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PAPER

The role of cyclobutenes in gold(I)-catalysed skeletal rearrangement of 1,6-enynes†‡

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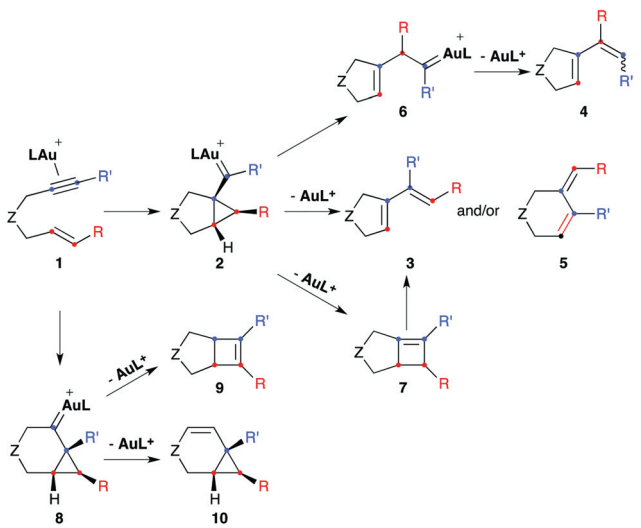
1,6-Enynes with electron-donating substituents at the alkyne undergo gold(I)-catalysed single cleavage skeletal rearrangement, whereas substrates with electron-withdrawing substituents evolve selectively to double cleavage rearrangement. Theoretical calculations provide a qualitative rationale for these effects, and suggest that bicyclo[3.2.0]hept-5-enes are involved as intermediates. We provide the first X-ray structural evidence for the formation of a product of this class in a cycloisomerisation of a 1,6-enyne.

Introduction

1,*n*-Enynes (*n* = 5–7) give rise to a series of fascinating skeletal rearrangements in the presence of gold(I) and other electrophilic metals as catalysts.[1–8] For gold(I), the rearrangement was proposed to be initiated by the activation of the alkyne in complexes **1** to form intermediates **2**, with highly distorted structures that are intermediate between cyclopropyl gold carbenes and gold-stabilized homoallylic carbocations.[2,9] These intermediates evolve to form two main types of dienes **3** (single *exo*-cleavage) and **4** (double *exo*-cleavage) (Scheme 1).[2,9–20] The involvement of intermediates **2** in skeletal rearrangements and other processes has been supported by different trapping experiments.[6,11,21,22] The initial step in the gold[23] or platinum catalysed[24] cyclisation of furanynes also proceeds by intermediates related to **2**.

A third type of product **5** (single *endo*-cleavage) was discovered using cationic gold(I) catalysts.[19,25] Products of type **5** were later found in reactions catalysed by $InCl_3$,[12e,f] Fe(III),[3b] or Ru(II).[26] In the single cleavage rearrangement, the alkene configuration of the starting enyne is preserved using gold(I) and other metal catalysts.[1,25] However, in cases where the alkene is substituted with strongly electron-donating groups, we have found that cationic gold(I) catalysts lead selectively to *cis*-configured products starting both from *cis*- or *trans*-enynes.[27]



Scheme 1 Main reaction pathways for the gold(I)-catalyzed cycloisomerization of 1,6-enynes.

The double *exo*-cleavage skeletal rearrangement leads to dienes **4** with predominant[1,10,11,25] or exclusive *Z*[28] configuration *via* rearranged carbenes **6**.[9]

Based on theoretical calculations on a 1,6-enyne model system bearing a *trans*-disubstituted alkene (**1**, Z = CH_2, R = Me, R′ = H), we proposed that the skeletal rearrangement to form single *exo*-cleavage products **3** can occur directly, bypassing involvement of bicyclo[3.2.0] hept-5-enes **7**.[9] These products could arise by expansion of *syn*-cyclopropyl gold(I) carbene intermediates.[9] Cyclobutenes of type **7** have been obtained in metal-catalyzed reactions of 1,7-,[12d,13,19,29] and 1,8-enynes.[30] Additionally, the *endo*-cyclization pathway *via* intermediates **8** can lead to regioisomeric cyclobutenes **9** or bicyclo-[4.1.0]hept-2-ene derivatives **10**.[5,31,32] Cyclobutenes **9** were also formed using palladium[10a,b] or platinum catalysts.[33]

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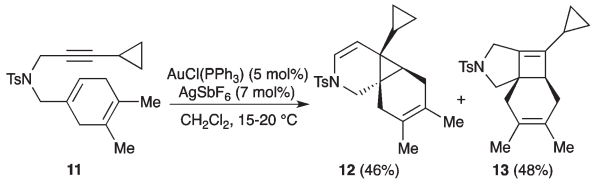


Scheme 2 Gold(I)-catalysed cycloisomerisation of **11**.[35]

In the case of 1,6-enynes, it has been argued that the formation of bicyclo[3.2.0] hept-5-enes **7** would be very unlikely due to their highly strained *trans*-cycloheptene structure, a species that is not stable at room temperature.[10d,34] However, a compound of this type was reported in the gold(I)-catalysed reaction of 1,6-enyne **11** that leads to a 1 : 1 mixture of *endo*-type cycloisomerization product **12** and cyclobutene **13** (Scheme 2).[35,36]

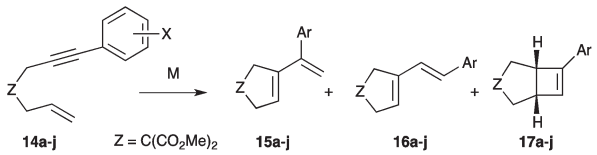
We have obtained the first X-ray structural evidence for the formation of a product of type **7** with a bicyclic skeleton embedded in a *trans*-cycloheptene. One important aspect that has not been addressed yet is the control of the single *vs.* double selectivity in the skeletal rearrangement of 1,*n*-enynes. Here we report the first examples in which the single *vs.* double skeletal rearrangement is controlled by the nature of the substituents at the alkyne. We also report a more comprehensive mechanistic study on the skeletal rearrangement of 1,6- and 1,7-enynes which concludes that cyclobutenes can indeed be intermediates in some of the rearrangements.

