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Gold- and Copper-Catalyzed Cycloisomerizations towards the Synthesis of Thujopsanone-Like Compounds

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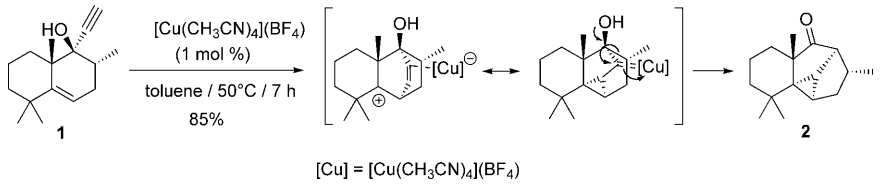
Abstract: In the search for a new access to thujopsanone related compounds by cycloisomerization reactions of unsaturated propargylic alcohols and acetates, we found several interesting reaction types and demonstrated the complementarity of Au, Pt, and Cu catalysts. Thus, 6-en-1-yn-3-ol **10a** underwent clean cyclization/ether formation to **16**, in particular using Au catalysts (76–98%) or a newly prepared Cu^{I}-triflimidate-catalyst (94%). The corresponding acetate **11a** underwent either the cycloisomerization with concomitant [1,2]-acyl shift (to **12**: 78% using $AuCl_3$) or an unprecedented rearrangement-cycloaddition leading to **20** (43% using [(*t*BuXPhos)$AuNTf_2$]), a strained fused tricyclic ring system containing a [2.2.0] bicyclic subunit.

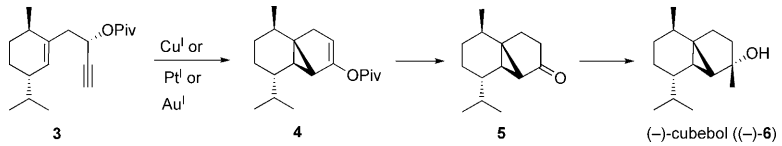
Keywords: copper · cycloisomerization · fragrances · gold · rearrangement

Introduction

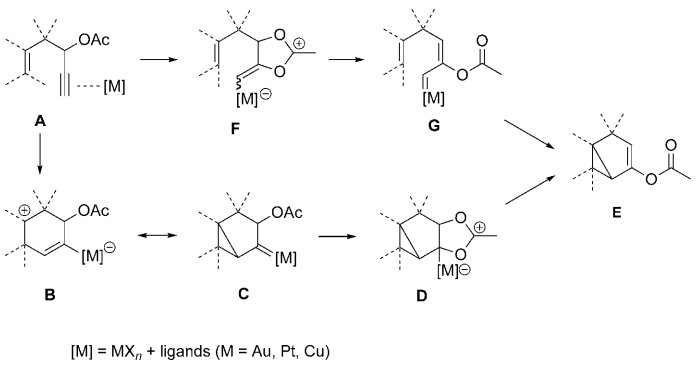
In 2006, we reported the copper-catalyzed cycloisomerization of 5-en-1-yn-3-ols (cyclopropanation/1,2-alkyl shift; Scheme 1)[1] and related enynol esters, as exemplified by the synthesis of (−)-cubebol (Scheme 2).[2] These cyclopropanation reactions,[3] leading selectively to complex polycyclic compounds, are generally catalyzed by platinum[4] or gold.[5] It has been demonstrated that esters of type **3** first undergo cyclization, then [1,2]-acyl migration, as the propargylic stereogenic center controls the stereochemical outcome of the cycloisomerization (Scheme 3; **A**→**B**→**C**). The alternative reaction pathway in which the [1,2]-acyl shift precedes the



Scheme 1. Cycloisomerization with concomitant 1,2-alkyl shift.[1]



Scheme 2. Cycloisomerization with concomitant 1,2-pivalate shift.[2]



Scheme 3. Cycloisomerizations of enynol esters with [1,2]-acyl shift: possible reaction pathways.

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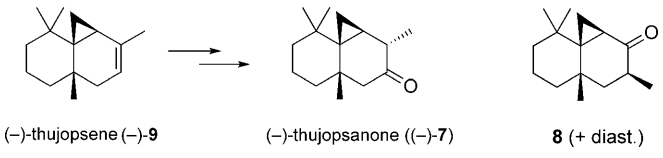
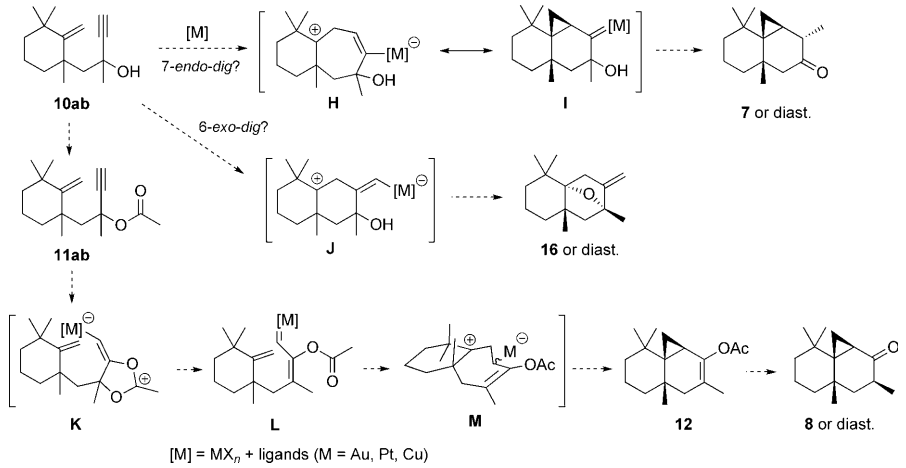
cyclization (Scheme 3; **A**→**F**→**G**) is only operative when the cyclization is slow enough to allow the [1,2]-acyl shift to occur first. This is the case in intermolecular reactions[5b,i] and medium-sized ring closures.[5c]

We recognized that these cycloisomerization reactions could be applied to the synthesis of sesquiterpenes such as thujopsanone **7** or the structurally related isomer **8**. Whereas (−)-**7** (used as a 1:1 mixture of diastereomers), prepared from (−)-thujopsene ((−)-**9**),[6] is an appreciated fragrance compound with woody, cedar-like, camphoraceous, ambery odor notes, **8** of undetermined configuration had only been prepared once in low yield and without any mention of the odor (Scheme 4).[7]



Scheme 4. Target compounds **7** and **8**.

Retrosynthetic analysis of thujopsanone **7** leads back to enynol **10**. A formal 7-*endo-dig* cycloisomerization reaction of **10** (via **H**/**I**) and subsequent [1,2]-methyl shift, would generate **7**. Of course, the 6-*exo-dig* reaction mode (via **J**) was expected to be kinetically favored, but as the cyclization step (to **H** or **J**) can be reversible, the outcome of the reaction may depend on the rate of the ensuing reactions (Scheme 5).

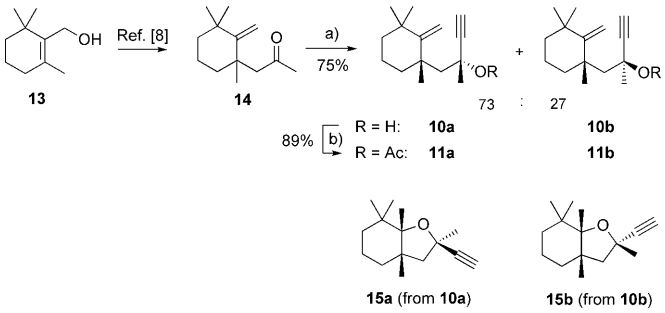


Scheme 5. Projected synthetic scheme: 7-*endo-dig* versus 6-*exo-dig* cyclization mode.

