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On the Mechanism of the Puzzling "Endocyclic" Skeletal Rearrangement of 1,6-Enynes

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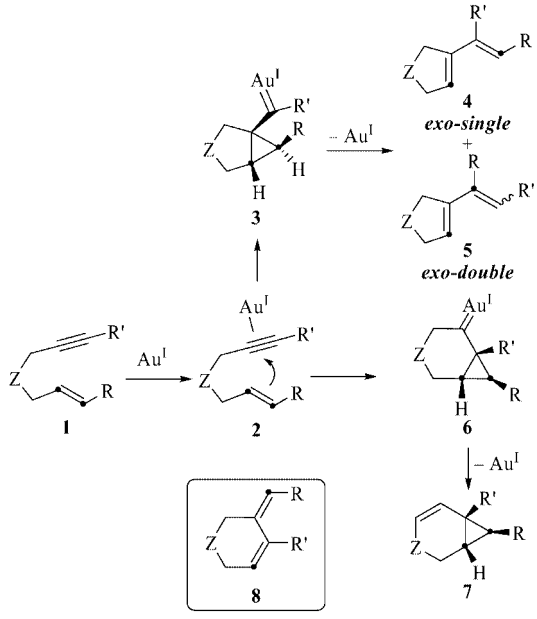
Skeletal rearrangements of simple 1,6-enynes have been studied in order to determine the factors that control the formation of five- or six-membered rings. Simple 1,6-enynes substituted only at C-4 preferentially give six-membered rings on skeletal rearrangement in the presence of gold(I) catalysts, whereas increasing electron-withdrawing character of substituents at C-4 leads to five-membered rings. Reactions of these simple enynes in the presence of $PtCl_4$ as catalyst give exclusively *exo-double* skeletal rearrangements. Enynes substituted at the alkyne also react with Au^I catalysts to give exclusively products of *exo-double* rearrangement. The different mechanisms have been analyzed by DFT calculations. Although a pathway for the formation of six-membered rings involving two steps in a ring-expansion/ring-contraction process was found, the activation energy of the first step is too high. Instead, this skeletal rearrangement appears to follow an *exo-single* skeletal rearrangement in which the initial cyclopropyl gold carbene opens to form a six-membered ring.

Introduction

Gold complexes are the most active catalysts for the cyclizations of enynes.[1–5] In the presence of gold(I), selective activation of the alkyne components of 1,6-enynes **1** via complexes **2** usually proceeds by an *exo* pathway to form cyclopropyl gold carbenes **3** (Scheme 1).[6] In the absence of nucleophiles, intermediates **3** evolve to give 1,3-dienes **4** and **5** by an intramolecular rearrangement process.[1,2,7–10] Skeletal rearrangement products **4** result from the cleavage of the alkene (*single-cleavage rearrangement*), whereas dienes **5** are formed by a more complex process in which both the alkene and the alkyne are cleaved (*double-cleavage rearrangement*). In the presence of alcohols or water, products of alkoxy- or hydroxycyclization are obtained.[11–13] Recently, the Au^I-catalyzed additions of carbon nucleophiles to 1,6-enynes via intermediates **3** have been described.[14,15]

A few unsubstituted 1,6-enynes (**1**, R′ = H), as well as those bearing alkyl or aryl substituents at the alkyne, can cyclize by *endo* pathways via intermediates **6** (Scheme 1) to give bicyclic compounds **7**.[11,16,17,18] We have found recently that opening of gold(I) intermediates **6** to form seven-membered ring products is also possible.[19]



Scheme 1. General scheme for the Au^I-catalyzed cyclization of 1,6-enynes in the absence of nucleophiles.

Using gold(I) catalysts we found a new rearrangement that affords dienes **8** (Scheme 1),[11] products of an apparent endocyclic skeletal rearrangement.[6] Only a few additional examples of this type of rearrangement have been reported: Miyanohana and Chatani reported the formation of dienes of type **8** as minor products when using $InCl_3$ as the cata-

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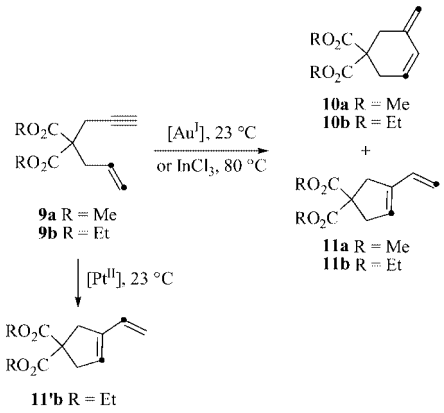
lyst,[20] while Faller and Fountaine found two additional examples when using a Ru^{II} catalyst.[21]

The mechanism by which dienes **8** are formed is still unknown,[6,22] although labeling experiments are consistent with an intramolecular process in which the terminal C atom of the alkene is finally attached to C-2 of the alkyne (Scheme 1).[11b,21] Interestingly, Kim and Lee reported the formation of products **8** in reactions of 1,6-enynes catalyzed by rhodium(I), although labeling experiments indicated that in that case the mechanism proceeds through vinylidene intermediates.[23]

