UNIVERSITAT ROVIRA I VIRGILI

NEW GOLD (I) ALKYNOPHILIC CATALYSTS

Mihai Raducan

ISBN: 978-84-694-0315-0
Dipòsit Legal: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Mihai Răducan

New Gold(I) Alkynophilic Catalysts

Doctoral Thesis

supervised by Prof. Antonio M. Echavarren

Institut Català d'Investigació Química

Universitat Rovira i Virgili
Tarragona
2010

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Institute of Chemical Research of Catalonia (ICIQ)
Av. Països Catalans 16 – 43007 Tarragona (Spain)
Tel.: +34 977 920 218
Fax.: +34 977 920 205

FAIG CONSTAR que aquest treball, titulat "New Gold(I) Alkynophilic Catalysts", que presenta Mihai Rãducan per a l'obtenció del títol de Doctor, ha estat realitzat sota la meva direcció al Departament de Química Analítica i Química Orgánica d'aquesta Universitat i que acompleix els requeriments per poder optar a Menció Europea.

Tarragona, 29 de octubre de 2010

El Director de la Tesi Doctoral

Prof. Antonio M. Echavarren

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Părinţilor mei

Sorei mele

Colegilor mei

Profesorilor mei

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Este trabajo de Tesis Doctoral se ha realizado en el Institut Català d'Ivnvestigació Química bajo la dirección del Profesor Antonio M. Echavarren, a quien quiero agradecer por todo el tiempo y confianza que ha depositado en mí durante estos años. He sido afortunado por haberle conocido y tenido como mentor. Pocos han tenido la suerte de aprender a superarse bajo su supervisión.

Estoy especialmente agradecido a las varias entidades que han financiado mi estancia aquí, tan lejos de mi país: al MEC (beca predoctoral FPU abril 2006 - diciembre 2009), al AGAUR (beca predoctoral FI enero - marzo 2006) y a la Fundación ICIQ (beca predoctoral noviembre – diciembre 2005, contrato de investigación enero-diciembre 2010).

Quiero agradecer también la amabilidad del Profesor Paul Knochel (Ludwig-Maximilians-Universität, München), en cuyo grupo de investigación he realizado una estancia breve (septiembre - diciembre 2008). Tuve la suerte de haber trabajado junto con Tobias Thaler, a quien le deseo mucha suerte en el futuro.

Un agradecimiento muy especial merece Sònia Gavaldà, por la pasión con la que me ayudó con los muchos problemas administrativos y logísticos que surgierón durante esta tesis. Sin dejar de nombrar a la técnico Vanessa Martínez, que siempre me ha atendido asap.

He sido muy afortunado por haber podido contar con el apoyo de unos técnicos tan profesionales como los del ICIQ: Kerman Gómez y Dr. Gabriel González de RMN; Eduardo Escudero y Dr. Jordi Benet-Buchholz del servicio de rayos X; Dra. Noemí Cabello y Alba González de espectrometría de masas; Enrique Cequier y Simona Curreli de la unidad de cromatografía del ICIQ; y finalmente a Ángel Mosquera y David Pena, los mas pacientes técnicos de informática.

Durante estos años he compartido la mayoría de mis proyectos con otros investigadores que me han enseñado una buena parte de las técnicas experimentales que conozco. Querría agradecerles por el apoyo y paciencia a Cati Ferrer, Verónica López-Carillo, Patrícia Pérez-Galán, Kian Molawi, Dr. Thorsten Lauterbach de nuestro grupo, a Xacobe Couso Cambeiro y a Carles Rodríguez Escrich del grupo del Profesor Miquel A. Pericas.

Finalmente querría mencionar a todos aquellos que con una sonrisa, un chiste o una fiesta han hecho mi estancia en Tarragona un poco mas feliz. No os olvidaré y seguramente nos veremos en el futuro. El mundo (de la química) es un pañuelo.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

At the printing of this manuscript, the results presented herein have yielded the publications presented below.

A Multipurpose Cationic Gold(I) Complex

Raducan, M.; Couso Cambeiro, X.; Rodríguez Escrich, C.; Pericás, M. A.; Echavarren A. M.

ICIQ **2008-2010**, in preparation.

Nitrogen Acyclic Gold(I) Carbenes: Excellent and Easily Accessible Catalysts in Reactions of 1,6-Enynes

Bartolomé, C.; Ramiro, Z.; García-Cuadrado, D.; Pérez-Galán, P.; Raducan, M.; Bour, C.; Echavarren, A. M.; Espinet, P.

Organometallics **2010**, *29*, 951-956.

Evolution of Propargyl Ethers to Allyl-Gold Cations in Cyclizations of Enynes

Jiménez-Núñez, E.; Raducan, M.; Lauterbach, T.; Molawi, K.; Solorio, C. R.; Echavarren A. M.

Angew. Chem. Int. Ed. **2009**, *48*, 6152-6155.

Gold(I) Complexes with Hydrogen-Bond Supported Heterocyclic Carbenes as Active Catalysts in Reactions of 1,6-Enynes

Bartolomé, C.; Ramiro, Z.; Perez-Galan, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P.

Inorg. Chem. **2008,** *47*, 11391-11397.

Gold(I)-Catalyzed Intermolecular Addition of Carbon Nucleophiles to 1,5- and 1,6-Enynes

Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M.

J. Org. Chem. **2008**, *73*, 7721-7730.

The results obtained between November 2005 – June 2007 were presented in the manuscript required for the obtention of the DEA (Diploma de Estudios avanzados,

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Universidad Rovira i Virgili, June 2007). Those results yielded the publication below and will not be detailed here.

Missing Cyclization Pathways and New Rearrangements Unveiled in the Gold(I) and Platinum(II)-Catalyzed Cyclization of 1,6-Enynes.

Ferrer, C.; Raducan, M.; Nevado, C.; Claverie, C. K.; Echavarren, A. M.

Tetrahedron **2007**, *63*, 6306-6316.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Contents

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

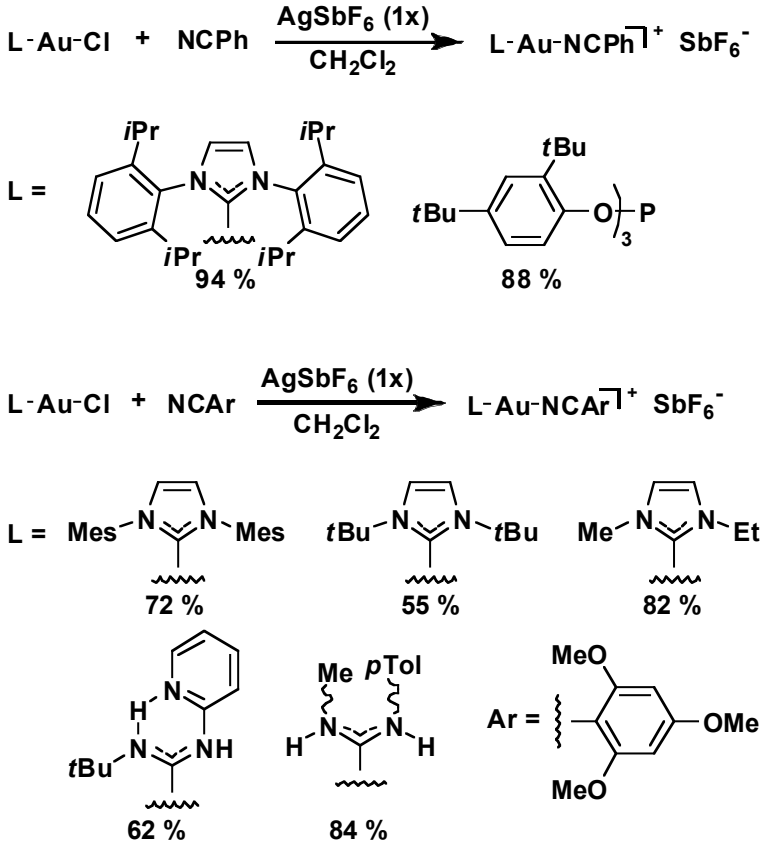
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Resumen

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

El uso de nitrilos aromáticos ricos en electrones permitió el aislamiento de nuevos catalizadores catiónicos de oro(I) como sólidos cristalinos estables al aire.[1,2,3]



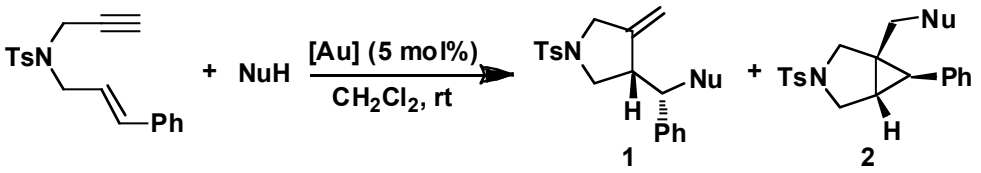
Los complejos catiónicos de oro(I) catalizan la adición de nucleófilos carbonados a 1,6-eninos.[1] La selectividad del ataque nucleofílico (frente al ciclopropano o al carbeno) puede ser controlada por el ligando no lábil del catalizador.

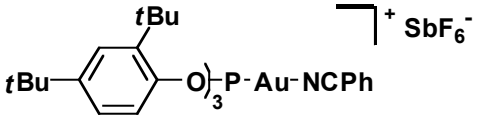
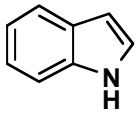
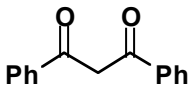
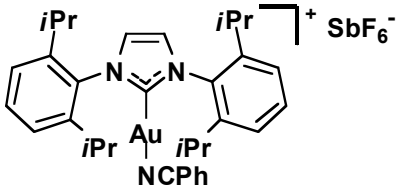
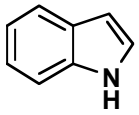
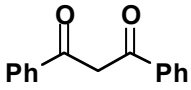
1. Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M. *J. Org. Chem*. **2008**, *73*, 7721-7730.

2. Bartolomé, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem*. **2008**, *47*, 11391-11397.

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

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

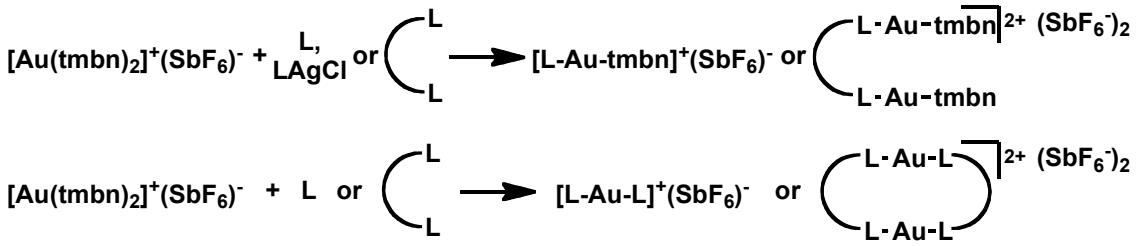


[Au]	NuH	time (h)	products	yield (%)
		1	1a + 2a (84 : 16)	71
		0.33	1b + 2b (77:23)	83
		17	1a + 2a (23 : 77)	57
		0.33	1b + 2b (2 : 98)	87

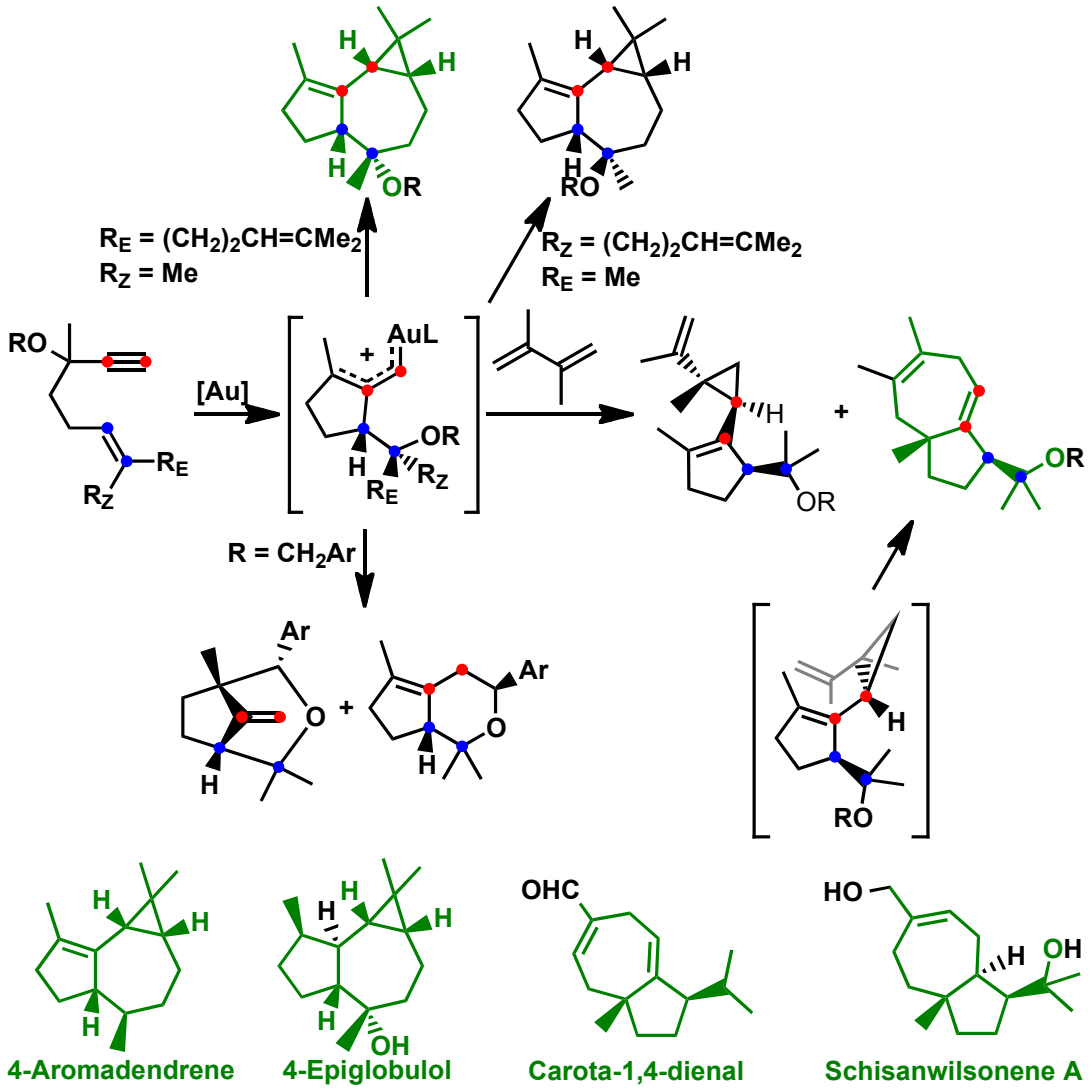
El complejo $[Au(tmbn)_2](SbF_6)$ (tmbn = 2,4,6-trimethoxybenzonitrilo) se puede sintetizar fácilmente a partir de AuCl y es estable indefinidamente al aire.[4] Usando cantidades estoiquiométricas de ligandos fosforados o nitrogenados uno o los dos ligandos tmbn pudieron ser sustituidos y los complejos resultantes se pudieron aislar mediante cristalización. La sustitución de sólo un ligando tmbn es posible usando ligandos voluminosos o pobres en electrones. Algunos de estos complejos fueron empleados *in situ* en la adición de dibenzoilmetano a un 1,6-enino y mostraron selectividades similares con los catalizadores ya publicados.[1,5]

4. Raducan, M.; Echavarren, A. M. unpublished results, **2009**, ICIQ.
5. Amijs, C. H. M.; Ferrer, C.; Echavarren, A. M. *Chem. Commun.* **2007**, 698-700.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



Tras la activación con complejos catiónicos de oro(I), los 1,6-eninos conteniendo alcoholes o éteres propargílicos sufren una migración 1,5 dando lugar a cationes de alil-oro. Estos intermedios se pueden atrapar intra- o intermolecularmente con alquenos o éteres bencílicos.[6] Esta reacción estereoespecífica da lugar a compuestos tricíclicos relacionados con los sesquiterpenos 4-epiglobulol and 4-aromadendreno.

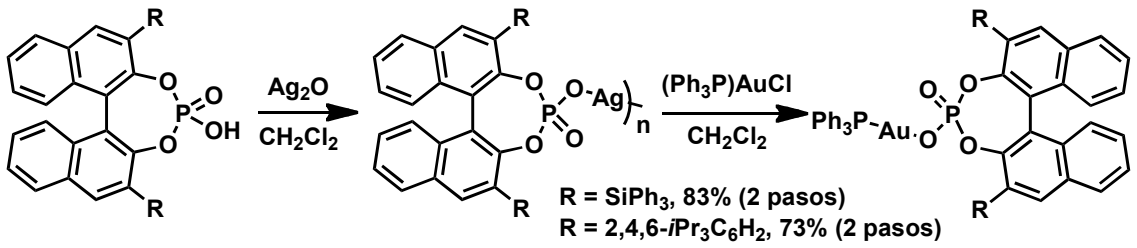


6. Jiménez-Núñez, E.; Raducan, M.; Lauterbach, T.; Molawi, K.; Solorio, C. R.; Echavarren A. M. *Angew. Chem. Int. Ed.* **2009**, *48*, 6152-6155.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

El atrapamiento con dienos puede llevar a compuestos bicíclicos relacionados con los carotanes y los schinsanwilsonenos.

Los complejos de oro conteniendo fosfatos quirales[7] se han sintetizado y caracterizado con el propósito de entender su comportamiento en catálisis.



7. Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste F. D. *Science* **2007**, *317*, 496-499.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

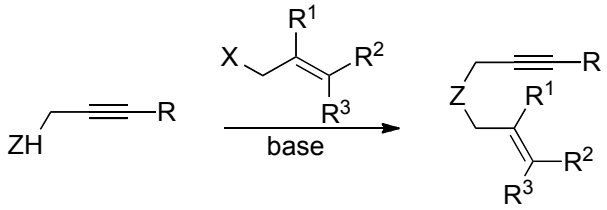
Introduction

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Transition metal catalyzed cyclizations of 1,6-enynes lead to towards highly functionalized carbo- and heterocycles.[1] These transformations usually proceed with high levels of atom economy[2] and selectivity.

One of the advantages of the cycloisomerization of enynes is the ease of synthesis of the starting compounds. Simple alkylation of malonic esters, bis-sulfones, tosylamides and alcohols allowed access to a large number of substrates from commercially available substances in one or two high yielding steps.[3]



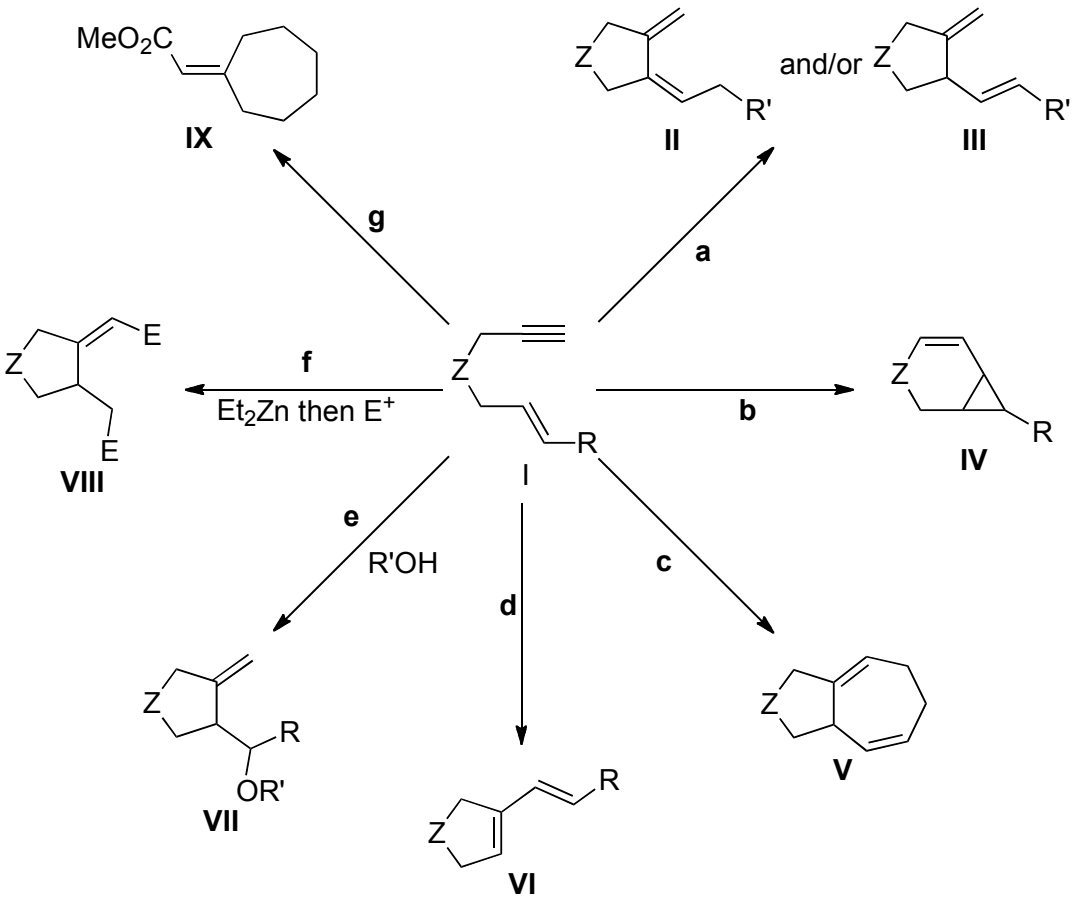
Z = $(COOMe)_2$, $(PhSO_2)_2C$, NTs, O
X = Br, Cl

The substitution pattern of the starting enyne, as well as the nature of the catalyst, influences significantly the outcome of the cycloisomerization process. Thus, simple enynes **I** react in the presence of different metals to give several types of carbo- and heterocyclic products (Scheme 1): (a) cyclopentane dienes **II** and/or **III** (with Pd,[4] Ru,[5] Rh,[6] Pt),[5b,7] (b) bicycloheptene[4.1.0] derivates **IV** (Pt,[8] Co),[9] (c) seven membered

1. Reviews on metal catalyzed cyclization of enynes: (a) Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34-42. (b) Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, *102*, 813-834. (c) Anorbe, L.; Dominguez, G.; Pérez-Castells, J. *Chem. Eur. J.* **2004**, *10*, 4938-4943. (d) Bruneau, C. *Angew. Chem. Int. Ed.* **2005**, *44*, 2328-2334. (e) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271-2296.
2. (a) Trost, B. M. *Science* **1991**, *254*, 1471. (b) Trost, B. M. *Acc. Chem. Res.* **2002**, *35*, 695-705.
3. For an outline of the strategies towards the most common enynes see: Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2002**, *124*, 5025-5036.
4. (a) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781-1783. (b) Trost, B. M.; Lautens, M. *Tetrahedron Lett.* **1985**, *26*, 4887-4890. (c) Trost, B. M.; Chen, S.-F. *J. Am. Chem. Soc.* **1986**, *108*, 6053-6054. (d) Trost, B. M.; Lautens, M.; Chan, C.; Jebaratnam, D. S.; Mueller, T. *J. Am. Chem. Soc.* **1991**, *113*, 636-644. (e) Trost, B. M.; Gelling, O. J. *Tetrahedron Lett.* **1993**, *34*, 8233-8236. (f) Wartenberg, F.-H.; Hellendahl, B.; Blechert, S. *Synlett* **1993**, 539-540. (g) Castro, J.; Balme, G.; Goré, J. *J. Chem. Res.* **1995**, 504-505.
5. (a) Paih, J. L.; Rodriguez, D. C.; Dérien, S.; Dixneuf, P. H. *Synlett* **2000**, 95-97. (b) Méndez, M.; Muñoz, M. P.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2001**, *123*, 10511-10520.
6. (a) Cao, P.; Wang, B.; Zhang, X. *J. Am. Chem. Soc.* **2000**, *122*, 6490-6491. (b) Cao, P.; Zhang, X. *Angew. Chem. Int. Ed.* **2000**, *39*, 4104-4106.
7. (a) Méndez, M.; Muñoz, M. P.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 11549-11550. (b) Muñoz, M. P.; Méndez, M.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Synthesis* **2003**, 2898-2902.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

ring cycloalkenes **V** (Rh,[10] Ru),[11] (d) vinylcycloalkenes via skeletal rearrangement **VI** (Ru,[12] Pt,[13] Ga,[14] other),[12b] (e) alkoxycyclopentane derivates containing an *exo* double bond **VII** (Au),[15] (f) cyclopentane derivates with an *exo* double bond **VIII** (RMgX/Ti(IV))[16] and (g) seven membered rings **IX** (Ru).[3]



Scheme 1.

8. (a) Blum, J.; Beer-Kraft, H.; Badrieh, Y. *J. Org. Chem.* **1995**, *60*, 5567-5569. (b) Fürstner, A.; Szillat, H.; Stelzer, F. *J. Am. Chem. Soc.* **2001**, *123*, 11863-11869. (c) Mainetti, E.; Mouries, V.; Fensterbank, L.; Malacria, M. *Angew. Chem. Int. Ed.* **2002**, *41*, 2132-2135.

9. Borodkin, V. S.; Shapiro, N. A.; Azoz, V. A.; Krochetkov, N. K. *Tetrahedron Lett.* **1996**, *37*, 1489-1492.

10. Wender, P. A.; Takahashi, H.; Witulski, B. *J. Am. Chem. Soc.* **1995**, *117*, 4720-4721.

11. Trost. B. M.; Toste, F. D.; Shen, H. *J. Am. Chem. Soc.* **2000**, *122*, 2379-2380.

12. (a) Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049-6050. (b) Chatani, N.; Kataoka. K.; Murai, S.; Furukawa, N.; Seki, Y. *J. Am. Chem. Soc.* **1998**, *120*, 9104-9105.

13. (a) Chatani, N.; Furukawa. N.; Sakurai, H.; Murai, S. *Organometallics* **1996**, *15*, 901-903. (b) Ho-Oh, C.; Youn-Bang, S.; Yun-Rhim, C. *Bull. Korean Chem. Soc.* **2003**, *24*, 887-888.

14. Chatani, N.; Inoue, H.; Kotsuma, T.; Murai, S. *J. Am. Chem. Soc.* **2002**, *124*, 10294-10295.

15. (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-Nuñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677-1693.

16. Montchamp, J. L.; Neghisi, E. *J. Am. Chem. Soc.* **1998**, *120*, 5345-5346.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Among the range of transition metal complexes capable of catalyzing enyne cycloisomerizations, gold and platinum complexes are particularly powerful as they are capable of delivering a diverse array of cyclic products that are produced under mild conditions, with excellent chemoselectivity and high synthetic efficiency.[1e] While the pioneering work in this area goes back to the 1990s, there has been an explosive increase of interest in Au and Pt catalysis during the last six years.

Scheme 2 summarizes the range of observed reaction topologies for gold and platinum cycloisomerizations of 1,6-enynes **X**. The process can furnish the six-membered carbocyclic or heterocyclic products **XI**[8a,8b,15a,17] and **XII**[15,18] . Alternatively, the cycloisomerization provides an efficient access to five-membered dienes **XIII**[13a,15a,19] and **XIV**[5b] or alkenes **XV**.[7a,15a,18,20] Compounds **XIIIa**,[13a,21] **XVI**[5b] and **XVII**[20b] have also been observed. Highly strained bicyclo[3.2.0]heptenes **XVIII**[22] can also be obtained as a result of this transformation. Incorporation of arene and alkene groups (**R**^{1}) at the terminal alkyne position provides access to bicyclic and tricyclic products **XIX**[23] as a result of a formal [4+2] cycloaddition.

1. (e) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271-2296.

5. (b) Méndez, M.; Muñoz, M. P.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2001**, *123*, 10511-10520.

7. (a) Méndez, M.; Muñoz, M. P.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 11549-11550.

8. (a) Blum, J.; Beer-Kraft, H.; Badrieh, Y. *J. Org. Chem.* **1995**, *60*, 5567-5569. (b) Fürstner, A.; Szillat, H.; Stelzer, F. *J. Am. Chem. Soc.* **2001**, *123*, 11863-11869.

13. (a) Chatani, N.; Furukawa. N.; Sakurai, H.; Murai, S. *Organometallics* **1996**, *15*, 901-903.

15. (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-Nuñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677-1693.

17. Fürtsner, A.; Szillat, H.; Stelzer, F. *J. Am. Chem. Soc.* **2000**, *122*, 6785-6786.

18. Nevado, C.; Ferrer, C.; Echavarren A. M. *Org. Lett.* **2004**, *6*, 3191-3194.

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

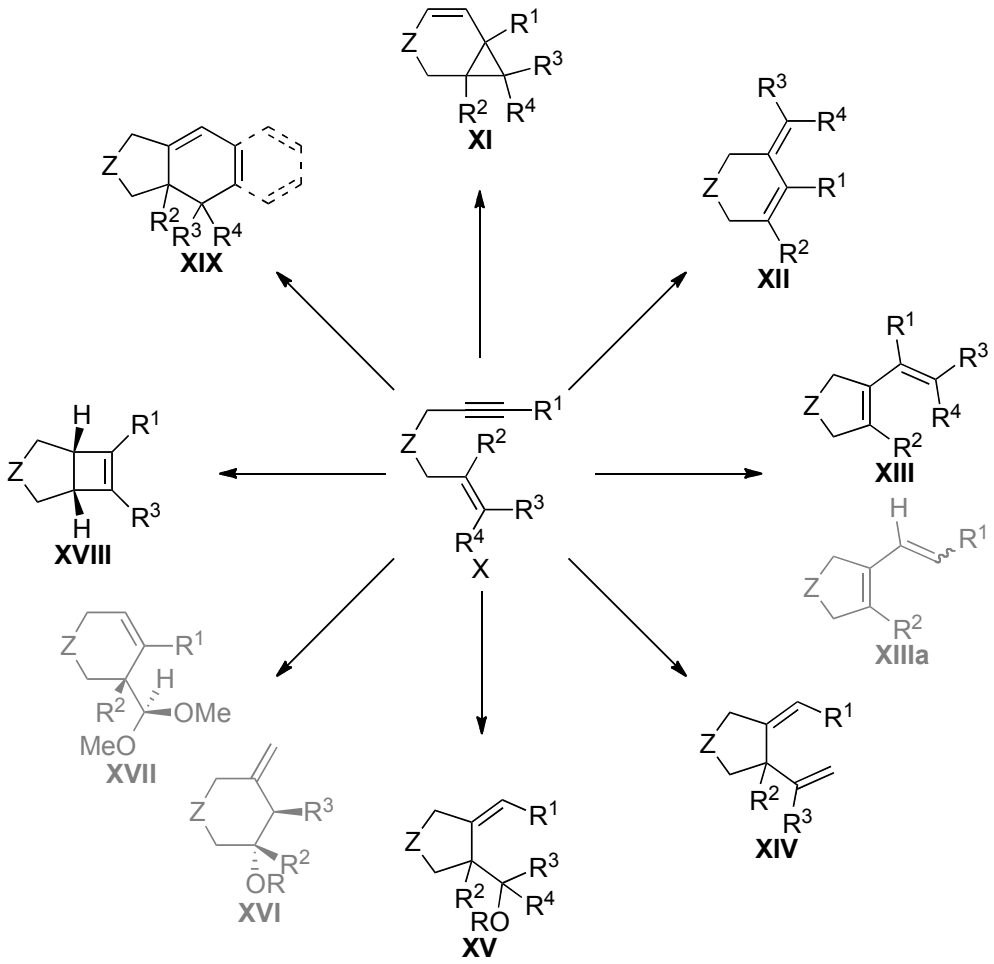
20. (a) Nevado, C.; Charruault, L.; Michelet, V.; Nieto-Oberhuber, C.; Muñoz, M. P.; Mendez, M.; Rager, M.; Genet, J.; Echavarren, A. M. *Eur. J. Org. Chem.* **2003**, *4*, 706-713. (b) Nevado, C.; Cardenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2003**, *9*, 2627-2635.

21. 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.

22. Fürstner, A.; Davies, P. W.; Gress, T. *J. Am. Chem. Soc.* **2005**, *127*, 8244-8245.

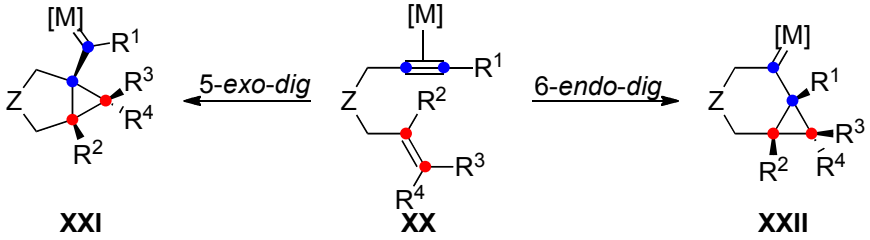
23. Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178-6179.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



Scheme 2. Observed reaction topologies in the cycloisomerisations of 1,6 enynes. Less common compounds are highlighted in grey.

The mechanistic scheme of gold and platinum catalyzed 1,6-enyne cyclization has been elucidated,[20b,24] with all observed products having been accounted for. Upon monocoordination of the metal fragment to the alkyne in **XX** two general manifolds have been revealed: a *5-exo-dig* cyclization via anti-cyclopropyl metal carbenes **XXI** and the relatively less common *6-endo-dig* cyclization via **XXII**.



Scheme 3. General manifolds in 1,6-enyne cyclization.

20. (b) Nevado, C.; Cardenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2003**, *9*, 2627-2635.
24. Echavarren, A.M.; Nevado, C. *Chem. Soc. Rev.* **2004**, *33*, 431-436.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Stereoselective attack at the cyclopropane carbons of intermediate **XXI** by alcohol or water could cleave bonds **a** or **b** yielding either the five- (**XXV**) or six-membered ring (**XXVI**) derivatives, respectively. Subsequent, protonolysis of the alkenylmetal bond by the alcohol or water would give cycles **XV** or **XVI**.[5b,20] In the absence of nucleophiles, ring opening of cyclopropyl carbene **XXI** could generate intermediate **XXIV** which, following deprotonation and protodemetallation, would yield diene **XIV**.[5b] Skeletal rearrangement of 1,6-enynes is best envisioned via the spirocycle **XXIa**[25] (**Scheme 4**): thus, cleavage of bond **a** of **XXIa** would form conjugated dienes **XIII**, while cleavage of bond **d** would furnish dienes **XIIIa**.[24]

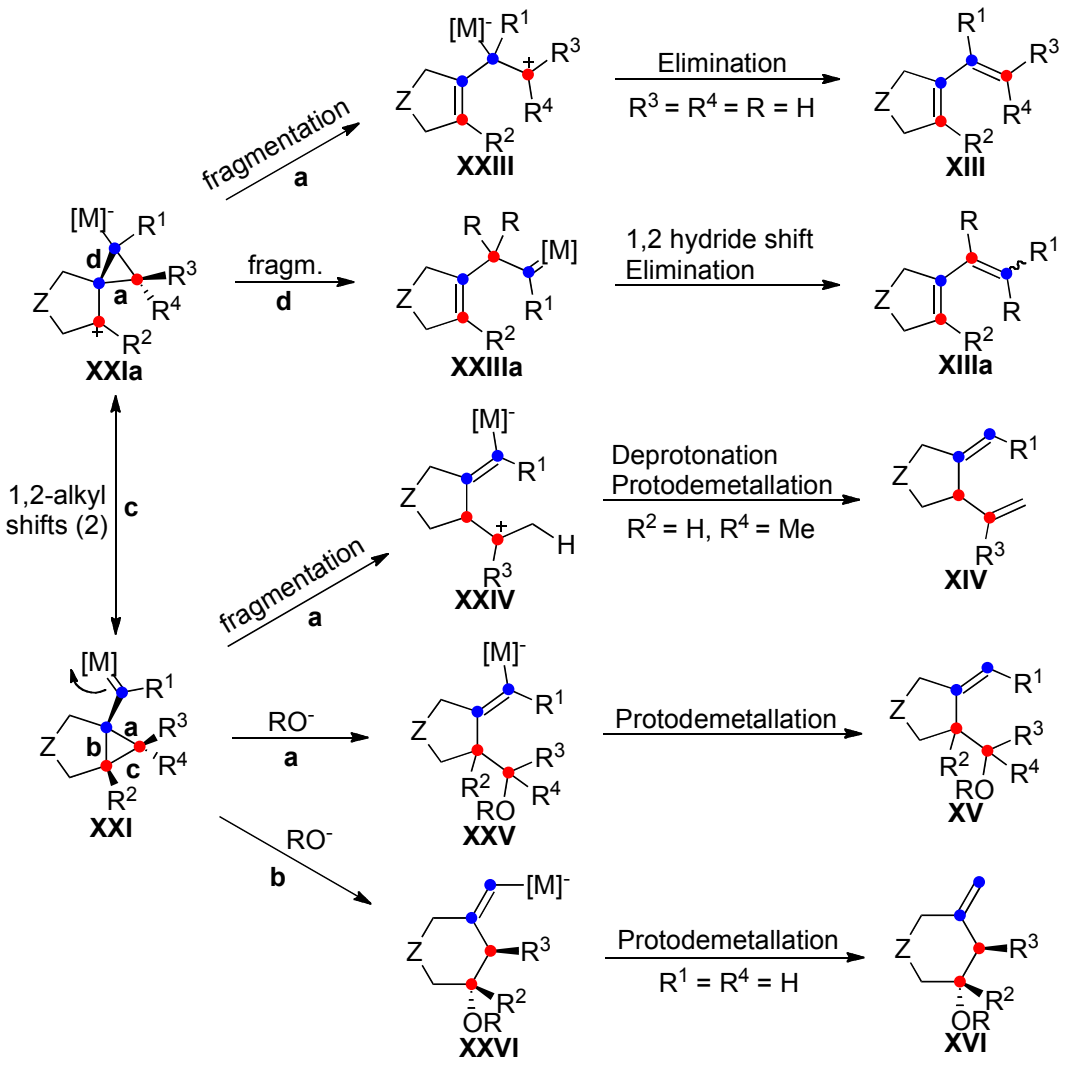
5. (b) Méndez, M.; Muñoz, M. P.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2001**, *123*, 10511-10520.

20. (a) Nevado, C.; Charruault, L.; Michelet, V.; Nieto-Oberhuber, C.; Muñoz, M. P.; Mendez, M.; Rager, M.; Genet, J.; Echavarren, A. M. *Eur. J. Org. Chem.* **2003**, *4*, 706-713. (b) Nevado, C.; Cardenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2003**, *9*, 2627-2635.

24. Echavarren, A.M.; Nevado, C. *Chem. Soc. Rev.* **2004**, *33*, 431-436.

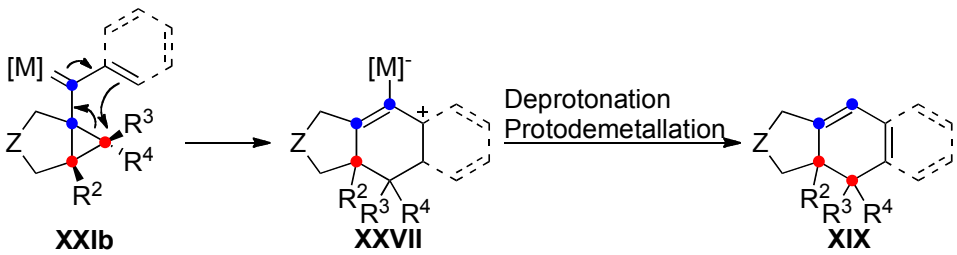
25. This is just for heuristics: DFT calculations showed that **XXI** evolves directly towards **XXIII** or **XXIIIa**, see ref. 21.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



Scheme 4. *5-exo-dig* pathways for 1,6-enyne cyclization.

Finally, cyclopropyl carbenes **XXIb** (R^1 = Aryl, vinyl) probably evolve by a Nazarov-type cyclization to form **XXVII**, which upon proton loss and protodemetallation furnish bi- or tricyclic products **XIX** (Scheme 5).[22.]

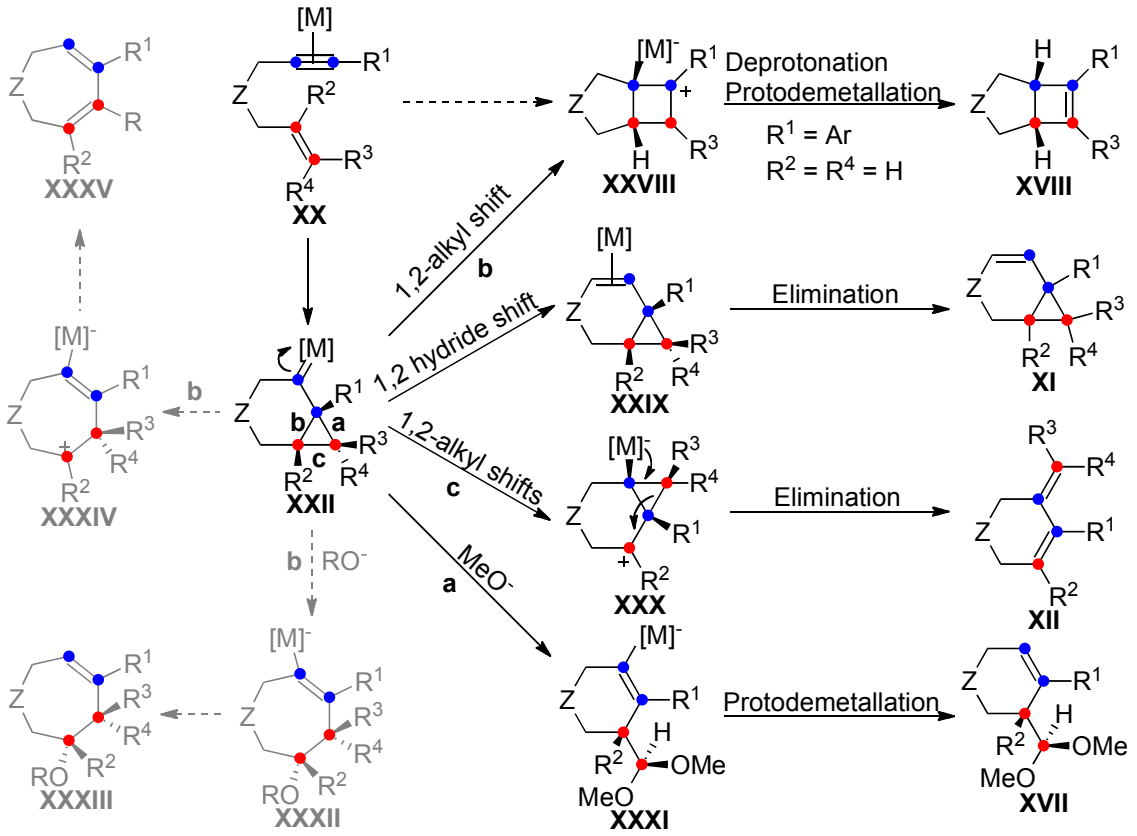


Scheme 5. Mechanism of Au-catalyzed intramolecular [4+2] cycloadditions.

22. Fürstner, A.; Davies, P. W.; Gress, T. *J. Am. Chem. Soc.* **2005**, *127*, 8244-8245.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Similarly, nucleophilic attack on *6-endo* intermediate **XXII** could cleave bond **a** yielding six-membered ring **XXXI**, which would generate cyclohexene **XVII** after protodemetallation.[20b,23] In the absence of nucleophiles, metal carbenes **XXII** typically undergo a [1,2] hydride shift followed by an elimination to produce [4,1,0] bicycloheptenes **XI**.[20b,24,26] Rearrangement of **XXII** could afford the cationic intermediate **XXX** which would undergo a concomitant fragmentation-elimination to produce the observed methylenecyclohexenes **XII**.[15b,24] Finally enynes with mono- or disubstituted alkenes and aryl alkynes can favour the formation of intermediate **XXVIII** in which the carbocation is stabilized by the neighbouring aryl group. Elimination of a proton followed by protodemetallation affords cyclobutenes **XVIII**.[1e,23]



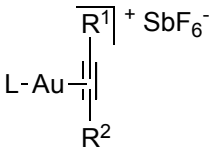
Scheme 6. Possible *6-endo-dig* pathways for the 1,6-enyne cyclization.

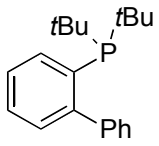
1. (e) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271-2296.
20. (b) Nevado, C.; Cardenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2003**, *9*, 2627-2635.
23. Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178-6179.
24. Echavarren, A.M.; Nevado, C. *Chem. Soc. Rev.* **2004**, *33*, 431-436.
26. Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333-346.

Seven membered ring compounds **XXXIII** and **XXXV** that could be formed by nucleophilic cleavage of bond **b** in **XXII** or by ring expansion of intermediates **XXII** and **XXX** had not been observed prior to the completion of this work.[27]

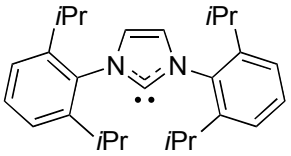
In our group, we had tried to obtain seven-membered ring compounds **XXXIII** or **XXXV** by using enol ethers as substrates (R^2 = alkoxy group) to facilitate cleavage of bond **b** in intermediates **XXII**.[20b] However, this strategy was not successful using $PtCl_2$ as catalyst.[18] We later proved that that by using more electrophilic catalysts, cleavage of bond **b** is possible, allowing acces to cycloheptadienes **XXXV**.[27]

The host of existing η^2-alkyne-Au(I)[28] and η^2-alkyne-Pt(II)[29] complexes effectively demonstrates that monocoordination is the first step in the enyne cycloisomerization process. The relative binding affinities of internal alkynes to L-Au^+ fragments (L = JOHNPHOS, IPr) have been recently determined.[30]





JOHNPHOS



IPr

Vinyl-gold(I) complexes are well known air-stable compounds and their synthesis and applications in catalysis still attract a great deal of interest.[31] More recently, vinyl-gold(I) complexes were obtained directly from the reaction of allenes[32]

18. Nevado, C.; Ferrer, C.; Echavarren A. M. *Org. Lett.* **2004**, *6*, 3191-3194.

20. (b) Nevado, C.; Cardenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2003**, *9*, 2627-2635.

27. Ferrer, C.; Raducan, M.; Nevado, C.; Claverie, C. K.; Echavarren, A. M. *Tetrahedron* **2007**, *63*, 6306-6316.

28. Some simple examples: (a) Carriedo, G. A.; Miguel, D.; Riera, V.; Soláns X.; Font-Altaba, M.; Coll, M. *J. Organomet. Chem.* **1986**, *299* (3), C43-C45. (b) Carriedo, G. A.; Miguel, D.; Riera, V.; Soláns X. *J. Chem. Soc., Dalton Trans.* **1987**, 2867-2873 (c) Schulte, P.; Behrens, U. *Chem. Commun.* **1998**, 1633-1634.

29. Some examples: (a) Gelmini, L.; Stephan, D. W. *Inorg. Chem.***1986,** *25,* 1225-1233. (b) Usón, R.; Forniés, J.; Tomás, M.; Menjón, B.; Fortuño, C.; Welch, A. J.; Smith, D. E. *J. Chem. Soc., Dalton Trans.* **1993**, 275-280. (c) De Felice, Vi.; De Renzi, A.; Giordano, F.; Tesauro, D. *J. Chem. Soc., Dalton Trans.* **1993**, 1927-1933. (d) Cucciolito, M. E.; De Felice, V.; Orabona, I.; Ruffo, F. *J. Chem. Soc., Dalton Trans.* **1997**, 1351-1354. (e) Fanizzi, F. P.; Natile, G.; Lanfranchi, M.; Tiripicchio, A.; Pacchioni, G. *Inorg. Chim. Acta* **1998**, *275-276*, 500-509. (f) Haskel, A.; Keinan, E. *Tetrahedron Lett.* **1999**, *40*, 7861-7865.

30. Brown, T. J.; Widenhoefer, R. A. *J. Organomet. Chem.* **2010**, DOI: 10.1016/j.jorganchem.2010.09.055.

31. Shi, Y.; Ramgren, S. D.; Blum, S. A. *Organometallics* **2009**, *28*, 1275-1277.

32. (a) Liu, L.-P.; Xu, B.; Mashuta, M. S.; Hammond, G. B. *J. Am. Chem. Soc.* **2008**, *130*, 17642-17643; (b) Weber, D.; Tarselli, M. A.; Gagné, M. R. *Angew. Chem. Int. Ed.* **2009**, *48*, 5733-5736.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

or alkynes[33] with cationic gold(I) complexes. Further insight into the mechanism of Au(I) catalyzed cyclization was provided by a study of the protodemetalation step. The relative kinetic basicities of a series of differently substituted and hybridized neutral organogold compounds were examined through competitive protodeauration experiments and were found to span 2 orders of magnitude.[34]

33. (a) Hashmi, A. S. K.; Schuster, A. M.; Rominger, F. *Angew. Chem. Int. Ed.* **2009**, *48*, 8247-8249; (b) Chen, Y.; Wang, D.; Petersen, J. L.; Akhmedov, N. G.; Shi, X. *Chem. Commun.* **2010**, ***46***, 6147-6149.

34. Roth, K. E.; Blum, S. A. *Organometallics* **2010**, *29*, 1712-1716.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Objectives

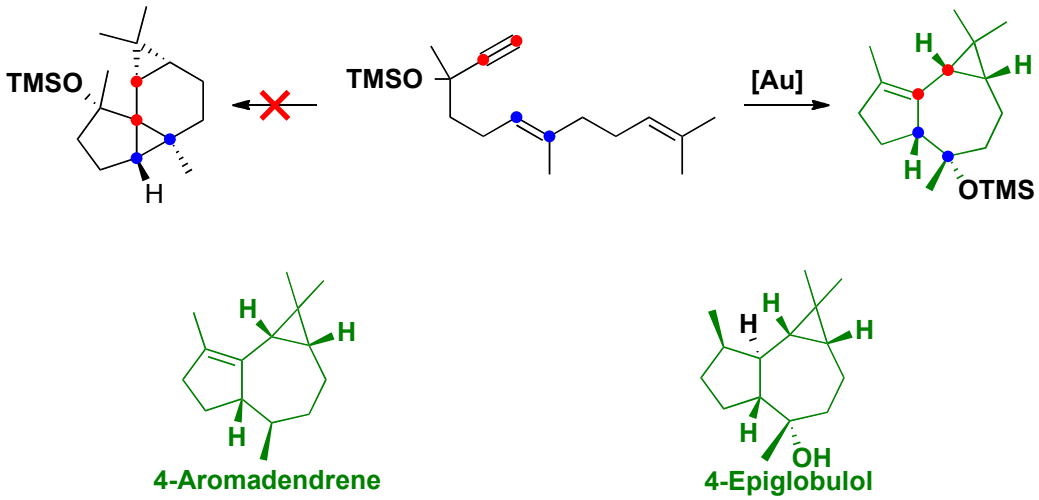
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

A major issue in gold catalyzed cyclization is substrate controlled selectivity. Furthermore, most Au(I) complexes require activation with Lewis or Brønsted acids in order to become catalytically active. One of the major goals of this Thesis was to design and synthesize new air stable Au(I) catalysts.

Screening different gold(I) catalysts in development of new methods or asymmetric catalysis requires the time-consuming preparation of a series of gold(I) complexes. It would be highly desirable to prepare in situ the desired gold(I) catalysts from a simple $[AuL_2]^+X^-$ precursor bearing two weakly bound ligands L. The search for such a complex constitutes the second main objective of this Thesis.

Finally, we would test the catalytic performance of the newly synthesized Au(I) complexes in previously described reactions where yield or selectivity needed improvement. We would also look for new reactivity for substrates containing a 1,6-enyne backbone. Of particular interest was the development of the novel cyclization of enynes bearing propargyl ethers (Scheme 7), a methodology that could provide a rapid acces to sesquiterpenes 4-epiglobulol and 4-aromadendrene.



Scheme 7.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

New air stable gold(I) catalysts

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Introduction

The ongoing search for more active and selective catalysts for the activation of alkynes yielded a plethora of Au(I) complexes during the last decade. Although most of the initial discoveries were done using phosphine ligands,[35,36,37] there has been an increasing interest in developing new N-heterocyclic (NHC)[38,39,40,41,42] and open[43,44,45] carbenes, and other related carbenes.[46] The highest reactivity can be achieved with less donating phosphite or phosphoramidite ligands.[47,48]

One major drawback of catalysis using Au(I) complexes is that the most common complexes require some form of activation in order to be able to function as efficient catalysts. Thus cationic Au(I) complexes can be generated in situ by several methods:[35] a) protonation of $[Au(CH_3)L]$ with a strong acid whose anion does not coordinate strongly to gold (i.e. MsOH, H_2SO_4 , HBF_4); b) [Au(X)L] + Ag(WCA), where X is Cl, Br, or I, and WCA is a weakly coordinating anion such as BF_4^-, PF_6^- or SbF_6^-; c) $[Au(Y)L] + BF_3{\cdot}OEt_2$, where Y is a hard anion such as NO_3^- , CF_3COO^-, $CH_3SO_3^-$, Cl^-; d) $[(AuL)_3O^+]$ or $[(AuL)_2Cl^+] + BF_3{\cdot}OEt_2$. Each of the activation methods mentioned above makes use of Lewis or Brønsted acids which are not innocent in the presence of alkynes or alkenes. For example silver salts of the type Ag(WCA)

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

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

37. Herrero-Gómez, E.; Nieto-Oberhuber, C.; López, S.; Benet-Buchholz, J.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 5455-5459.

