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Gold-Catalyzed Cycloisomerizations of Functionalyzed Cyclopropyl Alkynes: the Cases of Carboxamides and Alcohols

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Dedicated to honour the memory of Prof. J. Barluenga, deceased on September 7th, 2016.

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Abstract. Push-pull alkynylcyclopropane derivatives are claimed as suitable and active substrates for gold-catalyzed transformations. Thus, 2(3*H*)-azepinones can be readily prepared from alkynylcyclopropanecarboxamides through a nucleophilic addition/cyclopropane ring-opening cascade process and, in this manuscript, the scope and the limitations of such reaction sequence are reported. The cascade reaction is general and occurs with complete regio- and quimioselection to form the seven-membered heterocycles with the exception of primary alkyl-substituted alkynylcyclopropanecarboxamides that render 4-methoxy-6-oxo-4-enenitriles in moderate yields. Additionally, less activated alkynylcyclopropylmethanols undergo regioselective cycloisomerization at low temperature leading to oxabicyclo[4.1.0]heptanes. Notably, the cyclopropane ring opening of these adducts takes place under thermal conditions to form dihydropyranones.

Keywords: alkynes; gold; nucleophilic addition; ring expansion; seven-membered heterocycles; pyranones

Introduction

In recent years, the extremely active field of homogeneous metal catalysis has bloomed with the discovery and the establishment of gold catalysis as a powerful and versatile tool to induce molecular complexity.[1, 2] The soft, carbophilic Lewis acidic nature of Au(I) cations enables the mild activation (as π-Lewis acids) of unsaturated C–C bonds (alkynes, alkenes, allenes) toward nucleophilic attack, while a dual σ,π-activation has been observed for terminal alkynes.[3] Thus, carbon-carbon and carbon-heteroatom bond forming transformations have been developed, usually involving cycloaddition or cycloisomerization reactions. In this context, we have demonstrated the critical effect of donor-acceptor substituents in the outcome of gold-catalyzed reactions of enynes. In this way we have been able to prepare six-membered heterocycles (pyridines and dihydropyridones)[4] and carbocycles (phenols and terphenyls)[5] from push-pull conjugated dienynes.[6, 7] On the other hand, alkynyl cyclopropanes have also served as useful starting materials for gold-catalyzed transformations.[8, 9] Taking into account our previous experience, we wanted to assess the influence of donor-acceptor substituents in the cyclization of this kind of substrates. We hypothesised that readily accessible push-pull alkynyl cyclopropanes **1** and **2**[10, 11] could be suitable starting materials for a cascade reaction consisting on a sequential intramolecular nucleophilic addition/cyclopropane ring-opening (Figure 1). The presence of donor-acceptor (DA) substituents in the cyclopropane ring should facilitate the ring-opening leading to oxepin-2-ones **4** and azepin-2-ones **5**, whereas in the reaction of alkynylcyclopropane **3**, lacking an electron withdrawing group, the ring opening would probably be less favoured.

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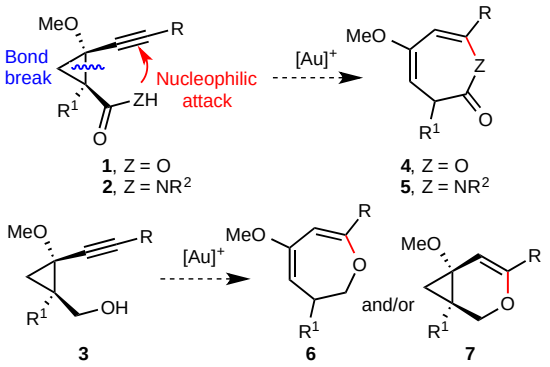
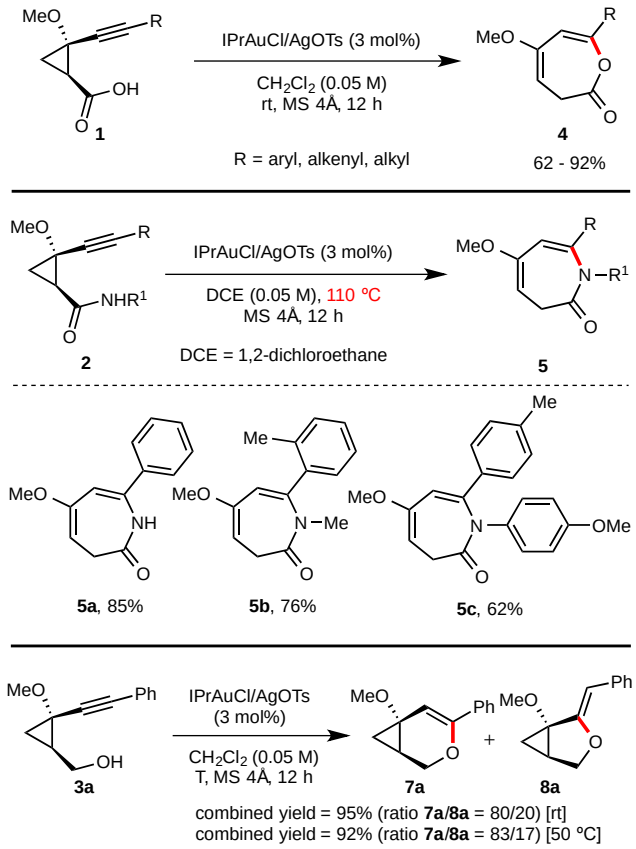


Figure 1. Working hypothesis.

Indeed, we have already disclosed the potential of the proposed route for the synthesis of oxepinones **4** in good to excellent yields[12] (Scheme 1, *top*). Remarkably, the cascade process takes place with complete regioselectivity under mild reaction conditions (room temperature) provided that the cyclopropane ring bears both donor and acceptor substituents, due to the known intrinsic vulnerability of DA cyclopropanes to undergo ring-opening reactions. We have also found mechanistic evidence proving that, for a particular substrate, the role of the gold catalyst is restricted to promote the nucleophilic addition step.[13]



Scheme 1. State of the Art: previous results (ref. 12).

Additionally, we have shown that our developed strategy towards oxepin-2-ones could be employed for the synthesis of isoelectronic azepin-2-ones, and azepinones bearing *N*-H (**5a**), *N*-alkyl (**5b**) and *N*-aryl (**5c**) groups have been prepared (Scheme 1, *middle*). Nevertheless, as expected, harsh conditions (warming at 110 °C) were required for the gold-catalyzed reaction sequence, probably due to difficulties associated with the intramolecular triple bond amidation step,[14] but in all cases the regioselectivity was complete towards the 6-*endo*-dig isomer.[15] In all these transformations, the combination IPrAuCl/AgOTs proved to be the best catalyst system.[16] These preliminary results are also remarkable because the generation of seven-membered heterocycles remains as a highly challenging task in organic synthesis.[17]

At this point it is worth to note that the azepin-2-one skeleton is present in both natural and synthetic products displaying useful biological and pharmacological activities, such as natural and synthetic ceratamines **9-11** (antimicotic and microtubule-stabilizing properties),[18] synthetic compound **12** (inhibitor of γ-secretase),[19] zatebradine **13** (specific bradycardic agent),[20] or allsterpaullone **14** (promising candidate for therapeutic treatment of type-1 diabetes)[21] (Figure 2). Azepinone derivatives have also been employed as useful synthetic intermediates.[22]

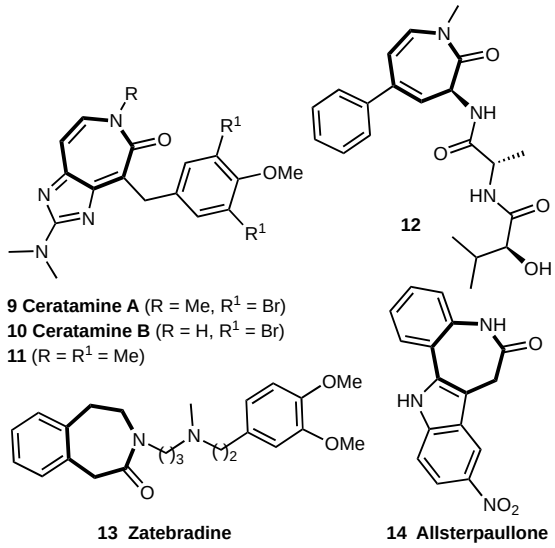


Figure 2. Natural and synthetic products bearing the azepin-2-one skeleton.

Interestingly, the gold-catalyzed synthesis of azepinone derivatives has some precedents, for instance, in the preparation of pyrroloazepinones[23] and azepino-[*c*,*d*]indolones.[24] In an example more closely related to our work, Liu has reported the regioselective synthesis of 3-benzoazepinones in moderate to excellent yields by a cationic Au(I)-catalyzed *7-endo*-dig hydroamidation of 2-(1-alkynyl)phenylacetamides.[25] This work represents

one of the scarce examples of direct gold-catalyzed hydroamidation of alkynes,[26] as carbamates[27] and tosylamides have been more often used as nitrogen nucleophiles.[28]

On the other hand, while checking the necessity of the "push-pull" nature of the substituents at the cyclopropane ring, we found that under the typical reaction conditions alkynylcyclopropylmethanol **3a**, which lacks of an acceptor group, does not experience ring-expansion, leading to bicyclic enol ethers **7a** and **8a** in excellent yield although with moderate regioselectivity.[12] A very similar result was also reached when warming at 50 ºC (Scheme 1, *bottom*).

In this regard, gold-catalyzed intramolecular hydroalkoxylations have allowed the blossoming of cascade reactions, mainly based in the facts that cycloisomerizations of alkynols are usually very efficient and take place under mild reaction conditions.[29] Remarkably, although two regioisomers can be formed, the cycloisomerization step may be highly regioselective toward either the *endo*-dig or the *exo*-dig adducts depending on the nature of the starting material, the catalyst employed or the size of the ring formed.[30]

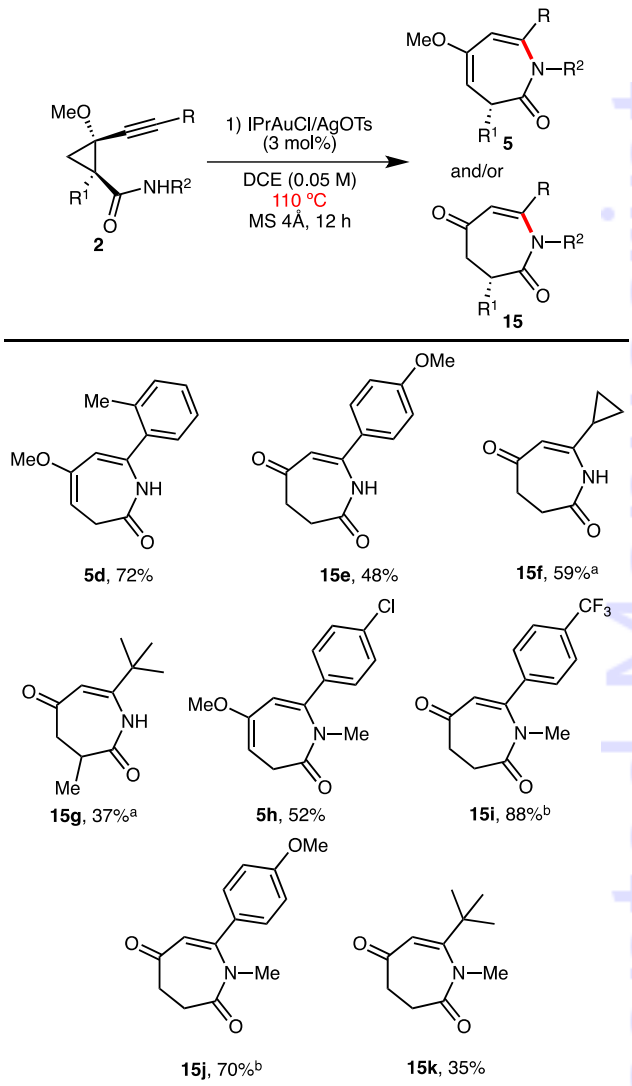
Based on all those precedents, in this manuscript we present an update on the gold-catalyzed reactivity of functionalized alkynylcyclopropanes **2** and **3**, including a novel synthesis of dihydropyranones discovered while assessing the influence of the electronic nature of the alkynylcyclopropane in the outcome of the reaction.

Results and Discussion

1. Cycloisomerizations and isomerizations on 2-methoxy-2-alkynylcyclopropanecarboxamides

In an aim to extend the scope of the synthesis of azepin-2-ones, primary and secondary 2-methoxy-2-alkynylcyclopropanecarboxamides bearing different substituents at the triple bond were treated under the previously established reaction conditions. It should be noted that, in general, the 5-methoxy-2-azepinone ring proved to be less stable than the isoelectronic 5-methoxy-2-oxepinone; thus, in some cases, the enol ether functionality underwent hydrolysis during purification and the corresponding azepin-2,5-dione **15** was isolated instead of or together with the corresponding 5-methoxy-azepinone **5** (Scheme 2). In all cases the regioselectivity was complete towards the 6-*endo*-dig isomer.

Good yields were achieved for primary carboxamides bearing aryl substituted groups at the triple bond (**5a**,**5d**). The *ortho*-substitution did not seem to be a handicap for this transformation (**5d**), but the electronic nature of the aryl-substituent at the triple bond did affect the stability of the seven-membered heterocyclic ring; thus, azepindione **15e** bearing strong electron-donating *p*-methoxyphenyl (PMP) group was the only product isolated in a moderate 48% yield. This was also the case of cyclopropyl substituted azepindione **15f**; remarkably the cyclopropyl substituent remained inert under the reaction conditions. Moreover, as observed before for the oxepinone series, a methyl group could be placed at position 3 of the azepindione skeleton (**15g**), starting from the corresponding cyclopropanecarboxamide **2g**.



Scheme 2. Scope of the reaction.

Regarding the reaction scope for secondary (*N*-Me) 2-alkynylcarboxamides, electron-withdrawing and electron-donating substituted aryl groups as well as a tertiary alkyl group were placed as substituents at the triple bond (**5b,h**, **15i-k**). Remarkably, although for CF_3-substituted and PMP-substituted *N*-Me alkynylcyclopropanecarboxamides **2i,j** mixtures of the corresponding azepinones and azepindiones were initially obtained, treatment of the crude reaction mixture with silica gel allowed the selective isolation of azepindiones **15i,j**. As expected, tertiary alkyl

group substituted azepinone also underwent enol ether hydrolysis and only 35% of azepindione **15k** was reached. An aromatic group has also been placed as nitrogen substituent, as in azepinone **5c** (Scheme 1).

