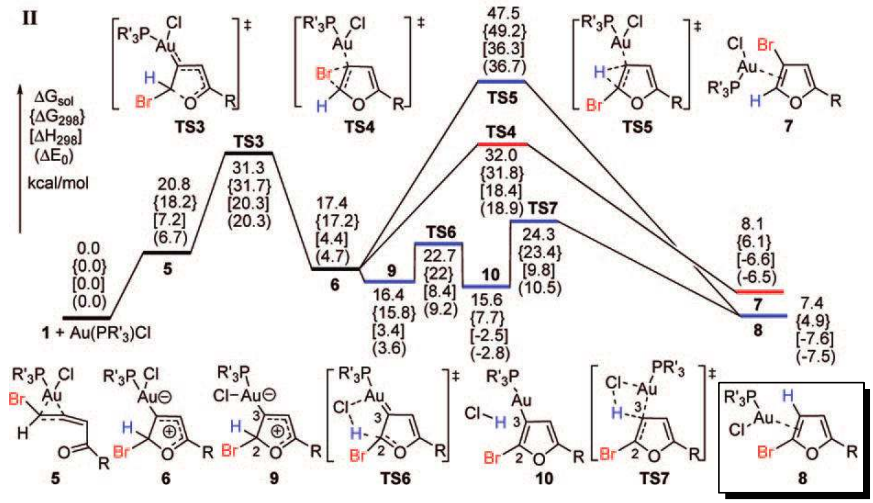


1,2-H shift : **2**→**TS2**→**4**

14.3 kcal/mol

1,2-Br migration : **2**→**TS1**→**3**

$Au(PH_3)Cl$-catalyzed cycloisomerization

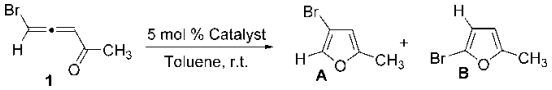


1,2-H shift : **6**→**TS5**→**8**

15.5 kcal/mol

1,2-Br migration : **6**→**TS4**→**7**

chloride-assisted H-migration: **9**→**8**
(only 8.7 kcal/mol)



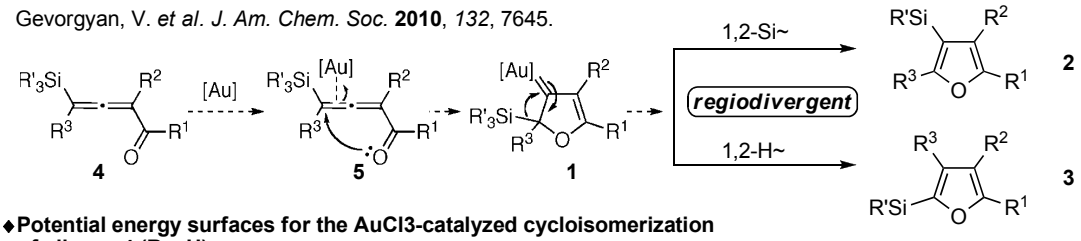
entry	Catalyst	A : B
1	$Au(PPh_3)BF_4$	>98 : 2
2	$Au(PPh_3)SbF_6$	100 : 0
3	$Au(PPh_3)OTf$	0 : 100
4	AuCl	80 : 20

- ♦**1,2-H shift in $Au(PR3)^+$-catalyzed reactions can be assisted by the counterions**
- ♦**OTf^--assisted 1,2-H shift :9.6 kcal/mol**
  BF_4^-: 20.2 kcal/mol
  SbF_6^-: 29 kcal/mol

(R = CH_3, R' = H).

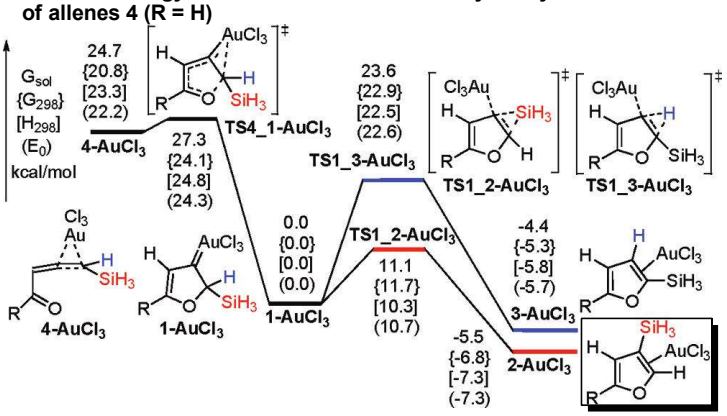
Au(III)-catalyzed 1,2-Si migration in allenes

Gevorgyan, V. *et al. J. Am. Chem. Soc.* **2010**, *132*, 7645.

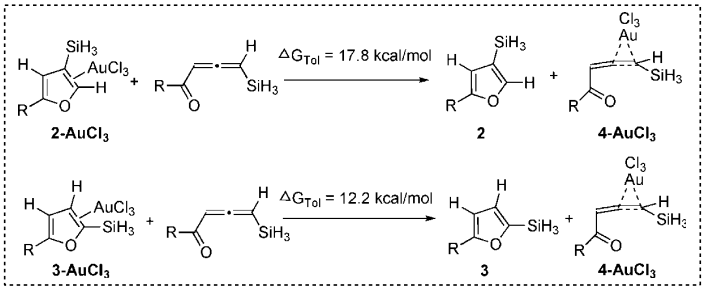


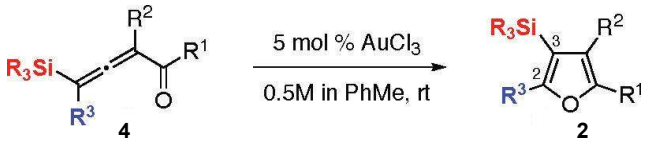
4 **5** **1** **2** **3**

♦**Potential energy surfaces for the AuCl3-catalyzed cycloisomerization of allenes 4 (R = H)**

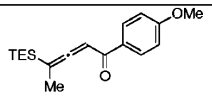
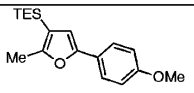
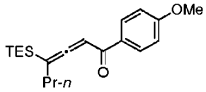
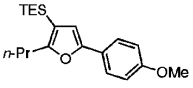
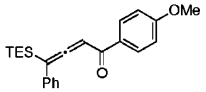
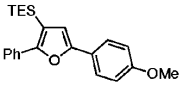
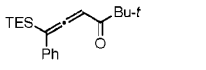
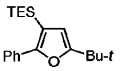
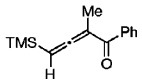
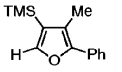


♦kinetically more favorable 1,2-Si migration over the 1,2-H shift led to the product complex **2-AuCl$_3$**.





4 **2**

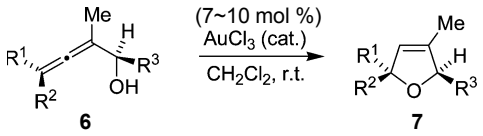
Entry	Substrate	Product	**2**, %[a]
1			**2a**, 90
2			**2b**, 80
3			**2c**, 82
4			**2d**, 87
5			**2e**, 82 (73)[b] [77][c]

[a] Isolated yield of product for reactions performed on 0.5 mmol scale.
[b] Isolated yield of **2e** for reaction performed in $MeNO_2$.
[c] Isolated yield of **2e** for reaction performed with 1 mol % of catalyst.

2.1.2. Isomerization of hydroxyallenes : **formation of chiral heterocycles**

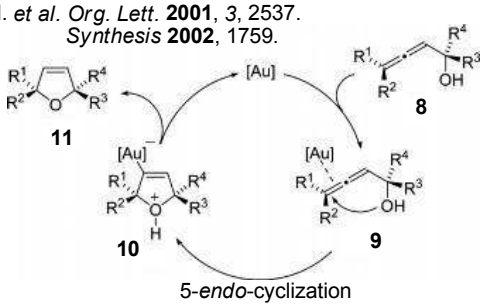
alkyl-substituted α-hydroxyallenes

Krause, N. *et al. Org. Lett.* **2001**, *3*, 2537.
Synthesis **2002**, 1759.



6 **7**

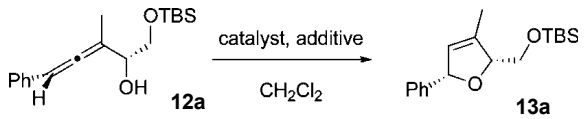
R^1	R^2	R^3	Yield (%)
t-Bu	Me	CO_2Et	94
t-Bu	H	CH_2OTBS	95
H	Me	CH_2OTBS	77
H_2C=$CHCH_2$	Me	CH_2OMe	86



♦the cyclization is accelerated in the presence of external proton donors(water, methanol)
♦this suggests that the protodeauration of **10** is the rate-limiting step.

hydroxyallenes substrates with phenyl or electron-rich aromatic substituents

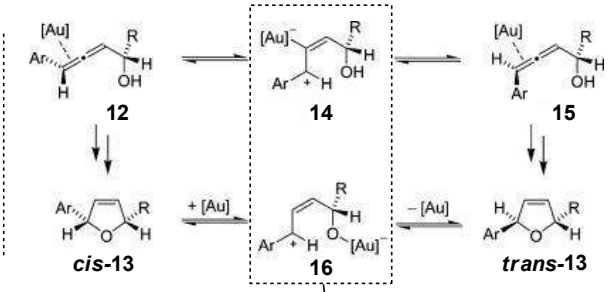
Krause, N. *et al*. *Synlett* **2007**, 1790.