On the other hand, acetate **11** is ideally suited for cycloisomerization through an [1,2]-acyl shift, as the metal carbenoid **L** should guarantee the desired cyclopropanation to **12**.[5c]

Results and Discussion

The synthesis of the key precursors **10ab** and **11ab** was straightforward (Scheme 6). Ketone **14**, obtained by Claisen rearrangement of β-cyclogeraniol **13**,[8] was treated with bromomagnesium acetylide in the presence of $CeCl_3$ and

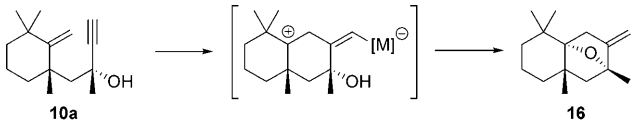


Scheme 6. Synthesis of **10ab** and **11ab**. a) $CeCl_3$ (1.2 equiv), LiCl (1.2 equiv), HCCMgBr (2.4 equiv), THF, RT. b) Ac_2O (2.5 equiv), NEt_3 (3.0 equiv), DMAP (0.3 equiv), CH_2Cl_2, RT.

LiCl.[9] The two diastereomers **10a** and **10b**, obtained in good yield in a 73:27 ratio, could be easily separated by chromatography. For the determination of their configurations, **10a** and **10b** were converted into the rigid bicyclic tetrahydrofurans **15a** and **15b** (cat. $BF_3{\cdot}Et_2O$, CH_2Cl_2, 5 min). The shown configurations are also consistent with the results discussed below.

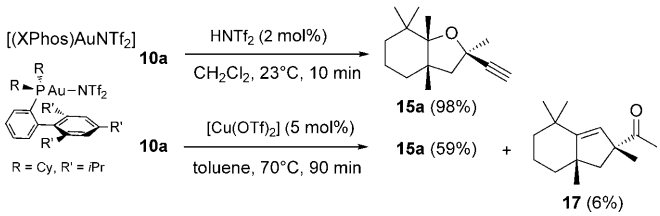
The major diastereomer **10a** was treated with a variety of Au, Pt, and Cu catalysts (Scheme 7). Unfortunately, the desired 7-*endo-dig* cyclization that should have afforded cyclopropane **7** was never observed. On the contrary, all catalysts induced the 6-*exo-dig* cycloisomerization, affording exclusively the bridged ether **16** (Scheme 7). The use of the more oxophilic $AuCl_3$ (entry 3) did not alter the cyclization mode.

Taking inspiration from Gagosz' gold triflimidate catalysts,[5n] we decided to test an analogous Cu catalyst. Interestingly, the highly electrophilic Cu^I-triflimidate of tentative structure $[Cu(CH_3CN)_4]NTf_2$, readily obtained from Cu_2O and $NHTf_2$ in CH_3CN (Scheme 7, entry 6),[10] showed dramatically increased reactivity as compared to $[Cu(CH_3CN)_4]BF_4$ (Scheme 7, entry 5) and afforded **16** after 15 minutes at room temperature in 94% yield. In a control experiment, the replacement of $[Cu(CH_3CN)_4]NTf_2$ (2 mol%) by the same amount of $HNTf_2$ led to **15a** in 98%. After completion of this study we tested the reactivity of $[(IPr)CuNTf_2]$.[11] Using $[(IPr)CuNTf_2]$ (5



Entry	Catalyst	mol%	Solvent	T[°C]	time [min]	Yield
1	[(PPh$_3$)AuCl] / AgBF$_4$	2	CH_2Cl_2	−10	120	87%
2	[(XPhos)AuNTf$_2$]	1	CH_2Cl_2	23	5	98%
3	$AuCl_3$	5	$(CH_2)_2Cl_2$	23	60	76%
4	$PtCl_2$	5	toluene	70	60	51%
5	[Cu(CH$_3$CN)$_4$]BF$_4$	5	toluene	70	60	49%
6	[Cu(CH$_3$CN)$_4$]NTf$_2$	2	CH_2Cl_2	23	15	94%

[Cu(CH$_3$CN)$_4$]NTf$_2$: from Cu_2O + 2 HNTf$_2$ in CH_3CN [M] = MX$_n$ + ligands (M = Au, Pt, Cu)



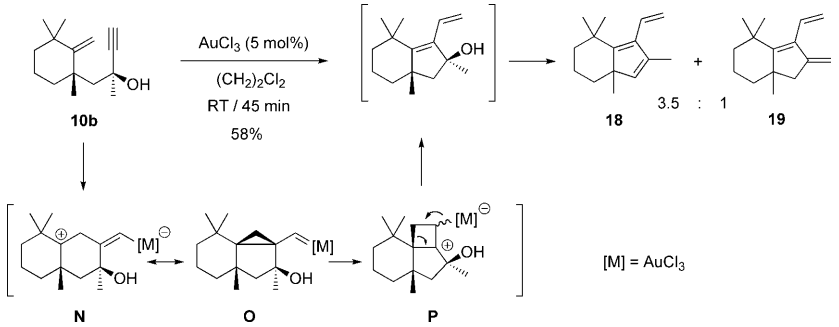
Scheme 7. Cycloisomerization of **10a**. Tf = triflyl.

mol%) in $(CH_2)_2Cl_2$ at 23°C for 15 minutes, **10a** produced **16** in 35% yield.

In sharp contrast to the Cu^I catalysts, in which the olefin reacts as the nucleophile, $[Cu(OTf)_2]$ activates the C=C bond for nucleophilic attack of the hydroxyl function towards the incipient carbocation, thus leading to the bridged ether **15a**. The formation of ketone **17** in 6% yield may be rationalized by an initial attack of the OH group onto the acetylene, followed by pentannulation.

The minor diastereomer **10b** was no better suited for cyclopropanation to give **7**. In the presence of $AuCl_3$, smooth formation of hydrocarbons **18** and **19** was exclusively observed (Scheme 8). Here, the intramolecular capture of the carbocationic species **N** by the OH group seems to be impeded for reasons of strain and the metathesis pathway (via **N**, **O** and **P**) is preferred.

We next focused on the synthesis of "regioiso-thujopsanone" **8** by cycloisomerization of propargylic acetate **11a** (Scheme 5 and Scheme 9).



Scheme 8. Metathesis of **10b**.

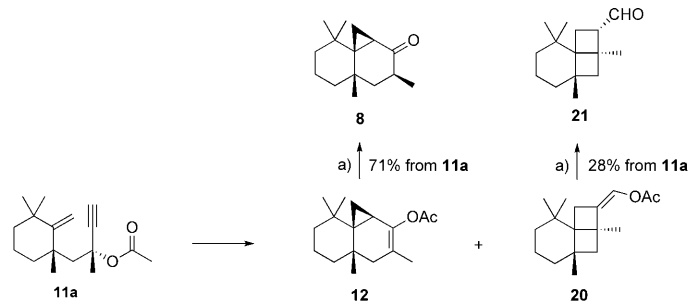
The desired cycloisomerization of **11a** to **12** was readily achieved with Au, Pt, or Cu catalysts (Scheme 9). Of all the catalysts tested, $AuCl_3$ proved to be the most efficient one in terms of selectivity and yield (Scheme 9, entries 1 and 2). [(Ph$_3$P)AuNTf$_2$], [(JohnPhos)AuNTf$_2$] and [(XPhos)-AuNTf$_2$][5n] were less selective and many unidentified side products were also formed (Scheme 9, entries 3–5). Much to our surprise, the structurally closely related [(*t*BuXPhos)-AuNTf$_2$] induced a completely different reaction to afford enol acetate **20** (Scheme 9, entry 6). Although the reaction appeared to be clean by GC (72% of **20** + 9% of **12**), pure **20** was isolated in only 43% yield, owing to its limited stability. We also tested the reactivity of a N-heterocyclic carbene bound gold catalyst ([(IPr)AuNTf$_2$]; Scheme 9, entry 7), but in addition to **12**, we observed the formation of nonvolatile products. $PtCl_2$ showed diminished reactivity. Using 5 mol% of catalyst, heating in dichloroethane at 70°C for 4 hours was necessary and afforded **12** in 43% yield (Scheme 9, entry 8). [Cu(CH$_3$CN)$_4$]BF$_4$ and [Cu-(CH$_3$CN)$_4$]NTf$_2$ promoted the reaction more efficiently and gave **12** in acceptable yield (Scheme 9, entries 9 and 10). Finally, [(IPr)CuNTf$_2$][11] led to **12** in good yield (Scheme 9, entry 11).

