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Stereoselective *cis*-Vinylcyclopropanation via a Gold(I)-Catalyzed Retro-Buchner Reaction under Mild Conditions

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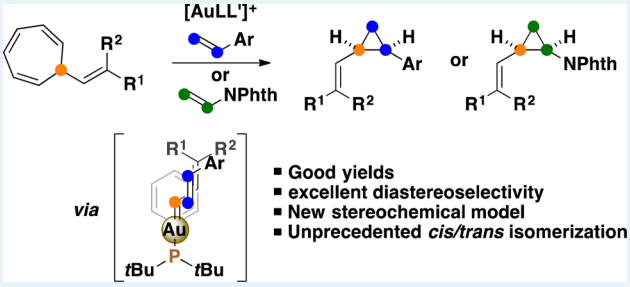
Supporting Information

ABSTRACT: A highly stereoselective gold(I)-catalyzed *cis*-vinylcyclopropanation of alkenes has been developed. Allylic gold carbenes, generated via a retro-Buchner reaction of 7-alkenyl-1,3,5-cycloheptatrienes, react with alkenes to form vinylcyclopropanes. The gold(I)-catalyzed retro-Buchner reaction of these substrates proceeds by simple heating at a temperature much lower than that required for the reaction of 7-aryl-1,3,5-cycloheptatrienes (75 °C vs 120 °C). A newly developed Julia−Kocienski reagent enables the synthesis of the required cycloheptatriene derivatives in one step from readily available aldehydes or ketones. On the basis of mechanistic investigations, a stereochemical model for the *cis* selectivity was proposed. An unprecedented gold-catalyzed isomerization of *cis*- to *trans*-cyclopropanes has also been discovered and studied by DFT calculations.



KEYWORDS: *cyclopropanation, vinylcyclopropanes, gold catalysis, retro-Buchner reaction, cycloheptatrienes*

INTRODUCTION

Vinylcyclopropanes are common motifs in natural products[1] and active pharmaceuticals.[2] Moreover, vinylcyclopropanes are of particular interest as synthetic intermediates[3] because of their rich downstream chemistry, undergoing rearrangements to cyclopentenes,[4] (3 + *n*) and (5 + *n*) cycloadditions,[5] or other transition-metal-catalyzed transformations,[6] providing ready access to molecular complexity.

Methods for the stereoselective cyclopropanation of alkenes by formal carbene transfer usually require directing groups and rely on the use of organometallic reagents or diazoalkanes,[7−9] which are hydrolytically unstable, pyrophoric, or potentially explosive. Recent efforts have led to the development of safer ways to access metal carbenes from stable precursors.[10] Thus, among others, metal carbenes or carbenoids have been generated from *α,β*-unsaturated carbonyl compounds,[11] tosyl hydrazones,[12] triazoles,[13] cyclopropenes,[14] and propargyl ethers[15] or esters,[16] as well as from alkynes by oxidative processes.[17] However, highly stereoselective methods for the synthesis of vinylcyclopropanes that do not rely on the use of diazo reagents remain scarce.[18] In general, diastereopure vinylcyclopropanes are accessed in a stepwise manner through derivatization of functionalized cyclopropane building blocks, by either Wittig olefination[19] or metal-catalyzed cross-couplings.[20,21]

Metal-catalyzed reactions of styryldiazoacetates efficiently give rise to 1-styrylcyclopropane-1-carboxylates.[22−24] However, the synthesis of simple vinylcyclopropanes not bearing ester groups requires the use of alkenyldiazomethanes, which are much less stable since they can easily give rise to pyrazoles[25,26] or undergo dimerization to form trienes.[27] This instability has been partially circumvented by performing the cyclopropanation under metal-free conditions with flow-generated alkenyldiazalkanes.[28]

We recently discovered that highly electrophilic gold(I) complexes are able to cleave two-carbon bonds of norcaradienes, which are in equilibrium with more stable cycloheptatrienes,[29] to form in situ gold(I) carbenes.[30−32] Starting from readily available 7-aryl substituted cycloheptatrienes, the retrocyclopropanation (decarbenation) reaction leads to aryl-substituted gold(I) carbenes, which undergo cyclopropanation with alkenes,[30b] intramolecular Friedel−Crafts-type reactions,[30c] and [4 + 1] cycloadditions with methylenecyclopropanes or cyclobutenes.[30d] In contrast to aryl derivatives, 7-alkynyl-1,3,5-cycloheptatrienes undergo cycloisomerization reactions at low temperature with gold(I) or gold(III) catalysts to give indenes via stabilized barbaralyl cations.[33,34]

The gold(I)-catalyzed retro-Buchner reaction requires relatively high temperatures (ca. 120 °C) for the efficient cleavage of the cyclopropane ring of norcaradienes,[30b,c,d] which results in low stereoselectivity in the subsequent trapping of the generated aryl-substituted gold(I) carbenes with alkenes.[30b] We

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envisaged that the retro-Buchner reaction of 7-alkenyl-1,3,5-cycloheptatrienes **1** would take place with gold(I) under milder conditions to form more stabilized α,β-unsaturated gold(I) carbenes **I**,[35] which could react with alkenes **2** to give rise to vinylcyclopropanes **3** (Scheme 1).

