

Cyclopropanation with Gold(I) Carbenes by Retro-Buchner Reaction from Cycloheptatrienes

César R. Solorio-Alvarado,[†] Yahui Wang,[†] and Antonio M. Echavarren^{*,†,‡}

[†]Institute of Chemical Research of Catalonia (ICIQ), Av. Països Catalans 16, 43007 Tarragona, Spain

[‡]Departament de Química Analítica i Química Orgànica, Universitat Rovira i Virgili, C/Marcel·lí Domingo s/n, 43007 Tarragona, Spain

S Supporting Information

ABSTRACT: Cationic gold(I) promotes the retro-Buchner reaction of 7-substituted 1,3,5-cycloheptatrienes, leading to gold(I) carbenes that cyclopropanate alkenes.

Gold(I)-catalyzed cyclization of 1,*n*-enynes proceeds through intermediates that can be viewed as highly distorted gold(I) carbenes,¹ which can be trapped by alkenes intra- or intermolecularly in cyclopropanation reactions.^{2,3} Cyclopropanation via gold(I) carbenes has been reported from propargylic carboxylates,⁴ vinyl allenes,⁵ and cyclopropenes.⁶ Diazo derivatives have also been commonly used for the cyclopropanation of alkenes in the presence of metal catalysts,⁷ including gold(I).⁸

We have recently found an example of a gold(I)-promoted retro-cyclopropanation in the context of a synthesis of 1,3-disubstituted naphthalenes.⁹ A similar process was also proposed in the gas-phase cleavage of 1-ethoxy-2-methoxycyclopropane with [AuIMes]⁺ [IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene] on the basis of CID experiments and theoretical calculations.¹⁰ Cleavage of cyclopropanes to form metal carbenes had only been reported previously using highly electrophilic PhWCl₃/AlCl₂ (R = Et, Cl)¹¹ or in reactions of strained bicyclo[1.1.0]butanes with Ni(0) or Rh(I) complexes.¹²

We have now found the first metal-promoted retro-Buchner reaction. 7-Substituted 1,3,5-cycloheptatrienes **1**, which are in equilibrium with norcaradienes **2**,¹³ react with cationic gold(I) catalysts to generate in situ gold(I) carbenes **3** that cyclopropanate alkenes (Scheme 1). Interestingly, the reverse process, formation of cycloheptatrienes, occurs as a side reaction in the gold(I)-catalyzed reaction between ethyl diazoacetate and arenes.¹⁴ In this retro-cyclopropanation, two C–C bonds in norcaradienes **2** are cleaved by Au(I), which is in contrast with that observed in the presence of strong electrophiles such as TeCl₄, wherein a single C–C bond of **2** is cleaved, leading to benzylic chlorides.^{15–18} This new catalytic process is a safe alternative to the use of diazo compounds¹⁹ as carbene precursors.²⁰

7-Substituted 1,3,5-cycloheptatrienes are easily prepared in one step by the addition of organolithium or Grignard reagents to commercially available tropylium tetrafluoroborate.²¹ We first studied the reaction between 7-phenyl-1,3,5-cycloheptatriene and *trans*-stilbene with different Au(I) catalysts A–E (Table 1).^{22,23} No reaction was observed with [Au(PPh₃)(MeCN)]SbF₆ at 23–80 °C. However, when the reaction was carried out in 1,2-dichloroethane (DCE) at 80–100 °C with catalyst A, 1,2,3-triphenylcyclopropane (**4a**) was obtained in 26–33% yield (entries 1–3).