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

39. Díez-González, S.; Marion, N.; Nolan, S. P. *Chem. Rev.* **2009**, *109*, 3612-3676.

40. Alcarazo, M.; Stork, T.; Anoop, A.; Thiel, W.; Fürstner, A. *Angew. Chem. Int. Ed.* **2010**, *49*, 2542-2546.

41. Gung, B. W.; Bailey, L. N.; Craft, D. T.; Barnes, C. L.; Kirschbaum, K. *Organometallics* **2010**, *29*, 3450-3456.

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

43. Bartolomé, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem.* **2008**, *47*, 11391-11397.

44. Bartolomé, C.; Ramiro, Z.; García-Cuadrado, D.; Pérez-Galán, P.; Raducan, M.; Bour, C.; Echavarren, A. M.; Espinet, P. *Organometallics* **2010**, *29(4)*, 951-956.

45. Hashmi, A. S. K.; Lothschütz, T. H. C.; Rominger, F. *Adv. Synth. Catal.* **2010**, *352*, 1315-1337.

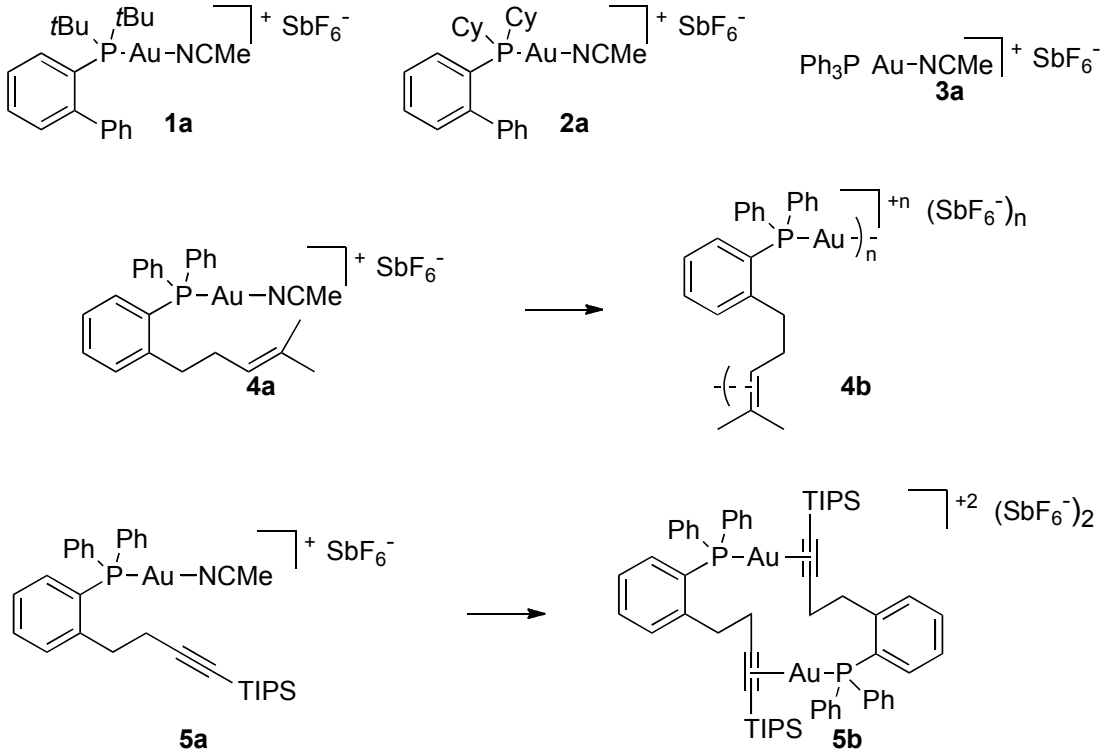
46. (a) Lavallo, V.; Frey, G. D.; Kousar, S.; Donnadieu, B.; Bertrand, G. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 13569-13573; (b) Frey, G. D.; Dewhurst, R. D.; Kousar, S.; Donnadieu, B.; Bertrand, G. *J. Organomet. Chem.* **2008**, *693*, 1674-1682; (c) Zeng, X.; Soleilhavoup, M.; Bertrand, G. *Org. Lett.* **2009**, *11*, 3166-3199; (d) Zeng, X.; Frey, G. D.; Kousar, S.; Bertrand, G. *Chem. Eur. J.* **2009**, *15*, 3056-3060.

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

48. Teller, H.; Flügge, S.; Goddard, R.; Fürstner, A. *Angew. Chem. Int. Ed.* **2010**, *49*, 1949-1953.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

were shown to catalyze the cyclization of 1,6-enynes,[49] although at a much slower rate than cationic Au(I) complexes.[36] These activating agents are usually highly hygroscopic and/or moisture sensitive and their handling typically requires more special precautions than the substrates and gold complexes themselves. Therefore there was a strong incentive for the design and isolation of new Au(I) complexes that would not require activation. Despite this fact, before the beginning of this work, there were few examples of isolated mononuclear Au(I) catalysts.



In our group we had previously prepared cationic Au(I) catalysts **1a**-**3a** bearing bulky phosphines and an acetonitrile as a labile ligand.[50,51] Complexes **4a** and **5a** were observed in solution and yielded complexes **4b** and **5b** upon concentration.[52] Although the latter were characterized by X-ray crystallography they were not stable in solution long enough for full characterization by NMR.

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

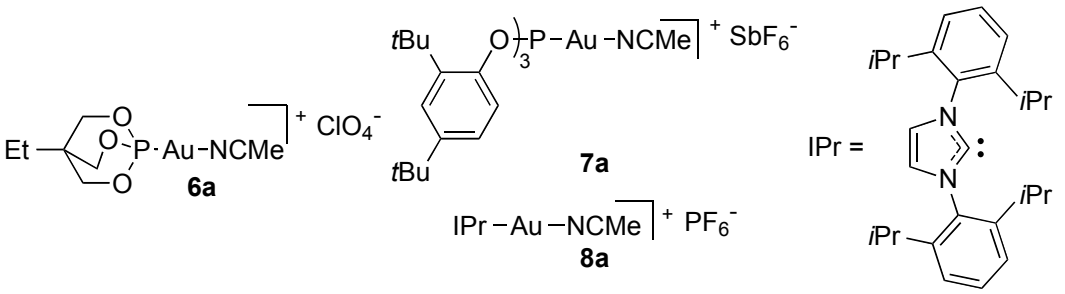
49. Porcel, S.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 2672-2676.

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

51. Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jimenez-Nuñez, E.; Nevado, C.; Herrero-Gómez, Elena; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677-1693.

52. Shapiro, N. D.; Toste, F. D *Proc. Natl. Acad. Sci. U.S.A* **2008**, *105*, 2779-2782.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



On the other hand, there were no known stable cationic Au(I) catalysts bearing phosphites or NHCs. Both complexes **6a**[53] and **8a**[54] decomposed within one day when stored in solid state under ambient conditions. Early attempts to isolate **7a** starting from the corresponding chloride led to an uncrystalizable oil that quickly decomposed.[47]

The use of NTf_2^- as a weakly coordinating anion allowed the isolation of neutral [Au(NTf_2)L] catalysts, with L being a either a phosphine[55,56,57,58] or a bulky NHC.[59,60] As a minor inconvenient, the required $AgNTf_2$ was not commercially available at the begining of this project and is now far more expensive than the more common $AgClO_4$, $AgPF_6$ or $AgSbF_6$. More importantly, catalysts bearing small NHCs or phosphites were unknown.

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

53. Fenske, G. P., Jr.; Mason, W. R. *Inorg Chem.* **1974**, *13*, 1783-6.

54. de Fremont, P.; Stevens, E. D.; Fructos, M R.; Díaz-Requejo, M. M.; Pérez, P. J.; Nolan, S. P. *Chem. Commun.* **2006**, *19*, 2045-2047.

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

56. Shin, S. *Bulletin of the Korean Chemical Society* **2005**, *26*, 1925-1926.

57. Buzas, A.; Istrate, F.; Gagosz, F. *Org. Lett.* **2006**, *8*, 1957-1959.

58. Buzas, A.; Gagosz, F. *J. Am. Chem. Soc.* **2006**, *128*, 12614-12615.

59. Ricard, L.; Gagosz, F. *Organometallics* **2007**, *26*, 4704-4707.

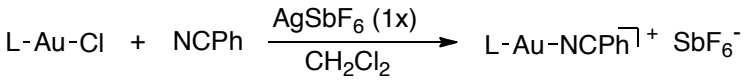
60. Li, G.; Zhang, L. *Angew. Chem. Int. Ed.* **2007**, *46*, 5156-5159.

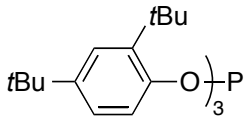
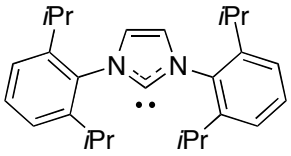
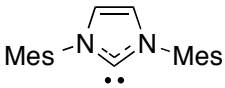
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Results and discussion

We were pleased to discover that employing benzonitrile as labile ligand allowed the isolation of complexes **7b** and **8b** as white air stable solids (Table 1, entries 1-2).[61] The use of a minimum excess of benzonitrile (5-10 mol%) was crucial for the successful isolation of the complexes as higher excesses led to uncrystalizable oils. Unfortunately complex **9b** was obtained as an uncrystalizable oil that decomposed within minutes under ambient conditions (Table 1, entry 3).

Table 1. Synthesis of cationic Au(I) complexes with NCPh as a labile ligand.



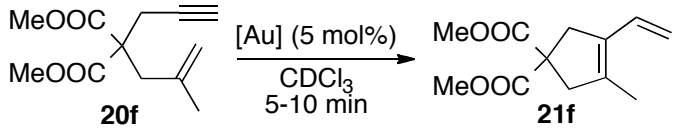
Starting complex	L	Cationic complex	Yield (%)
7		**7b**	88
8	 IPr	**8b**	94
9	 IMes	**9b**	-

Undeterred, we set to try a number of different labile ligands that could stabilize a cationic Au(I) complex containing a small strongly bonding ligand (Scheme 8). As a test of catalytic activity we chose the cyclization of enyne **20f**. Active cationic Au(I) complexes cleanly yield vinyl-cyclopentene **21f** within 5 minutes.[36]

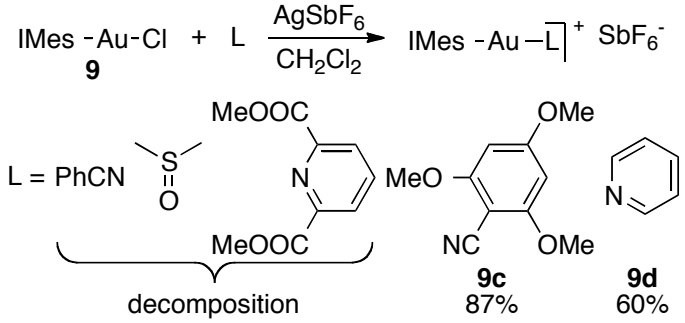
36. Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cardenas, D. J.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 2402-2406.

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

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



Just as in the benzonitrile case, the use of DMSO and dimethyl dipicolinate led to unstable cationic gold complexes as dark-grey solids. Pyridine binds too strongly to gold, resulting in catalytically inactive complex **9d**. However employing 2,4,6-trimethoxybenzonitrile (tmbn) allowed the isolation of complex **9c** as crystalline solid that is stable under ambient conditions yet catalytically active.



Scheme 8.

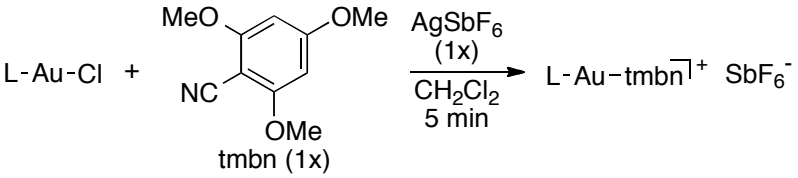
Gratifyingly, the use of tmbn as a labile ligand proved to be a general method for the synthesis of stable cationic Au(I) catalysts bearing strongly σ-donating ligands (Table 2). Steric shielding was not necessary (complex **11c**). Complexes containing hydrogen bond supported heterocyclic carbenes (HBHC, **12c**)[43] and nitrogen acyclic carbenes (NAC, **13c**)[44] were also obtained in this way.

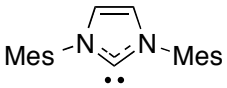
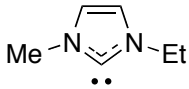
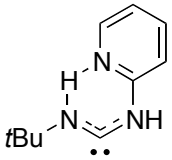
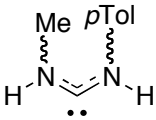
43. Bartolomé, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem.* **2008**, *47*, 11391-11397.

44. Bartolomé, C.; Ramiro, Z.; García-Cuadrado, D.; Pérez-Galán, P.; Raducan, M.; Bour, C.; Echavarren, A. M.; Espinet, P. *Organometallics* **2010**, *29(4)*, 951-956.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Table 2. Cationic Au(I) complexes with tmbn as a labile ligand.



Starting complex	L	Cationic complex	Yield (%)
9	 IMes	**9c**	87
10	 ItBu	**10c**	55
11		**11c**	82
12		**12c**	62
13		**13c**	84

We then set out to test the reactivity and selectivity of the newly synthesized catalysts in several known reactions. In addition to comparing them to the previously described catalytic systems, we also tested the recently discovered Au(I) complexes containing acyclic carbenes.[43,44.] A small library of these modular complexes were provided by the group of Prof. Espinet. Results are summarized in Tables 3-10.

43. Bartolomé, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem.* **2008**, *47*, 11391-11397.

44. Bartolomé, C.; Ramiro, Z.; García-Cuadrado, D.; Pérez-Galán, P.; Raducan, M.; Bour, C.; Echavarren, A. M.; Espinet, P. *Organometallics* **2010**, *29(4)*, 951-956.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

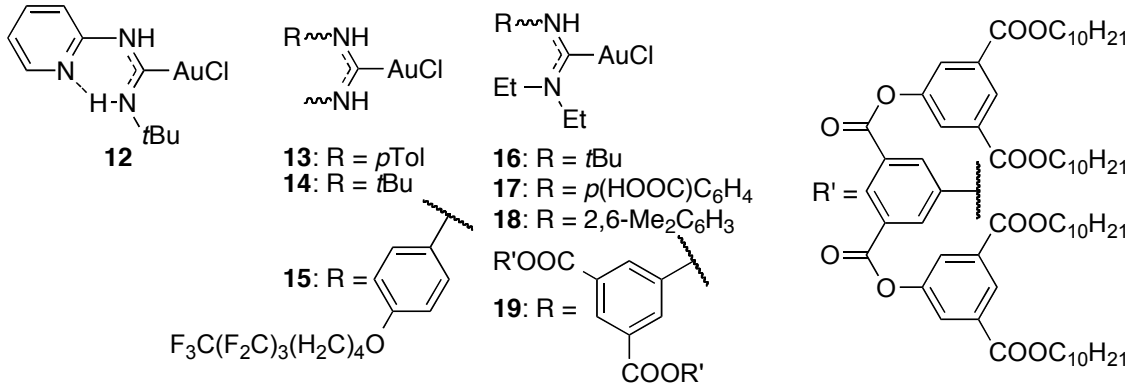
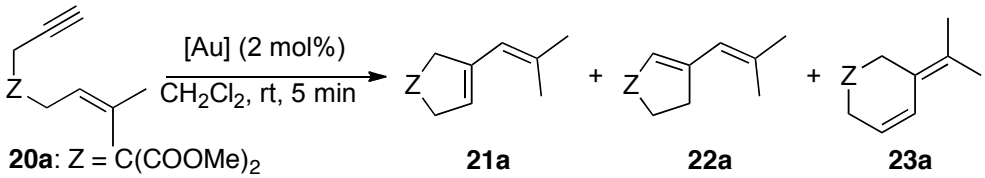


Table 3. Au(I) catalyzed skeletal rearrangement of enyne **20a**.[a]



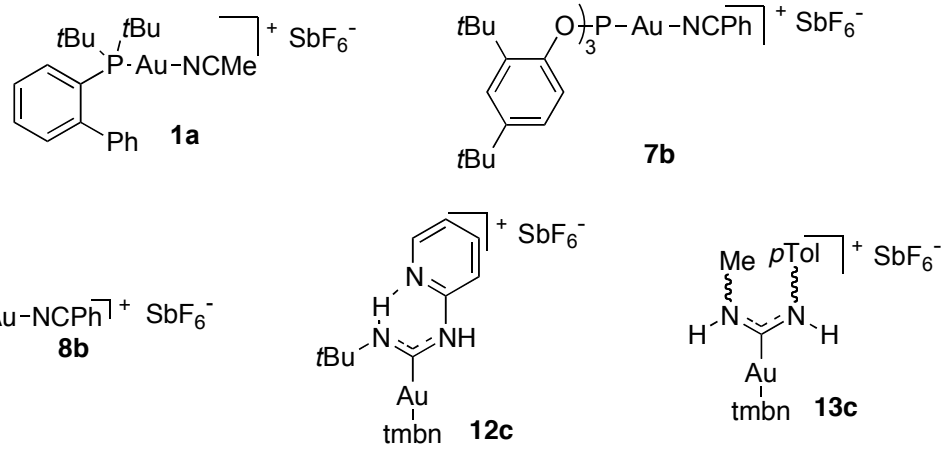
Entry	Catalyst	Product(s) (yield, %)
1[15b]	**1a**	**21a** (98)[b]
2	**7b**	**21a** (76)[b]
3	**8b**	**21a** (83)[b]
4[c,43]	**12**/$AgSbF_6$	**21a** (90) + **23a** (3)
5	**12c**	**21a** (92) + **23a** (2)
6[c,44]	**13**/$AgSbF_6$	**21a** (85) + **23a** (3)
7	**13c**	**21a** (89)+ **23a** (2)
8	**14**/$AgSbF_6$	**21a** (35) + **22a** (21) + **23a** (1)
9	**15**/$AgSbF_6$	**21a** (69) + **22a** (6) + **23a** (2)
10	**16**/$AgSbF_6$	**21a** (81) + **23a** (2)
11	**17**/$AgSbF_6$	**21a** (74) + **22a** (6) + **23a** (2)
12	**19**/$AgSbF_6$	**21a** (79) + **23a** (3)

a) yield determined by ^{1}H NMR against an internal standard; b) isolated yield; c) results obtained by Patricia Pérez-Galán and Dr. Christophe Bour.

15. (b) Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Nuñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677-1693.

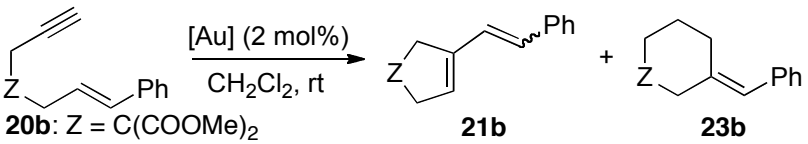
43. Bartolomé, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem.* **2008**, *47*, 11391-11397.

44. Bartolomé, C.; Ramiro, Z.; García-Cuadrado, D.; Pérez-Galán, P.; Raducan, M.; Bour, C.; Echavarren, A. M.; Espinet, P. *Organometallics* **2010**, *29(4)*, 951-956.



The yields and selectivities obtained with the cationic catalysts **7b-8b** and **9c-13c** were similar to those obtained by activation of the corresponding chloride complexes **7-13**. Acyclic carbene catalysts performed poorly in the cyclization of enyne **20a** (Table 3, entries 4-12), whereas cationic catalysts **1a**, **7b**, and **8b** selectively yielded vinylcyclopentadiene **21a**.[15b] The catalysts described here cyclized enynes **20b-d** (Tables 4-6) in a similar manner as [(Ph_3P)AuCl] (**3**) / $Ag^+(WCA)^-$ (WCA^- = SbF_6^- or BF_4^-).[15b,23,36]

Table 4. Au(I) catalyzed skeletal rearrangement of enyne **20b**.[a]



Entry	Catalyst	Yield (%)	**21b** / **23b**	**21b** *E*/*Z*
1[15b]	[(Ph_3P)AuCl] **3** / $AgSbF_6$	100	52 : 48	100 : 0
2	**7b**	73	69 : 31	22 : 1
3	**8b**	76	98 : 2	100 : 0
4[b,43]	**12**/$AgSbF_6$	100	26 : 74	100 : 0

a) isolated yield; b) results obtained by Patricia Pérez-Galán and Dr. Christophe Bour.

15. (b) Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Nuñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677-1693.

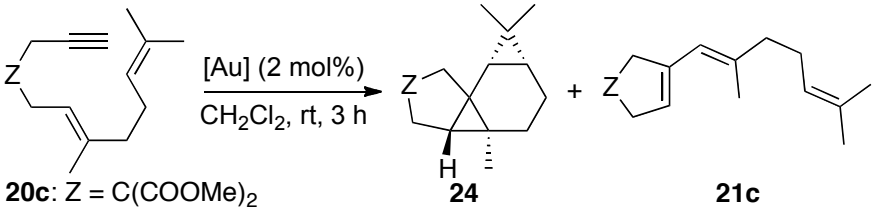
23. Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178-6179.

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

43. Bartolomé, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem.* **2008**, *47*, 11391-11397.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Table 5. Au(I) catalyzed skeletal rearrangement of enyne **20c**.[a]

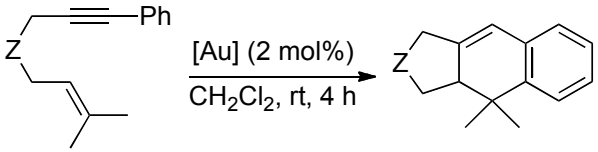


20c: Z = C(COOMe)$_2$ **24** **21c**

Entry	Catalyst	Product(s) (yield, %)
1[c,36]	**3**/AgBF$_4$	**24** (78) + **21c** (7)
2	**13c**	**24** (64)
3[b,44]	**13**/AgSbF$_6$	**24** (83)

a) isolated yield; b) results obtained by Patricia Pérez-Galán and Dr. Christophe Bour; c) reaction performed at -30 ºC, 20 min.

Table 6. Au(I) catalyzed skeletal rearrangement of enyne **20d**.[a]



20d: Z = C(COOMe)$_2$ **25**

Entry	Catalyst	Yield (%)
1[b,23]	**3**/AgSbF$_6$	83
2	**13c**	9[c]
3[d,44]	**13**/AgSbF$_6$	89

a) isolated yield; b) reaction time 12 h; c) 50% of the starting material was recovered; d) results obtained by Patricia Pérez-Galán and Dr. Christophe Bour.

However, **13c** showed a unexpectedly low reactivity in the cyclization of **20d**. On the other hand acyclic carbene proved to be very effective in the methoxycyclization of enyne **20a**,[15b] in most cases (Table 7, entries 4, 6, 15-17) even outperforming the corresponding cationic catalysts (Table 7, entries 2-3, 5, 7).

15. (b) Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Nuñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677-1693.

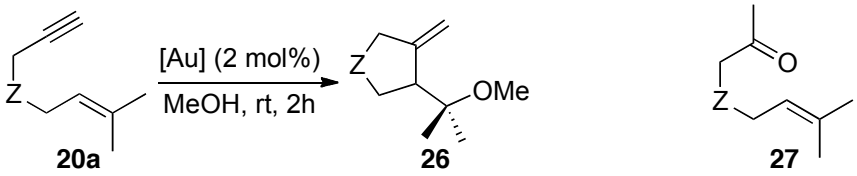
23. Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178-6179.

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

44. Bartolomé, C.; Ramiro, Z.; García-Cuadrado, D.; Pérez-Galán, P.; Raducan, M.; Bour, C.; Echavarren, A. M.; Espinet, P. *Organometallics* **2010**, *29(4)*, 951-956.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Table 7. Au(I) catalyzed methoxycyclization of enyne **20a**.[a]



Entry	Catalyst (mol%)	Time (h)	Conversion (%)	Yield (%)
1[15b]	**1a** (2)	0.25	>98	91
2	**7b** (5)	0.5	nd	68[b,c]
3	**8b** (5)	0.5	nd	76[b]
4[d,43]	**12**/$AgSbF_6$ (5)	3	nd	70[b]
5	**12c** (2)	2	58	56
6[d,44]	**13**/$AgSbF_6$ (2)	2	nd	83
7	**13c** (2)	2	68	65
8	**14**/$AgSbF_6$ (2)	2	65	65
9	**15**/$AgSbF_6$ (2)	2	76	72
10	**16**/$AgSbF_6$ (2)	2	88	83
11	**17**/$AgSbF_6$ (2)	2	90	85
12	**19**/$AgSbF_6$ (2)	2	11	0

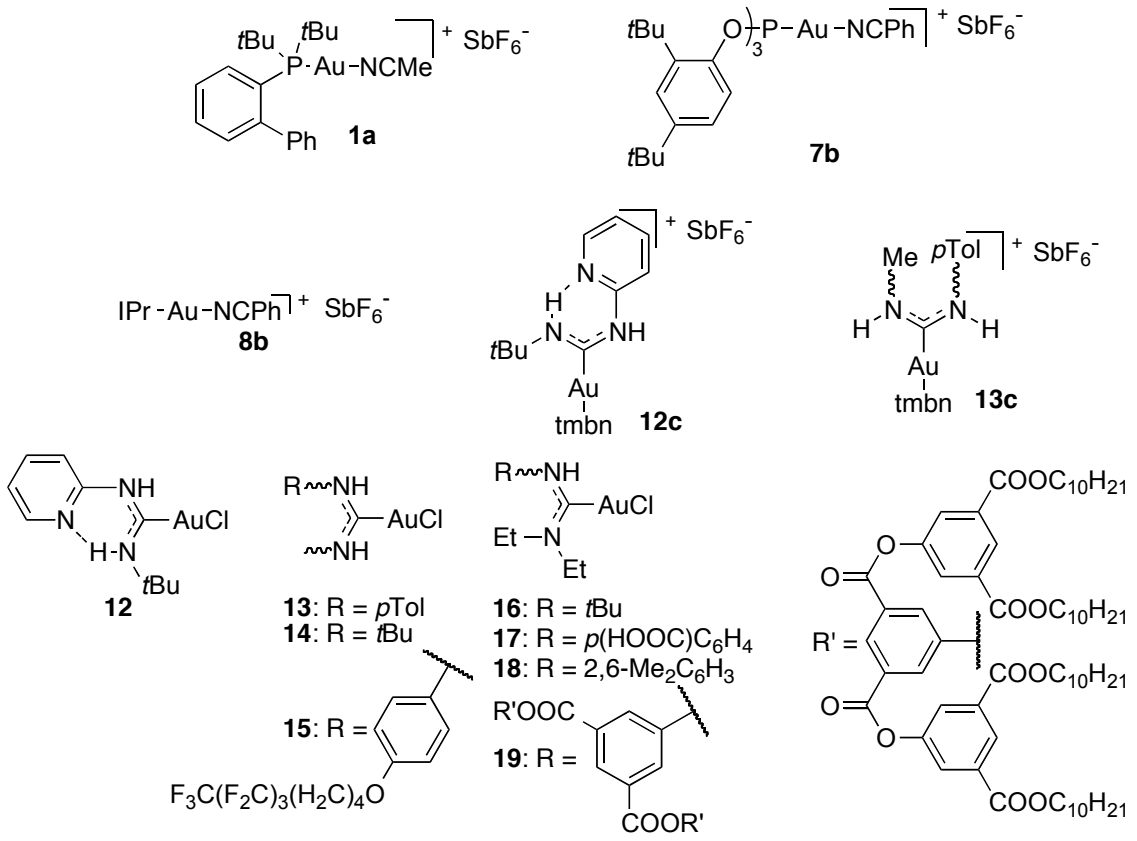
a) yield and conversion determined by ^{1}H NMR against an internal standard; b) reaction performed until completion (TLC), isolated yield; c) 10% of hydration product **27** was also isolated; d) results obtained by Patricia Pérez-Galán and Dr. Christophe Bour.

15. (b) Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Nuñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677-1693.

43. Bartolomé, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem.* **2008**, *47*, 11391-11397.

44. Bartolomé, C.; Ramiro, Z.; García-Cuadrado, D.; Pérez-Galán, P.; Raducan, M.; Bour, C.; Echavarren, A. M.; Espinet, P. *Organometallics* **2010**, *29(4)*, 951-956.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



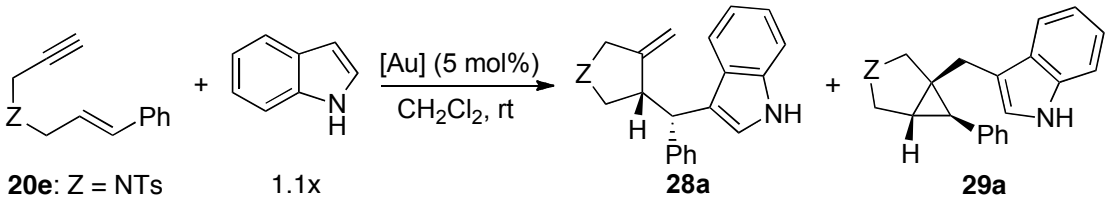
Gold(I) cationic complexes catalyze the addition of carbon nucleophiles to 1,6-enynes.[62,63] The cyclopropane vs. carbene site-selectivity can be controlled by the ligand on gold.[61] The complexes synthesized above were also tested in this reaction in an attempt to improve the site-selectivity (Tables 8-10). The yields and selectivities obtained with cationic complexes **7b**, **9c**, **13c** (Table 8, entries 3, 6; Table 10, entries 3, 6, 9) were similar to those obtained with chloro-complexes **7**, **9**, **13** (Table 8, entries 2, 5; Table 10, entries 2, 5, 8). NHC-Au(I) catalysts (Table 8, entries 4-8, Table 10 entries 4-10) seemed to favor the formation of cyclopropanes **29a-b**, whereas phosphite-Au(I) complexes generally favored the formation of methylene-cyclopentanes **28a-b** (Table 8, entries 2-3; Table 10, entries 2-3). Acyclic carbene complexes **13**, **18** are incompatible with indole (Table 8, entries 9-10). Reaction of enyne **20f** with indoles in the presence of phosphite or NHC catalyst yields double cleavage products **30a-b** (Table 9).

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

62. Amijs, C. H. M.; Ferrer, C.; Echavarren, A. M. Chem. Commun. 2007, 698-700.

63. Toullec, P. Y.; Genin, E.; Leseurre, L.; Genêt, J.-P.; Michelet, V. *Angew. Chem., Int. Ed.* **2006**, *45*, 7427-7430.

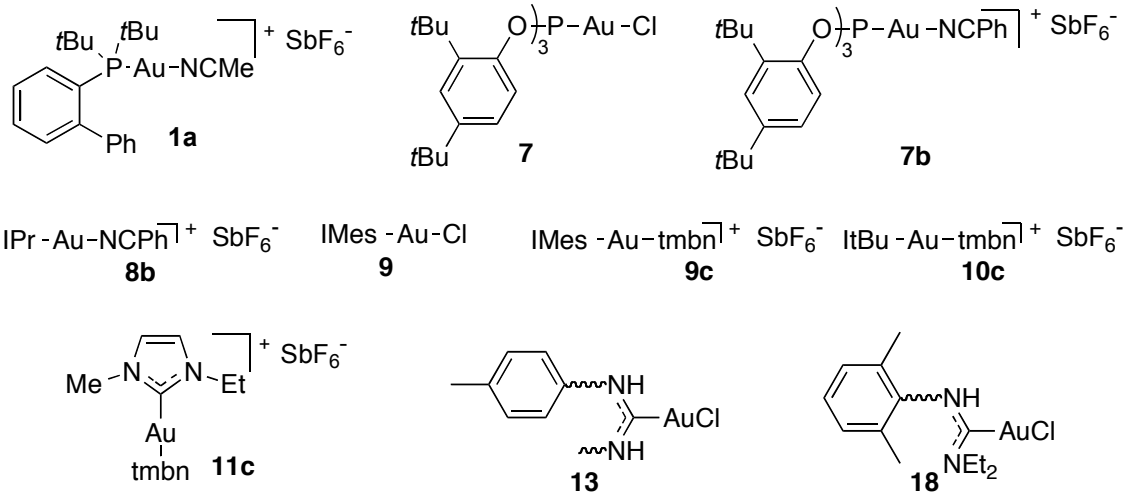
Table 8. Au(I) catalyzed addition of indole to enyne **20e**.[a]



20e: Z = NTs 1.1x **28a** **29a**

Entry	Catalyst	Time (h)	Selectivity (**28a** / **29a**)	Yield (%)
1[61,62]	**1a**	1	80 : 20	74
2[61,62]	**7**/$AgSbF_6$	1	91 : 9	68
3	**7b**	1	84 : 16	71
4	**8b**	17	25 : 75	57[b]
5[61,62]	**9**/$AgSbF_6$	19	45 : 55	72
6	**9c**	19	40 : 60	62[b]
7	**10c**	17	39 : 61	68
8	**11c**	47	84 : 16	33[c]
9	**13**/$AgSbF_6$	12	-	-[d]
10	**18**/$AgSbF_6$	12	-	-[d]

a) isolated yield; b) yield corrected against an internal stadard due to the presence of unknown isomers; c) a fraction containing 23% of the starting enyne and 25%of the starting indole was recovered; d) the indole-substrate mixture turned black upon the addition of the catalyst; no reaction observed after 12 h.

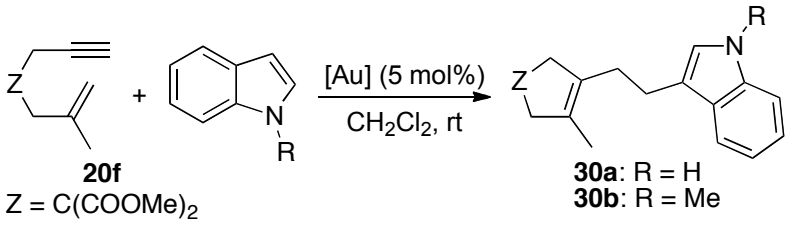


61. Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M. *J. Org. Chem.* **2008**, *73*, 7721-7730.

62. Amijs, C. H. M.; Ferrer, C.; Echavarren, A. M. Chem. Commun. 2007, 698-700.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Table 9. Au(I) catalyzed addition of indole to enyne **20f**.[a]

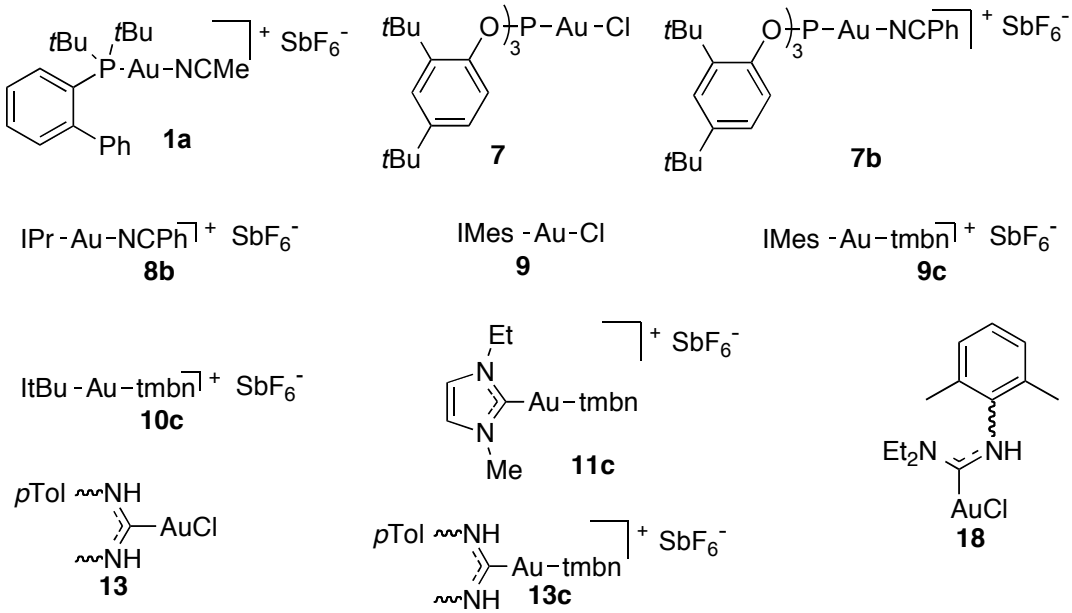


20f
Z = $C(COOMe)_2$

30a: R = H
30b: R = Me

Entry	R	Catalyst	Indole (mol%)	Time (min)	Product (yield, %)
1[62]	H	**7**/$AgSbF_6$	110	90	**30a** (56)
2	H	**7b**	110	60	**30a** (62)
3	H	**7b**	300	30	**30a** (71)
4	H	**8b**	300	45	**30a** (69)
5[62]	Me	**7**/$AgSbF_6$	110	90	**30b** (45)
6	Me	**7b**	300	90	**30b** (80)
7	Me	**8b**	300	60	**30b** (81)

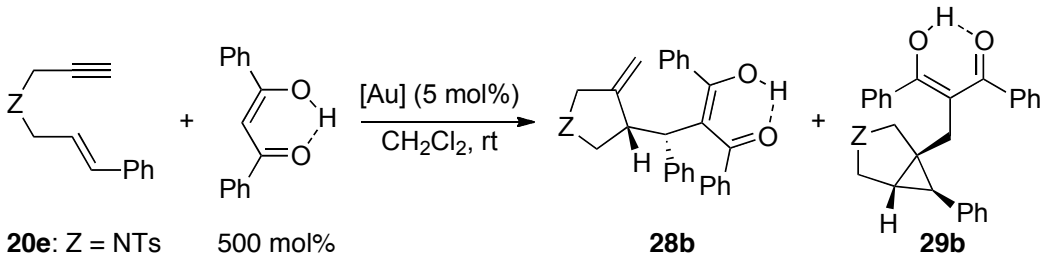
a) isolated yield.



62. Amijs, C. H. M.; Ferrer, C.; Echavarren, A. M. Chem. Commun. 2007, 698-700.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Table 10. Au(I) catalyzed addition of dibenzoylmethane to enyne **20e**.[a]

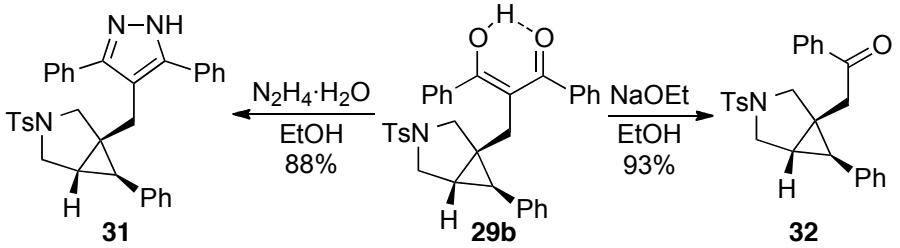


20e: Z = NTs 500 mol% **28b** **29b**

Entry	Catalyst	Time (min)	Selectivity (**28b** / **29b**)	Yield (%)
1[61,62]	**1a**	30	33 : 67	85
2[61,62]	**7**/$AgSbF_6$	30	75 : 25	77
3	**7b**	20	77 : 23	83
4	**8b**	30	<2 : 98	87
5[61,62]	**9**/$AgSbF_6$	30	2 : 98	99
6	**9c**	20	<1 : 99	86
7	**11c**	30	4 : 96	68
8	**13**/$AgSbF_6$	15	3 : 97	73
9	**13c**	15	4 : 96	79
10	**18**/$AgSbF_6$	15	<1 : 99	84

a) isolated yield.

Derivatization of one of the adducts was also briefly examined. Thus, condensation with hydrazine afforded pyrazole **31** in 88% yield. On the other hand, a retro-Claisen reaction was cleanly achieved with NaOEt in EtOH to give ketone **30** in 93% yield.



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

62. Amijs, C. H. M.; Ferrer, C.; Echavarren, A. M. Chem. Commun. 2007, 698-700.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Experimental Part

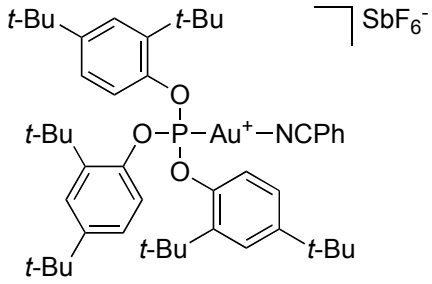
General methods

Unless otherwise specified, all reactions were carried out at room temperature, under Ar, using magnetic stirring and in solvents dried using a Solvent Purification System (SPS). Thin layer chromatography was carried out using TLC-aluminium 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 cromatographer CombyFlash Companion. NMR spectra were recorded at 23 ºC on a Bruker Avance 400 Ultrashield and Bruker Avance 500 Ultrashield apparatus. Mass spectra were recorded on a Waters LCT Premier (ESI) and Waters GCT (EI, CI) spectrometers. Elemental analyses were performed on a LECO CHNS 932 micro-analyzer at the Universidad Complutense de Madrid. Melting points were determined using a Büchi melting point apparatus.

NMR chemical shifts (δ) are expressed in ppm. ^{1}H NMR chemical shifts are referenced to TMS (in the case of $CDCl_3$) or to the solvent residual signal[64] (in the case of other NMR solvents). $^{13}C\{^{1}H\}$ NMR chemical shifts are referenced to the solvent signal.[64] $^{31}P\{^{1}H\}$ NMR chemical shifts are referenced to an external standard (85% aqueous H_3PO_4).

64. (a) Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512-7515; (b) Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. *Organometallics* **2010**, *29*, 2176-2179.

The Au(I) complexes: chloro[tris(2,4-di-*tert*-butylphenyl)phosphite]gold(I) **7**,[47] [(IPr)AuCl] **8**,[65] [(IMes)AuCl] **9**,[23] [(ItBu)AuCl] **10**,[66] and the 1,6-enynes **20a-b**,[27] **20c**,[36] **20d**,[23] **20e-f**,[27] were synthesized according to described procedures. Complexes **12-19**[43,44] were provided by the group of professor Pablo Espinet.



(Benzonitrile)[tris(2,4-di-*tert*-butylphenyl)phosphite]gold(I) hexafluoroantimonate (7b)

A solution of **7** (0.880 g, 0.500 mmol) and PhCN (0.11 mL, 1.1 mmol) in CH_2Cl_2 (10 mL + 1 mL washing) was added over a solution of $AgSbF_6$ (0.350 g, 1.00 mmol) in CH_2Cl_2 (6 mL). A white precipitate appeared immediately. After stirring for 5 min, the mixture was filtered (double filter paper), evaporated and vacuum dried (60ºC overnight). The cationic complex **7b** was obtained as a white, foamy solid (1.05 g, 88%): $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 90.88 (br s, 1P); $^1H\{^{31}P\}$ NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.0 Hz, 2H), 7.77 (t, J = 7.9 Hz, 1H), 7.57 (t, J = 8.0 Hz, 2H), 7.47 (d, J = 2.5 Hz, 3H), 7.43 (d, J = 8.5 Hz, 3H), 7.27 (dd, J = 8.4, 2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, PENDANT) δ 149.14 (C), 147.17 (d, J = 6.4 Hz, C), 139.29 (d, J = 7.2 Hz, C), 136.34 (CH), 134.46 (CH), 129.87 (CH), 125.88 (CH), 124.91 (CH), 120.80 (CN), 119.21 (d, J = 8.9 Hz, CH), 106.87 (C), 35.26 (C), 34.90 (C), 31.49

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

27. Ferrer, C.; Raducan, M.; Nevado, C.; Claverie, C. K.; Echavarren, A. M. *Tetrahedron* **2007**, *63*, 6306-6316.

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

43. Bartolomé, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem.* **2008**, *47*, 11391-11397.

44. Bartolomé, C.; Ramiro, Z.; García-Cuadrado, D.; Pérez-Galán, P.; Raducan, M.; Bour, C.; Echavarren, A. M.; Espinet, P. *Organometallics* **2010**, *29(4)*, 951-956.

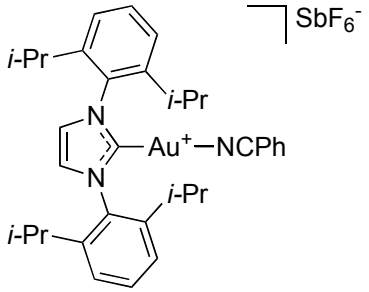
47. López, S.; Herrero-Gómez, E.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 6029-6032.

65. Fructos, M. R.; Belderrain, T. R.; de Frémont, P.; Scott, N. M.; Nolan, S. P.; Díaz-Requejo, M. M.; Pérez, P. J. *Angew. Chem. Int. Ed.* **2005**, *44*, 5284-5288.

66. Baker, M. V.; Barnard, P. J.; Brayshaw, S. K.; Hickey, J. L.; Skelton, B. W.; White, A. H. *Dalton Trans.* **2005**, 37-43.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

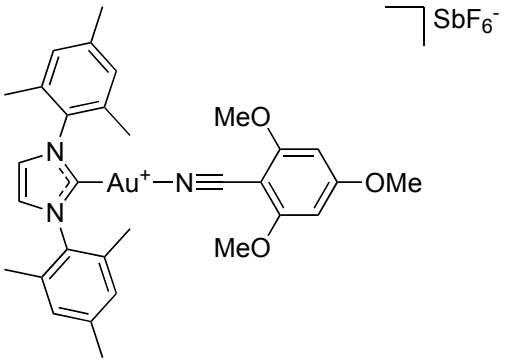
(CH_3), 30.67 (CH_3). Anal. Calcd for $C_{49}H_{68}AuF_6NO_3PSb \cdot 2H_2O$: C, 48.29; H, 5.95; N, 1.15; found: C, 48.26; H, 5.63; N, 1.33.



(Benzonitrile)[1,3-bis(2,6-diisopropyl-phenyl)imidazol-2-ylidene]gold(I) hexafluoroantimonate (8b)

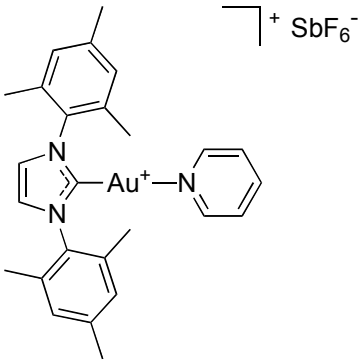
A solution of IPrAuCl **8** (497 mg, 0.800 mmol) and PhCN (0.9 mL, 0.9 mmol) in CH_2Cl_2 (10 mL) was added over a solution of $AgSbF_6$ (275 mg, 0.800 mmol) in CH_2Cl_2 (4 mL). A white precipitate appeared immediately. After stirring for 5 min, the mixture was filtered (double Teflon filter) and the solid was washed with CH_2Cl_2 (2 x 4 mL). The CH_2Cl_2 solution was evaporated to small volume (*ca.* 2 mL) and Et_2O (8 mL) was slowly added with shaking. The precipitate was decanted and washed with Et_2O (2 x 4 mL), then vacuum dried. The cationic complex **8b** was obtained as a white, air-stable crystalline solid (699 mg, 94%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.77 (m, 3H), 7.60 (t, J = 7.9 Hz, 2H), 7.58 (t, J = 7.9 Hz, 2H), 7.43 (s, 2H), 7.38 (d, J = 7.8 Hz, 4H), 2.51 (septet, J = 7.0 Hz, 4H), 1.34 (d, J = 6.9 Hz, 6H), 1.27 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, PENDANT) δ 165.72 (C), 145.81 (C), 136.69 (CH), 133.86 (CH), 133.25 (C), 131.51 (CH), 130.14 (CH), 125.29 (CH), 124.75 (CH), 119.80 (C), 106.55 (C), 29.03 (CH), 24.92 (CH_3), 24.12 (CH_3). Anal. Calcd for $C_{34}H_{41}AuF_6N_3Sb$: C, 44.17; H, 4.47; N, 4.55; found: C, 44.12; H, 4.43; N, 4.63.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



(2,4,6-Trimethoxybenzonitrile)[1,3-bis(2,4,6-trimethyl-phenyl)imidazol-2-ylidene]gold(I) hexafluoroantimonate (9c)

A solution of $AgSbF_6$ (210 mg, 0.600 mmol) in CH_2Cl_2 (6 mL) was added over IMesAuCl **9** (322 mg, 0.600 mmol) and 2,4,6-trimethoxybenzonitrile (116 mg, 0.600 mmol) in CH_2Cl_2 (6 mL) and the mixture was stirred for 5 min. The mixture was filtered (2 x HPLC Teflon filter) then Et_2O (6 mL) and hexane (6 mL) were added. Filtration and vacuum drying yielded a bright white solid which was vacuum dried at 100 ºC for 2 h (489 mg, 88%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (s, 2H), 7.07 (s, 4H), 6.10 (s, 2H), 3.90 (s, 3H), 3.87 (s, 6H), 2.39 (s, 6H), 2.13 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.18 (C), 165.76 (C), 165.21 (C), 140.55 (C), 134.79 (C), 134.19 (C), 129.82 (CH), 124.11 (CH), 118.39 (C), 91.31 (CH), 78.20 (C), 56.79 (CH_3), 56.61 (CH_3), 21.34 (CH_3), 17.86 (CH_3); HRMS-ESI *m/z* calcd for $C_{31}H_{35}AuN_3O_3$ $[M]^+$ 694.2344, found 694.2332. Anal. Calcd for $C_{31}H_{35}AuF_6N_3O_3Sb$: C, 40.02; H, 3.79; N, 4.52; found: C, 39.89; H, 3.79; N, 4.89.

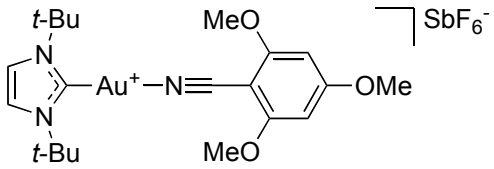


[1,3-Bis(2,4,6-trimethyl-phenyl)imidazol-2-ylidene](pyridine)gold(I) hexafluoroantimonate (9d)

A solution of IMesAuCl (54 mg, 0.10 mmol) and pyridine (0.04 mL, 0.50 mmol) in dry CH_2Cl_2 (1 mL) was added over $AgSbF_6$ (35 mg, 0.1 mmol) and stirred 5 min. Filtration (Teflon), evaporation to dryness and trituration with Et_2O and few drops of CH_2Cl_2 and

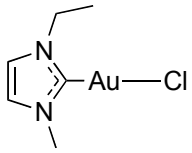
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

vacuum drying yielded a grey solid. This was dissolved in CH_2Cl_2, filtered through Celite then crystallized from $CHCl_3/Et_2O$ at 5-8 ^oC overnight (50 mg, 60% yield).
^1H NMR (400 MHz, $CDCl_3$) δ 8.09-8.07 (m, 2H), 7.98-7.93 (m, 1H), 7.58-7.55 (m, 2H), 7.27 (s, 2H), 7.09 (m, 4H), 2.39 (s, 6H), 2.16 (s, 12H).



(2,4,6-Trimethoxybenzonitrile)[1,3-di-*tert*-butyl-imidazol-2-ylidene]gold(I) hexafluoroantimonate (10c)

A solution of ItBuAuCl **10** (21.0 mg, 50.9 μmol) and 2,4,6-trimethoxybenzonitrile (9.8 mg, 50.9 μmol) in CH_2Cl_2 (0.5 mL) was added over solid $AgSbF_6$ (17.5 mg, 50.9 μmol). A white precipitate appeared immediately. After stirring for 5 min, the mixture was filtered (HPLC teflon filter) and the residue washed with CH_2Cl_2 (2 x 0.2 mL). Addition of Et_2O to the filtrate led to the formation of a white precipitate that was filtered and air-dried. The cationic complex **10c** was obtained as a bright white, air-stable solid (22.6 mg, 55%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (s, 2H), 6.17 (s, 2H), 3.97 (s, 6H), 3.95 (s, 3H), 1.89 (s, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.17 (C), 165.92 (C), 159.29 (C), 118.29 (CH), 91.30 (CH), 78.65 (C), 59.48 (C), 56.87 (CH_3), 56.58 (CH_3), 32.22 (CH_3); CN was not observed; HRMS-ESI *m/z* calcd for $C_{21}H_{31}AuN_3O_3$ $[M]^+$ 570.2031, found 570.2038. Anal. Calcd for $C_{21}H_{31}AuF_6N_3O_3Sb$: C, 31.29; H, 3.88; N, 5.21; found: C, 31.21; H, 4.18; N, 5.59.



