MASTERING THE REACTIVITY OF GOLD (I) CARBENES
Verónica López Carrillo

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Mastering the Reactivity of Gold(I) Carbenes

TESIS DOCTORAL

dirigida por el Prof. Antonio M. Echavarren

Institut Català d'Investigació Química (ICIQ)

UNIVERSITAT ROVIRA I VIRGILI

Tarragona
2010

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HAGO CONSTAR que este trabajo de investigación titulado "Mastering the Reactivity of Gold(I) Carbenes", que presenta Verónica López Carrillo para la obtención del título de doctor, ha sido realizado bajo mi dirección en el Institut Català d'Investigació Química vinculado a la Universidad Rovira i Virgili y que cumple los requisitos necesarios para poder optar a Mención Europea.

Tarragona, 30 de septiembre de 2010

El director de la Tesis Doctoral

Prof. Antonio M. Echavarren

No hay nada repartido de modo más equitativo que la razón: todo el mundo está convencido de tener suficiente.

René Descartes

Este trabajo de Tesis Doctoral se ha realizado en el Institut Català d'Investigació Química bajo la dirección del Profesor Antonio M. Echavarren, a quien quiero agradecer todo el tiempo y confianza que ha depositado en mí durante estos cuatro años.

El trabajo recogido en esta memoria se ha llevado a cabo gracias a una beca predoctoral del Institut Català d'Investigació Química desde octubre de 2006 hasta marzo de 2007 y una beca de Formación del Profesorado Universitario del Ministerio de Educación y Ciencia desde abril de 2007. Durante este periodo he realizado una estancia breve en el grupo de investigación del Profesor Kálmán Szabó (Stockholm University, Sweden, agosto-noviembre 2008) a quien agradezco su total disponibilidad y su acogida.

Por supuesto me gustaría agradecer el apoyo logístico de Sònia Gavaldà y Vanessa Martínez, si no fuera por su dedicación y lo bien que hacen las cosas todo habría sido mucho más difícil.

Mi trabajo de tesis habría durado algún año más sin la colaboración prestada por la Dra. Noemí Cabello y Alba González de espectrometría de masas; el Dr. Gabriel González y Kerman Gómez de RMN, el Dr. Jordi Benet-Buchholz y Eduardo Escudero del servicio de rayos X, y Enrique Cequier y Simona Curreli de la unidad de cromatografía del ICIQ. Sin dejar de nombrar a los técnicos de informática, Ángel Mosquera y David Pena, que siempre me han atendido ASAP. Gracias.

El dibujo de la portada se lo agradezco al artista y amigo Javier Burgos de Vergara; y a la ayuda logística de Laura y Mihai.

No puedo dejar de nombrar a todos mis compañeros tanto actuales como anteriores del laboratorio P2.2, P2.3 y de la fase II por todos los momentos compartidos. To my Swedish labmates: tack så mycket!! A mis compañeros y amigos del 101 (U.A.M.): gracias por apoyarme desde el principio. Al Profesor Diego J. Cárdenas y a la Dra. Elena Buñuel, les agradezco haberme dado la oportunidad de colaborar en su grupo de investigación y enseñarme a dar los primeros pasos en la química organometálica.

También quiero agradecer de forma muy especial a todos los que me han arropado con su amistad y cariño durante estos cuatro años: Mary, Noemí, Magda, mi comadre, Silvia Cura, Alla, mi mamá de Tarragona, Patri, Clau, Caroline, Madeleine, Marsha, Isabella, mi familia de la isla, Belen, Ramonjito, Henrick, Juhannes, Pavel,

Agradecimientos

cuasi-doctor Valencia, Mihai, Roy, Jose, Xacobe y Xisco. Lo mejor de haber hecho el doctorado aquí es haberme encontrado con vosotros.

Y por supuesto, gracias a todos mis amigos que en algún momento se han desplazado para acompañarme o recibieron grandes facturas telefónicas. A toda mi familia por estar siempre orgullosos y animarme a seguir adelante. A Rosa-Pink por recordarme que los buenos valores se tienen desde pequeña: nuestro cordón no se deteriora. A mis padres y mi hermano: sin vosotros no habría podido.

Hasta el momento de redactar esta memoria, los resultados aquí descritos han dado lugar a las siguientes publicaciones:

Gold(I)-Catalyzed [2+2] Cycloaddition of Alkynes with Alkenes
Verónica López-Carrillo, Antonio M. Echavarren.
J. Am. Chem. Soc. **2010**, *132*, 9292-9294.

Gold-Catalyzed Reactions of 1,5- and 1,6-Enynes with Carbonyl Compounds: Cycloadditions vs. Metathesis
Ana Escribano-Cuesta, Verónica López-Carrillo, Dominic Janssen, Antonio M. Echavarren.
Chem. Eur. J. **2009**, *15*, 5646-5650.

Gold(I)-Catalyzed Intermolecular Addition of Carbon Nucleophiles to 1,5- and 1,6-Enynes
Catelijne H. M. Amijs, Verónica López-Carrillo, Mihai Raducan, Patricia Pérez-Galán, Catalina Ferrer, Antonio M. Echavarren.
J. Org. Chem. **2008**, *73*, 7721-7730.

Gold(I)-Catalyzed Addition of Carbon Nucleophiles to Propargyl Carboxylates
Catelijne H. M. Amijs, Verónica López-Carrillo, Antonio M. Echavarren.
Org. Lett. **2007**, *9*, 4021-4024.

Por tener menos relación con el tema principal de esta memoria, no se han incluido los resultados aportados en la siguiente publicación:

Gold(I)-Catalyzed Allyl-Allyl Coupling
Susana Porcel, Verónica López-Carrillo, Cristina García-Yebra, Antonio M. Echavarren.
Angew. Chem. Int. Ed. **2008**, *47*, 1883-1886 (Hot paper).

Contents

Esta memoria del trabajo de Tesis Doctoral se ha dividido en siete partes: un resumen en castellano, una introducción general, tres capítulos de resultados y finalmente la parte experimental. Los capítulos 1 y 2 se dividen a su vez en tres secciones, una descripción de los objetivos del capítulo, un apartado de resultados y discusión, y por ultimo las conclusiones del capítulo. El tercer capítulo se ha dividido en cuatro apartados, tres de resultados y discusión, y un cuarto apartado con las conclusiones globales del capítulo.

En el apartado *Introduction* se recogen los principios básicos sobre catálisis homogénea de oro en las activaciones de alquinos, centrada principalmente en las reacciones de esters propargílicos y eninos, y en los aspectos mecanísticos de las mismas.

El trabajo recogido en el apartado *Chapter 2. Gold(I)-Catalyzed Addition of Carbon Nucleophiles to Propargyl Carboxylates* se ha realizado en colaboración con la Dra. Catelijne H. M. Amijs. Algunos de sus resultados se han incluido en forma de esquemas para asegurar la coherencia en el desarrollo de la discursión.

En el trabajo recogido en *Chapter 3.1. Ligand Controlled 1,5-Enyne Cyclization* han colaborado Ángeles Mosquera durante una estancia de tres meses y la doctoranda Nuria Huguet. Algunos de los resultados de Ángeles Mosquera se han incluido en forma de esquema para facilitar el desarrollo de la discursión.

Resumen

Durante los últimos años, nuestro grupo de investigación se ha centrado en el desarrollo de nuevos complejos de oro(I) y su aplicación en la activación de alquinos, en especial en el estudio de la ciclación de 1,6-[1] y 1,7-eninos.[2] De acuerdo con resultados teóricos y experimentales, la formación de los productos de ciclación de 1,6-eninos se puede explicar por activación del alquino al coordinarse el oro y ataque nucleófilo de la olefina, que pude dar lugar a dos intermedios según la ciclación sea 5-*exo*-dig o 6-*endo*-dig (*Esquema 1*).
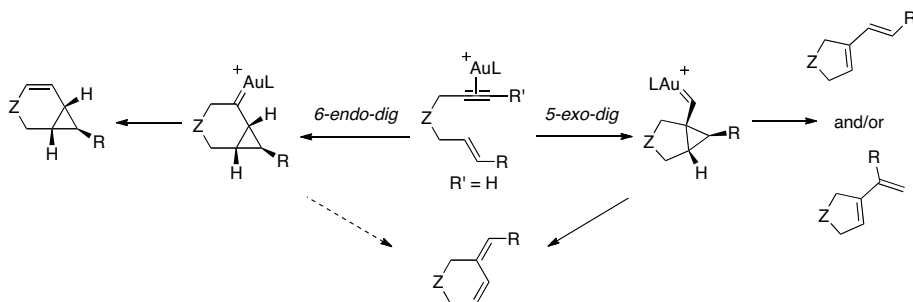
Esquema 1

La ciclación de 1,8-eninos también se ha descrito[3]. Hasta el inicio de esta tesis doctoral la máxima elongación descrita en la unión de alqueno y alquino era un único ejemplo de ciclación de 1,9-enino descrita por el grupo de Porco, en la que se utiliza un 50% de catalizador de oro(I) para obtener tan sólo 58% de un dieno cíclico (*Esquema 2*).[4]
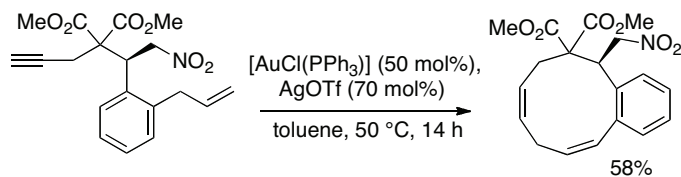
Esquema 2

Vista esta limitación en la ciclación de eninos, nos planteamos si sería posible desarrollar la versión intermolecular alquino/alqueno. En este trabajo se demuestra que la reacción intermolecular entre alquenos y alquinos catalizada por Au(I) es factible si se utilizan ligandos voluminosos de modo que el oro se coordine selectivamente al

1 Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326-3350.

2 Cabello, N.; Rodriguez, C.; Echavarren, A. M. *Synlett* **2007**, 1753-1758.

3 Odabachian, Y.; Gagosz, F. *Adv. Synth. Catal.* **2009**, *351*, 379-386.

4 Comer, E.; Rohan, E.; Deng, L.; Porco, J. A. *Org. Lett.* **2007**, *9*, 2123-2126.

Resumen

alquino y no al alqueno (*Esquema 3*). Es una reacción muy general que además abre nuevas oportunidades para el desarrollo de nuevos procesos intermoleculares catalizados por oro(I).
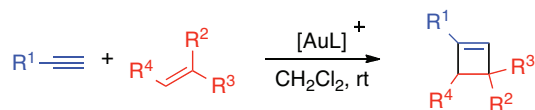
Esquema 3

Mecanísticamente se propone la participación de un ciclopropil carbeno de Au(I) muy distorsionado análogo al intermedio propuesto en la cicloisomerización de 1,6-eninos. El carácter carbénico de este intermedio se pone de manifiesto al aislar el producto de bisciclopropanación de alquinos con 1,5-dienos (*Esquema 4*).
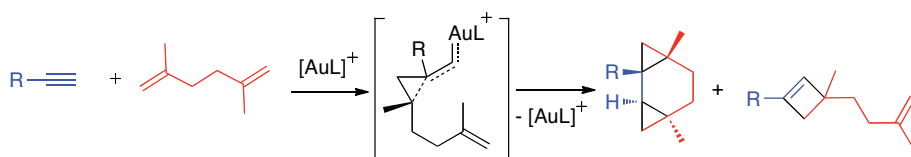
Esquema 4

En nuestro grupo de investigación se han obtenido evidencias sobre la formación de los ciclopropil carbenos de oro en la ciclación de 1,6-eninos al aislar los productos de ciclopropanación intra- e intermolecular en presencia de complejos de Au(I).[5] También se han utilizado nucleófilos carbonados como indol, trimetoxibenceno, compuestos 1,3-dicarbonílicos o alilsilanos para atrapar estos intermedios de reacción.[6]
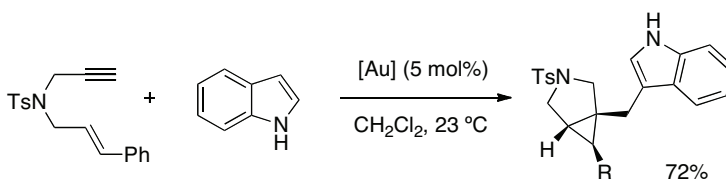
Esquema 5

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5 López, S.; Herrero-Gómez, H.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 6029-6032.

6 (a) Toullec, P. Y.; Genin, E.; Leseurre, L.; Genet, J.-P.; Michelet, *V. Angew. Chem. Int. Ed.* **2006**, *45*, 7427-7430. (b) Amijs, C. H. M.; Ferrer, C.; Echavarren, A. M. *Chem. Commun.* **2007**, 698-700. (c) Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M. *J. Org. Chem.* **2008**, *73*, 7721-7730. (d) Chao, C.M.; Vitale, M. R.; Toullec, P. Y.; Genêt, J.-P.; Michelet, V. *Chem. Eur. J.* **2009**, *15*, 1319-1323.

Como extensión de este proyecto nos propusimos atrapar los intermedios de reacción en la transposición de ésteres propargílicos catalizada Au(I). En esta Tesis Doctoral se describe la adición de compuestos 1,3-dicarbonílicos a los carbenos α,β-insaturados descritos como intermedios en la migración [1,2] de carboxilatos propargílicos, dando lugar a productos de adición de Michael o adición [1,2] sobre el carbono unido directamente al oro. Cuando la migración del éster es [1,3], se forman alenos que también pueden ser activados por oro y reaccionar con nucleófilos como compuestos 1,3-dicarbonílicos o anillos aromaticos ricos en electrones (*Esquema 6*).
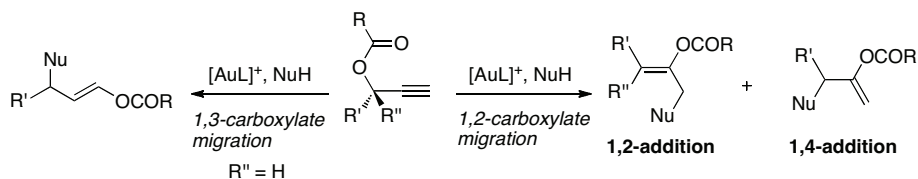
Esquema 6

Por otro lado, nos planteamos estudiar el mecanismo y reactividad de 1,5-eninos. La ciclación de 1,5-eninos catalizada por complejos de Au(I) ha demostrado ser un potente método para obtener diversidad estructural en condiciones de reacción muy suaves.[7] Sin embargo, la predictibilidad de la reacción es muy baja: pequeños cambios estructurales en el 1,5-enino dan lugar a productos de reacción completamente divergentes independientemente del catalizador de oro utilizado. Al introducir un grupo electroatrayente en la posición alílica del 1,5-enino hemos encontrado que se pueden obtener distintos productos al modular la electrofilia del catalizador (*Esquema 7*).
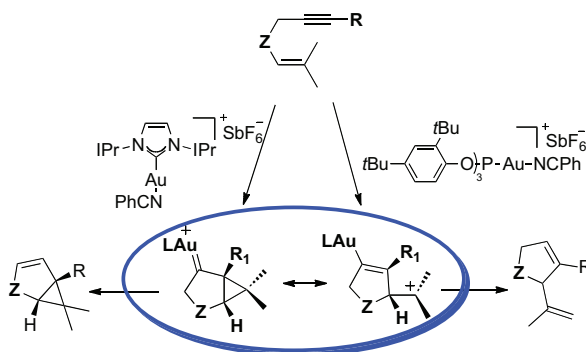
Esquema 7

7 Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271-2296. c) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351-3378.

La reacción catalizada por complejos de oro con fosfitos como ligandos da lugar a 1,4-dienos, sin embargo, los catalizadores con carbenos N-heterocíclicos (NHC) como ligandos dan lugar a la formación de biciclo[3.1.0]hexenes. Mecanísticamente se trata de un ataque intramolecular de la olefina sobre el alquino activado por Au(I) dando lugar a una ciclación 5-*endo-dig*, en la cual se forma un ciclopropil carbeno de Au(I) como intermedio. Cálculos DFT llevados a cabo sobre estos intermedios muestran que cuando el ligando es un fosfito el ciclopropilo está prácticamente abierto y tiene por tanto un carácter mucho más catiónico que en el caso de utilizar un carbeno N-heterocíclico como ligando.

Los intermedios ciclopropil carbeno de Au(I) propuestos es la ciclación de 1,5-eninos reaccionan de forma análoga a los intermedios en la ciclación de 1,6-eninos, de modo que pueden reaccionar in situ con alcoholes, agua o nucleófilos carbonados (*Esquema 8*).
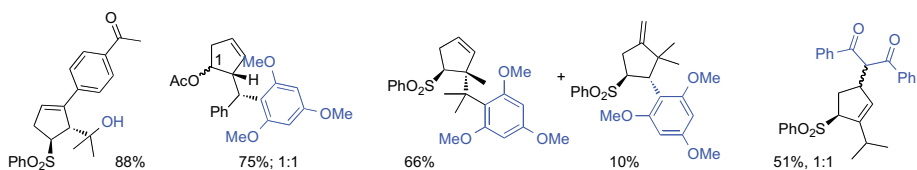
Esquema 8

Los intermedios de la ciclación de 1,5-eninos también se han podido interceptar con aldehídos y cetonas para obtener compuestos bicíclicos. En el caso de utilizar cinamaldehído con eninos aril sustituidos en el alquino, tiene lugar la fragmentación del intermedio formándose trienos conjugados tras extrusión de acetona (*Esquema 9*).
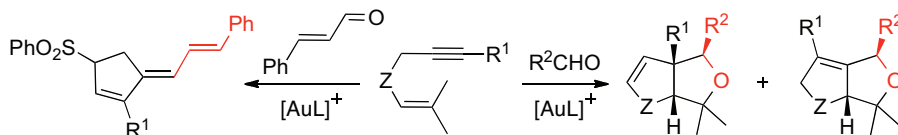
Esquema 9

Abbreviations and Acronyms

In this manuscript, the abbreviations and acronyms most commonly used in organic and organometallic chemistry have been used following the recommendations found in the on-line "Guidelines for authors" of the Journal of Organic Chemistry.

Additionally, I have also used the following abbreviations and acronyms:

BIPHEP	(Biphenyl-2,2′-diyl)bis(diphenylphosphine)
Bs	Brosyl (p-BrC$_6$H$_4$SO$_2$)
DFT	Density Funtional Theory
DNBS	2,4-Dinitrobenzenesulfonyl
DTBM	3,5-Di-*tert*-butyl-4-methoxyphenyl
Dppm	1,1-Bis(diphenylphosphino)methane
IMes	1,3-Bis(2,4,6-trimethylphenyl)imidazolidene
IPr	1,3-Bis(2,6-diisopropylphenyl)imidazolidene
PNBn	p-Nitrobenzyl
Tol	Tolyl

Introduction

Natural and synthetic alkynes are important molecules in our society. Alkyne moieties can be found in modern oral contraceptive pill that contains the synthetic strogen 17-ethinylestradiol (**I**), as well as in natural ocurring antibiotic and antitumoral drugs like calicheamicins (**II**). But the high importance of alkynes in our society relays on its reactivity, since they are strategic intermediates in total syntesis of bioactive compounds as well as monomers of useful polymers like polyacetylene. Therefore, organic chemists have a high interest on studying the reactivity of alkynes to develop new methods of functionalization under mild conditions.
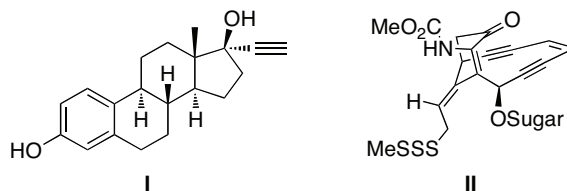
Figure I

Alkynes can react as nucleophiles by deprotonation of terminal alkynes by a strong base or with soft bases in the presence of a metal, since alkynes can also react as Lewis base donors towards metals. Bonding in metal-alkyne complexes can be explained by the Dewar-Chatt-Duncanson model. One of the π bonds of the alkyne can interact with a empty orbital on the metal to form a σ bond (**IV**), in the same way as a phosphine donates its lone pair to a metal. The second interaction in the metal-alkyne complex depends on the metal: (1) alkynes will behave as *σ donor/π donor* if the metal has empty d orbital to interact with the second π bond of the alkyne producing a metal-alkyne π bond (**III**); (2) alkynes can also be *σ donor/π acceptor* if the metal has a pair of electron in another d orbital that can overlap with the empty π* orbital on the alkyne producing a back-bonding interaction (**V**).
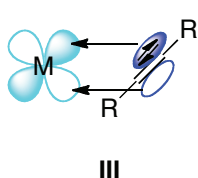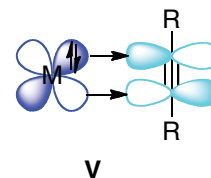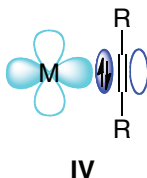
Figure II

The Dewar-Chatt-Duncanson model predicts an elongation of the triple bond by dumping electron density into the π^* orbital. As a consequence the alkyne is susceptible to nucleophilic attack to form alkenyl-metal complexes. A well known and generally used application of this metal-alkyne interaction is the addition of water to alkynes catalyzed by Hg(II)[1] salts under acidic conditions.[2] The mechanism starts by complexation of the alkyne by Hg(II) and subsequent Markovnikov addition of water to give a 2-hydroxy-1-alkenylmercury(II) compound. Protodemetalation occurs to give a metal-free enol which tautomerizes to the corresponding ketone.

Even though mercury(II)-catalyzed addition of water and alcohols to alkynes is well established, it has some serious drawbacks that under the reaction conditions Hg(II) is reduced to Hg(0), which is inactive in this reaction, and the high toxicity of Hg(II) salts and Hg(0). Alternative mercury-free catalysts using different metals have been studied.[3] In the industry, supported gold(III) catalyst has shown to be good substitute for $HgCl_2$ supported on carbon in the hydrochlorination of acetylene to form vinyl chloride (the precursor of polyvinylchloride). In organic synthesis, Hg(II) was also replaced by Au(III) in the hydration of alkynes (*Scheme I*).[4]

$$Ph\text{---}\!\!\!\equiv \quad \xrightarrow[\substack{MeOH/H_2O \\ 1\ h,\ reflux}]{NaAuCl_4\ (2\ mol\%)} \quad Ph\!\!\!\overset{O}{\underset{91\%}{\diagdown\!\!\diagup}} \quad (1)$$
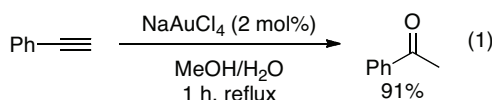
Scheme I

Laguna and co-workers identified possible intermediates in this reaction by spectroscopic methods.[5] At low temperatures, Au(III)-alkyne (**VI**) and Au(III)-alkenyl (**VII**) intermediates were detected in the hydration of phenyl acetylene, which were

1 Smith, M. B.; March, J. in *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*; Sixth Edition; Wiley, New York, **2007**.

2 The uncatalyzed hydration of alkynes is extremely difficult due to the instability of alkenyl cations, thus it has been described for terminal alkynes at 200ºC under microwave irradiation: Vasudevan, A.; Verzal, M. K. *Synlett* **2004**, 631-634.

3 (a) Halpern, J.; James, B. R.; Kemp, A. L. W. *J. Am. Chem. Soc.* **1961**, *83*, 4097-4098. (b) Halpern, J.; James, B. R.; Kemp, A. L. W. *J. Am. Chem. Soc.* **1966**, *88*, 5142-5147. (c) Hiscox, W.; Jennings, P. W. *Organometallics* **1990**, *9*, 1997-1999. (d) Hartman, J. W.; Hiscox, W. C.; Jennings, P. W. *J. Org. Chem.* **1993**, *58*, 7613-7614. (e) Baidossi, W.; Lahav, M.; Blum, J. *J. Org. Chem.* **1997**, *62*, 669-672. (f) Suzuki, T.; Tokunaga, M; Wakatsuki, Y *Org. Lett.* **2001**, *3*, 735-737.

4 Fukuda, Y.; Utimoto, K. *J. Org. Chem.* **1991**, *56*, 3729-3731.

5 Casado, R.; Contel, M.; Laguna, M.; Romero, P.; Sanz, S. *J. Am. Chem. Soc.* **2003**, *125*, 11925-11935.

consistent with the mechanism suggested for Hg(II). Based on these results, it was proposed that the terminal alkyne coordinates to Au(III) and nucleophilic attack of water leads to the Au(III)-alkenyl intermediate (**VII**). The final ketone was formed by keto-enol equilibrium, protonation of **VIII** and consequent regeneration of the catalyst (*Scheme II*).
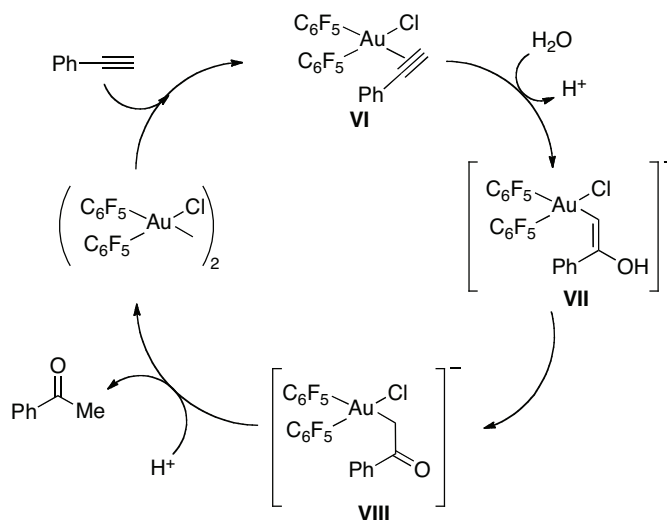
Scheme II

However, due to the instability of gold(III) the catalyst is quickly reduced to inactive metallic gold. An important improvement was reported by the group of Teles using air stable gold(I) complexes of the general type [AuMe(L)] (where L is phosphine, phosphite or arsine), which were activated in situ with protic acids.[6] Tanaka and co-workers also applied [AuMe(PPh₃)] in the presence of protic acids for the hydration of alkynes in methanol as solvent.[7] In both cases, the reaction can be applied for the synthesis of ketones in good yields from terminal and internal alkynes (*Scheme III*).

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6 Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem. Int. Ed.* **1998**, *37*, 1415-1418.

7 Mizushima, E.; Sato, K.; Hayashi, T.; Tanaka, M. *Angew. Chem. Int. Ed.* **2002**, *41*, 4563-4565.
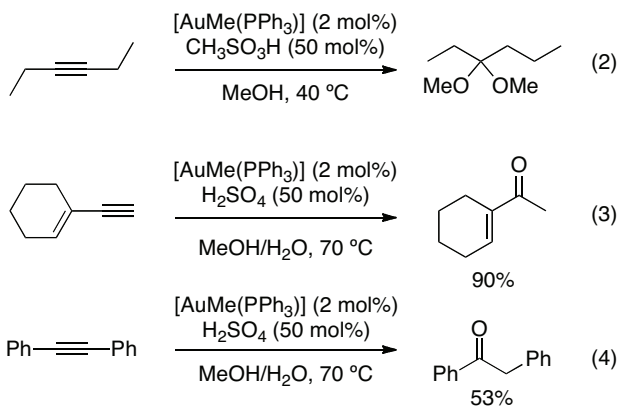
Scheme III

Gold(I) complexes for alkyne activation

Simple commercially available gold salts such as $NaAuCl_4$ or $AuCl$ are active enough to catalyze additions to alkynes but gold(III) can be reduced to gold(0) by easily oxidizable substrates and $AuCl$ tends to suffer desproportionation. To stabilize gold(I) oxidation state, donor ligands such as phosphines[6] are commonly used. The catalitically active species $[AuL]^+$ are generate in situ by cleavage of the Au-alkyl bond with a protic acid in complexes such as $[AuMe(PPh_3)]$.[6,7] Similarly, cationic gold(I) can be formed in situ by chloride abstraction from $[AuCl(L)]$ using one equivalent of a silver salt with a non-coordinating anion.[8] Different types of gold(I) complexes **A-D**[9] bearing bulky, biphenyl-based phosphines, which were developed as ligands for Pd-catalyzed

8 (a) Nieto-Oberhuber, C; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. _Angew. Chem. Int. Ed._ **2004**, _43_, 2402-2406. (b) Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Núñez, E.; Nevado, C.; Herrero-Gómez, E., Raducan, M.; Echavarren, A. M. _Chem. Eur. J._ **2006**, _12_, 1677-1693. (c) Ferrer, C.; Raducan, M.; Nevado, C.; Claverie, C. K.; Echavarren, A. M. _Tetrahedron_ **2007**, _63_, 6306-6316.

9 (a) **A-F** structures were confirmed by X-ray crystallography: Herrero-Gómez, E.; Nieto-Oberhuber, C.; López, S.; Benet-Buchholz, J.; Echavarren, A. M. _Angew. Chem. Int. Ed._ **2006**, _45_, 5455-5459. (b) Partyka, D. V.; Robilotto, T. J.; Zeller, M.; Hunter, A. D.; Gray, T. G. _Organometallics_ **2008**, _27_, 28-32.

reactions,[10] lead to very active catalysts upon being mixed with Ag(I) salts.[11] More convenient catalysts are the cationic derivatives of the general type [Au(S)(L)]X (L = phosphine ligand, S = solvent molecule) **E-F** since they do not require activation with silver salts and are stable crystalline solids that can be handled under ordinary conditions. Related complexes **G-H** with weakly coordinated bis(trifluoromethanesulfonyl)amide (NTf$_2$) have also been reported.[12]

Phosphite as ligand showed to form more active catalyst [AuL]$^+$ in the addition of methanol to propyne: Ph$_3$P (TOF= 610 h^{-1}) < (MeO)$_3$P (TOF = 1200 h^{-1}) < (PhO)$_3$P (TOF = 1500 h^{-1}).[6] Phosphite gold(I) complexes **J**[13] and its cationic derivative **K**,[14] bearing tris(2,6-di-*tert*-butylphenyl)phosphite are one of the most electrophilic cationic gold(I) catalysts.

Gold complexes with highly donating ligand such as **L-O** bearing N-heterocyclic ligands (NHC) are also good precatalysts.[11,15,16,17] Their cationic derivative **P-R**,[14,18] and those with NTf$_2$ as ligand (**S-T**) have also been reported.[19,20]

10 (a) Kaye, S.; Fox, J. M.; Hicks, F. A.; Buchwald, S. L. *Adv. Synth. Catal.* **2001**, *343*, 789-794. (b) Walker, S. D.; Barder, T. E.; Martinelli, J. R.; Buchwald, S. L. Angew. Chem. Int. Ed. **2004**, *43*, 1871-1876. (c) Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 13978-13980. (d) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685-4696. (e) Barder, T. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 5096-5101.

11 Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178-6179.

12 Mézailles, N.; Ricard, L.; Gagosz, F. *Org. Lett.* **2005**, *7*, 4133-4136.

13 (a) López, S.; Herrero-Gómez, H.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 6029. (b) **J** structure was confirmed by X-Ray crystallography: Nieto-Oberhuber, C.; Pérez-Galán, P.; Herrero-Gómez, E.; Lauterbach, T.; Rodríguez, C.; López, S.; Bour, C.; Rosellón, A.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2008**, *130*, 269-279.

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15 (a) Deetlefs, M.; Raubenheimer, H. G.; Esterhuysen, M. W. *Cat. Today.* **2002**, *72*, 29-41. (b) Schneider, S. K.; Herrmann, W. A.; Herdtrweck, E. Z. *Anorg. Allg. Chem.*, **2002**, *629*, 2363-2370.

16 de Frémont, P.; Scott, N. M.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2005**, *24*, 2411-2418.

17 For NHC-Au(III) complexes see: de Frémont, P.; Singh, R.; Stevens, E. D.; Petersen, J. L.; Nolan, S. P. *Organometallics* **2007**, *26*, 1376-1385.

18 de Frémont, P.; Stevens, E. D.; Fructos, M. R.; Diaz-Requejo, M. M.; Perez, P. J.; Nolan, S. P. *Chem Commun* **2006**, 2045-2047.

19 Li, G.; Zhang, L. *Angew. Chem. Int. Ed.* **2007**, *46*, 5156-5159.

20 Ricard, L.; Gagosz, F. *Organometallics* **2007**, *26*, 4704-4707.
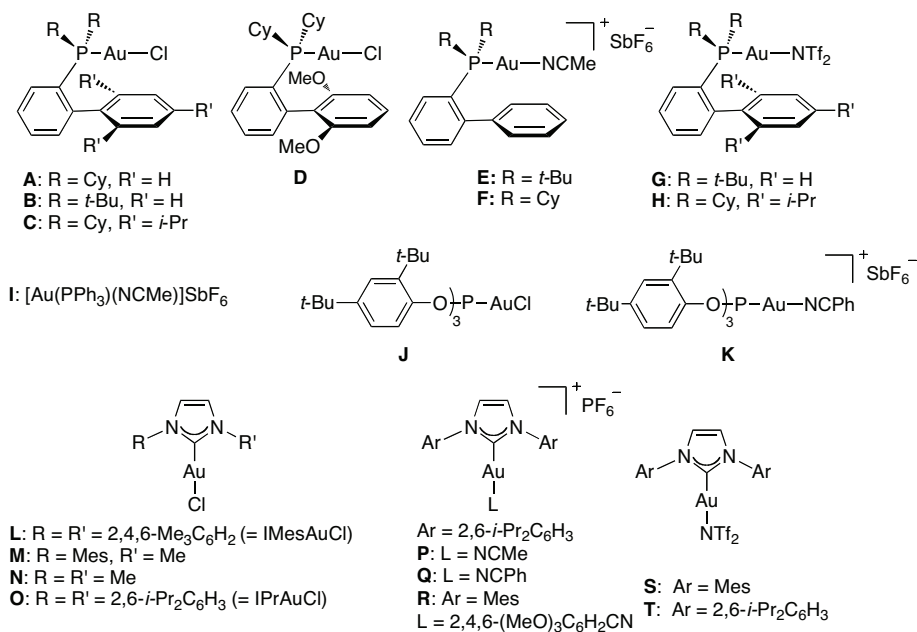
Figure III

Gold-catalyzed addition of heteronucleophiles to alkynes.

The utility of gold(I) complexes for the activation of alkynes towards inter- and intramolecular nucleophilic attack has been demonstrated for a wide range of heteronucleophiles such as amines,[21] imines,[22] azides,[23] sulfoxides,[24] or thiols.[25]

Intramolecular addition of nucleophiles to alkynes deserves special mention when the nucleophile is located at the propargylic position. Propargylic alcohols

---

21 (a) Mizushima, E.; Hayashi, T.; Tanaka, M. *Org. Lett.* **2003**, *5*, 3349-3352. (b) Istrate, F. M.; Gagosz, F. *Org. Lett.* **2007**, *9*, 3181-3184.

22 Kusama, H.; Miyashita, Y.; Takaya, J.; Iwasawa, N. *Org. Lett.* **2006**, *8*, 289-292.

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25 Nakamura, I.; Sato, T.; Yamamoto, Y. *Angew. Chem. Int. Ed.* **2006**, *45,* 4473-4475. (b) Nakamura, I.; Sato, T.; Yamamoto, Y. *Org. Lett.* **2007**, *9*, 4081-4083.

undergo gold-catalyzed Meyer-Schuster rearrangement[26] to yield α,β-unsaturated carbonyl compounds (*Scheme IV*).[27] In contrast, propargylic cyclopropanols and cyclobutanols undergo migration of a carbon-carbon σ bond onto the gold-activated alkyne leading to ring expansion (*Scheme IV*).[28] Similar alkyl migrations were observed in the gold-catalyzed intramolecular oxidation of propargyl alcohols with sulfoxides to form 1,3-dicarbonyl compounds.[29]
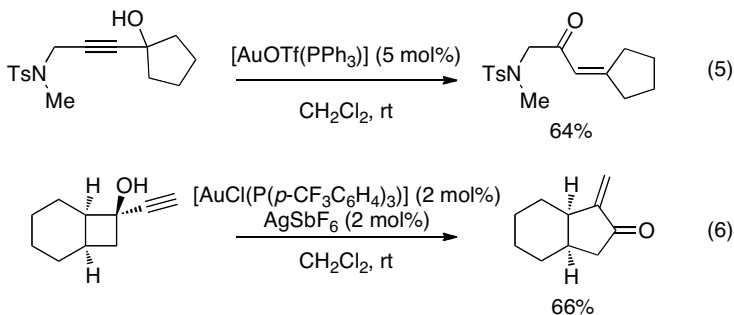
Scheme IV

Propargyl carboxylates in gold catalysis.

When the propargylic alcohol is protected as carboxylate,[30] carbamate or thiocarbamate,[31] more complex transformations are observed.[32]

Thus, gold(I) is an efficient catalyst for the rearrangement of propargylic esters (*Scheme V*),[33] a process known as the Rautenstrouch rearrangement that also occurs with other electrophilic metal salts and complexes.[32]

26 Swaminathan, S.; Narayan, K. V. *Chem. Rev.* **1971**, *71*, 429-438.

27 (a) Engel, D. A.; Dudley, G. B. *Org. Lett.* **2006**, *8*, 4027-4029. (b) Lee, S.-I.; Baek, J. Y.; Sim, S. H.; Chung, Y. K. *Synthesis* **2007**, 2107-2114. (c) López, S. S.; Engel, D. A.; Dudley, G. B. *Synlett* **2007**, 949-953.

28 Markham, J. P.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 9708-9709.

29 Li, G. T.; Zhang, L. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 5156-5159.

30 Marion, N.; Nolan, S. P. *Angew. Chem. Int. Ed.* **2007**, *46*, 2750-2752.

31 Ikeda, Y.; Murai, M.; Abo, T.; Miki, K.; Ohe, K. *Tetrahedron Lett.* **2007**, *48*, 6651-6654.

32 (a) Strickler, H.; Davis, J.B.; Ohloff, O. *Helv. Chim. Acta* **1976**, *59*, 1328-1332. (b) Rautenstrauch, V. *J. Org. Chem.* 1984, *49*, 950-952.

33 Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654-8655.
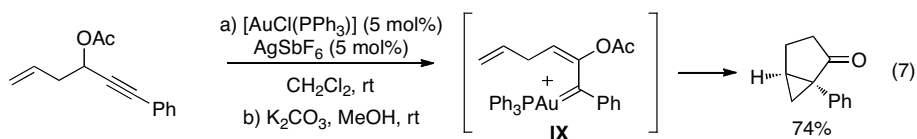
Scheme V

Gold(I) carbene intermediate **IX** was proposed as a reasonable intermediate in the postulated mechanism of Pd(II)-catalyzed Rautenstrauch rearrangement. Chirality transfer is possible in this rearrangement (*Scheme VI*).[34] Subsequent calculations predicted an asynchronous mechanism in which the C-O bond breaks immediately before bond formation, leading to a helical intermediate, in which the stereochemical information is retained.[35]
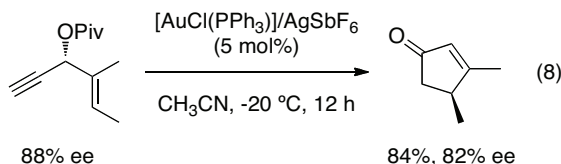
Scheme VI

Propargyl carboxylate migration has been applied in 1,n-enyne cyclization (n = 5,[33,36] 6,[37] 7 and 8[38] and 9[39]) as well as in the total synthesis of sesquiterpenes (*Scheme VII*).[37] In these cyclizations the alkene moiety was proposed to trap the carbene intermediate of type **IX** to form a cyclopropane ring.

34 Shi, X.; Gorin, D. J.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 5802-5803.

35 Faza, O. N.; López, C. S.; Álvarez, R.; de Lera, A. R. *J. Am. Chem. Soc.* **2006**, *128*, 2434-2437.

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37 (a) Fürstner, A.; Hannen, P. *Chem. Commun.* **2004**, 2546-2547. (b) Fürstner, A.; Hannen, P. *Chem. Eur. J.* **2006**, *12*, 3006- 3019. (c) Fürstner, A.; Schlecker, A. *Chem. Eur. J.* **2008**, *14*, 9181-9191. (d) Fehr, C.; Magpantay, I.; Arpagaus, A.; Marquet, X.; Vuagnoux, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 7221-7223. (e) Fehr, C.; Winter, B.; Magpantay, I. *Chem. Eur. J.* **2009**, *15*, 9773- 9784.

38 Moreau, X.; Goddard, J.-P.; Bernard, M.; Lemière, G.; López-Romero, J. M.; Mainetti, E.; Marion, N.; Mouriès, V.; Thorimbert, S.; Fensterbank, L.; Malacria, M. *Adv. Synth. Catal.* **2008**, *350*, 43-48.

39 Watson, I. D. G.; Ritter, S.; Toste, D. F. *J. Am. Chem. Soc.* **2009**, *131*, 2056–2057.
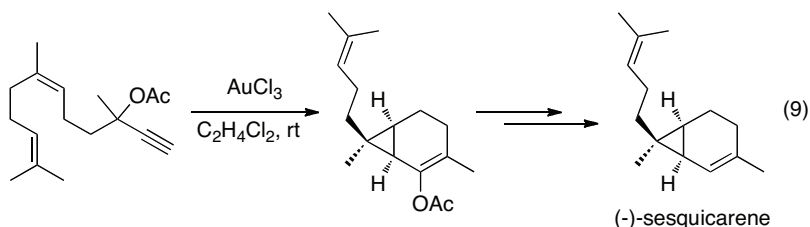
Scheme VII

The intermolecular trapping of gold(I) carbene proposed for the 1,2-migration of carboxylates has also been reported (*Scheme VIII*).[40] Intermediate gold(I) carbenes can also be oxidized with Ph₂SO to yield carbonyl compounds.[41]
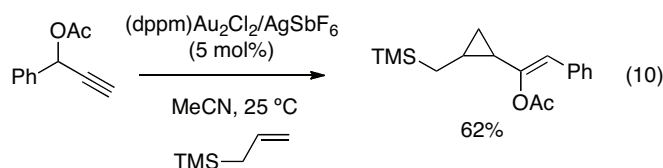
Scheme VIII

Gold(I) carbenes from propargyl esters can also be trapped intermolecularly with sulfides.[42] Analogous intramolecular trapping of the *α,β*-unsaturated gold(I) carbene was reported using ethers, which involves a reaction of an allyl carbocation with a chiral allyl gold(I) intermediate **X** (*Scheme IX*).[43]

40 Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002-18003.

41 Witham, C. A.; Mauleón, P.; Shapiro, N. D.; Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 5838-5839.

42 Davies, P. W.; Albrecht, S. J.-C. *Chem. Commun.* **2008**, 238-240.

43 Uemura, M.; Watson, I. D. G.; Katsukawa, M.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 3464–3465.

(11)

74%, 97% ee
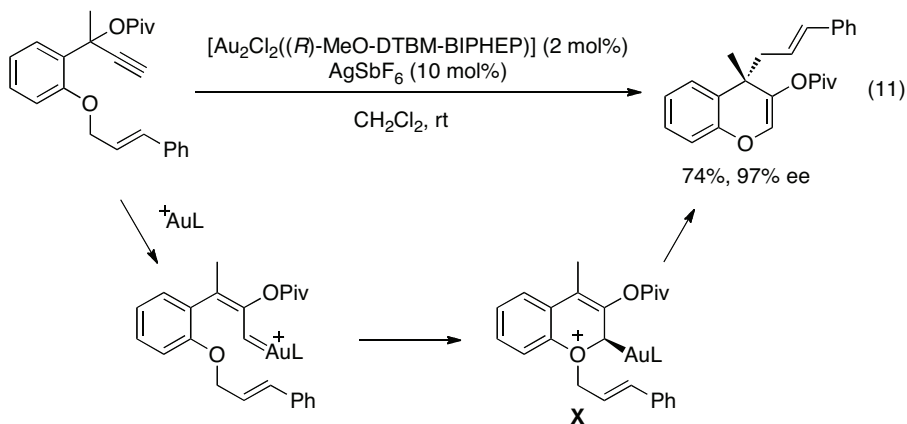
Scheme IX

Gold-catalyzed 1,3-enyne cyclization was reported using acetates at the propargylic position of the enyne to give α,β-unsaturated ketones.[44] The cyclization involves a 1,3-migration of the propargylic acetate, and subsequent Nazarov cyclization of **XI** (*Scheme X*).

(12)

92%
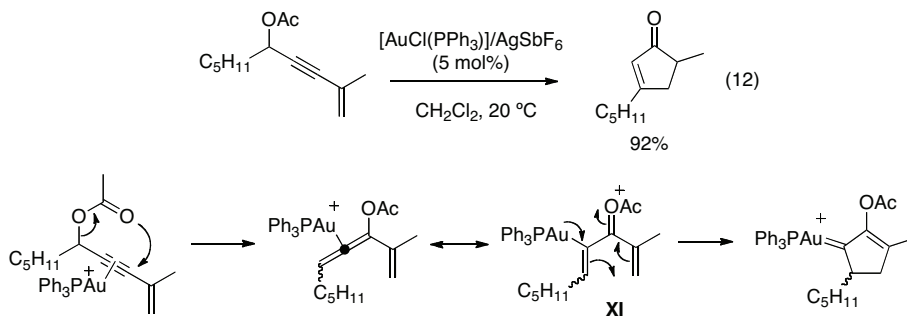
Scheme X

1,3-Shift of propargylic esters was also used to form in situ an allenyne that could undergo gold-catalyzed Myers-Saito cyclization (*Scheme XI*).[45,46] A [3,3]

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44 Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006**, *128*, 1442-1443.

45 Zhao, J.; Hughes, C. O.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 7436-7437.

46 For analogous cyclizations of diynes bearing propargyl carboxylates see: (a) Oh, C. H.; Kim, A. *New J. Chem.* **2007**, *31*, 1719-1721. (b) Luo, T.; Schreiber, S. L. *Angew. Chem. Int. Ed.* **2007**, *46*, 8250-8253.

rearrangement is also involved in the gold-catalyzed formation of alkenyl enol esters from trimethylsilylmethyl-substituted propargyl carboxylates.[47]

$$\text{(13)}$$
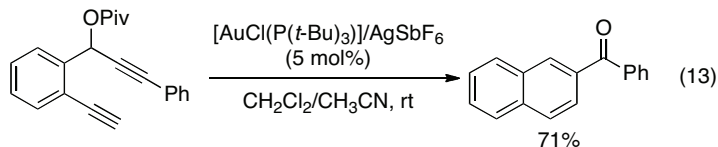
Scheme XI

1,3-Carboxylate migration has been reported in the cycloisomerization of aryl propargylic esters in which the gold(I)-activated allene suffers an intramolecular addition of an aryl moiety (*Scheme XII*). Depending on the substitution patterns 1,2- or 1,3-shift pathway controls the reaction products (*Scheme XII*).[48]

$$\text{(14)}$$

$$\text{(15)}$$
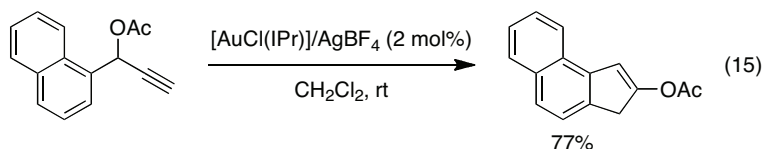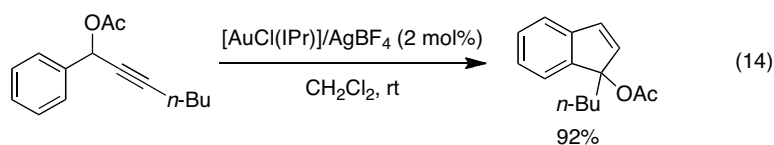
Scheme XII

DFT calculations showed that propargylic esters coordinated to gold(I) can undergo 1,2-acyl migration to form α,β-unsaturated gold(I) carbenes **XIII** or 1,3-acyl migration to give allene-gold complexes **XII**, via non-concerted mechanisms (*Scheme XIII*). Intermediates **XII** and **XIII** can interconvert by 1,2-acyl migration through the five member ring intermediate **XIV** (*Scheme XIII*).[49]

47 (a) Zhang, L.; Wang, S. *Org. Lett.* **2006**, *8*, 4585-4587. (b) Fu-Qiang Shi, F.-Q.; Xin Li, X.; Yuanzhi Xia, Y.; Liming Zhang,L.; Zhi-Xiang Yu, Z.-X. *J. Am. Chem. Soc.* **2007**, *129*, 15503–15512.

48 Marion, N.; Diez-Gonzalez, S.; de Fremont, P.; Noble, A. R.; Nolan, S. P. *Angew. Chem. Int. Ed.* **2006**, *45*, 3647-3650.

49 Correa, A.; Marion, N.; Fensterbank, L.; Malacria, M.; Nolan, S. P.; Cavallo, L. *Angew. Chem. Int. Ed.* **2008**, *47*, 718-721.

Scheme XIII

40
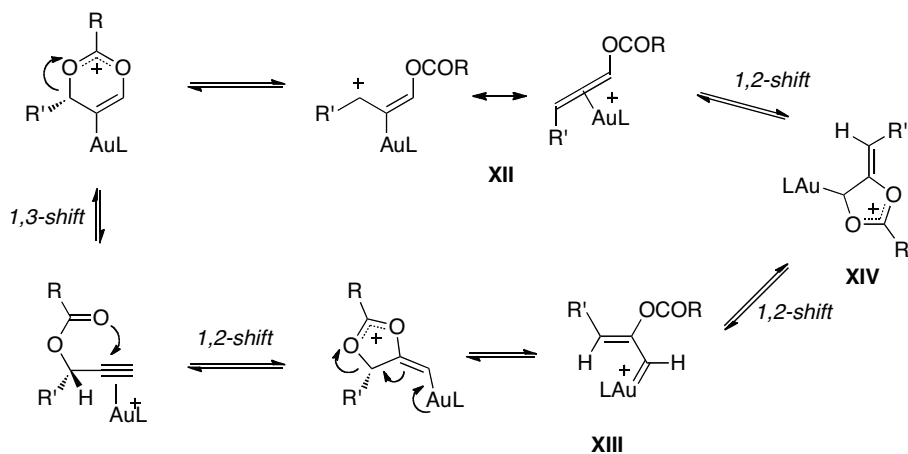
Gold-catalyzed addition of carbon nucleophiles to alkynes

Carbon nucleophiles can also attack alkyne-gold complexes. Gold-catalyzed reaction of arenes with alkynes catalyzed by gold has been extensively studied.[50] Intermolecular hydroarylation of alkynes catalyzed by gold leads to 1,1-disubstituted alkenes (*Scheme XIV*).[51] 1,2-Disubstituted alkenes can be obtained using alkynes with electron-withdrawing groups.[52] Direct auration of eletron-rich arenes is well-known,[53] but there is no experimental evidence for the involvement of the resulting arene-gold complex in the addition to alkynes (*Scheme XIV*). The generally accepted mechanism proceeds via alkyne-gold complexes and subsequent electrophilic substitution on the aromatic ring.

$$AuCl_3 \ (5 \ mol\%)$$
$$AgSbF_6 \ (10 \ mol\%)$$
$$CH_2Cl_2, \ 50 \ °C$$

(16)

84%
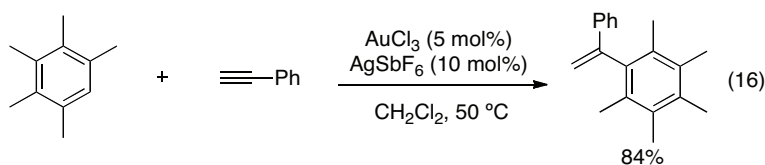
Scheme XIV

Intramolecular gold-catalyzed hydroarylation of alkynes in biphenyl systems lead to phenantrenes rings in excellent yield.[54] Interestingly, haloalkynes react with AuCl to yield the corresponding phenantrenes via a 1,2-halide shift (*Scheme XV*).[55] This result suggested the formation of gold(I) vinylidene intermediate **XV** and subsequent electrocyclization.[56]

50 Nevado, C.; Echavarren, A. M. *Synthesis* **2005**, 167-182.

51 Reetz, M. T.; Sommer, K. *Eur. J. Org. Chem.* **2003**, 3485-3496.

52 Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669-3671.

53 (a) Kharasch, M. S.; Isbell, H. S. *J. Am. Chem. Soc.* **1931**, *53*, 3053-3059. (b) Porter, K. A.; Schier, A.; Schmidbaur, H. *Organometallics* **2003**, *22*, 4922-4927. (c) Shi, Z.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 5964-5965. (d) Shi, Z.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 13596-13597. (e) Li, Z.; Ding, X.; He, C. *J. Org. Chem.* **2006**, *71*, 5876-5880.

54 Fürstner, A.; Mamane, V. *J. Org. Chem.* **2002**, *67*, 6264-6267.

55 Mamane, V.; Hannen, P.; Fürstner, A. *Chem. Eur. J.* **2004**, *10*, 4556-4575.

56 Soriano, E.; Marco-Cotelles, J. *Organometallics* **2006,** *25,* 4542-4553.

(17)

77%

XV
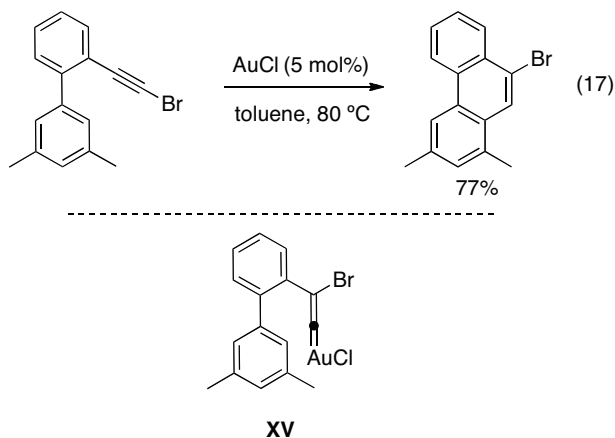
Scheme XV

In contrast to the Friedel-Crafts reaction of arenes with alkynes, intermolecular reaction of alkynes with heteroarenes such as pyrrol, indole,[57] and furane[58] results in a double addition to the internal carbon of the alkyne (*Scheme XVI*).

(18)

95%
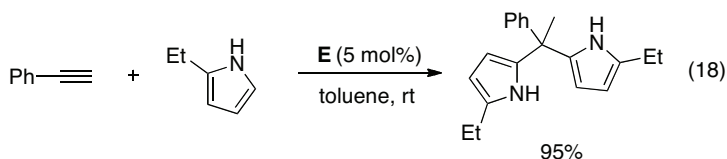
Scheme XVI

Intramolecular reaction of indole with alkynes can proceed by *exo* or *endo* cyclization depending on the gold catalyst (*Equation 19*).[57,59] Internal alkynes are also active in the intramolecular process leading to allenes and tetracyclic compounds (*Equation 20*). The proposed mechanism is shown in *Scheme XVII*. Protonation of intermediate **XVI** gives an opened intermediate (**XVII**) that can rearrange to the final allene **XVIII**. Intermediate **XVII** can also lead to an α,β-unsaturated gold(I) carbene (**XIX**) by nucleophilic attack of the vinylgold to the aza-fulvenium moiety. Michael-type cyclization and protodemetalation would lead to the final tetracycle **XX**.

57 Ferrer, C.; Amijs, C. H. M.; Echavarren, A. M. *Chem. Eur. J.* **2007**, *13*, 1358-1373.

58 Hashmi, A. S. K.; Blanco, M. C. *Eur. J. Org. Chem*. **2006**, 4340-4342.

59 Ferrer, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 1105-1109.

(19)

(20)

27%   36%

XVI

XVIII   - [AuL]$^+$ **XVII**

XX   - [AuL]$^+$ **XIX**
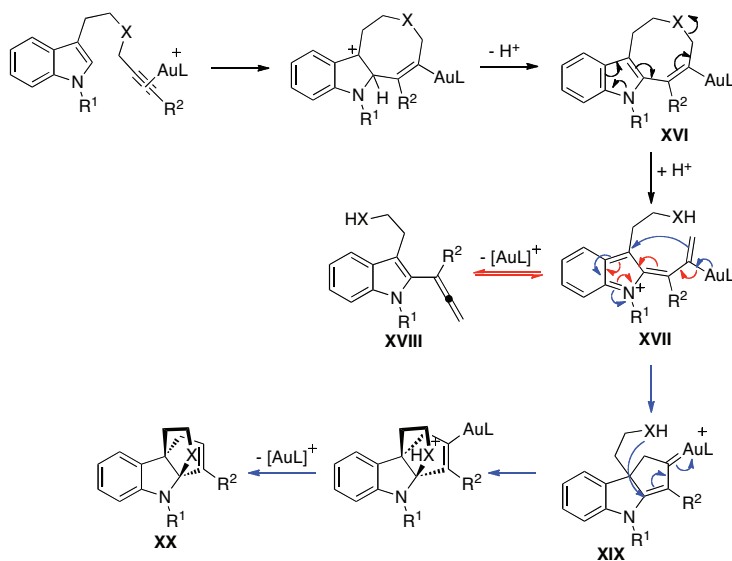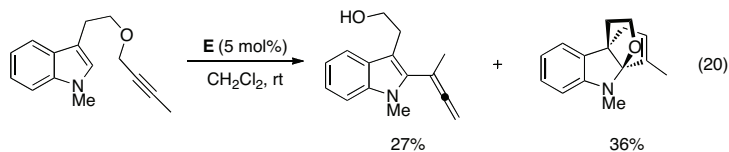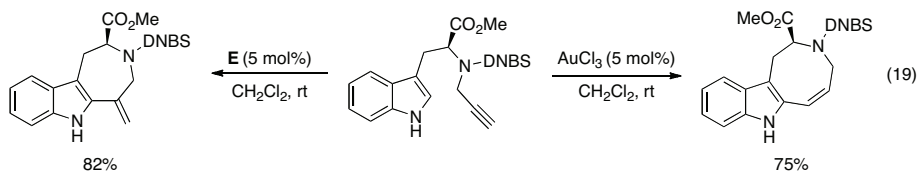
Scheme XVII

Intramolecular addition of furans catalyzed by gold(I),[60] AuCl$_3$[61] or heterogeneous gold[62] catalysts provides phenols in good to excellents yields (*Scheme XVIII*).

60 Hashmi, A. S. K.; Haufe, P.; Schmid, C.; Nass, A. R.; Frey, W. *Chem. Eur. J.* **2006**, *12*, 5376-5382.

61 (a) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *J. Am. Chem. Soc.* **2000**, *122*, 11553-11554. (b) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Org. Lett.* **2001**, *3*, 3769-3771. (c) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Catal. Today* **2001**, *72*, 19-27. (d) Hashmi, A. S. K.; Ding, L.; Bats, J. W.; Fischer, P.; Frey, W. *Chem. Eur. J.* **2003**, *9*, 4339-4345. (e) Hashmi, A. S. K.; Weyrauch, J. P.; Rudolph, M.; Kurpejovic, E. *Angew. Chem. Int. Ed.* **2004**, *43*, 6545-6547. (f) Hashmi, A. S. K.; Rudolph, M.; Weyrauch, J. P.; Wölfle, M.; Frey, W.; Bats, J. W. *Angew. Chem. Int. Ed.* **2005**, *44*, 2798-2801. (g)

$$(21)$$

62%
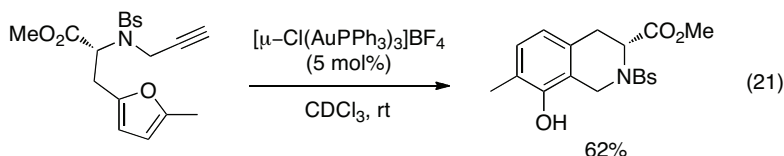
Scheme XVIII

The mechanistic proposal depicted in *Scheme XIX* is supported by experimental and theoretical studies on gold[61e-f] and platinum-catalyzed[63] additions of furans to alkynes. This reaction proceeds by nucleophilic attack of furan to the gold-alkyne complex to form cyclopropyl gold carbene **XXI** as intermediate. Electrocyclic ring opening of **XXI** leads to a new carbene intermediate (**XXII**) with a carbonyl moiety. Cyclization of **XXII** gives oxepin **XXIII**, which is in tautomeric equilibrium with the corresponding benzene oxide (**XXIII'**) (*Equation 22*).[61e] Intermediate **XXIII'** then opens to give the final phenols (*Scheme XIX*).

$$(22)$$
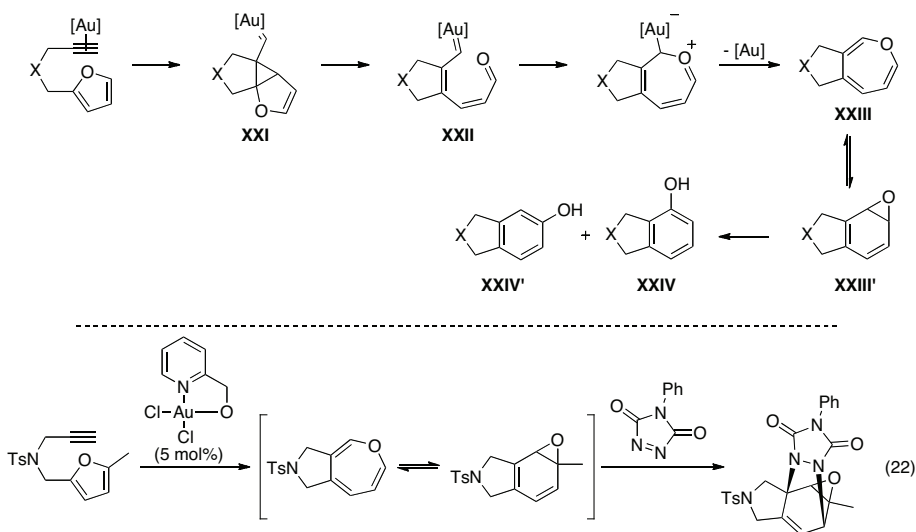
Scheme XIX

Hashmi, A. S. K.; Weyrauch, J. P.; Kurpejovic, E.; Frost, T. M.; Miehlich, B.; Frey, W. Bats, J. W. *Chem. Eur. J.* **2006**, *12*, 5806-5814. (h) Hashmi, A. S. K.; Kurpejovic, E.; Frey, W.; Bats, J. W. *Tetrahedron* **2007**, *63*, 5879-5885.

62 Carrettin, S.; Blanco, M. C.; Corma, A.; Hashmi, A. S. K. *Adv. Synth. Catal.* **2006**, *348*, 1283-1288.

63 Martín-Matute, B.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2003**, *125*, 557-5766.

Aside from arenes and heteroarenes, also 1,3-dicarbonyl compounds can be used as nucleophiles leading to the gold-catalyzed Conia-ene reaction (*Scheme XX*).[64]

Scheme XX
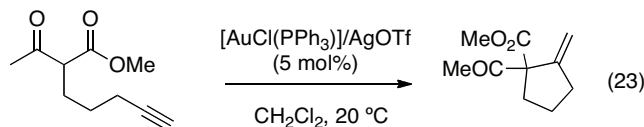
Gold-catalyzed cyclization of 1,6-enynes

In gold-catalyzed reactivity, alkenes are by far the most studied carbon nucleophiles in intramolecular reaction. This is known as enyne cycloisomerization and it can lead to a wide variety of carbo- and heterocycles.

Enyne cyclization has attracted much attention since in 1985 Trost reported the palladium catalyzed Alder-ene process using alkynes as enophiles.[65]

Depending on the metal, the ligands and the reaction conditions, enyne cyclizations can give different products.[66] The key step is the coordination of the metal to the enyne. Simultaneous complexation to the alkene and the alkyne leads preferentially to metallacyclopentenes which usually evolve to form 1,3- or 1,4-dienes (pathway **a**, *Scheme XXI*). Selective activation of the alkene takes place if there is a functional group at the allylic position or the metal can promote C-H allylic activation. This reaction proceeds through a π-allyl complex which can react with the alkyne (pathway **b**, *Scheme XXI*). The third possible pathway is the selective activation of the alkyne (pathway **c**, *Scheme XXI*).

64 Kennedy-Smith, J. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 4526-4527.

65 Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781-1783.

66 (a) Lloyd-Jones, G. C. *Org. Biomol. Chem*. **2003**, *1*, 215-236. (b) Michelet, V.; Toullec, P. Y.; Genêt, J.-P. *Angew. Chem. Int. Ed.* **2008**, *47*, 4268-4315.
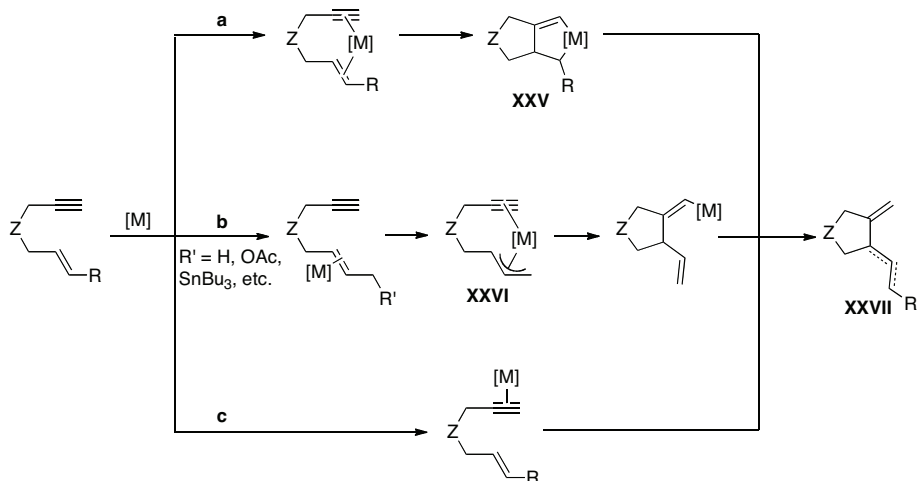
Scheme XXI

Gold(I) activates selectively the alkyne moiety of 1,6-enynes and the alkene acts as nucleophile leading to cyclization products by *5-exo-dig* or *6-endo-dig* pathways.[67] In both pathways, cyclopropyl gold(I) carbenes **XXIX** and **XXX** are generated as intermediates (*Scheme XXII*). These intermediates can undergo skeletal rearrangements (**XXXI**, **XXXII** and **XXXIV**)[8a] or yield cyclopropyl product **XXXIII**[68] by 1,2-hydrogen shift and demetalation.

---

67 Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326-3350.

