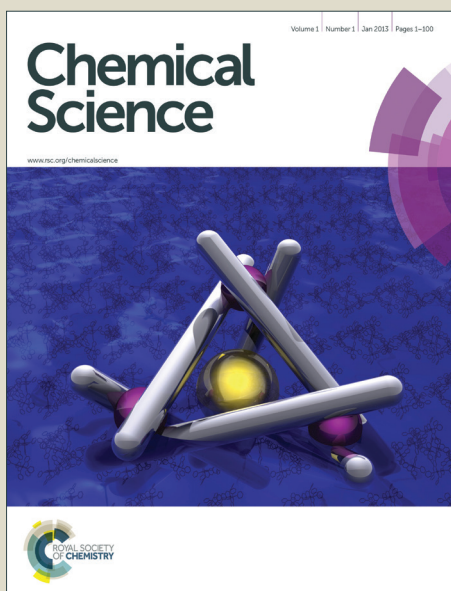


Chemical Science

Accepted Manuscript



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this *Accepted Manuscript* with the edited and formatted *Advance Article* as soon as it is available.

You can find more information about *Accepted Manuscripts* in the [Information for Authors](#).

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard [Terms & Conditions](#) and the [Ethical guidelines](#) still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

Cite this: DOI: 10.1039/coxx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

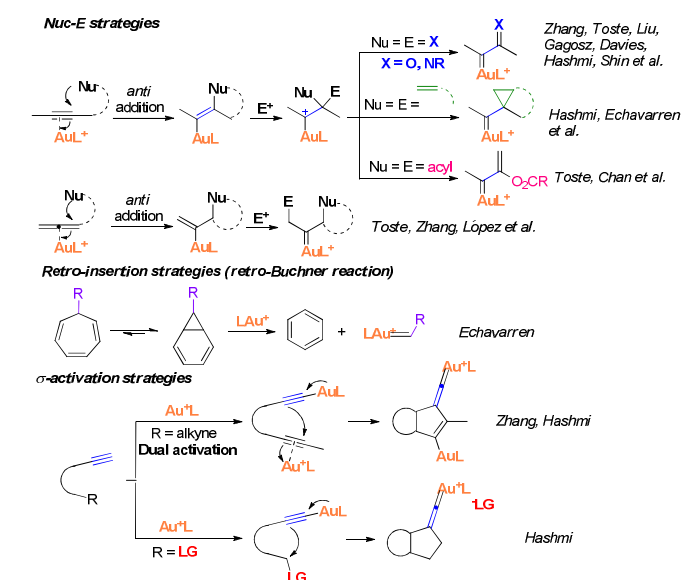
Gold(I)-Catalyzed Cycloisomerization of Vinylidenecyclopropane-enes *via* Carbene or non-Carbene Processes

De-Yao Li,[†] Yin Wei,[†] Ilan Marek,[‡] Xiang-Ying Tang,^{†*} Min Shi^{†*}

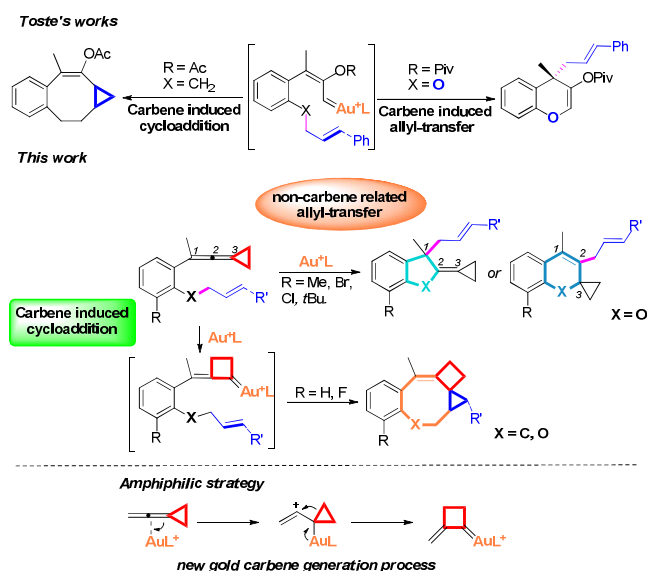
Received (in XXX, XXX) Xth XXXXXXXXXX 20XX, Accepted Xth XXXXXXXXXX 20XX
DOI: 10.1039/b000000x

Gold catalyzed cycloisomerization of aromatic ring tethered vinylidenecyclopropane-enes provides a divergent synthetic protocol for the construction of O-containing fused heterocycles through controllable carbene or non-carbene related processes. The carbene induced process features a new amphiphilic strategy to generate gold carbene via a rearrangement of vinylidenecyclopropane. Whereas, the electronic effect of *ortho*-substituents switches the reaction mode onto the non-carbene related process, from which five- or six-membered rings are selectively produced through allyl-migration.

