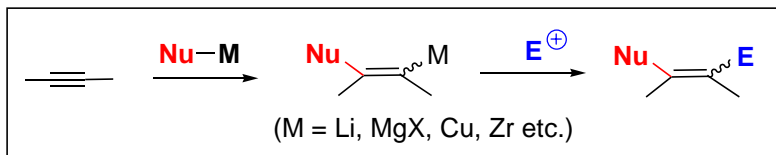
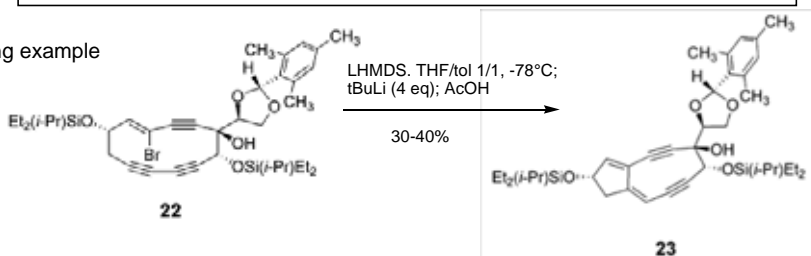


Cationic Phosphine-Gold(I) Catalysis for C-C Forming Reaction with $C\equiv C$ ~ Can relativistic effects rationalize its reactivity? ~

@ Carbometallation is powerful C-C bond formation although stoichiometric metal is needed.

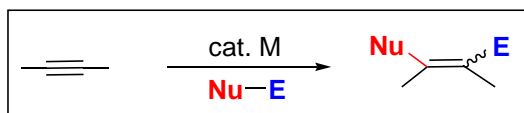


outstanding example



A.G. Myers et al.
(JACS 2006 14825)

@ Catalytic variant of this transformation is highly attractive



⇒ Electrophilic late transition-metals (easily forming π -complex) might be suitable for Nu addition.
But standard carbon Nu (enolate etc.) is difficult to apply

(oxi./red. stable but electrophilic metal is desirable)

problem : oxidative coupling of substrate etc. ←

⇒ Recently some transition metal catalysts (In^{III} , Au^I or III , Pd^{II} etc) are realized for this carbon Nu addition.

Among them, $[R_3P-Au^I]^+$ is one of the most powerful catalysts.

-1995	B.Sc. and M.Sc. / University of Toronto, Canada (Prof. Ian W. J. Still)
1995-2000	Ph.D. / Stanford University (Prof. Barry M. Trost) { asymmetric alkylation (Pd), cycloisomerization ($CpRu^+$), some total syntheses l. 21 papers (17 JACS !)
2001-2002	Post-Doctoral Fellow / Caltech (Prof. Robert H. Grubbs)
2002-2006	Assistant Professor / University of California, Berkeley
2006-	Associate Professor / University of California, Berkeley

F. Dean Toste

⇒ He utilizes **relativistic effect** to explain unique reactivities of gold.

↻ (相对論の効果) ↻

D. J. Gorin and F. D. Toste (*Nature* **2007**, 446, 395-403)

< Contents >

0. Preface (p2)

1. Theoretical chemistry of Gold

- 1-1. Relativistic effects (p3)
- 1-2. Other theoretical aspects (p4)

2. Nu addition toward $C=C$

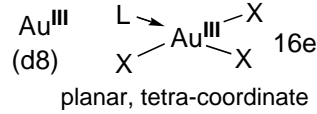
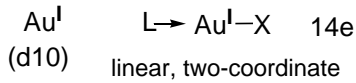
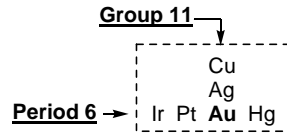
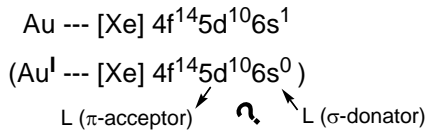
- 2-1. Heteroatom Nu (discovery of $[R_3PAu(I)]^+$) (p5)
- 2-2. Theoretical chemistry of cationic phosphineGold(I) (p6)
- 2-3. Carbon Nu ($Au(I)$ vs $Au(III)$) (p7-8)

3. Reaction after Nu addition (via carbenoid)

- 3-1. Generation of cationic intermediates (p9)
- 3-2. Investigation of cationic intermediate (p10)

0. Preface

> **Au**
(Z = 79)



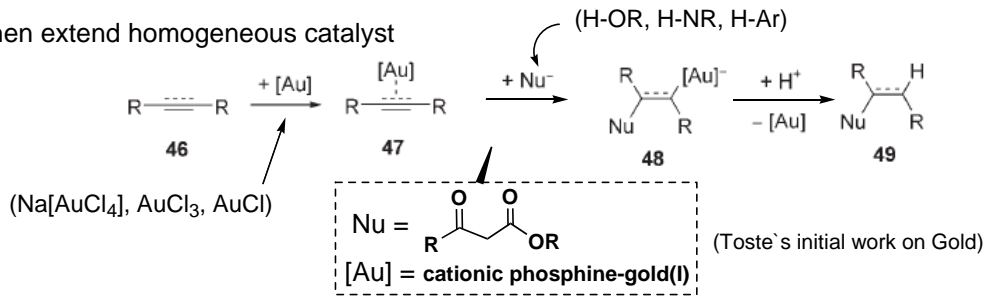
> intrinsically π -electrophilic

first recognized in heterogeneous catalyst

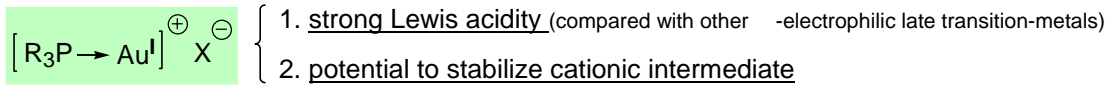


G. J. Hutchings (*J. Cat.* **1985**, 96, 292.)

then extend homogeneous catalyst



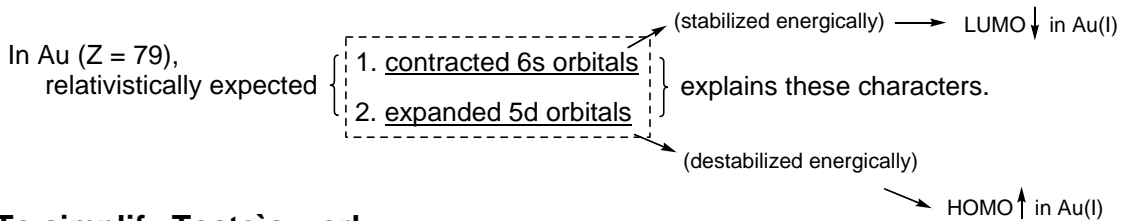
(His understanding from experiments)



