Tetrahedron 65 (2009) 1880–1888

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Gold-catalyzed reactivity of 3-silyloxy-1,5-enynes: a synthetic tool for the synthesis of complex structures and its limitations

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ARTICLE INFO

Article history:
Received 8 September 2008
Received in revised form 26 November 2008
Accepted 26 November 2008
Available online 24 December 2008

ABSTRACT

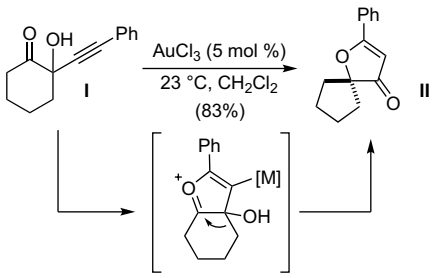
Gold-catalyzed reactions of 3-silyloxy-1,5-enynes in the presence of sterically demanding alcohols afford 4-acylcyclopentenes. The cascade process most likely proceeds through a 6-*endo-dig* carbocyclization and subsequent pinacol-type rearrangement. Studies that define scope and limitations of the cyclization–migration strategy are also described. An alternative cascade yields highly substituted aryls through an unprecedented cyclization–fragmentation pathway.

1. Introduction

The use of noble metal catalysts[1,2] to activate alkynes and to induce a cascade reaction that evolves complex and structurally diverse molecules is a steadily growing field of importance in synthetic chemistry.[3] Amongst other carbophilic Lewis acids, gold(I) and gold(III) complexes are particularly attractive due to the fact that they are typically employed under convenient and experimentally simple reaction conditions while showing outstanding functional group tolerance. As part of our ongoing research program that aims to construct heterocyclic[2n,4] and carbocyclic compounds with increased complexity and structural diversity using noble metal-catalyzed cascade strategies, we developed a powerful sequence for the construction of 3(2*H*)-furanones[5–7] and 3-pyrrolones.[8]

As shown for 2-hydroxy 2-alkynyl carbonyl compounds **I**, the internal oxygen nucleophile facilitates an initial cyclization that finally leads to the formation of spirocyclic 3-furanone **II** (Scheme 1). The putative oxonium ion is believed to undergo a 1,2-alkyl migration analogous to a formal α-ketol rearrangement. Encouraged by these results and the works by Echavarren et al.[9] and Toste et al.,[10] we envisaged an extension of the noble metal-catalyzed cascade strategy by combining an initial carbocyclization with a then pinacol-type rearrangement.[11]

Based on the typical reactivity of 1,5-enynes,[12] it was expected that 3-silyloxy-1,5-enynes of type **A** are ideal substrates for a cyclization–pinacol cascade (Fig. 1). The initial coordination of a soft gold complex to the alkynyl moiety would result in reactive intermediate **C** (or **D**) through 6-*endo-dig* carbocyclization. Due to the silyloxy group at C3, the intermediate cation should then trigger an irreversible 1,2-shift analogous to a pinacol rearrangement and subsequent protonation of the carbon–transition-metal bond should afford the 4-acylcyclopentene framework **F** and regenerate the catalyst. The realization of this concept was recently communicated in preliminary form.[13] We herein disclose full details on the reactivity of 3-silyloxy-1,5-enynes in the presence of gold catalysts. In particular with regard to the meanwhile reports of closely related noble metal-catalyzed cascade reactions involving carbocyclization and pinacol-type rearrangement,[14] we feel it might be beneficial to define the scope of the conversion **A**→**F** more precisely. Therefore, the focus lies on pointing out limitations and reaction pathways that are alternative to the one depicted in Figure 1.



Scheme 1. Gold-catalyzed synthesis of 3(2*H*)-furanones.

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doi:10.1016/j.tet.2008.11.103

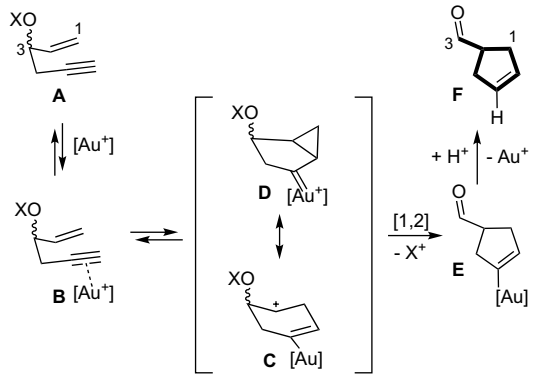


Figure 1. Projected cyclization–pinacol pathway for the synthesis of 4-acyl cyclopentenes.

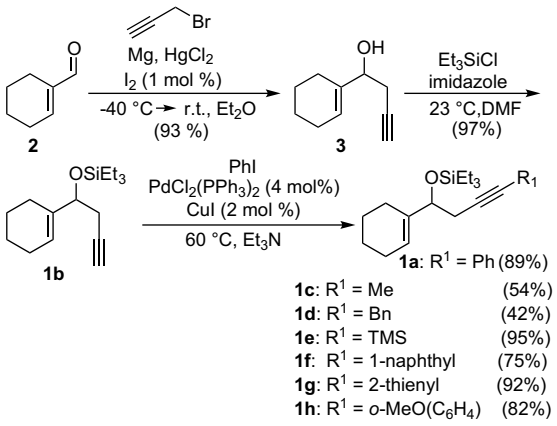
2. Results and discussion

2.1. Synthesis of 3-silyloxy-1,5-enynes

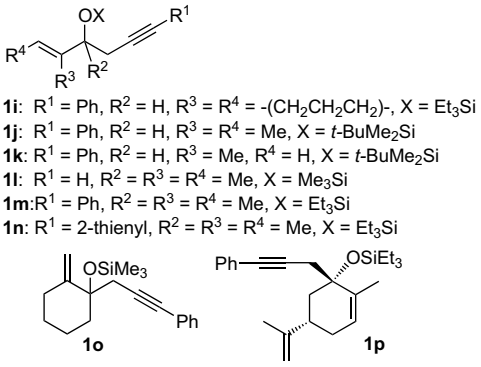
In the present study, we have utilized a general synthesis route to easily access a variety of 3-silyloxy-1,5-enynes **1** from enals and enones. As exemplified for the preparation of 3-silyloxy-1,5-enyne **1a**, 1,2-addition of the Grignard-reagent derived from propargyl bromide[15] in the presence of catalytic amounts of $HgCl_2$ and iodine gave secondary alcohol **3** in 93% yield. Protection of the free hydroxy group as triethylsilyl ether delivered the 3-silyloxy-1,5-enyne skeleton required for the planned investigations. Subsequent Sonogashira coupling[16] with iodobenzene transformed terminal alkyne **1b** into internal alkyne **1a**. Terminal alkyne **1b** was reacted to a series of 6-substituted 3-siloxy-1,5-enynes in large scale and good overall yields as shown in Scheme 2. Accordingly, a variety of acyclic 1,5-enynes **1i**–**1n** depicted in Scheme 3 were obtained from enals and enones other than cyclohex-1-enecarbaldehyde (**2**). Enyne **1p** was synthesized in enantiomerically pure form starting from commercially available (*S*)-(+)-carvone.

2.2. Optimization of reaction conditions

Our initial studies have been carried out on the transition metal-catalyzed conversion of 3-triethylsilyloxy-1,5-enyne **1a** into bicyclic aldehyde **4a** (Table 1). These results were promising, as product formation was observed in the presence of cationic triphenylphosphinegold(I) complex derived from activation of [AuCl(PPh_3)] with $AgSbF_6$ (Table 1, entry 3). The low yield was attributed to the fact that the mechanistic scheme discussed in Figure 1 requires an external proton source for the proto-demetalation step to



Scheme 2. Synthesis of 3-siloxy-1,5-enynes **1a**–**1h**.