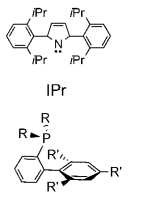
Using $AuCl_3$ (3 mol%) in dichloroethane at 0°C for 10 minutes, the minor diastereomer **11b** also gave **12**, although in slightly lower yield (66%).

The enol acetates **12** and **20** were readily transformed into the parent carbonyl compounds **8** and **21**, using K_2CO_3 in MeOH (Scheme 9). Ketone **8** was formed as a single diastereomer. Its configuration was determined by NOE experiments, and the spectral data are different from those reported earlier without defined configuration.[7] It possesses a pleasant, but faint woody, cedar-like, ambery odor. Aldehyde **21** was initially formed as a mixture of two epimers (58:42 after 5 min at 0°C) which underwent epimerization to afford **21** as the major isomer (91:9 after 20 min at RT). The aldehyde **21** is of limited stability. After chromatographic purification, a new unidentified by-product was formed, probably during concentration of the collected fractions. A pure sample of **21**, obtained after carefully repeated chromatography, showed an intense woody odor.

Whereas the formation of **12** can be rationalized by a [1,2]-acyl shift-cyclopropanation (via **K** and **L**), the formation of **20** may be the result of a non-concerted [2+2]-cycloaddition of an allenic species **Q** (Scheme 10).[12] Alternatively, a 6-*exo-dig* cyclization-[1,3]-acyl shift, (via **R**,**S**,**(U)** or via **R**,**T**,**U**) is also plausible.

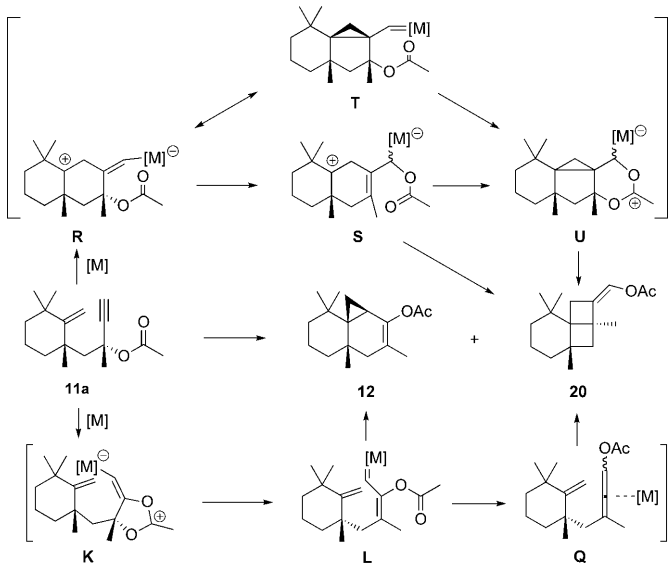
To support the hypothetic intermediacy of an allene of type **Q** during formation of **20**, we tried to prepare allene **22** from acetate **11a**. However, $AgBF_4$ (1 mol%) in 1,2-dimethoxyethane at RT gave no reaction, and upon heating at





Entry	Catalyst	mol%	Solvent	T [°C]	time [h]	Yield 12 % GC/isol.	Yield 20 % GC/isol.
1	$AuCl_3$	3	CH_2Cl_2	0	0.2	91/78	
2	$AuCl_3$	1	CH_2Cl_2	0	9	90/71[A]	
3	$[(Ph_3P)AuNTf_2]$	1	CH_2Cl_2	23	12	60/-	
4	[(JohnPhos)$AuNTf_2$]	1	CH_2Cl_2	23	24	41/-	
5	[(XPhos)$AuNTf_2$]	1	CH_2Cl_2	0	4	18/-	
6	[(tBuXPhos)$AuNTf_2$]	0.75	CH_2Cl_2	0	3	9/-	72/43
7	[(IPr)$AuNTf_2$]	3	CH_2Cl_2	23	3	50/-	
8	$PtCl_2$	5	$(CH_2)_2Cl_2$	78	4	56/43	
9	$[Cu(CH_3CN)_4]BF_4$	5	$(CH_2)_2Cl_2$	50	0.5	61/42	
10	$[Cu(CH_3CN)_4]NTf_2$	5	CH_2Cl_2	23	1	57/-	
11	[(IPr)$CuNTf_2$]	5	$(CH_2)_2Cl_2$	23	1	88/70	

Scheme 9. Cycloisomerization of **11a**. a) K_2CO_3 (1.5 equiv), MeOH, RT, 20 min. [A] Yield of **8** from **11a**.



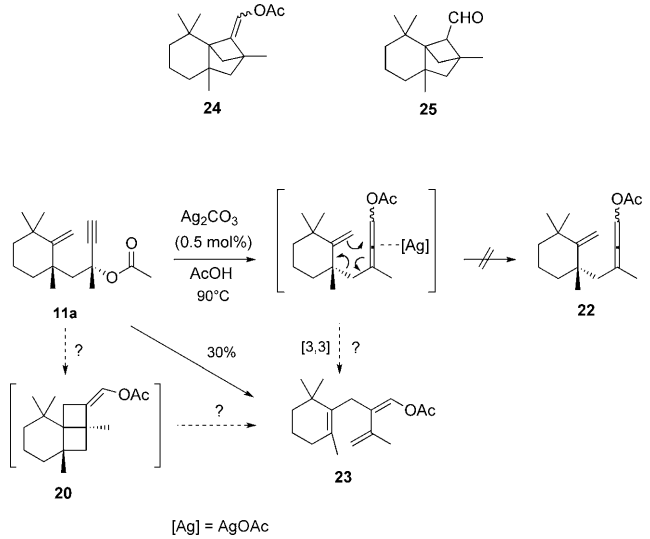
[M] = MX_n + ligands (M = Au, Pt, Cu, see Scheme 9)

Scheme 10. Mechanistic proposals for the formation of **12** and **20**.

60 °C nonvolatile products formed.[5e] Heating **11a** in AcOH in the presence of catalytic amounts of Ag_2CO_3[13] furnished exclusively the dienol acetate **23**, which formally is the Cope-rearrangement product of the expected allene **22**[14] (Scheme 11). **23** may also arise from **20** by retro-[2+2]-cycloaddition. Incidentally, **20** and **23** possess the same enol acetate configuration, and heating **20** in $(CH_2)_2Cl_2$ at 70 °C for 1 hour gave cleanly **23**, as shown by NMR analysis.

Finally, a pathway via **U** for the formation of **20** (Scheme 10) is favored for the following reasons. First, it would account for the (*Z*)-configuration of enol acetate **20**. Moreover, a side product obtained in approximately 10% yield together with **21** was identified as **25** of unknown configuration. Its formation may be explained by rearrangement of intermediate **U** (to give **24**) followed by hydrolysis. Therefore, the formation of both **20** and presumed enol acetate **24** would follow a common mechanism via **U**.[15]

In conclusion, we have found a direct access to tricyclic ketone **8** possessing the basic skeleton of thujopsanone by gold-, copper-, or platinum-catalyzed cycloisomerization of **11a**. In addition, we have discovered new reaction types and demonstrated that a variety of complex, highly functionalized compounds can be accessed selectively by the proper choice of catalyst (Scheme 12).