Scheme 1. Vinylcyclopropanation via Retro-Buchner Reaction of Alkenylcycloheptatrienes 1

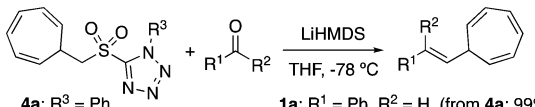
Here, we report the scope of this gold(I)-catalyzed vinylcyclopropanation that proceeds at moderate temperatures and for the first time allows preparing vinylcyclopropanes **3** with very good *cis* stereoselectivities. In contrast to the case for alkenyldiazomethanes, the required alkenylcycloheptatrienes **1** are perfectly stable compounds that can be obtained from commercially available tropylium salts or by a new procedure based on the Julia–Kocienski reaction. We have also found that *cis*-configured cyclopropanes can undergo isomerization to form *trans*-cyclopropanes by a reversible carbon–carbon bond cleavage promoted by gold(I).

RESULTS AND DISCUSSION

Synthesis of New Alkenylcycloheptatrienes. Alkenylcycloheptatrienes **1** can be obtained by the reaction of alkenyllithium or Grignard reagents with tropylium salts.[30b,36] In addition, we have found that alkenyl trifluoroborates can also be used as softer nucleophiles, which allow performing the addition reaction at room temperature in DMF.[37]

To further extend the scope of the cyclopropanation reaction by increasing the structural diversity on the alkenyl cycloheptatrienes, we also considered applying an olefination reaction as the ideal method considering the wide availability of aldehydes and ketones. Therefore, we prepared the bench-stable Julia–Kocienski reagents **4a,b** (Scheme 2).[38] These

Scheme 2. Formation of 7-Alkenyl-1,3,5-cycloheptatrienes 1a–g via Julia–Kocienski Reaction

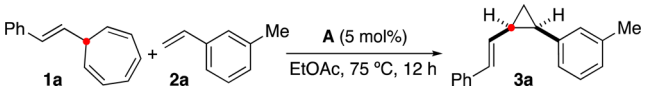


1a: R^1 = Ph, R^2 = H (from **4a**: 99%)
1b: R^1 = 4-$MeOC_6H_4$, R^2 = H (from **4a**: 92%)
1c: R^1 = 4-$CF_3C_6H_4$, R^2 = H (from **4a**: 82%)
1d: R^1 = 4-BrC_6H_4, R^2 = H (from **4a**: 85%)
1e: R^1 = 3,5-$MeO_2C_6H_4$, R^2 = H (from **4a**: 93%)
1f: R^1 = R^2 = Me (from **4b**: 75%)
1g: R^1, R^2 = -$(CH_2)_2O(CH_2)_2$- (from **4b**: 86%)

reagents allowed access to a wider variety of alkenylcycloheptatrienes in one step with excellent yields from commercially available carbonyl compounds. Aromatic aldehydes afforded the desired cycloheptatrienes **1a–e** with exclusive *E* selectivity from the lithium salt of **4a** at −78 °C. Although poor results were observed for ketones, due to the competing enolization, switching to the bulkier tetrazole **4b** led to cycloheptatrienes **1f,g** in good yields from acetone or cyclohexanone.

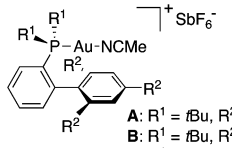
Development of the Vinylcyclopropanation Reaction. We started by reinvestigating the reaction conditions required to perform the retro-Bucher/cyclopropanation using *trans*-styrylcycloheptatriene **1a** (Table 1). In contrast with the initial conditions (120 °C, 1,2-dichloroethane),[30b] we found that the

Table 1. Retro-Buchner/Cyclopropanation To Form 3a

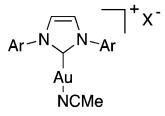


entry	deviation from standard conditions[a]	yield (%)[b]
1	none	75
2	DCE instead of EtOAc	68
3	toluene instead of EtOAc	16
4	THF instead of EtOAc.	46
5	catalyst **B** instead of **A**	38
6	catalyst **C** instead of **A**	–
7	catalyst **D** instead of **A**	–
8	catalyst **E** instead of **A**	14

[a]Standard conditions: cycloheptatriene **1**, styrene **2** (1.5 equiv), and [JohnPhosAu(MeCN)SbF_6] (**A**) (5 mol %) in EtOAc (0.25 M) at 75 °C for 12 h.