The factors that govern the selectivity in the skeletal rearrangement are not well understood. Thus, for example, although similar reactivities are observed on using gold(I) and platinum(II) complexes as catalysts,[24] different results are observed in the skeletal rearrangements. Indeed, formation of products of type **8** with many metal catalysts (Pd^{II}, Pt^{II}, Ru^{II}, Ir^{I}, Ga^{III}) has not been reported. Somewhat strikingly, similar results were obtained with gold(I) and indium(III) catalysts in these reactions. Thus, **9a** reacted in the presence of a cationic Au^{I} catalyst (2 mol-%) in CH_2Cl_2 at 23 °C to give a 2:1 mixture of the skeletal rearrangement products **10a** and **11a**,[7b] while **9b** in the presence of $InCl_3$ (10 mol-%) at 80 °C afforded a 1:5 mixture of **10b** and **11b**[20] (Scheme 2). Interestingly, in contrast with these results, the reaction of **9b** in the presence of a cationic Pt^{II} catalyst (2 mol-%) at room temperature provided exclusively **11′b**,[8] the product of a double-cleavage rearrangement. In the reaction of **9a** in the presence of a Ru^{II} complex only the exocyclic rearranged diene **11a** was detected in low yield.[21]



Scheme 2. Different outcomes of the skeletal rearrangements of 1,6-enynes **9a** and **9b** in the presence of cationic gold(I),[11] cationic platinum(II),[8] or $InCl_3$[20] as catalysts. $[Pt^{II}] = [Pt(dppe)(PhCN)_2]BF_4$.[8]

Reactions of **9a** in the presence of Au^{I} catalysts under different reaction conditions gave highly variable results, ranging from exclusive isolation of **10a** to the selective formation of **11a** as the major product. We therefore decided to carry out a detailed examination of the *endo*/*exo* selectivity in the Au^{I}-catalyzed rearrangement of **9a** and of related simple 1,6-enynes bearing substituents at C-4. We also report the first theoretical work on the mechanism of the endocyclic rearrangement that leads to dienes of type **8**.

Results and Discussion

Experimental Results

For the gold(I)-catalyzed skeletal rearrangements of 1,6-enynes we used the cationic complexes **12**[25] and **13**[26,27] and the precatalyst **14**,[28] which have been shown to be excellent catalysts for a variety of reactions of enynes (Figure 1).

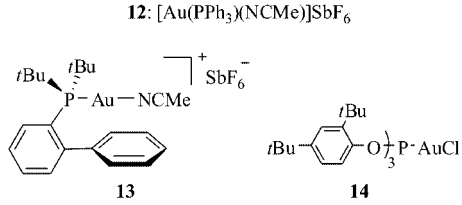


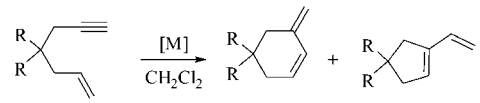
Figure 1. Au^{I} complexes used as catalysts for the skeletal rearrangement of 1,6-enynes.

The cyclization of enyne **9a** was found to be highly dependent on the reaction temperature. Thus, the reaction of **9a** at –15 °C in the presence of the cationic catalyst **12** afforded a 10:1 mixture of **10a** and **11a** (Table 1, Entry 1). At room temperature a 1:1 mixture of **10a** and **11a** was obtained (Table 1, Entry 3). Higher temperatures or catalyst loadings led to formation of the exocyclic rearrangement product **11a** as the major product, as a result of the decomposition of **10a**. As already reported, the reaction in the presence of $PtCl_4$ led only to the formation of **11a** (Table 1, Entry 6).[10] On the other hand, enyne **15**, with strongly electron-withdrawing substituents at C-4, afforded the exocyclic rearrangement product **17** as the major product (Table 1, Entries 7–12), while the reaction of **15** in the presence of $PtCl_4$ also led to *exo* product **17** (Table 1, Entry 13). Lower levels of conversion and/or longer reaction times were required in the reactions in the presence of AuCl or Pt^{II} complex **18**[19] as catalysts (Table 1, Entries 14 and 15). In these reactions, endocyclic rearrangement diene **16** was not detected in the crude reaction mixtures. In all cases, reactions catalyzed by gold(I) proceeded more readily than those catalyzed by platinum(II)[8] or indium(III).[20]

We next decided to study the reactions of enynes **19a** and **19b**, which possess electron-withdrawing substituents one carbon more distant than in **9a** and **15**. Enyne **19a** afforded endocyclic rearrangement diene **20a** as the major product in the presence of catalysts **12** or **13** (Table 2, Entries 1–7). In the case of the bis(trifluoroacetate) **19b**, a catalyst-dependent reversal in the *exo*/*endo* selectivity was observed (Table 2, Entries 9–11). The reactions of **19a** and **19b** in the presence of $PtCl_4$ led only to the formation of *exo* products **21a** and **21b** (Table 2, Entries 8 and 12).

To confirm that the above exocyclic skeletal rearrangements proceed by the single-cleavage mechanism (formation of products of type **4** in Scheme 1) we examined the reactions of 1,6-enynes **9a-d_1** and **15-d_1** in the presence of cationic complex **12** as catalyst (Scheme 2). In these reactions, the deuterated derivatives **10a-d_1**/**11a-d_1** and **16-d_1**/**17-d_1** were obtained, which is fully consistent with labeling experi-

Table 1. Skeletal rearrangement of 1,6-enynes **9a** and **15**.[a]