[Ag] = AgOAc

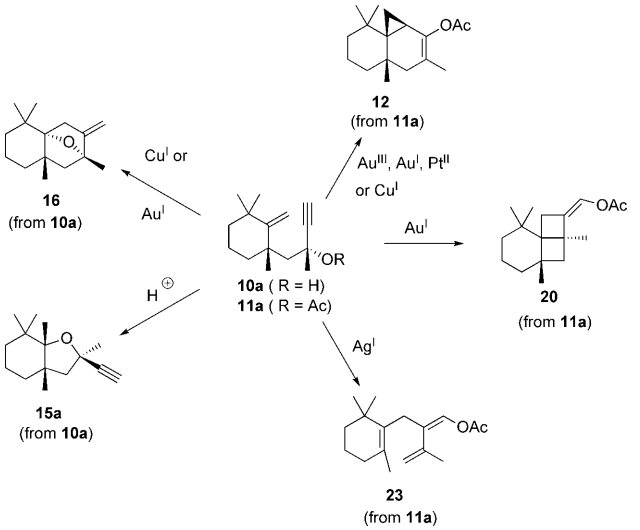
Scheme 11. Formation of **23** during attempted synthesis of allene **22**.

Experimental Section

General comments: Bulb-to-bulb distillation: Büchi GKR-51 glass-oven, b.p. correspond to the oven temp. TLC: silica gel F-254 plates (Merck); detection with EtOH/anisaldehyde/H_2SO_4 18:1:1. Column chromatography: silica gel 60 (Merck; 0.063–0.2 mm, 70–230 mesh, ASTM). GC: Varian instrument, model 3500; cap. columns: DB1 30 W (15 m × 0.319 mm), DB-WAX 15W (15 m × 0.32 mm); carrier gas He at 0.63 bar. ^{1}H- and ^{13}C NMR: Bruker AVANCE III 400 (400 MHz) and AVANCE I 500 (500 MHz). MS: Agilent MSD 5973N, electron energy 70 eV.

Preparation of the catalysts:

[Tetrakis(acetonitrile)]copper(I) bis(trifluoromethanesulfonyl)imidate ($[Cu(CH_3CN)_4]NTf_2$): $HNTf_2$ (0.5 M in CH_2Cl_2, 4 mL, 2 mmol) was added dropwise (not exothermic) to a mixture of copper(I) oxide (150 mg, 1 mmol) in acetonitrile (5 mL) (not completely soluble; fuchsia colored



Scheme 12. Summary of cycloisomerization reactions of **10a** and **11a**.

solution with a few crystals of Cu_2O). The resulting mixture, which turned from fuchsia to pale pink (containing trace amounts of solid Cu_2O) was stirred at RT for 15 min. The mixture was then stored in a closed vessel in the refrigerator for 5 days (no crystals observed). The mixture was filtered over Celite (to remove the remaining solid Cu_2O), and the resulting pale solution was evaporated under reduced pressure to give a pale pink–brown solid which was dried at reduced pressure and kept under nitrogen. The complex became oily after 30 min under N_2. Yield: 477 mg (94%). It was used as such, and its structure is not established.

[1,3-Bis(2,6-diisopropylphenyl)-2,3-dihydro-1*H*-imidazol-2-yl][1,1,1-trifluoro-*N*-(trifluoromethylsulfonyl)methylsulfonamido]gold ([(IPr)AuNTf$_2$]): $AgNTf_2$ (62 mg, 0.16 mmol) was added to a solution of [(IPr)AuCl] (100 mg, 0.16 mmol) in dry CH_2Cl_2 (3.2 mL). The resulting solution was stirred for 5 min and filtered over Celite. The pad of Celite was further washed twice with 3.2 mL of CH_2Cl_2 and the resulting solution was concentrated under vacuum to ca. 1.6 mL. Pentane (6.4 mL) was then added, which resulted in the immediate precipitation of a white solid. This solid was filtered and further washed with pentane (3× 3.2 mL), concentrated, and dried under high vacuum for 30 min. Yield: 111 mg (80%).

[P(*t*Bu)$_2$(*o*-biphenyl][bis(trifluoromethanesulfonyl)imidate]gold(I) ([(JohnPhos)AuNTf$_2$]): $AgNTf_2$ (62 mg, 0.16 mmol) was added to a solution of [(JohnPhos)AuCl] (85 mg, 0.16 mmol) in dry CH_2Cl_2 (4 mL), and the resulting solution was stirred for 15 min. The instantaneously formed AgCl precipitate was removed by filtration over Celite. The pad of Celite was further washed twice with 4 mL of CH_2Cl_2 and the resulting pale solution was evaporated under reduced pressure and dried under high vacuum to afford the title compound as a white solid. Yield: 101 mg (81%).

[(*t*BuXPhos)AuCl]: [$AuCl(SMe_2)$] (128 mg, 0.375 mmol) and the phosphine *t*Bu-XPhos (163 mg, 0.375 mmol) were weighed (in air) and placed under N_2. CH_2Cl_2 (10 mL) was added, which resulted in the dissolution of the starting material and the formation of a pale yellow solution. After stirring at RT for 45 min the solution was concentrated to 2 mL and hexane was added (10 mL). The complex was precipitated and filtered, washed with hexane, and dried under vacuum. Yield: 151 mg of a white solid (151 mg; 61%).

[Bis(trifluoromethanesulfonyl)imidate](*t*BuXphos)gold(I) ([(*t*BuXPhos)AuNTf$_2$]): The above [(*t*BuXPhos)AuCl] complex (151 mg, 0.230 mmol) was dissolved in CH_2Cl_2 (6 mL), and $AgNTf_2$ (90 mg, 0.23 mmol) was added, thus resulting in the instantaneous precipitation of AgCl. The mixture was stirred for an additional 15 min. After filtration over Celite the pale solution was evaporated and the white complex dried under vacuum (131 mg; 87%).

(*S*,*R*)-2-Methyl-1-[(*R*,*S*)-1,3,3-trimethyl-2-methylenecyclohexyl]but-3-yn-2-ol (10a) and (*S*,*R*)-2-methyl-1-[(*S*,*R*)-1,3,3-trimethyl-2-methylenecyclohexyl]but-3-yn-2-ol (10b): LiCl (2.64 g, 62.3 mmol) was added at RT to a solution of $CeCl_3$ (15.35 g, 62.3 mmol; dried under reduced pressure at 160°C in a bulb to bulb distillation apparatus for 2 h) in THF (54 mL) under nitrogen. The suspension was stirred for 50 min at RT (pale yellow color). Ethynylmagnesium bromide (125 mL; 0.5 M in THF) was then added in one portion (exothermic) and the resulting mixture was stirred 1 h at RT (solution became brown). 1-(1,3,3-Trimethyl-2-methylenecyclohexyl)propan-2-one (10.09 g, 51.9 mmol) in THF (80 mL) was then added dropwise. After stirring for 1 h, more ethynylmagnesium bromide (125 mL; 0.5 M in THF) was added and stirring continued for 90 min. The mixture was poured into 5% aqueous HCl/ice and extracted with Et_2O (3×150 mL). The combined organic layers were washed with water, saturated aqueous $NaHCO_3$ solution, and a saturated aqueous solution of NaCl, dried over Na_2SO_4, filtered and concentrated to afford 10.46 g of a yellow oil. Bulb to bulb distillation at 130°C and 3 mbar, followed by flash chromatography on SiO_2 (pentane/Et_2O=95:5) gave successively **10a** (6.12 g, 54%) and **10b** (2.5 g, 22%). **10a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.15 (s, 3H), 1.21 (s, 3H), 1.27–1.40 (m, 2H), 1.48 (s, 3H), 1.50 (s, 3H), 1.49–1.60 (m, 2H), 1.63–1.82 (m, 2H), 1.71 (d(AB), J_{AB}= 14.8 Hz, 1H), 2.34 (d(AB), J_{AB}=14.8 Hz, 1H), 2.50 (s, 1H), 5.22 (s, 1H), 5.34 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=18.0 (t), 30.5 (q), 31.2 (q), 32.9 (q), 33.9 (q), 36.8 (s), 40.0 (s), 40.6 (t), 42.2 (t), 51.0 (t), 66.9 (s), 72.1 (d), 89.7 (s), 110.9 (t), 164.2 ppm (s); MS (EI): *m*/*z* (%): 220 (4) $[M]^+$, 205 (11), 202 (9), 187 (50), 159 (51), 133 (53), 121 (51), 105 (51), 95 (100), 91 (57), 81 (65), 69 (76), 55 (42), 43 (65). **10b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.15 (s, 3H), 1.19 (s. 3H), 1.29 (s, 3H), 1.35–1.44 (m, 2H), 1.47–1.76 (m, 3H), 1.55 (s, 3H), 1.94 (d(AB), J_{AB}=15.0 Hz, 1H), 2.24 (d(AB), J_{AB}=15.0 Hz, 1H), 2.19–2.28 (m, 1H), 2.48 (s, 1H), 5.07 (s, 1H), 5.12 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=18.2 (t), 31.9 (q), 32.0 (q), 33.1 (q), 34.3 (q), 36.4 (s), 37.8 (t), 39.7 (s), 40.0 (t), 52.1 (t), 67.4 (s), 72.2 (d), 89.3 (s), 109.1 (t), 164.0 ppm (s); MS (EI): *m*/*z* (%): 220 (2) $[M]^+$, 205 (9), 202 (12), 187 (51), 95 (100), 91 (54), 81 (61), 69 (73), 43 (63).