Results and discussion

Skeletal rearrangement of 1,6-enynes

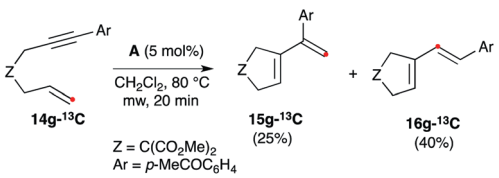
First we studied the rearrangement of 7-aryl-1,6-enynes **14a–j** with gold and platinum catalysts (Table 1). Due to the poor reactivity of enynes bearing terminal unsubstituted alkenes in metal-catalysed cycloisomerisations, the reactions were carried out by heating at 80 °C under microwave irradiation. Interestingly, single- or double-cleavage was observed as a function of the substituents at the aryl group. Parent enyne **14a** (X = H) leads to single cleavage product **15a** as the major product, along with cyclobutene **17a**, using gold(I) cationic catalyst **A**[5a] (Table 1, entry 1). Similar results were obtained with substrates bearing *p*-MeO and *m*-MeO groups using catalyst **A** (Table 1, entries 2 and 6). No reaction was observed using gold(I) complexes **B** and **C**[6b] (Table 1, entries 3 and 4), whereas platinacycle **D** led to diene **15b** in excellent yield (Table 1, entry 5). Reaction of enynes **14d–f** led to single cleavage products **15d–f** accompanied by cyclobutenes **17d–f** (Table 1, entries 7–9). In contrast, enynes **14g–j** bearing strongly withdrawing groups *p*-COMe, *p*-CF_3, *p*-CN, and *p*-NO_2 led preferentially or exclusively to double cleavage dienes **16g–j** (Table 1, entries 10–15). Surprisingly, in the case of 1,6-enyne **14j**, $PtCl_4$ as catalyst led exclusively to single cleavage diene **15j** in excellent yield (Table 1, entry 17). This total inversion of the selectivity confirms that platinum and gold behave differently in the skeletal rearrangement of enynes.[25]

Table 1 Gold(I)-catalyzed skeletal rearrangement of 1,6-enynes **14a–j** leading to single cleavage (**15**), double cleavage (**16**) rearrangement and cyclobutenes **17**[a]

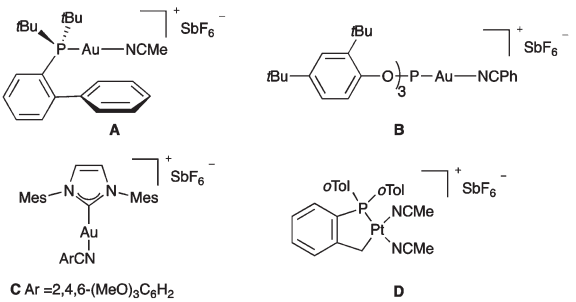


Entry	**14**	X	M	**15** (%)	**16** (%)	**17** (%)
1	a	H	**A**	73	3	23
2	b	*p*-MeO	**A**	78	2	10
3	b	*p*-MeO	**B**	—	—	—
4	b	*p*-MeO	**C**	—	—	—
5	b	*p*-MeO	**D**	96	—	—
6	c	*m*-MeO	**A**	70	2	0
7	d	*p*-AcO	**A**	63	—	25
8	e	*p*-BzO	**A**	45	—	38
9	f	Cl	**A**	55	—	40
10	g	COMe	**A**	30	40	—
11	h	CF_3	**A**	20	65	—
12	i	CN	**A**	11	70	—
13	j	NO_2	**A**	—	93	—
14	j	NO_2	**B**	—	90	—
15	j	NO_2	**C**	—	10	—
16	j	NO_2	$PtCl_4$	96	0	0

[a] Reactions carried out in CH_2Cl_2 with 5 mol% catalyst at 80 °C under microwave irradiation for 10–60 min.

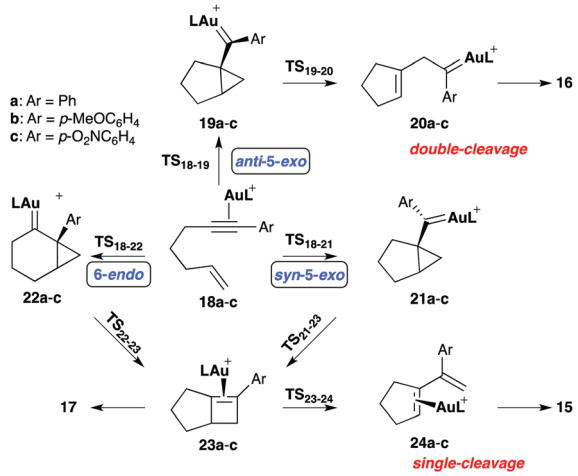


Scheme 3 Single- and double-cleavage rearrangement of **14g-^{13}C**.