12a **13a**

entry	cat.(mol %)	additive (%)	temp.	time (h)	% yield(*cis:trans*)
1	$AuCl_3$ (2)	-	rt	1	81 (75:25)
2	AuCl (2)	-	rt	1	85 (60:40)
3	$AuCl_3$ (2.5)	2,2-bipyridine (5)	rt	1	70 (>97:3)
4	AuCl (2.5)	2,2-bipyridine (3.8)	rt	10	96 (95:5)
5	$AuCl_3$ (1)	-	-30°C	2	92 (97:3)

Proposed mechanism



♠ epimerization during the gold-catalyzed cyclization of phenyl-substituted α-hydroxyallene **12** to dihydrofuran **13.**

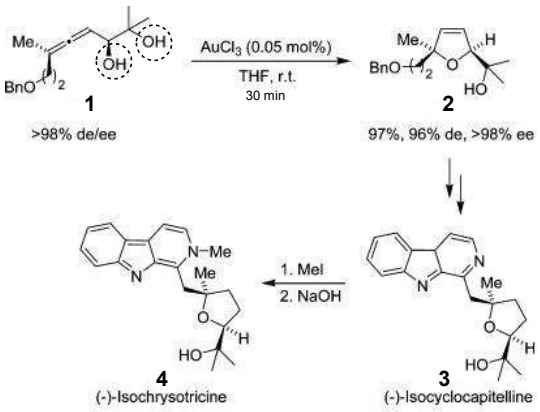
♦ $AuCl_3$ /CH_2Cl_2 epimerizes both the allene and the dihydrofuran.
♦ AuCl/CH_2Cl_2 epimerizes only the allene , but not the dihydrofuran.

zwitterionic intermediates (a planar benzyl cation substructure)

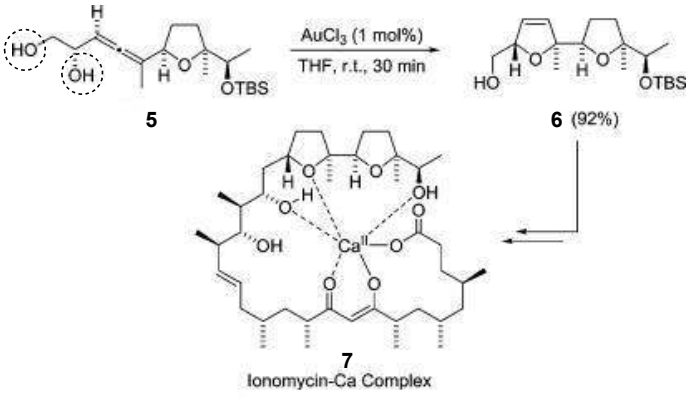
♠epimerization prevented if
♦the Lewis acidity of the gold catalyst is reduced so that the formation of zwitterionic intermediates **14/16** is disfavored;
♦weakly coordinating solvents decreased the reactivity of the gold catalyst only slightly and led to an improved diastereoselectivity;
♦original AuCl3/CH2Cl2 system at -30°C instead of room temperature.

cycloisomerization of α,β-dihydroxyallenes

Krause, N. *et al. Org. Biomol. Chem.* **2007**, *5*, 1519.
Tetrahedron **2009**, *65*, 1902.



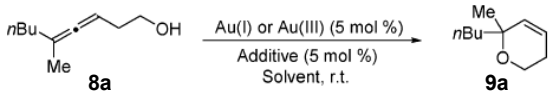
Kocienski, P. J. *et al. Angew. Chem., Int. Ed.* **2009**, *48*, 5022.



♦The gold-catalyzed cycloisomerization of α,β-dihydroxyallenes is not only **stereoselective** but also highly **chemoselective**.
(because no product resulting from nucleophilic attack of the β-hydroxy group was observed.)
♦Cycloisomerization of β-hydroxyallenes are often very slow, resulting in reaction times of several days.

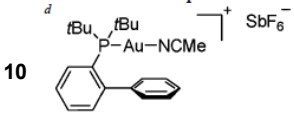
cycloisomerization of β-hydroxyallenes (6-*endo* cyclization)

Krause, N. *et al. Org. Lett.* **2006**, *8*, 4485.

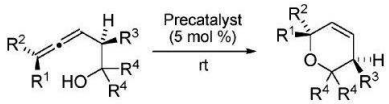


entry	Au salt	additive	solvent	time	yield (%)
1	$AuCl_3$[a]		toluene	6 d	58
2	$AuCl_3$[a]	3-hydroxy-propionitrile	toluene	1 d	62
3	AuCl		CH_2Cl_2	5 d	50
4	AuCl	$AgBF_4$	CH_2Cl_2	3 d	60
5	AuCl	$AgBF_4$	toluene	3 d	62
6	AuCl	pyridine	CH_2Cl_2	4.5 h	64
7	AuCl	2,2′-bipyridine	CH_2Cl_2	5 d	86
8		$AgBF_4$	toluene	5 d	–
9	$Au(OAc)_3$		toluene	14 d	–
10	Ph_3PAuCl		toluene	14 d	–
11	Ph_3PAuCl	$AgSbF_6$	toluene	25 min	54
12	Ph_3PAuCl	$AgBF_4$	toluene	1 h	60
13	Ph_3PAuCl	$AgBF_4$	CH_2Cl_2	1.5 h	60
14	Ph_3PAuCl	$AgBF_4$	THF	3 d	46
15	Ph_3PAuCl	$AgBF_4$	Et_2O	4 d	56
16	Ph_3PAuCl	$AgBF_4$	MeCN	27 d	62
17	Ph_3PAuCl	$AgBF_4$	toluene[b]	1.25 h	66
18	Ph_3PAuCl[c]	$AgBF_4$[c]	toluene	6.5 h	61
19	Au(I) complex **10**[c,d]		toluene	1.5 h	66

[a] 0.195 M solution in MeCN. [b] Temperature: 0 °C. [c] 1 mol %.



♦No trace of the 5-*exo* isomer could be detected
♦Addition of pyridine or 2,2-bipyridine induced a remarkable increase of the reactivity.
♦The yield was hardly affected by the solvent and the presence of silver salts. (leads to the formation of cationic gold species.)

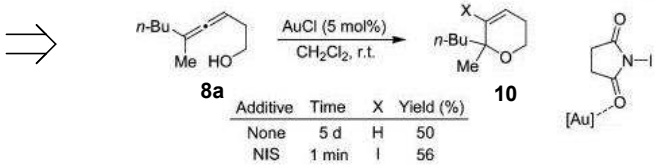


entry		R^1	R^2	R^3	R^4	conditions[a]	yield, %
1	**8a**	*t*Bu	Me	H	H	A	22 h	42
2	**8b**	*t*Bu	*n*Bu	H	H	A	10 d	36[b]
3	**8c**	Me	*n*Bu	H	Me	A	24 h	32
4	**8d**	Me	*n*Bu	H	Me	B	6 d	46
5	**8e**	Me	*n*Bu	COOEt	Me	A	4 h	–
6	**8f**	Me	*n*Bu	COOEt	Me	B	13 d	84[c]

[a] Conditions A: $Ph_3PAuCl/AgBF_4$ in toluene. Conditions B: AuCl/pyridine in CH_2Cl_2. [b] 67% conversion of **8b**. [c] dr = 70:30.

♦Addition of *N*-iodosuccinimide (NIS) to the reaction mixture induces a tremendous acceleration, leading to the formation of the corresponding iodinated dihydropyran.
♦This effect is probably caused by a very rapid iododeauration of a σ-gold intermediate(**10**, page 4) by NIS, which is activated by the gold catalyst.

Krause, N. *et al. Eur. J. Org. Chem.* **2010**, 311.



Additive	Time	X	Yield (%)
None	5 d	H	50
NIS	1 min	I	56

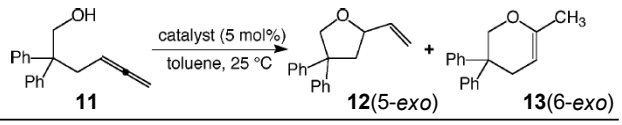
(NIS 1.1-1.5 equiv.)