68 Chao, C.-M.; Beltrami, D.; Toullec, P. Y.; Michelet, V. *Chem. Commun.* **2009**, *45*, 6988-6990.
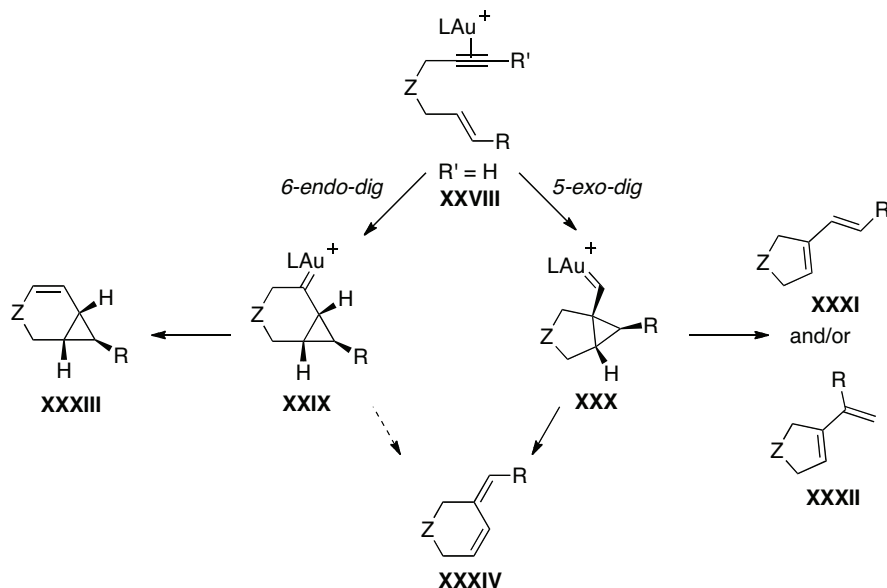
Scheme XXII

When the cyclization proceeds through the *5-exo-dig* pathway, three different 1,3-dienes **XXXI**, **XXXII**, and **XXXIV** can be obtained (*Scheme XXIII*).[8b,69] Dienes **XXXI** and **XXXII** were initially found in the palladium(II)-catalyzed cyclization of enynes and its connectivity was determined by ^{13}C-isotopic labelling.[70] Dienes **XXXI** are the products of single cleavage rearrangement, in which the external alkene carbon migrates to the terminus of the alkyne. On the other hand, dienes **XXXII** are the products of double cleavage rearrangement in which both the alkene and the alkyne are cleaved.
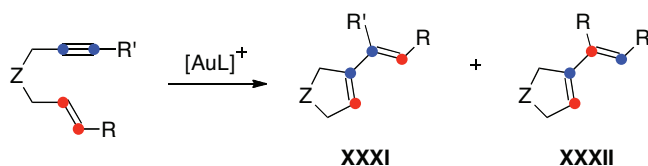
Scheme XXIII

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

70 (a) Trost, B. M.; Tanoury, G. J. *J. Am. Chem. Soc.* **1988**, *110*, 1636-1638. (b) Trost, B. M.; Trost, M. K. *Tetrahedron Lett.* **1991**, *32*, 3647-3650. (c) Trost, B. M.; Yanai, M.; Hoogsteed, K. *J. Am. Chem. Soc.* **1993**, *115*, 5294-5295.

The mechanistic proposals for both single and double cleavage rearrangement are explained in *Scheme XXIV* and are based on kinetic data and DFT calculations.[69] Thus, the *anti*-cyclopropyl gold carbene **XXX** rearranges to give **XXXV**, which can undergo demetalation (pathway **a**) to form single cleavage dienes **XXXII**. Alternatively, **XXXV** can undergo 1,2-shift (pathway **b**) to form a new gold carbene **XXXVI**, which yields the double cleavage dienes **XXXI** by 1,2-hydride shift and subsequent demetalation. This double cleavage can also occur directly from intermediate **XXX** to give intermediate **XXXVI**.
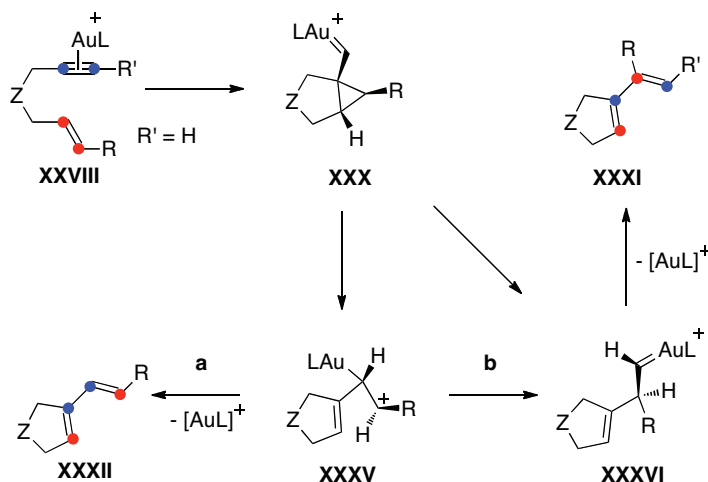
Scheme XXIV

On the other hand, formation of dienes **XXXIV** was initially explained by skeletal rearrangement through a 6-*endo-dig* pathway.[8a] However theoretical studies show that **XXXIV** is formed by a 5-*exo-dig* pathway from carbene **XXX** (*Scheme XXV*).[71]
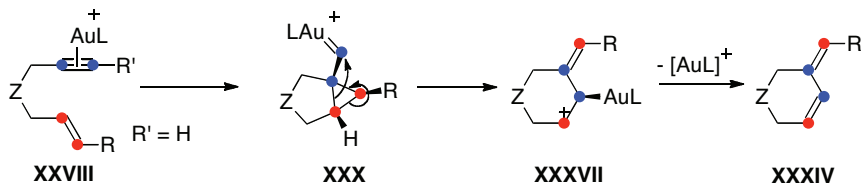
Scheme XXV

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

For convenience, intermediates **XXIX** and **XXX** are often represented as cyclopropyl gold(I) carbenes, although according to DFT calculations these species are distorted structures that can also be represented as gold-stabilized homoallylic carbocations. Evidence for this dualism between gold(I) carbenes and homoallylic carbocations was found in the single cleavage rearrangement of 1,6-enynes (*Scheme XXVI*). Cyclization of simple 1,6-enynes is stereospecific according to a concerted mechanism via cyclopropyl gold(I) carbenes **XXX** (*Equation 24*). In contrast, enynes substituted at the olefin with electron-donating groups give mixtures of *E* and *Z* isomers (*Equation 25*). This lack of stereospecificity in the cyclization suggests the formation of an open intemediate **XXXVIII** in which the rotational barrier for the *E/Z* interconversion is accessible at room temperature (*Scheme XXVI*).
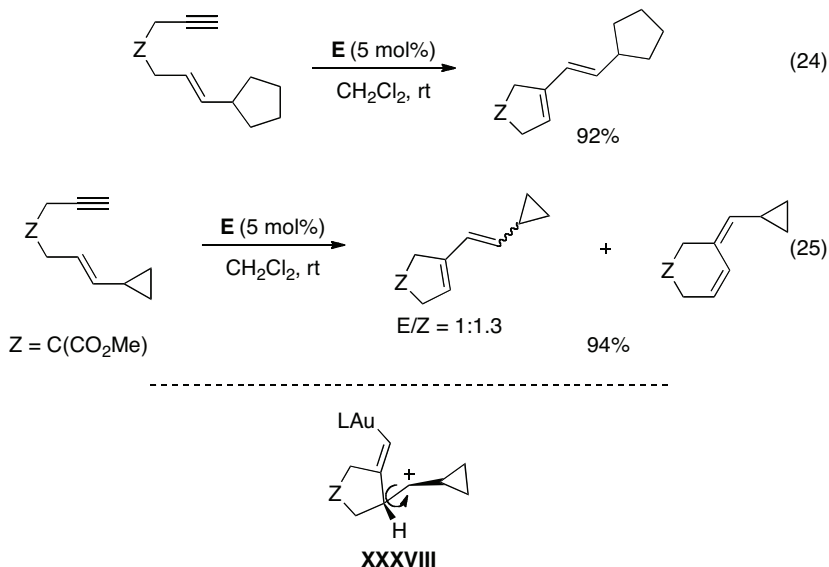
Scheme XXVI

DFT calculations show the cationic or carbenic character of the intermediates is highly influenced by the substitution pattern of the enyne and the nature of the ligand.[69,71,72] Thus, in enynes where R = H or Me, the most relevant resonance structure is **XXXIX** with a relatively long *b* bond. When the R group can stabilize a carbocation like R = *c*-C_3H_5, the more relevant canonical structure correspond more closely to the open intermediate **XXXVIII**, in which the long cyclopropane bond is now *c*. It is

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

important to note that a strongly electron-donating ligand such as Cl^- shows a more regular structure with similarly elongated *b* and *c* bonds, resembling the cyclopropyl gold intermediate **XXX** (*Table I*).

Table I
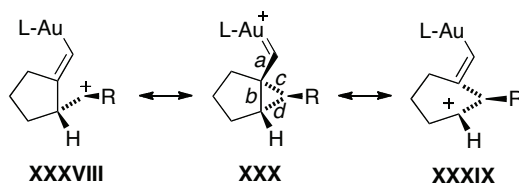
R	L	*a*	*b*	*c*
H	PH_3	1.378	1.742	1.569
Me	PH_3	1.372	1.720	1.622
c-C_3H_5	Cl^-	1.401	1.621	1.606
c-C_3H_5	PH_3	1.356	1.586	1.987

Bond distance in Å determined by DFT calculations at the B3LYP/6-31G(d) (C,H,P), LANL2DZ (Au) level.

Evidence for the carbenic character of the intermediates was observed by intra-[8a,73,74] and intermolecular[75] cyclopropanation of alkenes. The carbene intermediate **XXX** as well as the carbene **XXXVI** proposed for the double cleavage rearrangement were trapped by intermolecular cyclopropanation with styrene using a NHC as ligand in the gold(I) complex (*Scheme XXVII*).

73 Nieto-Oberhuber, C.; López, S.; Muñoz, M. P.; Jiménez-Núñez, E.; Buñuel, E.; Cárdenas; D.; Echavarren, A. M. *Chem. Eur. J.* **2006,** *11*, 1694-1702.

74 Kim, S. M.; Park, J. H.; Choi, S. Y.; Chung, Y. K. *Angew. Chem. Int. Ed.* **2007**, *46*, 6172-6175.

75 (a) López, S.; Herrero-Gómez, E.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 6029-6032. (b) Pérez-Galán, P.; Herrero-Gómez, E.; Hog, D. T.; Martin, N. J. A.; Echavarren, A. M. *Chem. Sci.* **2011**, DOI: 10.1039/COSC00335B.

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UNIVERSITAT ROVIRA I VIRGILI
MASTERING THE REACTIVITY OF GOLD (I) CARBENES
Verónica López Carrillo
ISBN:978/84-694-0328-0/DL:T-208-2011                                        Introduction
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(26)

75%

(27)

67%
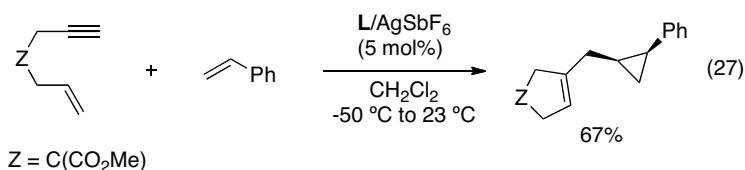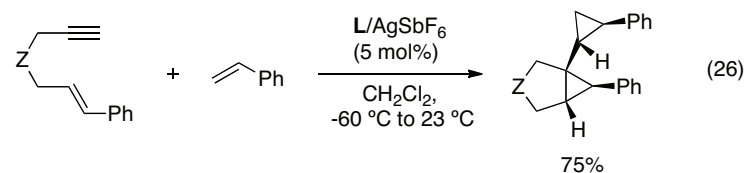
Z = C(CO₂Me)

Scheme XXVII

1,6-Enynes substituted at the alkyne with an aryl group undergo formal [4+2] cycloaddition in the presence of gold(I) complexes to yield tricyclic compounds in good to excellent yields (*Scheme XXVIII*).[11,13b] The reaction is stereospecific and tolerates both electron-withdrawing and electron-donating groups. However, the stereospecificity is lost in the cyclization of enynes substituted at the olefin with electron-donating groups, which give mixtures of stereoisomers (*Equation 30*).[72]

(28)

74%

(29)

85%

(30)

Z = C(CO₂Me)

trans/*cis* = 72:28
85%
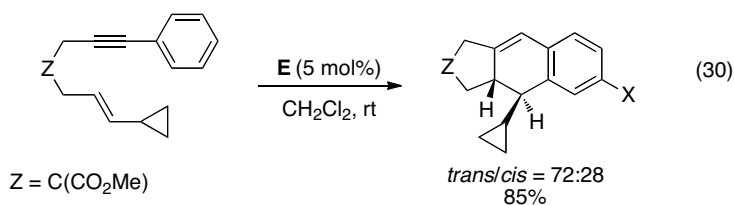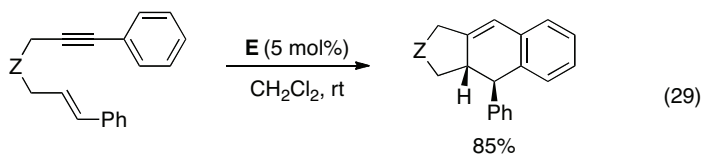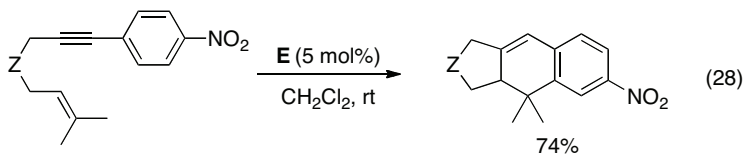
Scheme XXVIII

For this transformation, DFT caculations predict a Friedel-Crafts type process from the open structure **XXXVIII**, which is stabilized by the aryl ring. The cationic intermediate **XL** undergoes aromatization and protodemetalation to give the tricyclic **XLI** (*Scheme XXIX*).
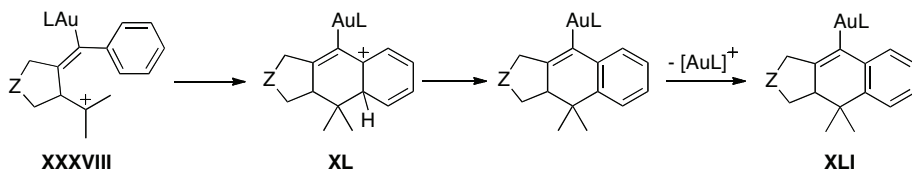
Scheme XXIX

Along with cyclopropanation reactions, the most caracteristic reactivity of cyclopropyl gold carbene intermediates is the addition of nucleophiles.[67] This process involves an opening of the cyclopropane intermediate, which results in a formal nucleophilic 1,4-addition. Two different adducts can be obtained from intermediate **XXX**. Cleavage of the *a* bond in **XXX** results in methylenecyclopentanes **XLII**, whereas clavage of bond *b* leads to methylenecyclohexane **XLIII**. Cyclohexenes **XLIV** are also obtained as a result of 6-*endo-dig* cyclization pathway (*Scheme XXX*).
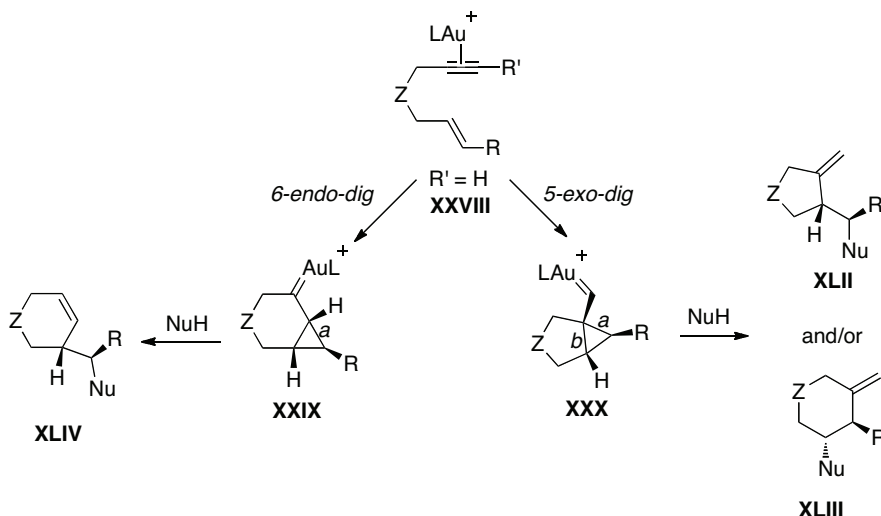
Scheme XXX

Alcohols and water have been widely studied as nucleophiles in reactions of 1,6-enynes leading to hydroxy- and alkoxycyclization reaction in both inter-[8a,76] and

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76 (a) Nieto-Oberhouber, C.; Muñoz, M. P.; Lopez, S.; Jiménez-Nuñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M. *Chem. Eur. J.* **2006**, *12*, 1677-1693. (b) Ricard, L.; Gagosz, F. *Organometallics* **2007**, *26*, 4704-4707. (c) Bartolomé, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem.* **2008**, *47*, 11391-11397. (d) Chao, C.-M.; Vitale, M. R.; Toullec, P. Y.; Michelet, V. *Tetrahedron Lett.* **2009**, *50*, 3719-3722. € Bartolomé, C.; Ramiro, Z.;

intramolecular[76a] fashion (*Scheme XXXI*). The reaction is stereospecific and compatible with many different substitutions paterns in the alkene and the alkyne. The asymmetric gold(I)-catalyzed hydroxy- and alcoxycyclization of 1,6-enynes has also been reported with good to excellent enantiomeric excesses (*Equation 32*).[77]

$$(31)$$

$$(32)$$
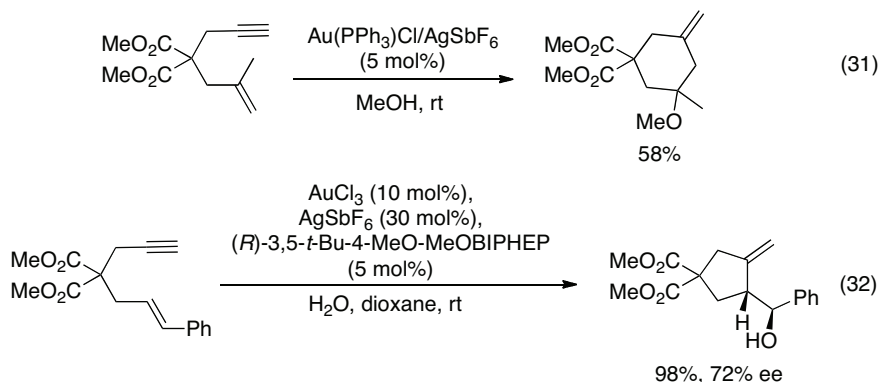
Scheme XXXI

The gold(I) catalyzed addition of carbon nucleophiles to 1,6-enynes has also been reported.[14,78] The reaction is very efficient for indole, electron-rich arenes, 1,3-dicarbonyl compounds and allylsilanes. In the addition of indole and dibenzoylmethane a strong effect of the ligands on the structure of the gold(I) intermediates was observed (*Scheme XXXII*). In this reaction, catalysts with more donating ligands led to 1,2-addition products, as a result of the direct trapping of the gold(I) carbene by the nucleophile. On the other hand, a more electrophilic catalyst **J**, with a phosphite as

García-Cuadrado, D.; Pérez-Galán, P.; Raducan, M.; Bour, C.; Echavarren, A. M.; Espinet, P. *Organometallics* **2010**, *29*, 951-956.

77 (a) Muñoz, M. P.; Adrio, J.; Carretero, J. C.; Echavarren, A. M. *Organometallics* **2005**, *24*, 1293-1300. (b) Chao, C.-M.; Genin, E.; Leseurre, L.; Toullec, P. Y.; Genêt, J.-P.; Michelet, V. *Synlett* **2007**, 1780-1784. (c) Chao, C.-M.; Genin, E.; Toullec, P. Y.; Genêt, J.-P.; Michelet, V. *Journal of Organometallic Chemistry* **2009**, *694*, 538-545. (d) Matsumoto, Y.; Selim, K. B.; Nakanishi, H.; Yamada, K.; Yamamoto, Y.; Tomioka, K. *Tetrahedron Letters* **2010**, *51*, 404-406.

78 (a) Toullec, P. Y.; Genin, E.; Leseurre, L.; Genet, J.-P.; Michelet, *V. Angew. Chem. Int. Ed.* **2006**, *45*, 7427-7430. (b) Amijs, C. H. M.; Ferrer, C.; Echavarren, A. M. *Chem. Commun.* **2007**, 698-700. (c) Chao, C.M.; Vitale, M. R.; Toullec, P. Y.; Genêt, J.-P.; Michelet, V. *Chem. Eur. J.* **2009**, *15*, 1319-1323.

ligand, led to the 1,4-addition product. Similar results were obtained using other carbene gold catalysts.[79]
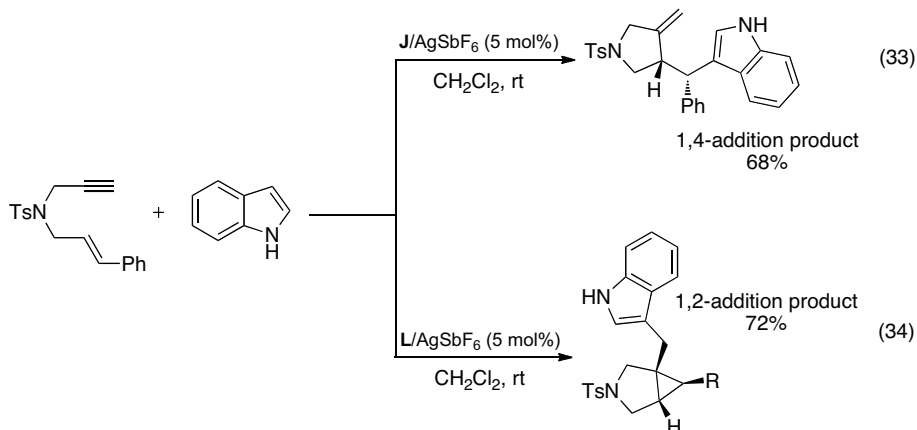
Scheme XXXII

Aldehydes and ketones can react as intramolecular nucleophiles in the gold(I)-catalyzed cyclization of 1,6-enynes in a formal [2+2+2] cycloaddition (*Scheme XXXIII*).[80] This transformation is a powerful method to increase molecular complexity in one step, which has been applied as key step in the total synthesis of natural products like (+)-orientalol F, (+)-pubinernoid B[81] and englerin A[82] (*Figure IV*).
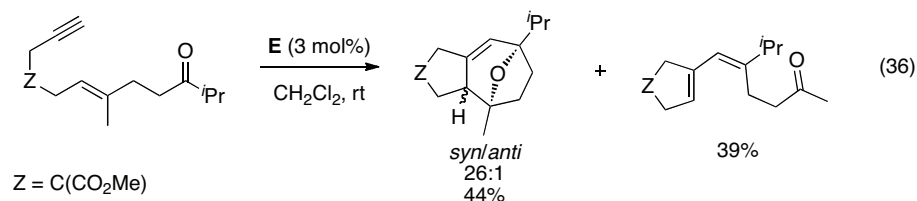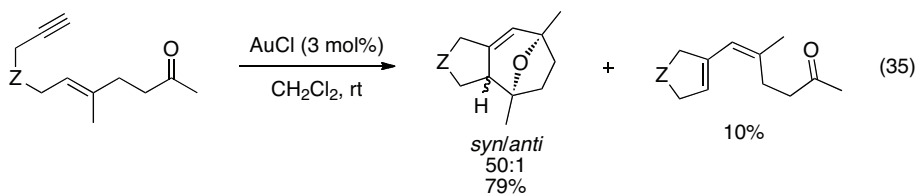
Scheme XXXIII

79 Seo, H.; Roberts, B. P.; Abboud, K. A.; Merz, K. M. Jr.; Hong, S. *Org. Lett.* **2010**, *12*, 4860-4863.

80 Jiménez-Núñez, E.; Claverie, C. K.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 5452-5455.

81 Jiménez-Núñez, E.; Molawi, K.; Echavarren, A. M. *Chem. Commun.* **2009**, 7327-7329.

82 Molawi, K.; Delpont, N.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2010**, *49*, 3517-3519.
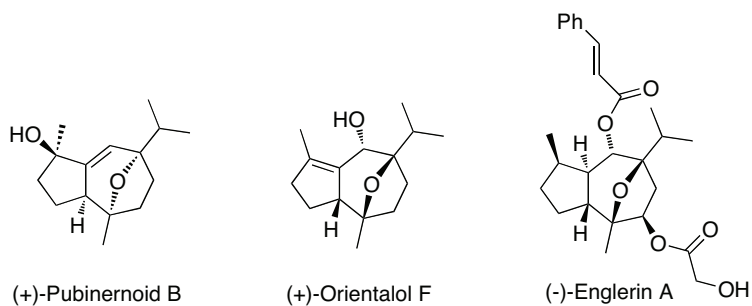
Figure IV

The mechanism proposed for this stereoselective cycloaddition is despicted in *Scheme XXXIV*. The carbonyl group opens the cyclopropyl gold(I) carbenes intermediates to form the oxonium cations **XLV**, which are attacked by the vinyl-gold moiety to give **XLVIa**. Demetalation can take place to yield the final oxatricyclic compound *syn*-**XLVII**. Alternatively, cleavage of the *a* bond in **XLVIa** can yield the unsaturated ketone **XLVIII** or might form a second oxonium cation **IL** that lead to **XLVII** (*Scheme XXXIV*).
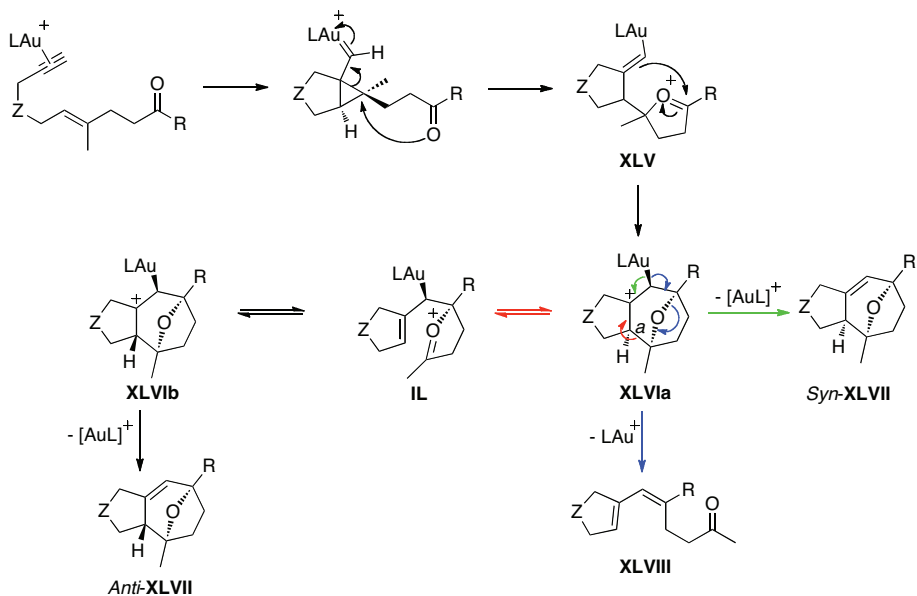
Scheme XXXIV

Intermolecular addition of aldehydes and ketones to 1,6-enynes is also feasible. In this case three main products are observed (*Scheme XXXV*). Products **L** are obtained

from 1,6-enynes unsubtituted at the alkene,[83] while mixtures of **LI** and **LII** were obtained with substituted alkenes.[84]
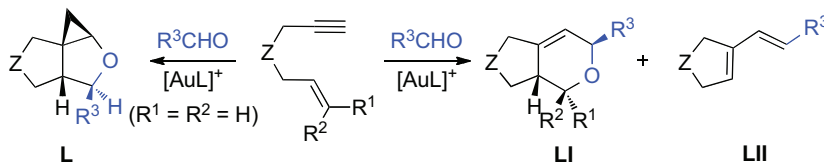
Scheme XXXV

Products **L** result from the attack of the carbonyl compound to the rearrange carbenes **XXXVI** to form **LIII**. Prins cyclization would then give cations **LIV** which evolve to product **L** (*Scheme XXXVI*). In contrast, products **LI** and **LII** result from the direct reaction of the aldehyde with cyclopropyl gold(I) intermediates **XXX** to form the oxonium cations **LV** which undergo Prins cyclization to give tetrahydropyranyl cations **LVI**. Intermediates **LVI** can evolve by demetalation to yield bicycles **LI** or by fragmentation reaction to form dienes **LII** (*Scheme XXXVI*).

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

84 Escribano-Cuesta, A.; López-Carrillo, V.; Janssen, D.; Echavarren, A. M. *Chem. Eur. J.* **2009**, *15*, 5646-5650.
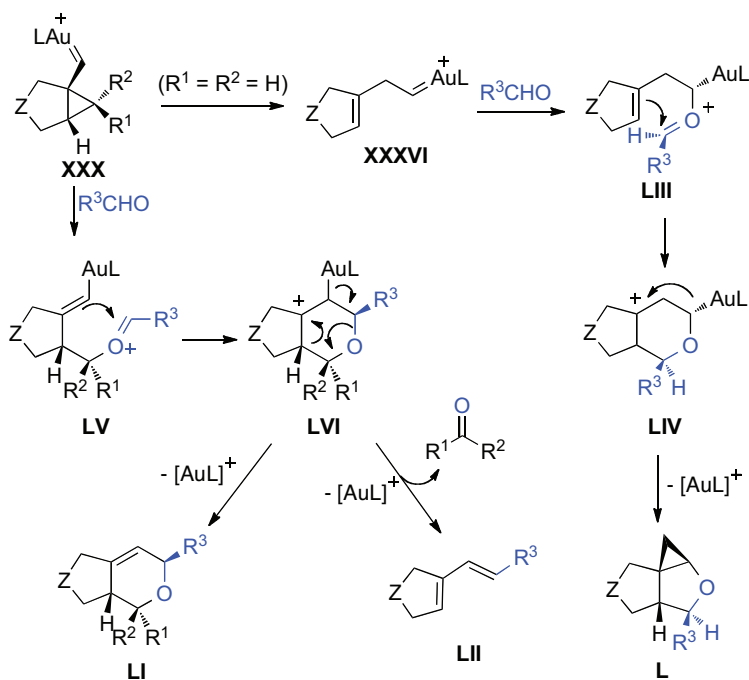
Scheme XXXVI

Double addition of aldehydes to alkene-substituted 1,6-enynes was found to give dioxolanes (*Equation 37*).[83b] Formation of dioxolanes of type **LVII** might proceed by trapping the cationic intermediate in the single cleavage rearrangement (**XXXV**). Addition of the carbonyl compound to the cation **XXXV** would give the oxonium cation **LVIII**. Subsequent Prins reaction of an allyl gold(I) intermediate leads to the gold(I) stabilized carbocation **LIX** which suffers nucleophilic attack by a second carbonyl compound. The new oxonium cation **LX** rearrange to the final dioxolane **LVII** (*Scheme XXXVII*).

$$(37)$$
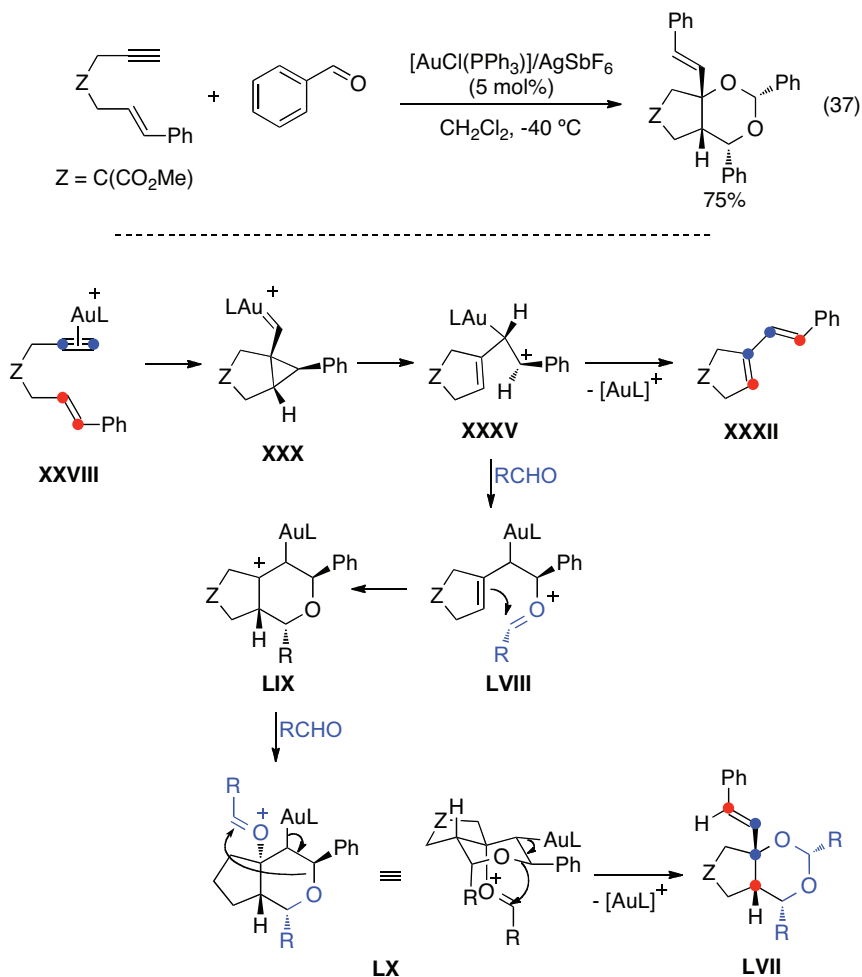
Scheme XXXVII

Oxonium cation can also react with η^1-allyl-gold(I) intermediates formed in the cyclization of 1,6-enynes bearing OR groups at the propargylic position (*Scheme XXXVIII*).[85] This cascade transformation starts by 5-*exo-dig* cyclization of the enyne to form the cyclopropyl gold(I) intermediate **XXX** which suffers intramolecular attack by the OR group at the cyclopropyl ring (**LXI**). Opening of **LXI** then gives a α,β-unsaturated gold carbene/allyl gold carbocation **LXIIa**, followed by a formal C-H insertion at the benzylic position of the ether to form the oxonium cation **LXIII**. The

85 Jiménez-Núñez, E.; Raducan, M.; Lauterbach, T.; Molawi, K.; Solorio, C. R.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2009**, *48*, 6152-6155.

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Verónica López Carrillo
ISBN:978/84-694-0328-0/DL:T-208-2011
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Introduction

η^1-allyl-gold(I) moiety in **LXIII** can react with the oxonium cation at C1 to form **LXIV** or at C3 to yield **LXV**.
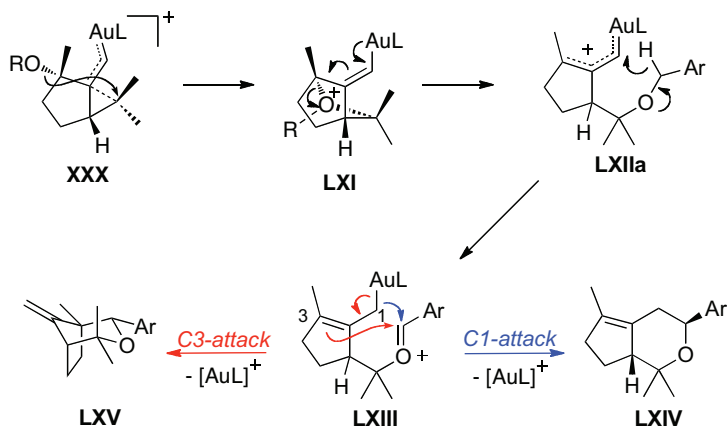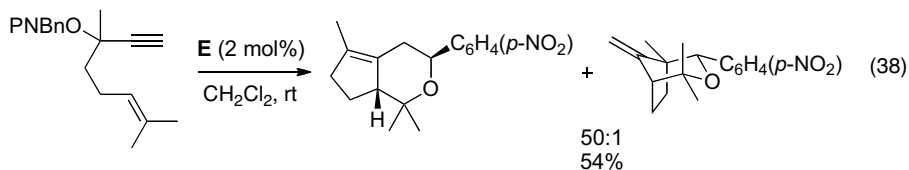
Scheme XXXVIII

This gold(I)-catalyzed cascade transformation is general for alcohols, ethers, and silyl ethers present at the propargylic position of 1,6-enynes.[85] In the case of dienynes **LVI**, the intramolecular 1,5-migration of the OR groups takes place to yield tricyclic compounds **LXVII** (*Scheme XXXIX*) in which the cyclopropyl ring comes from the reaction of the α,β-unsaturated gold carbene/allyl gold carbocation **LXII** with the alkene moiety.
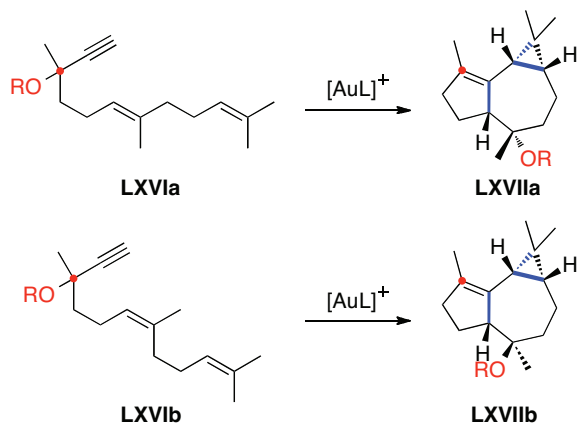
Scheme XXXIX

Gold-catalyzed cyclization of 1,5-enynes

Gold-catalyzed cyclization of 1,5-enynes (**LXVIII**) can also lead to a wide range of synthetically useful products (*Scheme XL*),[86] some of which resemble those that were obtained in cyclization of 1,6-enynes.
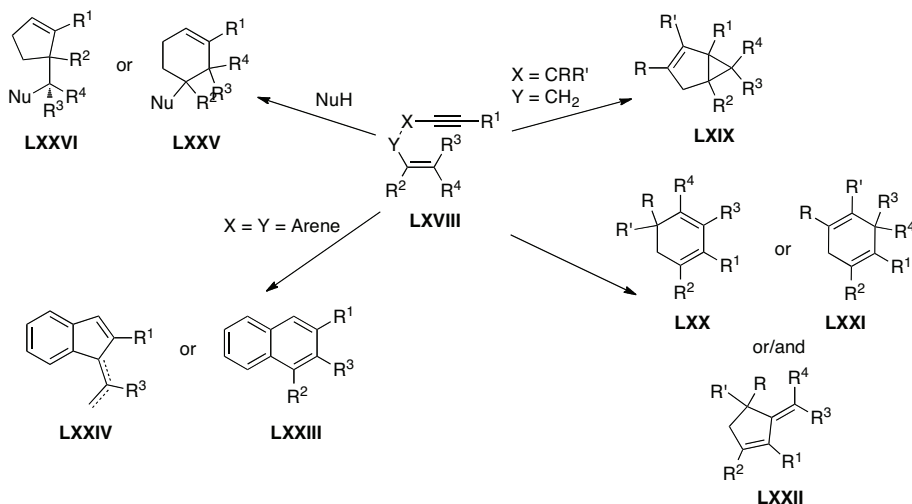
Scheme XL

1,5-Enyne cycloisomerization to bicyclo[3.1.0]hexenes (**LXIX**) was first reported using platinum complexes,[87] although immediately after gold(I) complexes were reported as the best catalyst for this reaction (*Scheme XLI*).[88] Thus, subjection of 1,5-enyne to 1 mol% of cationic gold complex at room temperature afforded the bicyclo[3.1.0]hexenes in good to excellent yields (*Equation 39*). The proposed mechanism for the formation of bicyclo[3.1.0]hexenes **LXIX** begins by 5-*endo-dig* cyclization to give an internal cyclopropyl gold-carbene which undergoes hydride or alkyl 1,2-shift to give **LXXVIII** (*Scheme XLI*). Demetalation results in the formation of the bicyclo **LXIX** and regeneration of the active catalyst.

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86 (a) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271-2296. (b) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351-3378.

87 (a) Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654-8655. (b) Harrak, Y.; Blaszykowski, C; Bernard, M.; Cariou, K.; Mainetti, E.; Mouries, V.; Dhimane, A. L.; Fensterbank, L.; Malacria, M. *J. Am. Chem. Soc.* **2004**, *126*, 8656-8657.

88 Luzung, M. R.; Markham, J. P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 10858-10859.

$$(39)$$

$$(40)$$
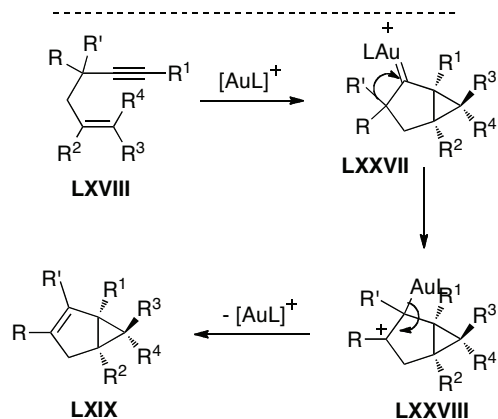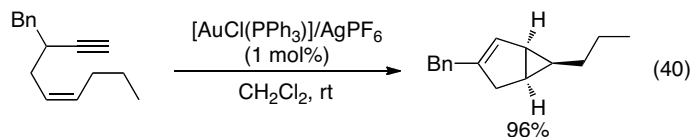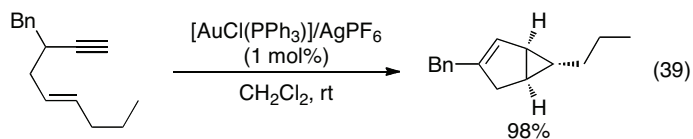
Scheme XLI

Evidence for this mechanism was found in the cyclization of 1,5-enynes deuterated at the propargylic position in which a 1,2-shift of deuterium was observed (*Equation 41*).[88] 1,5-Enynes disubtituted at the propargilyc position also cyclize in the presence of gold(I) complexes leading to 1,2-shift of alkyl groups (*Equation 42*).[88]

$$(41)$$

$$(42)$$
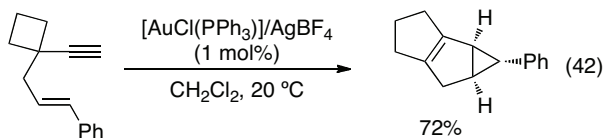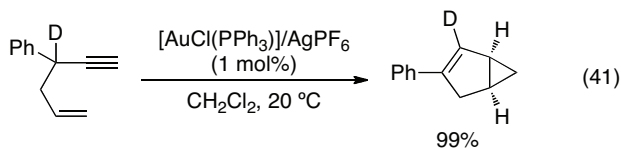
Scheme XLII

When the 1,2-shift of alkyl or hydride is not feasible, the cyclopropyl gold carbene intermediate **LXXVII** can open to form a cyclohexyl or cyclopentyl cation. 6-

Endo-dig[89] or 5-*endo-dig*[90] cyclization products are obtained after protodemetalation (*Scheme XLIII*).

LXXVII

(43)

83%

(44)

81%, 82% ee
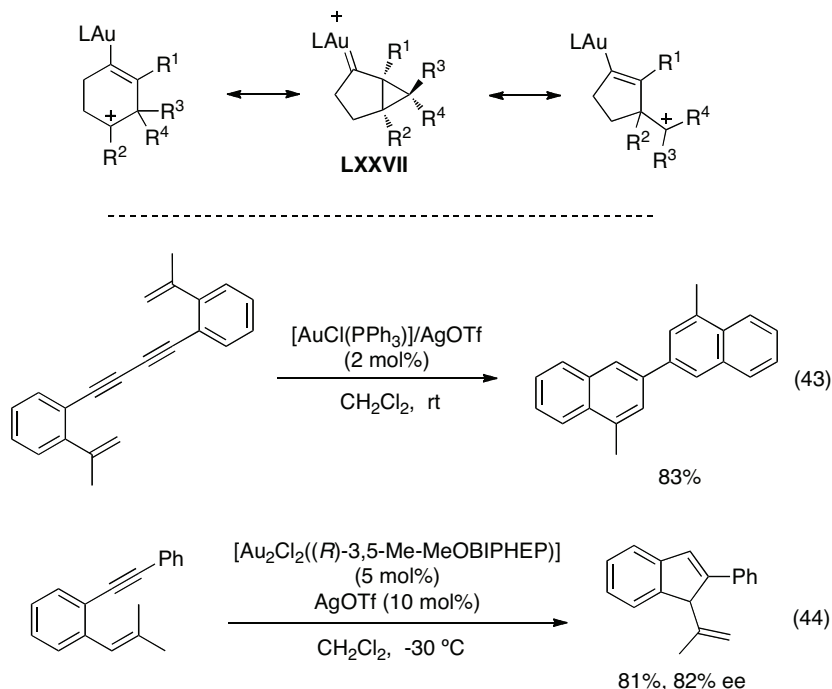
Scheme XLIII

The lack of stereospecificity observed in *Equation 45* can be explain by the opening of cyclopropyl gold(I) carbene **LXXVIIa** to the six-membered ring carbocation or the cyclopentenyl cation. Formation of the minor diasteroisomer is noteworthy since this bicyclo[3.1.0]hexene is the expected product from the *Z* isomer of the starting 1,5-enyne (*Scheme XLIV*).[91]

89 Shibata, T.; Ueno, Y.; Kanda, K. *Synlett* **2006**, 411-414.

90 Martínez, A.; García-García, P.; Fernández-Rodríguez, M. A.; Rodríguez, F.; Sanz, R. *Angew. Chem. Int. Ed.* **2010**, *49*, 4633-4637.

91 Gagosz, F. *Org. Lett.* **2005**, *7*, 4129-4132.

(45)
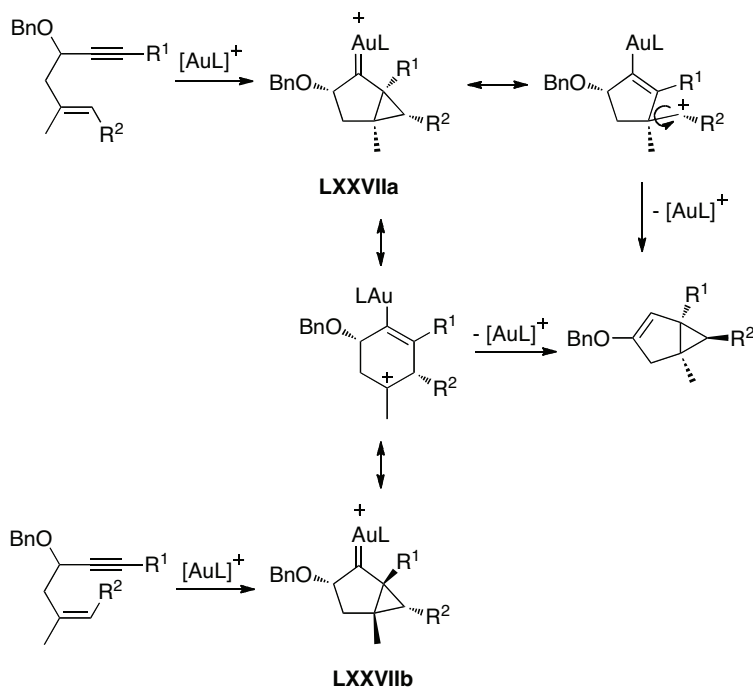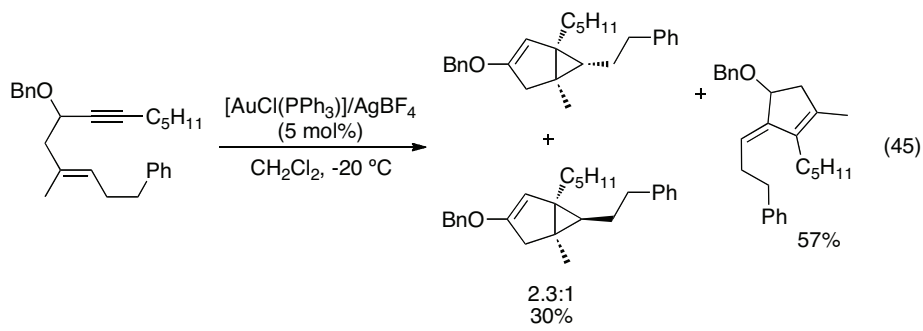
Scheme XLIV

The major product in *Equation 45* corresponds to the product of single cleavage rearrangement. The mechanism is analogous to the one proposed for 1,6-enynes. The internal gold(I) carbenes **LXXVII** intermediate can undergo a 1,2-shift of the alkyl group to afford carbocations **LXXIX**. Subsequent elimination of cationic gold would lead to dienes **LXXII** (*Scheme XLV*).
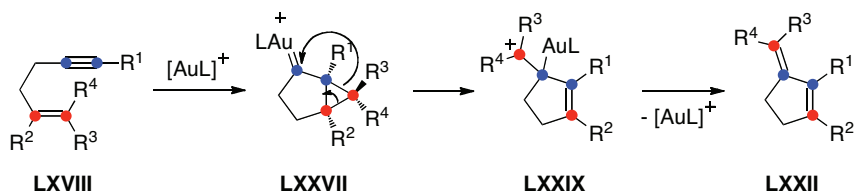
Scheme XLV

Double cleavage products have been obtained from aryl- and sililoxy-substituted 1,5-enynes (*Equation 46*).[92] The double cleavage rearrangement in 1,5-enynes occurs by reorganization of cyclopropyl gold(I) carbene intermediates **LXXVII** to form an internal gold(I) carbene (**LXXX**). Then 1,2-shift of the substituents at the α position and demetalation would form cyclohexadienes **LXX** and **LXXI** (*Scheme XLVI*).

92 (a) Zhang, L.; Kozmin, S. *J. Am. Chem. Soc.* **2004**, *126*, 11806-11807. (b) Sun, J.; Conley, M. P.; Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2006**, *128*, 9705-9710.
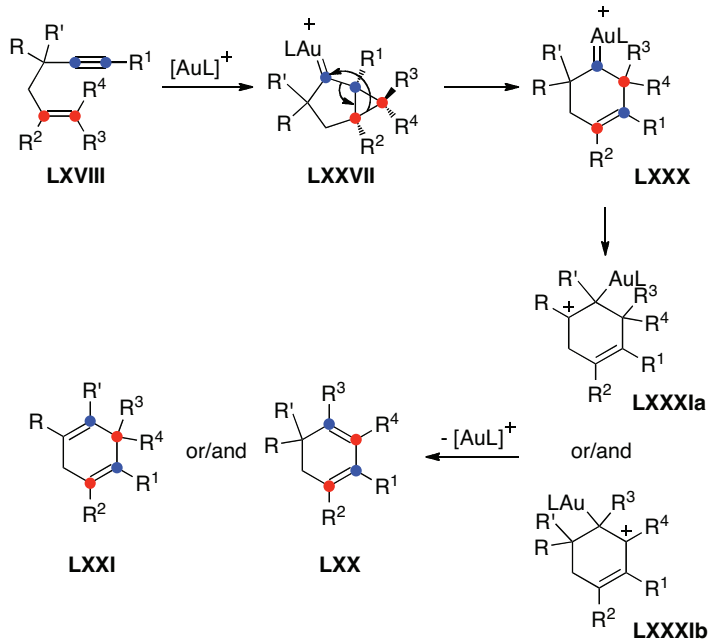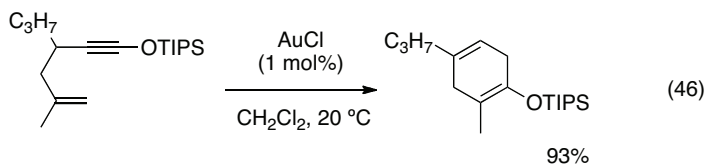
Scheme XLVI

The *exo* cyclization was also observed as a minor pathway in the gold(I)-catalyzed cyclization of 1,5-enynes with internal alkynes and as a major product for terminal or iodo-substituted alkyne moiety on the 1,5-enyne (*Scheme XLVII*).[89]

(47)

(48)

(49)
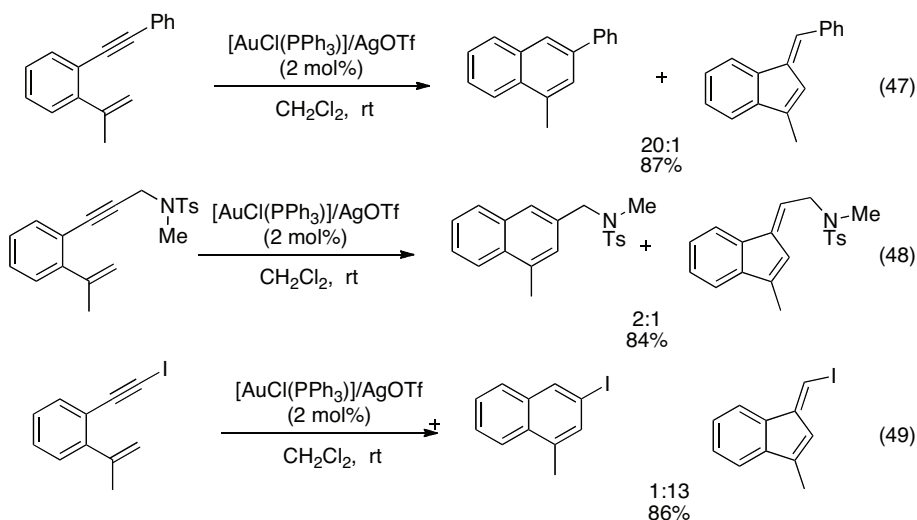
Scheme XLVII

Gold(I)-catalyzed intermolecular addition of nucleophiles such as H_2O or alcohols to 1,5-enynes give cyclic products of type **LXXV**[88] and **LXXVI**,[93] by a formal 1,4-intermolecular addition to the cyclopropyl gold carbene intermediate **LXXVII** (*Scheme XLVIII*).
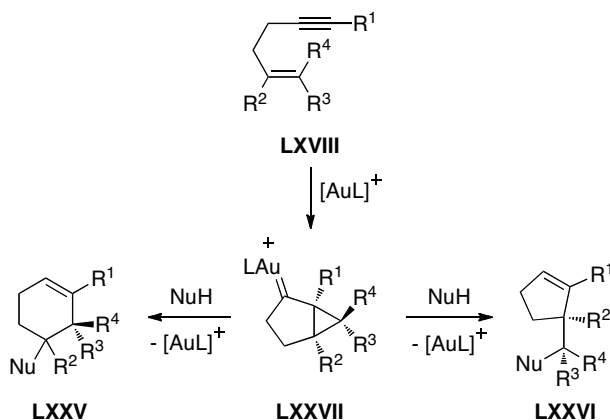
Scheme XLVIII

Hydroxy- and alkoxycyclization have been recently acomplished in a tandem nucleophilic addition process to give bicyclo[4.3.0]nonane (*Equation 50*). This transformation starts by 5-*endo-dig* cyclization to intermediate **LXXVIIc** which suffers intramolecular nucleophilic attack of the alkene moiety. The [4+2] annulation forms the

93 Buzas, A. K.; Istrate, F. M.; Gagosz, F. *Angew. Chem. Int. Ed.* **2007**, *46*, 1141-1144.

gold(I)-stabilyzed carbocation **LXXXII**, which react with ROH to form **LXXXIII** (*Scheme XLIX*).[94]

(50)
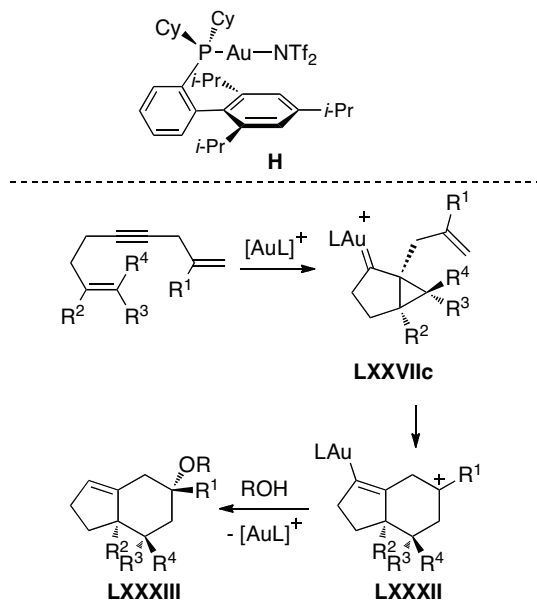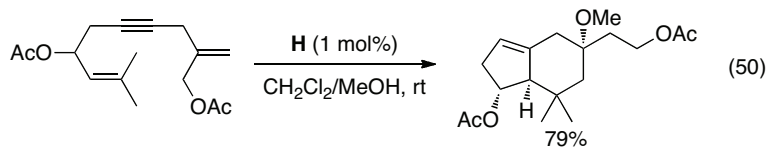
Scheme XLIX

3-Alkoxy-1,5-enynes bearing a cyclopropyl ring at the allylic position cyclize in the presence of gold(I) complexes to produce functionalized benzenes (*Equation 51*).[95] The presence of the cyclopropyl ring at the allylic position promotes the formation of a highly distorted gold carbene **LXXXIV** which suffers addition of alcohols to give cyclohexa-1,4-diene **LXXXV**. After gold-mediated aromatization, functionalized benzenes **LXXXVI** are obtained (*Scheme L*). Substituted benzenes are also obtained from 3-hydroxy-1,5-enynes in the absence of alcohols or water.[96]

---

94 Böhringer, S.; Gagosz, F. *Adv. Synth. Catal.* **2008**, *350*, 2617-2630.

95 Li, G.; Liu, Y. *J. Org. Chem.* **2010**, *75*, 2903-2909.

96 (a) Grisé, C. M.; Barriault, L. *Org. Lett.* **2006**, *8*, 5905-5908. (b) Grisé, C. M.; Rodrigue, E. M.; Barriault, L. *Tetrahedron* **2008**, *68*, 797-808.

$$\text{(51)}$$
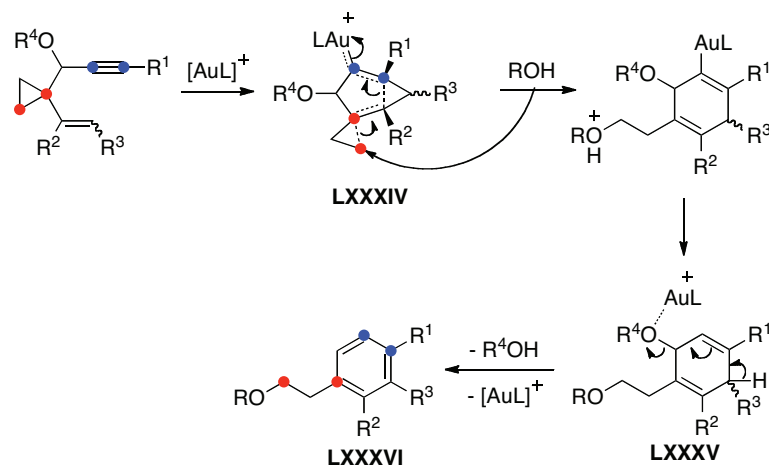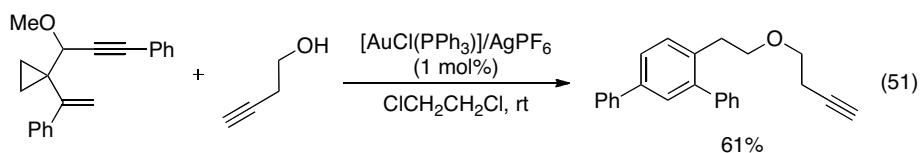
Scheme L

Gold(I)-catalyzed intramolecular addition of nucleophiles to cyclopropyl gold carbenes formed from 1,5-enynes has also been studied. 1,5-Enynes with hydroxy or amino groups at different chain positions can cyclize to fused,[97] bridged and spirocyclic systems[98] (*Scheme LI*). Cyclization of *O*-Boc substituted 1,5-enynes also take place by opening of the cyclopropyl gold(I) carbene intermediate to yield cyclohex-4-ene-1,2-diol derivatives.[99]

97 Toullec, P. Y.; Blarre, T.; Michelet, V. *Org. Lett.* **2009**, *11*, 2888-2891.

98 Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 6962-6963.

99 Lim, C.; Kang, J.-E.; Lee, J.-E.; Shin, S. *Org. Lett.* **2007**, *9*, 3539-3542.
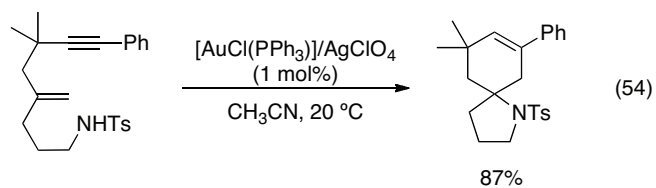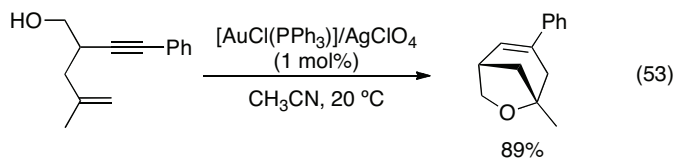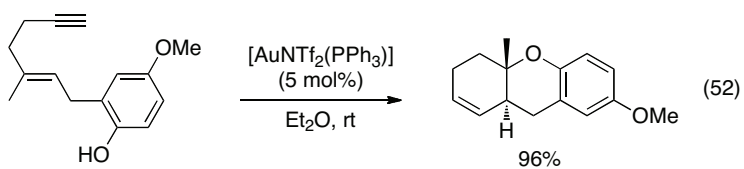
Scheme LI

Gold-catalyzed cyclization of 1,n-enynes (n > 6)

1,7-Enynes were usually presented as an extension of the 1,6-enynes cyclization studies.[100]

1,7-Enynes also undergo single cleavage rearrangement with different catalysts like Ga(III),[100e,h,i] Pt(II)[100b,g] or Rh(II),[100j] but only gold(I)-catalyzed cyclization of 1,7-enynes take place at room temperature with low catalyst loadings (*Scheme LII*).[101] Double cleavage rearrangement of 1,7-enynes is still unknown using gold catalysis but it has been reported in the presence of $Rh_2(O_2CCF_3)_4$.[100j]

$$Z = C(CO_2Me)$$
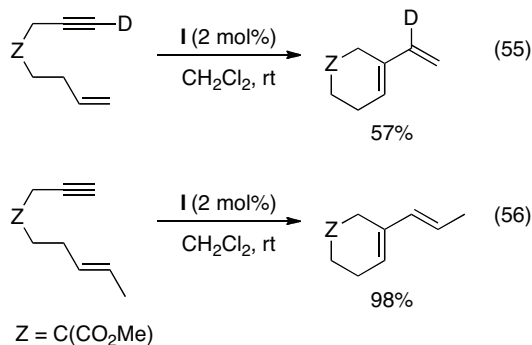
Scheme LII

The proposed mechanism for the gold(I)-catalyzed single cleavage rearrangement is analogous to the one proposed for 1,6-enynes. Nucleophilic attack to the alkyne coordinated to gold(I) leads to the exo carbene **LXXXVIII** which rearranges to the gold-stabilyzed carbocation **LXXXIX**, followed by demetalation to give 1,3-dienes **XC** (*Scheme LIII*).

---

100 (a) Chatani, N.; Morimoto, T.; Muto, T.; Murai, M. *J. Am. Chem. Soc.* **1994,** *116,* 6049-6050. (b) Chatani, N.; Furukawa, N.; Sakurai, H.; Murai, S. *Organometallics* **1996,** *15,* 901-903. (c) Trost, B. M.; Dean Toste, F. D. *J. Am. Chem. Soc.* **2000,** *122,* 714-715. (d) Chatani, N.; Inoue, H.; Morimoto, T.; Muto, T.; Murai, S. *J. Org. Chem.* **2001,** *66,* 4433-4436. (e) Chatani, N.; Inoue, H.; Kotsuma, T.; Murai, S. *J. Am. Chem. Soc.* **2002**, *124*, 10294-10295. (f) Hatano, M.; Mikami, K. *J. Am. Chem. Soc.* **2003**, *125*, 4704-4705. (g) Bajracharya, G. B.; Nakamura, I.; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 892-897. (h) Simmons, E. M.; Sarpong, R. *Org. Lett.* **2006**, *8*, 2883-2886. (i) Simmons, E. M.; Yen, J. R.; Sarpong, R. *Org. Lett.* **2007**, *9*, 2705-2708. (j) Ota, K.; Lee, S. I.; Tang, J.-M.; Takachi, M.; Nakai, H.; Morimoto, T.; Sakurai, H.; Kataoka, K.; Chatani, N. *J. Am. Chem. Soc.* **2009**, *131*, 15203-15211.

101 Cabello, N.; Rodríguez, C.; Echavarren, A. M. *Synlett.* **2007**, 1753-1758.
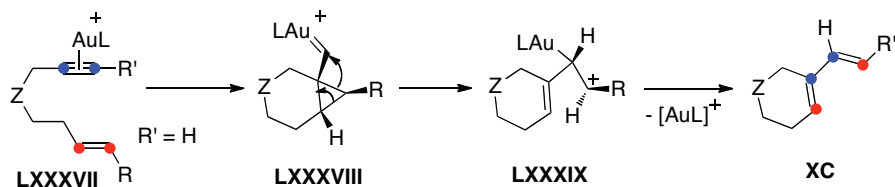
Scheme LIII

In the platinum(II)-catalyzed reaction of 1,7-enynes, cyclobutenes were found to be the primary products, which then would open to form 1,3-dienes (*Scheme LIV*).
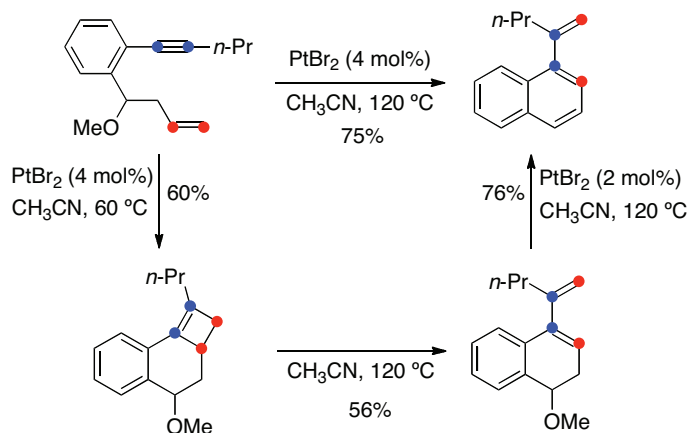
Scheme LIV

1,8-Enyne cyclization has also been reported using gold(I) complexes to form cyclobutenes as the main products.[102] Depending on the substitution pattern cyclobutenes are unstable in solution and open to form 1,3-dienes (*Equation 57*). Stable cyclobutenes can also open to dienes in the presence of gold(I) catalyst (*Equation 58*). In this case, formation of dienes is proposed to proceed by gold(I)-promoted opening of cyclobutenes via the cataionic intermediate **XCII** (*Scheme LV*).