To prove that the products formed in these rearrangements correspond to single and double cleavage, we repeated the result of entry 10 in Table 1 using **14g-^{13}C** labelled with ^{13}C at the terminal alkene carbon (Scheme 3). Under these conditions, single cleavage **15g-^{13}C** and double cleavage **16g-^{13}C** dienes were obtained.

A DFT study (B3LYP, 6-31G(d) (C, P, N, H) and LANL2DZ (Au)) was carried out on 1,6-enyne-gold(I) complexes **18a–c** (L PMe_3) in order to explain the observed selectivity



Scheme 4 Main reaction pathways for the cycloisomerization of **18a–c**.

Table 2 Relative energies of stationary points of Scheme 4[a]

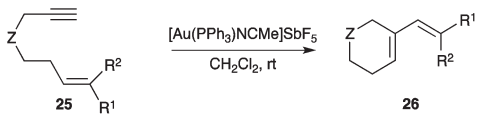
	H	*p*-MeO	*p*-NO_2
$TS_{18–19}$	16.04	17.71	13.61
19	−0.84	−2.30	−1.39
$TS_{19–20}$	11.92	13.10	8.79
20	−4.37	−8.86	−0.86
$TS_{18–21}$	23.87	27.77	23.16
21	0.51	−4.57	−0.49
$TS_{21–23}$	9.00	11.08	6.77
$TS_{18–22}$	17.41	17.73	16.93
22	0.85	3.27	0.18
$TS_{22–23}$	14.41	13.47	16.01
23	−10.82	−11.31	−10.75
$TS_{23–24}$	18.01	18.21	16.77
24	−22.80	−21.92	−25.92

[a] Relative free energies (kcal mol^{-1}) including solvation effects in dichloromethane. DFT calculations B3LYP, 6-31G(d) (H, C, N, O, P) and LANL2DZ (Au).

(Scheme 4). Three possible reaction pathways were considered: *anti*-5-*exo*-*dig*, *syn*-5-*exo*-*dig*, and 6-*endo*-*dig* cyclization. This study completes related work using more simple PH_3 as the model phosphine, in which we found that the *syn*-5-*exo*-*dig* pathway followed by cyclopropane expansion competes with the 6-*endo*-*dig* pathway for the formation of intermediates of type **23a–c**.[5b]

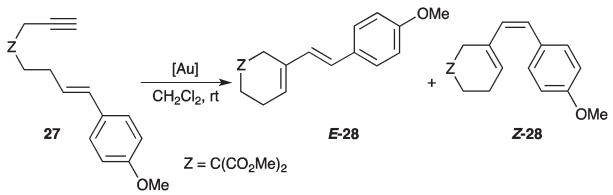
According to the calculations, the *syn*-5-*exo*-*dig* pathway proceeding through **$TS_{18–21}$** does not compete in any of the three cases considered (Table 2). For the parent (**18a**) and the *p*-nitro-substituted (**18c**) systems, calculations show that the *anti*-5-*exo*-*dig* pathway through **$TS_{19–20}$** to form carbene **20a**, precursor of double *exo*-cleavage rearranged product **16**, is the most favourable. On the other hand, although very similar energies of activation were calculated for the *anti*-5-*exo*-*dig* and 6-*endo*-*dig* cyclizations in the case of the enyne with an electron-donating OMe substituent in the aromatic ring, according to the potential energies,[37] the 6-*endo*-*dig* cyclization would be the most favourable reaction pathway for this system (14.00 *vs.* 16.19 kcal mol^{-1}). The potential energy for the formation of **23b** *via* **$TS_{22–23b}$** was also lower (15.06 kcal mol^{-1}) than that required for the *anti*-5-*exo* pathway.

While the energies of the transition states leading to the 6-*endo*-*dig* and *syn*-5-*exo*-*dig* pathways are quite similar for the three enyne-gold(I) complexes **18a–c**, substituents at the aryl cause a more significant effect on the transition states **$TS_{18–19}$** in the *anti*-5-*exo*-*dig* pathway.



Scheme 5 Gold(I)-catalyzed single-cleavage rearrangement of 1,7-enynes.

Table 3 Gold(I)-catalyzed rearrangement of 1,7-enyne **27**[a]



Entry	[Au]	Yield (%)	*E*/*Z* ratio
1	**A**	92	1 : 1.5
2	**B**	96	1 : 4
3	**C**	82	1.3 : 1

[a] Reactions carried out in CH_2Cl_2 with 5 mol% catalyst at 23 °C for 1 h. The starting enyne **27** was a 2.5 : 1 mixture of *E* and *Z* isomers.

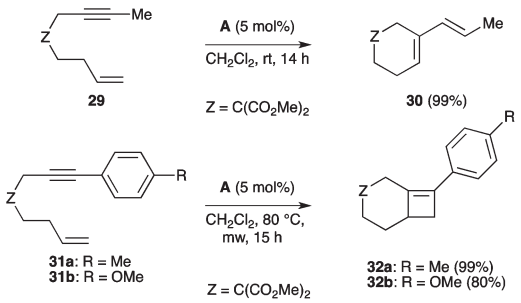
Skeletal rearrangement of 1,7-enynes

Cationic gold(I) complexes are the best catalysts for the skeletal rearrangement of 1,7-enynes **25** to form single cleavage 1,6-dienes **26** (Scheme 5).[38] Additional examples have been reported with Ru(II),[12a] Pt(II),[12b,e] Pt(IV),[10a] Ir(I),[12c] $GaCl_3$[12d,18,39,40] and $InCl_3$[12f] catalysts.