(*S*,*R*)-2-Methyl-1-[(*R*,*S*)-1,3,3-trimethyl-2-methylenecyclohexyl]but-3-yn-2-yl acetate (11a): Basic conditions: Et_3N (7.6 mL, 54.5 mmol), Ac_2O (4.3 mL, 45.4 mmol), and a catalytic amount of 4-dimethylaminopyridine (DMAP; 665 mg, 5.45 mmol) were added to a solution of **10a** (4.00 g, 18.15 mmol) in CH_2Cl_2 (20 mL), and the resulting mixture was stirred at RT over night. The mixture was poured into 5% HCl solution and extracted with Et_2O (2×30 mL). The combined organic layers were washed with water, a saturated aqueous $NaHCO_3$ solution, a saturated aqueous solution of NaCl, dried (Na_2SO_4), filtered, and concentrated to furnish a pale yellow oil (5.07 g). Flash chromatography on SiO_2 (pentane/Et_2O= 95:5) afforded **11a** as a pale yellow oil (4.38 g, 89%). Acidic conditions: A catalytic amount of *p*-TsOH (30 mg, 0.153 mmol) was added to a solution of **10a** (845 mg, 3.84 mmol) in Ac_2O (9 mL, 101.4 mmol), and the resulting mixture was stirred at RT overnight. The mixture was washed with water, a saturated aqueous $NaHCO_3$ solution, water, and a saturated aqueous solution of NaCl, dried (Na_2SO_4), filtered, and concentrated to afford **11a** as a yellow oil (10.06 g). Yield after chromatography: (9.22 g; 92%). **11a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.13 (s, 3H), 1.17 (s, 3H), 1.26–1.40 (m, 2H), 1.32 (s, 3H), 1.45–1.57 (m, 2H), 1.68–1.81 (m, 1H), 1.74 (s, 3H), 2.01 (s, 3H), 2.10 (mc, 1H), 2.19 (d(AB), J_{AB}=15.2 Hz, 1H), 2.26 (d(AB), J_{AB}=15.2 Hz, 1H), 2.61 (s, 1H), 4.97 (s, 1H), 5.03 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=18.5 (t), 22.2 (q), 29.3 (q), 30.3 (q), 31.3 (q), 33.2 (q), 36.4 (s), 38.8 (t), 40.0 (s), 40.7 (t), 50.2 (t), 74.5 (s), 74.6 (d), 84.8 (s), 108.8 (t), 162.9 (s), 169.2 ppm (s); MS (EI): *m*/*z* (%): 262 (2) $[M]^+$, 220 (34), 187 (75), 137 (64), 123 (75), 95 (100), 81 (62), 43 (86).

Compounds 15a and 17: [$Cu(OTf)_2$] (18.5 mg; 0.05 mmol) was added to **10a** in toluene (5 mL). The mixture was heated to 70°C for 90 min and cooled to RT. The dark grey mixture was filtered through a short pad of SiO_2 (4 g) using CH_2Cl_2. The solvents were removed under vacuum to give an orange colored oil (265 mg). Flash chromatography on SiO_2 (cy-

clohexane/AcOEt = 98:2) afforded successively **15a** (130 mg, 59%) and **17** (14 mg, 6%). Likewise, $BF_3(OEt)_2$ also afforded **15a. 15a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (s, 3H), 1.01 (s, 3H), 1.09 (s. 3H), 1.10–1.14 (m, 1H), 1.28–1.38 (m, 2H), 1.31 (s, 3H), 1.40–1.57 (m, 1H), 1.61 (s, 3H), 1.58–1.73 (m, 2H), 1.81 (d(AB), J_{AB} = 12.9 Hz, 1H), 2.36 (s, 1H), 2.42 ppm (d(AB), J_{AB} = 12.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5 (q), 18.9 (t), 22.9 (q), 25.0 (q), 27.4 (q), 31.1 (q), 36.5 (s), 37.5 (t), 38.0 (t), 44.5 (s), 56.0 (t), 68.9 (d), 70.4 (s), 89.1 (s), 92.2 ppm (s); MS (EI): *m/z* (%): 220 (0.2) $[M]^+$, 205 (19), 136 (100), 96 (14), 85 (38), 69 (16), 55 (16), 43 (28).

Compound 15b: $BF_3(OEt)_2$ (29 mg; 0.20 mmol) was added to a stirred solution of **10b** (100 mg; 0.45 mmol) in toluene (3 mL). After 2 min the red solution was quenched with ice and a solution of saturated aqueous $NaHCO_3$. Extraction (Et_2O) in the usual manner, concentration, and bulb-to-bulb distillation at 100°C and 0.1 mbar afforded **15b** (86 mg; 86%). **15b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (s, 3H), 0.99 (s, 3H), 1.07 (s, 3H), 1.09 (s, 3H), 1.11 (mc, 1H), 1.30 (mc, 1H), 1.35–1.44 (m, 1H), 1.51 (mc, 1H), 1.56 (s, 3H), 1.74 (ddd, *J* = 13.1/13.1/3.1 Hz, 1H), 2.04 (d(AB), J_{AB} = 12.7 Hz, 1H), 2.09 (d(AB), J_{AB} = 12.7 Hz, 1H), 2.39 (ddd, *J* = 13.6/13.6/4.06 Hz, 1H), 2.45 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.6 (t), 19.5 (q), 22.8 (q), 24.9 (q), 27.3 (q), 32.5 (q), 36.2 (t), 36.6 (s), 37.5 (t), 45.1 (s), 55.8 (t), 70.4 (d), 71.3 (s), 88.5 (s), 90.2 ppm (s); MS (EI): *m/z* (%): 205 (17), 136 (100), 121 (16), 91 (18), 85 (40), 55 (16), 43 (32), 41 (24). **17**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.11 (s, 3H), 1.12 (s, 3H), 1.15–1.23 (m, 2H), 1.25 (s, 3H), 1.29 (s, 3H), 1.44–1.53 (m, 2H), 1.61 (d(AB), J_{AB} = 13.3 Hz, 1H), 1.68–1.82 (m, 2H), 2.12 (s, 3H), 2.13 (d(AB), J_{AB} = 13.3 Hz, 1H), 5.26 ppm (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.5 (t), 24.5 (q), 25.6 (q), 27.2 (q), 28.7 (q), 31.4 (q), 34.3 (s), 41.5 (t), 42.8 (t), 46.8 (s), 52.8 (t), 58.9 (s), 124.3 (d), 158.6 (s), 212.9 ppm (s); MS (EI): *m/z* (%): 177 (100), 121 (30), 107 (23), 105 (10), 95 (16), 91 (15), 69 (17), 43 (13).