A: R^1 = *t*Bu, R^2 = H
B: R^1 = *t*Bu, R^2 = *i*Pr
C: R^1 = cyclohexyl, R^2 = H



D: Ar = mesityl, X = SbF_6
E: Ar = 2,6-diisopropylphenyl, X = BAr^F_4

[b]Determined by ^{1}H NMR with diphenylmethane as internal standard.

reaction of **1a** with styrene **2a** proceeds smoothly at 75 °C using ethyl acetate as the solvent in the presence of [(Johnphos)Au(MeCN)]SbF_6 (**A**) as catalyst (Table 1, entry 1). While the reaction in 1,2-dichloroethane proceeded in slightly lower yield, much lower catalytic activity was observed in toluene or THF (Table 1, entries 2–4). Increasing or decreasing the steric parameters of the ligand using complexes **B** and **C** (Table 1, entries 5 and 6) or changing to NHC-gold(I) complexes **D** and **E** had deleterious effects on the reaction outcome (Table 1, entries 7 and 8). When cycloheptatriene **1a** was used in excess, small quantities of an inseparable bis-cyclopropane were formed as a result of the cyclopropanation of product **3a**. The transformation proved to be robust, as similar yields were obtained when the reaction was performed in commercial ethyl acetate containing small amounts of water.

Reaction Scope. The intermolecular reaction of cycloheptatriene **1a** with a variety of *para*-, *meta*-, and *ortho*-substituted styrenes gave the corresponding *cis*-substituted cyclopropanes **3a–t** in moderate to high yields and with excellent *cis* selectivities (from 15:1 to more than 20:1) (Table 2). In general, electron-rich arenes were slightly better substrates for the reaction and led to higher yields of **3a,c,g,j**, whereas electron-poor arenes reacted more slowly, leading to lower yields of **3e,i,n,o**. Functional groups such as aldehydes (**3l**), esters (**3h,i**), and nitro groups (**3n**) were well tolerated, as were aryl halides (**3d,f,m,q,r**). However, traces or low yields of cyclopropanes were observed with non-aryl-substituted alkenes.

Disubstituted α-styrenes reacted efficiently to give cyclopropanes **3u,v**, albeit with a lower stereoselectivity in the former case. Adding one (**3w**) or two (**3x**) substituents to the β-position of the styrene resulted in a decrease in the yield. On the other hand, when cyclic alkenes such as indenes, 1,2-dihydronaphthalene, and 2*H*-chromene were used, *endo*-

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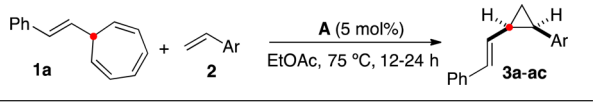
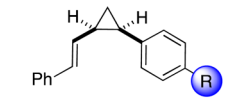
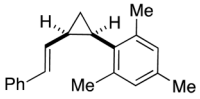
Table 2. Synthesis of *cis*-Arylcyclopropanes 3a–ac from 1a[d]

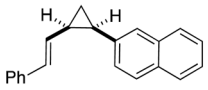




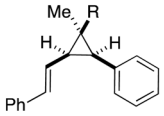
3b: R = H (65%, >20:1 dr)[a]
3c: R = Me (69%, >20:1 dr)[a]
3d: R = Cl (75%, >20:1 dr)[a]
3e: R = CF_3 (59%, 19:1 dr)
3f: R = F (65%, >20:1 dr)
3g: R = OMe (70%, 15:1 dr)
3h: R = OAc (68%, 19:1 dr)
3i: R = CO_2Me (54%, >20:1 dr)
3j: R = *t*Bu (70%, >20:1 dr)
3k: R = Ph (83%, >20:1 dr)



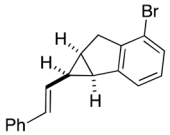
3s (47%, >20:1 dr)



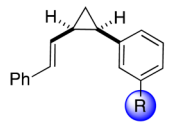
3t (73%, >20:1 dr)



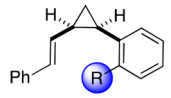
3w: R = H (45%, 3:1 dr)
3x: R = Me (35%, 8:1 dr)



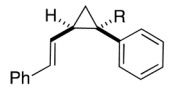
3aa (71%, >20:1 dr)



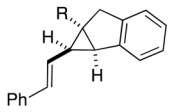
3a: R = Me (75%, >20:1 dr)[b]
3l: R = CHO (72%, >20:1 dr)
3m: R = Br (56%, >20:1 dr)[a]
3n: R = NO_2 (47%, >20:1 dr)
3o: R = CF_3 (52%, >20:1 dr)



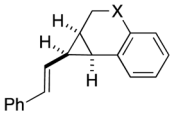
3p: R = Me (65%, >20:1 dr)
3q: R = F (60%, >20:1 dr)
3r: R = Br (71%, >20:1 dr)[c]



3u: R = Me (73%, 5:1 dr)
3v: R = Ph (73%)



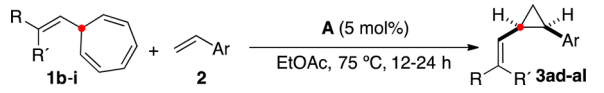
3y: R = H (85%, >20:1 dr)[a]
3z: R = Me (66%, >20:1 dr)

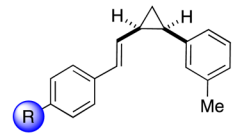


3ab: X = CH_2 (50%, >20:1 dr)[a]
3ac: X = O (56%, >20:1 dr)[a]

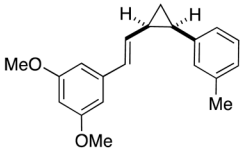
[a]2 equiv of styrene used. [b]Relative configuration confirmed by X-ray diffraction. [c]3 equiv of styrene used. [d]General conditions unless specified otherwise: cycloheptatriene **1** (0.25 mmol), styrene **2** (0.375 mmol), and **A** (0.0125 mmol, 5 mol %) in EtOAc (1 mL) at 75 °C for 12–24 h.