Recently, the field of gold catalysis has witnessed significant developments.^[1] The exploration of new reaction modes in this arena has emerged as one of the forefront of current research. Due to the relativistic effect observed with gold, gold carbene complexes,^[2] these species present unique properties and reactivities and impressive work has appeared recently,^[3] providing novel reaction pathways that could be summarized in Scheme 1: 1) Nuc-E strategies have been widely used to form α -functionalized gold carbenes;^[4] 2) Retro-Buchner reaction can be easily used *in situ* to generate gold carbenes as a potentially common method;^[5] 3) The Au- σ -activated alkynes could also produce gold vinylidene species, which can act as gold carbenes through versatile reaction pathways.^[6] However, to the best of our knowledge, there are barely any reports on one precursor being able to rapidly generate molecular complexity^[7] via either carbene or non-carbene pathways in gold catalysis.^[8] On the basis of our ongoing investigation on metal-catalyzed transformations of vinylidenecyclopropanes (VDCPs),^[9] we envisaged that VDCPs could be excellent candidates for the exploration of new reaction modes in gold catalysis because of its multiple reaction sites. Previously, Toste and co-workers reported novel intramolecular cyclopropanation and allyl-transfer both through gold carbene intermediates (Scheme 2).^[4q-4s] Interestingly, during our study on the gold catalyzed cycloisomerization of aromatic ring tethered VDCP-enes, we found that cyclopropanation



Scheme 1. Previous Strategies for the Generation of Gold Carbenes



Scheme 2. Modulable Reaction Processes of VDCP-enes Catalyzed by Gold(I) Complex along with A New Gold Carbene Generation Process

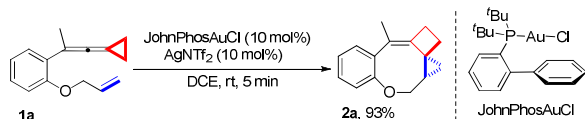
[†] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, P. R. China. E-mail: siocxiangying@mail.sioc.ac.cn; mshi@mail.sioc.ac.cn.

[‡] Schulich Faculty of Chemistry, Technion-Israel Institute of Technology, Technion City, Haifa 32000, Israel, Email: chilanm@tx.technion.ac.il

[†] Electronic Supplementary Information (ESI) available: Experimental procedures, characterization data of new compounds, and CCDC 996502, 980558, 997410 and 996499. See DOI: 10.1039/b000000x/

and allyl transfer through controllable carbene/non-carbene related processes could be achieved, respectively, featuring a new gold carbene generation process. The VDCP acts as a nucleophile under activation by gold(I) complex and then undergoes ring expansion as an electrophile due to its amphiphilic electronic nature to generate gold carbene species. Herein, we wish to report these intriguingly new gold-catalyzed transformations, which afford an easy and efficient access to fused five-, six- and eight-membered ring systems (Scheme 2).

Upon reaction condition screening (see SI for the details), we identified JohnPhosAuCl (10 mol%) as the best gold catalyst together with AgNTf₂ (10 mol%) to carry out the reaction of **1a**. Product **2a**^[10] was formed in 93% yield at ambient temperature in DCE within 5 minutes (Scheme 3).

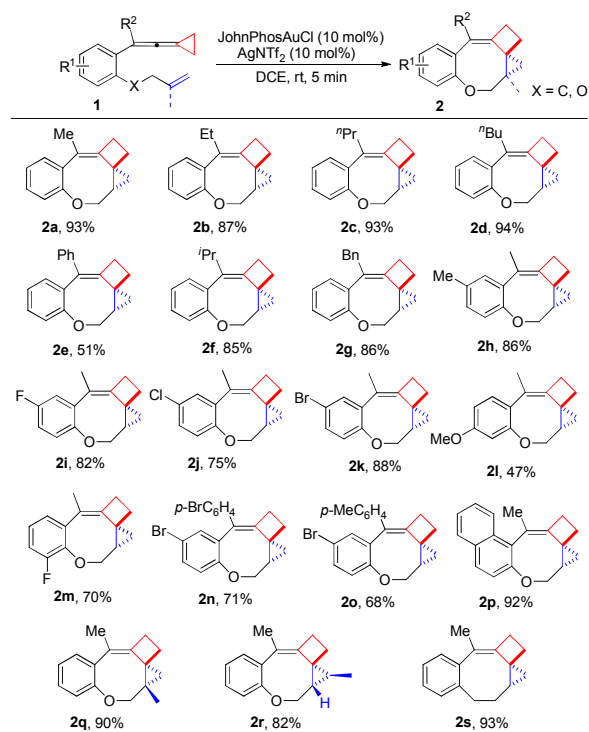


Scheme 3. Optimal Conditions for the Synthesis of **2a**.

Having the optimal reaction conditions in hand, we next investigated the scope of the reaction with respect to various VDCP-enes. As shown in Table 1, these cyclization reactions proceeded smoothly, affording the desired products in moderate to excellent yields. Although this transformation proceeds in high yields for alkyl-substituted VDCPs (R^2 = alkyl), yield is slightly lower for phenyl-substituted VDCP (R^2 = Ph, **2e**). As for the substituents at the benzene ring, no obvious erosion of yields was observed when different halogen atoms such as F, Cl or Br were introduced. Substrate **1l** with electron-donating substituent MeO at the benzene ring afforded product **2l** in 47% yield.^[11] Naphthalene tethered substrate gave the expected product **2p** in good yield. Substrates **1q** and **1r** bearing a methyl substituent at the allyl group also afforded the corresponding products **2q** and **2r** in 90% and 82% yields, respectively. When homoallylic group was introduced instead of allyloxy group, the desired product **2s** could be given in 93% yield. It should be noted that only product **2l** was obtained in lower yield but it may come from the instability of the starting material. The DFT calculation indicated that the formation of **2** is an exothermic process (see SI).