Entry	[Au]	mol-%	Solvent	Time	Yield [%]
1	$AuCl_3$[a]	5	CH_2Cl_2	1 min	67
2	$AuCl_3$[a]	0.5	CH_2Cl_2	1 min	50
3	$AuCl_3$[a]	0.05	CH_2Cl_2	15 min	42
4	$Ph_3PAuCl/AgBF_4$	5	toluene	1 min	52
5	$Ph_3PAuCl/AgBF_4$	0.5	toluene	15 min	42
6	AuCl	5	CH_2Cl_2	1 min	56
7	AuCl	0.5	CH_2Cl_2	20 min	49
8[b]	AuCl	5	CH_2Cl_2	1 h	47
9	AuCl/Pyridine	5	CH_2Cl_2	1 min	50
10	–	–	toluene	2 d	45

[a] 0.166 M solution in MeCN. [b] At –20 °C.

exo-hydroalkoxylation of hydroxyallenes

Widenhoefer, R. A. *et al. J. Am. Chem. Soc.* **2006**, *128*, 9066.



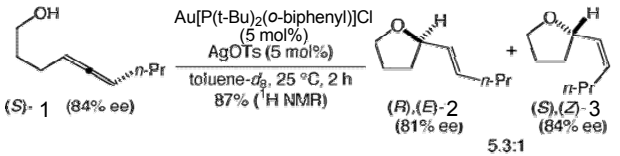
entry	catalyst	time	conv.	yield **12**[a]	yield **13**[a]
1	**14**/AgOTf	5 min	>99%	48%	37%
2	**14**/AgOTs	3 min	>99%	96%	≤1%
3	$AgNO_3$	16 h	17%	14%	0%
4	AgOTs	48 h	0%		
5	$[PtCl(H_2C{=}CH_2)]_2$/$P(C_6H_5CF_3)_3$	5 min	>99%	0%	49%

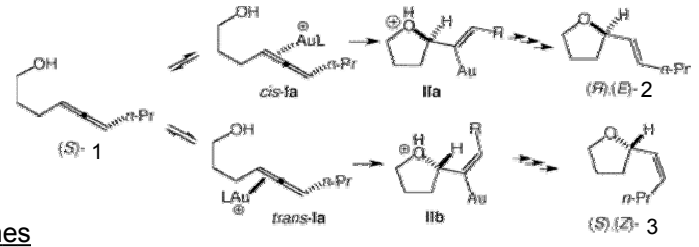
[a] Yield determined by GC analysis vs internal standard.

14 : Au[P(t-Bu)$_2$(*o*-biphenyl)]Cl

♦the regioselectivity of Au-catalyzed hydroalkoxylation depended strongly on the nature of the counterion. ?

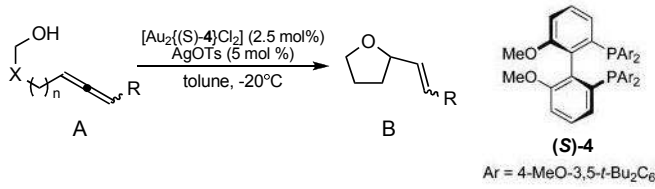
Mechanism.

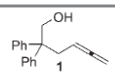
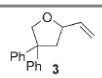
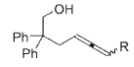
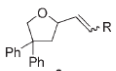
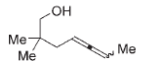
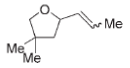
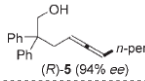
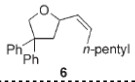
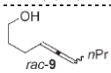
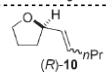
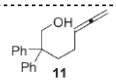
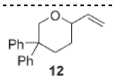
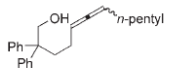
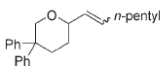
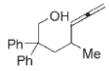
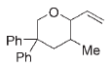
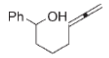
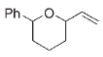




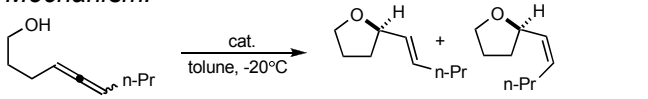
enantioselective *exo*-hydroalkoxylation of hydroxyallenes

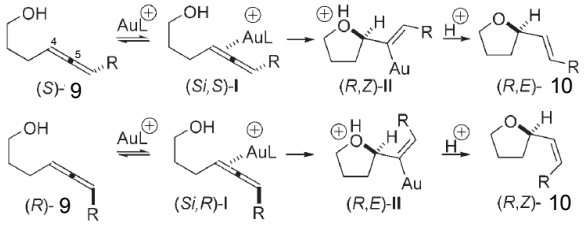
Widenhoefer, R. A. *et al. Angew. Chem., Int. Ed.* **2007**, *46*, 283.



Entry	Alkenyl alcohol	Product	Ratio of isomers[a]	Yield [%][b]	*ee* [%][c]
1	 1	 3	–	67	93
2	 *rac*-**5** (R = *n*-pentyl)	 6	1:1	94	>95/>95[d]
3	*rac*-**7** (R = Me)	8	1:1	96	97/99
4			1:1	95[e]	93/95
5	 (*R*)-**5** (94% *ee*)	 6	>20:1	88	>95[d]
6	 *rac*-**9**	 (*R*)-**10**	1.5:1	94[e]	28/39
7	 11	 12	–	96	88
8			1.5:1	92	67/93
9			1.3:1	99	81/82
10			1:3.3	95	88/45

Mechanism.

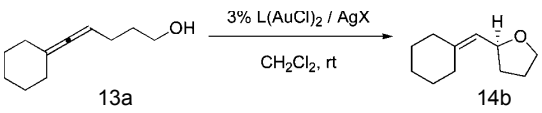




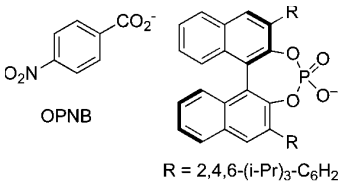
- In the major pathway, complexation of Au to the Si face of the C4=C5 bond of rac-**9** would form Au-allene complexes (*Si,S*)-**I** and (*Si,R*)-**I**.
- The minor enantiomers (*S,Z*)-**10** and (*S,E*)-**10** would be formed through outer-sphere cyclization of the Au-allene complexes (*Re*,S)-**I** and (*Re,R*)-**I**.

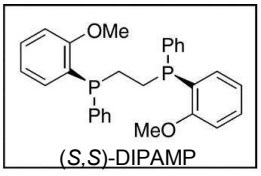
[a] Ratio of isomers refers to trans/cis or E/Z. [b] Combined yield of all diastereomers with >95% purity. [c] For reactions that form two diastereomers, ee values are reported as trans/cis or E/Z. [d] Determination of the enantiomeric purity was complicated by the coelution of one enantiomer of (E)-6 with one enantiomer of (Z)-6 in HPLC. [e] Yield determined by 1H NMR analysis with reaction carried out in [D8]toluene.

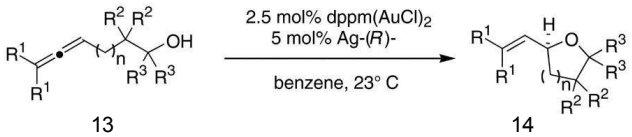
Toste, F. D. *et al. Science* **2007**, *317*, 496.



entry	ligand (L)	X	yield (%)	ee (%)
1	(*R*)-3,5-xylyl-BINAP	BF_4	68	0
2	(*R*)-3,5-xylyl-BINAP	OPNB	89	8
3	(*R*)-DTBMSegphos	BF_4	79	2
4	dppm	**15**	76	65







Entry	n	R^1	R^2	R^3	Time (h)	% Yield	% ee
1	1	$-(CH_2)_4-$	H	H	1	90	97
2	1	CH_3	H	H	1	91	95
3	1	CH_2CH_3	H	H	5	89	96
4	1	$-(CH_2)_4-$	H	CH_3	2	79	99
5	1	$-(CH_2)_4-$	H	Ph	30	86	92
6	1	$-(CH_2)_4-$	CH_3	H	13	90	90
7	2	CH_3	H	H	15	81	90
8	2	H	H	H	24	96	92 (80)

◆The use of chiral counterions, rather than chiral neutral ligands, could provide high enantioselectivity in additions of oxygen nucleophiles to allenes.

- Neither noncoordinating (BF_4) nor more coordinating (OPNB) counterions associated with dicationic chiral bisphosphine(digold) species induced significant enantioselectivity in the cyclization.
- Chiral Binol-derived phosphoric acid **15** in conjunction with the dppm ([bis(diphenyl)phosphino]methane) ligand proved optimal.
- more-polar solvents, such as nitromethane or acetone, gave significantly lower enantiomeric excess values.
- the less-polar benzene proved to be the optimal medium, providing the desired product in an exceptional 97% ee.