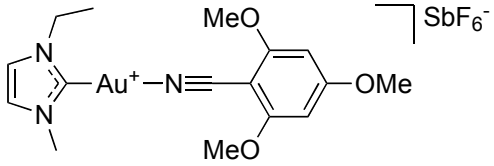
Chloro(1-ethyl-3-methyl-imidazol-2-ylidene)gold(I) (11)

Procedure similar to the synthesis of [Au(Me_2-bimy)Cl]:[67] Ag_2O (116 mg, 0.500 mmol) was added to a CH_2Cl_2 (50 mL) and EtOH (50 mL) mixed solution of 1-ethyl-3-methylimidazolium bromide (195 mg, 1.00 mmol). After stirring for 2 h at room temperature a grey precipitate was formed. Au(SMe_2)Cl (295 mg, 1.00 mmol) was then added (white precipitate appeared), and the resultant solution was stirred for an

67. Wang, H. M. J.; Chen, C. Y. L.; Lin I. J. B. *Organometallics* **1999**, *18*, 1216-1223.

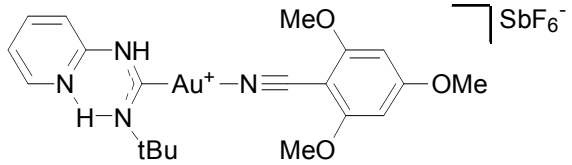
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

additional 2 h. After the white precipitate was filtered, the solvent was removed to give a yellow oil. Precipitation from CH_2Cl_2/Et_2O gave a yellow oil, which yielded an off-white solid by scratching (280 mg, 82%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, J = 1.9 Hz, 1H), 6.96 (d, J = 1.9 Hz, 1H), 4.23 (q, J = 7.3 Hz, 2H), 3.83 (s, 3H), 1.47 (t, J = 7.3 Hz, 3H); ^{13}C NMR (PENDANT, 100 MHz, $CDCl_3$) δ 170.66 (C), 121.97 (CH), 120.06 (CH), 46.52 (CH_2 sp^3), 38.38 (CH_3), 16.67 (CH_3); HRMS-ESI *m/z* calcd for $C_6H_{10}AuClN_2Na$ $[M+Na]^+$ 365.0096, found 365.0080.



(1-Ethyl-3-methyl-imidazol-2-ylidene)(2,4,6-trimethoxybenzonitrile)gold(I) hexafluoroantimonate (11c)

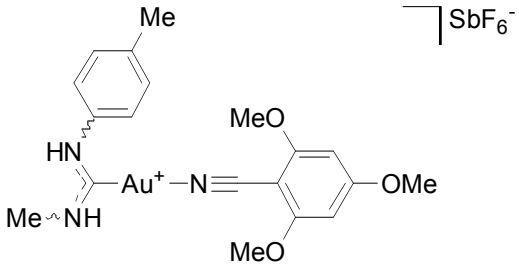
A solution of **11** (172 mg, 0.502 mmol) and 2,4,6-trimethoxybenzonitrile (99 mg, 0.502 mmol) in CH_2Cl_2 (5 mL) was added over a solution of $AgSbF_6$ (173 mg, 0.502 mmol) in CH_2Cl_2 (2.5 mL). A white precipitate appeared immediately. After stirring for 5 min, the mixture was filtered (double filter-paper) and the residue washed with CH_2Cl_2. Addition of Et_2O to the filtrate led to the formation of a white precipitate that was filtered and air-dried. The cationic complex **11c** was obtained as a bright white, air-stable solid (312 mg, 84%): ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.13 (d, J = 1.9 Hz, 1H), 7.11 (d, J = 1.9 Hz, 1H), 6.17 (s, 2H), 4.22 (q, J = 7.3 Hz, 2H), 3.94 (s, 6H), 3.92 (s, 3H), 3.85 (s, 3H), 1.49 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 169.38 (C), 166.21 (C), 162.86 (C), 123.61 (CH), 121.65 (CH), 118.80 (C), 91.48 (CH), 78.75 (C), 57.07 (CH_3), 56.72 (CH_3), 47.24 (CH_2), 38.82 (CH_3), 16.84 (CH_3); confirmed by PENDANT and HMBC; HRMS-ESI *m/z* calcd for $C_{16}H_{21}AuN_3O_3$ $[M+Na]^+$ 500.1249, found 500.1263. Anal Calcd. for $C_{16}H_{21}AuF_6N_3O_3Sb$: C, 26.11; H, 2.88; N, 5.71; found: C, 25.84; H, 2.93; N, 5.83.



(2,4,6-Trimethoxybenzonitrile)[(2-pyridylamino)(*tert*-butylamino)methylene] gold(I) hexafluoroantimonate (12c)

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

A solution of **12** (41 mg, 0.10 mmol) and 2,4,6-trimethoxybenzonitrile (59 mg, 0.30 mmol) in dry CH_2Cl_2 (1 mL) was added over a solution of $AgSbF_6$ (35 mg, 0.10 mmol) in CH_2Cl_2 (0.6 mL). A white precipitate appeared immediately. After stirring for 5 min, the mixture was filtered (double HPLC teflon filter). Addition of Et_2O (5 mL) led to the formation of a white precipitate (1 min) which filtered, washed with Et_2O (2x5mL) and air-dried. The cationic complex **12c** was obtained as a white, air-stable solid. (50 mg, 62%) ^{1}H NMR (400 MHz, CD_3CN) δ 13.29 (br s, 1H), 9.27 (br s, 1H), 8.32-8.31 (m, 1H), 7.87-7.83 (m, 1H), 7.20 (dd, J = 6.9, 5.6 Hz, 1H), 7.03 (d, J = 8.3 Hz, 1H), 6.23 (s, 2H), 3.88 (s, 6H), 3.86 (s, 3H), 1.63 (s, 9H); ^{13}C NMR (100 MHz, CD_3CN) δ 182.52 (C), 166.83 (C), 164.86 (C), 155.52 (C), 146.78 (CH), 140.50 (CH), 121.28 (CH), 115.53 (CN), 114.67 (CH), 91.87 (CH), 57.17 (CH_3), 56.78 (CH_3), 55.08 (C), 31.15 (CH_3); HRMS-ESI: 567.1698; Calcd for $C_{20}H_{26}AuN_4O_3$: 567.1671; Anal. Calcd for $C_{20}H_{26}AuF_6N_4O_3Sb$: C, 29.91; H, 3.26; N, 6.98; Found: C, 30.03; H, 3.26; N, 6.98. IR (neat): ν = 2261.07 cm^{-1} (CN).



(73 : 15 : 12 in CD_3CN)

(2,4,6-Trimethoxybenzonitrile)[(methylamino)(*p*-tolylamino)methylene] gold(I) hexafluoroantimonate (13c)

A solution of **13** (18 mg, 47 μmol) and 2,4,6-trimethoxybenzonitrile (9.3 mg, 47 μmol) in dry CH_2Cl_2 (0.5 mL) was added over solid $AgSbF_6$ (17 mg, 47 μmol). A white precipitate appeared immediately. After stirring for 5 min, the mixture was filtered (HPLC teflon filter) and the residue washed with CH_2Cl_2 (2x0.1 mL). Addition of Et_2O led to the formation of a white precipitate which was filtered and air-dried. The cationic complex **13c** was obtained as a white, air-stable solid. (31 mg, 84%) ^{1}H NMR (400 MHz, CD_3CN) δ major isomer: 8.63 (br s, 1H), 7.54 (br s, 1H), 7.34 (d, J = 8.3 Hz, 2H), 7.24 (d, J = 8.3 Hz, 2H), 6.22 (s, 2H), 3.88 (s, 6H), 3.86 (s, 3H), 2.91 (d, J = 5.3 Hz, 3H), 2.35 (s, 3H); ^{13}C NMR (400 MHz; CD_3CN) δ major isomer: 182.71 (C), 166.79 (C), 164.83 (C), 138.92 (C), 138.41 (C), 130.81 (CH), 125.87 (CH), 115.03 (CN, observed in HMBC), 91.86 (CH), 83.76 (C, observed in HMBC), 57.16 (CH_3), 56.78

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

(CH_3), 30.56 (CH_3), 21.00 (CH_3); stereoisomers ratio 6:1.2:1. HRMS-ESI: 538.1398; calcd for $C_{19}H_{23}AuN_3O_3$ (M-SbF_6): 538.1405; Anal. Calcd for $C_{19}H_{23}AuF_6N_3O_3Sb$: C, 29.48; H, 2.99; N, 5.43; found: C, 29.49; H, 3.00; N, 5.34. IR (neat): ν = 2255.30 cm^{-1} (CN).

General procedures for the skeletal rearrangement of 1,6-enynes.

Procedure A (activation with $AgSbF_6$): The enyne (0.2 mmol) and the gold complex (4 μmol) were dissolved with stirring in a solution of $AgSbF_6$ in CH_2Cl_2 (2 mM, 2 mL; 4 μmol of $AgSbF_6$). After 5 min, the reaction was quenched with a solution of Et_3N in hexanes (0.1 M, 2 mL) then filtered through a pad of silica which was washed with Et_2O. The internal standard was added, the mixture was evaporated, vacuum dried and analyzed by ^1H NMR ($CDCl_3$).

Procedure B (cationic catalysts): The enyne (0.2 mmol) ws dissolved with stirring in a solution of the cationic catalyst (4 μmol) in CH_2Cl_2 (2 mL). After 5 min, the reaction was quenched with a solution of Et_3N in hexanes (0.1 M, 2 mL) then filtered through a pad of silica which was washed with Et_2O. The internal standard was added, the mixture was evaporated, vacuum dried and analyzed by ^1H NMR ($CDCl_3$).

Procedure C (isolated products): the enyne (0.2 mmol) was dissolved in a solution of the catalyst (0.004 mmol) in dry CH_2Cl_2 (2 mL) and stirred for the indicated time. After quenching with Et_3N (0.1 M in hexanes, 1 mL), the mixture was concentrated on Celite and submitted to flash chromatography.

NMR data for the rearranged products **21a**,[68] **21b**,[69] **21c**,[70] **21f**,[71] **22a**,[15b] **23a**,[69] **23b**,[15b] **24**,[70] **25**,[23] was consistent with the literature.

General procedure for the methoxycyclization of 1,6-enynes.

Procedure A (activation with $AgSbF_6$): The enyne (0.2 mmol) and the gold complex (4 μmol) were dissolved with stirring in a solution of $AgSbF_6$ in MeOH (2 mM, 2 mL; 4 μmol of $AgSbF_6$). After 1 h, the reaction was quenched with a solution of Et_3N in

15. (b) Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Nuñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677-1693.

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

68. Hoye, T. R.; Suriano, J. A. *Organometallics* **1992,** *11*, 2044-2050.

69. Faller, J. W.; Fontaine, P. P. *J. Organomet. Chem.* **2006**, 691, 1912-1918.

70. Nieto-Oberhuber, C.; López, S.; Muñoz, M. P.; Jiménez-Nuñez, E.; Buñuel, E.; Cárdenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1694-1702.

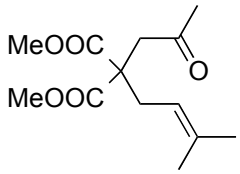
71. Steinig, A. G.; de Meijere, A. *Eur. J. Org. Chem.* **1999**, 1333-1344.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

hexanes (0.1 M, 2 mL) then filtered through a pad of silica which was washed with Et_2O. The internal standard was added, the mixture was evaporated, vacuum dried and analyzed by ^1H NMR ($CDCl_3$).

Procedure B (cationic catalysts): The enyne (0.2 mmol) ws dissolved with stirring in a solution of the cationic catalyst (4 μmol) in MeOH (2 mL). After 1 h, the reaction was quenched with a solution of Et_3N in hexanes (0.1 M, 2 mL) then filtered through a pad of silica which was washed with Et_2O. The internal standard was added, the mixture was evaporated, vacuum dried and analyzed by ^1H NMR ($CDCl_3$).

NMR data for product **26**[7a] was consistent with the literature.



Dimethyl 2-(3-methylbut-2-en-1-yl)-2-(2-oxopropyl)malonate 27

^1H NMR (400 MHz, $CDCl_3$) δ 4.90 (triple septuplet, J = 7.7, 1.5 Hz, 1H), 3.72 (s, 6H), 3.09 (s, 2H), 2.74 (d, J = 7.7 Hz, 2H), 2.13 (s, 3H), 1.70-1.69 (m, 3H), 1.56 (m, 3H).

General procedure for the reaction of 1,6-enynes with C-nucleophiles.[62] To a solution of enyne (65 mg, 0.20 mmol) and the nucleophile in CH_2Cl_2 (1.5 mL) was added a mixture of the gold catalyst (0.01 mmol, 5 mol%) and $AgSbF_6$ (3.4 mg, 0.01 mol, 5 mol%) in CH_2Cl_2 (0.5 mL). The reaction mixture was stirred at room temperature (unless stated otherwise) for the time indicated in Table. The mixture was filtered trough silica gel with CH_2Cl_2 and the solvents evaporated. The residue was chromatographed to give the desired product.

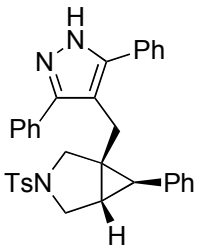
NMR data for products **28a-b, 29a-b, 30a-b**[61] was consistent with the literature.

7. (a) Méndez, M.; Muñoz, M. P.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 11549-11550.

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

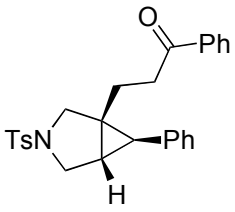
62. Amijs, C. H. M.; Ferrer, C.; Echavarren, A. M. Chem. Commun. 2007, 698-700.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



1-((3,5-Diphenyl-1*H*-pyrazol-4-yl)methyl)-6-phenyl-3-tosyl-3-azabicyclo[3.1.0]hexane (31)

A sample of **29b** (56 mg, 0.10 mmol) was dissolved in a solution of hydrazine hydrate (5.5 μL, 0.11 mmol) in EtOH (2 mL) and the mixture was heated at 48 ºC for 25 h. More hydrazine hydrate (5.5 μL, 0.11 mmol) was added and after 8 h at 48 ºC the solution was vacuum dried, evaporated on Celite from CH_2Cl_2 and submitted to flash chromatography (hexane/EtOAc = 3:2, 2x10 cm silica). The compound **31** was obtained as a white solid (49 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.2 Hz, 2H), 7.43-7.41 (m, 6H), 7.32 (d, J = 8.0 Hz, 2H), 7.26-7.15 (m, 7H), 6.82 (d, J = 7.0 Hz, 2H), 3.27 (d, J = 9.1 Hz, 1H), 3.17 (d, J = 9.4 Hz, 1H), 2.74 (d, J = 15.8 Hz, 1H), 2.70 (d, J = 9.4 Hz, 1H), 2.48 (dd, J = 9.1, 4.0 Hz, 1H), 2.46 (s, 3H), 2.38 (d, J = 15.8 Hz, 1H), 1.94 (d, J = 4.3 Hz, 1H), 0.97 (t, J = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4 (observed in HMBC, C), 143.61 (C), 136.84 (C), 133.25 (C), 132.19 (br s, C), 129.61 (2CH), 129.00 (4CH), 128.70 (2CH), 128.55 (2CH), 128.29 (6CH), 127.64 (2CH), 126.35 (1CH), 112.76 (C), 52.13 (CH_2), 50.42 (CH_2), 35.16 (C), 29.62 (CH), 26.49 (CH), 21.70 (CH_3), 20.76 (CH_2), (confirmed by PENDANT, HMQC, HMBC); HRMS-ESI *m/z* calcd for $C_{34}H_{32}N_3O_2S$ $[M+H]^+$ 546.2215, found 546.2216.



1-Phenyl-3-(6-phenyl-3-tosyl-3-azabicyclo[3.1.0]hexan-1-yl)propan-1-one (32)

A sample of **29b** (59 mg, 0.10 mmol) was dissolved in a solution of sodium ethoxide (8.2 mg, 0.11 mmol) in EtOH (2 mL) then heated at 48ºC. After 20 min a light yellow suspension appeared. After further heating for 7 h the mixture was vacuum dried, then partitioned between CH_2Cl_2 (4 mL) and saturated $NaHCO_3$ (1 mL). The organic layer was washed with H_2O (1 mL) and the combined aqueous layers were extracted with CH_2Cl_2 (2 mL). Evaporation of the organic extract, followed by flash chromatography

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

(hexane/EtOAc = 4:1; 1x15 cm SiO_2) yielded an off-white solid (41 mg, 93%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.3 Hz, 2H), 7.54-7.47 (m, 3H), 7.36-7.27 (m, 6H), 7.24-7.20 (m, 1H), 7.12-7.10 (m, 2H), 3.76 (d, J = 9.4 Hz, 1H), 3.68 (d, J = 9.2 Hz, 1H), 3.21 (dd, J = 9.2, 3.9 Hz, 1H), 3.07 (d, J = 9.4 Hz, 1H), 2.73 (ddd, J = 15.7, 10.4, 5.3 Hz, 1H), 2.61 (ddd, J = 15.9, 10.5, 5.6 Hz, 1H), 2.26 (d, J = 4.2 Hz, 1H), 1.89-1.82 (m, 2H), 1.63 (ddd, J = 14.6, 10.5, 5.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.57 (C), 143.80 (C), 136.76 (C), 136.33 (C), 133.46 (C), 133.21 (CH), 129.90 (CH), 128.72 (CH), 128.59 (CH), 128.40 (CH), 128.14 (CH), 127.74 (2CH), 126.51 (CH), 54.28 (CH_2), 50.62 (CH_2), 36.33 (CH_2), 34.89 (C), 29.57 (CH), 26.30 (CH), 23.50 (CH_2), 21.71 (CH_3) (confirmed by PENDANT, HSQCed, HMBC); IR (cm^{-1}) 1734 (CO); HRMS-ESI *m/z* calcd for $C_{27}H_{27}NO_3SNa$ $[M+Na]^+$ 468.1609, found 468.1620.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

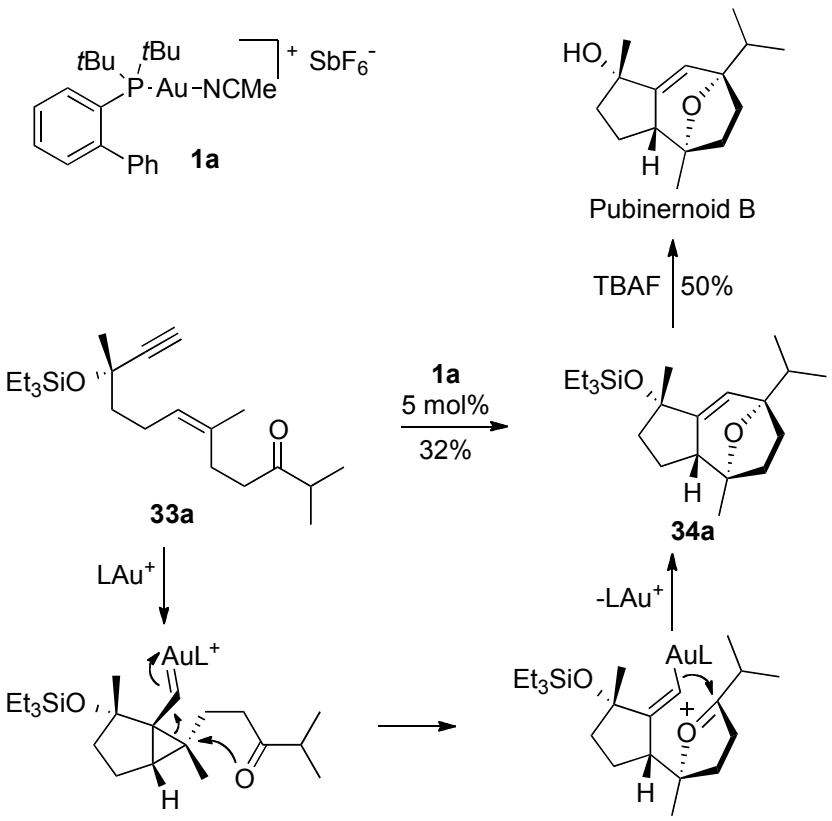
Intramolecular 1,5-migrations via allylgold cations

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Introduction

In recent years, Au(I) catalyzed activation of alkynes has made its way into total synthesis of natural compounds. For example, our group took advantage of the recently described formal [2+2+2] alkyne/alkene/carbonyl cycloaddition[72] and designed new syntheses for pubinernoid B (Scheme 9), orientalol F,[73] and englerin A, (Scheme 10)[74] a sesquiterpene that has been shown to selectively inhibit the growth of renal cancer cell lines at the nanomolar level.

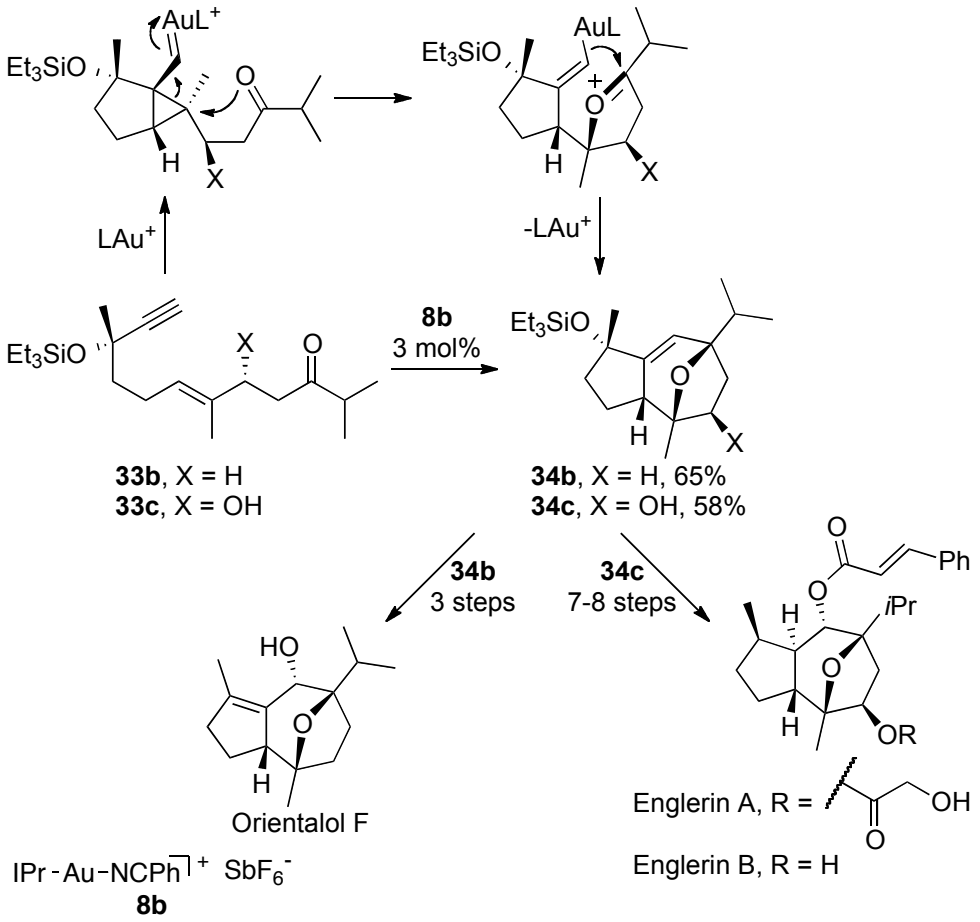


Scheme 9. Key steps in the syntheses of pubinernoid B.

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

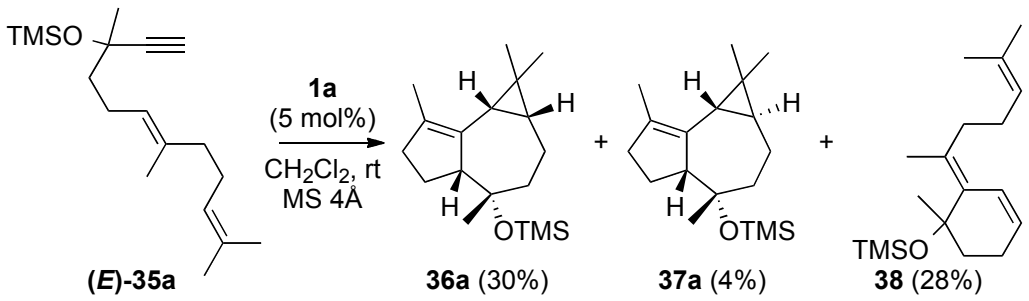
73. Jiménez-Núñez, E.; Molawi, K.; Echavarren A. M. *Chem. Commun.* **2009**, 7327-7329.

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



Scheme 10. Key steps in the syntheses of orientalol F and englerin A-B.

The key step in the above syntheses is the stereoselective cyclization of ketoenynes **33a-c** that leads to oxatricycles **34a-c** presumably via cyclopropyl carbene and vinyl-gold(I)/oxonium intermediates. We were intrigued to find out that similar dienyne **(*E*)-35a**, functionalized at the propargylic position showed a markedly different reactivity, yielding mainly tricyclic compounds **36-37** (Scheme 11).[75]

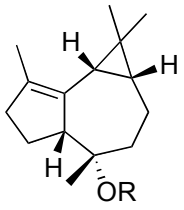


Scheme 11.

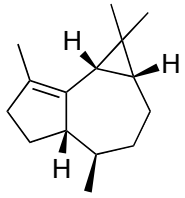
75. Compounds **35a-38a** were isolated and characterized by Eloisa Jiménez-Núñez.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

We set to further investigate this novel transformation[76] as it could provide a straightforward route to sesquiterpenes 4-epiglobulol and 4-aromadendrene.

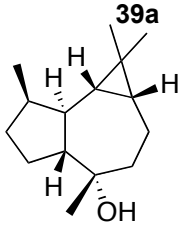


36a, R = TMS



4-Aromadendrene

39a

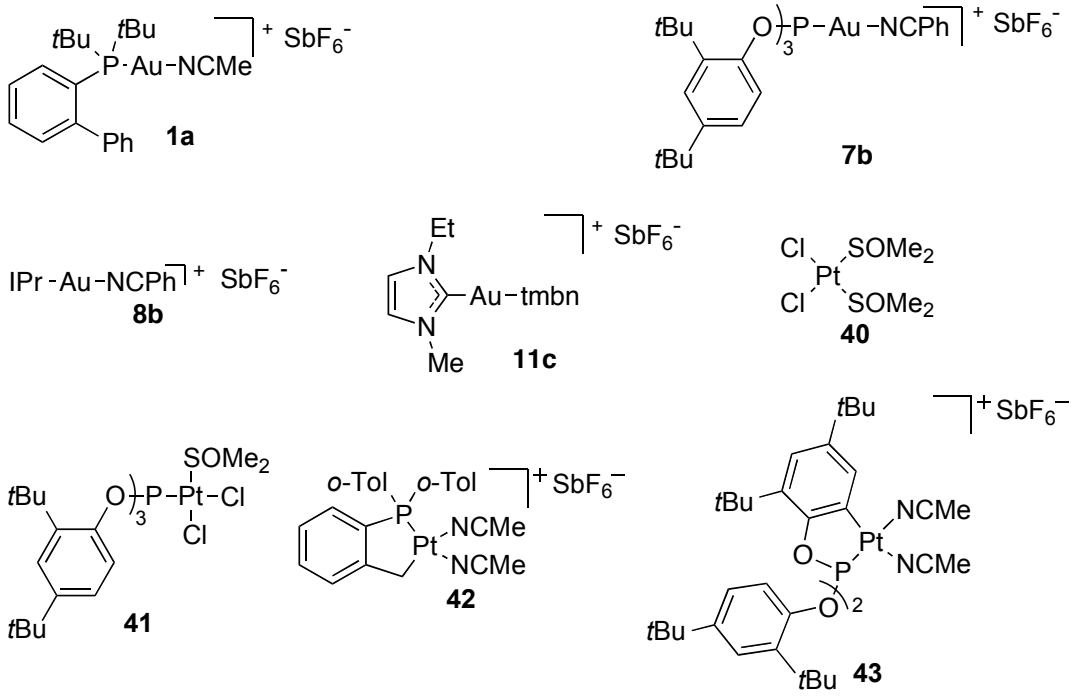


4-Epiglobulol

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

Results and discussion

The initial attempts at optimizing the formation of tricycle **36** were not encouraging. Regardless of the ligand on gold, the best yields achieved for **36a** stayed within 24-35% (Table 11, entries 1-3, 5). An additional rearrangement product **39a** was identified as a major product using NHC catalyst **11c** (Table 11, entries 6-7). Although the compound was unstable under flash chromatography conditions, it could be obtained pure enough (91%, Table 11, entry 7) for characterization by ^{1}H and ^{13}C NMR. This product of single-cleavage skeletal rearrangement shows some similarities with previously described diene **39b**.[73]



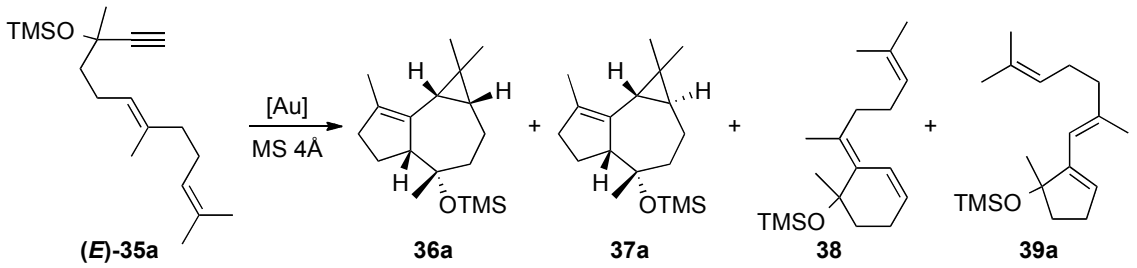
The apparent selectivity of the phosphite catalyst **7b** (Table 11, entries 2-3) is probably due to the instability of trienes **38**, **39a** in the presence of Lewis acids.[77] Reducing the temperature lowers the yield of tricycles (Table 11, entries 3, 7). The use of MeCN drastically reduces the activity of the catalysts (Table 11, entries 4, 8).

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

77. See for example the polymerization of styrenes using the catalytic system (NHC)$AuBr_3$/$NaBAr^F_4$ (Ar^F = 3,5-bis(trifluoromethyl)phenyl), Urbano, J.; Hormigo, A. J.; de Frémont, P.; Nolan, S. P.; Díaz-Requejo, M. M.; Pérez, P. J. *Chem. Commun.*, 2008, 759-761.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

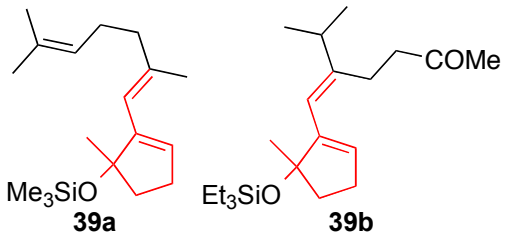
Table 11. Attempted optimization of the rearrangement of enyne **(*E*)-35a** towards tricycle **36**.[a]



(*E*)-35a **36a** **37a** **38** **39a**

Entry	Catalyst (mol%)	Solvent	Temperature (ºC)	Time (h)	Yield (%) **36a**, **37a**, **38**, **39a**	Conversion (%)
1	**1a** (2)	CH_2Cl_2	23	0.17	33, 5, 20, 14	100
2	**7b** (2)	CH_2Cl_2	23	0.17	35, 5, 0, 0	100
3	**7b** (5)	CH_2Cl_2	-40	0.28	24, <1, 0, 0	100
4	**7b** (5)	MeCN	45	72	1, 0, 0, <1	5
5	**8b** (2)	CH_2Cl_2	23	3	30, 4, 41, 7	100
6	**11c** (2)	CH_2Cl_2	23	0.33	5, 2, 4, 47	100
7	**11c** (5)	CH_2Cl_2	-40	0.67	3, 2, 3, 80	100
8	**11c** (5)	MeCN	45	72	1, 0, 0, 9	10
9	$AuCl_3$ (5)	CH_2Cl_2	23	14	4, <1, <1, 0	63
10	$PtCl_4$ (10)	CH_2Cl_2	23	72	<1, 0, 0, 0	98
11	AuCl (10)	CH_2Cl_2	23	72	2, 0, 0, 0[b]	92
12	AuCl (4)	toluene	90	47	<2, 0, <1, 0	12
13	$AuCl(SMe_2)$ (4)	toluene	90	47	<1, 0, 0, 0	15
14	$PtCl_2$ (4)	toluene	90	47	<2, 0, <1, 0	91
15	**40** (4)	toluene	90	47	<1, 0, 0, 0	100
16	**41** (4)	toluene	90	47	1, 0, <1, 0	100
17	**42** (2)	CH_2Cl_2	23	15	20, 1, 9, 0	100
18	**43** (2)	CH_2Cl_2	23	15	34, 0, 2, 0	100

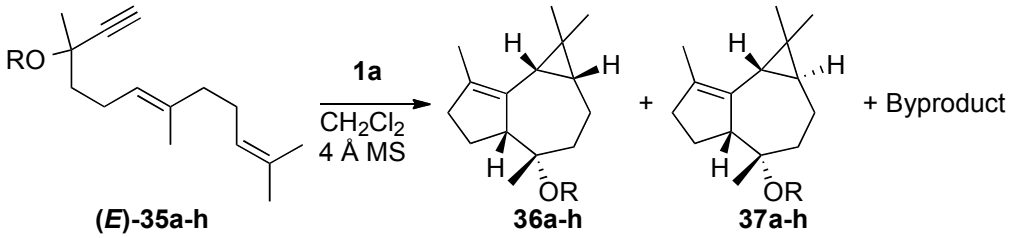
a) the reactions were followed by TLC; the yield and conversion were determined by ^{1}H NMR against an internal standard; b) TMS-deprotected starting material was observed (13%).



39a **39b**

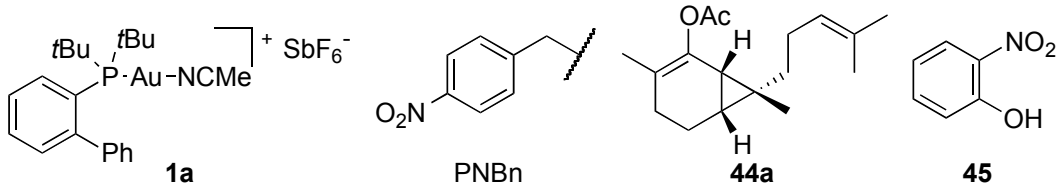
Simple Au(I), Au(III), Pt(II), Pt(IV) salts and complexes decompose the staring enyne **35a** (Table 11, entries 9-16). Finally, cationic platinacycle complexes **42** and **43** (Table 11, entries 17-18) showed similar reactivity to the active Au(I) complexes.

Table 12. Skeletal rearrangement of enynes **(*E*)-35a-h**.[a]



Entry	Enyne (R)	**1a** (mol%)	Time (min)	Yield (%)	Selectivity (**36** / **37**)	Byproducts (yield, %)
1	**(*E*)-35a** (TMS)	1	10	34	88 : 12[b]	**38** (28)
2[c,76]	**(*E*)-35b** (Me)	2	5	84	100 : 0	-
3	**(*E*)-35c** (MOM)	1	8	57	98 : 2	-
4	**(*E*)-35c** (MOM)	1	360[d]	52	98 : 2	**36b** (7)
5[c,76]	**(*E*)-35d** (Bn)	2	10	64	100 : 0	-
6	**(*E*)-35e** (PNBn)	2	15	74	94 : 6	-
7[c,76]	**(*E*)-35f** (Ac)	2	10	56	100 : 0	**44a** (40)
8	**(*E*)-35g** (*o*-$NO_2C_6H_4$)	5	30	56	96 : 4	**45**[e]
9[c,76]	**(*E*)-35h** (H)	2	5	14	88 : 12	-

a) reactions run at room temperature, isolated yields; b) the isomers could be separated by chromatography, yields: *cis* 30%, *trans* 4%; c) results obtained by Kian Molawi and Dr. Thorsten Lauterbach; d) reaction run at -40 ºC, 7% recovered starting material; d) detected in the crude by ^{1}H NMR and TLC.



The key to the success of this methodology proved to be changing the propargylic ether moiety. The best results were obtained with substrates bearing simple alkyl ethers **(*E*)-35b-e** (Table 12, entries 2-6) although phenyl ethers were also tolerated

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

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

(Table 12, entry 8). Once again, lowering the temperature slightly lowered the yield of the desired tricyclic product (Table 12, entry 4). The unprotected alcohol **(*E*)-35h** also reacted under these conditions, albeit affording the rearranged alcohols **36h**/**37h** in low yield (Table 12, entry 9). Interestingly, although acetate **(*E*)-35f** had been shown to react exclusively by 1,2-acyl migration to give **44a** with $AuCl_3$ or $PtCl_2$,[78] the 1,5-migration derivative **36f** was obtained as the major product using the gold(I) catalyst **1a** (Table 12, entry 7). The configuration of **36e** was confirmed by X-ray crystallography (Figure 1).

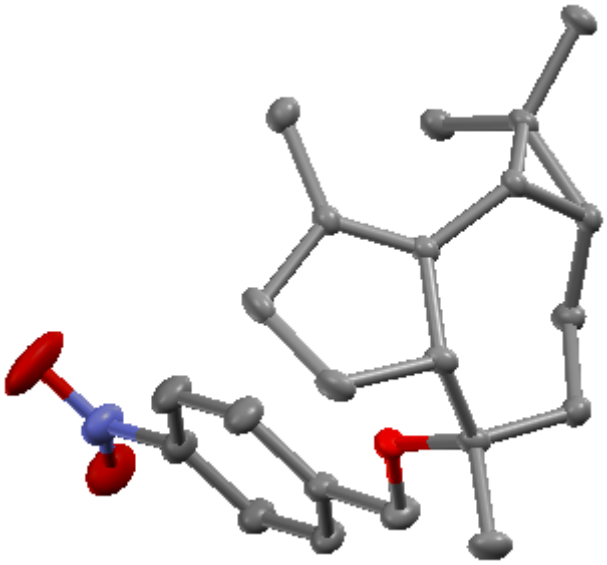


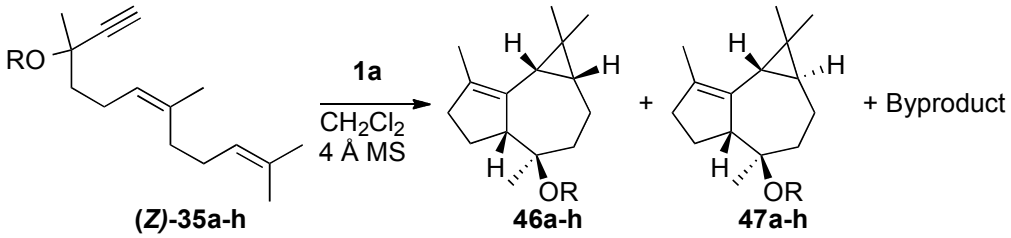
Figure 1. X-ray structure of **36e** (H atoms omitted for clarity).

Reactions of dienynes **(*Z*)-35a–h** with **1a** led to **46a–h** in 40–77% yield (Table 13). However the yield of the minor isomers **47a-h** was also higher, resulting in a lower selectivity when compared to dienynes **(*E*)-35a–h**. The configuration of **46e** was confirmed by X-ray crystallography (Figure 2).

78. (a) Fürstner, A.; Hannen, P. *Chem. Commun.* **2004**, 2546-2547; (b) Fürstner, A.; Hannen, P. *Chem. Eur. J.* **2006**, *12*, 3006-3019.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

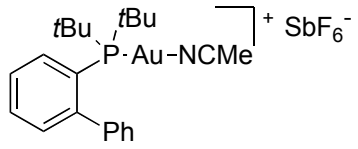
Table 13. Skeletal rearrangement of enynes **(*Z*)-35a-h**.[a]



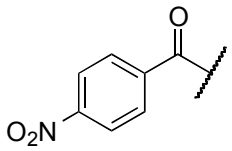
(*Z*)-35a-h **46a-h** **47a-h**

Entry	Enyne (R)	**1a** (mol%)	Time (min)	Yield (%)	Selectivity (**46** / **47**)	Byproducts (yield, %)
1	**(*Z*)-35a** (TMS)	1	8	46	86 : 14	-
2[b,76]	**(*Z*)-35b** (Me)	2	5	81	90 : 10	-
3	**(*Z*)-35c** (MOM)	1	7	72	88 : 12	**46b**[c]
4	**(*Z*)-35e** (PNBn)	1	36	87	88 : 12	-
5	**(*Z*)-35f** (PNBz)	1	12	48	88 : 12	**44b** (29)
6[b,76]	**(*Z*)-35h** (H)	2	5	52	92 : 8	-

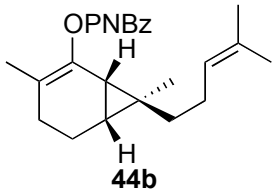
a) reactions run at room temperature, isolated yields; b) results obtained by Kian Molawi and Dr. Thorsten Lauterbach; c) observed by NMR in complex mixture fraction.



1a



PNBz



44b

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

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

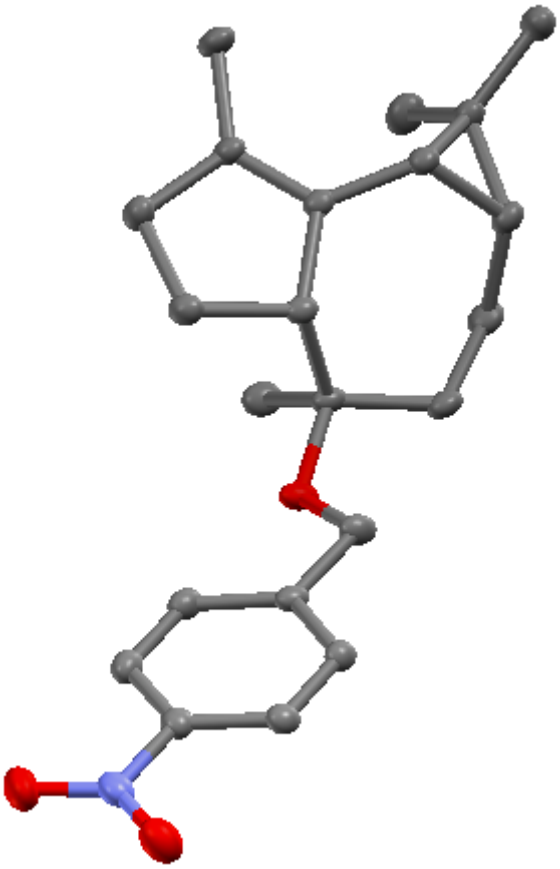
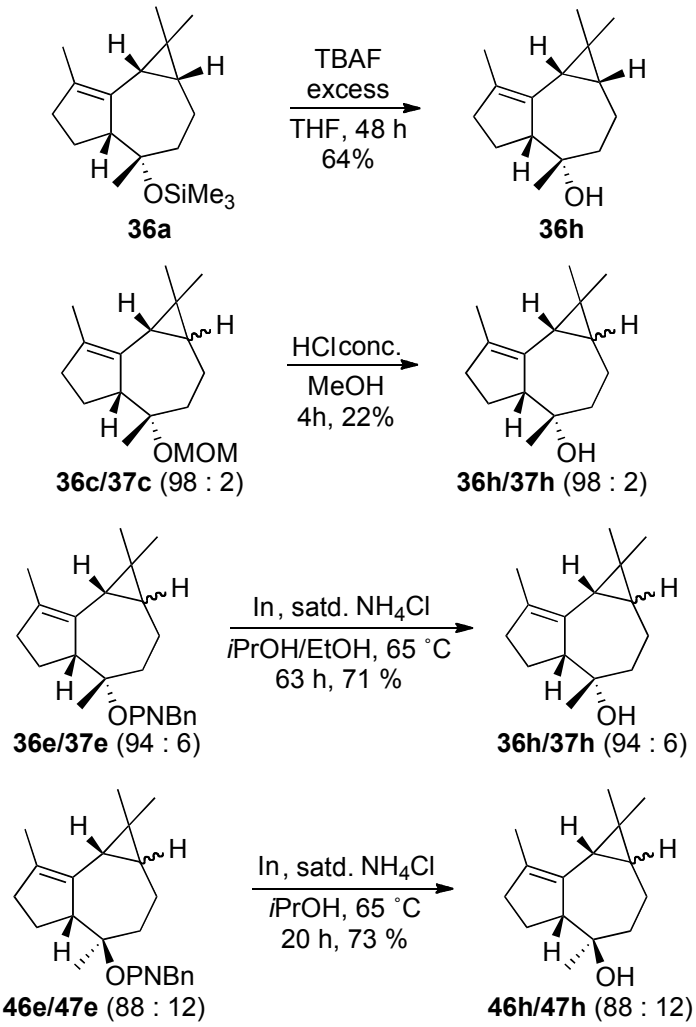


Figure 2. X-ray structure of **46e** (H atoms omitted for clarity).

The deprotection of the rearranged tricyclic products was also briefly investigated (Scheme 12). The *p*-nitrobenzyl and the TMS groups could be cleaved more efficiently than the MOM group.



Scheme 12. Methods for the deprotection of rearranged tricyclic products.

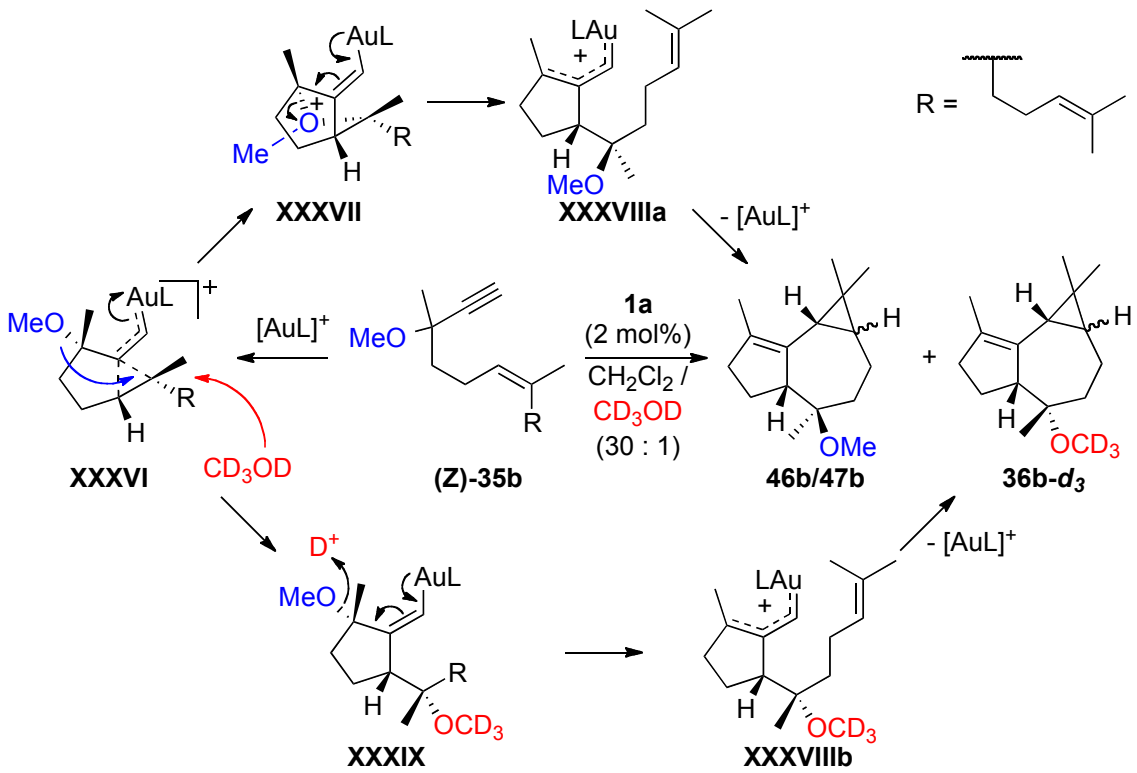
Reaction of dienyne **(*Z*)-35b** in a 30:1 mixture of CH_2Cl_2 and MeOH gave the ether **36b** in addition to **46b** and **47b**.[76,79] The ether **36b** was the product of the reaction of dienyne **35b** (Table 12, entry 2). When this reaction was performed with CD_3OD, **46b** and **47b** showed no deuterium incorporation, whereas the methoxy group of **36b** was deuterated (Scheme 13).[76,79] This experiment confirms that the 1,5-migration is an intramolecular transformation. Accordingly, upon activation of the alkyne with gold(I), an intermediate such as **XXXVI** is probably formed, which is not an open carbocation since the original configuration at the alkene is preserved. The OR group migrates to form **XXXVII**, which then opens to give allylgold cation **XXXVIIIa**. An intramolecular cyclopropanation with the alkene on the side chain then gives tricyclic

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

79. Experiments performed by Dr. Thorsten Lauterbach.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

compounds **46b** and **47b**. In the presence of CD_3OD, an alternative intermolecular addition to **XXXVI** gives **XXXIX**, which then forms **36b-*d*$_3$** via allylic carbocation **XXXVIIIb**. Remarkably, migration of the OR group is faster than the interception of the first intermediate of type **XXXVI** by the pendant alkene, which have been previously shown to be a fast process in dienynes leading to biscyclopropanation.[36,51]



Scheme 13. Mechanistic proposal for the 1,5-migration of OR groups.

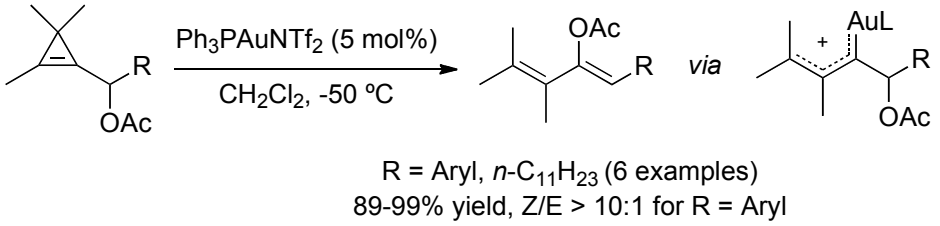
Allylgold cations intermendiates were proposed recently in the mechanism of the gold(I)-catalyzed rearrangement of cyclopropenylmethyl acetates to *Z*-acetoxydienes (Scheme 14).[80]

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

51. Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jimenez-Nuñez, E.; Nevado, C.; Herrero-Gómez, Elena; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677-1693.

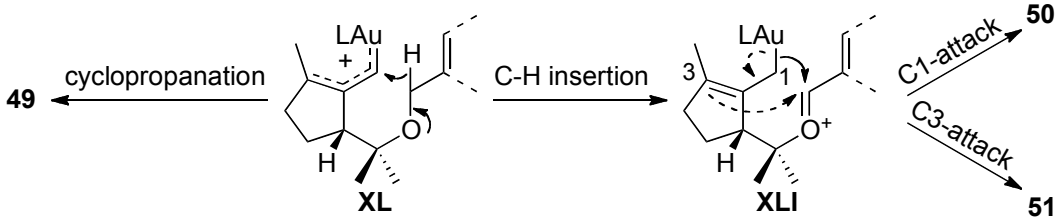
80. Seraya, E.; Slack, E.; Ariafard, A.; Yates, B. F.; Hyland, C. J. T. *Org. Lett.* **2010**, *12*, 4768-4771.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

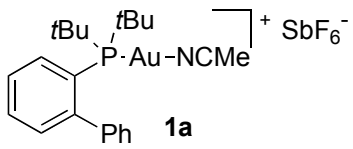


Scheme 14. Gold(I)-catalyzed rearrangement of cyclopropenylmethyl acetates to *Z*-acetoxydienes.

We then studied the scheletal rearrangement of enynes **48a-f** bearing an unsaturation on the propargylic ether moiety. Enyne **48a** predictably yielded tricycle **49** (Table 14, entry 1) via intramolecular cyclopropanation of an intermediate type **XL** (Scheme 15). Enynes **48b-e**, yielded formal C-H insertion products **50-51**, presumably via η^1-allyl-gold(I) intermediates type **XLI** (Scheme 15). The configuration of product **50** was confirmed by X-ray crystallography (Figure 3). On the other hand, enyne **48f** was rapidly decomposed by **1a** even at low temperatures (Table 14, entries 7-8).

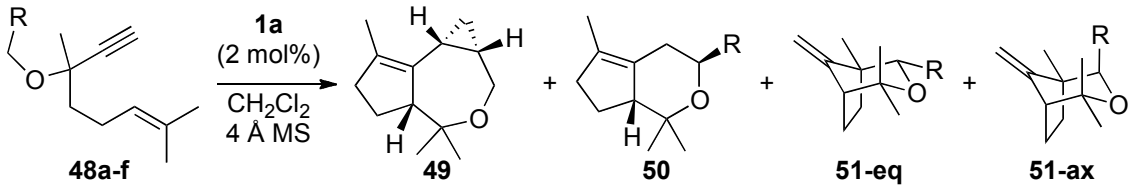


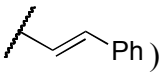
Scheme 15. Proposed mechanisms for the formation of rearranged products **49-51**.



UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Table 14. 1,5-migration of enynes **48a-f**.[a]



Entry	Enyne (R)	Time (min)	Products (selectivity)	Yield (%)
1[b,76]	**48a** (vinyl)	20	**49**	65
2	**48b** ()	10	**50b**/**51b-eq** (40 : 60)	42
3[b,76]	**48c** (Ph)	20	**50c/51c-eq/51c-ax** (75 : 18 : 7)	91
4	**48d** (*p*-NO_2-C_6H_4)	6	**50d/51d-eq** (98 : 2)	54
5	**48e** (*p*-MeO-C_6H_4)	20	**50e/51e-eq** (10 : 90)	91
6	**48e** (*p*-MeO-C_6H_4)	30[c]	**50e/51e-eq/51e-ax** (12 : 12 : 76)	72
7	**48f** (MeO)	12[d]	Complex mixture	-
8	**48f** (MeO)	6[e]	Complex mixture	-

a) reactions performed at room temperature, isolated yield (mixture of isomers); b) results obtained by Dr. Thorsten Lauterbach; c) reaction performed at -40 ºC; d) reaction performed using 1 mol% **1a**; e) reaction performed at -50 ºC using 5 mol% **1a**.