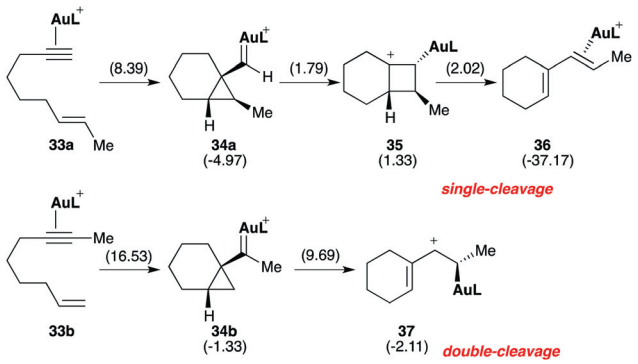
Interestingly, 1,7-enyne **27** (2.5 : 1 mixture of *E* and *Z* isomers) with an electron-rich group at the alkene terminus gives mixtures of diene **28** enriched in the *Z* stereoisomer (Table 3). The origin of this *cis*-selectivity, which is more significant with the most electrophilic gold(I) catalyst **B** (Table 3, entry 2), is still unclear although is related to that we found before for 1,6-enynes with electron-donating substituents at the alkene.[27]

In contrast with the exclusive formation of single cleavage rearrangement dienes **26** and **28**, the reaction of enyne **29** with a disubstituted alkyne using catalyst gold(I) **A** at room temperature gave only diene **30** by double cleavage rearrangement (Scheme 6). Less reactive substrates **31a–b** reacted at 80 °C to give cyclobutenes **32a–b**, which do not undergo conrotatory ring opening under these conditions.

Preliminary studies were performed using $[Au(PH_3)]^+$. In this case, a bifurcation on the reaction pathway was found depending on the conformation of the newly-formed six-membered ring (namely, two pseudo-chair and a boat type conformation).



Scheme 6 Cycloisomerisation of 1,7-enynes **29** and **31a–b**.



Scheme 7 Mechanism for the single- and double-cleavage rearrangement of 1,7-enynes.

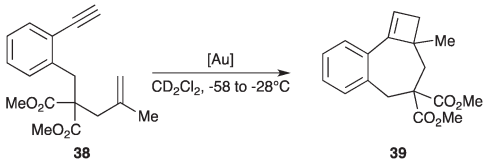
However, when the rearrangement was computed using [Au(PMe$_3$)]$^+$, the reaction takes place in all cases through a pseudo-chair conformation. The reaction pathway is slightly different for the gold(I) complexes of (*E*)-non-1-en-7-yne (**33a**) and (*E*)-oct-1-en-7-yne (**33b**) (Scheme 7). In the first case, formation of single cleavage rearranged dienes proceeds through cyclopropyl carbene **34a** that gives rise to **36** through a shallow potential surface in which bicyclo[4.2.0]octane **35** is an intermediate. In contrast, intermediate **37**, the precursor for double-cleavage diene, was formed directly *via* the opening of the cyclopropyl carbene intermediate **34b**.

Formation of strained cyclobutenes

Cyclobutenes are the products in the intermolecular reaction between alkenes and terminal alkynes in the presence of a cationic gold(I) catalyst.[41] To determine the activation energies required for the [2 + 2] cycloaddition between alkynes and alkenes in gold(I)-catalysed reactions, we decided to study the cycloisomerisation of 1,8-enyne **38**, which was reported to give stable cyclobutene **39**.[30] The kinetics of this reaction were studied using catalysts **A** and **C**. The reaction showed pseudo-first order behaviour between −58 and −28 °C, which allowed us to determine the thermodynamic parameters shown in Table 4.

Interestingly, although very similar free energies of activation were obtained, the enthalpies and entropies of activation were very different for the reactions with catalysts **A** or **C**. Particularly interesting is the large and negative activation entropy found for

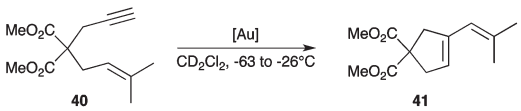
Table 4 Activation parameters for the [2 + 2] cycloaddition of 1,8-enyne **38**[a]



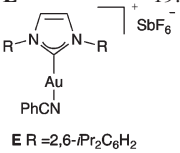
[Au]	$\Delta G^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$
A	21.2 ± 4.4	6.3 ± 0.4	−46.4 ± 4.0
C	19.2 ± 4.8	11.3 ± 0.3	−26.5 ± 4.5

[a] ($\Delta G_{298}^{\ddagger}$ and $\Delta H^{\ddagger}$ in kcal mol^{-1} and $\Delta S^{\ddagger}$ in cal K^{-1} mol^{-1}).