Interestingly, considering the two reactive alkynyl carbons and the bidentate nucleophilic nature of the carboxamide group, the most remarkable feature of this reaction sequence is its high selectivity: the fact that out of the four possible reaction products (imidates vs amides, *endo* vs *exo*), only one –the *endo*-amide product (Figure 3)– is obtained; therefore, *the reaction sequence takes place in all previous cases with a complete double selectivity*.

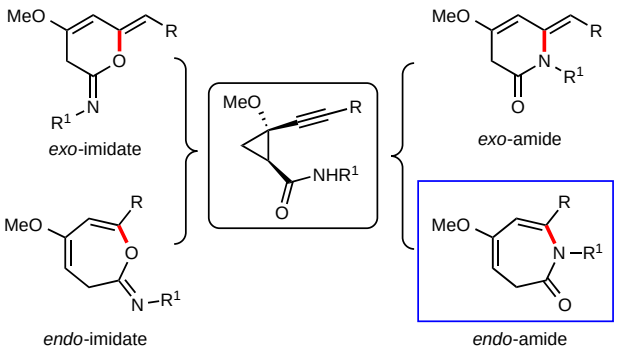
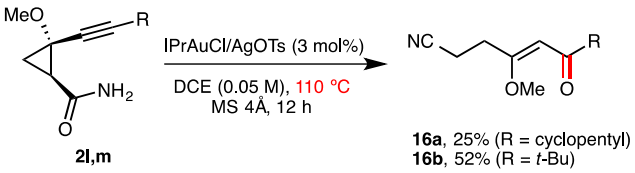


Figure 3. Double selectivity (*endo-exo*, amide-imidate) in the reaction sequence.

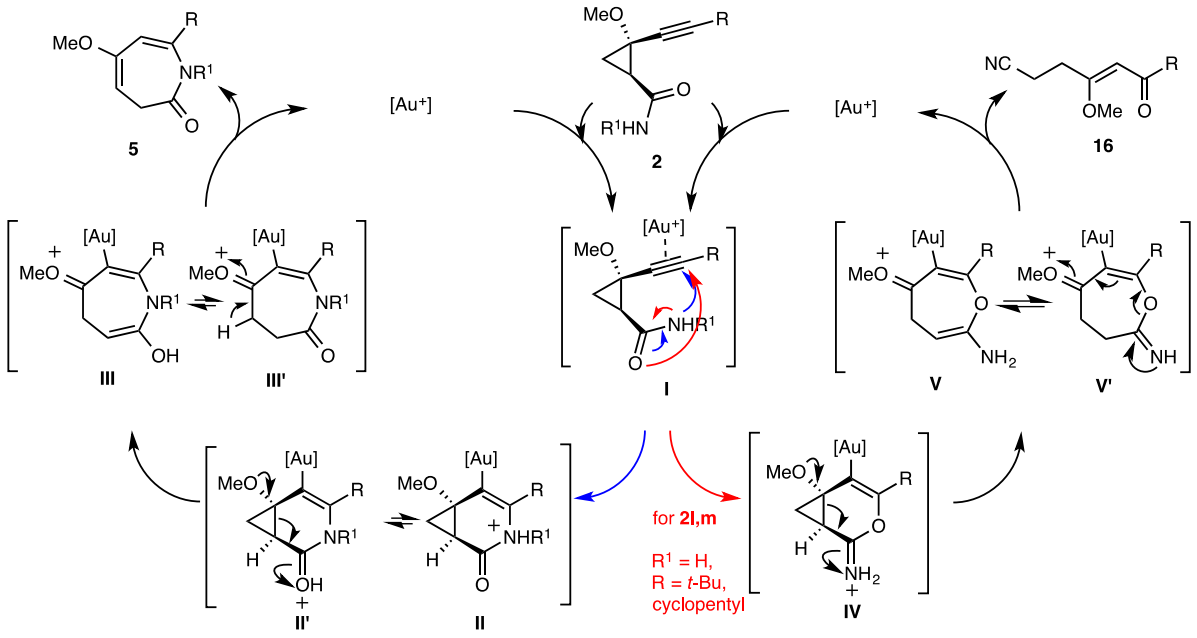
The only exception to this general behaviour was observed for primary alkynylcyclopropylcarboxamides **2l,m** bearing an alkyl group as substituent of the triple bond (R = cyclopentyl, *t*-Bu), which gave moderate yields of 4-methoxy-6-oxo-4-enenitriles **16** under the optimized reaction conditions (Scheme 3).



Scheme 3. Synthesis of 4-methoxy-6-oxo-4-enenitriles by isomerization of primary alkyl-substituted alkynylcyclopropylcarboxamides **2l,m**.

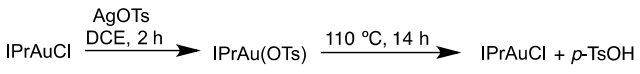
A mechanism to explain the formation of both azepinones and oxoenenitriles is depicted in Scheme 4. To account for the formation of azepinones, we suggest the commonly accepted initial activation of the triple bond of the alkynylcyclopropane by π–coordination of the gold cation[31] to form intermediate **I**. This intermediate[32] should evolve by a regioselective 6-*endo*-dig nucleophilic addition of the nitrogen of the carboxamide to the activated triple bond in **I** leading to **II** (Scheme 4, blue arrows). A subsequent cyclopropane ring-opening would render seven-membered ring intermediate **III**, which after a final protodemetalation would give products **5** and would regenerate the catalyst.

On the other hand, the formation of 4-methoxy-6-oxo-4-enenitriles **16** may be readily understood by considering the bidentate nucleophilic nature of the carboxamide group. In this regard, while the amide group was postulated as a nitrogen nucleophile to account for the formation of azepinones, its behaviour as an oxygen nucleophile would lead to oxoenenitriles **16**. Therefore, the nucleophilic attack of the amide oxygen atom to triple-bond activated intermediate **I** (Scheme 4, red arrows) would give bicyclic iminium-type cation **IV**, which should undergo an effortless cyclopropane ring-opening, due to the push-pull nature of the substituents at the cyclopropyl ring. Cyclic ketene aminal species **V** is then formed which should tautomerize to imidate intermediate **V'** and a final ring-opening would form the observed enenitriles **16**.



Scheme 4. Proposed reaction mechanisms for the synthesis of azepinones **5** and enenitriles **16**.

In order to address some concerns regarding gold catalyst stability under the harsh reaction conditions, the evolution of the catalyst was monitored by NMR using 1,2-dichlorethane as solvent.[33] AgOTs was added to a solution of IPrAuCl in 1,2-dichloroethane and the mixture was stirred at room temperature for 2 h. The ^{1}H-NMR spectrum then recorded showed the formation of IPrAu(OTs) as indicated by the presence of the *p*-tosyl moiety as well as by a slight shifting in the IPr signals; some IPrAuCl remained still as a minor component (for details of the aromatic region in ^{1}H NMR, see Figure 4a and 4b). The chemical shift of the carbene carbon in ^{13}C-NMR moved from 174.7 ppm in the chloride species to 163.1 ppm in the tosylate species; additionally, the diffusion coefficient of the NMR signals from the IPr and the OTs fragments were measured through a ^{1}H DOSY experiment. Their values were found identical (logD = –9.18 m^2/s), so the identity of the catalyst molecule IPrAu(OTs) was verified. The mixture was then heated at 110 ºC for 14 h; the spectra recorded at this stage showed the disappearance of IPrAu(OTs), the regeneration of IPrAuCl and the formation of *p*-TsOH (Figure 4c); as expected, the different measured diffusion coefficient values for the IPr (logD = –9.18 m^2/s) and the OTs (logD = –9.02 m^2/s) fragments agree with NMR signals belonging to hydrogen atoms located at different size molecules, thus proving that the gold species undergoes transformation upon the reaction conditions[34] (Scheme 5).



Scheme 5. Evolution of the gold species with the reaction conditions.

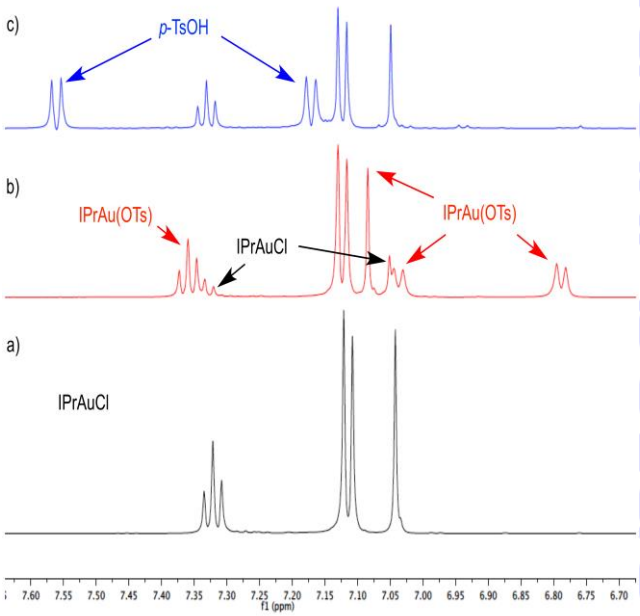


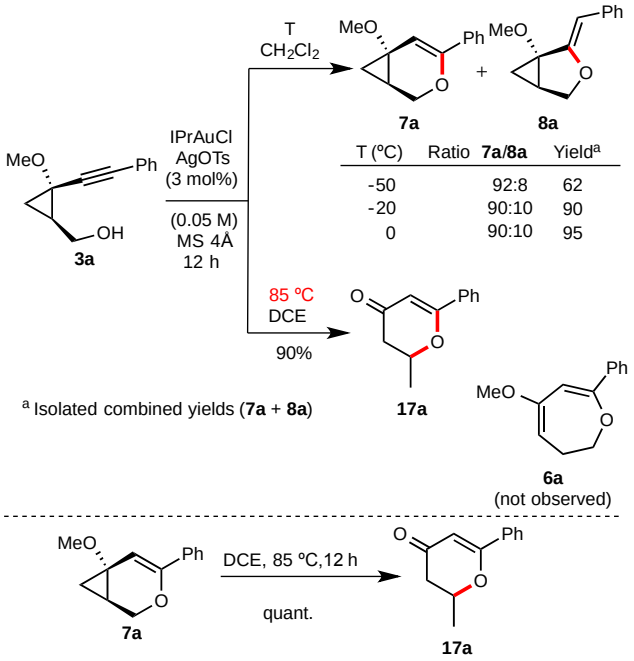
Figure 4. ^{1}H-NMR (600 MHz, 1,2-DCE[D_2O]) monitoring of the evolution of the gold species with the reaction conditions (details of the aromatic region): a) IPrAuCl. b) after stirring IPrAuCl + AgOTs, for 2h at rt. c) after heating at 110 ºC for 14 h.

The upon-heating-formed gold species have shown poor catalytic activity for the cycloisomerization reaction of amide **2a**, as approximately 65% starting material remained unreacted after 14 h at 110 ºC. Additionally, a blank test confirmed that *p*-TsOH is not able to catalyze the cycloisomerization reaction.

2. Cycloisomerizations on 2-methoxy-2-alkynylcyclopropylmethanols

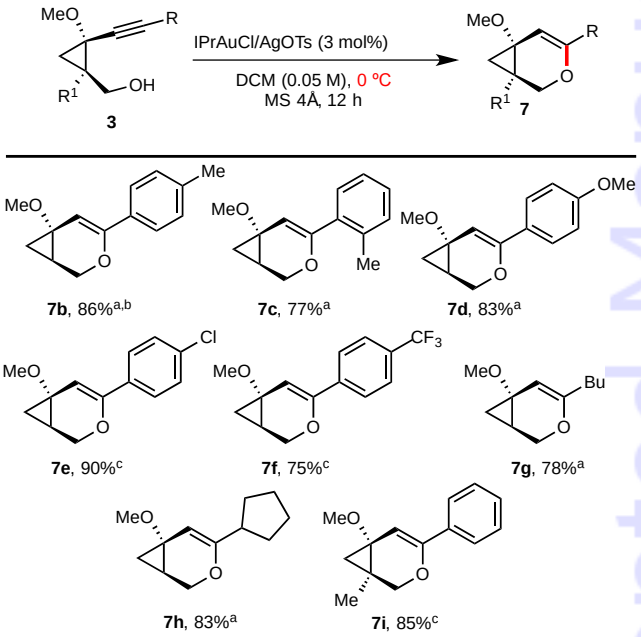
As stated in the manuscript introduction, 2-methoxy-2-alkynylcyclopropanemethanol **3a** did not experience cyclopropyl ring-expansion, neither under the previously optimized (for alkynylcyclopropane carboxylic acids **1**) reaction conditions nor when raising the temperature to 50 ºC (Scheme 1, *bottom*); lowering the temperature to 0 ºC or –20 ºC enhanced the regioisomeric ratio of bicyclic enol ethers **7a** and **8a**, which come from *6-endo*-dig and *5-exo*-dig intramolecular hydroalkoxylations, without compromising the reaction yield (Scheme 6, *top*). A further decrease of the temperature to –50 ºC led to a much slower reaction and only a 62% combined yield of cyclization products was isolated, although the regioselectivity was slightly improved. Surprisingly, dihydropyranone **17a**[35] was the only product obtained instead of the expected dihydrooxepine **6a** when the reaction was performed at a higher temperature (85 ºC) in an attempt to promote the opening of the cyclopropane ring.

To evaluate the role of the catalyst in the formation of **17a**, compound **7a** was warmed in absence of metal and led quantitatively to dihydropyranone **17a**, pointing out that this transformation is thermally promoted (Scheme 6, *bottom*). Therefore, the role of the gold catalyst is restricted to control the cyclization step to **7a**.



Scheme 6. Temperature-dependent cyclization of alkynylcyclopropylmethanol **3a**.