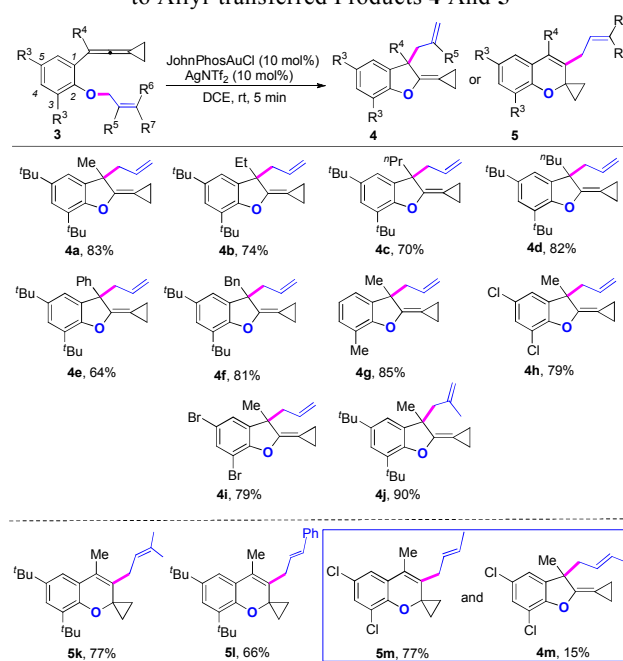
We next synthesized substrate **3a** from 3,5-di-*t*-butyl salicylaldehyde to examine the reaction outcome. However, we found that an allyl-transferred product **4a** derived from a non-carbene process was formed in 83% yield rather than the cyclopropanation product (Table 2).^[12] To have a better insight on the substituent effects, we synthesized a library of substrates to clarify the scope. Consistent with the above results, all of these VDCP-enes having a substituent such as *t*-Bu, Me or Cl at 3-position gave the allyl-transferred products in good yields. Only when a fluorine atom was introduced at the 3-position, the reaction proceeded via carbene process, giving **2m** in 70% yield as shown in Table 1. As for substrates **3k** and **3l** having two methyl groups or one phenyl group at the terminal position of alkene, another type of allyl-transfer took place, affording **5k**^[13] and **5l** in 77% and 66% yields, respectively (Table 2). In the case of **3m**, two types of allyl-transfers took place at the same time to give **5m** and **4m** in good total yield as a product mixture (Table 2). **3k**'s regioisomer, O-(1,1-dimethylprop-2-enyl) derivative, is unavailable via the present synthetic method (see Scheme at page S8 in SI for the details).

Table 1. Reaction Scope of VDCP-enes **1** to Polycyclic Products **2**.^a



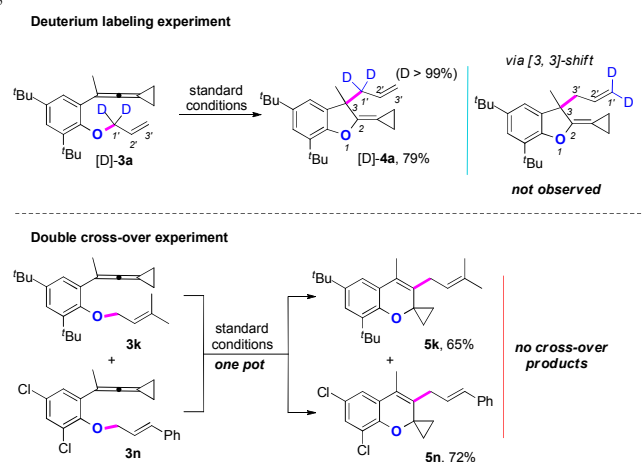
^a The reaction free energy $\Delta G_{\text{rxn}, 298}$ is -17.9 kcal/mol (obtained by DFT calculations, for details, see SI). This result suggests that the formation of product **2** is exothermic.

Table 2. Gold-catalyzed Cycloisomerization of VDCP-enes **3** to Allyl-transferred Products **4** And **5**



Two mechanistic experiments were conducted to clarify the allyl-transfer process of allyloxy group (Scheme 4). Treatment of [D]-**3a** under the standard conditions produced [D]-**4a** in 79% yield along with > 99% D content. The deuterium labeling experiments suggesting that the allyl-transfer might proceed through a 1, 3-shift of allylic oxonium intermediate rather than a 75 3, 3-shift^[18, 48] because none allylic inversion was observed. Furthermore, the double cross-over experiment using **3k** and **3n**

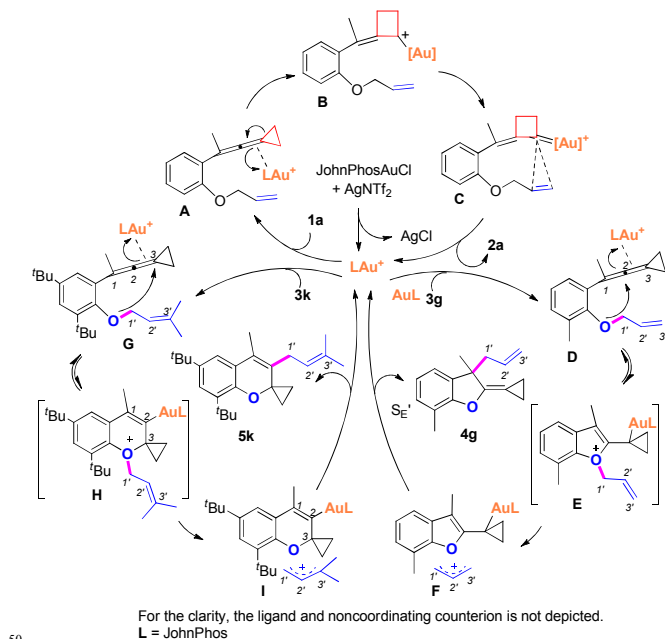
as substrates under the standard conditions only produced the corresponding products **5k** and **5n**, respectively and none cross-over products were observed, indicating that the allyl-transfer proceeded via an intimate ion-pair.