Scheme 1

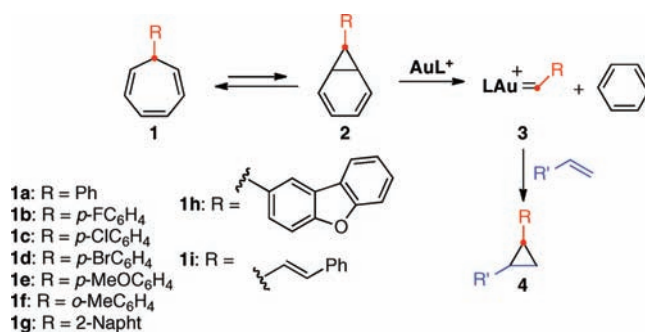
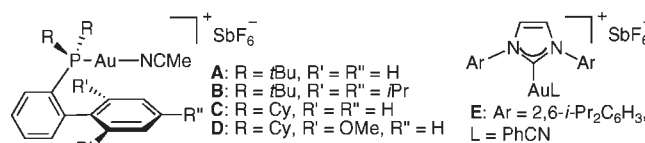


Table 1. Gold(I)-Catalyzed Cyclopropanation of *trans*-Stilbene with Cycloheptatriene 1a

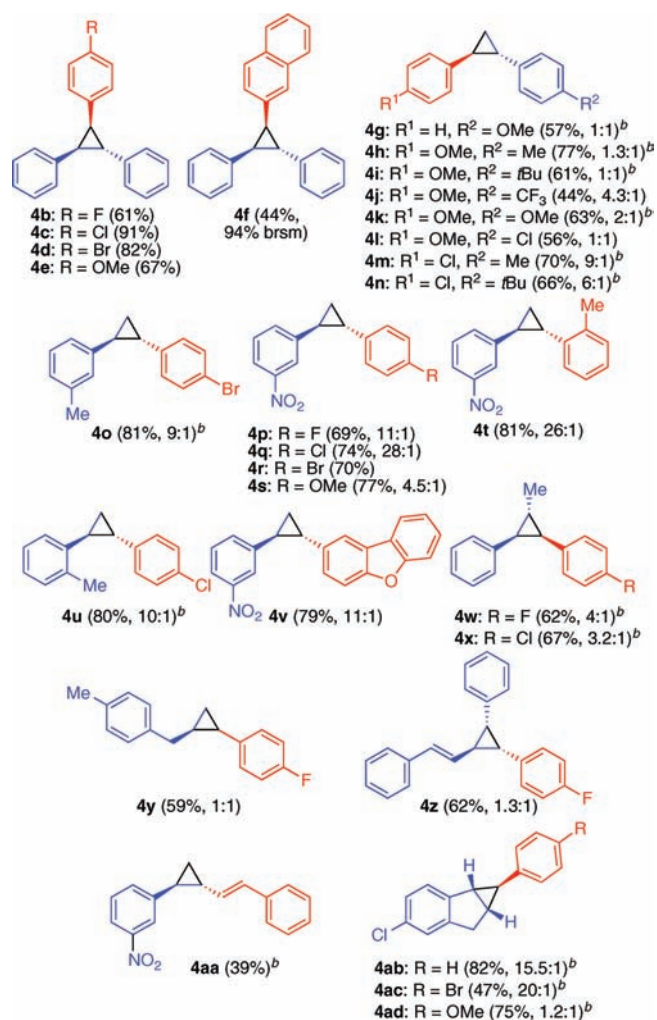
entry	[Au] (mol %)	T (°C)	time (h)	yield of 4a (%)
1	A (5)	80	8	26
2	A (5)	100	5	31
3	A (10)	100	5	33
4	B (5)	80	8	49
5	B (5)	100	5	73
6	B (5)	120	2.25	84
7	C (5)	80	8	5
8	C (5)	100	8	7
9	D (5)	80	10	– ^a
10	E (5)	80	8	43
11	E (10)	100	5	64
12	E (5)	120	1.75	70

^aNo reaction was observed.



Received: June 7, 2011

Published: July 15, 2011

Chart 1. Gold(I)-Catalyzed Cyclopropanation of Alkenes with Cycloheptatrienes **1** (Color Code as in Scheme 1)^a

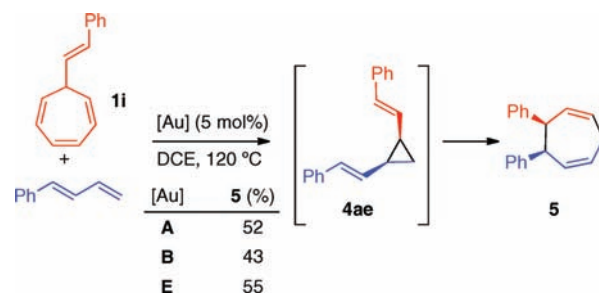
^aConditions: catalyst **B** (5 mol %) in DCE at 120 °C for 15–19 h.

