Formation of Cyclopropanes via Activation of (γ-Methoxy)alkyl Gold(I) Complexes with Lewis Acids

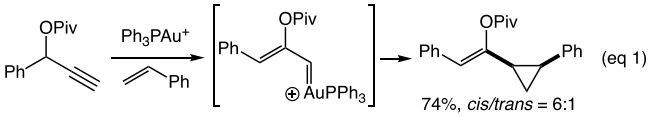
Nana Kim and Ross A. Widenhoefer*

Department of Chemistry, French Family Science Center, Duke University, Durham, North Carolina 27708, United States

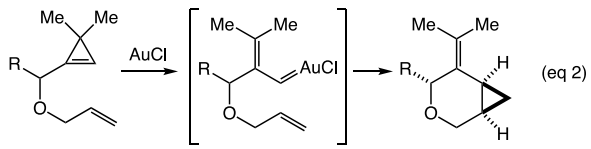
ABSTRACT: Treatment of the gold 3-methoxy-3-phenylpropyl complex (**P**)AuCH$_2$CH$_2$CH(OMe)Ph [**P** = P(*t*-Bu)$_2$*o*-biphenyl] with AlCl$_3$ at –78 °C led to immediate (≤5 min) formation of a 4:1 mixture of phenylcyclopropane and (1-methoxypropyl)benzene in 86 ± 5% combined yield. Lewis acid activation of the stereochemically pure isotopomer *erythro*-(**P**)AuCH$_2$CHDCH(OMe)Ph led to formation of *cis*-2-deuterio-1-phenylcyclopropane in 84 ± 5% yield as a single stereoisomer, which established that cyclopropanation occurred with inversion of the γ-stereocenter. Similarly, ionization of the stereochemically pure cyclohexyl gold complex *cis*-(**P**)AuCHCH$_2$CH(OMe)CH$_2$CH$_2$CH$_2$ at –78 °C formed bicyclo[3.1.0]hexane in 82% ± 5% yield, which validated a low energy pathway for cyclopropanation involving inversion of the α-stereocenter. Taken together, these observations are consistent with a mechanism for cyclopropane formation involving backside displacement of both the Cγ leaving group and the Cα (L)Au$^+$ fragment via a W-shaped transition state.

INTRODUCTION

Cationic gold(I) complexes have attracted considerable attention over the past decade owing to the ability of these complexes to catalyze a diverse range of transformations, many of which have been postulated to involve cationic gold carbene intermediates.[1] Of the transformations associated with cationic gold carbene complexes, gold to alkene carbene transfer (cyclopropanation) has perhaps generated the most interest (eqs 1 and 2).[2,3] This is due in part to the stereoselectivity of gold-catalyzed cyclopropanation, which occurs with retention of alkene configuration and often with high levels of diastereo- and enantioselectivity, and to the diverse range of carbene precursors including 1,*n*-enynes, diazo compounds, propargylic esters, cyclopropenes, 1,3,5-cycloheptatrienes, and simple alkynes in combination with nucleophilic oxidants. [2,3] There has likewise been considerable effort directed toward understanding the structure and behavior of cationic gold carbene complexes[4] and toward the synthesis of well-defined gold carbene complexes that undergo carbene transfer to alkenes.[5,6]



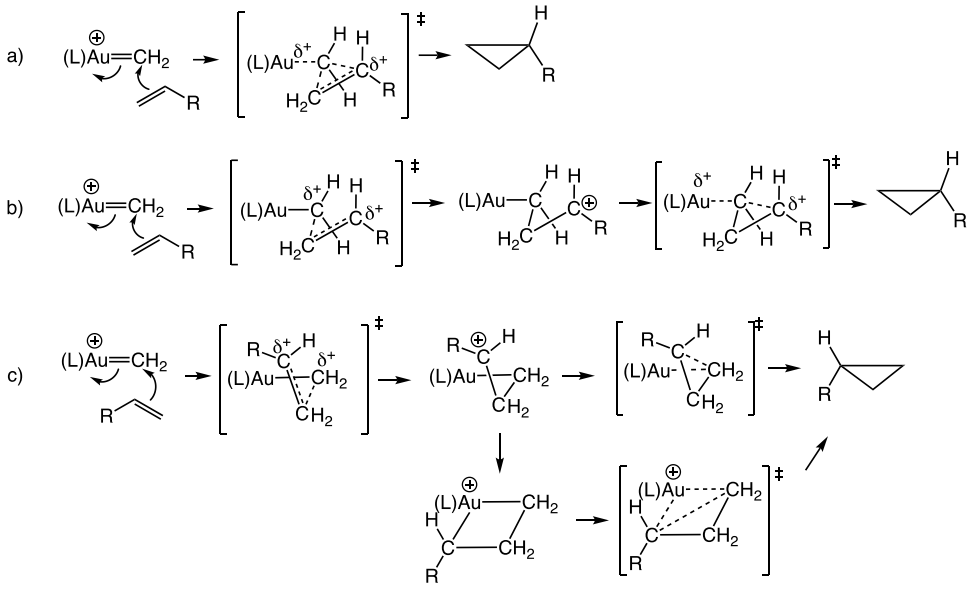
(eq 1)

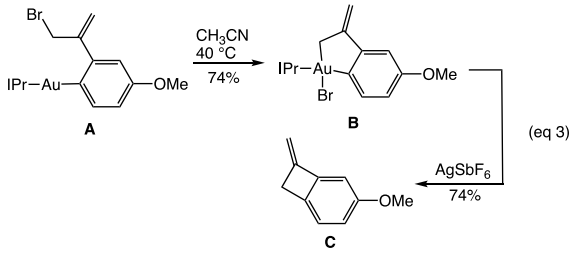


(eq 2)

Despite the prevalence of gold to alkene carbene transfer, the intimate mechanisms of these transformations remain unclear. Both computation[7-10] and experiment[7] point to mechanisms for gold to alkene carbene transfer initiated by nucleophilic attack of the alkene on the electrophilic carbene carbon, but within this framework of electrophilic cyclopropanation,[11] a number of alkene- and carbene-dependent mechanisms have been postulated. For example, computational analysis of carbene transfer from gold to aliphatic alkenes supports mechanisms involving concerted, asynchronous cyclopropane formation involving more advanced C–C formation to the less substituted alkene carbon atom coupled with backside displacement of the (L)Au$^+$ fragment (Scheme 1, path a). Conversely, computational analyses of carbene transfer to vinyl ethers or vinylarenes support stepwise mechanisms involving formation of a γ-carbenium ion intermediate that collapse via backside displacement of the (L)Au$^+$ fragment (Scheme 1, path b).[7-11] In the specific case of the cyclopropanation of styrene, calculations predict that the γ-carbenium ion intermediate collapses faster than C–C bond rotation, leading to retention of alkene configuration,[7] consistent with experimental observations.[2] However, these analyses also identified low-lying reaction pathways for cyclopropane formation involving cationic Au(III) metallacyclobutane intermediates, which form cyclopropanes via reductive elimination.[7-11] The viability of a metallacyclobutane pathway for gold-catalyzed alkene cyclopropanation is likewise supported by the oxidative addition of the gold(I) aryl complex **A** to form gold(III) metallacyclopentane **B** and facile silver-induced reductive elimination of **B** to form benzocyclobutene **C** (eq 3).[12]

Scheme 1. Representative potential reaction pathways for gold to alkene carbene transfer including (a) concerted with backside displacement, (b) stepwise with backside displacement, and (c) stepwise with frontside displacement.