Scheme 4. Mechanistic Experiments

Based on Toste's previous work and other groups' results, plausible mechanisms^[45, 14] for above gold-catalyzed carbene and non-carbene related processes are outlined in Scheme 5. As for substrate **1a**, upon coordination of gold catalyst with VDCP intermediate **A** was formed, which initiates a ring expansion to give gold stabilized cation **B** and then carbene species **C**. Subsequent cyclopropanation produces polycyclic adduct **2a**. When the *ortho*-position is substituted by a Me, Cl, Br or *t*Bu group, due to the increased nucleophilicity of the oxygen atom, **3g** attacks the middle carbon of the allenyl moiety in intermediate **D** to give the corresponding oxonium intermediate **E**, which undergoes S_E' allyl-transfer^[15] to afford product **4g** via an intimate ion-pair **F**. In the case of **3k**, the oxygen atom exclusively attacks the terminal carbon at the allene moiety of VDCP in intermediate **G** to give the corresponding oxonium intermediate **H** presumably due to the steric bulkiness at the alkene site, which similarly undergoes the allyl-transfer to give **5k** via an intimate ion-pair **I**. Overall, the gold species is finally quenched by allylic cation to give the allyl-transferred product. The allyl-migration mode is different from previous work,^[45, 15b-c] probably due to the steric hindrance of cyclopropane in the VDCP-type substrates.

The X-ray crystal structures of substrates **1n** and **3e** indicated that the distances between the oxygen and the central carbon of VDCP are very close (for details, see SI), suggesting that it is not the *ortho*-substituent that induces a proximity effect promoting the nucleophilic attack. We believe that the electronic effects of *ortho*-substituents in substrates influence the nucleophilicity of the oxygen atom, which is the origin for the different reactivity of substrates **2** and **3**. Calculation of Mulliken Charge on O atom influenced by X (a substituent or a substituted group at the *ortho*-position) was carried out on the basis of B3LYP/6-31+G(d) level, inferring that different substituents led to different electron density on the oxygen atom in the following order of *t*Bu > Br > Cl > H > F (Table 3). In the similar manner, Mulliken Charge on O atom influenced by Y (a substituent at the *para*-position) was also calculated at B3LYP/6-31+G(d) level, and the results show that the substituent at *para*-position does not influence the electron density on the oxygen atom significantly (Table 3). These results suggest that nucleophilicity of the oxygen is tunable by a judicious choice of substituents at the 3-position of the



Scheme 5. Proposed Mechanisms

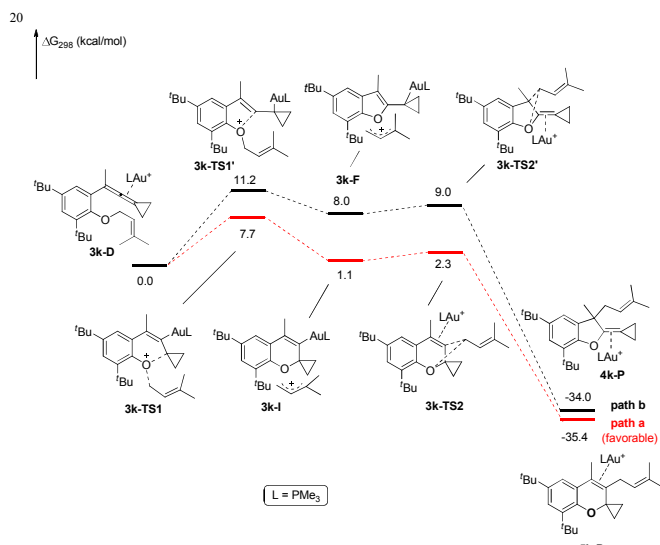
benzene ring, controlling therefore the carbene or non-carbene related processes at the very beginning. The thermodynamic stability of the subsequent oxonium intermediate **E** with different *ortho*-substituents was also investigated by DFT calculations (see SI for the details). The reactions were probably controlled by kinetic factors judged by the reaction conditions (5 minutes at room temperature). In order to understand why the substituents on terminal alkene can affect the reaction outcome, we did DFT calculations on key steps in the reaction of substrate **3k**. All calculations have been performed at B3LYP/6-31+G(d)/SDD level with Gaussian 09 program (see SI for the details). We investigated two reaction pathways starting from gold complex **3k-D** in Scheme 6. In **path a**, the oxygen atom in gold complex **3k-D** attacks the terminal carbon at the allene moiety to give an intermediate **3k-I** via transition state **3k-TS1** with an energy barrier of 7.7 kcal/mol. Subsequently, the intermediate **3k-I** passes through transition state **3k-TS2** with an energy barrier of 2.3 kcal/mol, giving product complex **5k-P**. On the other hand, in **path b**, the oxygen atom in gold complex **3k-D** attacks the middle carbon at the allene moiety to give an intermediate **3k-F** via transition state **3k-TS1'** with an energy barrier of 11.2 kcal/mol. The energy of **3k-TS1'** is higher than that of **3k-TS1** by 3.5 kcal/mol, presumably due to the steric repulsions among the substituents on terminal alkene, the *t*-Bu substituent, and the ligand (For optimized structures of **3k-TS1'** and **3k-TS1**, see Figure 1). Subsequently, the intermediate **3k-F** passes through transition state **3k-TS2'** with an energy barrier of 9.0 kcal/mol, giving product complex **4k-P**. The calculation results show that all intermediates along the **path a** are thermodynamically more stable than those along the **path b**, meanwhile the **path a** is also kinetically favourable, indicating that the product **5k** is the major product. The calculation results are in line with experimental results which obtained the product **5k** using **3k** as starting material. For comparison, we also investigated two pathways for the reaction of **3a**. The relative energies of all intermediates and transitional states along the reaction pathway for the reaction of **3a** are shown in Scheme 7. Similarly, the oxygen atom in gold complex **3a-D** attacks the terminal carbon at the allene moiety to give an intermediate **3a-I** via transition state **3a-TS1** with an energy barrier of 9.3 kcal/mol in **path a'**. Subsequently, the