Table 3. Synthesis of *cis*-Arylcyclopropanes with Cycloheptatrienes 1b–i

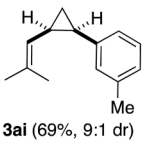




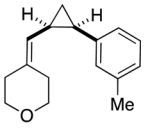
3ad: R = OMe (48%, 12:1 dr)
3ae: R = Ac (87%, >20:1 dr)
3af: R = CF_3 (79%, 17:1 dr)
3ag: R = Br (85%, >20:1 dr)



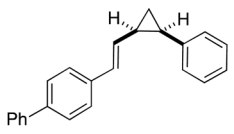
3ah (69%, >20:1 dr)



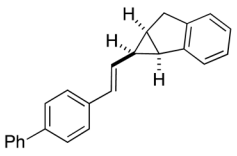
3ai (69%, 9:1 dr)



3aj (70%, 6:1 dr)



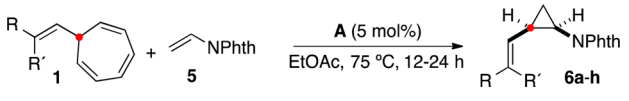
3ak (64%, >20:1 dr)

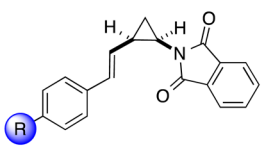


3al (76%, >20:1 dr)[a]

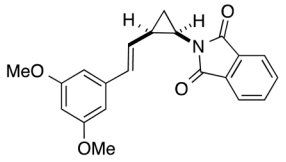
[a]Relative configuration confirmed by X-ray diffraction.

Table 4. Synthesis of N-Protected Aminocyclopropanes 6a–h from *N*-Vinylphthalimide (5)

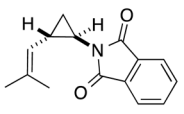




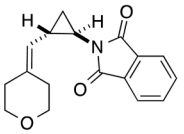
6a: R = H (75% (74%),[a] 6:1 dr)
6b: R = OMe (52%, 6:1 dr)
6c: R = Ac (63%, >20:1 dr)
6d: R = CF_3 (79%, 10:1 dr)
6e: R = Ph (69%, 2.6:1 dr)[b]



6f (60%, 6:1 dr)



6g (59%, 4.7:1 dr)[c]



6h (73%, 1.2:1 dr)[c]

[a]Isolated yield for reaction on 10 mmol scale, 2.1 g isolated with 7:1 d.r. See the Supporting Information for details. [b]Relative configuration (both *cis* and *trans*) confirmed by X-ray diffraction. [c]Major isomer depicted.

tricycles **3y–ac** were obtained essentially as single diastereomers in 50–85% yields.

Similarly, alkenylcycloheptatrienes **1b–i** gave rise to vinyl cyclopropanes **3ad–al** with good to excellent *cis* selectivities (from 6:1 to more than 20:1) (Table 3).

N-Vinylphthalimide (**5**) was also cyclopropanated to give products **6a–h** (Table 4). The robustness of the method was further demonstrated by the synthesis of **6a** on a multigram scale with identical high yield and similar diastereoselectivity (7:1 *cis*:*trans*). In general, lower *cis* stereoselectivities were observed using **5** as the alkene, with the exception of **6c**, and in the cases of **6g**,**h** the trans derivatives were obtained as the major isomers.

Application to the Synthesis of Diverse Cyclopropanes. The phthalimido protecting group of **6a** could be readily removed by treatment with $NaBH_4$ followed by addition of dry HCl to form the amine hydrochloride **7**,[39] which could be conveniently reprotected to form carbamate **8** (Scheme 3). Considering the importance of sterically constrained β-amino acids,[40,41] we developed a simple access to such building blocks containing a cyclopropane ring. Thus, ozonolysis of **6a** followed by reductive workup yielded *cis*-aldehyde **9a**. Subsequent formation of the ester proved challenging, as this push–pull substituted cyclopropane was prone to undergo opening under basic conditions, leading to the corresponding dihydrofuran. Acidic conditions, on the other hand, led to complete epimerization of the aldehyde, affording *trans*-cyclopropane **9b**. Finally, methyl ester **10** could be obtained by oxidation with hydrogen peroxide and vanadium oxide in methanol under mildly acidic conditions.[42]