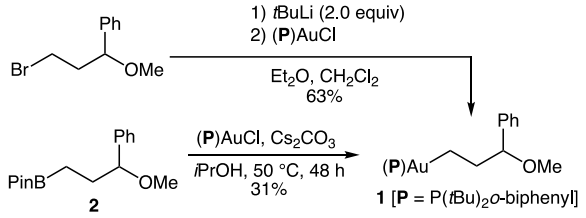
Common to the potential mechanisms for gold to alkene carbene transfer is the involvement of an intermediate and/or transition state possessing full or partial positive charge on the carbon atom γ to gold that collapses via electrophilic attack of Cγ on Cα with concomitant displacement of the (L)Au fragment (Scheme 1). Electrophilic attack of Cγ on Cα of a gold alkyl complex has also been invoked on the basis of DFT calculations as the product-releasing step in the gold-catalyzed cyclopropanation of alkenes and allenes with stabilized sulfonium ylides.[13] However, no direct experimental observations support the electrophilic attack of Cγ on Cα of a gold alkyl complex to form cyclopropane,[14] although analogous reactivity has been validated for iron,[15,16] platinum,[17] group IV[18-20] and other nontransition metals.[21-25]

We sought to validate the formation of cyclopropanes via the electrophilic attack of Cγ on Cα of a gold alkyl complex by independently generating gold alkyl complexes bearing an electrophilic γ-carbon atom. In addition to establishing the importance of an electrophilic carbon atom γ to gold in the carbene transfer process, stereochemical analysis of cyclopropane formation might provide additional insight into the intimate mechanism of gold to alkene carbene transfer, in particular by distinguishing between front side and backside displacement of the (L)Au fragment. Here we report that Lewis acid activation of gold (γ-methoxy)- and (γ-methylthio)propyl complexes forms cyclopropanes. Stereochemical analysis of cyclopropane formation supports a mechanism involving inversion of configuration of both the Cα and Cγ atoms, consistent with backside displacement of both the leaving group and (L)Au fragment via a W-shaped transition state.

RESULTS AND DISCUSSION

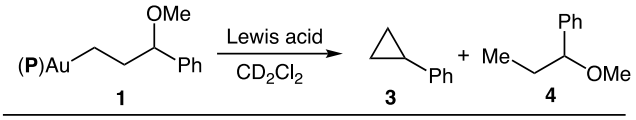
Lewis acid activation of a gold (γ-methoxy)propyl complex. We have previously demonstrated the Lewis acid-mediated ionization of gold acetylide and vinyl complexes bearing a γ-methoxy group to form thermally unstable cationic gold(I) allenylidene[26] and vinyl carbene[6] complexes, respectively. Similarly, Brookhart and Casey have independently demonstrated the Lewis acid-mediated ionization/cyclopropanation of (γ-methoxy)alkyl iron[15,16] and zirconium complexes.[20] On the basis of these precedents, we targeted the gold 3-methoxy-3-phenylpropyl complex (**P**)AuCH$_2$CH$_2$CH(OMe)Ph [**1**; **P** = P(*t*-Bu)$_2$*o*-biphenyl] as a precursor for Lewis acid-mediated cyclopropane formation, which would specifically model the intermediate and/or transition state for the cyclopropanation of styrene with the cationic gold methylidene complex [(**P**)Au=CH$_2$]$^+$. More practically, we hypothesized that the 3-phenyl group of **1** might facilitate both the displacement of the γ-leaving group and characterization of the resultant cyclopropane. Thermally stable **1** was synthesized via transmetallation of (**P**)AuCl with either (3-methoxy-3-phenylpropyl)lithium or (3-phenyl-3-phenylpropyl)pinacol borane (**2**) (Scheme 2) and was characterized by spectroscopy, mass spectrometry, and elemental analysis.[27] In particular, the ^{13}C NMR spectrum of **1** displayed a diagnostic doublet at δ 24.8 (J = 92.5 Hz) assigned to the gold-bound carbon atom.[27]

Scheme 2. Synthesis of 3-methoxy-3-phenylpropyl gold complex 1.



Treatment of **1** (24 mM) with $AlCl_3$ (1.6 eq) in CD_2Cl_2 at –78 °C led to immediate consumption of **1** to form a 4:1 mixture of phenylcyclopropane (**3**) and 1-methoxy-1-phenylpropane (**4**) in ≥86 ± 5% combined yield by ^{1}H NMR analysis (Table 1, entry 1). Although formation of the protodeauration product **4** points to the presence of trace amounts of Brønsted acid in the reaction mixture, efforts to diminish this side reaction, for example by employing silanized glassware, were largely unsuccessful. We then evaluated the efficiency of the cyclopropanation of **1** as a function of Lewis acid. TMSOTf and $BF_3{\cdot}OEt_2$ reacted rapidly (< 1 min) and quantitatively with **1** at –78 °C, but with diminished selectivity for cyclopropane **3** (Table 1, entries 2 and 3). Conversely, a mixture of TMSOTf (1.2 equiv) and pyridine (0.2 equiv) provided results comparable to $AlCl_3$, whereas $AlEt_2Cl$ activated **1** slowly at –35°C, but with enhanced (>85%) selectivity for **3** (Table 1, entries 5 and 6). Weaker Lewis acids such as CuOTf, AgOTf, $ZnCl_2$, $AlEt_3$, and PBr_3 showed no reactivity toward **1** at ambient temperature (Table 1, entries 7-12).

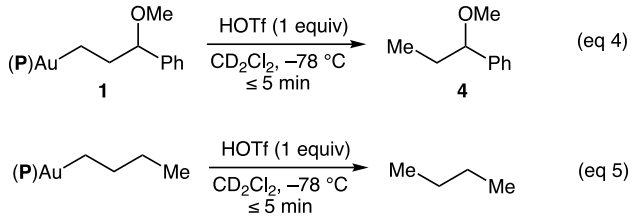
Table 1. Lewis acid-mediated cyclopropanation of 1 (~36 mM).



entry	T (°C)	time (min)	Lewis acid	yield **3** (%)[a]	yield **4** (%)[a]
1	–78	< 1 min	$AlCl_3$	69	17
2	–78	< 1 min	TMSCl	<2	>98
3	–78	< 1 min	TMSOTf	38	39
4	–78	< 1 min	TMSOTf/py	61	24
5	–78	< 1 min	$BF_3{\cdot}OEt_2$	52	26
6	–35	~ 1h	$AlEt_2Cl$	76	11
7	25	–	CuOTf	–	–
8	25	–	AgOTf	–	–
9	25	–	$ZnCl_2$	–	–
10	25	–	$AlEt_3$	–	–
11	25	–	$Al(OiPr)_3$	–	–
12	25	–	PBr_3	–	–

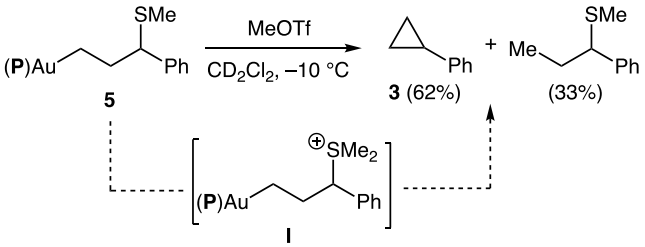
[a]Determined by ^{1}H NMR analysis of the crude reaction mixture versus internal standard.

We were surprised by the apparent high sensitivity of **1** toward protodeauration,[28] and questioned whether the γ-methoxy group facilitated protodeauration relative to a simple gold alkyl complex. However, a pair of control experiments argued against this contention as independent treatment of both **1** and the gold *n*-butyl complex (**P**)Au(CH_2CH_2 CH_2CH_3) with TfOH (24 mM; 1 equiv) at –78 °C led to immediate formation of **4** and *n*-butane, respectively as the exclusive organic products (eqs 4 and 5).



Cyclopropanation of a (γ-sulfonium)propyl gold complex. Maulide has recently reported the gold-catalyzed cyclopropanation of alkenes and allenes with stabilized sulfonium ylides.[13] DFT analysis of these transformations support mechanisms involving outer-sphere attack of ylide on a gold π-complex to form a gold (γ-sulfonium)alkyl complex followed by product-releasing electrophilic attack of Cγ on Cα with concomitant backside displacement of the (L)Au fragment.[13] We therefore sought to independently generate a gold (γ-sulfonium)alkyl complex and validate the cyclopropanation of this species. Indeed, *in situ* alkylation of the (3-methylthiol-3-phenylpropyl)gold complex **5** with methyl trifluoromethanesulfonate from –78 to –10 °C formed a 66:34 mixture of **3** and methyl(1-phenylpropyl)sulfane[29] in 95 ± 5% combined yield (^{1}H NMR) without observation of the presumed gold (γ-sulfonium) propyl intermediate **I** (Scheme 3).

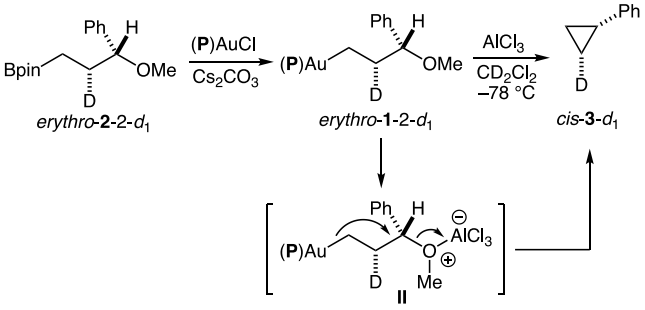
Scheme 3. Methyl triflouromethanesulfonate-mediated cyclopropanation of 5.