Scheme 3. 3-Siloxy-1,5-enynes **1i**–**1p** used in this study.

regenerate the catalyst. Therefore, the yield of 39% might result from the hygroscopicity of $AgSbF_6$ under the open-flask conditions employed for the transformations described in Table 1 (see Experimental). Our attempts to use the corresponding 3-hydroxy-1,5-enyne with a free hydroxy group as internal proton source failed due to competitive heterocyclizations.[17] Gratifyingly, the use of 1.1 equiv of isopropanol as external proton source led to the desired conversion into cis-fused carbocycle **4a** (Table 1, entry 3). Monitoring revealed that the reaction was completed after 10 min at room temperature in CH_2Cl_2. The reaction can be run at low catalyst loadings (2 mol % [AuCl(PPh_3)]/1 mol % $AgSbF_6$) to afford **4a** in 81% yield, although a significantly increased period of time (150 min) is required for the reaction to reach completion (Table 1, entry 4).

The use of proton sources other than isopropanol was also examined;[18] however, utilizing water led to diminished yields that lacked reproducibility. On the other hand, 1.1 equiv of *tert*-butyl alcohol as another sterically demanding proton source gave the desired product in good yields (Table 1, entry 8). The use of an excess of *t*-BuOH did not influence the reaction outcome (result not shown in Table 1). Unlike in the case of *i*-PrOH and *t*-BuOH, the addition of methanol did not result in a clean and rapid reaction providing instead a mixture of various unidentified compounds. This might be attributed to the enhanced nucleophilicity of MeOH leading to the trapping of intermediate **C**. However, compounds originating from such a trapping were not identified during this study.

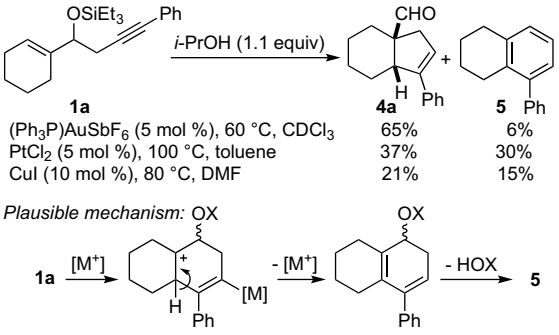
Of primary importance for the optimization of reaction conditions was the observation that even traces of $AgSbF_6$ led to the rapid and complete decomposition of both product and starting material. Therefore, we switched to gold catalysts that were activated prior to use by reaction with 0.5 equiv of $AgSbF_6$ in CH_2Cl_2 at room temperature followed by filtration of the resulting slurry over Celite (Table 1, footnote c). The reaction conditions shown in Schemes 5–8 signify that [AuCl(PPh_3)] was preactivated by the reaction with 0.5 equiv of $AgSbF_6$. Catalysts generated in situ by dechlorination of [AuCl(PPh_3)] with $AgSbF_6$ gave low yields. [AuCl(PPh_3)] is not an efficient catalyst for this conversion without counterion exchange (Table 1, entry 10). To our surprise activation of the gold(I)-source with $AgBF_4$ instead of $AgSbF_6$ under otherwise identical conditions did not produce the desired product (Table 1, entry 12). The gold–oxo complex, [{Au(PPh_3)}$_3$O]BF_4, was not an alternative electrophilic gold(I) species to catalyze the reaction (Table 1, entry 13).

Although not observed for the gold-catalyzed reactions at room temperature, a competing aromatization was found at higher temperatures leading to biaryl compound **5** (Scheme 4). Elimination in the proposed six-membered cationic intermediate **C** might explain the product formation.[19] However, gold complexes proved to be the most reliable catalysts even at elevated temperatures showing a much higher propensity for the 1,2-migration pathway than copper- and platinum-catalysis.

Table 1
Optimization of conditions for the cyclization–pinacol reaction of **1a**

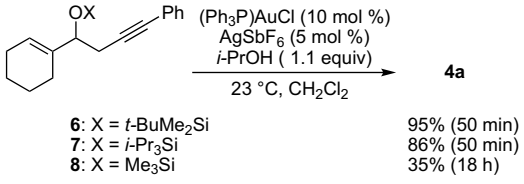
Entry	Catalyst (mol %)	Conditions	Yield[a] [%] **1a**[b]	Yield[a] [%] **4a**
1	AuCl (5)	Toluene, 80 °C, 24 h	>95	0
2	$KAu(CN)_2$ (5)	Toluene, 80 °C, 24 h	>95	0
3[c]	$[AuCl(PPh_3)]$ (10)/$AgSbF_6$ (10)	CH_2Cl_2, 23 °C, 30 min	0	39
4[c]	**$[AuCl(PPh_3)]$ (10)/$AgSbF_6$ (5)**	***i*-PrOH (1.1 equiv), CH_2Cl_2, 23 °C, 10 min**	**0**	**93**
5[c]	$[AuCl(PPh_3)]$ (2)/$AgSbF_6$ (1)	*i*-PrOH (1.1 equiv), CH_2Cl_2, 23 °C, 150 min	0	81
6[c]	$[AuCl(PPh_3)]$ (10)/$AgSbF_6$ (5)	CH_2Cl_2/H_2O (10:1), 23 °C, 60 min	0	39
7[c]	$[AuCl(PPh_3)]$ (10)/$AgSbF_6$ (5)	MeOH (1.1 equiv), CH_2Cl_2, 23 °C, 30 min	0	12
8[c]	$[AuCl(PPh_3)]$ (10)/$AgSbF_6$ (5)	*t*-BuOH (1.1 equiv), CH_2Cl_2, 23 °C, 10 min	0	86
9[c]	$[AuCl(PMe_3)]$ (10)/$AgSbF_6$ (5)	*i*-PrOH (1.1 equiv), CH_2Cl_2, 23 °C, 10 min	0	50
10	$[AuCl(PPh_3)]$ (5)	*i*-PrOH (1.1 equiv), CH_2Cl_2, 23 °C, 24 h	>95	0
11	$AgSbF_6$ (5)	*i*-PrOH (1.1 equiv), CH_2Cl_2, 23 °C, 60 min	0	0
12[c]	$[AuCl(PPh_3)]$ (10)/$AgBF_4$ (5)	*i*-PrOH (1.1 equiv), CH_2Cl_2, 23 °C, 30 min	>95	0
13	$[\{Au(PPh_3)\}_3O]BF_4$ (5)	*i*-PrOH (1.1 equiv), CH_2Cl_2, 23 °C, 24 h	>95	0

[a] Yield of pure product after column chromatography.
[b] Recovered starting material.
[c] The precatalyst $[AuCl(PPh_3)]$ was preactivated by reaction with 0.5 equiv of $AgSbF_6$ in CH_2Cl_2.



Scheme 4. Competing aromatization pathway at elevated temperatures.

The influence of other trialkylsilyl ethers was also examined to define the scope of cyclization–pinacol cascades of this type (Scheme 5). 3-Silyloxy-1,5-enynes with more robust silyl ethers such as **6** (X=*t*-$BuMe_2Si$) and **7** (X=*i*-Pr_3Si) gave aldehyde **4a** in competitive yields. In the case of trimethylsilyl ether **8** (X=Me_3Si) the partial loss of the $SiMe_3$ group under the reaction conditions is most likely responsible for the reduced yield.

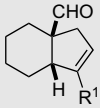
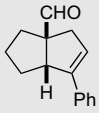
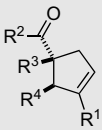
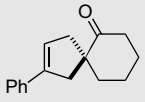
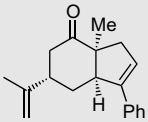


Scheme 5. Influence of the trialkylsilyl ether on the reaction outcome.