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102 Odabachian, Y.; Gagosz, F. *Adv. Synth. Catal.* **2009**, *351*, 379-386.

(57)

(58)

Z = C(CO$_2$Me)

XCI   **XCII**
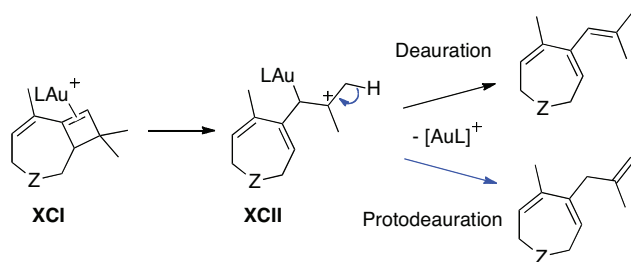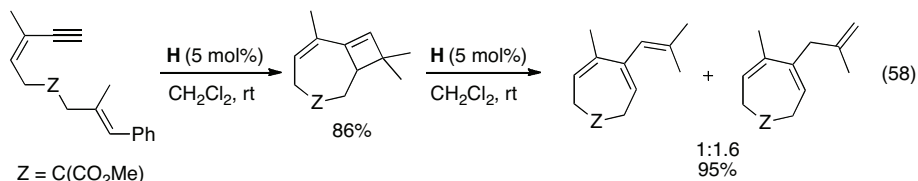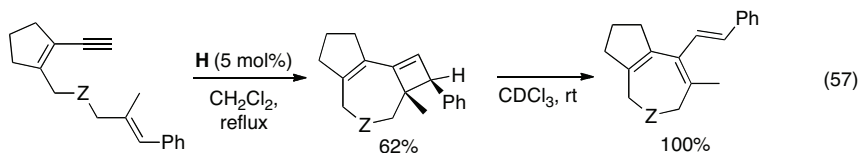
Scheme LV

There is only a single example of cyclization of 1,9-enynes.[103] However, this reaction requires 50 mol% of the gold complex and 70 mol% of silver salt to obtain a cyclic diene in 58% yield (*Equation 59*).

Z = C(CO$_2$Me)   (59)

58%

Scheme LVI

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103 Comer, E.; Rohan, E.; Deng, L.; Porco, J. A. *Org. Lett.* **2007**, *9*, 2123-2126.

Chapter 1

Gold(I)-Catalyzed Intermolecular Reaction of Alkynes with Alkenes

Objectives

Cyclizations of 1,n-enynes have been the benchmark for the development of gold-catalyzed reactions. Although much has been advanced in the understanding of the reactivity of alkynes with electrophilic catalysts, the intermolecular reaction of alkynes with alkenes catalyzed by gold is still unknown.[104]

Based on the general reactivity of 1,n-enynes with gold(I), the intermolecular reaction of alkynes with alkenes would be expected to proceed via regioisomeric cyclopropyl gold(I) carbenes **1a** and/or **1b** to give dienes **2a-c** or cyclobutenes **3** (*Scheme 1*).
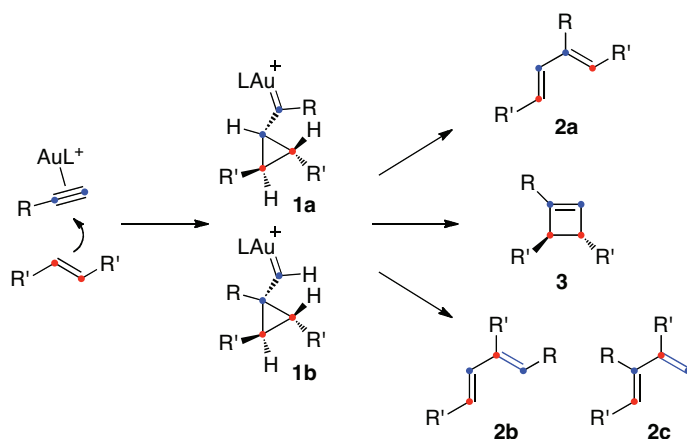
Scheme 1

The objective of this work was to develop the gold(I)-catalyzed intermolecular reaction of alkynes with alkenes.

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104 The only example of a somewhat related intermolecular reaction is the formation of a phenol in the reaction of 2,5-dimethylfuran with phenylacetylene (38% yield after 6 days): Hashmi, A. S. K.; Blanco, M. C.; Kurpejovic, E.; Frey, W.; Bats, J. W. *Adv. Synth. Catal.* **2006**, *348*, 709-713.

Results and Discussion

Gold(I)-Catalyzed Intermolecular Reaction of Alkynes with Alkenes

For the study on the alkyne/alkene intermolecular reaction we first selected as substrates phenylacetylene (**4a**) and α-methylstyrene (**5a**) (*Table 1*). No reaction was observed with AuCl as catalyst, whereas [AuCl(PPh$_3$)]/AgSbF$_6$ led only to indane **7** (in 43% yield) (*Table 1*, entries 1 and 2), which is a dimer formed by dimerization of **5a**.[105] The mechanism for this dimerization starts by coordination of the alkene to gold(I) and nucleophillic attack of a second molecule of alkene to form carbocation **9**. Subsequent Friedel-Crafts type precess produces intermediate **10**, which forms indane **7** after proton loss and protodemetalation (*Scheme 2*).
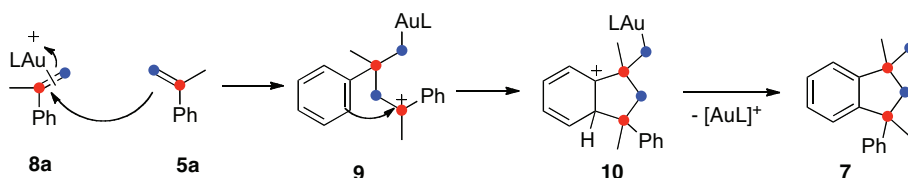
Scheme 2

Formation of **7** indicates that gold(I) coordinates preferentially to the alkene in the presence of the alkyne. To avoid complexation of alkene with gold(I), catalysts **E** and **U** bearing bulky dialkylbiarylphosphine ligands were tested in the presence of different alkenes. A rapid equilibrium was immediately established between catalyst **E** and **8ae** in CD$_2$Cl$_2$ at 23 °C (^{1}H and ^{31}P NMR analysis). However, even at 23 °C, this equilibrium was slow with catalyst **U** (*Scheme 3*). Isomerization of terminal alkenes **5b-d** () was observed with **E** at 23 °C, whereas this isomerization was very slow with **U**.

---

105 Acid-catalyzed formation of indanes from styrenes is a facile process: Sun, H.-B.; Li, B.; Hua, R.; Yin, Y. *Eur. J. Org. Chem.* **2006**, 4231-4236; and references therein.

Scheme 3
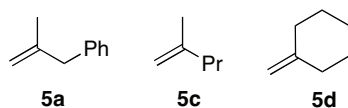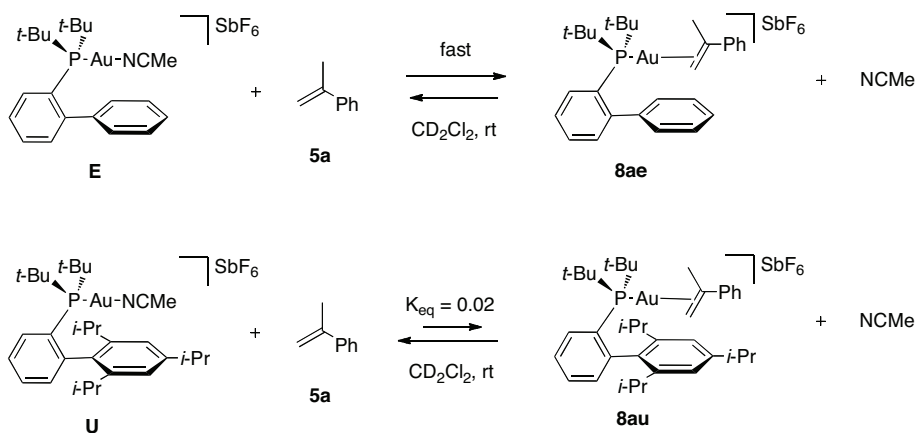
Figure 1

In the presence of catalysts **E** and **U-W** (*Figure 2*) cyclobutene **6a** was obtained as a single regioisomer (*Table 1*, entries 3-6). The best results were obtained using more crowded complex **U** (*Table 1*, entry 6). Less sterically hindered **W** led to lower yields (*Table 1*, entry 7). NHC-gold(I) complex **R** was not effective, whereas **Q** led to **6a** in 58% yield after 4 h (*Table 1*, entries 8 and 9), although in this case longer reactions times led to lower yields.

Table 1

entry	[M]	4a/5a	time (h)	6a (yield, %)[b]
1	AuCl	2:1	72	-[c]
2	[AuCl(PPh₃)]/AgSbF₆	2:1	16	-[d]
3	**E**	2:1	18	42
4	**E**	1:2	18	67 (60)
5	**U**	1:2	16	81 (80)
6	**V**	1:2	16	70
7	**W**	1:2	16	19
8	**R**	3:1	4	-[c]
9	**Q**	3:1	4	58

(a) 3 mol% catalyst, in CH_2Cl_2 at room temperature. (b) ^{1}H NMR yields. In parentheses isolated yields. (c) Complex mixture. (d) 1,1,3-trimethyl-3-phenyl-2,3-dihydro-1*H*-indene (**7**) was obtained (43%).
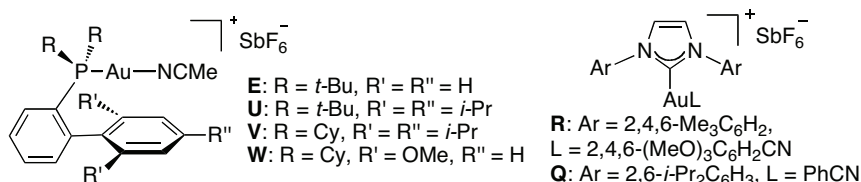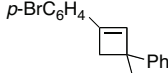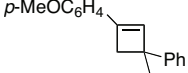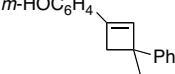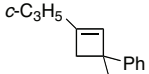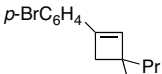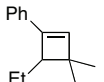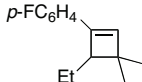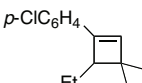
Figure 2
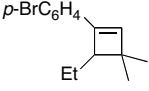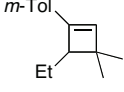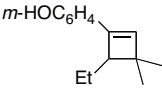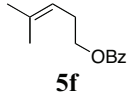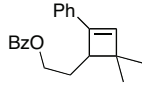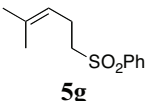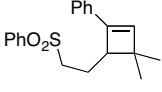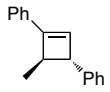
The scope in the substitution of alkyne and alkene is shown in *Table 2*. Reaction of **4a-h** with alkenes **5a-h** led to cyclobutenes **6a-u** in moderate to good yields using catalyst **U** (*Table 2*). The reaction proceeds satisfactorily with alkynes with both electron-rich and moderate electron-poor substituents at the aryl ring, including a free OH group (*Table 2*, entries 1-8). *p*-Nitrophenylacetylene and 1-ethynyl-3,5-bis(trifluoromethyl)benzene were recovered under the reaction conditions of *Table 2*. Alkyl substituted alkynes like 1-hexyne and ethynylcyclohexane were unreactive under

these conditions, whereas ethynylcyclopropane (**4i**) reacts with **5a** to yield the corresponding cyclobutene **6i** after 48 h at room temperature (*Table 2*, entry 9). Internal alkynes such as 1-phenyl-1-propyne and 1-phenyl-1-hexyne were recovered unchanged under these conditions. A single regioisomer was obtained with 1,1-disusbtituted alkenes (**5a-d**) (*Table 2*, entries 1-12), whereas trisubstituted alkenes led to **6m-r** as the major regioisomer (*Table 2*, entries 13-18). A single regioisomer can be obtained by introducing an electron-withdrawing group at one of the chain of trisubstituted alkenes (**5f-g**) but longer reaction times are requaried to form cyclobutenes **6s-t** in moderate yields (*Table 2*, entries 19-21). *Trans*-1,2-disubstituted alkenes such as *trans-β*-methylstyrene (**5h**) react stereospecifically with **4a** to yield a 4:1 mixture of regioisomers **6u/6u'** in moderate yield (*Table 2*, entry 21).

Table 2

Entry	Alkyne	Alkene	time (h)	Product (yield, %)[b]
1	**4a**	**5a**	16	**6a** (80)
2	**4b**	**5a**	40	**6b** (74)
3	**4c**	**5a**	4	**6c** (78)
4	**4d**	**5a**	6	**6d** (75)
5	**4e**	**5a**	25	

6	**4f**	**5a**	24	**6e** (61) — p-BrC$_6$H$_4$, Ph
7	**4g**	**5a**	24	**6f** (74) — p-MeOC$_6$H$_4$, Ph
8	**4h**	**5a**	26	**6g** (64) — m-HOC$_6$H$_4$, Ph
9	**4i**	**5a**	48	**6h** (74) — c-C$_3$H$_5$, Ph
10	**4a**	Ph **5b**	20	**6i** (46) — Ph, Ph
11	**4f**	Pr **5c**	20	**6j** (45) — p-BrC$_6$H$_4$, Pr
12	**4a**	**5d**	23	**6k** (45, **6k/6o** = 5:1) — Ph
13	**4a**	Et **5e**	20	**6l** (53) — Ph, Et
14	**4d**	**5e**	16	**6m** (74, 9:1) — p-FC$_6$H$_4$, Et
15	**4e**	**5e**	18	**6n** (73, 9:1) — p-ClC$_6$H$_4$, Et

				6p (62, 10:1) — p-BrC$_6$H$_4$, Et
16	**4f**	**5e**	16	
				6o (62, 12:1) — m-Tol , Et
17	**4c**	**5f**	7	
				6q (62, 7:1) — m-HOC$_6$H$_4$, Et
18	**4h**	**5e**	18	
				6r (60, 7:1) — Ph , BzO
19	**4a**	(structure, OBz) **5f**	14	
				6s (50) — Ph , PhO$_2$S
20	**4a**	(structure, SO$_2$Ph) **5g**	72	
				6t (44) — Ph
21	**4a**	Ph⌒ **5h**	58	
				6u (48, 4:1) — Ph , Ph

(a) Reactions with 2:1 alkyne/alkene ratio. (b) Isolated yields, regioisomeric ratio.

Biscyclobutenes **6v** and **6w** were also obtained from p- and m-diethynylbenzene, respectively. Similarly, reaction of m-di(prop-1-en-2-yl)benzene (**5j**) with phenylacetylene (**4a**) provided biscyclobutenes **6x** (*Figure 3*). Compounds **6v-x** were obtained as 1:1 mixtures of diasteroisomers.

6v (68%)   **6w** (53%)   **6x** (48%)

Figure 3

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UNIVERSITAT ROVIRA I VIRGILI
MASTERING THE REACTIVITY OF GOLD (I) CARBENES
Verónica López Carrillo
ISBN:978/84-694-0328-0/DL:T-208-2011
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Chapter 1. Results and Discussion
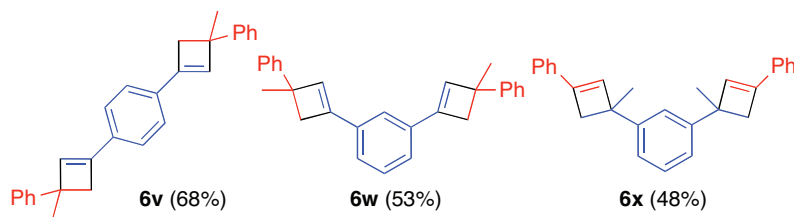
Reaction **4a** with *trans-β*-methylstyrene (**5h**) led to a 4:1 mixture of regioisomers **6u**/**6u'** with *trans* configuration (*Table 2*, entry 21), which suggest that the [2+2] cycloaddition is stereospecific. However, reaction of **4a** with (*E*)-**5a**-d_1 gave cycloadduct **6a**-d_1 as a 1:1 mixture of diasteroisomers (*Scheme 4*).
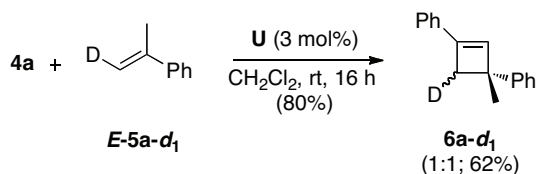
Scheme 4

These results are consistent with a reaction of Au(I)-alkyne complex **11** with the alkene **5** to form highly distorted cyclopropyl gold(I) carbenes **12**/**12'** as intermediates. Intemediate **12'** would form cyclobutene **6** via **13'** by migration of the C2-C3 bond. Intermediate **12** gives **6** via carbocation **13** by migration of the C2-C4 bond (*Scheme 5*). However, since both pathways proceeds trough carbocationic intermediates, formation of intermediate **13** is more reasonable due to the stabilization of the R^1 group (*Scheme 5*). Indeed, the group tolerance on the alkyne suggests that the mechanism proceeds through intermediate **13**, since the reaction only works for terminal alkynes bearing groups that can stabilize a carbocation such as aryl and cyclopropane (see *Table 2*).
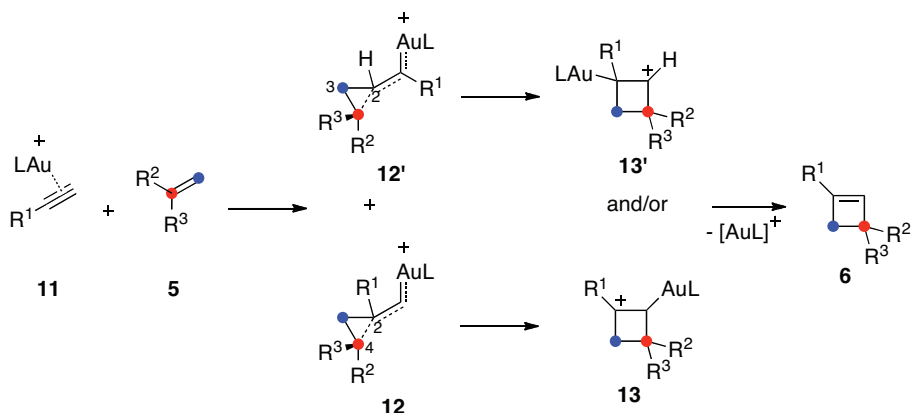
Scheme 5

Formation of intermediate **12** is analogue of the *exo*-type intermediates formed in the cyclization of 1,n-enynes,[69] which have been shown to undergo cyclopropanation

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

of alkenes in both intra-[73] and intermolecular[75] reactions. We reasoned that intermediate **12** could also form cyclopropanes in the presence of a second alkene moiety. Indeed, reaction of terminal alkynes with 2,5-dimethylpenta-1,5-diene in the presence of complex **U** gave biscyclopropyl derivatives **14a-e**, with an *anti*-relative configuration, in addition to cyclobutenes **6y-ac** (*Scheme 6*).

R = Ph (63%, 1:1)
R = *p*Tol (54%, 1.2:1)
R = *m*Tol (60%, 1.1:1)
R = 4-*t*-BuC$_6$H$_4$ (50%, 1.4:1)
R = 3-HOC$_6$H$_4$ (64%, 1.8:1)
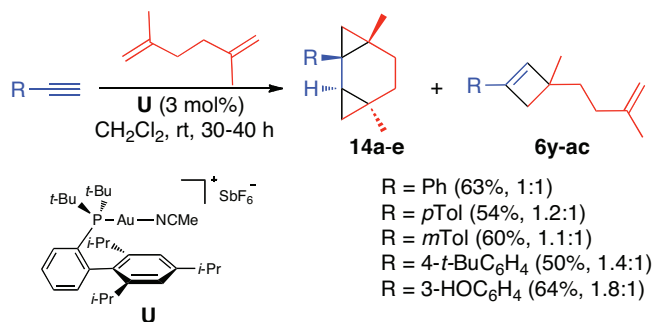
Scheme 6

Reaction of **4a** with **5j-d_2** gave stereospecifically **14a-d_2** and cyclobutene **6y-d_2** (1:1 ratio), which suggest that the reaction proceeds through intermediate **12-d_2** in which no free rotation occurs around the C3-C4 bond (*Scheme 7*).
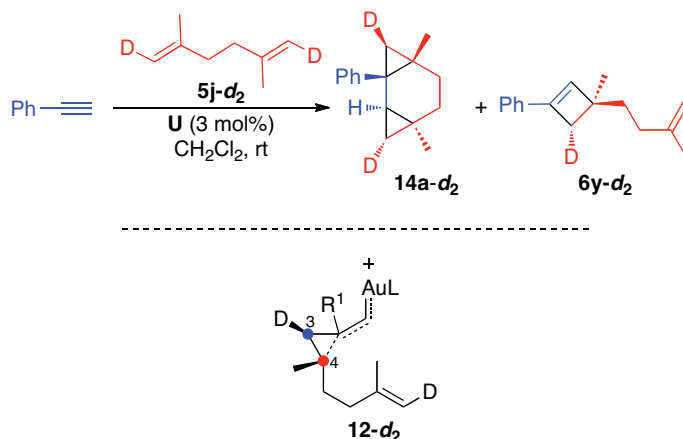
Scheme 7

73 Nieto-Oberhuber, C.; López, S.; Muñoz, M. P.; Jiménez-Núñez, E.; Buñuel, E.; Cárdenas; D.; Echavarren, A. M. *Chem. Eur. J.* **2006,** *11*, 1694-1702.

75 (a) López, S.; Herrero-Gómez, E.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 6029-6032. (b) Pérez-Galán, P.; Herrero-Gómez, E.; Hog, D. T.; Martin, N. J. A.; Echavarren, A. M. *Chem. Sci.* **2011**, DOI: 10.1039/COSC00335B.

Formation of biscyclopropyl derivatives **14a-e** and cyclobutenes **6v-z** (*Scheme 6*) could be explained by the different evolution of stereoisomeric intermediates **12a** and **12b**. Intermediate **12a** in which the gold(I) carbene is in *syn* disposition to the alkyl chain bearing the alkene, can lead to biscyclopropyl product **14**. In intermediate **12b**, cyclopropanation of the alkene is not feasible since the gold(I) carbene and the alkene are *anti*. Hence, ring-expansion takes place from intermediate **12b** to form cyclobutene **6** (*Scheme 8*).
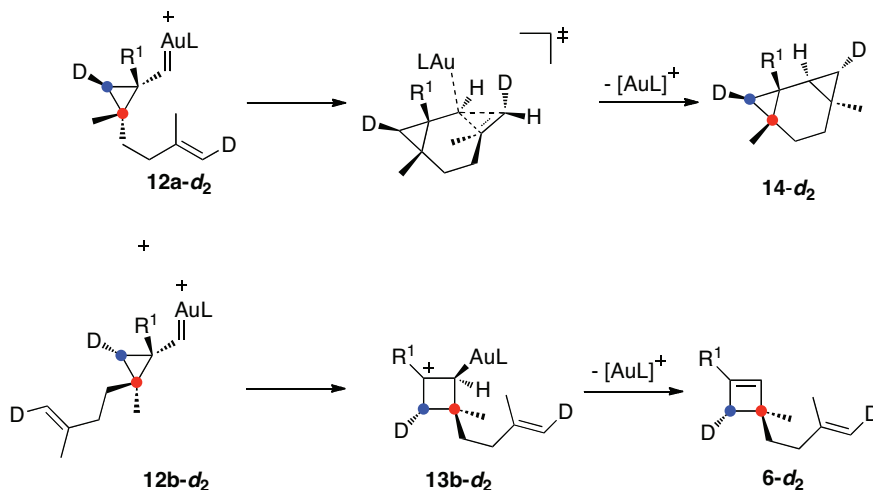
Scheme 8

The *exo*-type intermediates formed in 1,6-enyne cyclization can react with carbonyl compounds in both intra- and intermolecular fashion.[80-84] We reasoned that intermediate **12** might also be trapped with carbonyl compounds. Indeed, reaction of phenylacetylene with the unsaturated ketone **5k** under the optimal reaction conditions found in *Table 1* gave 39% yield of triciclic compound **15** (entry 4, *Table 3*). Performing the reaction under more diluted conditions resulted in an improvement on

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80 Jiménez-Núñez, E.; Claverie, C. K.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 5452-5455.

81 Jiménez-Núñez, E.; Molawi, K.; Echavarren, A. M. *Chem. Commun.* **2009**, 7327-7329.

82 Molawi, K.; Delpont, N.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2010**, *49*, 3517-3519.

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

84 Escribano-Cuesta, A.; López-Carrillo, V.; Janssen, D.; Echavarren, A. M. *Chem. Eur. J.* **2009**, *15*, 5646-5650.

the yield of **15** to 46% (37% isolated yield) (entry 5, *Table 3*). The screening of different gold(I) catalysts revealed the same pattern found in the formation of cyclobutene (*Table 1*), but no improvement in the reaction conversion.

Table 3

entry	[M]	**4a/5a**	[Limitant Reagent] (M)	time (h)	**15** (yield, %)[b]
1	**E**	1:2	0.4	24	19
2	**E**	2:1	0.5	24	15
3	**U**	1:2	0.5	24	13
4	**U**	2:1	0.5	24	39
5	**U**	2:1	0.25	24	46 (37)
6	**V**	2:1	0.25	24	25
7	**W**	2:1	0.25	24	-
8	**Q**	2:1	0.25	24	15

(a) 3 mol% catalyst, in CH_2Cl_2 at room temperature. (b) ^1H NMR yields. In parentheses isolated yields.
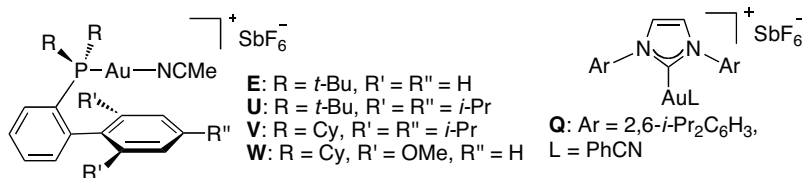
Figure 4

Formation of **15** corresponds to a formal [2+2+2] cycloaddition whose mechanism is despicted in *Scheme 9*. The reaction presumably starts with the formation of a distorted cyclopropyl gold(I) carbene **12c**, which is opened by the carbonyl group to form **16**. In intermediate **16** the vinyl gold(I) moiety can attack the oxonium cation in

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a Prins reaction to form **17**, which gives the tricyclic compound **15** after elimination of [AuL]$^{+}$ (*Scheme 9*).
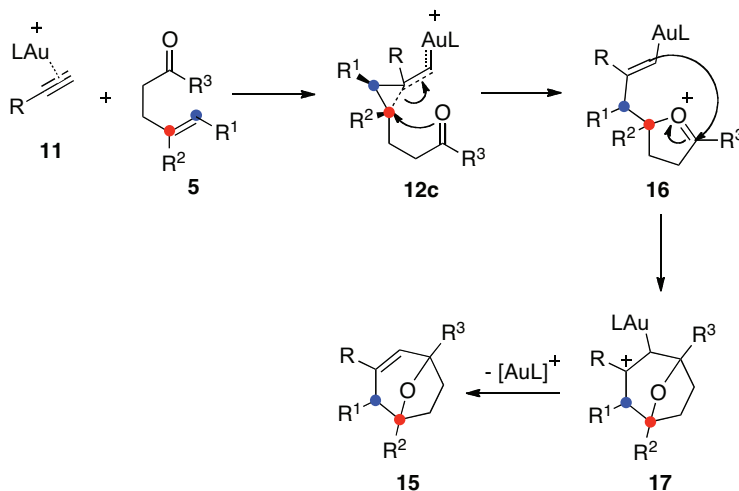
Scheme 9

Conclusions

This work shows that in the absence of the constrains imposed by the tethers in intramolecular processes (enyne cyclization), the gold(I)-catalyzed reaction of alkynes with alkenes leads to cyclobutenes in a stereospecific [2+2] cycloaddition. Key for the success of this reaction is the use of gold(I) complexes with bulky ligands that selectively activate alkynes in the presence of alkenes.
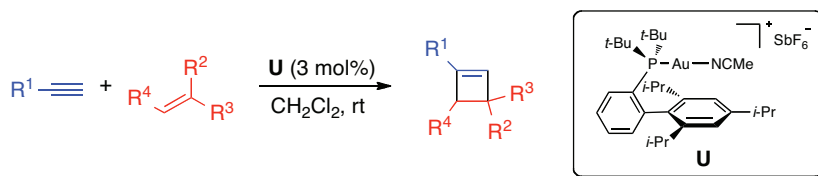
Scheme 10

This reactivity opens new opportunities for the invention of related intermolecular gold(I)-catalyzed processes, like cyclopropanation reaction or multicomponent reaction with carbonyl compounds (*Scheme 11*).
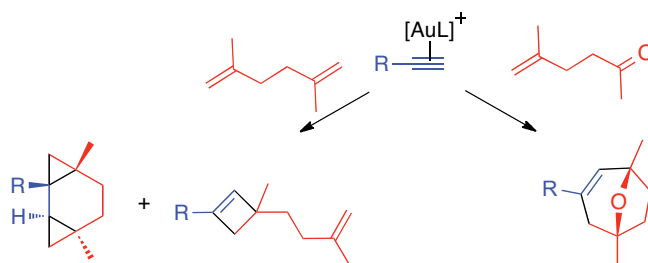
Scheme 11

This work shows that the gold(I)-catalyzed [2+2] cycloaddition is compatible with difunctionalyzed monomers which opens the door towards new polymerization strategies (Scheme 12).
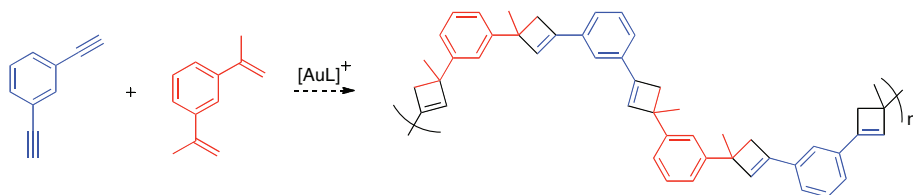
Scheme 12

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Chapter 2

Gold-Catalyzed Addition of Carbon Nucleophiles to Propargyl Carboxylates

Objectives

Propargyl esters **18** undergo 1,2- or 1,3-acyloxy migration with Au(I) complexes via intermediates **20** or **21** to form highly reactive α,β-unsaturated Au(I) carbenes **23** or Au(I)-coordinated allenes **22**, respectively (*Scheme 13*).[49]
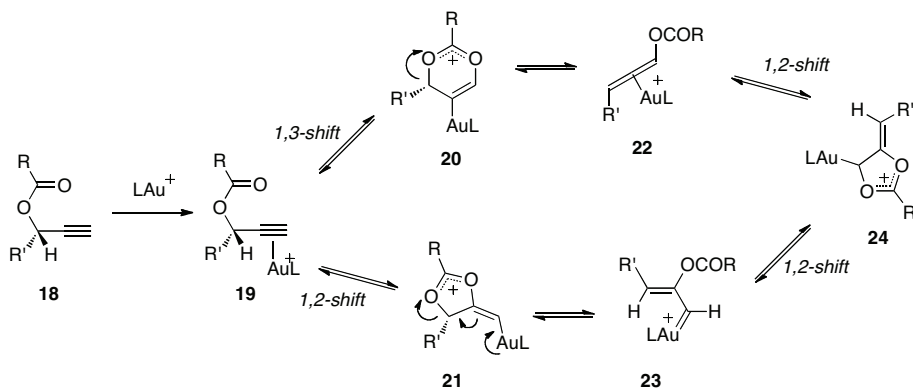
Scheme 13

Carbenes **23** formed from **18** by 1,2-acyloxy migration react with alkenes to give cyclopropanes.[40] Au(I) carbenes formed from 1,6-enynes have also been trapped in cyclopropanation reactions.[8a,73-75] Ongoing investigations in our group showed that Au(I)-catalyzed the addition of electron-rich aromatic compounds to 1,6-enynes, which proceeds by nucleophilic attack at the cyclopropane of intermediates **27** (*Scheme 14*).[14]

8a Nieto-Oberhuber, C; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 2402-2406.

14 Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M. *J. Org. Chem.* **2008**, *73*, 7721-7730.

40 Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002-18003.

49 Correa, A.; Marion, N.; Fensterbank, L.; Malacria, M.; Nolan, S. P.; Cavallo, L. *Angew. Chem. Int. Ed.* **2008**, *47*, 718-721.

73 Nieto-Oberhuber, C.; López, S.; Muñoz, M. P.; Jiménez-Núñez, E.; Buñuel, E.; Cárdenas; D.; Echavarren, A. M. *Chem. Eur. J.* **2006,** *11*, 1694-1702.

74 Kim, S. M.; Park, J. H.; Choi, S. Y.; Chung, Y. K. *Angew. Chem. Int. Ed.* **2007**, *46*, 6172-6175.

75 (a) López, S.; Herrero-Gómez, E.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 6029-6032. (b) Pérez-Galán, P.; Herrero-Gómez, E.; Hog, D. T.; Martin, N. J. A.; Echavarren, A. M. *Chem. Sci.* **2011**, DOI: 10.1039/COSC00335B.
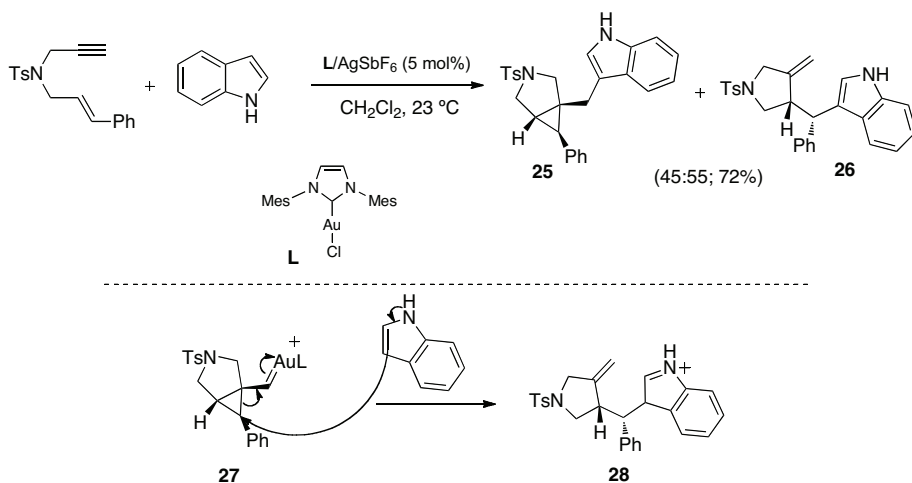
Scheme 14

We also observed examples of direct attack to the gold(I) carbene such as **25** (*Scheme 14*), which is formed by 1,2-addition of indole to the carbene in intermediate **27** (*Scheme 15*).
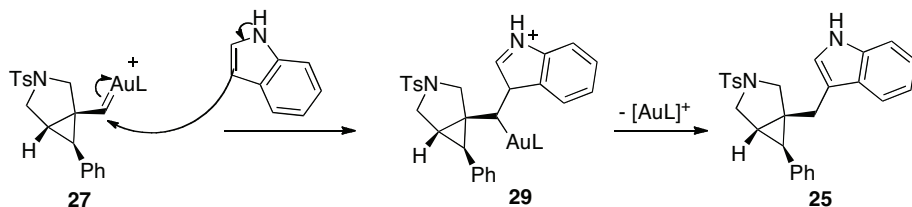
Scheme 15

In this context, we decided to study the reactivity of propargylic esters with carbon nucleophiles in the presence of gold(I) catalysts.

Results and Discussion

Gold-Catalyzed Addition of Carbon Nucleophiles to Propargyl Carboxylates

To study the rearrangement of propargyl carboxylates in the presence of carbon nucleophiles we first tested the reaction of propargyl acetate (**18a**) and dibenzoylmethane (**30a**) with AuCl, AuCl$_3$, cationic Au(I) complex **E**, precatalysts **J** and **L**, and cationic Ag(I) complex **33** (*Table 4*). Addition of **30a** to **18a** proceeded at room temperature to give enol acetate **31a** with all the gold catalysts (*Table 4*, entries 1-6). A mixture of *E* and *Z* isomers was obtained with AuCl and AuCl$_3$ (*Table 4*, entries 1 and 2), whereas cationic Au(I) catalysts provided pure *Z*-**31a**. The reaction was faster and cleaner with complex **E** (*Table 4*, entries 3 and 4). With **L** and AgSbF$_6$, a mixture of **31a** and the product of nucleophilic substitution **32** was obtained (*Table 4*, entry 6). Reaction of **18a** with cationic complex **33** or Sc(OTf)$_3$ as catalysts gave acetylene **32**, whereas with Cu(OTf)$_2$ a mixture of **32** and **34**, which is the product of hydration of **32**, (*Figure 6*) was obtained (*Table 4*, entries 7-9).

Table 4

Entry	[M]	Time (h)	31a (*Z/E*)	31a Yield (%)	20 Yield (%)
1	AuCl	15	79:21	60[a]	0[a]
2	AuCl$_3$	1	71:29	56	6
3	**E**	2.3	100:0	66	0
4	**E**	2.5	100:0	88	0
5	**J**/AgSbF$_6$	3	100:0	50	0
6	**L**/AgSbF$_6$ [a]	2.5	100:0	50	36
7	**33**	15.5	-	0	21
8	Sc(OTf)$_3$	1	-	0	98
9	Cu(OTf)$_2$	1.5	-	0	20[b]

(a) 2 mol% of catalyst. (b) The methyl ketone **34** (*Figure 6*) was also obtained (74%).

Figure 5

34
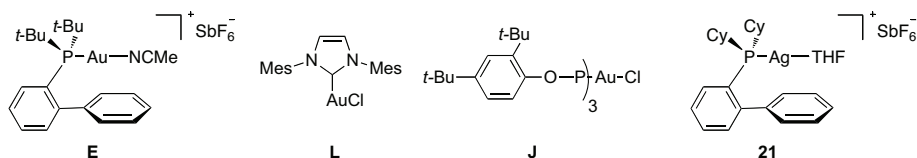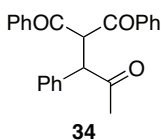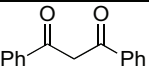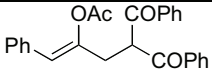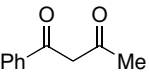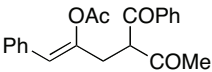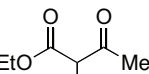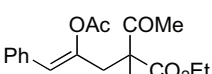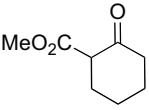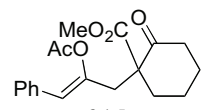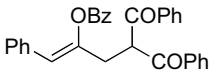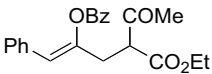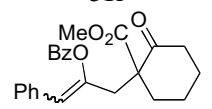
Figure 6

Propargylic esters **18a-b** react with a variety of 1,3-dicarbonyl compounds in the presence of catalyst **E** (*Table 5*) to give products of 1,2-addition to gold(I) carbene intermediates **23** (*Scheme 13*). A higher yield was obtained in the reaction of benzoate **18b** with dibenzoylmethane **30a** than that obtained with acetate **18a** under identical conditions (*Table 5*, entry 1, 5). The addition of α-ketoesters **30c-e** to **18a-b** had to be carried out in the presence of 5 mol% of Sc(OTf)$_3$ (*Table 5*, entries 3-4 and 7) or Cu(OTf)$_2$ (*Table 5*, entry 6) to give adducts **31c-d** and **31f-g** in moderate yields. It is important to note that in the presence of Sc(III) or Cu(II) as additives the major reaction pathway is dominated by Au(I). Cyclic 1,3-dicarbonyl compounds such as cyclopentane-1,3-dione and cyclohexane-1,3-dione gave the desired product in very low yields and most of the ester **18a** suffered decomposition. Meldrum's acid, dimethyl malonate and bis(phenylsulfonyl)methane failed to react with **18a** in the presence of catalyst **E**.

Table 5
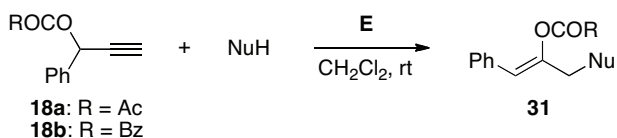
Entry	**18a-b**	NuH	Time (h)	Product	Yield (%)
1[a]	**18a**	**30a**	1	**31a**	88
2[a]	**18a**	**30b**	1.5	**31b**	57
3[b]	**18a**	**30c**	0.4	**31c**	37
4[b]	**18a**	**30d**	1.5	**31d**	36
5[a]	**18b**	**30a**	1	**31e**	92
6[c]	**18b**	**30e**	1.5	**31f**	43
7[b]	**18b**	**30d**	1	**31g**	51

(a) 5 mol% of **E**. (b) 2 mol% of **E** and 5 mol% of Sc(OTf)$_3$. (c) 2 mol% of **E** and 5 mol% of Cu(OTf)$_2$.

The reactions of substrates bearing *gem*-dimethyl substituents at the propargylic position with 1,3-dicarbonyl compounds also yielded product of 1,2-addition to

intermediate **16**. In these cases indole[106] was also a feasible nucleophile leading to products of type **31** (*Scheme 16*).[107]
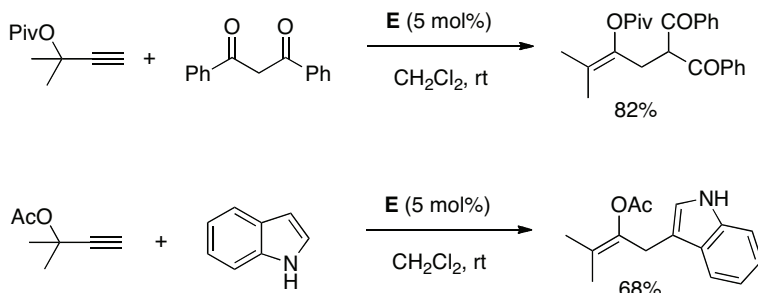
Scheme 16

Reaction of **18a** with 1,3,5-trimethoxybenzene (**35**) and catalyst **E** gave adduct **31h** (44%), the expected product of 1,2-addition to the gold carbene, along with 6% of a new product **36a** (*Scheme 17*). Formation of **36** corresponds to 1,4-addition of the nucleophile to intermediate **23** (*Scheme 18*).
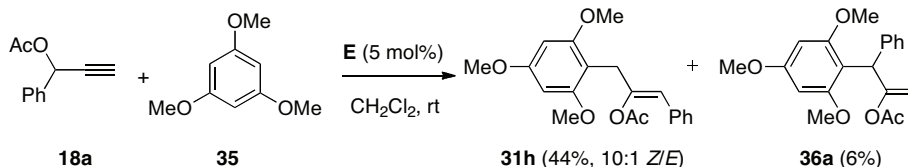
Scheme 17
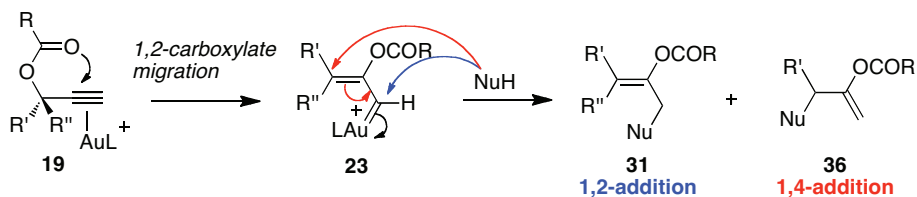
Scheme 18

Reactions of secondary propargylic esters (**18c-d**) with 1,3-dicarbonyl compounds afforded product **37** (*Table 6*, entries 1-2) resulting from 1,3-acyl migration

---

[106] Reaction of substrates **14a-b** with indole in the presence of catalyst **E** led to complex mixtures.

[107] Results by Catelijne H. M. Amijs published in: Amijs, C. H. M.; López-Carrillo, V.; Echavarren, A. M. *Org. Lett.* **2007**, *9*, 4021-4024.

to intermediates **22** (*Scheme 19*) and subsequent attack of the nucleophile. Reaction of **18e** with dibenzoylmethane (**30a**) using catalyst **E** gave **37c** in good yield (*Table 6*, entry 3). Primary propargylic esters (**18e-f**) react with α-ketoester **30c** or trimethoxybenzene (**35**) in the presence of complex **E** as catalyst to yield mixtures of two products (*Table 6*, entries 4-6): **37** and **36**. Product **36** results from 1,4-addition of the nucleophile to the α,β-unsaturated gold(I) carbene **23** (*Scheme 18*). Addition of 5 mol% of Sc(OTf)$_3$ or Cu(OTf)$_2$ led to improve results with α-ketoesters as nucleophiles. Reaction of 2-butynyl acetate (**18f**) with **35** using **E** as catalyst aforded a 2:1 mixture of **36d** and **37f** in a combined 59% yield. The *Z* configuration of adduct **37f** was assigned based on a NOE between the olefinic C-H and the methyl group. The *E* configurations of **37a-e** were assigned on the basis of the observed olefinic proton coupling constant (^3J = 12.3-12.6 Hz).[108] It should be mentioned that **37e** isomerize to **37e'** where the alkene is conjugated with the aromatic ring.
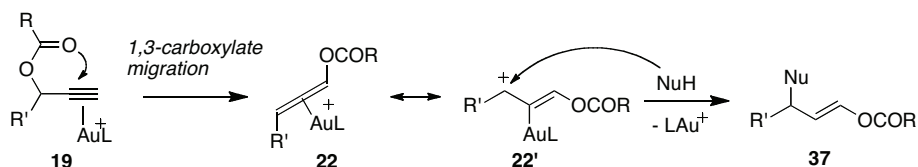
Scheme 19

108 (a) ^{1}H NMR data for *E*- and *Z*-enol esters: Doucet, H.; Höfer, J.; Bruneau, C.; Dixneuf, P. H. *Chem. Commun.* **1993**, 850-851. (b) ^{1}H NMR data for *Z*-enol esters: Doucet, H.; Martin-Vaca, B.; Bruneau, C.; Dixneuf, P. H. *J. Org. Chem.* **1995**, *60*, 7247-7255.

Table 6
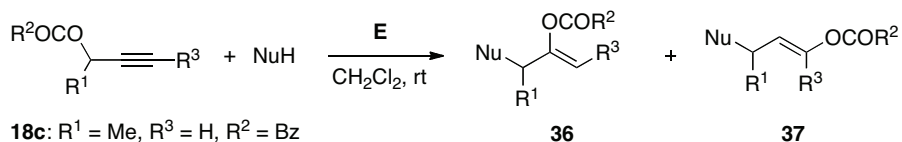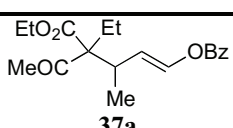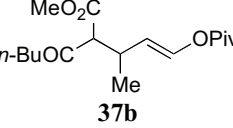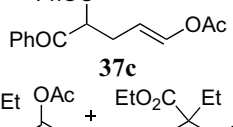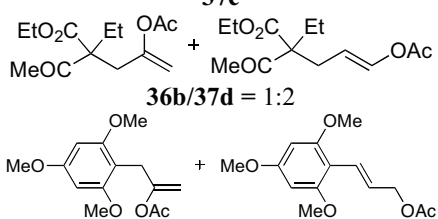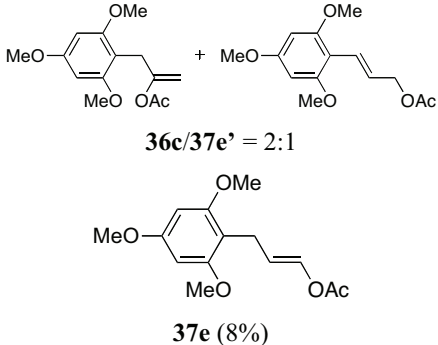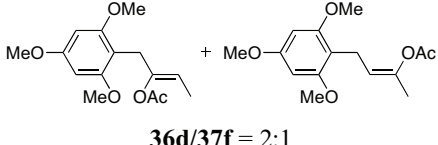
18c: R^1 = Me, R^3 = H, R^2 = Bz
18b: R^1 = Me, R^3 = H, R^2 = Piv
18e: R^1 = H, R^3 = H, R^2 = Ac
18f: R^1 = H, R^3 = Me, R^2 = Ac

Entry	**18c-e**	NuH	Time (h)	Products	Yield (%)
1[b,107]	**18c**	**30c**	9	**37a**	49
2[b,107]	**18d**	**30e**	0.5	**37b**	53
3[a]	**18e**	**30a**	4.5	**37c**	87
4[b]	**18e**	**30c**	2	**36b/37d** = 1:2	48
5[a]	**18e**	**22**	4	**36c/37e'** = 2:1 ; **37e** (8%)	69
6[a]	**18f**	**22**	1	**36d/37f** = 2:1	59

(a) 5 mol% of **E**. (b) 2 mol% of **E** and 5 mol% of Sc(OTf)$_3$.

E
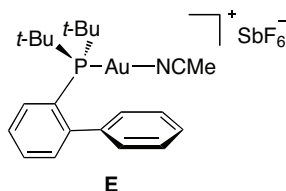
Figure 7

Since internal alkyl substituted alkynes are also able to undergo gold(I)-catalyzed rearrangement, the phenyl substituted analogs (**18g-j**) (*Figure 8*) were treated with **30a** and **35** with catalyst **E** and **J**/AgSbF$_6$ but no reaction was observed.

14g   **14h**   **14i**   **14j**
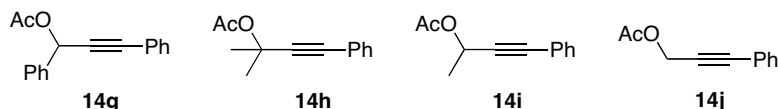
Figure 8

Experiments with deuterated substrates **30a-d_2** and **18e-d_1** are shown in *Scheme 20*. Formation of **31a-d_2** is consistent with the mechanistic hypotheses shown in *Scheme 18* in which the α,β-unsaturated gold(I) carbene **23** undergoes a 1,2-nucleophilic attack by the enol of the 1,3-dicarbonyl compound or the arene to give **31**. Nucleophilic addition of the enol of **30a** to the propargylic ester **18e** gave the expected product **37c-d_2** (*Scheme 20*).The deuterium labelled **18e-d_1** gave **37c-d_1**, which results from the addition of the nucleophile to the gold(I)-activated allene (**15'**) resulting from 1,3-acyloxy migration as shown in *Scheme 19*.
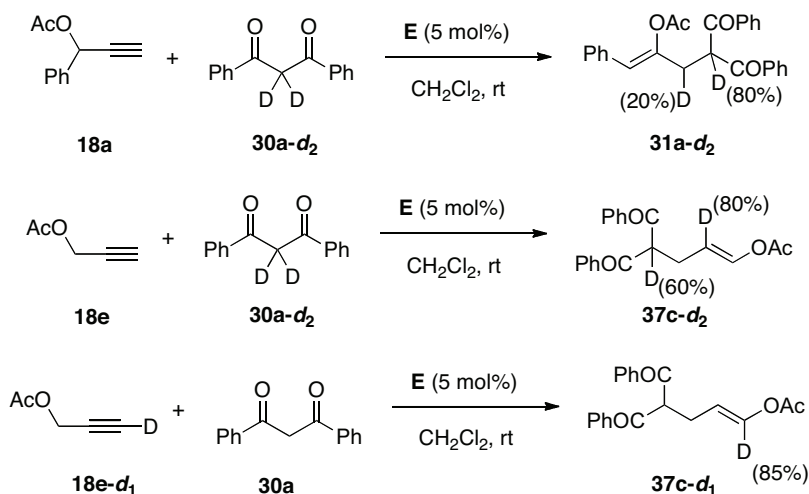
Scheme 20

103

Conclusions

This work shows that α,β-unsaturated gold(I) carbene **23** and gold(I)-coordinated allenes **22** formed in the rearrangement of propargylic esters react with 1,3-dicarbonyl compound and electron-rich arenes. The scope of this reaction has been studied. This represents a direct route for the synthesis of functionalized enol carboxylates under very mild conditions.
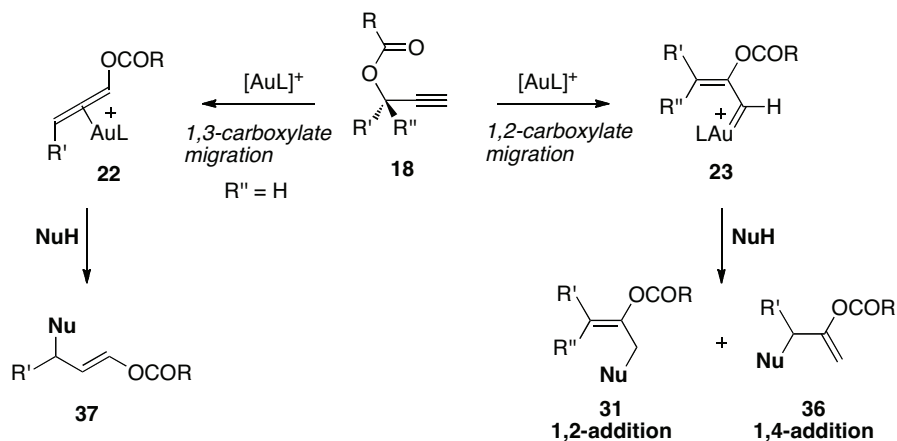
Scheme 21

These results also provide additional evidences for the existence of gold carbenes in the reaction of propargylic esters. In addition we have also described the first conjugate addition to α,β-unsaturated carbenes to form products of type **36** (*Scheme 36*).

Chapter 3

Gold-Catalyzed 1,5-Enyne Cyclization Reactions

3.1. Ligand Controlled 1,5-Enyne Cyclization

Objectives

Gold(I)-catalyzed cyclization of 1,5-enynes can lead to a range of synthetically useful products under mild conditions. However the predictability of the reaction is low since small changes in the 1,5-enyne structure lead to highly divergent products under identical reaction conditions.[86]
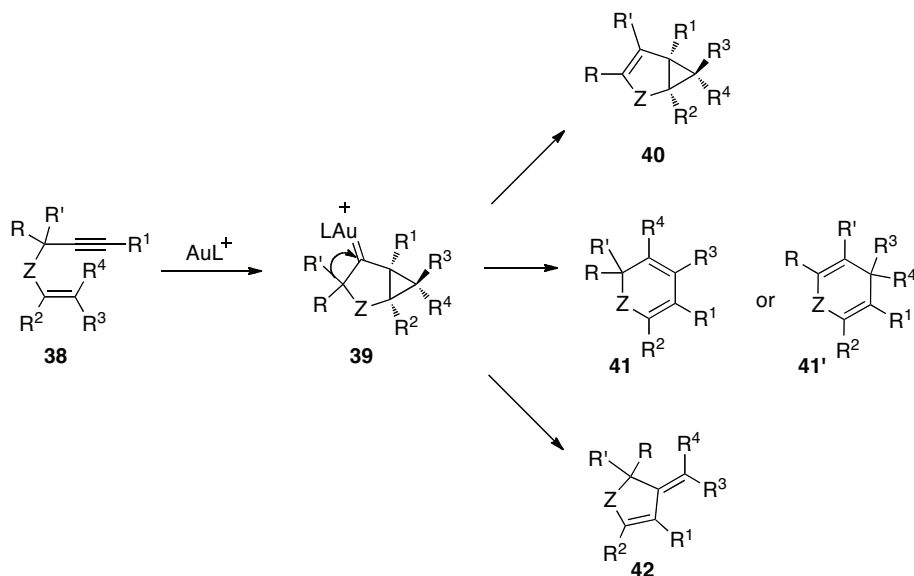
Scheme 22

In contrast to 1,6-enynes where the main cyclization pathway is *exo-dig*, for 1,5-enyne the *exo-dig* cyclization is less common[89] since the resulted bicyclo[2.1.0]pentane intermediate is highly strained. The proposed mechanism for the cyclization of 1,5-enynes begins with the intramolecular nucleophilic attack of the alkene to the alkyne-gold complex in a 5-*endo-dig* fashion. Intermediates of type **38** are formed wich can evolve to form bicyclo[3.1.0]hexane derivatives **40** or dienes **41-42** (*Scheme 22*).

Ligands can play a major role in the control of the regio- or site-selectivity in gold-catalyzed reactions.[86b] The objective of this work was to develop a cyclization of 1,5-enynes that could be controlled by the ligands on the gold catalyst.

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86 (a) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271-2296. (b) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351-3378.

89 Shibata, T.; Ueno, Y.; Kanda, K. *Synlett* **2006**, 411-414.

Results and Discussion

Most of the 1,5-enyne cyclization reactions are fast processes even at low temperature using less than 5 mol% of catalyst but proceed with low selectivity since small changes in the structure result in completely divergent products (*Scheme 23*).[86] We reasoned that the cyclization outcome could be controlled by tuning the electrophilicity of the gold catalyst.
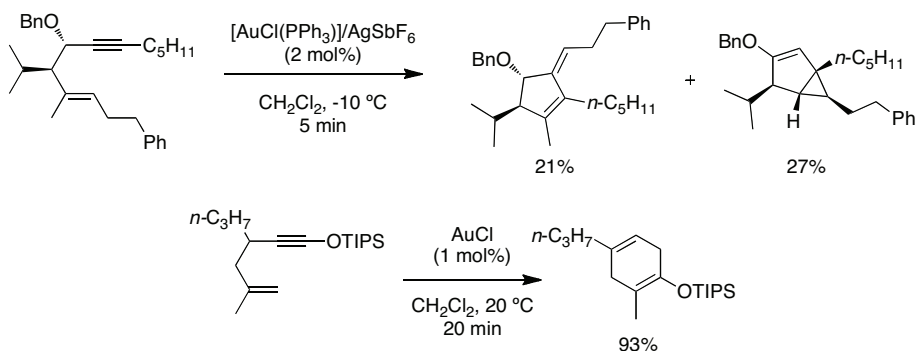
Scheme 23

We first synthesized protected 3-hydroxy-1,5-enynes **38a-e** (*Figure 9*) and tested their reactivity in the presence of 1-5 mol% of catalyst **E** in CH$_2$Cl$_2$ at room temperature or -20 ºC. However, under these conditions only complex mixtures of products were obtained.
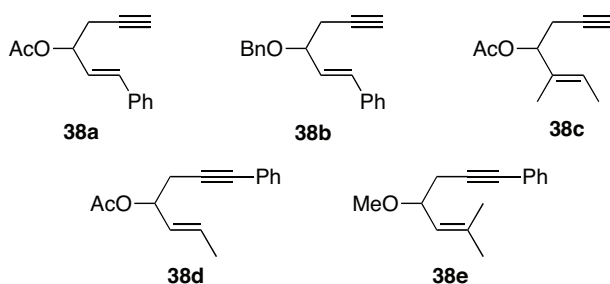
Figure 9

Since substrates **38a-e** could undergo decomposition by the ready formation of allyl cations, we decided to replace the alcoxy/acetoxy group by a sulfone. Thus,

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86 (a) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271-2296. (b) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351-3378.

reaction of 1,5-enyne **38f** bearing an allylic sulfone with 5 mol% of catalyst **E** in CH$_2$Cl$_2$ at room temperature gave unexpectedly cyclopentadiene **45a** in good yield after 2 days (*Table 7*, entry 1). Heating **38f** in the presence of **E** at 100 ºC under microwave irradiation afforded **45a** in 87% yield and reduced the reaction time to 20 minutes (*Table 7*, entry 2). Catalysts **K** and **X** (*Figure 10*) decomposed under the reaction conditions (*Table 7*, entries 3-5). Using catalyst **Q** bicyclo[3.1.0]hexane **43a** was obtained as the major product (*Table 7*, entry 6). Reaction with AuCl$_3$ as catalyst required heating at 80 ºC in toluene to give 51% of a 1:1 mixture of **43a** and **44a** (*Table 7*, entry 8). NaAuCl$_4$ in toluene at 50 ºC gave exclusively **44a** in poor yields (*Table 7*, entry 9). Platinum(II) complex **46** also led to **43a** as the major product, while a complex mixture was observed with PtCl$_4$ (*Table 7*, entries 10-11).

Table 7

Entry	[M]	T (ºC)	Time (h)	Product(s) (ratio)	Yield (%)
1	**E**	23	48	**45a**	51
2	**E**	100[b]	0.3[b]	**45a**	87
3[c]	**K**	23	1	**45a**	23
4[c]	**K**	23	48	**45a**	21
5[c]	**X**	23	8	-	-
6	**Q**	23	16	**43a/44a/45a** (10:1:4)	74
7[d,e]	AuCl	80	24	-	-
8[d]	AuCl$_3$	80	14	**43a/44a** (1:1.1)	51
9[d]	NaAuCl$_4$	50	16	**44a**	21
10	**46**	23	16	**43a/44a/45a** (10:2:1)	69
11[e]	PtCl$_4$	23	20	-	-

(a) 5 mol% catalyst in CH$_2$Cl$_2$. (b) Microwave heating. (c) Decomposition of the catalyst. (d) 10-20 mol% catalyst in toluene. (e) Complex mixture.
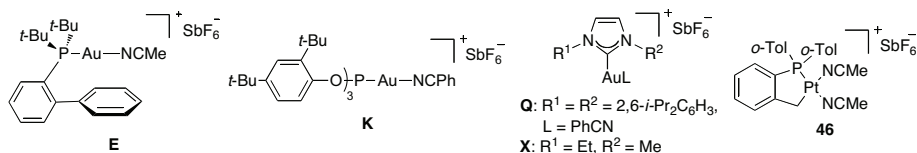
Figure 10

Formation of **43a** proceeds from intermediates **39** by 1,2-migration of hydrogen and demetalation (*Scheme 24*). A second type of hydride migration can take place from intermediates **39** leading to an α,β-unsaturated gold(I) carbene **34**. Subsequent loss of the allylic proton give the neutral intermediate **49** which form **45a** after protodemetalation. In a third reaction pathway, **39** might evolve by proton loss to form gold intermediates **36**, which undergoes protodemetalation to give **44a** (*Scheme 24*).
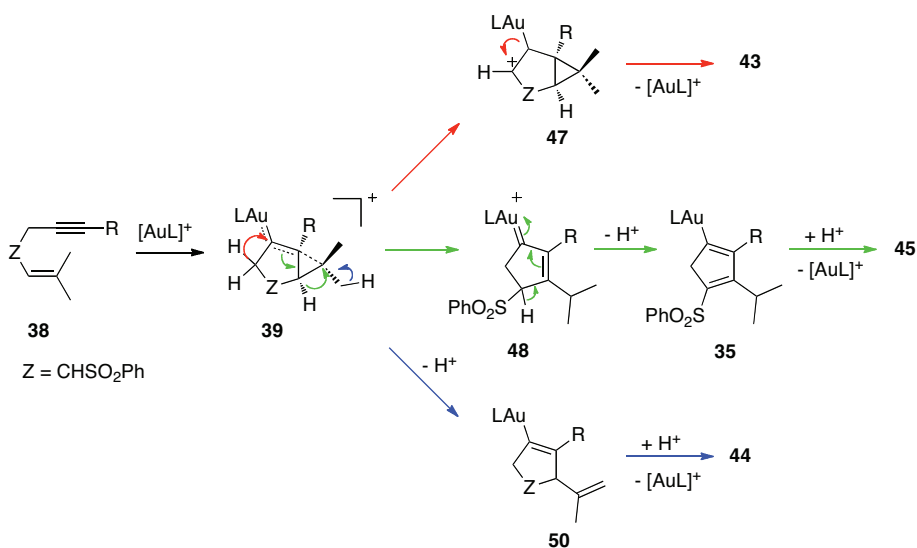
Scheme 24

Different substitutions in the alkyne were essayed. Methyl substituted enyne **38g** reacted with catalyst **Q** in CH_2Cl_2 at room temperature to form the corresponding bicyclo[3.1.0]hexane **43b** (*Table 8*, entry 2), while complex **E** and **46** failed to act as a catalyst in this cycloisomerization (*Table 8*, entries 1 and 4). Reaction of **38g** in the presence of catalyst **K** gave exclusively the 1,4-diene **44b** (*Table 8*, entry 3). Cycloisomerization of **38h** using **K** gave 1,4-diene **44** in moderate yield (*Table 8*, entries 4-5). Aryl substituted enynes were also tested with catalyst **Q** and **K**. As expected, phenyl substituted enyne **38i** cyclized to **43c** in the presence of catalyst **Q** (*Table 8*, entry 6). Reaction of **38i** with complex **K** led to **44d** along with 25% yield of

an unexpected diene **45'd**[109] (*Table 8*, entry 7). Cyclization of enynes **38j-k** in the presence of catalyst **K**, also gave mixtures of 1,4-dienes **44e-f** and cyclopentadienes **45'e-f** (*Table 8*, entry 8-9). In contrast, cyclization of enyne **38l** with catalyst **K** gave exclusively **44g** in 74% yield (*Table 8*, entry 10)

Table 8

38g: R = Me   **38j**: R = *p*-MeC$_6$H$_4$
38h: R = Et   **38k**: R = *p*-MeOC$_6$H$_4$
38i: R = Ph   **38l**: R = *p*-AcC$_6$H$_4$
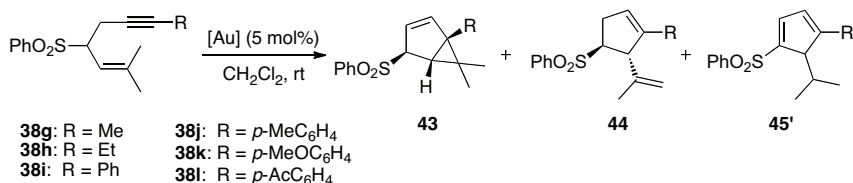
entry	Enyne	[Au]	time (h)	Product(s) (yield, %)
1[a]	**38g**	**E**	0.3	-
2	**38g**	**Q**	16	**43b** (50)
3	**38g**	**K**	24	**44b** (80)
4	**38g**	**46**	24	-
5	**38h**	**K**	24	**44c** (52)
6	**38i**	**Q**	18	**43d** (50)
7	**38i**	**K**	17	**44d** (67) + **45'd** (25)
8	**38j**	**K**	16	**44e** (58) + **45'e** (21)
9	**38k**	**K**	16	**44f** (58) + **45'f** (28)
10	**38l**	**K**	18	**44g** (85)

Formation of 1,3-diene **45'** can be explained by tautomerization of **45** or **45''** via [1,5]-H shift. Formation of **45** can also be explained by tautomerization of **45''**, which is formed by 1,2-migration of hydride in **48** followed by demetalation (*Scheme 25*).