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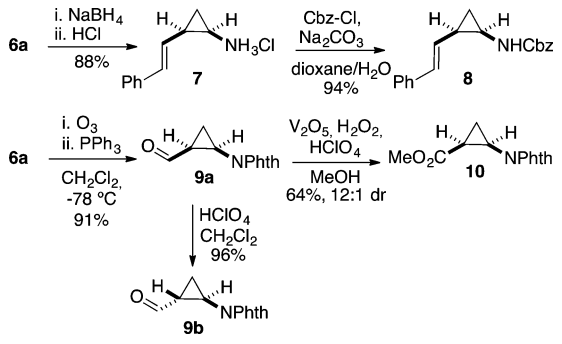
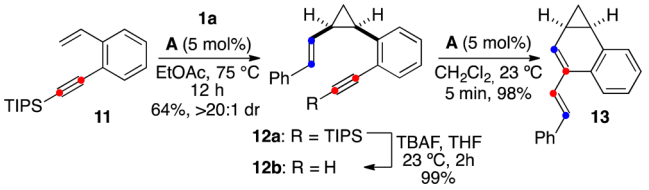
ACS Catal. 2017, 7, 3668–3675

Scheme 3. Deprotection of the Phthalimide and Oxidative Cleavage



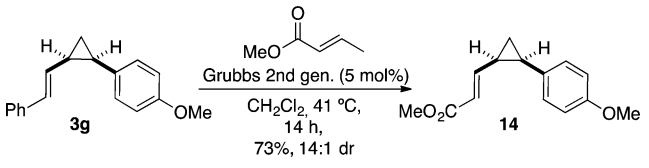
Gold(I)-catalyzed enyne cycloisomerizations are able to rapidly build up chemical complexity.[43] We wondered whether it would be possible to selectively cyclopropanate a 1,5-enyne to generate a new 1,7-enyne, which would then be cycloisomerized with the same gold(I) catalyst. To demonstrate this concept, 1,5-enyne **11** was first converted with remarkable chemo- and diastereoselectivity into *cis*-cyclopropane **12a** by reaction with cycloheptatriene **1a** in the presence of catalyst **A** (Scheme 4). After desilylation, 1,7-enyne **12b** was cleanly transformed by catalyst **A** at room temperature to furnish cyclopropyldiene **13** by a single cleavage rearrangement cascade.[44]

Scheme 4. Gold(I)-Catalyzed Cyclopropanation and 1,7-Enyne Cyclization



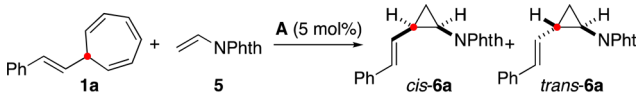
Finally, in order to access substrates bearing electron-withdrawing functional groups at the alkene that would otherwise be beyond the scope of our method, the feasibility of using cross-metathesis on styrylcyclopropanes was investigated. Apart from ring-closing metathesis[45] or cross-metathesis on terminal vinylcyclopropanes,[46] only a single example of a comparable reaction has been reported.[47] It is also important to note that *cis*−*trans* isomerization of cyclopropanes has been observed under the conditions of ring-closing metathesis in the presence of Grubbs carbenes via expansion of the intermediate cyclopropylruthenium(II) carbenes to form ruthenacyclopentenes.[45d] However, using the second-generation Grubbs catalyst,[48] cross-metathesis of **3g** with methyl crotonate proceeded smoothly to form *cis*-**14** without erosion of the diastereoselectivity (Scheme 5).

Scheme 5. Cross Metathesis of Vinylcyclopropane 3g



Mechanistic Investigations. The usually high *cis* stereoselectivities observed in this study are in contrast with the seemingly erratic stereoselectivities observed before in the cyclopropanation from arylcycloheptatrienes that had to be performed at higher temperatures (120 °C, 1,2-dichloroethane).[30b] At the same time, we were interested in the lower selectivity observed in the cyclopropanation of *N*-vinylphthalimide (**5**) (Table 4). Intriguingly, lower diastereoselectivities were observed when those reactions were performed for longer reaction times. The progress of the reaction between **1a** and **5** followed by ^{1}H NMR revealed a fast consumption of the cycloheptatriene **1a** along with the formation of *cis*-**6a**, which was then followed by a slow isomerization of *cis*-**6a** to from *trans*-**6a**, until an equilibrium was reached (Scheme 6).

Scheme 6. *cis*−*trans* Isomerization of Vinylcyclopropanes[a]



T (solvent)	time (h)	*cis*-**6a**	*trans*-**6a**
75 °C (EtOAc)	12	71%	10%
75 °C (EtOAc)	168	23%	62%

[a]Yields determined by ^{1}H NMR (diphenylmethane as internal standard).