intermediate **3a-I** passes through transition state **3a-TS2** with an energy barrier of 8.4 kcal/mol, giving product complex **5a-P**. On the other hand, in **path b'**, the oxygen atom in gold complex **3a-D** attacks the middle carbon at the allene moiety to give an intermediate **3a-F** via transition state **3a-TS1'** with an energy barrier of 8.9 kcal/mol. The energy of **3a-TS1'** is slightly lower than that of **3a-TS1** by 0.9 kcal/mol, probably due to no steric repulsions among the substituents on terminal alkene, the *t*-Bu substituent, and the ligand. Subsequently, the intermediate **3a-F** passes through transition state **3a-TS2'** with an energy barrier of 6.3 kcal/mol, giving product complex **4a-P**, which is lower than that of product complex **5a-P** by 1.8 kcal/mol. The calculation results show that the **path b'** is also kinetically favourable, indicating that the product **4a** is the major product. The calculation results are in line with experimental results which obtained the product **4a** using **3a** as starting material.

Table 3. *Ortho*- and *Para*-substituent Effects.

X	Y	Mulliken Charge on O atom ^a
F	H	-0.244
H	H	-0.301
Cl	H	-0.308
Br	H	-0.315
<i>t</i> Bu	H	-0.347
H	F	-0.242
H	Cl	-0.247
H	Br	-0.248

^a Calculated at B3LYP/6-31+G(d) level



Scheme 6. DFT studies on key reaction steps of the reaction of **3k**.

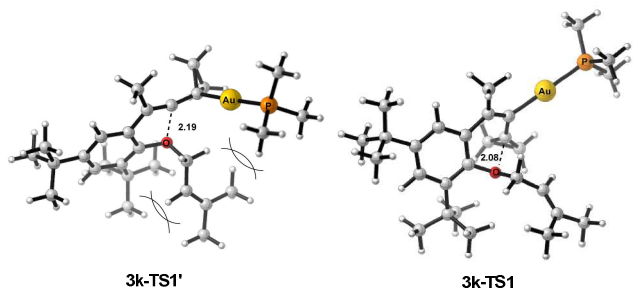
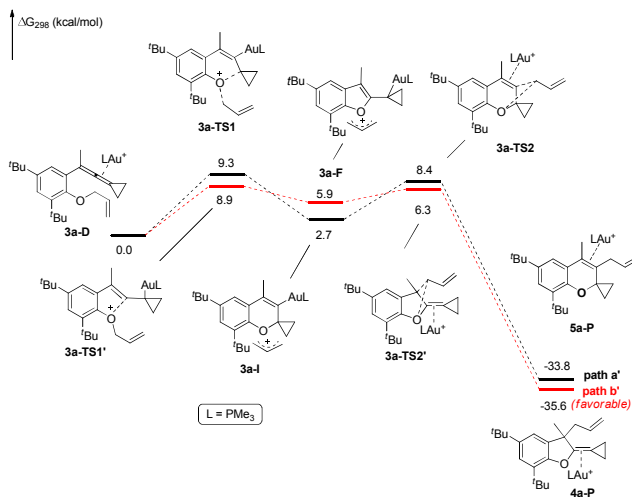
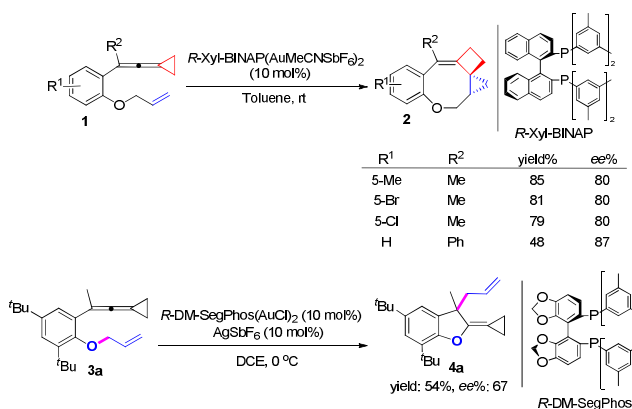


Figure 1. Optimized structures of **3k-TS1'** and **3k-TS1**.



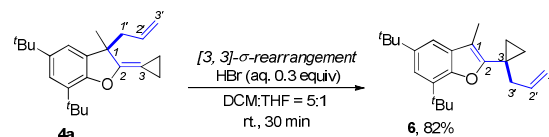
Scheme 7. DFT studies on key reaction steps of the reaction of **3a**.