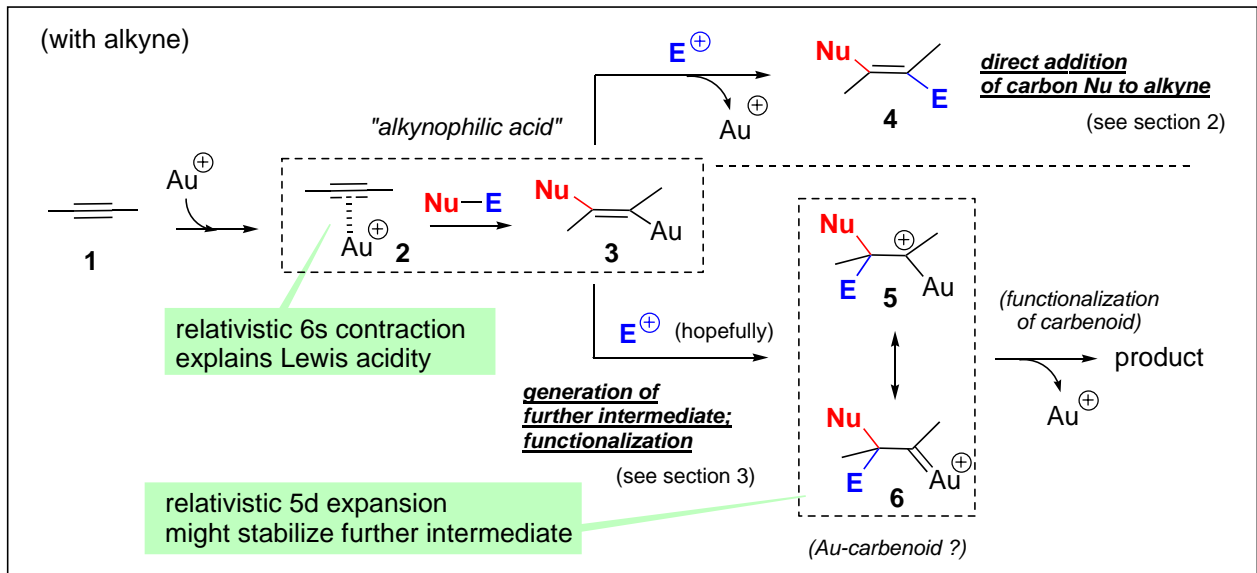
> Relativistic effect

(量子化学の世界において相対性理論を加味した場合に出てくる効果...らしい)

should be considered when investigating (calculating) the electronic structure of heavy atoms (> 5th-row)



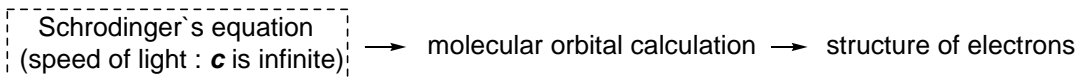
> To simplify Toste's work



1. Theoretical chemistry of Gold

1-1 Relativistic effects

> quantum mechanics + special relativity



· the average radial v of the 1s electrons

$$v = Z \text{ au}$$

Z: atomic number
($c = 137 \text{ au}$)

⇒ In heavy atom ($Z > 4-50$), v has significant value relative to c

↓
consideration of special relativity

Dirac's equation (c is finite)

The term "relativistic effects" refers to any phenomenon resulting from the need to consider velocity as significant relative to the speed of light.

> one basic consequence of special relativity

$$m = m_0 / \sqrt{1 - (v/c)^2}$$

m : corrected mass
 m_0 : non-relativistic (rest) mass

mass increases towards infinity as a body's v approaches c

> effects

Effect 1: The Relativistic Contraction

Bohr radius: $a_0 = 4\pi\epsilon_0\hbar^2 / mZe^2 = \frac{\hbar^2}{mc^2}$

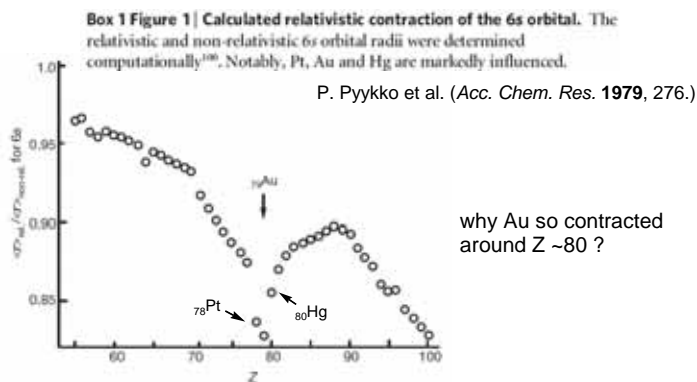
m が相対論の効果で増加
 a_0 は減少

(supported by calculation)

(expected r for valence s)

	Cu(4s)	Ag(5s)	Au(6s)
r [au]	3.2	3.4	3

P. S. BAGUS (Chem. Phys. Lett. 1975, 408.)



· contraction of the 1s and all s and p orbitals.



Stabilization of orbital energies

Practically, contraction is only significant for elements in which the 4f and 5d orbitals are filled

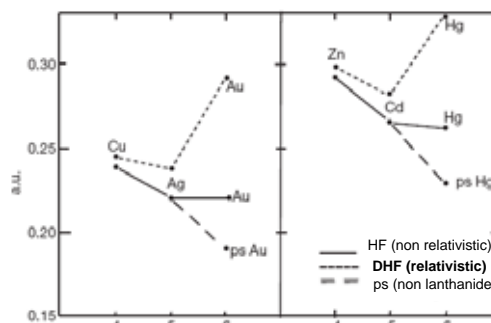
why Au so contracted around $Z \sim 80$?

· **electrons are closer to the nucleus; have greater ionization energies.**

(supported by calculation) →

	10	11	12
4	28 Ni 58.69 4s ² 3d ⁸ 7.635	29 Cu 63.546 4s ¹ 3d ¹⁰ 7.726	30 Zn 65.39 4s ² 3d ¹⁰ 9.394
5	46 Pd 106.42 4d ¹⁰ 8.34	47 Ag 107.8682 5s ¹ 4d ¹⁰ 7.576	48 Cd 112.411 5s ² 4d ¹⁰ 8.993
6	78 Pt 195.08 6s ⁴ 5d ⁸ 9.0	79 Au 196.96654 6s ¹ 5d ¹⁰ 9.225	80 Hg 200.59 6s ² 4f ¹⁴ 5d ¹⁰ 10.437

(experimental values)



Effect 2: The Relativistic Self-Consistent Expansion

The d and f orbitals are not contracted. (higher angular momentum, seldom descend to nucleus)

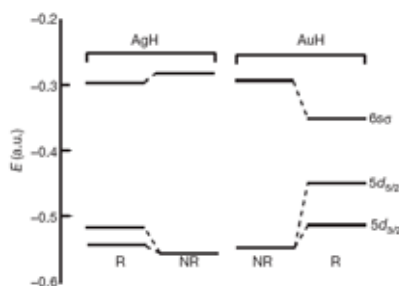
Instead, { better shielded by contracted s and p orbitals
see a weaker nuclear attraction

↓
Expansion of d and f orbitals ⇒ Destabilization of orbital energies

Effect 3: The Spin-Orbit splitting

Au	relativistic effects	↙	6s orbitals contracted	→	stabilizing
	↘	5d orbitals expanded	→	destabilizing (and splitting)	

> these effects are reflected in MO calculation



P. Pyykko et al. (*Acc. Chem. Res.* **1979**, 276.)

Figure 1 | Comparison of AuH and AgH bond energies. Calculated (Hartree-Fock) molecular orbital energies for AgH and AuH are shown with (R) and without (NR) consideration of relativistic effects⁵. In the non-relativistic calculation, the two molecules had similar bond energies. In the relativistic calculation, the 6s contraction resulted in a far stronger AuH σ -bond. (Reprinted from ref. 4, with permission from the American Chemical Society.)