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109 Compound **45'd** was observed by 1H NMR in the reaction crude as a single tautomer but after purification by column chromatography a 3.6:1:1 mixture of **45'/45/45''d** was isolated.
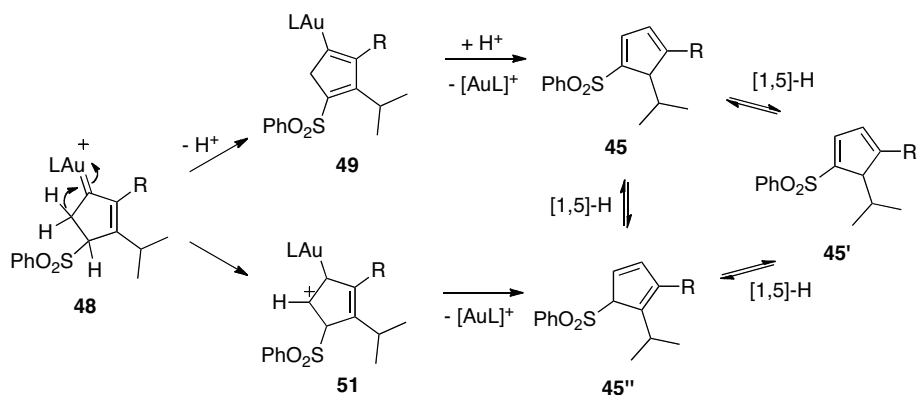
Scheme 25

Enynes with a different substitution pattern at the alkene **38m-o** also react with catalyst **Q** to form tricyclic products **43e-g** in good yields (*Scheme 26*). Enyne **38n** was also tested with catalyst **K** giving a complex mixture of products, while in the presence of Pt(II) complex **46**, compound **43f** was obtained in 78% yield after 12 h. The structure of tricyclic compound **43f** was confirmed by X-ray diffraction (*Figure 11*).

Scheme 26

Figure 11
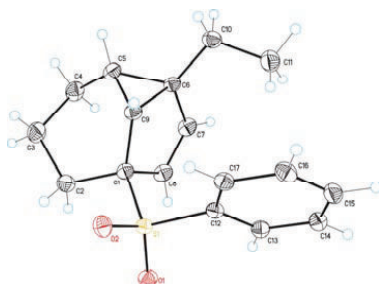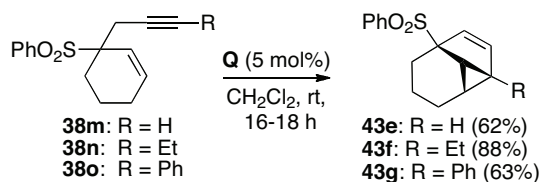
The different results observed with catalysts **Q** and **K** can be explained by the strong influence of the ligand in the structure of the reaction intermediates. Highly donating ligands such as NHC ligand in complex **Q** increase the electron density at the metal center, increasing the carbene character of intermedites **39**. Catalyst **K** whith less

donating phosphite ligand would lead to more distorted intermediates resembling open carbocation **39'** (*Scheme 27*).
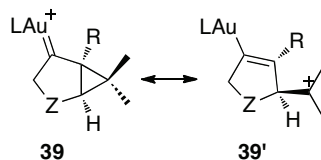
Scheme 27

DFT caculations on simple 1,5-enyne models show the distortion trend on intermediate **39** depending on the ligand on gold(I) (*Figure 12*). For comparison, Pt(II) intermediates **52** and free carbocations **53a** and **53b** were also included for this study. Calculations show that metal-stabilized intermediates are significantly different from single homoallylic carbocations **53a-b**. When intermediate **39** was calculated for P(OPh)$_3$ as ligand L, the structure corresponds more closely to the open intermediate **39'**, but the bond *d* is still 0.3 Å shorter than a classic carbocation such as **53a**. In contrast, intermediate **39a** with a strongly electron-donating ligand such as Cl$^-$ presents the shortest *d* bond, resembling the cyclopropyl gold(I) structure **39**.
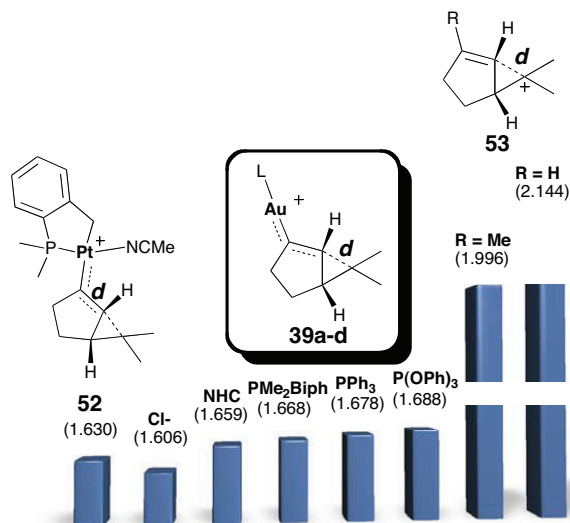
Variation of distance *d* (Å) in gold intermediates **39a-d** as a function of L ligand. (NHC = N,N'-diphenylimidazolydene). Platinum intermediate **52** and carbocation **53a-b** are included for comparison. The y axis has its origin at 1.40 Å to highligt the differences between the cationic species. [DFT, B3LYP/6-31G**, LANL2DZ (Au)].

Figure 12

According to theoretical calculations we should be able to trap the cyclopropyl gold(I) intermediates **39** using NHC ligands on gold(I). To test this hypothesis enynes **54**, which bear a second alkene moiety to react with gold(I) carbene, were tested using both catalysts **Q** and **K**. With catalyst **K** most of the enyne **54a** was decomposed and only 30% of the unexpected trycicle compound **56** was isolated, while in the presence of **Q** enyne **54** gave 76% of the pentacycle **55a**. Enyne **54b** also cyclized in the presence of **Q** to form cyclopropyl product **55b**, while in the presence of **K** enyne **54b** was decomposed (*Scheme 28*). Methoxycyclization of **54a** in the presence of catalyst **Q** leads to a 1:1.4 mixture of **57a** and **57b**. In the presence of catalyst **K** the methoxycyclization reaction gave a 1:5 mixture of products of **57a** and **57b** (*Scheme 28*).[110]
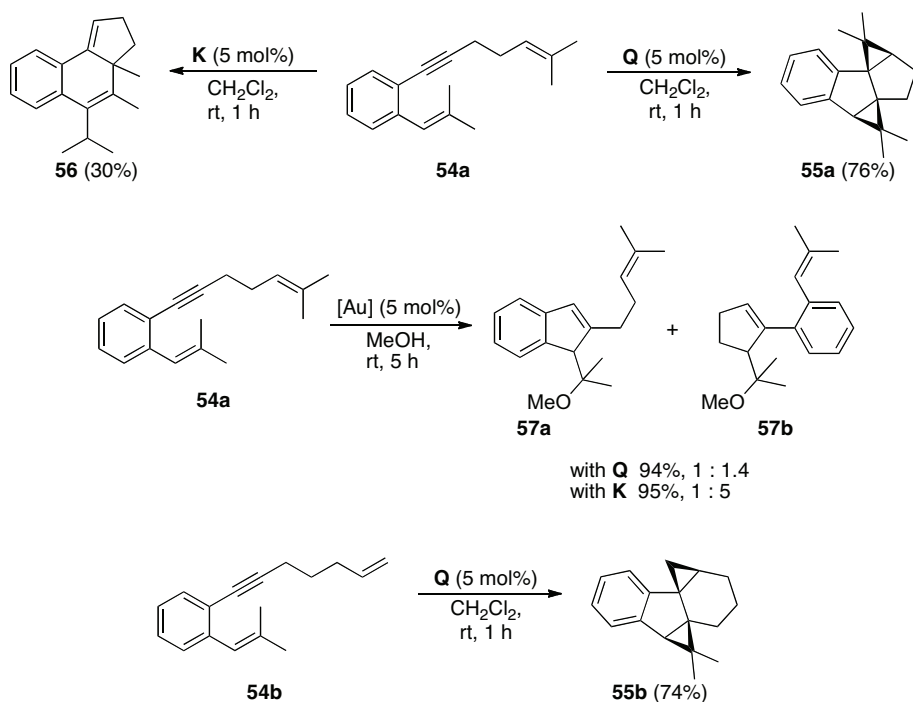
Scheme 28

A mechanistic proposal for this cyclization is despicted in *Scheme 29*. The gold-activated alkyne moiety in **54a** can suffer attack from the two alkenes to form intermediates **39f** and **39g**. In both intemediates, the gold(I) carbene can undergoes

110   Results carried out in collaboration with Ángeles Mosquera, visiting student from Universidad de A
        Coruña (August-September 2009).

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cyclopropanation of the second alkene moiety to form the policycle **55a**. Methoxycicyzation can also take place from both intermediates **39f** and **39g**, as we observed in the presence of catalyst **Q** that led to a 1:1.4 mixture of **57a** and **57b** (*Scheme 28*). While in the presence of catalyst **K** the main reaction pathway is formation of **39g** as shown in the methoxycyclization reaction that gave a 1:5 mixture of **57a** and **57b**. Therefore, formation of **56** is explained through intermediate **39g** which can react intramolecularly with the second alkene to form a tertiary cabocation **58**. Subsequent [1,5]-H shift would form the α,β-unsaturated gold carbene **59**. [1,2]-Methyl shift could form a second tertiary carbocation **60** which give the product **56** after proton loss and protodemetalation.

Scheme 29

118
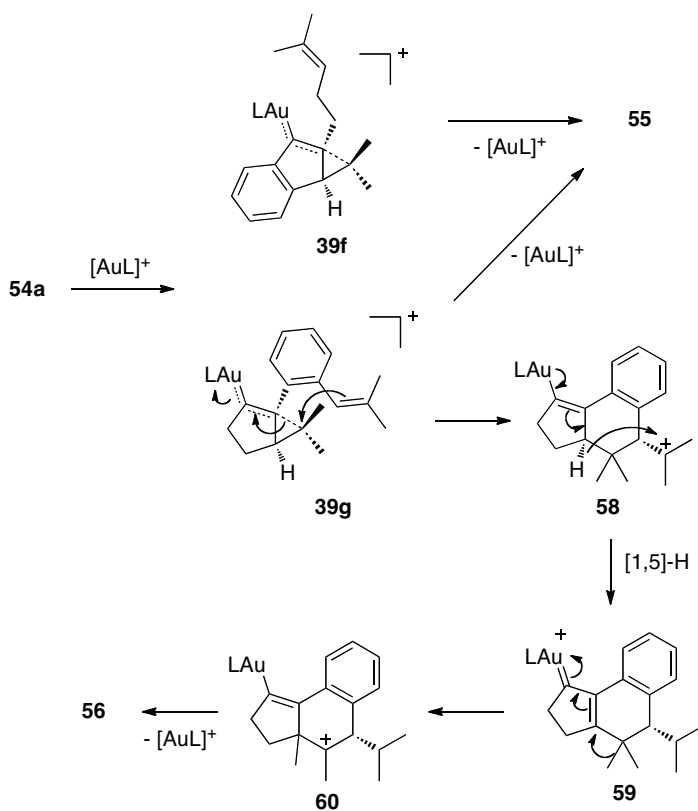
3.2. Gold-Catalyzed Addition of Nucleophiles to 1,5-Enynes

Objectives

Inter-[88,93] and intramolecular[97,98] reaction of 1,5-enynes with ROH nucleophiles in the presence of gold(I) complexes has been reported. The intramolecular amination of 1,5-enynes has also been described.[98]

Intermolecular addition of heteronucleophiles to 1,5-enynes leads to cyclopentenes **53**[93] when the nucleophile attacks the carbon labeled as *a* on intermediates **39** or cyclohexenes **54**[88] when the addition occurs on the carbon labeled as *b* (*Scheme 30*).
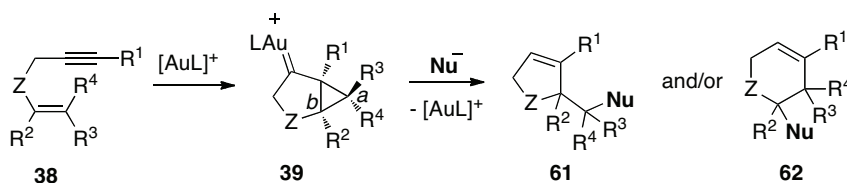
Scheme 30

Addition of electron rich arenes and heteroarenes to 1,6-enynes has been reported by the group of Genêt and by our group using different gold(I) complexes (*Scheme 31*).[14,78] 1,3-Dicarbonyl compounds can also be added to 1,6-enynes in the presence of gold(I) catalyst (*Scheme 31*).[14]

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14 Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M. *J. Org. Chem.* **2008**, *73*, 7721-7730.

78 (a) Toullec, P. Y.; Genin, E.; Leseurre, L.; Genet, J.-P.; Michelet, *V. Angew. Chem. Int. Ed.* **2006**, *45*, 7427-7430. (b) Amijs, C. H. M.; Ferrer, C.; Echavarren, A. M. *Chem. Commun.* **2007**, 698-700. (c) Chao, C.M.; Vitale, M. R.; Toullec, P. Y.; Genêt, J.-P.; Michelet, V. *Chem. Eur. J.* **2009**, *15*, 1319-1323.

88 Luzung, M. R.; Markham, J. P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 10858-10859.

93 Buzas, A. K.; Istrate, F. M.; Gagosz, F. *Angew. Chem. Int. Ed.* **2007**, *46*, 1141-1144.

97 Toullec, P. Y.; Blarre, T.; Michelet, V. *Org. Lett.* **2009**, *11*, 2888-2891.

98 Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 6962-6963.
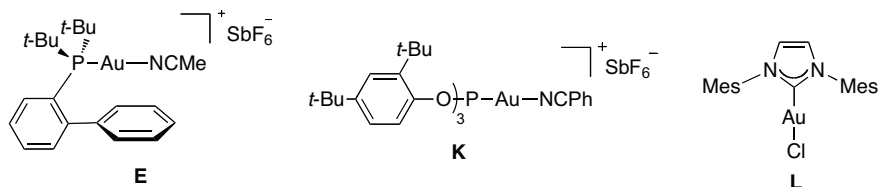
Figure 13
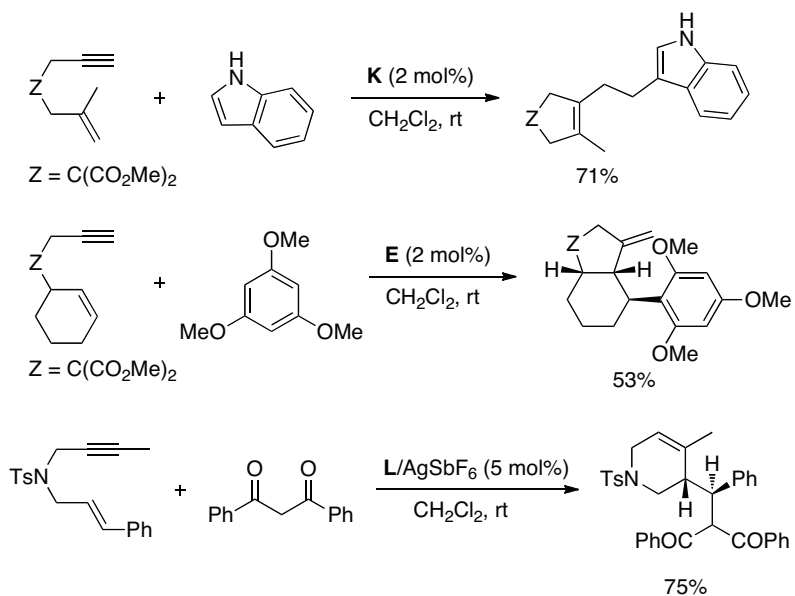
Scheme 31

As another objective of this work, we decided to use carbon nucleophiles to trap the intermediates in the gold(I)-catalyzed cyclization of 1,5-enynes.

Results and Discussion

To study the addition of carbon nucleophiles to 1,5-enynes we first tested **38a** with dibenzoylmethane (**30a**) in the presence of neutral complex **J** activated with AgSbF$_6$ and catalyst **E**. These reactions led to complex mixtures (*Table 9*, entries 1-2). Reaction of enyne **38a** with trimethoxybenzene **(35)** with **J**/AgSbF$_6$ in the presence of AgSbF$_6$ was also unproductive, while using complex **E** as catalyst compound **61a** was isolated in 75% yield as a 1:1 mixture of diasteroisomers (*Table 9*, entries 3-4). Adducts **61a** were shown to be epimers at C-1 by methanolysis. Thus, treatment of **61a** with K$_2$CO$_3$ in methanol led to selective cleavage of the acetate of the *trans* isomer to give alcohol **62** (46% yield) and *cis*-**61a** (54% yield) (*Scheme 32*).
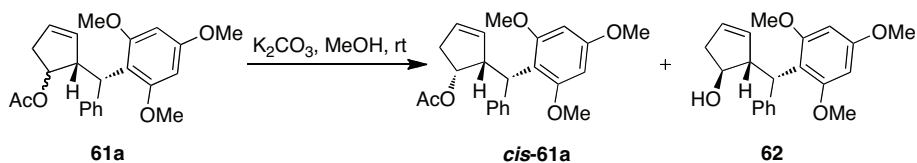
Scheme 32

Reaction of **38a** with indole catalyzed by complex **E** gave the desired product **61b** in low yield along with bisindolyl derivative **64** (*Table 9*, entry 5). Formation of **64** can be explained by the nucleophilic addition of indole to the alkyne moiety in **38a** and subsequent activation of the alkene by gold(I) to promote a second addition of indole (*Scheme 33*). The addition of indole to alkynes was already reported by our research group.[57,59]

Table 9

Entry	NuH	[Au]	Time (h)	Product(s) (ratio)	Yield (%)
1	30a	**J**/AgSbF$_6$	26	-	- [a]
2	30a	**E**	24	-	- [a]
3	35	**J**/AgSbF$_6$	10	-	- [a]
4	35	**E**	29	61a (1:1)	75
5	63	**E**	48	61b	17
				56	15

(a) Complex mixture.
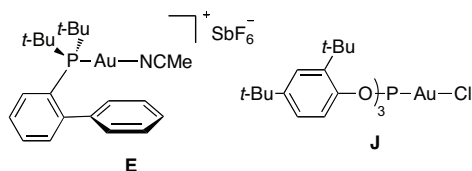
Figure 14
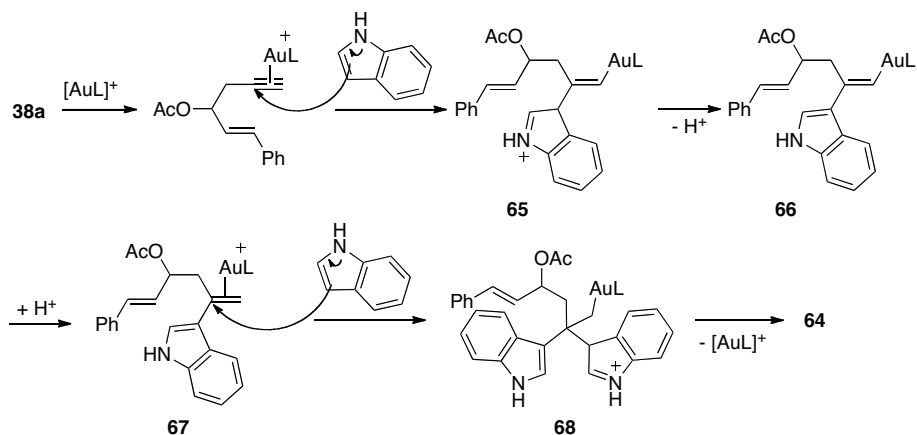
Scheme 33

Addition of heteronucleophiles to 1,5-enynes **38f-i** bearing a sulphone group at the allylic position was not reported so we first tested hydroxy- and alkoxycyclization of these substrates. Enynes **38f-g** with catalyst **E** in a 1:3 mixture of H_2O and CH_2Cl_2 to give the hydroxycyclization products **61c-d** in excellent yields (*Table 10*, entries 1-2). Reaction of **38i** with catalyst **E** using a 1:10 mixture of H_2O and CH_2Cl_2 as solvent gave 60% of the hydroxycyclization product **61e** (*Table 10*, entry 3). Enynes **38m-o** (*Figure 15*) gave complex mixture using **E** as catalyst in H_2O/CH_2Cl_2 or MeOH as solvents.

38m: R = H
38n: R = Et
38o: R = Ph

Figure 15

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Table 10

38f: R = H
38g: R = Me
38i: R = Ph
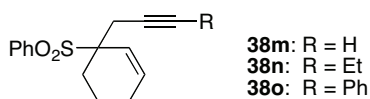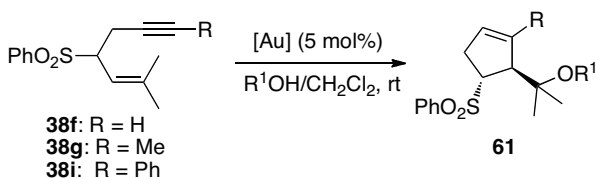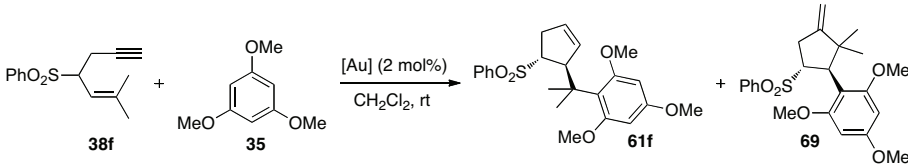
Entry	Enyne	R^1OH/CH_2Cl_2 (ratio)	[Au]	Time (h)	Product (Yield, %)
1	**38f**	H_2O (1:3)	**E**	16	**61c** (92)
2	**38g**	H_2O (1:3)	**E**	16	**61d** (91)
3	**38i**	H_2O (1:2)	**E**	10	**61e** (60)

1,5-Enynes bearing a sulphone group at the allylic position also reacted with trimethoxybenzene (**35**) in the presence of gold(I) complexes. Reaction of **38f** with **35** using complex **E** as catalyst led to 76% of the expected adduct **61f** together with **69** as a 7:1 mixture (*Table 11*, entry 1). A 2:1 mixture of **61f** and **69** was observed when the reaction was carried out with **K** as catalyst (*Table 11*, entry 2). When complex **Q** was used as catalyst, 34% of **61f** was observed with no formation of **69** (*Table 11*, entry 3). Adduct **69** corresponds to a rare *exo* cyclization of 1,5-enyne **38f** via intermediate **70** and subsequent addition of **35** (*Scheme 34*).

Table 11

Entry	[Au]	Time (h)	**61f/69**	Yield (%)
1	**E**	6	7:1	76[a]
2	**K**	1	2:1	54[a]
3	**Q**	18	1:0	34[b]

(a) Formation of diene **45a** was observed. (b) The starting 1,5-enyne was recovered.
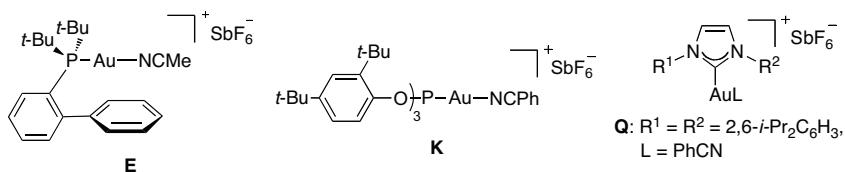
Figure 16
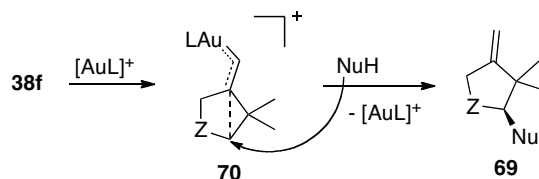
Scheme 34

Reaction of 1,5-enynes **38g** and **38i** with **35** in the presence of **E** as catalyst provided adducts **61f-g** in moderate yields (*Scheme 35*).
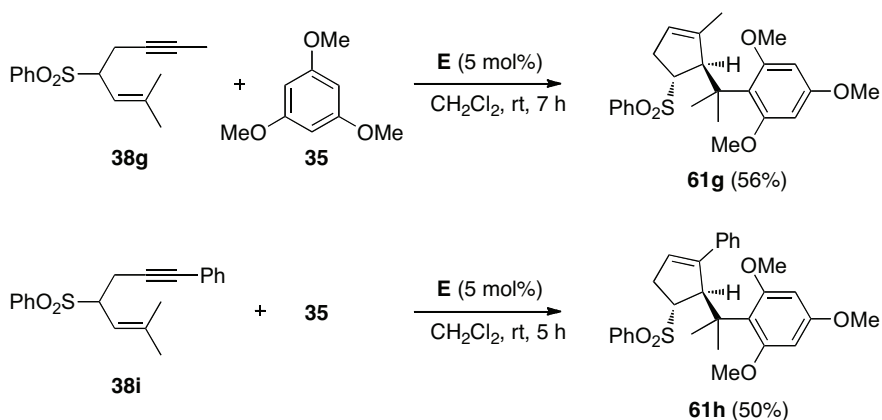
Scheme 35

Dibenzoylmethane (**30a**) was also tested as the nucleophile in the cyclization of 1,5-enynes bearing a sulphone group at the allylic position using complex **E** as catalyst. The unexpected adduct **71** was isolated as a 1:1 mixture of diasteroisomers in the reaction of **38f** with **30a** using Sc(OTf)$_3$ as additive (*Scheme 36*). Formation of **71** demostrates the involvement of the proposed intermediate **48** in the formation of **45a** (*Scheme 36*). The alternative formation of **71** by addition of dibenzoylmethane (**30a**) to the diene **45a** was excluded by permorming the control experiment under the same reaction conditions shown in *Scheme 36*.
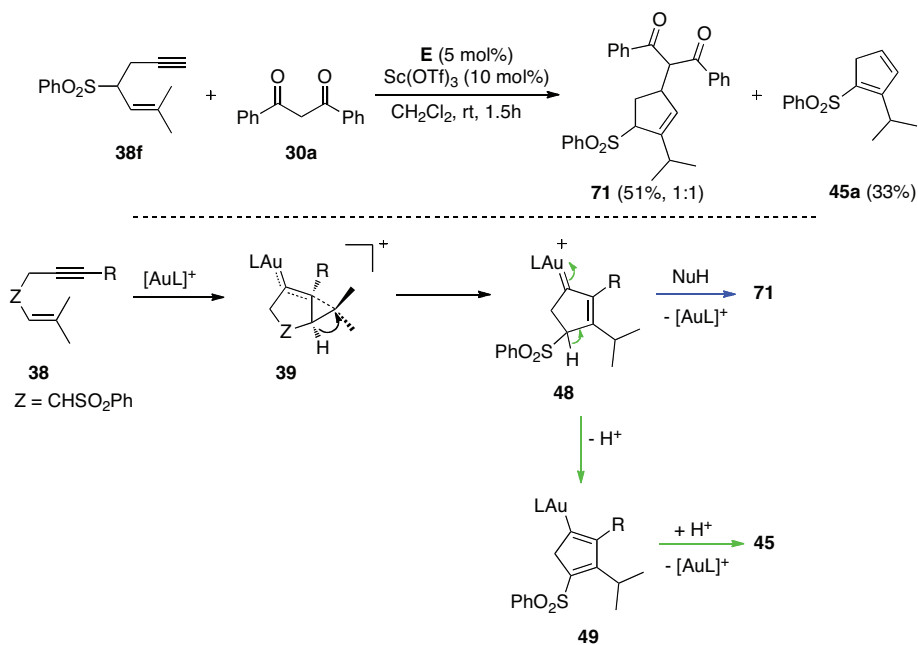
Scheme 36

3.3. Gold-Catalyzed Reactions of 1,5-Enynes with Carbonyl Compounds

Objectives

Carbonyl compounds also act as intramolecular nucleophiles in the cyclization of 1,6-enynes via the opening of cyclopropil gold(I) carbenes **73**. The resulting oxonium cations suffer nucleophilic attack by the vinylgold intermediates (**74**) in a Prins reaction that gives **75** in a tandem process (*Scheme 37*).[80] This reaction has already shown to be a powerfull method for total synthesis of complex molecules like orientalol F (**76**)[81] and englerin A (**77**).[82]
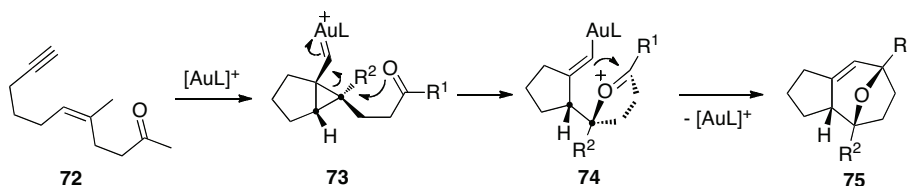
Scheme 37
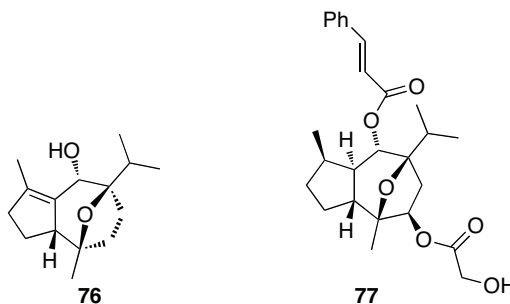
Figure 17

Gold(I)-catalyzed intermolecular reaction of carbonyl compounds with 1,6-enynes unsubstituted at the alkene has also been reported to yield tricyclic compounds

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80 Jiménez-Núñez, E.; Claverie, C. K.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 5452-5455.

81 Jiménez-Núñez, E.; Molawi, K.; Echavarren, A. M. *Chem. Commun.* **2009**, 7327-7329.

82 Molawi, K.; Delpont, N.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2010**, *49*, 3517-3519.

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

83. The mechanism proceeds by nucleophilic attack of the carbonyl group to the rearrange carbene **80** and subsequent reaction of the oxonium cation with the alkene in **81** (*Scheme 38*).[83]
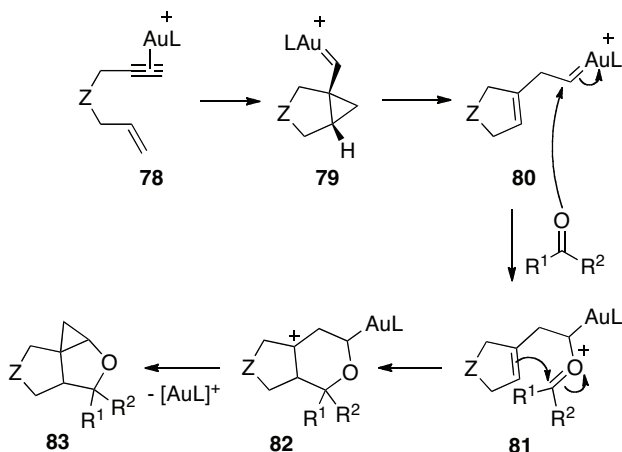
Scheme 38

Analogous reactions of 1,6-enynes substituted at the alkene with aldehydes led to products different from **83**. Products **84** of formal [2+2+2] cycloaddition were indeed obtained together with unexpected 1,4-dienes **85** which correspond to a formal metathesis between alkene and aldehyde (*Scheme 39*).[84]
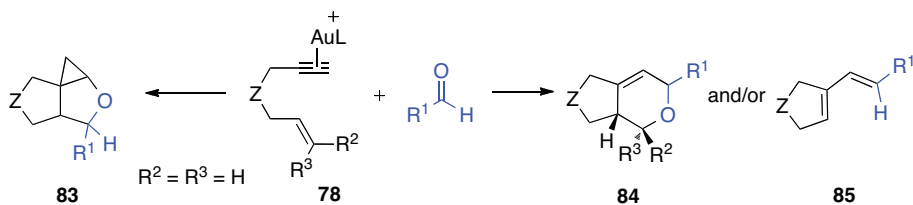
Scheme 39
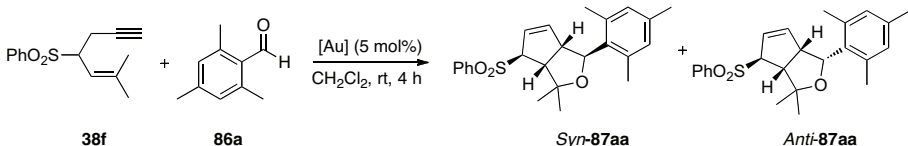
The objective of this work was to study the intermolecular reaction of 1,5-enynes with carbonyl compounds in the presence of gold(I) complexes.

84 Escribano-Cuesta, A.; López-Carrillo, V.; Janssen, D.; Echavarren, A. M. *Chem. Eur. J.* **2009**, *15*, 5646-5650.

Results and Discussion

To study the reactivity of 1,5-enynes in the presence of carbonyl compounds and gold(I) complexes we used enyne **38f** and 2,4,6-trimethylbenzaldehyde (**86a**). Reaction of **38f** gave adduct **87aa** as a single diasteroisomer in excellent yields using complexes **E** and **Q** as catalysts. When using complex **K** as catalyst the conversion was not complete and **87aa** was isolated as mixture of diasteroisomers.

Table 12

Entry	[Au]	**87aa** (*Syn*/*Anti* ratio)	Yield (%)
1	**E**	1:0	85
2	**K**	7:1	74
3	**Q**	1:0	95
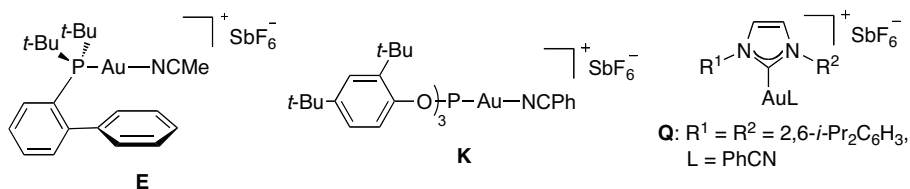
Figure 18

Bicyclic compound **87aa** is the product of a formal [2+2+2] cycloaddition. We reasoned that the aldehyde would open the distorted cyclopropyl gold(I) intermediate **39** to form an oxonium cation **88** which suffers the intramolecular attack of the vinylgold(I). The resulted gold carbene intermediate **89** undergoes 1,2-shift of hydrogen and demetalation to give **87** (*Scheme 40*).
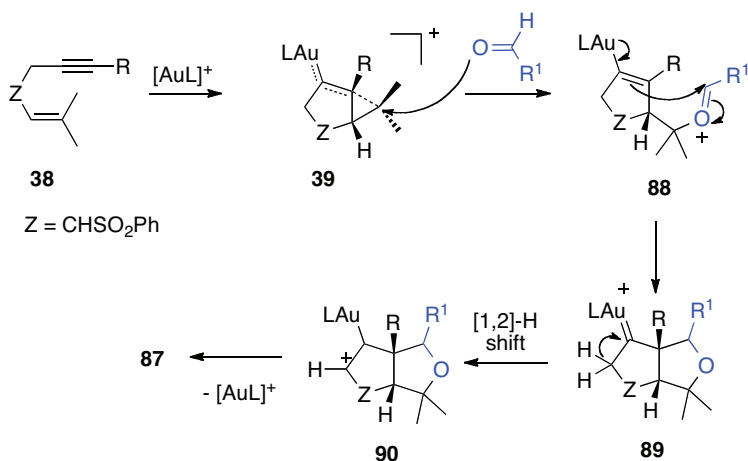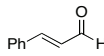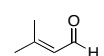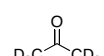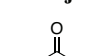
Scheme 40

The scope of the reaction is shown in *Table 13*. Reaction of 1,5-enyne **38f** with aldehyde **86b** using complex **E** as catalyst led to a 7:1 mixture of *syn/anti*-**87ab** in 81% yield while catalyst **Q** gave **87ab** in good yield together with an unexpected adduct **87'ab** (*Table 13*, entries 2-3). Complex **E** catalyzes the reaction of **38f** with aldehyde **86c** to yield 66% of adduct **87ac** as a 2.7:1 mixture of *syn* and *anti*. 4-Bromobenzaldehyde reacted with **38f** in the presence of complex **Q** to form a 1:1 mixture of *syn/anti*-**87ad** and 3-bromobenzaldehyde to give a 1:1 mixture of *syn/anti*-**87ae** in 62% yield; while 2-bromobenzaldehyde gave both isomers **87af** and **87'af** (*Table 13*, entries 5-7). Reaction of **38f** and aldehyde **86g** with catalyst **Q** led to 51% of a 2.5:1 mixture of *syn/anti*-**87ag** together with **87'ag** in 7% yield (*Table 13*, entry 8). When using cinnamaldehyde with **38f**, **87ah** was the only adduct observed in just 30 min with catalyst **Q** and 7 h using complex **E** as catalyst (*Table 13*, entries 9-10). α,β-Unsaturated aldehyde **86i** and enyne **38f** also reacted in 30 min with complex **Q** as catalyst to yield a 3:1 mixture of *syn/anti*-**87ai** (*Table 13*, entry 11). Long reaction times were required for the reaction of **38f** with acetone or cyclohexanone to form mixtures of adducts **87aj-ak** and **87'aj-ak** (*Table 13*, entries 12-13).

Table 13
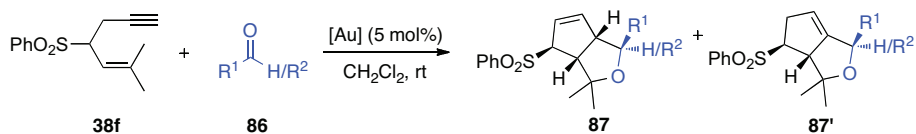
Entry	Carbonyl Compound[a]	[Au]	Time (h)	Product(s) (ratio,[b] yield [%])
1	**86a**	**Q**	4	**87aa** (95)
2	**86b**	**E**	30	**87ab** (7:1; 81)
3	**86b**	**Q**	2.5	**87ab** (7.5:1; 79) + **87'ab** (15)
4	**86c**	**E**	7	**87ac** (2.7:1; 66)
5	**86d**	**Q**	2.5	**87ad** (1:1; 78)
6	**86e**	**Q**	1	**87ae** (1:1; 62)
7	**86f**	**Q**	1	**87af** (1:1; 59) + **87'af** (9)
8	**86g**	**Q**	2.5	**87ag** (2.5:1; 51) + **87'ag** (7)

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9	**86h**	**E**	7	**87ah** (2:1; 59)
10	**86h**	**Q**	0.5	**87ah** (1.5:1; 72)
11	**86i**	**Q**	0.5	**87ai** (3:1; 58)
12	**86j**	**Q**	32	**87aj + 87'aj** (1:1; 55)
13	**86k**	**Q**	20	**87ak + 87'ak** (1:2; 67)

(a) The reaction was carried out with 2 equivalents of aldehyde or 4 equivalents of ketone. (b) The ratios for **87ab-ai** refer to epimers at C1.
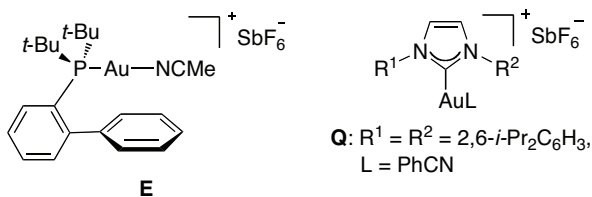
Figure 19
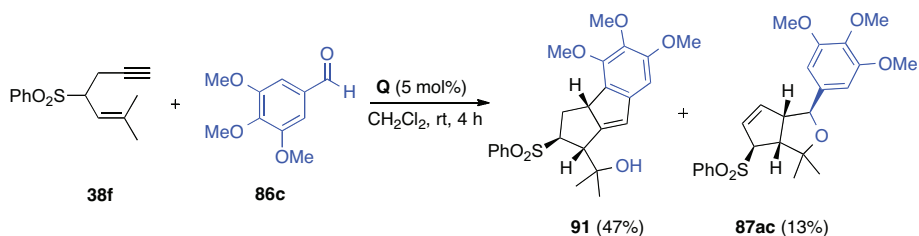
Scheme 41
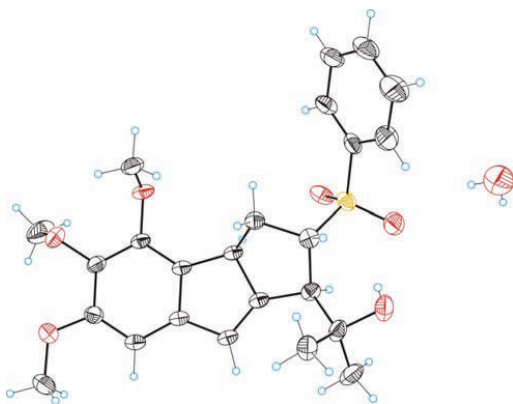
Figure 20

Interestingly reaction of **38f** and 3,4,5-trimethoxybenzaldehyde (**86c**) in the presence of complex **Q** led to an unexpected tricyclic product **91** in 47% yield, along with *syn*-**87ac** in 13% yield (*Scheme 41*). The structure of **91** was confirmed by X-ray diffraction (*Figure 20*). The mechanism for the formation of **91** may involve an intramolecular trapping of the gold(I) carbene in intermediate **89ac** to give **92** in a Friedel-Crafts type process, followed by a proton promoted cleavage (*Scheme 42*).

Scheme 42

135
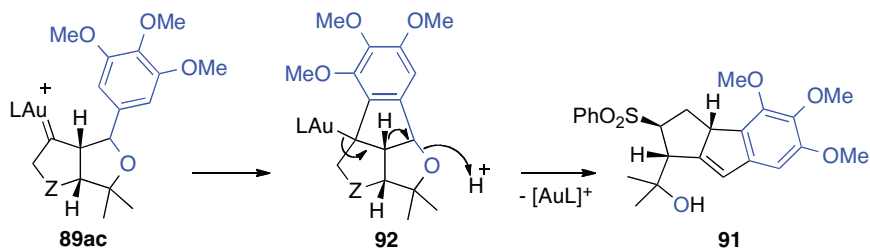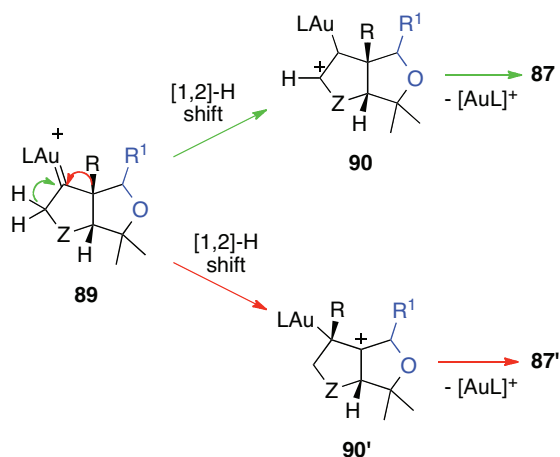
Scheme 43

Formation of adducts **87'** is explained by another 1,2-shift of hydrogen in carbene intermediate **89** as shows *Scheme 43*. According to this proposal, reaction of 1,5-enynes substituted at the alkyne would lead to adduct **87'** by 1,2-migration of alkyl or aryl groups. Indeed, reaction of **38g** and cinnamaldehyde with complex **Q** gave a 1:4.7 mixture of **87ba** and **87'ba** (*Scheme 44*).
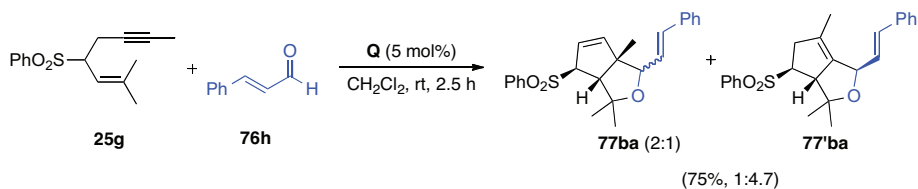
Scheme 44

Adduct **87'** was not observed in the reactions of ethyl substituted enyne **38h** with aldehydes (*Scheme 45*). 1,5-Enyne **38h** reacted with mesitaldehyde (**86a**) in the presence of **Q** to yield **94** as a single diasteroisomer in 43% yield. Using cyclopropanecarbaldehyde under identical reaction conditions, adduct **87ca** (1.5:1 mixture of epimers, 41%) was formed in addition to 30% of a new tricyclic product **94**. Tricyclic compounds **93** and **94** are formed by formal insertions of carbenes intermediates **79b-c** into C-H bonds of neighboring groups[111] (*Scheme 46*).

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[111] Fon analogous C-H insertion see: Horino, Y.; Yamamoto, T.; Ueda, K.; Kuroda, S.; Toste, D. F. *J. Am. Chem. Soc.* **2009**, *131*, 2809–2811.
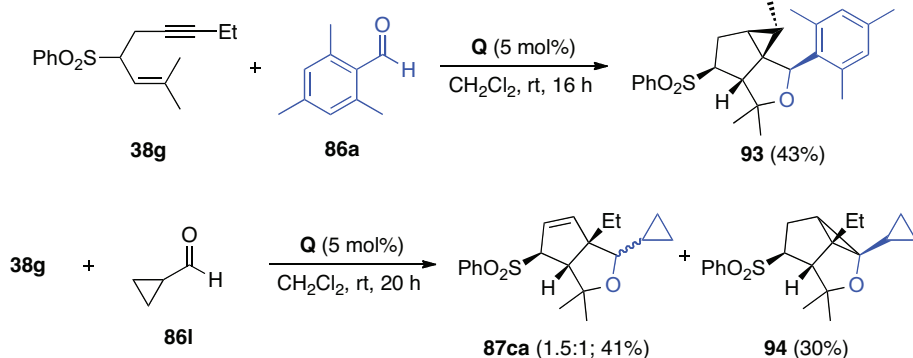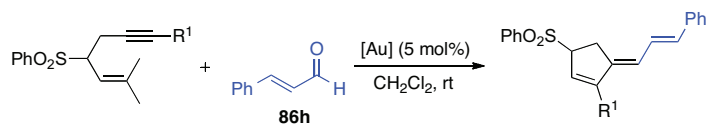
Scheme 45
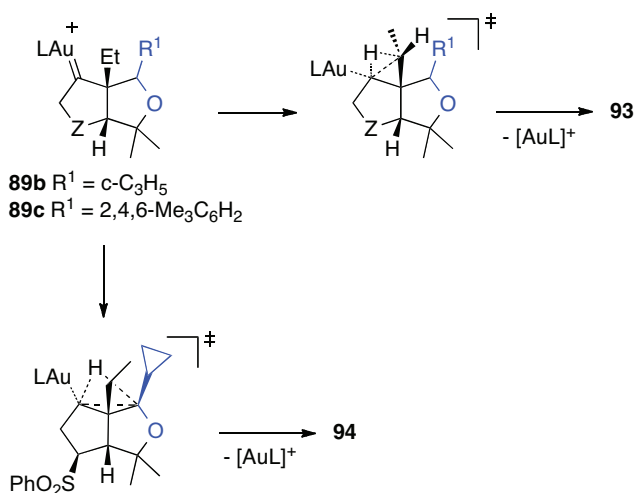
Scheme 46

Gold(I)-catalyzed reactions of aryl-substituted 1,5-enynes with aldehydes is despicted in *Table 14*. Reaction of enyne **38i** with mesitaldehyde (**86a**) was unproductive using complexes **E**, **K** or **Q** in CH₂Cl₂ at room temperature. In contrast, reaction of **38i** with cinnamaldehyde gave triene **95a** in moderate yield with complex **K** as catalyst and 75% yield using catalysts **E** or **Q** (*Table 14,* entries 1-3).

Table 14

38i: R = Ph
38j: R = *p*-MeC$_6$H$_4$ **38l**: R = *p*-AcC$_6$H$_4$
38k: R = *p*-MeOC$_6$H$_4$ **38p**: R = *p*-ClC$_6$H$_4$

Entry	Enyne	[Au]	Time (h)	Product (yield [%])
1	**38i**	**Q**	2	**95a** (75)
2	**38i**	**E**	1	**95a** (75)
3	**38i**	**K**	1	**95a** (50)
4	**38j**	**Q**	1	**95b** (80)
5	**38k**	**K**	1	**95c** (79)
6	**38l**	**Q**	1	**95d** (78)
7	**38p**	**Q**	2	**95e** (67)

Formation of **95** is explained in *Scheme 47*. The aldehyde would open intermediate **39** to form oxonium cation **88**. Subsequent Prins reaction affords cation **96**[112] which would fragmentate to give dienes **95** and release acetone (*Scheme 47*).

38i-l, p   **39**   **88**

Z = CHSO$_2$Ph

96   **95**
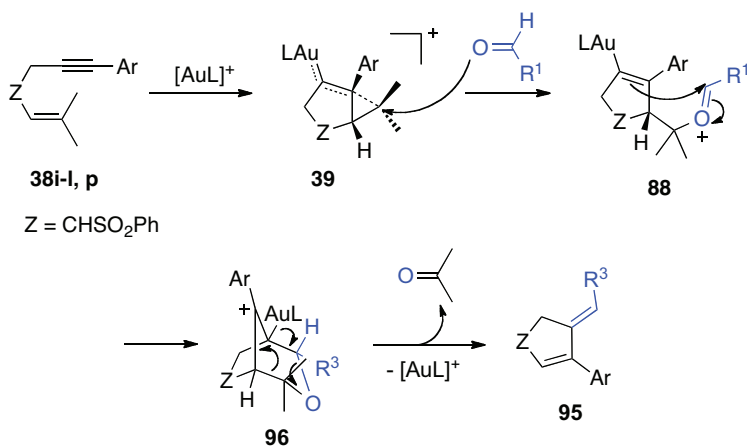
Scheme 47

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112 4-Tetrahydropyranyl cation is a delocalized species with aromatic stabilization: Alder, R. W.; Harvey, J. N.; Oakley, M. T. *J. Am. Chem. Soc.* **2002**, *124*, 4960-4961.

Conclusions

This work demonstrates that different products can be obtained from 1,5-enynes by tuning the electrophilicity of the gold(I) catalyst. The reaction catalyzed by gold(I) complexes with a bulky phosphite as ligand proceed through highly gold(I) stabilized carbocations to yield 1,4-dienes, whereas catalysts with NHC ligands give rise bicyclo[3.1.0]hexenes through intermediates that are better described as gold(I) carbenes (*Scheme 48*).
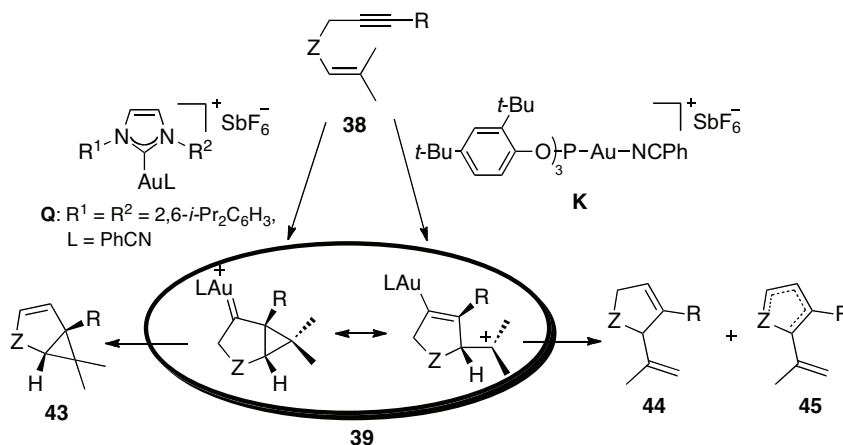
Scheme 48

These results also show 1,5-enynes can react with carbon nucleophiles in the presence of gold(I) complexes by addition to the cyclopropyl gold carbenes **50** formed through 5-*endo*-dig cyclization. The *exo* cyclization was also observed as a minor reaction pathway.
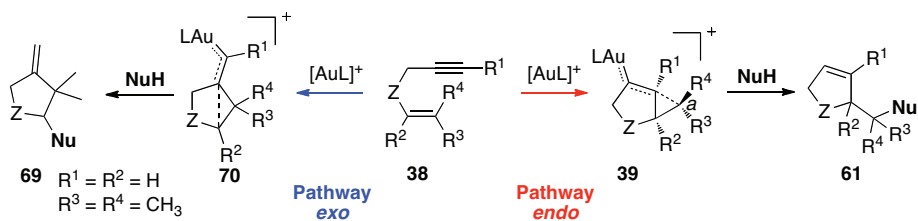
Scheme 49

The mechanism proposed for the formation of **45a** is supported by trapping the α,β-unsaturated gold(I) carbene **48** proposed as intermediate with a carbon nucheophile (*Scheme 50*).
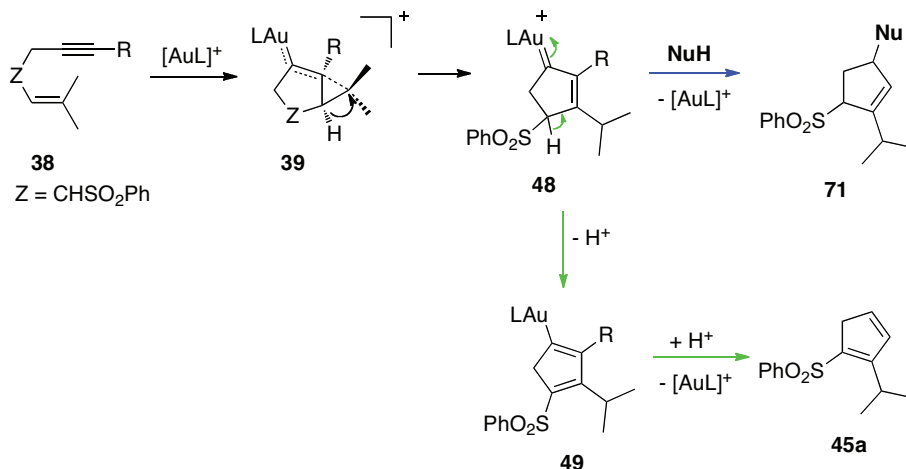
Scheme 50

The reaction of 1,5-enynes with carbonyl compounds gives the expected products of [2+2+2] cycloaddition. Fragmentation of the intermediates can occur in a few cases.
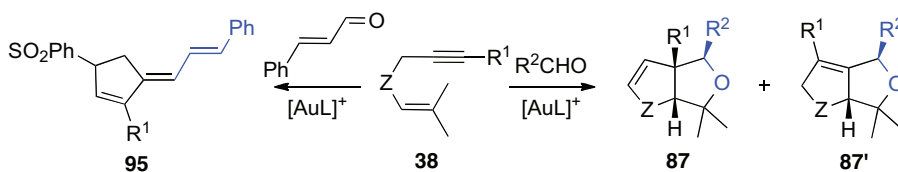
Scheme 51

This work also shows that the intermediate gold(I) carbenes can undergo formal C-H insertion or electrophilic aromatic substitution to form complex carbocyclic skeletons in a stereoselective manner.

Scheme 52

140

Experimental Section

Methods

All reactions were carried out under Ar in solvents dried using a Solvent Purification System (SPS). Thin layer chromatography was carried out using TLC-aluminum sheets with 0.2 mm of silica gel (Merck GF$_{234}$). Chromatography purifications were carried out using flash grade silica gel (SDS Chromatogel 60 ACC, 40-60 μm) or automated flash chromatographer CombyFlash Companion. Melting points were determined using a Büchi-B450 apparatus.

NMR spectra was recorded at 23ºC on a Bruker Avance 400 Ultrashield and Bruker Avance 500 Ultrashield apparatus. Mass spectra was recorded on a Waters Micromass LCT Premier (ESI), Waters Micromass GCT (EI, CI) and Bruker Daltonics Autoflex (MALDI) spectrometers. Elemental analyses were performed on a LECO CHNS 932 micro-analyzer at the Universidad Complutense de Madrid.

Crystal structure determinations were carried out using a Bruker-Nonius diffractometer equipped with an APPEX 2 4K CCD area detector, a FR591 rotating anode with MoK$_{\alpha}$ radiation, Montel mirrors as monochromator and a Kryoflex low temperature device (T = -173 $^{\circ}$C). Full-sphere data collection was used with ω and φ scans. *Programs used:* Data collection APEX-2,[113] data reduction Bruker Saint[114] V/.60A and absorption correction SADABS.[115] Structure Solution and Refinement: Crystal structure solution was achieved using direct methods as implemented in SHELXTL[116] and visualized using the program XP. Missing atoms were subsequently located from difference Fourier synthesis and added to the atom list. Least-squares refinement on F^{2} using all measured intensities was carried out using the program SHELXTL. All non hydrogen atoms were refined including anisotropic displacement parameters.

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113 Data collection with APEX II versions v1.0-22, v2009.1-0 and v2009.1-02. Bruker (2007). Bruker AXS Inc., Madison, Wisconsin, USA.

114 Data reduction with Bruker SAINT versions V.2.10(2003), V/.60A and V7.60A. Bruker (2007). Bruker AXS Inc., Madison, Wisconsin, USA.

115 SADABS: V.2.10(2003); V2008 and V2008/1 Bruker (2001). Bruker AXS Inc., Madison, Wisconsin, USA. Blessing, Acta Cryst. (1995) A51 33-38.

116 Sheldrick, G.M. *Acta Cryst.* **2008**, A*64*, 112-122. SHELXTL versions V6.12 and 6.14.

Synthesis of Catalysts.

The following complexes were used as received from the commercial sources: $PtCl_4$, $NaAuCl_4$ (Johnson Matthey), $AuCl_3$, AuCl, [AuCl(PPh$_3$)] (Stream), Sc(Otf)$_3$, AgSbF$_6$, and complex **E**[69] (Aldrich). Complexes [PdCl$_2$(PPh$_3$)$_2$],[117] **33**,[118] **46**, **J**,[13] **K**,[14] **L**[11] and **Q-R**[14] were synthesized according to the described procedures.

Complex V.

Cy Cy
P—Au—NCMe [ ]+ SbF$_6^-$
iPr
iPr
iPr
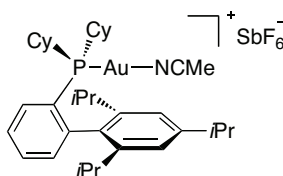
Complex **V** was prepared by addition of 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenylgold chloride (553 mg, 0.779 mmol) to a solution of AgSbF$_6$ (321.2 mg, 0.935 mmol) in MeCN (10 mL) and stirred for 4h at r.t. After evaporation the solid was dissolved in CH$_2$Cl$_2$ (5 mL) and filtered through SiO$_2$. After evaporation complex **V** was obtained as a white solid (625 mg, 84%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91-7.79 (m, 1H), 7.78-7.62 (m, 2H), 7.39-7.30 (m, 1H), 7.26 (s, 2H), 3.08 (dt, J = 13.8, 6.9 Hz, 1H), 2.37 (s, 3H), 2.32 (dt, J = 13.5, 6.8 Hz, 2H), 2.19 (m, 2H), 2.00 (m, 2H), 1.87 (m, 6H), 1.62-1.31 (m, 12H), 1.44 (d, J = 6.9 Hz, 6H), 1.40 (d, J = 6.9 Hz, 6H), 1.07 (d, J = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 149.7 (C), 146.8 (C), 135.7 (d, J = 6.4 Hz, C), 133.6 (d, J = 8.2 Hz, CH), 132.1 (d, J(^{13}C-^{31}P) = 4.3 Hz, CH), 131.4 (d, J(^{13}C-^{31}P) = 1.8 Hz, CH), 128.0 (d, J(^{13}C-^{31}P) = 8.3 Hz, CH), 124.6 (d, J(^{13}C-^{31}P) = 58.7 Hz,

11 Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178-6179.

13 (a) López, S.; Herrero-Gómez, H.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 6029. (b) **J** structure was confirmed by X-Ray crystallography: Nieto-Oberhuber, C.; Pérez-Galán, P.; Herrero-Gómez, E.; Lauterbach, T.; Rodríguez, C.; López, S.; Bour, C.; Rosellón, A.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2008**, *130*, 269-279.

14 Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M. *J. Org. Chem.* **2008**, *73*, 7721-7730.

117 Cotton, F. A. *Inorg. Synth.* **1972**, *13*, 121.

118 Porcel, S.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 2672-2676.

C), 121.7 (CH), 119.3 (C), 36.8 (d, $J(^{13}C-^{31}P)$ = 35.2 Hz, CH), 34.1 (CH), 31.1 (d, $J(^{13}C-^{31}P)$ = 11.9 Hz, CH$_2$), 30.2 (CH), 26.9 (d, $J(^{13}C-^{31}P)$ = 13.8 Hz, CH$_2$), 26.5 (d, $J(^{13}C-^{31}P)$= 13.6 Hz, CH) 25.6 (CH$_3$), 24.1 (CH$_3$), 23.16 (CH$_3$), 2.6 (CH$_3$); ^{31}P NMR (162 MHz, CDCl$_3$) δ 32.82.

Chapter 1. Experimental Section

Alkynes and Alkenes.

Alkynes **4a-k** were used as received from Alfa Aesar and/or Aldrich. Alkenes **5a-j** were used as received from Aldrich and compound **5i-d$_1$** was prepared according to the described procedure.[119]

4-Methylpent-3-en-1-yl Benzoate (5f).
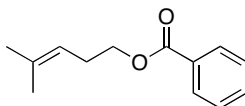
Compound **5e** was prepared by addition of 4-methylpent-3-en-1-ol (0.9 mL, 7.709 mmol) to a suspension of NaH (60% in mineral oil, 370 mg, 9.25 mmol) in THF (30 mL) at 0 ºC. After 20 min benzoyl chloride (1.324 g, 9.25 mmol) was added. The reaction mixture was stirred at r.t. for 3 h. After work-up **5e** was isolated by column chromatography (Hexane/EtOAc 6:1) (868 mg, 55%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04 (dd, J = 8.2, 1.0, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 5.20 (t, J = 7.2 Hz, 1H), 4.29 (t, J = 7.0 Hz, 2H), 2.46 (q, J = 7.0 Hz, 2H), 1.73 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 166.8 (C), 134.9 (C), 132.9 (CH), 130.7 (C), 129.7 (CH), 128.5 (CH), 119.4 (CH), 64.8 (CH$_2$), 27.9 (CH$_2$), 25.9 (CH$_3$), 18.0 (CH$_3$); HRMS-APCI *m/z* calculated for C$_{13}$H$_{17}$O$_2$ [*M*+H]$^+$ 205.1229, found 205.1233.

(4-Methylpent-3-enylsulfonyl)benzene (5g).

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119 Lipshutz, B. H.; Butler, T.; Lower, A.; Servesko, J. *Org. Lett.* **2007**, *9*, 3737-3740.
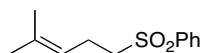
Over a stirring suspension of sodium benzylsulfonate (1.5 equiv) in DMF (20 mL) 5-bromo-2-methylpent-2-ene (4.500 g) was added at room temperature. The reaction mixture was stirred for 8 hours. After extractive work-up (10% HCl solution and Et_2O) the corresponding sulfone **5f** was isolated and used without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (m, 2H), 7.69-7.62 (m, 1H), 7.61-7.52 (m, 2H), 4.97 (dddd, J = 7.2, 5.9, 2.8, 1.4, 1H), 3.16-2.94 (m, 2H), 2.40 (dd, J = 16.0, 7.4, 2H), 1.63 (d, J = 0.8, 3H), 1.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4 (C), 135.2 (C), 133.8 (CH), 129.4 (CH), 128.2 (CH), 119.4 (CH), 56.1 (CH_2), 25.7 (CH_2), 21.8 (CH_3), 17.8 (CH_3); HRMS-ESI m/z calculated for $C_{12}H_{16}O_2SNa$ $[M+Na]^+$ 247.0769, found 247.0767.

((1*E*,5*E*)-1,6-Dideutero-2,5-dimethylhexa-1,5-diene (5i-d_2).
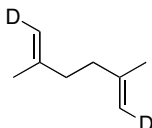
Compound **5h-d_2** was prepared following the procedure described by Negishi and co-workers.[120] To a suspension of Cp_2ZrCl_2 (402 mg, 1.37 mmol) in CH_2Cl_2 (10 mL) Al_2Me_6 2M in toluene (1.4 mL, 2.74 mmol) was added under argon at 0 ºC. After 10 min Cp_2ZrCl_2 was dissolved to give a yellow solution. Then 1,5-hexadyne (50% in pentane, 215.2 mg, 1.37 mmol) was added at r.t. and the reaction mixture was stirred at r.t. for 16 h. The reaction mixture was quenched by adding 2 mL of D_2O at 0 ºC and 25 mL of Et_2O. After filtration the organic layer was washed with water (3x10 mL), dried with $MgSO_4$ and evaporated at 100 mbar and 35 ºC. **5h-d_2** (25% in toluene) was used without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.68 (s, 2H), 2.15 (s, 4H), 1.73 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.7 (C), 109.7 (CD), 36.1 (CH_2), 22.5 (CH_3).

General procedure for the gold(I)-catalyzed [2+2] cycloaddition of alkynes with alkenes. A solution of alkyne (1 equiv) and alkene (2 equiv) in CH_2Cl_2 (0.53M) was

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120 Negishi, E.; Van Horn, D. E.; Yoshida, T. *J. Am. Chem. Soc.* **1985**, *107*, 6639-6647.

added to a solution of gold(I) catalyst **U** (0.03 mol%) in CH$_2$Cl$_2$ (0.08M). The reaction was stirred at room temperature for the time indicated in Tables **1-2** (GC-MS monitoring). Et$_3$N (0.05 mL) was added and the solvent was evaporated.