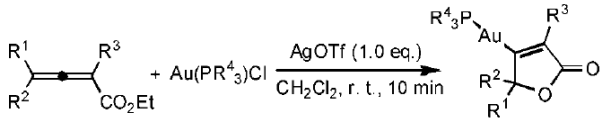
◆These findings are consistent with an ion-pair model, in which the degree of enantioinduction depends on the proximity of the counteranion to the cationic gold center

◆The chiral counterion can be combined additively with chiral ligands to enable an asymmetric transformation that cannot be achieved by either method alone.
- For the terminal allene(Entry 8), the enantiomeric excess could be improved from 80 to 92% by using a chiral gold catalyst [(S,S)-*D*IPAMP]$(AuCl)_2$ together with the chiral silver salt.

2.1.3. Isomerization of allenic esters : **formation of lactones**

cyclization of allenic esters

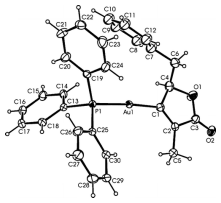
Hammond, G. B. *et al. J. Am. Chem. Soc.* **2008**, *130*, 17642.



1 2 3

entry	$R^1/R^2/R^3/R^4$	3, yield[% b]
1	n-C_6H_{13}/H/Me/C_6H_5	**3a**, 85
2	^{i}Pr/H/Me/C_6H_5	**3b**, 82
3	Me/H/Me/C_6H_5	**3c**, 75
4	Bn/H/Me/C_6H_5	**3d**, 81
5	Me/H/H/C_6H_5	**3e**, 46
6	Me/Me/Me/C_6H_5	**3f**, 68
7	Ph/H/Me/C_6H_5	no reaction
8	n-C_6H_{13}/H/Me/o-$CH_3C_6H_4$	**3g**, 71
9	n-C_6H_{13}/H/Me/m-$CH_3C_6H_4$	**3h**, 68
10	n-C_6H_{13}/H/Me/p-$CH_3C_6H_4$	**3i**, 70
11	n-C_6H_{13}/H/Me/p-$CH_3OC_6H_4$	**3j**, 62
12	n-C_6H_{13}/H/Me/cyclohexyl	**3k**, 54

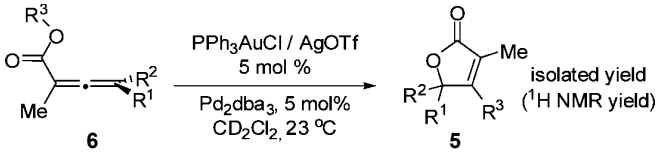
[a] General conditions: allenoate **1** 0.24 mmol, Au(PR3)Cl **2** 0.2 mmol, AgOTf 0.2 mmol, CH_2Cl_2 2.0 mL. [b] Isolated yields.



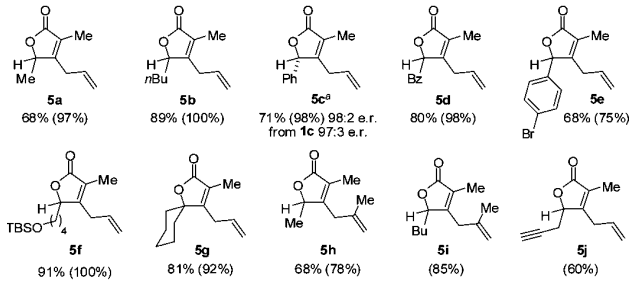
♦The structure of 3 was determined by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopic data and X-ray crystallography of complex **3d**.

dual-catalytic C-C bond formation as an alternative to protodemetalation

Blum, S. A. *et al. J. Am. Chem. Soc.* **2009**, *131*, 18022.

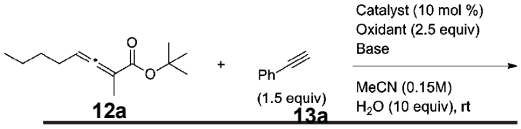


6 5

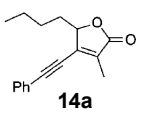


cyclization-oxidative alkynylation of allenic esters

Gouverneur, V. *et al. Org. Lett.* **2010**, *12*, 4904.



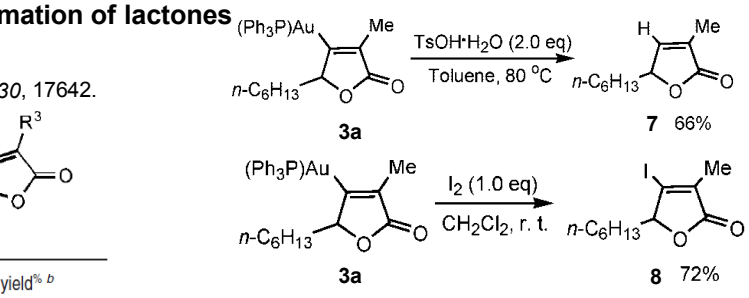
12a 13a



14a

entry	catalyst	oxidant	base	time	yield[a]
1	$Ph_3PAuNTf_2$	Selectfluor	none	4 d	44%
2	$Ph_3PAuNTf_2$	Selectfluor	K_3PO_4	4 h	94%
3	no catalyst	Selectfluor	K_3PO_4	10 d	NR
4	AuCl[b]	Selectfluor	K_3PO_4	48 h	NR
5	AgOTf	Selectfluor	K_3PO_4	10 d	NR
6	$PtCl_2$	Selectfluor	K_3PO_4	10 d	NR
7	CuOAc	Selectfluor	K_3PO_4	10 d	NR
8	H_2SO_4	Selectfluor	K_3PO_4	10 d	NR
9	SIPrAuCl/AgOTf[c]	Selectfluor	K_3PO_4	10 d	NR
10	$Pd(OAc)_2$/ CuOAc	Selectfluor	K_3PO_4	24 h	decomp.
11	$AuCl_3$	Selectfluor	K_3PO_4	6 d	22%
12	$Ph_3PAuNTf_2$[b]	Selectfluor	K_3PO_4	24 h	72%
13	$Ph_3PAuNTf_2$	no oxidant	K_3PO_4	5 d	NR
14	$Ph_3PAuNTf_2$	PhI(OAc)$_2$	K_3PO_4	7 d	NR
15	$Ph_3PAuNTf_2$	tBuOOH	K_3PO_4	7 d	NR
16	$Ph_3PAuNTf_2$	Oxone[d]	K_3PO_4	7 d	NR
17	$Ph_3PAuNTf_2$	NFSI[e]	K_3PO_4	7 d	54%[f]

[a] Isolated yield. [b] 5 mol%. [c] SIPr = 1,3-Bis(2,6-diisopropylphenyl) imidazolin-2-ylidene. [d] Oxone = $KHSO_5$·1/2$KHSO_4$·1/2K_2SO_4. [e] NFSI = *N*-Fluorobenzenesulfonimide. [f] Conversion estimated by ^{1}H NMR.

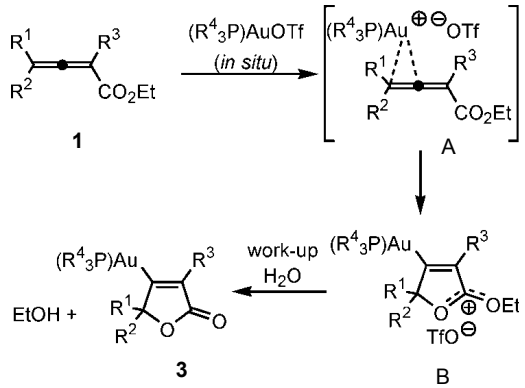


3a 7 66%

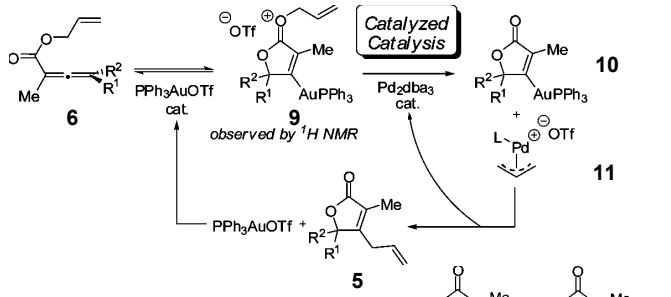
3a 8 72%

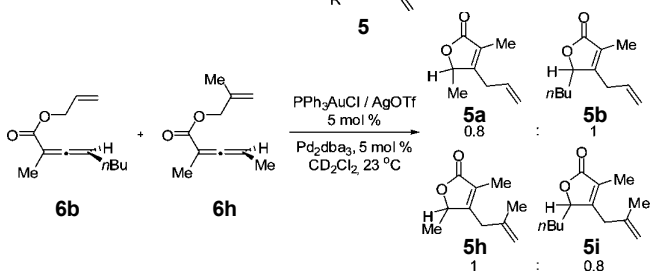
♦In the presence of triflic acid or iodine, vinylgold compounds **3a** undergo protodeauration or iododeauration to the corresponding butenolides.