1-2 Other theoretical aspects

> aurophilicity

the tendency for Au–Au interactions to be stabilizing on the order of hydrogen bonds (might be important for neutral complex (LAgX etc..))

> [Me₂Au^I][⊖]

not particularly nucleophilic relative to the corresponding Cu^I (and Ag^I) complexes.

E. Nakamura et al. (*J. Am. Chem. Soc.* **2005**, 127, 1446.)

> Me₂RAu^{III}L (R = Me or allyl, L = PMe₃)

reductive elimination is relatively disfavoured as well.

{
 ⇒ Au^I and Au^{III} complexes do not readily cycle between oxidation states.
 (of course exception exists)
 (+ from experiments)
 ⇒ tolerate both oxygen and acidic protons,

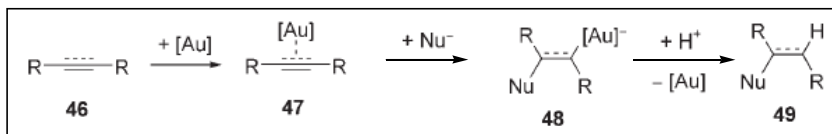
@ With its unique properties strongly influenced by relativistic effects, theoretical chemists have much attention to gold.

review P. Pyykko (*Angew. Chem. Int. Ed.* **2004**, 43, 4412.)

(pp 4424) one can regard the moiety [AuPR₃]⁺ as a σ -acceptor in analogy to H⁺.

quite a lot ! review

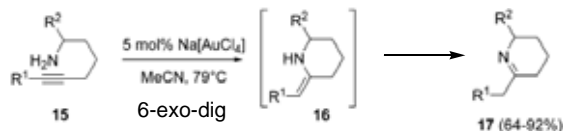
- A. S. K. Hashmi (*Angew. Chem. Int. Ed.* **2005**, *44*, 6990-6993)
- A. S. K. Hashmi and G. J. Hutchings (*Angew. Chem. Int. Ed.* **2006**, *45*, 7896-7936)
- A. S. K. Hashmi (*Chem. Rev.* **2007**, *107*, 3180-3211)
- D. J. Gorin and F. D. Toste (*Nature* **2007**, *446*, 395-403)



2-1 Heteroatom Nu

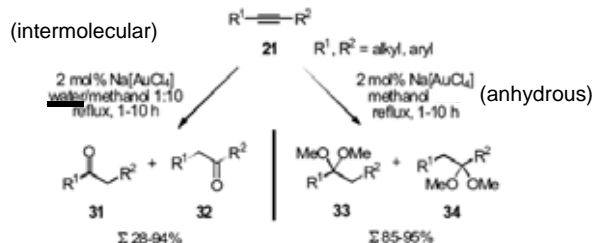
> initially Au^{III} halide

(intramolecular)



@ Pd^{II} unsatisfactory results

Utimoto. K. et al. (*Heterocycle*. **1987**, *96*, 292.)



@ internal --- regio mixture, terminal --- Markovnikov

@ K[Au(CN)₂] is inactive

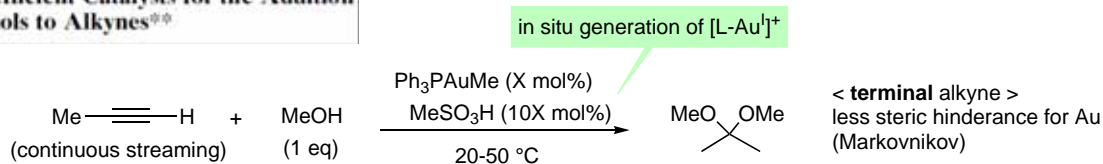
@ Na[AuCl₄] quickly reduced to metallic Au (TON >50)

Utimoto. K. et al. (*J. Org. Chem.* **1991**, *96*, 292.)

> cationic phosphineAu^I

Cationic Gold⁰ Complexes: Highly Efficient Catalysts for the Addition of Alcohols to Alkynes^{φφ}

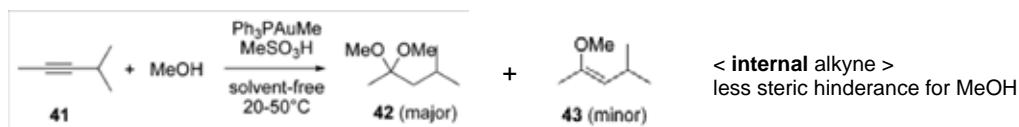
J. H. Teles et al. (*Angew. Chem. Int. Ed.* **1998**, *37*, 1415)



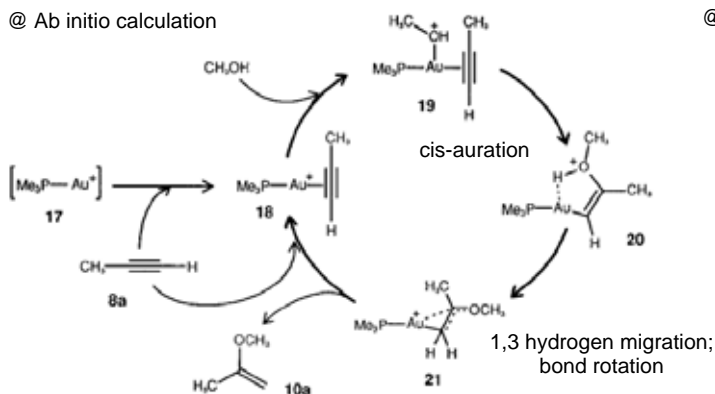
→ TON up to 50000! (0.00002 mol%), TOF up to 5400 h⁻¹ (cf Hg^{II} quickly reduced to metallic Hg (TON ~100))

[L-Au]^{I+} → the initial TOFs [h⁻¹]: Ph₃As (430) < Et₃P (550) < Ph₃P (610) < (4-F-C₆H₄)₃P (640) < (MeO)₃P (1200) < (PhO)₃P (1500)
electron-poor ligands lead to an increase in activity, but the stability decreases.

[Ph₃PAu^IX] → the initial TOFs [h⁻¹]: I⁻ (2) < Cl⁻ (7) < NO₃⁻ ~ CF₃COO⁻ ~ CH₃SO₃⁻ (700)
progresses from soft to hard anions

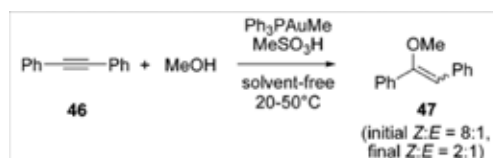


@ Ab initio calculation



Scheme 3. Proposed mechanism for the addition of methanol to propyne catalyzed by the trimethylphosphane-gold(I) cation.