Stereochemistry of cyclopropane formation. Two general mechanisms exist for the electrophilic attack of Cγ on Cα of a gold alkyl complex leading to cyclopropane formation via Cα–Cγ bond formation and Cα–Au bond cleavage. One mechanism involves the backside displacement of the (L)Au$^+$ fragment leading to inversion of configuration at Cα and the second involves frontside displacement of (L)Au$^+$, either by a concerted pathway or a stepwise mechanism involving a metallacyclobutane intermediate, with retention of configuration at Cα (Scheme 1). We also considered two mechanisms for Cγ–O bond cleavage involving either concerted backside displacement of the oxonium leaving group by the Au–Cα electron pair leading to inversion of configuration at Cγ or a stepwise mechanism involving ionization followed by trapping of the resultant γ-carbenium ion, which would likely lead to partial to complete loss of configuration at Cγ. Therefore, in an effort to distinguish between these potential reaction manifolds, we investigated the stereochemistry of Lewis acid-mediated cyclopropanation of γ-methoxy gold alkyl complexes.

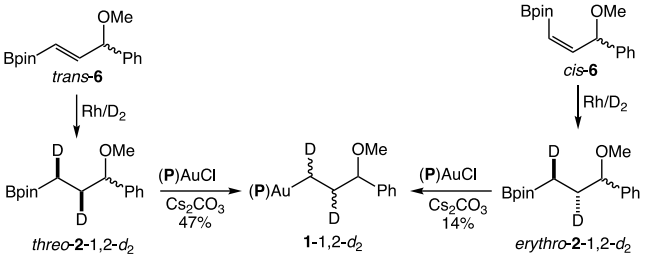
Our first objective in this area was to determine stereochemistry of the Lewis acid-mediated cyclopropanation of (3-phenyl-3-methoxy)propyl gold complexes with respect to the γ-position, which also proved critical to the determination of stereochemistry with respect to the α-position (see below). To this end, we targeted the stereochemically pure 2-deuterio-3-phenyl-3-methoxypropyl gold isotopomer *erythro*-(**P**)AuCH$_2$CHDCH(OMe)Ph (*erythro*-**1**-2-d_1), generated via transmetallation of *erythro*-(Bpin)CH$_2$CHDCH(OMe)Ph (*erythro*-**2**-2-d_1) with (**P**)AuCl (Scheme 4). Treatment of *erythro*-**1**-2-d_1 (≥95% d) with $AlCl_3$ at –78 °C led to formation of a 4.4:1 mixture of *cis*-2-deuterio-1-phenylcyclopropane (*cis*-**3**-2-d_1) and 2-deuterio-1-methoxy-1-phenylpropane (**4**-2-d_1) in 103 ± 5% combined (Scheme 4). Formation of *cis*-**3**-2-d_1 as a single stereoisomer (≥95%) was established by ^{1}H NMR analysis and homonuclear ^{1}H-^{1}H decoupling experiments. The stereoselective conversion of *erythro*-**1**-2-d_1 to *cis*-**3**-2-d_1 established that cyclopropanation occurred with inversion of configuration of the γ-stereocenter. This result is consistent with concerted backside displacement of the oxonium group of intermediate **II** and argues strongly against a stepwise mechanism involving a free carbenium ion, which would be expected to occur with loss of configuration of the γ-stereocenter (Scheme 4). However, we cannot rule out a mechanism involving a tight carbenium-oxonium ion pair that retains configuration of the Cγ stereocenter.[30]

Scheme 4. Synthesis and cyclopropanation of *erythro*-1-2-d_1.



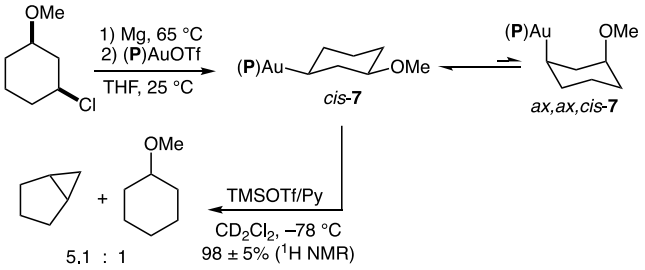
Having established the net inversion of the γ-stereocenter in the cyclopropanation of *erythro*-**1**-2-d_1, we sought to determine the stereochemistry of cyclopropanation with respect to Cα. In an initial attempt toward this objective, we targeted the diastereomeric 1,2-dideuterated gold alkyl complexes *threo*- and *erythro*- (**P**)AuCHDCHDC(OMe)Ph, which we reasoned could be generated via transmetallation of (**P**)AuCl with the appropriate 1,2-dideuterio-3-methoxy-3-phenylpropyl pinacol boranes *threo*-**2**-1,2-d_2 and *erythro*-**2**-1,2-d_2, respectively (Scheme 5). The stereochemically pure boronic esters *threo*-**2**-1,2-d_2 and *erythro*-**2**-1,2-d_2 were synthesized via rhodium-catalyzed deuteration of vinylboronic esters *trans*-**6** and *cis*-**6**, respectively.[31] Independent transmetallation of (**P**)AuCl with *threo*-**2**-1,2-d_2 and *erythro*-**2**-1,2-d_2 led to isolation of the gold propyl complex **1**-1,2-d_2 in 47% and 14 % yield, respectively (Scheme 5). Unfortunately, ^{1}H NMR analysis of the gold complexes **1**-1,2-d_2 generated from *threo*-**2**-1,2-d_2 and *erythro*-**2**-1,2-d_2 were indistinguishable, indicating that transmetallation had occurred with loss of configuration at the Cα.

Scheme 5. Synthesis of 1-1,2-d_2 with loss of configuration at Cα.



As an alternative approach to determine the stereochemistry of cyclopropanation with respect to Cα, we targeted the *cis*-3-methoxycyclohexyl gold complex *cis*-(**P**)AuCHCH$_2$CH(OMe)CH$_2$CH$_2$CH$_2$ (*cis*-**7**). This approach was inspired by the work of Glueck, who reported the stereoselective formation of the all equatorial gold menthyl complex (PPh$_3$)AuCHCH$_2$CH(Me)CH$_2$CH$_2$CH(CHMe$_2$) via transmetallation of Ph$_3$PAuCl with the Grignard reagent derived from (–)menthyl chloride.[32] Because both the (**P**)Au moiety and methoxy groups of *cis*-**7** would presumably occupy equatorial orientations, *cis*-**7** would be particularly susceptible to cyclopropanation via a double inversion mechanism upon treatment with Lewis acid (Scheme 6). Conversely, although complex *cis*-**7** could potentially access the higher-energy axial-axial conformation in solution (*ax,ax,cis*-**7**), this conformer would not allow for cyclopropanation via a Cα retention/Cγ inversion pathway, the latter of which was established for the cyclopropanation of *erythro*-**1**-2-*d*. For this reason, efficient Lewis acid-mediated cyclopropanation of *cis*-**7** would validate cyclopropanation with inversion of the Cα stereocenter.

Scheme 6. Synthesis and Lewis acid-mediated cyclopropanation of *cis*-7 to form bicyclo[3.1.0]hexane.



Transmetallation of (**P**)AuCl with the Grignard reagent generated from *cis*-1-chloro-3-methoxycyclohexane led to isolation of *cis*-**7** in 20% yield as a single diastereomer as determined by ^{1}H and ^{31}P NMR analysis. The ^{13}C NMR spectrum of *cis*-**7** displayed a diagnostic doublet at δ 42.7 (d, J = 99.2 Hz) assigned to the gold-bound carbon atom.[27,32] The equatorial orientation of both the (**P**)Au and methoxy groups of *cis*-**7** was established by the presence of large $^3J_{HH}$

axial–axial coupling constants for both the Hα (δ 0.65, *J* = 12.5 Hz) and Hγ protons (δ 2.83, *J* = 10.3) in the ^{1}H NMR spectrum. Treatment of *cis*-**7** with TMSOTf/pyridine (10:1) at –78 °C led to immediate formation of a 5.1:1 mixture of bicyclo[3.1.0]hexane and cyclohexyl methyl ether in 98 ± 5% combined yield as determined by ^{1}H NMR spectroscopy (Scheme 6), thereby validating a double inversion mechanism for the cyclopropanation of γ-methoxy gold alkyl complexes. As a caveat, we acknowledge that *cis*-**7** represents a biased system because cyclization with retention of Cα configuration is precluded from the outset. Therefore, although the selective conversion of *cis*-**7** to bicyclo[3.1.0]hexane validates the double inversion mechanism for cyclopropanation, this observation does not rule out the possibility that cyclopropanation might also occur through a competing pathway involving retention of configuration at Cα, although we do not consider this a likely scenario.