◆Thus, the mechanism of the gold-catalyzed cyclization of allenic esters is similar to that proposed for α-hydroxyallenes

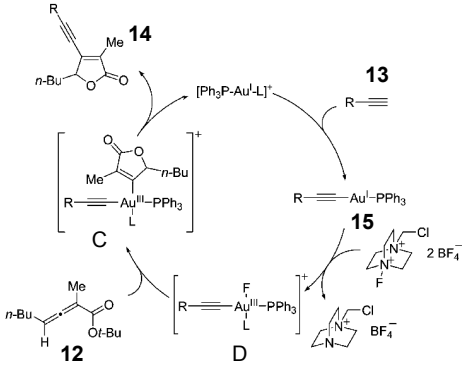


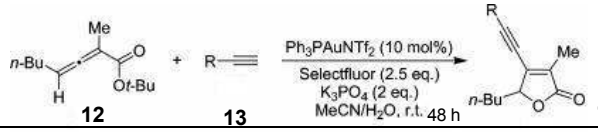
1 A 3 B





♦The observed crossover is consistent with the intermediacy of **10** and **11** followed by intermolecular transmetalation and reductive elimination.





12 13 14

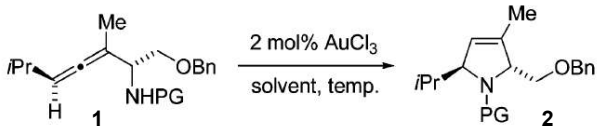
entry	R	yield (%)	entry	R	yield (%)
1	Ph	94	6	4-FC_6H_4	78
2	2-MeC_6H_4	42	7	4-$CF_3C_6H_4$	63
3	3-MeC_6H_4	72	8	4-$NO_2C_6H_4$	45
4	4-MeC_6H_4	98	9	H	16
5	4-$MeOC_6H_4$	88	10	*n*-Pr	28

2.2. Nitrogen Nucleophiles

2.1.1. *endo*-selective hydroamination

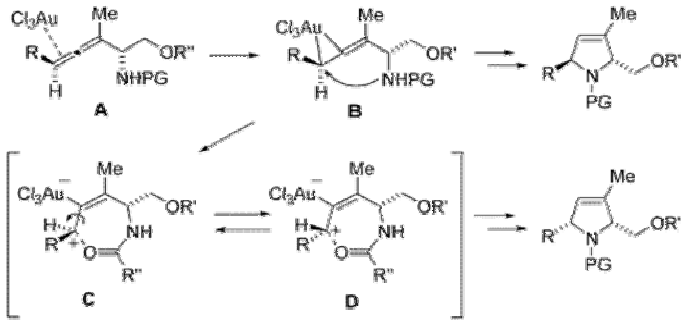
first intramolecular *endo*-selective hydroamination of allenes

Krause, N. *et al. Org. Lett.* **2004**, *6*, 4121.



entry	PG	solvent	T (°C)	time	yield, %	dr
1	H	CH_2Cl_2	rt	5 days	74	>99:1
2	Ms	CH_2Cl_2	rt	30 min	77	94:6
3	Ts	CH_2Cl_2	rt	30 min	93	95:5
4	Ts	CH_2Cl_2	0	1 h	95	96:4
5	Ts	THF	rt	1.5 h	95	93:7
6	Ac	CH_2Cl_2	rt	30 min	80	70:30
7	Boc	CH_2Cl_2	rt	30 min	69	46:54

♦the diminished reactivity of unprotected aminoallene is probably due to deactivation of the gold catalyst by the Lewis-basic amino group.

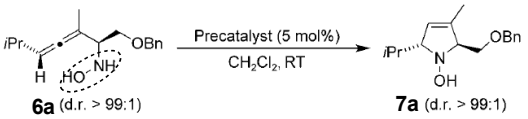


♦An oxygen atom of the protecting group could stabilize the zwitterionic complex **C** by coordination, and the cyclization would proceed with partial isomerization (via single bond rotation) to complex **D**, leading to a diminished diastereoselectivity.

cycloisomerization of allenic hydroxylamine or hydroxylamine ether

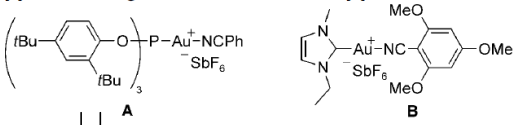
Krause, N. *et al. Angew. Chem., Int. Ed.* **2009**, *48*, 6339.

♦**all cycloisomerizations proceeded with exclusive 5-endo regioselectivity.**



Entry	Precatalyst	t [h]	Yield [%]
1	$AuCl_3$	0.5	77
2	AuCl	0.5	94
3[a]	AuCl	7	87
4	**A**	18	40[b]
5	**B**	1	62[c]
6	$[AuCl(PPh_3)]/AgBF_4$	16	43
7	$AgBF_4$	2	88
8[d]	$HAuCl_4/LiCl$	2	64

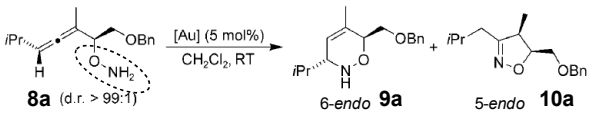
[a] 1 mol% of AuCl was used. [b] 7% starting material was recovered. [c] 37% starting material was recovered. [d] Water was used as solvent.



♦allenic substrates in which the heteroatom positions were exchanged.

♦**cyclization proceeded by the nucleophilic attack of the nitrogen atom**

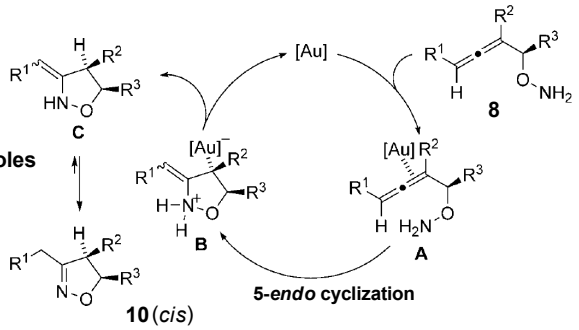
♦**afforded a mixture of the 3,6-dihydro-1,2-oxazine and the 4,5-dihydroisoxazole**



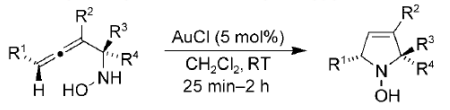
Entry	Precatalyst	t [h]	**9a**: Yield [%] (d.r.)	**10a**: Yield [%] (d.r.)	**9a/10a**
1	AuCl	2.5	47 (>99:1)	19 (87:13)	71:29
2	$AuCl_3$	2.5	49 (>99:1)	15 (89:11)	77:23
3[a]	$AuCl_3$	3.0	35 (>97:3)	16 (87:13)	69:31
4[b]	$AuCl_3$	62	40 (>98:2)	26 (87:13)	61:39
5	$[Au(PPh_3)]BF_4$[c]	1.5	3 (n.d.)[d]	69 (79:21)	4:96
6	**A**	1.5	3 (n.d.)[d]	81 (94:6)	4:96

[a] A stock solution of $AuCl_3$ in MeCN was used. [b] Reaction performed in THF. [c] Prepared in situ from $[AuCl(PPh_3)]$ and $AgBF_4$. [d] Not determined.

♦highly regioselective cyclization of the allenic hydroxylamine ether **8a** to 4,5-dihydroisoxazole **10a** could be achieved in the presence of cationic gold(I) complexes



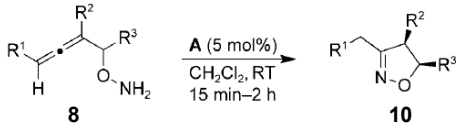
Gold-catalyzed synthesis of *N*-hydroxypyrrolines



Entry	R^1	R^2	R^3	R^4	(Yield [%])
1	*i*Pr	Me	H	CH_2OBn	(76)
2	*n*Bu	Me	CH_2OBn	H	(80)
3	Ph	Me	CH_2OBn	H	(73)
4	*n*Bu	Me	CH_2OH	H	(67)
5[a]	Me	H	H	$(CH_2)_2Ph$	(78)
6	*i*Pr	H	H	$(CH_2)_2CO_2Et$	(77)

[a] was used as a diastereomeric mixture (1:1).