Table 5 Activation parameters for the skeletal rearrangement of 1,6-enyne **40**[a]



[Au]	$\Delta G^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$
A[9]	21.7 ± 1.1	3.7 ± 0.3	−60.6 ± 4.0
C	19.9 ± 2.1	13.1 ± 0.5	−22.8 ± 2.1
E	19.3 ± 1.5	11.1 ± 0.3	27.5 ± 1.4



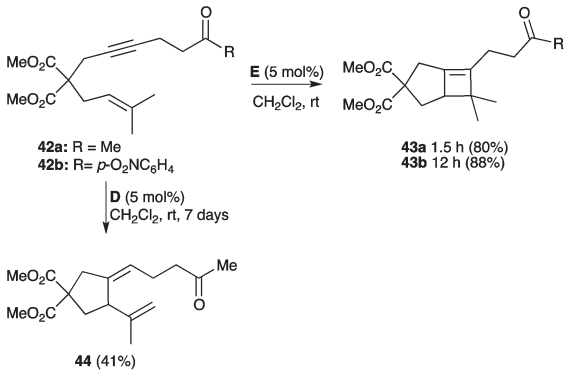
E R =2,6-*i*Pr$_2$C$_6$H$_2$

[a] ($\Delta G_{298}^{\ddagger}$ and $\Delta H^{\ddagger}$ in kcal mol^{-1} and $\Delta S^{\ddagger}$ in cal K^{-1} mol^{-1}).

the reaction with catalyst **A**, which is similar to those determined for the skeletal rearrangement of 1,6-enyne **40** and its cyclohexyl analogue using the same catalyst.[9] We repeated the experiments with 1,6-enyne **40** using gold(I) catalysts **C** and **E** with more donating NHC ligands (Table 5). Again, although the free energies of activation are almost the same with the three catalysts, the activation enthalpies with **C** and **E** are higher and the entropic terms lower than those with phosphine gold(I) complex **A**.

As previously suggested,[9] these experimental activation parameters probably correspond to a rate-determining ligand exchange that is outside of the catalytic cycle, in which the diene- or cyclobutene-gold(I) complex equilibrates with the starting enyne. This reasoning is supported by the observation of a low enthalpy of activation (5 kcal mol^{-1}) and large negative entropic term (−33 eu) in the intermolecular isobutylene exchange processes of a [*o*-biphenylP(*t*-Bu)$_2$]Au complex, which occur by an associative mechanism.[42]

Although we had never before detected bicyclo[3.2.0]hept-5-enes of type **7** in the skeletal rearrangement and related reactions of many 1,6-enynes,[2,5,6,9,19] when substrates **42a–b** were allowed to react in the presence of catalyst **E**, bicyclo[3.2.0]hept-5-ene derivatives **43a–b** were isolated in good yields (Scheme 8). The bicyclo[3.2.0]hept-5-ene structure of **43b** was



Scheme 8 Cycloisomerisation of 1,6-enynes **42a–b**.

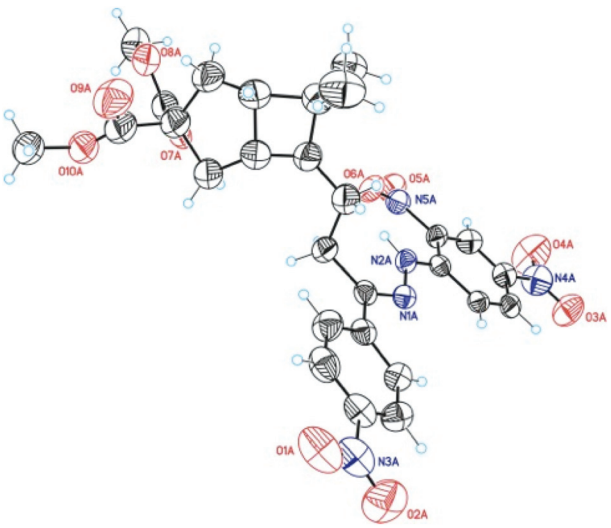
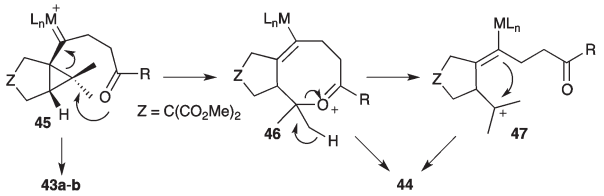


Fig. 1 X-Ray crystal structure for the 2,4-dinitrophenylhydrazone of bicyclo[3.2.0]hept-5-ene derivative **43b**.

definitively confirmed by X-ray diffraction of its crystalline 2,4-dinitrophenylhydrazone (Fig. 1).[43]

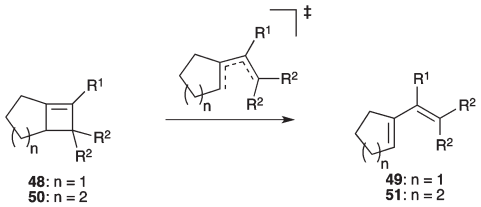
Lower yields or complex reaction mixtures were obtained in the presence of other gold(I) catalysts. However, using platinum(II)-catalyst **D**, **42a** led to 1,4-diene **44**. We[19b] and others[44] have obtained related products, which result *via* the opening of intermediate **2** to form carbocationic species that evolve by proton loss to give products of formal Alder-type cycloisomerization. In this case, an intermediate like **46** might be involved as an intermediate by an intramolecular attack of the carbonyl group to cyclopropyl carbene **45**.[45] Proton loss from **46** or **57** would give **44**, whereas cyclobutene formation might occur by direct ring expansion from **45** (Scheme 9).

The computed free energies of activation for the thermal conrotatory opening of a series of bicyclo[3.2.0]hept-5-enes (**48**) and bicyclo[4.2.0]oct-6-enes (**50**) to form dienes **49** and **51**, respectively, range between 24 and 41 kcal mol^{-1}, with entropic terms that are almost negligible (Table 6).[37] For 6-phenylbicyclo-[3.2.0]hept-5-ene, the barrier is 25.20 kcal mol^{-1} (Table 6, entry 4), slightly lower than that calculated for the opening of the corresponding gold(I) complex **23a** (28.83 kcal mol^{-1}). In general, coordination to gold(I) was calculated to increase the barrier for



Scheme 9 Proposed mechanism for the cycloisomerisation of 1,6-enynes **42a–b**.