2.3. Reactivity of 3-silyoxy-1,5-enynes with different substitution patterns

To probe the scope and limitations of the gold-catalyzed cyclization–pinacol reactions, enynes **1b**–**1p** were allowed to react. As illustrated in Table 2, the cascade reaction is general for a range of substrates bearing different aryl substituents (R^1=aryl) at the alkyne terminus (Table 2, entries 1–3). Unfortunately, substrates containing alkyl substituents (R^1=Me or benzyl) reacted considerably less clean than their aryl analogues. Treatment of TMS-substituted enyne **1e** did not afford the expected cyclopentene (Table 2, entry 4). This novel cyclization–migration reaction is also applicable to acyclic systems, although the yields were modest. Substrates derived from both secondary and tertiary allylic alcohols react with equal facility, the latter producing ketones. As exemplified through the construction of complex spirocyclic (Table 2, entry 14) or bicyclic compounds (Table 2, entry 15), a definite feature of this route to complex 4-acylcyclopentene of type **F** is that all-carbon quaternary stereocenters are created through the 1,2-shift. In all cases, the isolated cyclopentenes **4a**–**4p** were efficiently

Table 2
Gold-catalyzed cyclization–pinacol reactions

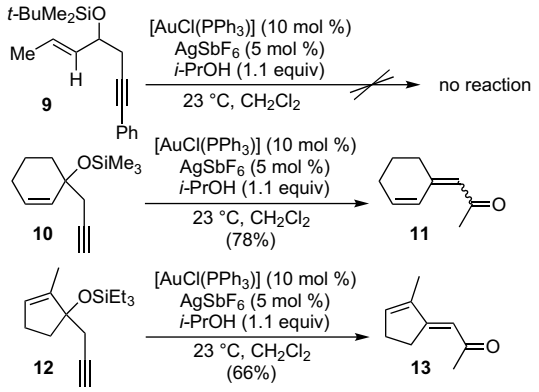
Entry	Substrate	Product[a]		Yield[b] [%]
1	**1h**	 R^1=*o*-MeO(C_6H_4)	**4h**	83
2	**1g**	R^1=2-thienyl	**4g**	81
3	**1f**	R^1=1-naphthyl	**4f**	71
4[c]	**1e**	R^1=TMS	**4e**	—
5	**1b**	R^1=H	**4b**	68
6	**1d**	R^1=CH_2Ph	**4d**	35
7	**1c**	R^1=Me	**4c**	54
8	**1i**		**4i**	73
9	**1j**	 R^1=Ph, R^2=H, R^3=R^4=Me	**4j**	72
10	**1k**	R^1=Ph, R^2=H, R^3=Me, R^4=H	**4k**	28
11	**1l**	R^1=H, R^2=R^3=R^4=Me	**4l**	50
12	**1m**	R^1=Ph, R^2=R^3=R^4=Me	**4m**	55
13	**1n**	R^1=2-thienyl, R^2=R^3=R^4=Me	**4n**	58
14	**1o**		**4o**	65
15	**1p**		**4p**	67

[a] The relative configuration was determined by ^{1}H NMR NOE experiments.
[b] Yield of pure product after column chromatography.
[c] In this case, complete decomposition was observed.

produced as a single diastereoisomer (d.r. >95:5). Diastereomeric products were not evident by ^{1}H NMR analysis of crude reaction mixtures. Notably, the carvone-derived substrate **1p** was converted into the enantiomerically pure bicycle **4p**.

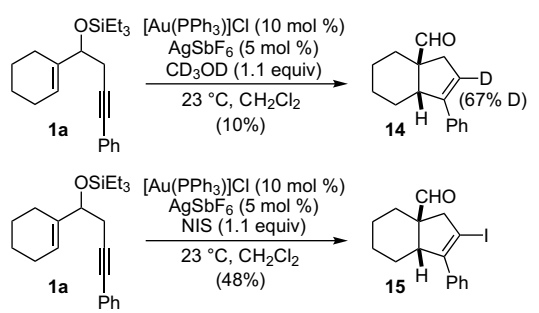
Noteworthy, 3-siloxy-1,5-enynes bearing a tetra-substituted double-bond did not react in the gold-catalyzed cascade process. Instead, starting material was completely recovered without loss under the reaction conditions [5 mol % [AuCl(PPh$_3$)]/10 mol % AgSbF$_6$; *i*-PrOH, CH_2Cl_2, 23 °C].

Presumably due to the crucial stabilization of cationic intermediate **C**, the reaction proved strictly limited to 1,5-enynes possessing a substituent at the C2-position. Product formation that is consistent with an initial 6-*endo-dig* carbocyclization was not obtained from 3-siloxy-1,5-enynes lacking an additional substituent at C2. Instead, in most cases, enynes of this type were inert to the reaction conditions as illustrated for the failed conversion of enyne **9** (Scheme 6). Interestingly, enyne **10** gave 2,4-dienone **11** as an inseparable mixture of diastereoisomers in 78% yield under the reaction conditions. The occurrence of **11** can be rationalized by a sequence consisting of triple-bond hydration[20] and subsequent elimination. Alternatively, an initial elimination might be followed by the hydration step. A similar reaction outcome was observed for the conversion of enyne **12**. In this case, the formation of the corresponding cyclization–pinacol product was not found despite the *C*2-methyl group. This might be attributed to structural restraints during the carbocyclization event resulting from the five-membered ring system.



Scheme 6. Importance of the *C*2-substituent.

These results indicate that the behavior of the putative intermediate **C**/**D** can be better understood in terms of a cation **C** rather than a gold–carbenoid of type **D**, although a strictly carbenoid description cannot be ruled out.[21,22] However, considering the latter, it would be hard to explain the massive difference in reactivity between C2-substituted and C2-unsubstituted substrates. More specifically, the 1,2-migration appears to be the result of



Scheme 7. Electrophilic trapping.

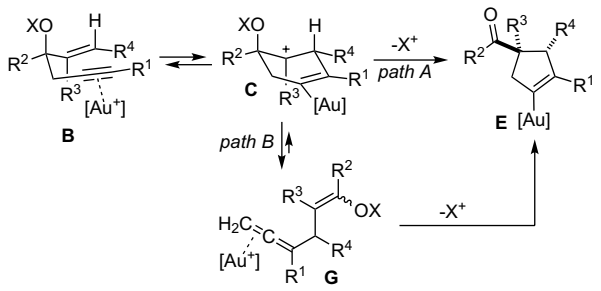


Figure 2. Plausible pathways for the formation of vinylgold species **E**.

a rearrangement that is close to the classical semipinacol rearrangement. However, an alternative mechanism in which the six-membered intermediate **C** collapses into the allenic compound **G** is also plausible (path *B*). In this case, enyne **A** would undergo a formal [3,3]-sigmatropic rearrangement based on a gold-catalyzed cyclization-induced rearrangement (CIR)[23] mechanism.[4,18] An intramolecular 5-*endo-trig* cyclization then gives vinylgold intermediate **E**.[18]

We have briefly examined the proposed proto-demetalation step to set free the gold catalyst. When triethylsilyl ether **1a** was subjected to the standard gold-catalyzed conditions using an excess of CD_3OD as additive instead of *i*-PrOH, deuterium incorporation into the cyclopentene core at C5 was observed (Scheme 7). This result is consistent with the cyclization–migration mechanism as proposed in Figures 1 and 2 in which the proto demetalation at C5 is believed to be the final step in the domino process. Nevertheless, deuterium incorporation did not exceed 67%, a fact that we attributed to both proton residues in CD_3OD and experimental problems to ensure water-free conditions when a mixture of [AuCl(PPh$_3$)] and AgSbF$_6$ was used as catalytic system. We also examined the use of other electrophiles.[24] A useful iodine-incorporation results when *N*-iodosuccinimide (NIS) is added to the reaction mixture instead of isopropyl alcohol as a proton source (Scheme 7).[25] Due to low yields and various by-products, a similar reaction in the presence of *N*-bromosuccinimide or *N*-chlorosuccinimide that aimed to synthesize the corresponding alkenyl bromides and chlorides was not of synthetic value.