9a R = CO_2Me
15 R = SO_2Ph

10a
16

11a
17

Entry	Enyne	[M]	*T* (°C)	Time	*endo*/*exo* ratio	Yield (%)
1	**9a**	**12**	–15	5.5 h	10:1	100[b]
2	**9a**	**12**	0	30 min	4:1	100[b]
3	**9a**	**12**	23	20 min	1:1	100[b]
4	**9a**	**13**	0	30 min	3:1	100[b]
5	**9a**	**13**	23	5 min	2:1	97
6	**9a**	$PtCl_4$	23	1 h	<1:100	70
7	**15**	**12**	0	1 h	1:10	100
8	**15**	**12**	23	5 min	1:8	100
9	**15**	**13**	0	1.5 h	1:62	96[b]
10	**15**	**13**	23	10 min	1:54	100
11[c]	**15**	**14**/Ag^I	–20	1 h	1:12	99
12[c]	**15**	**14**/Ag^I	23	2 min	1:10	89
13	**15**	$PtCl_4$	23	45 min	<1:100	98
14	**15**	AuCl	23	5 h	<1:100	30[b]
15	**15**	**18**	23	20 h	<1:100	91

[a] Reactions in the presence of 2 mol-% catalyst. [b] Determined by ^1H NMR spectroscopy. [c] Ag^I: $AgSbF_6$.

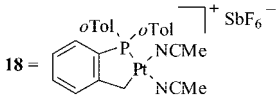
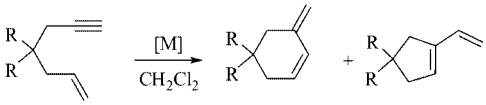


Table 2. Skeletal rearrangements of 1,6-enynes **19a** and **19b**.[a]



19a R = CH_2OAc
19b R = CH_2OCOCF_3

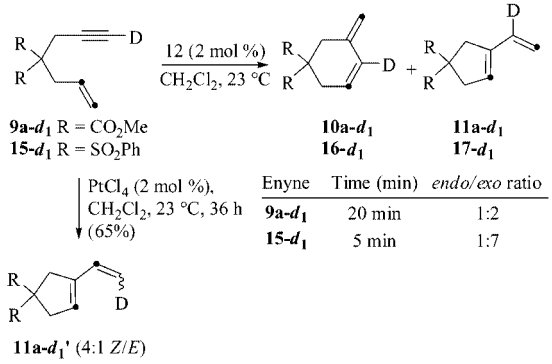
20a
20b

21a
21b

Entry	Enyne	[M]	*T* (°C)	Time	*endo*/*exo* ratio	Yield (%)
1	**19a**	**12**	–15	12 h	>100:1	95
2	**19a**	**12**	23	20 min	5:1	100[b]
3	**19a**	**12**	40	5 min	3:1	–[c]
4	**19a**	**13**	–15	12 h	3:1	89
5	**19a**	**13**	0	30 min	3:1	100[b]
6	**19a**	**13**	23	20 min	2:1	95
7	**19a**	**13**	40	5 min	2:1	84
8	**19a**	$PtCl_4$	23	1 h	<1:100	60
9	**19b**	**12**	23	20 min	2:1	100[b]
10	**19b**	**13**	23	20 min	1:1.6	100
11	**19b**	**13**	40	5 min	1:1.6	60
12	**19b**	$PtCl_4$	23	1 h	<1:100	80

[a] Reactions in the presence of 2 mol-% catalyst. [b] Yield determined by ^1H NMR spectroscopy. [c] Not determined. Decomposition was observed.

ments on related rearrangements.[11b,21] On the other hand, the reaction of **9a**-d_1 in the presence of $PtCl_4$ provided exclusively **11a**-d_1′ [(*Z*)/(*E*) 4:1], the products of a double skeletal rearrangement (Scheme 3).



9a-d_1 R = CO_2Me
15-d_1 R = SO_2Ph

10a-d_1
16-d_1

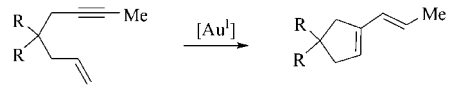
11a-d_1
17-d_1

11a-d_1′ (4:1 *Z*/*E*)

Scheme 3. Skeletal rearrangements of 1,6-enynes **9a**-d_1 and **15**-d_1 in the presence of cationic complex **12** or $PtCl_4$ as catalyst.

Finally, substrates **22** and **23**, each possessing a methyl group at C-1 of the alkyne component, were examined in their reactions in the presence of cationic Au^I complexes. As shown in Table 3, the skeletal rearrangements of **22** and **23** both proceed exclusively by the double-cleavage mechanism to give selectively **24** and **25**, respectively, which is consistent with previous observations in Au^I-catalyzed reactions of similar substrates.[7] Interestingly, the reaction of the diethyl ester analogue of **22** in the presence of a cationic Pt^{II} catalyst has been reported to give a 3:7 (*E*)/(*Z*) mixture of products of double cleavage,[8] whereas use of $PtCl_2$[9b] and $PtCl_4$[10] gave mixtures of the single-/double-cleavage rearranged products (8:1 and 1:9, respectively). In contrast with the platinum catalysts, gold(I) catalysts give **24** and **25** exclusively as the (*E*) isomers.