The double inversion mechanism validated for the conversion of *cis*-**7** to bicyclo[3.1.0]hexane is consistent with a W-shaped transition state where the back lobe of the Au–Cα σ-bond attacks the back lobe of the Cγ–O σ-bond of the oxonium intermediate (Figure 1). W-shaped transition states have been invoked on the basis of stereochemical analysis for a number of similar cyclopropane forming transformations including the Lewis acid-mediated 1,3-elimination of γ-trialkylstannyl alcohols[21] and 3-methoxy-3-phenylpropyl zirconocene complexes,[20] the solvolysis of γ-trialkylstannyl mesylates[22] and γ-trimethylsilyl sulfonates,[23] the base-promoted 1,3-elimination of γ-haloalkylboranes[24] and γ-sulfonylalkylboranes,[25] and the 1,3-elimination of γ-functionalized alkyl iron complexes.[15,16] There are however exceptions to the preferential inversion of the Cα stereocenter in the formation of cyclopropanes via 1,3-elimination. Most notably, Jennings showed that platinum (γ-pyridinium)alkyl complexes formed cyclopropanes via reductive elimination from a metallacyclobutane intermediate.[17] Similarly, Grubbs demonstrated that thermolysis of γ-iodo titanium alkyl complexes formed cyclopropanes with retention of configuration at Cα.[18] Casey showed that Lewis acid-mediated cyclopropanation of alkyltitanium species possessing a γ-oxo group, generated as an intermediate in the Kulinkovich hydroxycyclopropanation,[33,34] occurs with retention of configuration at Cα, consistent with a front-side mechanism for ring closure.[20] Interestingly, the corresponding cyclopropanation of alkyltitanium species possessing a γ-iminium group generated as intermediates in the de Meijere cyclopropylamine synthesis[34,35] occurs with inversion of configuration at Cα.[19,20]

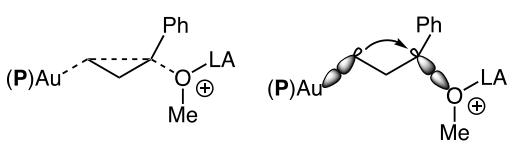


Figure 1. Representations of the proposed W-shaped transition state for Lewis acid-mediated cyclopropanation of 3-methoxy-3-phenylpropyl gold complexes.

CONCLUSIONS

The Lewis acid activation of gold γ-methoxy and γ-(thiomethyl) alkyl complexes forms cyclopropanes, suggesting that gold to alkene carbene transfer similarly involves intermediates and/or transition states bearing full or partial positive charge at the γ-carbon atom. The Lewis acid-mediated cyclopropanation of *erythro*-**1**-2-d_1 to form *cis*-**3**-2-d_1 established inversion of the γ-stereocenter, consistent with backside displacement of the γ-oxonium leaving group by the Au–C electron pair as opposed to formation of a free carbenium ion intermediate. This observation, coupled with the facile Lewis acid mediated cyclopropanation of *cis*-**7** to form bicyclo[3.1.0]hexane validated a double inversion mechanism for cyclopropane formation consistent with a W-shaped transition state where the back lobe of the Au–Cα σ-bond attacks the back lobe of the Cγ–O σ-bond (Figure 1). The Lewis acid mediated cyclopropanation of 3-phenyl-3-(thiomethyl)propyl gold complexes also supports Maulide's proposed mechanism for the gold-catalyzed cyclopropanation of alkenes and allenes with stabilized sulfonium ylides involving the electrophilic attack of Cγ on Cα of a gold (γ-sulfonium)alkyl intermediate.[13]

EXPERIMENTAL SECTION

General methods. Reactions were performed under a nitrogen atmosphere in flame dried glassware. Room temperature is 25 °C. NMR spectra were obtained on a Varian spectrometer operating at 400 and 500 MHz for ^{1}H, 125 MHz for ^{13}C, and 162 or 202 MHz for ^{31}P at 25 °C unless noted otherwise. ^{13}C NMR spectra were referenced relative to CD_2Cl_2 (δ 53.8) or $CDCl_3$ (δ 77.2), ^{1}H NMR spectra were referenced relative to residual $CHCl_3$ (δ 7.26) or $CHDCl_2$ (δ 5.32). ^{31}P NMR spectra were referenced relative to an external solution of triphenylphosphine oxide in CD_2Cl_2 (δ 26.9). NMR probe temperatures were measured from a single scan of neat methanol.[36]NMR tubes used for cyclopropanation experiments were silanized before use.[37] Flash column chromatography was performed employing 200-400 mesh silica gel 60 (EM). Thin layer chromatography (TLC) was performed on silica gel 60 F254. CD_2Cl_2 was dried over CaH_2 and degassed prior to use. Ether, methylene chloride, and THF were purified by passage through columns of activated alumina under nitrogen. Reagents and other materials were obtained through major chemical suppliers and were used as received unless noted otherwise. Boronic ester **2** was synthesized employing a modified version of the procedure reported by Liu.[38] *erythro*-**2**-2-d_1 Was prepared in two steps from cis-β-deuterio-styrene oxide[39] employing the procedure reported by Fu.[40] *threo*- And *erythro*-**2**-1,2-d_2 were prepared employing modified version of the procedures reported by Morken.[41] Vinyl boronic esters (*E*)-**6** and (*Z*)-**6** were prepared employing modified versions of the procedures reported by Frost,[42] and Miyaura,[43] respectively. 3-Bromo-1-methoxypropyl)benzene,[44] 3-methylthio-3-phenyl-1-propanol,[45]*cis*-1-chloro-3-methoxycyclohexane[46] and 1-methoxy-1-phenylpropyne[47] were prepared by employing known procedures.

Synthesis of Gold Alkyl Complexes

[P(*t*Bu)$_2$*o*-biphenyl]AuCH$_2$CH$_2$C(OMe)Ph (1), Procedure 1. A solution of (3-bromo-1-methoxypropyl)benzene (81.6 mg, 0.30 mmol) in diethyl ether (1.5 mL) was added dropwise to a solution of *t*BuLi (0.59 mmol) in diethyl ether (0.5 mL) at –78 °C to give a bright yellow solution which was stirred for 5 min. To this, a solution of (**P**)AuCl (157 mg, 0.30 mmol) in CH_2Cl_2 (1.5 mL) was

added dropwise at −78 °C to form a colorless solution that was warmed slowly to 0 °C and then stirred at 4 °C for 15 h. The resulting slightly murky solution was concentrated under vacuum. The resulting white solid was dissolved in hexanes–EtOAc = 9:1 and filtered through basic alumina. The filtrate was concentrated, triturated with pentanes, and dried under vacuum to give **1** (119 mg, 63%) as white solid.

Complex 1, Procedure 2. Complex **1** was synthesized employing a procedure similar to that reported by Hashmi.[48] A solution of **2** (59 mg, 0.21 mmol), (**P**)AuCl (113.0 mg, 0.21 mmol) and Cs_2CO_3 (69 mg, 0.21 mmol) in *i*PrOH (2.1 mL) was stirred at 50 °C for two days. The reaction mixture was cooled to room temperature and concentrated under vacuum. The resulting white solid was dissolved in hexanes–EtOAc = 9:1 and filtered through thin pad of basic alumina, concentrated, and the procedure was repeated. The resulting oil was triturated with pentane to give **1** (46 mg, 33 %) as a white solid.