@ experimental data



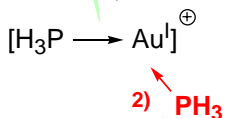
intuitively, trans-auration acceptable

theoretically, cis-auration



far more covalent robust

in reaction
2nd PH_3 is \equiv



$Au(I)^+$ is a large, diffuse cation sharing positive charge with the phosphine ligand,

one might expect **orbital rather than charge interactions** in binding a second ligand. "soft"

6s orbital of $[R_3PAu]^+$ can further accept electrons (contracted 6s)
keep strong Lewis acidity

Table 3. NBO Population Analysis for $[M(PH_3)_n]^+$ (M = Cu, Ag, Au)^a

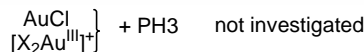
compd	q(M)	q(P)	n(d)	n(s)	n(p)
AuPH ₃ ⁺	0.66	0.25	9.890	0.438	0.011
Au(PH ₃) ₂ ⁺	0.36	0.27	9.875	0.796	0.011
Au(PH ₃) ₃ ⁺	0.55	0.16	9.833	0.519	0.003
AgPH ₃ ⁺	0.47	0.18	9.858	0.627	0.030
Ag(PH ₃) ₂ ⁺	0.65	0.11	9.901	0.423	0.010
Ag(PH ₃) ₃ ⁺	0.50	0.16	9.854	0.584	0.051
AgPH ₃ ⁺	0.64	0.11	9.893	0.417	0.024
Ag(PH ₃) ₂ ⁺	0.86	0.07	9.973	0.156	0.005
Ag(PH ₃) ₃ ⁺	0.61	0.15	9.923	0.449	0.006
Ag(PH ₃) ₄ ⁺	0.63	0.12	9.938	0.405	0.014
Ag(PH ₃) ₅ ⁺	0.60	0.12	9.939	0.417	0.025
CuPH ₃ ⁺	0.85	0.07	9.971	0.168	0.007
Cu(PH ₃) ₂ ⁺	0.61	0.15	9.936	0.444	0.009
Cu(PH ₃) ₃ ⁺	0.60	0.13	9.940	0.430	0.020
Cu(PH ₃) ₄ ⁺	0.56	0.15	9.931	0.456	0.033

^a Nonrelativistic values are set in italics. Charges q and metal orbital populations n.

Table 4. NBO Population Analysis for $[MCl(PH_3)_n]$ (M = Cu, Ag, Au)^a

compd	q(M)	q(P)	q(Cl)	n(d)	n(s)	n(p)
ClAuPH ₃	0.40	0.30	-0.64	9.763	0.772	0.046
ClAu(PH ₃) ₂	0.59	0.18	-0.73	9.849	0.590	0.042
ClAu(PH ₃) ₃	0.40	0.31	-0.65	9.766	0.774	0.043
ClAu(PH ₃) ₄	0.59	0.19	-0.74	9.851	0.507	0.029
ClAg(PH ₃) ₃	0.51	0.21	-0.82	9.845	0.548	0.059
ClAg(PH ₃) ₄	0.64	0.16	-0.84	9.886	0.390	0.041
ClAg(PH ₃) ₅	0.60	0.17	-0.73	9.892	0.447	0.041
ClAg(PH ₃) ₆	0.64	0.17	-0.78	9.921	0.379	0.023
ClAg(PH ₃) ₇	0.61	0.16	-0.83	9.932	0.371	0.039
ClCuPH ₃	0.61	0.18	-0.74	9.905	0.421	0.050
ClCu(PH ₃) ₂	0.63	0.17	-0.80	9.931	0.376	0.040
ClCu(PH ₃) ₃	0.60	0.19	-0.82	9.929	0.398	0.031

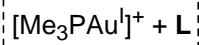
^a Nonrelativistic values are set in italics. Charges q and metal orbital populations n.



P. Schwerdtfeger et al. (*Inorg. Chem.* **2003**, *42*, 1334.)

> Stability of $[R_3PAu]^+ + L$

1) with several ligand



stability [kJ/mol]:

CH_2Cl_2 (+63) < H_2O (+44) < acetylene (+38) < MeOH ~ 1,4-dioxane (+24)
< **propyne** (+18) < THF (+2) < **2-butyne** (0) < Me_2S (-18) < Ph_3P (-114)

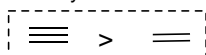
carbophilic rather than oxophilic

substituted alkynes are better ligands than MeOH or dioxane

J. H. Teles et al. (*Angew. Chem. Int. Ed.* **1998**, *37*, 1415)

2) alkyne vs alkene

Experimentally, reactivity of Nu is



but theoretical stability is inverse

$E(Au^+-alkyne) < E(Au^+-alkene)$ (~10 kcal/mol)

alkynes LUMOs intrinsically lower than alkenes (~0.5eV)
That is important for Nu addition.

W. Koch et al. (*J. Phys. Chem.* **1996**, *100*, 12253)

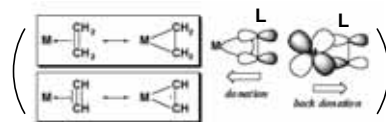
V. M. Rayon et al. (*J. Phys. Chem. A* **2004**, *108*, 3134)

> Backdonation from $[R_3PAu]^+$

1) to alkyne / alkene (by calculation)

Backbonding to antibinding orbital (of alkene / alkyne) is poor (smaller than Cu)

render alkyne / alkene more electron deficient



2) to carbene (their explanation, not by calculation ?)

Backbonding to antibinding orbital also might be poor

but backbonding (from Au^I 5d) to **lower-energy (than antibonding) non-bonding p-orbitals** (of carbene) might be suitable

relativistically expanding (destabilizing)

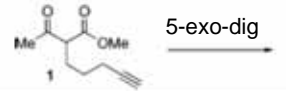
This can stabilize carbenoid intermediate in the Au^I catalyzed reaction

> (Nu = β -keto ester)

Gold(I)-Catalyzed Conia-Ene Reaction of β -Ketoesters with Alkynes
 Joshua J. Kennedy-Smith, Steven T. Staben, and F. Dean Toste*
 Center for New Directions in Organic Synthesis, Department of Chemistry, University of California, Berkeley, California 94720

(*J. Am. Chem. Soc.* **2004**, 126, 4526)

Table 1. Efficiency of Group XI Metal Catalysts in the Conia-Ene Reaction



entry	conditions	time	% conv. to 2 ^a
1	10 mol % AgOTf, DCE, rt	18 h	50
2	10 mol % AgOTf, 10 mol % PPh ₃ , DCE, rt	18 h	0
3	10 mol % AuCl ₃ , DCE, R.T.	30 min	30 ^b
4	10 mol % (PPh ₃)AuCl, DCE, 60 °C	6 h	0
5	10 mol % (PPh ₃)AuOTf, DCE, rt	<15 min	>95
6	10 mol % [(CyNC) ₂ Au]PF ₆ , DCE, rt	14 h	0
7	1 mol % (PPh ₃ Au) ₂ O]BF ₄ , DCE, 60 °C	1 h	0
8	1 mol % [(RNC) ₂ Au] ⁺ OTf, DCE, rt	<15 min	>95

^a As judged by ¹H NMR. ^b No starting material (1) remained.