Table 6 Calculated energies for the conrotatory opening of bicyclo-[3.2.0]hept-5-enes (**48**) and bicyclo[4.2.0]oct-6-enes (**50**)[a]



Entry	*n*	R^1	R^2	$\Delta G^{\ddagger}$	ΔG
1	1	H	H	33.38	−14.67
2	1	H	Me	23.90	−26.89
3	1	Me	Me	39.88	−5.35
4	1	Ph	H	25.20	−16.40
5	1	Ph	Me	41.06	−1.74
6	2	H	H	30.52	−13.60
7	2	H	Me	29.51	−16.79
8	2	Me	Me	31.64	−9.84
9	2	Ph	H	31.06	−7.46
10	2	Ph	Me	30.18	−9.29

[a] Free energies (kcal mol^{-1}). DFT calculations B3LYP, 6-31G(d) (H, C).

cyclobutene opening.[37] In the case of 7-phenylbicyclo[4.2.0]oct-6-enes (Table 6, entry 9) that barrier was found to be 5.9 kcal mol^{-1} higher, in agreement with the isolation of derivatives **32a–b** in the cycloisomerisation of 1,7-enynes **31a–b** (Scheme 6). Finally, the conrotatory opening of 6,7,7-trimethylbicyclo[3.2.0]hept-5-ene was calculated to be more difficult ($\Delta G^{\ddagger}$ = 39.88 kcal mol^{-1}) (Table 6, entry 3), which is consistent with the isolation of bicyclo[3.2.0]hept-5-ene derivatives **43a–b**.

Conclusions

The mechanistic scenario for the cycloisomerisation of 1,*n*-enynes is rather complex, with several competing pathways whose relative rates depend highly on the substitution pattern of the starting substrates. Here we have found the first examples in which the single *vs.* double skeletal rearrangement is controlled by the substituents at the alkyne, which has been rationalized theoretically. In this study, we propose that products of single cleavage rearrangement can be formed *via* the opening of the gold(I) complexes of bicyclo[3.2.0]hept-5-enes. We also report the first theoretical study of the skeletal rearrangement of 1,7-enynes. Finally, we have obtained for the first time X-ray structural evidence for the formation of a strained bicyclo[3.2.0]-hept-5-enes, which has a bicyclic skeleton embedded in a *trans*-cycloheptene.

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Notes and references

1 (*a*) E. Jiménez-Núñez and A. M. Echavarren, *Chem. Commun.*, 2007, 333–346; (*b*) E. Jiménez-Núñez and A. M. Echavarren, *Chem. Rev.*, 2008, **108**, 3326–3350; (*c*) D. J. Gorin, B. D. Sherry and F. D. Toste, *Chem. Rev.*, 2008, **108**, 3351–3378; (*d*) V. Michelet, P. Y. Toullec and J.-P. Genêt, *Angew. Chem., Int. Ed.*, 2008, **47**, 4268–4315; (*e*) A. S. K. Hashmi, *Chem. Rev.*, 2007, **107**, 3180–3211; (*f*) A. Fürstner and P. W. Davies, *Angew. Chem., Int. Ed.*, 2007, **46**, 3410–3449; (*g*) L. Zhang, J. Sun and S. A. Kozmin, *Adv. Synth. Catal.*, 2006, **348**, 2271–2296.

2 C. Nieto-Oberhuber, S. López, E. Jiménez-Núñez and A. M. Echavarren, *Chem.–Eur. J.*, 2006, **12**, 5916–5923.

3 (*a*) C. Nieto-Oberhuber, M. P. Muñoz, E. Buñuel, C. Nevado, D. J. Cárdenas and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2004, **43**, 2402–2406; (*b*) C. Nieto-Oberhuber, M. P. Muñoz, S. López, E. Jiménez-Núñez, C. Nevado, E. Herrero-Gómez, M. Raducan and A. M. Echavarren, *Chem.–Eur. J.*, 2006, **12**, 1677–1693. Corrigendum: C. Nieto-Oberhuber, M. P. Muñoz, S. López, E. Jiménez-Núñez, C. Nevado, E. Herrero-Gómez, M. Raducan and A. M. Echavarren, *Chem.–Eur. J.*, 2008, **14**, 5096; (*c*) C. Nevado, D. J. Cárdenas and A. M. Echavarren, *Chem.–Eur. J.*, 2003, **9**, 2627–2635.

4 (*a*) L. Zhang and S. A. Kozmin, *J. Am. Chem. Soc.*, 2005, **127**, 6962–6963; (*b*) A. K. Buzas, F. M. Istrate and F. Gagosz, *Angew. Chem., Int. Ed.*, 2007, **46**, 1141–1144; (*c*) B. D. Sherry, L. Maus, B. N. Laforteza and F. D. Toste, *J. Am. Chem. Soc.*, 2006, **128**, 8132–8133; (*d*) S. Park and D. Lee, *J. Am. Chem. Soc.*, 2006, **128**, 10664–10665; (*e*) Y. Horino, M. R. Luzung and F. D. Toste, *J. Am. Chem. Soc.*, 2006, **128**, 11364–11365; (*f*) C. A. Witham, P. Mauleón, N. D. Shapiro, B. D. Sherry and F. D. Toste, *J. Am. Chem. Soc.*, 2007, **129**, 5838–5839; (*g*) A. Fürstner and L. Morency, *Angew. Chem., Int. Ed.*, 2008, **47**, 5030–5033.