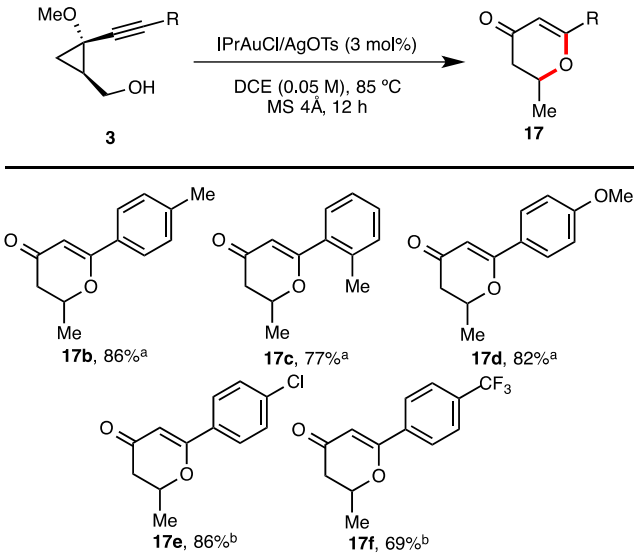
The scope of the cyclization was then analyzed at 0 ºC to find that only oxabicyclo[4.1.0]heptenes **7** were obtained in high yields (77-86%) when the substituent at the triple bond (R) was an alkyl group or an electron-donating substituted aryl group (**7b-d,g,h**), while mixture of both regioisomeric cyclopropyl enol ethers **7** and **8** was observed for R being electron-withdrawing substituted aryl groups (**7e-f**) (Scheme 7). Such results reflect an important electronic effect for the nucleophilic addition of the hydroxyl group to the triple bond. As expected, only one diastereomer (the *Z* isomer) of the *5-exo*-dig cyclization derived bicyclic enol ether **8** was formed in those cases, as established by NOESY experiments. Steric effects also proved to be crucial: the reaction was completely inhibited by the presence of bulky groups linked to the alkyne; for instance, no reaction was observed for alkynylcyclopropylmethanols **3j,k** (R = *t*-Bu, TMS) (not even at 110 ºC). Additionally, the presence of an all carbon quaternary stereocenter seems to affect the regioselectivity of the reaction: the cyclization of alkynylcyclopropylmethanol **3i** at 0 ºC lead to a mixture of oxabicyclic enol ethers, **7i** and **8i**, with much lower regioselectivity than for the reaction performed with **3a** (4.1/1 vs 9/1).



Scheme 7. Scope of the cyclization at 0 ºC.

It is worth to note that pyran ring derivatives are important intermediates for the synthesis of biologically active compounds.[36] In this sense, the direct gold-catalyzed reaction of alkynylcyclopropanemethanols **3** at 85 ºC provided dihydropyranones (**17a-d**) as the only compounds, without traces of oxabicyclo[3.1.0]hexane byproducts, for alkynylcyclopropylmethanols bearing alkyl groups or aryl groups with electron-donating substitutents at the acetylene (Scheme 8). On the contrary, substrates **5e,f** possessing electron-withdrawing aryl groups at

this position produced mixtures of dihydropyranones **17** and oxabicyclo[3.1.0]hexanes **8**.

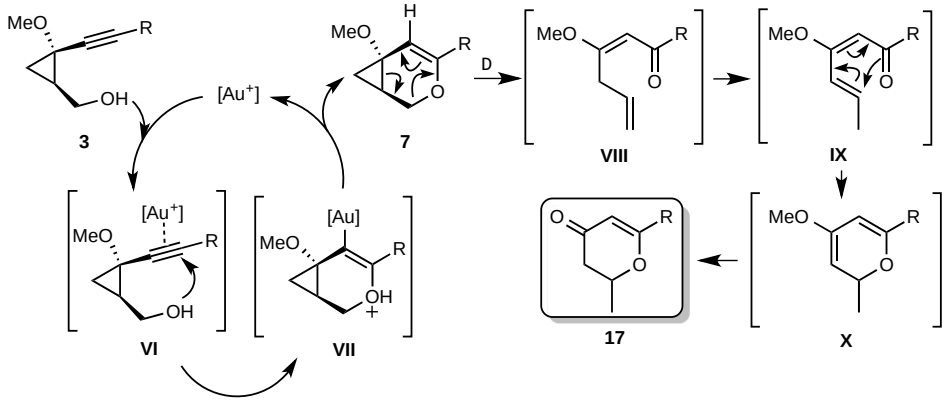


[a] Isolated yield of compounds **17**
[b] Combined isolated yield of compounds **17** + 5-*exo*-adducts **8** (ratio **17e**/**8e** = 1.6:1; **17f**/**8f** = 2.3:1)

Scheme 8. Scope of the reaction at 85 ºC.

Regarding the cycloisomerization mechanism, it is assumed a nucleophilic attack of the hydroxy group to the gold-activated triple bond in intermediate **VI** leading to oxabicyclospecies **VII**, which then should undergo a hydrodemetalation step to form oxabicyclo[4.1.0]hexanes **7** (Scheme 9). The lower regioselectivity observed in the cyclization reaction when the triple bond substituent is an electron-withdrawing group can be understood considering the slippage of the electron density in π-activated alkynes.

On the other hand, to explain the formation of dihydropyranones **17**, oxabicyclo[4.1.0] enol ethers **7** would undergo a thermal electrocyclic ring opening to form conjugated enone-type intermediates **VIII**, which should suffer a 1,3-H migration leading to isomeric dienones **IX**. A 6π electrocyclization would form 4-methoxy-2*H*-pyranes **X**, which would be readily hydrolyzed to the final dihydropyranones **8**.



Scheme 9 Proposed reaction mechanisms for the formation of oxabicyclo[3.1.0]heptenes **7** and dihydropyranones **17**.

Conclusion

In conclusion, we have developed a general and efficient synthesis of azepin-2-ones by gold-catalyzed completely regioselective cycloisomerization of 2-methoxy-2-alkynylcyclopropane carboxamides. Remarkably, a double selectivity (*endo*/*exo*, amide/imidate) was observed with the only exception of particular substrates being primary amides and bearing alkyl substituents at the triple bond that furnished oxoenenitriles, in moderate yields. On the other hand, the gold-catalyzed cycloisomerization of 2-methoxy-2-alkynylcyclopropylmethanols, without push-pull character, led to the regioselective synthesis of oxabicyclo[4.1.0]heptenes in good yields at 0 ºC. However, dihydropyranones were formed instead at 85 ºC through a thermal rearrangement of the initially formed oxabicycles.

Experimental Section

General Methods. All reactions involving air sensitive compounds were carried out under inert atmosphere (Ar or N_2, ≥ 99.99%). All glassware was oven-dried (120 °C), evacuated and purged with nitrogen. All common reagents and solvents were obtained from commercial suppliers and used without any further purification unless otherwise indicated. IPrAuCl and AgOTs were purchased from commercial supplies and lyophilized prior to use.

Fischer methoxy cyclopropylethynyl chromium carbene complex,[37] alkynylcyclopropanecarboxylic esters, [10, 12] alkynylcyclopropanecarboxylic acids **1**,[12] alkynylcyclopropanecarboxamides **2a-c**,[12] and alcohol **3a**[12] have been previously synthesized and were prepared as described. Azepinones **5a-c** and bicyclic enol ethers **7a** and **8a** have been previously reported by us,[12] and dihydropyranones **17a,d** have also been described.[35] Solvents were dried by standard methods.[38] Hexane (HxH), ethyl acetate and triethylamine were purchased as extra pure grade reagents and used as received. TLC was performed on aluminium-backed plates coated with silica gel 60 with F_{254} indicator; the chromatograms were visualized under ultraviolet light and by staining with $KMnO_4$ reagent and subsequent heating. R_f values are reported on silica gel. Column chromatography was carried out on silica gel 60, 230-240 mesh. Routine NMR measurements were recorded on Bruker AV-400 or DPX-300 spectrometers. The values of δ are expressed in ppm and referred to the residual signal of the solvent ($CDCl_3$). The coupling constants values *J* are expressed in Hz. ^{1}H NMR: splitting pattern abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; sext, sextet; at, apparent triplet; dd, double doublet; ddd, double doublet of doublet; adt, apparent double triplet; m, multiplet. ^{13}C NMR: multiplicities were determined by DEPT, abbreviations are: q, CH_3; t, CH_2; d, CH; s quaternary carbons, except for compounds bearing fluorine atoms **2i, 15i, 3f, 7f, 8f** and **17f** (see below). For these compounds, the abbreviation (q) regarding the carbon multiplicity refers to the F-C coupling and there will be no abbreviation if there is no F-C coupling; the number of hydrogen atoms linked to a determined carbon atom is indicated as C, CH, CH_2 or CH_3. In the cases where a mixture of two diastereomers was observed, the abbreviation "min" refers to the signals assigned to the minor diastereomer and the abbreviation "maj" to the signals belonging to the major one; in the cases where nothing is specified, either it hasn't been possible to assign the signal to any of the diastereomers or it belongs to both of them. ^{19}F NMR: Trichlorofluoromethane ($CFCl_3$) was employed as reference standard (δ = 0). COSY, HSQC, HMBC, NOESY and DOSY experiments were carried out on Bruker AV-400 or on Bruker AV-600 spectrometers. Standard pulse sequences were employed for the DEPT experiments. NMR-experiments involving gold catalysts have been performed in 1,2-dichloroethane with D_2O-insert. Mass spectra were determined by Universidad de Vigo (CACTI) with a VG AutoSpec M, Universidad de Burgos with a Micromass Autospec, and Universidad de Oviedo with a Bruker model Impact II mass spectrometers respectively for high resolution mass spectra (HRMS); low resolution mass spectra were obtained on a gas chromatograph mass spectrometer Shimadzu QP2010 Plus with auto injector AOC-20i. Electron ionization (70 eV) or electrospray ionization (ESI) were employed.

(1*R,2*R**)-2-[(Cyclopropyl)ethynyl]-2-methoxy-cyclopropanecarboxylic acid (1p).** In a sealed tube methyl acrylate (6.80 mL, 15 equiv, 75 mmol) was added to a solution of Fischer methoxy cyclopropylethynyl chromium carbene complex (1.50 g, 1 equiv, 5 mmol) in dry THF (100 mL). The mixture was stirred at 90 ºC until complete disappearance of the carbene complex was observed by TLC (~12 h). Solvent was removed under reduced pressure, and the residue was purified by flash chromatography (hexane/AcOEt); methyl 2-methoxy-2-[(cyclopropyl)ethynyl]cyclopropanecarboxylate was isolated as a yellow liquid in 40% yield [0.39 g, dr = 4.7:1, the major isomer has a *cis* relationship between alkynyl and ester substituents - (1*R**,2*R**)-isomer].

$LiOH{\cdot}H_2O$ (6 equiv, 12 mmol, 0,50 g) was added to a solution of methyl (1*R**,2*R**)-2-methoxy-2-[(cyclopropyl)ethynyl]cyclopropanecarboxylate (2 mmol, 0.39 g) in $MeOH/H_2O$ 1:1 mixture (35 mL) in a 250 mL flask. The mixture was stirred during 2 hr at room temperature, the final of the reaction was verified by TLC. The solution was extracted with ether (2 x 25 mL) and the combined organic phase was discarded; the resulting aqueous layer was neutralized with HCl 1N and was extracted employing ether (3 x 25 mL). The combined organic phase was dried over Na_2SO_4, filtered and solvents were removed under vacuum. The resulting alkynylcyclopropanecarboxylic acid **1p** was isolated as yellow-orange solid oil, which did not require further purification (0.24 g, 66% yield); R_f = 0.28 (HxH/AcOEt: 7/3); the following data have been obtained from a 3.5:1 mixture of diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.45 (bs, 1 H, maj + 1 H, min), 3.41 (s, 3 H, maj), 3.39 (s, 3 H, min), 2.09 – 2.02 (m, 1H, min), 2.04 (dd, *J* = 9.3, 7.4 Hz, 1 H, maj), 1.82 (dd, *J* = 7.3, 5.8 Hz, 1H, min), 1.63 (dd, *J* = 7.3, 5.7 Hz, 1 H, maj), 1.56 (dd, *J* = 9.3, 5.7 Hz, 1 H, maj), 1.45 (dd, *J* = 8.8, 5.8 Hz, 1 H, min), 1.34 – 1.21 (m, 1H maj + 1 H min), 0.86 –0.74 (m, 2H maj + 2H min), 0.74 – 0.64 (m, 2H maj + 2H min); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 175.6 (s, maj), 174.6 (s, min), 90.9 (s, maj), 88.5 (s, min), 72.2 (s, maj), 68.7 (s, min), 59.9 (s, maj), 59.0 (s, min), 56.0 (q, min), 55.7 (q, maj), 29.4 (d, min), 29.2 (d, maj), 22.5 (t, maj), 22.1 (t, min), 8.5 (t, maj), 8.40 (t, 2 CH_2, maj + min), 8.37 (t, min), –0.5 (d, maj), –0.6 (d, min); HRMS: (ESI) Calculated for $C_{10}H_{12}NaO_3$ $[M]^+$: 203.0679, found: 203.0689.

General procedure for the synthesis of alkynylcyclopropanecarboxamides 2: A solution of the corresponding alkynylcyclopropanecarboxylic acid **1** (1 mmol) in THF (15 mL) under inert atmosphere was cooled to –15 ºC with stirring. Et_3N (1 equiv, 1 mmol, 0.14 mL) and ethyl chloroformate (1 equiv, 1 mmol, 0.096 mL) were sequentially added; a white precipitate was formed. Stirring was maintained for 1h at that temperature and, then, the corresponding amine (or ammonium hydroxide) (2 equiv) was added. Stirring was continued for 15 min at –15 ºC, before removing the cooling bath and allowing the mixture to reach room temperature. Solvent was evaporated under vacuum; ethyl acetate (25 mL) and 5% sodium bicarbonate solution (15 mL) were added. After shaking and separation, the ethyl acetate layer was sequentially washed with water (15 mL), 1*N* hydrochloric acid (15 mL), and finally, water (15 mL). After drying over anhydrous sodium sulphate, evaporation of the ethyl acetate solution led to amides **2**. Some of them were pure enough to be used without further purification, while some others required chromatographic purification. No epimerization was observed under the reaction conditions.