- #1 [Ag^I]⁺ weak Lewis acidity
- #2 [R₃PAg^I]⁺ insufficient
- #3 [Au^{III}X₃] sufficient Lewis acidity (?) but undesired path
- #4 [R₃PAu^IX] insufficient
- #5 [R₃PAu^I]⁺ sufficient Lewis acidity
- #6 [(RNC)₂Au^I]⁺ insufficient

Table 2. Gold(I)-Catalyzed Conia-Ene Reaction^a

entry	substrate	time	product	yield (d.r.)
1	R = Me, R' = Me (1)	15 min	(2)	94%
2	R = Ph, R' = Et (3)	18 h	(4)	93%
3	R = Me, R' = ^t Bu (5)	30 min	(6)	81%
4	R = Me, R' = CH ₂ CCH (7)	60 min	(8)	79%
5	n = 1 (9)	1 h	(10)	90%
6	n = 2 (11)	18h	(12)	90% ^b
7	(13)	16 h	(14)	88%
11	(21)	5 min	(22)	99%

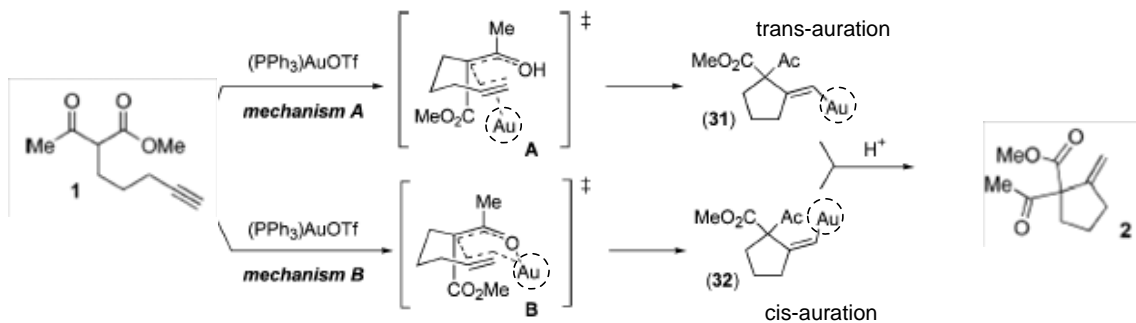
^a Reaction Conditions: 1 mol % (PPh₃)AuCl, 1 mol % AuOTf, 0.4 M (ketoester) in dichloromethane, rt. ^b 5 mol % (PPh₃)AuCl and 5 mol % AgOTf.

terminal alkyne only

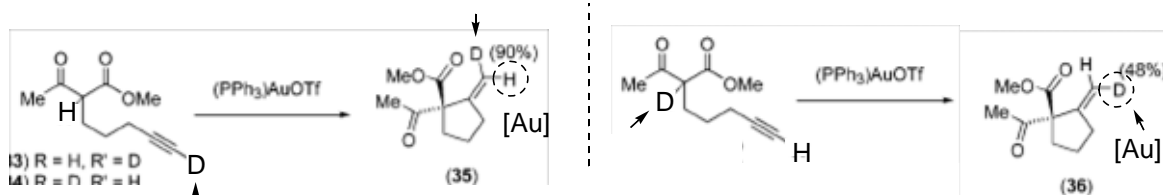
cationic - Au^I - mono-phosphine

- ⊙ Au vs Ag --- relativistic contraction of s orbital
- ⊙ [Au^I]⁺ vs Au^I --- aurophilicity (?)
- ⊙ Au^I vs Au^{III} --- unknown (for regio, see (Nu = Ar-H))
- ⊙ Au vs Pt --- not mentioned (possible?)

nucleophilic attack on a Au(I)-alkyne complex by enol



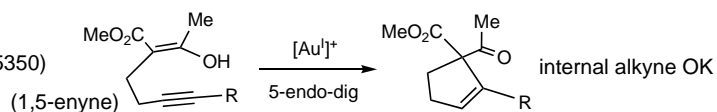
formation of a Au-enolate followed by a cis-carboauration



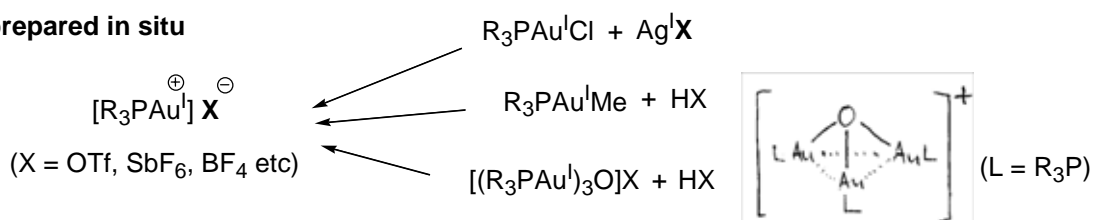
Trans-auration → **Now generally accepted.**

(mechanism A)

5-endo-dig (*Angew. Chem. Int. Ed.* **2004**, 43, 5350)



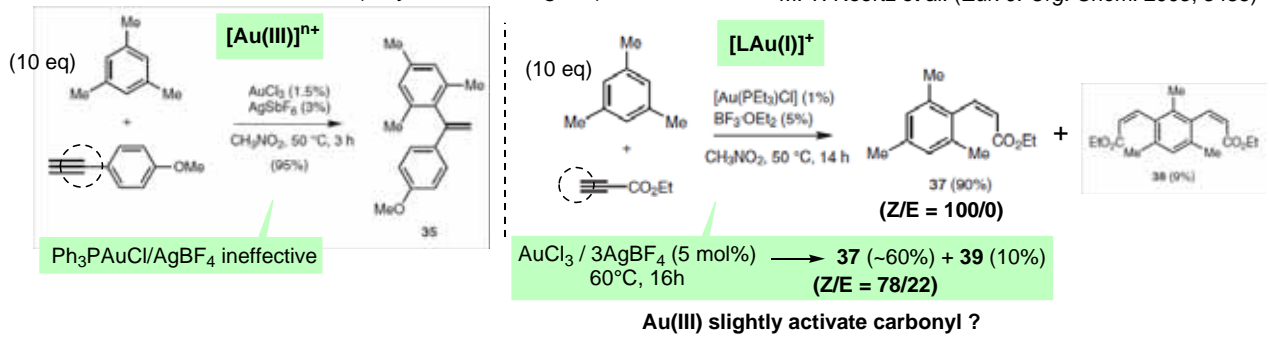
> usually prepared in situ



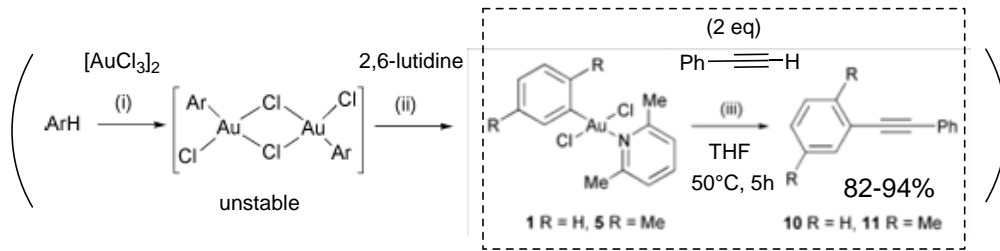
@ Regioselectivity is inverted between Au(I) and Au(III) with terminal alkyne,

(only intrinsical regio ?)