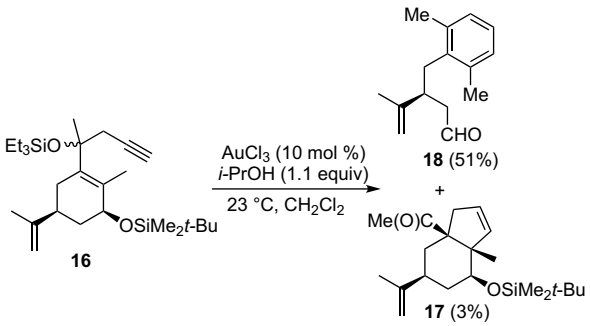
To further expand the scope of the gold-catalyzed process, we investigated the possibility of chirality transfer from enantiomerically pure 3-silyloxy-1,5-enynes. To this end, the enantioenriched 3-siloxy-1,5-enynes (*S*)-**1a** (95% ee) and (*R*)-**1a** (99% ee) were treated with isopropanol and catalytic amounts of silver-free [(Ph$_3$P)Au]SbF$_6$ in CH_2Cl_2 at room temperature.[26] Surprisingly, the rearrangement products were obtained as racemic mixtures in both cases (Scheme 8). This demonstrates that **B** most likely does not possess a preferred conformation, as shown in Figure 2, in which hyperconjugative interactions between $\pi^*_{C=C}$ and the allylic σ_{C-R} are maximized and interactions between the allylic σ^*_{C-O} and the alkene $\pi_{C=C}$ are minimized.[27] The observed complete loss of chirality limits future applications in total syntheses.[28] Bicyclic compound **4p** was the only enantiomerically enriched cyclization–pinacol product that was achieved during the course of this study. In the case of its precursor **1p**, the fact that the stereogenic center

Scheme 8. Attempted chirality transfer starting from **1a**.

within the 1,5-enyne system is part of a ring system leads to a clean chirality transfer. To reveal additional 3-silyloxy-1,5-enynes bearing a backbone that gives chirality transfer, further investigations are ongoing and will be reported in due course.

2.4. Alternative C–C-bond scission

While investigating 3-silyloxy-1,5-enynes with tetra-substituted alkene moieties, we found that enyne **16** underwent an unprecedented transformation into the aryl-containing aldehyde **18** in the presence of $AuCl_3$ (Scheme 9; Table 3, entry 1). This reaction took place in modest yield, whereas the cyclization–pinacol product **17** was obtained in only 3% yield. As for all 3-silyloxy-1,5-enynes with tetra-substituted alkenes, the formation of the cyclization–pinacol product **17** was not observed employing the standard catalyst system [5 mol% [AuCl(PPh_3)]/10 mol% $AgSbF_6$; *i*-PrOH, CH_2Cl_2, 23 °C]. Instead, aldehyde **18** was afforded in low yield (12%) under these conditions (Table 3, entry 2). The best conditions we found for this interesting aryl formation utilize $PtCl_2$ as catalyst in the presence of CO to give aldehyde **18** in 67% yield (Table 3, entry 6).[29] It should be noted that internal alkynes (derived from **16** through Sonogashira cross-couplings) do not react under these conditions.



Scheme 9. Alternative aromatization.

Table 3
Optimization of conditions for the formation of **18**

Entry	Catalyst (mol%); conditions[a]	Yield[b] of **18** [%]
1[c]	$AuCl_3$ (10); A	51
2	[AuCl(PPh_3)] (10)/$AgSbF_6$ (10); A	12
3	AuCl (10); A	21
4[d]	$KAuCl_4$ (10); A	11
5[e]	CuI (10); B	—
6	$PtCl_2$ (10); C	67

[a] Conditions: A: *i*-PrOH (1.1 equiv), CH_2Cl_2, 23 °C; B: *i*-PrOH (1.1 equiv), DMF, 80 °C; C: CO (1 atm), *i*-PrOH (1.1 equiv), toluene, 80 °C.
[b] Yield of pure product after column chromatography.
[c] Compound **17** was isolated in 3% yield.
[d] Traces of **17** were detected.
[e] Compound **16** was recovered in 98% yield.

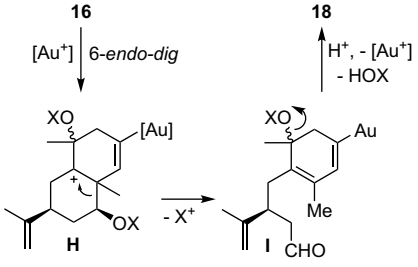


Figure 3. Plausible mechanism for the synthesis of **18**.

As illustrated in Figure 3, this result may be rationalized through an initial C–C-bond formation between C1 and C6. Instead of favoring the pinacol-type 1,2-migration, intermediate **H** appears to undergo a Grob-type fragmentation followed by elimination and proto demetalation.[30] The aromatic core created through this sequence features three substituents in a 1,2,3-assembly.

3. Conclusions

In summary, as predicted by the mechanistic scheme originally proposed for the gold-catalyzed reactivity of 3-silyloxy-1,5-enynes, 3-silyloxy-1,5-enynes are readily transformed into a variety of 4-acylcyclopentenes possessing challenging elements of structure. This reaction has been realized by using silver-free gold(I) complexes (e.g., [(Ph_3P)Au]SbF_6) in the presence of sterically demanding proton sources such as isopropanol. The overall sequence can be understood best as a cascade consisting of a 6-*endo-dig* carbocyclization followed by a pinacol-type 1,2-shift within the cationic intermediate. This mechanism is in agreement with the observation that the reaction proved strictly limited to 1,5-enynes possessing a substituent at the C2-position. A more severe limitation comes from the fact that efficient chirality transfer depends on the enyne structure. For example, **1p** rearranged smoothly to give the product in enantiomerically pure form, whereas the reaction of (*S*)-**1a** resulted in a racemic mixture. Gold(I) also triggers a remarkable rearrangement involving a Grob-type fragmentation that finally leads to complex aryl systems such as **18**. From a synthetic point of view, the results described herein provide a convenient access to structural units, which could find wide application in the design of pharmaceutically active compounds.

4. Experimental

4.1. Synthesis of the 3-silyloxy1,5-enynes

*4.1.1. 1-Cyclohexenylbut-3-yn-1-ol (**3**)*

In a flame dried flask magnesium (500 mg, 20 mmol, 2.0 equiv), mercury dichloride (5 mg, 0.02 mmol, 0.5 mg/mmol aldehyde), and iodine (10 mg) were dissolved in 10 mL diethyl ether. Some drops of propargylbromide were added to start the reaction. The reaction mixture was then cooled to −10 °C and a solution of propargylbromide (1190 mg, 10 mmol, 1.0 equiv) and cyclohex-1-encarbaldehyde (1100 mg, 10 mmol) in 10 mL diethyl ether was quickly added via syringe. The reaction mixture was stirred at 0 °C for 20 min and then at room temperature for additional 4 h. Saturated aqueous NH_4Cl solution (20 mL) and HCl (1 M, 20 mL) is carefully added to quench the reaction and the resulting biphasic mixture was stirred for 1 h. The mixture was extracted with diethyl ether (3×15 mL) and the combined organic solution was washed with saturated aqueous NaCl solution, dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (pentanes/EtOAc=9:1) to afford 1-cyclohexenylbut-3-yn-1-ol (1400 mg, 93%) as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.51–1.69 (m, 4H), 1.94–2.06 (m, 6H), 2.44–2.48 (m, 2H), 4.14 (m, 1H), 5.75 (m, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=22.4, 22.5, 23.8, 24.9, 25.8, 70.5, 74.1, 81.1, 123.8, 138.0; LRMS (EI): 150 (1%) (M^+), 132 (20%), 111 (100%), 104 (34%), 91 (48%).

*4.1.2. (1-Cyclohexenylbut-3-ynyloxy)triethylsilane (**1b**)*

Imidazole (1120 mg, 16.4 mmol, 1.8 equiv) and triethylsilyl chloride (2000 mg, 13.3 mmol, 1.5 equiv) were added to a solution of 1-cyclohexenylbut-3-yn-1-ol (1370 mg, 9.1 mmol) in 10 mL DMF. The solution was stirred for 30 min at room temperature. Then, the reaction was quenched by addition of water (100 mL). The mixture was extracted with diethyl ether (3×20 mL) and the combined organic phases were washed with saturated aqueous NaCl solution,

dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (pentanes/EtOAc=98:2) to afford the title compound (2350 mg, 97%) as colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.59 (q, J=5.5 Hz, 6H), 0.95 (t, J=5.5 Hz, 9H), 1.49–1.71 (m, 4H), 1.85–2.12 (m, 4H), 1.94 (t, J=1.8 Hz, 1H), 2.37–2.40 (m, 2H), 4.13 (t, J=4.8 Hz, 1H), 5.64 (m, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=4.9, 7.0, 22.7, 22.8, 22.9, 25.1, 26.9, 69.5, 76.1, 82.2, 123.7, 139.0; LRMS (EI): 264 (1%) (M^+), 235 (17%), 225 (100%), 115 (19%), 103 (22%).