(1*R,2*R**)-2-Methoxy-2-(*o*-tolylethynyl)cyclopropanecarboxamide (2d).** Colorless liquid; 227 mg, 99% yield, of a mixture of diastereomers 6.7:1; R_f = 0.06 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41 – 7.37 (m, 2 H, min + maj), 7.24 – 7.07 (m, 6 H, min + maj), 6.21 (bs, 2 H, min + maj), 6.07 (s, 2 H, min + maj), 3.53 (s, 3 H, min), 3.48 (s, 3 H, maj), 2.41 (s, 6 H, min + maj), 2.11 (dd, *J* = 9.5, 7.3 Hz, 1 H, maj + 1 H, min), 1.70 (dd, *J* = 7.3, 5.8 Hz, 1 H, maj + 1 H min), 1.53 (dd, *J* = 9.5, 5.8 Hz, 1 H, maj + 1 H min) –the values of the coupling constants correspond to the major isomer–; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.3 (s, min), 170.6 (s, maj), 140.4 (s, maj), 140.3 (s, min), 132.2 (d, maj), 132.0 (d, min), 129.5 (d, min), 129.4 (d, maj), 128.7 (d, min), 128.5 (d, maj), 125.6 (d, min), 125.5 (d, maj), 122.1 (s, maj), 121.8 (s, min), 90.2 (s, min),

87.5 (s, maj), 85.7 (s, maj), 83.2 (s, min), 58.8 (s, maj), 57.8 (s, min), 56.3 (q, min), 55.8 (q, maj), 31.3 (t, min), 31.1 (t, maj), 22.0 (d, min), 21.1 (d, maj), 20.7 (q, maj), 20.6 (q, min); LRMS: (EI) *m/z* (%) = 229 ([M]$^+$, 7), 214 (10), 185 (43), 167 (34), 143 (41), 115 (100); HRMS: (EI) calculated for $C_{14}H_{15}NO_4$ [M]$^+$: 229.1103, found: 229.1107.

(1*R,2*R**)-2-Methoxy-2-[(4-methoxyphenyl)ethynyl]cyclopropanecarboxamide (2e).** Yellow liquid; 105 mg, 43% yield, of a mixture of diastereomers 4:1; the following data have been obtained from that mixture and correspond to the major isomer: R_f = 0.06 (Hex/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37 (d, *J* = 8.5 Hz, 2 H), 6.80 (d, *J* = 8.5 Hz, 2 H), 5.94 (bs, 1 H), 3.78 (s, 3 H), 3.46 (s, 3 H), 2.08 (dd, *J* = 9.4, 7.4 Hz, 1 H), 1.66 (dd, *J* = 7.4, 5.8 Hz, 1 H), 1.54 (dd, *J* = 9.4, 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.5 (s), 159.8 (s), 133.4 (d, 2 CH), 114.3 (s), 113.9 (d, 2 CH), 87.0 (s), 82.1 (s), 58.7 (s), 55.8 (q), 55.3 (q), 31.0 (d), 21.4 (t); LRMS: (EI) *m/z* (%) = 245 ([M]$^+$, 16), 201 (100), 187 (27), 159 (35); HRMS: (EI) calculated for $C_{14}H_{15}NO_3$ [M]$^+$: 245.1052, found: 245.1051.

(1*R,2*R**)-2-[(Cyclopropyl)ethynyl]-2-methoxycyclopropanecarboxamide (2f).** Yellow-orange solid; 136 mg, 76% yield of a mixture of diastereomers 3:1. R_f = 0.06 (HxH /AcOEt: 1/1); the following data have been obtained from that mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.45 (s, 3 H, min), 3.40 (s, 3 H, maj), 1.98 – 1.93 (m, 1 H, min), 1.96 (dd, *J* = 9.8, 7.3 Hz, 1 H, maj), 1.64 (bs, 2 H, maj + 2 H, min), 1.59 – 1.42 (m, 2 H, maj + 2 H, min), 1.37 – 1.24 (m, 1 H, maj + 1 H, min), 0.88 – 0.65 (m, 4 H, maj + 4 H, min); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 171.5 (s, min), 170.8 (s, maj), 91.5 (s, maj), 88.5 (s, min), 72.3 (s, maj), 69.4 (s, min), 58.4 (s, maj), 57.6 (s, min), 56.0 (q, min), 55.5 (q, maj), 31.0(d, min), 30.7(d, maj), 21.9 (t, min), 21.3 (t, maj), 8.65 (t, maj), 8.58 (t, maj), 8.4 (t, 2 CH_2, min), –0.43 (d, maj), –0.65 (d, min); HRMS: (ESI) Calculated for $C_{10}H_{13}NNaO_2$ [M+Na]$^+$: 202.0838, found: 202.0846.

(1*R,2*R**)-2-(3,3-Dimethylbut-1-yn-1-yl)-1-methyl-2-methoxycyclopropanecarboxamide (2g).** Colorless liquid; 208 mg, 99.5% yield; R_f = 0.04 (HxH/AcOEt: 7/3); ^{1}H NMR (300 MHz) δ = 6.10 (bs, 1 H), 5.84 (bs, 1 H), 3.40 (s, 3 H), 1.56 (d, *J* = 5.9 Hz, 1 H), 1.44 (s, 3 H), 1.20 (s, 9 H), 1.00 (d, *J* = 5.9 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 174.0 (s), 95.8 (s), 74.0 (s), 59.7 (s), 55.6 (q), 34.9 (s), 30.8 (q, 3 CH_3), 27.5 (s), 26.1 (t), 15.4 (q); HRMS: (ESI) Calculated for $C_{12}H_{19}NNaO_2$ [M+Na]$^+$: 232.1308, found: 232.1300.

(1*R,2*R**)-2-[(4-Chlorophenyl)ethynyl)]-2-methoxy-*N*-methylcyclopropanecarboxamide (2h).** Yellow solid; 216 mg, 82% yield, of a mixture of diastereomers 5:1; after chromatographic separation 200 mg, 77% yield, of a 89:11 mixture of diastereoisomers was isolated; the following data have been obtained from that mixture and correspond to the major isomer: R_f = 0.02 (HxH/AcoEt: 5/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35 (d, *J* = 8.5 Hz, 2 H), 7.25 (d, *J* = 8.5 Hz, 2 H), 5.93 (bs, 1 H), 3.45 (s, 3 H), 2.84 (d, *J* = 4.4 Hz, 3 H), 2.05 (dd, *J* = 9.6, 7.3 Hz, 1H), 1.71 (dd, *J* = 7.3, 5.7 Hz, 1H), 1.50 (dd, *J* = 9.6, 5.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.3 (s), 134.4 (d), 133.0 (d, 2 CH), 128.6 (d, 2 CH), 120.95 (s), 85.5 (s), 85.1 (s), 58.2 (s), 55.9 (q), 31.5 (q), 26.7 (d), 20.7 (t); LRMS: (EI) *m/z* (%) = 265 ([M]$^+$, 5), 263 ([M]$^+$, 16), 250 (19), 248 (83), 217 (52), 205 (100), 191 (84), 163 (99), 141 (25), 139 (76), 112 (94); HRMS: (EI) calculated for $C_{14}H_{14}ClNO_2$ [M]$^+$: 263.0713, found: 263.0709.

(1*R,2*R**)-2-Methoxy-*N*-methyl-2-{[4-(trifluoromethyl)phenyl]ethynyl}cyclopropane carboxamide (2i).** White solid; 250 mg, 84% yield, of a mixture of diastereomers 5:1; R_f = 0.08 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60 – 7.48 (m, 8 H, maj + min), 6.04 (bs, 1 H, min), 5.76 (bs, 1 H, maj), 3.51 (s, 3 H, min), 3.48 (s, 3 H, maj), 2.87 (d, *J* = 4.8 Hz, 3 H, maj), 2.85 (d, *J* = 4.9 Hz, 3 H, min), 2.21 (dd, *J* = 9.4, 7.5 Hz, 1 H, min), 2.05 (dd, *J* = 9.6, 7.3 Hz, 1 H, maj), 1.79 (dd, *J* = 7.5, 5.9 Hz, 1 H, min), 1.77 (dd, *J* = 7.3, 5.7 Hz, 1 H, maj), 1.68 (dd, *J* = 9.4, 5.9 Hz, 1 H, min), 1.53 (dd, *J* = 9.6, 5.7 Hz, 1 H, maj); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.5 (C, min), 168.1 (C, maj), 132.0 (2 CH, maj), 131.9 (2 CH, min), 130.1 (q, $^2J_{C\text{-}F}$ = 32.7 Hz, C, maj), 126.3 (C, maj), 125.3 (q, $^3J_{C\text{-}F}$= 3.8 Hz, C, min), 125.1 (q, $^3J_{C\text{-}F}$ = 3.7 Hz, C, maj), 123.9 (q, $^1J_{C\text{-}F}$ = 271.0 Hz, C, maj), 89.2 (C, min), 86.8 (C, maj), 85.2 (C, maj), 82.7 (C, min), 59.6 (C, min), 58.2 (C, maj), 56.5 (CH_3, min), 55.9 (CH_3, maj), 31.6 (CH_3, maj + min), 26.7 (CH, maj), 26.5 (CH, min), 22.8 (CH_2, maj), 21.0 (CH_2, min) [three signals corresponding to -CF_3, to F_3C-C-, and to C*sp*–C*sp*^{2} of the minor isomer were not observed]; LRMS: (EI) *m/z* (%) = 297 ([M]$^+$, 50), 282 (64), 251 (53), 239 (100), 197 (91), 112 (66); HRMS: (EI) calculated for $C_{15}H_{14}F_3NO_2$ [M]$^+$: 297.0977, found: 297.0975.

(1*R,2*R**)-2-Methoxy-2-[(4-methoxyphenyl)ethynyl]-*N*-methylcyclopropanecarboxamide**. **(2j).** Yellow solid; 205 mg, 79% yield, of a mixture of diastereomers 4:1; R_f = 0.08 (Hex/AcoEt: 5/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36 (d, *J* = 8.5 Hz, 2 H, maj + 2 H, min), 6.81 (d, *J* = 8.5 Hz, 2 H, maj + 2 H, min), 6.13 (bs, 1 H, min), 5.93 (bs, 1 H, maj), 3.80 (s, 3 H, min), 3.79 (s, 3 H, maj), 3.48 (s, 3 H, min), 3.45 (s, 3 H, maj), 2.84 (d, *J* = 4.7 Hz, 3 H, maj), 2.82 (d, *J* = 4.2 Hz, 3 H, min), 2.08 (dd, *J* = 9.7, 7.7 Hz, 1 H, min), 2.04 (dd, *J* = 9.8, 7.1 Hz, 1 H, maj), 1.69 – 1.61 (dd, *J* = 7.1, 5.8 Hz, 1 H, maj + 1 H, min), 1.52 – 1.45 (dd, *J* = 9.8, 5.8 Hz, 1 H, maj + 1 H, min); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.6 (s, maj), 159.8 (s, maj), 133.5 (d, 2 CH, min), 133.3 (d, 2 CH, maj), 114.0 (d, 2 CH, min), 113.9 (d, 2 CH, maj), 110.0 (d, maj), 109.5 (d, min), 86.8 (s, maj), 82.5 (s, maj), 58.2 (s, maj), 55.7 (q, maj), 55.3 (q, maj), 31.6 (q, min), 31.5 (q, maj), 26.6 (d, maj), 21.2 (t, min), 20.9 (t, maj) – signals not listed of minor isomer either are superimposed or have not been observed –; LRMS: (EI) *m/z* (%) = 259 ([M]$^+$, 18), 244 (19), 202 (40), 201 (100), 187 (43), 159 (49), 112 (39); HRMS: (EI) calculated for $C_{15}H_{17}NO_3$ [M]$^+$: 259.1208, found: 259.1211.

(1R*,2R*)-2-(3,3-Dimethylbut-1-yn-1-yl)-2-methoxy-*N*-methylcyclopropanecarboxamide. (2k). Yellow liquid; 142 mg, 68% yield, of a mixture of diastereomers 5:1; R_f = 0.10 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.93 (bs, 2 H, min + maj), 3.40 (s, 3 H, min), 3.37 (s, 3 H, maj), 2.83 – 2.79 (d, *J* = 4.9 Hz, 3 H, maj + m, 3 H, min), 1.96 (dd, *J* = 10.0, 7.5 Hz, 1H, maj + m, 1 H, min), 1.45 – 1.39 (m, 4 H, min + maj), 1.22 (s, 9 H, maj), 1.21 (s, 9 H, min) –the values of the coupling constants correspond to the major isomer–; ^{13}C NMR (reported data correspond to major isomer) (100 MHz, $CDCl_3$) δ = 168.9 (s), 96.3 (s), 73.3 (s), 57.5 (s), 55.4 (q), 31.1 (q), 30.8 (q, 3 CH_3), 27.5 (s), 26.4 (d), 20.9 (t); LRMS: (EI) *m/z* (%) = 209 ([M]$^+$, 3), 194 (100), 151 (28), 91 (45), 79 (30); HRMS: (ESI) calculated for $C_{12}H_{20}NO_2$ [M+H]$^+$: 210.1489, found: 210.1486.

(1*R,2*R**)-2-[(Cyclopent-1-yl)ethynyl]-2-methoxycyclopropanecarboxamide (2l).** Yellow liquid; 182 mg, 88% yield, of a mixture of diastereomers 5:1; R_f = 0.07 (Hex/AcOEt: 5/1); the following data have been obtained from that mixture and correspond to the major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.17 (bs, 1 H), 6.06 (bs, 1 H), 3.36 (s, 3 H), 2.68 – 2.59 (m, 1 H), 1.99 – 1.92 (m, 1 H), 1.92 – 1.82 (m 2 H), 1.72 – 1.63 (m, 2 H), 1.62 – 1.49 (m, 4 H), 1.49 – 1.43 (m, 1 H) 1.40 (dd, *J* = 9.6, 5.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.1 (s), 92.4 (s), 73.8 (s), 58.3 (s), 55.4 (q), 33.8 (t, 2 CH_2), 30.7 (d), 30.1 (d), 24.9 (t, 2 CH_2), 21.0 (t); LRMS: (EI) *m/z* (%) = 207 ([M]$^+$, 5), 192

(63), 163 (81), 91 (100), 55 (50); HRMS: (EI) calculated for $C_{12}H_{17}NO_2$ $[M]^+$: 207.1259, found: 207.1265.