Scheme 8. Asymmetric Versions of The Two Processes

On the basis of the above results, we also attempted to develop an asymmetric variant for the two intramolecular cyclizations. The optimization of these asymmetric gold catalyses revealed that xyl-BINAP ligand coordinated gold complex gave the highest ee values in the carbene induced process, while DM-SegPhos ligand coordinated gold complex was the best one for the other (see SI for the details). As shown in Scheme 8, the corresponding product **2** could be obtained in good yields along with 80-87% ee values whereas the allyl-transferred product **4a** was obtained in moderate yield along with 67% ee value. Using 20 mol% of AgSbF₆ did not improve the ee value of **4a** (see SI).

The product **4a** could be easily transformed into benzofuran derivative **6** in 82% yield in the presence of a Brønsted acid such as HBr via a [3, 3]-sigmatropic rearrangement (Scheme 9) (see SI for the details on screening of the reaction conditions).^[16] The compound **6** could be easily transformed to the masked alcoholic products via normal processes (see SI for the details).^[17]



Scheme 9. Further Transformation of **4a**

In a summary, we have explored a novel gold(I)-catalyzed cycloisomerization of VDCP-ene derivatives via carbene or non-carbene processes, in which a substituent adjacent to the oxygen

atom could switch the reaction modes. The reaction features a new amphiphilic strategy for gold carbene generation. For non-carbene cyclization, the regioselectivity is dependent upon the steric effect at the alkene moiety. These carbene or non-carbene processes can provide a new synthetic protocol for the divergent synthesis of O-containing heterocyclic scaffolds including a fused tricyclic system and fused five-, and six-membered ring systems. Further investigations to examine the mechanistic details more extensively and exploration of new methodology based on gold catalyzed transformations of VDCPs as well as their asymmetric variants are currently underway in our laboratory.

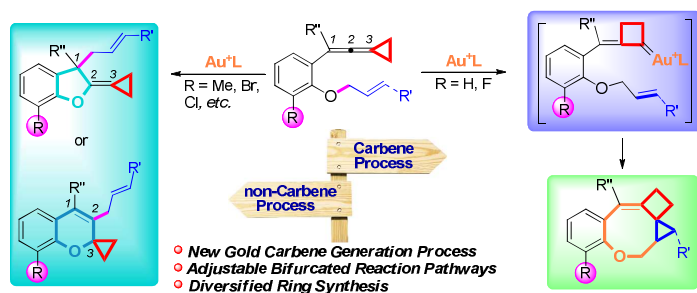
Acknowledgement: We are grateful for the financial support from the National Basic Research Program of China (973)-2015CB856603, and the National Natural Science Foundation of China (20472096, 21372241, 21361140350, 20672127, 21421091, 21372250, 21121062, 21302203 and 20732008).