Gold-catalyzed synthesis of dihydroisoxazoles

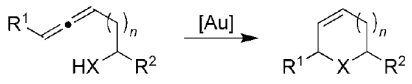


Entry	R^1	R^2	R^3	(Yield [%])	d.r.
1	*n*Bu	Me	CH_2OBn	(77)	95:5
2	H	Me	CH_2OBn	(72)	95:5
3	H	Me	CH_2OTBS	(78)	51:49
4	Me	H	$(CH_2)_2Ph$	(87)	
5	Me	H	Me	(86)	
6	*i*Pr	H	$(CH_2)_2CO_2Et$	(86)	

◆**Proposed mechanism for the formation of *cis*-substituted dihydroisoxazoles**

- ♦coordination of the gold catalyst to the allenic double bond adjacent to the hydroxylamine moiety affords π complex **A**
- ♦complex **A** undergoes a 5-*endo* cyclization to the zwitterionic species **B**.
- ♦the bulky gold moiety is preferentially situated trans to the group R3

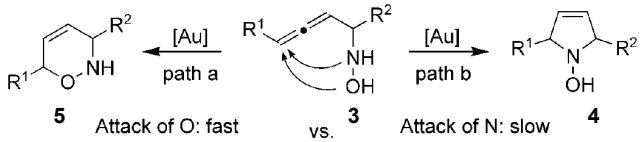
■Different reaction rates in the endo cycloisomerization



k_{rel} (n = 0) > k_{rel} (n = 1)

k_{rel} (X = O) > k_{rel} (X = NH)

■possible consequences for the cyclization of *N*-hydroxy-a-aminoallenes

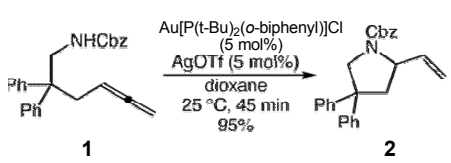


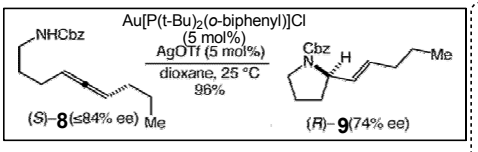
Attack of O: fast
6-membered ring: slow
vs.
Attack of N: slow
5-membered Ring: fast

2.1.2. *exo*-selective hydroamination

exo-selective hydroamination of *N-allenyl carbamates*

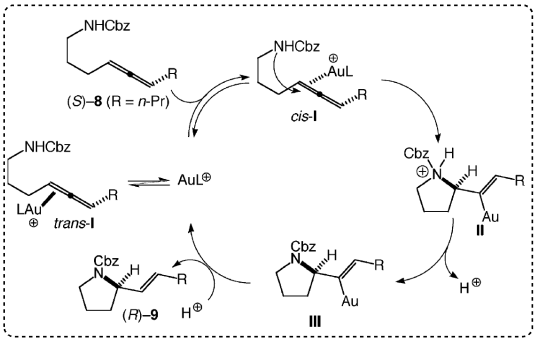
Widenhoefer, R. A. *et al*. *J. Am. Chem. Soc*. **2006**, *128*, 9066.





entry	allenyl carbamate	heterocycle	yield (%)[a]
1	R = Boc		94
2	R = Fmoc		88
3			80 (16:1)
4			90 (4:1)
5			97
6	R = Me (**6**)	**7**	92 (≥50:1)
7	R = *n*-Pr (**8**)	**9**	98 (≥50:1)
8			96
9			92 (7.0:1)[b]
10			96 (≥50:1)

10 **11** **12** **13**



♦formation of the *E*-alkene moiety of (*R*)-9 requires selective cyclization of gold-allene intermediate cis-**I**

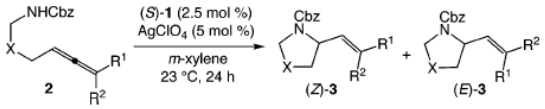
♦Au-catalyzed conversion of (*S*)-8 to (*R*)-9 presumably involves rapid and reversible formation of *trans*-**I** followed by irreversible cyclization of *cis*-**I** to form **II.**

♦the transition state for C-N bond formation is destabilized to a greater extent by a cis arrangement of the carbamate moiety and *n*-propyl group (*trans*-**I** → **II**) than by a cis arrangement of the Au[P(*t*-Bu)2-(*o*-biphenyl)] moiety and the *n*-propyl group (*cis*-**I**→**II**).

dynamic kinetic enantioselective hydroamination(DKEH) of allenes

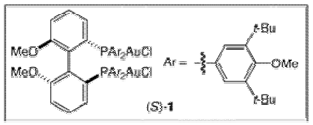
Widenhoefer, R. A. *et al*. *J. Am. Chem. Soc*. **2007**, *129*, 14148.

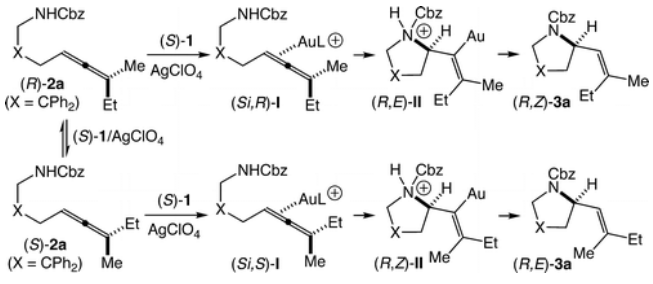
Table 1. Dynamic Kinetic Enantioselective Hydroamination (DKEH) of *N*-(γ-Allenyl) Carbamates Catalyzed by a Mixture of (*S*)-**1** (2.5 mol %) and $AgClO_4$ (5 mol %) in *m*-Xylene at 23 °C



entry	allene	yield (*Z*)-3 + (*E*)-3 (%)[a]	(*Z*)-3/ (*E*)-3	ee (*Z*)-3 (%)	ee (*E*)-3 (%)
1	**2a** (X = CPh_2, R^1 = Me, R^2 = Et)	94	3.1:1	96	76
2	**2b** (X = CPh_2, R^1 = Me, R^2 = *n*-hexyl)	99	10.1:1	91	9
3[b]	**2c** (X = CPh_2, R^1 = Me, R^2 = *i*-Bu)	99	2.6:1	87	54
4	**2d** (X = CPh_2, R^1 = Me, R^2 = *i*-Pr)	94	2.0:1	95	67
5[c]	**2e** (X = CPh_2, R^1 = Me, R^2 = *t*-Bu)	52	≤1:25	2	–
6	**2f** (X = CPh_2, R^1 = Et, R^2 = *n*-hexyl)	86	4.3:1	84	47
7	**2g** (X = CH_2, R^1 = Me, R^2 = *n*-hexyl)	87	2.4:1	75	45

[a] Yield of isolated material of > 95% purity. [b] Reaction run at 0 °C for 24 h followed by 23 °C for 24 h. [c] Reaction run at 60 °C for 212 h followed by 100 °C for 48 h.





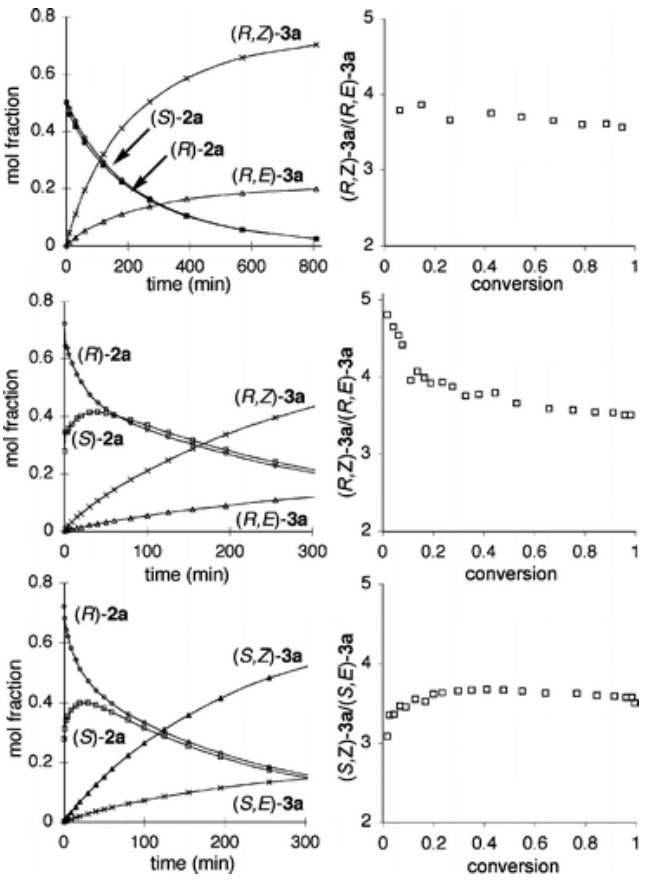
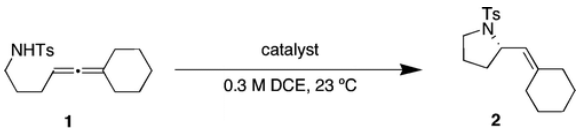


Figure 1. Plots of concentration versus time (left-hand column, minor enantiomers omitted for clarity) and *Z*/*E* ratio versus conversion (right-hand column) for the cyclization of *rac*-**2a** catalyzed by (*S*)-**1**/$AgClO_4$ (top plots), a ~3:1 mixture of (*R*)-**2a** and (*S*)-**2a** catalyzed by (*S*)-**1**/$AgClO_4$ (middle plots), and a ~3:1 mixture of (*R*)-**2a** and (*S*)-**2a** catalyzed by (*R*)-**1**/$AgClO_4$ (bottom plots) in *m*-xylene at 23 °C. Catalyst loading: **1** = 2.5 mol %; $AgClO_4$ = 5 mol %.