Table 3. Skeletal rearrangements of 1,6-enynes **22** and **23** catalyzed by Au^I.[a]



22 R = CO_2Me
23 R = SO_2Ph

24 R = CO_2Me
25 R = SO_2Ph

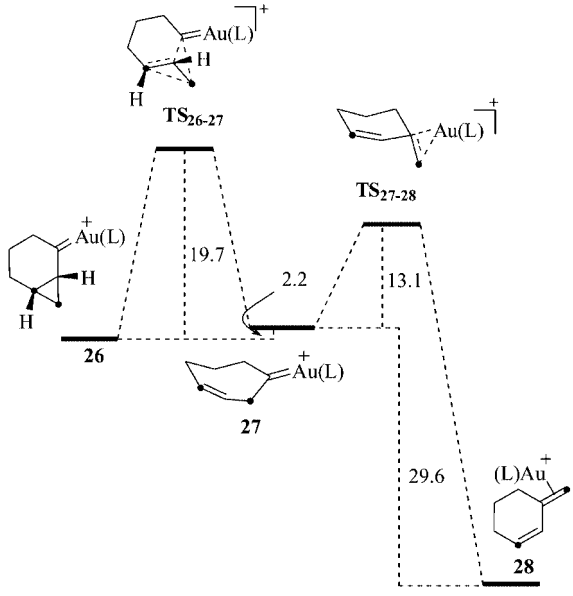
Entry	Enyne	[Au^I]	*T* (°C)	Time	Yield (%)
1	**22**	**12**	23	24 h	91[b]
2	**23**	**12**	23	20 h	70[b]
3[c]	**23**	**12**	50	50 min	99
4[d]	**23**	**14**/Ag^I	23	5 min	100

[a] Reactions with 2 mol-% catalyst in CH_2Cl_2. [b] Determined by ^1H NMR spectroscopy. [c] Reaction in 1,2-dichloroethane. [d] Ag^I: $AgSbF_6$.

Theoretical Results

We first considered the possibility that the formation of compounds **8** may be the result of endocyclic rearrangements via intermediates **6** (Scheme 1). According to DFT calculations [B3LYP/6-31G(d) (C, H, P), LANL2DZ (Au) level] performed on model system **26** (Scheme 4), rearrangement does not occur in a single step.[29] Instead, intermediate **26** (i.e., **6** in Scheme 1) undergoes a ring expansion via $\mathbf{TS_{26-27}}$ to form a seven-membered ring intermediate **27**, which then undergoes a ring contraction to give **28**. Elimi-

nation of $[AuL]^+$ from **28** would then afford the six-membered ring diene. Although in Scheme 4 the final complex **28** is depicted as an η^2-1,3-dienegold(I) complex, bond lengths and angles indicate that its structure actually corresponds to an allyl carbocation stabilized by an α η^1-alkylgold. Very similar results were obtained for the analogous system with a terminal *trans*-disubstituted alkene with a Me group (activation energies of 21.2 and 7.6 kcal mol^{-1} for the two steps).

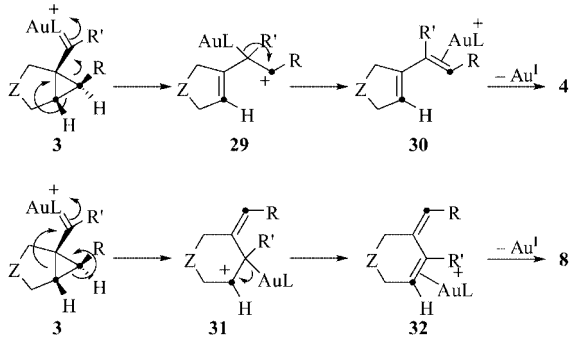


Scheme 4. Reaction pathway and energies for the Au^I-catalyzed endocyclic rearrangement calculated at the B3LYP/6-31G(d) (C, H, P), LANL2DZ (Au) level (+ ZPE-corrected electronic energies are given in kcal mol^{-1}). L = PH_3.

The activation energy for the transformation of **26** into **27** is relatively high (19.7 kcal mol^{-1}), although formation of **26** from the first η^2-alkynegold(I) complex (transformation **2** into **6** in Scheme 1) is exothermic (ca. 19.7 kcal mol^{-1}). Overall, the rearrangement is an exothermic process (ca. –47 kcal mol^{-1}). A very similar pathway was found for the Pt^{II}-catalyzed reaction, with even higher activation energies for the two-step process (32.6 and 19.5 kcal mol^{-1}).[29]

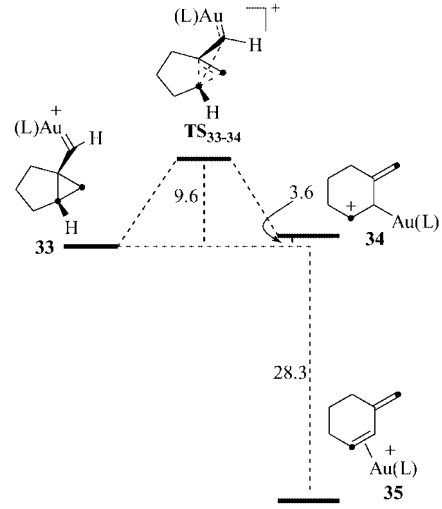
As an endocyclic process for this rearrangement requires a relatively high activation for the first step, we also considered an alternative based on an exocyclic transformation (Scheme 5). Thus, in analogy to the known *exo* single-cleavage rearrangement of intermediates **3** via **29** and **30**,[7] a similar opening of **3** with cleavage of the endocyclic cyclopropane bond would form six-membered ring intermediate **31**. Metal elimination from cation **31** via **32** would then give **8**.

DFT calculations support this hypothesis (Scheme 6). Thus, cyclopropyl gold(I) carbene **33** rearranges with ring-opening via $\mathbf{TS_{33–34}}$ to give cation **34** in a moderately endothermic process with an activation energy of only 9.6 kcal mol^{-1}, much lower than that calculated for the first step in Scheme 4. We have calculated activation energies for



Scheme 5. The two alternative single-cleavage rearrangements of intermediate **3**: exo- and endocyclic cleavage mechanisms.

the rearrangement of **3** to **29** (Z = CH_2, R = Me, R′ = H) of 9.1 kcal mol^{-1}, similar to that found here for the opening of **33** to **34**.[7] Elimination of the metal from **34** is a highly exothermic process. Overall, formation of **35** from the enyne coordinated to $[Au^IL]^+$ is an exothermic process (ca. –44 kcal mol^{-1}).