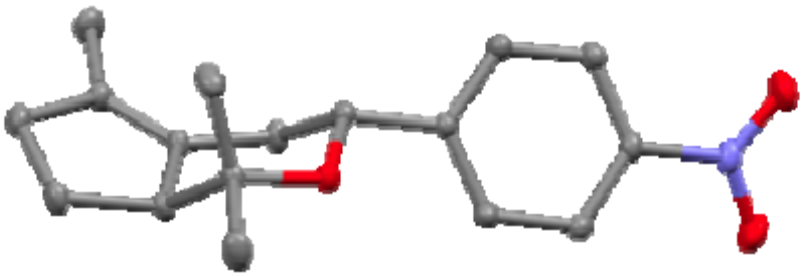
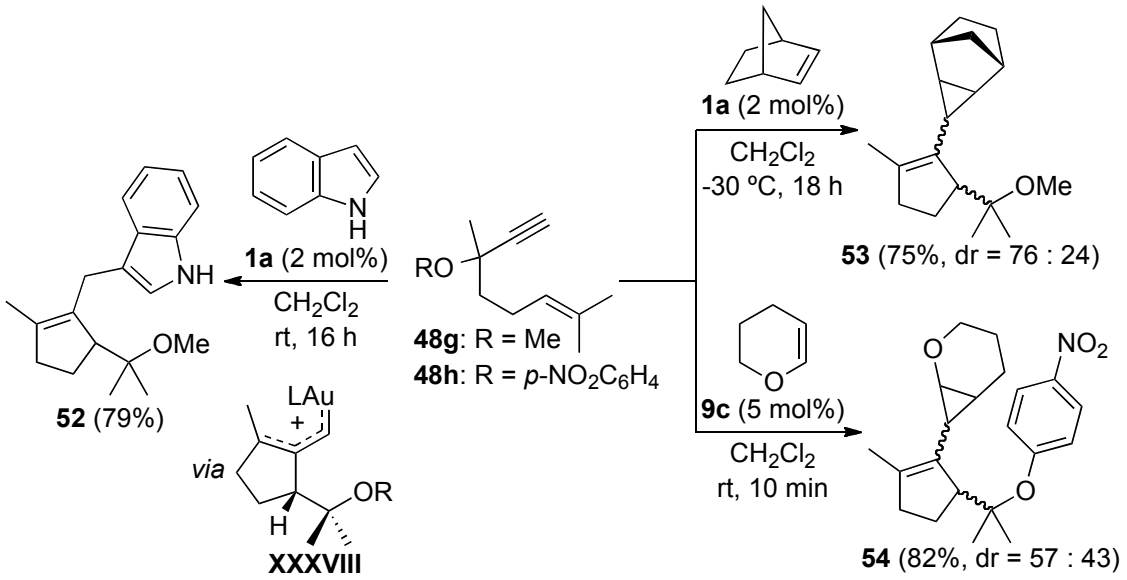


Figure 3. X-ray structure of **50** (H atoms ommited for clarity).

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

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



Scheme 16. Trapping of alyl-gold(I) cations with indole, norbornene and dihydropyrane.

To confirm the involvement of allylgold cations in these migrations, we examined the reactions of enynes **48g-h** in the presence of reagents known to react with Au(I) carbenes (Scheme 16).[81] Thus, trapping of the migration intermediate from **48g** a using indole[61] led to adduct **52**. The gold-catalyzed reaction of **48g** in the presence of norbornene gave cyclopropane **53**. Similary, the gold catalyzed reaction of **48h** yielded cyclopropanes **54** as mixture of isomers that could not be separated by flash chromatography. Surprisingly, only 2 out of 4 possible diastereomers of cyclopropanes **54** were observed (Figure 4). Due to significant overlapping in their ^{1}H NMR spectrum, their relative configuration could not assigned.

An intermolecular cyclopropanation also occurred in the reaction of enynes **48** with 2,3-dimethyl-1,3-butadiene using NHC-Au(I) catalysts **8b** or **9c**. In this case, a mixture of **55** and **56** was obtained (Table 15). Hexahydroazulene **56** presumably arises by a Cope rearrangement[82] of a *cis*-divinylcyclopropane diastereomer of **55**.

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

81. Products **48g**, **52** and **53** were syntehesized and characterized by Dr. Thorsten Lauterbach, ref. 76.

82. Divinylcyclopropane-cycloheptadiene rearrangement: Hudlicky, T.; Fan, R.; Reed, J.W.; Gadamasetti, K. G. *Org. React.* **1992**, *41*, 1-133.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

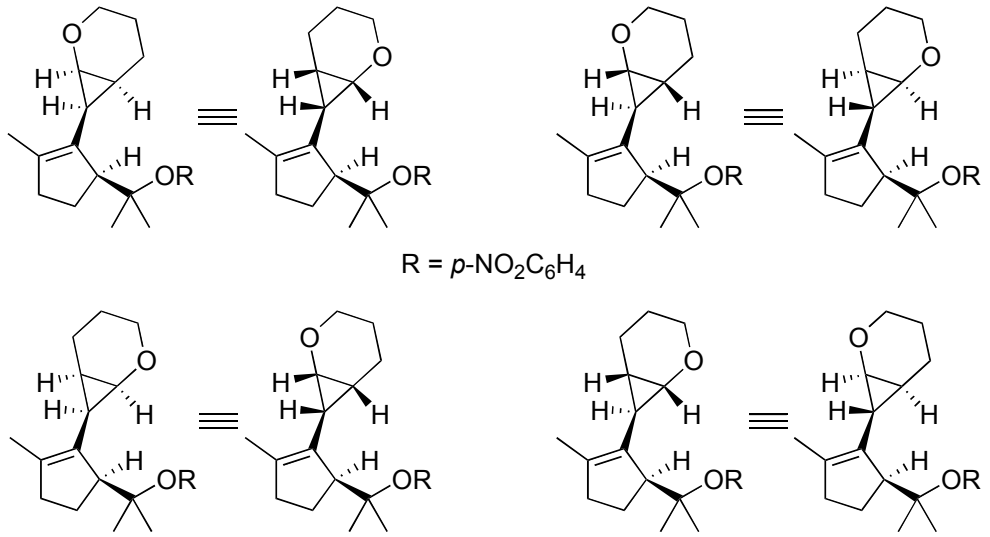
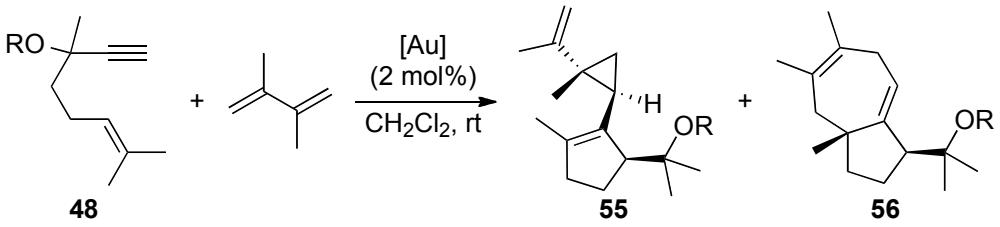


Figure 4. Possible diastereomers for structure **54**.

Table 15. Au(I) catalyzed reaction of enynes with 2,3-dimethyl-1,3-butadiene.[a]



Entry	Enyne (R)	Catalyst	Time (h)	Products (selectivity)	Yield (%)
1	**48d** (PNBn)	**9c**	0.20	**55a/56a** (77 : 23)[b]	73
2	**48e** (PMBn)	**9c**	0.33[c]	**55b/56b** (76 : 24)	62
3	**48f** (MOM)	**8b**	4[c]	Complex mixture	-
4	**48h** (*p*-NO_2-C_6H_4)	**8b**	2.33	**55c/56c** (72 : 28)	71
5	**48i** (H)	**9c**	0.33[c]	Complex mixture	-
6	**48i** (H)	**8b**	3[d]	Complex mixture	-

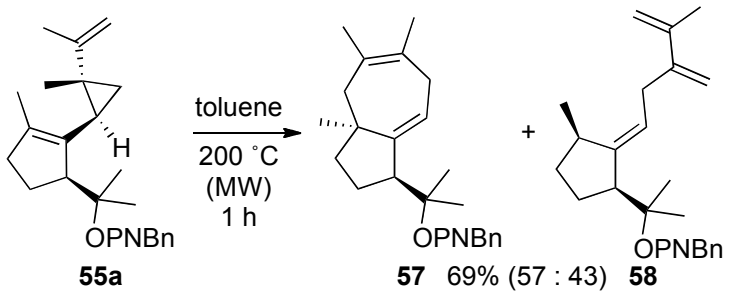
a) reaction performed in the presence of 5 equivalents of 2,3-dimethylbuta-1,3-diene, isolated yields (mixture of isomers); b) the two isomers could be separated by chromatography, **55a** 56%, **56a** 17%; c) reaction performed at 0 ºC; d) reaction performed at -60 ºC using 5 mol% **8b**.

8b **9c**

Whereas the relative configuration of **56b** could be determined by GOESY experiments, this approach was ineffective for **55a** due to the rotation around the cyclopropyl-cyclopentenyl bond. However, the relative configuration of **58** (Scheme 17)

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

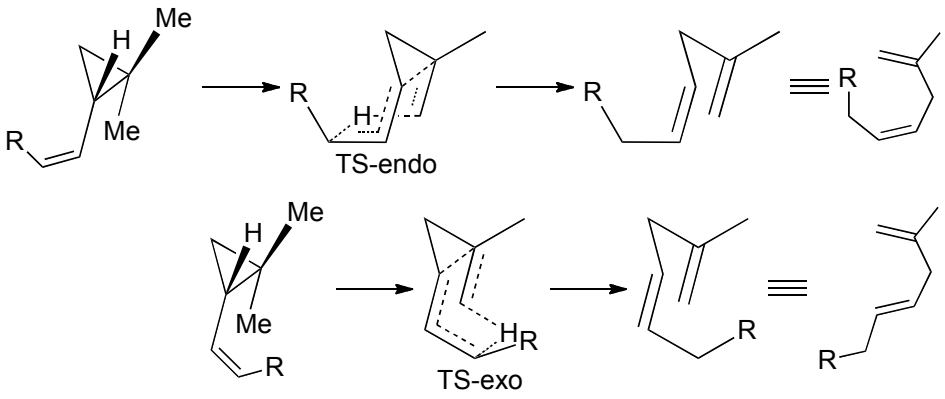
could be determined by GOESY experiments, and this, in turn, allowed us to determine the configuration of **55a**.



55a **57** 69% (57 : 43) **58**

Scheme 17. Thermal rearrangement of **55a**.

Triene **58** is the product of a homodienyl 1,5-sigmatropic hydrogen shift, also known as a retro-ene reaction. This reaction can occur through two different transition states (both allowed thermally) leading to two different geometries around the newly formed internal double bond (Scheme 18).[83] It has been shown experimentally[84] and theoretically[83] that the endo pathway is favored even against strong steric bias (R = *t*Bu).



Scheme 18. Transition states (TS) for the homodienyl 1,5-sigmatropic hydrogen shift.

More importantly, the reaction is stereospecific,[85] meaning that each one of the two possible *trans*-cyclopentenyl-propenyl-cyclopropanes **55a** would lead to only one

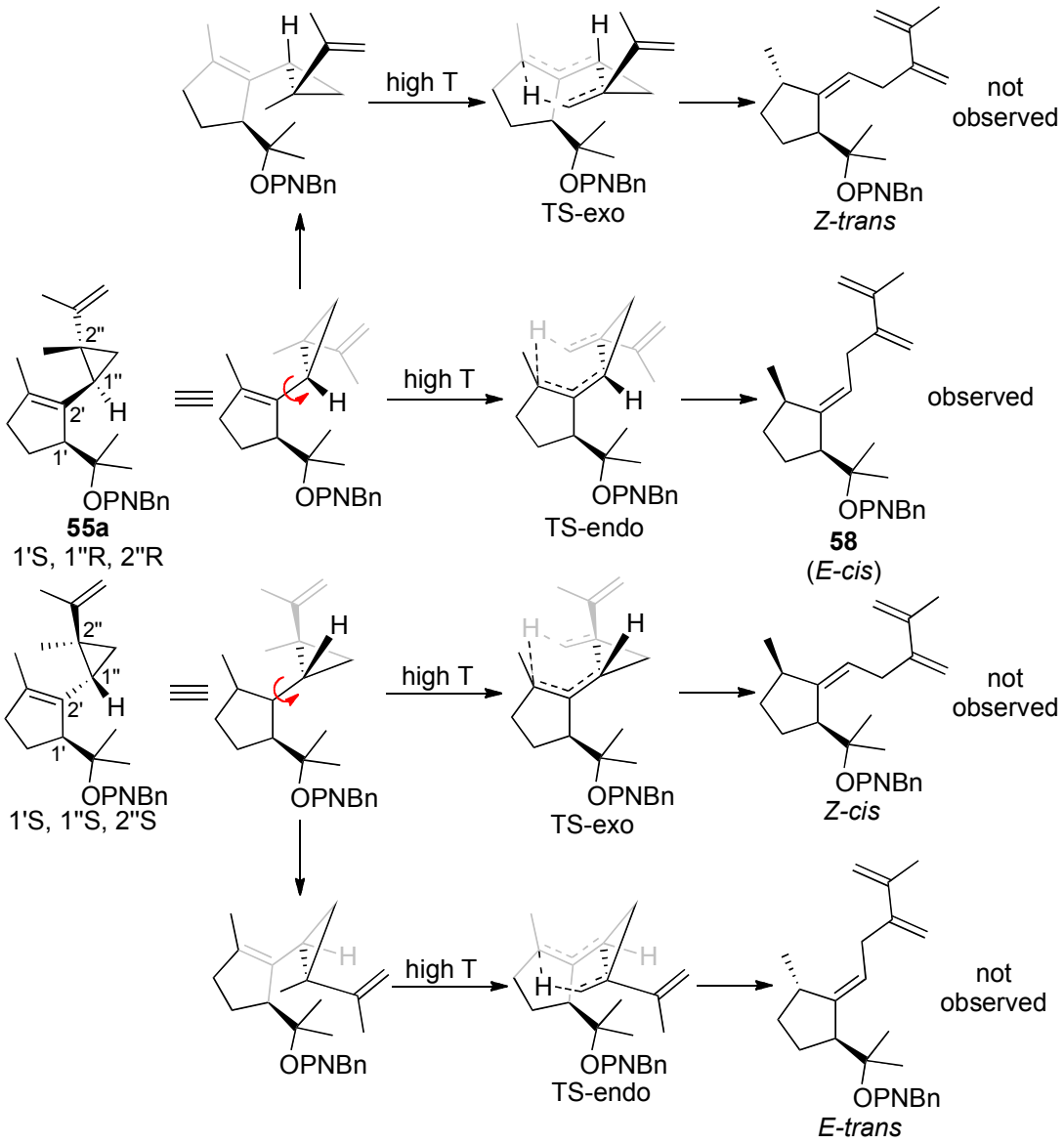
83. For a detailed computational study of the mechanism see: R. J. Loncharich, K. N. Houk *J. Am. Chem. Soc.* **1988**, *110*, 2089-2092.

84. Daub, J. P.; Berson, I. A. *Tetrahedron Lett.* **1984**, *25,* 4463-4466.

85. For one example of stereogenicity transfer in this reaction see: Parziale, P. A.; Berson, J. A. *J. Am. Chem. Soc.* **1991**, *113*, 4595-4606.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

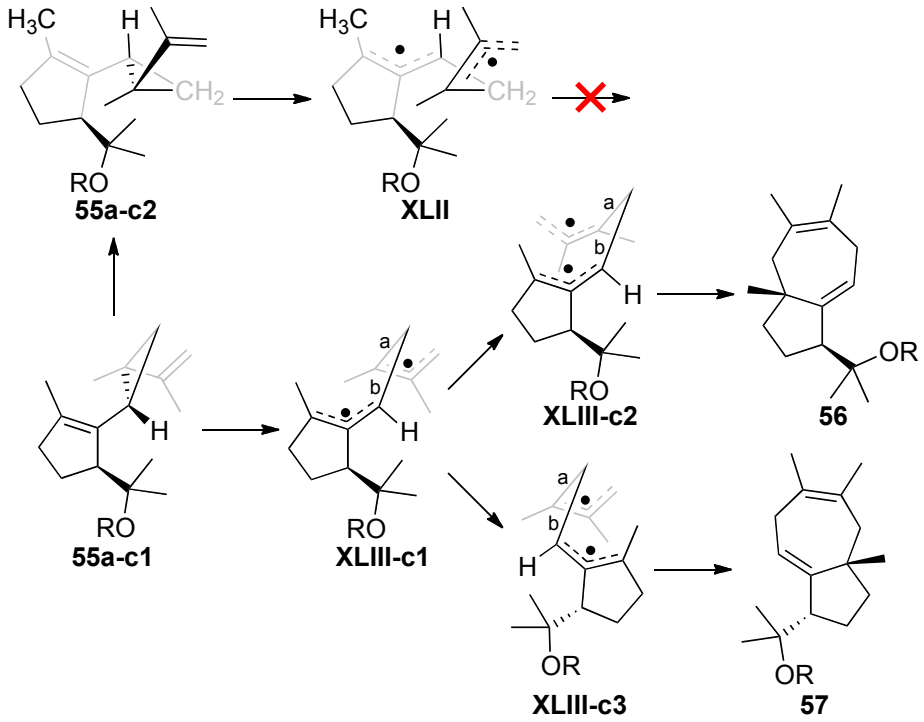
of the 4 possible dialkyl-alkylidene-cyclopentanes **58**, taking into account the two allowed transition states (Scheme 19).



Scheme 19. Deduction of the structure of **55a** starting from the known structure of **58**.

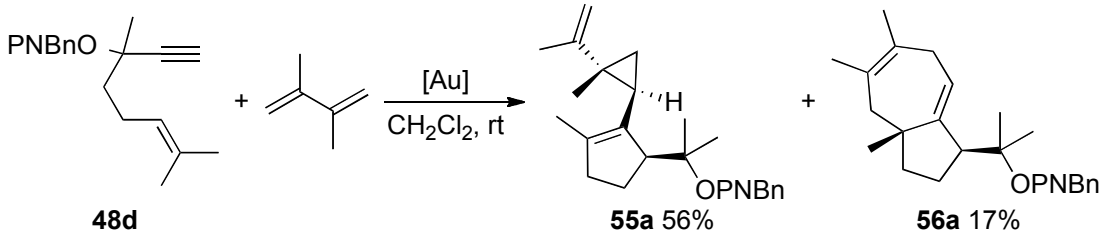
The formation of the cycloheptadiene **57** from **55a** probably occurs through a homolythic cleavage of the cyclopropane bond leading to a bis-allyl radical followed by reorganization and radical recombination (Scheme 20). Cleavage of the less stable rotamer **55a-c2** is unproductive as it leads to an "*E*" allyl radical (**XLII**) around the exocyclic double bond. On the other hand, after cleavage of the **55a-c1** conformer followed by rotation around the least sterically hindered Csp^3-Csp^3 bond (b) of intermediate **XLIII** leads to **57**.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



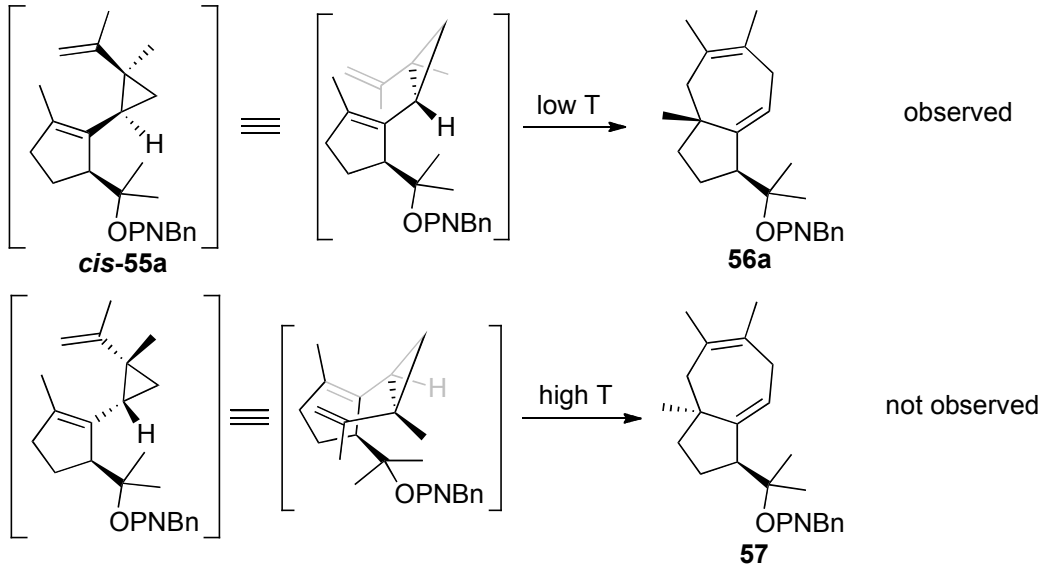
Scheme 20. Mechanistic proposal for the formation of **57** from **55a**.

Considering the steric constraints associated with the Cope rearrangement[86] the relative configuration of the transient *cis*-cyclopentenyl-propenyl-cyclopropane ***cis*-55a** can also be assigned (Scheme 21).



86. This reaction takes place exclusively through an endo transition state similar to the shown structures. An exo transition state would lead to to a highly strained *trans,trans*-1,4-bicycloheptadiene, see reference 82.

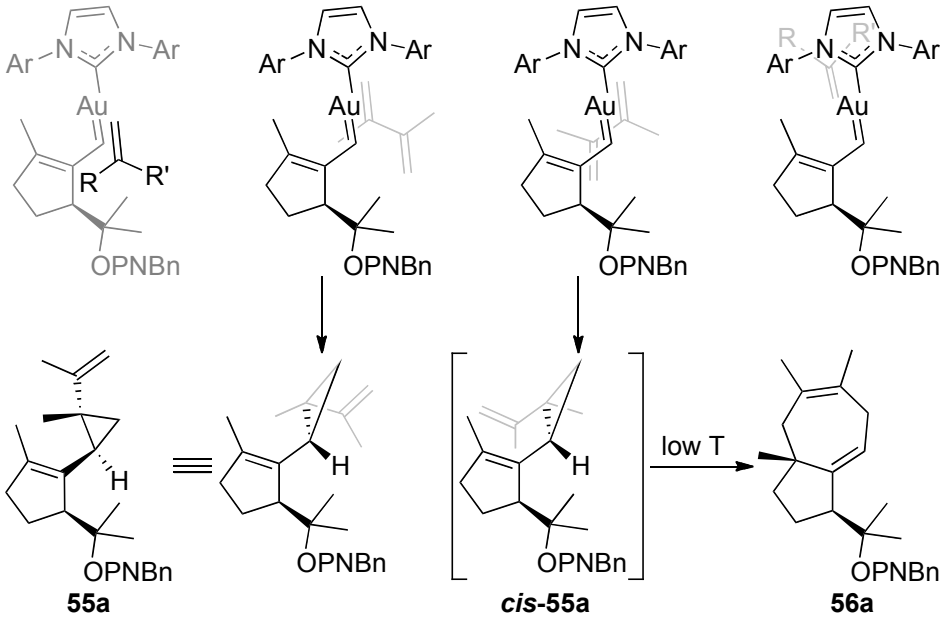
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



Scheme 21. Proposal for the assignment of the configuration of ***cis*-55a**.

A mechanistic explanation for the formation of only two isomers in this reaction is shown in Scheme 22. Considering the NHC ring and the allyl-gold(I) to be near planar, there are only two sterically favorable approaches of the incoming diene. One of the faces of the allyl-gold(I) is blocked by the bulky tertiary ether. The top half-space is inaccessible due to the presence of the aryl rings which are perpendicular to the NHC ring. Finally, this proposal also explains the observed selectivity. The approach leading to the minor isomer requires the bulkier 2-propenyl moiety to come close to the cyclopentene ring. Obviously the approach facing the 2-propenyl with the proton and the methyl with the ring would be favored.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



Scheme 22. Proposed justification for the observed stereoselectivity of the trapping of allyl-gold(I) cations with 2,3-dimethyl-1,3-butadiene.

We were interested in further developing this reaction as it could provide straightforward access to a plethora of carotane sesquiterpenoids.[87] The most appealing targets, schinsanwilsonenes A-C (Figure 6), were shown to exhibit anti-HBV activity in the μM range.[88] Cycloheptadiene **56a** also has a similar structure to the pseudolaric acids,[89] tormesol (Figure 5)[90] and other related diterpenes (Figure 6).[91]

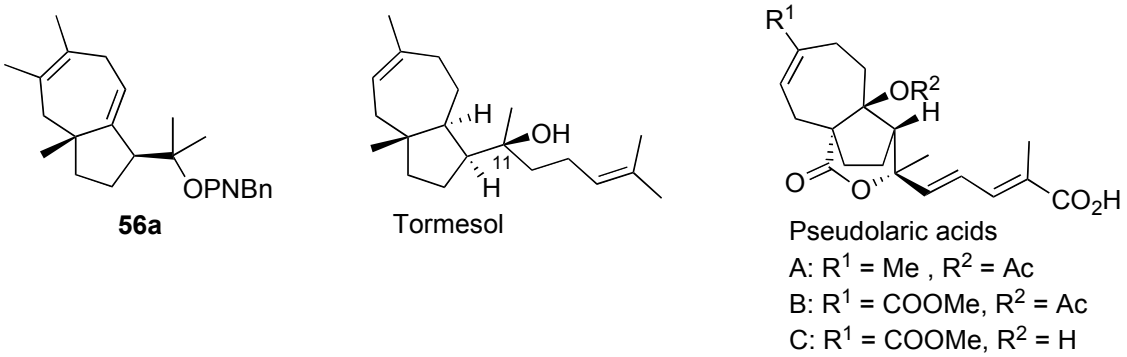


Figure 5.

87. Hashidoko, Y.; Tahara, S.; Mizutani J. *Phytochemistry* **1991**, *30*, 3729-3739.
88. Ma, W.-H.; Huang, H.; Zhou, P.; Chen D.-F. *J. Nat. Prod.* **2009**, *72,* 676-678.
89. Zhon, B. N.; Ying, B. P.; Song, G. C.; Chen, Z. Y.; Han, J.; Yan, Y. F.; *Planta Med.* **47**, 35.
90. Urones, J. G.; Sánchez Marcos, I.; Martín Garrido, N.; de Pascual Teresa, J.; San Feliciano Martín, A. *Phytochemistry* **1989**, *28*, 183-187.
91. Beyer, J.; Becker, H.; Toyota, M.; Asakawa Y. *Phytochemistry* **1987**, *26*, 1085-1089.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

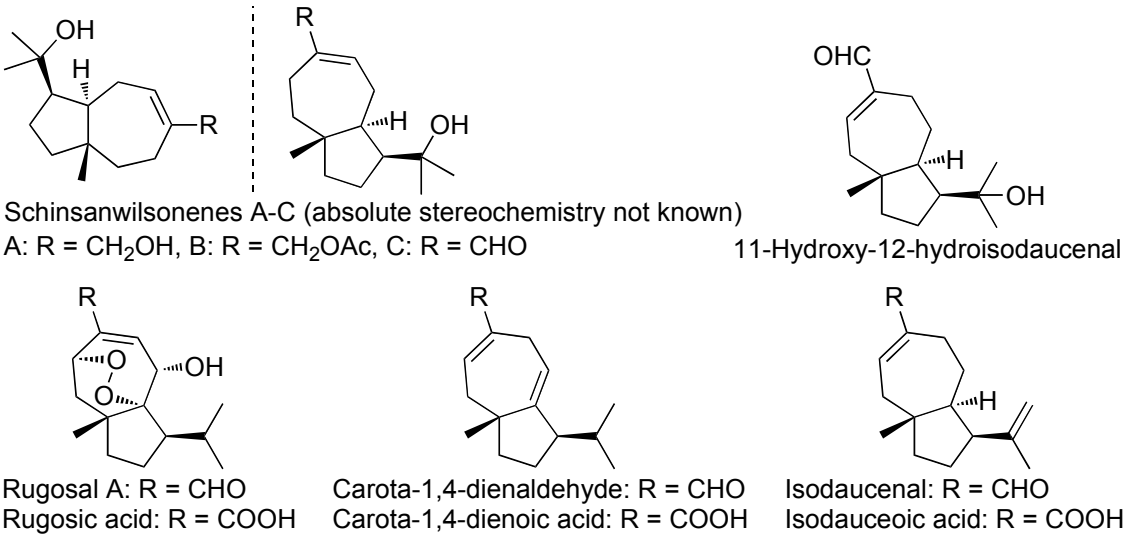
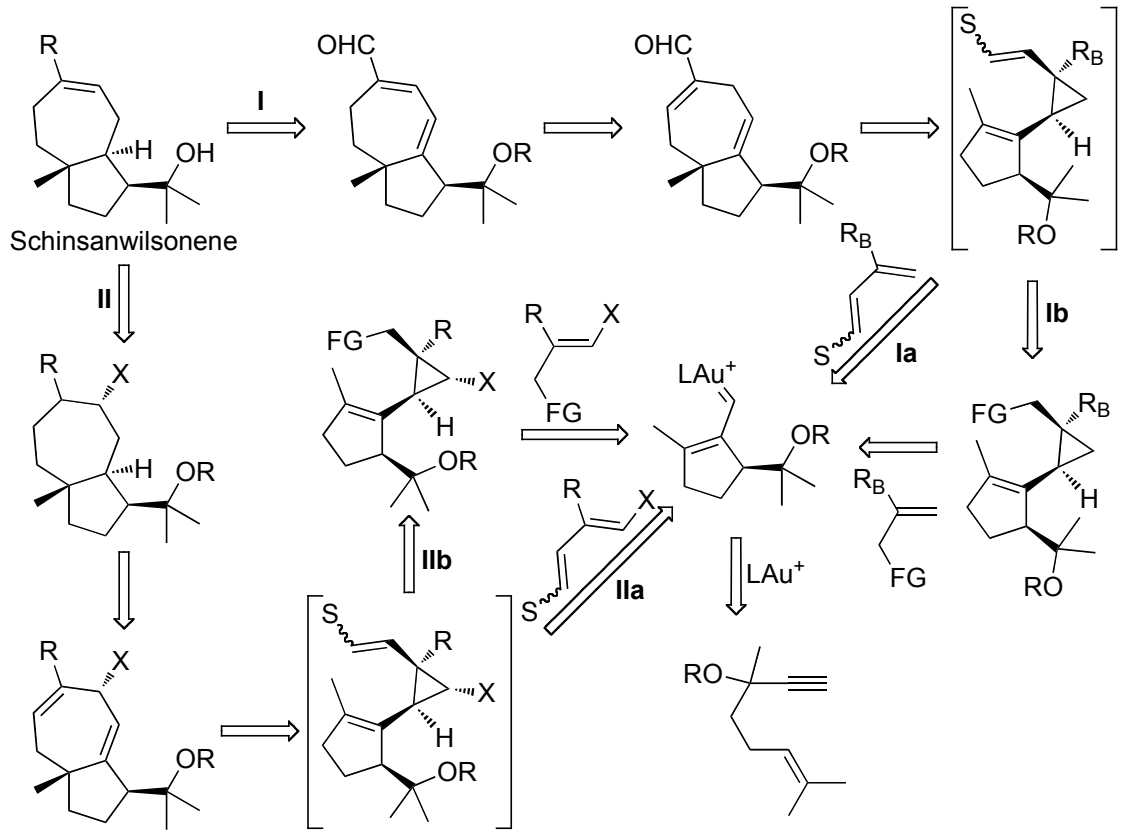


Figure 6.

There two main issues when designing a synthesis for schinsanwilsonene based on a Au(I) carbene trapping approach: achieving a high *cis* selectivity for the transient vinyl-cyclopentenyl-cyclopropane and setting the correct regiochemistry for the cycloheptene double bond. In order to deal with the regiochemistry issue we envisioned two possible pathways (Scheme 23). Pathway **I** would would require an isomerisation of the trapping product to a conjugated cycloheptadiene followed by a chemoselective hydrogenation. Pathway **II** would proceed through a saturated bicycloalkane followed by an elimination step. In both pathways the bulky tertiary ether is expected to control the hydrogenation of the bridgehead double bond leading to the required *trans* ring junction.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

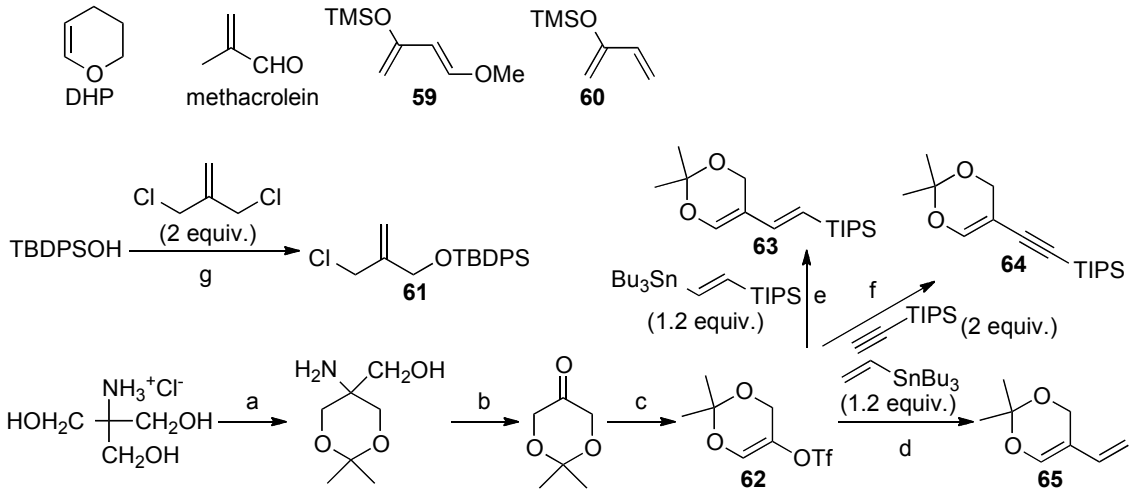


Scheme 23.

The transient *cis*-vinyl-cyclopentenyl-cyclopropane could result directly from trapping with a suitable diene (pathways **a**) or through functional group manipulations of the product resulting from the trapping with a suitable alkene (pathways **b**). Considering the previously proposed mechanism, we hoped to achieve the desired *cis* selectivity in pathway **I** by choosing alkenes/alkadienes with bulky R_B groups. Using the same reasoning for pathway **II**, the use of alkenes/alkadienes in which X and R are *cis* would also favor the formation of the *cis*-cyclopropane.

Scheme 24 summarizes the synthesis of some of the alkenes/alkadienes designed for the schinsanwilsonene synthesis.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



Scheme 24.

a)[92] $Me_2C(OMe)_2$ (1.1 equiv.), $TsOH{\cdot}H_2O$ (5 mol%), DMF, room temperature, 12 h; then Et_3N (1 equiv.), EtOAc, 86%; b)[92] $NaIO_4$ (1.0 equiv.), KH_2PO_4 (1.0 equiv), H_2O, 5 ºC, 4 h, then room temperature, 5 h; then $Na_2S_2O_3$ (1.0 equiv.), 85%; c)[93] Tf_2O (1.0 equiv.), Et_3N (1 equiv.), DMAP (1 equiv.), CH_2Cl_2, -23 ºC, 24 h, 63%; d) $Pd_2(dba)_3$ (1 mol%), $AsPh_3$ (8 mol%), NMP, room temperature, 21 h, 54%; e) LiCl (3 equiv.), $PdCl_2(PPh_3)_2$ (10 mol%), DMF/Et_2O/THF, room temperature, 87 h, 32%; f)[93] CuI (6 mol%), $PdCl_2(PPh_3)_2$ (3 mol%), Et_3N, room temperature, 20 h, 61%. g. NaH (1.1 equiv), $Bu_4N^+I^-$ (6 mol%), THF, 60 ºC (MW), 5 h, 50%.

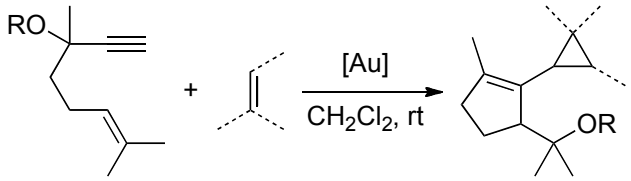
Unfortunately trapping with most of the additional alkenes and dienes failed to proceed towards the desired products (Table 16). Methacrolein is probably too electron poor to react under this conditions (Table 16, entry 2). On the other hand very electron rich dienes **59-60** can either completely inhibit the reaction (Table 16, entries 3-4) or yield complex mixtures (Table 16, entry 5). The failure of enol-ethers **63-65** (Table 16, entries 7-9) seems to indicate that tertiary substituted alkenes are too sterically hindered to be reactive under these conditions. The failure of alkene **61** can be explained by both steric and electronic reasons. Additional alkenes have been synthesized in our laboratory and successfully used for the trapping of allyl-gold(I) carbocations.

92. Forbes, D. C.; Ene, D. G.; Doyle, M. P. *Synthesis* **1998**, 879-882.

93. Fearnley, S. P.; Funk, R. L.; Gregg, R. J. *Tetrahedron* **2000**, *56*, 10275-10281.

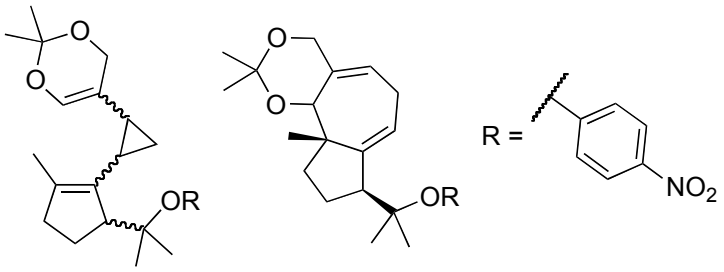
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Table 16.

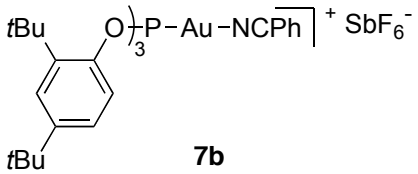


Entry	Enyne (R)	Alkene (mol%)	Catalyst (mol%)	Time (min)	Products (selectivity)
1	**48h** (*p*-$NO_2C_6H_4$)	DHP (500)	**9c** (5)	10	**54** (57 : 43)[b]
2	**48h** (*p*-$NO_2C_6H_4$)	methacrolein (500)	**9c** (2)	5	Complex mixture
3	**48d** (PNBn)	**59** (500)	**7b** (10)	24	No reaction
4	**48d** (PNBn)	**59** (500)	**9c** (10)	24	No reaction
5	**48d** (PNBn)	**60** (500)	**9c** (5)	29	Complex mixture
6	**48d** (PNBn)	**61** (200)	**9c** (2)	12	Complex mixture
7	**48h** (*p*-$NO_2C_6H_4$)	**63** (160)	**9c** (2)	0.33	Complex mixture
8	**48d** (PNBn)	**64** (200)	**9c** (10)	4	Complex mixture
9	**48h** (*p*-$NO_2C_6H_4$)	**65** (160)	**8b** (2)	0.25	**66/67** (89 : 11)[c]

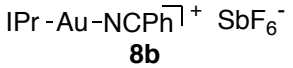
a) reactions run at room temperature, isolated yield (inseparable mixture of isomers); b) 82% yield; c) 66% yield, the cyclopropanation occurs exclusively at the exocyclic double bond; 3 diastereomeric cyclopropanes observed (61 : 15 : 13).



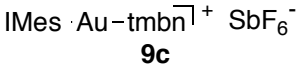
66 (61 : 15 : 13) / **67** (11)



7b



8b



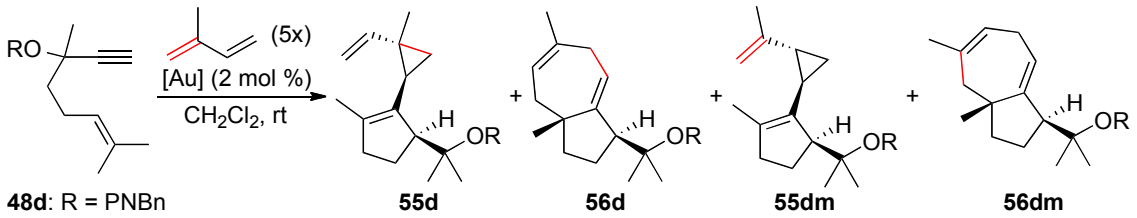
9c

When using isoprene, cyclopropanation occurred selectively at the disubstituted, more electron rich double bond (Table 17). The structural assignments were based on ^{1}H NMR signal multiplicity in the olefin region and comparison with the trapping products using 2,3-dimethyl-1,3-butadiene. Phosphine-Au(I) (Table 17, entry 5) or phosphite-Au(I) (Table 17, entry 6) catalysts yielded more than 4 trapping products.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

The cationic platinacycle complex **42** (Table 17, entry 4) showed very reduced activity in this reaction.

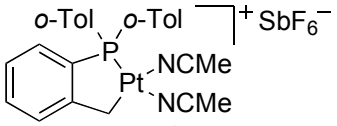
Table 17. Au(I) catalyzed reaction of enyne **48d** with isoprene.[a]



48d: R = PNBn **55d** **56d** **55dm** **56dm**

Entry	Catalyst	Time (min)	Selectivity (A/B/C/D)	Yield (%)
1	**9c**	20	41 : 44 : 13 : 2	72
2	**8b**	40	41 : 45 : 11 : 2	78
3	**11c**	20	44 : 44 : 7 : 5	68
4	**42**	48 h	51 : 49 : 0 : 0	18[b]
5	**1a**	20	Complex mixture	-
6	**7b**	6	Complex mixture	-

a) the yield was determined by ^{1}H NMR against an internal standard of 1,3,5-trimethoxybenzonitrile after reaction completion; b) conversion 56%.

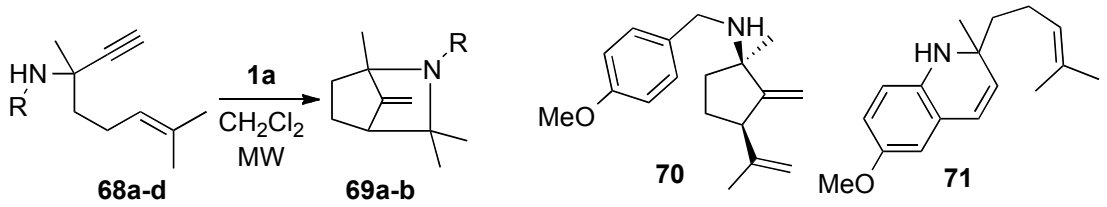


42

The initial attempts to form allyl-gold(I) cations via migration of an amine group were delayed by difficulties associated with the synthesis of suitable starting materials (see: *Synthesis of the substrates* below). We found that anilines show the desired reactivity, yielding the desired product in low to moderate yield (Table 18, entries 2-6). Blocking the ortho positions resulted in an unreactive substrate (Table 18, entries 6-9). The structure of **69b** was confirmed by X-ray crystallography (Figure 7).

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

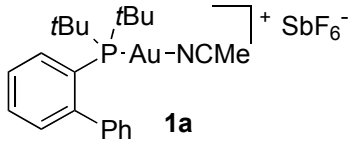
Table 18. Au(I) catalyzed rearrangement of amino-enynes **68a-d**.[a]



68a-d **69a-b** **70** **71**

Entry	Enyne (R)	**1a** (mol%)	t (º C)	Time (h)	Product (yield, %)
1	**68a** (PMBn)	10	80	6	**70** (36%)
2	**68b** (4-MeO-C_6H_4)	5	rt	40	**69a** (2), **71** (66%)
3	**68b** (4-MeO-C_6H_4)	5	rt[a]	2.5	decomposition
4	**68c** (4-NO_2-C_6H_4)	10[b]	rt	21	**69b** (39)
5	**68c** (4-NO_2-C_6H_4)	10	rt	21	**69b** (36)
6	**68c** (4-NO_2-C_6H_4)	30	-10	13	**69b** (10)
7	**68d** (2,3-Me_2-4-MeO-C_6H_2)	5	(MW)	1	No reaction
8	**68d** (2,3-Me_2-4-MeO-C_6H_2)	5	80	1	No reaction
9	**68d** (2,3-Me_2-4-MeO-C_6H_2)	5	120	1	Decomposition

a. reaction carried out in the presence of TfOH (2 equivalents), rt = room temperature; the catalyst was added portionwise: 5 mol%, 17 h, another 5 mol%, 4 h.



1a

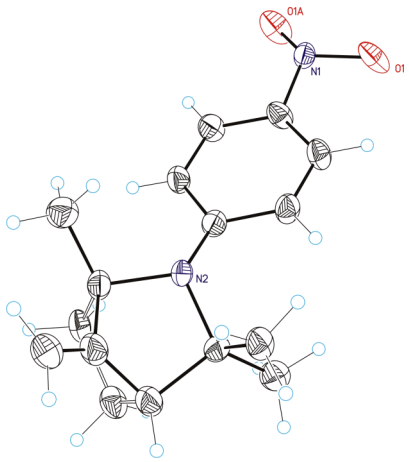
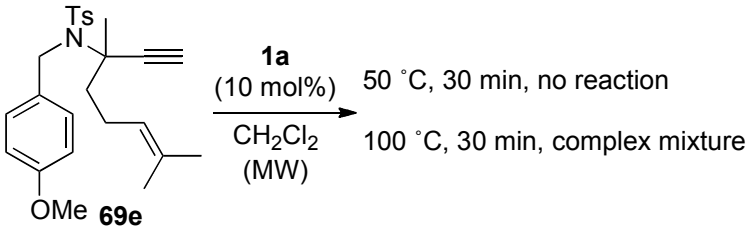


Figure 7. X-ray structure of **69b**.

In the presence of catlyst **1a** (10 mol%) the tosylamine **69e** yielded a complex mixture that could not be separated by HPLC.

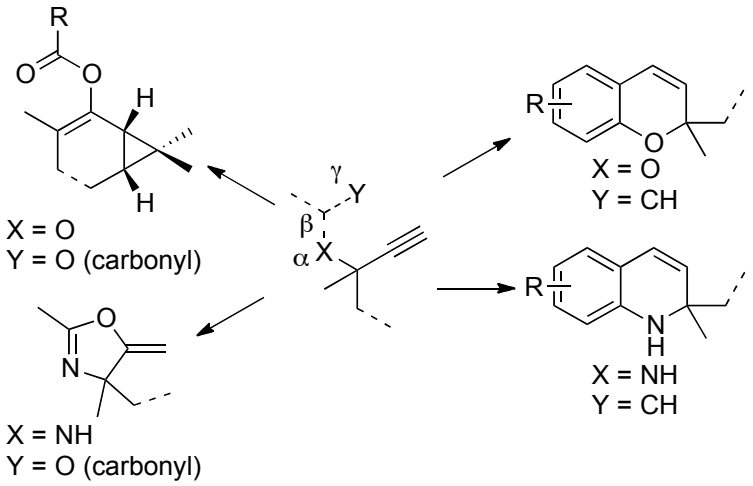
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Synthesis of the substrates

From the previous results it would seem that the most suitable groups for 1,5-migration must contain electron withdrawing groups. More importantly, in order to avoid side reactions, high electron density in the γ position must be avoided. For example propargyl carboxylates[78] and propargyl amides[94] are known to undergo facile 1,2-migration in the presence of Au(I) and Au(III) catalysts (Scheme 25). Propargyl-aryl ethers and amines can also yield 2*H*-chromenes[95] and 1,2-dihydroquinolines[95b,95d,96] respectively. Last but not least, in the context of a total synthesis, the groups that facilitated the 1,5-migration should be easily cleavable under mild conditions.



Scheme 25. Pathways competing with the 1,5-migration.

The synthesis of suitably functionalized enynes can prove to be a challenge in its own right. Tertiary propargylic alkoxides show reduced reactivity towards most soft electrophiles and may not react at all with weak electrophiles (Table 21, entries 8-12).

78. (a) Fürstner, A.; Hannen, P. *Chem. Commun.* **2004**, 2546-2547; (b) Fürstner, A.; Hannen, P. *Chem. Eur. J.* **2006**, *12*, 3006-3019.

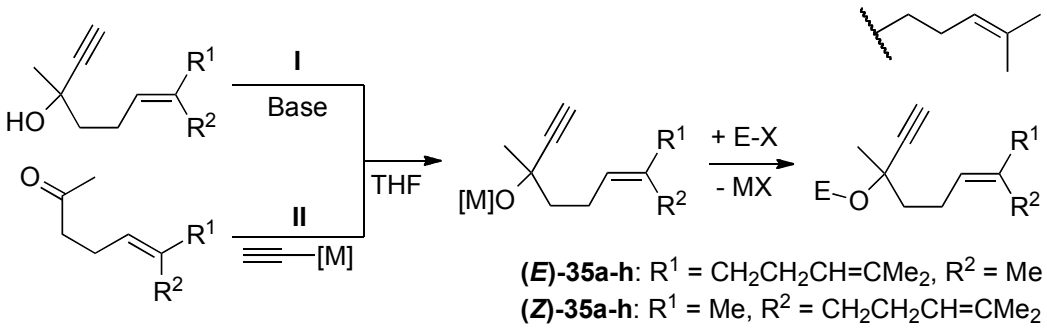
94. (a) Hashmi, A. S. K.; Weyrauch, J. P.; Frey, W.; Bats, J. W. *Org. Lett.* **2004**, *6*, 4391-4394; (b) Liu, Y.; Xu, W.; Wang, X. Org. Lett. **2010**, *12*, 1448-1451.

95. (a) Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669-3671; (b) Nevado, C.; Echavarren, A. M. *Chem. Eur. J.* **2005**, *11*, 3155-3164; (c) Curtis, N. R.; Prodger, J. C.; Rassias, G.; Walker, A. J. *Tetrahedron Lett.* **2008**, *49*, 6279-6281; (d) Menon, R. S.; Findlay, A. D.; Bissember, A. C.; Banwell, M. G. *J. Org. Chem.* **2009**, *74*, 8901-8903.

96. Liu, X.-Y.; Ding, P.; Huang, J.-S.; Che, C.-M. *Org. Lett.* **2007**, *9*, 2645-2648.

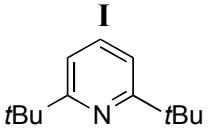
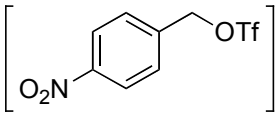
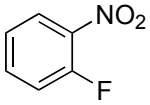
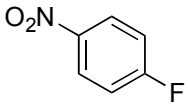
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Arylation with C_6Cl_6,[97] C_6F_6[98] or *p*-nitrophenyl fluoride[99] could not be achieved (Table 19, entries 5-8; Table 20, entry 5; Table 21, entries 5-7). The *p*-nitrobenzyl ethers could only be obtained using *p*-nitrobenzyl trifluoromethanesulfonate (Table 19, entry 3; Table 20, entry 3; Table 21, entry 2).[76]



(*E*)-35a-h: $R^1 = CH_2CH_2CH{=}CMe_2$, $R^2 = Me$
(*Z*)-35a-h: $R^1 = Me$, $R^2 = CH_2CH_2CH{=}CMe_2$
48a-f: $R^1 = Me$, $R^2 = Me$

Table 19. Synthesis of enynes **(*E*)-35a-h** via nucleophilic substitution (selected examples).[a]

Entry	Method (reagent)	E-X	Product (yield, %)
1	**I** (Et_3N)	TMSOTf	**(*E*)-35a** (91)
2	**II** (HC_2Na)	MOMBr	**(*E*)-35c** (65)
3	**I** 		**(*E*)-35e** (65)
4	**II** (HC_2Na)		**(*E*)-35g** (77)
5	**II** (HC_2Na)	C_6Cl_6	-
6	**II** (HC_2Na)		-
7	**I** (NaH)[b]		-
8	**I** (KHMDS)		-

a) isolated yields; b) the reaction did not proceed even after addition of TMEDA.

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

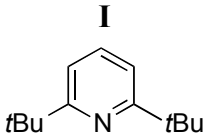
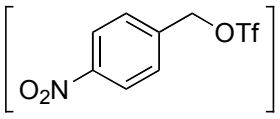
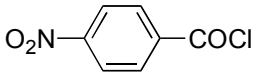
97. Brady, J. H.; Wakefield, B. J. *Synthesis* **1984**, 33-34.