M. T. Reertz et al. (*Eur. J. Org. Chem.* **2003**, 3485)



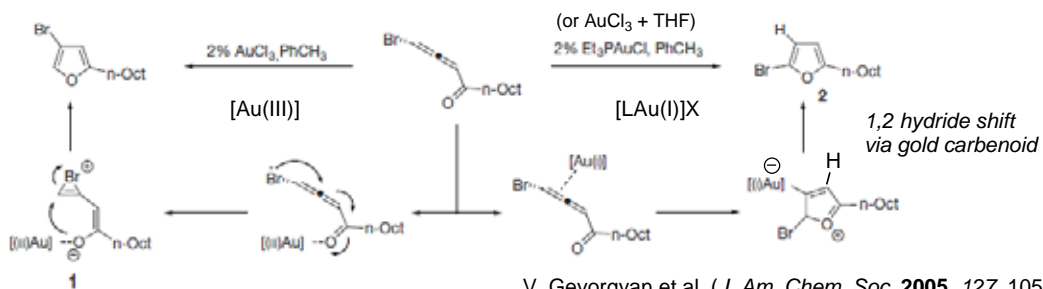
@ Ar-[Au] might be unlikely instead of electrophilic activation of alkyne



Y. Fuchita et al. (*J. Chem. Soc., Dalton. Trans.* **2001**, 2330)

> Au^I vs Au^{III} (Nu = -C=O)

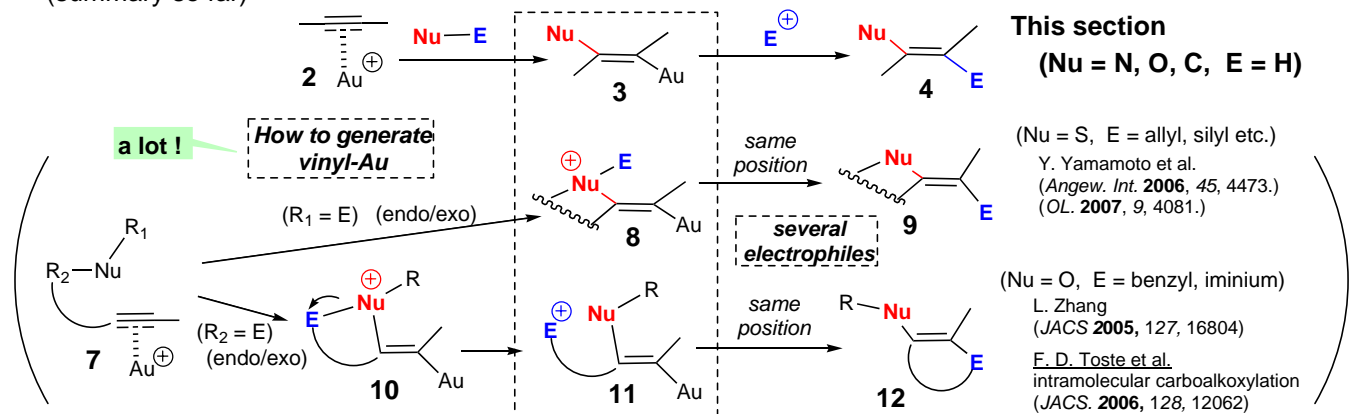
@ They said "oxophilic Au^{III} species" and "π-philic Au^I species"



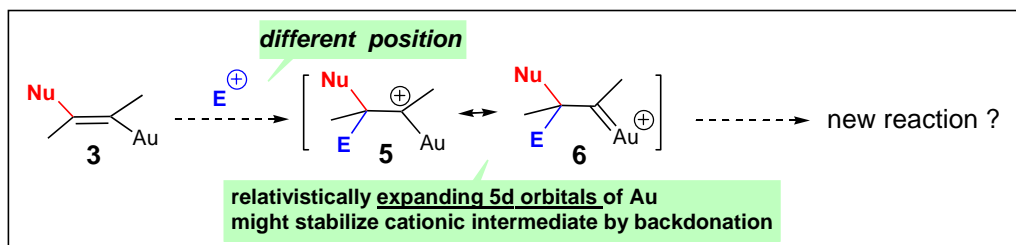
V. Gevorgyan et al. (*J. Am. Chem. Soc.* **2005**, 127, 10500)

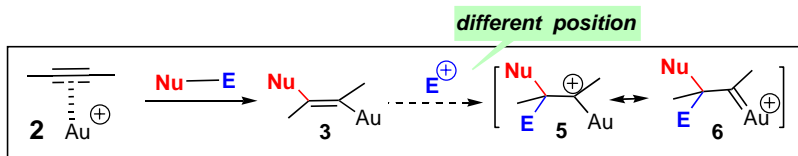
(my opinion) ⇒ Basically both Au(I) and Au(III) are π-philic
But Au(III) is slightly more oxophilic than Au(I)

(summary so far)



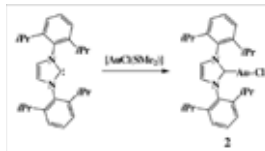
Next section
(Toste's plan)





3-1 Generation of cationic intermediates

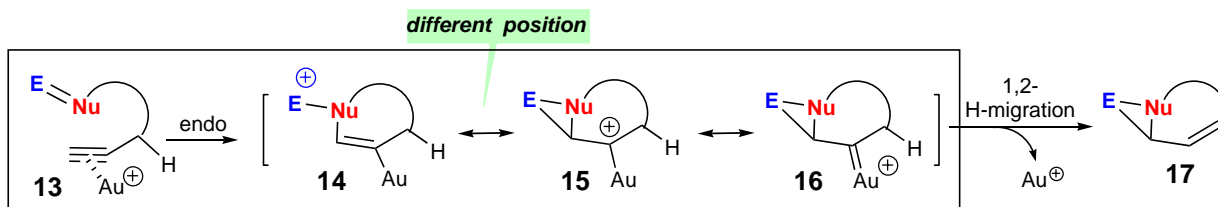
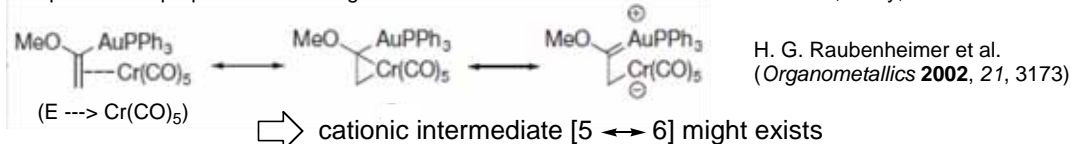
@ Au^I-NHC complexes are known



can catalyze cyclopropanation of styrene with ethyldiazoacetate

S. P. Nolan et al.
(*Angew. Chem. Int. Ed.* **2005**, *44*, 5284)

@ vinyl Au species was proposed to have significant Au carbene character on the basis of NMR, X-ray, and calculations



@ initial work of Toste

Catalytic Isomerization of 1,5-Enynes to Bicyclo[3.1.0]hexenes

Michael R. Luzung, Jordan P. Markham, and F. Dean Toste*

(*J. Am. Chem. Soc.* **2004**, *126*, 10858)

same intermediates (14-16) was proposed with Au^I

{ Nieto-Oberhuber, C. et al.
(*Angew. Chem. Int. Ed.* **2004**, *43*, 2402)
(*Chem. Eur. J.* **2006**, *12*, 1677.)
Furstner, A. et al.
(*J. Am. Chem. Soc.* **2004**, *126*, 8654)