Scheme 6. Reaction pathway and energies for the Au^I-catalyzed single-cleavage rearrangement by endocyclic cleavage of **33** calculated at the B3LYP/6-31G(d) (C, H, P), LANL2DZ (Au) level (+ ZPE-corrected electronic energies are given in kcal mol^{-1}). L = PH_3.

Conclusions

The gold(I)-catalyzed skeletal rearrangement of 1,6-enyne **9a** preferentially gives the six-membered ring skeletal rearrangement product **10a**, whereas the 1,6-enyne **15**, with more strongly electron-withdrawing substituents at the tether (C-4), preferentially gives the five-membered ring skeletal rearrangement product **17**. This trend is reproduced by diacetate **19a** and bistrifluoroacetate **19b**. Enynes **22** and **23**, substituted at the alkyne, react in the presence of Au^I catalysts to give exclusively five-membered ring products. So far, all the reported examples of formation of six-membered rings by rearrangement of 1,6-enynes correspond to enynes that are unsubstituted at the alkyne.

Reactions in the presence of $PtCl_4$ as catalyst did not provide any six-membered ring products by skeletal rearrangement, which is in line with previous observations made with Pt^{II} catalysts. These results underline the difference between Au^{I} and less reactive catalysts.

DFT calculations indicate that an endocyclic rearrangement should proceed in two steps through a ring-expansion that requires high activation energy (ca. 20 kcal mol^{-1}). A more probable pathway is shown in Schemes 5 and 6. Accordingly, this rearrangement of 1,6-enynes leading to the formation of six-membered rings is a variant of the single-cleavage mechanism in which the endocyclic cyclopropane bond undergoes cleavage to afford a ring-expanded product. These theoretical results show that with some 1,6-enynes the two types of single-cleavage rearrangement could compete, which is consistent with the experimental results reported above with substrates **9a**, **15**, **19a**, and **19b**.

Experimental Section

All reactions were carried out under Ar under anhydrous conditions. Chromatographic purifications were carried out with flash grade silica gel (40–60 μm). Solvents were dried using a Solvent Purification System (SPS).

General Procedure for Cyclization Reactions: The enyne (0.10–0.50 mmol) in dry CH_2Cl_2 (1 mL) or 1,2-dichloroethane (1 mL) was added to a solution of Au or Pt catalyst (2 mol-%) in CH_2Cl_2 or 1,2-dichloroethane (1 mL). When precatalyst **14** was employed, the solution of enyne was added to a mixture of $AgSbF_6$ (2 mol-%) and compound **14** (2 mol-%) in dry CH_2Cl_2. This mixture was stirred for the time and at the temperature stated in the tables and quenched with NEt_3, and then water was added. After the usual extractive workup, the mixtures were purified by flash column chromatography (hexane/EtOAc mixtures).

Compounds **9a**,[30] **10a**,[31] **10a-*d*$_1$**,[23] **11a**,[11b,21] **15**,[32] **17**,[17a] **19a**,[33] **22**,[34] **24**,[9a] and **25**[12b] have been described previously.

Dimethyl 3-(Vinyl-*2-d*)cyclopent-3-ene-1,1-dicarboxylate (11a-*d*$_1$′): 4:1 (*Z*)/(*E*) mixture (96% d_1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.46 (d, J = 10.9 Hz, 1 H), 5.57 (t, J = 1.8 Hz, 1 H), 5.08 [d, J = 16.7 Hz, 0.2 H, (*E*)], 5.08 [overl.d, J = 10.0 Hz, 0.8 H, (*Z*)], 3.75 (s, 6 H), 3.13–3.11 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.57 (CO), 140.08 (C), 132.37 (CH), 126.92 (CH), 114.92 (t, $^1J_{C,D}$ = 23.8 Hz, CHD), 58.80 (C), 52.98 (CH_3), 40.98 (CH_2), 39.34 (CH_2) ppm. HMRS-ESI calcd. for $C_{11}H_{13}DO_4Na$ [M + Na]$^+$: 234.0853; found: 234.0843.

4,4-Bis(phenylsulfonyl)hept-1-en-6-yne-*7-d* (15-*d*$_1$): 4,4-Bis(phenylsulfonyl)hept-1-en-6-yne (300 mg, 0.80 mmol) was partially dissolved in THF (5 mL) and the solution was cooled down to –78 °C. Then a *n*BuLi solution (2.4 M in hexane, 0.4 mL, 0.96 mmol) was added and the solution turned red. The cooling bath was removed and the reaction mixture was stirred at room temperature for 10 min. Then it was cooled down again to –78 °C and D_2O was added dropwise. Finally the cooling bath was removed and the mixture was extracted with CH_2Cl_2 and a saturated aqueous NH_4Cl solution. The crude residue was purified by column chromatography to give **15-*d*$_1$** as a white solid (220 mg, 73% yield, 92% deuteration). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, J = 7.4 Hz, 4 H), 7.72 (t, J = 7.4 Hz, 2 H), 7.59 (t, J = 7.8 Hz, 4 H), 6.08 (ddt, J = 17.1, 9.7, 7.0 Hz, 1 H), 5.35–5.30 (m, 1 H), 5.29 (br. s, 1 H), 3.18 (s, 2 H), 3.11 (d, J = 6.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.44 (2 C), 134.82 (2 CH), 131.56 (4 CH), 129.43 (CH), 128.60 (4 CH), 121.19 (CH_2), 88.76 (C), 75.26 (t, $^2J_{C,D}$ = 6.9 Hz, C), 74.13 (t, $^1J_{C,D}$ = 38.3 Hz, CD), 33.24 (CH_2), 20.70 (CH_2) ppm. HRMS-ESI calcd. for $C_{19}H_{17}DO_4S_2Na$ [M + Na]$^+$: 398.0607; found: 398.0599.