98. Cheong, C. L.; Wakefield, B. J. *J. Chem. Soc. Perkin. Trans. I* **1988**, 3301-3305.

99. Woiwode, T. F.; Rose, C.; Wandless, T. J. *J. Org. Chem.* **1998**, *63*, 9594-9596.

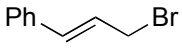
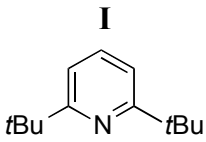
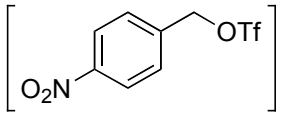
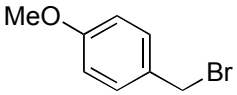
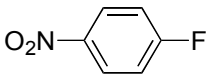
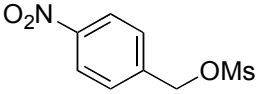
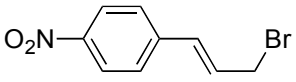
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Table 20. Synthesis of enynes **(*Z*)-35a-h** via nucleophilic substitution (selected examples).[a]

Entry	Method (reagent)	E-X	Product (yield, %)
1	**I** (Et_3N)	TMSOTf	**(*Z*)-35a** (88)
2	**II** (HC_2Na)	MOMBr	**(*Z*)-35c** (65)
3	**I** 		**(*Z*)-35e** (68)
4	**I** (NaH)		**(*Z*)-35f** (41)
5	**II** (HC_2Na)	C_6Cl_6	-

a) isolated yields; b) yield based on recovered starting material: 85%.

Table 21. Synthesis of enynes **48a-f** via nucleophilic substitution (selected examples).[a]

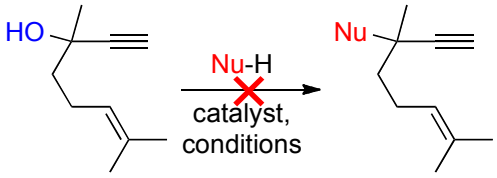
Entry	Method (reagent)	E-X	Product (yield, %)
1	**I** (NaH)[b]		**48b** (28)
2	**I** 		**48d** (64)
3	**I** (NaH)		**48e** (80)
4	**I** (iPr_2EtN)[c]	MOMBr	**48f** (78)
5	**II** (HC_2Na)	C_6Cl_6	-
6	**II** (HC_2Na)	C_6F_6	-
7	**II** (HC_2Na)		-
8	**I** (Et_3N)[d]		-
9	**I** (NaH)[d,e]		-
10	**I** (BuLi)[e]		-
11	**I** (BuLi)[e]		-
12	**I** (NaH)[b,d,e]		-

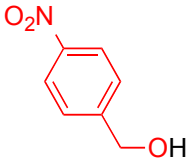
a) isolated yields; b) reaction performed in the presence of TBAI (1 equiv.); c) reaction performed in CH_2Cl_2; d) the reaction did not proceed in DMF either; e) the alkylating agent decomposes after a while.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Methodologies for Brønsted acid,[100] Bi(III),[101] Cu(II)[102] and Au(III)[103] catalyzed functionalization of unprotected propargyl alcohols were recently developed (Scheme 26). However, when we tried to apply them to our substrate (an aliphatic propargyl alcohol), we observed no reaction (Table 22). This decrease in reactivity is due to the absence of a phenyl group (either R^1, R^2 or R^3) that stabilizes the propargyl carbocation in these reactions.

Table 22.



NuH	Catalyst, conditions	Observations
	$CuBr_2$ (5 mol%), $MeNO_2$, room temperature, 12 h[102]	No reaction
	$NaAuCl_4 \cdot 2H_2O$ (5 mol%), CH_2Cl_2, room temperature, 24 h[103]	No reaction, gold mirror
	$CuBr_2$ (5 mol%), $MeNO_2$, room temperature, 12 h[102]	No reaction
	$NaAuCl_4 \cdot 2H_2O$ (5 mol%), CH_2Cl_2, room temperature, 24 h[103]	No reaction, gold mirror
	CSA (10 mol%), MeCN, 140 ºC, 20 min[100]	No reaction
	CSA (20 mol%), MeCN, 200 ºC, 40 min	Complex mixture
	$Bi(OTf)_3$ (5 mol%), KPF_6 (5 mol%), drierite, dioxane, room temperature 18 h[101]	No reaction
	$Bi(OTf)_3$ (5 mol%), KPF_6 (5 mol%), drierite, dioxane, room temperature 8 days	Partial decomposition

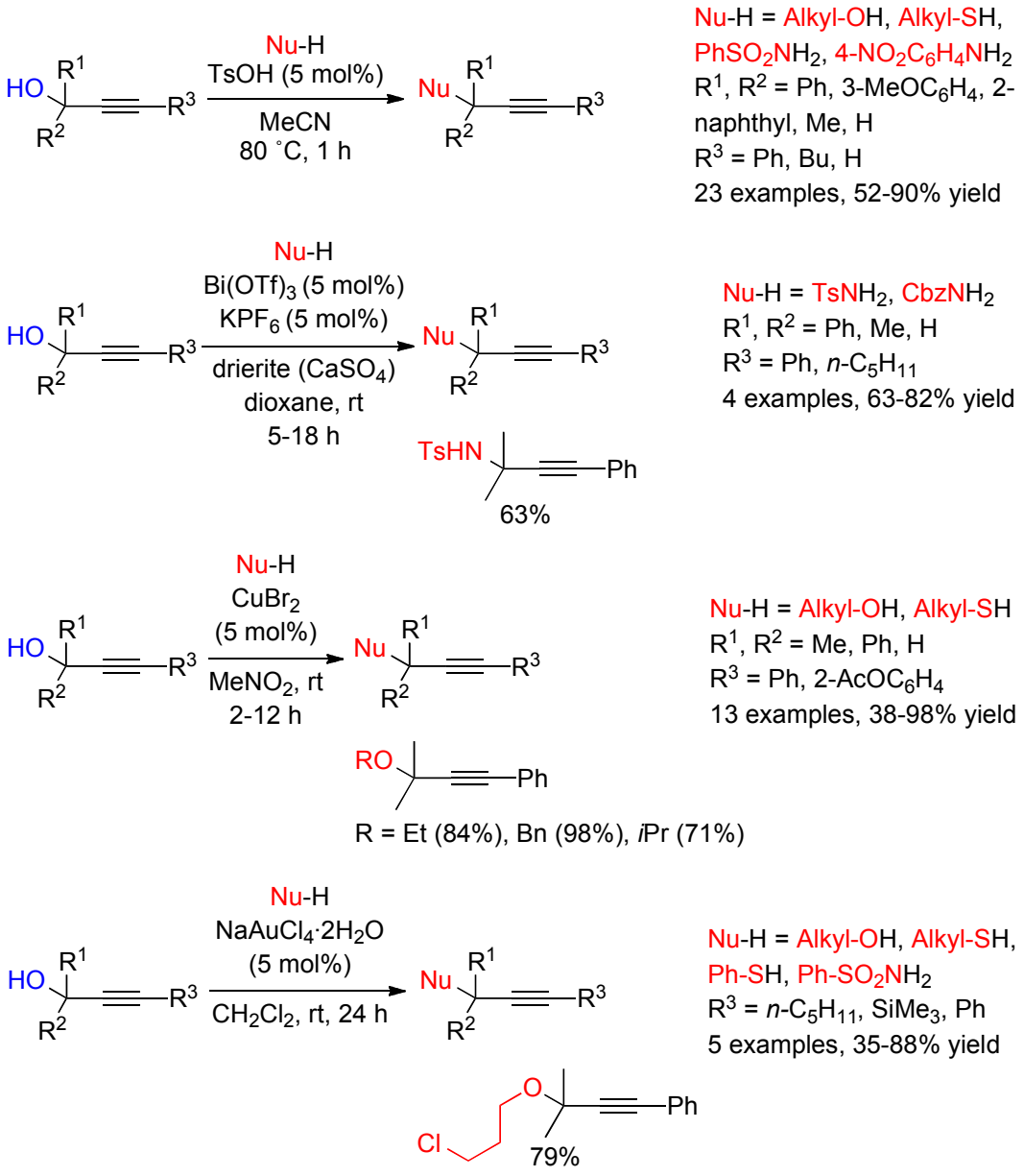
100. Sanz, R.; Martínez, A.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Eur. J. Org. Chem.* **2006**, 1383-1386.

101. Qin, H.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. *Angew. Chem. Int. Ed.* **2007**, *46*, 409-413.

102. Hui, H.; Zhao, Q.; Yang, M.; She, D.; Chen, M.; Huang, G. *Synthesis* **2008**, *2*, 191-196.

103. Georgy, M.; Boucard, V.; Debleds, O.; Zotto, C. D.; Campagne, J.-M. *Tetrahedron* **2009**, *65*, 1758-1766.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



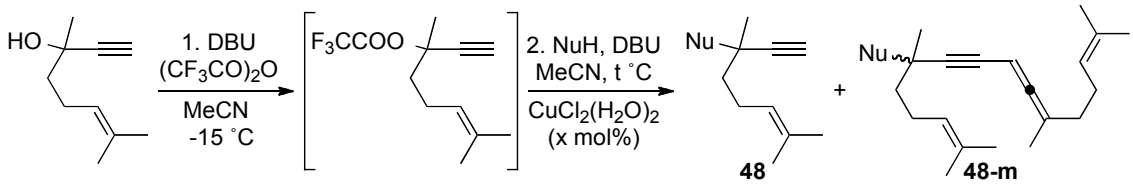
Scheme 26.

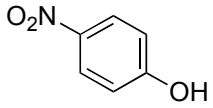
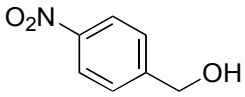
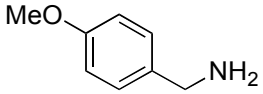
The reported method for the preparation of aryl-propargyl ethers[104] (Table 23, entry 1) could not be extended to benzyl ethers (entry 2), amines (entry 3), or imides (entry 4).

104. Godfrey, J. D. Jr.; Mueller, R. H.; Sedergran, T. C.; Soundararajan, N.; Colandrea, V. J. *Tetrahedron Lett*. **1994**, *35*, 6405-6408.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Table 23. Synthesis of functionalized enynes via Cu catalysis.[a]



Entry	NuH	x (mol%)	t (º C)	Time (h)	Products (yield, %)
1		1	-5	24	**48h** (68), **48h-m** (8)
		1	rt	24	**48h** (37), **48h-m** (6)
2		2	rt[b]	24	No reaction
3		1	50 (MW)	4	No reaction[c]
4	Phthalimide	1	100[d] (MW)	12	Partial decomposition

a) reactions run with 1 mol% $CuCl_2(H_2O)_2$, isolated yields, rt = room temperature; b) reactions run with 2 mol% $CuCl_2(H_2O)_2$; c) formation of the starting alcohol was observed after the addition of the amine; d) the phthalimide was added as a solution in dioxane.

The reported method for the preparation of propargyl-amines[105] (Table 24, entry 1) worked well for propargyl-anilines (entries 2-4), but it could not be extended to HMDS (entry 6), sulfonamides (entrues 7-9) or potassium phthalimide (entries 10-11).

Tertiary propargyl alcohols were described to give tertiary propargyl acetamides under Ritter conditions.[106,107] Unfortunately our substrate yielded a complex mixture under these conditions (Table 25).

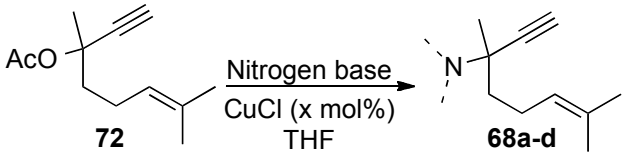
105. Imada, Y.; Yuasa, M.; Nakamura, I.; Murahashi, S.-I. *J. Org. Chem.* **1994**, *59*, 2282-2284.

106. Schmidt, E. Y.; Vasil'tsov, A. M.; Mikhaleva, A. I.; Zaitsev, A. B.; Afonin, A. V.; Toryashinova, D.-S. D.; Klyba, L. V.; Arndt, J.-D.; Henkelmann, J. ARKIVOC **2003**, *xiii*, 35-44.

107. Xu, X.; Weitzberg, M.; Keyes, R. F.; Li, Q.; Wang, R.; Wang, X.; Zhang, X.; Frevert, E. U.; Camp, H. S.; Beutel, B. A.; Sham, H. L.; Gu, Y. G. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1803-1807.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

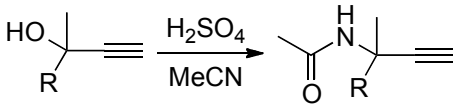
Table 24. Synthesis of amino-enynes **68a-d**.[a]

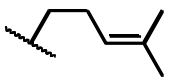


Entry	Nitrogen base (mol%)	x (mol%)	t (º C)	Time (h)	Products (yield, %)
1	PMBn-NH_2 (400)	10	80	38	**68a** (57)
2	4-methoxyaniline (300)	5	50	8	**68b** (68), **71** (8)
3	4-nitroaniline (400)	5	50	4	**68c** (83)
4	4-methoxy-2,6-dimethylaniline (300)	5	50	4	**68d** (46)
5		5	50	8	Decomposition
6	$(TMS)_2NH$ (300)	10	70 (MW)	2	Complex mixture
7	$TsNH_2$ (400)	10	100 (MW)	6	Complex mixture
8	$MsNH_2$ (200)	5	rt	14	No reaction
9		5[b]	50 (MW)	3	Complex mixture
10	Potassium phthalimide (200)[c]	5	100 (MW)	2	No reaction
11		25		24	Complex mixture

a) isolated yields, rt = room temperature; b) reaction performed in the presence of DBU (300 mol%); c) reactions run in MeCN in the presence of 18-crown-6 (400 mol%).

Table 25.



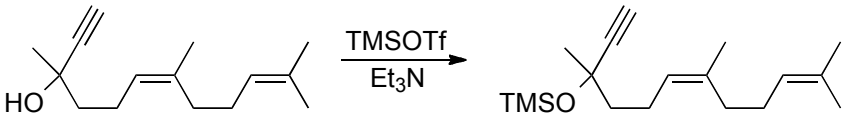
Entry	R	Conditions	Yield (%)
1	Me[106]	H_2SO_4 (0.9 equiv.), MeCN (1-10 equiv.), -40 ºC to 10 ºC	38-54
2	Me[107]	Na_2SO_4 (1 equiv.), H_2SO_4 (5 equiv.), MeCN, -20 ºC to room temperature	50-74
3		Na_2SO_4 (1 equiv.), H_2SO_4 (1.1 equiv.), MeCN (10 equiv.), -25 ºC to room temperature	Complex mixture

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Experimental Part

Synthesis of the substrates

The general considerations from the previous chapter still apply. Enynes **(*E*)-35a**,[108] **(*E*)-35b**, **(*E*)-35d**, **(*E*)-35f**, **(*Z*)-35b**, **48a**, **48c**, **48g**,[109] were synthesized by coworkers and their ^{1}H and ^{13}C NMR data was published.[76] **(*Z*)-35h** and **(*E*)-35h** were synthesized according to a published procedure.[78]



(*Z*)-Trimethyl(3,7,11-trimethyldodeca-6,10-dien-1-yn-3-yloxy)silane ((*Z*)-35a)

Over a 0ºC solution of **(*Z*)-35h** (0.630 g, 2.86 mmol) and Et_3N (0.73 mL, 5.2 mmol) in CH_2Cl_2 (29 mL), TMSOTf (0.63 mL, 3.4 mmol) was added dropwise. After stirring for 10 min, the solution was washed with NH_4Cl pH = 8 buffer solution (6 mL), water (6 mL) and brine (6 mL). The combined washings were extracted with CH_2Cl_2 (2x15 mL) and the combined organic layers were dried on Na_2SO_4, evaporated and submitted to flash-chromatography (hexane). (*Z*)-trimethyl(3,7,11-trimethyldodeca-6,10-dien-1-yn-3-yloxy)silane was obtained as a colourless liquid (0.739 g, yield 88%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (some signals overlap) 5.16-5.13 (m, 2H), 2.43 (s, 1H), 2.22-2.11 (m, 2H), 2.06-2.05 (m, 4H),1.69-1.56 (m, 2H), 1.69 (br, 6H), 1.62 (br, 3H), 1.46 (s, 3H), 0.18 (s, 9H); ^{13}C NMR (PENDANT, $CDCl_3$, 101 MHz) δ 135.55 (C sp^2), 131.67 (C sp^2), 124.89 (CH sp^2), 124.52 (CH sp^2), 88.13 (C sp), 72.41 (CH sp), 69.30 (C sp^3), 45.40 (CH_2 sp^3), 32.08 (CH_2 sp^3), 31.23 (CH_3), 26.75 (CH_2 sp^3), 25.88 (CH_3), 23.56 (CH_3), 23.35 (CH_2 sp^3), 17.79 (CH_3), 2.05 (CH_3); HRMS-ESI Calcd. for $C_{18}H_{32}OSiNa$ ($M+Na^+$): 315.2120. Found: 315.2105.

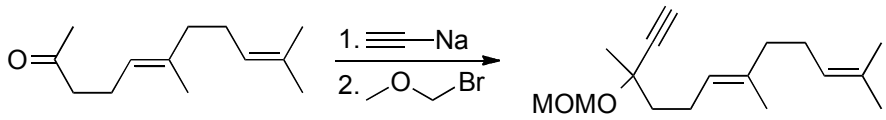
76. Jiménez-Núñez, E.; Raducan, M.; Lauterbach, T.; Molawi, K.; Solorio, C. R.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2009**, *48*, 6152-6155.

78. (a) Fürstner, A.; Hannen, P. *Chem. Commun.* **2004**, 2546-2547; (b) Fürstner, A.; Hannen, P. *Chem. Eur. J.* **2006**, *12*, 3006-3019.

108. Product(s) synthesized and characterized by Eloísa Jiménez-Núñez.

109. Product(s) synthesized and characterized by Dr. Thorsten Lauterbach, Kian Molawi.

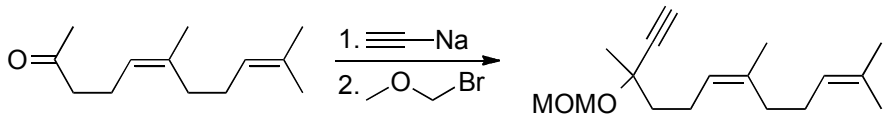
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



(*E*)-3-(Methoxymethoxy)-3,7,11-trimethyldodeca-6,10-dien-1-yne ((*E*)-35c)

Over a solution of geranylacetone (0.47 mL, 2.0 mmol) in THF (20 mL), a well homogenized slurry of sodium acetylide in xylene/light mineral oil (18%, 0.50 mL, 2.2 mmol) was added. After 2 h 45 min, more sodium acetylide was added (1x, 0.45 mL) and again after 23 h (2x, 0.9 mL). After 33 h MOMBr (0.88 mL, 9.7 mmol, 4.8x) was added and the mixture was cooled with an ice-bath when mild refluxing ensued. Et_3N (2.4 mL, 10 mmol) was added, the mixture was concetrated over Celite (8g) and submitted to flash chromatography (hexane/EtOAc = 50 : 1, 5x15 cm silica). The desired compound was obtained as a light yellow oil. (347 mg, 65%)

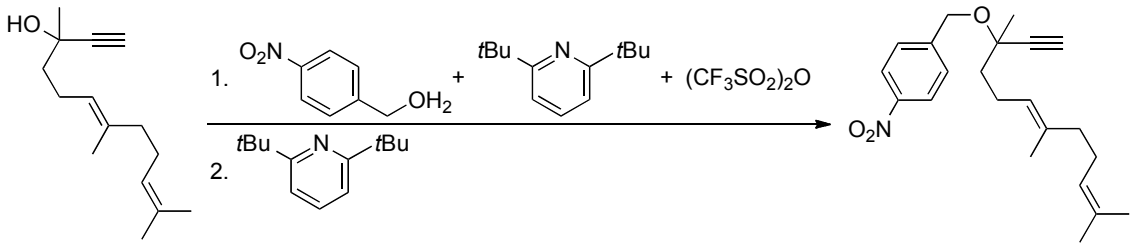
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.15-5.08 (m, 2H), 5.0 (d, J = 7.0 Hz, 1H), 4.83 (d, J = 7.0 Hz, 1H), 3.40 (s, 3H), 2.51 (s, 1H), 2.24-2.13 (m, 2H), 2.09-2.04 (m, 2H), 2.00-1.96 (m, 2H), 1.82-1.74 (m, 1H), 1.72-1.64 (m, 1H), 1.68 (br s, 3H), 1.62 (br s, 3H), 1.60 (br s, 3H), 1.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.64 (C), 131.47 (C), 124.47 (CH), 123.76 (CH), 93.23 (CH_2), 84.86 (C), 74.02 (CH), 73.95 (C), 55.76 (CH_3), 42.73 (CH_2), 39.82 (CH_2), 28.00 (CH_3), 26.84 (CH_2), 25.83 (CH_3), 23.17 (CH_2), 17.82 (CH_3), 16.11 (CH_3); HRMS-ESI Calcd for $C_{17}H_{28}O_2Na$ ($M+Na^+$): 287.1987. Found: 287.1969.



(*Z*)-3-(Methoxymethoxy)-3,7,11-trimethyldodeca-6,10-dien-1-yne ((*Z*)-35c)

This compound was prepared from nerylacetone in a similar manner to the *E* isomer. The desired compound was obtained as a light yellow oil (349 mg, 65%).

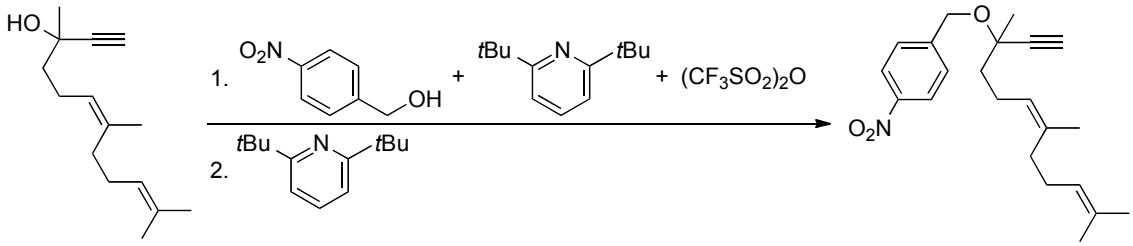
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.15-5.11 (m, 2H), 4.99 (d, J = 7.0 Hz, 1H), 4.82 (d, J = 7.0 Hz, 1H), 3.39 (s, 3H), 2.50 (s, 1H), 2.25-2.10 (m, 2H), 2.09-2.04 (m, 4H), 1.80-1.73 (m, 1H), 1.70-1.62 (m, 1H), 1.69 (m, 6H), 1.61 (br s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.74 (C), 131.69 (C), 124.59 (CH), 124.46 (CH), 93.20 (CH_2), 84.78 (C), 74.03 (CH), 73.91 (C), 55.73 (CH_3), 42.99 (CH_2), 32.05 (CH_2), 28.01 (CH_3), 26.71 (CH_2), 25.86 (CH_3), 23.52 (CH_3), 23.07 (CH_2), 17.76 (CH_3); HRMS-ESI Calcd for $C_{17}H_{28}O_2Na$ ($M+Na^+$): 287.1987. Found: 287.1995.



(*E*)-1-Nitro-4-((3,7,11-trimethyldodeca-6,10-dien-1-yn-3-yloxy)methyl)benzene ((*E*)-35e)

This compound was prepared from the corresponding alcohol in a similar manner to the *Z* isomer. The desired compound was obtained as a yellow oil (0.463 g, 65%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.7 Hz, 2H), 7.52 (d, J = 8.6 Hz, 2H), 5.16 (br t, J = 7.0 Hz, 1H), 5.09 (br t, J = 6.8 Hz, 1H), 4.78 (d, J = 12.8 Hz, 1H), 4.71 (d, J = 12.8 Hz, 1H), 2.52 (s, 1H), 2.32-2.15 (m, 2H), 2.10-2.04 (m, 2H), 2.00-1.97 (m, 2H), 1.88-.173 (m, 2H), 1.68 (s, 3H), 1.63 (s, 3H), 1.60 (s, 3H), 1.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.30 (C), 147.00 (C), 135.91 (C), 131.54 (C), 127.75 (CH), 124.40 (CH), 123.63 (CH), 123.53 (CH), 84.77 (C), 74.15 (CH), 74.14 (C), 65.20 (C), 41.70 (CH_2), 39.81 (CH_2), 26.82 (CH_2), 26.38 (CH_3), 25.83 (CH_3), 23.09 (CH_2), 17.82 (CH_3), 16.14 (CH_3); HRMS ESI calcd for $C_{22}H_{29}NO_3Na$ $(M+Na)^+$: 378.2045; found: 378.2064.



(*Z*)-1-Nitro-4-((3,7,11-trimethyldodeca-6,10-dien-1-yn-3-yloxy)methyl)benzene ((*Z*)-35e)[110]

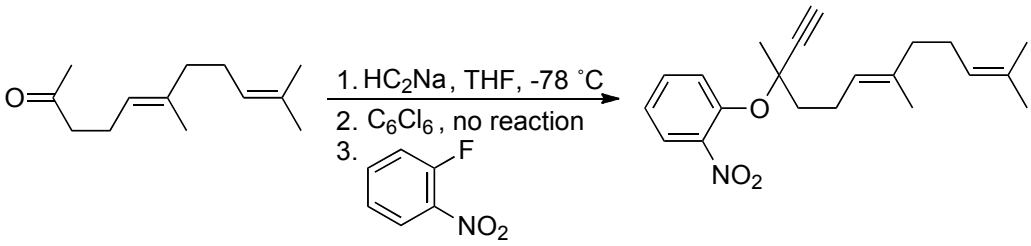
Over a solution of $(CF_3SO_2)_2O$ (0.40 mL, 2.4 mmol) in CH_2Cl_2 (2.4 mL), with ice-bath cooling, a solution of 4-nitrobenzyl alcohol (0.372 g, 2.4 mmol) and 2,6-di-*tert*-butylpyridine (0.56 mL, 2.4 mmol) in CH_2Cl_2 (7.2 mL) was slowly added. The mixture was then allowed to reach room temperature. After 100 min a solution of dienynol (0.441 g, 2.00 mol) and 2,6-di-*tert*-butylpyridine (0.56 mL, 2.4 mmol) in CH_2Cl_2 (2 mL) was added and the mixture was stirred for an additional 8 h. The mixture was concentrated over Celite (4.9 g) with Et_3N (1.4 mL) then purified by flash

110. For the synthesis of other nitrobenzyl ethers see: Wheeler, T. N.; Craig, T. A.; Morland, R. B.; Ray, J. A. *Synthesis* **1987**, 883-887.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

chromatography (hexane/EtOAc/Et_3N = 100 : 2 : 1, 5x15 cm silica) to yield the desired compound as a yellow oil (0.481 g, 68%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.7 Hz, 2H), 7.52 (d, J = 8.6 Hz, 2H), 5.18-5.11 (m, 2H), 4.77 (d, J = 12.9 Hz, 1H), 4.70 (d, J = 12.8 Hz, 1H), 2.51 (s, 1H), 2.31-2.15 (m, 2H), 2.07-2.06 (m, 4H), 1.87-1.72 (m, 2H), 1.70 (s, 3H), 1.68 (s, 3H), 1.60 (s, 3H), 1.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.29 (C), 147.00 (C), 136.00 (C), 131.78 (C), 127.73 (CH), 124.40 (CH), 124.39 (CH), 123.62 (CH), 84.72 (C), 74.16 (CH), 74.08 (C), 65.17 (CH_2), 41.97 (CH_2), 32.09 (CH_2), 26.71 (CH_2), 26.39 (CH_3), 25.87 (CH_3), 23.53 (CH_3), 22.99 (CH_2), 17.78 (CH_3); HRMS ESI calcd for $C_{22}H_{29}NO_3Na$ $(M+Na)^+$: 378.2045; found: 378.2048.



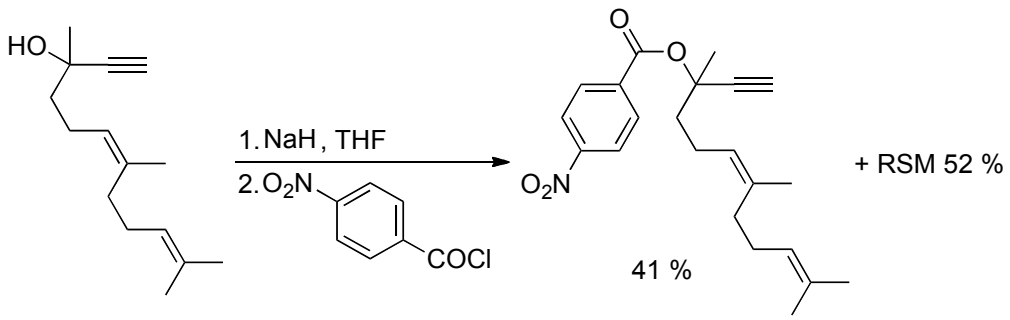
(*E*)-1-Nitro-2-((3,7,11-trimethyldodeca-6,10-dien-1-yn-3-yl)oxy)benzene ((*E*)-35g)

Over a -90 ºC solution of geranylacetone (0.47 mL, 2.0 mmol) in THF (10 mL), a well homogenized slurry of sodium acetylide in xylene/light mineral oil (18%, 0.50 mL, 2.2 mmol) was added. After 30 min no reaction was observed (TLC) and the cold bath was removed and the mixture was allowed to reach room temperature (aprox 1 h, no reaction), then more sodium acetilyde (0.50 mL) was added. After 24 h (complete consumption of the geranylacetone), the mixture was cooled to -78 ºC and C_6Cl_6 (1.28 g, 4.46 mmol) was added. The cold bath was removed. After 23 h no reaction was observed. The mixture was cooled to 0 ºC then 1-fluoro-2-nitrobenzene (0.47 mL, 4.46 mmol) was added; after stirring 1 h at 0 ºC the ice-bath was removed and the mixture was stirred for a further 1 h (the reaction completed). The mixture was treated with Et_3N (1.8 mL) and AcOH (0.25 mL), concetrated over Florisil (6.91 g) and submitted to flash chromatography (hexane/EtOAc = 100 : 5, 5x30 cm SiO_2). A second chromatography (hexane/$CHCl_3$ = 3 : 1, 5x15 cm SiO_2) was required to remove a small excess of C_6Cl_6 which nonpolar and is insoluble in the first eluent. **(*E*)-35g** was obtained as an orange oil (0.523 mg, 77%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76-7.72 (m, 2H), 7.48 (ddd, J = 8.4, 7.4, 1.8 Hz, 1H), 7.10 (ddd, J = 8.1, 7.4, 1.2 Hz, 1H), 5.17-5.13 (m, 1H), 5.12-5.07 (m, 1H), 2.68 (s, 1H),

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

2.38-2.19 (m, 2H), 2.10-1.98 (m, 2H), 1.90 (ddd, J = 13.5, 11.7, 5.3 Hz, 1H), 1.68 (m, 3H), 1.65 (s, 3H), 1.63 (m, 3H), 1.60 (br s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.06 (C), 143.61 (C), 136.29 (C), 132.84 (CH), 131.54 (C), 125.14 (CH), 124.44 (CH), 123.06 (CH), 122.29 (CH), 121.85 (CH), 84.22 (C), 77.88 (C), 76.46 (CH), 42.66 (CH_2), 39.82 (CH_2), 26.82 (CH_2), 26.53 (CH_3), 25.84 (CH_3), 23.03 (CH_2), 17.83 (CH_3), 16.11 (CH_3); HRMS calcd. for: $C_{21}H_{27}NO_3Na$ (M+Na): 364.1889; found: 364.1895.

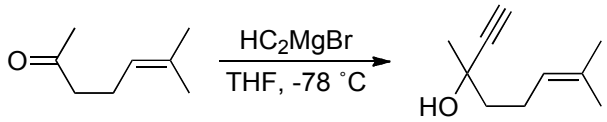


(*Z*)-3,7,11-Trimethyldodeca-6,10-dien-1-yn-3-yl 4-nitrobenzoate ((*Z*)-35f)

A solution of the dieninol (330 mg, 1.50 mmol) in THF (3 mL) was added over a suspension of NaH (60% in mineral oil, 66 mg, 1.65 mmol) in THF (3 mL) and the mixture was stirred for 1 h. A solution of *p*-nitrobenzoyl chloride (417 mg, 2.25 mmol) in THF (3 mL) was added. Color change and H_2 evolution started to ocurr. The mixture was stirred at room temperature for 17 h then at 45 ºC for 21 h. The mixture was cooled, treated with Et_3N (0.1 mL) and AcOH (0.3 mL) then it was concentrated over Florisil (2.45 g) and submitted to flash chromatography (hexane/EtOAc = 100 : 5 to 10 : 1, 5 x 15 cm silica) to yield the desired **(*Z*)-35f** as a clear yellow oil that solidified in the fridge (8 ºC) (226 mg, 41%). Starting material was recovered (173 mg, 52%).

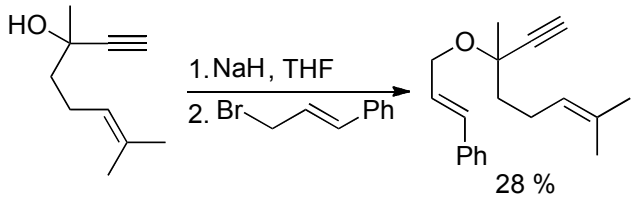
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29-8.26 (m, 2H), 8.19-8.16 (m, 2H), 5.20-5.17 (m, 1H), 5.11 (br s, 1H), 2.66 (s, 1H), 2.37-2.22 (m, 2H), 2.17-1.95 (m, 8H), 1.85 (s, 3H), 1.70 (m, 3H), 168 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.95 (C), 150.64 (C), 136.52 (C), 136.42 (C), 131.88 (C), 130.82 (CH), 124.29 (CH), 123.73 (CH), 123.62 (CH), 83.08 (C), 76.81 (C), 74.46 (CH), 41.98 (CH_2), 32.12 (CH_2), 26.67 (CH_2), 26.59 (CH_3), 25.87 (CH_3), 23.52 (CH_3), 22.96 (CH_2), 17.80 (CH_2); HRMS calcd. for $C_{22}H_{27}NO_4Na$ (M+Na): 392.1838; found: 392.1848.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



3,7-Dimethyloct-6-en-1-yn-3-ol (48i)

This product was synthesized according to a modified procedure:[78] over a -78 ºC solution of 6-methylhept-5-en-2-one (11.6 mL, 75.0 mmol) in Et_2O (150 mL), ethynylmagnesium bromide (0.5 M in THF, 195 mL, 97.5 mmol) was added dropwise (20 min addition time). The mixture allowed to slowly thaw to room temperature overnight (without removing the cold bath). The mixture was cooled with an ice bath then it was quenched with AcOH (6.4 mL, 112 mmol) and Et_3N (4.2 mL, 30 mmol). The suspension was filtered through a wide pad of sand (5x5 cm) and silica (5x5 cm) then the filtrate was concentrated over neutral alumina (40 g). Flash chromatography (gradient elution, CombiFlash) yielded **48i** (pure fraction: 7.94 g, 70%). The last traces of solvent were removed by sonication under vacuum (1 h). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.19-5.14 (m, 1H), 2.46 (s, 1H), 2.34-2.25 (m, 1H), 2.23-2.13 (m, 2H), 1.72-1.68 (m, 5H), 1.66 (s, 3H), 1.50 (s, 3H).

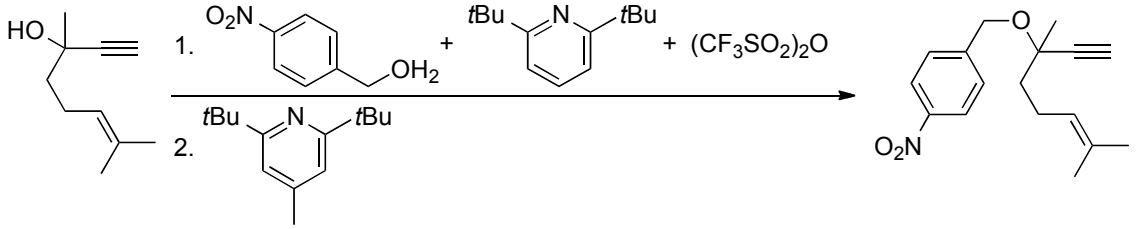


(*E*)-(3-((3,7-Dimethyloct-6-en-1-yn-3-yl)oxy)prop-1-en-1-yl)benzene (48b)

Over a suspension of NaH (18 mg, 0.44 mmol) in THF (2 mL) a solution of 3,7-dimethyloct-6-en-1-yn-3-ol (63 mg, 0.40 mmol) in THF (0.8 mL) was rappidly added. After 5 min stirring, cinnamyl bromide (0.07 mL, 0.48 mmol) was added, followed by TBAI (15 mg, 0.040 mmol). After 21 h Et_3N (0.06 mL) was added to the mixture then it was concentrated over Florisil (352 mg) and submitted to flash chromatography (hexane/EtOAc/Et_3N = 100 : 1 : 1, 3x15 cm SiO_2). **48b** was obtained as a clear colorless oil (30 mg, 28%). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.41-7.38 (m, 2H), 7.33-7.29 (m, 2H), 7.25-7.21 (m, 1H), 6.64-6.59 (m, 1H), 6.32 (dt, J = 15.9, 5.7 Hz, 1H), 5.18-5.13 (m, 1H), 4.30-4.21 (m, 2H), 2.54 (s, 1H), 2.27-2.11 (m, 2H), 1.81-1.67 (m, 2H), 1.70-1.69 (m, 3H), 1.64 (m, 3H), 1.48 (s, 3H).

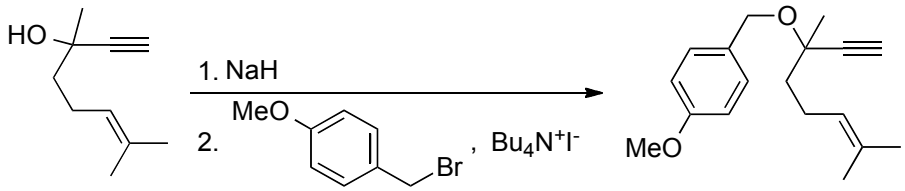
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

1-((3,7-Dimethyloct-6-en-1-yn-3-yloxy)methyl)-4-nitrobenzene (48d)



Over a solution of $(CF_3SO_2)_2O$ (1.00 mL, 6.00 mmol) in CH_2Cl_2 (6 mL), with ice-bath cooling, a solution of 4-nitrobenzyl alcohol (0.930 g, 6.00 mmol) and 2,6-di-*tert*-butylpyridine (1.39 mL, 6.00 mmol) in CH_2Cl_2 (18 mL) was slowly added. The mixture was then allowed to reach room temperature. After 90 min a solution of enynol (0.610 g, 4.00 mol) and 2,6-di-*tert*-butyl-4-metylpyridine (1.26 g, 6.00 mmol) in CH_2Cl_2 (4 mL) was added and the mixture was stirred for an additional 19 h (a white precipitate appeared after 15 min). The mixture was concentrated over Florisil with Et_3N (2.8 mL) then purified by flash chromatography (hexane/EtOAc/Et_3N = 100 : 2 : 1) to yield **48d** as a light yellow oil (0.738 g, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21-8.18 (m, 2H), 7.52 (d, J = 8.8 Hz, 2H), 5.17-5.13 (m, 1H), 4.78 (AB system, J = 12.8 Hz, 1H), 4.71 (AB system, J = 12.9 Hz, 1H), 2.52 (s, 1H), 2.30-2.14 (m, 2H), 1.87-1.72 (m, 2H), 1.70-1.69 (m, 3H), 1.63 (s, 3H), 1.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.31 (C), 147.00 (C), 132.28 (C), 127.75 (CH), 123.70 (CH), 123.64 (CH), 84.75 (C), 74.15 (CH), 74.14 (C), 65.21 (CH_2), 41.71 (CH_2), 26.39 (CH_3), 25.82 (CH_3), 23.21 (CH_2), 17.80 (CH_3); HRMS-ESI calcd for $C_{17}H_{22}NO_3$ (M^+): 288.1600; found: 288.1591.

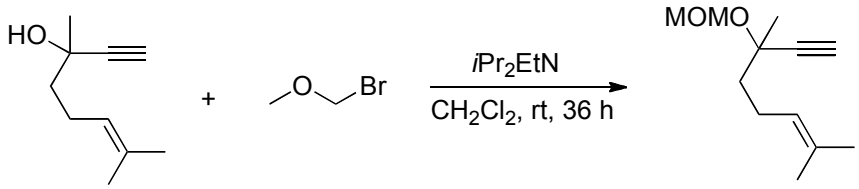
1-((3,7-Dimethyloct-6-en-1-yn-3-yloxy)methyl)-4-methoxybenzene (48e)



Over a stirred suspension of NaH (60% in mineral oil, 96 mg, 2.4 mmol) in THF (2 mL) a solution of the dienynol (305 mg, 2.00 mmol) in THF (2 mL) was added and the mixure was stirred at room temperature for 30 min. A solution of 4-methoxybenzyl bromide (0.36 mL, 2.4 mmol) and $Bu_4N^+I^-$ (89 mg, 0.24 mmol) in THF (2 mL) was added. After 38 h the mixture was quenched with Et_3N (0.7 mL, 4.8 mmol) and AcOH (0.14 mL, 2.4 mmol), concentrated over Florisil and purified by flash chromatography (hexane/EtOAc/Et_3N = 100 : 2 : 1) to yield **48e** as a colorless oil (444 mg, 80%).

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.3 Hz, 2H), 5.15-5.12 (m, 1H), 4.60 (AB system, J = 10.6 Hz, 1H), 4.53 (AB system, J = 10.6 Hz, 1H), 3.79 (s, 3H), 2.50 (s, 1H), 2.28-2.13 (m, 2H), 1.84-1.69 (m, 2H), 1.69 (s, 3H), 1.63 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$, PENDANT) δ 159.13 (C), 131.99 (C), 131.35 (C), 129.27 (CH), 124.01 (CH), 113.87 (CH), 85.51 (C), 73.49 (CH), 73.46 (C), 66.04 (CH_2), 55.43 (CH_3), 41.64 (CH_2), 26.53 (CH_3), 25.83 (CH_3), 23.19 (CH_2), 17.81 (CH_3); HRMS-ESI calcd. for $C_{18}H_{25}O_2$ $(M+H)^+$: 273.1855; found: 273.1842.

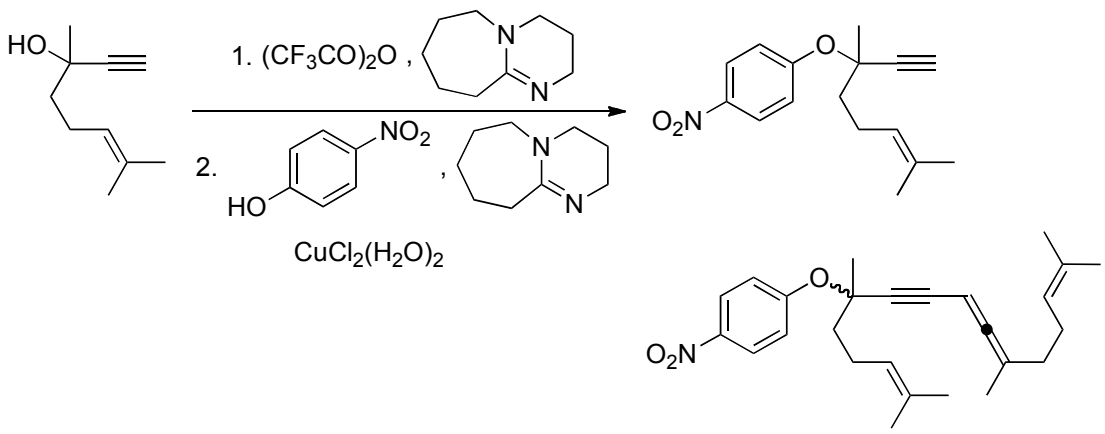


3-(Methoxymethoxy)-3,7-dimethyloct-6-en-1-yne (48f)

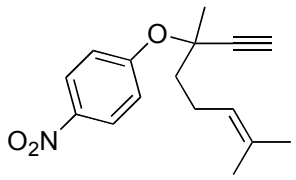
Over a solution of the enynol (314 mg, 2.00 mmol) in CH_2Cl_2 (10 mL), MOMBr (0.22 mL, 2.4 mmol) and DIPEA (0.42 mL, 2.4 mmol) were slowly and succesively added (mild refluxing occurs). After 17 h an additional amount of MOMBr (0.11 mL) and DIPEA (0.21 mL) was added and the mixture was stirred for 31 h. Et_3N (1 mL) was added, the mixture was concentrated over Florisil (1.92 g) and purified by flash chromatography (hexane/EtOAc = 100 : 2) to yield **48f** as a clear colorless oil (306 mg, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.14-5.10 (m, 1H), 4.99 (d, J = 7.0 Hz, 1H), 4.83 (d, J = 7.0 Hz, 1H), 3.40 (s, 3H), 2.50 (s, 1H), 2.24-2.10 (m, 2H), 1.80-1.73 (m, 1H), 1.71-1.65 (m, 1H), 1.69 (s, 3H), 1.63 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.04 (C), 123.89 (CH), 93.23 (CH_2), 84.83 (C), 74.02 (CH), 73.94 (C), 55.78 (CH_3), 42.73 (CH_2), 28.01 (CH_3), 25.82 (CH_3), 23.29 (CH_2), 17.78 (CH_3); HRMS Calcd for $C_{12}H_{20}O_2Na$ (M+Na): 219.1361; found: 219.1365.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



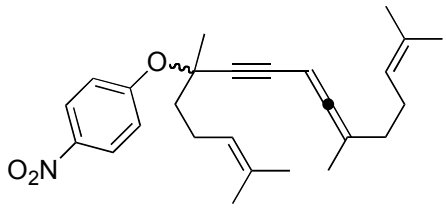
This procedure is similar to the previously described synthesis of aryl-propargyl ethers.[104] To a solution of enynol (0.305 g, 2.00 mmol) in MeCN (SPS, 2 mL) at -15 ºC, were added dropwise DBU (0.40 mL, 2.6 mmol) then $(CF_3CO)_2O$ (0.34 mL, 2.4 mmol). The solution was warmed to -5 ºC and stirred for 15 min, then a solution of p-nitrophenol (0.310 g, 2.20 mmol) and $CuCl_2 \cdot 2H_2O$ (3.4 mg, 0.02 mmol) in MeCN (1 mL) (prepared almost under air) was added. The mixture was stirred at -5 ºC for 24 h (overnight). Et_3N (0.29 mL) was added, the mixture was concentrated over Florisil (3.75 g) then purified by flash chromatography (hexane/EtOAc/Et_3N = 100 : 2 : 1, 5x30 cm silica). The desired compound was obtained as a pale orange oil (0.374 g, 68%, fraction 2); additionally a homocoupling allenynol ether was also isolated (31 mg, 8%, fraction 1).



1-((3,7-Dimethyloct-6-en-1-yn-3-yl)oxy)-4-nitrobenzene (48h)

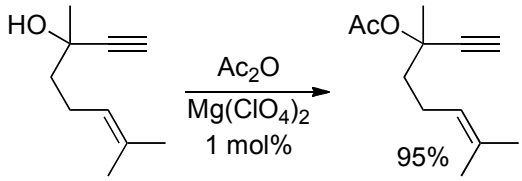
Pale orange oil (hexane/EtOAc/Et_3N = 100 : 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20-8.16 (m, 2H), 7.32-7.28 (m, 2H), 5.16-5.11 (m, 1H), 2.71 (s, 1H), 2.35-2.17 (m, 2H), 2.00 (ddd, J = 13.6, 11.1, 5.3 Hz, 1H), 1.90 (ddd, J = 13.6, 11.5, 5.4 Hz, 1H), 1.70 (m, 3H), 1.68 (s,3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.46 (C), 142.23 (C), 132.76 (C), 125.37 (CH), 123.07 (CH), 119.20 (CH), 83.69 (C), 76.78 (CH), 76.13 (C), 42.58 (CH_2), 26.80 (CH_3), 25.81 (CH_3), 23.06 (CH_2), 17.78 (CH_3); HRMS calcd. for $C_{16}H_{19}NO_3Na$ (M+Na): 296.1263; found: 296.1265.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



1-Nitro-4-((2,6,11,15-tetramethylhexadeca-2,9,10,14-tetraen-7-yn-6-yl)oxy)benzene (48h-m)

Pale orange oil (hexane/EtOAc/Et_3N = 100 : 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17-8.13 (m, 2H), 7.30-7.26 (m, 2H), 5.29 (sextuplet, J = 2.9, 2.9 Hz, 1H), 5.17-5.08 (m, 2H), 2.33-2.16 (m, 2H), 2.12-2.06 (m, 2H), 2.03-1.96 (m, 3H), 1.89 (ddd, J = 13.5, 11.4, 5.5 Hz, 1H), 1.73-1.72 (m, 3H), 1.69 (m, 3H), 1.67 (s, 6H), 1.62 (br s, 3H), 1.59 (br s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; some signals are splitted due to the presence of 2 diastereomers) δ 210.48 (C), 161.85 (C), 141.95 (C), 132.50 (C), 132.30 (C), 125.27 (CH), 123.64 (CH), 123.37 (CH), 119.17 (CH), 102.45 (102.44) (C), 88.03 (C), 83.20 (C), 77.13 (C), 74.02 (74.01) (CH), 42.84 (42.83) (CH_2), 33.78 (CH_2), 26.90 (26.89) (CH_3), 26.09 (26.07) (CH_2), 25.84 (25.82) (2xCH_3), 23.27 (CH_2), 18.63 (CH_3), 17.85 (CH_3), 17.72 (CH_3); HRMS-ESI Calcd for $C_{26}H_{33}NO_3Na$ (M+Na): 430.2358; found: 430.2367;



3,7-Dimethyloct-6-en-1-yn-3-yl acetate (72)

This compound was synthesized similarly to a described procedure.[111,112] The enynol (762 mg, 5.00 mmol) was added dropwise to a solution of $Mg(ClO_4)_2$ (11 mg, 50 μmol) in Ac_2O (0.57 mL, 6.0 mmol) at room temperature with stirring. After additional stirring for 1.5 h the mixture was diluted with Et_2O (6 mL) and added over a solution of Na_2CO_3 (637 mg, 6 mmol) in H_2O (30 mL). The mixture was stirred vigorously for 30 min, then after separation, the aqueous phase was extracted with Et_2O (3x30 mL). The organic layer was dried over Na_2SO_4, then after filtration and evaporation of the solvent the product was vacuum dried on the rotaevaporator (40 ºC, 100 mbar, 1 h). Acetate **72**

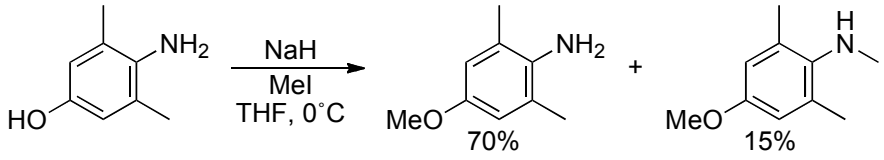
111. Gabriele, B.; Plastina, P.; Salerno, G.; Mancuso, R.; Costa, M. *Org. Lett.* **2007**, *9*, 3319-3322.

112. Bartoli, G.; Bosco, M.; Dalpozzo, R.; Marcantoni, E.; Massaccesi, M.; Rinaldi, S.; Sambri, L. *Synlett* **2003**, 39-42.

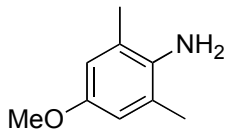
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

was obtained as a yellow oil (921 mg, 95%) which was used as such for the amination step. ^{1}H NMR data was consistent with the bibliography.[113]

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.12 (t septuplet, J = 7.1, 1.4 Hz, 1H), 2.56 (s, 1H), 2.21-2.14 (m, 2H), 2.03 (s, 3H), 2.00-1.92 (m, 1H), 1.85-1.78 (m, 1H), 1.69-1.68 (m, 6H), 1.63 (m, 3H).



A solution of 4-amino-3,5-dimethylphenol (5.60 g, 40.0 mmol) in DMF (20 mL) was added over a 0 ºC stirred suspension of NaH (60% in mineral oil, 1.76 g, 44 mmol) in DMF (20 mL). The ice bath was removed and the suspenion was stirred at room temperature for 4 h. The thick paste was thinned with DMF (40 mL) and the mixture was stirred at 50 ºC for another 1.5 h to complete the deprotonation. The resulting mixture was cooled to 0 ºC and MeI (2.8 mL, 44 mmol) was added dropwise. After 5 min (elution of one TLC plate) Et_3N (6.3 mL, 44 mmol) was added, the mixture was concentrated over Florisil (30 g) and submitted to flash chromatography (gradient elution with Combiflash). The resulting products were **4-methoxy-2,6-dimethylaniline** (4.26 g, 70%, brown solid) and **4-methoxy-N,2,6-trimethylaniline** (1.02 g, 15%, brown oil, elutes first).



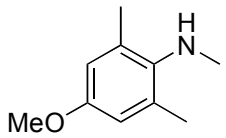
4-Methoxy-2,6-dimethylaniline[114]

^{1}H NMR (400 MHz, C_6D_6) δ 6.63 (m, 2H), 3.45 (s, 3H), 2.74 (br s, 2H), 1.90-1.89 (m, 6H); ^{13}C NMR (100 MHz, C_6D_6) δ 152.70 (C), 137.10 (C), 122.90 (C), 114.40 (CH), 55.29 (CH_3), 17.92 (CH_3).