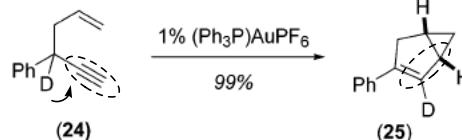
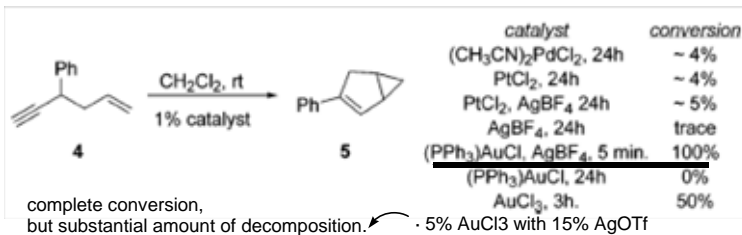
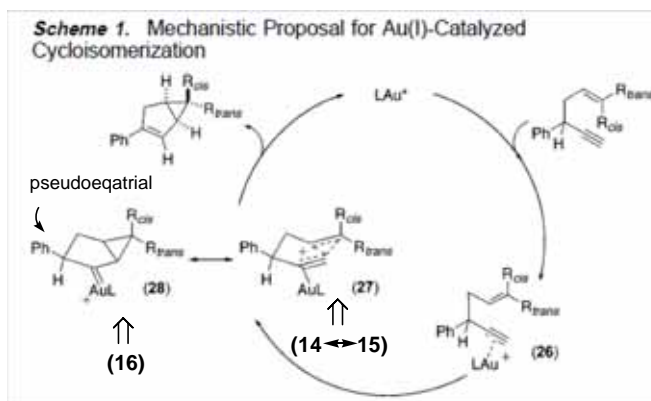


Table 1. Au(I)-Catalyzed Synthesis of Bicyclo[3.1.0]hexenes^a

entry	substrate	(mol%) catalyst	product	yield
1	Ar = Ph (4)	1% (Ph ₃ P)AuPF ₆	(5)	99%
2	Ar = MeO (6)	2% (Ph ₃ P)AuPF ₆	(7)	99%
3	Ar = Br (8)	1% (Ph ₃ P)AuBF ₄	(9)	95%
4	Ph (10)	1% (Ph ₃ P)AuBF ₄	(11)	94%
5	Ph (12)	3% (Ph ₃ P)AuBF ₄	(13)	96%
6	Ph (14)	1% (Ph ₃ P)AuBF ₄	(15)	99% (>99:1 dr) ^b
7	Ph (16)	1% (Ph ₃ P)AuBF ₄	(17)	96% (97:3 dr) ^b

^a Reaction conditions: 0.5 M 1,5-enyne in dichloromethane, rt.

stereospecific



• Au might lower the barrier to cationic intermediate by backbonding.

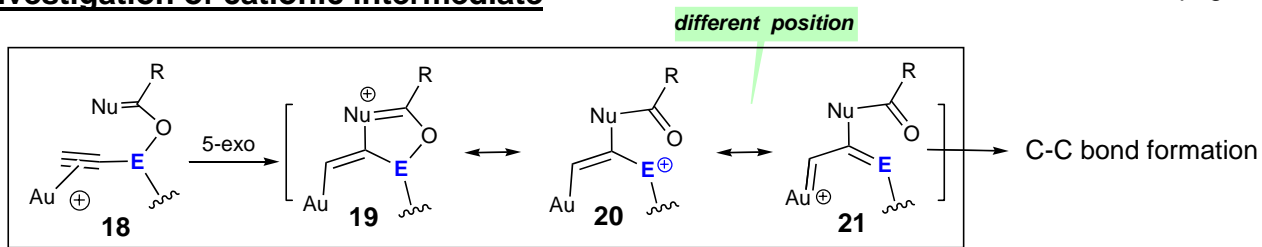
"expanded 5d"

Anyway... carbenoid or cationic ?

• With Au(III), analogous intermediates were proposed.

• Pt(II) shows similar reactivity (relativistic effect also influence Pt)

activation of alkynes { cationic Au(I) --- even in the presence of strongly donating ligands, such as phosphines
Pt(II) --- simple salts or CO complex reactivity tuning, stereoselectivity

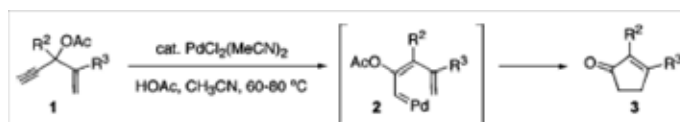


Synthesis of 2-Cyclopentenones by Gold(I)-Catalyzed Rautenstrauch Rearrangement

(*J. Am. Chem. Soc.* **2005**, *127*, 5802)

Xiaodong Shi, David J. Gorin, and F. Dean Toste*

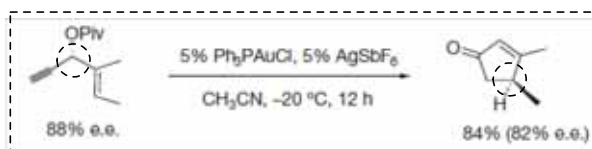
Original Rautenstrauch rearr.



(*J. Org. Chem.* **1984**, *49*, 950)

metal carbene intermediate proposed

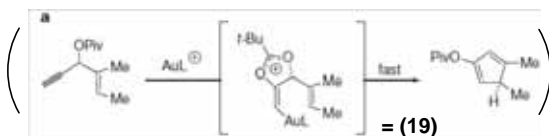
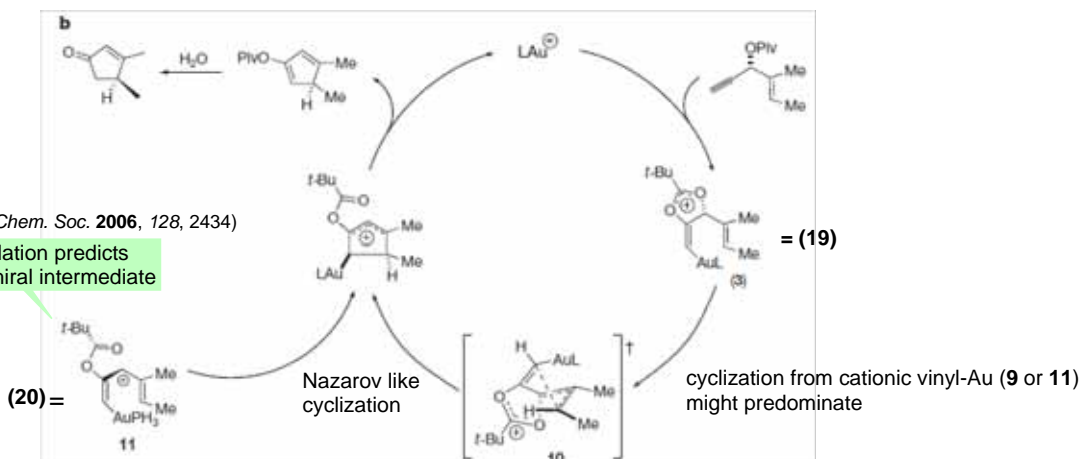
"a method for generation of metal-carbenoid"



Toste's case
chirality transfer
not Au-carbene (21)

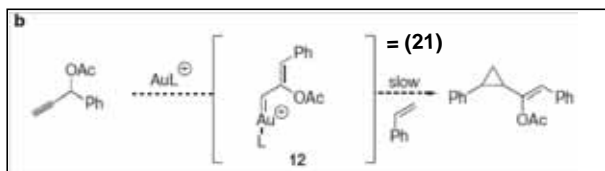
A. R. de Lera (*J. Am. Chem. Soc.* **2006**, *128*, 2434)

DFT calculation predicts
helically chiral intermediate



carbenoid or cationic? ⇔ cationic

on a fast time scale
(intramolecular reaction)