3-Methylene-5,5-bis(phenylsulfonyl)cyclohex-1-ene (16): This compound was characterized from an enriched mixture (1.7:1 ratio) together with 4,4-bis(phenylsulfonyl)-1-vinylcyclopent-1-ene (**17**), previously described.[17a] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05–7.98 (m, 4H **16**, 4H **17**), 7.74–7.66 (m, 2H **16**, 2H **17**), 7.59–7.52 (m, 4H **16**, 4H **17**), 6.16 (dd, J = 17.5, 10.7 Hz, 1H **17**), 6.02 (dt, J = 10.1, 1.9 Hz, 1H **16**), 5.56–5.49 (m, 1H **16**), 5.22 (br. s, 1H **17**), 5.08 (d, J = 10.7 Hz, 1H **17**), 5.02 (d, J = 17.5 Hz, 1H **17**), 4.98 (br. s, 1H **16**), 4.89 (br. s, 1H **16**), 3.45 (br. s, 2H **17**), 3.40 (br. s, 2H **17**), 3.19 (br. s, 2H **16**), 3.05–3.01 (m, 2H **16**) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.67 (C **17**), 136.77 (C **17**), 136.52 (C **16**), 135.91 (C **16**), 134.63 (2 CH **17**), 134.61 (2 CH **16**), 131.39 (4 CH **16**), 131.17 (CH **17**), 130.78 (4 CH **17**), 128.81 (4 CH **17**), 128.59 (CH **16**), 128.49 (4 CH **16**), 125.44 (CH **17**), 123.02 (CH **16**), 116.21 (CH_2 **17**), 115.50 (CH_2 **16**), 91.10 (C **17**), 86.83 (C **16**), 38.87 (CH_2 **17**), 37.39 (CH_2 **17**), 30.95 (CH_2 **16**), 26.39 (CH_2 **16**) ppm.

6-Methylene-4,4-bis(phenylsulfonyl)cyclohex-1-ene-*1-d* (16-*d*$_1$): This compound was characterized from a 1:1 mixture together with 4,4-bis(phenylsulfonyl)-1-(vinyl-*1-d*)cyclopent-1-ene (**17-*d*$_1$**), described below. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05–7.98 (m, 4H **16**, 4H **17**), 7.73–7.66 (m, 2H *endo*, 2H *exo*), 7.58–7.52 (m, 4H **16**, 4H **17**), 5.52 (t, J = 3.8 Hz, 1H **16**), 5.22 (t, J = 1.8 Hz, 1H **17**), 5.07 (br. s, 1H **17**), 5.01 (br. s, 1H **17**), 4.98 (br. s, 1H **16**), 4.89 (br. s, 1H **16**), 3.45 (q, J = 1.8 Hz, 2H **17**), 3.40 (br. s, 2H **17**), 3.19 (t, J = 1.5 Hz, 2H **16**), 3.03 (d, J = 4.1 Hz, 2H **17**) ppm. ^{13}C NMR (100 MHz, $CDCl_3$; HSQC): δ = 139.67 (C **17**), 136.77 (C **17**), 136.52 (C **16**), 135.91 (C **16**), 134.63 (2CH **17**), 134.61 (2CH **16**), 131.39 (4CH **16**), 130.78 (4CH **17**), 128.81 (4CH **17**), 128.49 (4CH **16**), 125.44 (CH **17**), 123.02 (CH **16**), 116.21 (CH_2 **17**), 115.50 (CH_2 **16**), 91.10 (C **17**), 86.83 (C **16**), 38.87 (CH_2 **17**), 37.39 (CH_2 **16**), 30.95 (CH_2 **17**), 26.39 (CH_2 **17**) ppm. The two signals corresponding to the deuterated carbon atoms are missing, due to their lower intensities.

1,1-Bis(phenylsulfonyl)-3-(vinyl-*1-d*)-3-cyclopentene (17-*d*$_1$): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03–7.97 (m, 4 H), 7.69 (t, J = 7.4 Hz, 2 H), 7.55 (t, J = 7.9 Hz, 4 H), 5.22 (br. s, 1 H), 5.07 (br. s, 1 H), 5.01 (br. s, 1 H), 3.45 (m, 2 H), 3.40 (br. s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.67 (C), 136.77 (C), 134.63 (2 CH), 130.87 (t, $^1J_{C,D}$ = 23.3 Hz, CD) 130.78 (4 CH), 128.81 (4 CH), 125.45 (CH), 116.21 (CH_2), 91.10 (C), 38.87 (CH_2), 37.39 (CH_2) ppm.