*4.1.3. (1-Cyclohexenyl-4-phenylbut-3-ynyloxy)triethylsilane (**1a**)*

Under argon atmosphere, iodobenzene (1000 mg, 4.9 mmol, 1.3 equiv), copper iodide (15 mg, 0.08 mmol, 2 mol %), and $PdCl_2(PPh_3)_2$ (112 mg, 0.16 mmol, 4 mol %) were mixed in triethylamine (15 mL). The mixture was degassed with argon to remove oxygen and heated to 60 °C until the solids were dissolved. Compound **1b** (1000 mg, 3.79 mmol, 1.0 equiv) was added, and the mixture was stirred at 60 °C for 10 h. The resulting black reaction mixture was cooled to room temperature and quenched with 30 mL saturated $NHCl_4$ solution. The mixture was extracted three times with 15 mL ethyl acetate, not dissolvable solids were removed by filtration, and the combined organic phases were washed with saturated aqueous NaCl solution, dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (pentanes/EtOAc=99:1) to afford the title compound **1a** (1147 mg, 89%) as yellowish oil. ^{1}H NMR (360 MHz, $CDCl_3$): δ=0.57–0.64 (m, 6H), 0.95 (t, J=7.9 Hz, 9H), 1.49–1.71 (m, 4H), 1.89–2.17 (m, 4H), 2.56 (dd, J=6.3, 16.6 Hz, 1H), 2.62 (dd, J=7.0, 16.6 Hz, 1H), 4.21 (t, J=6.7 Hz, 1H), 5.66–5.69 (m, 1H), 7.25–7.28 (m, 3H), 7.34–7.37 (m, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=5.0, 7.0, 22.8, 22.9, 23.1, 25.2, 28.0, 76.4, 81.9, 88.1, 123.6, 124.3, 127.6, 128.3, 131.6, 139.3; LRMS (EI): 311 (5%) ($M^+-C_2H_5$), 225 (100%), 208 (10%), 180 (12%), 165 (15%); HRMS 311.1826 [311.1831 calcd for $C_{22}H_{32}OSi$ ($M^+-C_2H_5$)].

*4.1.4. ((1R,5S)-2-Methyl-1-(3-phenylprop-2-ynyl)-5-(prop-1-en-2-yl)cyclohex-2-enyloxy)-triethylsilane (**1p**)*

Using the identical sequence that has been employed for the preparation of compound **1a**, the corresponding enyne **1p** was obtained from (*S*)-(+)-carvone as a yellow oil (65% over three steps) after flash chromatography on silica (pentanes/EtOAc=95:5). ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.61–0.74 (m, 6H), 1.01 (t, J=7.9 Hz, 9H), 1.70 (app t, J=13.1 Hz, 1H), 1.79–1.80 (m, 6H), 1.94–2.00 (m, 1H), 2.12–2.16 (m, 1H), 2.48–2.53 (m, 2H), 2.71 (d, J=16.9 Hz, 1H), 2.88 (d, J=16.9 Hz, 1H), 4.79 (s, 2H), 5.47–5.48 (m, 1H), 7.29–7.33 (m, 3H), 7.41–7.43 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=6.9, 7.3, 17.5, 21.0, 31.2, 32.4, 40.1, 41.7, 83.2, 87.7, 109.0, 123.2, 124.4, 127.6, 128.3, 131.6, 139.0, 149.2.

4.2. Cyclization–pinacol reactions of 3-silyloxy1,5-enynes

4.2.1. General procedure for the gold(I)-catalyzed cyclization–pinacol reaction

*4.2.1.1. 1-Phenyl-3a,4,5,6,7,7a-hexahydro-3H-indene-3a-carbaldehyde (**4a**).* A solution of $(Ph_3P)AuCl$ (22.4 mg, 10 mol %) in CH_2Cl_2 (0.3 mL) was added to a solution of $AgSbF_6$ (7.8 mg, 5 mol %) in CH_2Cl_2 (0.3 mL), and the mixture was stirred at room temperature for 10 min. The resulting suspension was filtered through Celite and concentrated under reduced pressure. To this residue, a solution of **1a** (156 mg, 0.45 mmol) and *i*-PrOH (0.04 mL, 0.50 mmol) in CH_2Cl_2 (4.5 mL) was added. The pale purple solution was stirred at room temperature for 10 min. The mixture was concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel (pentanes/EtOAc=98:2) gave **4a** as a colorless oil (94.7 mg, 0.42 mmol, 93%). R_f=0.42 (pentanes/EtOAc=95:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.20–1.26 (m, 2H), 1.43–1.45 (m, 1H), 1.57–1.66 (m, 3H), 1.68–1.72 (m, 1H), 2.06–2.10 (m, 1H), 2.53 (d, J=16.7 Hz, 1H), 2.70 (dd, J=16.7, 2.7 Hz, 1H), 3.16 (t, J=5.8 Hz, 1H), 6.02 (s, 1H), 7.23 (t, J=7.3 Hz, 1H), 7.32 (t, J=7.4 Hz, 2H), 7.41 (d, J=7.6 Hz, 2H), 9.52 (s, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 21.9, 22.9, 27.1, 28.5, 36.3, 44.1, 56.7, 123.5, 126.1, 127.4, 128.6, 135.4, 148.0, 205.6; LRMS (EI): 226 (58%) [M^+], 197 (100%), 156 (52%); HRMS 226.1356 [226.1358 calcd for $C_{16}H_{18}O$ (M^+)].

*4.2.1.2. 3a,4,5,6,7,7a-Hexahydro-3H-indene-3a-carbaldehyde (**4b**).* Following the general procedure, **4b** was obtained as a colorless liquid (68%) after flash chromatography on silica (pentanes/Et_2O=98:2). R_f=0.44 (pentanes/EtOAc=95:5); ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.23–1.54 (m, 6H), 1.60–1.83 (m, 2H), 2.16 (d, J=16.0 Hz, 1H), 2.57 (d, J=16.0 Hz, 1H), 2.82–2.95 (m, 1H), 5.64–5.71 (m, 2H), 9.55 (s, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=22.0, 22.1, 27.4, 27.9, 39.1, 44.3, 56.6, 128.4, 135.8, 205.6; LRMS (EI): 150 (26%) [M^+], 135 (19%), 121 (100%), 107 (38%); HRMS 150.1041 [150.1045 calcd for $C_{10}H_{14}O$ (M^+)].

*4.2.1.3. 1-Methyl-3a,4,5,6,7,7a-hexahydro-3H-indene-3a-carbaldehyde (**4c**).* Following the general procedure, **4c** was obtained as a colorless liquid (54%) after flash chromatography on silica (pentanes/Et_2O=98:2). R_f=0.51 (pentanes/EtOAc=95:5); ^{1}H NMR (360 MHz, $CDCl_3$): δ=1.28–1.37 (m, 2H), 1.39–1.52 (m, 4H), 1.63–1.80 (m, 5H), 2.09 (dq, J=15.7, 2.0 Hz, 1H), 2.46 (dq, J=15.7, 2.2 Hz, 1H), 2.62–2.71 (m, 1H), 5.27 (t, J=1.6 Hz, 1H), 9.54 (s, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=14.9, 22.3, 26.2, 27.8 (2×C), 38.1, 46.6, 57.1, 121.8, 143.6, 205.6; LRMS (EI): 164 (6%) [M^+], 149 (31%), 135 (100%), 121 (42%); HRMS 164.1203 [164.1201 calcd for $C_{11}H_{16}O$ (M^+)].