113. Anjum, S.; Marco-Contelles, J. *Tetrahedron* **2005**, *61* (20), 4793-4803.

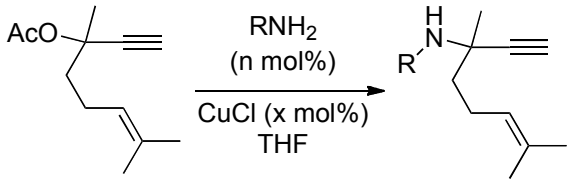
114. Leuthäußer, S.; Schmidts, V.; Thiele, C. M.; Plenio, H. *Chem. Eur. J.* **2008**, *14*, 5465-5481

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



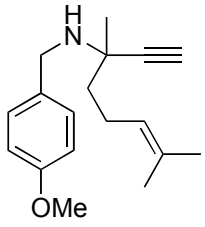
4-Methoxy-N,2,6-trimethylaniline

^{1}H NMR (400 MHz, C_6D_6) δ 6.65 (s, 2H), 3.42 (s, 3H), 2.44 (s, 3H), 2.40 (br s, 1H), 2.12 (m, 6H); ^{13}C NMR (100 MHz, C_6D_6) δ 155.63 (C), 141.32 (C), 132.16 (C), 114.36 (CH), 54.95 (CH_3), 35.76 (CH_3), 18.31 (CH_3); HRMS calcd. for $C_{10}H_{16}NO$ (M+H): 166.1232, found: 166.1231.



General procedure for the synthesis of Cu(I) catalyzed synthesis of the propargylamines[105]

A solution of the enynol acetate (195 mg, 1.00 mmol), the corresponding N-nucleophile and CuCl (5-10 mol%) in anhydrous THF (2.0 mL) was heated at the indicated temperature in a sealed tube for the indicated time. After cooling the mixture was treated with Et_3N (same number of equivalents as the N-nucleophile), concentrated over Florisil and purified by flash chromatography.



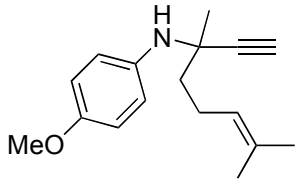
N-(4-Methoxybenzyl)-3,7-dimethyloct-6-en-1-yn-3-amine (68a)

Pale yellow oil (hexane/EtOAc/Et_3N = 100 : 9 : 1). ^{1}H NMR (400 MHz, C_6D_6) δ 7.33-7.30 (m, 2H), 6.84-6.81 (m, 2H), 5.19 (triple septuplet, J = 7.2, 1.4 Hz, 1H), 3.92 (AB system, J = 12.0 Hz, 1H), 3.87 (AB system, J = 12.0 Hz, 1H), 3.33 (s, 3H), 2.31-2.26 (m, 2H), 2.11 (s, 1H), 1.71-1.66 (m, 2H), 1.65-1.64 (m, 3H), 1.57 (s, 3H), 1.31 (s, 3H), 1.09 (br s, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 159.33 (C), 133.60 (C), 131.53 (C), 129.85 (CH), 124.82 (CH), 114.16 (CH), 88.55 (C), 71.17 (CH), 54.81 (CH_3), 53.67

105. Imada, Y.; Yuasa, M.; Nakamura, I.; Murahashi, S.-I. *J. Org. Chem.* **1994**, *59*, 2282-2284.

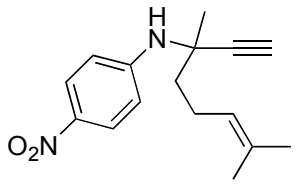
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

(C), 48.33 (CH_2), 42.26 (CH_2), 27.16 (CH_3), 25.83 (CH_3), 23.59 (CH_2), 17.71 (CH_3); HRMS calcd. for $C_{18}H_{26}NO$ (M+H): 272.2014, found: 272.2017.



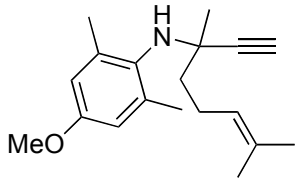
N-(3,7-Dimethyloct-6-en-1-yn-3-yl)-4-methoxyaniline (68b)

Golden oil (hexane/EtOAc/Et_3N = 100 : 6 : 1). ^{1}H NMR (400 MHz, C_6D_6) δ 6.98-6.94 (m, 2H), 6.82-6.78 (m, 2H), 5.17 (triple septuplet, J = 7.1 Hz, 1.4 Hz, 1H), 3.37 (s, 3H), 3.06 (br s, 1H), 2.38-2.21 (m, 2H), 2.06 (s, 1H), 1.82-1.67 (m, 2H), 1.65 (m, 3H), 1.56 (m, 3H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 154.81 (C), 139.58 (C), 131.88 (C), 124.46 (CH), 121.48 (CH), 114.57 (CH), 88.04 (C), 71.95 (CH), 55.12 (CH_3), 53.11 (C), 42.69 (CH_2), 28.03 (CH_3), 25.83 (CH_3), 23.78 (CH_2), 17.70 (CH_3); HRMS calcd. for $C_{17}H_{24}NO$ (M+H): 258.1858, found: 258.1846.



N-(3,7-Dimethyloct-6-en-1-yn-3-yl)-4-nitroaniline (68c)

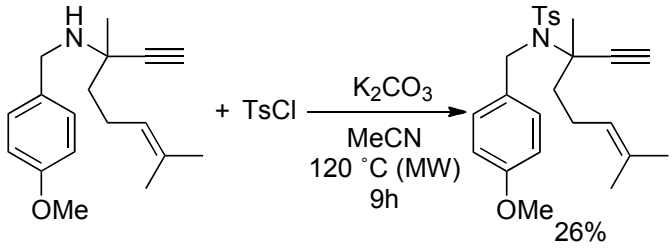
Orange oil after vacuum drying overnight at 50 ºC (hexane/EtOAc/Et_3N = 100 : 12 : 1 to 100 : 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11-8.07 (m, 2H), 6.87-6.83 (m, 2H), 5.17-5.12 (m, 1H), 4.61 (br s, 1H), 2.50 (s, 1H), 2.33-2.14 (m, 2H), 1.95-1.82 (m, 2H), 1.71 (m, 3H), 1.63 (s, 3H), 1.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.15 (C), 138.69 (C), 133.39 (C), 125.96 (CH), 123.08 (CH), 113.66 (CH), 84.92 (C), 73.16 (CH), 51.81 (C), 41.99 (CH_2), 27.77 (CH_3), 25.83 (CH_3), 23.29 (CH_2), 17.86 (CH_2); HRMS calcd. for $C_{16}H_{20}N_2O_2Na$ (M+Na): 295.1422, found: 295.1415.



N-(3,7-Dimethyloct-6-en-1-yn-3-yl)-4-methoxy-2,6-dimethylaniline (68d)

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Yellow oil (hexane/EtOAc/Et_3N = 100 : 3 :1). ^{1}H NMR (400 MHz, C_6D_6) δ 6.70 (s, 2H), 5.25 (triple septuplet, J = 7.0, 1.4 Hz, 1H), 3.40 (s, 3H), 2.78 (br s, 1H), 2.55-2.45 (m, 1H), 2.43-2.34 (m, overlapped with 6H singlet, 1H), 2.36 (s, 6H), 1.96 (s, 1H), 1.85 (ddd, J = 13.1, 11.4, 5.3 Hz, 1H), 1.75 (ddd, J = 13.1, 11.6, 5.3 Hz, 1H), 1.68 (m, 3H), 1.63-1.62 (m, 3H), 1.31 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 156.76 (C), 137.77 (C), 135.86 (C), 131.69 (C), 124.75 (CH), 114.02 (CH), 89.47 (C), 71.87 (CH), 55.84 (C), 54.77 (CH_3), 44.78 (CH_2), 28.04 (CH_3), 25.86 (CH_3), 24.38 (CH_2), 20.73 (CH_3), 17.77 (CH_3); HRMS calcd. for $C_{19}H_{28}NO$ (M+H): 286.2171, found: 286.2176



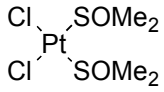
N-(3,7-Dimethyloct-6-en-1-yn-3-yl)-N-(4-methoxybenzyl)-4-methylbenzenesulfonamide (69e)

The starting benzyl-alkylamine (79 mg, 0.29 mmol) was dissolved in MeCN (1.5 mL) then TsCl (83 mg, 0.44 mmol) and K_2CO_3 (80 mg, 0.58 mmol) were added. No reaction was observed after heating at 60 ºC (MW) for 1 h. The mixture was heated at 120 ºC (MW) for 6 h then (after cooling) additional TsCl (83 mg, 0.44 mmol) and K_2CO_3 (80 mg, 0.58 mmol) were added. The mixture was heated at 120 ºC (MW) for an additional 3 h then it was concentrated over Florisil (0.81 g) and submitted to flash chromatography (3x15 cm SiO_2, toluene/Et_3N = 100 : 1 to toluene/EtOAc = 20 :1). The resulting material was submitted to a second flash chromatography (2x15 cm SiO_2, toluene/hexane/Et_3N = 100 : 50 : 1) to yield **69e** as a pale yellow oil (33 mg, 26%). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.62-7.59 (m, 2H), 7.39-7.36 (m, 2H), 7.25-7.23 (m, 2H), 6.86-6.83 (m, 2H), 4.93-4.89 (m, 1H), 4.82 (AB system, J = 16.5 Hz, 1H), 4.68 (AB system, J = 16.5 Hz, 1H), 3.79 (s, 3H), 2.42 (s, 1H), 2.40 (s, 3H), 2.04-1.99 (m, 2H), 1.93-1.83 (m, 2H), 1.64 (m, 3H), 1.62 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 159.21 (C), 143.50 (C), 140.18 (C), 132.45 (C), 131.65 (C), 129.62 (CH), 129.57 (CH), 127.62 (CH), 123.47 (CH), 113.83 (CH), 85.58 (C), 74.43 (CH), 61.52 (C), 55.58 (CH_3), 51.86 (CH_2), 42.21 (CH_2), 28.14 (CH_3), 25.67 (CH_3), 24.11 (CH_2), 21.55 (CH_3), 17.70 (CH_3); HRMS calcd. for $C_{25}H_{31}NNaO_3S$ (M+Na): 448.1922, found: 448.1936.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Synthesis of platinum complexes

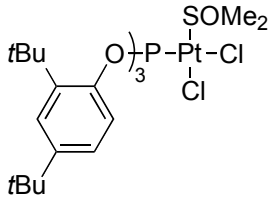
Cationic platinacycle **42** was synthesized according to a published procedure.[27]



***cis*-[Dichloro-bis(dimethylsulfoxide)platinum(II)] (40)**

Solid $PtCl_2$ (1.332 g, 5.000 mmol) was slowly and carefully added over DMSO (25 mL) with sonication and and shaking. The reaction was completed by stirring the mixture at 70 º C until all the solid had dissolved. (*ca* 5 min). Upon cooling, water (50 mL) was added and the precipitate was filtered, washed with water, Et_2O (3x) and air dried. *cis*-$PtCl_2(DMSO)_2$ was obtained as pale yellow crystals (1.84 g, 87%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.54 (s with Pt satellites, J = 22.0 Hz, 6H)



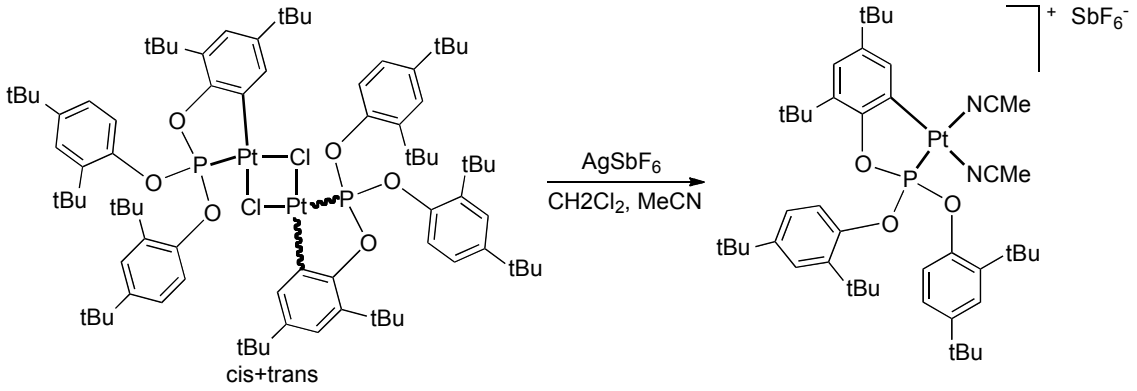
***cis*-[Dichloro(dimethylsulfoxide)(tris(2,4-di-*tert*-butylphenyl)phosphite)platinum(II)] (41)**

cis-$PtCl_2(DMSO)_2$ **40** (128 mg, 0.300 mmol) and tris(2,4-di-*tert*-butylphenyl) phosphite (198 mg, 0.300 mmol) were stirred in CH_2Cl_2 (3 mL, SPS grade) under air for 30 min (a clear soln. is obtained after 7 min). EtOH (6 mL) was added then the mixture was evaporated to a small volume; filtration and washing with EtOH yielded a white solid which was air dried then vacuum dried (276 mg, 93%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, J = 8.6, 1.5 Hz, 3H), 7.37-7.36 (m, 3H), 7.12 (dd, J = 8.6, 2.6 Hz, 3H), 3.16 (s, 6H), 1.43 (s, 27H), 1.26 (s, 27H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 48.6 (s with Pt satelites, $J_{P\text{-}Pt}$ = 6147 Hz).

27. Ferrer, C.; Raducan, M.; Nevado, C.; Claverie, C. K.; Echavarren, A. M. *Tetrahedron* **2007**, *63*, 6306-6316.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



Cationic platinacycle (43)

Over a solution of the chloro-platinacycle dimer[115] (100 mg, 0.055 mmol) in CH_2Cl_2 (2 mL) was added a solution of $AgSbF_6$ (39 mg, 0.11 mmol) in MeCN (2 mL). A white suspension formed immediately; after 1 h 30 min a grey precipitate appeared. ^{31}P NMR of an aliquot showed completion after 30 min. The mixture was filtered through a pad of silica which was subsequently washed with $CHCl_3$. The combined filtrates were evaporated to yield a colorless oil which slowly solidified at room temperature. (yield 114 mg, 89%).

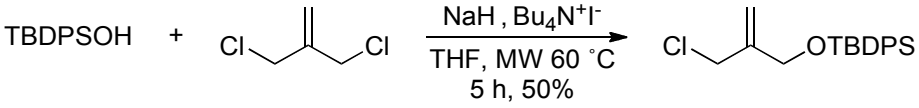
^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (m, 2H), 7.23 (ABX system, J = 8.5, 1.5 Hz, 2H), 7.19 (br s, 1H), 7.17 (apparent t, J = 2.2 Hz, 1H), 7.10 (ABX system, J = 8.5, 2.5 Hz, 2H), 2.60 (br s, 3H), 2.29 (s, 3H), 1.44 (s, 18 H), 1.33 (s, 9H), 1.30 (s, 18 H), 1.16 (s, 9H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 83.72 (s with Pt satelites J = 7322 Hz, 1P).

Synthesis of the trapping reagents

DHP, methacrolein **59** and **60** are commercially available and were used as received. 2,2-Dimethyl-1,3-dioxan-5-one was synthesized in two steps from TRIZMA™ hydrochloride according to a described procedure.[92] Triflate **62** was synthesized from 2,2-dimethyl-1,3-dioxan-5-one according to a described procedure.[93] Enyne **64** was synthesized from **62** according to a described procedure.[93] TBDPSOH was prepared from TBDPSCl according to the described procedure,[116] followed by flash chromatography (hexane/EtOAc = 10 : 1) (yield: 1.98 g, 85%).

92. Forbes, D. C.; Ene, D. G.; Doyle, M. P. *Synthesis* **1998**, 879-882.
93. Fearnley, S. P.; Funk, R. L.; Gregg, R. J. *Tetrahedron* **2000**, *56*, 10275-10281.
115. Bedford, R. B.; Hazelwood, S. L.; Albisson D. A. *Organometallics* **2002,** *21,* 2599-2600.
116. Mullen, D. G.; Barany, G. *J. Org. Chem.* **1988**, *53*, 5240-5248.

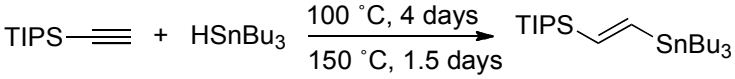
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



***tert*-Butyl(2-(chloromethyl)allyloxy)diphenylsilane (61)**

A solution of TBDPSOH (512 mg, 2.0 mmol) in THF (2 mL) was added over a suspension of NaH (60% in mineral oil, 88 mg, 2.2 mmol) in THF (2 mL) then 3-chloro-2-(chloromethyl)prop-1-ene (0.37 mL, 3 mmol) and TBAI were succesively added. The final solution was transferred to a sealed vial and heated at 60 ºC (MW) for 3 h. More 3-chloro-2-(chloromethyl)prop-1-ene (0.12 mL, 1 mmol) was adde and the solution was further heated at 60 ºC for 2 h. Finally the mixture was concentrated over Florisil (3.5 g) and purified by flash chromatography (5x15 cm SiO_2, hexane/$CHCl_3$ = 10 : 1 to 5 : 1) to yield **61** as a colorless oil (347 mg, 50%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.66 (m, 4H), 7.45-7.36 (m, 6H), 5.30 (q, J = 1.5 Hz, 1H), 5.24 (m, 1H), 4.27 (m, 2H), 4.11 (m, 2H), 1.07 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, PENDANT) δ 144.29 (C), 135.67 (CH), 133.45 (C), 129.90 (CH), 127.88 (CH), 114.63 (CH_2), 64.26 (CH_2), 45.18 (CH_2), 26.93 (CH_3), 19.43 (C).



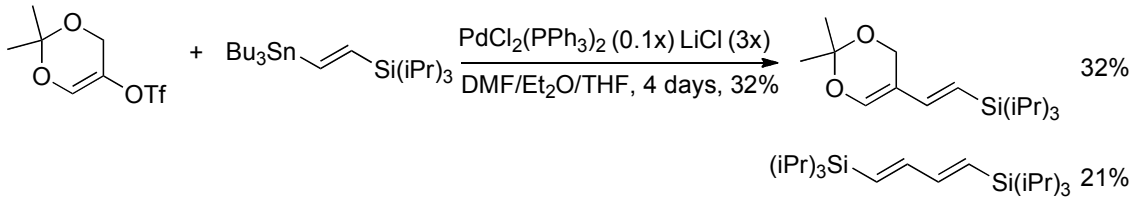
Triisopropyl(2-(tributylstannyl)vinyl)silane

A mixture of Bu_3SnH (0.56 mL, 2.0 mmol) and ethynyltriisopropylsilane (0.69 mL, 3.0 mmol) wass heated at 100 ºC for 4 days, then at 150 ºC for 1.5 days. The conversion of the starting Bu_3SnH was checked from time to time by ^{1}H NMR of an aliquot (C_6D_6). The excess alkyne was distilled (8-9 mbar, 200 ºC too high) to yield **(*E*)-triisopropyl(2-(tributylstannyl)vinyl)silane** as a colorless oil (631 mg, 81% purity, 66% yield). The purity was determined by ^{1}H NMR using an internal standard.

^{1}H NMR (400 MHz, C_6D_6) δ 7.26 (d, J = 23.0 Hz, with Sn satelites, J = 108, 103 Hz, 1H), 6.78 (d, J = 23.0 Hz, with Sn satelites, J = 106, 102 Hz, 1H), 1.68-1.61 (m, 6H), 1.39 (sextuplet, J = 7.3 Hz, 6H), 1.15 (s, 21H), 1.04-1.00 (m, 6H), 0.95 (t, J = 7.3 Hz, 9H); in agreement with lit.[117] ^{13}C NMR (100 MHz, C_6D_6) δ 152.28 (CH), 148.95 (CH), 28.70 (CH_2), 26.67 (CH_2), 17.92 (CH), 13.02 (CH_3), 10.10 (CH_3), 8.96 (CH_2).

117. Jones, T. K.; Denmark, S. E. *Helv. Chim. Acta* **1983**, *66*, 2397-2411.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



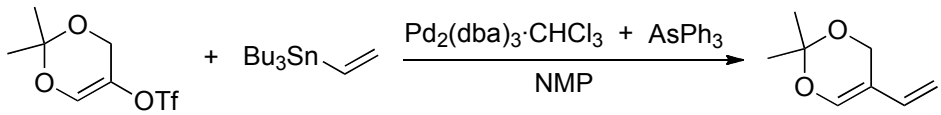
Over a solution of $PdCl_2(PPh_3)_2$ (18 mg, 25 μmol) and LiCl (64 mg, 1.5 mmol) in DMF (0.5 mL), a solution of the triflate (140 mg, 0.502 mmol) in DMF (1 mL) and a solution of the stannane *E*-$Bu_3SnCH{=}CHSi(iPr)_3$ (236 mg, 0.602 mmol) in DMF (1 mL) / Et_2O (1 mL) were sequentially added. The resulting mixture was stirred at room temperature for 22 h during which time the mixture separated in two phases. THF (2 mL) was added resulting in the formation of a clear solution. After 17 h more $PdCl_2(PPh_3)_2$ (18 mg, 25 μmol) was added and the reaction was allowed to continue for 48 h. The resulting mixture was partitioned between H_2O (4 mL) and hexane (4 mL) and the aqueous layer extracted with hexane (2x4 mL). The combined organic layers were washed with brine (4 mL), concentrated on Florisil (1.18 g) and submitted to flash chromatography (3x15 cm SiO_2, pentane/CH_2Cl_2 = 3 : 1). The desired coupled product was obtained as a yellow oil (48 mg, 32%, fraction 2) that slowly decomposed at room temperature. Additionally, (1E,3E)-1,4-bis(triisopropylsilyl)buta-1,3-diene was isolated as a white wax (23 mg, 21% based on starting stannane).

(*E*)-(2-(2,2-Dimethyl-4H-1,3-dioxin-5-yl)vinyl)triisopropylsilane (63)

^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.58 (s, 1H), 6.41-6.36 (m, 1H), 5.21-5.16 (m, 1H), 4.37 (m, 2H), 1.45 (s, 6H), 1.06-1.02 (m, 21H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 143.18 (CH), 141.59 (CH), 116.43 (CH), 114.16 (C), 99.98 (C), 59.56 (CH_2), 24.59 (CH_3), 18.87 (CH_3), 11.40 (CH); ESI-MS calcd. for $C_{17}H_{31}O_2Si^+$ $[M-H]^+$: 295.2, found: 295.2

(1E,3E)-1,4-Bis(triisopropylsilyl)buta-1,3-diene

^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.66-6.58 (m, 2H), 5.84-5.76 (m, 2H), 1.11-1.05 (m, 42H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 149.82 (CH), 128.98 (CH), 18.87 (CH_3), 11.43 (CH); HRMS calcd for $C_{22}H_{47}Si_2^+$ $[M]^+$: 367.3216, found: 367.3223.



2,2-Dimethyl-5-vinyl-4H-1,3-dioxine (65)

This product was synthesized similarly to a described procedure.[93] To a stirred solution of triflate (147 mg, 0.527 mmol) in Ar purged N-methyl pyrrolidinone (dry, 2.5 mL),

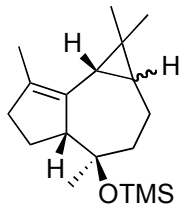
was added $AsPh_3$ (13 mg, 0.042 mmol) and $Pd_2(dba)_3{\cdot}CHCl_3$ (5.5 mg, 0.0053 mmol) at room temperature. After 10 min, $Bu_3SnCH{=}CH_2$ (0.19 mL, 0.63 mmol) was added. After 21 h the reaction was completed (NMR of an aliquot). Water (6 mL) was added and the resultant mixture extracted with hexanes (2x6 mL). The combined organic fractions were washed with water (6 mL), stirred over sat. KF (12 mL) for 30 min, washed with brine (6 mL), dried ($MgSO_4$), filtered and reduced in vacuo to yield a black oil. Further purification by flash chromatography (2x15 cm silica, pentane/CH_2Cl_2 = 3 : 1) yielded **65** as a colorless volatile oil (40 mg, 54%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (s, 1H), 6.15 (dd, J = 17.7, 11.0 Hz, 1H), 4.80 (d, J = 11.0 Hz, 1H), 4.73 (d, J = 17.7 Hz, 1H), 4.36 (s, 2H), 1.47 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, PENDANT) δ 142.15 (CH), 132.24 (CH), 112.03 (C), 107.69 (CH_2), 99.58 (C), 59.08 (CH_2), 24.47 (CH_3); MS calcd for: $C_8H_{13}O_2$ (M+H): 141; found; 141.

General procedure for the cycloisomerization (trapping) of 1,6-enynes

The solid catalyst was added over a solution of the substrate (0.1 M) (and trapping reagent – as indicated in the tables) in dry CH_2Cl_2 and the mixture was stirred at the indicated temperature for the indicated time. After quenching with Et_3N (>1 equiv.), the mixture was concentrated over Florisil and submitted to flash chromatography.

Rearranged products **36a**, **37a**, **38**,[108] **36b**, **36b-*d3***, **36d**/**37d**, **36f**/**37f**, **36h**/**37h**, **46b**/**47b**, **46h**/**47h**, **49**, **50c/51c-eq/51c-ax** and addition products **52** and **53**[109] were synthesized by coworkers and their ^{1}H and ^{13}C NMR data was published.[76]



***rac*-Trimethyl((4R,4aR,7bS)-1,1,4,7-tetramethyl-1a,2,3,4,4a,5,6,7b-octahydro-1H-cyclopropa[e]azulen-4-yloxy)silane (46a/47a)**

(hexane) colorless oil.

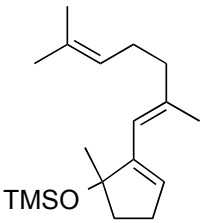
76. Jiménez-Núñez, E.; Raducan, M.; Lauterbach, T.; Molawi, K.; Solorio, C. R.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2009**, *48*, 6152-6155.

108. Product(s) synthesized and characterized by Eloísa Jiménez-Núñez.

109. Product(s) synthesized and characterized by Dr. Thorsten Lauterbach, Kian Molawi.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64 (br d, J = 9.3 Hz, 1H), 2.37-2.29 (br m, 1H), 2.05-1.97 (m, 2H), 1.91-1.78 8 (m, 2H), 1.75-1.66 (m, 2H), 1.64 (br, 3H), 1.10 (s, 3H), 1.01 (s, 3H), 0.98 (br, 1H), 0.94 (s, 3H), 0.86-0.77 (m, 1H), 0.67 (td, J = 10.0, 7.2 Hz, 1H), 0.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.56 (C), 132.96 (C), 80.92 (C), 62.91 (CH), 44.26 (CH_2), 37.30 (CH_2), 28.82 (CH_3), 26.49 (CH), 26.36 (CH_2), 25.66 (CH), 21.50 (CH_3), 20.59 (CH_2), 20.00 (C), 17.99 (CH_3), 16.18 (CH_3), 3.05 (3xCH_3); Minor isomer (selected signals): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.87-2.82 (m, 1H), 2.24-2.11 (m, 2H), 1.59 (br, 3H), 1.34-1.21 (m, 3H), 1.25 (s, 3H), 1.22 (s, 3H), 0.36 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 67.67, 36.74, 31.96, 29.86, 25.59, 22.01, 16.28, 3.16; HRMS-EI calcd for $C_{15}H_{23}$ $(M\text{-}OTMS)^{+}$: 203.1794; found: 203.1792.



(*E*)-(2-(2,6-Dimethylhepta-1,5-dienyl)-1-methylcyclopent-2-enyloxy)trimethylsilane (39a)

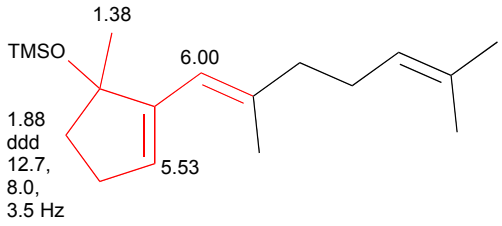
This compound was obtained as the major isomer following the general procedure for cyclization (5 mol% [(EMI)Au(tmbn)](SbF_6), 4Å MS, -50ºC). It decomposed in flash chromatography conditions. It was also impurified with traces of 2,4,6-trimetoxybenzonitrile.

^{1}H NMR (400 MHz, C_6D_6) δ 6.00 (br, 1H), 5.53 (br, 1H), 5.24-5.19 (m, 1H), 2.39-2.32 (m, 1H), 2.23-2.12 (m, 5H), 2.10-2.03 (m, 1H), 1.88 (ddd, J = 12.7, 8.0, 3.5 Hz, 1H), 1.78 (br, 3H), 1.67 (br, 3H), 1.55 (br, 3H), 1.38 (br, 3H), 0.20 (s, 9H); ^{13}C NMR (100 MHz, C_6D_6) δ 147.05 (C), 140.57 (C), 131.38 (C), 126.47 (CH), 124.72 (CH), 118.88 (CH), 86.84 (C-O), 41.49 (CH_2), 40.58 (CH_2), 29.92 (CH_2), 28.55 (CH_3), 27.24 (CH_2), 25.89 (CH_3), 18.89 (CH_3), 17.75 (CH_3), 2.44 (CH_3).

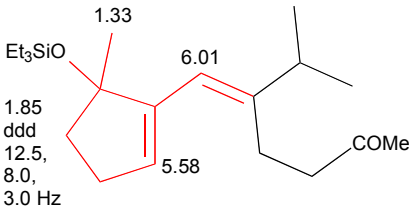
The structure was confirmed by PENDANT, HMQC, HMBC and comparison with a known compound 39b.[73]

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

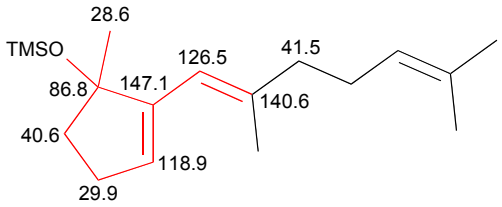
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



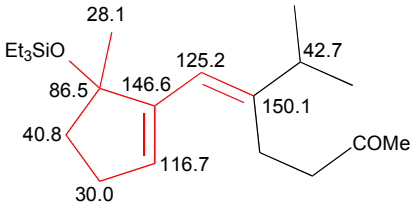
39a



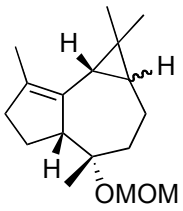
39b



39a



39b

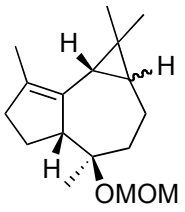


***rac*-(4S,4aR,7bS)-4-(Methoxymethoxy)-1,1,4,7-tetramethyl-1a,2,3,4,4a,5,6,7b-octahydro-1H-cyclopropa[e]azulene (36c/37c)**

(hexane/EtOAc = 100 : 1) colorless oil.

Major isomer **36c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.64 (d, J = 7.0 Hz, 1H), 4.55 (d, J = 7.0 Hz, 1H), 2.53-2.47 (m, 1H), 2.47-2.38 (m, 1H), 2.07-1.97 (m, 2H), 1.92-1.82 (m, 2H), 1.65-1.59 (m, 4H), 1.50 (ddd, J = 14.7, 11.8, 1.1 Hz, 1H), 1.32-1.22 (m, 1H), 1.21 (s, 3H), 1.11 (s, 3H), 1.00-0.95 (m, 4H), 0.70 (ddd, J = 10.4, 9.4, 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.63 (C), 132.86 (C), 90.95 (CH_2), 80.46 (C), 61.68 (CH), 55.53 (CH_3), 37.78 (CH_2), 36.98 (CH_2), 28.76 (CH_3), 27.11 (CH_3), 26.88 (CH), 26.66 (CH), 25.32 (CH_2), 21.18 (C), 19.15 (CH_2), 17.66 (CH_3), 16.17 (CH_3); Minor isomer **37c** (selected signals): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.87 (d, J = 7.0 Hz, 1H), 4.67 (d, J = 7.0 Hz, 1H), 3.39 (s, 3H), 0.26-0.23 (m, 1H); HRMS ESI Calcd for $C_{17}H_{28}O_2Na$ ($M+Na^+$): 287.1987. Found: 287.1976.

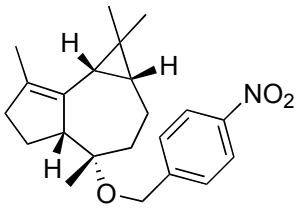
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



***rac*-(4R,4aR,7bS)-4-(Methoxymethoxy)-1,1,4,7-tetramethyl-1a,2,3,4,4a,5,6,7b-octahydro-1H-cyclopropa[e]azulene (46c/47c)**

(hexane/EtOAc = 50 : 1) colorless oil.

Major isomer **46c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.78 (AB system, J = 7.3 Hz, 1H), 4.73 (AB system, J = 7.3 Hz, 1H), 3.39 (s, 3H), 2.81 (br d, J = 9.1 Hz, 1H), 2.41-2.31 (m, 1H), 2.09-1.75 (m, 6H), 1.66 (br s, 3H), 1.11 (s, 3H), 1.06 (s, 3H), 1.02-1.00 (m, 1H), 0.96 (s, 3H), 0.88-0.78 (m, 1H), 0.71 (ddd, J = 10.3, 9.4, 6.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.05 (C), 132.42 (C), 90.73 (CH_2), 83.24 (C), 59.90 (CH), 55.48 (CH_3), 39.95 (CH_2), 37.33 (CH_2), 28.76 (CH_3), 26.40 (CH), 25.91 (CH_2), 25.79 (CH), 20.16 (C), 20.09 (CH_2), 18.28 (CH_3), 17.97 (CH_3), 16.18 (CH_3); Minor isomer **47c** (selected signals): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.80 (d, J = 7.2 Hz, 1H), 4.69 (d, J = 7.2 Hz, 1H), 3.37 (s, 3H), 3.00-2.96 (m, 1H), 2.24-2.18 (m, 3H), 1.60 (br, 3H), 1.29 (s, 3H), 1.26 (br, 3H), 1.23 (s, 3H), 0.36-0.34 (m, 1H), 0.14-0.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 90.65, 55.59, 55.34, 39.87, 36.82, 31.98, 28.76, 25.65, 25.55, 21.97, 16.23; HRMS ESI Calcd for $C_{15}H_{23}$ (M-MOMO)$^{+}$: 203.1800; found: 203.1801.



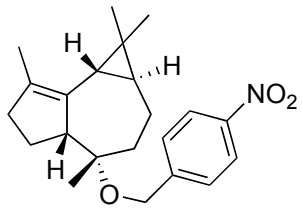
***rac*-(1a*R*,4*S*,4a*R*,7b*S*)-1,1,4,7-Tetramethyl-4-(4-nitrobenzyloxy)-1a,2,3,4,4a,5,6,7b-octahydro-1*H*-cyclopropa[e]azulene (36e)**

Flash chromatography (hexane/Et_3N = 100:1) followed by semipreparative HPLC, yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 8.2 Hz, 2H), 4.47 (d, J = 13.6 Hz, 1H), 4.34 (d, J = 13.6 Hz, 1H), 2.60 (d, J = 8.8 Hz, 1H), 2.52-2.43 (m, 1H), 2.12-1.86 (m, 4H), 1.68 (s, 3H), 1.64-1.51 (m, 2H), 1.26-1.15 (m, 1H), 1.23 (s, 3H), 1.10 (s, 3H), 1.03-1.01 (m, 1H), 0.95 (s, 3H), 0.75-0.69 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.30 (C), 146.74 (C), 139.54 (C), 132.49 (C), 126.60 (CH), 123.34

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

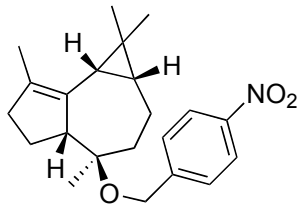
(CH), 79.69 (C), 61.72 (CH_2), 61.40 (CH), 37.13 (CH_2), 36.12 (CH_2), 28.59 (CH_3), 26.55 (CH), 26.48 (CH), 25.43 (CH_3), 25.37 (CH_2), 21.16 (C), 18.88 (CH_2), 17.50 (CH_3), 16.13 (CH_3). HRMS-ESI calcd for $C_{22}H_{29}NO_3Na$ $(M+Na)^+$: 378.2045; found: 378.2059.



***rac*-(1a*S*,4*S*,4a*R*,7b*S*)-1,1,4,7-Tetramethyl-4-(4-nitrobenzyloxy)-1a,2,3,4,4a,5,6,7b-octahydro-1*H*-cyclopropa[e]azulene (37e)**[118]

Flash chromatography (hexane/Et_3N = 100 : 1) followed by semipreparative HPLC, yellow solid.

^1H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 8.8 Hz, 2H), 7.50 (d, J = 8.9 Hz, 2H), 4.67 (d, J = 13.6 Hz, 1H), 4.63 (d, J = 13.7 Hz, 1H), 2.67 (t, J = 8.2 Hz, 1H), 2.28-2.17 (m, 2H), 2.15-2.11 (m, 1H), 2.06-1.97 (m, 2H), 1.91-1.85 (m, 2H), 1.62 (s, 3H), 1.42-1.35 (m, 1H), 1.23 (s, 3H), 1.21 (s, 3H), 1.11 (s, 3H), 0.76-0.71 (m, 1H), 0.30-0.27 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.29 (C), 146.92 (C), 137.52 (C), 127.11 (CH), 125.59 (C), 123.44 (CH), 80.32 (C), 65.27 (CH), 63.57 (CH_2), 36.85 (CH_2), 36.25 (CH_2), 31.04 (CH), 29.70 (C), 28.37 (CH), 26.71 (CH_3), 25.14 (CH_3), 24.30 (CH_2), 23.44 (CH_2), 21.57 (CH_3), 16.04 (CH_3). HRMS-ESI calcd for $C_{22}H_{29}NO_3Na$ $(M+Na)^+$: 378.2045; found: 378.2059.



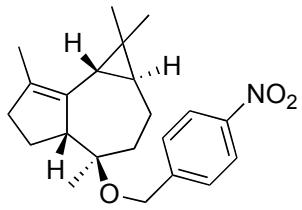
***rac*-(1a*R*,4*R*,4a*R*,7b*S*)-1,1,4,7-Tetramethyl-4-(4-nitrobenzyloxy)-1a,2,3,4,4a,5,6,7b-octahydro-1*H*-cyclopropa[e]azulene (46e)**

Flash chromatography (hexane/EtOAc = 25:1) followed by semipreparative HPLC, yellow solid.

118. Work done in collaboration with Kian Molawi.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.6 Hz, 2H), 7.51 (d, J = 8.5 Hz, 2H), 4.59 (d, J = 13.0 Hz, 1H), 4.55 (d, J = 13.1 Hz, 1H), 2.92 (d, J = 9.3 Hz, 1H), 2.44-2.36 (m, 1H), 2.12-2.05 (m, 2H), 1.94-1.75 (m, 4H), 1.78 (s, 3H), 1.13 (s, 3H), 1.09 (s, 3H), 1.05-1.03 (m, 1H), 0.98 (s, 3H), 0.94-0.82 (m, 1H), 0.76-0.70 (m, 1H). ^{13}C NMR (100 MHz, PENDANT, $CDCl_3$) δ 148.08 (C), 146.97 (C), 139.92 (C), 132.12 (C), 127.51 (CH), 123.43 (CH), 82.22 (C), 61.95 (CH_2), 58.43 (CH), 38.14 (CH_2), 37.26 (CH_2), 28.62 (CH_3), 26.26 (CH), 25.56 (CH), 25.28 (CH_2), 20.00 (C), 19.91 (CH_2), 18.59 (CH_3), 17.79 (CH_3), 15.99 (CH_3). HRMS-ESI calcd for $C_{22}H_{29}NO_3Na$ $(M+Na)^+$: 378.2045; found: 378.2068.



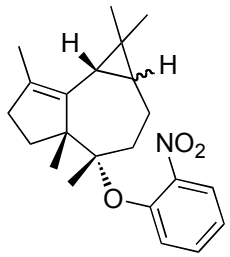
***rac*-(1a*S*,4*R*,4a*R*,7b*S*)-1,1,4,7-Tetramethyl-4-(4-nitrobenzyloxy)-1a,2,3,4,4a,5,6,7b-octahydro-1*H*-cyclopropa[e]azulene (47e)**[118]

Flash chromatography (hexane/EtOAc = 25:1) followed by semipreparative HPLC, yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 8.7 Hz, 2H), 7.50 (d, J = 8.7 Hz, 2H), 4.61 (d, J = 13.3 Hz, 1H), 4.56 (d, J = 13.3 Hz, 1H), 3.12 (t, J = 8.0 Hz, 1H), 2.31-2.18 (m, 2H), 2.05-1.92 (m, 4H), 1.81-1.73 (m, 1H), 1.62 (s, 3H), 1.44-1.36 (m, 1H), 1.30 (s, 3H), 1.25 (s, 3H), 1.12 (s, 3H), 0.37 (d, J = 7.9 Hz, 1H), 018-014 (m, 1H). ^{13}C NMR (100 MHz, PENDANT, $CDCl_3$) δ 148.23 (C), 146.96 (C), 136.17 (C), 127.30 (CH), 125.37 (C), 123.46 (CH), 82.36 (C), 63.38 (CH), 61.86 (CH_2), 37.99 (CH_2), 36.77 (CH_2), 32.27 (CH), 29.669 (C), 28.71 (CH), 25.40 (CH_3), 24.00 (CH_2), 21.85 (CH_3), 20.56 (CH_2), 20.07 (CH_3), 16.08 (CH_3). HRMS-ESI calcd for $C_{22}H_{29}NO_3Na$ $(M+Na)^+$: 378.2045; found: 378.2068.

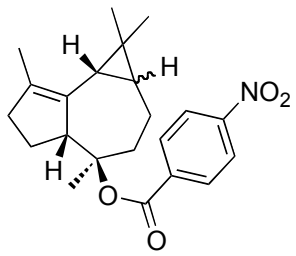
118. Work done in collaboration with Kian Molawi.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



***rac*-(4S,4aR,7bS)-1,1,4,4a,7-Pentamethyl-4-(2-nitrophenoxy)-1a,2,3,4,4a,5,6,7b-octahydro-1H-cyclopropa[e]azulene (36g/37g)**

orange solid (hexane/EtOAc/Et_3N = 100 : 3 : 1) Major isomer **36g**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, J = 8.0, 1.8 Hz, 1H), 7.37-7.33 (m, 1H), 7.10-7.07 (m, 1H), 6.99-6.95 (m, 1H), 2.67-2.64 (m, 1H), 2.57-2.50 (m, 1H), 2.32 (dd, J = 15.2, 7.3 Hz, 1H), 208-1.89 (m, 3H), 1.79-1.69 (m, 2H), 1.69 (s, 3H), 1.36 (s, 3H), 1.36-1.27 (m, 1H), 1.11 (s, 3H), 1.05-1.02 (m, 1H), 1.00 (s, 3H), 0.80-0.73 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.35 (C), 144.29 (observed in HMBC) (C), 141.74 (C), 132.11 (CH), 131.01 (C), 124.50 (CH), 120.64 (CH), 120.49 (CH), 88.79 (C), 62.97 (CH), 38.57 (CH_2), 36.72 (CH_2), 28.81 (CH_3), 26.92 (CH), 26.70 (CH), 26.31 (CH_3), 25.35 (CH_2), 21.61 (C), 19.54 (CH_2), 17.40 (CH_3), 16.21 (CH_3); Minor isomer **37g**: ^{1}H NMR (400 MHz, $CDCl_3$, selected signals) δ 0.33-0.30 (m, 1H); HRMS calcd. for $C_{21}H_{27}NO_3Na$ (M+Na): 364.1889; found: 364.1904.

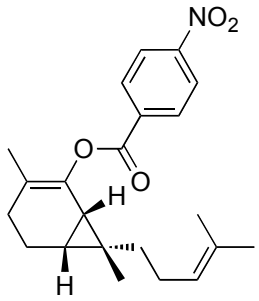


***rac*-(4R,4aR,7bS)-1,1,4,7-Tetramethyl-1a,2,3,4,4a,5,6,7b-octahydro-1H-cyclopropa[e]azulen-4-yl 4-nitrobenzoate (46f/47f)**

yellow solid (hexane/EtOAc = 100 : 3) Major isomer **46f**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28-8.24 (m, 2H), 8.15-8.11 (m, 2H), 3.37-3.35 (m, 1H), 2.48-2.39 (m, 2H), 2.17-2.09 (m, 2H), 2.05-1.92 (m, 3H), 1.70 (s, 3H), 1.47 (s, 3H), 1.14 (s, 3H), 1.11-1.05 (m, 1H), 0.99 (s, 3H), 0.96-0.89 (m, 1H), 0.82-0.75 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.67 (C), 150.35 (C), 141.24 (C), 138.00 (C), 131.48 (C), 130.57 (CH), 123.52 (CH), 92.58 (C), 59.67 (CH), 37.83 (CH_2), 37.38 (CH_2), 28.73 (CH_3), 26.32 (CH), 25.81 (CH_2), 25.71 (CH), 20.40 (C), 20.00 (CH_2), 18.43 (CH_3), 17.91 (CH_3), 16.14 (CH_3);

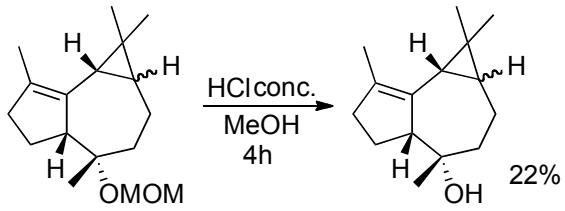
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Minor isomer **47f**: ^{1}H NMR (400 MHz, $CDCl_3$, selected signals) δ 3.53-3.48 (m, 1H), 2.65-2.60 (m, 1H), 0.45-0.43 (m, 1H), 0.18-0.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, selected signals) δ 38.08 (CH_2), 36.90 (CH_2), 28.94 (CH); HRMS calcd. for $C_{22}H_{27}NO_4Na$ (M+Na): 392.1838; found: 392.1852;



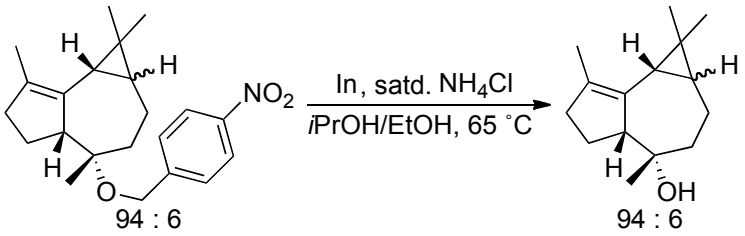
***rac*-(1S,6R,7R)-3,7-Dimethyl-7-(4-methylpent-3-en-1-yl)bicyclo[4.1.0]hept-2-en-2-yl 4-nitrobenzoate (44b)**

yellow wax (hexane/EtOAc = 100 : 3) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34-8.31 (m, 2H), 8.30-8.27 (m, 2H), 5.20-5.16 (m, 1H), 2.38-2.31 (m, 1H), 2.16-1.99 (m, 2H), 1.98-1.82 (m, 2H), 1.77-1.71 (m, 1H), 1.71 (s, 3H), 1.64 (s, 3H), 1.59 (s, 3H), 1.48-1.32 (m, 2H), 1.26-1.19 (m, 2H), 1.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.21 (C), 150.77 (C), 141.45 (C), 135.80 (C), 131.38 (C), 131.17 (CH), 125.08 (CH), 123.74 (CH), 120.68 (C), 30.30 (CH_2), 30.17 (CH_2), 29.18 (C), 25.88 (CH_3), 25.50 (CH_2), 25.45 (CH), 25.33 (CH_3), 24.17 (CH), 18.15 (CH_2), 17.70 (CH_3), 16.33 (CH_3); HRMS calcd. for $C_{22}H_{27}NO_4Na$ (M+Na): 392.1838; found: 392.1848.

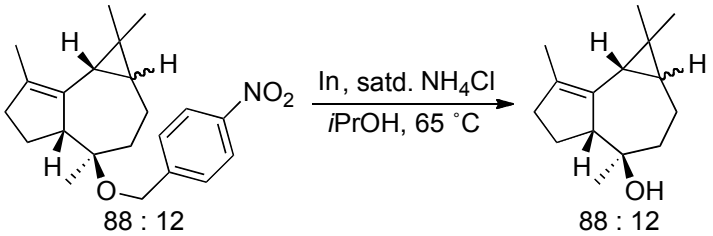


Over a solution of **36c/37c** (42.7 mg, 0.162 mmol) in MeOH (1.6 mL), HCl conc (37%, 0.02 mL, 0.2 mmol) was added. After stirring for 4 h at room temperature, the mixture was quenched with Et_3N 0.1 M in hexane (4 mL), concentrated over Celite and purified by flash chromatography (hexane/EtOAc = 15 : 1) to yield the deprotected alcohol **36h/37h** as a colorless oil (8 mg, 22%). Additionally, a fraction containing 4% of the starting material was recovered.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

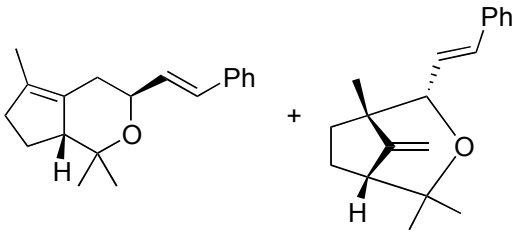


To a 65 ºC solution of the substrate (**36e/37e** 107 mg, 0.3 mmol) in *i*PrOH (3 mL) and EtOH (1.5 mL), saturated NH_4Cl solution (0.9 mL) was added (a white precipitate appeared) then indium powder (100 mesh, 0.3 g) was added. After 24 h, more EtOH (1.5 mL), In (0.3 g) and satd. NH_4Cl (0.9 mL) were added. After another 17 h, more In (0.3 g) and satd. NH_4Cl (0.9 mL) were added and the mixture was further kept at 65 ºC for 22 h. The cooled reaction mixture was filtered through Celite which was washed with CH_2Cl_2 (4 x 3 ml). The aqueous layer was separated and extracted with CH_2Cl_2 (3 mL). The combined organic layers were dried (Na_2SO_4), concentrated over Celite and submitted to flash chromatography (hexane/EtOAc = 20 : 1, 3 x 15 cm silica) to yield **36h/37h** as an yellow oil (47 mg,71%).



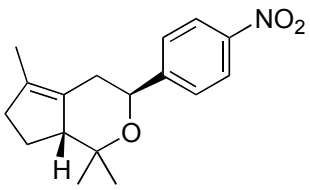
To a 65 ºC solution of the substrate (**46e**/**47e**, 71 mg, 0.2 mmol) in *i*PrOH (2 mL) saturated NH_4Cl solution (0.6 ml) and indium powder (100 mesh, 0.2 g) were sequentially added. After 3 h EtOH (1 mL) was added and the mixture was further kept at 65 ºC for 20 h. The cooled reaction mixture was filtered through Celite which was washed with CH_2Cl_2 (3 x 2 ml). The resulting solution was dried (Na_2SO_4), concentrated over Celite and submitted to flash chromatography (hexane/EtOAc = 8 : 1, 1 x 15 cm silica) to yield **46h**/**47h** as an off-white solid (32 mg, 73%).

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



***rac*-(3S,7aR)-1,1,5-Trimethyl-3-((*E*)-styryl)-1,3,4,6,7,7a-hexahydrocyclopenta[c]pyran (50b)** and ***rac*-(1S,2S,5R)-1,4,4-trimethyl-8-methylene-2-((*E*)-styryl)-3-oxabicyclo[3.2.1]octane (51b-eq)**

Colorless oil (hexane/EtOAc/Et_3N = 100 : 1 : 1) Major isomer **51b-eq**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.38 (m, 2H), 7.31-7.27 (m, 2H), 7.23-7.19 (m, 1H), 6.59 (d, J = 15.9 Hz, 1H), 6.20 (dd, J = 15.8, 7.3 Hz, 1H), 4.73 (s, 1H), 4.71 (s, 1H), 3.97 (d, J = 7.3 Hz, 1H), 2.21 (d, J = 6.7 Hz, 1H), 2.02-1.87 (m, 3H), 1.26 (s, 3H), 1.24 (s, 3H), 1.14 (dd, J = 12.3, 9.1 Hz, 1H), 0.96 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.11 (C), 137.16 (C), 133.13 (CH), 128.55 (CH), 127.62 (CH), 127.12 (CH), 126.74 (CH), 100.78 (CH_2), 82.75 (CH), 76.84 (C, oscured by the $CDCl_3$ signal, observed by HMBC), 52.97 (CH), 45.97 (CH), 28.78 (CH_2), 27.20 (CH_3), 23.70 (CH_3), 23.61 (CH_2), 18.13 (CH_3); Minor isomer **50**: ^{1}H NMR (400 MHz, $CDCl_3$, selected signals) δ 7.40-7.38 (m, 2H), 7.31-7.27 (m, 2H), 7.23-7.19 (m, 1H), 6.59 (d, J = 15.9 Hz, 1H), 6.27 (dd, J = 16.0, 6.4 Hz, 1H), 4.11-4.06 (m, 1H), 2.58 (br s, 1H), 2.49 (dd, J = 13.6, 3.1 Hz, 1H), 2.37-2.23 (m, 2H), 1.67 (s, 3H), 1.62-1.57 (m, 1H), 1.42-1.36 (m, 1H), 1.26 (s, 3H), 1.08 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 137.13 (C), 131.49 (CH), 130.89 (CH), 130.65 (C), 130.45 (C), 128.56 (CH), 127.57 (CH), 126.65 (CH), 76.84 (C, oscured by the $CDCl_3$ signal, observed by HMBC), 71.11 (CH), 55.93 (CH), 37.60 (CH_2), 33.20 (CH_2), 29.47 (CH_3), 23.62 (CH_2), 18.83 (CH_3), 13.58 (CH_3); HRMS calcd. for $C_{19}H_{24}ONa^+$ $(M+Na)^+$: 291.1731, found: 291.1725.