highly enantioselective hydroamination of allenes

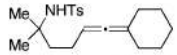
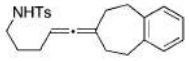
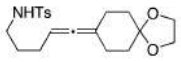
Toste, F. D. *et al. J. Am. Chem. Soc.* **2007**, *129*, 2452.



entry	catalyst	time (h)	yield[a]	ee[b] (%)
1	3 mol % (*R*)-xylyl-BINAP(AuCl)$_2$; 6 mol % AgBF$_4$[c]	0.5	82	1
2	3 mol % (*R*)-xylyl-BINAP(AuCl)$_2$; 3 mol % AgBF$_4$[c]	0.5	81	51
3	3 mol % (*R*)-xylyl-BINAP(AuCl)$_2$; 6 mol % AgOBz[c]	24	27	98
4	3 mol % (*R*)-xylyl-BINAP(AuCl)$_2$; 6 mol % AgOPNB[c,d]	24	76	98
5	3 mol % (*R*)-xylyl-BINAP(AuCl)$_2$; 6 mol % AgODNB[c]	17	82	95
6	3 mol % (*R*)-xylyl-BINAP(AuOPNB)$_2$ (**4**)	17	88	98
7	3 mol % (*R*)-BINAP(AuOPNB)$_2$ (**5**)	15	82	93
8	3 mol % (*S*)-BINAP(AuOPNB)$_2$ (**6**)	15	86	94[f]
9	3 mol % (*R*)-SEGPHOS(AuOPNB)$_2$ (**7**)	24	57	83
10	3 mol % (*R*)-SYNPHOS(AuOPNB)$_2$ (**8**)	24	47	92
11	3 mol % (*R*)-ClMeOBiPHEP(AuOPNB)$_2$ (**9**)	15	85	97

[a] Isolated yield after column chromatography. [b] Determined by HPLC. [c] Catalyst prepared in situ by stirring for 5 min in DCE before addition to substrate. [d] OPNB = *p*-nitrobenzoate. [e] ODNB = 3,5-dinitrobenzoate. [f] *ent*-**2**.

Table 2. Scope of Gold(I)-Catalyzed Hydroamination of Allenes

entry	substrate	conditions[a]	time (h)	product	% yield[b]	% ee[c]
1	**10** R_1 = Me; R_2 = H	A	15	**11**	98	99
2	**12** R_1 = Et; R_2 = H	A[d]	17	**13**	90	99
3	**14** R_1 = -CH$_2$(CH$_2$)$_2$CH$_2$-; R_2 = H	A	15	**15**	75	83
4	**1** R_1 = -CH$_2$(CH$_2$)$_3$CH$_2$-; R_2 = H	A	17	**2**	88	98
5	**16** R_1 = -CH$_2$(CH$_2$)$_4$CH$_2$-; R_2 = H	A	15	**17**	88	98
6	**18** R_1 = Me; R_2 = Me	B	15	**19**	94	93
7	**20** R_1 = Me; R_2 = -CH$_2$(CH$_2$)$_3$CH$_2$-	B	15	**21**	99	70
8	**22** R_1 = Me; R_2 = Ph	C	15	**23**	99	87
9	**24** 	D	17	**25**	76	96
10	**26** 	A	25	**27**	80	98
11	**28** 	A[e]	25	**29**	79	98
12	**30** R_1 = Me; R_2 = H	D	15	**31**	88	81
13	**32** R_1 = Et; R_2 = H	D	24	**33**	41	74
14	**34** R_1 = Me; R_2 = Me	D	24	**35**	70	98
15	**36** R_1 = Me; R_2 = Ph	D	24	**37**	70	88
16	**38** R_1 = Me; R_2 = -CH$_2$(CH$_2$)$_3$CH$_2$-	D	17	**39**	66	97

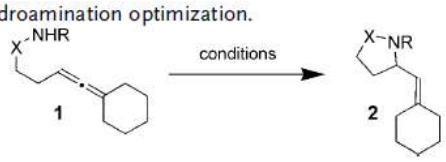
[a] Reaction conditions: A = 3 mol % of **4**, 0.3 M in DCE, 23 °C; B = 5 mol % of **4**, 0.3 M in $MeNO_2$, 50 °C; C = 5 mol % of 7, 0.3 M in $MeNO_2$, 50 °C; D = 5 mol % of **9**, 0.3 M in $MeNO_2$, 50 °C. [b] Isolated yield after column chromatography. [c] Determined by HPLC. [d] 5 mol % of catalyst. [e] At 50 °C.

- the remaining coordinated counterion was crucial for stereoinduction.
- replacing chloride with a larger coordinated counterion could further increase the transmission of chiral information.

enantioselective hydroaminations and hydroalkoxylations of allenes with hydroxylamines and hydrazines

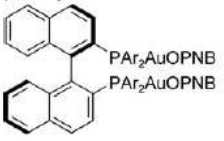
Toste, F. D. *et al. Angew. Chem., Int. Ed.* **2010**, *49*, 598.

Table 1: Hydroamination optimization.

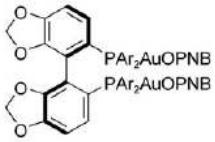


Entry	**1**; X	R	Cond.[a]	**2**; Yield[b] [%]	*ee*[c] [%]
1	**1a**; NBoc	H	A	**2a**; 46	5
2	**1b**; NBoc	Boc	A	**2b**; >98[d]	70
3	**1c**; NBoc	Mts	A	**2c**; >98[d]	80
4	**1c**; NBoc	Mts	A[e]	**2c**; 78	97
5	**1d**; O	H	B[f]	**2d**; 92	10
6	**1e**; O	Cbz	B	**2e**; 8[d]	–
7	**1f**; O	Boc	B	**2f**; 93	93

[a] Reaction Conditions: A = Catalyst **I** (5 mol%), 0.3 M in $MeNO_2$, 50 °C, 15 h; B = Catalyst **I** (3 mol%), 0.1 M in CH_2Cl_2, 23 °C, 24 h; [b] Yield of product isolated after column chromatography. [c] Determined by HPLC methods. [d] Conversion determined by ^{1}H NMR analysis. [e] Catalyst **II**. [f] 18 h. Boc = *tert*-butoxycarbonyl, Cbz = benzyloxycarbonyl, Mts = 2-mesitylsulfonyl, binap = 2,2-bis(diphenylphosphanyl)-1,1-binaphthyl, DTBM-Segphos = 5,5'-bis{di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino}-4,4'-bi-1,3-benzodioxole.

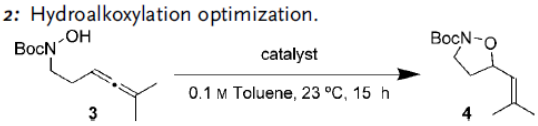


Catalyst **I**
Ar = 3,5-xylyl
[(*R*)-xylyl-binap(AuOPNB)$_2$]



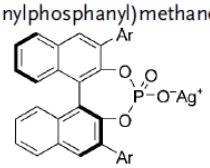
Catalyst **II**
Ar = 3,5-di-*tert*-butyl-4-methoxyphenyl
[(*R*)-DTBM-Segphos(AuOPNB)$_2$]

Table 2: Hydroalkoxylation optimization.

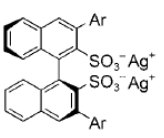


Entry	Catalyst[a]	Yield [%][b]	*ee* [%][c]
1	**I**	0	–
2	3 mol% [dppm(AuCl)$_2$] 3 mol% **IV**	98[d]	65
3	3 mol% [(*R*)-binap(AuCl)$_2$] 3 mol% **IV**	98[d]	8
4	3 mol% [(*S*)-binap(AuCl)$_2$] 3 mol% **IV**	98	42
5	3 mol% [dppm(AuCl)$_2$] 6 mol% **III**	98	98

[a] Reaction Conditions: 0.1 M in toluene, 23 °C, 15 h; [b] Yield of product isolated after column chromatography. [c] Determined by HPLC methods. [d] Conversion determined by ^{1}H NMR analysis. dppm = bis(diphenylphosphanyl)methane.

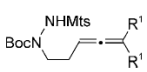
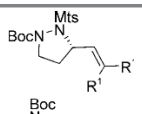
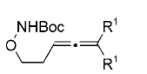
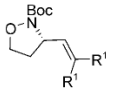
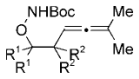
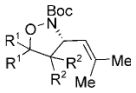
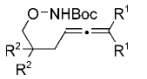
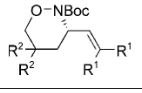


(*S*)-TriPAg (**III**)
Ar = 2,4,6-triisopropylphenyl



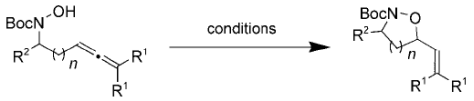
(*S*)-(**5**) Ag (**IV**)
Ar = 3,5-ditrifluoromethylphenyl

Table 3: Hydrazine and hydroxylamine hydroamination scope.