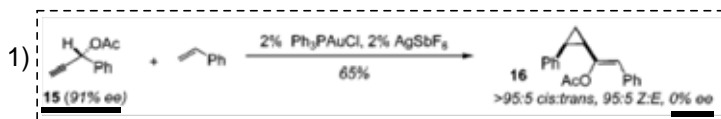


toward highly carbenoid character

Gold(I)-Catalyzed Stereoselective Olefin Cyclopropanation

Magnus J. Johansson, David J. Gorin, Steven T. Staben, and F. Dean Toste*

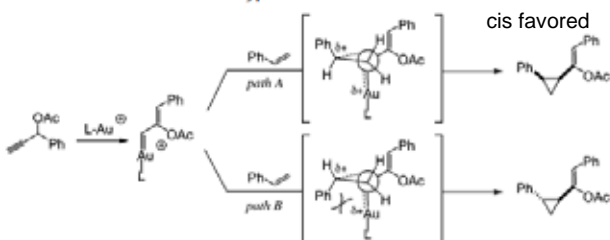
(*J. Am. Chem. Soc.* **2005**, *127*, 18002)



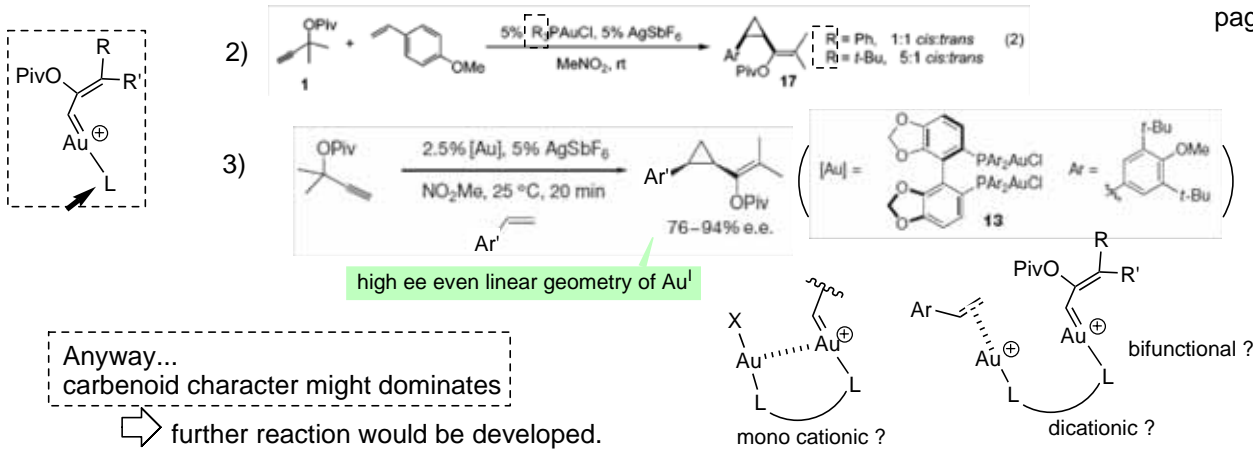
stereochemical information
was not conserved.

"carbenoid"

Scheme 1. Mechanistic Hypothesis



might be concerted mechanism

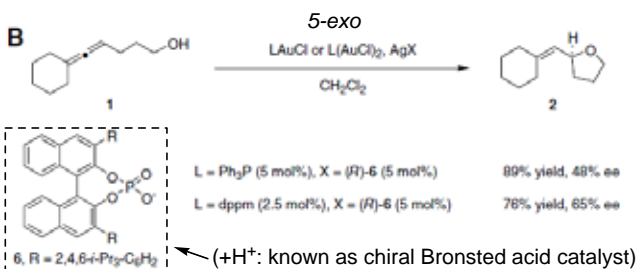
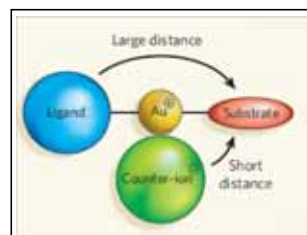



> to conquer demerit of linear coordination geometry of Au^I for ee

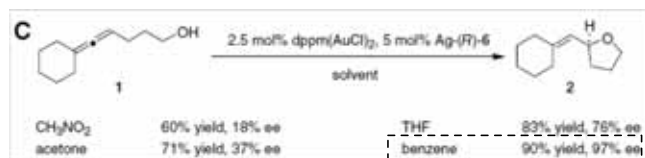
A Powerful Chiral Counterion Strategy for Asymmetric Transition Metal Catalysis

(*Science*, 2007, 317, 496)

Gregory L. Hamilton, Eun Joo Kang, Miriam Mba, F. Dean Toste*



- @ standard chiral phosphine poor ee (<10%ee)
- @ only PPh₃AuCl or Ag-6 or  : no rxn
- @ dinuclear Au^I better
- @ less polar solvent best
- ee depends on the proximity of the counterion to the cationic gold center



@ match-mismatch pairing between chiral phosphine and chiral counterion observed in other systems.

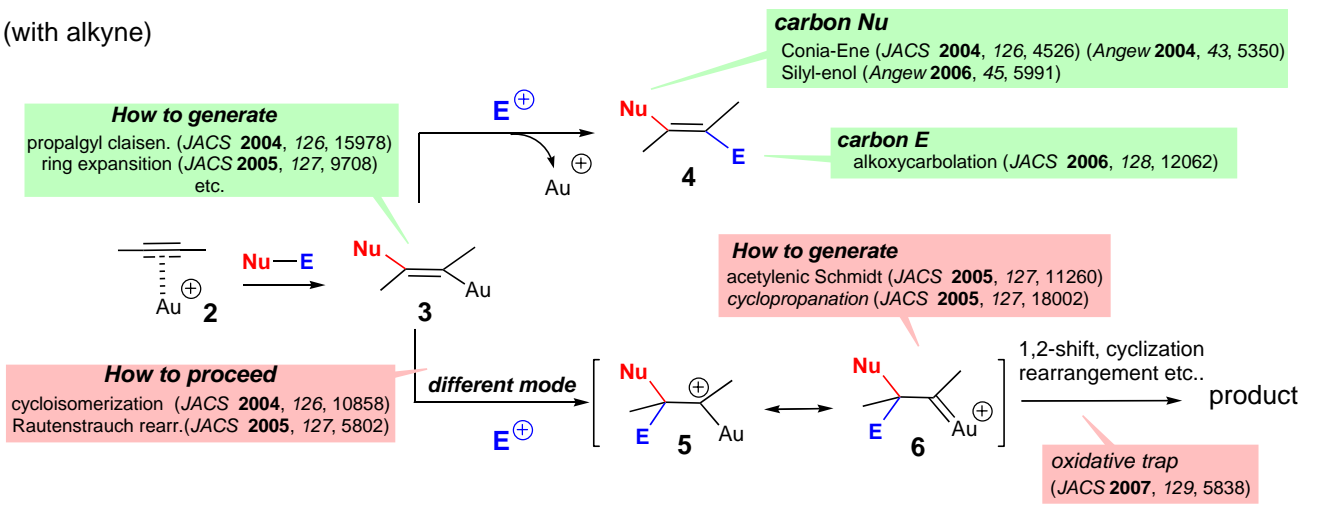
might extend standard transition metal catalysed process

cf) hydroamination of allene with chiral phosphine gold (*J. Am. Chem. Soc.* 2007, 129, 2452)

< summary >

Au^I 6s contraction strong Lewis acidity (Nature 2007, 446, 395-403)
 5d expansion backdonation for carbenoid

(with alkyne)



other works about Au { (with allene)
 (cycloaddition)
 (asymmetric variants)