For 1: ^{1}H NMR: δ 7.85 (t, *J* = 6.5, 1H), 7.41 (p, *J* = 7.4, 2H), 7.36 – 7.17 (m, 8H), 7.15 – 7.07 (m, 3H), 3.97 (dd, *J* = 6.2, 7.2 Hz, 1H), 3.20 (s, 3H), 2.10 – 1.96 (m, 1H), 1.82 – 1.69 (m, 1H), 1.38 (d, *J* = 14.1 Hz, 18H), 0.38 – 0.19 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 143.8, 143.4 (d, *J* = 5.1 Hz), 135.5, 132.9 (d, *J* = 7.8 Hz), 129.7, 129.4 (d, *J* = 2.4 Hz), 128.0 (d, *J* = 5.4 Hz), 127.9, 127.0, 126.5, 126.4 (d, *J* = 4.5 Hz), 90.1, 56.8, 40.3, 37.30 (d, *J* = 16.4 Hz), 37.26 (d, *J* = 16.4 Hz), 31.1 (d, *J* = 7.2 Hz), 24.8 (d, *J* = 92.5 Hz). ^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$): δ 65.5. Anal calcd. (found) for $C_{30}H_{40}AuOP$: C, 55.90 (55.72); H, 6.26 (6.24). HRMS (ESI) calcd. (found) for $C_{30}H_{40}AuOP$ $(MH)^+$: 645.2555 (645.2549).

***erythro*-(P)AuCH$_2$CHDCH(OMe)Ph (*erythro*-1-2-*d*$_1$).** A solution of *erythro*-**2**-2-*d*$_1$ (55 mg, 0.20 mmol), (**P**)AuCl (105 mg, 0.20 mmol) and Cs_2CO_3 (65 mg, 0.20 mmol) in *i*PrOH (2.3 mL) and CH_2Cl_2 (0.2 mL) was stirred at 50 °C for 24 h. The reaction mixture was cooled to room temperature and concentrated under vacuum. The resulting white solid was dissolved in hexanes–EtOAc = 9:1 and filtered through a thin pad of basic alumina, concentrated, and the procedure was repeated. The resulting oil was triturated with pentane to give *erythro*-**1**-2-*d*$_1$ as white solid (22 mg, 17 %). ^{1}H NMR (400 MHz, $CDCl_3$; selected peaks): δ 3.96 (d, *J* = 6.0 Hz, 1H), 2.01 (m, 1H), 0.36-0.18 (m, 2H). Comparison of the intensity of the resonances at δ 2.01 and δ 1.76 corresponding to the diastereotopic protons β to gold established ≥95% deuterium incorporation at one of the two positions β to gold.

(P)AuCHDCHDCH(OMe)Ph (1-1,2-*d*$_2$). Isotopomer **1**-1,2-*d*$_2$ was synthesized from boronic esters *threo*-**2**-1,2-*d*$_2$ or *erythro*-**2**-1,2-*d*$_2$ employing procedures analogous to that used to synthesize *erythro*-**1**-2-*d*$_1$ in 72% yield (from *threo*-**2**-1,2-*d*$_2$) and 14% yield (from *erythro*-**2**-1,2-*d*$_2$) as white solids. The ^{1}H NMR spectra of 1-**1**,2-*d*$_2$ prepared from both *threo*-**2**-1,2-*d*$_2$ and *erythro*-**2**-1,2-*d*$_2$ were indistinguishable as were homonuclear ^{1}H-^{1}H decoupling experiments, thus confirming the scrambling of the Cα stereocenter. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (dd, *J* = 7.5, 4.9 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.34 – 7.18 (m, 8H), 7.16 – 7.06 (m, 3H), 3.96 (d, *J* = 6.8 Hz, 1H), 3.20 (s, 3H), 2.06 – 1.97 (m, 0.5H), 1.80 – 1.70 (m, 0.5H), 1.38 (d, *J* = 14.2 Hz, 18H), 0.36 – 0.27 (m, 0.5H), 0.27 – 0.17 (m, 0.5H).

(P)AuCH$_2$CH$_2$CH(SMe)Ph (5). A solution of (3-bromo-1-phenylpropyl)(methyl)sulfane (50.1 mg, 0.20 mmol) in diethyl ether (0.8 mL) was added dropwise to a solution of *t*BuLi (0.40 mmol) in diethyl ether (0.7 mL) at −78 °C and stirred for 5 min. To the resulting light yellow solution, a solution of (**P**)AuCl (16.2 mg, 0.20 mmol) in CH_2Cl_2 (0.7 mL) was added dropwise at −78 °C to form a colorless solution that was warmed slowly to 0 °C and stirred at room temperature for 30 min. The resulting slightly murky solution was concentrated under vacuum to give white solid. The crude solid was dissolved in hexanes–EtOAc = 9:1 and the resulting mixture was filtered through basic alumina. The filtrate was concentrated, triturated with pentanes, and dried under vacuum to give **5** (46.4 mg, 35 %) as white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (ddd, *J* = 7.6, 5.8, 1.8 Hz, 1H), 7.46 – 7.37 (m, 2H), 7.33 – 7.14 (m, 9H), 7.10 (d, *J* = 7.4 Hz, 1H), 7.08 (d, *J* = 7.4 Hz, 1H), 3.55 (dd, *J* = 8.3, 6.0 Hz, 1H), 2.01 (dtd, *J* = 11.9, 8.2, 5.9 Hz, 2H), 1.85 (s, 3H), 1.38 (d, *J* = 14.1 Hz, 8H), 1.37 (d, *J* = 14.1 Hz, 9H), 0.42 – 0.31 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.6 (d, *J* = 17.4 Hz), 144.1, 143.4, 135.5, 132.9 (d, *J* = 7.8 Hz), 129.8, 129.5, 128.6, 128.1, 127.1, 126.5 (d, *J* = 3.8 Hz), 126.4, 57.9 (d, *J* = 6.9 Hz), 37.4 (d, *J* = 17.3 Hz), 37.3 (d, *J* = 16.5 Hz), 31.2 (d, *J* = 4.6 Hz), 31.1, 27.7 (d, *J* = 91.6 Hz), 14.9. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 65.5. HRMS (ESI) calcd. (found) for $C_{30}H_{41}AuPS$ $(MH)^+$: 661.2327 (661.2326).

***cis*-(P)AuCHCH$_2$CH(OMe)CH$_2$CH$_2$CH$_2$ (*cis*-7).** A slurry of magnesium powder (100 mg. 4.1 mmol) and 1,2-dibromoethane (30 μL) in THF (1 mL) was stirred at 50 °C for 20 min. A solution of *cis*-1-chloro-3-methoxycyclohexane (300 mg, 2.0 mmol) in THF (0.8 mL) was added to the slurry and the resulting suspension was heated at reflux for 5 h. After cooling to room temperature and allowing the excess Mg to settle, 0.6 mL of the dark gray solution was transferred to a solution of (**P**)AuOTf (120 mg, 0.19 mmol) in THF (10 mL), and stirred for 12 h. The resulting mixture was concentrated, filtered through a thin pad of basic alumina with hexanes–EtOAc = 9:1, concentrated, redissolved in pentane, and recrystallized at −20 °C to give *cis*-**7** as slightly off white solid (23.0 mg, 20 % from (**P**)AuOTf). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (ddd, *J* = 7.5, 5.5, 2.1 Hz, 1H), 7.45 – 7.34 (m, 5H), 7.20 (ddd, *J* = 7.5, 4.1, 1.9 Hz, 1H), 7.15 (dd, *J* = 7.0, 2.3 Hz, 2H), 3.33 (s, 3H), 2.76 (tt, *J* = 10.3, 3.6 Hz, 1H), 2.09 (dq, *J* = 12.4, 3.1 Hz, 1H), 1.93 – 1.84 (m, 1H), 1.70 (dq, *J* = 9.3, 3.1 Hz, 1H), 1.35 (dt, *J* = 14.0, 2.4 Hz, 17H), 0.58 (tdt, *J* = 12.5 Hz, 9.0, 3.1 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 143.2, 135.6, 132.8 (d, *J* = 7.4 Hz), 129.9 (d, J = 25 Hz), 129.8, 129.6, 128.5 (d, *J* = 5.2 Hz), 128.1, 127.1, 126.4 (d, *J* = 3.3 Hz), 83.3 (d, *J* = 9.4 Hz), 55.5, 42.7 (d, *J* = 99.2 Hz), 42.3, 37.2 (d, *J* = 16.1 Hz), 36.3 (d, *J* = 4.5 Hz), 33.8, 31.2 (d, *J* = 7.7 Hz), 29.5 (d, *J* = 9.3 Hz). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 63.5.