Entry	Substrate		R^1	R^2	Cond.[a]	Product		Yield [%][b]	*ee* [%][c]
1		**6**	Me	–	A		**7**	98	99
2		**8**	-$(CH_2)_4$-	–	A		**9**	90	83
3		**1c**	-$(CH_2)_5$-	–	A		**2c**	75	97
4		**10**	Me	–	B		**11**	91	98
5		**12**	-$(CH_2)_4$-	–	B		**13**	98	91
6		**1f**	-$(CH_2)_5$-	–	B		**2f**	93	93
7		**14**	Me	H	C		**15**	94	63
8		**16**	H	Me	C		**17**	73	99
9		**18**	-$(CH_2)_5$-	H	D[d]		**19**	63	89
10		**20**	-$(CH_2)_5$-	Me	D		**21**	85	89
11		**22**	Me	Me	D		**23**	79	89

[a] Reaction Conditions: A = [(*R*)-DTBM-Segphos(AuOPNB)$_2$] (5 mol%), 0.3 M in $MeNO_2$, 50 °C, 15 h; B = **I** (3 mol%), 0.1 M in CH_2Cl_2, 23 °C, 24 h; C = [(*R*)-DM-MeOBiPhep(AuOPNB)$_2$] (5 mol%), 0.1 M in $MeNO_2$, 50 °C, 24 h; D = **I** (5 mol%), 0.3 M in $MeNO_2$, 50 °C, 24 h. [b] Yield of the product isolated after column chromatography. [c] Determined by HPLC methods. [d] 36 h, 65 °C. DM-MeOBiPhep = 2,2′-bis[di(3,5-xylyl)phosphino]-6,6′-dimethoxy-1,1′-biphenyl.

Table 4: Hydroxylamine hydroalkoxylation scope.



Entry	Substr.	*n*	R^1; R^2	Cond.[a]	Prod.	Yield [%][b]	*ee* [%][c]
1	**26**	1	Me; H	A	**27**	98	98
2	**3**	1	-$(CH_2)_5$-; H	A	**4**	75	99
3	**28**	1	Me; Me	A	**29**	99[d]	40/97
4	**30**	2	Me; H	A[e]	**31**	66	50
5	**30**	2	Me; H	B	**31**	94	87
6	**30**	2	Me; H	C	**31**	36	45

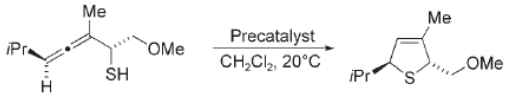
[a] Reaction Conditions: A = [dppm(AuCl)$_2$] (3 mol%), **III** (6 mol%), 0.1 M in toluene, 23 °C, 18 h; B = [(*S*,*S*)-dipamp(AuCl)$_2$] (3 mol%), **III** (6 mol%), 0.1 M in toluene, 23 °C, 18 h; C = [(*S*,*S*)-dipamp(AuCl)$_2$] (3 mol%), (*R*)-AgTriP (6 mol%), 0.1 M in toluene, 23 °C, 18 h. [b] Yield of product isolated after column chromatography. [c] Determined by HPLC methods. [d] 5:1 d.r. [e] 60 h. dipamp = 1.

2.3. Sulfur Nucleophiles

cycloisomerization of α-thioallenes

Krause, N. *et al. Angew. Chem., Int. Ed.* **2006**, *45*, 1897.

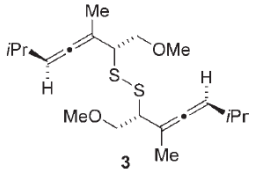
Table 1: Cycloisomerization of α-thioallene **1a** to 2,5-dihydrothiophene **2a**.

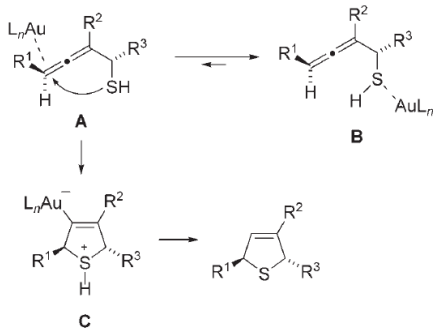


1a (d.r. > 99:1) **2a** (d.r. > 99:1)

Entry	Precatalyst (mol%)	*t*	Yield (**2a**) [%]
1	$AuCl_3$ (5)	3 h	58[a]
2	$AuBr_3$ (5)	20 min	56[a]
3	AuCl (5)	1.5 h	88
4	AuI (5)	5 min	88
5	AuI (1)	1.5 h	64
6	[Ph_3PAuCl] (5)	7 days	trace
7	[Ph_3PAuCl] (5)/ $AgBF_4$ (10)	4 h	52
8	$AgBF_4$ (15)	2 days	trace
9	AgCl (15)	2 days	no reaction
10	CuCl (20)	1 h	trace
11	CuI (20)	2 days	no reaction

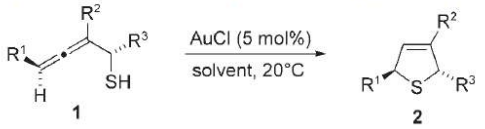
[a] Small amounts of disulfide **3** were formed as side product.





Scheme 3. Proposed mechanism of the gold-catalyzed cycloisomerization of α-thioallenes to 2,5-dihydrothiophenes.

Table 2: Scope of the cycloisomerization of α-thioallenes **1** to 2,5-dihydrothiophenes **2**.



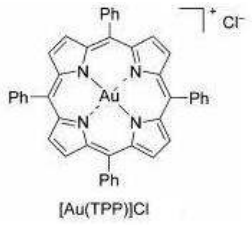
Entry	**1**	R^1	R^2	R^3	d.r. (**1**)	Solvent	*t*	**2** (Yield)	d.r. (**2**)
1	**1b**	*i*Pr	Me	CH_2OBn	95:5	CH_2Cl_2	1.5 h	**2b** (86%)	95:5
2	**1b**	*i*Pr	Me	CH_2OBn	95:5	THF	2 days	**2b** (24%)	95:5
3	**1b**	*i*Pr	Me	CH_2OBn	95:5	toluene	1 days	**2b** (55%)	95:5
4	**1b**	*i*Pr	Me	CH_2OBn	95:5	hexane	2 days	**2b** (trace)	–
5[a]	**1b**	*i*Pr	Me	CH_2OBn	95:5	CH_2Cl_2	5 min	**2b** (87%)	95:5
6	**1c**	*i*Pr	Me	4-$CF_3C_6H_4OCH_2$	>99:1	CH_2Cl_2	4 h	**2c** (67%)	>99:1
7	**1d**	*n*-hexyl	Me	CH_2OBn	>99:1	CH_2Cl_2	2 h	**2d** (82%)	>99:1
8	**1e**	$H_2C{=}CH(CH_2)_7$	H	H	–	CH_2Cl_2	1.5 h	**2e** (43%)	–

[a] AuI (5 mol%) was used instead of AuCl.

3. Conclusion

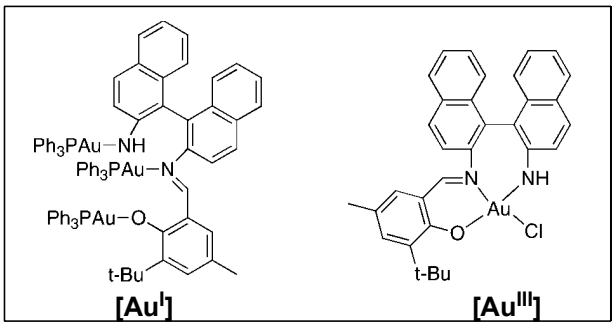
(1) For carbophilic activation with Au(I), the reactivity and selectivity of cationic Au(I) complexes may be tuned by switching the ligand. Biphenyl-substituted phosphines ligands have repeatedly been observed to induce greater reactivity and modulate selectivity among competing reaction pathways.

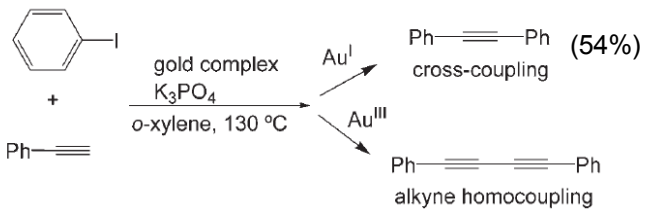
(b) The stability of Au(III) catalysts may be greatly improved with *N*-donor ligands. In some cases, the reactivity of the Au(III) center may be attenuated. Such ligands have also been successfully employed with Au(I) precatalysts in oxidation and group transfer reactions.



[Au(TPP)]Cl

Corma, A. *et al*. *Angew*. *Chem., Int. Ed*. **2007**, *46*, 1536.





- The homogeneous catalysis studies show us that **Au^{I}**, which has the same d^{10} electronic configuration as Pd metal and Cu^{I}, is active and very selective for performing the Sonogashira reaction.
- **Au^{III}** does not catalyze the cross-coupling reaction but does catalyze the homocoupling condensation.