(1*R,2*R**)-2-(3,3-Dimethylbut-1-yn-1-yl)-2-methoxycyclopropanecarboxamide (2m).** Colorless liquid; 172 mg, 88% yield, of a mixture of diastereomers 5:1; R_f = 0.08 (HxH/AcOEt: 5/1); the following data have been obtained from that mixture and correspond to the major isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ = 5.72 (bs, 1 H), 5.42 (bs, 1 H), 3.41 (s, 3 H), 1.99 (t, *J* = 8.8 Hz, 1 H), 1.50 (d, *J* = 8.8 Hz, 2 H), 1.25 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.7 (s), 96.7 (s), 72.9 (s), 58.1 (s), 55.4 (q), 30.8 (q, 3 CH_3), 30.0 (s), 27.6 (d), 21.5 (t); LRMS: (EI) *m/z* (%) = 195 ($[M]^+$, 2), 180 (100), 163 (18), 151 (25), 91 (45), 55 (21); HRMS: (ESI) calculated for $C_{11}H_{18}NO_2$ $[M]^+$: 193.1332, found: 196.1337.

General procedure for the synthesis of (1*R,2*S**)-[2-methoxy-2-(alkynyl)cyclopropyl]methanols (3).** The corresponding alkynylcyclopropanecarboxylic ester[10, 25] [1 mmol, used as mixture of diastereomers] was dissolved in THF (10 mL) in a 50 mL round bottomed flask under inert atmosphere. Then $LiBEt_3H$ [2 equiv, 2 mmol, 2.0 mL (1.0 M solution in THF] was added at –78 ºC and the mixture was stirred for 12 hr. When the end of the reaction was observed by TLC NaOH 1M (25 mL) was added. THF was removed by evaporation under reduced pressure, the crude was extracted with ether (2 x 25 mL) and the combined organic layer was dried with Na_2SO_4. The ether was removed by evaporation under reduced pressure leading to the corresponding alcohol **3** as a liquid in the yield indicated below. Alcohols **3** were used without further purification when clean crude ^{1}H-NMR spectra where obtained and purified by column chromatography (HxH/EtOAc 5/1) when necessary.

(1*R,2*S**)-[2-Methoxy-2-(*p*-tolylethynyl)cyclopropyl]methanol (3b).** Colorless liquid; 212 mg, 98% yield, of a mixture of diastereomers 5:1; R_f = 0.09 (Hexane/AcOEt, 5/1); ^{1}H NMR (401 MHz, $CDCl_3$) δ = 7.33 (d, *J* = 8.0 Hz, 2 H maj + 2 H min), 7.12 (d, *J* = 8.0 Hz, 2 H maj + 2 H min), 3.95 (dd, *J* = 11.6, 5.0 Hz, 1 H, min), 3.83 (dd, *J* = 11.9, 5.8 Hz, 1 H, maj), 3.65 (dd, *J* = 11.6, 8.4 Hz, 1 H, min), 3.57 (dd, *J* = 11.9, 8.9 Hz, 1 H, maj), 3.50 (s, 3 H, min), 3.45 (s, 3 H, maj), 2.35 (s, 6 H, min + maj), 2.06 (sa, 2 H, min + maj), 1.72 – 1.65 (m, 2 H, min + maj), 1.32 (dd, *J* = 10.0, 5.6 Hz, 1 H, maj), 1.17 (dd, *J* = 9.6, 5.6 Hz, 1 H, min), 0.99 – 0.89 (m, 2 H, min + maj); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 138.7 (s, maj), 138.4 (s, min), 131.7 (d, 2 CH, maj), 131.6 (d, 2 CH, min), 129.1 (d, 2 CH, maj), 129.0 (d, 2 CH, min), 119.6 (s, min), 119.3 (s, maj), 87.5 (s, min), 85.8 (s, maj), 85.1 (s, maj), 83.9 (s, min), 63.4 (t, maj), 61.3 (t, min), 57.1 (s, maj), 56.1 (s, min), 56.0 (q, min), 55.7 (q, maj), 29.8 (d, min), 28.9 (d, maj), 21.5 (t, 2 CH_2, min + maj), 20.3 (q, maj), 18.7 (q, min); LRMS: (EI) *m/z* (%)= 216 ($[M]^+$, 1), 185 (100), 169 (29), 155 (68), 143 (95), 129 (47); HRMS: (EI) calculated for $C_{14}H_{16}O_2$ $[M]^+$: 216.1150, found: 216.1154.

(1*R,2*S**)-[2-Methoxy-2-(*o*-tolylethynyl)cyclopropyl]metanol (3c).** Colorless liquid; 214 mg, 99% yield, of a mixture of diastereomers 6.7:1; R_f = 0.09 (Hexane/AcOEt, 5/1); ^{1}H NMR (401 MHz, $CDCl_3$) δ= 7.43 – 7.37 (m, 2 H, min + maj), 7.23 – 7.18 (m, 4 H, min + maj), 7.16 – 7.11 (m, 2 H, min + maj), 4.00 – 3.91 (m, 1 H, min), 3.90 – 3.80 (m, 1 H, maj), 3.65 – 3.57 (m, 1 H, min), 3.56 – 3.46 (m, 1 H, maj), 3.53 (s, 3 H, min), 3.48 (s, 3 H, maj), 2.44 (s, 6 H, min + maj), 1.76 – 1.62 (m, 2 H, min + maj), 1.36 (dd, *J* = 9.5, 5.6 Hz, 1 H, maj), 1.20 (dd, *J* = 9.5, 5.6 Hz, 1 H, min), 0.98 – 0.90 (m, 1 H, maj), 0.83 – 0.74 (m, 1H, min), the signal corresponding to OH group was not observed; ^{13}C NMR (75 MHz, $CDCl_3$) (data for major isomer) δ = 140.5 (s), 132.4 (d), 129.8 (d), 128.6 (d), 125.9 (d), 123.1 (s), 90.4 (s), 84.8 (s), 64.1 (t), 57.9 (s), 56.0 (q), 28.2 (d), 21.1 (t), 20.8 (q); HRMS: (EI) calculated for $C_{14}H_{16}O_2$ $[M]^+$: 216.1150, found: 216.1155.

(1*R,2*S**)-[2-Methoxy-2-(4-methoxyphenylethynyl)cyclopropyl]methanol (3d).** Colorless liquid; 228 mg, 98% yield, of a mixture of diastereomers 4:1; R_f = 0.09 (Hexane/AcOEt, 5/1); ^{1}H NMR (401 MHz, $CDCl_3$) δ = 7.37 (d, *J* = 8.6 Hz, 2 H maj + 2H min), 6.83 (d, *J* = 8.6 Hz, 2 H maj + 2H min), 3.98 – 3.92 (m, 1 H, min), 3.86 – 3.74 (m, 1 H, maj), 3.79 (s, 6 H, min + maj), 3.72 – 3.66 (m, 1 H, min), 3.56 (dd, *J* = 11.6, 9.0 Hz, 1 H, maj), 3.48 (s, 3 H, min) 3.44 (s, 3H, maj), 2.41 (bs, 2 H, min + maj), 1.72 – 1.61 (m, 2 H, min + maj), 1.34 – 1.18 (m, 2 H, min + may), 0.92 – 0.87 (m, 2 H, min + maj); ^{13}C NMR (101 MHz, $CDCl_3$) δ (data for major isomer) = 159.8 (s), 133.3 (d, 2 CH), 114.5 (s), 114.0 (d, 2 CH), 85.6 (s), 84.4 (s), 63.4 (t), 57.2 (s), 55.6 (q), 55.3 (q), 28.9 (d), 20.2 (t); LRMS: (EI) *m/z* (%) = 232 ($[M]^+$, 3), 201 (100), 171 (11), 159 (40), 55 (18); HRMS: (EI) calculated for $C_{14}H_{16}O_3$ $[M]^+$: 232.1099, found: 232.1096.

(1*R,2*S**)-[2-(4-Chlorophenylethynyl)-2-methoxycyclopropyl]methanol (3e).** Yellow liquid; 166 mg, 70% yield, of a mixture of diastereomers 5:1; R_f = 0.10 (Hexane/AcOEt, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.36 (d, *J* = 8.4 Hz, 2 H maj + 2 H min), 7.28 (d, *J* = 8.4 Hz, 2 H maj), 7.27 (d, *J* = 8.4 Hz, 2 H min), 3.95 (dd, *J* = 11.6, 5.1 Hz, 1 H min), 3.81 (dd, *J* = 11.9, 5.9 Hz, 1 H maj), 3.65 – 3.52 (m, 2 H, maj + min), 3.49 (s, 3 H, min), 3.45 (s, 3 H, maj), 2.28 (bs, 2 H, maj + min), 1.81 – 1.60 (m, 2 H, maj + min), 1.34 (dd, *J* = 10.0, 5.6 Hz, 1 H maj), 1.18 (dd, *J* = 9.6, 5.7 Hz, 1 H min), 1.00 – 0.89 (m, 2 H, maj + min); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 134.5 (s, maj), 134.3 (s, min), 133.0 (d, 2 CH maj + 2 CH min), 128.7 (d, 2 CH, maj), 128.6 (d, 2 CH, min), 121.2 (s, min), 120.9 (s, maj), 89.4 (s, min), 87.0 (s, maj), 84.6 (s, maj), 82.7 (s, min), 63.3 (t, maj), 61.2 (t, min), 59.2 (s, min), 57.1 (s, maj), 56.1 (q, min), 55.8 (q, maj), 29.9 (d, min), 29.0 (d, maj), 20.3 (t, maj), 18.7 (t, min); HRMS: (EI) calculated for $C_{13}H_{13}ClO_2$ $[M]^+$: 236.0604, found: 236.0600.

(1*R,2*S**)-[2-Methoxy-2-(4-trifluoromethylphenylethynyl)-cyclopropyl]methanol (3f).** Yellow liquid; 243 mg, 90% yield, of a mixture of diastereomers 5:1; R_f = 0.11 (Hexane/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60 – 7. 51 (m, 4 H maj + 4 H min), 4.01 – 3.93 (m, 1 H min), 3.85 (dd, *J* = 11.8, 5.8 Hz, 1 H maj), 3.69 – 3.62 (m, 1 H, min), 3.57 (dd, *J* = 11.8, 9.0 Hz, 1 H maj), 3.47 (s, 3 H, maj), 3.45 (s, 3 H, min), 1.78 – 1.55 (m + bs, 4 H, maj + min), 1.38 (dd, *J* = 10.0, 5.7 Hz, 1 H maj), 1.25 – 1.18 (m, 1 H min), 1.06 – 0.88 (m, 2 H, maj + min); ^{13}C NMR data from the major isomer: ^{13}C NMR (100 MHz, $CDCl_3$) δ = 131.9 (2 CH), 130.2 (q, $^2J_{C\text{-}F}$ = 33.0 Hz, C), 126.2 (C), 125.3 (q, $^3J_{C\text{-}F}$ = 3.6 Hz, 2 CH), 123.8 (q, $^1J_{C\text{-}F}$ = 272.1 Hz, C), 88.7 (C), 84.4 (C), 63.3 (CH_2), 57.1 (C), 55.9 (CH_3), 29.0 (CH), 20.4 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ = –62.86 (min), –62.89 (maj); LRMS: (EI) *m/z* (%) = 270 ($[M]^+$, <3), 239 (100), 197 (24), 183 (14), 155 (15); HRMS: (ESI) calculated for $C_{14}H_{13}F_3NaO_2$ $[M+Na]^+$: 293.0760, found: 293.0759.

(1*R,2*S**)-[2-(Hex-1-yn-1-yl)-2-methoxycyclopropyl]methanol (3g).** Colorless liquid; yield = 173 mg, 95% yield, of a mixture of diastereomers 5:1; R_f = 0.09 (Hexane/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.87 (dd, *J* = 11.7, 5.2 Hz, 1 H, min), 3.76 (dd, *J* = 11.9, 5.7 Hz, 1 H, maj), 3.57 (dd, *J* = 11.7, 8.3 Hz, 1 H, min), 3.42 (dd, *J* = 11.9, 9.0 Hz, 1 H, maj), 3.39 (s, 3 H, min), 3.35 (s, 3 H, maj), 2.24 (t, *J* = 7.0 Hz, 2 H, maj), 2.20 (t, *J* = 7.1 Hz, 2 H, min), 1.95 (bs, 2 H, min + maj), 1.57 – 1.34 (m, 10 H, min + maj), 1.17 (dd, *J* = 10.0, 5.6 Hz, 1 H, maj), 0.99 (dd, *J* = 9.5, 5.6 Hz, 1 H, min), 0.90 (t, *J* = 7.2 Hz, 3 H, maj), 0.89 (t, *J* = 7.1 Hz, 3 H,

min), 0.82 (dd, *J* = 6.8, 5.6 Hz, 1 H, min), 0.74 (dd, *J* = 6.7, 5.6 Hz, 1 H maj); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 86.4 (s, maj), 84.4 (s, min), 79.0 (s, min), 76.5 (s, maj), 63.5 (t, maj), 61.4 (t, min), 56.8 (s, maj), 56.0 (s, min), 55.6 (q, min), 55.2 (q, maj), 30.8 (t, maj), 29.3 (d, min), 28.2 (d, maj) , 21.9 (t, maj), 19.8 (t, maj), 18.4 (t, maj), 18.3 (t, min), 13.5 (q, maj) –several signals of the minor diastereomer were not observed–; HRMS: (ESI) calculated for $C_{11}H_{19}O_2$ $[M+H]^+$: 183.1380, found: 183.1377.

(1*R,2*S**)-{2-[(Cyclopent-1-yl)ethynyl]-2-methoxycyclopropyl}methanol (3h).** Colorless liquid; 179 mg, 92% yield, of a mixture of diastereomers 5:1; R_f = 0.11 (Hexane/AcOEt, 5/1); the following data have been obtained from that mixture and correspond to the major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.77 (dd, *J* = 12.0, 5.7 Hz, 1 H), 3.41 (dd, *J* = 12.0, 9.1 Hz, 1 H), 3.35 (s, 3 H), 2.72 – 2.58 (m, 1 H), 1.97 – 1.79 (m, 3 H), 1.77 – 1.65 (m, 2 H), 1.64 – 1.47 (m, 5 H), 1.17 (dd, *J* = 9.9, 5.5 Hz, 1 H), 0.75 (at, *J* = 6.2, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 90.8 (s), 76.0 (s), 63.6 (t), 56.8 (s), 55.2 (q), 34.0 (t, 2 CH_2), 30.2 (d), 28.3 (d), 24.9 (t, 2 CH_2), 20.0 (t); HRMS: (EI) calculated for $C_{12}H_{18}O_2$ $[M]^+$: 194.1307, found: 194.1313. HRMS: (ESI) Calculated for $C_{12}H_{18}NaO_2$ $[M+Na]^+$: 217.1199, found: 217.1197.