Performing the reaction at 120 °C in *i*PrOAc allowed for the isolation of *trans*-**6a** in a synthetically relevant yield of 55%. When pure *cis*-**6a** was heated with catalyst **A** in EtOAc at 75 °C for 132 h, a 1.6:1 mixture of *trans*-**6a** and *cis*-**6a** was obtained. No isomerization was observed in the absence of the gold(I) catalyst, which excludes a radical background reaction.[49−51]

We examined theoretically the complete reaction pathways for the formation of **3b** and **6a**,**g** by DFT calculations at the M06/6-31G(d)/M06/6-311+G(2d,p) (C, H, N, O, P) and SDD (Au) levels, taking into account the solvent effect (SMD = dichloromethane) and employing JohnPhos as the phosphine ligand.[52]

The reaction to form **3b** starts with the retro-Buchner reaction of **1a**, which involves the stepwise cleavage of two C−C bonds in complex **II** (Figure 1a). The cleavage of the second bond determines the activation barrier for the generation of gold(I) carbene **V**, which was calculated to be 25.1 kcal mol^{-1},[53] corresponding to the experimentally estimated value of 27 kcal mol^{-1}.[54,55] The cyclopropanation of styrene by **V** proceeds through an asynchronous concerted mechanism, with an energy difference of 3.1 kcal mol^{-1} between the *cis* and *trans* pathways (Figure 1b).

The cyclopropanations of alkene **5** also favor the *cis* product,[52] through closely similar transition states (Figure 1c,d). Electronic noncovalent interactions, namely $\pi-\pi$ interactions in the *cis*-TS and the lack thereof in the *trans*-TS, provide an explanation for the preferred formation of *cis* products[56] since the interplanar distances and stabilization energies for the *cis*-TS are within the typical range for such stabilizing interactions (3.6 Å, 5 kcal mol^{-1}).[57] Additionally, calculations corroborate that dispersion interactions are responsible for a significant stabilization of the *cis* transition states (Table 5, compare rows 2 and 3 for PBE and PBE-D3(BJ) functionals, respectively). Finally, the color-filled reduced density gradient (RDG) isosurface identified the weak van der Waals interactions (in green) between the π

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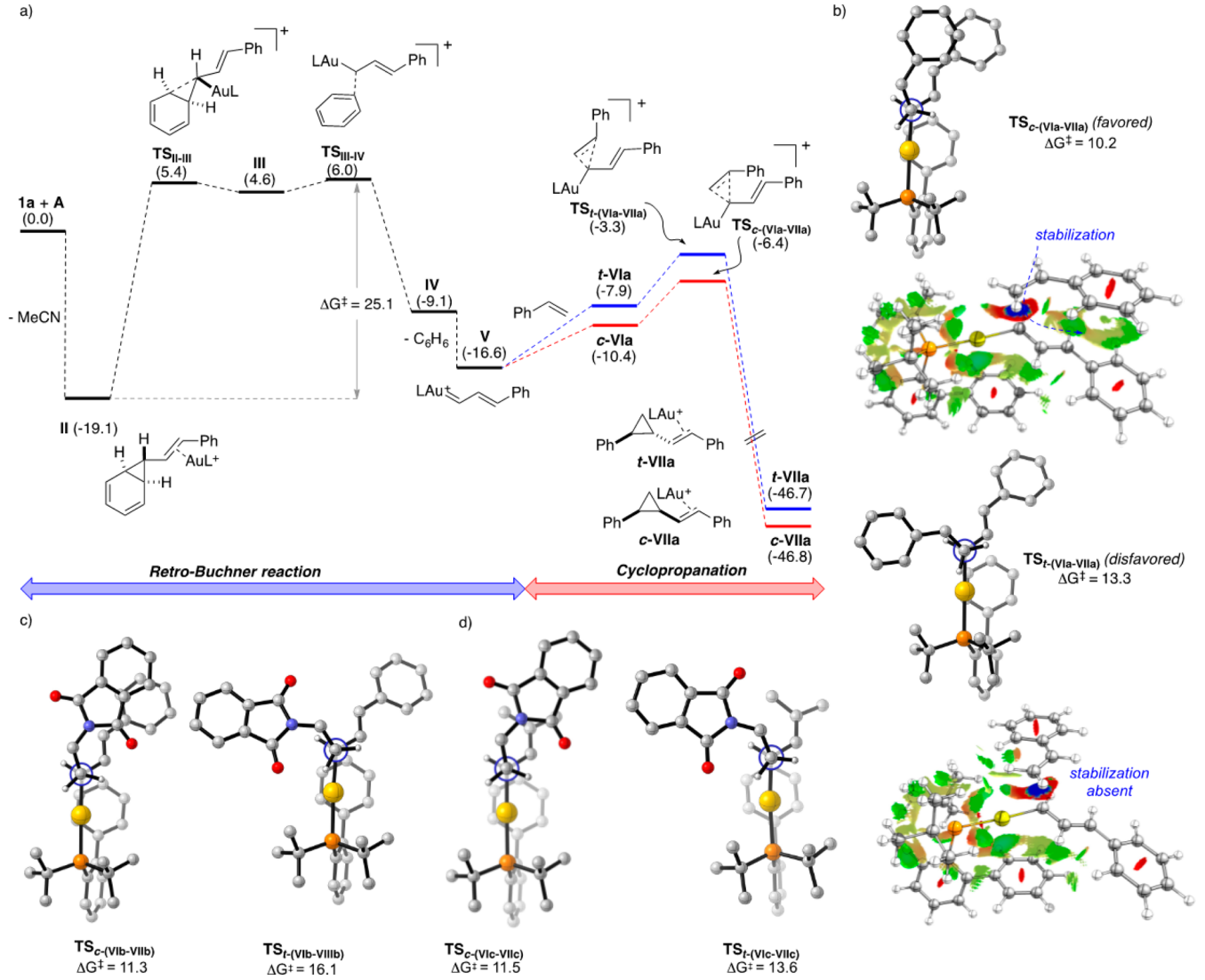