*4.2.1.4. 1-Benzyl-3a,4,5,6,7,7a-hexahydro-3H-indene-3a-carbaldehyde (**4d**).* Following the general procedure, **4d** was obtained as a colorless liquid (35%) after flash chromatography on silica (pentanes/Et_2O=98:2). R_f=0.52 (pentanes/EtOAc=95:5); ^{1}H NMR (360 MHz, $CDCl_3$): δ=1.21–1.31 (m, 2H), 1.37–1.50 (m, 3H), 1.56–1.64 (m, 1H), 1.65–1.78 (m, 2H), 2.15–2.21 (m, 1H), 2.49–2.55 (m, 1H), 2.67 (t, J=5.84 Hz, 1H), 3.25–3.33 (m, 1H), 3.47 (d, J=15.71 Hz, 1H), 5.26 (s, 1H), 7.16–7.24 (m, 3H), 7.28–7.32 (m, 2H), 9.48 (s, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=22.2, 22.5, 26.6, 27.7, 36.1, 37.4, 45.1, 57.1, 123.5, 126.3, 128.5, 129.0, 139.3, 147.3, 205.7; HRMS 240.1520 [240.1514 calcd for $C_{17}H_{20}O$ (M^+)].

*4.2.1.5. 1-(Naphthalen-1-yl)-3a,4,5,6,7,7a-hexahydro-3H-indene-3a-carbaldehyde (**4f**).* Following the general procedure, **4f** was obtained as a pale yellow liquid (71%) after flash chromatography on silica (pentanes/Et_2O=80:20). R_f=0.37 (pentanes/Et_2O=80:20); ^{1}H NMR (500 MHz, $CDCl_3$): δ=1.10–1.34 (m, 2H), 1.35–1.58 (m, 4H), 1.68–1.80 (m, 1H), 1.84–1.96 (m, 1H), 2.47 (dt, J=16.3 Hz, J=1.9 Hz, 1H), 2.82 (dt, J=16.3 Hz, J=1.9 Hz, 1H), 3.42−3.54 (m, 1H), 5.76–5.85 (m, 1H), 7.31 (dd, J=7.0 Hz, J=1.2 Hz, 1H), 7.40–7.58 (m, 3H), 7.78 (d, J=8.2 Hz, 1H), 7.81–7.92 (m, 1H), 8.03–8.13 (m, 1H), 9.78 (s, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=22.2, 22.4, 26.5, 28.1, 38.7, 47.5, 57.2, 125.3, 125.8, 125.9, 126.1, 127.5, 127.6, 128.5, 131.9, 133.9, 135.3, 146.9, 205.4; LRMS (EI): 276 (99%) [M^+], 247 (100%), 165 (43%), 84 (43%); HRMS 276.1518 [276.1514 calcd for $C_{20}H_{20}O$ (M^+)].

*4.2.1.6. 1-(Thiophen-2-yl)-3a,4,5,6,7,7a-hexahydro-3H-indene-3a-carbaldehyde (**4g**).* Following the general procedure, **4g** was obtained as a yellow oil (81%) after flash chromatography on silica (pentanes/EtOAc=97:3). ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.20–1.23 (m, 2H), 1.37–1.47 (m, 1H), 1.55–1.64 (m, 3H), 1.67–1.73 (m, 1H), 2.04–2.10 (m, 1H), 2.52 (d, J=17.0 Hz, 1H), 2.67 (dd, J=3.0, 17.0 Hz, 1H), 3.08 (dd, J=6.2, 9.4 Hz, 1H), 5.89 (t, J=2.5 Hz, 1H), 6.95–6.97 (m, 2H), 7.15 (dd, J=2.0, 4.1 Hz, 1H), 9.47 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=21.9, 23.1, 26.8, 29.2, 35.8, 45.5, 56.8, 123.0, 124.0, 124.3,

127.4, 139.7, 142.2, 205.4; HRMS (EI): 232 (100%) [M^+], 203 (60%), 189 (51%), 161 (39%), 97 (31%); HRMS 232.0919 [232.0922 calcd for $C_{14}H_{16}OS$ (M^+)].

*4.2.1.7. 1-(2-Methoxyphenyl)-3a,4,5,6,7,7a-hexahydro-3H-indene-3a-carbaldehyde (**4h**).* Following the general procedure, **4h** was obtained as a yellow oil (83%) after flash chromatography on silica (pentanes/EtOAc=95:5). ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.20–1.23 (m, 2H), 1.37–1.47 (m, 1H), 1.55–1.64 (m, 3H), 1.67–1.73 (m, 1H), 2.04–2.10 (m, 1H), 2.52 (d, J=16.6 Hz, 1H), 2.67 (dd, J=2.9, 16.6 Hz, 1H), 3.08 (dd, J=6.8, 8.4 Hz, 1H), 3.80 (s, 3H), 5.88 (t, J=2.4 Hz, 1H), 6.84–6.86 (m, 2H), 7.33–7.36 (m, 2H), 9.50 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=22.0, 23.0, 27.0, 28.7, 36.1, 44.2, 55.4, 56.6, 114.0, 121.3, 127.3, 128.2, 147.5, 159.1, 206.0; LRMS (EI): 256 (11%) [M^+], 120 (48%), 105 (100%), 84 (44%), 43 (57%); HRMS 256.1461 [256.1463 calcd for $C_{17}H_{20}O_2$ (M^+)].

*4.2.1.8. 6-Phenyl-1,2,3,3a,4,6a-hexahydropentalene-3a-carbaldehyde (**4i**).* Following the general procedure, **4i** was obtained as a colorless liquid (73%) after flash chromatography on silica (pentanes/EtOAc=95:5). R_f=0.33 (pentanes/EtOAc=95:5); ^{1}H NMR (360 MHz, $CDCl_3$): δ=1.59–1.79 (m, 4H), 1.87–2.02 (m, 1H), 2.09–2.22 (m, 1H), 2.33 (dt, J=18.2, 2.7 Hz, 1H), 3.18 (dd, J=18.2, 1.8 Hz, 1H), 3.74 (d, J=8.9 Hz, 1H), 5.98–6.04 (m, 1H), 7.20–7.25 (m, 1H), 7.29–7.36 (m, 2H), 7.39–7.45 (m, 2H), 9.68 (s, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=26.3, 32.5, 36.1, 40.4, 53.6, 64.2, 124.1, 126.4, 127.4, 128.6, 135.5, 143.7, 203.0; LRMS (EI): 212 (100%) [M^+], 183 (42%), 155 (52%), 141 (26%); HRMS 212.1201 [212.1201 calcd for $C_{15}H_{16}O$ (M^+)].

*4.2.1.9. 1,2-Dimethyl-3-phenylcyclopent-3-enecarbaldehyde (**4j**).* Following the general procedure, **4j** was obtained as a yellow oil (72%) after flash chromatography on silica (pentanes/EtOAc=99:1). R_f=0.4 (pentanes/EtOAc=90:10); ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.07 (d, J=7.0 Hz, 3H), 1.19 (s, 3H), 2.41 (dt, J=17.3, 2.0 Hz, 1H), 2.81 (dd, J=17.3, 3.2 Hz, 1H), 3.33 (q, J=6.9 Hz, 1H), 5.97 (s, 1H), 7.20–7.26 (m, 1H), 7.29–7.36 (m, 2H), 7.36–7.45 (m, 2H), 9.56 (s, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=14.2, 16.1, 39.7, 42.7, 56.1, 123.2, 126.3, 127.5, 128.6, 135.5, 147.8, 205.1; LRMS (EI): 200 (23%) [M^+], 185 (60%), 171 (100%), 157 (40%); HRMS 200.1202 [200.1201 calcd for $C_{14}H_{16}O$ (M^+)].

*4.2.1.10. 1-Methyl-3-phenylcyclopent-3-enecarbaldehyde (**4k**).* Following the general procedure, **4k** was obtained as a colorless liquid (28%) after flash chromatography on silica (pentanes/Et_2O=98:2). R_f=0.64 (pentanes/EtOAc=90:10); ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.32 (s, 3H), 2.38 (dq, J=17.5, 2.2 Hz, 1H), 2.56 (dq, J=16.2, 2.1 Hz, 1H), 2.97 (dq, J=17.5, 2.3 Hz, 1H), 3.18 (dq, J=16.0, 2.2 Hz, 1H), 6.04–6.09 (m, 1H), 7.22–72.7 (m, 1H), 7.29–7.36 (m, 2H), 7.39–7.44 (m, 2H), 9.64 (s, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=21.9, 41.6, 41.7. 52.9, 123.2, 125.7, 127.6, 128.5, 135.8, 140.5, 203.9; LRMS (EI): 186 (92%) [M^+], 171 (100%), 157 (46%), 143 (94%); HRMS 186.1042 [186.1045 calcd for $C_{13}H_{14}O$ (M^+)].