Compound 16 by Cu-catalysis: $[Cu(CH_3CN)_4]NTf_2$ (2 mol%, 5.1 mg, 0.01 mmol) was added to a solution of **10a** (110 mg, 1.00 mmol) in CH_2Cl_2 (1 mL), and the resulting mixture was stirred at RT for 15 min, filtered on a pad of SiO_2 using CH_2Cl_2 and concentrated to afford **16** (103 mg; 94%) as a pale yellow oil.

Compound 16 by Au-catalysis: [(XPhos)AuNTf$_2$] (1 mol%, 9.5 mg, 0.01 mmol) was added to a solution of **10a** (220 mg, 1.00 mmol) in CH_2Cl_2 (1 mL), and the resulting mixture was stirred at RT for 5 min, filtered on a pad of SiO_2 using CH_2Cl_2, and concentrated to afford **16** (216 mg; 98%) as a pale yellow oil. **16**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (s, 3H), 1.01 (s, 3H), 1.17 (s, *J* = 0.5 Hz, 3H), 1.23–1.31 (m, 1H), 1.34–1.45 (m, 3H), 1.43 (s, 3H), 1.49–1.72 (m, 4H), 2.41–2.58 (m, 2H), 4.62 (t, *J* = 2.0 Hz, 1H), 4.69 ppm (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.5 (q), 19.2 (t), 23.9 (q), 24.8 (q), 27.0 (q), 34.2 (s), 35.2 (t), 38.3 (t), 40.9 (t), 43.7 (s), 56.4 (t), 84.5 (s), 90.2 (s), 98.4 (t), 155.9 ppm (s); MS (EI): *m/z* (%):220 (81) $[M]^+$, 205 (54), 177 (47), 147 (83), 137 (100), 123 (61), 107 (50), 95 (47), 69 (37), 43 (70).

Compounds 18/19: A solution of **10b** (440 mg, 2.00 mmol) in $(CH_2)_2Cl_2$ (20 mL) was treated with $AuCl_3$ (35.0 mg, 0.115 mmol). After 20 min, the mixture was quenched with a solution of saturated aqueous $NaHCO_3$. Extraction (Et_2O) in the usual manner, concentration (413 mg), and bulb-to-bulb distillation at 100°C and 0.1 mbar afforded a mixture of **18** and **19** (290 mg; 63+18% by GC; 58%). **18/19** of higher purity (70+18%) was obtained by flash chromatography on SiO_2 (cyclohexane/AcOEt = 95:5). **18**: (characteristic signals): ^{1}H NMR (400 MHz, $CDCl_3$): δ of Me-signals: δ = 1.13 (s), 1.19 (s), 1.28 (s), 1.86 ppm (s), olefinic CH: 5.11 (d,d, *J* = 18.0/2.1 Hz, 1H), 5.21 (d,d, *J* = 11.0/2.1 Hz, 1H), 5.79 (br s, 1H), 6.67 ppm (d,d, *J* = 18.0/11.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.4 (q), 19.3 (t), 22.3 (q), 26.4 (q), 33.8 (q), 35.5 (t), 36.7 (s), 43.8 (t), 52.2 (s), 117.0 (t), 134.2 (d), 134.4 (s), 137.5 (s), 141.0 (d), 155.8 ppm (s); MS (EI): *m/z* (%): 202 (29) $[M]^+$, 187 (100), 159 (14), 145 (19), 133 (28), 115 (13), 105 (16), 91 (13), 77 (7).

Compound 12: A solution of **11a** (100 mg, 0.377 mmol) in CH_2Cl_2 (2 mL), was cooled at 0°C and treated with $AuCl_3$ (3.43 mg, 0.011 mmol; weighted in the glove box). The color turned immediately to purple. After 10 min, the mixture was filtered through a cartridge of SiO_2 (4 g) and concentrated (90 mg). Bulb-to-bulb distillation at 130°C and 0.06 mbar afforded **12** (83 mg; 93% pure; 78%). Likewise, a solution of **11a** (655 mg, 2.49 mmol) in CH_2Cl_2 (3 mL), was cooled at 0°C and treated with $AuCl_3$ (7.57 mg, 0.025 mmol; weighted in the glove box). The color turned immediately to purple. After 9 h, the mixture was filtered through a cartridge of SiO_2 (4 g) and concentrated (640 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.58 (s, 3H), 0.74 (dd, *J* = 8.8/5.0 Hz, 1H), 0.83 (t, *J* = 5.0 Hz, 1H), 1.09 (s, 3H), 1.14 (s, 3H), 1.14–1.19 (m, 1H), 1.28–1.59 (m, 6H), 1.46 (d, *J* = 1.3 Hz, 3H), 1.78 (mc, 1H), 1.97 (mc, 1H), 2.18 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.6 (t), 16.0 (q), 19.4 (t), 20.4 (d), 20.8 (q), 26.4 (q), 27.8 (q), 29.0 (q), 32.6 (s), 33.6 (s), 35.0 (s), 36.4 (t), 40.0 (t), 45.8 (t), 112.2 (s), 141.7 (s), 169.2 ppm (s); MS: *m/z* (%): 262 (9) $[M]^+$, 220 (100), 205 (17), 149 (19), 135 (60), 123 (57), 121 (34), 109 (30), 69 (20), 43 (25).

Compound 8: The above crude product **12** (640 mg, max.2.44 mmol) was dissolved in methanol (7 mL), treated with K_2CO_3 (506 mg, 3.66 mmol) at RT, and stirred for 20 min. The mixture was poured into water and extracted with Et_2O (3×20 mL). The combined organic phases were washed with a solution of saturated aqueous NaCl, dried over Na_2SO_4, filtered, and concentrated to afford **8** (447 mg ; 87% pure; 71% from **11a**). Pure **8** (>97%) was obtained by flash chromatography on SiO_2 (cyclohexane/AcOEt = 95:5). M.p. 64–66°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.60 (s, 3H), 0.95 (ddd, *J* = 10.8/5.1/0.9 Hz, 1H), 1.04 (d, *J* = 6.9 Hz, 3H), 1.11 (s, 3H), 1.14 (ddd, *J* = 5.1/5.1/0.5 Hz, 1H), 1.20 (d, *J* = 0.6 Hz, 3H), 1.26 (dd, *J* = 14.7/6.3 Hz, 1H), 1.27–1.31 (m, 1H), 1.31–1.37 (m, 1H), 1.40 (dd, *J* = 14.7/13.1 Hz, 1H), 1.50 (mc, 1H), 1.56 (mc, 1H), 1.67 (td, *J* = 13.1/3.9 Hz, 1H), 1.85 (mc, 1H), 1.95 (dd, *J* = 10.8/5.1 Hz, 1H), 2.25 ppm (ddq, *J* = 13.1/6.9/6.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.0 (t), 15.8 (q), 18.8 (t), 27.2 (q), 28.4 (q), 28.6 (q), 32.0 (d), 33.3 (s), 33.6 (s), 36.0 (t), 37.1 (d), 38.5 (s), 40.2 (t), 44.0 (t), 212.2 ppm (s); MS (EI): *m/z* (%): 220 (15) $[M]^+$, 205 (9), 178 (14), 137 (100), 123 (17), 107 (17), 93 (18), 79 (13), 55 (12).