Figure 1. (a) Calculated energies for the gold(I)-catalyzed retro-Buchner reaction and cyclopropanation reaction using SMD(CH_2Cl_2)-M06/6-311+G(2d,p), SDD(Au, ζ_f = 1.05)//SMD(CH_2Cl_2)-M06/6-31G(d), SDD(Au) at the standard state ([Au] = Au-JohnPhos). For the full PES see the Supporting Information. Energies are given in kcal mol^{-1}. (b–d) Newman projections of the cyclopropanation transition states (most hydrogen atoms are omitted for clarity) and color-filled RDG isosurface for $TS_{(VIa\text{-}VIIa)}$ (isovalue set to 0.5): (blue) areas of attraction (covalent bonding); (green) vdW interaction; (red) areas of repulsion (steric and ring effects).

Table 5. Calculation of Difference in Activation Energies ($\Delta\Delta E$) between *cis*- and *trans*-Cyclopropanation[a]

functional	$TS_{t\text{-}(VIa\text{-}VIIa)} - TS_{c\text{-}(VIa\text{-}VIIa)}$	$TS_{t\text{-}(VIb\text{-}VIIIb)} - TS_{c\text{-}(VIb\text{-}VIIb)}$	$TS_{t\text{-}(VIc\text{-}VIIc)} - TS_{c\text{-}(VIc\text{-}VIIc)}$
M06	3.1	5.8	3.9
PBE	1.3	1.7	0.7
PBE-D3(BJ)	3.2	6.0	3.7

[a]Values given in kcal mol^{-1}.

systems (Figure 1b).[52,58] Remarkably, even in the case of $TS_{c\text{-}(VIc\text{-}VIIc)}$ (Figure 1d) lacking the phenyl substituent at the carbene, $\pi-\pi$ interactions between the alkene and the phthalimide result in the stabilization of the *cis*-TS.

The calculated mechanisms reveal a unified stereomodel for all three reactions, explaining the diastereoselectivity in the cyclopropanation step, which we consider relevant for other gold-catalyzed cyclopropanation reactions.[14a,16b,30b] Our model distinguishes itself from a previous proposal[16b] by considering noncovalent interactions to explain the high diastereoselectivity of the reaction and also takes into account the steric bulk of the phosphine ligand, which forces the substrates to adopt a particularly rigid geometry.

For the subsequent isomerization of the *cis*-cyclopropanes to the corresponding *trans* isomers, we identified two transition states with a linear carbocationic structure resulting from the cleavage of the C1–C2 bond (Figure 2).[59] As expected, the stability of the transition states depends on the stabilization of the carbocation. For the most favorable pathway, natural bond orbital analysis showed that the positive charge is stabilized as an allylic carbocation in $TS_{c\text{-}Xb\text{-}t\text{-}Xb}$, resulting in an activation barrier of 29.4 kcal mol^{-1}, which agrees well with the experimentally determined value of 29 kcal mol^{-1}.[54] The alternative regioisomeric cleavage of the cyclopropane requires a much higher activation energy (38.4 kcal mol^{-1}) through $TS_{c\text{-}VIIIb\text{-}t\text{-}VIIIb}$, where the positive charge is stabilized through participation of the nitrogen lone pair leading to an iminium-like structure, as demonstrated by natural population analysis.