^bReaction was carried out with catalyst **A** (5 mol %).

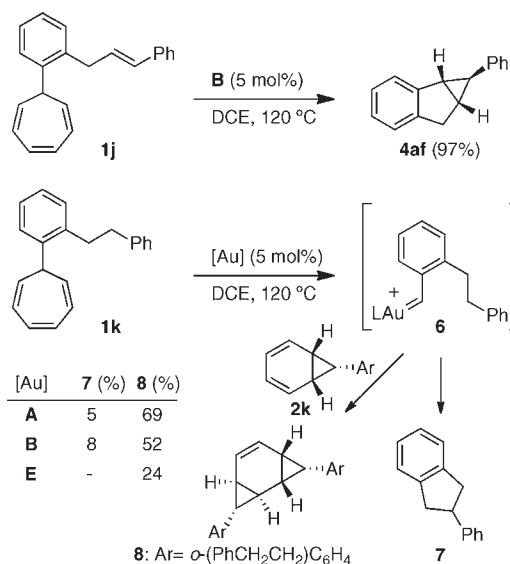
The best yield was obtained using catalyst **B** with a more sterically hindered phosphine ligand (entries 5 and 6). Complexes **C** and **D** did not perform satisfactorily, whereas complex **E** with a bulky NHC ligand gave **4a** in slightly lower yields than **B** (entries 10–12). No reaction was observed in the absence of gold(I) catalysts or when the Ag(I) complex analogous to **B** was used.^{22b}

Reactions of cycloheptatrienes **1b–e** and **1g** with *trans*-stilbene led to the formation of cyclopropanes **4b–f** in as single stereoisomers using gold(I) catalyst **B** (5 mol %) at 120 °C in DCE (Chart 1). Substituted styrenes provided the corresponding cyclopropanes with *trans* stereoselectivities, although **4g**, **4i**, and **4l** were obtained as 1:1 mixtures of *trans* and *cis* isomers. The *trans* selectivity was confirmed by the X-ray crystal structure of *trans*-**4s**. The reaction also proceeded with 1-allyl-4-methylbenzene to give **4y** in 59% yield. In the case of (*E,E*)-1,4-diphenyl-1,3-butadiene, only the monoadduct **4z** could be obtained. The cyclopropanation using vinyl cycloheptatriene **1i** provided **4aa** in moderate yield using catalyst **A**. The cyclopropanations of 6-chloro-1*H*-indene with **1a**, **1d**, and **1e** led selectively to *exo*-tetrahydrocyclopropa[*a*]indenes **4ab–ad**.

Scheme 2



Scheme 3

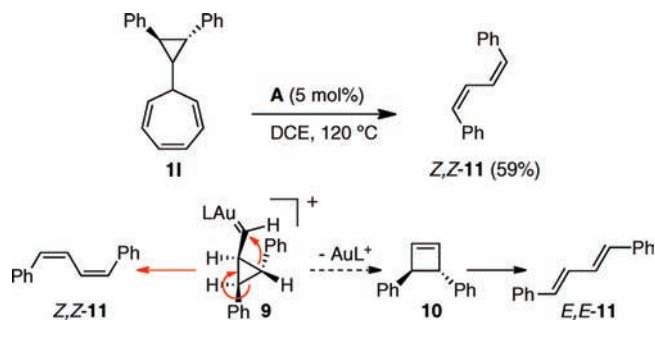


The reaction of 1-phenyl-1,3-butadiene with cycloheptatriene **1i** in the presence of gold(I) catalysts led to *cis*-6,7-diphenylcyclohepta-1,4-diene (**5**) in 43–55% yield as the only isolated product as a result of the cyclopropanation at the least-substituted double bond to form **4ae** followed by a Cope rearrangement (Scheme 2).