1,3-Diphenyl-3-methylcyclobut-1-ene (6a).
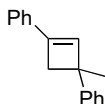
Compound **6a** was synthesized following the general procedure starting from phenylacetylene (28.8 μL, 0.263 mmol) and α-methylstyrene (72 μL, 0.526 mmol) with catalyst **U** (7.8 mg, 0.009). The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6a** as a colorless oil (46.1 mg, 80%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.39 (d, J = 7.2 Hz, 4H), 7.32 (dd, J = 13.7, 7.2 Hz, 4H), 7.27-7.22 (m, 1H), 7.21-7.15 (m, 1H), 6.72 (s, 1H), 2.93 (q, J = 12.5 Hz, 2H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 147.8 (C), 143.9 (C), 134.8 (C), 133.9 (CH), 128.4 (CH), 128.2 (CH), 127.9 (CH), 126.0 (CH), 125.8 (CH), 124.7 (CH), 46.1 (C), 44.4 (CH$_2$), 27.7 (CH$_3$); HRMS-ESI *m/z* calculated for C$_{17}$H$_{17}$ $[M+H]^+$ 221.1330, found 221.1335.

4-Deutero-1,3-Diphenyl-3-methylcyclobut-1-ene (6a-d$_1$).
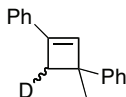
Compound **6a-d$_1$** was synthesized following the general procedure starting from phenylacetylene (28.8 μL, 0.263 mmol) and α-methylstyrene-d$_1$ (62.2 mg, 0.522 mmol) with catalyst **U** (7.6 mg, 0.008). The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6a-d$_1$** as a colorless oil (35.6 mg, 61%): ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.44-7.37 (m, 4H), 7.36-7.29 (m, 4H), 7.21-7.17 (m, 2H), 6.72 (s, 1H), 2.95 (m, 0.5H), 2.89 (m, 0.5H), 1.63 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 147.8 (C), 143.9 (C), 134.9 (C), 133.9 (CH), 128.5 (CH), 128.3 (CH), 127.9 (CH), 126.0 (CH), 125.8 (CH), 124.7 (CH), 46.0 (CH$_2$), 44.3 (t, J = 21.9 Hz, CDH), 44.0 (t, J = 20.7 Hz, CDH), 27.7 (CH$_3$); HRMS-APCI *m/z* calculated for C$_{17}$DH$_{16}$ $[M+H]^+$ 222.1393, found 222.1396.

1-(4-Methylphenyl)-3-methyl-3-phenylcyclobut-1-ene (6b).
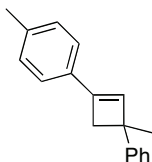
Compound **6b** was synthesized following the general procedure starting from **4b** (30.1 mg, 0.259 mmol) and α-methylstyrene (72 μL, 0.526 mmol) with catalyst **U** (7.7 mg, 0.008 mmol). The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6b** as a colorless oil (45.1 mg, 74%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.39 (dm, J = 8.1, 2H), 7.33-7.26 (m, 4H), 7.21-7.15 (m, 1H), 7.13 (dm, J = 7.8 Hz, 2H), 6.65 (s, 1H), 2.94 (d, J = 12.5 Hz, 1H), 2.88 (d, J = 12.5 Hz, 1H), 2.34 (s, 3H), 1.61 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 148.0 (C), 143.8 (C), 137.7 (C), 132.7 (CH), 132.2 (C), 129.1 (CH), 128.2 (CH), 126.0 (CH), 125.75 (CH), 124.7 (CH), 46.0 (C), 44.4 (CH$_2$), 27.7 (CH$_3$), 21.5 (CH$_3$); HRMS-APCI m/z calculated for C$_{18}$H$_{19}$ $[M$+H$]^+$ 235.1487, found 235.1486.

1-(3-Methylphenyl)-3-methyl-3-phenylcyclobut-1-ene (6c).
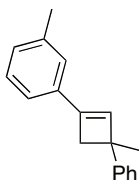
Compound **6c** was synthesized following the general procedure starting from **4c** (30.3 mg, 0.261 mmol) and α-methylstyrene (72 μL, 0.526 mmol) with catalyst **U** (7.9 mg, 0.009 mmol). The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6c** as a colorless oil (42.7 mg, 70%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.42-7.34 (m, 2H), 7.31 (m, 2H), 7.20 (m, 4H), 7.07 (dm, J = 6.9 Hz, 1H), 6.69 (s, 1H), 2.95 (d, J = 12.5 Hz, 1H), 2.89 (d, J = 12.5 Hz, 1H), 2.34 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 147.9 (C), 144.1 (C), 138.0 (C), 134.8 (C), 133.7 (CH), 128.7 (CH), 128.38 (CH), 128.2 (CH), 125.9 (CH), 125.8 (CH), 125.4 (CH), 121.8 (CH), 46.1 (C), 44.5

(CH$_2$), 27.7 (CH$_3$), 21.5 (CH$_3$); HRMS-APCI *m/z* calculated for C$_{18}$H$_{19}$ [*M*+H]$^+$ 235.1487, found 235.1487.

1-(4-Fluorophenyl)-3-methyl-3-phenylcyclobut-1-ene (6d).
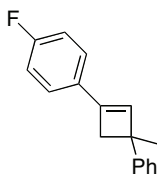
Compound **6d** was synthesized following the general procedure starting from **4d** (32.8 mg, 0.277 mmol) and α-methylstyrene (72 μL, 0.526 mmol) with catalyst **U** (7.7 mg, 0.008 mmol). The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6d** as a colorless oil (49.7 mg, 75%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37 (m, 2H), 7.35-7.10 (m, 5H), 7.01 (t, *J* = 8.7 Hz, 2H), 6.66 (s, 1H), 2.95 (d, *J* = 12.5 Hz, 1H), 2.88 (d, *J* = 12.5 Hz, 1H), 1.62 (s, 3H); 13C NMR (101 MHz, CDCl3) δ 162.6 (d, *J* = 247.2 Hz, C), 147.7 (C), 142.9 (C), 133.3 (d, *J* = 2.3 Hz, CH), 131.2 (d, *J* = 3.3 Hz, C), 128.3, 126.5 (d, J = 8.1 Hz, CH), 126.0(CH), 125.9 (CH), 115.4 (d, *J* = 21.7 Hz, CH), 46.1 (C), 44.4 (CH$_2$), 27.8 (CH$_3$); HRMS-APCI *m/z* calculated for C$_{17}$H$_{16}$F [*M*+H]$^+$ 239.1236, found 239.1245.

1-(4-Chlorophenyl)-3-methyl-3-phenylcyclobut-1-ene (6e).
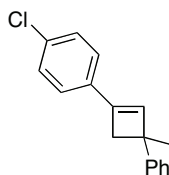
Compound **6e** was synthesized following the general procedure starting from **4e** (36.3 mg, 0.266 mmol)) and α-methylstyrene (72 μL, 0.526 mmol) with catalyst **U** (7.9 mg, 0.009 mmol). The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6e** as a colorless oil (41.5 mg, 61%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.34 (m, 2H), 7.32-7.23 (m, 5H), 7.23-7.12 (m, 2H), 6.69 (s, 1H), 2.92 (d, *J* = 12.5 Hz, 1H), 2.85 (d, *J* = 12.5 Hz, 1H), 1.58 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 147.6 (C), 142.9 (C), 134.6 (CH), 133.6 (C), 133.3 (C), 128.7 (CH), 128.3 (CH), 126.1 (CH), 125.9 (CH),

125.9 (CH), 46.2 (C), 44.3 (CH$_2$), 27.7 (CH$_3$); HRMS-APCI *m/z* calculated for C$_{17}$H$_{16}$Cl [*M*+H]$^+$ 255.0941, found 255.0942.

1-(4-Bromophenyl)-3-methyl-3-phenylcyclobut-1-ene (6f).
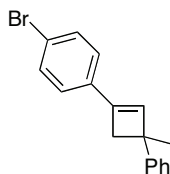
Compound **6f** was synthesized following the general procedure starting from **4f** (48.3 mg, 0.267 mmol) and α-methylstyrene (72 µL, 0.526 mmol) with catalyst **U** (7.6 mg, 0.008 mmol). The residue was purified by preparative TLC (9:1 pentane/CH$_2$Cl$_2$) to give **6f** as a colorless oil (59.4 mg, 74%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.49 (d, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 8.2 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.26 (dd, *J* = 13.7, 8.1 Hz, 3H), 6.78 (s, 1H), 2.99 (d, *J* = 12.5 Hz, 1H), 2.92 (d, *J* = 12.5 Hz, 1H), 1.65 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 147.4 (C), 142.8 (C), 134.7 (CH), 133.6 (C), 131.5 (CH), 128.2 (CH), 126.2 (CH), 125.9 (CH), 125.8 (CH), 121.7 (C), 46.2 (C), 44.2 (CH$_2$), 27.6 (CH$_3$); HRMS-APCI *m/z* calculated for C$_{17}$H$_{16}$Br [*M*+H]$^+$ 299.0435, found 299.0444.

1-(4-Methoxyphenyl)-3-methyl-3-phenylcyclobut-1-ene (6g).
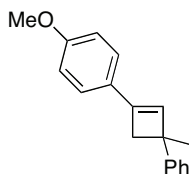
Compound **6g** was synthesized following the general procedure starting from **4g** (34 µL, 0,263 mmol) and α-methylstyrene (72 µL, 0.526 mmol) with catalyst **U** (7.7 mg, 0.008 mmol). The residue was purified by preparative TLC (9:1 pentane/CH$_2$Cl$_2$) to give **6g** as a white solid (42.1 mg, 64%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.45-7.35 (m, 2H), 7.31 (m, 4H), 7.17 (t, *J* = 7.3 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 2H), 6.57 (s, 1H), 3.79 (s, 3H), 2.93 (d, *J* = 12.5 Hz, 1H), 2.87 (d, *J* = 12.4 Hz, 1H), 1.61 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 159.5 (C), 148.1 (C), 143.4 (C), 131.3 (CH), 128.2 (CH), 128.0 (C), 126.1 (CH), 126.0 (CH), 125.7 (CH), 113.9 (CH), 55.4 (CH$_3$), 45.9 (C), 44.4

(CH$_2$), 27.9 (CH$_3$); HRMS-ESI *m/z* calculated for C$_{18}$H$_{19}$O [*M*+H]$^+$ 251.1436, found 251.1441.

3-(3-Methyl-3-phenylcyclobut-1-enyl)phenol (6h).
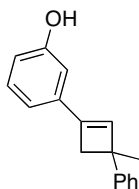
Compound **6h** was synthesized following the general procedure starting from **4h** (33.5 mg, 0.286 mmol) and α-methylstyrene (72 μL, 0.526 mmol) with catalyst **U** (7.7 mg, 0.008 mmol). The residue was purified by preparative TLC (1:8 pentane/CH$_2$Cl$_2$) to give **6h** as a colorless oil (50.3 mg, 74%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.40-7.34 (m, 2H), 7.34-7.26 (m, 2H), 7.21-7.13 (m, 2H), 6.99-6.92 (m, 1H), 6.83 (dd, *J* = 2.6, 1.5 Hz, 1H), 6.71 (ddd, *J* = 8.1, 2.6, 0.9 Hz, 1H), 6.69 (s, 1H), 2.92 (d, *J* = 12.5 Hz, 1H), 2.85 (d, *J* = 12.5 Hz, 1H), 1.60 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 155.8 (C), 147.7 (C), 143.5 (C), 136.5 (C), 134.5 (CH), 129.7 (CH), 128.3 (CH), 125.9 (CH), 125.8 (CH), 117.5 (CH), 115.0 (CH), 111.5 (CH), 46.1 (C), 44.4 (CH$_2$), 27.6 (CH$_3$); HRMS-ESI *m/z* calculated for C$_{17}$H$_{15}$O [*M*+H]$^+$ 235.1123, found 235.1121.

1-Cyclopropyl-3-methyl-3-phenylcyclobut-1-ene (6i).
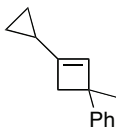
Compound **6i** was synthesized following the general procedure starting from **4a** (34.8 mg, 0.526 mmol) and α-methylstyrene (35.5 μL, 0.263 mmol) with catalyst **U** (7.8 mg, 0.009 mmol). The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6i** as a colorless oil (22.4 mg, 46%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.33-7.22 (m, 4H), 7.23-7.08 (m, 1H), 6.13 (s, 1H), 2.41 (d, *J* = 12.5 Hz, 1H), 2.35 (d, *J* = 12.5 Hz, 1H), 1.49 (s, 3H), 1.46 (m, 1H), 0.73-0.59 (m, 2H), 0.53-0.39 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 149.0 (C), 148.5 (C), 131.8 (CH), 128.1 (CH), 125.9 (CH), 125.54

(CH), 45.5 (C), 43.9 (CH$_2$), 28.1 (CH$_3$), 11.6 (CH), 5.6 (CH$_2$), 5.5 (CH$_2$); HRMS-APCI
m/z calculated for C$_{14}$H$_{17}$ [*M*+H]$^+$ 185.1330, found 185.1331.

1-Phenyl-3-methyl-3-phenylmethylcyclobut-1-ene (6j).

Compound **6j** was synthesized following the general procedure starting from **4a** (28.8
µL, 0.263 mmol) and (2-methylallyl)benzene (**5b**) (69.5 mg, 0.526 mmol) with catalyst
U (7.1 mg, 0.008 mmol). The residue was purified by preparative TLC (99:1
pentane/CH$_2$Cl$_2$) to give **6j** as a colorless oil (27.6 mg, 45%): ^{1}H NMR (400 MHz,
CDCl$_3$) δ 7.42-7.17 (m, 11H), 6.48 (s, 1H), 2.95-2.79 (m, 2H), 2.72 (d, *J* = 12.6 Hz,
1H), 2.53 (d, *J* = 12.5 Hz, 1H), 1.22 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 142.3 (C),
140.1 (C), 135.3 (CH), 135.2 (C), 129.9 (CH), 128.4 (CH), 128.1 (CH), 127.7 (CH),
125.9 (CH), 124.6 (CH), 46.8 (CH$_3$), 43.6 (C), 41.3 (CH$_2$), 23.9 (CH$_3$); HRMS-APCI
m/z calculated for C$_{18}$H$_{18}$ [*M*+H]$^+$ 235.1487, found 235.1498.

1-Bromo-4-(3-methyl-3-propylcyclobut-1-enyl)benzene (6k).
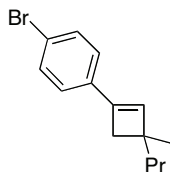
Compound **6k** was synthesized following the general procedure starting from **4f** (47.7
mg, 0.263 mmol) and 2-methylpent-1-ene (**5c**) (100 µL, 0.0.810 mmol) with catalyst **U**
(7.7 mg, 0.008 mmol). The residue was purified by preparative TLC (99:1
pentane/CH$_2$Cl$_2$) to give **6k** and **6o** as 5:1 mixture of isomers (27.6 mg, 45%): ^{1}H NMR
(400 MHz, CDCl$_3$) δ 7.43 (d, *J* = 8.5 Hz, 3H), 7.19 (d, *J* = 8.5 Hz, 2H), 6.44 (s, 1H),
2.51 (d, *J* = 12.5 Hz, 1H), 2.39 (d, *J* = 12.5 Hz, 1H), 1.51 (ddd, *J* = 6.9, 5.4, 2.0 Hz,
2H), 1.42-1.32 (m, 2H), 1.22 (s, 3H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz,
CDCl$_3$) δ 141.5 (C), 137.1 (CH), 134.3 (C), 131.5 (CH), 126.1 (CH), 121.3 (C), 43.2
(C), 42.5 (CH$_2$), 41.1 (CH$_2$), 24.1 (CH$_2$), 19.3 (CH$_3$), 14.9 (CH$_3$); HRMS-APCI *m/z*
calculated for C$_{14}$H$_{30}$Br [*M*+H]$^+$ 265.0592, found 265.0594.

2-Phenylspiro[3.5]non-1-ene (6l).

Compound **6k** was synthesized following the general procedure starting from **4a** (58.0 µL, 0.526 mmol) and methylenecyclohexane (**5c**) (31.6 µL, 0.263 mmol) with catalyst **-U** (7.1 mg, 0.008 mmol). The residue was purified by preparative TLC (pentane) to give **6k** as a colorless oil (27.7 mg, 53%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38-7.28 (m, 4H), 7.23 (dt, J = 9.3, 4.3 Hz, 1H), 6.54 (s, 1H), 2.43 (s, 2H), 1.39-1.59 (m, 10H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 143.6 (C), 135.7 (CH), 135.5 (C), 128.4 (CH), 127.5 (CH), 124.5 (CH), 44.5 (C), 40.3 (CH$_2$), 36.6 (CH$_2$), 26.1 (CH$_2$), 24.7 (CH$_2$); HRMS-APCI *m/z* calculated for C$_{15}$H$_{19}$ [*M*+H]$^+$ 199.1487, found 199.1489.

4-Ethyl-3,3-dimethyl-1-phenylcyclobut-1-ene (6m).
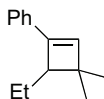
Compound **6l** was synthesized following the general procedure starting from **4a** (28.8 µL, 0.263 mmol) and 2-methylpent-2-ene (**5d**) (64.5 µL, 0.526 mmol) with catalyst **U** (7.7 mg, 0.009 mmol). The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6l** as a 9:1 mixture of regioisomers (36.0 mg, 74%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.43-7.30 (m, 4H), 7.26 (dd, J = 5.0, 3.2 Hz, 1H), 6.33 (s, 1H), 2.70 (dd, J = 10.6, 4.1 Hz, 1H), 1.84 (m, 1H), 1.59-1.45 (m, 1H), 1.29 (s, 3H), 1.21 (s, 3H), 1.04 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 146.1 (C), 136.4 (CH), 135.2 (C), 128.4 (CH), 127.3 (CH), 125.2 (CH), 53.9 (CH), 43.0 (C), 28.1 (CH$_3$), 22.4 (CH$_2$), 21.9 (CH$_3$), 13.5 (CH$_3$); HRMS-APCI *m/z* calculated for C$_{14}$H$_{19}$ [*M*+H]$^+$ 187.1487, found 187.1487.

3,3-Dimethyl-4-ethyl-1-(4-fluorophenyl)cyclobut-1-ene (6n).
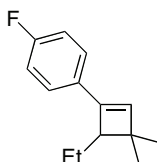
Compound **6m** was synthesized following the general procedure starting from **4c** (29.9 mg, 0.249 mmol) and 2-methylpent-2-ene (**5d**) (64.5 μL, 0.526 mmol) with catalyst **U** (7.4 mg, 0.008 mmol). The residue was purified by preparative TLC (99:1 pentane/CH_2Cl_2) to give **6m** as a colorless oil 9:1 mixture of regioisomers (37.1 mg, 73%): ^1H NMR (400 MHz, CDCl$_3$) δ 7.33-7.22 (m, 2H), 7.03-6.93 (m, 2H), 6.22 (s, 1H), 2.62 (dd, J = 10.6, 4.1 Hz, 1H), 1.77 (ddd, J = 14.2, 7.5, 4.1 Hz, 1H), 1.46 (ddd, J = 14.2, 10.6, 7.1 Hz, 1H), 1.24 (s, 3H), 1.16 (s, 3H), 0.98 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 162.1 (d, J = 246.3 Hz, C), 145.1 (C), 135.9 (d, J = 2.2 Hz, CH), 131.3 (d, J = 3.3 Hz, C), 126.9 (d, J = 7.9 Hz, CH), 115.32 (d, J = 21.5 Hz, CH), 53.9 (CH), 43.0 (C), 28.0 (CH$_3$), 22.3 (CH$_2$), 21.8 (CH$_3$), 13.4 (CH$_3$); HRMS-EI$^+$ *m/z* calculated for C$_{14}$H$_{17}$F $[M]^+$ 204.1314, found 204.1320.

1-(4-Chloro)-3,3-dimethyl-4-ethylcyclobut-1-en (6p).
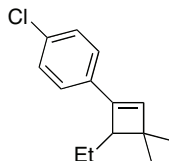
Compound **6p** was synthesized following the general procedure starting from **4e** (32.5 mg, 0.259 mmol) and 2-methylpent-2-ene (**5e**) (64.5 μL, 0.526 mmol) with catalyst **U** (7.7 mg, 0.009 mmol). The residue was purified by preparative TLC (99:1 pentane/CH_2Cl_2) to give **6p** as a 10:1 mixture of regioisomers (29.1 mg, 51%): ^1H NMR (400 MHz, CDCl$_3$) δ 7.28-7.22 (m, 4H), 6.28 (s, 1H), 2.62 (dd, J = 10.6, 4.1 Hz, 1H), 1.84-1.69 (m, 1H), 1.51-1.40 (m, 1H), 1.24 (s, 3H), 1.16 (s, 3H), 0.98 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 145.0 (C), 137.1 (CH), 133.6 (C), 132.9 (C), 128.6 (CH), 126.6 (CH), 53.8 (CH), 43.2 (C), 28.0 (CH$_2$), 22.3 (CH$_3$), 21.7 (CH$_3$), 13.4 (CH$_3$); HRMS-APCI *m/z* calculated for C$_{14}$H$_{17}$Cl $[M+H]^+$ 220.1019, found 220.1019.

1-(4-Bromophenyl)-3,3-dimethyl-4-ethylcyclobut-1-en (6o).
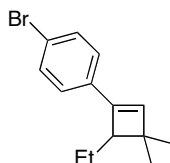
Compound **6o** was synthesized following the general procedure starting from **4f** (46.9 mg, 0.259 mmol) and 2-methylpent-2-ene (**5e**) (64.5 µL, 0.526 mmol) with catalyst **U** (7.7 mg, 0.009 mmol). The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6o** as a 12:1 mixture of regioisomers (42.6 mg, 62%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.46-7.37 (m, 2H), 7.18 (d, J = 8.4 Hz, 2H), 6.30 (s, 1H), 2.62 (dd, J = 10.6, 4.1 Hz, 1H), 1.83-1.69 (m, 1H), 1.52-1.38 (m, 1H), 1.24 (s, 3H), 1.16 (s, 3H), 0.98 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 144.9 (C), 137.2 (CH), 133.9 (C), 131.4 (CH), 126.7 (CH), 120.9 (C), 53.6 (CH), 43.0 (C), 27.8 (CH$_2$), 22.2 (CH$_3$), 21.6 (CH$_3$), 13.3 (CH$_3$); HRMS-APCI m/z calculated for C$_{14}$H$_{18}$Br [M+H]$^+$ 265.0592, found 265.0594.

3,3-Dimethyl-4-ethyl-1-(3-methylphenyl)cyclobut-1-en (6q).
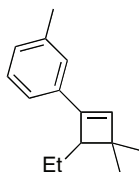
Compound **6q** was synthesized following the general procedure starting from **4c** (33.4 mg, 0.287 mmol) and 2-methylpent-2-ene (**5e**) (64.5 µL, 0.526 mmol) with catalyst **U** (7.7 mg, 0.008 mmol). The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6q** as a 7:1 mixture of regioisomers (40.1 mg, 60%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.17 (dt, J = 21.8, 9.4 Hz, 3H), 7.03 (d, J = 7.5 Hz, 1H), 6.27 (s, 1H), 2.64 (dd, J = 10.6, 4.0 Hz, 1H), 2.33 (s, 3H), 1.81 (ddd, J = 14.3, 7.4, 4.1 Hz, 1H), 1.47 (ddd, J = 10.8, 10.3, 4.9 Hz, 1H), 1.24 (s, 3H), 1.16 (s, 3H), 0.99 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 146.2 (C), 137.9 (C), 136.3 (CH), 135.1 (C), 128.3 (CH), 128.1 (CH), 125.8 (CH), 122.4 (CH), 53.9 (CH$_2$), 42.9 (C), 28.1 (CH$_3$), 22.4 (CH$_2$), 21.9 (CH$_3$), 21.6 (CH$_3$), 13.5 (CH$_3$); HRMS-APCI m/z calculated for C$_{15}$H$_{21}$ [M+H]$^+$ 201.1643, found 201.1645.

3-(4-Ethyl-3,3-dimethylcyclobut-1-en-1-yl)phenol (6r).
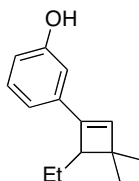
Compound **6r** was synthesized following the general procedure starting from **4h** (31.0 mg, 0.263 mmol) and 2-methylpent-2-ene (**5e**) (64 μL, 0.526 mmol) with catalyst **U** (7.1 mg, 0.008 mmol). The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6r** as a 7:1 mixture of regioisomers (40.0 mg, 60%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.18 (t, J = 7.8 Hz, 1H), 6.92 (d, J = 7.6 Hz, 1H), 6.79 (s, 1H), 6.69 (dd, J = 8.0, 2.5 Hz, 1H), 6.36 (s, 1H), 6.28 (s, 1H), 4.75 (s, 1H), 2.62 (dd, J = 10.6, 4.0 Hz, 1H), 1.86-1.72 (m, 1H), 1.52-1.41 (m, 1H), 1.25 (s, 3H), 1.16 (s, 3H), 0.99 (t, J = 7.4 Hz, 4H); ^{13}C NMR (100 MHz, CDCl$_3$); HRMS-APCI m/z calculated for C$_{14}$H$_{18}$ $[M+H]^+$ 202.1358, found 202.1358.

2-(4,4-Dimethyl-2-phenylcyclobut-2-en-1-yl)ethyl Benzoate (6s).
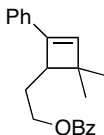
Compound **6s** was synthesized following the general procedure starting from **4a** (28.8 μL, 0.263 mmol) and **5f** (107.4 mg, 0.526 mmol) with catalyst **U** (7.4 mg, 0.008 mmol). The residue was purified by preparative TLC (6:1 hexane/EtOAc) to give **6s** as a single regioisomer with non-separable traces of **5f** (39.8 mg, 50%): ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.06 (dd, J = 8.3, 1.3 Hz, 2H), 7.60-7.54 (m, 1H), 7.47-7.42 (m, 2H), 7.36-7.29 (m, 4H), 7.25-7.20 (m, 1H), 6.32 (s, 1H), 4.49-4.35 (m, 2H), 2.93 (dd, J = 10.2, 4.3 Hz, 1H), 2.32-2.19 (m, 1H), 2.03-1.90 (m, 1H), 1.27 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 166.8 (C), 145.1 (C), 136.9 (CH), 134.6 (C), 133.0 (CH), 130.6 (C), 129.7 (CH), 128.6 (CH), 128.5 (CH), 127.6 (CH), 125.1 (CH), 64.4 (CH$_2$), 48.3

(CH), 43.0 (C), 28.6 (CH$_2$), 27.8 (CH$_3$), 22.3 (CH$_3$); HRMS-ESI *m/z* calculated for C$_{21}$H$_{22}$O$_2$Na [*M*+Na]$^+$ 329.1517, found 329.1503.

((2-(4,4-Dimethyl-2-phenylcyclobut-2-en-1-yl)ethyl)sulfonyl)benzene (6t).
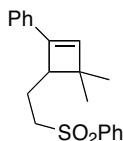
Compound **6t** was synthesized following the general procedure starting from **4a** (57.6 μL, 0.526 mmol) and **5g** (58.9 mg, 0.257 mmol) with catalyst **U** (7.7 mg, 0.008 mmol). The residue was purified by preparative TLC (6:1 hexane/EtOAc) to give **6t** as a single regioisomer with non-separable traces of **5f** (37.7 mg, 44%): ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.90 (dd, *J* = 11.7, 4.3 Hz, 2H), 7.72-7.61 (m, 1H), 7.60-7.51 (m, 2H), 7.33-7.27 (m, 2H), 7.25-7.17 (m, 3H), 6.25 (s, 1H), 3.21-3.15 (m, 2H), 2.76 (dd, *J* = 10.6, 4.2 Hz, 1H), 2.27-2.15 (m, 1H), 1.86-1.74 (m, 1H), 1.20 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 144.6 (C), 139.1 (C), 136.9 (CH), 134.2 (C), 133.8 (CH), 129.4 (CH), 128.6 (CH), 128.3 (CH), 128.2 (CH), 125.1 (CH), 55.4 (CH$_2$), 49.8 (CH), 42.9 (C), 27.8 (CH$_3$), 22.8 (CH$_2$), 21.7 (CH$_3$); HRMS-ESI *m/z* calculated for C$_{20}$H$_{22}$O$_2$SNa [*M*+Na]$^+$ 349.1235, found 349.1238.

((1*R**,4*R**)-4-Methylcyclobut-2-ene-1,2-diyl)dibenzene   compound   (6u)   with ((3*R**,4*S**)-4-methylcyclobut-1-ene-1,3-diyl)dibenzene (6u') (4:1).
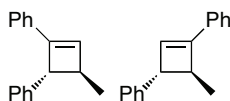
Compound **6u/6u'** was synthesized following the general procedure starting from **4a** (86.6 μL, 0.789 mmol) and **5h** (34.2 μL, 0.263 mmol) with catalyst **U** (7.1 mg, 0.008 mmol). The residue was purified by preparative TLC (6:1 hexane/EtOAc) to give a **6u**/**6u'** 4:1 mixture of regioisomers (27.9 mg, 48%). Regioisomer **6u**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.40-7.14 (m, 10H), 6.48 (d, *J* = 1.1 Hz, 1H), 3.43 (s, 1H), 2.96 (qd, *J* = 6.9, 1.6 Hz, 1H), 1.41 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 151.1 (C), 143.4 (C), 134.0 (C), 128.6 (CH), 128.47 (CH), 127.9 (CH), 127.8 (CH), 126.9 (CH),

126.4 (CH), 125.3 (CH), 52.6 (CH), 47.4 (CH), 17.9 (CH$_3$); Regiosiomer **6u'**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.40-7.14 (m, 10H), 6.56 (d, J = 0.9 Hz, 1H), 3.64 (d, J = 1.6 Hz, 1H), 2.60 (q, J = 6.9 Hz, 1H), 1.28 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 151.12, 143.37, 133.1 (C), 128.6 (CH), 128.41 (CH), 128.39 (CH), 127.7 (CH), 127.1 (CH), 126.41 (CH), 125.17 (CH), 54.8 (CH), 46.1 (CH), 18.8 (CH$_3$); HRMS-EI *m/z* calculated for C$_{17}$H$_{16}$ $[M]^+$ 220.1252, found 220.1246.

1,4-Bis(3-methyl-3-phenylcyclobut-1-en-1-yl)benzene (6v).
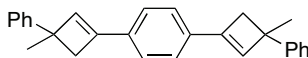
Compound **6v** was synthesized following the general procedure starting from 1,4-diethynylbenzene (**4i**) (32.3 mg, 0.256 mmol) and α-methylstyrene (108.4 μL, 0.789 mmol) with catalyst **U** (7.1 mg, 0.008 mmol) stirring at r.t. for 15 h. The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6v** as a pale yellow solid (64.8 mg, 68%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.46-7.31 (m, 6H), 7.27-7.19 (m, 2H), 6.76 (s, 1H), 3.00 (d, J = 12.5 Hz, 1H), 2.94 (d, J = 12.5 Hz, 1H), 1.66 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 147.8 (C), 143.7 (C), 134.2 (C), 134.0 (CH), 128.3 (CH), 126.0 (CH), 125.8 (CH), 124.7 (CH), 46.2 (C), 44.3 (CH$_2$), 27.8 (CH$_3$); HRMS-MALDI *m/z* calculated for C$_{28}$H$_{26}$ $[M]^+$ 362.2035, found 362.2014.
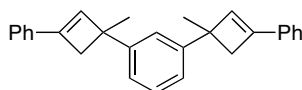
1,3-Bis(3-methyl-3-phenylcyclobut-1-en-1-yl)benzene (6w).

Compound **6w** was synthesized following the general procedure starting from 1,3-diethynylbenzene (**4j**) (35 μL, 0.263 mmol) and α-methylstyrene (108.4 μL, 0.789 mmol) with catalyst **U** (7.6 mg, 0.008 mmol) stirring at r.t. for 20 h. The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **6w** as a yellow solid (50.7 mg, 53%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.40 (m, 3H), 7.37-7.28 (m, 4H), 7.20 (m, 2H), 6.75 (s, 1H), 2.99 (d, J = 12.8, 1H), 2.93 (d, J = 12.5 Hz, 0.5H), 2.92 (d, J = 12.5 Hz, 0.5H), 1.64 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 147.8 (C), 143.8 (C), 134.9 (C),

(CH$_2$), 42.6 (C), 40.9 (CH$_2$), 38.2 (CH$_2$), 34.1 (CH$_2$), 24.1 (CH$_3$), 22.7 (CH$_3$); HRMS-APCI *m/z* calculated for C$_{16}$H$_{20}$ [*M*+H]$^+$ 212.1565, found 212.1564.

cis-(E)-(4-Deutero-3-methyl-3-(4-deutero-3-methylbut-3-en-1-yl)-1-phenylcyclobut-1-ene (6y-d$_2$).
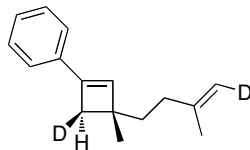
Compound **6y-d$_2$** was synthesized following the general procedure starting from **4a** (28.8 μL, 0.263 mmol) and **5g-d$_2$** (25% in toluene, 256 mg, 0.571 mmol) with catalyst **U** (7.4 mg, 0.008 mmol) stirring at r.t. for 34 h. The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give a 1:1 mixture of **6y-d$_2$** and **11a-d$_2$** (21,4 mg, 38%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.40 –7.12 (m, 5H), 6.43 (s, 1H), 4.67 (br s, 1H), 2.54 (s, 1H), 2.10-2.01 (m, 2H), 1.76 (s, 3H), 1.72-1.67 (m, 2H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 146.6 (C), 142.5 (C), 135.6 (CH), 135.1 (C), 128.3 (CH), 127.5 (CH), 124.4 (CH), 109.1 (t, *J* = 26.1 Hz, CDH), 42.5 (C), 40.5 (t, *J* = 29.4 Hz, CDH), 38.2 (CH$_2$), 34.1 (CH$_2$), 24.0 (CH$_3$), 22.5 (CH$_3$).

(3-Methyl-3-(3-methylbut-3-enyl)-1-(4-methylphenyl)cyclobut-1-ene (6z).
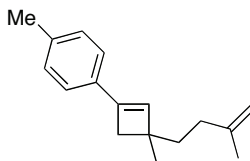
Compound **6z** was synthesized following the general procedure starting from **4b** (34.6 mg, 0.297 mmol) and 2,5-dimethylhexa-1,5-diene (78.0 μL, 0.526 mmol) with catalyst **U** (7.1 mg, 0.008 mmol) stirring at r.t. for 40 h. The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give a 1.2:1 mixture of **6z** and **11b** (36.2 mg, 54%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.27 (m, 2H), 7.14 (m, 2H), 6.39 (d, *J* = 1.0 Hz, 1H), 4.72 (s, 2H), 2.57 (d, *J* = 12.5 Hz, 1H), 2.44 (d, *J* = 12.5 Hz, 1H), 2.37 (s, 3H), 2.14-2.04 (m, 2H), 1.77 (s, 3H), 1.73-1.67 (m, 2H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 146.8 (C), 142.6 (C), 137.4 (C), 134.5 (CH), 132.6 (C), 129.1 (CH), 124.5 (CH), 109.4 (CH),

42.7 (C), 41.0 (CH$_2$), 38.4 (CH$_2$), 34.3 (CH$_2$), 26.41 (CH$_3$), 22.83 (CH$_3$), 21.5 (CH$_3$); HRMS-MALDI *m/z* calculated for C$_{16}$H$_{20}$ [*M*]$^+$ 226.1722, found 226.1710.


(3-Methyl-3-(3-methylbut-3-enyl)-1-(3-methylphenyl)cyclobut-1-ene (6aa).
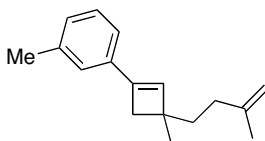
Compound **6aa** was synthesized following the general procedure starting from **4c** (32.0 mg, 0.275 mmol) and 2,5-dimethylhexa-1,5-diene (78.0 μL, 0.526 mmol) with catalyst **U** (7.1 mg, 0.008 mmol) stirring at r.t. for 40 h. The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give a 1.1:1 mixture of **6aa** and **11c** (37.2 mg, 60%): ^{1}H NMR (400 MHz, CDCl$_3$) *δ* 7.25-7.11 (m, 3H), 7.00 (dm, *J* = 6.4 Hz, 1H), 6.41 (s, 1H), 4.69 (d, *J* = 0.9 Hz, 2H), 2.55 (d, *J* = 12.5 Hz, 1H), 2.42 (d, *J* = 12.5 Hz, 1H), 2.34 (s, 3H), 2.06 (dd, *J* = 10.1, 6.5 Hz, 2H), 1.73 (s, 3H), 1.70-1.63 (m, 2H), 1.24 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) *δ* 146.8 (C), 142.8 (C), 137.9 (C), 135.5 (CH), 135.2 (C), 128.4 (CH), 128.3 (CH), 125.2 (CH), 121.6 (CH), 109.5 (CH), 42.7 (C), 41.0 (CH$_2$), 38.3 (CH$_2$), 34.3 (CH$_2$), 24.2 (CH$_3$), 22.8 (CH$_3$), 21.5 (CH$_3$); HRMS-MALDI *m/z* calculated for C$_{16}$H$_{20}$ [*M*]$^+$ 226.1722, found 226.1694.


1-(4-*tert*-Butylphenyl)-3-methyl-3-(3-methylbut-3-enyl)cyclobut-1-ene (6ab).
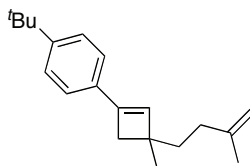
Compound **6ab** was synthesized following the general procedure starting from alkyne **4k** (41.6 mg, 0.263 mmol) and 2,5-dimethylhexa-1,5-diene (78.0 μL, 0.526 mmol) with catalyst **U** (7.4 mg, 0.008 mmol + 7.1 mg, 0.008 mmol after 15 h) stirring atroom temperaturefor 30 h. The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give a **6ab** with traces of **11d** (20.8 mg, 29%): ^{1}H NMR (400 MHz, CDCl$_3$) *δ* 7.35 (d, *J* = 8.2 Hz, 2H), 7.32-7.27 (m, 2H), 6.37 (s, 1H), 4.68 (bs, 2H), 2.54

(d, J = 12.5 Hz, 1H), 2.42 (d, J = 12.5 Hz, 1H), 2.11-1.98 (m, 2H), 1.73 (s, 3H), 1.71-1.60 (m, 2H), 1.31 (s, 9H), 1.24 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 150.7 (C), 146.9 (C), 142.5 (C), 134.8 (CH), 132.6 (C), 125.3 (CH), 124.3 (CH), 109.4 (CH), 42.8 (C), 41.0 (CH$_2$), 38.4 (CH$_2$), 34.8 (CH$_2$), 34.3 (C), 31.6 (CH$_2$), 31.5 (CH$_3$), 24.3 (CH$_3$), 22.8 (CH$_3$); HRMS-APCI m/z calculated for C$_{20}$H$_{19}$ [M+H]$^+$ 269.2269, found 269.2272.

3-(3-Methyl-3-(3-methylbut-3-en-1-yl)cyclobut-1-en-1-yl)phenol (6ac).
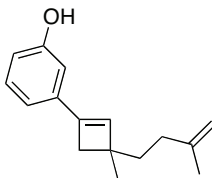
Compound **6ac** was synthesized following the general procedure starting from **4h** (31.0 mg, 0.263 mmol) and 2,5-dimethylhexa-1,5-diene (78.0 μL, 0.526 mmol) with catalyst **U** (7.1 mg, 0.008 mmol) stirring at r.t. for 34 h. The residue was purified by preparative TLC (5:1 hexane/EtOAc) to give a 1:1 mixture of **6ac** and **11e** (38.1 mg, 64%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.19 (t, J = 7.8 Hz, 1H), 6.96-6.89 (m, 1H), 6.83-6.79 (m, 1H), 6.72 (dd, J = 7.7, 2.3 Hz, 1H), 6.42 (s, 1H), 4.85 (br s, 1H), 4.69 (d, J = 0.9 Hz, 2H), 4.67 (s, 1H), 2.53 (d, J = 12.5 Hz, 1H), 2.41 (d, J = 12.5 Hz, 1H), 2.06 (dd, J = 9.9, 6.9 Hz, 2H), 1.73 (s, 3H), 1.70-1.63 (m, 2H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 155.7 (C), 146.8 (C), 142.3 (C), 137.1 (C), 136.3 (CH), 129.7 (CH), 117.3 (CH), 114.7 (CH), 111.3 (CH), 109.5 (CH), 42.8 (C), 41.0 (CH$_2$), 38.2 (CH$_2$), 34.2 (CH$_2$), 24.1 (CH$_3$), 22.8 (CH$_3$); HRMS-ESI m/z calculated for C$_{16}$H$_{19}$O [M-H]$^-$ 227.1436, found 227.1446.

1,1,3-Trimethyl-3-phenyl-2,3-dihydro-1H-indene (7).
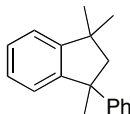
Compound **7** was synthesized following the general procedure starting from phenylacetylene (50 μL, 0.526 mmol) and α-methylstyrene (36 μL, 0.263 mmol) with Ph$_3$PAuCl (3.9 mg, 0.008 mmol) and AgSbF$_6$ (3.0 mg, 0.009 mmol) as catalyst. The

residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **7** as a colorless oil (11.8 mg, 43%): ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.32-7.26 (m, 1H), 7.26-7.10 (m, 8H), 2.42 (d, J = 13.0 Hz, 1H), 2.20 (d, J = 13.0 Hz, 1H), 1.69 (s, 3H), 1.35 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 152.2 (C), 151.0 (C), 148.7 (C), 128.0 (CH), 127.2 (CH), 126.7 (CH), 126.6 (CH), 125.5 (CH), 125.0 (CH), 122.6 (CH), 59.2 (CH$_2$), 50.8 (C), 42.9 (C), 30.9 (CH$_3$), 30.7 (CH$_3$), 30.4 (CH$_3$).

Syn-4,7-Dimethyl-1-phenyltricyclo[5.1.0.0^{2,4}]octane (11a).

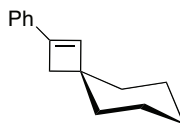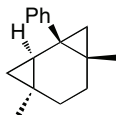Compound **11a** was synthesized following the general procedure starting from **4a** (28.8 μL, 0.263 mmol) and 2,5-dimethylhexa-1,5-diene (78.0 μL, 0.526 mmol) with catalyst **U** (7.1 mg, 0.008 mmol) stirring at r.t. for 34 h. The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give a 1:1 mixture of **6y** and **11a** (35.1 mg, 63%). Subsequent column chromatography (pure pentane) gave product **11a** as colorless oil (16.9 mg): ^{1}H NMR (400 MHz, C$_6$D$_6$) *δ* 7.41-7.28 (m, 2H), 7.23 (dd, J = 10.7, 4.4 Hz, 2H), 1.67-1.39 (m, 4H), 1.02 (dd, J = 8.0, 4.7 Hz, 1H), 0.89 (s, 3H), 0.85 (d, J = 4.3 Hz, 1H), 0.74 (s, 3H), 0.71 (m, 2H), 0.28 (dd, J = 8.1, 4.3 Hz, 1H); ^{1}H NMR (400 MHz, CDCl$_3$) *δ* 7.38 (dd, J = 8.2, 1.3 Hz, 2H), 7.31 (dd, J = 8.2, 6.8 Hz, 2H), 7.26-7.15 (m, 1H), 1.77 (td, J = 5.6, 3.1 Hz, 2H), 1.68-1.51 (m, 2H), 1.09-1.03 (m, 3H), 1.03 (s, 3H), 0.93 (d, J = 4.4 Hz, 1H), 0.81-0.69 (m, 2H), 0.75 (s, 3H), 0.39 (dd, J = 8.0, 4.3 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 145.2 (C), 129.2 (CH), 127.9 (CH), 125.7 (CH), 31.8 (C), 28.6 (CH), 27.4 (CH$_2$), 26.6 (CH$_2$), 26.3 (CH$_3$), 23.7 (CH$_3$), 22.3 (C), 19.9 (CH$_2$), 16.9 (C), 15.6 (CH$_2$); HRMS-APCI *m/z* calculated for C$_{16}$H$_{21}$ [*M*+H]$^+$ 212.1565, found 212.1564.

11a-d_2.
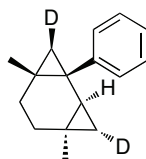
Compound **11a** was synthesized following the general procedure starting from **4a** (28.8 µL, 0.263 mmol) and **5h-d_2** (25% in toluene, 256 mg, 0.571 mmol) with catalyst **U** (7.4 mg, 0.008 mmol) stirring at r.t. for 34 h. The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give a 1:1 mixture of **6y-d_2** and **11a-d_2** (21,4 mg, 38%): ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.40 –7.12 (m, 5H), 2.10-1.56 (m, 4H), 1.04 (d, J = 5.2 Hz, 1H), 1.02 (s, 3H), 0.91 (br s, 1H), 0.75 (d, J = 5.1 Hz, 1H), 0.74 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.3, 129.3 (CH), 128.0 (CH), 125.9 (CH), 30.5 (C), 128.6 (CH), 27.5 (CH$_2$), 26.7 (CH$_2$), 26.4 (CH$_3$), 23.8 (CH$_3$), 22.4 (C), 19.6 (t, J = 21.8 Hz, CDH), 16.9 (C), 15.4 (t, J = 24.2 Hz, CDH); HRMS-APCI m/z calculated for C$_{16}$H$_{18}$D$_2$ $[M+$H$]^+$ 215.1769, found 215.1769.

Syn-4,7-Dimethyl-1-(p-tolyl)tricyclo[5.1.0.0^{2,4}]octane (11b).
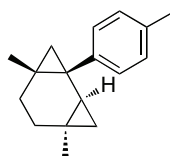
Compound **11b** was synthesized following the general procedure starting from **4b** (34.6 mg, 0.297 mmol) and 2,5-dimethylhexa-1,5-diene (78.0 µL, 0.526 mmol) with catalyst **U** (7.1 mg, 0.008 mmol) stirring at r.t. for 40 h. The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give a 1.2:1 mixture of **6z** and **11b** (36.2 mg, 54%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.27 (m, 2H), 7.14 (m, 2H), 2.36 (s, 3H), 1.76-1.64 (m, 2H), 1.64-1.51 (m, 2H), 1.02 (s, 3H), 1.04-1.01 (m, 3H), 0.91 (d, J = 4.1 Hz, 1H), 0.75 (s, 3H), 0.77-0.74 (m, 1H), 0.71 (d, J = 4.2 Hz, 1H), 0.37 (dd, J = 7.9, 4.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 142.3 (C), 135.3 (C), 129.2 (CH), 128.7 (CH), 31.5 (C), 28.9 (CH), 27.5 (CH$_2$), 26.8 (CH$_2$), 24.3 (CH$_2$), 23.9 (CH$_2$), 22.4 (C), 21.2 (CH$_3$), 20.0 (CH$_2$), 17.0 (C), 15.7 (CH$_2$); HRMS-MALDI m/z calculated for C$_{16}$H$_{20}$ $[M]^+$ 226.1722, found 226.1710.

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Syn-4,7-Dimethyl-1-(m-tolyl)tricyclo[5.1.0.02,4]octane (11c).
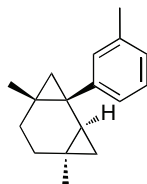
Compound **11c** was synthesized following the general procedure starting from **4c** (32.0 mg, 0.275 mmol) and 2,5-dimethylhexa-1,5-diene (78.0 μL, 0.526 mmol) with catalyst **U** (7.1 mg, 0.008 mmol) stirring at r.t. for 40 h. The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give a 1.1:1 mixture of **6aa** and **11c** (37.2 mg, 60%). Subsequent column chromatography (pure pentane) gave product **11c** as colorless oil (17.2 mg): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.22-7.13 (m, 3H), 7.05-7.00 (m, 1H), 2.36 (s, 3H), 1.79-1.71 (m, 2H), 1.65-1.51 (m, 2H), 1.03 (d, J = 4.7 Hz, 1H), 1.01 (s, 3H), 0.90 (d, J = 4.2 Hz, 1H), 0.79-0.73 (m, 1H), 0.74 (s, 3H), 0.71 (d, J = 4.4 Hz, 1H), 0.36 (dd, J = 8.0, 4.3 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 145.3 (C), 137.4 (C), 130.1 (CH), 127.9 (CH), 126.7 (CH), 126.4 (CH), 31.9 (C), 28.8 (CH), 27.5 (CH$_2$), 26.8 (CH$_2$), 26.4 (CH$_3$), 23.9 (CH$_3$), 22.4 (C), 21.7 (CH$_3$), 20.0 (CH$_2$), 17.0 (C), 15.7 (CH$_2$); HRMS-MALDI *m/z* calculated for C$_{16}$H$_{20}$ [*M*]$^+$ 226.1722, found 226.1694.

Syn -1-(4-(tert-Butyl)phenyl)-4,7-dimethyltricyclo[5.1.0.0^{2,4}]octane (11d).
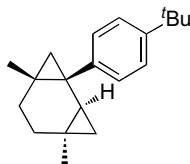
Compound **11d** was synthesized following the general procedure starting from **4k** (41.6 mg, 0.263 mmol) and 2,5-dimethylhexa-1,5-diene (78.0 μL, 0.526 mmol) with catalyst **U** (7.4 mg, 0.008 mmol + 7.1 mg, 0.008 mmol after 15 h) stirring at r.t. for 30 h. The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **11d** with traces of **6ab** (15.0 mg, 21%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.58-7.00 (m, 5H), 1.81-1.70 (m, 0H), 1.59 (ddd, J = 13.1, 10.0, 3.4 Hz, 1H), 1.34 (s, 5H), 1.08-1.01 (m, 0H), 1.02 (s, 0H), 0.90 (d, J = 4.3 Hz, 1H), 0.75 (s, 3H), 0.72 (d, J = 4.3 Hz, 1H), 0.38 (dd, J = 8.0,

4.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 148.3 (C), 142.0 (C), 128.7 (CH), 124.7 (CH), 31.3 (C), 28.6 (CH), 27.4 (CH$_2$), 26.7 (CH$_2$), 26.3 (CH$_3$), 23.7 (CH$_3$), 22.3 (C), 19.8 (CH$_2$), 16.8 (C), 15.5 (CH$_2$); HRMS-APCI m/z calculated for C$_{16}$H$_{20}$ [M+H]$^+$ 212.1565, found 212.1564.

Syn-3-(4,7-dimethyltricyclo[5.1.0.0^{2,4}]octan-1-yl)phenol (11e).
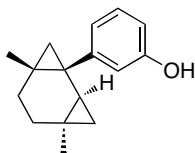
Compound **11e** was synthesized following the general procedure starting from **4h** (31.0 mg, 0.263 mmol) and 2,5-dimethylhexa-1,5-diene (78.0 µL, 0.526 mmol) with catalyst **U** (7.1 mg, 0.008 mmol) stirring at r.t. for 34 h. The residue was purified by preparative TLC (5:1 hexane/EtOAc) to give a 1:1 mixture of **6ac** and **11e** (38.1 mg, 64%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.14 (t, J = 7.8 Hz, 1H), 6.97-6.89 (m, 1H), 6.89-6.82 (m, 1H), 6.66 (dd, J = 8.0, 1.8 Hz, 1H), 4.60 (s, 1H), 1.72-1.65 (m, 2H), 1.60-1.50 (m, 2H), 1.04-1.01 (m, 1H), 0.99 (s, 3H), 0.88 (d, J = 4.4 Hz, 1H), 0.73 (s, 3H), 0.72-0.67 (m, 2H), 0.36 (dd, J = 8.0, 4.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 155.2 (C), 147.3 (C), 129.1 (CH), 121.9 (CH), 116.31 (CH), 112.8 (CH), 31.8 (C), 28.5 (CH), 27.5 (CH$_2$), 26.7 (CH$_2$), 26.3 (CH$_3$), 23.7 (CH$_3$), 22.7 (C), 20.0 (CH$_2$), 16.9 (C), 15.7 (CH$_2$); HRMS-ESI m/z calculated for C$_{16}$H$_{19}$O [M-H]$^-$ 227.1436, found 227.1446.

1,5-Dimethyl-3-phenyl-8-oxabicyclo[3.2.1]oct-3-ene (15).
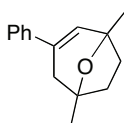
Compound **15** was synthesized following the general procedure starting from **4a** (58 µL, 0.526 mmol) and 2,5-dimethylhexa-1,5-diene (34 µL, 0.263 mmol) with catalyst **U** (7.3 mg, 0.008 mmol) in 1.0 mL of CH$_2$Cl$_2$ stirring at r.t. for 24 h. The residue was purified by preparative TLC (99:1 pentane/CH$_2$Cl$_2$) to give **15** (21.1 mg, 37%): ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.42-7.37 (m, 2H), 7.32 (s, 2H), 7.25 (s, 1H), 6.23 (t, J = 1.6 Hz, 1H), 2.70 (d, J = 16.7, 1H), 2.29 (d, J = 16.6 Hz, 1H), 2.06 (d, J = 9.1 Hz, 1H),

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ISBN:978/84-694-0328-0/DL:T-208-2011
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Experimental Section

1.94-1.89 (m, 1H), 1.85-1.78 (m, 2H), 1.51 (s, 3H), 1.49 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 139.9 (C), 133.6 (C), 131.1 (CH), 128.5 (CH), 127.4 (CH), 125.0 (CH), 79.7 (C), 79.5 (C), 42.4 (CH$_2$), 42.2 (CH$_2$), 37.5 (CH$_2$), 27.4 (CH$_3$), 23.8 (CH$_3$); HRMS-APCI *m/z* calculated for C$_{15}$H$_{19}$O [*M*+H]$^+$ 215.1436, found 215.1437.

Chapter 2. Experimental procedures

Synthesis of propargylic esters.

Propargyl acetate **18e** was used as received from Aldrich and **18f** was used as received from Alfa Aesar.

General procedure for acetylation. The propargylic alcohol (8 mmol) is added to an ice-cooled solution of Ac$_2$O (2 equiv), pyridine (1.5 equiv) and DMAP (0.05 mol%) in ether (15 ml) and stirred at room temperature for 4-8 hours.

1-Phenylprop-2-ynyl ethanoate (18a).
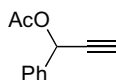
Compound **18a** was synthesized following the general procedure for acetylation reaction starting from 1-phenyl-2-propyn-1-ol (2.35 mL, 18.5 mmol), Ac$_2$O (3.78 mg, 37.1 mmol), pyridine (2.25 mL, 27.8 mmol) and DMAP (115 mg, 0.926 mmol). The residue was purified by chromatography (3:1 hexane-EtOAc) to give **18a** (2.6 g, 82%) as a yellow oil: ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.50 (m, 2H), 7.39 (m, 3H), 6.45 (m, 1H), 2.65 (m, 1H), 2.11 (s, 3H).[121]

1-Phenylprop-2-ynyl benzoate (18b).

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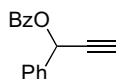
[121] NMR data agreed with: Marcel, K. K.; Kahle, G. G. *J. Am. Chem. Soc.* **1977**, *99*, 6038.

Compound **18b** was prepared by addition of 1-phenyl-2-propyn-1-ol (0.45 mL, 3.71 mmol) to a suspension of NaH (60% in mineral oil, 178 mg, 4.45 mmol) in THF (20 mL) at 0 ºC. After 20 min benzoyl chloride (625.5 mg, 4.45 mmol) was added. The reaction mixture was stirred at r.t. for 3 h. After work-up **18b** was isolated as a white solid (699 mg, 80%) by column chromatography (4:1 Hexane/EtOAc): ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.06 (m, 2H), 7.61 (m, 2H), 7.54 (m, 2H), 7.41 (m, 4H), 6.69 (d, J = 1.9 Hz, 1H), 2.67 (d, J = 1.9 Hz, 1H).[122]
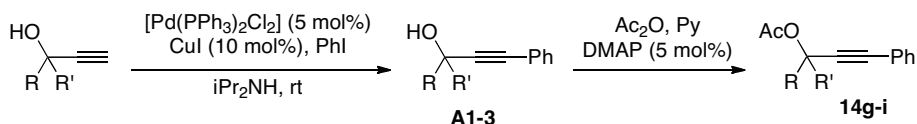
Scheme 53

General procedure for the Sonogashira reaction of propargylic alcohols. A mixture of [Pd(PPh$_3$)$_2$Cl$_2$] (0.05 mol%), PhI (1.2 equiv), CuI (10 mol%), the corresponding propargylic alcohol (1 mmol) and ^{i}Pr$_2$NH or piperidine (3-5 mL) was stirred atroom temperaturefor 18-20 h. After extractive work-up (Et$_2$O) the residue was purified by column chromatography (hexane/EtOAc).

3-Diphenylprop-2-ynyl ethanoate (18g).
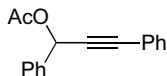
Compound **18g** was was synthesized following *Scheme 53*. A mixture of [Pd(PPh$_3$)$_2$Cl$_2$] (0.05 mol%), PhI (1.2 equiv), CuI (10 mol%), 1-phenyl-2-propyn-1-ol (1.2 mL, 9.27 mmol) and ^{i}Pr$_2$NH (15 mL) was stirred atroom temperaturefor 18 h. After extractive work-up (Et$_2$O) the residue was purified by column chromatography (6:1 hexane/EtOAc) to give **A1** (1.63 g, 82%).[123] Alcohol **A1** (600 mg, 2.87 mmol) was acetylated following the general procedure to obtained **18g** (657 mg, 95%) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.60 (m, 2H), 7.48 (m, 2H), 7.43-7.36 (m, 3H), 7.34-7.28 (m, 3H), 6.70 (s, 1H), 2.13 (s, 3H).[124]

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122 NMR data agreed with: Rodriguez, D.; Pérez Sestelo, J.; Sarandeses, L. A. *J. Org. Chem*. **2003**, *68*, 2518-2520.

123 NMR data of **A1** agreed with: Engel, D. A.; Dudley, G. B. *Org. Lett*. **2006**, *8*, 4027-4029.

124 NMR data agreed with: Wang, S.; Zhang, L. *J. Am. Chem. Soc.* **2006**, *128*, 8414-8415.

2-Methyl-4-phenylbut-3-yn-2-yl ethanoate (18h).
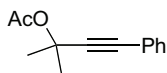
Compound **18h** was was synthesized following *Scheme 53*. A mixture of [Pd(PPh$_3$)$_2$Cl$_2$] (0.05 mol%), PhI (1.2 equiv), CuI (10 mol%), 2-methylbut-3-yn-2-ol (1 mL, 10.32 mmol) and piperidine (18 mL) was stirred atroom temperaturefor 18 h. After extractive work-up (Et$_2$O) the residue was purified by column chromatography (6:1 hexane/EtOAc) to give **A2** (1.11 g, 68%).[125] Alcohol **A2** (1.11 g, 6.94 mmol) was acetylated following the general procedure to obtained **18h** (1.13 g, 87%) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.43 (m, 2H), 7.30-7.26 (m, 3H), 2.04 (s, 3H), 1.75 (s, 6H).[126]

4-Phenylbut-e-yn-2-yl ethanoate (18i).
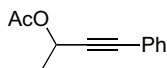
Compound **18h** was was synthesized following *Scheme 53*. A mixture of [Pd(PPh$_3$)$_2$Cl$_2$] (0.05 mol %), PhI (1.2 equiv), CuI (10 mol %), 3-butyn-2-ol (1.4 mL, 17.86 mmol) and piperidine (20 mL) was stirred atroom temperaturefor 18 h. After extractive work-up (Et$_2$O) the residue was purified by column chromatography (6:1 hexane/EtOAc) to give **A3** (1.87 g, 72%).[127] Alcohol **A3** (1.2 g, 8.74 mmol) was acetylated following the general procedure to obtained **18h** (1.48 g, 90%) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.44 (m, 2H), 7.32-7.27 (m, 3H), 5.68 (q, *J* = 6.6 Hz, 1H), 2.10 (s, 3H), 1.58 (d, *J* = 6.6 Hz, 3H).[124]

3-Phenylprop-2-ynyl ethanoate (18j).
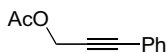
125 NMR data of **A2** agreed with: Rahman, T.; Fukuyama, T.; Ryu, I.; Suzuki, K.; Yonemura, K.; Hughes, P. F.; Nokihara, K. *Tetrahedron Lett.* **2006**, *47*, 2703-2706.

126 NMR data agreed with: Mahrwald, R.; Quint, S.; Scholtis, S. *Tetrahedron* **2002**, *58*, 9847-9851.

127 NMR data of **A3** agreed with: Burgess, K.; Jennings, L. D. *J. Am. Chem. Soc.* **1991**, *113*, 6129-6139.

Ester **18j** was synththesized following the general procedure for acetylation, starting from 3-phenylprop-2-yn-1-ol (0.45 mL, 3.61 mmol) to obtained **18j** (614 mg, 98%) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.45 (m, 2H), 7.34-7.28 (m, 3H), 4.90 (s, 2H), 2.13 (s, 3H).[128]

General procedure for the reaction with propargyl carboxylates. A solution of propargyl ester and nucleophile in CH$_2$Cl$_2$ (1.5 mL) was slowly added to a previously prepared mixture of the gold catalyst (2 or 5 mol% rel. to the propargyl carboxylate) and, if necessary, AgSbF$_6$ (2 or 5 mol% rel. to the propargyl ester) and/or M(OTf)$_n$ (5 mol% rel. to the propargyl ester) in CH$_2$Cl$_2$ (0.5 mL). The reaction mixture was stirred at room temperature for the time indicated in Tables 3-5, and *Scheme 13Scheme 16*. The mixture was filtered through silica gel with CH$_2$Cl$_2$ and the solvents were evaporated. The residue was chromatographed to give the desired product.

(*Z*)-5-Oxo-1,5-diphenyl-4-(phenylcarbonyl)pent-1-en-2-yl Acetate (31a).
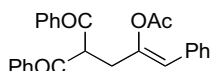
Compound **31a** was synthesized following the general procedure (*Table 4*, entry 1) starting from **18a** (49 mg, 0.28 mmol) and **30a** (94 mg, 0.42 mmol). The residue was purified by chromatography (hexane/EtOAc 8:1) to give **31a** (97 mg, 88%) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.0 (d, J = 8.6 Hz, 4H), 7.59 (m, 2H), 7.47 (m, 5H), 7.28 (m, 4H), 6.11 (s, 1H), 5.60 (t, J = 6.5 Hz, 1H), 3.24 (d, J = 6.5 Hz, 2H), 2.12 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 195.3 (C), 165.9 (C), 134.1 (CH), 131.2 (C), 129.3 (CH), 128.7 (CH), 128.6 (CH), 128.0 (CH), 127.8 (CH), 119.4 (CH), 55.5 (CH), 34.8 (CH$_2$), 21.3 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{26}$H$_{22}$O$_4$Na [M+Na]$^+$ 421.1416, found 421.1406.

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[128] NMR data agreed with: Imagawa, H.; Asai, Y.; Takano, H.; Hamagaki, H. ; Nishizawa, M. *Org. Lett.* **2006**, *8*, 447.

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ISBN:978/84-694-0328-0/DL:T-208-2011
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Experimental Section
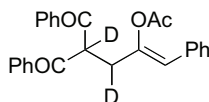
31a-d_2.

Compound **31a-d_2** was synthesized following the general procedure (*Scheme 16*) starting from **18a** (50 mg, 0.28 mmol) and **30a-d_2** (97 mg, 0.43 mmol). The residue was purified by chromatography (hexane/EtOAc 8:1) to give **31a-d_2** (88.0 mg, 77%) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.0 (d, J = 8.6 Hz, 4H), 7.59 (m, 2H), 7.47 (m, 5H), 7.28 (m, 4H), 6.11 (s, 1H), 5.60 (t, J = 6.5 Hz, 0.2H), 3.24 (m, 1.6H), 2.12 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 195.3 (C), 165.9 (C), 134.1 (CH), 131.2 (C), 129.3 (CH), 128.7 (CH), 128.6 (CH), 128.0 (CH), 127.8 (CH), 119.4 (CH), 55.0 (CH), 54.7 (t, J = 19.9 Hz, CD), 34.3 (CH$_2$), 33.9 (t, J = 20.8 Hz, CHD), 21.3 (CH$_3$).

(Z)-5-Oxo-1-phenyl-4-(phenylcarbonyl)hex-1-en-2-yl Acetate (31b).
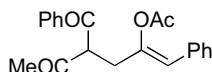
Compound **31b** was synthesized following the general procedure (*Table 4*, entry 2) starting from **18a** (50 mg, 0.29 mmol) and **30b** (61 mg, 0.37 mmol). The residue was purified by chromatography (8:1 hexane/EtOAc) to give **31b** (55 mg, 57%) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.02 (d, J = 7.5 Hz, 2H), 7.62 (m, 2H), 7.50 (m, 2H), 7.29-7.46 (m, 3H), 7.20 (m, 1H), 6.06 (s, 1H), 4.80 (t, J = 6.9 Hz, 1H), 3.13 (dd, J = 15.5, 7.5 Hz, 1H), 3.06 (dd, J = 15.5, 6.9 Hz, 1H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) 202.7 (C), 195.7 (C), 168.8 (C), 146.4 (C), 136.5 (C), 134.3 (CH), 133.7 (C), 129.0 (CH), 128.9 (CH), 128.4 (CH), 128.3 (CH), 127.5 (CH), 118.8 (CH), 60.8 (CH), 33.8 (CH$_2$), 28.5 (CH$_3$), 20.9 (CH$_3$); HRMS-ESI m/z calcd for C$_{21}$H$_{20}$O$_4$Na [M+Na]$^+$ 359.1259, found 359.1261.

(Z)-Ethyl 2-ethanoyl-4-(ethanoyloxy)-2-ethyl-5-phenylpent-4-enoate (31c).
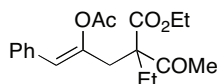
Compound **31b** was synthesized following the general procedure (*Table 4*, entry 3) starting from **18a** (50.1 mg, 0.285 mmol), **30c** (65 μL, 0.40 mmol) and Sc(OTf)$_3$ (5.6 mg, 0.011 mmol). The residue was purified by chromatography (hexane/EtOAc 4:1) to give **31c** (35 mg, 37%) as a colorless oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.32-7.19 (m, 5H), 6.03 (s, 1H), 4.19 (m, 2H), 3.01 (d, J = 15.2 Hz, 1H), 2.96 (d, J = 15.2 Hz, 1H), 2.15 (s, 3H), 2.09 (s, 3H), 2.03 (m, 2H), 1.25 (t, J = 6.8 Hz, 3H), 0.80 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 204.4 (C), 168.2 (C), 145.3 (C), 134.0 (C), 128.4 (CH), 128.3 (CH), 127.5 (CH), 120.3 (CH), 63.4 (C), 61.5 (CH$_2$), 36.3 (CH$_2$), 26.8 (CH$_3$), 25.0 (CH$_2$), 21.0 (CH$_3$), 14.1 (CH$_3$), 8.4 (CH$_3$).