*4.2.1.11. 1-(1,2-Dimethylcyclopent-3-enyl)ethanone (**4l**).* Following the general procedure, **4l** was obtained as a colorless oil (50%) after flash chromatography on silica (pentanes/EtOAc=80:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.99 (d, J=7.3 Hz, 3H), 1.11 (s, 3H), 2.14 (s, 3H), 2.82 (dq, J=16.6, 2.1 Hz, 1H), 3.01–3.06 (m, 1H), 5.47–5.48 (m, 1H), 5.56–5.58 (m, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=14.9, 19.3, 25.8, 43.9, 44.6, 57.4, 127.0, 135.4, 212.6.

*4.2.1.12. 1-(1,2-Dimethyl-3-phenylcyclopent-3-enyl)ethanone (**4m**).* Following the general procedure, **4m** was obtained as a colorless oil (55%) after flash chromatography on silica (pentanes/EtOAc=80:20). ^{1}H NMR (360 MHz, $CDCl_3$): δ=1.06 (d, J=7.0 Hz, 3H), 1.26 (s, 3H), 2.21 (s, 3H), 2.34 (dt, J=17.0, 2.1 Hz, 1H), 1.82 (dt, J=17.0, 2.1 Hz, 1H), 3.50 (q, J=7.1 Hz, 1H), 5.91 (s, 1H), 7.27 (dt, J=31.2, 7.3 Hz, 3H), 7.38 (d, J=7.3 Hz, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=14.4, 19.5, 25.5, 42.1, 44.2, 58.1, 123.6, 126.4, 127.3, 128.5, 136.2, 147.5, 212.5; LRMS (EI) 214 (6%) [M^+], 199 (12%), 185 (14%), 171 (100%), 143 (15%), 91 (15%), 43 (22%); HRMS 214.1357 [214.1358 calcd for $C_{15}H_{18}O$ (M^+)].

*4.2.1.13. 1-(1,2-Dimethyl-3-(thiophen-2-yl)cyclopent-3-enyl) (**4n**).* Following the general procedure, **4n** was obtained as a pale yellow oil (58%) after flash chromatography on silica (pentanes/EtOAc=97:3). ^{1}H NMR (360 MHz, $CDCl_3$): δ=1.15 (d, J=7.0 Hz, 3H), 1.25 (s, 3H), 2.19 (s, 3H), 2.34 (td, J=17.3, 2.1 Hz, 1H), 2.95 (dd, J=17.4, 3.1 Hz, 1H), 3.37 (q, J=7.1 Hz, 1H), 5.86–5.85 (m, 1H), 6.98–6.96 (m, 2H), 7.15 (dd, J=3.9, 2.3 Hz, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=14.8, 19.3, 25.4, 41.6, 45.5, 58.4, 123.5, 123.7, 124.1, 127.4, 140.1, 141.6, 212.2.

*4.2.1.14. 2-Phenyl-spiro[4.5]dec-2-en-6-one (**4o**).* Following the general procedure, **4o** was obtained as a pale yellow liquid (65%) after flash chromatography on silica (pentanes/Et_2O=80:20). R_f=0.37 (pentanes/Et_2O=80:20); ^{1}H NMR (500 MHz, $CDCl_3$): δ=1.77–1.83 (m, 2H), 1.85–1.94 (m, 4H), 2.44 (d, J=17.3 Hz, 1H), 2.49 (dt, J=6.6, 1.7 Hz, 2H), 2.55 (d, J=16.1 Hz, 1H), 3.03 (dd, J=17.5, 2.2 Hz, 1H), 3.33 (dd, J=15.9, 2.2 Hz, 1H), 5.98 (s, 1H), 7.20–7.25 (m, 1H), 7.31 (t, J=7.4 Hz, 2H), 7.41 (d, J=7.4 Hz, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=22.4, 27.5, 39.7, 40.5, 42.1, 42.3, 56.0, 122.7, 125.6, 127.3, 128.5, 136.3, 139.7, 213.0; LRMS (EI): 226 (100%) [M^+], 211 (66%), 198 (37%), 169 (50%), 156 (80%), 142 (70%); HRMS 226.1358 [226.1358 calcd for $C_{16}H_{18}O$ (M^+)].

*4.2.1.15. (3aS,6S,7aR)-3a-Methyl-1-phenyl-6-(prop-1-en-2-yl)-3,3a,-5,6,7,7a-hexahydroinden-4-one (**4p**).* Following the general procedure, **4p** was obtained as a pale yellow solid (67%) after flash chromatography on silica (pure pentanes, then pentanes/EtOAc=95:5). $[\alpha]_D^{20}$ +6.7 (*c* 0.51, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ=1.31 (s, 3H), 1.64 (s, 3H), 1.84–1.94 (m, 2H), 2.28 (d, J=17.0 Hz, 1H), 2.40–2.46 (m, 2H), 2.61 (q, J=10.1 Hz, 1H), 2.98 (d, J=17.0 Hz, 1H), 3.24 (br s, 1H), 4.63 (s, 1H), 4.76 (s, 1H), 6.04 (s, 1H), 7.26–7.29 (m, 1H), 7.34–7.39 (m, 4H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=21.1, 24.1, 30.7, 38.9, 43.5, 43.6, 52.2, 54.0, 110.2, 125.5, 126.4, 127.4, 128.6, 135.9, 145.5, 147.3, 215.8; LRMS (EI) 266 (100%) [M^+], 223 (32%), 197 (36%), 185 (55%), 157 (88%), 155 (58%); HRMS 266.1671 [266.1671 calcd for $C_{19}H_{22}O$ (M^+)].

*4.2.1.16. 1-(Cyclohex-2-enylidene)propan-2-one (**11**).* Following the general procedure, a 5:3 mixture of diastereoisomers **11** was obtained as a pale yellow oil (78%) after flash chromatography on silica (pentanes/EtOAc=95:5). ^{1}H NMR (360 MHz, $CDCl_3$): δ=(5:3 mixture of diastereoisomers) 1.67 (qn, J=6.3 Hz, 2H), 1.76 (qn, J=6.2 Hz, 1H), 2.14–2.20 (m, 8H), 2.32 (td, J=6.4, 1.4 Hz, 1H), 2.88–2.92 (m, 2H), 5.82 (br s, 0.5H), 5.92 (br s, 1H), 6.03 (dt, J=9.8, 1.7 Hz, 1H), 6.20–6.29 (m, 1.5H), 7.42–7.45 (m, 0.5H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=21.9, 22.9, 25.7, 26.4, 26.8, 31.9, 32.0, 32.6, 121.0, 122.7, 125.9, 130.6, 139.7, 139.8, 150.7, 152.4, 198.7, 199.1. The double-bond configuration was not assigned.

*4.2.1.17. (1Z)-1-(2-Methylcyclopent-2-enylidene)propan-2-one (**13**).* Following the general procedure, **13** was obtained as a pale yellow oil (66%) after flash chromatography on silica (pentanes/EtOAc=95:5). ^{1}H NMR (360 MHz, $CDCl_3$): δ=1.81–1.82 (m, 3H), 2.23 (s, 3H), 2.47–2.51 (m, 2H), 3.06 (td, J=4.3, 2.3 Hz, 2H), 6.06 (s, 1H), 6.44 (s, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=12.7, 31.5, 31.8, 32.0, 114.4, 141.2, 146.3, 167.6, 198.5. The double-bond configuration was assigned according to NOE experiments.