(1*R,2*S**)-[2-Methoxy-1-methyl-2-(phenylethynyl)-cyclopropyl]methanol (3i).** Colorless liquid; 167 mg, 77% yield = 77% (one diastereomer); R_f = 0.49 (Hexane/AcOEt, 7/3); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.52 – 7.41 (m, 2 H), 7.36 – 7.30 (m, 3 H), 3.78 (d, *J* = 11.8, 1 H), 3.59 (d, *J* = 11.8, 1 H), 3.50 (s, 3 H), 1.60 (br s, 1H) 1.77 (bs, 1 H), 1.38 (s, 3 H), 1.06 (d, *J* = 5.6 Hz, 1 H), 0.97 (d, *J* = 5.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 131.6 (d, 2 CH), 128.42 (d), 128.35 (d, 2 CH), 122.4 (s), 86.8 (s), 85.2 (s), 68.6 (t), 59.7 (s), 56.1 (q), 32.4 (s), 25.8 (t), 14.3 (q); HRMS: (ESI) Calculated for $C_{14}H_{16}NaO_2$ $[M+Na]^+$: 239.1042, found: 239.1044.

(1*R,2*R**)-2-(3,3-Dimethylbut-1-yn-1-yl)-2-methoxycyclopropylmethanol (3j).** Colorless liquid; 49 mg, 27% yield, of a mixture of diastereomers 14:1; R_f = 0.39 (HxH/AcOEt, 7/3); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.77– 3.65 (m, 1 H, maj + 1 H, min), 3.47 – 3.36 (m, 1 H, maj + 1 H, min), 3.33 (s, 3 H, min), 3.32 (s, 3 H, maj), 2.19 (bs, 1 H, maj + 1 H, min), 1.93 – 1.77 (m, 1 H, min), 1.59 – 1.41 (m, 1 H, maj), 1.22 – 1.12 (m, 1 H, maj + 1 H, min), 1.20 (s, 9 H, maj), 1.18 (s, 9 H, min), 1.02 – 0.83 (m, 1 H, min), 0.77 – 0.69 (m, 1 H, maj); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 94.7 (s), 74.9 (s), 63.5 (t), 56.6 (s), 55.1 (q), 30.9 (q), 28.1 (d), 27.5 (s), 20.0 (t); HRMS: (EI) Calculated for $C_{11}H_{18}NaO_2$ $[M+Na]^+$: 205.1199, found: 205.1193.

(1*R,2*R**)-2-Methoxy-2-(trimethylsilylethynyl)cyclopropylmethanol (3k).** Colorless liquid; 147 mg, 74% yield, of a mixture of diastereomers 12:1; R_f = 0.22 (HxH/AcOEt, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.77 – 3.69 (m, 1 H, maj + 1 H, min), 3.55 – 3.39 (m, 1 H, maj + 1 H, min), 3.40 (s, 3 H, min), 3.37 (s, 3 H, maj), 2.44 (bs, 1 H, min), 2.20 (bs, 1 H, maj) 1.62 – 1.45 (m, 1 H, maj + 1 H, min), 1.27 – 1.10 (m, 1 H, maj + 1 H min), 0.89 – 0.76 (m, 1 H, maj + 1 H, min) 0.20 (s, 9 H, min), 0.16 (s, 9 H, maj); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 102.4 (s, maj), 90.8 (s), 63.2 (t), 57.0 (s), 55.5 (q), 28.7 (d), 20.3 (t), –0.1 (q, 3 CH_3); HRMS: (ESI) Calculated for $C_{10}H_{19}O_2Si$ $[M + H]^+$: 199.1149, found: 199.1153.

General procedure for the synthesis of azepinones 5 and/or azepindiones 15: A solution of freshly lyophilized IPrAuCl (3 mol%, 0.015 mmol, 9.3 mg) and AgOTs (3 mol%, 0.015 mmol, 4.2 mg) in 1,2-dichloroethane (5 mL) was placed in a sealed tube under Ar atmosphere and protected from light. The mixture was stirred during 30 min, and a solution of the corresponding alkynylcyclopropanecarbamide **2** (0.5 mmol) in CH_2Cl_2 (5 mL) was then added; stirring was maintained for 12 h at 110 ºC (at 80 ºC, for azepindione **15f,g**). End of reaction was monitored by TLC; solvents were removed under vacuum and the crude reaction mixture was purified by flash chromatography using hexane/AcOEt (5:1) as eluent to give the corresponding azepinone **5** and/or azepindione **15** in the yield indicated in Scheme 2.

For starting alkynylcyclopropanecarboxamides **3i** and **3j**, mixtures of azepinones **5i,j** and azepindiones **15i,j** were obtained under the general procedure. The reaction crude was then dissolved in dichloromethane, silica-gel was added and the mixture was allowed to stir overnight at room temperature. The reaction mixture was filtered, solvents were evaporated under vacuum and tresidue was purified by flash chromatography using hexane/AcOEt (5:1) as eluent to give the corresponding azepindione **15i,j** in the yield indicated in Scheme 2.

5-Methoxy-7-(*o*-tolyl)-1*H*-azepin-2(3*H*)-one (5d). Colorless liquid; 83 mg, 72 % yield; R_f = 0.27 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35 – 7.19 (m, 4 H), 7.02 (bs, 1 H), 5.76 (s, 1 H), 4.73 (t, *J* = 7.1 Hz, 1 H), 3.62 (s, 3 H), 2.93 (d, *J* = 7.1 Hz, 2 H), 2.35 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.0 (s), 156.1 (s), 139.3 (s), 137.3 (s), 135.9 (s), 130.7 (d), 129.5 (d), 129.3 (d), 126.2 (d), 111.8 (d), 89.8 (d), 55.6 (q), 33.2 (t), 19.9 (q); LRMS: (EI) *m/z* (%) = 229 ($[M]^+$, 100), 215 (60), 200 (58), 160 (44), 130 (85); HRMS: (EI) calculated for $C_{14}H_{15}NO_2$ $[M]^+$: 229.1103, found: 229.1103.

7-(4-Methoxyphenyl)-3,4-dihydro-1*H*-azepin-2,5-dione (15e). Yellow oil; 55 mg, 48% yield; R_f = 0.13 (HxH/AcOEt: 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.50 (d, *J* = 8.8 Hz, 2 H), 6.97 (d, *J* = 8.8 Hz, 2 H), 5.83 (s, 1 H), 3.87 (s, 3 H), 2.93 – 2.86 (m, 2 H), 2.84 – 2.77 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 197.9 (s), 174.6 (s), 162.5 (s), 147.2 (s), 129.2 (s), 129.0 (d, 2 CH), 115.0 (d, 2 CH), 110.9 (d), 55.9 (q), 36.8 (t), 31.0 (t); LRMS: (EI) *m/z* (%) = 231 ($[M]^+$, 90), 202 (34), 189 (61), 175 (69), 134 (100); HRMS: (EI) calculated for $C_{13}H_{13}NO_3$ $[M]^+$: 231.0895, found: 231.0900.

7-(Cyclopropyl)-3,4-dihydro-1*H*-azepin-2,5-dione (15f) Yellow-orange oil; 49 mg, 59% yield; R_f = 0.28 (HxH/AcOEt: 7/3); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.77 (s, 1 H), 5.39 (s, 1 H), 2.83 – 2.74 (m, 2 H), 2.74 – 2.65 (m, 2 H), 1.61 – 1.51 (m, 1 H), 1.05 – 0.90 (m, 2 H), 0.88 – 0.67 (m, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 197.2 (s), 174.2 (s), 151.1 (s), 108.0 (d), 35.8 (t), 30.4 (t), 17.5 (d), 7.7 (t, 2 CH_2); HRMS: (ESI) Calculated for $C_9H_{11}NNaO_2$ $[M+Na]^+$: 188.0682, found: 188.0686.

7-(*tert*-Butyl)-3,4-dihydro-3-methyl-1*H*-azepin-2,5-dione (15g) Yellow-orange liquid; 36 mg, 37% yield; R_f = 0.28 (HxH/AcOEt: 7/3); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.68 (s, 1 H), 2.93 – 2.81 (m, 1 H), 2.78 – 2.53 (m, 2 H), 1.70 (bs, 1 H), 1.27 (d, *J* = 7.2 Hz, 3H), 1.25 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 198.1 (s), 176.5 (s), 155.8 (s), 108.6 (d), 44.6 (t), 37.1 (s) 33.4 (d), 28.6 (q, 3 CH_3), 15.5 (q); HRMS: (ESI) Calculated for $C_{11}H_{18}NO_2$ $[M+H]^+$: 196.1332, found: 196.1337.

7-(4-Chlorophenyl)-5-methoxy-1-methyl-1*H*-azepin-2(3*H*)-one (5h). Yellow liquid; 69 mg, 52% yield; R_f = 0.10 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38 (d, *J* = 8.6 Hz, 2 H), 7.33 (d, *J* = 8.6 Hz, 2 H), 6.10 (s, 1 H), 4.60 (t, *J* = 7.0 Hz, 1 H), 3.62 (s, 3 H), 2.85 (s, 3 H), - a signal, which should appear as a doublet, corresponding to CH_2 was not observed-; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.1 (s), 155.1 (s), 144.1 (s), 135.7 (s), 134.9 (s), 129.1 (d, 2 CH), 128.7 (d, 2 CH), 115.3 (d), 93.7 (d), 55.5 (q), 35.0 (q), 33.7 (t); LRMS: (EI) *m/z* (%) = 265 (27), 264 (33), 263 ($[M]^+$, 80), 262 (100), 236 (17), 234 (50), 152 (22), 55 (23);

HRMS: (EI) calculated for $C_{14}H_{14}ClNO_2$ $[M]^+$: 263.0713, found: 263.0713.

1-Methyl-7-(4-trifluoromethylphenyl)-3,4-dihydro-1*H*-azepin-2,5-dione (15i). Yellow liquid; 125 mg, 88% yield; R_f = 0.32 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.72 (d, *J* = 8.2 Hz, 2 H), 7.51 (d, *J* = 8.2 Hz, 2 H), 5.87 (s, 1 H), 3.06 – 3.01 (m, 2 H), 2.92 (s, 3 H), 2.87 – 2.82 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 199.8 (C), 173.7 (C), 150.4 (C), 140.6 (C), 132.2 (q, $^2J_{C-F}$ = 32.8 Hz, C), 127.9 (2 CH), 126.1 (q, $^3J_{C-F}$ = 3.6 Hz, 2 CH), 123.6 (q, $^1J_{C-F}$ = 272.4 Hz, C), 118.8 (CH), 39.3 (CH_2), 36.3 (CH_3), 31.2 (CH_2); LRMS: (EI) *m/z* (%) = 283 ($[M]^+$, 63), 254 (50), 228 (100), 186 (95), 145 (37). HRMS: (EI) calculated for $C_{14}H_{12}F_3NO_2$ $[M]^+$: 283.0820, found: 283.0821.

7-(4-Methoxyphenyl)-1-methyl-3,4-dihydro-1*H*-azepin-2,5-dione (15j). Yellow oil; 86 mg, 70% yield; R_f = 0.19 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.31 (d, *J* = 8.8 Hz, 2 H), 6.95 (d, *J* = 8.8 Hz, 2 H), 5.85 (s, 1 H), 3.86 (s, 3 H), 3.06 – 2.97 (m, 2 H), 2.95 (s, 3H), 2.83 – 2.79 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 200.5 (s), 174.1 (s), 161.3 (s), 133.3 (s), 129.0 (d, 2 CH), 117.2 (d), 114.4 (d, 2 CH), 55.5 (q), 39.5 (t), 36.7 (q), 31.5 (t); LRMS: (EI) *m/z* (%) = 245 ($[M]^+$, 72), 216 (35), 204 (45), 148 (100), 190 (38); HRMS: (EI) calculated for $C_{14}H_{15}NO_3$ $[M]^+$: 245.1052, found: 245.1053.

7-(*tert*-Butyl)-1-methyl-3,4-dihydro-1*H*-azepin-2,5-dione (15k) Yellow liquid; 22 mg, 35% yield; R_f = 0.18 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.84 (s, 1 H), 3.31 – 3.22 (m, 2 H), 3.03 (s, 3H), 2.61 – 2.51 (m, 2H), 1.18 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 204.9 (s), 177.3 (s), 161.3 (s), 95.4 (d), 43.5 (s), 28.8 (q) 28.1 (t), 27.0 (q, 3 CH_3), 25.7 (t); LRMS: (EI) *m/z* (%) = 195 ($[M]^+$, 3), 152 (3), 138 (100), 82 (27); HRMS: (EI) calculated for $C_{11}H_{17}NO_2$ $[M]^+$: 195.1259, found: 195.1256.

General procedure for the synthesis of 4-methoxy-6-oxo-4-enenitriles 16. A solution of freshly lyophilized IPrAuCl (3 mol%, 0.015 mmol, 9.3 mg) and AgOTs (3 mol%, 0.015 mmol, 4.2 mg) in CH_2Cl_2 (5 mL) was placed in a sealed tube under Ar atmosphere and protected from light. The mixture was stirred during 30 min, and a solution of the corresponding alkynylcyclopropanecarbamide **2l,m** (0.5 mmol) in CH_2Cl_2 (5 mL) was then added; stirring was maintained for 12 h at 110 ºC. End of reaction was monitored by TLC; solvents were removed under vacuum and the crude reaction mixture was purified by flash chromatography using hexane/AcOEt (5:1) as eluent to give the corresponding oxoenenitrile **16** in the yield indicated in Scheme 3.