5 (*a*) C. Nieto-Oberhuber, S. López and A. M. Echavarren, *J. Am. Chem. Soc.*, 2005, **127**, 6178–6179; (*b*) C. Nieto-Oberhuber, P. Pérez-Galán, E. Herrero-Gómez, T. Lauterbach, C. Rodríguez, S. López, C. Bour, A. Rosellón, D. J. Cárdenas and A. M. Echavarren, *J. Am. Chem. Soc.*, 2008, **130**, 269–279.

6 (*a*) C. H. M. Amijs, C. Ferrer and A. M. Echavarren, *Chem. Commun.*, 2007, 698–700; (*b*) C. H. M. Amijs, V. López-Carrillo, M. Raducan, P. Pérez-Galán, C. Ferrer and A.M. Echavarren, *J. Org. Chem.*, 2008, **73**, 7721–7730.

7 P. Y. Toullec, E. Genin, L. Leseurre, J.-P. Genêt and V. Michelet, *Angew. Chem., Int. Ed.*, 2006, **45**, 7427–7430.

8 A. K. Buzas, F. M. Istrate and F. Gagosz, *Angew. Chem., Int. Ed.*, 2007, **46**, 1141–1144.

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

10 (*a*) B. M. Trost and G. J. Tanoury, *J. Am. Chem. Soc.*, 1988, **110**, 1636–1638; (*b*) B. M. Trost and M. K. Trost, *Tetrahedron Lett.*, 1991, **32**, 3647–3650; (*c*) B. M. Trost and G. A. Doherty, *J. Am. Chem. Soc.*, 2000, **122**, 3801–3810; (*d*) B. M. Trost, M. Yanai and K. Hoogsteed, *J. Am. Chem. Soc.*, 1993, **115**, 5294–5295; (*e*) B. M. Trost and A. S. K. Hashmi, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 1085–1087.

11 S. I. Lee and N. Chatani, *Chem. Commun.*, 2009, 371–384.

12 (*a*) N. Chatani, T. Morimoto, T. Muto and S. Murai, *J. Am. Chem. Soc.*, 1994, **116**, 6049–6050; (*b*) N. Chatani, N. Furukawa, H. Sakurai and S. Murai, *Organometallics*, 1996, **15**, 901–903; (*c*) N. Chatani, H. Inoue, T. Morimoto, T. Muto and S. Murai, *J. Org. Chem.*, 2001, **66**, 4433–4436; (*d*) N. Chatani, H. Inoue, T. Kotsuma and S. Murai, *J. Am. Chem. Soc.*, 2002, **124**, 10294–10295; (*e*) Y. Miyanohana, H. Inoue and N. Chatani, *J. Org. Chem.*, 2004, **69**, 8541–8543; (*f*) Y. Miyanohana and N. Chatani, *Org. Lett.*, 2006, **8**, 2155–2158; (*g*) H. Nakai and N. Chatani, *Chem. Lett.*, 2007, 1494–1495.

13 (*a*) A. Fürstner, H. Szillat and F. Stelzer, *J. Am. Chem. Soc.*, 2000, **122**, 6785–6786; (*b*) A. Fürstner, F. Stelzer and H. Szillat, *J. Am. Chem. Soc.*, 2001, **123**, 11863–11869; (*c*) A. Fürstner, H. Szillat, B. Gabor and R. Mynott, *J. Am. Chem. Soc.*, 1998, **120**, 8305–8314.

14 S. Oi, I. Tsukamoto, S. Miyano and Y. Inoue, *Organometallics*, 2001, **20**, 3704–3709.

15 C. H. Oh, S. Y. Bang and C. Y. Rhim, *Bull. Korean Chem. Soc.*, 2003, **24**, 887–888.

16 G. B. Bajracharya, I. Nakamura and Y. Yamamoto, *J. Org. Chem.*, 2005, **70**, 892–897.

17 (*a*) M. Méndez, M. P. Muñoz and A. M. Echavarren, *J. Am. Chem. Soc.*, 2000, **122**, 11549–11550; (*b*) M. Méndez, M. P. Muñoz, C. Nevado, D. J. Cárdenas and A. M. Echavarren, *J. Am. Chem. Soc.*, 2001, **123**, 10511–10520.

18 S. M. Kim, S. I. Lee and Y. K. Chung, *Org. Lett.*, 2006, **8**, 5425–5427.

19 (*a*) C. Nieto-Oberhuber, M. P. Muñoz, E. Buñuel, C. Nevado, D. J. Cárdenas and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2004, **43**, 2402–2406; (*b*) C. Nieto-Oberhuber, M. P. Muñoz, S. López, E. Jiménez-Núñez, C. Nevado, E. Herrero-Gómez, M. Raducan and A. M. Echavarren, *Chem.–Eur. J.*, 2006, **11**, 1677–1693; (*c*) C. Ferrer, M. Raducan, C. Nevado, C. K. Claverie and A. M. Echavarren, *Tetrahedron*, 2007, **63**, 6306–6316.

20 (*a*) E. Soriano, P. Ballesteros and J. Marco-Contelles, *Organometallics*, 2005, **24**, 3172–3181; (*b*) E. Soriano, P. Ballesteros and J. Marco-Contelles, *Organometallics*, 2005, **24**, 3182–3195; (*c*) E. Soriano and J. Marco-Contelles, *Acc. Chem. Res.*, 2009, **42**, 1026–1036.