Cyclopropanation of Gold Alkyl Complexes

General procedure for cyclopropanation of 1. A solution of **1** (14.4 mg, 2.23 × 10^{-2} mmol) in CD_2Cl_2 (0.25 mL) was added dropwise with constant agitation to a silanized NMR tube containing Lewis acid (1.5 - 2.0 equiv) and nitrobenzene or CH_2Br_2 (internal standard) in CD_2Cl_2 (0.35 mL) at −78 °C to give a colorless solution. The tube was placed in the probe of an NMR spectrometer precooled at −78 °C and analyzed by ^{1}H NMR spectroscopy. The yields for cyclopropanation and protodeauration were determined by integrating the ^{1}H NMR resonances for **3** at δ 0.93 or δ 0.63 and for **4** at δ 3.99 relative to the resonance of nitrobenzene at δ 8.20 or CH_2Br_2 at δ 4.96 in the ^{1}H NMR spectrum. The ^{1}H NMR spectroscopy of **3** and **4** were consistent with published data.[49,50]

For 3: ^{1}H NMR (−20 °C, 500 MHz, CD_2Cl_2; aliphatic resonances): δ 1.85 (tt, *J* = 8.8, 5.1 Hz, 1H), 0.94 (m, 2H), 0.65 (m, 2H).

For 4: ^{1}H NMR (−20 °C, 500 MHz, CD_2Cl_2; aliphatic resonances): δ 3.97 (t, *J* = 6.7 Hz, 1H), 3.13 (s, 3H), 1.73 (m, 2H), 0.83 (m, 3H).

Cyclopropanation of *erythro*-1-2-*d*$_1$. A solution of *erythro*-**1**-2-*d*$_1$ (11 mg, 1.7 × 10^{-2} mmol) in CD_2Cl_2 (0.2 mL) was added via syringe to an NMR tube containing a solution of CH_2Br_2 (2.5 × 10^{-3} mmol; internal standard) and $AlCl_3$ (2.7 mg, 2.0 × 10^{-2} mmol) in CD_2Cl_2 (0.3 mL) at −78 °C and the tube was washed with additional CD_2Cl_2 (0.2 mL). The tube was placed in the probe of an NMR spectrometer precooled at −78 °C. The yields of *cis*-**3**-*d*$_1$ and **4**-2-*d*$_1$ were determined by integrating the resonances at δ 1.84 and δ 0.82 corresponding to the benzylic proton of *cis*-**3**-*d*$_1$ and the methyl resonance of **4**-2-*d*$_1$, respectively, relative to the resonance of CH_2Br_2 at δ 4.96 in ^{1}H NMR spectrum. Integration of the resonances at δ 1.84 and δ 0.66 corresponding to the benzylic and cis hydrogen resonances of *cis*-**3**-*d*$_1$ gave a ratio of 1.00: 1.01, indicating complete deuteration of one of the positions cis to the phenyl group.[51] The relative configuration of *cis*-**3**-*d*$_1$ was further established by comparison of the ^{1}H NMR data to the reported

values[15] and by selective homonuclear ^{1}H-^{1}H decoupling experiments (see SI).

Cyclopropanation of *cis*-7. A solution of CH_2Br_2 (0.73 mg, 4.2 × 10^{-3} mmol; internal standard), TMSOTf (3.5 mg, 1.6 × 10^{-2} mmol), and pyridine (0.20 μL, 2.6 × 10^{-3} mmol) in CD_2Cl_2 (0.3 mL) was added to a solution of *cis*-**7** (8 mg, 1.3 × 10^{-2} mmol) in CD_2Cl_2 (0.2 mL) at –78 °C and the tube was washed with additional CD_2Cl_2 (0.15 mL). The tube was placed in the probe of an NMR spectrometer precooled at –78 °C and monitored by ^{1}H NMR spectroscopy. Consumption of *cis*-**7** was complete within 15 min to form a mixture of TMSOMe, bicyclo[3.1.0]hexane (82%), and cyclohexyl methyl ether (16%). The yield of bicyclo[3.1.0]hexane and cyclohexyl methyl ether were determined by integrating the *exo* cyclopropyl proton of bicyclo[3.1.0]hexane[52] at δ 0.26 and the methoxy resonance of cyclohexyl methyl ether[53] δ 3.28 relative to the resonance of CH_2Br_2 at δ 4.96 in ^{1}H NMR spectrum.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information material is available free of charge via the Internet at http://pubs.acs.org.
Experimental procedures, spectroscopic data, and scans of NMR spectra.

AUTHOR INFORMATION

Corresponding Author

Ross A. Widenhoefer – *Department of Chemistry, Duke University, Durham, North Carolina 27708, United States;* orcid.org/0000-0002-5349-8477; Email: rwidenho@chem.duke.edu

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

We thank the NSF (CHE-1800273) for support of this research.

REFERENCES

(1) (a) Zi, W.; Toste, F. D. Recent advances in enantioselective gold catalysis. *Chem. Soc. Rev.* **2016**, *45,* 4567–4589. (b) Dorel, R.; Echavarren, A. M. Gold(I)-catalyzed activation of alkynes for the construction of molecular complexity. *Chem. Rev.* **2015**, *115*, 9028–9072. (c) Asiri, A. M.; Hashmi, A. S. K. Gold-catalysed reactions of diynes. *Chem. Soc. Rev.* **2016**, *45*, 4471–4503. (d) Goodwin, J. A.; Aponick, A. Regioselectivity in the Au-catalyzed hydration and hydroalkoxylation of alkynes. *Chem. Commun.* **2015**, *51*, 8730–8741. (e) Jia, M.; Bandini, M. Counterion effects in homogeneous gold catalysis. *ACS Catal.* **2015**, *5,* 1638–1652. (f) Furstner, A. Gold catalysis for heterocyclic chemistry: a representative case study on pyrone natural products. *Angew. Chem., Int. Ed.* **2018**, *57*, 4215–4233. (g) Akram, M. O.; Banerjee, S.; Saswade, S. S.; Bedi, V.; Patil, N. T. Oxidant-free oxidative gold catalysis: the new paradigm in cross-coupling reactions. *Chem. Commun.* **2018**, *54*, 11069–11083.

(2) Qian, D.; Zhang, J. Gold-catalyzed cyclopropanation reactions using a carbenoid precursor toolbox. *Chem. Soc. Rev.* **2015**, *44*, 677–698.

(3) Liu, L.; Zhang, J. Gold-catalyzed transformations of α-diazocarbonyl compounds: selectivity and diversity. *Chem. Soc. Rev.* **2016**, *45*, 506–516.

(4) (a) Wang, Y.; Muratore, M. E.; Echavarren, A. M. Gold carbene or carbenoid: is there a difference? *Chem. Eur. J.* **2015,** *21*, 7332–7339; (b) Harris, R. J.; Widenhoefer, R. A. Gold carbenes, gold-stabilized carbocations, and cationic intermediates relevant to gold-catalyzed cycloaddition. *Chem. Soc. Rev*. **2016**, *45*, 4533 - 4551.

(5) (a) Seidel, G.; Fürstner, A. Structure of a reactive gold carbenoid. *Angew. Chem. Int. Ed.* **2014**, *53*, 4807-4811. (b) Werlé, C.; Goddard, R.; Fürstner, A. The first crystal structure of a reactive dirhodium carbene complex and a versatile method for the preparation of gold carbenes by rhodium-to-gold transmetalation. *Angew. Chem. Int. Ed*. **2015**, *54*, 15452-15456. (c) Garcìa-Morales, C.; Pei, X.-L.; Sarria Toro, J. M.; Echavarren, A. M. Direct observation of aryl gold(I) carbenes that undergo cyclopropanation, C-H insertion, and dimerization reactions. *Angew. Chem. Int. Ed*. **2019**, *58*, 3957–3961.

(6) Kim, N.; Widenhoefer, R. A. Ionization of gold (γ-methoxy)vinyl complexes generates reactive gold vinyl carbene complexes. *Chem. Sci*. **2019**, *10*, 6149-6156.

(7) Pérez-Galán, P.; Herrero-Gómez, E.; Hog, D. T.; Martin, N. J. A.; Maseras, F.; Echavarren, A. M. Mechanism of the gold-catalyzed cyclopropanation of alkenes with 1,6-enynes. *Chem. Sci.* **2011**, *2*, 141–149.

(8) Nieto-Oberhuber, C.; Lopez, S.; Munoz, M. P.; Jiménez-Núñez, E.; Buñuel, E.; Cárdenas, D. J.; Echavarren, A. M. Gold(I)-catalyzed intramolecular cyclopropanation of dienynes. *Chem. Eur. J.* **2006**, *12,* 1694–1702.