(*Z*)-6-Cyclopentyl-4-methoxy-6-oxohex-4-enenitrile (16a). Yellow liquid; 26 mg, 25% yield; R_f = 0.12 (HxH/AcOEt: 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.56 (s, 1 H), 3.71 (s, 3 H), 3.07 (t, *J* = 7.2 Hz, 2 H), 2.89 (p, *J* = 7.8 Hz, 1 H), 2.62 (t, *J* = 7.2 Hz, 2 H), 1.89 – 1.55 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 202.0 (s), 170.9 (s), 119.0 (s), 99.6 (d), 55.8 (q), 52.9 (d), 29.4 (t, 2 CH), 28.7 (t), 26.1 (t, 2 CH), 14.9 (t); LRMS: (EI) *m/z* (%) = 207 ($[M]^+$, 5), 166 (3), 138 (100), 69 (6); HRMS: (EI) calculated for $C_{12}H_{17}NO_2$ $[M]^+$: 207.1259, found: 207.1258.

(*Z*)-4-Methoxy-7,7-dimethyl-6-oxooct-4-enenitrile (16b) Yellow liquid; 51 mg, 52 % yield; R_f = 0.14 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.76 (s, 1 H), 3.71 (s, 3 H), 3.02 (t, *J* = 7.2 Hz, 2 H), 2.61 (t, *J* = 7.2 Hz, 2 H), 1.16 (s, 9 H);^{13}C NMR (100 MHz, $CDCl_3$) δ = 204.5 (s), 171.6 (s), 119.0 (s), 95.7 (d), 55.7 (q), 43.9 (s) 28.9 (t), 27.0 (q, 3 CH_3), 14.9 (t); LRMS: (EI) *m/z* (%) = 195 ($[M]^+$, <3), 138 (100), 69 (10); HRMS: (EI) calculated for $C_{11}H_{17}NO_2$ $[M]^+$: 195.1259, found: 195.1254.

Chloro[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]gold(I) – [IPrAuCl]. Commercial IPrAuCl (0.06 mmol, 37.3 mg) was dissolved in dry 1,2-dichloroethane (15 ml) in a Schlenk flask under Ar. An aliquot was then taken and analyzed by NMR. ^{1}H NMR (600 MHz, 1,2-dichloroethane with D_2O insert) δ = 7.32 (t, *J* = 8.0 Hz, 2 H), 7.11 (d, *J* = 8.0 Hz, 4 H), 7.04 (s, 2 H), 2.34 – 2.28 (m, 2 H), 1.09 (d, *J* = 7.3 Hz, 6 H), 0.99 (d, *J* = 7.4 Hz, 6 H).^{13}C NMR (150 MHz, 1,2-dichloroethane-[D_2O]) δ = 174.7 (C, carbene), 145.5 (2 CH_{Ar}), 133.8 (2 C_{Ar}), 130.5 (2 CH_{Ar}), 124.0 (2 CH_{Ar}), 123.2 (2 CH_{Im}), 28.5 (2 CH), 23.9 (2 CH_3), 23.4 (2 CH_3).

[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]gold(I) tosylate – [IPrAu(OTs)]. Freshly lyophilized AgOTs (0.06 mmol, 16.8 mg) is added to a solution of commercial IPrAuCl (0.06 mmol, 37.3 mg) in 1,2-dichloroethane (15 ml) in a Schlenk flask under Ar and protected from light. The mixture was stirred during 2 h at room temperature. An aliquot was then taken and analyzed by NMR (600 MHz), which confirmed the formation of the title compound. ^{1}H NMR (600 MHz, 1,2-dichloroethane with D_2O insert) δ = 7.36 (t, *J* = 8.1 Hz, 2 H), 7.12 (d, *J* = 8.2 Hz, 4 H), 7.08 (s, 2 H), 7.04 (d, *J* = 8.3 Hz, 2 H), 6.79 (d, *J* = 8.4 Hz, 2 H), 2.28 – 2.21 (m, 2 H), 1.04 (d, *J* = 7.4 Hz, 6 H), 0.99 (d, *J* = 7.7 Hz, 6 H).^{13}C NMR (150 MHz, 1,2-dichloroethane-[D_2O]) δ = 163.1 (C, carbene), 145.45 (2 CH_{Ar}), 140.4 (2 C_{Ts}), 133.5 (2 C_{Ar}), 130.6 (2 CH_{Ar}), 128.6 (2 CH_{Ts}), 125.6 (2 CH_{Ts}), 124.1 (2 CH_{Ar}), 123.6 (2 CH_{Im}), 30.2 (CH_3), 28.6 (2 CH), 23.7 (2 CH_3), 23.2 (2 CH_3).

Cycloisomerization of 2-alkynylcyclpropylmethanols 3. Synthesis of 6-methoxy-3-oxabicyclo[4.1.0]hept-4-enes 7. A solution of freshly lyophilized IPrAuCl (3 mol%, 0.015 mmol, 9.3 mg) and AgOTs (3 mol%, 0.015 mmol, 4.2 mg) in CH_2Cl_2 (5 mL) was placed in a sealed tube under Ar atmosphere and protected from light. The mixture was stirred during 30 min, and a solution of the corresponding alkynylcyclopropylmethanol **3** (0.5 mmol) in CH_2Cl_2 (5 mL) was then added at 0ºC; stirring was maintained for 12 h at that temperature. End of reaction was monitored by TLC; solvents were removed under vacuum and the crude reaction mixture was purified by flash chromatography using hexane/AcOEt mixtures as gradient eluent to give the corresponding 6-methoxy-3-oxabicyclo[4.1.0]hept-4-enes **7** in the yield indicated in Scheme 6.

(1*R,6*S**)-6-Methoxy-4-(4-methylphenyl)-3-oxabicyclo[4.1.0]hept-4-ene (7b).** Colorless liquid; 93 mg, 86% yield; R_f = 0.61 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.44 (d, *J* = 8.1 Hz, 2 H), 7.13 (d, *J* = 8.1 Hz, 2 H), 6.01 (s, 1 H), 4.26 (dd, *J* = 10.4, 1.3 Hz, 1 H), 3.97 (dd, *J* = 10.4, 2.1 Hz, 1 H), 3.40 (s, 3 H), 2.35 (s, 3 H), 1.82 – 1.73 (m, 1 H), 1.30 (dd, *J* = 9.9, 5.1 Hz, 1 H), 1.07 (at, *J* = 5.7 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.6 (s), 137.9 (s), 132.2 (s), 128.9 (d, 2 CH), 124.2 (d, 2 CH), 102.0 (d), 63.9 (t), 57.5 (s), 55.4 (q), 24.6 (t), 21.2 (q), 19.6 (d); LRMS: (EI) *m/z* (%) = 216 ($[M]^+$, 14), 143 (10), 132 (10), 120 (16), 119 (100), 91 (29); HRMS: (EI) calculated for $C_{14}H_{16}O_2$ $[M]^+$: 216.1150, found: 216.1147.

(1*R,6*S**)-6-Methoxy-4-(2-methylphenyl)-3-oxabicyclo[4.1.0]hept-4-ene (7c).** Colorless liquid; 83 mg, 77 % yield; R_f = 0.48 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.31 – 7.28 (m, 1 H), 7.24 – 7.21 (m, 1 H), 7.19 – 7.16 (m, 2 H), 5.66 (s, 1 H), 4.21 (dd, *J* = 10.2, 1.3 Hz, 1 H), 4.02 (dd, *J* = 10.2, 1.9 Hz, 1 H), 3.41 (s, 3 H), 2.36 (s, 3 H), 1.80 – 1.74 (m, 1 H), 1.34 (dd, *J* = 9.9, 5.1 Hz, 1 H), 1.10 (at, *J* = 5.6, Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 151.7 (s), 136.4 (s), 136.1 (s), 130.4 (d), 128.8 (d), 128.4 (d), 125.5 (d), 106.1 (d), 63.5 (t), 57.1 (s), 55.4 (q), 24.3 (t), 20.4 (d), 19.8 (q); HRMS: (EI) calculated for $C_{14}H_{16}O_2$ $[M]^+$: 216.1150, found: 216.1149.

(1*R,6*S**)-6-Methoxy-4-(4-methoxyphenyl)-3-**

oxabicyclo[4.1.0]hept-4-ene (7d). Colorless liquid; 96 mg, 83 % yield; R_f = 0.58 (HxH/AcOEt, 5/1); ^{1}H NMR (401 MHz, $CDCl_3$) δ = 7.48 (d, *J*= 8.9 Hz, 2 H), 6.86 (d, *J* = 8.9 Hz, 2 H), 5.92 (s, 1 H), 4.24 (dd, *J* = 10.4, 1.4 Hz, 1 H), 3.98 (dd, *J* = 10.4, 2.2 Hz, 1 H), 3.81 (s, 3 H), 3.39 (s, 3 H), 1.78 – 1.71 (m, 1 H), 1.29 (dd, *J* = 9.9, 5.1 Hz, 1 H), 1.05 (at, *J* = 5.7 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.6 (s), 149.4 (s), 131.0 (s), 127.8 (s), 125.6 (d, 2 CH), 114.0 (s), 113.6 (d, 2 CH), 101.0 (d), 64.0 (t), 57.5 (s), 55.4 (q), 55.3 (q), 24.4 (t), 19.6 (d); HRMS: (EI) calculated for $C_{14}H_{16}O_3$ $[M]^+$: 232.1099, found: 232.1094.

(1*R,6*S**)-4-(4-Chlorophenyl)-6-methoxy-3-oxabicyclo[4.1.0]hept-4-ene (7e).** Yellow liquid; 107 mg, 90% yield, of a 4/1 mixture of regioisomers (*endo*:*exo*); 86 mg, 72% yield, of *endo* regioisomer, after column chromatography; R_f = 0.53 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.47 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 6.06 (s, 1H), 4.26 (d, *J* = 10.4, 1.4 Hz, 1H), 3.96 (dd, *J* = 10.4, 1.6 Hz, 1H), 3.39 (s, 3H), 1.82 – 1.76 (m, 1H), 1.32 (dd, *J* = 9.9, 5.1 Hz, 1H), 1.07 (at, *J* = 5.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.4 (s), 133.8 (s), 133.4 (s), 128.4 (d, 2 CH), 125.5 (d, 2 CH), 103.6 (d), 63.9 (t), 57.6 (s), 55.5 (q), 24.8 (d), 19.7 (t); HRMS: (EI) Calculated for $C_{13}H_{13}ClO_2$ $[M]^+$: 236.0604, found: 236.0597.

(1*R,6*S**)-6-Methoxy-4-(4-trifluoromethylphenyl)-3-oxabicyclo[4.1.0]hept-4-ene (7f).** Yellow liquid; 101 mg, 75% yield, of a 1.2:1 mixture of regioisomers (*endo*:*exo*); 8 mg, 6% yield, of pure *endo* regioisomer + 72 mg, 53% yield, a 1.8:1 mixture of regioisomers obtained after column chromatography; R_f: 0.53 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.69 – 7.63 (m, 2 H), 7.57 (d, *J* = 8.3 Hz, 2 H), 6.22 (s, 1 H), 4.30 (d, *J* = 10.3 Hz, 1 H), 3.97 (d, *J* = 10.3 Hz, 1 H), 3.41 (s, 3 H), 1.87 – 1.79 (m, 1 H), 1.36 (dd, *J* = 9.7, 5.1 Hz, 1 H), 1.12 (at, *J* = 5.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) (data retrieved from a 1.8:1 mixture of regioisomers) δ = 148.0 (C), 138.3 (C), 129.7 (q, $^2J_{C\text{-}F}$ = 32.4 Hz, C), 125.2 (q, $^3J_{C\text{-}F}$ = 3.9 Hz, 2 CH), 124.4 (2 CH), 124.2 (q, $^1J_{C\text{-}F}$ = 271.2 Hz, C), 105.5 (d), 63.8 (t), 57.5 (s), 55.5 (q), 25.1 (d), 19.8 (t); ^{19}F NMR (282 MHz, $CDCl_3$) δ = –62.5; LRMS: (EI) *m/z* (%) = 270 ($[M]^+$, 2), 269 (8), 255 (100), 173 (15), 145 (19); HRMS: (ESI) calculated for $C_{13}H_{12}F_3O_2$ $[M–CH]^+$: 257.0784, found: 257.0785.

(1*R,6*S**)-4-Butyl-6-methoxy-3-oxabicyclo[4.1.0]hept-4-ene (7g).** Yellow liquid; 71 mg, 78% yield; R_f = 0.56 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.17 (s, 1 H), 4.02 (dd, *J* = 10.5, 1.3 Hz, 1 H), 3.85 (dd, *J* = 10.5, 2.4 Hz, 1 H), 3.31 (s, 3 H), 2.00 – 1.93 (m, 2 H), 1.44 – 1.24 (m, 5 H), 1.17 (dd, *J* = 9.9, 5.0 Hz, 1 H), 0.89 (t, *J* = 7.2 Hz, 3 H), 0.80 (at, *J* = 5.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.2 (s), 100.4 (d), 63.7 (t), 56.4 (s), 55.0 (q), 33.5 (t), 28.8 (t), 22.9 (d), 22.1 (t), 19.7 (t), 13.9 (q); LRMS: (EI) *m/z* (%) = 182 ($[M]^+$, 3), 167 (100), 125 (99), 97 (26), 59 (16); HRMS: (ESI) calculated for $C_{11}H_{19}O_2$ $[M+H]^+$: 183.1380, found: 183.1377.

(1*R,6*S**)-4-Cyclopentyl-6-methoxy-3-oxabicyclo[4.1.0]hept-4-ene (7h).** Yellow liquid; 81 mg, 83% yield; R_f = 0.54 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.21 (s, 1 H), 4.02 (d, *J* = 10.5 Hz, 1 H), 3.80 (dd, *J* = 10.5 Hz, 1 H), 3.31 (s, 3 H), 2.39 (p, *J* = 7.9 Hz, 1 H), 1.80 – 1.40 (m, 9 H), 1.16 (dd, *J* = 9.8, 5.0 Hz, 1 H), 0.80 (at, *J* = 5.3 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.1 (s), 99.0 (d), 63.9 (t), 56.5 (s), 55.0 (q), 43.7 (d), 30.3 (t), 30.2 (t), 25.38 (t), 25.36 (t), 23.2 (d), 19.4 (t); LRMS: (EI) *m/z* (%) = 194 ($[M]^+$, 5), 179 (42), 125 (100), 97 (22), 82 (12); HRMS: (EI) calculated for $C_{12}H_{18}O_2$ $[M]^+$: 194.1307, found: 194.1309.