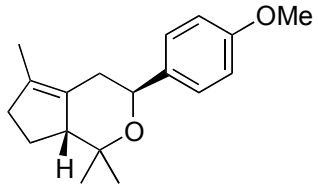


***rac*-(3S,7aR)-1,1,5-Trimethyl-3-(4-nitrophenyl)-1,3,4,6,7,7a-hexahydrocyclopenta[c]pyran (50d)**

(hexane/EtOAc/Et_3N = 100 : 2 : 1) yellow solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21-8.18 (m, 2H), 7.59-7.57 (m, 2H), 4.56 (dd, J = 11.5, 3.2 Hz, 1H), 2.65 (dd, J = 13.6, 3.2

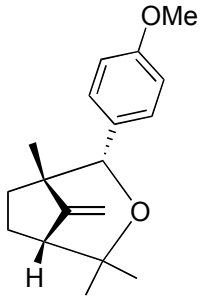
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Hz, 1H), 2.67-2.62 (br s, 1H), 2.37-2.25 (m, 2H), 2.00-1.88 (m, 2H), 1.69 (s, 3H), 1.47-1.39 (m, 1H), 1.31 (s, 3H), 1.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.29 (C), 147.06 (C), 131.29 (C), 130.25 (C), 126.68 (CH), 123.57 (CH), 77.59 (C), 71.23 (CH), 55.68 (CH), 37.50 (CH_2), 35.03 (CH_2), 29.27 (CH_3), 23.40 (CH_2), 18.56 (CH_3), 13.50 (CH_3); HRMS-ESI calcd for $C_{17}H_{22}NO_3$ $(M+H)^+$: 288.1600; found: 288.1588.



***rac*-(3S,7aR)-3-(4-Methoxyphenyl)-1,1,5-trimethyl-1,3,4,6,7,7a-hexahydrocyclopenta[c]pyran (50e)**

(hexane/Et_3N = 100 : 1, partial separation from **51e-eq**) colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.31 (m, 2H), 6.89-6.85 (m, 2H), 4.40 (dd, J = 11.6, 3.1 Hz, 1H), 3.79 (s, 3H), 2.65-2.61 (m, 1H), 2.56 (dd, J = 13.6, 3.2 Hz, 1H), 2.34-2.50 (m, 2H), 2.05-1.98 (m, 1H), 1.98-1.88 (m, 1H), 1.67 (s, 3H), 1.44-1.38 (m, 1H), 1.27 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.01 (C), 136.10 (C), 131.72 (C), 130.27 (C), 127.51 (CH), 113.91 (CH), 77.20 (C), 71.90 (CH), 56.02 (CH), 55.48 (CH_3), 37.68 (CH_2), 35.17 (CH_2), 29.60 (CH_3), 23.62 (CH_2), 18.80 (CH_3), 13.59 (CH_3); HRMS-ESI calcd. for $C_{18}H_{25}O_2$ $(M+H)^+$: 273.1855; found: 273.1841.

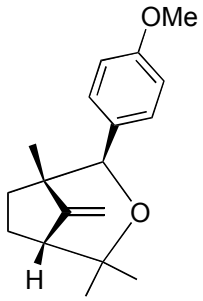


***rac*-(1S,2S,5R)-2-(4-Methoxyphenyl)-1,4,4-trimethyl-8-methylene-3-oxabicyclo[3.2.1]octane (51e-eq)**

(hexane/Et_3N = 100 : 1, partial separation from **50e**) colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.25 (m, 2H), 6.87-6.83 (m, 2H), 4.78 (s, 1H), 4.74 (s, 1H), 4.41 (s, 1H), 3.79 (s, 3H), 2.26 (d, J = 6.8 Hz, 1H), 2.08-1.94 (m, 2H), 1.65-1.58 (m, 1H), 1.29 (s, 3H), 1.26 (s, 3H), 0.90 (td, J = 12.3, 4.0 Hz, 1H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.05 (C), 158.51 (C), 132.34 (C), 129.16 (CH), 113.09 (CH), 100.87 (CH_2),

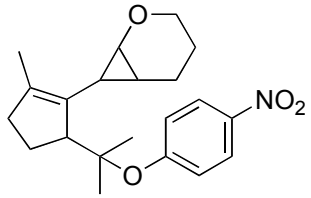
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

83.07 (CH), 76.69 (C), 55.39 (CH_3), 52.85 (CH), 46.51 (C), 27.67 (CH_2), 27.13 (CH_3), 23.51 (CH_3), 23.46 (CH_2), 18.76 (CH_3); HRMS-ESI calcd. for $C_{18}H_{25}O_2$ $(M+H)^+$: 273.1855; found: 273.1846.



***rac*-(1S,2R,5R)-2-(4-Methoxyphenyl)-1,4,4-trimethyl-8-methylene-3-oxabicyclo[3.2.1]octane (51e-ax)**

(hexane/EtOAc/Et_3N = 100 : 2 : 1) colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.50-7.46 (m, 2H), 6.80-6.77 (m, 2H), 5.02 (s, 1H), 4.99-4.98 (m, 1H), 4.50 (s, 1H), 3.78 (s, 3H), 2.33 (d, J = 6.2 Hz, 1H), 2.10-2.02 (m, 2H), 1.64-1.53 (m, 2H), 1.18 (s, 3H), 1.05 (s, 3H), 1.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.64 (C), 155.23 (C), 134.88 (C), 130.67 (CH), 113.01 (CH), 104.19 (CH_2), 87.07 (CH), 78.87 (C), 55.28 (CH_3), 53.58 (CH), 44.78 (C), 39.52 (CH_2), 27.86 (2xCH_3), 22.73 (CH_2), 20.18 (CH_3); HRMS-ESI calcd. for $C_{18}H_{25}O_2$ $(M+H)^+$: 273.1855; found: 273.1844.

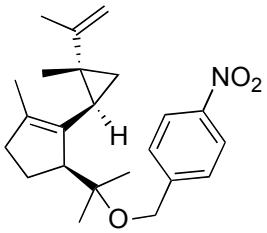


7-(2-Methyl-5-(2-(4-nitrophenoxy)propan-2-yl)cyclopent-1-en-1-yl)-2-oxabicyclo[4.1.0]heptane (54)

Light yellow oil (hexane/EtOAc/Et_3N = 100 : 9 : 1). Major isomer: ^1H NMR (400 MHz, $CDCl_3$, selected signals) δ 8.15-8.11 (m, 2H), 7.12-7.08 (m, 2H), 3.60-3.56 (m, 1H), 3.40 (dd, J = 7.2, 2.6 Hz, 1H), 3.31 (td, J = 11.0, 2.3 Hz, 1H), 3.05 (br d, J = 9.0 Hz, 1H), 2.33-2.27 (m, 1H), 2.15-2.07 (m, 2H), 2.02-1.94 (m, 1H), 1.92-1.81 (m, 2H), 1.69 (s, 3H), 1.53 (s, 3H), 1.40 (s, 3H), 1.03-0.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.42 (C), 141.98 (C), 141.12 (C), 133.57 (C), 125.31 (CH), 121.17 (CH), 86.66 (C), 65.55 (CH_2), 57.75 (CH), 56.92 (CH), 37.37 (CH_2), 25.27 (CH_2), 25.12 (CH_3), 24.36 (CH), 24.16 (CH_3), 22.77 (CH_2), 21.41 (CH), 19.98 (CH_2), 15.04 (CH_3); minor isomer:

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

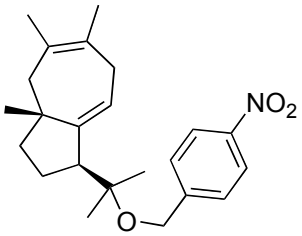
^{1}H NMR (400 MHz, $CDCl_3$, selected signals) δ 7.08-7.04 (m, 2H), 2.95-2.93 (m, 1H), 1.83 (m, 3H), 1.41 (s, ·H), 1.33 (s, 3H), 0.89-0.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.28 (C), 142.46 (C), 141.30 (C), 132.66 (C), 125.30 (CH), 122.05 (CH), 87.03 (C), 64.37 (CH_2), 59.72 (CH), 57.21 (CH), 37.60 (CH_2), 25.34 (CH_2), 25.32 (CH_3), 24.14 (CH), 24.09 (CH_3), 22.49 (CH_2), 19.34 (CH_2), 17.63 (CH), 15.18 (CH_3); HRMS calcd. for $C_{21}H_{27}NO_4Na$ (M+Na): 380.1838; found: 380.1827.



***rac*-1-((2-((S)-3-Methyl-2-((1S,2S)-2-methyl-2-(prop-1-en-2-yl)cyclopropyl)cyclopent-2-enyl)propan-2-yloxy)methyl)-4-nitrobenzene (55a)**

Flash chromatography (hexane/EtOAc = 100 : 3), light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18-8.14 (m, 2H), 7.50-7.47 (m, 2H), 4.77-4.75 (m, 1H), 4.68-4.67 (m, 1H), 4.56 (AB system, J = 13.4 Hz, 1H), 4.51 (AB system, J = 13.3 Hz, 1H), 2.85 (br s, 1H), 2.36-2.27 (m, 1H), 2.18-2.11 (m, 1H), 1.88-1.83 (m, 2H), 1.75 (m, 3H), 1.65 (br s, 1H), 1.46-1.45 (m, 3H), 1.26 (s, 3H), 1.20 (dd, J = 8.8, 4.5 Hz, 1H), 1.20 (s, 3H), 1.15 (s, 3H), 0.59 (dd, J = 6.6, 4.5 Hz, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 149.73 (C), 148.37 (C), 147.04 (C), 139.84 (C), 134.29 (C), 127.46 (CH), 123.46 (CH), 108.70 (CH_2), 80.06 (C), 62.41 (CH_2), 57.70 (CH), 37.95 (CH_2), 25.41 (C), 25.22 (CH_2), 24.08 (CH_3), 23.90 (CH), 23.65 (CH_3), 20.67 (CH_2), 19.71 (CH_3), 18.83 (CH_3), 15.41 (CH_3); HRMS-ESI calcd for $C_{23}H_{32}NO_3$ $(M+H)^+$: 370.2382; found: 370.2383. The structure was also confirmed by thermal rearrangement (see below).

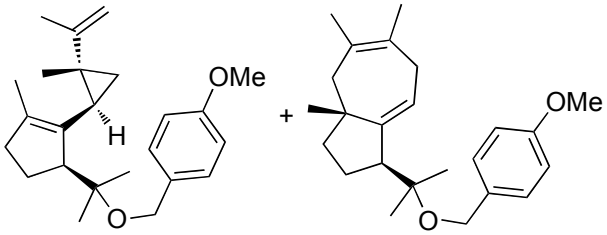


***rac*-(1S,3aR)-3a,5,6-Trimethyl-1-(2-(4-nitrobenzyloxy)propan-2-yl)-1,2,3,3a,4,7-hexahydroazulene (56a)**

Flash chromatography (hexane/EtOAc = 100:3), light yellow oil.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

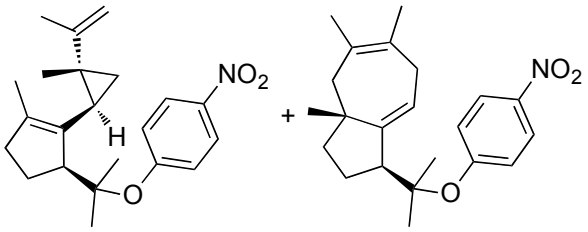
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20-8.16 (m, 2H), 7.53-7.49 (m, 2H), 5.54 (td, J = 4.8, 2.0 Hz, 1H), 4.57 (s, 2H), 2.98-2.90 (m, 2H), 2.69-2.63 (m, 1H), 2.45 (d, J = 14.7 Hz, 1H), 1.92 (d, J = 14.2 Hz, 1H), 1.74-1.65 (m, 1H), 1.71 (m, 3H), 1.65 (s, 3H), 1.60-1.51 (m, 1H), 1.50-1.38 (m, 2H), 1.24 (s, 3H), 1.23 (s, 3H), 1.02 (s, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ149.14 (C), 147.99 (C), 147.14 (C), 127.95 (C), 127.60 (CH), 126.95 (C), 123.61 (CH), 121.24 (CH), 78.97 (C), 62.46 (CH_2), 52.89 (CH), 48.30 (CH_2), 45.56 (C), 41.33 (CH_2), 36.88 (CH_2), 26.08 (CH_2), 24.61 (CH_3), 23.46 (2xCH_3), 22.71 (CH_3), 21.79 (CH_3); HRMS-ESI: expected for $C_{16}H_{25}$ (M-PNBnO)$^+$: 217.1956; found: 217.1963. The structure was also confirmed by a GOESY experiment.



***rac*-1-Methoxy-4-(((2-((S)-3-methyl-2-((1R,2R)-2-methyl-2-(prop-1-en-2-yl)cyclopropyl)cyclopent-2-en-1-yl)propan-2-yl)oxy)methyl)benzene (55b) and *rac*-(1S,3aR)-1-(2-((4-methoxybenzyl)oxy)propan-2-yl)-3a,5,6-trimethyl-1,2,3,3a,4,7-hexahydroazulene (56b)**

Light yellow oil (hexane/EtOAc/Et_3N = 100 : 2 : 1). Major isomer **55b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.22 (m, 2H), 6.86-6.82 (m, 2H), 4.76-4.75 (m, 1H), 4.71-4.70 (m, 1H), 4.39-4.33 (m, 2H), 3.79 (s, 3H), 2.85 (br d, J = 9.2 Hz, 1H), 2.35-2.26 (m, 1H), 2.15-2.07 (m, 1H), 1.98-1.92 (m, 1H), 1.86-1.80 (m, 1H), 1.74-1.73 (m, 3H), 1.63 (br s, 1H), 1.55 (dd, J = 1.3, 0.6 Hz, 3H), 1.27 (s, 3H), 1.22-1.19 (m, 1H), 1.15 (s, 3H), 1.14 (s, 3H), 0.57 (dd, J = 6.6, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.80 (C), 149.85 (C), 139.67 (C), 134.50 (C), 132.50 (C), 128.88 (CH), 113.74 (CH), 108.58 (CH_2), 79.17 (C), 63.04 (CH_2), 57.81 (CH), 55.42 (CH_3), 38.00 (CH_2), 25.29 (C), 25.19 (CH_2), 24.71 (CH_3), 24.02 (CH), 23.45 (CH_3), 20.75 (CH_2), 19.83 (CH_3), 18.89 (CH_3), 15.43 (CH_3); minor isomer **56b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.63-5.60 (m, 1H), 3.79 (s, 3H), 2.98-2.91 (m, 2H), 2.72-2.65 (m, 1H), 2.47-2.44 (m, 1H), 1.71-1.70 (m, 3H), 1.65 (s, 3H), 1.55 (s, 3H), 1.22 (s, 3H), 1.21 (s, 3H), 1.01 (s, 3H); HRMS calcd. for $C_{24}H_{34}O_2Na$ (M+Na): 377.2457; found: 377.2459. The minor (cycloheptadiene) isomer autooxidized before its ^{13}C NMR could be acquired. The peroxo-hydroperoxide and the peroxide-alcohol were observed by MS (425.2, 441.2).

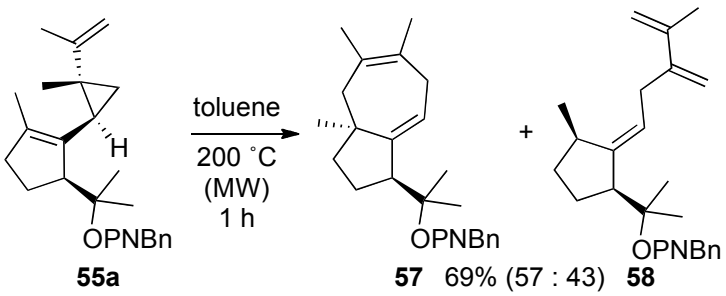
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



***rac*-1-((2-((S)-3-Methyl-2-((1R,2R)-2-methyl-2-(prop-1-en-2-yl)cyclopropyl)cyclopent-2-en-1-yl)propan-2-yl)oxy)-4-nitrobenzene (55c) and *rac*-(1S,3aR)-3a,5,6-trimethyl-1-(2-(4-nitrophenoxy)propan-2-yl)-1,2,3,3a,4,7-hexahydroazulene (56c)**

Light yellow oil (hexane/EtOAc/Et_3N = 100 : 2 : 1). Major isomer **55c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13-8.10 (m, 2H), 7.03-6.99 (m, 2H), 4.72-4.71 (m,1H), 4.67-4.65 (m,1H), 3.09-3.06 (m,1H), 2.39-2.29 (m, 1H), 2.22-2.15 (m,1H), 1.97-1.87 (m,1H), 1.81-1.76 (m, 1H), 1.78-1.76 (m,3H), 1.55 (m,3H), 1.38 (s, 3H), 1.36 (s, 3H), 1.22 (dd, J = 8.7, 4.5 Hz, 1H), 1.14 (s, 3H), 0.60 (dd, J = 6.6, 4.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.22 (C), 149.55 (C), 142.22 (C), 140.75 (C), 133.94 (C), 125.27 (CH), 121.57 (CH), 108.82 (CH_2), 87.08 (C), 59.48 (CH), 36.84 (C), 37.81 (CH_2), 25.67 (CH_2), 24.79 (CH_3), 24.60 (CH_3), 24.07 (CH), 20.72 (CH_2), 19.81 (CH_3), 18.90 (CH_3), 15.44 (CH_3); minor isomer **56c**: ^{1}H NMR (400 MHz, $CDCl_3$, selected signals) δ 8.17-8.13 (m, 2H), 7.07-7.03 (m,2H), 5.62 (ddd, J = 5.3, 4.3, 2.0 Hz, 1H), 2.72-2.65 (m, 1H), 2.50-2.46 (m, 1H), 1.84 (t, 2.8 Hz, 1H), 1.83 (t, J = 2.7 Hz, 1H), 1.73 (m, 3H), 1.37 (s, 3H), 1.38 (s, 3H), 1.37 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.16 (C), 148.62 (C), 142.46 (C), 128.21 (C), 127.09 (C), 125.34 (CH), 122.15 (CH), 121.99 (CH), 85.82 (C), 54.76 (CH), 48.17 (CH_2), 45.59 (C), 41.12 (CH_2), 25.94 (CH_3), 25.86 (CH_2), 25.32 (CH_2), 23.95 (CH_3), 23.54 (CH_3), 23.41 (CH_3), 21.75 (CH_3); HRMS calcd. for $C_{22}H_{29}NO_3Na$ (M+Na): 378.2045; found: 378.2041.

Thermal rearrangement of 55a



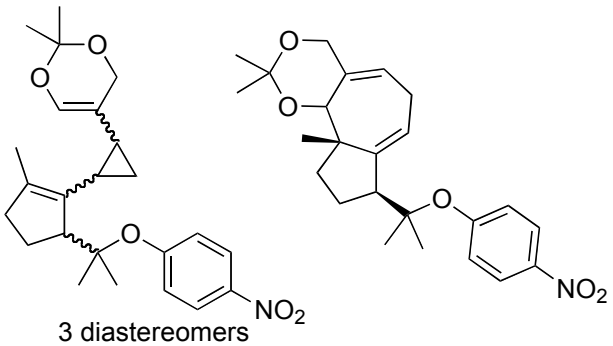
55a **57** 69% (57 : 43) **58**

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

A solution of **55a** (38 mg, 0.10 mmol) in toluene (5 mL) was heated at 90 ºC under Ar for 22 h; no reaction was observed by TLC or by ^{1}H NMR of an aliquote. The solution was then transferred to a sealed vial and heated for 1 h at 200 ºC under microwave irradiation. Flash chromatography (hexane/EtOAc = 100 : 3) yielded a mixture of isomers as a light yellow oil (**57**/**58** = 57 : 43) (26 mg, 69%). Compound **57** is unstable when concentrated and decomposes overnight in a $CDCl_3$ solution. The flash chromatography was repeated acordingly in order to get clean NMR spectra (**58** becames major isomer, while traces of **57** remain visible).

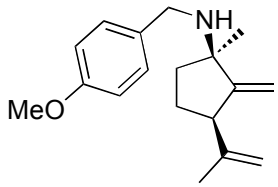
***rac*-(1S,3aS)-3a,5,6-Trimethyl-1-(2-(4-nitrobenzyloxy)propan-2-yl)-1,2,3,3a,4,7-hexahydroazulene (57) and *rac*-1-((2-((1S,3R,*E*)-3-methyl-2-(4-methyl-3-methylenepent-4-enylidene)cyclopentyl)propan-2-yloxy)methyl)-4-nitrobenzene (58)** **57**: ^{1}H NMR (400 MHz, $CDCl_3$, selected signals) δ 5.74 (td J = 5.3, 2.3 Hz, 1H), 4.55 (s, 2H), 2.99-2.94 (m, 1H), 2.76-2.70 (m, 1H), 2.50 (d, J = 15.9 Hz, 1H), 1.68 (s, 3H), 1.65 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.54 (C), 147.85 (C), 147.17 (br, C), 127.75 (CH), 127.44 (C), 126.90 (C), 123.62 (CH), 119.61 (CH), 79.33 (C), 62.35 (CH_2), 50.51 (CH), 46.66 (CH_2), 45.13 (C), 41.26 (CH_2), 35.90 (CH_2), 25.93 (CH_2), 25.49 (CH_3), 24.78 (CH_3), 23.14 (CH_3), 22.41 (CH_3), 21.88 (CH_3); **58**: ^{1}H NMR (400 MHz, $CDCl_3$, selected signals) δ 8.18-8.14 (m, 2H), 7.50-7.48 (m, 2H), 5.64 (tt, J = 7.0, 2.0 Hz, 1H), 5.07-5.06 (m, 2H), 4.97 (s, 1H), 4.94 (s, 1H), 4.60-4.53 (m, 2H), 3.01 (d, J = 7.1 Hz, 2H), 2.90-2.84 (m, 2H), 1.90 (m, 3H), 1.79-1.73 (m, 1H), 1.27 (s, 6H), 0.98 (d, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.79 (C), 147.69 (C), 147.42 (C), 147.17 (br, C), 143.08 (C), 127.84 (CH), 123.59 (CH), 122.55 (CH), 112.91 (CH_2), 112.42 (CH_2), 78.94 (C), 62.49 (CH_2), 51.55 (CH), 36.48 (CH), 33.93 (CH_2), 32.67 (CH_2), 27.69 (CH_2), 24.98 (CH_3), 22.31 (CH_3), 21.29 (CH_3), 19.61 (CH_3); HRMS-ESI calcd for $C_{23}H_{31}NO_3Na$ $(M+Na)^+$: 392.2202; found: 392.2197.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



2,2-Dimethyl-5-(2-(2-methyl-5-(2-(4-nitrophenoxy)propan-2-yl)cyclopent-1-en-1-yl)cyclopropyl)-4H-1,3-dioxine (66) and *rac*-(8S,10aS)-2,2,10a-trimethyl-8-(2-(4-nitrophenoxy)propan-2-yl)-6,8,9,10,10a,10b-hexahydro-4H-azuleno[4,5-d][1,3]dioxine (67)

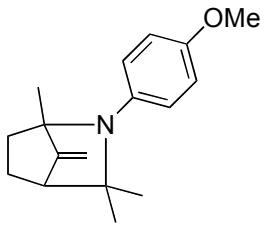
Pale yellow oil (hexane/EtOAc/Et_3N = 100 : 9 : 1). ^1H NMR (400 MHz, $CDCl_3$, selected signals) δ 6.29 (m, 1H, minor cyclopropane isomer), 6.19 (m, 1H, major cyclopropane isomer), 6.09 (br s, 1H, minor cyclopropane isomer), 6.05-6.03 (m, 1H, minor cycloheptadiene isomer), 5.75-5.73 (m, 1H, minor cycloheptadiene isomer); HRMS calcd. for $C_{24}H_{31}NNaO_5$ (M+Na): 436.2100, found: 436.2104.



***rac*-(1*R*,3*R*)-N-(4-Methoxybenzyl)-1-methyl-2-methylene-3-(prop-1-en-2-yl)cyclopentanamine (70)**

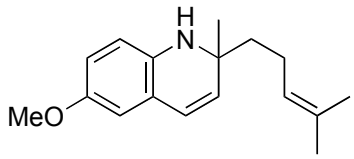
Pale yellow oil (hexane/EtOAc/Et_3N = 100 : 15 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.33-7.30 (m, 2H), 6.87-6.83 (m, 2H), 5.04 (d, J = 2.5 Hz, 1H), 5.02 (d, J = 2.8 Hz, 1H), 4.91-4.90 (m, 1H), 4.88-4.87 (m, 1H), 3.62 (AB system, J = 12.2 Hz, 1H), 3.57 (AB system, J = 12.2 Hz, 1H), 3.35 (s, 3H), 3.22-3.17 (m, 1H), 1.81-1.71 (m, 2H), 1.68 (m, 3H), 1.63-1.58 (m, 1H), 1.40-1.32 (m, 1H), 1.22 (s, 1H), 0.77 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.25 (C), 158.05 (C), 147.35 (C), 134.16 (C), 129.71 (CH), 114.10 (CH), 112.43 (CH_2), 106.69 (CH_2), 63.13 (C), 54.83 (CH_3), 53.01 (CH), 46.73 (CH_2), 38.85 (CH_2), 28.20 (CH_2), 26.01 (CH_3), 18.66 (CH_3); HRMS calcd. for $C_{18}H_{26}NO^+$ $[M]^+$: 272.014, found: 272.2013. The configuration was determined by GOESY experiments.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



2-(4-Methoxyphenyl)-1,3,3-trimethyl-7-methylene-2-azabicyclo[2.2.1]heptane (69a)

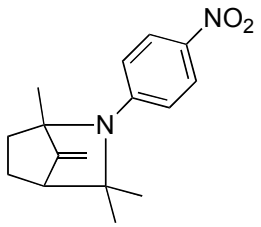
Colorless oil (hexane/EtOAc/Et_3N = 100 : 5 : 1). ^1H NMR (400 MHz, C_6D_6) δ 6.96-6.92 (m, 2H), 6.80-6.76 (m, 2H), 4.75 (s, 1H), 4.66 (s, 1H), 3.40 (s, 3H), 2.26 (ddd, J = 12.1, 9.5, 4.8 Hz, 1H), 2.05 (d, J = 4.2 Hz, 1H), 1.80 (ddd, J = 12.3, 9.5, 3.9 Hz, 1H), 1.46 (tt, J = 12.1, 4.6 Hz, 1H), 1.36-1.32 (m, overlapped with 2 Me signals, 1H), 1.34 (s, 3H), 1.33 (s, 3H), 1.07 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 158.83 (C), 154.39 (C), 139.28 (C), 124.39 (CH), 114.06 (CH), 94.65 (CH_2), 64.98 (C), 62.99 (C), 55.06 (CH_3), 53.50 (CH), 31.48 (CH_2), 31.43 (CH_3), 24.06 (CH_2), 23.31 (CH_3), 16.41 (CH_3); HRMS calcd. for $C_{17}H_{24}NO$ (M+H): 258.1858, found: 258.1846.



6-Methoxy-2-methyl-2-(4-methylpent-3-en-1-yl)-1,2-dihydroquinoline (71)

Brownish yellow oil (hexane/EtOAc/Et_3N = 100 : 5 : 1). ^1H NMR (400 MHz, C_6D_6) δ 6.67 (dd, J = 8.5, 2.8 Hz, 1H), 6.55 (d, J = 2.8 Hz, 1H), 6.18 (d, J = 9.8 Hz, 1H), 6.15 (d, J = 8.5 Hz, 1H), 5.23 (d, J = 9.7 Hz, 1H), 5.19-5.15 (m, 1H), 3.40 (s, 3H), 2.91 (br s, 1H), 2.24-2.14 (m, 1H), 2.11-2.02 (m, 1H), 1.67 (s, 3H), 1.53 (s, 3H), 1.40 (ddd, J = 13.6, 11.2, 5.5 Hz, 1H), 1.30 (ddd, J = 13.6, 11.3, 5.3 Hz, 1H), 1.06 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 152.49 (C), 138.28 (C), 131.12 (C), 130.59 (CH), 125.29 (CH), 125.13 (CH), 121.04 (C), 115.08 (CH), 113.56 (CH), 112.62 (CH), 55.47 (CH_3), 55.09 (C), 43.97 (CH_2), 29.74 (CH_3), 25.88 (CH_3), 23.87 (CH_2), 17.72 (CH_3); HRMS calcd. for $C_{17}H_{24}NO$ (M+H): 258.1858, found: 258.1850.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



1,3,3-Trimethyl-7-methylene-2-(4-nitrophenyl)-2-azabicyclo[2.2.1]heptane (69b)

Orange solid (hexane/EtOAc/Et_3N = 100 : 5 : 1). ^{1}H NMR (400 MHz, C_6D_6) δ 8.03-7.99 (m, 2H), 6.38-6.34 (m, 2H), 4.63 (s, 1H), 4.56 (s, 1H), 1.85 (ddd, J = 12.3, 9.4, 4.5 Hz, 1H), 1.79 (d, J = 4.4 Hz, 1H), 1.51 (ddd, J = 12.8, 9.4, 4.4 Hz, 1H), 1.33-1.25 (m, 1H), 1.17 (s, 3H), 1.12 (s, 3H), 1.07 (td, J = 12.1, 4.4 Hz, 1H), 0.89 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 156.49 (C), 150.86 (C), 138.61 (C), 124.93 (CH), 117.00 (CH), 97.27 (CH_2), 65.60 (C), 65.34 (C), 53.31 (CH), 30.51 (CH_2), 29.38 (CH_3), 23.28 (CH_2), 22.38 (CH_3), 15.80 (CH_3); HRMS calcd for $C_{16}H_{20}N_2NaO_2$ (M+Na): 295.1422, found: 295.1426. X-ray quality crystals were obtined by slow evaporation of a pentane solution of the product.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Towards a general Au(I) precatalyst

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Introduction

Screening different gold(I) catalysts in total synthesis, development of new methods, or asymmetric catalysis requires the time-consuming preparation of a series of gold(I) complexes. It would be highly desirable to prepare in situ the desired gold(I) catalysts from a simple $[AuL_2]^+X^-$ precursor bearing two L weakly ligands. Bisnitrile complexes $[Au(RCN)_2]^+WCA^-$ (**72** WCA = weakly coordinating ligand) appeared as the best candidates for the preparation of a wide variety of cationic gold(I) complexes. However, these complexes have been prepared in only low yields and, unfortunately, none is stable under ordinary conditions.

$[Au(NCMe)_2]^+(ClO_4)^-$ was originally obtained by treating $NOClO_4$ with an excess of gold powder in MeCN.[119] The complex $[Au(NCMe)_2]^+(SbF_6)^-$ was later isolated and characterized as the solvolysis product of $[Au(CO)_2]^+(Sb_2F_{11})^-$.[120] Alternatively, $[Au(NCMe)_2]^+(SbCl_6)^-$ was obtained by chloride abstraction from AuCl with $SbCl_5$ in acetonitrile.[121] Salts containing the $[Au(NCMe)_2]^+$ cation were used for the synthesis of other bis-nitrile gold(I) complexes.[122,123] Acetonitrile solutions of Au^+ with weakly coordinating anions were obtained by electrochemical methods.[124] The oxidation of Au metal with nitrosonium salts was recently revisited in the "high yielding" (brsm) synthesis of $[Au(NCPh)_2]^+$ with BF_4^- and SbF_6^- as counteranions.[125]

The greatest limitation of all the previously described $[(RCN)_2Au](WCA)$ complexes is their instability to ambient conditions. $[(MeCN)_nAu]^+$ containing solutions obtained by electrolythic methods and are also used immediately after their preparation.[126] Because of this reason the applications of these complexes are scarce.[125]

119. Bergerhoff, G. *Z. Anorg. Allg. Chem.* **1964**, 327, 139.

120. Willner, H.; Schaebs, J.; Hwang, G.; Mistry, F.; Jones, R.; Trotter, J.; Aubke, F. *J. Am. Chem. Soc.* **1992**, *114*, 8972-8980.

121. Zuur, A. P.; Groeneveld, W. L. *Recl. Trav. Chim. Pay. B.***1967**, *86*, 1089-1102.

122. Farha, F.; Iwamoto, R. T. *Inorg. Chem.* **1965**, 844-848.

123. Shimizu; K. D.; Rebek, J. Jr. *Proc. Natl. Acad. Sci. USA* **1996**, *93*, 4257-4260.

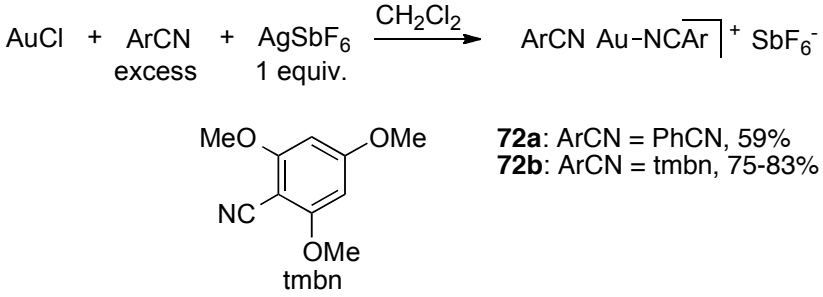
124. Kissner, R.; Latal P.; Geier, G.; *J. Chem. Soc., Chem. Commun.* **1993**, 136-137 and references cited therein.

125. Yau, J.; Mingos, D.M.P. *J. Chem. Soc*., *Dalton Trans*. **1997**, 1103-1111.

126. Fischbach, U.; Ruegger, H.; Grutzmacher, H. *Eur. J. Inorg. Chem*. **2007**, *18*, 2654-2667.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Results and discussion



We prepared complex $[Au(NCPh)_2]^+(SbF_6)^-$ **72a** in 59% yield by treatment of AuCl with $AgSbF_6$ (1 equiv) and PhCN in CH_2Cl_2 at room temperature for 43 h. However this complex is unstable to air and moisture and readily decomposes to form 2,4,6-triphenyl-1,3,5-triazine when treated with moist $MeNO_2$ or triphenylphosphine. Unfortunately attempts to use gold dinitrile complexes as a catalysts for the trimerization of benzonitrile proved unsuccesful. Although the sample of **72a** we prepared by chloride abstraction yielded the expected elemental analysis and could be characterized by ^1H and ^{13}C NMR, we could not observe the $[Au(NCPh)_2]^+$ cation by MS.[127]

We reasoned that a more robust complex could be prepared by using more electron-donating 2,4,6-trimethoxybenzonitrile (tmbn) as the ligand. Indeed, $[Au(tmbn)_2]^+(SbF_6)^-$ **72b** was obtained from the reaction of AuCl and $AgSbF_6$ in the presence of tmbn and is stable under ambient conditions for months.

The increased donor capacity from MeCN to tmbn not only increases the stability of the resulting complex but also reduces the reaction time. Whereas the synthesis of **72b** requires 20 min at room temperature, almost 2 days were required for the corresponding benzonitrile complex **72a**. Treatment of a AuCl solution in dry MeCN with one equivalent of $AgSbF_6$ resulted in an initial turbidity followed by slow deposition of metallic Au.

127. It is intriguing to notice that the authors of ref. 125 failed to obtain correct elemental analysis for complex **72a** prepared by the Au(0) oxidation method. NMR data was not provided either.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

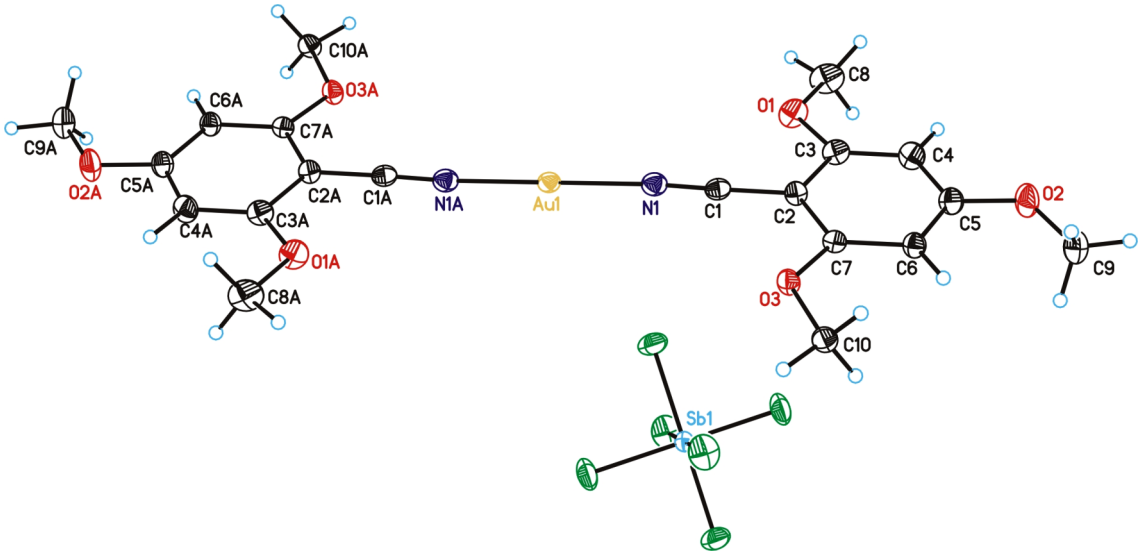


Figure 8. X-ray structure of **72b**.

The first attempts at synthesizing **72b** were made difficult by the occasional coprecipitation of the silver complex $[Ag(tmbn)_2]^+(SbF_6)^-$ **73a**. Dry and highly pure nitriles and AuCl as well as absence of light are crucial for the high yield synthesis of $[(RCN)_2Au]^+(SbF_6)^-$ complexes. However, most of the **72b** can be recovered by precipitation from mixtures impurified with up to 25 mol% **73a**. New complex $[Ag(MeCN)_2]^+(SbF_6)^-$ **73b** was also prepared as a relatively non-hygroscopic and light stable crystalline complex.

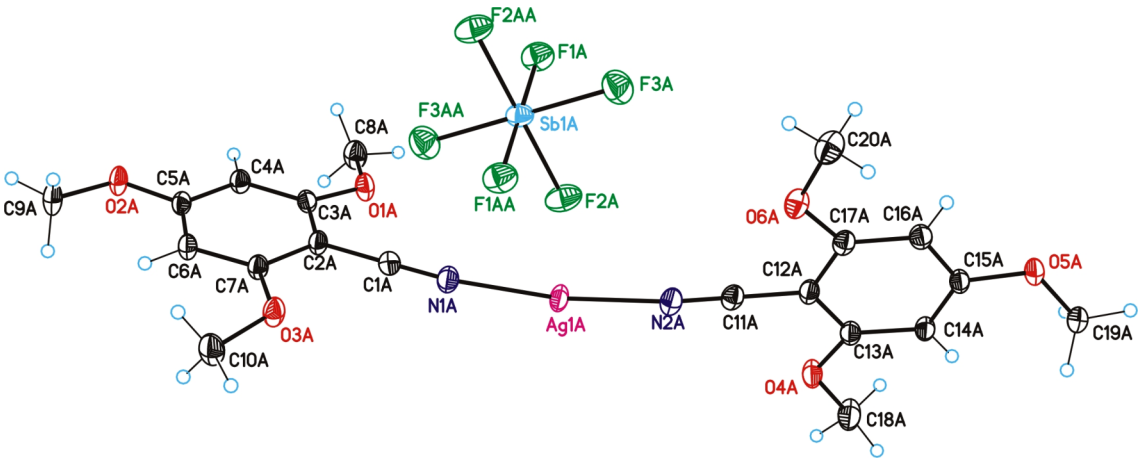


Figure 9. X-ray structure of **73a**.

Complexes **72b** (Figure 8) and **73a-b** (Figure 9, Figure 10) were characterized by X-ray diffraction. All three complexes show a perfect linear coordination around the

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

metal (N-Au-N and N-Ag-N angles of 180.0º).[128] As expected, the N-Au bond length in **72b** is considerably shorter (1.95 Å) that the N-Ag bond in **73a** (2.10 Å) **a**nd **73b** (2.11 Å).

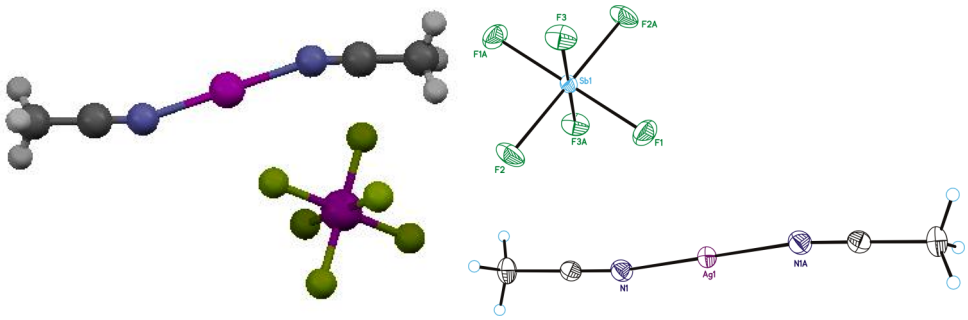
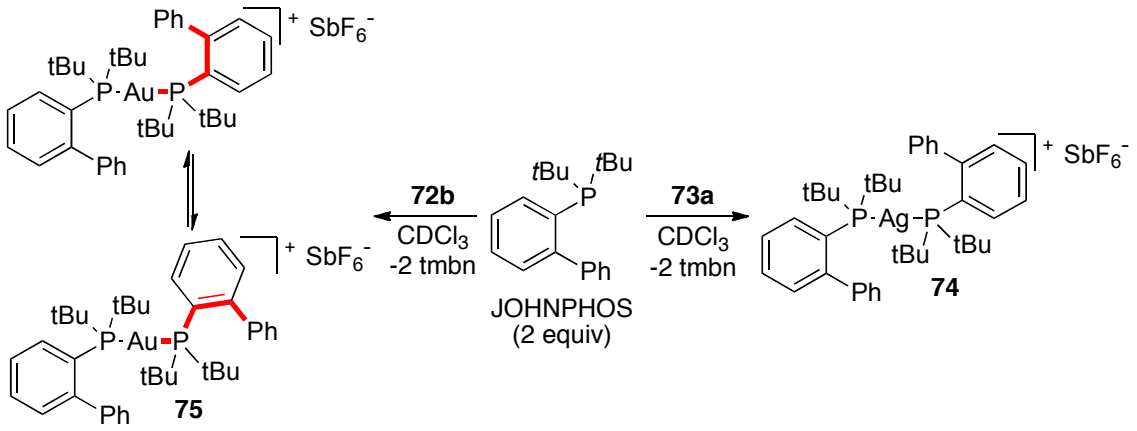


Figure 10. X-ray structure of **73b**.

Fortunately both complexes react within time of mixing with 2-di-*tert*-butylphosphinobiphenyl (JOHNPHOS, Scheme 27) and therefore a simple test for detecting the presence of silver was made possible using ^{31}P NMR. In the case of **75**, two isomers were observed by NMR corresponding to the symmetrical and unsymmetrical conformers. Only the symmetrical conformer of complex **74** was observed by NMR. In the solid state (Figure 11), the $[(JOHNPHOS)_2Ag]^+$ cation is bent (P-Ag-P angles 154.2º, 155.4º, 157.2º), with the substituents around the P-P axis set in a gauche conformation. This is possibly due to attractive CH-π interactions between the *t*Bu hydrogens and the phenyl ring.



Scheme 27.

128. There are two types of cations in the unit cell of **73a**. The second cation is not planar and the slight bending (N-Ag-N angle 171.4º) result from the asymmetric packing around one of the arene rings and around the Ag atom. See the experimental part for additional information.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

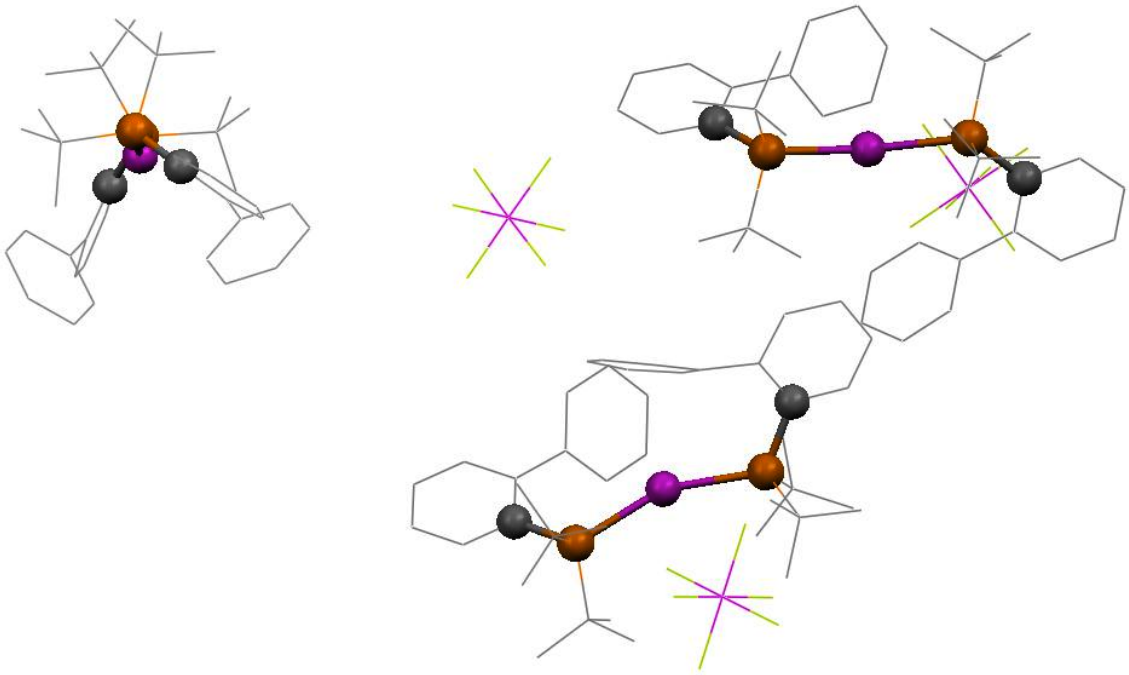


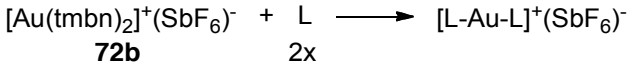
Figure 11. X-ray structure of **74**. The H atoms were ommited for clarity. The Ag, P and C_{ipso} atoms are highlighted.

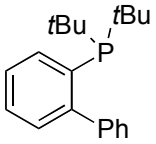
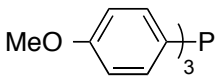
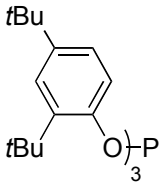
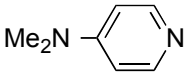
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Applications: synthesis of new complexes

Unsurprisingly, complex **72b** reacts cleanly within time of mixing with 1 or 2 equivalents of either phosphines, pyridines, phosphites or NHC-AgCl complexes. However, from NMR experiments, it seemed that only bulky or π-acidic ligands could lead cleanly to monosusbtitution. In the more general case, substitution of both tmbn ligands took place. Thus Au(I) complexes bearing two phosphine (**75-76**), phosphites (**77**) or DMAP ligands (**78**) were synthesized in good yields (Table 26).

Table 26. Synthesis of $[AuL_2]^+(SbF_6)^-$ complexes **75-78**.[a]



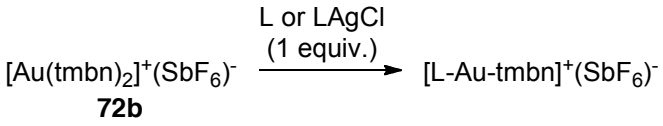
L	Cationic complex	Yield (%)
	**75**	87
	**76**	91
	**77**	76
	**78**	91

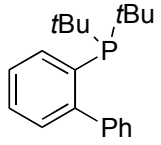
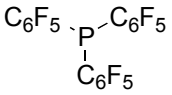
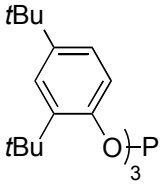
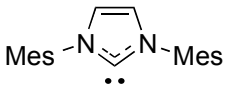
a) reactions performed in CH_2Cl_2 under air; isolated yields.

Gratifyingly, substitution of only one tmbn ligand could also be achieved yielding potentially catalitically active complexes $[Au(L)(tmbn)]^+(SbF_6)^-$ (Table 27). NHC complexes **8c**, **9c** could be conveniently obtained by transmetallation from the corresponding NHC-AgCl complex under ambient conditions. The phosphite complex **7c** could not be separated from the excess tmbn. Phosphite complexes **7c** and **7d** were synthesized by a conventional procedures for comparison purposes.

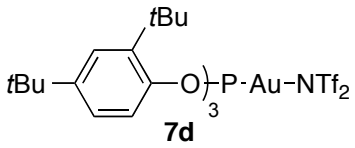
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Table 27. Synthesis of $[Au(L)(tmbn)]^+(SbF_6)^-$ complexes.[a]



L	Cationic complex	Yield (%)
	**1c**	90
	**79**	79
	**7c**	quant.[b]
	**8c**	85
	**9c**	70

a) a solution of the ligand was added over a solution of **72b**; isolated yields; b) NMR yield; c) a solution of the [(NHC)AgCl] was added over a solution of **72b**; DIPP = 2,6-*i*$Pr_2C_6H_3$.

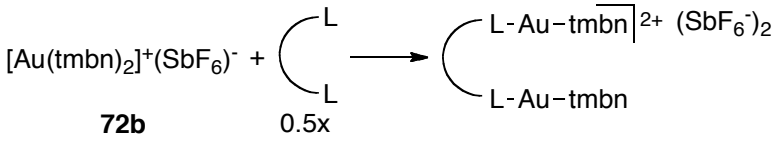


7d

Substitution of only one tmbn ligand was also possible using bulky bidentate ligands. Mixing complex **72b** with 0.5 equivalents of (*R*)-DTBM-SEGPHOS or (*R*)-DTBM-MeO-BIPHEP led to complexes $[Au_2(L\text{-}L)(tmbn)_2](SbF_6)_2$ such as **80** and **81** (Table 28).

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

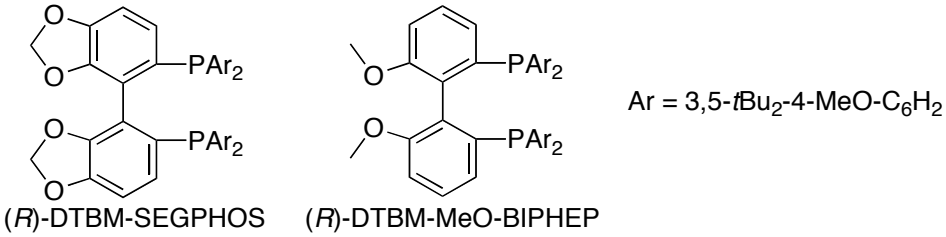
Table 28. Synthesis of $[Au_2(L\text{-}L)(tmbn)_2](SbF_6)_2$ complexes.[a]



72b 0.5x

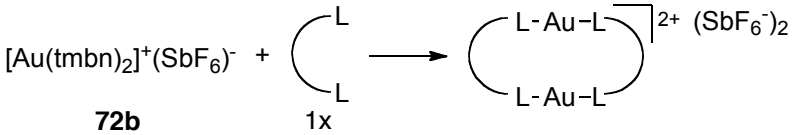
L	Cationic complex	Yield (%)
(*R*)-DTBM-SEGPHOS	**80**	71
(*R*)-DTBM-MeO-BIPHEP	**81**	44

a) a solution of the ligand was added over a solution of **72b**; isolated yields.



Once again, in the more general case, reaction of **72b** with bidentate ligands leads to macrocyclic $[Au_2(L\text{-}L)_2](SbF_6)_2$ complexes **82-86 (**Table 29).