We observed the formation of benzene by ¹H NMR spectroscopy when cycloheptatriene **1e** was heated in tetrachloroethane-*d*₂ at 70–80 °C with complex **B** (5 mol %).²⁴ On the other hand, when the reaction of **1e** was carried out in DCE at 120 °C for 3 h with Ph₂SO (6 equiv) using catalyst **E** (5 mol %), *p*-methoxybenzaldehyde was obtained 34% yield through oxidation of the gold(I) carbene formed in the retro-cyclopropanation.²⁵

The intermediate gold(I) carbenes could also be cleanly trapped intramolecularly. Thus, cycloheptatriene derivative **1j**, which was prepared from tropylium tetrafluoroborate in 71% yield, gave exclusively **4af** with an *exo* configuration in 97% yield (Scheme 3). Similarly, we envisioned that a gold(I) carbene formed by retro-cyclopropanation could undergo intramolecular C–H insertion.²⁶ For this purpose, we chose cycloheptatriene **1k** as a substrate that could form 2-phenylindane (**7**) via gold(I) carbene **6**. Interestingly, although **7** was indeed obtained in this reaction, the major product was the unsymmetrical bicyclic product **8**, which was formed by trapping of gold(I) carbene **6** with *endo*-norcaradiene **2k**. This result highlights the high propensity

Scheme 4



of gold(I) carbenes to react with alkenes in cyclopropanation reactions.

We expected that a retro-Buchner reaction of (*trans*-2,3-diphenylcyclopropyl)cyclohepta-1,3,5-triene (**11**) would generate cyclopropyl gold(I) carbene **9**, which could evolve to cyclobutene **10**²⁷ and subsequently (*E,E*)-**11** by thermal conrotatory opening (Scheme 4).²⁸ However, reaction of **11** with catalyst **A** led exclusively to (*Z,Z*)-**11**. This surprising result suggests that intermediate **9** evolves by a mechanism analogous to the skeletal rearrangement of 1,6-enynes,²⁹ bypassing the formation of cyclobutene **10**.

In summary, we have found that cationic Au(I) complexes promote the retro-Buchner reaction of 1,3,5-cycloheptatrienes to form substituted gold(I) carbenes that can be trapped by alkenes in a new cyclopropanation reaction. 1,2,3-Trisubstituted cyclopropanes, which are not easily prepared by other methods, can be synthesized from 1,2-substituted alkenes and readily available 7-substituted 1,3,5-cycloheptatrienes as a safe alternative to the use of explosive diazo compounds.

■ ASSOCIATED CONTENT

S Supporting Information. Additional data, experimental details, characterization data, and crystallographic data (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Author
aechavarren@icqi.es

■ ACKNOWLEDGMENT

We thank the MICINN (CTQ2010-16088/BQU, Consolider Ingenio 2010 Grant CSD2006-0003, and FPI Predoctoral Fellowship to C.R.S.-A.), the AGAUR (2009 SGR 47), and the ICIQ Foundation for financial support.

■ REFERENCES

- (1) (a) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326–3350. (b) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351–3378. (c) Michelet, V.; Toullec, P. Y.; Genêt, J.-P. *Angew. Chem., Int. Ed.* **2008**, *47*, 4268–4315. (d) Fürstner, A. *Chem. Soc. Rev.* **2009**, *38*, 3208–3221.
- (2) (a) López, S.; Herrero-Gómez, E.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 6029–6032. (b) Nieto-Oberhuber, C.; López, S.; Muñoz, M. P.;

Jiménez-Núñez, E.; Buñuel, E.; Cárdenas, D. J.; Echavarren, A. M. *Chem.—Eur. J.* **2006**, *12*, 1694–1702. (c) Jiménez-Núñez, E.; Raducan, M.; Lauterbach, T.; Molawi, K.; Solorio, C. R.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2009**, *48*, 6152–6155. (d) Pérez-Galán, P.; Herrero-Gómez, E.; Hog, D. T.; Martin, N. J. A.; Maseras, F.; Echavarren, A. M. *Chem. Sci.* **2011**, *2*, 141–149.