(*Z*)-5-Oxo-1,5-diphenyl-4-(phenylcarbonyl)pent-1-en-2-yl Benzoate (31e).
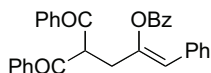
Compound **31e** was synthesized following the general procedure (*Table 4*, entry 5) starting from **18b** (50 mg, 0.21 mmol) and **30a** (58 mg, 0.25 mmol). The residue was purified by chromatography (hexane/EtOAc 8:1) to give **31e** (90 mg, 92%) as a pale yellow solid: mp 110-111ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.02 (dm, J = 8.2 Hz, 2H), 7.94 (dm, J = 8.3 Hz, 4H), 7.63 (m, 1H), 7.54-7.45 (m, 4H), 7.37 (m, 4H), 7.27 (m, 2H), 7.19- 7.11 (m, 3H), 6.22 (s, 1H), 5.66 (t, J = 6.4 Hz, 1H), 3.36 (d, J = 6.4 Hz, 2H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 194.9 (C), 164.4 (C), 146.0 (C), 136.0 (CH), 133.8 (CH), 133.6 (CH), 130.2 (CH), 128.9 (CH), 128.7 (CH), 128.4 (CH), 127.5 (CH), 119.6 (CH), 54.8 (CH), 34.6 (CH$_2$); HRMS-ESI m/z calcd for C$_{31}$H$_{24}$O$_4$Na [M+Na]$^+$ 483.1572, found 483.1573.

(*Z*)-4-(Ethoxycarbonyl)-5-oxo-1-phenylhex-1-en-2-yl benzoate (31f).
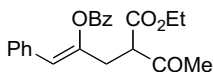
Compound **31e** was synthesized following the general procedure (*Table 4*, entry 6) starting from **18b** (50.1 mg, 0.212 mmol) and **30e** (32.7 μL, 0.254 mmol). The residue was purified by chromatography (hexane/EtOAc 4:1) to give **31f** (33.2 mg, 43%) as a pale yellow solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.10 (m, 2H), 7.62 (m, 1H), 7.50 (m, 2H), 7.37-7.12 (m, 5H), 6.16 (s, 1H), 4.14 (q, J = 6.7 Hz, 2H), 3.83 (t, J = 7.3 Hz, 1H),

2.29 (s, 3H), 1.22 (t, J = 7.0, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 198.2 (C), 168.8 (C), 146.0 (C), 133.9 (C), 130.2 (CH), 130.1 (CH), 128.7 (CH), 128.5 (CH), 128.3 (CH), 127.5 (CH), 119.1 (CH), 61.7 (CH$_2$), 57.5 (CH), 33.2 (CH$_2$), 29.4 (CH$_3$), 14.0 (CH$_3$).

(Z)-3-(1-(Methoxycarbonyl)-2-oxocyclohexyl)-1-phenylprop-1-en-2-yl Benzoate (31g).
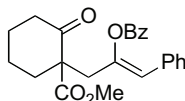
Compound **31g** was synthesized following the general procedure (*Table 4*, entry 7) starting from **18b** (50 mg, 0.21 mmol) and **30d** (52 mg, 0.33 mmol). The residue was purified by chromatography (hexane/EtOAc 8:1) to give **31g** (41 mg, 51%) as a white solid: mp 125-126ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.08 (m, 2H), 7.61 (m, 1H), 7.48 (m, 2H), 7.35 (m, 2H), 7.23-7.12 (m, 3H), 6.13 (s, 1H), 3.48 (s, 3H), 3.29 (d, J = 14.7, Hz, 1H), 2.80 (d, J = 14.7 Hz, 1H), 2.73 (dm, J = 13.9 Hz, 1H), 2.47-2.31 (m, 2H), 2.02 (m, 1H), 1.80-1.77 (m, 2H), 1.63 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$, Pendant) δ 206.3 (C), 171.4 (C), 164.1 (C), 145.4 (C), 134.0 (CH), 133.6 (C), 130.1 (CH), 129.3 (C), 128.6 (CH), 128.4 (CH), 128.4 (CH), 127.4 (CH), 120.8 (CH), 60.5 (C), 52.4 (CH$_3$), 40.9 (CH$_2$), 39.7 (CH$_2$), 35.7 (CH$_2$), 27.6 (CH$_2$), 22.4 (CH$_2$); HRMS-ESI *m/z* calcd for C$_{24}$H$_{24}$O$_5$Na [M+Na]$^+$ 415.1521, found 415.1520.

(E)-1-Phenyl-3-(2,4,6-trimethoxyphenyl)prop-1-en-2-yl Acetate (31h) and 3-Phenyl-3-(2,4,6-trimethoxyphenyl)prop-1-en-2-yl Acetate (36a).

31h   **36a**
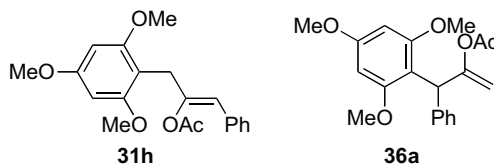
Compound **31h** was synthesized following the general procedure (*Scheme 13*) starting from **18a** (50 mg, 0.28 mmol) and **35** (73 mg, 0.43 mmol). The residue was purified by chromatography (hexane/EtOAc 6:1) to give compound **E-31h** (40 mg, 40%) as a yellow-orange oil and a 3:1 mixture of **Z-31h** and **36a** (10 mg, 10%) as a yellow oil. **E-31h:** ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.20-7.30 (m, 5H), 6.10 (s, 2H), 5.93 (s, 1H), 3.86

(s, 2H), 3.80 (s, 3H), 3.76 (s, 6H), 1.91 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 169.42 (C), 160.72 (C), 158.64 (C), 148.71 (C), 137.86 (C), 129.08 (CH), 128.31 (CH), 126.39 (CH), 109.38 (CH), 90.44 (CH), 55.65 (CH$_3$), 55.26 (CH$_3$), 40.02 (CH$_2$), 21.01 (CH$_3$). HRMS-ESI calculated for C$_{20}$H$_{22}$O$_5$Na [M+Na]$^+$ 365.1365, found 365.1366. **Z-31h:** ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.36-7.34 (m, 2H), 7.23-7.10 (m, 3H), 6.10 (s, 2H), 5.56 (m, 1H), 4.89 (m, 1H), 4.58 (m, 1H), 3.77 (s, 3H), 3.69 (s, 6H), 1.91 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, Pendant) δ 169.1 (C), 160.8 (C), 159.2 (C), 149.6 (C), 141.3 (C), 129.2 (CH), 127.6 (CH), 126.0 (C), 125.8 (CH), 110.1 (CH), 91.3 (CH), 55.7 (CH$_3$), 55.6 (CH$_3$), 43.7 (CH$_2$), 21.0 (CH$_3$). **36a:** ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.23-7.10 (m, 5H), 6.13 (s, 2H), 6.04 (m, 1H), 3.80 (s, 3H), 3.75 (s, 6H), 1.96 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, Pendant) δ 169.4 (C), 160.9 (C), 158.6 (C), 137.6 (C), 128.9 (CH), 128.0 (CH), 110.6 (C), 102.3 (CH$_2$), 90.6 (CH$_2$), 55.3 (CH$_3$), 55.2 (CH$_3$), 36.5 (CH), 20.8 (CH$_3$); HRMS-ESI calculated for C$_{20}$H$_{22}$O$_5$Na [M+Na]$^+$, 365.1365, found: 365.1360.

3-(2,4,6-Trimethoxyphenyl)prop-1-en-2-yl acetate (36d) and **(Z)-3-(2,4,6-trimethoxyphenyl)allyl acetate (37c')** (2:1).
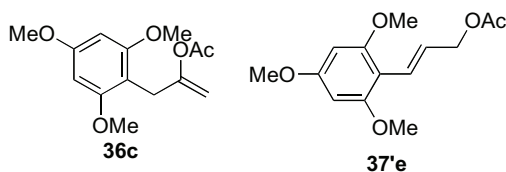
Compounds **36d** and **37c'** were synthesized following the general procedure (*Table 5*, entry 5) starting from **18e** (50.0 mg, 0.49 mmol) and **35** (127.3 mg, 0.75 mmol). The residue was purified by chromatography (8:1, hexane:EtOAc) to give a mixture 2:1 mixture of compounds **36d** and **37c'** (81 mg, 69%) as a pail yellow oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.14 (s, 2H, **36d**), 6.13 (s, 2H, **37c'**), 6.38 (dm, J = 11.5 Hz, 1H, **37c'**), 5.82 (dt, J = 11.3, 6.3 Hz, 1H, **37c'**), 5.57 (m, 1H, **36d**), 5.11 (m, 1H, **36d**), 4.73 (m, 2H, **36d**), 4.50 (dd, J = 6.2, 2.4 Hz, 2H, **37c'**), 3.82 (m, 9H, **37c'**), 3.80 (s, 3H, **36d**), 3.77 (s, 6H, **36d**), 2.05 (s, 3H, **36d**), 2.02 (s, 3H, **37c'**); ^{13}C NMR (100 MHz, CDCl$_3$) δ 161.1 (C), 160.7 (C), 158.9 (C), 158.6 (C), 158.3 (C), 137.6 (C), 126.5 (CH), 123.2 (CH), 117.3 (C), 90.6 (CH), 90.4 (CH), 66.4 (CH$_2$), 63.4 (CH$_2$), 55.8 (CH$_3$), 55.6 (CH$_3$), 55.32 (CH$_3$), 55.30 (CH$_3$), 21.0 (CH$_3$), 20.9 (CH$_3$); Elemental analysis calculated C 63.15%, H 6.81%, O 30.04%; found C 63.72%, H 7.42% , N 0.03%.

1-(2,4,6-Trimethoxyphenyl)but-2-en-2-yl Acetate (36d).
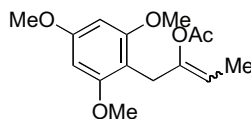
Compound **36d** was synthesized following the general procedure (*Table 5*, entry 6) starting from **18f** (51 mg, 0.45 mmol) and **35** (113 mg, 0.67 mmol). The residue was purified by chromatography (8:1 hexane-EtOAc) to give compound **36d** as a 2:1 mixture of isomers *Z* and *E* as a pale yellow oil (47 mg, 38%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.10 (s, 4H), 5.18 (t, *J* = 7.8 Hz, 1H, *E*), 8.09 (t, *J* = 7.7Hz, 1H), 3.78 (s, 12H), 3.77 (s, 6H), 3.28 (d, *J* = 7.8 Hz, 2H, *E*), 3.22 (d, *J* = 7.8 Hz, 2H, *Z*), 2.19 (s, 3H, *Z*), 2.05 (s, 3H, *E*), 1.99 (s, 3H, *E*), 1.85 (s, 3H, *Z*); ^{13}C NMR (100 MHz, CDCl$_3$) δ 169.7 (C, *E*), 169.0 (C, *Z*), 159.5 (C, *E*), 159.4 (C, *Z*), 145.2 (C, *E*), 144.1 (C, *Z*), 116.4 (CH, *E*), 115.8 (CH, *Z*), 109.1 (C, *E*), 108.9 (C, *Z*), 90.62 (CH, *Z*), 90.60 (CH, *E*), 55.68 (CH$_3$), 55.65 (CH$_3$), 21.0 (CH$_3$, *E*), 20.8 (CH$_3$, *Z*), 20.2 (CH$_2$, *E*), 19.4 (CH$_3$, *Z*), 18.9 (CH$_2$, *Z*), 15.0 (CH$_3$, *Z*); HRMS-ESI *m/z* calcd for C$_{30}$H$_{40}$O$_{10}$Na [M+Na]$^+$ 560.2600, found 560.2600.

(Z)-3-(2,4,6-Trimethoxyphenyl)prop-1-enyl acetate (37e).
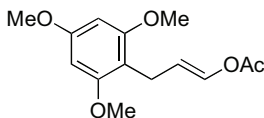
Compounds **37e** was synthesized following the general procedure (*Table 5*, entry 5) starting from **18e** (50.0 mg, 0.49 mmol) and **35** (127.3 mg, 0.75 mmol). The residue was purified by chromatography (hexane/EtOAc 8:1) to give compound **37e** (10.5 mg, 8%) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.10 (dm, *J* = 12.5 Hz, 1H), 6.11 (s, 2H), 5.52 (dt, *J* = 12.3, 7.0 Hz, 1H), 3.79 (s, 9H), 3.24 (dd, *J* = 7.1, 1.4 Hz, 2H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 168.2 (C), 159.8 (C), 158.7 (C), 135.9 (CH), 113.6 (CH), 108.7 (C), 90.8 (CH), 55.8 (CH$_3$), 55.3 (CH$_3$), 20.8 (CH$_3$), 20.5 (CH$_2$); Elemental analysis calculated C 63.15%, H 6.81%, O 30.04%; found C 63.71%, H 7.21%, N 0.04%.

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(*Z*)-5-Oxo-5-phenyl-4-(phenylcarbonyl)pent-1-enyl Acetate (37c).
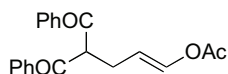
Compound **37c** was synthesized following the general procedure (*Table 5*, entry 7) starting from **18e** (0.054 mL, 0.48 mmol) and **30a** (154 mg, 0.67 mmol). The residue was purified by chromatography (hexane/EtOAc 10:1) to give **37c** (136 mg, 87%) as a white solid: mp 160-162ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.94 (m, 4H), 7.57 (m, 2H), 7.45 (m, 4H), 7.15 (dm, J = 12.5 Hz, 1H), 5.50 (dt, J = 12.5, 7.9 Hz, 1H), 5.23 (t, J = 6.6 Hz, 1H), 2.80 (m, 2H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 195.7 (C), 168.1 (C), 137.6 (CH), 135.7 (C), 133.9 (CH), 128.9 (CH), 128.5 (CH), 111.36 (CH), 57.3 (CH), 27.4 (CH$_2$), 20.5 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{20}$H$_{18}$O$_4$Na [M+Na]$^+$ 345.1103, found 345.1107.

37c-*d*$_1$.
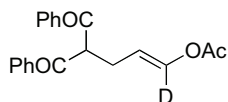
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.94 (m, 4H), 7.57 (m, 2H), 7.45 (m, 4H), 7.15 (d, J = 12.5 Hz, 0.**38h**), 5.50 (m, 1H), 5.23 (t, J = 6.6 Hz, 1H), 2.80 (m, 2H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 195.7 (C), 168.1 (C), 137.6 (CH), 135.7 (C), 133.9 (CH), 128.9 (CH), 128.5 (CH), 111.35 (t, CD), 111.36 (CH), 57.3 (CH), 27.4 (CH$_2$), 20.5 (CH$_3$).

37c-*d*$_2$.
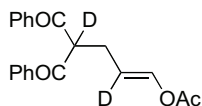
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.94 (d, J = 7.8 Hz, 4H), 7.56 (td, J = 7.4 Hz, 4H), 7.46-7.42 (m, 4H), 7.17-7.14 (m, 1H), 5.54-5.47 (m, 0.24H), 5.25 (t, J = 6.6 Hz, 0.43H), 2.81-2.79 (m, 2H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 195.4 (C), 195.4 (C), 168.1 (C), 137.4 (CH), 137.3 (CH), 135.9 (C), 133.8 (CH), 129.1 (CH), 128.7 (CH),

111.5 (CH), 111.5 (CH), 111.2 (t, J = 24.2 Hz, CD), 57.4 (CH), 57.0 (t, J = 19.2 Hz, CD), 27.54 (CH$_2$), 27.47 (CH$_2$), 20.7 (CH$_3$).

(Z)-4-(2,4,6-Trimethoxyphenyl)but-2-en-2-yl acetate (37f).
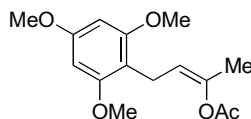
Compound **37f** was synthesized following the general procedure (*Table 5*, entry 6) starting from **18f** (51 mg, 0.45 mmol) and **35** (113 mg, 0.67 mmol). The residue was purified by chromatography (8:1 hexane-EtOAc) to give **37f** (26 mg, 21%) as a pale yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.13 (s, 2H), 5.74 (t, J = 6.4 Hz, 1H), 4.29 (d, J = 6.4 Hz, 2H), 3.82 (s, 6H), 2.15 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 167.6 (C), 158.6 (C), 144.2 (C), 122.6 (CH), 109.0 (C), 92.2 (CH), 90.7 (C), 55.3 (CH$_3$), 20.8 (CH$_3$), 19.4 (CH$_3$), 18.9 (CH$_2$); HRMS-ESI *m/z* calcd for C$_{30}$H$_{40}$O$_{10}$Na [M+Na][+] 560.2600, found 560.2600.

1,3-Diphenyl-2-(1-phenylprop-2-ynyl)propane-1,3-dione (32).
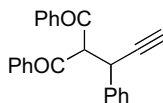
Compound **13** was synthesized following the general procedure (*Table 3*, entry 8) starting from **18a** (30 mg, 0.10 mmol) and **30a** (35 mg, 0.16 mmol). The residue was purified by chromatography (hexane/EtOAc 8:1) to give **20** (35 mg, 98%) as a white solid. The spectroscopic data are consistent with those described.[129]

2-Benzoyl-1,3-diphenylpentane-1,4-dione (34).
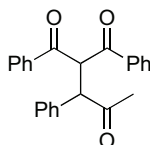
129 Sanz, R.; Miguel, D.; Martínez, A.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Org. Lett.* **2007**, *9*, 727-730.

Compound **34** was synthesized starting from **18a** (30 mg, 0.10 mmol) and **30a** (35 mg, 0.16 mmol) in CH_2Cl_2 (1.5 mL) with $AgSbF_6$ (5 mol%). The reaction mixture was stirred at room temperature for 32 h. The mixture was filtered trough silica gel with CH_2Cl_2 and the solvents evaporated. The residue was chromatographed (8:1 hexane-EtOAc) to give compound **34** (36 mg, 97%) as a pale yellow solid: mp 160-162ºC. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (m, 2H), 7.64 (m, 1H), 7.47 (m, 1H), 7.41 (m, 1H), 7.33 (m, 2H), 7.25 (m, 2H), 7.21-7.07 (m, 5H), 6.13 (d, J = 10.9 Hz, 1H), 4.94 (d, J = 10.9 Hz, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, Pendant) δ 206.46 (C), 195.44 (C), 194.45 (C), 136.59 (C), 136.25 (C), 134.04 (C), 133.33 (CH), 133.26 (CH), 129.10 (CH), 128.96 (CH), 128.62 (CH), 128.59 (CH), 128.57 (CH), 128.37 (CH), 127.97 (CH), 59.95 (CH), 59.85 (CH), 29.12 (CH); HRMS-ESI *m/z* calcd for $C_{24}H_{20}O_3Na$ [M+Na]$^+$ 356.1421, found 356.14.

Chapter 3. Experimental procedures

Synthesis of 1,5-enynes

General procedure for the synthesis of 3-acetoxy-1,5-enyne. To Mg turnings (2 equiv), I_2 (0.05) and $HgCl_2$ (0.02) under N_2, dry ether (0.4 equiv) was added. The reaction was started with a few drops of propargyl bromide. The mixture was allowed to reflux for 2 minutes, then cooled to 40 ºC below zero (Haake EK 90 immersion cooler). A pre-cooled mixture of aldehyde (4-6 mmol) and propargyl bromide (1.7 equiv) in ether was added dropwise. After stirring for 8 hours saturated NH_4Cl and HCl 1N were added and the mixture was stirred for 1h.[130] After extractive work-up and without further purification the 1,5-enyn-3-ol is added to an ice-cooled solution of Ac_2O (2 equiv), pyridine (1.5 equiv) and DMAP (0.05 mol%) in ether and stirred at room temperature for 4-8 hours. After extractive work-up (Et_2O) desired product was isolated by chromatography (hexane/EtOAc 4:1).

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130 Procedure described at: Rhode, O.; Hoffmann, H. M. R. *Tetrahedron* **2000**, *56*, 6479.

(*E*)-1-Phenylhex-1-en-5-yn-3-ol (A38a).
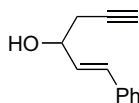
Compound **A38a** was synthesized following the general procedure described above, starting from cinnamaldehyde (0.50 mL, 3.59 mmol) and propargyl bromide (0.40 mL, 3.59 mmol). The residue was purified by chromatography (5:1 hexane/EtOAc) to give the desired alcohol **A38a** as a yellow oil (640 mg, 93%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.39 (d, J = 7.4 Hz, 2H), 7.32 (d, J = 7.2 Hz, 2H), 7.25 (m, 1H), 6.67 (d, J = 15.7 Hz, 1H), 6.28 (dd, J = 15.7, 6.7 Hz, 1H), 4.47 (m, 1H), 2.56 (m, 2H), 2,12 (s, 1H), 2.09 (t, J = 2.9 Hz).[131]

(*E*)-1-Phenylhex-1-en-5-yn-3-yl ethanoate (38a).
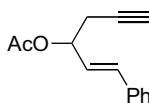
Compound **38a** was synthesized following the general procedure for the synthesis of 3-acetoxy-1,5-enynes, starting from cinnamaldehyde (0.50 mL, 3.59 mmol) and propargyl bromide (0.40 mL, 3.59 mmol). The residue was purified by chromatography (4:1 hexane/EtOAc) to give **38a** as a yellow oil (476 mg, 61%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.40 (m, 2H), 7.32 (m, 2H), 7.27 (m, 1H), 6.69 (d, J = 15.3, 6.23 Hz, 1H), 6.23 (dd, J = 15.3, 6.8 Hz, 1H), 5.53 (q, J = 6.8 Hz, 1H), 2.63 (m, 2H), 2.11 (s, 3H), 2.03 (m, 1H) ; ^{13}C NMR (100 MHz, CDCl$_3$) δ 170.0 (C), 136.0 (CH), 133.6 (C), 128.6 (CH), 128.2 (CH), 126.7 (CH), 125.7 (CH), 79.3 (C), 77.2 (CH), 72.2 (CH), 70.7 (CH), 24.9 (CH$_2$), 21.2 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{18h14}$O$_2$Na [M+Na]$^+$ 237.0891, found 237.0881.

(*E*)-(3-(Benzyloxy)hex-1-en-5-ynyl)benzene (38b).
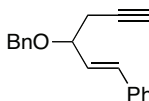
To Mg turnings (2 equiv), I$_2$ (0.05) and HgCl$_2$ (0.02) under N$_2$, dry ether (2 mL) was added. The reaction was started with a few drops of propargyl bromide. The mixture

131 NMR data agreed with: Hirayama, L. C.; Dunham, K. K.; Singaram, B. *Tetrahedron Lett.* **2006**, *47*, 5173.

was allowed to reflux for 2 minutes, and then cooled to 40 ºC below zero (Haake EK 90 immersion cooler). A pre-cooled mixture of the aldehyde (2.5 mmol) and propargyl bromide (1.7 equiv) in ether was added dropwise. After stirring for 8 hours saturated NH$_4$Cl and HCl 1N were added and the mixture was stirred for 1h. After extractive work-up and without further purification, **A38a** (266 mg, 1.39 mmol) was added to an ice-cooled solution of Ac$_2$O (2 equiv), pyridine (1.5 equiv) and DMAP (0.05 mol%) in ether and stirred at room temperature for 4-8 hours. After extractive work-up (Et$_2$O) the desired acetate is isolated and without further purification it was added to an ice-cooled suspension of sodium hydride (60% in mineral oil, 1.2 equiv) in THF. After stirring for 10 min benzyl chloride (1.2 equiv) was added and stirred overnight. Saturated NaOH was added and stirred 20 min. After extractive work-up (HCl 10%/Et$_2$O) **38b** was isolated by chromatography (8:1 hexane/EtOAc) as a yellow oil (233.9 mg, 64%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.43-7.27 (m, 5H), 6.62 (d, J = 15.5 Hz, 1H), 6.20 (dd, J = 15.5, 7.7 Hz, 1H), 4.67 (d, J = 12.4 Hz, 1H), 4.49 (s, 2H), 4.48 (d, J = 12.4 Hz, 1H), 4.1 (q, J = 6.2 Hz, 1H), 2.63 (ddd, J = 16.6, 5.7, 2.5 Hz, 1H), 2.54 (ddd, J = 16.6, 6.7, 2.7 Hz, 1H), 2.01 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 133.5 (C), 129.8 (C), 128.6 (CH), 128.5 (CH), 128.4 (CH), 127.9 (CH), 127.8 (CH), 127.6 (CH), 126.7 (CH), 77.9 (CH), 70.4 (C), 63.6 (CH), 57.9 (CH$_2$); HRMS-ESI m/z calcd for C$_{31h18}$ONa [M+Na]$^+$ 285.1255, found: 285.1254.

(*E*)-5-Methylhept-5-en-1-yn-4-yl ethanoate (38c).
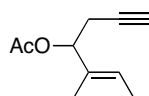
Compound **38c** was synthesized following the general procedure for the synthesis of 3-acetoxy-1,5-enyne, starting from tiglic aldehyde (0.58 mL, 5.83 mmol) and propargyl bromide (0.80 mL, 9.14 mmol). The residue was purified by chromatography (hexane/EtOAc 4:1) to give **38c** as a yellow oil (928.5 mg, 96%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.62 (m, 1H), 5.28 (t, J = 6.6 Hz, 1H), 2.56 (ddd, J = 16.7, 7.1, 2.7 Hz, 1H), 2.48 (ddd, J = 16.7, 6.7, 2.7 Hz, 1H), 2.07 (s, 3H), 1.96 (t, J = 2.7 Hz, 1H), 1.63 (m, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 170.4 (C), 132.7 (C), 124.4 (CH), 80.3 (C), 77.1 (CH), 70.5 (CH), 23.6 (CH$_2$), 21.5 (CH), 13.5 (CH$_3$), 11.9 (CH$_3$); HRMS-ESI m/z calcd for C$_{10}$H$_{14}$O$_2$Na [M+Na]$^+$ 189.0891, found 189.0900.

(*E*)-1-Phenylhept-5-en-1-yn-4-yl acetate (**38d**).
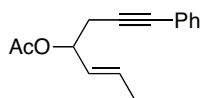
To Mg turnings (2 equiv), I_2 (0.05) and $HgCl_2$ (0.02) under N_2, dry ether (2 mL) was added. The reaction was started with a few drops of propargyl bromide. The mixture was allowed to reflux for 2 min, and then cooled to 40 ºC below zero (Haake EK 90 immersion cooler). A pre-cooled mixture of (*E*)-but-2-enal (0.49 mL, 5.8 mmol) and propargyl bromide (1.7 equiv) in ether was added dropwise. After stirring for 8 hours saturated NH_4Cl and HCl 1N were added and the mixture was stirred for 1h. After extractive work-up and without further purification **A38d** was added to an ice-cooled solution of Ac_2O (2 equiv), pyridine (1.5 equiv) and DMAP (0.05 mol%) in ether and stirred at room temperature for 4-8 hours. After extractive work-up (Et_2O) the desired acetate is isolated and without further purification **B38d** (230 mg, 1.51 mmol) was added to a bottom flask containing $[Pd(PPh_3)_2Cl_2]$ (0.05 mol%), PhI (4 mmol), propargylic alcohol (9.6 mmol) and Et_3N (1.4 mL, 10 mmol). The reaction mixture was stirred for 18h at room temperature. After extractive work-up (Et_2O) and column chromatography (6:1 toluene/EtOAc) **38d** was isolated as a yellow oil (165.3 mg, 48%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 2H), 7.26 (m, 3H), 5.83 (dq, J = 15.1, 6.5 Hz, 1H), 5.57 (ddm, J = 15.6, 7.6, 1H), 5.38 (q, J = 7.0 Hz, 1H), 2.70 (dd, J = 6.2, 2.3 Hz, 2H), 2.07 (s, 3H), 1.72 (dd, J = 6.5, 1.3 Hz, 3H); HRMS-ESI *m/z* calcd for $C_{15}H_{16}O_2Na$ [M+Na]$^+$ 251.1048, found 251.1051.

(4-Methoxy-6-methylhept-5-en-1-yn-1-yl)benzene (**38e**).
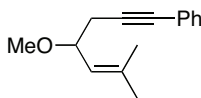
To Mg turnings (2 equiv), I_2 (0.05) and $HgCl_2$ (0.02) under N_2, dry ether (2 mL) was added. The reaction was started with a few drops of propargyl bromide. The mixture was allowed to reflux for 2 min, and then cooled to 40 ºC below zero (Haake EK 90 immersion cooler). A pre-cooled mixture of 3-methyl-but-2-enal (1.08 mL, 10.9 mmol) and propargyl bromide (1.7 equiv) in ether was added dropwise. After stirring for 8 hours saturated NH_4Cl and HCl 1N were added and the mixture was stirred for 1h. After extractive work-up and without further purification **A38e** (2.5g, 10.7 mmol) was added

to a bottom flask containing [Pd(PPh$_3$) $_2$Cl$_2$] (0.05 mol%), PhI (4 mmol), propargylic alcohol (9.6 mmol) and Et$_3$N (1.4 mL, 10 mmol). The reaction mixture was stirred for 18h at room temperature. After extractive work-up (Et$_2$O) and column chromatography (6:1 toluene/EtOAc) **B38e** was isolated as a yellow oil (1.179 g, 55%). Alcohol **B38e** (700 mg, 3.49 mmol) was added to an ice-cooled suspension of NaH (60% dispersion in mineral oil) in THF. Then dimethylsulfate was added over 20 min and stirred overnight. The reaction mixture was quenched with saturated NH$_4$Cl and stirred during 2 h. The mixture was diluted with Et$_2$O and washed with saturated NaCl. After column chromatography (8:1 hexane/EtOAc) **38e** was isolated as a dark yellow oil (520.5 mg, 69%): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38 (m, 2H), 7.27 (m, 3H), 5.15 (dd, J = 9.1, 1.3 Hz, 1H), 4.19-4.06 (m, 1H), 3.32 (s, 3H), 2.70 (dd, J = 16.6, 5.7 Hz, 1H), 2.56 (dd, J = 16.6, 6.9 Hz, 1H), 1.80 (d, J = 0.9 Hz, 3H), 1.76 (d, J = 1.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.5 (C), 131.8 (CH), 128.3 (CH), 127.7 (CH), 124.9 (CH), 124.0 (C), 86.9 (C), 81.8 (C), 76.1 (CH), 56.2 (CH$_3$), 26.6 (CH$_2$), 26.1 (CH$_3$), 18.7 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{15}$H$_{16}$O$_2$Na [M+Na]$^+$ 251.1048, found 251.1051.

General procedure for the synthesis of 3-phenylsulfonyl-1,5-enynes. Over a stirring solution of the allyl bromide (1M) in DMF sodium benzylsulfonate (1.5 equiv) was added at room temperature. The reaction mixture was stirred for 4-8 h. After extractive work-up (10% HCl solution and Et$_2$O) the corresponding allyl sulfone was isolated and used without further purification. A solution of the allylsulfone in THF was cooled to -78ºC and *n*-BuLi was slowly added. After stirring for 20 minutes the corresponding propargyl bromide was added. The reaction mixture was allowed to warm to room temperature and stirred for 6-10 h (^{1}H NMR monitoring).

(6-Methylhept-5-en-1-yn-4-ylsulfonyl)benzene (38f).
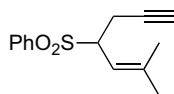
Compound **38f** was synthesized following the general procedure, starting from (3-methylbut-2-enylsulfonyl)benzene (820 mg, 3.90 mmol) in THF (20 mL) and propargyl bromide (0.6 mL, 6.73 mmol). The residue was purified by automated flash chromatography (120g RediSep flash column, hexane/EtOAc: 20 min gradient 0-20%

EtOAc) to yield **38f** (550 mg, 57%) as a white solid: mp 82-83ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.84 (dm, J = 8.5 Hz, 2H), 7.64 (m, 1H), 7.53 (m, 2H), 5.06 (dm, J = 10.3 Hz, 1H), 3.94 (td, J = 10.2, 3.8 Hz, 1H), 2.99 (ddd, J = 16.8, 3.8, 2.7 Hz, 1H), 2.62 (ddd, J = 16.7, 10.0, 2.7 Hz, 1H), 1.96 (t, J = 2.7 Hz, 1H), 1.72 (d, J = 1.5 Hz, 3H), 1.28 (d, J = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 143.3 (C), 137.3 (C), 133.7 (CH), 129.2 (CH), 128.8 (CH), 115.7 (CH), 79.1 (C), 70.7 (CH), 63.2 (CH), 25.8 (CH$_2$), 18.7 (CH$_3$). HRMS-ESI *m/z* calcd for C$_{18h16}$O$_2$NaS [M+Na]$^+$ 271.0769, found: 271.0773.

(2-Methyloct-2-en-6-yn-4-ylsulfonyl)benzene (38g).
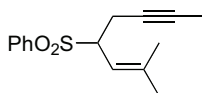
Compound **38g** was synthesized following the general procedure, starting from (3-methylbut-2-enylsulfonyl)benzene (799 mg, 3.42 mmol) in THF (20 mL) and 1-bromo-2-butyne (0.6 mL, 5.20 mmol). The residue was purified by column chromatography (hexane/EtOAc 8:1) to yield **38g** (535 mg, 60%) as a white solid: mp 83-84ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.84 (dm, J = 8.1 Hz, 2H), 7.62 (m, 1H), 7.52 (m, 1H), 5.05 (d, J = 10.3 Hz, 1H), 3.89 (td, J = 10.3, 3.9 Hz, 1H), 2.90 (dm, J = 16.5 Hz, 1H), 2.59-2.51 (m, 1H), 1.73 (d, J = 1.1 Hz, 3H), 1.69 (t, J = 2.5 Hz, 3H), 1.31 (d, J = 1.3 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 142.8 (C), 137.7 (C), 133.5 (CH), 129.2 (CH), 128.7 (CH), 116.1 (CH), 78.2 (C), 73.8 (C), 63.7 (CH), 25.96 (CH$_2$), 19.2 (CH$_3$), 18.2 (CH$_2$). HRMS-ESI *m/z* calcd for C$_{15}$H$_{18}$O$_2$NaS [M+Na]$^+$ 285.0925, found: 285.0938.

(2-Methylnon-2-en-6-yn-4-ylsulfonyl)benzene (38h).
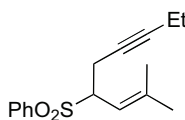
1,5-Enyne **38h** was synthesized following the general procedure, starting from (3-methylbut-2-enylsulfonyl)benzene (500 mg, 2.14 mmol) in THF (10 mL), *n*-BuLi (0.8 equiv) and 1-bromo-2-pentyne (0.25 mL, 2.35 mmol). The residue was purified by automated flash chromatography (120 g RediSep flash column, hexane/EtOAc 20 min gradient 0-20% EtOAc) to yield **38h** (380 mg, 64%) as a white solid: mp 61-62ºC; [1]H

NMR (400 MHz, CDCl$_3$) δ 7.83 (m, 2H), 7.62 (m, 1H), 7.52 (m, 2H), 5.05 (dm, J = 10.7 Hz, 1H), 3.90 (dd, J = 3.7, 9.6 Hz, 1H), 2.92 (dm, J = 16.6 Hz, 1H), 2.55 (ddm, J = 9.6, 16.6 Hz, 1H), 2.09-2.02 (m, 2H), 1.72 (s, 3H), 1.32 (s, 3H), 1.02 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 142.63 (C), 137.7 (C), 133.5 (CH), 129.3 (CH), 128.7 (CH), 116.1 (CH), 84.3 (C), 74.1 (C), 63.8 (CH), 25.8 (CH$_2$), 19.1 (CH$_2$), 18.1 (CH$_3$), 13.9 (CH$_3$), 12.3 (CH$_3$); HRMS-ESI m/z calcd for C$_{16}$H$_{20}$O$_2$NaS [M+Na]$^+$ 299.1082, found 299.1074.

(6-Methyl-1-phenylhept-5-en-1-yn-4-ylsulfonyl)benzene (38i).
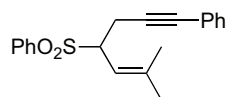
Enyne **38i** was synthesized by Sonogashira coupling of enyne **38f** and IPh. A mixture of [Pd(PPh$_3$)$_2$Cl$_2$] (0.05 mol%), PhI (1.2 equiv), CuI (10 mol%), 1,5-enyne **38f** (294 mg, 1.18 mmol) and ^{i}Pr$_2$NH (3 mL) was stirred atroom temperaturefor 18 h. After extractive work-up (Et$_2$O) the residue was purified by column chromatography (8:1 hexane/EtOAc) to give **38i** (280 mg, 73%) as a yellow solid: mp 108-110ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.92 (dm, J = 7.6 Hz, 2H), 7.68 (m, 1H), 7.58 (m,2H), 7.35-7.29 (m, 5H), 5.18 (dm, J = 10.4 Hz, 1H), 4.08 (td, J =10.2, 3.8 Hz, 1H), 3.25 (dd, J = 16.8, 3.8 Hz, 1H), 2.88 (dd, J = 16.8, 10.0Hz, 1H), 1.79 (d, J = 1.2 Hz, 3H), 1.4 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 143.0 (CH), 137.6 (C), 133.6 (C), 131.5 (CH), 129.2 (CH), 128.8 (CH), 128.1 (CH), 128.0 (CH), 123.2, 116.0 (CH), 84.7 (C), 82.8 (C), 63.6 (CH), 25.9 (CH$_2$), 19.8 (CH$_3$), 18.2 (CH$_3$); HRMS-ESI m/z calcd for C$_{22}$H$_{20}$O$_2$NaS [M+Na]$^+$ 347.1082, found 347.1091.

1-Methyl-4-(6-methyl-4-(phenylsulfonyl)hept-5-en-1-ynyl)benzene (38j).
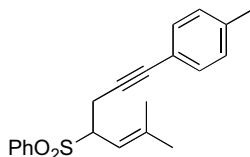
1,5-Enyne **5d** was synthesized by Sonogashira coupling of 1,5-enyne **38f** and p-iodotoluene. A mixture of [Pd(PPh$_3$)$_2$Cl$_2$] (5 mol%), p-iodotoluene (1.2 equiv), CuI (10

mol%), 1,5-enyne **38f** (200 mg, 0.80 mmol) and Et$_3$N (4 mL) was stirred at room temperature for 16 h. The solvent was removed under vacuum and the crude was purified by flash chromatography (toluene 100%, then 5:1 hexane/EtOAc) to yield **38j** (160 mg, 0.47 mmol, 59%) as a light yellow solid: mp 95-97ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89-7.86 (m, 2H), 7.65-7.61 (m, 1H), 7.55-7.51 (m, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 5.13 (dquintuplet, J = 10.4, 1.4 Hz, 1H), 4.02 (td, J = 10.2, 3.8 Hz, 1H), 3.18 (dd, J = 16.8, 3.8 Hz, 1H), 2.38 (dd, J = 16.9, 9.9 Hz, 1H), 2.32 (s, 3H), 1.74 (d, J = 1.3 Hz, 3H), 1.35 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 143.1 (C), 138.2 (C), 137.7 (C), 133.8 (CH), 131.5 (CH), 129.3 (CH), 129.1 (CH), 129.0 (CH), 120.2 (C), 116.2 (CH), 84.0 (C), 83.0 (C), 63.8 (CH), 26.1 (CH$_3$), 21.5 (CH$_3$), 20.0 (CH$_3$), 18.4 (CH$_2$); HRMS-ESI *m/z* calcd for C$_{21}$H$_{22}$NaO$_2$S $[M+Na]^+$ 361.1238, found 361.1238.

1-Methoxy-4-(6-methyl-4-(phenylsulfonyl)hept-5-en-1-ynyl)benzene (38k).
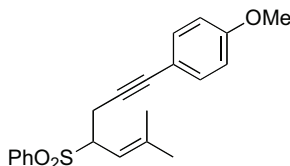
1,5-Enyne **38k** was synthesized by Sonogashira coupling of 1,5-enyne **38f** and *p*-iodomethoxybenzene. A mixture of [Pd(PPh$_3$)$_2$Cl$_2$] (5 mol%), *p*-iodomethoxybenzene (1.2 equiv), CuI (10 mol%), 1,5-enyne **38f** (200 mg, 0.805 mmol) and ^{i}Pr$_2$NH (2 mL) was stirred at room temperature for 18 h. After extractive work-up (Et$_2$O) the residue was purified by flash chromatography (8:1 hexane/EtOAc) to yield **38k** (131 mg, 51%) as a light yellow solid: mp 127-129ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.87 (d, J = 8.1 Hz, 2H), 7.63 (m, 1H), 7.53 (m, 2H), 7.22 (d, J = 8.8 Hz, 1H), 6.78 (d, J = 8.8 Hz, 1H), 5.12 (dm, J = 10.1 Hz, 1H), 4.01 (dt, J = 4.0, 10.1 Hz, 1H), 3.78 (s, 3H), 3.17 (dd, J = 4.0, 16.9 Hz, 1H), 2.81 (dd, J = 10.1, 16.9 Hz, 1H), 1.74 (d, J = 1.0 Hz, 3H), 1.34 (d, J = 1.3 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 142.9 (C), 137.6 (C), 133.6 (C), 132.9 (CH), 129.2 (CH), 128.8 (CH), 116.0 (CH), 115.3 (C), 113.8 (CH), 83.1 (C), 77.1 (C), 63.6 (CH), 55.2 (CH$_3$), 25.8 (CH$_2$), 19.8 (CH$_3$), 18.2 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{21}$H$_{22}$O$_3$NaS $[M+Na]^+$ 377.1187, found 377.1172.

1-(4-(6-Methyl-4-(phenylsulfonyl)hept-5-en-1-ynyl)phenyl)ethanone (38l).
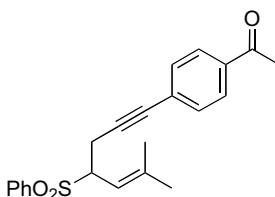
1,5-Enyne **38l** was synthesized by Sonogashira coupling of 1,5-enyne **38f** and *p*-iodoacetophenone. A mixture of [Pd(PPh$_3$)$_2$Cl$_2$] (5 mol%), *p*-iodoacetophenone (1.2 equiv), CuI (10 mol%), 1,5-enyne **38f** (200 mg, 0.805 mmol) and ^{i}Pr$_2$NH (2 mL) was stirred at room temperature for 18 h. After extractive work-up (Et$_2$O) the residue was purified by flash chromatography (8:1 hexane/EtOAc) to yield **38l** (210 mg, 71%) as a light yellow solid: mp 139-140ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.88-7.83 (m, 4H), 7.63 (m, 1H), 7.53 (m, 2H), 7.36 (d, *J* = 8.3 Hz, 2H), 5.13 (dm, *J* = 10.5 Hz, 1H), 4.03 (dt, *J* = 4.6, 10.5 Hz, 1H), 3.21 (dd, *J* = 4.6, 17.1 Hz, 1H), 2.87 (dd, *J* = 10.5, 17.1 Hz, 1H), 2.57 (s, 3H), 1.73 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 197.4 (C), 143.2 (C), 137.5 (C), 136.0 (C), 133.7 (CH), 131.7 (CH), 129.2 (CH), 128.9 (CH), 128.14 (CH), 128.09(C), 115.9 (CH), 88.5 (C), 82.3 (C), 63.3 (CH), 26.6 (CH$_3$), 25.9 (CH$_3$), 19.9 (CH$_2$), 18.2 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{22}$H$_{22}$O$_3$NaS [*M*+Na]$^+$ 389.1187, found 389.1184.

1-Chloro-4-(6-methyl-4-(phenylsulfonyl)hept-5-en-1-ynyl)benzene (38p).
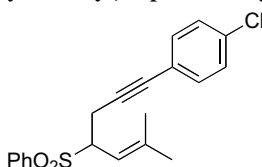
1,5-Enyne **38p** was synthesized by Sonogashira coupling of 1,5-enyne **38f** and *p*-iodochlorobenzene. A mixture of [Pd(PPh$_3$)$_2$Cl$_2$] (5 mol%), *p*-iodochlorobenzene (1.2 equiv), CuI (10 mol%), 1,5-enyne **38f** (200 mg, 0.805 mmol) and ^{i}Pr$_2$NH (2 mL) was stirred at room temperature for 18 h. After extractive work-up (Et$_2$O) the residue was purified by flash chromatography (8:1 hexane/EtOAc) to yield **38p** (198 mg, 69%) as a light yellow solid: mp 101ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.86 (d, J = 8.0 Hz, 2H), 7.63 (m, 1H), 7.53 (m, 2H), 7.24-7.19 (m, 4H), 5.12 (dm, *J* = 10.9 Hz, 1H), 4.01 (dt, *J* = 4.3, 10.9 Hz, 1H), 3.18 (dd, *J* = 4.0, 16.9 Hz, 1H), 2.83 (dd, *J* = 10.9, 16.9 Hz, 1H), 1.73

(s, 3H), 1.32 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 143.0 (C), 133.9 (C), 133.6 (C), 132.7 (CH), 129.2 (CH), 128.8 (CH), 128.5 (CH), 121.6 (C), 115.9 (CH), 85.8 (C), 81.8 (C), 63.4 (CH), 25.9 (CH$_2$), 19.7 (CH$_3$), 18.2 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{20}$H$_{31}$ClO$_2$ONaS [*M*+Na]$^+$ 381.0692, found 381.0687.

(1-(Prop-2-ynyl)cyclohex-2-enylsulfonyl)benzene (38m).
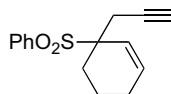
1,5-Enyne **38m** was synthesized following the general procedure, starting from (cyclohex-2-enylsulfonyl)benzene[132] (700 mg, 2.83 mmol) in THF (15 mL), *n*-BuLi (1 equiv) and propargyl bromide (0.4 mL, 3.59 mmol). The residue was purified by automated flash chromatography (120 g RediSep flash column, hexane/EtOAc 20 min gradient 0-20% EtOAc) to yield **38m** (567,0 mg, 77%) as a white solid: mp 120-121ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.87 (m, 2H), 7.64 (m, 1H), 7.53 (m, 2H), 6.92 (dt, *J* = 4.0, 9.8 Hz, 1H), 5.63 (d, *J* = 9.8 Hz, 1H), 2.78 (dd, *J* = 2.7, 16.8 Hz, 1H), 2.72 (dd, *J* = 2.7, 16.8 Hz, 1H), 2.24-2.15 (m, 1H), 2.05-1.85 (m, 3H), 1.96 (t, *J* = 2.7 Hz, 1H), 1.68-1.60 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 136.9 (CH), 136.1 (C), 133.9 (CH), 130.7 (CH), 128.8 (CH), 122.4 (CH), 78.7 (C), 71.7 (CH), 65.2 (C), 27.1 (CH$_2$), 26.3 (CH$_2$), 23.9 (CH$_2$); HRMS-ESI *m/z* calcd for C$_{15}$H$_{16}$O$_2$NaS [*M*+Na]$^+$ 283.0769, found 283.0782.

(1-(Pent-2-ynyl)cyclohex-2-enylsulfonyl)benzene (38n).
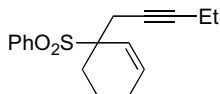
1,5-Enyne **38n** was synthesized following the general procedure, starting from (cyclohex-2-enylsulfonyl)benzene (700 mg, 2.83 mmol) in THF (15 mL), *n*-BuLi (1 equiv) and 1-bromo-2-pentyne (0.5 mL, 3.59 mmol). The residue was purified by

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132 (Cyclohex-2-enylsulfonyl)benzene was synthesized following the general procedure, the NMR data was in agreement with those reported: Trost, B.M.; Schmuff, N. R., Miller, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 5981-5983.

automated flash chromatography (120 g RediSep flash column, hexane/EtOAc 20 min gradient 0-20% EtOAc) to yield **38n** (488 mg, 60%) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89 (dm, J = 8.6 Hz, 2H), 7.65 (m, 1H), 7.55 (m, 2H), 6.22 (dt, J = 3.8, 10.1 Hz, 1H), 5.64 (d, J = 10.1 Hz, 1H), 2.74 (dt, J = 2.4, 16.5 Hz, 1H), 2.69 (dd, J = 2.4, 16.5 Hz, 1H), 2.27-2.18 (m, 1H), 2.11-1.93 (m, 5H), 1.75-1.62 (m, 2H), 1.04; ^{13}C NMR (100 MHz, CDCl$_3$) δ 136.4 (CH), 136.3 (C), 133.7 (CH), 130.7 (CH), 128.6 (CH), 122.9 (CH), 85.4 (C), 74.4 (C), 65.5 (C), 27.0 (CH$_2$), 26.7 (CH$_2$), 24.1 (CH$_2$), 18.6 (CH$_2$), 13.9 (CH$_3$), 12.3 (CH$_2$); HRMS-ESI m/z calcd for C$_{17}$H$_{20}$O$_2$NaS [M+Na]$^{+}$ 311.1082, found 311.1071.

(1-(3-Phenylprop-2-ynyl)cyclohex-2-enylsulfonyl)benzene (38o).
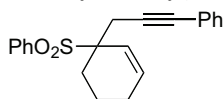
1,5-Enyne **38o** was synthesized by Sonogashira coupling of 1,5-enyne **38m** and IPh. A mixture of [Pd(PPh$_3$)$_2$Cl$_2$] (5 mol%), PhI (1.2 equiv), CuI (10 mol%), 1,5-enyne **38m** (200 mg, 0.769 mmol) and ^{i}Pr$_2$NH (2 mL) was stirred at room temperature for 18 h. After extractive work-up (Et$_2$O) the residue was purified by automated flash chromatography (12 g RediSep flash column, hexane/EtOAc 20 min gradient 0-20% EtOAc) to yield **38o** (131 mg, 51%) as a yellow solid: mp 76-77ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (dt, J = 8.5, 1.7 Hz, 2H), 7.70-7.59 (m, 1H), 7.59-7.48 (m, 2H), 7.36-7.17 (m, 5H), 6.25 (dt, J = 10.1, 4.0 Hz, 1H), 5.71 (dd, J = 10.2, 1.9 Hz, 1H), 3.11-2.82 (m, 2H), 2.29 (dt, J = 14.5, 5.7 Hz, 1H), 2.08 (dt, J = 20.7, 6.7 Hz, 1H), 2.04-1.88 (m, 2H), 1.75-1.64 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 136.7 (CH), 136.1 (C), 133.7 (CH), 131.5 (CH), 130.6 (CH), 128.7 (CH), 128.2 (CH), 127.9 (CH), 123.2 (C), 122.7 (CH), 84.2 (C), 83.9 (C), 65.5 (C), 27.30 (CH$_2$), 27.26 (CH$_2$), 24.1 (CH$_2$), 18.6 (CH$_2$); HRMS-ESI m/z calcd for C$_{21}$H$_{20}$O$_2$NaS [M+Na]$^{+}$ 359.1082, found 359.1075.

1,5-Enyne Cyclization

2-(Propan-2-ylidene)cyclopent-3-enylsulfonylbenzene (43a).
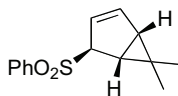
Compound **43a** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **38f** (40.9 mg, 0.142 mmol) with catalyst **Q**. The residue was purified by column chromatography (6:1 hexane/EtOAc) to give compound **43a** (35.8 mg, 88%) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.88 (m, 2H), 7.69-7.61 (m, 1H), 7.55 (m, 2H), 5.96 (dt, J = 5.5, 2.1, 1H), 5.64-5.55 (m, 1H), 3.87 (bs, 1H), 1.80 (d, J = 5.7, 1H), 1.71-1.64 (m, 1H), 1.11 (s, 3H), 0.78 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 139.0 (CH), 136.9 (C), 133.5 (CH), 129.3 (CH), 128.6 (CH), 124.0 (CH), 71.5 (CH), 36.6 (CH), 28.9 (CH), 26.0 (CH), 23.9 (C), 13.2 (CH); HRMS-ESI *m/z* calcd for C$_{20}$H$_{20}$O$_2$NaS [*M*+Na]$^{+}$ 347.1082, found 347.1084.

6,6-Dimethyl-1-phenyl-4-(phenylsulfonyl)bicyclo[3.1.0]hex-2-ene (43d).
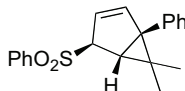
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.99-7.92 (m, 2H), 7.67 (m, 1H), 7.60-7.52 (m, 2H), 7.17 (dd, J = 6.4, 3.7 Hz, 3H), 6.83-6.73 (m, 2H), 6.04 (dd, J = 5.4, 2.0 Hz, 1H), 5.65 (dt, J = 5.4, 1.8 Hz, 1H), 2.01 (s, 1H), 1.02 (s, 3H), 0.92-0.77 (m, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 143.5 (CH), 137.6 (C), 137.0 (C), 133.7 (CH), 129.4 (CH), 129.1 (CH), 129.0 (CH), 128.6 (CH), 128.0 (CH), 126.5 (CH), 122.6 (CH), 71.8 (CH), 50.5 (C), 33.3 (CH), 29.1 (C), 23.8 (CH$_3$), 14.9 (CH$_3$); HRMS-ESI m/z calcd for C$_{20}$H$_{20}$O$_2$NaS [*M*+Na]$^{+}$ 347.1082, found 347.1084.

Compound 43e.
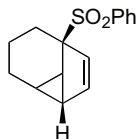
Compound **43e** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **38m** (23.0 mg, 0.088 mmol) with catalyst **Q**. The residue was purified by column chromatography (6:1 hexane/EtOAc) to give compound **43e** (14.2

mg, 62%) as a white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91-7.84 (m, 2H), 7.64-7.58 (m, 1H), 7.53-7.47 (m, 2H), 5.74 (dd, J = 5.4, 2.3 Hz, 1H), 5.34 (dd, J = 5.3, 1.1 Hz, 1H), 2.27 (ddd, J = 13.3, 8.0, 5.4 Hz, 1H), 2.07 (ddd, J = 8.6, 5.7, 1.3 Hz, 1H), 1.86-1.65 (m, 3H), 1.65-1.48 (m, 2H), 1.48-1.34 (m, 2H), 1.14 (ddd, J = 19.7, 9.9, 5.0, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 136.2 (C), 135.7 (CH), 133.3 (CH), 131.9 (CH), 130.1 (CH), 128.2 (CH), 74.9 (C), 27.9 (CH), 21.7 (CH$_2$), 20.8 (CH), 20.6 (CH), 19.8 (CH$_2$), 15.5 (CH$_2$); HRMS-ESI m/z calcd for C$_{15}$H$_{16}$O$_2$NaS [M+Na]$^+$ 283.0769, found 283.0767.

Compound 43f.
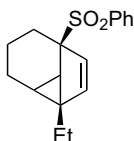
Compound **43f** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **43f** (40.9 mg, 0.142 mmol) with catalyst **Q**. The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **43f** (35.8 mg, 88%) as a off-white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89-7.84 (m, 2H), 7.62-7.57 (m, 1H), 7.52-7.47 (m, 2H), 5.64 (d, J = 5.4 Hz, 1H), 5.38 (dd, J = 5.4, 1.4 Hz, 1H), 2.28 (ddd, J = 13.3, 8.0, 5.3 Hz, 1H), 1.82-1.68 (m, 3H), 1.63-1.53 (m, 1H), 1.46-1.35 (m, 1H), 1.33-1.10 (m, 3H), 0.98 (dq, J = 14.7, 7.4 Hz, 1H), 0.42 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.1 (CH), 136.1 (C), 133.3 (CH), 131.2 (CH), 130.4 (CH), 128.2 (CH), 75.3 (C), 41.4 (C), 26.5 (CH), 25.5 (CH$_2$), 25.3 (CH), 21.2 (CH$_2$), 19.8 (CH$_2$), 16.1 (CH$_2$), 11.0 (CH$_3$); HRMS-ESI m/z calcd for C$_{17}$H$_{20}$O$_2$NaS [M+Na]$^+$ 311.1082, found 311.1080.

Compound 43g.

Compound **43g** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **38o** (40.9 mg, 0.142 mmol) with catalyst **Q**. The residue was

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purified by column chromatography (8:1 hexane/EtOAc) to give compound **43g** (35.8 mg, 88%) as a off-white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89- 7.80 (m, 2H), 7.61 (m, 1H), 7.45 (m, 2H), 7.14-7.04 (m, 3H), 6.56-6.46 (m, 2H), 5.83 (d, *J* = 5.3 Hz, 1H), 5.56 (dd, *J* = 5.3, 1.3 Hz, 1H), 2.37 (ddd, *J* = 13.2, 8.0, 5.4 Hz, 1H), 2.19- 2.12 (m, 1H), 2.03- 1.82 (m, 3H), 1.75- 1.63 (m, 1H), 1.57- 1.44 (m, 1H), 1.36 (tdd, *J* = 13.6, 8.5, 4.7 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.0 (C), 135.9 (CH), 133.3 (C), 132.0 (CH), 130.4 (CH), 128.5 (CH), 128.0 (CH), 127.1 (CH), 126.3 (CH), 75.3 (C), 43.9 (C), 29.6 (CH), 27.3 (CH), 21.1 (CH$_2$), 19.7 (CH$_2$), 16.0 (CH$_2$); HRMS-ESI m/z calcd for C$_{21}$H$_{20}$O$_2$NaS [*M*+Na]$^+$ 359.1082, found 359.1097.

3-Methyl-2-(prop-1-en-2-yl)cyclopent-3-enylsulfonylbenzene (44b).

Compound **44b** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **38g** (21.0 mg, 0.048 mmol) with catalyst **K** (3.4 mg, 0.003 mmol). The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **44b** (10.0 mg, 80%) as a off-white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.00-7.74 (m, 2H), 7.69-7.59 (m, 1H), 7.58-7.50 (m, 2H), 5.41-5.31 (m, 1H), 4.66 (dd, *J* = 3.1, 1.5, 1H), 4.54-4.49 (m, 1H), 3.61 (dt, *J* = 9.2, 4.5, 1H), 3.55 (s, 1H), 2.98-2.79 (m, 1H), 2.76-2.55 (m, 1H), 1.56-1.50 (m, 3H), 1.48 (dd, *J* = 1.3, 0.8, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 143.2 (C), 139.9 (C), 138.2 (C), 133.5 (CH), 129.0 (CH), 128.7 (CH), 123.3 (CH), 113.7 (CH$_2$), 66.9 (CH), 57.8 (CH), 32.8 (CH$_2$), 18.4 (CH$_3$), 14.5 (CH$_3$); HRMS-ESI m/z calcd for C$_{15}$H$_{18}$O$_2$NaS [*M*+Na]$^+$ 285.0925, found 285.0919.

((3-Ethyl-2-(prop-1-en-2-yl)cyclopent-3-en-1-yl)sulfonyl)benzene (44c).
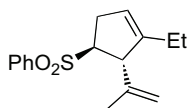
Compound **44c** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **38h** (59.5 mg, 0.216 mmol) with catalyst **K** (9.3 mg, 0.008

mmol). The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **44c** (42.8 mg, 72%) as a off-white sticky solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (m, 2H), 7.63 (m, 1H), 7.54 (m, 2H), 5.34 (d, J = 1.7 Hz, 1H), 4.71-4.62 (m, 1H), 4.53 (s, 1H), 3.62 (m, 1H), 2.90 (d, J = 17.6 Hz, 1H), 2.80-2.57 (m, 1H), 1.95-1.84 (m, 1H), 1.83-1.71 (m, 1H), 1.49 (s, 3H), 0.96 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 146.2 (C), 143.7 (C), 138.4 (C), 133.7 (CH), 129.2 (CH), 128.9 (CH), 121.3 (CH), 113.9 (CH), 67.1 (CH), 56.9 (CH), 32.9 (CH$_2$), 22.1 (CH$_2$), 18.7 (CH$_3$), 11.9 (CH$_3$).

((3-Phenyl-2-(prop-1-en-2-yl)cyclopent-3-en-1-yl)sulfonyl)benzene (44d).
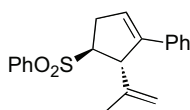
Compound **44d** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **38i** (40.9 mg, 0.124 mmol) with catalyst **K** (8.6 mg, 0.007 mmol). The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **43f** (27.1 mg, 67%) as a off-white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.94 (dt, J = 8.5, 1.8 Hz, 2H), 7.62 (ddd, J = 6.7, 3.9, 1.3 Hz, 1H), 7.58-7.46 (m, 2H), 7.36-7.12 (m, 6H), 6.06 (d, J = 0.7 Hz, 1H), 4.78-4.65 (m, 1H), 4.58 (d, J = 0.7 Hz, 1H), 4.19 (s, 1H), 3.65 (dt, J = 9.2, 3.3 Hz, 1H), 3.08 (dt, J = 18.8, 3.1 Hz, 1H), 2.88 (ddt, J = 18.8, 9.2, 2.3 Hz, 1H), 1.55 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 144.0 (C), 142.7 (C), 137.9 (C), 134.7 (C), 133.8 (CH), 129.3 (CH), 129.1 (CH), 128.4 (CH), 127.7 (CH), 126.2 (CH), 124.8 (CH), 114.0 (CH), 68.2 (CH), 54.8 (CH), 33.3 (CH$_2$), 19.7 (CH$_3$).

1-Methyl-4-(4-(phenylsulfonyl)-5-(prop-1-en-2-yl)cyclopent-1-en-1-yl)benzene (44e).
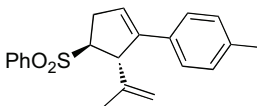
Compound **45'e** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **38j** (56.5 mg, 0.167 mmol) with catalyst **K** (10.1 mg, 0.008 mmol). The residue was purified by column chromatography (8:1 hexane/EtOAc) to

give compound **45'e** (32.8 mg, 58%) as a dark yellow solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.93 (m, 2H), 7.67-7.58 (m, 1H), 7.53 (m, 2H), 7.19 (d, J = 8.1 Hz, 2H), 7.06 (d, J = 8.1 Hz, 2H), 5.99 (d, J = 2.8 Hz, 1H), 4.77-4.63 (m, 1H), 4.58 (s, 1H), 4.17 (s, 1H), 3.64 (dt, J = 9.2, 3.3 Hz, 1H), 3.06 (dt, J = 18.7, 3.1 Hz, 1H), 2.87 (ddt, J = 18.8, 9.2, 2.3 Hz, 1H), 2.30 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 144.12 (C), 142.53 (C), 137.89 (C), 137.52 (C), 133.81 (CH), 131.94 (C), 129.25 (CH), 129.05 (CH), 126.11 (CH), 123.83 (CH), 113.90 (CH), 68.19 (CH), 54.82 (CH), 33.28 (CH$_2$), 21.30 (CH$_3$), 19.63 (CH$_3$); HRMS-ESI m/z calcd for C$_{15}$H$_{18}$O$_2$NaS [M+Na]$^+$ 285.0925, found 285.0919.

1-Methoxy-4-(4-(phenylsulfonyl)-5-(prop-1-en-2-yl)cyclopent-1-en-1-yl)benzene (44f).
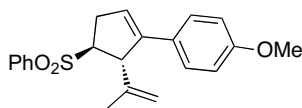
Compound **44f** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **38k** (40.5 mg, 0.114 mmol) with catalyst **K** (7.2 mg, 0.006 mmol). The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **44f** (23.6 mg, 58%) as a orange solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.01-7.85 (m, 2H), 7.70-7.60 (m, 1H), 7.56 (t, J = 7.6 Hz, 2H), 7.26 (d, J = 8.8 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 5.95 (s, 1H), 4.80-4.67 (m, 1H), 4.60 (s, 1H), 4.17 (d, J = 1.8 Hz, 1H), 3.80 (s, 3H), 3.65 (dd, J = 6.2, 2.9 Hz, 1H), 3.08 (dt, J = 18.7, 3.1 Hz, 1H), 2.88 (ddt, J = 18.7, 9.2, 2.3 Hz, 1H), 1.57 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 159.2 (C), 144.2 (C), 142.0 (C), 137.9 (C), 133.8 (CH), 129.2 (CH), 129.0 (CH), 127.5 (C), 127.4 (CH), 122.7 (CH), 113.9 (CH), 113.7 (CH), 68.2 (CH), 55.3 (CH$_3$), 54.9 (CH), 33.3 (CH$_2$), 19.6 (CH$_3$).

1-(4-(4-(Phenylsulfonyl)-5-(prop-1-en-2-yl)cyclopent-1-enyl)phenyl)ethanone (44g).
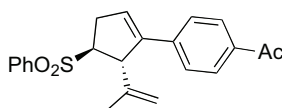
Compound **44g** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **38l** (30.0 mg, 0.082 mmol) with catalyst **K** (4.8 mg, 0.004 mmol). The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **43f** (25.6 mg, 85%) as a dark yellow sticky solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.02-7.88 (m, 3H), 7.86 (d, J = 8.5, 2H), 7.65 (t, J = 7.4, 1H), 7.55 (t, J = 7.6, 2H), 7.39 (d, J = 8.4, 2H), 6.24 (s, 1H), 4.78-4.64 (m, 1H), 4.59 (s, 1H), 4.22 (s, 1H), 3.66 (d, J = 9.2, 1H), 3.12 (dt, J = 19.0, 3.1, 1H), 2.91 (dd, J = 19.2, 9.2, 1H), 2.57 (s, 3H), 1.57 (s, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 197.6 (C), 143.6 (C), 141.9 (C), 139.2 (C), 137.7 (C), 136.1 (CH), 134.0 (CH), 129.4 (CH), 129.0 (CH), 128.6 (CH), 127.8 (CH), 126.3 (CH), 114.3 (CH), 68.0 (CH), 54.62 (CH), 33.5 (CH$_2$), 26.7 (CH$_3$), 19.7 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{15}$H$_{18}$O$_2$NaS [M+Na]$^+$ 285.0925, found 285.0919.

(2-Isopropylcyclopenta-1,3-dienylsulfonyl)benzene (45a).
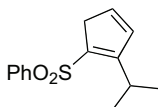
A solution of the enyne **45a** (10.3 mg, 0.042 mmol) and **E** (1.5 mg, 0.002 mmol) in CH$_2$Cl$_2$ under Ar was stirred under microwave irradiation (Initiator^{TM} 2.0 Biotage) at 100ºC for 20 min (Scheme 9). Celite was added and CH$_2$Cl$_2$ was evaporated. After column chromatography (6:1 hexane/EtOAc), compund **45a** (9.0 mg, 87%) was isolated as a sticky solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (m, 2H), 7.58-7.47 (m, 3H), 6.69 (dm, J = 5.4 Hz, 1H), 6.58 (dm, J = 5.4 Hz, 1H), 3.84 (septuplet, J = 6.7 Hz, 1H), 3.41 (m, 2H), 1.12 (d, J = 6.7 Hz, 6H). ^{13}C NMR (100 MHz, CDCl$_3$, PENDANT) δ 163.8 (C), 142.9 (C), 139.5 (CH), 134.1 (C), 132.7 (CH), 132.1 (CH), 129.1 (CH), 126.9 (CH), 43.2 (CH$_2$), 26.3 (CH), 21.5 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{24}$H$_{16}$O$_2$NaS [M+Na]$^+$ 271.0769, found 271.0770.