(9) Batiste, L.; Fedorov, A.; Chen, P. Gold carbenes via 1,2-dialkoxycyclopropane ring-opening: a mass spectrometric and DFT study of the reaction pathways. *Chem. Commun.* **2010**, *46*, 3899–3901.

(10) Fedorov, A.; Batiste, L.; Bach, A.; Birney, D. M.; Chen, P. Potential energy surface for (retro-)cyclopropanation: metathesis with a cationic gold complex. *J. Am. Chem. Soc*. **2011**, *133*, 12162–12171.

(11) (a) Brookhart, M.; Studabaker, W. B. Cyclopropanes from reactions of transition-metal-carbene complexes with olefins. *Chem. Rev.* **1987**, *87*, 411–432. (b) Doyle, M. P.; Griffin, J. H.; Bagheri, V.; Dorow, R. L. Correlations between catalytic reactions of diazo compounds and stoichiometric reactions of transition-metal carbenes with alkenes. mechanism of the cyclopropanation reaction. *Organometallics* **1984**, *3*, 53–61. (c) Doyle, M. P. Catalytic methods for metal carbene transformations. *Chem. Rev*. **1986**, *86*. 919–939.

(12) Levin, M. D.; Toste, F. D. Gold-catalyzed allylation of aryl boronic acids: accessing cross- coupling reactivity with gold. *Angew. Chem. Int. Ed*. **2014**, *53*, 6211–6215.

(13) (a) Klimczyk, S.; Huang, X.; Kählig, H.; Veiros, L. F.; Maulide, N. Stereoselective gold(I) domino catalysis of allylic isomerization and olefin cyclopropanation: mechanistic studies. *J. Org. Chem.* **2015**, *80*, 5719-5729. (b) Huang, X.; Klimczyk, S.; Veiros, L. F.; Maulide, N. Stereoselective intramolecular cyclopropanation through catalytic olefin activation. *Chem. Sci.* **2013**, *4*, 1105-1110. (c) Sabbatani, J.; Huang, X.; Veiros, L. F.; Maulide, N. Gold-catalyzed intermolecular synthesis of alkylidenecyclopropanes through catalytic allene activation. *Chem. Eur. J.* **2014**, *20*, 10636-10639. (d) Klimczyk, S.; Misale, A.; Huang, X.; Maulide, N. Dimeric TADDOL Phosphoramidites in asymmetric catalysis: domino deracemization and cyclopropanation of sulfonium ylides. *Angew. Chem. Int. Ed.* **2015**, *54*, 10365-10369.

(14) Bertrand has demonstrated the formation of cationic gold π-complexes via the β-hydride abstraction of gold alkyl complexes: Ung, G.; Bertrand, G. β- and α-Hydride abstraction in gold(I) alkyl complexes. *Angew. Chem. Int. Ed.* **2013**, *52*, 11388–11391.

(15) (a) Brookhart, M.; Liu, Y. When phenylcyclopropanes are generated by γ-ionization of *erythro*- and *threo-d*$_2$-$C_5H_5(CO)_2FeCHDCHDCH(OCH_3)C_6H_5$, cleavage of the Fe-$C_\alpha$ bond occurs with inversion of configuration of C_α. *Organometallics* **1989**, *8*, 1569–1572. (b) Brookhart, M.; Liu, Y. Investigation of the stereochemistry of Fe-C_α bond cleavage when phenylcyclopropane is generated by γ-ionization of stereospecifically deuterated $C_5H_5(CO)_2FeCHDCHDCH(OCH_3)C_6H_5$ complexes. A transition-state

model for transfer of the carbene ligand from $C_5H_5(CO)_2Fe{=}CHR^+$ to alkenes. *J. Am. Chem. Soc.* **1991**, *113*, 939–944.

(16) (a) Casey, C. P.; Smith, L. J. Inversion of stereochemistry at the carbon bound to iron in cyclopropane formation from *threo*-$C_5H_5(CO)2FeCHDCHDCH_2S(CH_3)C_6H_5^+$. *Organometallics* **1989**, *8*, 2289–2290. (b) Casey, C. P.; Smith, L. J. Cyclopropane formation from the reaction of (γ-haloalkyl)lron compounds with silver(1+). *Organometallics* **1988,** *7*, 2419–2421. (c) C. P. Casey, L.S. Vosjepka, Stereochemistry and mechanism of cyclopropane formation from ionization of $C_5H_5(CO)_2Fe(CH_2)_3X$. *Organometallics* **1992**, *11*, 738–744.

(17) Hanks, T. W.; Jennings, P. W. Platinacyclobutanes on the route to cyclopropanation. *J. Am. Chem. Soc.* **1987**, *109*, 5023–5025.

(18) Ho, S. C. H.; Straus, D. A.; Grubbs, R. H. An alternate path to reductive elimination for group 4B metals; mechanism of cyclopropane formation from titanacyclobutanes. *J. Am. Chem. Soc.* **1984**, *106*, 1533–1534.

(19) Ouhamou, N.; Six, Y. Studies on the intramolecular Kulinkovich–de Meijere reaction of disubstituted alkenes bearing carboxylic amide groups. *Org. Biomol. Chem*. **2003**, *1*, 3007–3009.

(20) Casey, C. P.; Strotman, N. A. Stereochemistry of cyclopropane formation involving group IV organometallic complexes. *J. Am. Chem. Soc.* **2004**, *126*, 1699–1704.

(21) (a) Fleming, I.; Urch, C. J.; Stereospecific cyclopropane synthesis from γ-stannyl alcohols. *Tetrahedron Lett.* **1983**, *24*, 4591–4594. (b) Fleming, I.; Urch, C. J.; stereospecific cyclopropane synthesis from γ-stannyl alcohols. *J. Organomet. Chem.* **1985**, *285*, 173-191.

(22) Davis, D. D.; Johnson, H. T. Stereospecific cyclopropane-ring formation by 1,3-deoxymetalation of trimethyltin-substituted norbornyl mesylates. *J. Am. Chem. Soc.* **1974**, *96*, 7576–7577.

(23) (a) Shiner, V. J. Jr.; Ensinger, M. W.; Kriz, G. S. β-Silicon stabilization of carbonium ions in solvolysis. 1. Solvolysis of *cis*- and *trans*-3-(trimethylsilyl)cyclohexyl *p*-bromobenzenesulfonates. *J. Am. Chem. Soc.* **1986**, *108*, 842–844. (b) Shiner, V. J. Jr.; Ensinger, M. W.; Huffman, J. C. γ-Silicon stabilization of carbonium ions in solvolysis. 3. Solvolysis of 4-(trimethylsilyl)-3-methyl-2-butyl *p*-bromobenzenesulfonates. *J. Am. Chem. Soc.* **1989**, *111*, 7199–7205.

(24) Goering, H. L.; Trenbeath, S. L.; On the stereochemistry of conversion of allylic halides to cyclopropanes via 7-haloalkylboranes. *J. Am. Chem. Soc.* **1976**, *98*, 5016–5017.

(25) Marshall, J. A.; Babler, J. H. The stereochemistry of alkylboronate 1,3-elimination reactions. *Chem. Commun.* **1968**, 993–994.

(26) Kim, N.; Widenhoefer, R. A. Synthesis, characterization, and reactivity of cationic gold diarylallenylidene complexes. *Angew. Chem. Int. Ed*. **2018**, *57*, 4722–4726.

(27) Wang, C.; Han, Z.-Y.; Luo, H.-W.; Gong L.-Z. Highly Enantioselective Relay Catalysis in the Three-Component Reaction for Direct Construction of Structurally Complex Heterocycles. *Org. Lett*. **2010**, *12*, 2266-2269.

(28) (a) Roth, K. E.; Blum, S. A. Relative Kinetic Basicities of Organogold Compounds. *Organometallics* **2010**, *29*, 1712–1716. (b) BabaAhmadi, R.; Ghanbari, P.; Rajabi, N. A.; Hashmi, A. S. K.; Yates, B. F.; Ariafard, A. A Theoretical Study on the Protodeauration Step of the Gold(I)-Catalyzed Organic Reactions. *Organometallics* **2015**, *34*, 3186–3195.

(29) Hideyuki, I.; Shigeo, T.; Tatsuo, O. The Lithium Diisopropylamide-induced Fragmentation of 1,3-Dithiolane Derivatives of Several Ketones Having α-Hydrogen. *B. Chem. Soc. Jpn*. **1983**, *56*, 2537 - 2538.