(3) Kim, S. M.; Park, J. H.; Choi, S. Y.; Chung, Y. K. *Angew. Chem., Int. Ed.* **2007**, *46*, 6172–6175.

(4) (a) Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002–18003. (b) Gorin, D. J.; Watson, I. D. G.; Toste, F. D. *J. Am. Chem. Soc.* **2008**, *130*, 3736–3737.

(5) (a) Lemièrre, G.; Gandon, V.; Cariou, K.; Fukuyama, T.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *Org. Lett.* **2007**, *9*, 2207–2209. (b) Lemièrre, G.; Gandon, V.; Cariou, K.; Hours, A.; Fukuyama, T.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *J. Am. Chem. Soc.* **2009**, *131*, 2993–3006.

(6) For a review, see: Miege, F.; Meyer, C.; Cossy, C. *Beilstein J. Org. Chem.* **2011**, *7*, 717–734.

(7) (a) Forbes, D. C.; Doyle, M. P. *Chem. Rev.* **1998**, *98*, 911–935. (b) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977–1050. (c) Lindsay, V. N. G.; Nicolas, C.; Charette, A. B. *J. Am. Chem. Soc.* **2011**, *133*, 8972–8981.

(8) Prieto, A.; Fructos, M. R.; Díaz-Requejo, M. M.; Pérez, P. J.; Pérez-Galán, P.; Delpont, N.; Echavarren, A. M. *Tetrahedron* **2009**, *65*, 1790–1793.

(9) Solorio-Alvarado, C. R.; Echavarren, A. M. *J. Am. Chem. Soc.* **2010**, *132*, 11881–11883.

(10) (a) Batiste, L.; Fedorov, A.; Chen, P. *Chem. Commun.* **2010**, *46*, 3899–3901. (b) Fedorov, A.; Chen, P. *Organometallics* **2010**, *29*, 2994–3000. (c) For other metal-promoted gas-phase retro-cyclopropanations, see: Eller, K.; Schwarz, H. *Chem. Rev.* **1991**, *91*, 1121–1177.

(11) (a) Gassman, P. G.; Johnson, T. H. *J. Am. Chem. Soc.* **1976**, *98*, 6057–6058. (b) Gassman, P. G.; Johnson, T. H. *J. Am. Chem. Soc.* **1976**, *98*, 6058–6059. (c) For reductive retro-cyclopropanation in fullerenes, see: Herranz, M. Á.; Cox, C. T.; Echegoyen, L. *J. Org. Chem.* **2003**, *68*, 5009–5012.

(12) (a) Ni(0): Takaya, H.; Suzuki, T.; Kumagai, Y.; Hosoya, M.; Kawauchi, H.; Noyori, R. *J. Org. Chem.* **1981**, *46*, 2854–2861. (b) Rh(I): Walczak, M. A. A.; Wipf, P. *J. Am. Chem. Soc.* **2008**, *130*, 6924–6925.

(13) (a) Daub, J.; Lüdemann, H.-D.; Michna, M.; Strobl, R. M. *Chem. Ber.* **1985**, *118*, 620–633. (b) McNamara, O. A.; Maguire, A. R. *Tetrahedron* **2011**, *67*, 9–40.

(14) (a) Fructos, M. R.; Belderrain, T. R.; de Frémont, P.; Scott, N. M.; Nolan, S. P.; Díaz-Requejo, M. M.; Pérez, P. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 5284–5288. (b) Rivilla, I.; Gómez-Emeterio, B. P.; Fructos, M. R.; Díaz-Requejo, M. M.; Pérez, P. J. *Organometallics* **2011**, *30*, 2855–2860.

(15) Albeck, M.; Tamari, T.; Sprecher, M. *J. Org. Chem.* **1983**, *48*, 2276–2278.