(5-Isopropyl-4-(phenylsulfonyl)cyclopenta-1,3-dien-1-yl)benzene (45'd).

Compound **44d** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **38i** (40.9 mg, 0.124 mmol) with catalyst **K** (8.6 mg, 0.007 mmol). The residue was purified by column chromatography (8:1 hexane/EtOAc) to

give compound **45'e** as a mixture of tautomers (10.2 mg, 25%) as a dark orange oil: 1H NMR (400 MHz, CDCl$_3$) δ 8.01-7.96 (m, 2H), 7.66-7.53 (m, 3H), 7.40-7.30 (m, 7H), 6.56 (d, J = 2.4 Hz, 1H), 3.92 (s, 1H), 2.47 (dseptuplet, J = 7.0, 2.6 Hz, 1H), 0.75 (d, J = 7.0 Hz, 3H), 0.69 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 160.0 (C), 146.3 (C), 144.3 (CH), 141.6 (C), 136.0 (C), 133.1 (CH), 129.2 (CH), 128.7 (CH), 128.6 (CH), 127.9 (CH), 127.8 (CH), 126.6 (CH), 59.1 (CH), 29.5 (CH), 19.1 (CH$_3$), 18.2 (CH$_3$).

1-(5-Isopropyl-4-(phenylsulfonyl)cyclopenta-1,3-dien-1-yl)-4-methylbenzene (45'e)
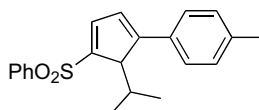
Compound **45'e** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **38j** (56.5 mg, 0.167 mmol) with catalyst **K** (10.1 mg, 0.008 mmol). The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **45'e** (11.6 mg, 21%) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.99-7.92 (m, 2H), 7.59-7.50 (m, 3H), 7.32 (ddd, J = 2.6, 1.5, 0.5 Hz, 1H), 7.20 (d, J = 8.1 Hz, 2H), 7.15 (d, J = 8.1 Hz, 2H), 6.50 (d, J = 2.5 Hz, 1H), 3.86 (m, 1H), 2.42 (dseptuplet, J = 7.0, 2.6 Hz, 1H), 2.38-2.27 (m, 3H), 0.74 (d, J = 7.0 Hz, 3H), 0.66 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 160.2 (C), 145.7 (C), 144.5 (CH), 141.7 (C), 138.7 (C), 133.2 (C), 133.1 (CH), 129.4 (CH), 129.2 (CH), 127.9 (CH), 127.8 (CH), 125.8 (CH), 58.9 (CH), 29.6 (CH), 21.4 (CH$_3$), 18.9 (CH$_3$), 18.4 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{15}$H$_{18}$O$_2$NaS [*M*+Na]$^+$ 285.0925, found 285.0919.

1-(5-isopropyl-4-(phenylsulfonyl)cyclopenta-1,3-dien-1-yl)-4-methoxybenzene (45'f).
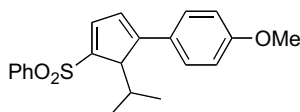
Compound **45'f** was synthesized following the general procedure for the cyclization of 1,5-enynes, starting from **38k** (40.5 mg, 0.114 mmol) with catalyst **K** (7.2 mg, 0.006 mmol). The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **45'f** (11.3 mg, 28%) as a orange oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.98 (dd, J = 8.3, 1.2 Hz, 3H), 7.61-7.53 (m, 4H), 7.35 (dd, J = 2.5, 1.5 Hz, 1H), 7.27

(d, J = 8.7 Hz, 3H), 6.90 (d, J = 8.7 Hz, 2H), 6.48 (d, J = 2.5 Hz, 1H), 3.86 (s, 1H), 3.84 (s, 3H), 2.43 (dseptuplet, J = 2.5, 7.0 Hz, 1H), 0.78 (d, J = 7.0 Hz, 3H), 0.68 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 160.1 (C), 159.9 (C), 145.1 (C), 144.7 (CH), 141.7 (C), 133.0 (CH), 129.2 (CH), 129.2 (CH), 128.6 (C), 127.9 (CH), 125.0 (CH), 114.1 (CH), 58.9 (CH), 55.5 (CH$_3$), 29.8 (CH), 18.8 (CH$_3$), 18.5 (CH$_3$).

General procedure for the reaction of 1,5-enynes with arenes. The starting enyne was dried before the reaction by repetitive evaporation of a solution of the compound in toluene (1 mL/10 mg of 1,5-enyne, 3x) under vacuum. A solution of the 1,5-enyne (30 mg) in 1.5 mL of CH$_2$Cl$_2$ was dropwise added in 30 min at room temperature to a solution of the nucleophile (2.5-5 equiv) and the gold complex **E** in 0.5 mL of CH$_2$Cl$_2$. The reaction mixture was monitored by TLC till complete conversion.

2-(Phenyl(2,4,6-trimethoxyphenyl)methyl)cyclopent-3-enyl ethanoate (61a).
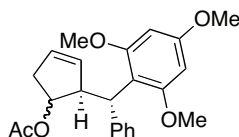
Compound **61a** was synthesized following the general procedure for the reaction of 1,5-enynes with arenes, starting from **38a** (50 mg, 0.233 mmol) and 1,3,5-trimethoxybenzene (100 mg, 0.582 mmol) (*Table 8*, entry 4). The residue was purified by column chromatography (6:1 hexane/EtOAc) to give **61a** (75 mg, 75% 1:0.7 Diasteromers *cis/trans*) as a yellow oil. Diasteromer *cis*: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.50 (m, 2H), 7.24 (m, 2H), 7.12 (m, 1H), 6.05 (s, 2H), 5.71 (m, 1H), 5.58 (m, 1H), 5.27 (t, J = 6.5 Hz, 1H), 4.65 (d, J = 11.9 Hz, 1H), 4.30 (dm, J = 13.0 Hz, 1H), 3.80 (s, 6H), 3.74 (s, 3H), 2.67 (dm, J = 17.4 Hz, 1H), 2.35 (d, J = 17.4 Hz, 1H), 1.76 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 179.58 (C), 159.29 (C), 145.33 (C), 133.96 (CH), 128.97 (CH), 128.36 (CH), 127.64 (CH), 126.03 (CH), 105.63 (C), 91.55 (CH), 76.00 (CH), 55.51 (CH$_3$), 50.99 (CH), 41.09 (CH$_2$), 40.48 (CH), 21.02 (CH$_3$). Diasteromer *trans*: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.43 (m, 2H), 7.25 (m, 2H), 7.11 (m, 1H), 6.03 (s, 2H), 5.64 (m, 2H), 4.98 (m, 1H), 4.30 (d, J = 12.2 Hz, 1H), 4.13 (d, J = 11.3 Hz, 1H), 3.74 (s, 3H), 3.73 (s, 6H), 2.80 (dm, J = 17.6 Hz, 1H), 2.22 (d, J = 17.6 Hz, 1H), 1.76 (s, 3H);

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.05 (C), 158.72 (C), 144.50 (C), 134.02 (CH), 129.20 (CH), 128.05 (CH), 127.96 (CH), 125.76 (CH), 113.04 (C), 91.49 (CH), 79.39 (CH), 55.92 (CH$_3$), 51.62 (CH), 44.21 (CH), 39.63 (CH$_2$), 21.40 (CH$_3$); HRMS-ESI calculated for C$_{23}$H$_{26}$O$_5$Na [M+Na]$^+$ 405.1678, found 405.1677.

2-((1*H*-Indol-3-yl)(phenyl)methyl)cyclopent-3-enyl ethanoate (61b).
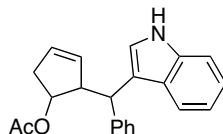
Compound **61f** was synthesized following the general procedure general procedure for the reaction of 1,5-enynes with arenes, starting from **38a** (32.3 mg, 0.151 mmol) and indole (22.1 mg, 0.188 mmol) with catalyst **E** (10.6 mg, 0,014 mmol). The residue was purified by column chromatography (8:1 hexane/EtOAc) to give the starting matirial (15.8 mg, 43% recovered) and isolate compound **61b** (8.3 mg, 17%) as a dark-yellow sticky solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.98 (s, 1H), 7.54 (d, J = 8.2 Hz, 1H), 7.38 (m, 2H), 7.30-7.21 (m, 2H), 7.16-7.08 (m, 3H), 7.04-6.95 (m, 2H), 5.76 (m, 1H), 5.46 (m, 1H), 5.58 (tm, J = 5.5 Hz, 1H), 4.38 (d, J = 11,9 Hz, 1H), 3.66 (m, 1H), 2.75 (dm, J = 16.8 Hz, 1H), 2.37 (dm, J = 16.8 Hz, 1H), 2.04 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 177.9 (C), 144.4 (C), 135.5 (C), 132.3 (CH), 128.4 (CH), 128.3 (CH), 126.1 (CH), 125.1 (C), 122.0 (CH), 119.2 (CH), 118.8 (CH), 117.6 (CH), 110.9 (CH), 77.2 (CH), 73.8 (CH), 54.5 (CH), 40.5 (CH$_2$), 20.6 (CH$_3$).

General procedure for the hydroxycyclization reaction. A solution of the gold complex **E** (5 mol%) in 0.2 mL of CH$_2$Cl$_2$ was added to a 1:3 mixture of H$_2$O and CH$_2$Cl$_2$ (2 mL) containing the 1,5-enyne (40-50 mg) opened to air at room temperature. The reaction mixture was monitored by TLC till complete conversion.

**2-(5-(Phenylsulfonyl)cyclopent-2-enyl)propan-2-ol (61c).**
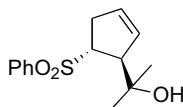
Compound **61c** was synthesized following the general procedure for the hydroxycyclization of 1,5-enynes, starting from **38f** (45.7 mg, 0.184 mmol) with

catalyst **E**. The residue was purified by column chromatography (3:1 hexane/EtOAc) to give compound **61c** (44.9 mg, 92%) as a white solid: mp 127-130 ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.93 (d, J = Hz, 2H), 7.66 (m, 1H), 7.57 (m, 2H), 5.79-5.76 (m, 1H), 5.65-5.64 (m, 1H), 3.86 (dt, J = 9.4, 3.2 Hz, 1H), 3.38 (m, 1H), 2.82 (dm, J = 18.3 Hz, 1H), 2.65-2.56 (m, 1H), 1.84 (bs, 1H), 1.23 (s, 3H), 1.07 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.0 (C), 133.8 (CH), 131.0 (CH), 129.8 (CH), 129.3 (CH), 129.0 (CH), 72.0 (C), 63.2 (CH), 58.4 (CH), 34.8 (CH$_2$), 28.8 (CH$_3$), 26.0 (CH$_3$); HRMS-ESI *m/z* calculated for C$_{18h18}$O$_3$NaS $[M+$Na$]^+$ 289.0874, found 289.0874; Anal calcd for C$_{18h18}$O$_3$S: C, 63.13; H, 6.81; S, 12.04; found C, 61.74; H, 6.58; S, 11.38.

### 2-(2-Methyl-5-(phenylsulfonyl)cyclopent-2-enyl)propan-2-ol (61d).
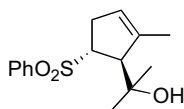
Compound **61d** was synthesized following the general procedure for the hydroxycyclization of 1,5-enynes, starting from **38g** (40.2 mg, 0.153 mmol) with catalyst **E**. The residue was purified by column chromatography 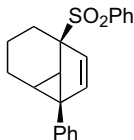(3:1 hexane/EtOAc) to give compound **61d** (39.2 mg, 91%) as a yellow solid: mp 165-166 ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.96 (dm, J = 8.5 Hz, 2H), 7.69 (m, 1H), 7.60 (m, 2H), 5.39 (m, 1H), 3.98 (dt, J = 9.1, 3.0 Hz, 1H), 3.24 (m, 1H), 2.71 (dm, 18.8 Hz, 1H), 2.58-2.49 (m, 1H), 2.09 (bs, 1H), 1.79 (m, 3H), 1.38 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 139.4 (C), 133.9 (CH), 129.3 (CH), 129.0 (CH), 126.6 (CH), 72.4 (CH), 65.3 (CH), 60.8 (C), 33.1 (CH$_2$), 29.9 (CH$_3$), 25.5 (CH$_3$), 17.8 (CH$_3$); HRMS-ESI *m/z* calculated for C$_{15}$H$_{20}$O$_3$NaS $[M+$Na$]^+$ 303.1031, found 303.1037.

2-(2-Phenyl-5-(phenylsulfonyl)cyclopent-2-enyl)propan-2-ol (61e).
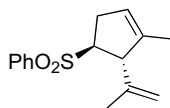

Compound **61e** was synthesized following the general procedure for the hydroxycyclization of 1,5-enynes, starting from **38h** (40.0 mg, 0.123 mmol) with catalyst **E**. The residue was purified by column chromatography (4:1 hexane/EtOAc) to

give compound **61e** (25.4 mg, 60%) as a yellow solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.97 (dm, J = 8.3 Hz, 2H), 7.62 (m, 1H), 7.55 (m, 2H), 7.31-7.22 (m, 5H), 5.77 (m, 1H), 4.07 (dt, J = 8.7, 2.3 Hz, 1H), 3.82 (m, 1H), 2.94 (dt, J = 18.8, 2.6 Hz, 1H), 2.77 (ddm, J = 18.8, 8.9, 2.3 Hz, 1H), 1.06 (s, 3H), 0.97 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.5 (C), 133.7 (CH), 129.1 (CH), 128.9 (CH), 128.3 (CH), 127.6 (C), 126.7 (CH), 73.2, 65.1 (CH), 58.3 (CH), 33.8 (CH$_2$), 29.7 (CH$_3$), 26.1 (CH$_3$); HRMS-ESI m/z calculated for C$_{20}$H$_{22}$O$_3$NaS $[M$+Na$]^+$ 365.1187, found 365.1195.

1,3,5-Trimethoxy-2-(2-(5-(phenylsulfonyl)cyclopent-2-enyl)propan-2-yl)benzene (61f).
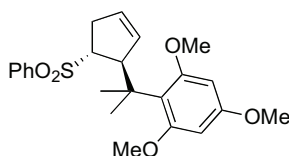
Compound **61f** was synthesized following the general procedure for the reaction of 1,5-enynes with arenes, starting from **38f** (40 mg, 0.161 mmol) and 1,3,5-trimethoxybenzene (135 mg, 0.806 mmol). After column chromatography (hexane/EtOAc 8:1), a 6:1 mixture of **61f** and **61**. The mixture was purified by semi-preparative HPLC (MeCN/H$_2$O: 15 min isocratic 45% MeCN, then 20 min gradient 45-100% MeCN; Ret. Time 23.851 min) to give **61f** (44.9 mg, 66%) as a white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.71 (dm, J = 7.9 Hz, 2H), 7.56 (m, 1H), 7.42 (m, 2H), 6.01 (s, 2H), 5.77 (m, 1H), 5.57 (m, 1H), 4.09 (m, 1H), 3.83 (s, 3H), 3.74 (m, 1H), 3.73 (s, 6H), 3.06 (dm, J = 18.4 Hz, 1H), 2.79 (dm, J = 18.3 Hz, 1H), 1.39 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 160.5, 159.2, 138.2 (C), 133.0 (CH), 131.8 (CH), 129.4 (CH), 128.7 (CH), 115.5 (CH), 92.7 (CH), 64.7 (CH), 55.8 (CH), 55.2 (CH$_3$), 54.8 (CH$_3$), 42.9 (CH), 34.6 (CH$_2$), 28.1 (CH$_3$), 26.7 (CH$_3$); HRMS-ESI m/z calculated for C$_{23}$H$_{29}$O$_5$S $[M$+H$]^+$ 417.1736, found: 417.1743.

1,3,5-Trimethoxy-2-(2-(2-methyl-5-(phenylsulfonyl)cyclopent-2-enyl)propan-2-yl)benzene (61g).
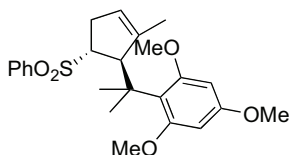
Compound **61g** was synthesized following the general procedure for the reaction of 1,5-enynes with arenes, starting from **38g** (40 mg, 0.152 mmol) and 1,3,5-trimethoxybenzene (128 mg, 0.763mmol). The residue was purified by column chromatography (hexane/EtOAc 8:1) to give compound **61g** (37.0 mg, 56%) was isolated as a yellow solid: m.p. 150-151 ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.80 (dm, J = 7.7 Hz, 2H), 7.60 (m, 1H), 7.48 (m, 1H), 6.11 (s, 2H), 5.26 (m, 1H), 4.14 (s, 1H), 3.84 (s, 3H), 3.80 (s, 6H), 3.70 (dt, J = 8.3, 1.8 Hz, 1H), 2.78 (dm, J = 18.0 Hz, 1H), 2.69-2.61 (m, 1H), 1.45 (s, 3H), 1.44 (s, 3H), 1.36 (m, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 160.2 (C), 159.1 (C), 141.9 (C), 138.3 (C), 132.9 (CH), 128.7 (CH), 128.6 (CH), 124.7 (CH), 116.7 (C), 92.5 (CH), 67.1 (CH), 56.2 (CH$_3$), 55.7 (CH$_3$), 55.0 (CH), 42.7 (C), 33.6 (CH$_2$), 28.2 (CH$_3$), 27.9 (CH$_3$), 17.0 (CH$_3$); HRMS-ESI *m/z* calculated for C$_{24}$H$_{30}$O$_5$NaS [M+Na]$^+$ 453.1712, found 453.1701.

1,3,5-Trimethoxy-2-(2-(2-phenyl-5-(phenylsulfonyl)cyclopent-2-enyl)propan-2-yl)benzene (61h).
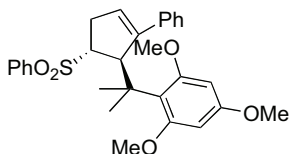
Compound **61h** was synthesized following the general procedure for the reaction of 1,5-enynes with arenes, starting from **38i** (29.8 mg, 0.089 mmol) and 1,3,5-trimethoxybenzene (48 mg, 0.285 mmol). The residue was purified by column chromatography (hexane/EtOAc 8:1) to give compound **61h** (49.6 mg, 50%) was isolated as a yellow solid: mp 127-129 ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.33 (dm, J = 7.4Hz, 2H), 7.49 (m, 1H), 7.38 (m, 2H), 7.16-7.05 (m, 5H), 5.87 (br s, 2H), 5.76 (m, 1H), 4.65 (m, 1H), 3.78 (d, J = 8.4 Hz, 1H), 3.74 (s, 3H), 3.69 (s, 6H), 3.07 (dm, J = 19.2Hz, 1H), 2.89 (ddm, J = 19.2, 8.4 Hz, 1H), 1.41 (s, 3H), 1.12 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, 100ºC) δ 160.2 (C), 159.2 (C), 145.7 (C), 138.4 (C), 138.1 (C),

133.1 (CH), 128.8 (CH), 128.7 (CH), 127.6 (CH), 127.4 (CH), 126.7 (CH), 115.7 (CH), 92.3 (CH), 67.2 (CH), 55.2 (CH_3), 53.6 (CH_3), 44.1 (C), 34.4 (CH_2), 29.4 (CH_3), 27.4 (CH_3); ^{1}H NMR (500 MHz, $C_6D_5CD_3$, 100ºC) δ 7.5 (m, 1H), 6.8 (m, 2H), 6.8-6.7 (5H), 6.6 (m, 1H), 5.6 (s, 2H), 5.2 (m, 1H), 4.7 (m, 1H), 3.5 (dt, J = 8.5, 1.6 Hz, 1H), 3.20 (s, 3H), 3.19 (s, 6H), 2.7 (ddd, J = 18.4, 3.2, 1.6 Hz, 1H), 2.4 (ddt, J = 18.4, 8.5, 2.3 Hz, 1H), 1.3 (s, 3H), 1.0 (s, 3H); ^{13}C NMR (125 MHz, $C_6D_5CD_3$) δ 146.7 (C), 137.5 (C), 132.5 (C), 129.1 (CH), 128.5 (CH), 127.6 (CH), 127.5 (CH), 126.9 (CH), 126.6 (CH), 92.5 (CH), 67.4 (CH), 54.5 (CH_3), 53.9 (CH_3), 34.8 (CH_2), 29.2 (CH_3), 28.1 (CH_3); HRMS-ESI *m/z* calculated for $C_{29}H_{32}O_3NaS$ [M+Na]$^+$ 515.1868, found 515.1883.

2-(Phenyl(2,4,6-trimethoxyphenyl)methyl)cyclopent-3-enol (62).
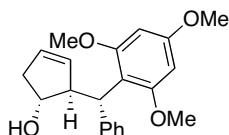
K_2CO_3 (3 equiv) was added to a solution of **61a** (48.9 mg, 0.128mmol) in MeOH (8mL) and stirred atroom temperaturefor 2 days (*Scheme 32*). MeOH was evaporated and after extractive work-up the residue was purified by column chromatography (hexane/EtOAc 8:1) to give one diasteroisomer of *cis*-**61a** (27mg, 54%) and **62** (20mg, 46%) as a white solid: mp 118-119 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dm, J = 7.5 Hz, 2H), 7.21 (tm, J = 7.5 Hz, 2H), 7.10 (m, 1H), 6.11 (s, 2H), 5.62 (m, 2H), 5.30 (s, 1H), 4.26 (d, J = 12.5 Hz, 1H), 4.06 (m, 1H), 3.88 (dm, J = 12.0 Hz, 1H), 3.774 (s, 3H), 3.770 (s, 6H), 2.73 (ddm, J = 17.0, 7.0 Hz, 1H), 2.29 (dm, J = 17.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8 (C), 158.9 (C), 144.0 (C), 133.3 (CH), 128.7 (CH), 127.8 (CH), 127.6 (CH), 125.3 (CH), 112.8 (C), 91.4 (CH), 77.5 (CH), 55.7 (CH), 55.4 (CH_3), 55.2 (CH_3), 44.1 (CH_2), 41.0 (CH); HRMS-ESI *m/z* calculated for $C_{21}H_{38o4}$ [M+H]$^+$ 341.1753, found 341.1756. Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11; O, 18.80; found: C, 73.38; H, 7.24; N, 0.02.

(*E*)-5,5-Di(1*H*-indol-3-yl)-1-phenylhex-1-en-3-yl acetate (56).
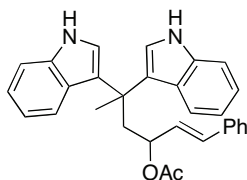
Compound **61f** was synthesized following the general procedure general procedure for the reaction of 1,5-enynes with arenes, starting from **38a** (32.3 mg, 0.151 mmol) and indole (22.1 mg, 0.188 mmol) with catalyst **E** (10.6 mg, 0,014 mmol). The residue was purified by column chromatography (4:1 hexane/EtOAc) to give the starting matirial (15.8 mg, 43% recovered) and isolate compound **56** (10.1 mg, 15%) as a dark-orange sticky solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.93 (s, 1H), 7.38 (m, 2H), 7.31-7.17 (m, 5H), 7.14-7.05 (m, 6H), 6.87 (m, 2H), 6.32 (d, J = 14.6 Hz, 1H), 5.91 (dd, J = 15.8, 7.2 Hz, 1H), 5.49 (m, 1H), 2.95 (dd, J = 14.5, 7.2 Hz, 1H), 2.77 (dd, J = 14.5, 3.8 Hz, 1H), 1.94 (s, 3H), 1.25 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 160.0 (C), 137.2 (C), 137.1 (C), 130.8 (CH), 128.9 (CH), 128.4 (CH), 127.6 (CH), 126.4 (CH), 123.3 (C), 123.0 (C), 121.6 (CH), 121.5 (CH), 121.4 (CH), 121.2 (CH), 121.2 (CH), 118.9 (CH), 118.8 (CH), 111.6 (CH), 111.0 (CH), 72.2 (CH), 44.7 (CH$_2$), 37.8 (C), 27.6 (CH$_3$), 20.6 (CH$_3$).

2-(2,2-Dimethyl-3-methylene-5-(phenylsulfonyl)cyclopentyl)-1,3,5-trimethoxybenzene (69).
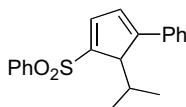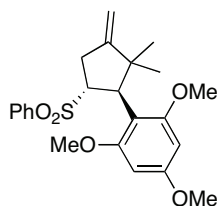

Compound **69** was synthesized following the general procedure for the reaction of 1,5-enynes with arenes, starting from **38f** (40 mg, 0.161 mmol) and 1,3,5-trimethoxybenzene (135 mg, 0.806 mmol). After column chromatography (hexane/EtOAc 8:1), a 6:1 mixture of **61f** and **69** was isolated. The mixture was purified by semi-preparative HPLC (MeCN-H$_2$O: 15 min isocratic 45% MeCN, then 20 min gradient 45-100% MeCN; Ret. Time 21.984 min) to give **69** (7.2 mg, 10%) as a white solid. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.77 (dm, J = 7.5Hz, 2H), 7.58 (m, 1H), 7.47 (m, 2H), 6.06 (s, 2H), 5.25 (m,1H), 4.94 (m, 1H), 4.86 (dm, J = 10.1 Hz, 1H), 3.80 (s,

3H), 3.71 (ddd, J = 12.4, 10.1, 2.3 Hz, 1H), 3.67 (s, 6H), 3.33 (dm, J = 13.9 Hz, 1H), 2.60 (dd, J = 13.9, 11.4 Hz, 1H), 1.59 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 158.3 (C), 141.9 (C), 138.6 (C), 137.6 (C), 133.1 (CH), 129.2 (CH), 128.6 (CH), 118.5 (CH), 117.4 (CH), 90.3 (CH), 63.8 (CH$_2$), 56.2 (CH$_3$), 55.6 (CH$_3$), 55.4 (C), 35.2 (CH$_2$), 25.9 (CH$_3$), 17.9 (CH$_3$); HRMS-ESI m/z calculated for C$_{23}$H$_{29}$O$_5$S [M+H]$^+$ 417.1736, found 417.1741.

2-(3-Isopropyl-4-(phenylsulfonyl)cyclopent-2-enyl)-1,3-diphenylpropane-1,3-dione (71).
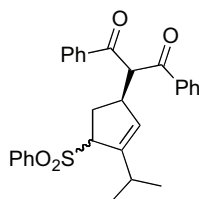
A solution of the enyne **38f** (30 mg, 0.120 mmol) in DCM under Ar was slowly added (1h addition) to a solution of dibenzoylmethane (135 mg, 0.806 mmol), scandium triflate (9.7 mg, 0.019) and catalyst **E** (5.9, 0.008 mmol) in CH$_2$Cl$_2$ (0.5 mL). After stirring atroom temperaturefor 1.5 h (*Scheme 32*), CH$_2$Cl$_2$ was evaporated and the residue was purified by column chromatography (hexane/EtOAc 8:1) to give compound **71** (29 mg, 51%, 1:1 Diasteromers *cis/trans*) was isolated as a white solid: m.p. 153-155 ºC; Diasteromer *trans*: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.17 (dm, J = 7.8 Hz, 2H), 7.95 (dm, J = 7.8 Hz, 2H), 7.74 (dm, J = 7.8 Hz, 2H), 7.63-7.51 (m, 5H), 7.45-7.40 (m, 4H), 5.94 (d, J = 10.7 Hz, 1H), 5.53 (m, 1H), 4.31 (dm, J = 9.7 Hz, 1H), 3.74 (dd, J = 10.7, 9.7 Hz, 1H), 2.78 (m, 1H), 2.46 (ddd, J = 15.7, 9.6, 9.1 Hz, 1H), 1.82 (dt, J = 15.7, 2 Hz, 1H), 1.02 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 195.6 (C), 194.7 (C), 145.6 (C), 138.6 (CH), 136.4 (CH), 136.3 (CH), 133.8 (CH), 133.6 (CH), 133.4 (CH), 129.2 (CH), 129.0 (CH), 128.6 (CH), 128.3 (CH), 128.1 (CH), 70.9 (CH), 61.3 (CH), 45.1 (CH), 32.0 (CH), 28.3 (CH$_2$), 20.6 (CH$_3$), 20.3 (CH$_3$). Diasteromer *cis*: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.93 (dm, J = 8.3 Hz, 2H), 7.89-7.86 (m, 4 H), 7.70 (m, 1H), 7.60-7.56 (m, 4H), 7.48-7.43 (m, 4H), 5.47 (m, 1H), 4.99 (d, J = 9.4 Hz, 1H), 3.25 (m, 1H), 2.88 (m, 1H), 2.64 (ddd, J = 15.1, 7.5, 2.3 Hz, 1H), 1.99 (ddd, J = 15.1, 9.4, 7.6 Hz, 1H), 1.04 (d, J = 6.9 Hz, 3H), 1.03 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 194.8 (C), 194.5 (C), 146.2 (C), 137.0 (C), 136.29 (C),

136.22 (C), 133.8 (CH), 133.7 (CH), 132.7 (CH), 129.1 (CH), 128.96 (CH), 128.90 (CH), 128.8 (CH), 128.6 (CH), 71.4 (CH), 62.7 (CH), 44.1 (CH), 32.8 (CH), 28.0 (CH$_2$), 21.8 (CH$_3$), 20.8 (CH$_3$); HRMS-ESI *m/z* calculated for C$_{29}$H$_{28}$O$_4$NaS [M+Na]$^+$ 495.1606, found: 495.1591.

General procedure for the reaction of 1,5-enynes with aldehydes and ketones The starting enyne was dried before the reaction by repeated evaporation of a solution of the compound in toluene (1 mL/10 mg of 1,5-enyne, 3 times) under vacuum. A solution of the 1,5-enyne (30 mg) and the corresponding aldehyde (1.5-2 equiv) or ketone (4 equiv) in 1 mL of CH$_2$Cl$_2$ was slowly added at room temperature to a solution of the gold complex **E, K** or **Q** in 0.5 mL of CH$_2$Cl$_2$. The reaction mixture was stirred for the time indicated in *Table 11-Table 13* and *Scheme 37,Scheme 40Scheme 41* (TLC monitoring).

1-Mesityl-3,3-dimethyl-4-(phenylsulfonyl)-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan (87aa).
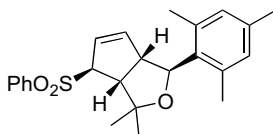
Compound *Syn*-**87aa** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (30.0 mg, 0.120 mmol) and 2,4,6-trimethylbenzaldehyde (35 μL, 0.240 mmol) with catalyst **Q**. The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87aa** (45.0 mg, 95%) as a white solid: mp 75-77 ºC; ^{1}H NMR (400 MHz, CDCl$_3$, HMQC) δ 7.88 (m, 2H), 7.63 (m, 1H), 7.53 (m, 2H), 6.79 (s, 2H), 6.03 (dt, J = 1.6, 5.7 Hz, 1H), 5.79 (dt, J = 2.1, 5.7 Hz, 1H), 4.94 (d, J = 7.4 Hz, 1H), 4.14 (m, 1H), 3.26-3.20 (m, 1H), 3.17 (dd, J = 2.1, 7.4 Hz, 1H), 2.30 (s, 6H), 2.22 (s, 3H), 1.34 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 141.2 (CH), 137.2 (C), 136.6 (C), 133.9 (CH), 132,15 (C), 132.10 (C), 130.2 (CH), 129.3 (CH), 128.9 (CH), 125.0 (CH), 81.7 (C), 78.5 (CH), 73.9 (CH), 58.8 (CH), 54.3 (CH), 28.4 (CH$_3$), 21.4 (CH$_3$), 20.7 (CH$_3$), 20.6 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{24}$H$_{28}$O$_3$NaS [*M*+Na]$^+$ 419.1657, found 419.1647.

1-(2,4-Dimethylphenyl)-3,3-dimethyl-4-(phenylsulfonyl)-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan (87ab).
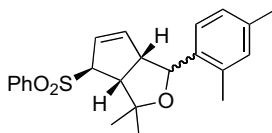
Compound **87ab** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (30.8 mg, 0.124 mmol) and 2,4-dimethylbenzaldehyde (32.0 mg, 0.238 mmol) with catalyst **E.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87ab** (37.0 mg, 81% 7:1 mixture of diastereoisomers *syn/anti*) as a white solid: mp 137-138ºC; ^{1}H NMR (400 MHz, CDCl$_3$, PENDANT) δ 7.89 (m, 2H), 7.64 (m, 1H), 7.55 (m, 2H), 7.26 (d, J = 7.8 Hz, 1H), 6.99 (d, J = 7.8 Hz, 1H), 6.93 (s, 1H), 6.13 (dt, J = 1.8, 5.6 Hz, 1H), 5.77 (dt, J = 2.2, 5.6 Hz, 1H), 4.72 (d, J = 6.9 Hz, 1H), 4.16 (m, 1H), 3.25-3.19 (m, 1H), 3.12 (dd, J = 2.1, 9.2 Hz, 1H), 2.28 (s, 6H), 1.28 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 141.1 (CH), 137.2 (C), 137.0 (C), 135.9 (C), 134.8 (C), 133.9 (CH), 131.3 (CH), 129.1 (CH), 129.0 (CH), 126.9 (CH), 126.2 (CH), 124.8 (CH), 81.7 (C), 80.0 (CH), 73.8 (CH), 60.7 (CH), 53.9(CH), 28.7 (CH$_3$), 21.7 (CH$_3$), 20.9 (CH$_3$), 19.3 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{23}$H$_{26}$O$_3$NaS [M+Na]$^+$ 405.1500, found 405.1489.

1-(2,4-Dimethylphenyl)-3,3-dimethyl-4-(phenylsulfonyl)-3,3a,4,5-tetrahydro-1H-cyclopenta[c]furan (87'ab).

Compound **87'ab** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (31.1 mg, 0.125 mmol) and 2,4-dimethylbenzaldehyde (32.5 mg, 0.240 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87'ab** (7.0 mg, 15%) as a sticky solid (NMR spectrum contain not separable impurities of *syn*-**87ab**): ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.29 (m, 2H), 7.67 (m, 1H), 7.60-7.53 (m, 2H), 7.27 (m,

1H), 7.00 (d, J = 8.3 Hz, 1H), 6.94 (br s, 1H), 5.47 (br s, 1H), 5.41 (br s, 1H), 3.76-3.66 (m, 2H), 3.25-3.16 (m, 1H), 2.80-2.73 (m, 1H), 2.33 (s, 3H), 2.28 (s, 3H), 1.32 (s, 3H), 1.18 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$ HMQC) δ 151.9 (C), 138.5 (C), 137.2 (C), 135.5 (C), 134.8 (C), 133.9 (CH), 131.2 (CH), 129.4 (CH), 128.7 (CH), 126.8 (CH), 125.8 (CH), 116.4 (CH), 79.6 (C), 72.0 (CH), 65.0 (CH), 59.7 (CH), 40.4 (CH$_2$), 27.2 (CH$_3$), 22.2 (CH$_3$), 21.0 (CH$_3$), 19.4 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{23}$H$_{26}$O$_3$NaS [*M*+Na]$^+$ 405.1500, found 405.1489.

3,3-Dimethyl-4-(phenylsulfonyl)-1-(3,4,5-trimethoxyphenyl)-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan (87ac).
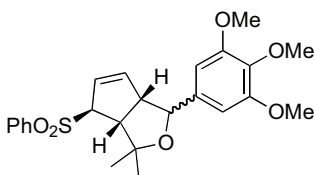
Compound **87ac** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (30.8 mg, 0.124 mmo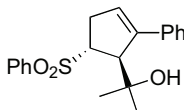l) and 3,4,5-trimethoxybenzaldehyde (47.3 mg, 0.241 mmol) with catalyst **E.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87ac** (35.0 mg, 66%) as a white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (d, J = 8.2 Hz, 2H), 7.66 (m, 1H), 7.57 (m, 2H), 6.53 (s, 2H), 6.15 (dm, J = 5.6 Hz, 1H), 5.75 (dm, J = 5.6 Hz, 1H), 4.45 (d, J = 7.0 Hz, 1H), 4.17 (m, 1H), 3.86 (s, 6H), 3.81 (s, 3H), 3.30 (m, 1H), 3.13 (dd, J = 2.6, 9.7 Hz, 1H), 1.27 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 153.9 (C), 140.6 (CH), 137.6 (C), 137.2 (C), 136.7 (CH), 133.9 (CH), 129.1 (CH), 129.0 (CH), 124.83 (C), 103.0 (CH), 83.1 (CH), 82.1 (C), 73.9 (CH), 61.5 (CH$_3$), 60.8 (CH), 56.1 (CH$_3$), 53.7 (CH), 28.9 (CH$_3$), 21.9 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{24}$H$_{28}$O$_6$NaS [*M*+Na]$^+$ 467.1504, found 467.1518.

1-(4-Bromophenyl)-3,3-dimethyl-4-(phenylsulfonyl)-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan (87ad).
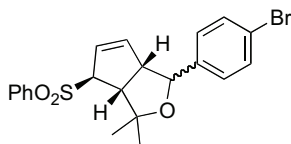
Compound **87ad** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (30.2 mg, 0.121 mmol) and *p*-bromobenzaldehyde (45.0 mg, 0.243 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87ad** (40.7 mg, 78%, 1:1 mixture of diastereoisomers) as a yellow solid: mp 163-165ºC; *Syn*-diastereoisomer*:* ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (m, 2H), 7.68 (m, 1H), 7.58 (m, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 6.15 (dt, J = 1.9, 5.4 Hz, 1H), 5.79 (dt, J = 2.1, 5.4 Hz, 1H), 4.51 (d, J = 7.1 Hz, 1H), 4.18 (m, 1H), 3.24-3.18 (m, 1H), 3.12 (dd, J = 9.3, 2.1 Hz, 1H), 1.27 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 140.4 (CH), 140.3 (C), 137.0 (C), 133.9 (CH), 131.6 (CH), 129.1 (CH), 127.5 (CH), 125.0 (CH), 121.5 (C), 82.25 (C), 82.21 (CH), 73.9 (CH), 61.6 (CH), 53.7 (CH), 28.8 (CH$_3$), 21.9 (CH$_3$). *Anti*-diastereoisomer*:* ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.86 (m, 2H), 7.67 (m, 1H), 7.56 (m, 2H), 7.47 (d, J = 8.6 Hz, 2H), 7.05 (d, J = 8.6Hz, 2H), 5.51 (dt, J = 2.1, 5.7 Hz, 1H), 5.24 (dt, J = 1.9, 5.7 Hz, 1H), 5.01 (d, J = 6.8 Hz, 1H), 4.36 (m, 1H), 3.57-3.52 (m, 1H), 3.08 (dd, J = 7.6, 2.4 Hz, 1H), 1.33 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 139.1 (CH), 137.6 (C), 137.3 (C), 133.8 (CH), 131.2 (CH), 129.1 (CH), 127.8 (CH), 124.5 (CH), 121.1 (C), 81.2 (C), 78.7 (CH), 74.9 (CH), 57.2 (CH), 52.1 (CH), 28.0 (CH$_3$), 25.3 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{21}$H$_{21}$O$_3$NaSBr $[M+$Na$]^+$ 455.0292, found 455.0285.

1-(3-Bromophenyl)-3,3-dimethyl-4-(phenylsulfonyl)-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan (87ae).

Compound **87ae** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (30.0 mg, 0.120 mmol) and *m*-bromobenzaldehyde (28 µL, 0.240 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87ae** (31.9 mg, 62%, 1:1 mixture of diastereoisomers) as a yellow solid: *Syn*-diastereoisomer: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (m, 2H), 7.68 (m, 1H), 7.59 (m, 2H), 7.37 (m, 1H), 7.34 (br s, 1H), 7.25-7.10 (m, 2H), 5.55 (dm, J = 5.6Hz, 1H), 5.27 (dm, J = 5.6Hz, 1H), 5.03 (d, J = 6.8Hz, 1H), 4.39 (m, 1H), 3.57 (m, 1H), 3.11 (dd, J = 2.6, 7.9Hz, 1H), 1.35 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 141.0 (C), 139.0 (CH), 137.3 (C), 133.8 (CH), 130.5 (CH), 129.7 (CH), 129.15 (CH), 129.12 (CH), 129.10 (CH), 124.8 (CH), 124.7 (CH), 122.4 (C), 81.4 (C), 78.7 (CH), 75.0 (CH), 57.4 (CH), 52.3 (CH), 28.1 (CH$_3$), 25.3 (CH$_3$); *Anti*-diastereoisomer: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.88 (m, 2H), 7.68 (m, 1H), 7.59 (m, 2H), 7.48 (bs, 1H), 7.41 (m, 1H), 7.25-7.10 (m, 2H), 6.17 (dm, J = 5.6 Hz, 1H), 5.80 (dm, J = 5.6 Hz, 1H), 4.52 (d, J = 7.2 Hz, 1H), 4.18 (m, 1H), 3.24 (m, 1H), 3.12 (dd, J = 2.6, 9.4 Hz, 1H), 1.28 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 143.6 (C), 140.3 (CH), 137.0 (C), 134.0 (CH), 130.8 (CH), 130.1 (CH), 129.18 (CH), 129.14 (CH), 128.8 (CH), 125.13 (CH), 124.4 (CH), 122.7 (C), 82.3 (C), 82.1 (CH), 73.9 (CH), 61.6 (CH), 53.7 (CH$_2$), 28.86 (CH$_3$), 21.9 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{21}$H$_{21}$O$_3$NaSBr [*M*+Na]$^+$ 455.0292, found 455.0271.

1-(2-Bromophenyl)-3,3-dimethyl-4-(phenylsulfonyl)-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan (87af).
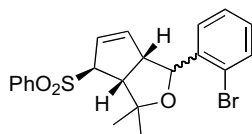
Compound **87af** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (30.2 mg, 0.121 mmol) and *o*-bromobenzaldehyde (28 µL, 0.240 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87af** (28.9 mg, 56%, 1:1 mixture of diastereoisomers) as a yellow solid: *Syn*-diastereoisomer: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.87 (m, 2H), 7.67 (m, 1H), 7.57 (m, 2H), 7.49 (m, 1H), 7.28-7.19 (m, 2H), 7.09 (m, 1H), 5.45 (dm, J = 5.7 Hz, 1H), 5.24 (d, J = 7.0 Hz, 1H), 5.17 (dm, J =

5.7 Hz, 1H), 4.36 (m, 1H), 3.97 (m, 1H), 3.11 (dd, J = 3.1, 8.3Hz, 1H), 1.36 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 138.9 (CH), 138.3 (C), 137.3 (C), 133.8 (CH), 132.2 (CH), 129.1 (CH), 128.7 (CH), 128.0 (CH), 127.0 (CH), 124.2 (CH), 121.1 (C), 80.9 (C), 78.5 (CH), 74.8 (CH), 54.87 (CH), 52.2 (CH), 27.9 (CH$_3$), 25.0 (CH$_3$); *Anti*-diastereoisomer: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.92-7.84 (m, 2H), 7.69-7.62 (m, 1H), 7.60-7.47 (m, 3H), 7.31-7.06 (m, 3H), 6.48 (dm, J = 5.4 Hz, 1H), 5.72 (dm, J = 5.4 Hz, 1H), 4.99 (d, J = 6.5 Hz, 1H), 4.11 (m, 1H), 3.20-3.14 (m, 1H), 3.11, 1.32 (s, 3H), 1.17 (s, 3H), ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 142.0 (CH), 141.0 (C), 137.1 (C), 133.9 (CH), 132.6 (CH), 129.3 (CH), 128.8 (CH), 128.5 (CH), 126.6 (CH), 124.4 (CH), 121.7 (C), 80.9 (C), 78.5 (CH), 73.6 (CH), 61.4 (CH), 53.6 (CH), 28.5 (CH$_3$), 21.7 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{21}$H$_{21}$O$_3$NaSBr [M+Na]$^+$ 455.0292, found 455.0281.

1-(2-Bromophenyl)-3,3-dimethyl-4-(phenylsulfonyl)-3,3a,4,5-tetrahydro-1H-cyclopenta[c]furan (87'af).
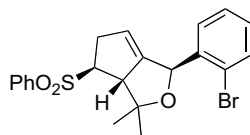
Compound **87'af** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (30.0 mg, 0.120 mmol) and *o*-bromobenzaldehyde (28 µL, 0.240 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87'af** (4.5 mg, 9%) as a yellow solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.92-7.84 (m, 2H), 7.69-7.62 (m, 1H), 7.60-7.47 (m, 3H), 7.31-7.06 (m, 3H), 5.77 (bs, 1H), 5.65 (bs, 1H), 3.71-3.64 (m, 2H), 3.20-3.14 (m, 1H), 2.76-2.68 (m, 1H), 1.41 (s, 3H), 1.20 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 150.5 (C), 141.0 (C), 137.1 (C), 133.8 (CH), 132.5 (CH), 129.0 (CH), 128.9 (CH), 128.5 (CH), 127.8 (CH), 127.5 (CH), 127.3 (CH), 121.2 (C), 117.9 (CH), 82.2 (C), 74.8 (CH), 73.8 (CH), 64.8 (CH), 40.4 (CH$_2$), 27.1 (CH$_3$), 22.3 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{21}$H$_{21}$O$_3$NaSBr [M+Na]$^+$ 455.0292, found 455.0273.

3,3-Dimethyl-1-(naphthalen-2-yl)-4-(phenylsulfonyl)-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan (87ag).
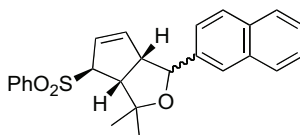
Compound **87ag** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (30.0 mg, 0.120 mmol) and 2-naphtaldehyde (38.2 mg, 0.240 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87ag** (24.8 mg, 51% 2.5:1 mixture of diastereoisomers) as a white solid: *Syn*-diastereoisomer*:* ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (m, 2H), 7.84-7.45 (m, 4H), 7.64 (m, 1H), 7.55 (m, 2H), 7.48-7.40 (m, 3H), 6.19 (m, 1H), 5.80 (m, 1H), 4.71 (d, J = 7.2 Hz, 1H), 4.21 (m, 1H), 3.32 (m, 1H), 3.16 (dd, J = 2.4, 9.6 Hz, 1H), 1.32 (s, 3H), 1.21 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 140.7 (CH), 138.5 (C), 137.0 (C), 133.8 (CH), 133.1 (C), 133.0 (C), 129.1 (CH), 129.0 (CH), 128.5 (CH), 127.8 (CH), 127.6 (CH), 126.1 (CH), 125.8 (CH), 124.8 (CH), 124.6 (CH), 123.7 (CH), 83.0 (C), 82.2 (CH), 74.0 (CH), 61.6 (CH), 53.8 (CH), 28.9 (CH$_3$), 22.0 (CH$_3$); *Anti*-diastereoisomer (NMR spectrum with **87'ag**)*:* ^{1}H NMR (400 MHz, CDCl$_3$, HMQC) δ 7.87 (m, 2H), 7.82-7.74 (m, 4H), 7.63-7.54 (m, 3H), 7.48-7.42 (m, 3H), 5.50 (m, 1H), 5.24 (m, 1H), 5.23 (d, J = 6.7Hz, 1H), 4.42 (m, 1H), 3.64 (m, 1H), 3.13 (dd, J = 2.5, 7.6Hz, 1H), 1.39 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 139.6 (CH), 137.3 (C), 136.1 (C), 133.8 (CH), 133.1 (C), 132.8 (C), 129,1 (CH), 129.0 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 126.0 (CH), 125.7 (CH), 124.6 (CH), 124.3 (CH), 124.2 (CH), 81.2 (C), 79.3 (CH), 75.0 (CH), 57.4 (CH), 52.2 (CH), 28.1 (CH$_3$), 25.4 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{38h24}$O$_3$NaS $[M$+Na$]^+$ 427.1344, found 427.1341.

3,3-Dimethyl-1-(naphthalen-2-yl)-4-(phenylsulfonyl)-3,3a,4,5-tetrahydro-1H-cyclopenta[c]furan (87'ag).
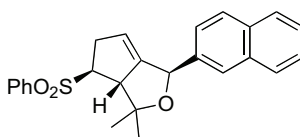
Compound **87'ag** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (30.0 mg, 0.120 mmol) and 2-naphtaldehyde (38.2 mg, 0.240 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87'ag** (3.2 mg, 7%) as a sticky solid: ^{1}H NMR (400 MHz, CDCl$_3$, HMQC) δ 7.96 (m, 2H), 7.82-7.74 (m, 2H), 7.69-7.60 (m, 5H), 7.38 (m, 1H), 7.28 (m, 2H), 5.52 (br s, 1H), 5.09 (bs, 1H), 3.88-3.74 (m, 2H), 3.27-3.19 (m, 1H), 2.76-2.68 (m, 1H), 1.30 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 151.3 (C), 138.4 (C), 137.6 (C), 133.9 (CH), 133.1 (C), 132.9 (C), 129.4 (CH), 128.6 (CH), 128.1 (CH), 127.9 (CH), 126.0 (CH), 125.8 (CH), 124.8 (CH), 124.0 (CH), 118.1 (CH), 79.1 (CH), 75.4 (C), 65.1 (CH), 60.3 (CH), 39.5 (CH$_2$), 28.3 (CH$_3$), 25.0 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{38h24}$O$_3$NaS $[M$+Na]$^+$ 427.1344, found 427.1333.

3,3-Dimethyl-4-(phenylsulfonyl)-1-styryl-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan (87ah).
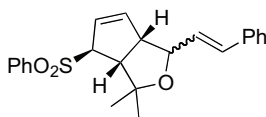
Compound **87ah** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (30.1 mg, 0.121 mmol) and cinnamaldehyde (30 µL, 0.238 mmol) with catalyst **E.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87ah** (27 mg, 59% 2:1 mixture of diastereoisomers *syn/anti* with 6% of unknown side product not separable) as a yellow sticky solid: *Syn*-diastereoisomer*:* ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (m, 2H), 7.69-7.65 (m, 1H), 7.60-7.55 (m, 2H), 7.38-7.21 (m, 5H), 6.58 (d, *J* = 15.2 Hz, 1H), 6.18 (dd, *J* = 7.2, 15.2 Hz, 1H), 6.10 (dm, *J* = 5.8 Hz, 1H), 5.76 (dm, *J* = 5.8 Hz, 1H), 4.18-4.13 (m, 2H), 3.17 (m, 1H), 3.07-3.02 (m, 1H), 1.22 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, PENDANT) δ 140.6 (C), 138.9 (C), 133.9 (CH), 132.1 (CH), 129.1 (CH), 128.5 (CH), 127.9 (CH), 127.8 (CH), 127.9 (CH), 126.6 (CH), 126.3 (CH), 124.8 (CH), 82.2 (CH), 81.9 (C), 74.0 (CH), 59.4 (CH), 53.6 (CH), 29.0 (CH$_3$), 25.3 (CH$_3$); *Anti*-diastereoisomer: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.88 (m, 2H), 7.69-7.65 (m, 1H), 7.60-7.55 (m, 2H), 7.38-7.21 (m, 5H), 6.60 (d, *J* = 15.9 Hz, 1H), 6.02 (dd, *J* = 7.4,

15.9Hz, 1H), 5.94 (dm, J = 5.5 Hz, 1H), 5.67 (dm, J = 5.5 Hz, 1H), 4.58 (t, J = 7.1 Hz, 1H), 4.36 (m, 1H), 3.45 (m, 1H), 3.07-3.02 (m, 1H), 1.29 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, PENDANT) δ 142.9 (C), 139.4 (C), 133.8 (CH), 132.6 (CH), 129.2 (CH), 129.1 (CH), 128.8 (CH), 128.5 (CH), 127.8 (CH), 126.5 (CH), 126.3 (CH), 124.9 (CH), 82.2 (CH), 81.9 (C), 78.8 (CH), 56.9 (CH), 52.4 (CH), 28.1 (CH$_3$), 22.1 (CH$_3$); HRMS-ESI m/z calcd for C$_{23}$H$_{24}$O$_3$NaS $[M$+Na$]^+$403.1344, 403.1346 found.

3,3-Dimethyl-1-(2-methylprop-1-enyl)-4-(phenylsulfonyl)-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan (87ai).
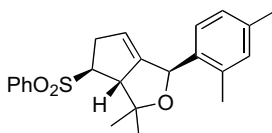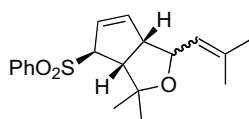

Compound **87ai** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (32.0 mg, 0.129 mmol) and 3-methylbut-2-enal (24 μL, 0.240 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87ai** (25.0 mg, 58% 2:1 mixture of diastereoisomers) as a yellow oil: *Syn*-diastereoisomer: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89 (m, 2H), 7.67 (m, 1H), 7.57 (m, 2H), 6.04 (dm, J = 5.7 Hz, 1H), 5.72 (dm, J = 5.7Hz, 1H), 5.18 (dm, J = 8.7 Hz, 1H), 4.23 (dd, J = 6.2, 8.7 Hz, 1H), 4.12 (m, 1H), 3.00-2.95 (m, 2H), 1.71 (s, 3H), 1.66 (s, 3H), 1.15 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, PENDANT) δ 140.9 (CH), 137.3 (C), 137.1 (C), 133.8 (CH), 129.2 (CH), 129.0 (CH), 124.6 (CH), 124.4 (CH), 81.2 (C), 77.6 (CH), 74.0 (CH), 59.8 (CH), 53.7 (CH), 28.9 (CH$_3$), 25.8 (CH$_3$), 21.9 (CH$_3$), 18.3 (CH$_3$); *Anti*-diastereoisomer: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89 (m, 2H), 7.67 (m, 1H), 7.57 (m, 2H), 5.93 (dm, J = 5.8 Hz, 1H), 5.63 (dm, J = 5.8 Hz, 1H), 5.02 (dm, J = 7.7 Hz, 1H), 4.65 (dd, J = 7.1, 7.7 Hz, 1H), 4.33 (m, 1H), 3.36-3.30 (m, 1H), 3.00-2.95 (m, 1H), 1.71 (s, 3H), 1.66 (s, 3H), 1.15 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, PENDANT) δ 139.4 (CH), 137.3 (C), 137.0 (C), 133.7 (CH), 129.1 (CH), 129.0 (CH), 124.2 (CH), 121.7 (CH), 81.2 (C), 74.8 (CH), 74.5 (CH), 56.0 (CH), 52.2 (CH), 28.0 (CH$_3$), 25.8 (CH$_3$), 25.2 (CH$_3$), 18.5 (CH$_3$); HRMS-ESI m/z calcd for C$_{31h24}$O$_3$NaS $[M$+Na$]^+$ 355.1344, found 355.1354.

**1,1-Bis(trideuteromethyl)-3,3-dimethyl-4-(phenylsulfonyl)-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan (87aj).**
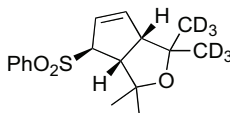
Compound **87aj** was synthesized following the general procedure for the reaction of 1,5-enynes with carbonyl compounds, starting from **38f** (30.5 mg, 0.121 mmol) and acetone-d6 (20 μL, 0.480 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87aj** (21.1 mg, 55% 1:1 mixture of **87aj**/**87'aj**) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.93 (m, 2H), 7.69-7.65 (m, 1H), 7.61-7.54 (m, 2H), 6.07 (dt, J = 1.9, 5.7 Hz, 1H), 5.66 (dt, J = 2.4, 5.7 Hz, 1H), 4.20 (m, 1H), 3.19-3.11 (m, 2H), 1.23 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 141.1 (CH), 138.6 (C), 133.81 (CH), 129.05 (CH), 128.5 (CH), 124.3 (CH), 81.5 (C), 74.6 (CH), 62.3 (CH), 53.78 (C), 53.75 (CH), 31.9 (CH$_3$), 26.7 (CH$_3$), the CD$_3$ signals were not observed; HRMS-ESI *m/z* calcd for C$_{17}$H$_{16}$D$_6$O$_3$NaS [*M*+Na]$^+$ 335.1564, found 335.1551.

1,1-Bis(trideuteromethyl)-3,3-dimethyl-4-(phenylsulfonyl)-3,3a,4,5-tetrahydro-1H-cyclopenta[c]furan (87'aj).

Compound **87'aj** was synthesized following the general procedure for the reaction of 1,5-enynes with carbonyl compounds, starting from **38f** (30.5 mg, 0.121 mmol) and acetone-d6 (20 μL, 0.480 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87'aj** (21.1 mg, 55% 1:1 mixture of **87aj**/**87'aj**) as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (m, 2H), 7.69-7.65 (m, 1H), 7.61-7.54 (m, 2H), 5.24 (m, 1H), 3.76-3.68 (m, 2H), 3.26-3.19 (m, 1H), 2.79-2.71 (m, 1H), 1.12 (s, 3H), 1.03 (s, 3H), the CD$_3$ signals were not observed; ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 156.2 (C), 137.5 (C), 133.89 (CH), 129.3 (CH), 129.06 (CH), 114.5 (CH), 78.3 (C), 65.1 (CH), 59.5 (CH), 39.7 (CH$_2$), 28.7 (CH$_3$), 24.2 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{17}$H$_{16}$D$_6$O$_3$NaS [*M*+Na]$^+$ 335.1564, found 335.1551.

3',3'-Dimethyl-4'-(phenylsulfonyl)-3',3a',4',6a'-tetrahydrospiro[cyclohexane-1,1'-cyclopenta[c]furan] (87ak).
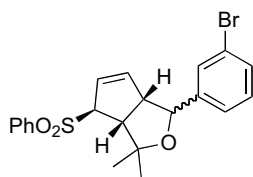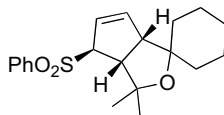

Compound **87ak** was synthesized following the general procedure for the reaction of 1,5-enynes with carbonyl compounds, starting from **38f** (30.9 mg, 0.124 mmol) and cyclohexanone (50 µL, 0.483 mmol) with catalyst **Q**. The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87ak** (28.9 mg, 67% 1:2 mixture of **87ak**/**87'ak**) as a yellow oil: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.89 (dm, J = 7.8 Hz, 2H), 7.68-7.64 (m, 1H), 7.59-7.55 (m, 2H), 6.14 (dm, J = 5.4 Hz, 1H), 5.65 (dm, J = 5.4 Hz, 1H), 4.16 (m, 1H), 3.13 (bs, 2H), 1.69-1.59 (m, 2H), 1.55-1.28 (m, 8H), 1.21 (s, 3H), 1.05 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$, HMQC) δ 141.0 (CH), 137.6 (C), 133.7 (CH), 129.05 (CH), 129.03 (CH), 124.5 (CH), 83.5 (C), 77.7 (C), 74.5 (CH), 60.6 (CH), 53.1 (CH), 38.0 (CH$_2$), 36.0 (CH$_2$), 32.2 (CH$_3$), 27.0 (CH$_3$), 25.4 (CH$_2$), 25.3 (CH$_2$), 23.0 (CH$_2$).

3',3'-Dimethyl-4'-(phenylsulfonyl)-3',3a',4',5'-tetrahydrospiro[cyclohexane-1,1'-cyclopenta[c]furan] (87'ak).
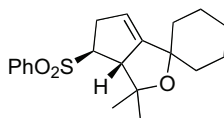
Compound **87'ak** was synthesized following the general procedure for the reaction of 1,5-enynes with carbonyl compounds, starting from **38f** (30.9 mg, 0.124 mmol) and cyclohexanone (50 µL, 0.483 mmol) with catalyst **Q**. The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87'ak** (28.9 mg, 67% 1:2 mixture of **87ak**/**87'ak**) as a yellow oil: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.92 (dm, J = 7.8 Hz, 2H), 7.68-7.64 (m, 1H), 7.59-7.55 (m, 2H), 5.36 (m, 1H), 3.73-3.65 (m, 2H), 3.22 (ddm, J = 8.6, 15.8 Hz, 2H), 2.72 (ddt, J = 2.9, 8.2, 15.8 Hz, 2H), 1.69-1.59 (m, 2H), 1.55-1.28 (m, 8H), 1.12 (s, 3H), 1.03 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$, HMQC) δ 155.2 (CH), 138.7 (C), 133.8 (CH), 129.3 (CH), 128.5 (CH), 114.9 (CH), 81.0 (C), 77.7

(C), 64.6 (CH), 59.9 (CH), 40.3 (CH$_2$), 39.9 (CH$_2$), 37.9 (CH$_2$), 28.8 (CH$_3$), 25.2 (CH$_2$), 24.6 (CH$_3$), 23.4 (CH$_2$).

### 3,3,6a-Trimethyl-4-(phenylsulfonyl)-1-styryl-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan (87ba).
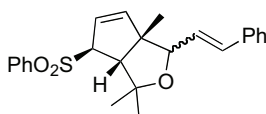
Compound **87ba** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38g** (29.3 mg, 0.112 mmol) and cinnamaldehyde (29 μL, 0.224 mmol). The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87ba** (2:1 *Syn*/*Anti*) (33.1 mg, 75% 4.7:1 mixture of **87'ba**/**87ba**) as a yellow solid: *Syn*-diastereoisomer: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89 (m, 2H), 7.67 (m, 1H), 7.60 (m, 2H), 7.35 (m, 2H), 7.26-7.27 (m, 2H), 7.22-7.16 (m, 1H), 6.59 (d, *J* = 14.9 Hz, 1H), 6.01-5.93 (m, 1H), 5.70 (dd, *J* = 2.3, 5.8 Hz, 1H), 5.61 (dd, *J* = 2.3, 5.8 Hz, 1H), 4.39 (m, 1H), 4.24 (d, *J* = 8.1 Hz, 1H), 1.73 (d, *J* = 5.8 Hz, 1H), 1.59 (s, 3H), 1.25 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 145.0 (CH), 137.1 (C), 136.4 (C), 133.9 (CH), 132.6 (CH), 129.2 (CH), 129.11 (CH), 127.7 (CH), 126.52 (CH), 125.63 (CH), 122.6 (CH), 84.8 (CH), 80.5 (C), 74.4 (CH), 64.2 (C), 61.2 (CH), 30.0 (CH$_3$), 26.8 (CH$_3$), 21.7 (CH$_3$); *Anti*-diastereoisomer: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89 (m, 2H), 7.67 (m, 1H), 7.60 (m, 2H), 7.35 (m, 2H), 7.26-7.27 (m, 2H), 7.22-7.16 (m, 1H), 6.59 (d, *J* = 14.9 Hz, 1H), 6.16 (dd, *J* = 7.3, 14.9 Hz, 1H), 5.91 (dd, *J* = 2.2, 5.6 Hz, 1H), 5.67 (dd, *J* = 2.2, 5.6 Hz, 1H), 4.26-4.24 (m, 1H), 4.12 (d, *J* = 7.3 Hz, 1H), 1.73 (d, *J* = 5.8 Hz, 1H), 1.59 (s, 3H), 1.30 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 143.4 (CH), 137.2 (C), 136.3 (C), 133.8 (CH), 132.7 (CH), 129.18 (CH), 129.0 (CH), 127.8 (CH), 126.50 (CH), 125.68 (CH), 122.7 (CH), 85.6 (CH), 80.8 (C), 75.1 (CH), 63.5 (C), 58.2 (CH), 27.7 (CH$_3$), 25.4 (CH$_3$), 23.6 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{24}$H$_{26}$O$_3$NaS [*M*+Na]$^+$ 417.1500, found 417.1498.

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3,3,6-Trimethyl-4-(phenylsulfonyl)-1-styryl-3,3a,4,5-tetrahydro-1H-cyclopenta[c]furan (87'ba).
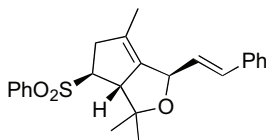
Compound **87'ba** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38g** (29.3 mg, 0.112 mmol) and cinnamaldehyde (29 μL, 0.224 mmol). The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87'ba** (33.1 mg, 75% 4.7:1 mixture of **87'ba**/**87ba**) as a yellow solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89 (m, 2H), 7.67 (m, 1H), 7.60 (m, 2H), 7.35 (m, 2H), 7.26-7.27 (m, 2H), 7.22-7.16 (m, 1H), 6.8 (d, J = 15.5 Hz, 1H), 5.95 (d, J = 15.5 Hz, 1H), 3.49 (d, J = 7.3 Hz, 1H), 2.74 (d, J = 1.6 Hz, 1H), 2.59-2.53 (m, 1H), 2.13 (dd, J = 7.6, 14.9 Hz, 1H), 1.68 (d, J = 6.1 Hz, 1H), 1.51 (s, 3H), 1.33 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 138.1 (C), 137.1 (C), 133.7 (CH), 129.3 (CH), 128.6 (CH), 128.4 (CH), 128.2 (C), 127.2 (CH), 127.0 (C), 126.0 (CH), 88.7 (C), 75.2 (CH), 70.6 (CH), 58.7 (CH), 40.1 (CH$_2$), 27.0 (CH$_3$), 26.3 (CH$_3$), 23.0 (CH$_3$); HRMS-ESI m/z calcd for C$_{24}$H$_{26}$O$_3$NaS $[M$+Na$]^+$ 417.1500, found 417.1498.