21 S. López, E. Herrero-Gómez, P. Pérez-Galán, C. Nieto-Oberhuber and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2006, **45**, 6029–6032.

22 (*a*) M. Schlwies, A. L. Dempwolff, F. Rominger and G. Helmchen, *Angew. Chem., Int. Ed.*, 2007, **46**, 5598–5601; (*b*) M. Schlwies, R. Moser, A. L. Dempwolff, F. Rominger and G. Helmchen, *Chem.–Eur. J.*, 2009, **15**, 10888–10900.

23 (*a*) A. S. K. Hashmi, T. M. Frost and J. W. Bats, *J. Am. Chem. Soc.*, 2000, **122**, 11553–11554; (*b*) A. S. K. Hashmi, *Pure Appl. Chem.*, 2010, **82**, 1517–1528.

24 (*a*) B. Martín-Matute, D. J. Cárdenas and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2001, **40**, 4754–4757; (*b*) B. Martín-Matute, C. Nevado, D. J. Cárdenas and A. M. Echavarren, *J. Am. Chem. Soc.*, 2003, **125**, 5757–5766.

25 N. Cabello, E. Jiménez-Núñez, E. Buñuel, D. J. Cárdenas and A. M. Echavarren, *Eur. J. Org. Chem.*, 2007, 4217–4223.

26 J. W. Faller and P. P. Fontaine, *J. Organomet. Chem.*, 2006, **691**, 1912–1915.

27 E. Jiménez-Núñez, C. K. Claverie, C. Bour, D. J. Cárdenas and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2008, **47**, 7892–7895.

28 K. Ota and N. Chatani, *Chem. Commun.*, 2008, 2906–2907.

29 (*a*) A. Fürstner, A. Schlecker and C. W. Lehmann, *Chem. Commun.*, 2007, 4277–4279; (*b*) G. B. Bajracharya, I. Nakamura and Y. Yamamoto, *J. Org. Chem.*, 2005, **70**, 892–897.

30 Y. Odabachian and F. Gagosz, *Adv. Synth. Catal.*, 2009, **351**, 379–386.

31 Y. T. Lee, Y. K. Kang and Y. K. Chung, *J. Org. Chem.*, 2009, **74**, 7922–7934.

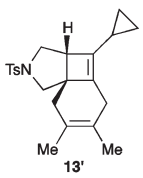
32 (*a*) F. Marion, J. Coulomb, C. Courillon, L. Fernsternbank and M. Malacria, *Org. Lett.*, 2004, **6**, 1509–1511; (*b*) S. Couty, C. Meyer and J. Cossy, *Angew. Chem., Int. Ed.*, 2006, **45**, 6726–6730; (*c*) S. Couty, C. Meyer and J. Cossy, *Tetrahedron*, 2009, **65**, 1809–1832.

33 A. Fürstner, P. W. Davies and T. Gress, *J. Am. Chem. Soc.*, 2005, **127**, 8244–8245.

34 B. M. Trost, A. C. Gutierrez and E. M. Ferreira, *J. Am. Chem. Soc.*, 2010, **132**, 9206–9218.

35 S. I. Lee, S. M. Kim, M. R. Choi, S. Y. Kim and Y. K. Chung, *J. Org. Chem.*, 2006, **71**, 9366–9372.

36 It is interesting to note that the alternative structure **13′** is 11 kcal mol^{-1} more stable (PM6 semi-empirical calculations, Spartan 10)



13′

37 See ESI† for additional details.

38 N. Cabello, C. Rodríguez and A. M. Echavarren, *Synlett*, 2007, 1753–1758.
39 E. M. Simmons and R. Sarpong, *Org. Lett.*, 2006, **8**, 2883–2886.
40 E. M. Simmons, J. R. Yen and R. Sarpong, *Org. Lett.*, 2007, **9**, 2705–2708.
41 V. López-Carrillo and A. M. Echavarren, *J. Am. Chem. Soc.*, 2010, **132**, 9292–9294.
42 T. J. Brown, M. G. Dickens and R. A. Widenhoefer, *Chem. Commun.*, 2009, 6451–6453.
43 The asymmetric unit is made up of two molecules. One molecule presents disorder in the di-methylbicycle with 70 : 30 occupation ratio, and two oxygens of the ester groups with 50 : 50 occupation ratio. The other molecule is also disordered, the di-methylbicycle over two positions with 50 : 50 occupation ratio and the two esters over three positions with 50 : 30 : 20 occupation ratio. For the resolution the SIR2008 program was used: R. Caliandro, B. Carrozzini, G. L. Cascarano, L. De Caro, C. Giacovazzo and D. Siliqi, *J. Appl. Crystallogr.*, 2007, **40**, 883–890. For the absorption correction, the TWINABS Version 2008/4 Bruker AXS program was used: Blessing, R. Caliandro, B. Carrozzini, G. L. Cascarano, L. De Caro, C. Giacovazzo and D. Siliqi, *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 1995, **A51**, 33–38.
44 S. I. Lee, S. M. Kim, S. Y. Kim and Y. K. Chung, *Synlett*, 2006, 2256–2260. Corrigendum: S. I. Lee, S. M. Kim, S. Y. Kim and Y. K. Chung, *Synlett*, 2009, 1355.
45 E. Jiménez-Núñez, C. K. Claverie, C. Nieto-Oberhuber and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2006, **45**, 5452–5455.