(16) For the formation of benzyl-Rh(II) from cycloheptatrienyl-Rh(I) by a metalloradical process, see: Chan, Y. W.; Chan, K. S. *Chem. Commun.* **2011**, *47*, 4802–4804.

(17) The reaction of 7-ethynylcyclohepta-1,3,5-triene with trifluoroacetic acid gives phenylallene by protonation of the alkyne in the norcaradiene tautomer followed by cyclopropane cleavage to form the arenium cation. See: (a) Kitagawa, T.; Kamada, J.; Minegishi, S.; Takeuchi, K. *Org. Lett.* **2000**, *2*, 3011–3013. (b) Minegishi, S.; Kamada, J.; Takeuchi, K.; Komatsu, K.; Kitagawa, T. *Eur. J. Org. Chem.* **2003**, 3497–3504.

(18) 2-Ethoxyethylidene carbene has been generated by photochemical cleavage of a cyclopropanated phenanthrene. See: Graves, K. S.; Thamattoor, D. M.; Rablen, P. R. *J. Org. Chem.* **2011**, *76*, 1584–1591.

(19) (a) Phenyl diazomethane is explosive at room temperature and should be stored between –20 and –80 °C under N₂ or Ar. See: Creary, X. *Org. Synth.* **1986**, *64*, 207–216. (b) Electron-rich *p*-methoxyphenyl diazomethane is shock-sensitive and can detonate. It slowly decomposes at –80 °C. See: Closs, G. L.; Moss, R. A. *J. Am. Chem. Soc.* **1964**, *86*, 4042–4053.

(20) For the use of tosylhydrazone salts as a safe alternative to handling diazo compounds, see: (a) Aggarwal, V. K.; Alonso, E.; Fang, G. Y.; Ferrara, M.; Hynd, G.; Porcelloni, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1433–1436. (b) Fulton, J. R.; Aggarwal, V. K.; de Vicente, J. *Eur. J. Org. Chem.* **2005**, 1479–1492.

(21) Picotin, G.; Faye, A.; Miginiac, P. *Bull. Soc. Chim. Fr.* **1990**, *127*, 245–251.

(22) (a) Herrero-Gómez, E.; Nieto-Oberhuber, C.; López, S.; Benet-Buchholz, J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 5455–5459. (b) Pérez-Galán, P.; Delpont, N.; Herrero-Gómez, E.; Maseras, F.; Echavarren, A. M. *Chem.—Eur. J.* **2010**, *16*, 5324–5332.

(23) Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M. *J. Org. Chem.* **2008**, *73*, 7721–7730.

(24) Preliminary calculations [DFT B3LYP, 6-31G(d) (C, P, H) and SDD (Au and Ag), CH₂Cl₂] performed with 7-phenylnorcaradiene (**2a**) and [Au(PMe₃)]⁺ and [Ag(PMe₃)]⁺ showed that the metal is directly involved in the electrophilic cleavage of the cyclopropane ring, leading to [PhCHAu(PMe₃)]⁺ and [PhCHAg(PMe₃)]⁺ with free energies of activation of 19.62 and 31.71 kcal/mol, respectively. The much higher barrier observed for silver is consistent with the lack of reactivity observed at 100–120 °C in DCE when the Ag(I) analogue of complex **B** was used.

(25) Witham, C. A.; Mauleón, P.; Shapiro, N. D.; Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 5838–5839.

(26) Horino, Y.; Yamamoto, T.; Ueda, K.; Kuroda, S.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 2809–2811.

(27) López-Carrillo, V.; Echavarren, A. M. *J. Am. Chem. Soc.* **2010**, *132*, 9292–9294.

(28) Wilcox, C. F.; Carpenter, B. K. *J. Am. Chem. Soc.* **1979**, *101*, 3897–3905.

(29) Nieto-Oberhuber, C.; López, S.; Muñoz, M. P.; Cárdenas, D. J.; Buñuel, E.; Nevado, C.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 6146–6148.