(30) Raber, D. J.; Harris, J. M. Nucleophilic substitution reactions at secondary carbon atoms. A modification of accepted views. *J. Chem. Ed.* **1972**, *49*, 60–64.

(31) Moran, W. J.; Morken, J. P. Rh-catalyzed enantioselective hydrogenation of vinyl boronates for the construction of secondary boronic esters. *Org. Lett.* **2006**, *8*, 2413–2415.

(32) Zuzek, A. A.; Reynolds, S. C.; Glueck, D. S.; Golen, J. A.; Rheingold, A. L. Synthesis and structure of gold and platinum menthyl complexes. *Organometallics* **2011**, *30*, 1812–1817.

(33) (a) Cha, J. K.; Kulinkovich, O. G. The Kulinkovich Cyclopropanation of Carboxylic Acid Derivatives. *Org. React*. **2012**, *77*, 1-160. (b) Brimble, M. A.; Haym, I. The Kulinkovich hydroxycyclopropanation reaction in natural product synthesis. *Org. Biomol. Chem*. **2012**, 10, 7649-7665. (c) Kulinkovich, O. G. Synthetic Applications of Intermolecular Cyclopropanation of Carboxylic Esters with Dialkoxytitanacyclopropane Reagents. *Eur. J. Org. Chem.* **2004**, 4517-4529.

(34) Kulinkovich, O. G.; de Meijere, A. 1,n-Dicarbanionic Titanium Intermediates from Monocarbanionic Organometallics and Their Application in Organic Synthesis. *Chem. Rev.* **2000**, *100*, 2789–2834.

(35) (a) Chaplinski, V.; de Meijere, A. A Versatile New Preparation of Cyclopropylamines from Acid Dialkylamide. *Angew. Chem., Int. Ed. Engl*. **1996**, *35*, 413-414. (b) de Meijere, A.; Williams, C. M.; Kourdioukov, A.; Sviridov, S. V.; Chaplinski, V.; Kordes, M.; Savchenko, A. I.; Stratmann, C.; Noltemeyer, M. Mono- and Disubstituted N,N-Dialkylcyclopropylamines from Dialkylformamides via Ligand-Exchanged Titanium-Alkene Complexes. *Chem. Eur. J.* **2002**, *8*, 3789-3801.

(36 Amman, C.; Meier P.; Merbach, A. E. A simple multinuclear NMR thermometer. *J. Magn. Reson*. **1982**, *46*, 319–321.

(37) Seed, B. Silanizing Glassware. *Curr. Protoc. Mol. Biol*. **1994**, A.3B.1–A.3B.2.

(38) Yang, C. T.; Zhang, Z. Q.; Tajuddin, H.; Wu, C. C.; Liang, J.; Liu, J. H.; Fu, Y.; Czyzewska, M.; Steel, P. G.; Marder, T. B.; Liu, L. Alkylboronic esters from copper-catalyzed borylation of primary and secondary alkyl halides and pseudohalides. *Angew. Chem. Int. Ed.* **2012,** *51*, 528–532.

(39) Capriati, V.; Florio, S.; Perna, F. M.; Salomone, A.; Abbotto, A.; Amedjkouh, M.; Nilsson Lill, S. O. On the dichotomic reactivity of lithiated styrene oxide: a computational and multinuclear magnetic resonance investigation. *Chem. Eur. J.* **2009**, *15*, 7958–7979.

(40) Ebrahim-Alkhalil, A.; Zhang, Z.-Q.; Gong, T.-J.; Su, W.; Lu, X.-Y.; Xiao, B.; Fu, Y. Copper-catalyzed cross-coupling reactions of epoxides with gem-diborylmethane: access to γ-hydroxyl boronic esters. *Chem. Commun*. **2016**, *52*, 4891–4893.

(41) (a) Moran, W. J.; Morken, J. P. Rh-Catalyzed Enantioselective Hydrogenation of Vinyl Boronates for the Construction of Secondary Boronic Esters. *Org. Lett*. **2006**, *8*, 2413-2415. (b) Morgan, J. B.; Morken, J. P. Catalytic Enantioselective Hydrogenation of Vinyl Bis(boronates). *J. Am. Chem. Soc.* **2004**, *126*, 15338-15339.

(42) Frost, C. G.; Edwards, H. J.; Penrose, S. D.; Gleave, R. Exploring rhodium-catalysed conjugate addition of chiral alkenylboronates using chiral olefin ligands. *Synthesis* **2010**, 3243–3247.

(43) Ohmura, T.; Yamamoto, Y.; Miyaura, N. Rhodium- or iridium-catalyzed trans-hydroboration of terminal alkynes, giving (Z)-1-alkenylboron compounds. *J. Am. Chem. Soc.* **2000**, *122*, 4990–4991.

(44) LaLonde, R. T.; Ferrara, P. B. Reactions of arylcyclopropanes with *N*-bromosuccinimide in hydroxylic solvents. *J. Org. Chem*. **1972**, *37*, 2502–2505.

(45) Kostas, I. D.; Steele, B. R.; Terzis, A.; Amosova, S. V. A palladium complex with a new hemilabile amino-and sulfur-containing phosphinite ligand as an efficient catalyst for the Heck reaction of aryl bromides with styrene. The effect of the amino group. *Tetrahedron* **2003**, *59*, 3467–3473.

(46) de Oliveira, P. R.; Rittner, R. 1,3-Diaxial steric effects and intramolecular hydrogen bonding in the conformational equilibria of new *cis*-1,3-disubstituted cyclohexanes using low temperature NMR spectra and theoretical calculations. *Spectrochim. Acta. A.* **2005**, *62*, 30–37.

(47) Yang, L.; Zeng, Q. Metal- and acid-free methyl triflate catalyzed Meyer-Schuster rearrangement. *Synthesis* **2017**, *49*, 3149–3156.

(48) Hashmi, A. S. K.; Ramamurthi, T. D.; Rominger, F. Synthesis, structure and reactivity of organogold compounds of relevance to homogeneous gold catalysis. *J. Organomet. Chem.* **2009**, *694*, 592-597.

(49) Li, H.; Breen, C. P.; Seo, H.; Jamison, T. F.; Fang, Y.-Q.; Bio, M. M. Ni-catalyzed Electrochemical Decarboxylative C−C couplings in Batch and Continuous Flow. *Org. Lett.* **2018**, *20*, 1338–1341.

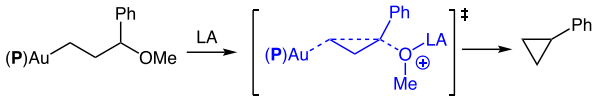
(50) Ayub, R.; Papadakis, R.; Jorner, K.; Zietz, B.; Ottosson, H. Cyclopropyl Group: An Excited-State Aromaticity Indicator? *Chem. Eur. J.* **2017**, *23*, 13684 – 13695.

(51) Casey, C. P.; Scheck, D. M., Shusterman, A. J. Mechanism of Rearrangement of Platinacyclobutanes. *J. Am. Chem. Soc.* **1979**, *101*, 4233-4236.

(52) (a) Shustov, G. V.; Denisenko, S. N., Chervin, I. I.; Asfandiarov, N. L., Kostyanovsky, R. G. Stereochemistry of bicyclic 1,2-*cis*-diaziridines. *Tetrahedron* **1985**, *23*, 5719–5731. (b) Hoffmann J.; Voss, J. Darstellung von Bicyclo[n.1.0]alkanen durch elektrochemische 1,3-Dibrorncycloalkanen. *Chem. Ber*. **1992**, *125*, 1415- 1419. (c) D. L. Muck and E. R. Wilson Synthesis and Nuclear Magnetic Resonance Analysis of Cyclopropyl- and 1-Bicyclo[n.1.0]alkylamines. *J. Org. Chem*. **1968**, *33*, 419-422.

(53) Miyamura, H.; Suzuki, A.; Yasukawa, T.; Kobayashi, S. Polysilane-Immobilized Rh-Pt Bimetallic Nanoparticles as Powerful Arene Hydrogenation Catalysts: Synthesis, Reactions under Batch and Flow Conditions, and Reaction Mechanism. *J. Am. Chem. Soc.* **2018**, *140*, 11325–11334.

.


Ph
(P)Au
OMe
LA
Ph
(P)Au
LA
O
Me
‡
Ph