4,4-Bis(trifluoroacetoxymethyl)hept-6-en-1-yne (19b): Pyridine (0.3 mL, 4 mmol) and a catalytic amount of DMAP were added at 0 °C to the crude diol 4,4-bis(hydroxymethyl)hept-6-en-1-yne[33] (0.311 g, 2.0 mmol). Then trifluoroacetic anhydride (1 mL, 8 mmol) was added dropwise at the same temperature. The mixture was stirred at room temperature overnight. Water was added, and the mixture was extracted with CH_2Cl_2, dried with $MgSO_4$, and evaporated under reduced pressure. Purification by chromatography (hexane to hexane/EtOAc 20:1) afforded **19b** as a colorless oil (0.416 g, 1.2 mmol, 60% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.73 (ddt, J = 7.6, 10.0, 16.8 Hz, 1 H), 5.24 (d, J = 10.0 Hz, 1 H), 5.20 (dq, J = 1.5, 16.8 Hz, 1 H), 4.35/4.32 (AB system, J = 11.3 Hz, 4 H), 2.35 (d, J = 2.7 Hz, 2 H), 2.31 (d, J = 7.6 Hz, 2 H), 2.11 (t, J = 2.7 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.03 (q, $^2J_{C,F}$ = 43 Hz, CO), 130.29 (CH), 121.26 (CH_2), 114.49

(q, CF_3, $^1J_{C,F}$ = 284 Hz), 77.62 (C), 72.71 (CH), 68.53 (CH_2), 40.48 (C), 35.82 (CH_2), 22.00 (CH_2) ppm. HMRS-ESI calcd. for $C_{13}H_{13}O_4F_6$ $[M + H]^+$: 347.0718; found: 347.0707.

5,5-Bis(acetoxymethyl)-3-methylenecyclohex-1-ene (20a): This compound was characterized from a 5:1 **20a/21a** mixture. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.49 (dd, J = 17.4 Hz, 10.7, 1H **21a**), 6.14 (dt, J = 9.7, 2.2 Hz, 1H **20a**), 5.65 (dt, J = 9.7, 4.1 Hz, 1H **20a**), 5.58 (s, 1H **21a**), 5.07–5.01 (m, 2H **21a**), 4.88 (s, 1H **20a**), 4.82 (s, 1H **20a**), 4.05/4.03 (AB system, J = 10.9 Hz, 4H **21a**), 3.94/3.91 (AB system, J = 11.1 Hz, 4H **20a**), 2.36–2.34 (m, 4H **21a**), 2.28 (t, J = 1.4 Hz, 2H **20a**), 2.07–2.06 (m, 2H **20a**), 2.06 (s, 6H **21a**), 2.03 (s, 6H **20a**) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.21 (CO **21a**), 170.95 (CO **20a**), 140.82 (C **21a**), 139.33 (C **20a**), 133.21 (CH **21a**), 129.24 (CH **20a**), 128.05 (CH **21a**), 126.12 (CH **20a**), 114.63 (CH_2 **21a**), 113.79 (CH_2 **20a**), 67.22 (CH_2 **21a**), 66.47 (CH_2 **20a**), 44.84 (C **21a**), 39.18 (CH_2 **21a**), 37.35 (CH_2 **21a**), 36.97 (CH_2 **20a**), 35.02 (CH_2 **20a**), 29.63 (C **20a**), 20.93 (CH_3 **21a**), 20.82 (CH_3 **20a**) ppm.

3-Methylene-5,5-bis(trifluoroacetoxymethyl)cyclohex-1-ene (20b): This compound was characterized from a 1:1.7 **20b/21b** mixture. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.51 (dd, J = 17.5 Hz, 10.8, 1H **21b**), 6.23 (dt, J = 9.9, 2.0 Hz, 1H **20b**), 5.70 (dt, J = 9.9, 4.1 Hz 1H **20b**), 5.62 (s, 1H **21b**), 5.13 (d, J = 10.8 Hz, 1H **21b**), 5.08 (d, J = 17.5 Hz, 1H **21b**), 5.00 (s, 1H **20b**), 4.93 (s, 1H **20b**), 4.36/4.34 (AB system, J = 11.1 Hz, 4H **21b**), 4.26/4.25 (AB system, J = 11.4 Hz, 4H **20b**), 2.45 (s, 4H **21b**), 2.37 (t, J = 1.1 Hz, 2H **20b**), 2.17–2.16 (m, 2H **20b**) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.38 (q, $^2J_{C,F}$ = 42 Hz **21b**, CO), 157.24 (q, $^2J_{C,F}$ = 43 Hz **20b**, CO), 140.50 (CH_2 **21b**), 137.62 (C **20b**), 132.52 (CH **21b**), 129.67 (CH **20b**), 127.01 (CH **21b**), 124.85 (CH **20b**), 115.67 (C **21b**), 115.63 (CH_2 **20b**), 114.52 (q, $^1J_{C,F}$ = 285 Hz **21b**, CF_3), 69.98 (CH_2 **21b**), 69.43 (C **20b**), 45.13 (C **21b**), 38.73 (CH_2 **21b**), 37.56 (C **20b**), 37.21 (CH_2 **21b**), 34.56 (CH_2 **20b**), 29.51 (CH_2 **20b**) ppm.

4,4-Bis(acetoxymethyl)-1-vinylcyclopent-1-ene (21a): Cyclization of enyne **19a** (48 mg, 0.20 mmol) in CH_2Cl_2 in the presence of $PtCl_4$ (1.3 mg, 0.004 mmol) afforded **21a** as a colorless oil (28 mg, 60% yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 6.49 (dd, J = 10.7, 17.4 Hz, 1 H), 5.58 (s, 1 H), 5.07–5.01 (m, 2 H), 4.05/4.03 (AB system, J = 10.9 Hz, 4 H), 2.36–2.34 (m, 4 H), 2.06 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.21 (CO), 140.82 (C), 133.21 (CH), 128.05 (CH), 114.63 (CH_2), 67.22 (CH_2), 44.84 (C), 39.18 (CH_2), 37.35 (CH_2), 20.93 (CH_3) ppm. HMRS-ESI calcd. for $C_{13}H_{18}O_4Na$ $[M + Na]^+$: 261.1103; found: 261.1112.