### 1-Cyclopropyl-6-ethyl-3,3-dimethyl-4-(phenylsulfonyl)-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan (87ca).
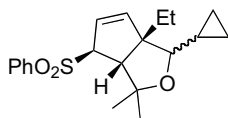
Compound **87ca** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38h** (30.1mg, 0.108 mmol) and (16μL, 0.216 mmol) with catalyst **E.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **87ca** (49.6 mg, 71% 2.7:1 mixture of **87ca**/**84**) as a colorless oil. Compound **87ca** was isolated pure after semi-preparative HPLC (H$_2$O/THF 60:40) as a colorless oil (1:1 mixture of diastereoisomers *syn/anti*): *Syn*-diastereoisomer: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (m, 2H), 7.71-7.66 (m, 1H), 7.62-7.57 (m, 2H), 5.81 (d, J = 2.3, 5.6 Hz, 1H), 5.64 (d, J = 2.2, 5.6 Hz, 1H), 4.32 (m, 1H),

2.64 (d, J = 5.6 Hz, 1H), 2.54 (d, J = 9.5 Hz, 1H), 1.69-1.50 (m, 2H), 1.207 (s, 3H), 1.200 (s, 3H), 0.93 (m, 1H), 0.80 (t, J = 7.2Hz, 3H), 0.65-0.47 (m, 4H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 142.7 (CH), 138.0 (C), 133.7 (CH), 129.2 (CH), 129.1 (CH), 122.9 (CH), 91.3 (CH), 79.6 (C), 74.3 (CH), 67.2 (C), 55.9 (CH), 27.1 (CH$_3$), 25.4 (CH$_2$), 25.3 (CH$_3$), 9.2 (CH$_3$), 4.4 (CH), 1.3 (CH$_2$), 1.0 (CH$_2$); *Anti*-diastereoisomer: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.92 (m, 2H), 7.71-7.66 (m, 1H), 7.62-7.57 (m, 2H), 5.85 (d, J = 2.2, 5.6 Hz, 1H), 5.64 (d, J = 2.2, 5.6 Hz, 1H), 4.39 (m, 1H), 2.91 (d, J = 8.8 Hz, 1H), 2.70 (d, J = 5.2 Hz, 1H), 1.69-1.50 (m, 2H), 1.17 (s, 3H), 1.13 (s, 3H), 0.68 (t, J = 7.6 Hz, 3H), 0.65-0.47 (m, 1H), 0.31-0.21 (m, 3H), 0.076 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 143.6 (CH), 137.1 (C), 133.8 (CH), 129.1 (CH), 129.0 (CH), 122.8 (CH), 88.3 (CH), 79.4 (C), 74.9 (CH), 67.5 (C), 57.0 (CH), 31.2 (CH$_2$), 30.4 (CH$_3$), 23.7 (CH$_3$), 9.5 (CH$_3$), 3.5 (CH), 1.3 (CH$_2$), 1.0 (CH$_2$); HRMS-ESI *m/z* calcd for C$_{20}$H$_{26}$O$_3$NaS [M+Na]$^+$ 369.1500, found 369.1508.

### 3,3-Dimethyl-5-(phenylsulfonyl)-7-(3,4,5-trimethoxybenzylidene)-2-oxabicyclo[2.2.1]heptane (91).
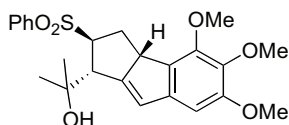
Compound **91** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38f** (30.0 mg, 0.120 mmol) and 3,4,5-trimethoxybenzaldehyde (47.5 mg, 0.242 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1-4:1 hexane/EtOAc) to give compound **91** (25.0 mg, 47%) as a orange solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.03 (m, 2H), 7.70 (m, 1H), 7.62 (m, 2H), 6.63 (s, 1H), 6.42 (m, 1H), 4.19 (dd, J = 8.6, 13.2 Hz, 1H), 4.10 (dd, J = 4.0, 8.6 Hz, 1H), 3.92 (s, 3H), 3.85 (s, 3H), 3.83 (s, 3H), 3.80 (m, 1H), 2.55 (dd, J = 8.0, 13.7 Hz, 1H), 2.48 (br s, 1H), 1.51 (s, 3H), 1.35-1.26 (m, 1H), 1.15 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 156.3 (C), 153.8 (C), 149.8 (C), 143.3 (C), 139.2 (C), 137.8 (C), 133.9 (CH), 129.4 (CH), 128.8 (CH), 127.7 (C), 122.12 (CH), 100.9 (CH), 72.0 (C), 71.6 (CH), 61.1 (CH$_3$), 60.4 (CH$_3$), 56.2 (CH$_3$), 53.9 (CH), 49.2 (CH), 30.0 (CH$_3$), 28.8 (CH$_2$), 24.5 (CH$_3$); HRMS-ESI *m/z* calcd for C$_{24}$H$_{28}$O$_6$NaS [M+Na]$^+$ 467.1504, found 467.1481.

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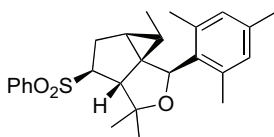
Compound 93.

Compound **93** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38h** (29.0 mg, 0.105 mmol) and and 2,4,6-trimethylbenzaldehyde (32 µL, 0.216 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **93** (19.0 mg, 43%) as a white solid: mp 143-145ºC; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (m, 2H), 7.67 (m, 1H), 7.59 (m, 2H), 6.79 (s, 1H), 6.95 (s, 1H), 5.44 (s, 1H), 3.51 (m, 1H), 3.03 (d, $J = 2.7$ Hz, 1H), 2.56 (m, 1H), 2.51 (s, 3H), 2.24 (s, 3H), 2.20 (s, 3H), 1.54 (dq, $J = 4.3, 6.2$ Hz, 1H), 1.21 (s, 3H), 0.93 (m, 1H), 0.87 (s, 3H), 0.37 (d, $J = 6.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 138.8 (C), 137.7 (C), 137.1 (C), 136.1 (C), 133.7 (CH), 131.8 (C), 130.8 (CH), 129.3 (CH), 128.9 (CH), 128.7 (CH), 80.2 (C), 74.9 (CH), 68.1 (CH), 60.3 (CH), 45.8 (C), 32.5 (CH$_2$), 31.6 (CH$_3$), 25.7 (CH$_3$), 22.0 (CH), 21.0 (CH$_3$), 20.77 (CH$_3$), 20.72 (CH$_3$), 20.6 (CH$_3$), 14.3 (CH); HRMS-ESI m/z calcd for C$_{26}$H$_{32}$O$_3$NaS [M+Na]$^+$ 447.1970, found 447.1969.

Compound 94.
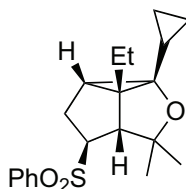
Compound **94** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38h** (30.1mg, 0.108 mmol) and (16µL, 0.216 mmol) with catalyst **Q.** The residue was purified by column chromatography (8:1 hexane/EtOAc) to give compound **94** (49.6 mg, 71% 2:1.6 mixture of isomer **87ca/94**) as a colorless oil. Compuond **94** was isolated pure after semi-preparative HPLC (H$_2$O/THF 60:40) as a white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89 (m, 2H), 7.65 (m, 1H), 7.57 (m, 2H), 3.45 (d, $J = 7.3$ Hz, 1H), 2.78 (d, $J = 1.7$ Hz, 1H), 2.38 (dd, $J = 6.5, 15.2$ Hz, 1H), 2.19 (dq, $J = 7.6, 14.9$ Hz, 1H), 1.91 (dd, $J = 7.3, 15.2$ Hz, 1H), 1.66 (dq, $J = 7.6, 14.9$ Hz, 1H), 1.32 (s, 3H), 1.21 (br d, $J = 6.5$Hz, 1H), 1.11 (t, $J = 7.6$ Hz,

3H), 1.11-1.06 (m, 1H), 1.06 (s, 3H), 0.57 (m, 1H), 0.45 (m, 1H), 0.36 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$, HMQC) δ 138.6 (C), 133.5 (CH), 129.2 (CH), 128.4 (CH), 86.7 (C), 76.8 (C), 71.7 (CH), 59.9 (CH), 46.6 (C), 33.6 (CH), 27.6 (CH$_3$), 25.8 (CH$_2$), 23.4 (CH$_3$), 22.3 (CH$_2$), 13.0 (CH$_3$), 11.1 (CH), 2.8 (CH$_2$), 2.4 (CH$_2$); HRMS-ESI *m/z* calcd for C$_{20}$H$_{26}$O$_3$NaS [*M*+Na]$^+$ 369.1500, found 369.1508.

((*E*)-3-Phenyl-4-((*E*)-3-phenylallylidene)cyclopent-2-enylsulfonyl)benzene (95a).
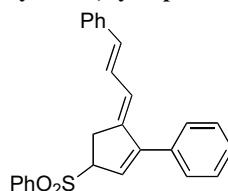
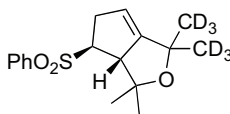

Compound **95a** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38i** (33 mg, 0.10 mmol) and cinnamaldehyde (26 µL, 0.20 mmol). The residue was purified by column chromatography (10:1 hexane/EtOAc) to give compound **95a** (30 mg, 75%) as a yellow oil: ^{1}H NMR (400 MHz, C$_6$D$_6$) δ 7.82-7.80 (m, 2H), 7.22 (d, *J* =7.5 Hz, 2H), 7.15-7.11 (m, 7H), 7.04 (t, *J* = 7.2 Hz, 1H), 6.92-6.83 (m, 3H), 6.74 (dd, *J* = 15.4, 11.4 Hz, 1H), 6.12 (dt, *J* = 15.3, 2.3 Hz, 1H), 6.06 (dt, *J* = 11.3, 2.3 Hz, 1H), 5.93 (d, *J* = 2.9 Hz, 1H), 4.20 (dt, *J* = 8.4, 2.4 Hz, 1H), 3.41 (dt, *J* = 17.9, 2.2 Hz, 1H), 2.74 (ddd, *J* = 18.0, 8.2, 2.3 Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, C$_6$D$_6$) δ 153.3 (C), 143.6 (C), 138.0 (C), 137.8 (C), 134.9 (C), 134.2 (CH), 133.4 (CH), 129.7 (CH), 129.0 (CH), 128.8 (CH), 128.8 (CH), 128.6 (CH), 128.2 (CH), 128.0 (CH), 126.9 (CH), 125.7 (CH), 123.1 (CH), 70.1 (CH), 30.8 (CH$_2$).

1-Methyl-4-((*E*)-5-((*E*)-3-phenylallylidene)-3-(phenylsulfonyl)cyclopent-1-enyl)benzene (95b).
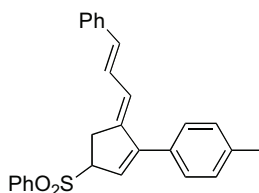
Compound **95b** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38j** (34 mg, 0.10 mmol) and cinnamaldehyde (26 μL, 0.20 mmol). The residue was purified by column chromatography (10:1 hexane/EtOAc) to give compound **95b** (33 mg, 80%) as a yellow oil: ^{1}H NMR (400 MHz, , C_6D_6) δ 7.83-7.80 (m, 2H), 7.22 (d, J =7.4 Hz, 2H), 7.13-7.02 (m, 5H), 7.00 (d, J =7.8 Hz, 2H), 6.91-6.82 (m, 3H), 6.75 (dd, J = 15.4, 11.4 Hz, 1H), 6.16 (d, J = 15.7 Hz, 1H), 6.12 (d, J = 11.4 Hz, 1H), 5.96 (d, J = 2.7 Hz, 1H), 4.21 (dt, J = 8.4, 2.4 Hz, 1H), 3.41 (dt, J = 18.1, 2.1 Hz, 1H), 2.74 (ddd, J = 18.0, 8.4, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, , C_6D_6) δ 153.3 (C), 143.8 (C), 138.4 (C), 138.0 (C), 137.9 (C), 134.1 (CH), 133.3 (C), 132.0 (CH), 129.7 (CH), 129.5 (CH), 129.0 (CH), 128.8 (CH), 128.6 (CH), 128.0 (CH), 126.9 (CH), 125.8 (CH), 123.1 (CH), 70.2 (CH), 30.8 (CH_2), 21.2 (CH_3).

**1-Methoxy-4-((*E*)-5-((*E*)-3-phenylallylidene)-3-(phenylsulfonyl)cyclopent-1-enyl)benzene (95c).**
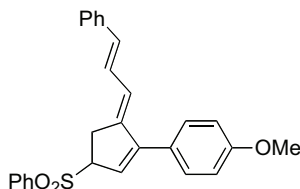
Compound **95c** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38k** (30.1 mg, 0.085 mmol) and cinnamaldehyde (22 μL, 0.171 mmol) with catalyst **K**. The residue was purified by column chromatography (6:1 hexane/EtOAc) to give compound **95c** (25.1 mg, 67%) as a yellow solid: ^{1}H NMR (400 MHz, C_6D_6) δ 7.81 (dm, J = 8.8 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 7.17-7.01 (m, 4H), 6.89-6.82 (m, 4H), 6.77 (dm, J = 8.8 Hz, 2H), 6.74 (d, J = 11.6 Hz, 1H), 6.19 (d, J = 11.6 Hz, 1H), 6.12 (dm, J = 15.8 Hz, 1H), 5.94 (d, J = 2.7 Hz, 1H), 4.21 (dm, J = 8.4 Hz, 1H), 3.40 (dm, J = 18.1 Hz, 1H), 3.31 (s, 3H), 2.74 (ddd, J = 2.7, 8.4, 18.1 Hz, 1H); ^{13}C NMR (100 MHz, CD_2Cl_2, HMQC) δ 160.2 (C), 153.1 (C), 143.6 (C), 137.7 (C), 137.2 (C), 134.1 (CH), 133.8 (CH), 129.7 (CH), 129.5 (CH), 129.3 (CH), 129.0 (CH), 128.0 (CH), 126.7 (CH), 126.63 (C), 126.61 (CH), 125.9 (CH), 122.8 (CH), 114.29 (CH), 70.1 (CH), 55.6 (CH_3), 30.8 (CH_2); HRMS-ESI *m/z* calcd for $C_{27}H_{24}O_3NaS$ [*M*+Na][+] 451.1344, found 451.1353.

**1-Chloro-4-((*E*)-5-((*E*)-3-phenylallylidene)-3-(phenylsulfonyl)cyclopent-1-enyl)benzene (95e).**
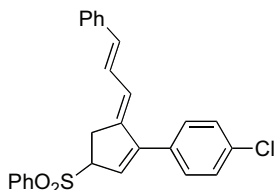
Compound **95e** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38p** (30.0 mg, 0.084 mmol) and cinnamaldehyde (35 µL, 0.275 mmol). The residue was purified by column chromatography (6:1 hexane/EtOAc) to give compound **95e** (25.1 mg, 67%) as a yellow solid: ^{1}H NMR (400 MHz, C_6D_6) δ 7.89 (dm, J = 8.2 Hz, 2H), 7.34 (m, 2H), 7.22 (m, 2H), 7.16 (m, 1H), 7.02-6.91 (m, 5H), 6.82 (dd, J = 11.3, 15.4 Hz, 1H), 6.32 (d, J = 15.4 Hz, 1H), 6.03 (dm, J = 11.3 Hz, 1H), 5.95 (d, J = 2.8 Hz, 1H), 4.27 (dm, J = 8.4 Hz, 1H), 3.48 (dm, J = 18.1 Hz, 1H), 2.79 (ddd, J = 2.8, 8.5, 18.1 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6, HMQC) δ 151.6 (C), 142.9 (C), 137.7 (C), 137.8 (C), 134.3 (C), 134.2 (CH), 133.1 (CH), 132.7 (C), 129.6 (CH), 129.2 (CH), 128.7 (CH), 128.5 (CH), 126.6 (CH), 125.1 (CH), 122.8 (CH), 69.7 (CH), 30.5 (CH_2); HRMS-ESI *m/z* calcd for $C_{26}H_{21}O_2ClONaS$ [*M*+Na][+] 455.0848, found 455.0854.

1-(4-((*E*)-5-((*E*)-3-Phenylallylidene)-3-(phenylsulfonyl)cyclopent-1-enyl)phenyl)ethanone (95d).
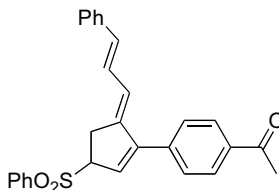
Compound **95d** was synthesized following the general procedure for the reaction of 1,5-enynes with aldehydes, starting from **38l** (29.8 mg, 0.081 mmol) and cinnamaldehyde (35 µL, 0.265 mmol). The residue was purified by column chromatography (6:1 hexane/EtOAc) to give compound **95d** (28.0 mg, 78%) as a yellow solid: ^{1}H NMR (400

MHz, C_6D_6) δ 7.81-7.76 (m, 4H), 7.23 (d, J = 7.6 Hz, 2H), 7.12 (d, J = 7.6 Hz, 2H), 7.05 (m, 3H), 6.93-6.84 (m, 3H), 6.74 (dd, J = 11.4, 15.4 Hz, 1H), 6.23 (d, J = 15.4 Hz, 1H), 6.00 (dm, J = 11.4 Hz, 1H), 5.93 (d, J = 2.8 Hz, 1H), 4.20 (dm, J = 8.2 Hz, 1H), 3.41 (dm, J = 17.7 Hz, 1H), 2.72 (ddd, J = 2.6, 8.2, 17.7 Hz, 1H); ^{13}C NMR (100 MHz, CD_2Cl_2, HMQC) δ 197.6 (C), 152.7 (C), 142.9 (CH), 139.1 (C), 137.5 (C), 137.4 (C), 137.1 (C), 134.3 (CH), 134.2 (CH), 129.5 (CH), 129.4 (CH), 129.0 (CH), 128.78 (CH), 128.73 (CH), 128.5 (CH), 128.2 (CH), 126.7 (C), 125.6 (CH), 123.2 (CH), 70.1 (CH), 30.8 (CH_2), 26.8 (CH_3); HRMS-ESI m/z calcd for $C_{28}H_{24}O_3NaS$ $[M+Na]^+$ 463.1344, found 463.1360.

Crystallographic Data.

Crystallographic data for compound 43f.
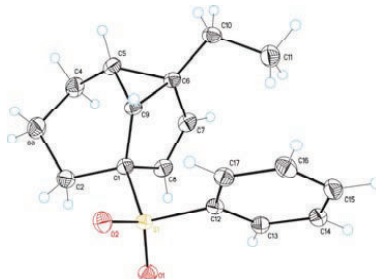
Table 15. **Crystal data and structure refinement for 43f.**

Empirical formula	C17 H20 O2 S
Formula weight	288.39
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/c
Unit cell dimensions	a = 8.2782(14) Å a= 90.00 °.
	b = 11.908(2) Å b = 103.858(6) °.
	c = 15.333(3) Å g = 90.00 °.
Volume	1467.5(4) Å^3
Z	4
Density (calculated)	1.305 Mg/m^3
Absorption coefficient	0.219 mm^{-1}
F(000)	616
Crystal size	0.35 x 0.15 x 0.10 mm^3
Theta range for data collection	2.74 to 32.50 °.
Index ranges	-12 <=h<=12 ,-14 <=k<=17 ,-22 <=l<=23
Reflections collected	4972
Independent reflections	4300 [R(int) = 0.0259]
Completeness to theta =32.50 °	0.938 %
Absorption correction	Empirical
Max. and min. transmission	0.9784 and 0.9272
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4972 / 0 / 182
Goodness-of-fit on F^2	1.096

Final R indices [I>2sigma(I)]	R1 = 0.0406 , wR2 = 0.1136
R indices (all data)	R1 = 0.0484 , wR2 = 0.1238
Largest diff. peak and hole	0.591 and -0.524 e.Å^{-3}

Table 16. **Bond lengths [Å] and angles [°] for 43f.**

_____

Bond lengths

S1-O1	1.4508(9)
S1-O2	1.4538(9)
S1-C12	1.7711(11)
S1-C1	1.819(12)
C1-C8	1.5229(16)
C1-C9	1.5252(15)
C1-C2	1.5619(16)
C2-C3	1.546(18)
C3-C4	1.537(18)
C4-C5	1.5207(18)
C5-C9	1.5199(16)
C5-C6	1.5295(17)
C6-C7	1.4857(16)
C6-C10	1.5138(16)
C6-C9	1.5335(15)
C7-C8	1.337(16)
C10-C11	1.5312(19)
C12-C17	1.3963(16)
C12-C13	1.3973(17)
C13-C14	1.3953(16)
C14-C15	1.3956(17)
C15-C16	1.3941(19)
C16-C17	1.3958(16)

Angles

O1-S1-O2	118.00(5)
O1-S1-C12	107.84(5)
O2-S1-C12	107.41(5)
O1-S1-C1	107.32(5)
O2-S1-C1	108.43(5)
C12-S1-C1	107.41(5)

C8-C1-C9	103.67(9)
C8-C1-C2	111.95(10)
C9-C1-C2	113.78(10)
C8-C1-S1	109.67(8)
C9-C1-S1	112.05(8)
C2-C1-S1	105.82(7)
C3-C2-C1	112.37(9)
C4-C3-C2	112.47(11)
C5-C4-C3	108.11(10)
C9-C5-C4	117.61(10)
C9-C5-C6	60.38(7)
C4-C5-C6	125.31(11)
C7-C6-C10	121.55(10)
C7-C6-C5	114.73(10)
C10-C6-C5	117.87(10)
C7-C6-C9	104.85(9)
C10-C6-C9	122.55(10)
C5-C6-C9	59.50(7)
C8-C7-C6	112.15(10)
C7-C8-C1	111.82(10)
C5-C9-C1	111.69(9)
C5-C9-C6	60.12(8)
C1-C9-C6	107.30(9)
C6-C10-C11	112.98(10)
C17-C12-C13	121.61(10)
C17-C12-S1	119.25(9)
C13-C12-S1	118.93(8)
C14-C13-C12	119.04(11)
C13-C14-C15	119.88(11)
C16-C15-C14	120.50(11)
C15-C16-C17	120.30(11)
C16-C17-C12	118.66(11)

Table 17. **Torsion angles [°] for 43f.**

_____

O1-S1-C1-C8	-51.50(9)
O2-S1-C1-C8	-179.99(7)
C12-S1-C1-C8	64.22(9)
O1-S1-C1-C9	-166.05(8)
O2-S1-C1-C9	65.46(9)
C12-S1-C1-C9	-50.33(9)
O1-S1-C1-C2	69.42(9)
O2-S1-C1-C2	-59.06(9)
C12-S1-C1-C2	-174.85(8)
C8-C1-C2-C3	-88.80(13)
C9-C1-C2-C3	28.33(14)
S1-C1-C2-C3	151.77(9)
C1-C2-C3-C4	29.82(15)
C2-C3-C4-C5	-62.93(14)
C3-C4-C5-C9	37.34(15)
C3-C4-C5-C6	109.10(13)
C9-C5-C6-C7	93.21(10)
C4-C5-C6-C7	-11.31(15)
C9-C5-C6-C10	-113.25(12)
C4-C5-C6-C10	142.23(12)
C4-C5-C6-C9	-104.52(12)
C10-C6-C7-C8	148.06(12)
C5-C6-C7-C8	-59.47(14)
C9-C6-C7-C8	3.40(14)
C6-C7-C8-C1	-0.64(15)
C9-C1-C8-C7	-2.40(14)
C2-C1-C8-C7	120.65(12)
S1-C1-C8-C7	-122.21(10)
C4-C5-C9-C1	18.86(14)
C6-C5-C9-C1	-98.08(10)
C4-C5-C9-C6	116.93(12)
C8-C1-C9-C5	68.38(11)
C2-C1-C9-C5	-53.46(13)
S1-C1-C9-C5	-173.45(8)
C8-C1-C9-C6	4.33(12)
C2-C1-C9-C6	-117.51(10)

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S1-C1-C9-C6	122.51(9)
C7-C6-C9-C5	-110.26(10)
C10-C6-C9-C5	105.53(12)
C7-C6-C9-C1	-4.74(12)
C10-C6-C9-C1	-148.95(11)
C5-C6-C9-C1	105.52(10)
C7-C6-C10-C11	-44.59(16)
C5-C6-C10-C11	163.76(10)
C9-C6-C10-C11	93.86(13)
O1-S1-C12-C17	-147.09(9)
O2-S1-C12-C17	-18.94(11)
C1-S1-C12-C17	97.52(10)
O1-S1-C12-C13	27.71(11)
O2-S1-C12-C13	155.86(9)
C1-S1-C12-C13	-87.68(10)
C17-C12-C13-C14	0.61(17)
S1-C12-C13-C14	-174.07(9)
C12-C13-C14-C15	-0.39(17)
C13-C14-C15-C16	-0.24(18)
C14-C15-C16-C17	0.67(18)
C15-C16-C17-C12	-0.45(18)
C13-C12-C17-C16	-0.19(17)
S1-C12-C17-C16	174.47(9)

Crystalographic data for 91.
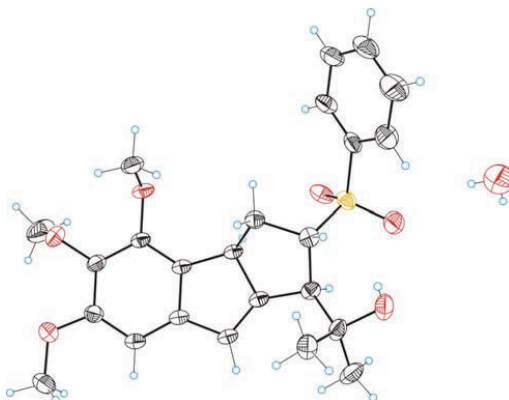
Table 18. Crystal data and structure refinement for **91.**

Empirical formula	C24 H29 O6.50 S
Formula weight	453.53
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/n
Unit cell dimensions	a = 8.1471(7) Å a= 90°.
	b = 10.2854(7) Å b= 97.371(4)°.
	c = 26.8670(18) Å g = 90°.
Volume	2232.7(3) Å^3
Z	4
Density (calculated)	1.349 Mg/m^3
Absorption coefficient	0.186 mm^{-1}
F(000)	964
Crystal size	0.40 x 0.40 x 0.20 mm^3
Theta range for data collection	3.06 to 35.07°.
Index ranges	-6<=h<=12, -16<=k<=13, -43<=l<=41
Reflections collected	25735
Independent reflections	8748 [R(int) = 0.0459]
Completeness to theta = 35.07°	88.5 %
Absorption correction	None
Max. and min. transmission	0.9638 and 0.9294
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8748 / 3 / 301
Goodness-of-fit on F^2	1.081

Final R indices [I>2sigma(I)]	R1 = 0.0802, wR2 = 0.2134
R indices (all data)	R1 = 0.1072, wR2 = 0.2389
Largest diff. peak and hole	0.866 and -1.403 e.Å^{-3}

Table 19. Bond lengths [Å] and angles [°] for **91.**

S(1)-O(1)	1.4451(14)
S(1)-O(2)	1.4515(16)
S(1)-C(20)	1.7599(17)
S(1)-C(1)	1.7966(17)
C(1)-C(12)	1.542(2)
C(1)-C(2)	1.563(2)
C(2)-C(3)	1.496(2)
C(2)-C(13)	1.550(2)
C(3)-C(4)	1.344(2)
C(3)-C(11)	1.510(2)
O(3)-C(7)	1.365(2)
O(3)-C(17)	1.428(2)
C(4)-C(5)	1.466(2)
O(4)-C(8)	1.376(2)
O(4)-C(18)	1.410(3)
C(5)-C(6)	1.392(2)
C(5)-C(10)	1.407(2)
O(5)-C(9)	1.3744(18)
O(5)-C(19)	1.440(2)
C(6)-C(7)	1.390(2)
O(6)-C(13)	1.443(2)
C(7)-C(8)	1.413(2)
C(8)-C(9)	1.395(2)
C(9)-C(10)	1.374(2)
C(10)-C(11)	1.499(2)
C(11)-C(12)	1.530(2)
C(13)-C(16)	1.521(2)
C(13)-C(15)	1.524(3)
C(20)-C(21)	1.385(3)
C(20)-C(25)	1.385(3)
C(21)-C(22)	1.388(3)
C(22)-C(23)	1.380(4)

C(23)-C(24)	1.390(3)
C(24)-C(25)	1.398(3)
O(1)-S(1)-O(2)	118.03(9)
O(1)-S(1)-C(20)	108.88(9)
O(2)-S(1)-C(20)	107.53(8)
O(1)-S(1)-C(1)	109.48(7)
O(2)-S(1)-C(1)	106.93(9)
C(20)-S(1)-C(1)	105.25(8)
C(12)-C(1)-C(2)	108.28(12)
C(12)-C(1)-S(1)	112.07(12)
C(2)-C(1)-S(1)	107.53(11)
C(3)-C(2)-C(13)	117.54(13)
C(3)-C(2)-C(1)	102.32(12)
C(13)-C(2)-C(1)	113.17(14)
C(4)-C(3)-C(2)	137.92(15)
C(4)-C(3)-C(11)	111.29(14)
C(2)-C(3)-C(11)	109.61(12)
C(7)-O(3)-C(17)	116.56(15)
C(3)-C(4)-C(5)	108.81(13)
C(8)-O(4)-C(18)	114.22(18)
C(6)-C(5)-C(10)	121.28(14)
C(6)-C(5)-C(4)	130.29(14)
C(10)-C(5)-C(4)	108.34(13)
C(9)-O(5)-C(19)	112.14(13)
C(7)-C(6)-C(5)	118.32(14)
O(3)-C(7)-C(6)	124.80(15)
O(3)-C(7)-C(8)	114.65(15)
C(6)-C(7)-C(8)	120.55(15)
O(4)-C(8)-C(9)	119.21(15)
O(4)-C(8)-C(7)	120.49(15)
C(9)-C(8)-C(7)	120.18(15)
O(5)-C(9)-C(10)	120.47(14)
O(5)-C(9)-C(8)	120.06(14)
C(10)-C(9)-C(8)	119.45(14)
C(9)-C(10)-C(5)	120.21(14)
C(9)-C(10)-C(11)	130.83(13)
C(5)-C(10)-C(11)	108.93(13)

C(10)-C(11)-C(3)	102.29(12)
C(10)-C(11)-C(12)	122.74(13)
C(3)-C(11)-C(12)	102.22(12)
C(11)-C(12)-C(1)	103.08(12)
O(6)-C(13)-C(16)	105.76(15)
O(6)-C(13)-C(15)	108.33(15)
C(16)-C(13)-C(15)	111.68(16)
O(6)-C(13)-C(2)	107.80(14)
C(16)-C(13)-C(2)	113.83(14)
C(15)-C(13)-C(2)	109.19(15)
C(21)-C(20)-C(25)	121.95(17)
C(21)-C(20)-S(1)	117.90(16)
C(25)-C(20)-S(1)	120.15(13)
C(20)-C(21)-C(22)	118.6(2)
C(23)-C(22)-C(21)	120.6(2)
C(22)-C(23)-C(24)	120.23(19)
C(23)-C(24)-C(25)	120.0(2)
C(20)-C(25)-C(24)	118.55(18)

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Table 20. Torsion angles [°] for **91**.

O(1)-S(1)-C(1)-C(12)	-45.72(13)
O(2)-S(1)-C(1)-C(12)	-174.67(11)
C(20)-S(1)-C(1)-C(12)	71.17(12)
O(1)-S(1)-C(1)-C(2)	73.17(13)
O(2)-S(1)-C(1)-C(2)	-55.78(13)
C(20)-S(1)-C(1)-C(2)	-169.95(11)
C(12)-C(1)-C(2)-C(3)	1.80(16)
S(1)-C(1)-C(2)-C(3)	-119.49(11)
C(12)-C(1)-C(2)-C(13)	-125.67(14)
S(1)-C(1)-C(2)-C(13)	113.05(13)
C(13)-C(2)-C(3)-C(4)	-19.3(3)
C(1)-C(2)-C(3)-C(4)	-143.9(2)
C(13)-C(2)-C(3)-C(11)	146.62(14)
C(1)-C(2)-C(3)-C(11)	22.00(16)
C(2)-C(3)-C(4)-C(5)	163.94(18)
C(11)-C(3)-C(4)-C(5)	-1.80(18)

C(3)-C(4)-C(5)-C(6)	-178.67(17)
C(3)-C(4)-C(5)-C(10)	-2.09(18)
C(10)-C(5)-C(6)-C(7)	-1.1(2)
C(4)-C(5)-C(6)-C(7)	175.12(16)
C(17)-O(3)-C(7)-C(6)	-1.5(3)
C(17)-O(3)-C(7)-C(8)	179.23(16)
C(5)-C(6)-C(7)-O(3)	-178.61(16)
C(5)-C(6)-C(7)-C(8)	0.6(2)
C(18)-O(4)-C(8)-C(9)	100.6(2)
C(18)-O(4)-C(8)-C(7)	-83.4(2)
O(3)-C(7)-C(8)-O(4)	4.1(2)
C(6)-C(7)-C(8)-O(4)	-175.24(16)
O(3)-C(7)-C(8)-C(9)	179.99(15)
C(6)-C(7)-C(8)-C(9)	0.7(3)
C(19)-O(5)-C(9)-C(10)	-97.61(18)
C(19)-O(5)-C(9)-C(8)	83.92(19)
O(4)-C(8)-C(9)-O(5)	-7.1(2)
C(7)-C(8)-C(9)-O(5)	176.95(15)
O(4)-C(8)-C(9)-C(10)	174.46(15)
C(7)-C(8)-C(9)-C(10)	-1.5(3)
O(5)-C(9)-C(10)-C(5)	-177.42(14)
C(8)-C(9)-C(10)-C(5)	1.1(2)
O(5)-C(9)-C(10)-C(11)	0.3(3)
C(8)-C(9)-C(10)-C(11)	178.82(16)
C(6)-C(5)-C(10)-C(9)	0.3(2)
C(4)-C(5)-C(10)-C(9)	-176.69(14)
C(6)-C(5)-C(10)-C(11)	-177.95(14)
C(4)-C(5)-C(10)-C(11)	5.10(17)
C(9)-C(10)-C(11)-C(3)	176.22(16)
C(5)-C(10)-C(11)-C(3)	-5.82(16)
C(9)-C(10)-C(11)-C(12)	62.8(2)
C(5)-C(10)-C(11)-C(12)	-119.24(15)
C(4)-C(3)-C(11)-C(10)	4.66(17)
C(2)-C(3)-C(11)-C(10)	-165.25(12)
C(4)-C(3)-C(11)-C(12)	132.50(14)
C(2)-C(3)-C(11)-C(12)	-37.41(16)
C(10)-C(11)-C(12)-C(1)	149.39(14)
C(3)-C(11)-C(12)-C(1)	35.93(15)

C(2)-C(1)-C(12)-C(11)	-23.85(16)
S(1)-C(1)-C(12)-C(11)	94.59(12)
C(3)-C(2)-C(13)-O(6)	-163.40(14)
C(1)-C(2)-C(13)-O(6)	-44.38(18)
C(3)-C(2)-C(13)-C(16)	-46.4(2)
C(1)-C(2)-C(13)-C(16)	72.59(19)
C(3)-C(2)-C(13)-C(15)	79.12(18)
C(1)-C(2)-C(13)-C(15)	-161.87(15)
O(1)-S(1)-C(20)-C(21)	-166.81(16)
O(2)-S(1)-C(20)-C(21)	-37.85(19)
C(1)-S(1)-C(20)-C(21)	75.89(17)
O(1)-S(1)-C(20)-C(25)	12.45(17)
O(2)-S(1)-C(20)-C(25)	141.41(15)
C(1)-S(1)-C(20)-C(25)	-104.85(16)
C(25)-C(20)-C(21)-C(22)	-1.1(3)
S(1)-C(20)-C(21)-C(22)	178.2(2)
C(20)-C(21)-C(22)-C(23)	1.7(4)
C(21)-C(22)-C(23)-C(24)	-1.0(4)
C(22)-C(23)-C(24)-C(25)	-0.4(3)
C(21)-C(20)-C(25)-C(24)	-0.3(3)
S(1)-C(20)-C(25)-C(24)	-179.52(14)
C(23)-C(24)-C(25)-C(20)	1.0(3)

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THEORETICAL CALCULATIONS

All calculations were carried out with DFT using the B3LYP functional[133] as implemented in Gaussian 03.[134] The 6-31G(d) basis set[135] was used for all atoms except gold and platinum, which was treated with SDD and the associated effective core potential.[136] Frequency calculations were performed to characterize the stationary points as minima.
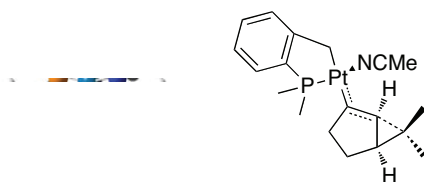
Scheme 54. Cartesian coordinates for **52a** (E = -1255.57049781 u.a.).

Coordinates (Å)

133 (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648-5652. (b) Lee, C. T.; Yang, W. T.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785-789. (c) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623-11627.

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135 (a) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; Defrees, D. J.; Pople, J. A. *J. Chem. Phys.* **1982**, *77*, 3654-3665. (b) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257-2261.

136 Andrae, D.; Haussermann, U.; Dolg, M.; Stoll, H.; Preuss, H. *Theor. Chim. Acta* **1990**, *77*, 123–141.

Atom	X	Y	Z
C	4.02915300	-0.99016900	-0.81602500
C	2.46260500	-1.30663600	-0.49471200
C	1.74869200	-0.48760700	0.41795800
C	3.70349600	-1.96231700	0.22879000
C	3.64927300	-1.48415000	1.67640500
C	2.49449200	-0.44346100	1.72856000
H	2.81295300	0.58748700	1.94190400
H	1.78513200	-0.67278500	2.53418500
H	3.43463400	-2.32935500	2.33696900
H	4.60678200	-1.06204300	1.99902800
H	3.89123500	-3.01495300	0.02903100
C	4.40867000	-1.53347300	-2.18500900
C	4.62448700	0.37711900	-0.53713100
H	1.97165900	-1.74073500	-1.35810400
H	4.33874400	1.08757400	-1.31998000
H	4.34502600	0.79712700	0.42964800
H	5.71799500	0.29032000	-0.55409200
H	4.07810300	-0.86300000	-2.98563600
H	5.50071500	-1.61465400	-2.24687800
H	3.98841600	-2.52694900	-2.36764700
Pt	-0.04236700	0.46616800	0.10734900
P	-1.37773100	-1.36327200	0.10255800
C	-3.06655300	-0.74287300	-0.10016200
C	-3.14888000	0.65194600	-0.22724200
C	-4.20923700	-1.55862300	-0.13282600
C	-4.42441900	1.21748900	-0.38928800
C	-5.46148000	-0.97539600	-0.29428400
H	-4.12688100	-2.63845300	-0.03157600
C	-5.56328700	0.41579100	-0.42237800
H	-4.51991900	2.29588200	-0.48958000
H	-6.35299100	-1.59458900	-0.31983900
H	-6.54018000	0.87432400	-0.54832700

C	-1.89064600	1.49493300	-0.18729500
H	-1.98293800	2.24599400	0.61051300
H	-1.80172700	2.05792300	-1.12835500
C	-1.07429700	-2.58138100	-1.24424800
H	-1.84528000	-3.35885900	-1.22912000
H	-1.10416600	-2.07227500	-2.21119500
H	-0.09575500	-3.05357000	-1.11638300
C	-1.33929400	-2.38508200	1.63356300
H	-1.54825700	-1.75224500	2.50019300
H	-2.09475600	-3.17615600	1.58247700
H	-0.35401000	-2.84555400	1.75717700
N	0.83506100	2.36058600	0.06449400
C	1.19969300	3.45743700	0.02577000
C	1.64779000	4.84383300	-0.02445300
H	1.37448900	5.28613200	-0.98778400
H	1.17047900	5.41651600	0.77711500
H	2.73409200	4.89646700	0.09727300
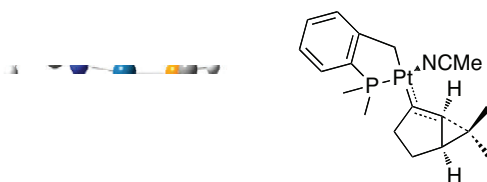
Scheme 55. Cartesian coordinates for **52b** (E = -1255.57053250 u.a.).

Coordinates (Å)

Atom	X	Y	Z
C	-3.66544400	-1.80668300	-0.37985200
C	-2.66853700	-0.58819800	-0.78693200
C	-1.89194900	0.10718300	0.17767800

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C	-4.20199100	-0.44719800	-0.41780300
C	-4.25914200	0.35880000	0.87618700
C	-2.78100700	0.54242800	1.31724800
H	-2.50286000	-0.01115600	2.22678500
H	-2.55929600	1.58776500	1.56454000
H	-4.72214900	1.33086200	0.68204400
H	-4.86832700	-0.13867800	1.63809500
H	-4.87365900	-0.18246400	-1.23110000
C	-3.94353400	-2.69807600	-1.58128900
C	-3.46541500	-2.59035100	0.90424600
H	-2.31600500	-0.68140800	-1.80852800
H	-2.68293500	-3.34696100	0.77924600
H	-3.21703700	-1.97746500	1.77161700
H	-4.39589600	-3.12313500	1.13649100
H	-3.12538200	-3.40634100	-1.75399300
H	-4.85202700	-3.28239800	-1.39192000
H	-4.10057900	-2.12089200	-2.49719600
Pt	0.07328900	0.67974900	0.02478600
P	1.02573500	-1.36888800	0.11152100
C	2.81268500	-1.09215700	0.02005900
C	3.17344300	0.26057700	-0.07225100
C	3.77431500	-2.11548100	0.04016800
C	4.54231800	0.56714400	-0.14382600
C	5.12390900	-1.78711800	-0.03265300
H	3.47721400	-3.15931200	0.11225000
C	5.50290500	-0.44175500	-0.12425400
H	4.85232900	1.60681300	-0.21503400
H	5.87742200	-2.56868600	-0.01799400
H	6.55644800	-0.18239100	-0.18067900
C	2.10280100	1.33245900	-0.08877100
H	2.20024800	1.92808300	-1.00863700
H	2.27191800	2.02926800	0.74508200
C	0.69817100	-2.34977500	1.63477000

Atom	X	Y	Z
H	1.28716200	-3.27290400	1.62760100
H	0.97592500	-1.75993500	2.51239300
H	-0.36325700	-2.60676600	1.70122700
C	0.57282400	-2.50833700	-1.26127400
H	0.80103300	-2.03118400	-2.21803500
H	1.14204800	-3.44066500	-1.18480200
H	-0.49594500	-2.73830700	-1.22402000
N	-0.43447400	2.70427800	-0.12170300
C	-0.60165300	3.84281200	-0.23738800
C	-0.80310200	5.27893500	-0.38560600
H	0.00830000	5.70601000	-0.98350900
H	-1.75648600	5.47612900	-0.88556900
H	-0.80900000	5.75779100	0.59871300
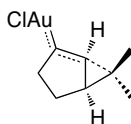
Scheme 56. Cartesian coordinates for **39a** (E = -908.044506574 u.a.).

Coordinates (Å)

Atom	X	Y	Z
C	-3.03535200	-0.70160500	0.09726900
C	-1.75064400	-0.28874500	-0.77282400
C	-0.73020200	0.50087100	-0.16064100
C	-3.10444200	0.49719800	-0.75610700
C	-2.81097700	1.85568900	-0.12701700
C	-1.32917500	1.78708700	0.34223500
Au	1.17355400	0.03762500	-0.04270300
Cl	3.41823500	-0.52002800	0.13393600
H	-1.18058800	1.87284300	1.42783900
H	-0.73648300	2.61105400	-0.07701100

H	-2.94117000	2.64466200	-0.87388100
H	-3.49576100	2.07779000	0.69874500
H	-3.72009800	0.45605100	-1.65168700
C	-3.66988400	-1.97501000	-0.44257200
C	-3.01174200	-0.65512500	1.61469700
H	-1.49345700	-1.03714700	-1.51367500
H	-2.47934200	-1.52343600	2.01693900
H	-2.54904200	0.24272000	2.02646500
H	-4.04355600	-0.69618100	1.98617700
H	-3.12782400	-2.86308300	-0.09927700
H	-4.70196600	-2.05002100	-0.07771000
H	-3.69695700	-1.98930300	-1.53651900
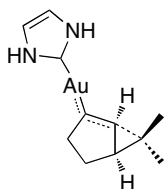
Scheme 57. Cartesian coordinates (E = -673.849832279 u.a.).

Coordinates (Å)

Atom	X	Y	Z
H	3.65572600	-2.33677400	-1.25097500
H	4.23934300	-2.01002000	0.37744400
C	3.51894200	-1.68849900	-0.38128500
C	3.74143200	-0.23451100	-0.78571400
H	4.29734700	-0.02106700	-1.69619600
C	3.68545800	0.79494500	0.24069500
C	3.68581000	0.51053000	1.72811100
H	3.27712500	-0.46246800	2.00103900
H	4.72614800	0.53922600	2.07640000
H	3.13580000	1.28445200	2.27225100
C	4.20357100	2.17820600	-0.11024400

248

H	4.20166200	2.36401100	-1.18797600
H	5.23863800	2.26141300	0.24393000
H	3.62069800	2.96180400	0.38486900
C	2.32120100	0.46600700	-0.67395700
H	2.03589900	1.34323200	-1.24193400
C	1.37974900	-0.45798400	-0.20220200
H	1.93818100	-1.98969100	1.19682400
C	2.05052900	-1.76337400	0.12590400
H	1.49777900	-2.56706300	-0.37873800
Au	-0.62290200	-0.15276400	-0.08555500
C	-2.66446200	0.15028600	0.04372400
N	-3.37421400	1.25611000	-0.28755600
H	-2.94393500	2.09426800	-0.65376500
C	-4.73190300	1.09274300	-0.06842200
H	-5.45428500	1.86651300	-0.27471600
C	-4.88529900	-0.16621700	0.42141500
H	-5.76769200	-0.70595000	0.72672700
N	-3.61428700	-0.71320300	0.47811500
H	-3.39987200	-1.64663200	0.80161200
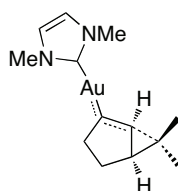
Scheme 58. Cartesian coordinates (E = -752.475928359 u.a.).

Coordinates (Å)

Atom	X	Y	Z
H	3.90810900	-2.13978700	-1.59913700
H	4.47983800	-2.08227300	0.06470400
C	3.76717000	-1.63860300	-0.63767600

249

C	4.00002800	-0.13990400	-0.80127900
H	4.56468200	0.21436100	-1.66093700
C	3.93975900	0.71128500	0.37822600
C	3.92738300	0.18930200	1.80017000
H	3.51008200	-0.81199900	1.90766000
H	4.96445400	0.15421300	2.15761000
H	3.37604100	0.86793600	2.45836100
C	4.47153400	2.12864700	0.25957300
H	4.47661200	2.48727400	-0.77356100
H	5.50535400	2.14463000	0.62625600
H	3.89203100	2.82643300	0.87293600
C	2.58471800	0.54325200	-0.58400100
H	2.30780000	1.50088000	-1.00822600
C	1.63189000	-0.43841900	-0.27477200
H	2.17275800	-2.18153000	0.85927100
C	2.29427400	-1.78415200	-0.15950000
H	1.74119700	-2.49077500	-0.79268200
Au	-0.37068100	-0.14847200	-0.12136400
C	-2.42122500	0.13560800	0.04690100
N	-3.10937000	1.30454200	-0.05196200
C	-4.46554800	1.09288000	0.11962600
H	-5.18559500	1.89550200	0.07550500
C	-4.63010800	-0.23926300	0.33121000
H	-5.52107900	-0.82174500	0.50884600
N	-3.37076900	-0.80918400	0.28266600
C	-2.52217700	2.61864700	-0.31173700
H	-1.44056300	2.50727200	-0.38643600
H	-2.91133600	3.02214000	-1.25041100
H	-2.76147500	3.30108200	0.50808600
C	-3.12227600	-2.23802000	0.47414200
H	-2.06007100	-2.43035600	0.32396800
H	-3.40552900	-2.53450100	1.48776100
H	-3.70108200	-2.81456300	-0.25203800
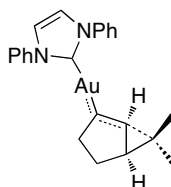
Scheme 59. Cartesian coordinates for **39b** (E = -1135.94548850 u.a.).

	Coordinates (Å)		
Atom	X	Y	Z
H	4.21158800	-1.96532700	-2.45383100
H	4.57484900	-2.87223600	-0.98939400
C	4.04187700	-1.99682900	-1.37408900
C	4.54758800	-0.70655200	-0.73642100
H	5.27222800	-0.10084300	-1.27617600
C	4.48065500	-0.57017800	0.71331000
C	4.20640600	-1.72154100	1.65994700
H	3.61259000	-2.52738100	1.22762900
H	5.16987600	-2.14951400	1.96464700
H	3.70285500	-1.36710700	2.56484100
C	5.26226100	0.56283100	1.35587700
H	5.45864700	1.38069500	0.65685500
H	6.22848800	0.17225300	1.69833900
H	4.73769600	0.96442200	2.22913700
C	3.25875800	0.05549000	-0.21919300
H	3.20019200	1.13056100	-0.09769800
C	2.11737300	-0.72478800	-0.47231000
H	2.20165800	-2.87041600	-0.40687100
C	2.51839000	-2.04731600	-1.06440100
H	1.93104500	-2.19688500	-1.98046000
Au	0.19962900	-0.13516600	-0.20469200
C	-1.76878500	0.45666900	0.07330200

N	-2.25573200	1.72710300	0.14676900
C	-3.63188600	1.72019300	0.33510500
H	-4.20277900	2.63267400	0.40269000
C	-4.01426600	0.41878600	0.37728100
H	-4.98234100	-0.03475700	0.51967700
N	-2.86322000	-0.34180300	0.21737400
C	-2.85309200	-1.78133400	0.21688800
C	-3.60246600	-2.46313900	-0.74394900
C	-2.12584500	-2.47144600	1.18940400
C	-3.61687900	-3.85862900	-0.73257100
H	-4.15562500	-1.90803100	-1.49582400
C	-2.14173900	-3.86723000	1.18618700
H	-1.57300900	-1.92121000	1.94396700
C	-2.88580800	-4.56067200	0.22858000
H	-4.19627800	-4.39469500	-1.47796600
H	-1.58537000	-4.41104100	1.94378900
H	-2.90153900	-5.64634500	0.23533500
C	-1.47424400	2.93026500	0.03162600
C	-1.48828500	3.84982200	1.08234600
C	-0.74525800	3.17651200	-1.13414400
C	-0.75495200	5.03128100	0.96361800
H	-2.05624200	3.63677800	1.98317000
C	-0.00921600	4.35805300	-1.23824900
H	-0.77125400	2.46188100	-1.95043900
C	-0.01404000	5.28492100	-0.19312100
H	-0.76116000	5.74994600	1.77738800
H	0.55376400	4.55983700	-2.14463100
H	0.55278800	6.20672700	-0.28264600
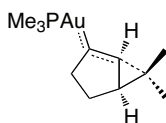
Scheme 60. Cartesian coordinates (E = -908.746645423 u.a.).

Coordinates (Å)

Atom	X	Y	Z
C	2.06741300	-1.75469700	0.35449300
C	1.41344000	-0.49447200	-0.13827500
C	2.35425400	0.34613300	-0.73565300
C	3.75636600	0.76778000	0.10660100
C	3.76743800	-0.38648000	-0.77399000
C	3.52880300	-1.77099400	-0.17867600
C	4.28007800	2.08498400	-0.43471400
C	3.77535900	0.68224100	1.61774200
Au	-0.60134600	-0.14812200	-0.05595600
P	-2.94294600	0.24280800	0.05175800
H	1.96802100	-1.83291600	1.44757100
H	1.49643000	-2.61083100	-0.02885900
H	3.64159700	-2.52938600	-0.95796000
H	4.25695500	-2.00256900	0.60493700
H	4.30241700	-0.30462500	-1.71789300
H	2.07642500	1.15359500	-1.40200300
H	3.25522600	1.53584400	2.06280900
H	3.34897200	-0.23535100	2.02301500
H	4.82280700	0.72970800	1.94250900
H	3.71642500	2.93469900	-0.03607500
H	5.32292400	2.19968300	-0.11360900
H	4.25833300	2.12613100	-1.52716200
C	-3.57065600	1.38695700	-1.24485600
C	-3.95605900	-1.28128100	-0.13308000
C	-3.49282600	0.98690300	1.64217500

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H	-4.65258000	1.52427300	-1.14442600
H	-3.07693800	2.35899600	-1.15380900
H	-3.35293800	0.98043000	-2.23694900
H	-5.02355200	-1.04316800	-0.07727900
H	-3.74519500	-1.75262500	-1.09759300
H	-3.70607700	-1.99184900	0.66030100
H	-4.57615300	1.14759100	1.63670800
H	-3.23417200	0.32325900	2.47255200
H	-2.99007100	1.94615200	1.79674200
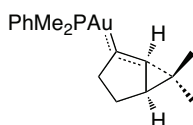
Scheme 61. Cartesian coordinates (E = -1100.47629664 u.a.).

Coordinates (Å)

Atom	X	Y	Z

C	-2.46596100	1.95511500	0.25757900
C	-2.10160400	0.56206400	-0.17225000
C	-3.21470200	-0.09305900	-0.70427500
C	-4.64067700	-0.17308400	0.19486300
C	-4.44710000	0.91133100	-0.75220100
C	-3.91010800	2.24602800	-0.24360100
C	-5.44380500	-1.37925200	-0.25498100
C	-4.58727200	-0.00587900	1.69813000
Au	-0.20444600	-0.19809800	-0.09101400
P	1.98445500	-1.12680300	0.02063900
H	-2.31464900	2.07186900	1.34116600
H	-1.74428200	2.65080900	-0.19116000
H	-3.89091900	2.96978100	-1.06272400

H	-4.54833000	2.66353200	0.54142200
H	-5.02216300	0.89344000	-1.67566700
H	-3.12947000	-0.97346800	-1.32950100
H	-4.23227300	-0.92229200	2.17927500
H	-3.97051200	0.82654900	2.03676500
H	-5.61007500	0.17675300	2.05220900
H	-5.05441400	-2.30556800	0.17974700
H	-6.47597200	-1.25699200	0.09655700
H	-5.46981000	-1.48210300	-1.34325700
C	2.34003900	-2.25904000	-1.38975800
C	2.21959800	-2.18202800	1.51357100
H	3.33936100	-2.69617900	-1.29946700
H	1.59891400	-3.06417300	-1.40789100
H	2.27893100	-1.70451800	-2.33030700
H	3.22199500	-2.62104300	1.52683700
H	2.08438400	-1.57858700	2.41541400
H	1.47778000	-2.98668100	1.51408400
C	3.33852500	0.09691900	0.04604100
C	4.67816000	-0.32214800	0.12101800
C	3.05007000	1.46884400	-0.00849100
C	5.70691100	0.61767300	0.14083000
H	4.92739400	-1.37934400	0.16504000
C	4.08353300	2.40729000	0.01181400
H	2.01765600	1.80332400	-0.06686400
C	5.41045500	1.98277700	0.08643700
H	6.73916700	0.28559400	0.19902300
H	3.85082300	3.46715900	-0.03081500
H	6.21449400	2.71259400	0.10229400
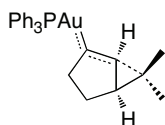
Scheme 62. Cartesian coordinates for **39d** (E = -1483.93692105 u.a.).

| | Coordinates (Å) | | |
| Atom | X | Y | Z |

C	3.59361300	-1.84745000	0.29143300
C	2.90872000	-0.59709300	-0.18379700
C	3.83483300	0.27970300	-0.75858100
C	5.20208700	0.72824300	0.10484500
C	5.26599800	-0.41287400	-0.79315200
C	5.06265100	-1.81158400	-0.21948200
C	5.69971500	2.06733000	-0.40877800
C	5.20969100	0.61996200	1.61530000
Au	0.89021900	-0.29771600	-0.10493700
P	-1.46732500	0.05293400	0.00593200
H	3.47941600	-1.95407400	1.38041200
H	3.05211900	-2.70980300	-0.12005100
H	5.21089000	-2.55646700	-1.00582700
H	5.78562300	-2.03030300	0.57289400
H	5.81445400	-0.30032100	-1.72598300
H	3.53835700	1.08430300	-1.42041700
H	4.66241100	1.45315100	2.06667700
H	4.80117700	-0.31359700	2.00223400
H	6.25162300	0.68863500	1.95356500
H	5.10829100	2.89518700	-0.00435800
H	6.73549400	2.20472100	-0.07406200
H	5.68891300	2.12553700	-1.50070300
C	-1.93970200	1.74713900	-0.50291900
C	-2.95922800	2.45792900	0.14851500
C	-1.26803800	2.33804000	-1.58620900

C	-3.29958500	3.74190200	-0.28251800
H	-3.48164400	2.01620900	0.99126600
C	-1.61614900	3.61805100	-2.01515600
H	-0.47557300	1.79586300	-2.09643000
C	-2.63100800	4.32186800	-1.36213000
H	-4.08780900	4.28790800	0.22770700
H	-1.09297200	4.06727100	-2.85440800
H	-2.89727500	5.32194900	-1.69172800
C	-2.12072900	-0.18929500	1.69999100
C	-3.35372400	-0.81768800	1.93216500
C	-1.36898900	0.28159100	2.79025800
C	-3.82645500	-0.96803400	3.23736000
H	-3.94263500	-1.19477400	1.10169300
C	-1.84959600	0.13339900	4.09088300
H	-0.40980800	0.76576000	2.62302500
C	-3.07808600	-0.49318800	4.31559200
H	-4.78052500	-1.45776700	3.40930100
H	-1.26308500	0.50100600	4.92796200
H	-3.44859300	-0.61395500	5.32938800
C	-2.38372600	-1.10185400	-1.08121100
C	-3.51389100	-0.69420000	-1.80564300
C	-1.94956300	-2.43580000	-1.16565700
C	-4.20098300	-1.61318700	-2.60119100
H	-3.85470100	0.33483700	-1.75172100
C	-2.64264700	-3.34947000	-1.95793600
H	-1.07231300	-2.75872300	-0.61013100
C	-3.76831200	-2.93799400	-2.67704100
H	-5.07422400	-1.29165500	-3.16127700
H	-2.30192300	-4.37893700	-2.01884900
H	-4.30450500	-3.64909200	-3.29879400
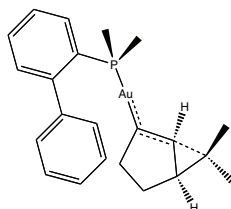
Scheme 63. Cartesian coordinates for **39c** (E = -1331.52469353 u.a.).

| | Coordinates (Å) | | |
Atom	X	Y	Z
C	-2.94242700	1.20217600	0.88188500
C	-2.31700400	0.17564500	-0.01652700
C	-3.16882800	-0.12260000	-1.08843500
C	-4.73595300	-0.60320300	-0.77978900
C	-4.45582400	0.80627500	-1.01025200
C	-4.23827300	1.71829000	0.19310300
C	-5.25184000	-1.42529300	-1.94762800
C	-5.09564500	-1.18476000	0.57203000
Au	-0.42643400	-0.53542800	0.25288300
P	1.72748000	-1.47482400	0.62640000
H	-3.07915600	0.79650200	1.89523100
H	-2.20967500	2.01122800	1.01149300
H	-4.10629800	2.74949600	-0.14579200
H	-5.10104300	1.70824700	0.86677600
H	-4.77459700	1.24489200	-1.95332700
H	-2.80887100	-0.58104000	-2.00170600
H	-4.76464900	-2.22524600	0.64658300
H	-4.69218700	-0.63225900	1.42080700
H	-6.18917100	-1.17889200	0.66429600
H	-4.87145400	-2.45150600	-1.91379800

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H	-6.34587900	-1.47441000	-1.88292300
H	-4.99187500	-0.98477200	-2.91426600
C	1.74178700	-3.24612100	0.11238900
C	2.19115300	-1.56449200	2.41129000
H	2.65168100	-3.76405700	0.42889000
H	0.88325600	-3.74101800	0.57624900
H	1.63959200	-3.32225300	-0.97362600
H	3.18529600	-2.00864800	2.52440300
H	2.19288600	-0.56584900	2.85332000
H	1.45771000	-2.17907500	2.94308600
C	3.13132100	-0.67509500	-0.25146300
C	4.19960000	-1.48394500	-0.67814300
C	3.14891900	0.70977600	-0.55083800
C	5.26663000	-0.95348900	-1.39964400
H	4.20394800	-2.54581500	-0.45686800
C	4.22713300	1.21905500	-1.29278700
C	5.27509400	0.40413500	-1.71574100
H	6.07930500	-1.60009500	-1.71638600
H	4.24354200	2.28054900	-1.52156400
H	6.09666700	0.83076200	-2.28350800
C	2.10295600	1.68490400	-0.11421200
C	1.95334700	2.03553700	1.23777600
C	1.32746000	2.36024100	-1.07310600
C	1.04610400	3.02532800	1.62329500
H	2.58743200	1.56756400	1.98572000
C	0.42208200	3.35112700	-0.68838400
H	1.44797600	2.11314800	-2.12441300
C	0.27868200	3.68669300	0.66088300
H	0.96202700	3.29966700	2.67120000
H	-0.15525600	3.87461500	-1.44568300
H	-0.40398100	4.47830500	0.95785900

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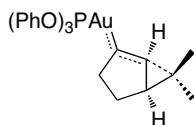
Scheme 64. Cartesian coordinates for **39e** (E = -1709.63187571 u.a.).

Coordinates (Å)

Atom	X	Y	Z
C	4.71091700	-1.21566300	-2.24363400
C	3.28123100	-1.53704500	-1.72156200
C	2.82940600	-0.37721300	-0.88155300
C	3.87707400	0.52068900	-0.67329800
C	5.34326700	-0.04061100	-0.05306500
C	5.15448000	0.03572100	-1.49084100
Au	0.90087900	-0.10892700	-0.26961900
P	-1.32948200	0.18309800	0.42698100
O	-1.96478800	-0.88761400	1.45705800
C	6.05946700	1.10597300	0.63601300
C	5.37666200	-1.33505500	0.73060500
O	-1.66822000	1.49785200	1.31054700
O	-2.26387600	0.21539200	-0.88587900
H	3.18786900	-2.47639100	-1.15633200
H	2.57239300	-1.65334400	-2.55237100
H	4.68731100	-1.00888200	-3.31684200
H	5.40808900	-2.04526100	-2.08979700
H	5.67753600	0.81959400	-2.03463700
H	3.71469200	1.54316600	-0.35490800
H	5.00379700	-1.18356200	1.74811100
H	4.81946700	-2.15276900	0.27375400
H	6.42441200	-1.65307100	0.80769200
H	5.64198200	1.30039900	1.62927200
H	7.11196900	0.82563200	0.76821400
H	6.02842600	2.02974800	0.05173900

C	-1.05789200	2.74178800	1.05347900
C	-3.67534200	0.19916600	-0.99250100
C	-1.65357100	-2.26105700	1.36367500
C	-0.34287800	3.32428200	2.09741200
C	0.23071700	4.58142700	1.89915900
C	0.09008700	5.23604400	0.67219000
C	-0.63478100	4.63561600	-0.35890600
C	-1.22212800	3.38064200	-0.17465200
H	-0.25848100	2.80318800	3.04566300
H	0.78166100	5.05081800	2.70879000
H	0.53334300	6.21623200	0.52524000
H	-0.76001200	5.14702700	-1.30869400
H	-1.81481100	2.92286400	-0.95970900
C	-4.16841700	-0.28682500	-2.20136300
C	-5.54881500	-0.31650600	-2.40241600
C	-6.41539200	0.13260200	-1.40330100
C	-5.89713500	0.61651700	-0.20115800
C	-4.51763700	0.65929500	0.01769800
H	-3.47570900	-0.62587700	-2.96496600
H	-5.94323300	-0.69098500	-3.34226900
H	-7.48901500	0.10735500	-1.56178900
H	-6.56573600	0.96938700	0.57831800
H	-4.12083800	1.04479800	0.94923200
C	-0.83212800	-2.80686200	2.34734500
C	-0.55432900	-4.17475300	2.30626700
C	-1.09294700	-4.97334400	1.29381300
C	-1.91977000	-4.40521800	0.32220500
C	-2.21091900	-3.03874200	0.35124900
H	-0.43983200	-2.17065700	3.13440900
H	0.07606000	-4.61563900	3.07284000
H	-0.87913500	-6.03756500	1.26990800
H	-2.35265100	-5.02552800	-0.45696000
H	-2.87707800	-2.59215700	-0.37973200
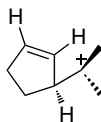
Scheme 65. Cartesian coordinates for **53b** (E = -312.329115163 u.a.).

Coordinates (Å)

Atom	X	Y	Z
C	-0.79936200	-2.96040900	0.81478000
C	-0.43884400	-1.23385600	-0.40563300
C	0.64877600	-0.45956900	-0.14016500
C	-1.20569400	-1.54738600	0.93975000
C	-0.50179300	-0.64781800	1.98927100
C	0.81550800	-0.12864800	1.32312400
H	1.72947700	-0.58756500	1.73110800
H	0.94411900	0.95166500	1.46324800
H	-1.16103700	0.19554200	2.21424100
H	-0.31839700	-1.17100100	2.93307500
H	-2.28288400	-1.39299600	0.84220500
C	-1.63922700	-3.88952900	-0.00506500
C	0.39319300	-3.53118300	1.51067100
H	-0.79969000	-1.54078000	-1.37975700
H	0.86777100	-4.33363800	0.93814300
H	1.13465600	-2.78788600	1.80569600
H	0.01636500	-3.98884600	2.44498800
H	-1.03982600	-4.47178000	-0.71582600
H	-2.07963300	-4.62903100	0.68703300
H	-2.45873500	-3.38999700	-0.52655600
H	1.29772100	-0.05459000	-0.91327000
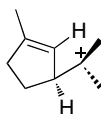
Scheme 66. Cartesian coordinates for **53a** (E = -351.651546227 u.a.).

Atom	Coordinates (Å)		
	X	Y	Z

Atom	X	Y	Z
C	-0.75997300	-2.90352800	0.78738800
C	-0.48043300	-1.30499500	-0.37450200
C	0.62413100	-0.51312900	-0.14879200
C	-1.26524300	-1.53302700	0.97272100
C	-0.56597700	-0.60128700	1.98867600
C	0.75987800	-0.12861600	1.31139600
H	1.66625100	-0.57528800	1.74830800
H	0.89881200	0.95599400	1.40540800
H	-1.21606900	0.25867000	2.17397500
H	-0.39555100	-1.09106700	2.95268500
H	-2.34543700	-1.41808100	0.87793000
C	-1.58076600	-3.88116700	-0.01249600
C	0.44927500	-3.45526200	1.48897600
H	-0.85119000	-1.60076800	-1.34770100
H	1.01071200	-4.14767900	0.85366300
H	1.12120800	-2.69889600	1.89397100
H	0.07400200	-4.04364300	2.34418000
H	-0.97165200	-4.45795200	-0.71768000
H	-2.00706100	-4.60888500	0.69777900
H	-2.41328100	-3.41227400	-0.54345900
C	1.55131900	0.00516800	-1.20175800
H	1.51921600	1.10349200	-1.23438100
H	2.59079600	-0.25751200	-0.95396100
H	1.32092900	-0.38103800	-2.19809400