Notes and references

- [1] For selected reviews, see: (a) A. S. K. Hashmi, *Chem. Rev.*, 2007, **107**, 3180; (b) A. S. K. Hashmi and M. Rudolph, *Chem. Soc. Rev.*, 2008, **37**, 1766; (c) E. Jiménez-Núñez and A. M. Echavarren, *Chem. Rev.*, 2008, **108**, 3326; (d) M. Rudolph and A. S. K. Hashmi, *Chem. Soc. Rev.*, 2012, **41**, 2448; (e) D. J. Gorin, B. D. Sherry and F. D. Toste, *Chem. Rev.*, 2008, **108**, 3351; (f) S. P. Nolan, *Acc. Chem. Res.*, 2011, **44**, 91; (g) Y.-M. Wang, A. D. Lackner and F. D. Toste, *Acc. Chem. Res.*, 2014, **47**, 889-901; (h) C. Obradors and A. M. Echavarren, *Acc. Chem. Res.*, 2014, **47**, 902; (i) L. Zhang, *Acc. Chem. Res.*, 2014, **47**, 877; (j) C. M. Friend and A. S. K. Hashmi, *Acc. Chem. Res.*, 2014, **47**, 729; (k) A. S. K. Hashmi, *Acc. Chem. Res.*, 2014, **47**, 864; (l) H.-S. Yeom and S. Shin, *Acc. Chem. Res.*, 2014, **47**, 966; (m) A. Fürstner, *Acc. Chem. Res.*, 2014, **47**, 925.
- [2] (a) P. Pyykko and J. P. Desclaux, *Acc. Chem. Res.*, 1979, **12**, 276; (b) D. J. Gorin and F. D. Toste, *Nature* 2007, **446**, 395; (c) H. G. Raubenheimer and H. Schmidbaur, *Organometallics* 2012, **31**, 2507.
- [3] For evidence of gold carbenoids, see (a) A. M. Echavarren, *Nat. Chem.*, 2009, **1**, 431; (b) G. Seidel and A. Fürstner, *Angew. Chem., Int. Ed.*, 2014, **53**, 4807; (c) P. Nösel, T. Laura Nunes dos Santos Comprido, Lauterbach, M. Rudolph, F. Rominger and A. S. K. Hashmi, *J. Am. Chem. Soc.*, 2013, **135**, 15662; (d) T. Wang, S. Shi, M. M. Hansmann, E. Rettenmeier, M. Rudolph and A. S. K. Hashmi, *Angew. Chem. Int. Ed.*, 2014, **53**, 3715.
- [4] For O as Nuc and E, see: (a) B. Lu, Y. Li, Y. Wang, D. H. Aue, Y. Luo and L. Zhang, *J. Am. Chem. Soc.*, 2013, **135**, 8512; (b) Z. Wang, Y. Wang and L. Zhang, *J. Am. Chem. Soc.*, 2014, **136**, 8887; (c) N. D. Shapiro and F. D. Toste, *J. Am. Chem. Soc.*, 2007, **129**, 4160; (d) S. Ghorpade, M.-D. Su and R.-S. Liu, *Angew. Chem., Int. Ed.*, 2013, **52**, 4229; (e) D. Vasu, H.-H. Hung, S. Bhunia, S. A. Gawade, A. Das and R.-S. Liu, *Angew. Chem., Int. Ed.*, 2011, **50**, 6911; (f) S. Bhunia, S. Ghorpade, D. B. Huple and R.-S. Liu, *Angew. Chem., Int. Ed.*, 2012, **51**, 2939; (g) H. S. Yeom, Y. Lee, J. Jeong, E. So, S. Hwang, J. E. Lee, S. S. Lee and S. Shin, *Angew. Chem., Int. Ed.*, 2010, **49**, 1611; (h) P. W. Davies, A. Cremonesi and N. Martin, *Chem. Commun.*, 2011, **47**, 379; (i) G. Henrion, T. E. J. Chavas, X. Le Goff and F. Gagosz, *Angew. Chem., Int. Ed.*, 2013, **52**, 6277; (j) A. S. K. Hashmi, T. Wang, S. Shi and M. Rudolph, *J. Org. Chem.*, 2012, **77**, 7761; (k) S. Shi, T. Wang, W. Yang, M. Rudolph and A. S. K. Hashmi, *Chem. Eur. J.*, 2013, **19**, 6576; For alkene/aryl as Nuc and E, see: (l) A. S. K. Hashmi, T. M. Frost and J. W. Batsin, *J. Am. Chem. Soc.*, 2000, **122**, 11553; (m) A. S. K. Hashmi, M. Rudolph, H. Siehl, M. Tanaka, J. W. Bats and W. Frey, *Chem. Eur. J.*, 2008, **14**, 3703; (n) V. Lopez-Carrillo and A. M. Echavarren, *J. Am. Chem. Soc.*, 2010, **132**, 9292; (o) P. Perez-Galan, E. Herrero-Gomez, D. T. Hog, N. J. A. Martin, F. Maseras and A. M. Echavarren, *Chem. Sci.*, 2011, **2**, 141; (p) Y. Wang, M. E. Muratore, Z. Rong and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2014, **53**, 14022; For acyl group as a strategy for gold carbene generation, see: (q) M. J. Johansson, D. J. Gorin, S. T. Staben and F. D. Toste, *J. Am. Chem. Soc.*, 2005, **127**, 17616; (r) I. D. G. Watson, S. Ritter and F. D. Toste, *J. Am. Chem. Soc.*, 2009, **131**, 2056; (s) M. Uemura, I. D. G. Watson, M. Katsukawa and F. D. Toste, *J. Am. Chem. Soc.*, 2009, **131**, 3464; (t) Y. Shi, K. E. Roth, S. D. Ramgren and S. A. Blum, *J. Am. Chem. Soc.*, 2009, **131**, 18022; (u) W. Rao, M. J. Koh, D. Li, H. Hirao and P. W. H. Chan, *J. Am. Chem. Soc.*, 2013, **135**, 7926; For allene as carbene precursor, see: (v) M. R. Luzung, P. Mauleón and F. D. Toste, *J. Am. Chem. Soc.*, 2007, **129**, 12402; (w) G. Zhang, V. J. Catalano and L. Zhang, *J. Am. Chem. Soc.*, 2007, **129**, 11358; (x) I. Alonso, B. Trillo, F. López, S. Montserrat, G. Ujaque, L. Castedo, A. Lledós and J. L. Mascareñas, *J. Am. Chem. Soc.*, 2009, **131**, 13020; (y) F. López and J. L. Mascareñas, *Chem. Eur. J.*, 2011, **17**, 418.
- [5] (a) C. R. Solorio-Alvarado and A. M. Echavarren, *J. Am. Chem. Soc.*, 2010, **132**, 11881; (b) C. R. Solorio-Alvarado, Y.-H. Wang and A. M. Echavarren, *J. Am. Chem. Soc.*, 2011, **133**, 11952; (c) Y. Wang, P. R. McGonigal, B. Herle, M. Besora and A. M. Echavarren, *J. Am. Chem. Soc.*, 2014, **136**, 801.
- [6] (a) L. Ye, Y. Wang, D. H. Aue and L. Zhang, *J. Am. Chem. Soc.*, 2012, **134**, 31; (b) J. Bucher, T. Wurm, K. S. Nalivela, M. Rudolph, F. Rominger and A. S. K. Hashmi, *Angew. Chem., Int. Ed.*, 2014, **53**, 3854; (c) M. M. Hansmann, M. Rudolph, F. Rominger and A. S. K. Hashmi, *Angew. Chem., Int. Ed.*, 2013, **52**, 2593; (d) A. S. K. Hashmi, I. Braun, P. Noesel, J. Schaedlich, M. Wietek, M. Rudolph and F. Rominger, *Angew. Chem., Int. Ed.*, 2012, **51**, 4456; (e) A. S. K. Hashmi, T. Haefner, M. Rudolph and F. Rominger, *Chem., Eur. J.*, 2011, **17**, 8195; (f) A. S. K. Hashmi, M. Wietek, I. Braun, P. Noesel, L. Jongbloed, M. Rudolph and F. Rominger, *Adv. Synth. Catal.*, 2012, **354**, 555; (g) A. S. K. Hashmi, M. Wietek, I. Braun, M. Rudolph and F. Rominger, *Angew. Chem., Int. Ed.*, 2012, **51**, 10633; (h) M. H. Vilhelmsen and A. S. K. Hashmi, *Chem., Eur. J.*, 2014, **20**, 1901; (i) Y. Yu, W. Yang, F. Rominger and A. S. K. Hashmi, *Angew. Chem., Int. Ed.*, 2013, **52**, 7586; (j) A. S. K. Hashmi, I. Braun, M. Rudolph and F. Rominger, *Organometallics* 2012, **31**, 644; (k) M. M. Hansmann, S. Tšupova, M. Rudolph, F. Rominger and A. S. K. Hashmi, *Chem., Eur. J.*, 2014, **20**, 2215; (l) M. Wietek, Y. Tokimizu, M. Rudolph, F. Rominger, H. Ohno, N. Fujii and A. S. K. Hashmi, *Chem., Eur. J.*, 2014, **20**, 16331; (m) P. Nösel, V. Müller, S. Mader, S. Moghimi, M. Rudolph, I. Braun, F. Rominger and A. S. K. Hashmi, *Adv. Synth. Catal.*, 2015, DOI: 10.1002/adsc.201400749; The possibility of gold allenylidene complexes, the higher homologues, have also been investigated: (n) M. M. Hansmann, F. Rominger and A. S. K. Hashmi, *Chem. Sci.*, 2013, **4**, 1552.
- [7] (a) K. C. Nicolaou, C. R. H. Hale, C. Nilewski and H. A. Ioannidou, *Chem. Soc. Rev.*, 2012, **41**, 5185; (b) M. M. Hann, A. R. Leach and G. Harper, *J. Chem. Inf. Comput. Sci.*, 2001, **41**, 856.
- [8] For carbene or non-carbene processes involved in propargylic ester substrates, see: (a) L. Zhang, *J. Am. Chem. Soc.*, 2005, **127**, 16804; (b) J. Zhao, C. O. Hughes and F. D. Toste, *J. Am. Chem. Soc.*, 2006, **128**, 7436; (c) A. Buzas and F. Gagosz, *J. Am. Chem. Soc.*, 2006, **128**, 12614; (d) A. Correa, N. Marion, L. Fensterbank, M. Malacria, S. P. Nolan and L. Cavallo, *Angew. Chem., Int. Ed.*, 2008, **47**, 718.
- [9] For selected reviews, and articles, see (a) A. Brandi, S. Cicchi, F. M. Cordero and A. Goti, *Chem. Rev.*, 2014, **114**, 7317; (b) G. Audran and H. Pellissier, *Adv. Synth. Catal.*, 2010, **352**, 575; (c) M. Shi, L.-X. Shao, J.-M. Lu, Y. Wei, K. Mizuno and H. Maeda, *Chem. Rev.*, 2010, **110**, 5883.
- [10] The unambiguous structure of **2** has been assigned by X-ray diffraction of **2n**.
- [11] The low yield for product **2l** is probably due to the instability of starting materials **1l** under the standard conditions since we found that it partially decomposed under acidic conditions.
- [12] The structure of **4a** has been confirmed by NMR spectroscopic analysis (NOESY, DEPT, gCOSY, HSQC and HMBC), see SI for the details.
- [13] The structure of **5k** has been unambiguously determined by X-ray crystal structure analysis.