Compound 20: [(*t*BuXPhos)AuNTf$_2$] (25 mg, 0.0285 mmol) was added to a solution of **11a** (1.50 g, 5.72 mmol) in CH_2Cl_2 (5.7 mL) under nitrogen at 0°C, and the resulting mixture was stirred at 0°C for 45 min. As GC showed incomplete conversion, more [(*t*BuXPhos)AuNTf$_2$] (13 mg, 0.014 mmol) was added and the mixture (which turned from yellow to dark orange) was stirred for 2 h at 0°C. Filtration over a SiO_2 pad impregnated with CH_2Cl_2 and concentration afforded a pale yellow oil. Flash chromatography on SiO_2 (cyclohexane/Et_2O = 95:5) gave **20** (660 mg, 43%) of limited stability. In another experiment, the reaction of **11a** (200 mg) went to completion with only 0.5 mol% of [(*t*BuXPhos)AuNTf$_2$] (1 h; 0°C). Yield of **20** after filtration (SiO_2/CH_2Cl_2): 168 mg (67% by GC). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.70 (s, 3H), 0.93 (s, 3H), 1.02 (s, 3H), 1.33–1.49 (m, 4H), 1.53 (s, 3H), 1.54–1.65 (m, 1H), 1.66 (d(AB), J_{AB} = 11.6 Hz, 1H), 1.77–1.84 (m, 1H), 2.04 (d(AB), J_{AB} = 11.6 Hz, 1H), 2.08 (s, 3H), 2.54 (dd, *J* = 16.2/2.0 Hz, 1H), 2.78 (dd, *J* = 16.2/2.0 Hz, 1H), 6.66 ppm (t, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.3 (t), 20.8 (q), 21.0 (q), 22.1 (q), 24.1 (q), 25.7 (q), 27.6 (t), 33.7 (s), 37.5 (s), 39.9 (t), 41.1 (t), 47.7 (t), 48.5 (s), 55.0 (s), 123.9 (d), 132.7 (s), 168.3 ppm(s); MS (EI): *m/z* (%): 262 (6) $[M]^+$, 220 (100), 205 (22), 149 (36), 135 (48), 123 (65), 109 (86), 91 (28), 43 (62).

Compound 21: Repetition of the above conditions starting from **11a** (262 mg; 1.00 mmol) afforded crude **20** (210 mg), which was dissolved in methanol (2 mL), treated with K_2CO_3 (166 mg, 1.20 mmol) at RT, and stirred for 20 min. The mixture was poured into aqueous 5% HCl and extracted with Et_2O (3×10 mL). The combined organic phases were washed with a solution of saturated aqueous NaCl, dried over Na_2SO_4, filtered, and concentrated to afford the title compound as a pale yellow oil. Flash chromatography on SiO_2 (cyclohexane/Et_2O = 90:10) furnished **21** (85 mg; 3 isomers (by MS)): 4%; 59%; 9% by increasing retention times on a DB-1 column; 28% from **11a**). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.68 (s, 3H), 0.98 (d, *J* = 0.8 Hz, 3H), 1.01 (s, 3H), 1.34 (dd, *J* = 12.0/1.0 Hz, 1H), 1.36–1.46 (m, 4H), 1.54 (s, 3H), 1.56–1.65 (m, 1H), 1.70–1.82 (m, 1H), 1.92 (dd, *J* = 13.0/9.9 Hz, 1H), 1.99 (d, 12 Hz, 1H), 2.56 (dd, *J* = 13.0/9.0 Hz, 1H), 2.86 (ddt, *J* = 9.9/9.0/1.0 Hz, 1H), 9.74 ppm (d, *J* = 1.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.2 (t), 21.2 (q), 22.2 (t), 23.4 (q), 24.7 (q), 26.1 (q), 33.5 (s), 39.2 (s), 39.6 (t), 40.4 (t), 42.3 (t), 45.8 (s), 53.8 (d), 54.5 (s), 204.0 ppm (d) ; MS (EI): *m/z* (%): 220 (2)

$[M]^+$, 163 (13), 137 (100), 121 (27), 109 (30), 95 (83), 91 (29), 81 (55), 69 (27), 41 (29).

Compound 23: A mixture of Ag_2CO_3 (14 mg; 0.05 mmol), AcOH (0.58 mL; 0.59 g; 9.90 mmol), and **11a** (500 mg; 1.87 mmol) was heated at 90°C for 8 h. The cooled mixture was quenched with ice and a solution of saturated aqueous $NaHCO_3$. Extraction (Et_2O) in the usual manner, concentration (430 mg), and flash chromatography on SiO_2 (cyclohexane/AcOEt = 98:2) gave **23** (149 mg, 30%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (s, 6H), 1.45–1.51 (m, 2H), 1.55 (s, 3H), 1.57–1.66 (m, 2H), 1.97 (dd, J = 1.6/0.8 Hz, 3H), 1.99 (br t, J = 6.6 Hz, 2H), 2.10 (s, 3H), 2.81 (br s, 2H), 4.92 (mc, 1H), 5.00 (mc, 1H), 6.70 ppm (t, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4 (t), 20.3 (q), 20.9 (q), 22.7 (q), 28.4 (q), 31.4 (t), 32.4 (t), 34.9 (s), 39.6 (t), 113.7 (t), 124.3 (s), 130.7 (s), 132.3 (d), 132.6 (s), 142.6 (s), 168.0 ppm (s); MS (EI): m/z (%): 262 (5) $[M]^+$, 220 (86), 205 (19), 149 (37), 135 (50), 123 (71), 109 (95), 91 (34), 81 (29), 69 (29), 55 (27), 43 (100).

Compound 25: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (s, 3H), 1.05 (s, 3H), 1.10–1.18 (m, 2H), 1.18 (s, 3H), 1.21 (s, 3H), 1.32–1.40 (m, 3H), 1.41–1.52 (m, 2H), 1.53–1.63 (m, 1H), 1.64–1.80 (m, 1H), 2.03 (dd, J = 11.6/2.0 Hz, 1H), 2.09–2.11 (m, 1H), 9.95 ppm (d, J = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.8 (q), 19.7 (t), 23.7 (q), 26.6 (q), 31.7 (q), 33.6 (s), 36.9 (t), 37.5 (t), 40.1 (t), 41.2 (s), 43.1 (s), 48.4 (t), 64.0 (d), 70.7 (s), 204.4 ppm (d) ; MS (EI): m/z (%): 220 (7) $[M]^+$, 205 (100), 177(15), 165 (23), 149 (23), 135 (28), 121 (34), 109 (47), 107 (37), 95 (40), 91 (26), 81 (21), 69 (25), 55 (18), 41 (24).

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[1] C. Fehr, I. Farris, H. Sommer, *Org. Lett.* **2006**, *8*, 1839; C. Fehr, I. Magpantay, J. Arpagaus, X. Marquet, M. Vuagnoux, *Angew. Chem.* **2009**, *121*, 7357; *Angew. Chem. Int. Ed.* **2009**, *48*, 7221.

[2] a) C. Fehr, J. Galindo, *Angew. Chem.* **2006**, *118*, 2967; *Angew. Chem. Int. Ed.* **2006**, *45*, 2901; b) C. Fehr, B. Winter, I. Magpantay, *Chem. Eur. J.* **2009**, *15*, 9773; c) For a closely related synthesis, see: A. Fürstner, P. Hannen, *Chem. Eur. J.* **2006**, *12*, 3006.