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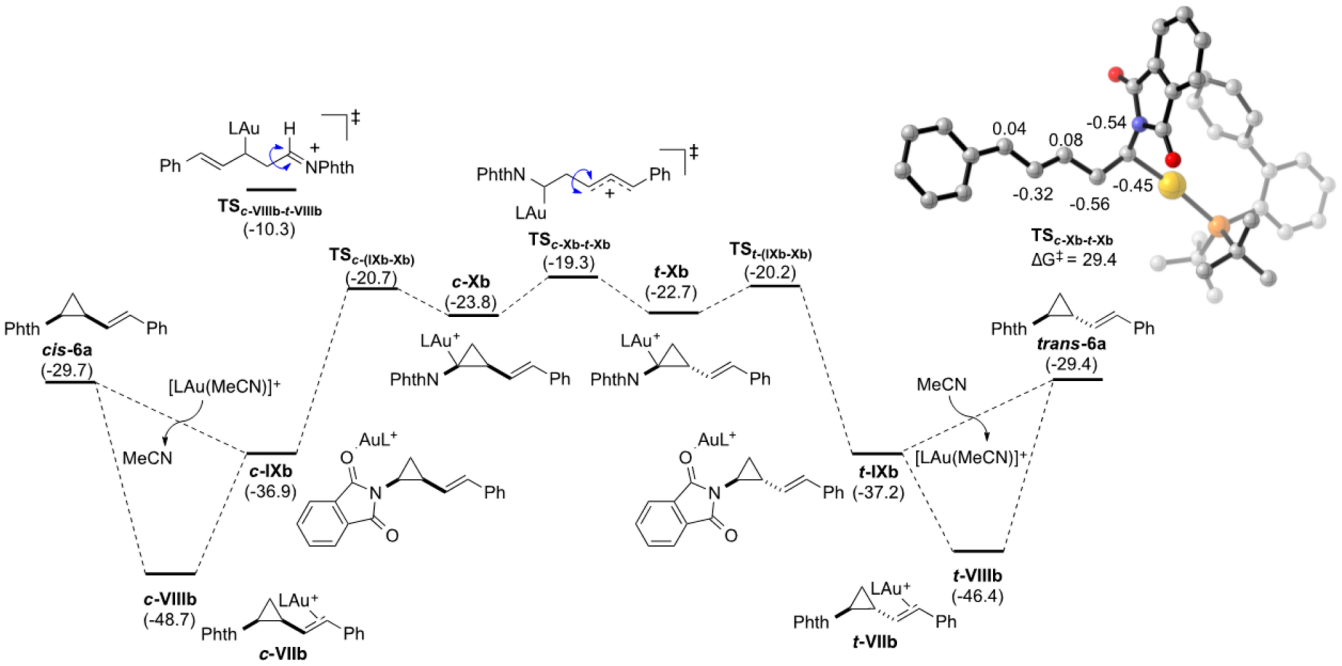
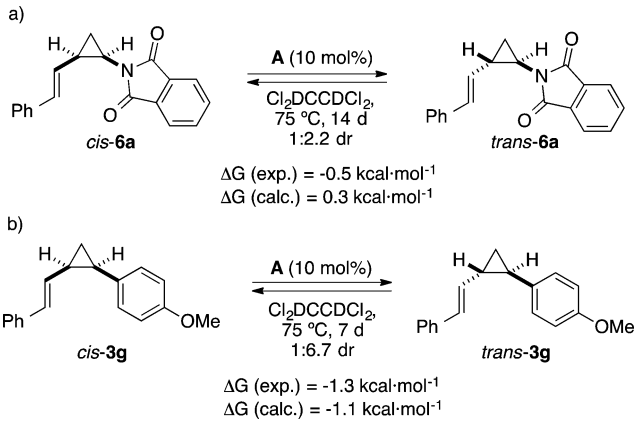


Figure 2. Calculated energies for the gold-catalyzed *cis*−*trans* isomerization and NPA charges of $TS_{cXb\text{-}tXb}$ (hydrogen atoms are omitted for clarity). Computational details are identical with those in Figure 1. Energies are given in kcal mol^{-1}. For the full PES see the Supporting Information.

In analogy to the isomerization pathway of *cis*-**6a**, a linear, carbocationic transition state with a relatively low activation energy of 25.9 kcal mol^{-1} was also identified for the isomerization of cyclopropane *cis*-**6g**.[52]

The isomerization reaction of a phthalimide-substituted cyclopropane such as **6a** was found to be more general (Scheme 7).[60] Thus, for example, *p*-methoxy-substituted substrate *cis*-**3g** could be isomerized to form *trans*-**3g** by heating in the presence of gold(I) complex **A**.

Scheme 7. Experimental and Theoretical Determination of the *cis*−*trans* Equilibration of Cyclopropanes 3g and 6a[37]



CONCLUSIONS

We have developed a highly *cis* selective gold-catalyzed cyclopropanation for the formation of vinylcyclopropanes and vinylaminocyclopropanes using stable and readily available 7-alkenyl-1,3,5-cycloheptatrienes as the source of the reactive metal carbenes. Remarkably, the decarbenation takes place at 75 °C, under conditions much milder than those required for other cycloheptatrienes. Our method allows for the preparation of diversely functionalized *cis*-cyclopropanes in diastereomerically pure form. Combined experimental and computational investigations of the reaction mechanism led to a refined stereochemical model for the cyclopropanation, in which stabilizing $\pi-\pi$ interactions account for the excellent *cis* selectivity. In addition, the mechanism of an unprecedented gold(I)-catalyzed *cis*−*trans* isomerization of cyclopropanes has been elucidated, which also allows for the preparation of *trans*-cyclopropanes. With a more clear understanding of the selectivity-determining elements, we are currently pursuing the development of enantioselective cyclopropanation reactions based on the retro-Buchner reaction.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.7b00737.

All procedures and characterization data for new compounds and full details on the theoretical calculations (PDF)

Crystallographic data (CIF)

Crystallographic data (CIF)

Crystallographic data (CIF)

Crystallographic data (CIF)

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Notes

The authors declare no competing financial interest.

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ACS Catal. 2017, 7, 3668−3675