- [14] (a) J. Fu, H. Shang, Z. Wang, L. Chang, W. Shao, Z. Yang and Y. Tang, *Angew. Chem., Int. Ed.*, 2013, **52**, 4198; (b) L. P. Liu, B. Xu, M. S. Mashuta and G. B. Hammond, *J. Am. Chem. Soc.*, 2008, **130**, 17642.
- [15] (a) A. S. K. Hashmi, A. M. Schuster, S. Litters, F. Rominger and M. Pernpointner, *Chem. Eur. J.*, 2011, **17**, 5661; (b) A. S. K. Hashmi, C. Lothschütz, R. Döpp, M. Ackermann, A. D. B. Becker, M. Rudolph, C. Scholz and F. Rominger, *Adv. Synth. Catal.*, 2012, **354**, 133; (c) M. Ackermann, J. Bucher, M. Rappold, K. Graf, F. Rominger and A. S. K. Hashmi, *Chem. Asian J.*, 2013, **8**, 1786; (d) A. S. K. Hashmi, K. Graf,
- 10 M. Ackermann and F. Rominger, *ChemCatChem* 2013, **5**, 1200.
- [16] (a) H. Zheng, L. L. Adduci, R. J. Felix, M. R. Gagné, *Angew. Chem., Int. Ed.*, 2014, **53**, 7904; (b) R. J. Felix, D. Weber, O. Gutierrez, D. J. Tantillo and M. R. Gagné, *Nat. Chem.*, 2012, **4**, 405; (c) R. J. Felix, O. Gutierrez, D. J. Tantillo and M. R. Gagné, *J. Org. Chem.*, 2013, **78**,
- 15 5685.
- [17] The structure of **6** has been confirmed by NMR spectroscopic analysis (NOESY, gCOSY, HSQC and HMBC), see SI for the details.

Gold(I)-Catalyzed Cycloisomerization of Vinylidenecyclopropanes via Carbene or non-Carbene Processes



Gold catalyzed cycloisomerization of aromatic ring tethered vinylidenecyclopropane-enes provides a divergent synthetic protocol for the construction of O-containing fused heterocycles through controllable carbene or non-carbene related processes. The carbene induced process features a new amphiphilic strategy to generate gold carbene via a rearrangement of vinylidenecyclopropane.

De-Yao Li,[†] Yin Wei,[†] Ilan Marek,[‡] Xiang-Ying Tang,^{†,*} Min Shi^{†,*}