(1*R,6*S**)-1-methyl-6-methoxy-4-phenyl-3-oxabicyclo[4.1.0]hept-4-ene (7i).** Colorless liquid corresponding to a 4.1:1 mixture of regioisomeric bicyclic ethers **7i** and **28i**; 90 mg, 83% combined yield. The following data have been retrieved from the mixture of regioisomers: R_f = 0.42 (HxH/AcOEt, 5/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.57 (d, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2 H), 7.32 - 7.27 (m, 1 H), 6.11 (s, 1 H), 4.18 (d, *J* = 10.1 Hz, 1 H), 3.71 (d, *J* = 10.1 Hz, 1 H), 3.47 (s, 3 H), 1.34 (s, 3 H), 1.26 (d, *J* = 5.0 Hz, 1 H), 1.01 (d, *J* = 5.0 Hz, 1 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.1 (s), 134.9 (s), 128.2 (d, 2 CH), 127.9 (d), 124.2 (d, 2 CH), 103.6 (d), 68.7 (t), 61.4 (s), 56.1 (q), 31.0 (s), 23.8 (t), 13.6 (q); HRMS: (ESI) Calculated for $C_{14}H_{16}NaO_2$ $[M+Na]^+$: 239.1042, found: 239.1034.

(1*R,5*S**,*Z*)-1-Methoxy-2-(4-methylbenzylyden)-3-oxabicyclo[3.1.0]hexane (8b).** Colorless liquid; 18 mg, 17 % yield; R_f = 0.61 (HxH/AcOEt, 5/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.48 (d, *J*= 8.1 Hz, 2 H), 7.12 (d, *J* = 8.1 Hz, 2 H), 5.47 (s, 1 H), 4.41 (dd, *J* = 8.8, 4.3 Hz, 1 H), 4.07 (d, *J* = 8.8 Hz, 1 H), 3.47 (s, 3 H), 2.34 (s, 3 H), 2.09 (ddd, *J* = 9.3, 5.4, 4.3 Hz, 1 H), 1.60 (dd, *J* = 9.3, 5.4 Hz, 1 H), 0.97 (t, *J* = 5.4 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 152.6 (s), 134.7 (s), 133.3 (s), 128.9 (d, 2 CH), 127.3 (2 CH), 97.2 (d), 72.5 (t), 70.9 (s), 56.8 (q), 21.4 (d), 21.2 (q), 20.9 (t); HRMS: (EI) calculated for $C_{14}H_{16}O_2$ $[M]^+$: 216.1150, found: 216.1153.

(1*R,5*S**,*Z*)-2-(4-Chlorobenzylydene)-1-methoxy-3-oxabicyclo[3.1.0]hexane (8e).** Yellow liquid; 19 mg, 16% yield in the reaction at 0ºC; 39 mg, 33% yield in the reaction at 85ºC; R_f = 0.59 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.50 (d, *J* = 8.6 Hz, 2 H), 7.24 (d, *J* = 8.6 Hz, 2 H), 5.44 (s, 1 H), 4.41 (dd, *J* = 8.9, 4.3 Hz, 1 H), 4.07 (d, *J* = 8.9 Hz, 1 H), 3.44 (s, 3 H), 2.13 – 2.07 (m, 1 H), 1.63 – 1.54 (m, 1 H), 0.95 (at, *J* = 5.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.1 (s), 134.7 (s), 130.3 (s), 128.6 (d, 2 CH), 128.3 (d, 2 CH), 96.3 (d), 72.8 (t), 71.0 (s), 56.8 (q), 21.4 (d), 21.0 (t); HRMS: (EI) Calculated for $C_{13}H_{13}ClO_2$ $[M]^+$: 236.0604, found: 236.0598.

(1*R,5*S**,*Z*)-6-Methoxy-4-(4-trifluoromethylphenyl)-3-oxabicyclo[4.1.0]hept-4-ene (8f).** Yellow liquid; 22 mg, 17% yield in the reaction at 0 ºC; 27 mg, 21% yield in the reaction at 85 ºC R_f = 0.53 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.69 – 7.63 (m, 2 H), 7.53 (d, *J* = 8.1 Hz, 2 H), 5.55 (s, 1 H), 4.44 (dd, *J* = 9.0, 4.3 Hz, 1 H), 4.10 (d, *J* = 9.0 Hz, 1 H), 3.45 (s, 3 H), 2.13 (adt, *J* = 9.1, 4.6 Hz, 1 H), 16.2 (dd, *J* = 9.1, 5.4 Hz, 1 H), 0.96 (at, *J* = 5.1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.3 (C), 140.2 (C), 129.6 (q, $^2J_{C\text{-}F}$ = 32.4 Hz, C), 127.7 (2 CH), 125.4 (q, $^3J_{C\text{-}F}$ = 4.1 Hz, 2 CH), 124.9 (q, $^1J_{C\text{-}F}$ = 270.9 Hz, C), 96.6 (d), 73.6 (t), 71.6 (s), 57.3 (q), 21.9 (d), 21.5 (t); ^{19}F NMR (282 MHz, $CDCl_3$) δ = –62.1; LRMS: (EI) *m/z* (%) = 270 ($[M]^+$, 100), 255 (25), 241 (24), 210 (25), 186 (25), 173 (25), 158 (54); HRMS: (ESI) Calculated for $C_{14}H_{14}F_3O_2$ $[M+H]^+$: 271.0940, found: 271.0939.

(1*R,5*S**)-1-methyl-5-methoxy-4-phenylethenylidene-3-oxabicyclo[3.1.0]hexane (8i).** Colorless liquid corresponding to a 4.1:1 mixture of regioisomeric bicyclic ethers **7i** and **8i**; 90 mg, 83% combined yield. The following data have been retrieved from the mixture of regioisomers: R_f = 0.42 (HxH/AcOEt, 5/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.60 (d, *J* = 7.5 Hz, 2 H), 7.32 - 7.27 (m, 2 H), 7.14 (t, *J* = 7.4 Hz, 1H), 5.48 (s, 1 H), 4.21 (d, *J* = 8.7 Hz, 1 H), 4.16 (d, *J* = 8.7 Hz, 1 H), 3.54 (s, 3 H), 1.45 (s, 3 H), 1.28 (d, *J* = 5.3 Hz, 1 H), 1.02 (d, *J* = 5.3 Hz, 1 H).^{13}C NMR (151 MHz, $CDCl_3$) δ 154.4 (s), 136.2 (s), 127.9 (d, 2 CH), 127.4 (d, 2 CH), 125.0 (d), 97.3 (d), 77.5 (t), 72.3 (s), 57.2 (q), 28.5 (s), 25.1 (t), 13.9 (q); HRMS: (ESI) Calculated for $C_{14}H_{16}NaO_2$ $[M+Na]^+$: 239.1042, found: 239.1034.

General procedure for the synthesis of 2-methyl-2,3-dihydropyran-4-ones 17. A solution of freshly lyophilized IPrAuCl (3 mol%, 0.015 mmol, 9.3 mg) and AgOTs (3 mol%, 0.015 mmol, 4.2 mg) in 1,2-dichloroethane (5 mL) was placed in a carousel tube under Ar atmosphere and protected from light. The mixture was stirred during 30 min, and a solution of the corresponding alkynylcyclopropylmethanol **3** (0.5 mmol) in CH_2Cl_2 (5 mL) was then added. Stirring was maintained at 85 ºC for approximately 12 h. (end of reaction was monitored by TLC). Solvents were removed under vacuum and the crude reaction mixture was purified by flash chromatography using hexane/AcOEt mixtures as gradient eluent to give the corresponding 2-methyl-2,3-dihydropyran-4-ones **17** in the yield indicated in Scheme 7.

Synthesis of 2-methyl-6-phenyl-2,3-dihydropyran-4-one 17a from 6-methoxy-4-phenyl-3-oxabicyclo[4.1.0]hept-4-ene 7a. A solution of 6-methoxy-4-phenyl-3-oxabicyclo[4.1.0]hept-4-ene **7a** (101 mg, 0.5 mmol) in 1,2-dichloroethane (5 mL) was placed under Ar atmosphere in an Schlenk flask equipped with a reflux condenser. Stirring was maintained at 85 ºC for approximately 12 h. (end of reaction was monitored by TLC). Solvents were removed under vacuum and the crude reaction mixture was purified by flash chromatography using hexane/AcOEt (5:1) as eluent to give 2-methyl-6-phenyl-2,3-dihydropyran-4-one **17a** in quantitative yield (94 mg).

2-Methyl-6-phenyl-2*H*-pyran-4(3*H*)-one (17a).[35] Colorless liquid; 85 mg, 90% yield, from alcohol **3a**; 94 mg, quantitative yield, from 2-methyl-6-phenyl-2,3-dihydropyran-4-one **7a**; R_f = 0.40 (Hexane/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.79 – 7.70 (m, 2 H), 7.50 – 7.40 (m, 3 H), 6.01 (s, 1 H), 4.77 – 4.62 (m, 1 H), 2.61 – 2.44 (m, 2 H), 1.58 (d, *J* = 6.3 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 193.5 (s), 170.4 (s), 132.8 (s), 131.6 (d), 128.7 (d, 2 CH), 126.5 (d, 2 CH), 101.9 (d), 76.0 (d), 42.9 (t), 20.5 (q); LRMS: (EI) *m/z* (%)= 188 ([M]$^+$, 43), 147 (15), 105 (100), 77 (22); HRMS: (EI) calculated for $C_{12}H_{12}O_2$ [M]$^+$: 188.0837, found: 188.0835.

2-Methyl-6-(4-methylphenyl)-2*H*-pyran-4(3*H*)-one (17b). Colorless liquid; 87 mg, 86% yield; R_f = 0.43 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64 (d, *J* = 8.1 Hz, 2 H), 7.23 (d, *J* = 8.1 Hz, 2 H), 5.98 (s, 1 H), 4.74 – 4.64 (m, 1 H), 2.61 – 2.45 (m, 2 H), 2.40 (s, 3 H), 1.58 (d, *J* = 6.3 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 193.5 (s), 170.6 (s), 142.2 (s), 130.0 (s), 129.4 (d, 2 CH), 126.5 (d, 2 CH), 101.3 (d), 75.9 (d), 43.0 (t), 21.5 (q), 20.5 (q); LRMS: (EI) *m/z* (%)= 202 ([M]$^+$, 21), 160 (9), 120 (6), 119 (100), 91 (11); HRMS: (EI) calculated for $C_{13}H_{14}O_2$ [M]$^+$: 202.0994, found: 202.0997.

2-Methyl-6-(2-methylphenyl)-2*H*-pyran-4(3*H*)-one (17c). Colorless liquid; 78 mg, 77 % yield; R_f = 0.43 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41 – 7.31 (m, 2 H), 7.26 – 7.19 (m, 2 H), 5.62 (s, 1 H), 4.80 – 4.66 (m, 1 H), 2.64 – 2.47 (m, 2 H), 2.42 (s, 3 H), 1.55 (dd, *J* = 6.4, 0.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 193.2 (s), 173.7 (s), 136.7 (s), 133.8 (s), 131.1 (d), 130.5 (d), 128.8 (d), 125.9 (d), 106.2 (d), 76.1 (d), 42.9 (t), 20.53 (q), 20.50 (q); HRMS: (EI) calculated for $C_{13}H_{14}O_2$ [M]$^+$: 202.0994, found: 202.0999.

2-Methyl-6-(4-methoxyphenyl)-2*H*-pyran-4(3*H*)-one (17d).[35] Colorless liquid; 94 mg, 83 % yield; R_f = 0.49 (HxH/AcOEt, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.70 (d, *J* = 8.9 Hz, 2 H), 6.92 (d, *J* = 8.9 Hz, 2 H), 5.93 (s, 1 H), 4.72 – 4.62 (m, 1 H), 3.85 (s, 3 H), 2.58 – 2.43 (m, 2 H), 1.56 (d, *J* = 6.3 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 193.3 (s), 170.3 (s), 162.4 (s), 128.3 (d, 2 CH), 125.0 (s), 114.0 (d, 2 CH), 100.6 (d), 75.8 (d), 55.4 (q), 42.9 (t), 20.5 (q).

6-(4-Chlorophenyl)-2-methyl-2*H*-pyran-4(3*H*)-one (17e). Colorless liquid; 59 mg, 53% yield; R_f = 0.41 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$): 7.67 (d, *J* = 8.7 Hz, 2 H), 7.40 (d, *J* = 8.7 Hz, 2 H), 5.97 (s, 1 H), 4.75 – 4.64 (m, 1 H), 2.61– 2.47 (m, 2 H), 1.58 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 193.2 (s), 169.1 (s), 137.7 (s), 131.3 (s), 128.9 (d, 2 CH), 127.8 (d, 2 CH), 102.0 (d), 76.1 (d), 42.9 (t), 20.4 (q); HRMS: (EI) calculated for $C_{12}H_{11}ClO_2$ [M]$^+$: 222.0448, found: 222.0447.

2-Methyl-6-(4-trifluoromethylphenyl)-2*H*-pyran-4(3*H*)-one (17f). Colorless liquid; 61 mg, 48 % yield; R_f = 0.45 (HxH/AcOEt: 5/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.2 Hz, 2 H), 7.70 (d, *J* = 8.2 Hz, 2 H), 6.05 (s, 1H), 4.90 – 4.61 (m, 1 H), 2.76 – 2.40 (m, 2 H), 1.61 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 193.2 (C), 168.5 (C), 136.2 (C), 127.8 (q, $^2J_{C\text{-}F}$ = 36.8 Hz, C), 126.8 (2 CH), 125.6 (q, $^3J_{C\text{-}F}$ = 3.8 Hz, 2 CH), 123.7 (q, $^1J_{C\text{-}F}$ = 273.8 Hz, C), 103.1 (CH), 76.4 (CH), 42.9 (CH_2), 20.4 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ = –63.0; LRMS: (EI) *m/z* (%) = 256 ([M]$^+$, 22), 215 (33), 173 (100), 145 (32), 69 (12); HRMS: (ESI) calculated for $C_{13}H_{12}F_3O_2$ [M+H]$^+$: 257.0784, found: 257.0783.

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UPDATE

Gold-Catalyzed Cycloisomerizations of Functionalyzed Cyclopropyl Alkynes: the Cases of Carboxamides and Alcohols

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