[3] Recent reviews on enyne cycloisomerizations: a) S. P. Nolan, *Acc. Chem. Res.* **2011**, *44*, 91; b) A. M. Echavarren, E. Jiménez-Nunez, *Top. Catal.* **2010**, *53*, 924; c) A. Fürstner, *Chem. Soc. Rev.* **2009**, *38*, 3208; d) H. C. Shen, *Tetrahedron* **2008**, *64*, 7847; e) E. Jiménez-Nunez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326; f) V. Michelet, P. Y. Toullec, J.-P. Genêt, *Angew. Chem.* **2008**, *120*, 4338; *Angew. Chem. Int. Ed.* **2008**, *47*, 4268; g) B. Crone, S. F. Kirsch, *Chem. Eur. J.* **2008**, *14*, 3514; h) A. Fürstner, P. W. Davies, *Angew. Chem.* **2007**, *119*, 3478; *Angew. Chem. Int. Ed.* **2007**, *46*, 3410; i) E. Jiménez-Nunez, A. M. Echavarren, *Chem. Commun.* **2007**, 333; j) D. J. Gorin, D. Toste, *Nature* **2007**, *446*, 395; k) N. Marion, S. P. Nolan, *Angew. Chem.* **2007**, *119*, 2806; *Angew. Chem. Int. Ed.* **2007**, *46*, 2750; l) J. Marco-Contelles, E. Soriano, *Chem. Eur. J.* **2007**, *13*, 1350; m) L. Zhang, J. Sun, S. A. Kozmin, *Adv. Synth. Catal.* **2006**, *348*, 2271; n) C. Nieto-Oberhuber, S. Lopez, E. Jiménez-Nunez, A. M. Echavarren, *Chem. Eur. J.* **2006**, *12*, 5916; o) S. Ma, S. Yu, Z. Gu, *Angew. Chem.* **2006**, *118*, 206; *Angew. Chem. Int. Ed.* **2006**, *45*, 200; p) C. Bruneau, *Angew. Chem.* **2005**, *117*, 2380; *Angew. Chem. Int. Ed.* **2005**, *44*, 2328; q) A. M. Echavarren, C. Nevado, *Chem. Soc. Rev.* **2004**, *33*, 431; r) C. Aubert, O. Buisine, M. Malacria, *Chem. Rev.* **2002**, *102*, 813.

[4] C. Blaszykowski, Y. Harrak, C. Brancour, K. Nakama, A.- L. Dhimane, L. Fensterbank, M. Malacria, *Synthesis* **2007**, 2037; E. Soriano, J. Marco-Contelles, *J. Org. Chem.* **2007**, *72*, 2651; J. Barluenga, L. Riesgo, R. Vicente, L. A. Lopez, M. Tomas, *J. Am. Chem. Soc.* **2007**, *129*, 7772 (Pt and Cu); S. Anjum, J. Marco-Contelles, *Tetrahedron* **2005**, *61*, 4793; E. Soriano, P. Ballesteros, J. Marco-Contelles, *Organometallics* **2005**, *24*, 3182; E. Soriano, J. Marco-Contelles, *J. Org. Chem.* **2005**, *70*, 9345; C. Blaszykowski, Y. Harrak, M.-H. Gonçalves, J.- M. Cloarec, A.- L. Dhimane, L. Fensterbank, M. Malacria, *Org. Lett.* **2004**, *6*, 3771; Y. Harrak, C. Blaszykowski, M. Bernard, K. Cariou, E. Mainetti, V. Mouriès, A.- L. Dhimane, L. Fensterbank, M. Malacria, *J. Am. Chem. Soc.* **2004**, *126*, 8656; V. Mamane, T. Gress, H. Krause, A. Fürstner, *J. Am. Chem. Soc.* **2004**, *126*, 8654.

[5] a) N. Marion, G. Lemière, A. Correa, C. Costabile, R. S. Ramon, X. Moreau, P. de Frémont, R. Dahmane, A. Hours, D. Lesage, J.-C. Tabet, J.-P. Goddard, V. Gandon, L. Cavallo, L. Fensterbank, M. Malacria, S. P. Nolan, *Chem. Eur. J.* **2009**, *15*, 3243; b) I. D. G. Watson, S. Ritter, F. D. Toste, *J. Am. Chem. Soc.* **2009**, *131*, 2056; c) X. Moreau, J.-P. Goddard, M. Bernard, G. Lemière, J. M. López-Romero, E. Mainetti, N. Marion, V. Mouriès, S. Thorimbert, L. Fensterbank, M. Malacria, *Adv. Synth. Catal.* **2008**, *350*, 43 (Au and Pt); d) A. Fürstner, A. Schlecker, *Chem. Eur. J.* **2008**, *14*, 9181; e) A. Fürstner, P. Hannen, *Chem. Eur. J.* **2006**, *12*, 3006; f) G. Lemière, V. Gandon, K. Cariou, T. Fukuyama, A.- L. Dhimane, L. Fensterbank, M. Malacria, *Org. Lett.* **2007**, *9*, 2207; g) A. Buzas, F. Gagosz, *J. Am. Chem. Soc.* **2006**, *128*, 12614; h) E. J. Cho, M. Kim, D. Lee, *Org. Lett.* **2006**, *8*, 5413; i) M. J. Johansson, D. J. Gorin, S. T. Staben, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 18002; j) M. R. Luzung, J. P. Markham, F. D. Toste, *J. Am. Chem. Soc.* **2004**, *126*, 10858; k) F. Gagosz, *Org. Lett.* **2005**, *7*, 4129; l) A. Correa, N. Marion, L. Fensterbank, M. Malacria, S. P. Nolan, L. Cavallo, *Angew. Chem.* **2008**, *120*, 730; *Angew. Chem. Int. Ed.* **2008**, *47*, 718; see also: m) C. M. Grisé, E. M. Rodrigue, L. Barriault, *Tetrahedron* **2008**, *64*, 797; n) For the seminal work on the development of [(PR$_3$)AuNTf$_2$] catalysts, see: N. Mézailles, L. Richard, F. Gagosz, *Org. Lett.* **2005**, *7*, 4133; o) D. Garayalde, K. Krüger, C. Nevado, *Angew. Chem.* **2011**, *123*, 941; *Angew. Chem. Int. Ed.* **2011**, *50*, 911; p) Y. Harrak, M. Makhlouf, S. Azzaro, E. Mainetti, J. M. L. Romero; K. Cariou, V. Gandon, J.-P. Goddard, M. Malacria, L. Fensterbank, *J. Organomet. Chem.* **2011**, *696*, 388; K. Cariou, V. Gandon, J.-P. Goddard, M. Malacria, L. Fensterbank, *J. Organomet. Chem.* **2011**, *696*, 388.

[6] G. Ohloff, H. Strickler, B. Willhalm, C. Borer, M. Hinder, *Helv. Chim. Acta* **1970**, *53*, 623.

[7] T. Hatsui, N. Suzuki, H. Takeshita, *Chem. Lett.* **1985**, 639.

[8] A. Srikrishna, K. Krishnan, *J. Org. Chem.* **1993**, *58*, 7751.

[9] A. Krasovskiy, F. Kopp, P. Knochel, *Angew. Chem.* **2006**, *118*, 511; *Angew. Chem. Int. Ed.* **2006**, *45*, 497.

[10] This synthesis is analogous to the one described for [Cu(CH$_3$CN)$_4$]PF$_6$: G. J. Kubas, *Inorg. Synth.* **1979**, *19*, 90; For the synthesis of CuNTf$_2$ from mesityl copper and NHTf$_2$: S. H. Strauss, O. G. Polyakov, J. W. Hammel, S. M. Ivanova, S. V. Ivanov, M. D. Havighurst, US 6114266, **2000**.

[11] A sample of [(IPr)CuNTf$_2$] was kindly obtained by Professor Steven P. Nolan (University of St. Andrews, St. Andrews, UK). For the preparation of [(IPr)CuNTf$_2$]: G. C. Fortman, A. M. Z. Slawin, S. P. Nolan, *Organometallics* **2010**, *29*, 3966.

[12] M. R. Luzung, P. Mauleon, F. D. Toste, *J. Am. Chem. Soc.* **2007**, *129*, 12402; N. D. Shapiro, F. D. Toste, *Synlett* **2010**, 675; B. Alcaide, P. Almendros, C. Aragoncillo, *Chem. Soc. Rev.* **2010**, *39*, 783.

[13] G. Saucy, R. Marbet, H. Lindlar, O. Isler, *Helv. Chim. Acta* **1959**, *42*, 1945.

[14] E. Vedejs, A. Cammers-Goodwin, *J. Org. Chem.* **1994**, *59*, 7541.

[15] We cannot exclude that **25** is formed by a stepwise formal [2+2]-cycloaddition of **Q**, followed by hydrolysis of the intermediate enol acetate **24**.

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