*4.2.1.18. 2-Iodo-1-phenyl-3a,4,5,6,7,7a-hexahydro-3H-indene-3a-carbaldehyde (**15**).* Following the general procedure, **15** was

obtained as a yellow oil (48%) after flash chromatography on silica (pentanes/EtOAc=97:3). ^{1}H NMR (360 MHz, $CDCl_3$): δ=1.27–1.30 (m, 2H), 1.45–1.50 (m, 3H), 1.62–1.70 (m, 2H), 1.79–1.86 (m, 1H), 2.71 (dd, J=1.6, 16.1 Hz, 1H), 3.02 (dd, J=1.8, 16.1 Hz, 1H), 3.25 (t, J=6.4 Hz, 1H), 7.29–7.40 (m, 5H), 9.63 (s, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=21.8, 21.9, 26.6, 27.8, 47.3, 50.3, 57.2, 89.2, 128.0, 128.2, 128.4, 136.7, 151.4, 203.6; LRMS (EI): 352 (20%) [M^+], 225 (35%), 197 (100%), 115 (25%), 91 (31%); HRMS 352.0320 [352.0324 calcd for $C_{16}H_{17}IO$ (M^+)].

4.3. Aromatization reactions of 3-silyloxy1,5-enynes

*4.3.1. (1S,5S)-3-(2-Triethylsilyloxypent-4-yn-2-yl)-2-methyl-5-(prop-1-en-2-yl)cyclohex-2-enyloxy(tert-butyl)dimethylsilane (**16**)*

To a solution of the alcohol precursor (1.00 g, 2.87 mmol) in DMF (5.7 mL) were added imidazole (449.0 mg, 6.60 mmol) and triethylsilyl chloride (0.97 mL, 5.74 mmol) in two portions. The reaction mixture was stirred at room temperature for 3 h and then quenched with water. The aqueous layer was extracted with Et_2O and the combined organic layer dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified on a silica gel column (from 1% Et_2O/pentanes) to provide compound **16** (922.0 mg, 1.99 mmol, 69% mixture of diastereoisomers, ratio 1:1) as a light yellow oil. *Diastereoisomer **1***: ^{1}H NMR (250 MHz, $CDCl_3$): δ=4.73 (br s, 2H), 4.17 (dd, J=9.7, 6.1 Hz, 1H), 2.56 (t, J=2.8 Hz, 2H), 2.36–2.29 (m, 1H), 2.14–2.04 (m, 1H), 1.99–1.92 (m, 2H), 1.93 (t, J=2.6 Hz, 1H), 1.86 (br s, 3H), 1.74 (s, 3H), 1.53 (s, 3H), 1.42 (app td, J=12.4, 10.3 Hz, 1H), 0.95 (t, J=7.8 Hz, 9H), 0.91 (s, 9H), 0.62 (q, J=8.0 Hz, 6H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=149.2, 137.0, 133.1, 109.1, 82.2, 77.1, 74.6, 69.8, 40.5, 38.1, 34.3, 33.7, 28.3, 26.1, 20.5, 18.3, 17.5, 7.3, 6.8, −3.7, −4.6. *Diastereoisomer **2***: ^{1}H NMR (250 MHz, $CDCl_3$): δ=4.73–4.72 (m, 2H), 4.21–4.17 (m, 1H), 2.65 (dd, J=16.4, 2.6 Hz, 1H), 2.49 (dd, J=16.4, 2.7 Hz, 1H), 2.17–2.07 (m, 1H), 2.02–1.95 (m, 2H), 1.92 (t, J=2.4 Hz, 1H), 1.89 (br s, 3H), 1.73 (s, 3H), 1.50 (s, 3H), 1.45–1.32 (m, 1H), 0.95 (t, J=7.8 Hz, 9H), 0.89 (s, 9H), 0.65–0.56 (m, 6H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=149.6, 136.7, 134.1, 109.0, 82.0, 74.4, 70.0, 40.0, 38.2, 35.5, 33.4, 27.0, 25.9, 20.7, 18.2, 17.8, 7.3, 6.7, −3.7, −4.8. MS (EI, 70 eV), m/z (%): 462 (1) [M^+], 423 (49) [$M^+-C_3H_3$], 291 (100), 265 (21), 197 (13), 159 (20), 115 (30), 87 (41), 73 (39), 59 (15); HRMS 423.3112 [423.3115 calcd for $C_{24}H_{47}O_2Si_2$ ($M^+-C_3H_3$)].

*4.3.2. (S)-3-(2,6-Dimethylbenzyl)-4-methylpent-4-enal (**18**)*

Method C using $PtCl_2$: to a solution of enyne **16** (80.0 mg, 0.17 mmol) in dry toluene (8.5 mL) was added platinum(II) chloride (12.6 mg, 0.04 mmol). The suspension was then purged under CO atmosphere and isopropanol (0.08 mL, 1.04 mmol) was added. The resulting mixture was stirred at 80 °C for 1 h. Then the reaction mixture was quenched with water, extracted with Et_2O, dried over Na_2SO_4, and concentrated under reduced pressure.

Method A using $AuCl_3$: to a solution of enyne **16** (50.0 mg, 0.11 mmol) in dry toluene (5.4 mL) was added a solution of pre-diluted gold(III) chloride (3.3 mg, 0.01 mmol) in MeCN (0.05 mL). Then, isopropanol (0.05 mL, 0.65 mmol) was added and the resulting mixture stirred at room temperature for 1 h. The reaction mixture was quenched with water, extracted with Et_2O, dried over Na_2SO_4, and concentrated under reduced pressure.

The residue was purified on a silica gel column (from 2% to 5% Et_2O/pentanes) to provide compound **18** (12.1 mg, 0.056 mmol, 51%) as a pale yellow oil. $[\alpha]_D^{20}$ +0.89 (c 0.63, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ=1.79 (s, 3H), 2.33 (ddd, J=15.8, 5.0, 1.5 Hz, 1H), 2.34 (br s, 6H), 2.54 (ddd, J=16.0, 10.1, 3.3 Hz, 1H), 2.73 (dd, J=13.9, 9.8 Hz, 1H), 2.83 (dd, J=13.9, 5.4 Hz, 1H), 2.95 (tt, J=10.0, 5.0 Hz, 1H), 4.80 (s, 1H), 4.83–4.84 (m, 1H), 7.00–7.05 (m, 3H), 9.46 (dd, J=3.1, 1.5 Hz, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=20.6, 20.2, 20.6, 32.3, 41.8, 46.0, 112.0, 126.4, 128.7, 136.7, 136.9, 147.0, 202.3; LRMS (EI): 216 (2) [M^+], 198 (1) [M^+-H_2O], 175 (1), 172 (5), 120 (11), 119 (100), 97 (11), 43 (12).

*4.3.3. 1-((3aS,4S,6S,7aR)-3a,4,5,6,7,7a-Hexahydro-4-(tert-butyl)dimethylsilyloxy-3a-methyl-6-(prop-1-en-2-yl)-1H-inden-7a-yl)ethanone (**17**)*

Obtained in 3% yield in the $AuCl_3$-catalyzed reaction of **16**. The relative configuration was assigned according to NOE experiments. ^{1}H NMR (500 MHz, $CDCl_3$): δ=5.91 (dd, J=5.8, 2.2 Hz, 1H), 5.56–5.55 (m, 1H), 4.66 (S, 1H), 4.63 (s, 1H), 4.00 (dd, J=11.5, 4.6 Hz, 1H), 2.91 (app dt, J=15.3, 1.8 Hz, 1H), 2.19 (dd, J=15.5, 2.8 Hz, 1H), 2.16 (s, 3H), 2.11–2.05 (m, 1H), 1.73–1.70 (m, 1H), 1.65 (s, 3H), 1.53–1.49 (m, 2H), 1.27–1.23 (m, 1H), 0.93 (s, 3H), 0.89 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ=211.6, 149.2, 137.9, 125.5, 109.1, 74.8, 62.3, 54.3, 42.3, 38.2, 38.0, 37.9, 28.8, 26.0, 20.9, 20.5, 18.2, −3.8, −4.6. MS (EI, 70 eV), m/z (%): 348 (19) [M^+], 291 (100) [M^+-t-Bu], 249 (14), 211 (15), 199 (23), 157 (40), 119 (50), 75 (100), 43 (51); HRMS 348.2482 [348.2485 calcd for $C_{21}H_{36}O_2Si$ (M^+)].

Acknowledgements

This project was supported by the Fonds der Chemischen Industrie (FCI) and the Deutsche Forschungsgemeinschaft (DFG). We thank Prof. Dr. Th. Bach and his group for helpful discussions and generous support.

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