4,4-Bis(trifluoroacetoxymethyl)-1-vinylcyclopent-1-ene (21b): Cyclization of enyne **19b** (52 mg, 0.15 mmol) in CH_2Cl_2 in the presence of $PtCl_4$ (1.0 mg, 0.003 mmol) afforded **21b** as a pale yellow oil (42 mg, 80% yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 6.51 (dd, J = 10.8, 17.5 Hz, 1 H), 5.62 (s, 1 H), 5.13 (d, J = 10.8 Hz, 1 H), 5.08 (d, J = 17.5 Hz, 1 H), 4.36/4.34 (AB system, J = 11.1 Hz, 4 H), 2.45 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.38 (q, $^2J_{C,F}$ = 42 Hz, CO), 140.50 (CH_2), 132.52 (CH), 127.01 (CH), 115.67 (C), 114.52 (q, $^1J_{C,F}$ = 285 Hz, CF_3), 69.98 (CH_2), 45.13 (C), 38.73 (CH_2), 37.21 (CH_2) ppm. HMRS-CI calcd. for $C_{13}H_{13}O_4F_6$ $[M + H]^+$: 347.0718; found: 347.0719.

4,4-Bis(phenylsulfonyl)oct-1-en-6-yne (23). Step i: A solution of bis(phenylsulfonyl)methane (1.50 g, 5.06 mmol) in DMF (5 mL) was added at 0 °C to a cooled suspension of NaH (60% in mineral oil, 223 mg, 5.57 mmol) in DMF (5 mL). When a clear solution was obtained, a solution of 1-bromobut-2-yne (0.462 mL, 5.56 mmol) in DMF (4 mL) was added by cannula. The mixture was stirred overnight at 50 °C. Then the mixture was cooled to room temperature and quenched with saturated aqueous solution of NH_4Cl and extracted with EtOAc. After being dried ($MgSO_4$), the solvents were removed under reduced pressure. The crude mixture was chromatographed (hexanes/EtOAc 2:1) to give 5,5-bis(phenylsulfonyl)-pent-2-yne as very thick, colorless oil (740 mg, 42% yield; 52% corrected based on conversion), together with 5,5-bis(phenylsulfonyl)nona-2,7-diyne as a white solid (436 mg, 23% yield; 28% corrected yield) and the starting material (294 mg, 20% yield).

5,5-Bis(phenylsulfonyl)pent-2-yne: ^1H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, J = 7.5 Hz, 4 H), 7.71 (t, J = 7.5 Hz, 2 H), 7.59 (t, J = 7.5 Hz, 4 H), 4.54 (t, J = 6.0 Hz, 1 H), 3.08 (dq, J = 6.0, 2.5 Hz, 2 H), 1.53 (t, J = 2.5 Hz, 3 H) ppm. ^{13}C NMR PENDANT (100 MHz, $CDCl_3$): δ = 138.10 (2C), 134.70 (2CH), 129.84 (4CH), 129.03 (4CH), 82.43 (CH), 80.12 (C), 71.87 (C), 17.04 (CH_2), 3.49 (CH_3) ppm. HRMS-ESI calcd. for $C_{17}H_{16}O_4S_2Na$ $[M + Na]^+$ 371.0388; found: 371.0375.

Step ii: A solution of 5,5-bis(phenylsulfonyl)pent-2-yne (730 mg, 2.09 mmol) in DMF (7 mL) was added by cannula to a suspension of sodium hydride (60% in mineral oil, 85 mg, 2.12 mmol) in DMF (3 mL). The mixture was stirred until it became a clear solution, and allyl bromide (200 μL, 2.30 mmol) was then added by syringe. The mixture was warmed up to 50 °C and was stirred at that temperature for 16 h. Then the reaction mixture was allowed to cool to room temperature and a saturated aqueous NH_4Cl solution was added (10 mL). The mixture was extracted with EtOAc and the combined organic layers were dried with anhydrous Na_2SO_4. After evaporation of the solvents, the crude residue was chromatographed (4:1 to 3:1 hexanes/EtOAc) to give **22** as a white solid (757 mg, 93% yield). m.p. 132–137 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.10 (m, 4 H), 7.70 (t, J = 7.4 Hz, 2 H), 7.58 (m, 4 H), 6.08 (ddt, J = 7.0, 9.1, 16.0 Hz, 1 H), 5.31–5.23 (m, 2 H), 3.16 (q, J = 2.5 Hz, 2 H), 3.07 (d, J = 7.0 Hz, 2 H), 1.63 (t, J = 2.5 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.02 (2 C), 134.61 (2 CH), 131.54 (4 CH), 129.94 (CH), 128.46 (4 CH), 120.57 (CH_2), 89.18 (C), 81.92 (C), 70.67 (C), 33.64 (CH_2), 21.18 (CH_2), 3.59 (CH_3). HRMS-ESI calcd. for $C_{20}H_{20}O_4S_2Na$ $[M + Na]^+$: 411.0701; found: 411.0698.

Supporting Information (see also the footnote on the first page of this article): Additional calculations, atomic Cartesian coordinates, and computed energies for the stationary points.

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