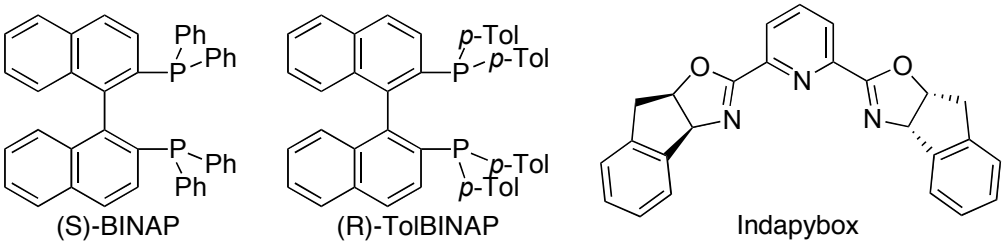
Table 29. Synthesis of $[Au_2(L\text{-}L)_2](SbF_6)_2$ complexes.[a]



72b 1x

L-L	Cationic complex	Yield (%)
(*S*)-BINAP	**82**	90
(*R*)-TolBINAP	**83**	87
(*R*)-DTBM-SEGPHOS	**84**	30
(*R*)-DTBM-MeO-BIPHEP	**85**	78
Indapybox	**86**	74

a) reactions performed in CH_2Cl_2 under air; isolated yields.



UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

The structures of dinuclear gold(I) complexes **80**, **82**, **84** and **86** were confirmed by X-ray diffraction. $[Au_2(\mu\text{-}S\text{-binap})_2](SbF_6)_2$ **82** shows a strong aurophilic interaction (Au-Au distance: 2.870 Å, Figure 13).[129] Interestingly, complex **86** with two indapybox ligands shows coordination of Au^I with the oxazolidinyl nitrogens and not with the pyridine (Figure 15). Although the Au-Au distances in complexes **80** (Figure 12), **84** (Figure 14) and **86** (Figure 15) are outside the rage (2.5-3.5 Å) considered significant for aurophilic interactions[130] there are significant deviations from the linear coordination, with the two Au(I) centers pointing in the same direction.

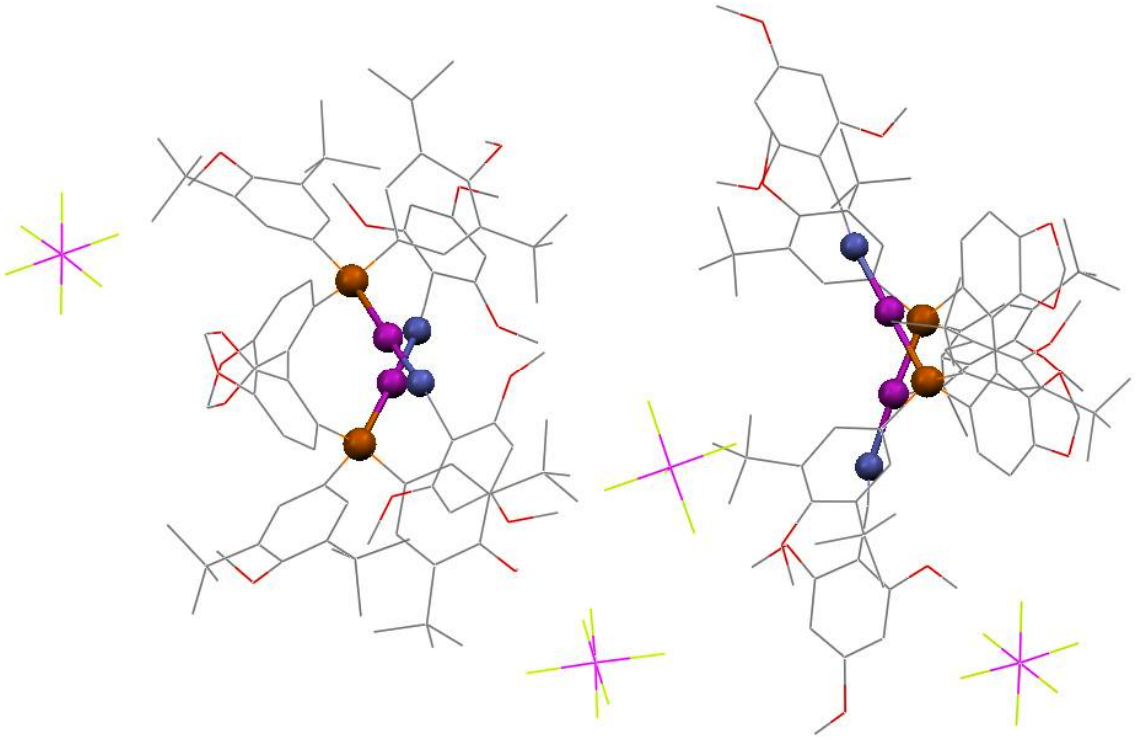


Figure 12. X-ray structure of complex **80**. Solvent molecules and H atoms omitted; P, N and Au atoms highlighted; Au-Au distances: 3.740 Å, 3.754 Å; P-Au-N angles 173.1º, 173.9º, 170.4º, 179.7º.

129. Meso complex $[Au_2(\mu\text{-}R\text{-binap})(\mu\text{-S-binap})](CF_3CO_2)_2$ also showed a strong aurophilic interaction. The unit cell of this complex contains two similar but independent macrocycles, each containing one *R*-binap and one *S*-binap ligand, with the distance Au-Au = 2.8700(4) Å in one complex, identical to that of **12**, whereas the in the second complex this interaction was slightly weaker (Au-Au = 2.9125(4) Å): Wheaton, C. A.; Jennings, M. C.; Puddephatt, R. J. *Z. Naturforsch.* **2009**, *64b*, 1469-1477.

130. (a) Schmidbaur, H.; Schier, A. *Chem. Soc. Rev.* **2008**, *37*, 1931-1951; (b) Schmidbaur, H.; Graf, W.; Müller, G. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 417-419.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

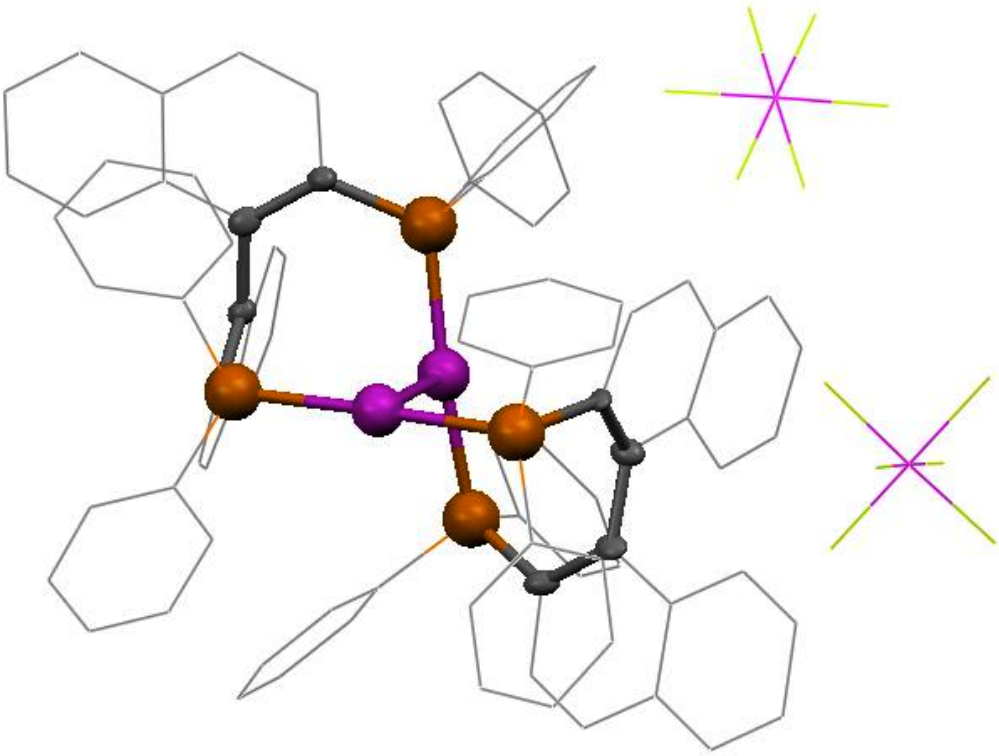


Figure 13. X-ray structure of complex **82**; H atoms and solvent molecules omitted; core macrocycle highlighted; Au-Au distance 2.87 Å; P-Au-P angles 166.9º, 173.7º.

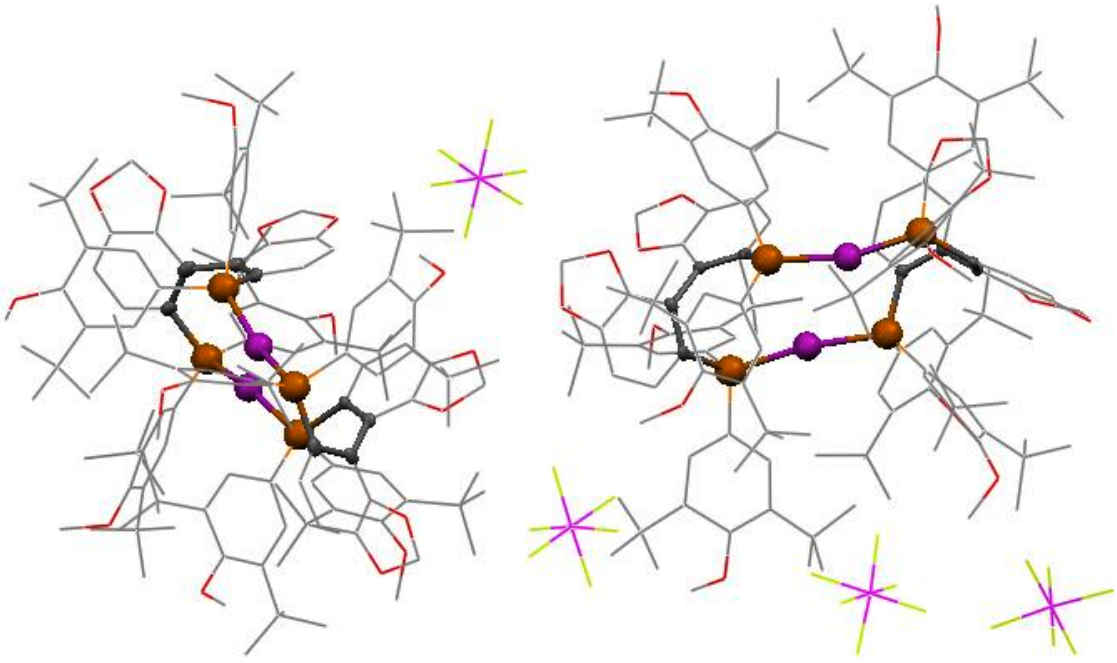


Figure 14. Xray structure of complex **84**; core macrocycle highlighted; solvent molecules and H atoms omitted; Au-Au distances 3.752 Å, 3.821 Å; P-Au-P angles 159.7º, 162.0º, 162.3º, 159.3º.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

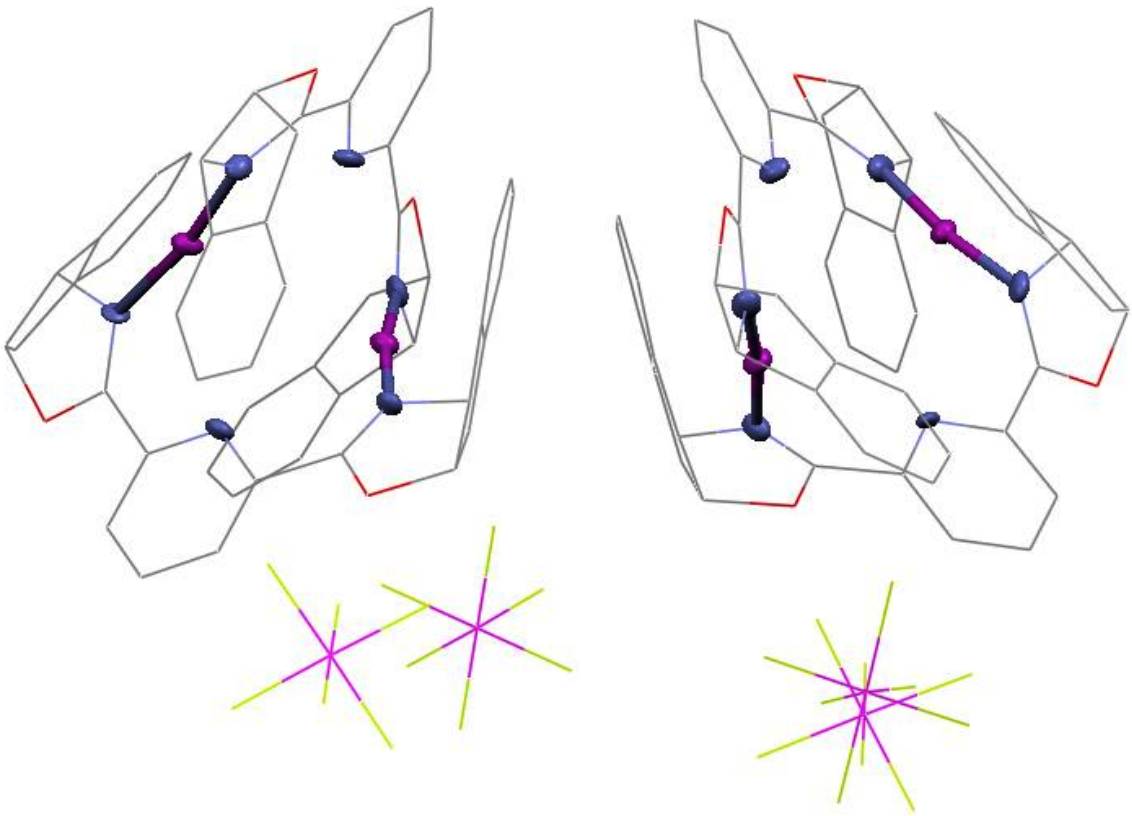


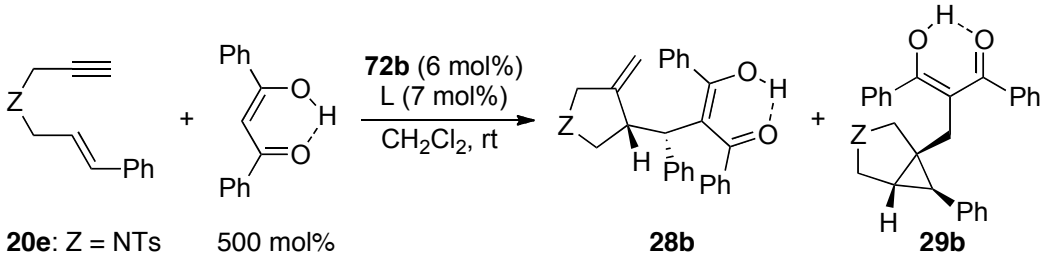
Figure 15. X-ray structure of complex **86**; solvent molecules and H atoms omitted for clarity; Au-Au distances: 3.627 Å, 3.757 Å; N-Au-N angles: 169.9 º, 171.1 º 172.9º, 173.0º.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Applications: catalysis

The complexes thus formed in situ were tested as catalysts for the addition of dibenzoylmethane to an enyne (Table 30).[61,131]

Table 30. Addition of dibenzoylmethane to **20e** using Au(I) catalysts prepared *in situ*.[a]



20e: Z = NTs 500 mol% **28b** **29b**

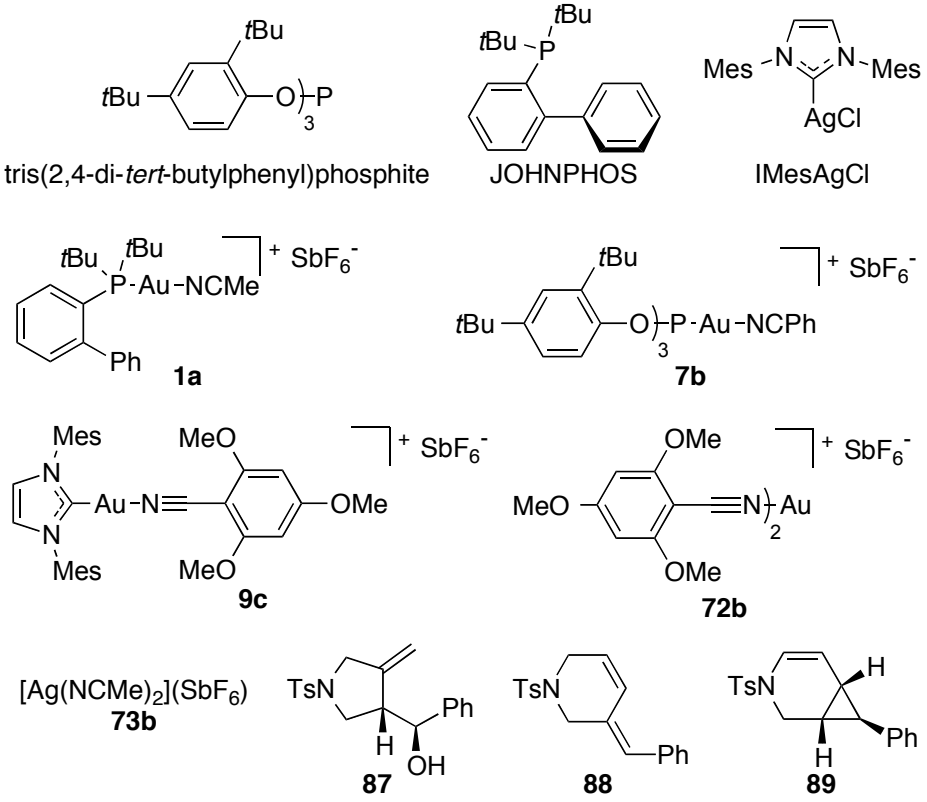
Entry	Catalyst	Additive (mol%)	Time (h)	Conv. (%)	Selectivity (**28b** / **29b**)	Yield (%)
1	JOHNPHOS + **72b**	-	14	95	36 : 64	43[b]
2	JOHNPHOS + **72b**	**73b** (6)	0.5	100[c]	35 : 65	53[c]
3	**1a**[d]	-	0.5	100[c]	33 : 67	85[c]
4	tris(2,4-di-*tert*-butylphenyl)phosphite + **72b**	-	216	35	100 : 0	14[e]
5	tris(2,4-di-*tert*-butylphenyl)phosphite + **72b**	$AgNTf_2$ (12)	0.25	100[c]	75 : 25	69[c]
6	**7b**[d]	-	0.33	100[c]	77 : 23	83[c]
7	IMesAgCl + **72b**	-	0.5	100	2 : 98	84[f]
8	**9c**[d]	-	0.33	100[c]	<1 : 99	86[c]
9	-[g]	$AgNTf_2$ (12)	5	84	100 : 0	2[h]
10	**7** (5 mol%)[g]	**73b** (5)	0.1	100[c]	77 : 23	76[c]

a) The catalytic mixture was prepared under air and added over the solution of the enyne under air; dry CH_2Cl_2 was used; yields and conversions determined by NMR; b) additional products were observed: **87** (4%), **88** (9%), **89** (4%); c) the completion of the reaction was determined by TLC, isolated yields; d) the isolated catalys (5 mol% was used); e) **87** (3%) was also observed; f) **89** (4%) was also observed; g) reation performed in the absence of **72b**; h) **89** (29%) was also observed.

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

131. Table 10 entries 1, 3, 6.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



However, it was found out that tmbn had an inhibiting effect for this reaction. Whereas in the case of the IMes ligand, the reaction took slightly longer to finish (Table 30, entry 7), in the case of JOHNPHOS (entry 1) the effect was more significant and the reaction with a phosphite-gold complex was almost completely stopped (entry 4). After trying several additives[132] it was found that silver salts could successfully trap the excess tmbn and revert the phosphite-Au system to its original reactivity and selectivity (Table 30, entries 2, 5). Due to its reduced sensitivity to moisture, $[Ag(NCMe)_2](SbF_6)$ **73b** was particularly useful for this methodology. This complex can also successfully activate gold precatalyst **7** (Table 30, entry 10).

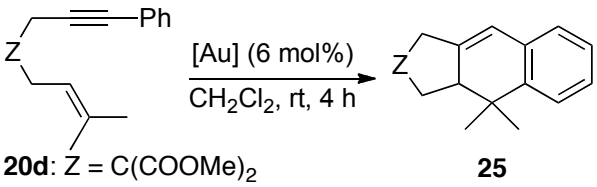
The catalyst loading of (n+1) mol% **72b** / (n+2) mol% L was meant to ensure (n) mol% [L-Au] while making sure that even after experimental errors during weighing, there will be no unreacted **72b** left, as this complex decomposes in the presence of most enynes.

132. $LiNTf_2$, $LiSbF_6$, $TlPF_6$ and $NaBAr^F$ were also tested. These additives fail to compete with gold for the tmbn ligand either due to poor solubility of weak Lewis acidity.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

The gold complexes formed in situ were also tried in the [4+2] cycloaddition of aryl-enynes,[23] with hopes of developing its enantioselective version. Dimeric $[Au_2(L\text{-}L)_2](SbF_6)_2$ complexes **83** and **86** proved totally unreactive in this reaction. However, $[Au_2(L\text{-}L)(tmbn)_2](SbF_6)_2$ **80-81** complexes did catalyze this transformation (Table 31). The complexes formed in situ performed similarly to the isolated ones. A similar inhibiting effect of tmbn could be observed.

Table 31. Au(I) catalyzed enantioselective scheletal rearrangement of enyne **20d**.[a]



20d: Z = $C(COOMe)_2$ **25**

Catalyst (system)	Time (days)	Yield (%)	ee
72b + 73b + (R)-DTBM-SEGPHOS[b]	7	84	67±2
80[c]	4	92	61±2
72b + 73b + (R)-DTBM-MeO-BIPHEP[b]	17	73	68±1
81[c]	10	86	64±3

a) isolated yield; b) L-L (4 mol%) and **73b** (7 mol%) were successively added over **72b** (7 mol%), see experimental part; c) 3 mol% $[Au_2(L\text{-}L)(tmbn)_2](SbF_6)_2$ catalyst.

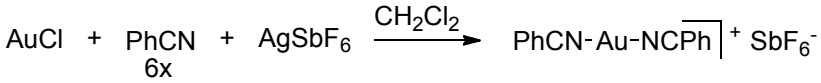
23. Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178-6179.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Experimental Part

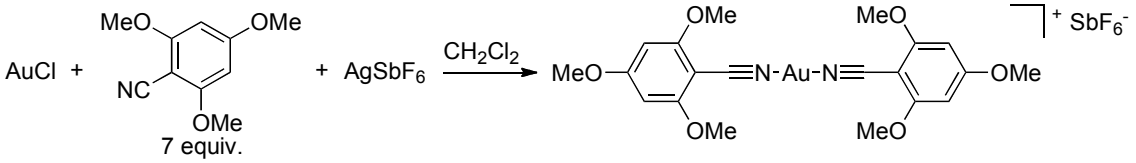
Unless otherwise specified: all experiments were perfomed under ambient conditions (atmosphere, lighting, temperature) in closed flasks or vials using magnetic stirring; CH_2Cl_2 and Et_2O were dried under N_2 using a solvent purification system (SPS); all other solvents and reagents were used as received. 2,4,6-trimetoxybenzonitrile (**tmbn**) from Alfa Aesar (yellow) was purified by short column flash chromatography (CH_2Cl_2) to yield a white crystalline solid.

Bis(benzonitrile)gold(I) hexafluoroantimonate (72a)



This complex was synthesized and stored under Ar. Dry PhCN (0.31 mL, 3.0 mmol) was added over a suspension of AuCl (116 mg, 0.500 mmol) in CH_2Cl_2 (5 mL) resulting in an immediate color change from orange to yellow. The suspension was stirred vigorously for 5 min in the dark then a solution of $AgSbF_6$ (175 mg, 0.500 mmol) in CH_2Cl_2 (5 mL) was added. The mixture was stirred vigorously at room temperature for 43 h in the absence of light and under positive Ar pressure. The precipitate was filtered off (suction through Teflon) then over the resulting CH_2Cl_2 solution (aprox 5 mL) Et_2O (10 mL) was added. The resulting white precipitate was decanted under Ar, washed with Et_2O (2x5 mL) and vacuum dried. It turned pale purple during vacuum drying and subsequent storage in the glovebox. Yield 188 mg (59%). IR: 2296 cm^{-1} (CN); ^1H NMR (400 MHz, CD_2Cl_2) δ 7.97 (d, J = 7.7 Hz, 4H), 7.92 (t, J = 7.7 Hz, 2H), 7.69 (t, J = 8.0 Hz, 4H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 137.38 (CH), 134.56 (CH), 130.49 (CH), 119.85 (CN), 106.57 (C); Anal. calcd. for $C_{14}H_{10}AuF_6N_2Sb \cdot 0.5H_2O$: C, 25.95; H, 1.71; N, 4.32; found: C, 25.78; H, 1.61; N, 4.87; MS (TOF MS ES+) peak corresponding to $[Au(PhCN)_3]^+$ observed at 506.0.

Bis(2,4,6-trimethoxybenzonitrile)gold(I) hexafluoroantimonate (72b)



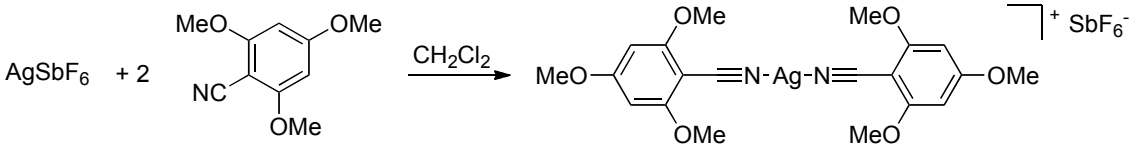
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Under an Ar atmosphere, AuCl (466 mg, 2.00 mmol) and tmbn (2.77 g, 14.0 mmol) were vigorously stirred in CH_2Cl_2 (20 mL) in the dark for 10 min then a solution of $AgSbF_6$ (703 mg, 2.00 mmol) in CH_2Cl_2 (20 mL) was added. The mixture was stirred in the dark for 20 min, then it was filtered through 2 Teflon filters (under air) and $CHCl_3$ (comerial grade, 40 mL) and Et_2O (40 mL) were added. The precipitate was filtered, air dried and vacuum dried (65 ºC, overnight) to yield a white solid (1.23-1.37 g, 75-83%). mp 226-231 (dec); IR: 2278 cm^{-1} (CN); ^1H NMR (400 MHz, CD_2Cl_2) δ 6.16 (s, 4H), 3.94 (s, 12H), 3.93 (s, 6H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 169.91 (C), 166.61 (C), 118.89 (CN), 91.57 (CH), 78.30 (C), 57.19 (CH_3), 56.85 (CH_3); MALDI-MS calcd. for $C_{20}H_{22}AuN_2O_6^+$ $[M\text{-}SbF_6]^+$: 583.1; found: 583.1; anal. calcd. for: $C_{20}H_{22}AuF_6N_2O_6Sb$: C, 29.33; H, 2.71; N, 3.42;. Found: C, 29.26; H, 2.87; N, 3.47.

Phosphine test: the nitrile complex (7.3 mg for tmbn or 5.5 mg for PhCN) and 6.6 mg 2-(di-*t*-Bu-phosphino)biphenyl were dissolved in 0.5 mL $CDCl_3$ and the ratio Au:Ag was determined by integration of the ^{31}P NMR spectra. The results were in concordance with the ones obtained by integration of the ^1H NMR spectra.

Recovery of the desired complex from a compromised sample: 1.18 g sample prepared as above was found to contain silver (mol ratio Au : Ag = 3 : 1). This solid was precipitated from CH_2Cl_2 (40 mL)/$CHCl_3$ (40 mL)/Et_2O (20 mL) and dried as above in order to obtain the desired complex, free of silver (0.63 g, 39%).

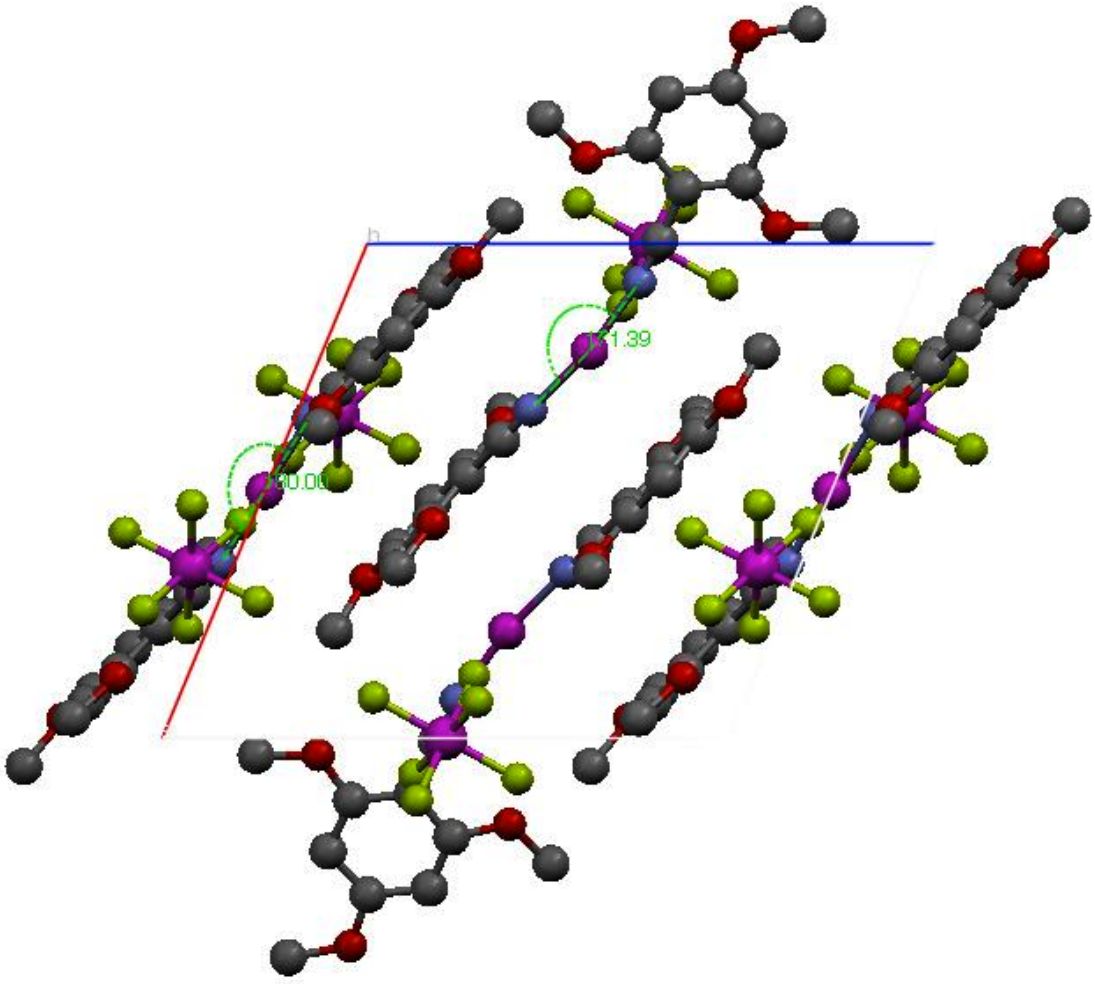
Bis(2,4,6-trimethoxybenzonitrile)silver(I) hexafluoroantimonate (73a)



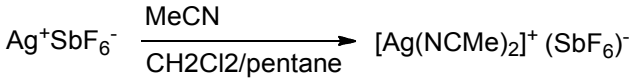
2,4,6-trimethoxybenzonitrile (213 mg, 1.10 mmol) was dissolved in a solution of $AgSbF_6$ (176 mg, 0.500 mmol) in CH_2Cl_2 (5 mL) then the mixture was filtered (Teflon) and Et_2O (10 mL) was added. The resulting precipitate was filtered and vacuum dried (50 ºC, 5 h). Yield: 315 mg (86%) bright white solid. X ray quality crystals were obtained by slow diffusion of Et_2O over a solution of the complex in CH_2Cl_2. ^1H NMR (400 MHz, CD_2Cl_2) δ 6.15 (s, 4H), 3.92 (s, 12H), 3.91 (s, 6H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 168.56 (C), 165.73 (C), 118.77 (C), 91.33 (CH), 80.09 (C), 56.98 (CH_3), 56.61 (CH_3); MS ESI calcd for $C_{20}H_{22}AgN_2O_6$ (M-SbF_6): 493.1, found: 493.0. Elem.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Anal. calcd for $C_{20}H_{22}AgF_6N_2O_6Sb$: C, 32.91; H, 3.04; N, 3.84; found: C, 33.05; H, 3.11; N, 3.92.



Bis(acetonitrile)silver(I) hexafluoroantimonate (73b)

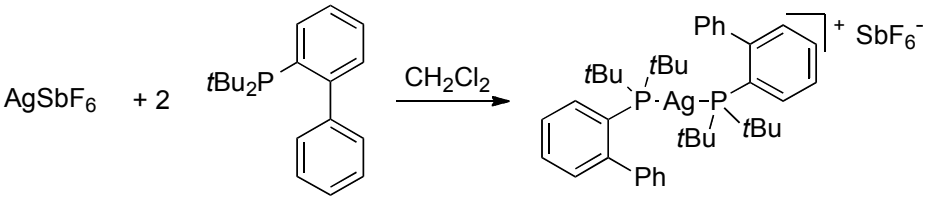


The following operations were performed in a glovebox, under Ar. A solution of $AgSbF_6$ (0.702 g, 2.00 mmol) in dry CH_2Cl_2 10 mL, was suction filtered (through a Teflon HPLC filter) and transferred to a vial, then 0.23 mL dry MeCN (0.23 mL, 4.4 mmol) was added. The resulting clear solution was carefully layered with pentane (10 mL) and allowed to stand; after 24 hours large crystals had formed. The mixture was shaked until the liquid phase homogenized, and the turbid solution was allowed to stand over the large crystals for another 24 h. The resulting crop of crystals were separated by decantation and vacuum dried (739 mg, 90%). The crystalline complex didn't change in

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

aspect or NMR properties after being stored for a week under ambient moisture and lighting; afterwords it was stored in a aluminium covered vial in a dessicator and weighed under air when needed. At least one of the resulting crystals was of X-ray quality. ^{1}H NMR (500 MHz, CD_2Cl_2) δ 2.29 (s, 6H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 120.38 (C), 2.62 (CH_3); Anal. calcd. for $C_4H_6AgF_6N_2Sb$: C, 11.29; H, 1.42; N, 6.58; found: C, 10.86; H, 1.40; N, 6.56.

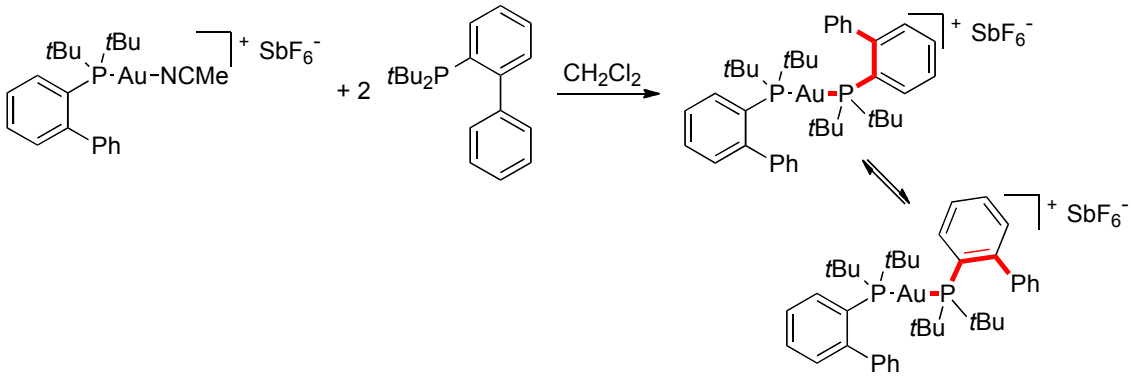
[(JohnPHOS)$_2$Ag]$^+$(SbF$_6$)$^-$ (74)



o-biphenylyl-di-*tert*-butylphosphine (306 mg, 1.00 mmol) was dissolved in a solution of $AgSbF_6$ (176 mg, 0.500 mmol) in CH_2Cl_2 (5 mL) then the mixture was filtered over a 1 cm pad of Celite which was washed with CH_2Cl_2 (2x5 mL). The combined solution was evaporated to dryness then the complex was precipitated from CH_2Cl_2 (2mL) / Et_2O (6 mL), filtered and vacuum dried (50 ºC, 4 h). Yield: 442 mg (94%) white solid. X Ray quality crystals were obtained by slow diffusion of Et_2O over a solution of the complex in CH_2Cl_2. ^{1}H{^{31}P} NMR (400 MHz, $CDCl_3$) δ 7.88-7.86 (m, 2H), 7.58-7.48 (m, 8H), 7.41 (t, J = 7.5 Hz, 2H), 7.32-7.30 (m, 4H), 7.15-7.12 (m, 2H), 1.21 (s, 36H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.69-148.51 (m, C), 142.87-142.82 (m, C), 135.16 (d, J = 6.0 Hz, CH), 133.90 (t, J = 3.4 Hz, CH), 131.19 (s, CH), 129.93 (br s, CH), 129.58 (br s, CH), 129.02 (s, CH), 127.19-127.13 (m, CH), 125.92-125.63 (m, C), 35.61-35.57 (m, C), 31.32 (br s, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ 48.2 (two centered d, J = 566, 491 Hz, 2P); HRMS ESI calcd for $C_{40}H_{54}AgP_2$ (M-SbF_6): 703.2752, found: 703.2739. Elem. Anal. Calcd for $C_{40}H_{54}AgF_6P_2Sb$: C, 51.09; H, 5.79; found: C, 50.98; H, 5.74.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

[(JohnPHOS)$_2$Au]$^+$(SbF$_6$)$^-$ (75)



Method a. A mixture of the cationic acetonitrile complex (77 mg, 0.10 mmol) and 2-di-*t*-butylphosphinobiphenyl (30 mg, 0.10 mmol) were dissolved in CH_2Cl_2 (1 mL) then Et_2O (2 mL) anf hexane (1 mL) were added. The precipitate was filtered and vacuum dried (50 ºC, 5 h) to yield the desired complex as a white solid (81 mg, 79%). $^1H\{^{31}P\}$ NMR (500 MHz, $CDCl_3$, -50 ºC) δ symetrical isomer: 7.85-7.84 (m, 2H), 7.61-7.51 (m, 8H), 7.46-7.43 (m, 2H), 7.37-7.33 (m, 4H), 7.14-7.10 (m, 2H), 1.23 (s, 36 H); unsymetrical isomer (selected signals): 8.00 (d, J = 7.8 Hz, 1H), 7.81 (d, J = 7.9 Hz, 1H), 7.67 (t, J = 7.8 Hz, 1H), 7.21 (d, J = 7.4 Hz, 2H), 6.95 (t, J = 7.6 Hz, 2H), 6.81 (t, J = 7.5 Hz, 1H), 1.56 (s, 18 H), 1.07 (s, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$, -50 ºC) could not be assigned due to the coupling with ^{31}P, broadening and overlapping of the signals (PENDANT, 1024 scans). ^{31}P NMR (202 MHz, $CDCl_3$, -50 ºC) δ symetrical isomer: 71.8 (s, 2P); unsymetrical isomer: 107.9 (d, J = 275 Hz, 1P), 70.4 (d, J = 275 Hz, 1P); HRMS ESI calcd. for $C_{40}H_{54}AuP_2$ (M-SbF_6): 793.3366, found: 793.3394. Anal. calcd. for $C_{40}H_{54}AuF_6P_2Sb$: C, 46.67; H, 5.29; found: C, 46.53; H, 5.05.

Ratio Symmetrical/unsymmetrical:

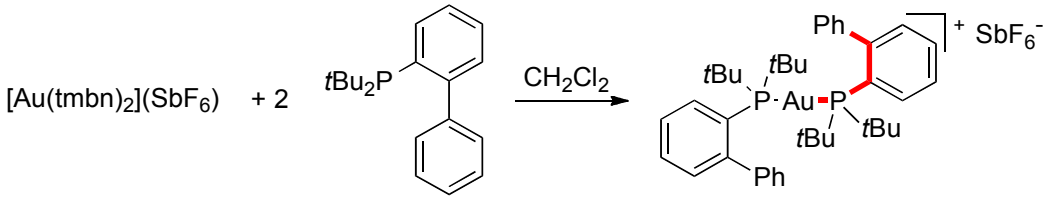
In CD_3CN, room temperature: 1.3 : 1

In $CDCl_3$, room temperature: 1.4 : 1

In $CDCl_3$, -20 ºC: 2 : 1

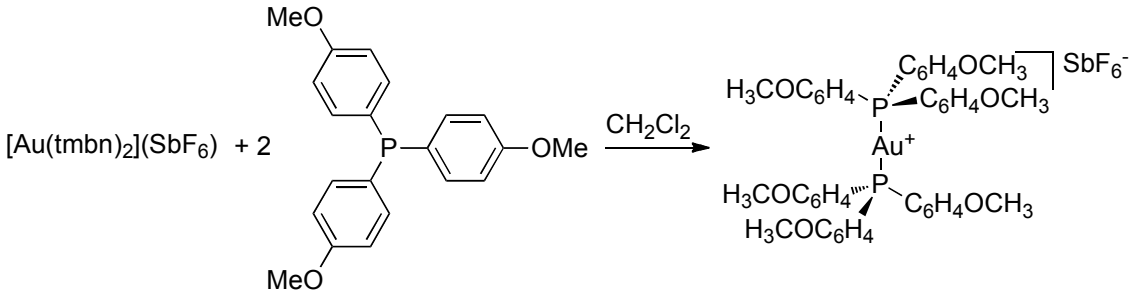
In $CDCl_3$, -50 ºC: 3 : 1

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



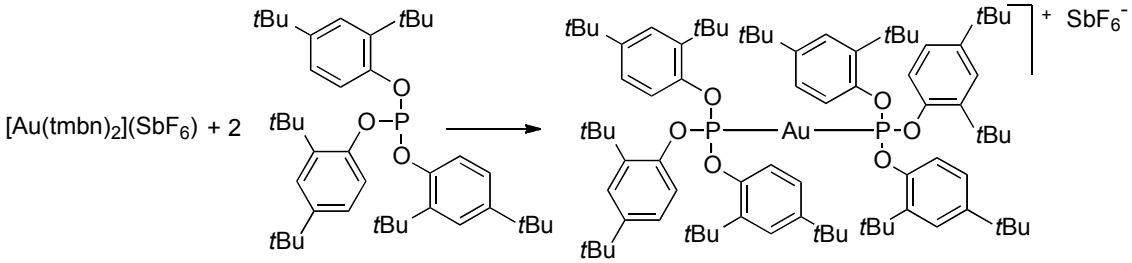
Method b. Over a solution of $[Au(tmbn)_2](SbF_6)$ (82 mg, 0.10 mmol) in CH_2Cl_2 (2 mL), solid 2-di-*t*-butylphosphinobiphenyl (60 mg, 0.20 mmol) was added. Upon complete dissolution, addition of Et_2O (12 mL) resulted in the formation of a white precipitate which was allowed to stand overnight, then it was filtered and vacuum dried (50 ºC, 2 h). (89 mg, 87%)

Bis(tris(4-methoxyphenyl)phosphine)gold(I) hexafluoroantimonate (76)



A solution of $[Au(tmbn)_2](SbF_6)$ (41 mg, 50 μmol) in CH_2Cl_2 (1 mL) of was added with shaking over a solution tris(4-methoxyphenyl)phosphine (35 mg, 0.1 mmol) in CH_2Cl_2 (0.5 mL) then Et_2O (12 mL) was added and the mixture was allowed to stand for 3 days in a closed vial. The resulting crystaline solid was filtered and vacuum dried (52 mg, 91% yield). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.47-7.40 (m, 12H), 7.09-7.06 (m, 12H), 3.87 (2, 18H); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 163.02 (C), 135.55 (t, J = 8.3 Hz, CH), 118.79 (t, J = 32.8 Hz, C), 115.4 (t, J = 6.5 Hz, CH), 55.64 (CH_3); ^{31}P NMR (162 MHz, CD_2Cl_2) δ 44.9 (s, 2P); MALDI-MS calcd. for $C_{42}H_{42}AuO_6P_2^+$ $[M\text{-}SbF_6]^+$: 901.2; found 901.2; anal. calcd. for $C_{42}H_{42}AuF_6O_6P_2Sb$: C, 44.35; H, 3.72; found: C, 44.27; H, 3.63.

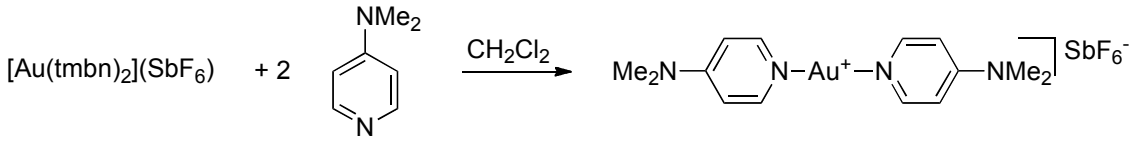
Bis(tris(2,4-di-*tert*-butylphenyl)phosphite)gold(I) hexafluoroantimonate (77)



UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

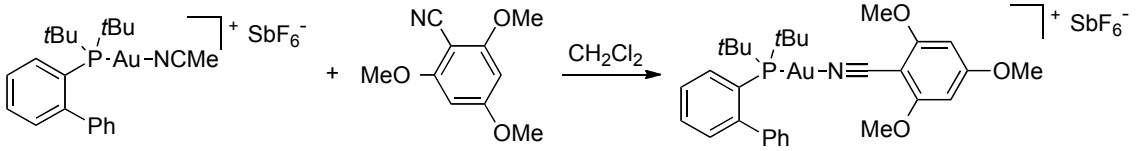
A solution of $[Au(tmbn)_2](SbF_6)$ (41 mg, 50 μmol) in CH_2Cl_2 (1 mL) was added over a solution of tris(2,4-di-*tert*-butylphenyl) phosphite (67 mg, 0.10 mmol) in CH_2Cl_2 (0.5 mL) then MeOH (9 mL) was added. The mixture was allowed to stand overnight resulting in the formation of small crystals. After sonication/homogenization (5 s), the mixture was allowed to stand 24 h. The resulting crystals were separated by decantation, washed with MeOH (2x0.5 mL) and vacuum dried at 60 ºC overnight (66 mg, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 1.9 Hz, 6H), 7.07-7.01 (m,12H), 1.30 (s, 54H), 1.29 (s, 54H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.83 (C), 146.75 (t, J = 2.8 Hz, C), 139.51 (t, J = 3.4 Hz, C), 126.29 (CH), 124.51 (CH), 119.06 (t, J = 4.1 Hz, CH), 35.15 (C), 34.94 (C), 31.49 (CH_3), 30.54 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ 123.0 (s, 2P); ESI-MS calcd. for $C_{84}H_{126}AuO_6P_2^+$ $[M\text{-}SbF_6]^+$: 1489.9; found: 1489.6; Anal. calcd. for $C_{84}H_{126}AuF_6O_6P_2Sb$: C, 58.43; H, 7.36; found: C, 58.37; H, 6.91.

$[Au(DMAP)_2](SbF_6)$ (78)



A solution of $[Au(tmbn)_2]SbF_6$ (0.164 g, 0.200 mmol) in CH_2Cl_2 (4 mL) was mixed with a solution of DMAP (49 mg, 0.40 mmol) in CH_2Cl_2 (4 mL) then Et_2O (4 mL) was added. The precipitate was filtered and vacuum dried (50 ºC, 5 h) to yield the desired complex as a lilac solid (0.123 g, 91%). ^{1}H NMR (400 MHz, CD_3CN) δ 8.05-8.02 (m, 4H), 6.68-6.65 (m,4H), 3.06 (s, 12H); ^{13}C NMR (100 MHz, CD_3CN) δ 156.32 (C), 151.56 (CH), 108.92 (CH), 39.77 (CH_3); HRMS-ESI calcd for $C_{14}H_{20}N_4Au^+$ $(M\text{-}SbF_6)^+$: 441.1354; found: 441.1348. Anal. Calcd. for $C_{14}H_{20}AuF_6N_4Sb$: C, 24.84; H, 2.98; N, 8.28; found: C, 24.89; H, 2.95; N, 8.35;

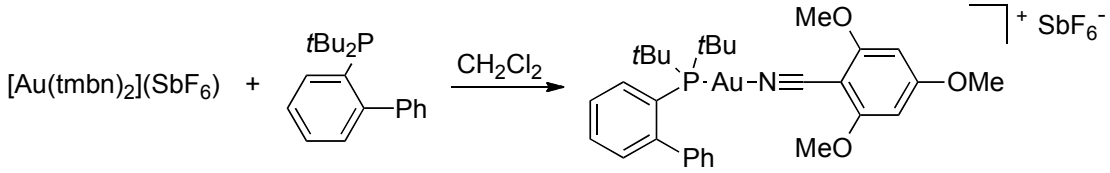
$[Au(JohnPHOS)(MeCN)](SbF_6)$ (1c)



Method a. A mixture of the cationic acetonitrile complex **1a** (77 mg, 0.10 mmol) and 2,4,6-trimethoxybenzonitrile (20 mg, 0.10 mmol) were dissolved in CH_2Cl_2 (1 mL). After evaporation and vacuum drying (50 ºC, 5 h) desired complex was obtained as a

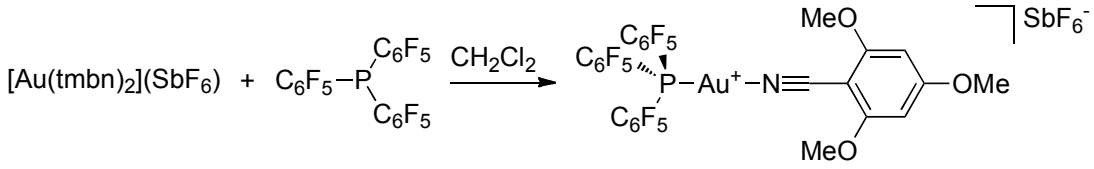
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

white foamy solid (93 mg, 100%). $^{1}H\{^{31}P\}$ NMR (400 MHz, $CDCl_3$) δ 7.91-7.89 (m, 1H), 7.62-7.58 (m, 2H), 7.49-7.45 (m, 2H), 7.42-7.38 (m, 1H), 7.35-7.33 (m, 1H), 7.20 (d, J = 7.2 Hz, 2H), 6.21 (s, 2H), 4.01 (s, 6H), 3.96 (s, 3H), 1.45 (s, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.01 (C), 165.75 (C), 149.15 (d, J = 12.1 Hz, C), 142.52 (d, J = 6.8 Hz, C), 133.33 (d, J = 5.4 Hz, CH), 133.27 (d, J = 1.9 Hz, CH), 131.67 (d, J = 2.4 Hz, CH), 129.60 (CH), 129.09 (CH), 128.44 (CH), 127.83 (d, J = 7.7 Hz, CH), 123.95 (d, J = 51.2 Hz, C), 117.05 (br s, C), 91.40 (CH), 77.36 (C), 56.81 (CH_3), 56.62 (CH_3), 38.23 (d, J = 27.3 Hz, C), 31.02 (d, J = 6.1 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ 60.6 (s, 1P); HRMS ESI calcd. for $C_{30}H_{38}AuNO_3P$ ($M\text{-}SbF_6$): 688.2, found: 688.0; Anal. calcd. for $C_{30}H_{38}AuF_6NO_3PSb$: C, 38.98; H, 4.14; N, 1.52; found: C, 39.42; H, 4.03; N, 1.70.



Method b. A solution of 2-di-tBu-phosphinobiphenyl (30 mg, 0.10 mmol) in CH_2Cl_2 was added dropwise with shaking over a solution of $[Au(tmbn)_2](SbF_6)$ (82 mg, 0.10 mmol) in CH_2Cl_2 (2 mL), then Et_2O was added until turbidity was observed (15 mL). The mixture was allowed to stand overnight at room temperature, then 4 h at 10 ºC (fridge) then 24 h at room temperature. The resulting white microcrystalline powder was filtered and vacuum dried (50 ºC, 5 h) (76 mg, 90% yield).

(Tris(perfluorophenyl)phosphine)(2,4,6-trimethoxybenzonitrile)gold(I) hexafluoroantimonate (79)

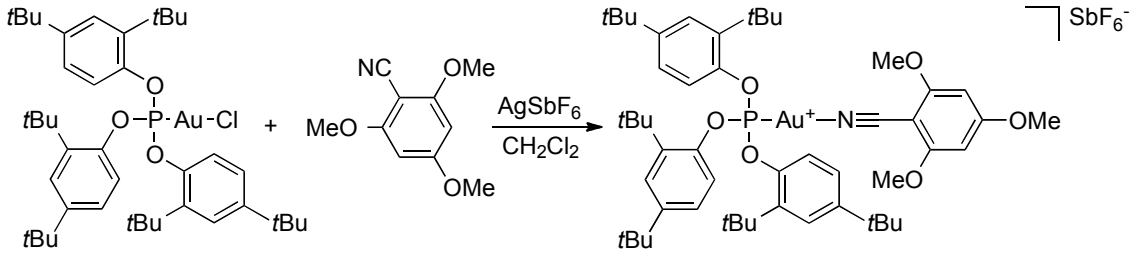


A solution of tris(pentafluorophenyl)phosphine (27 mg, 0.05 mmol) in CH_2Cl_2 (0.25 mL) was added over a stirred solution of $[Au(tmbn)_2](SbF_6)$ (41 mg, 0.05 mmol) in CH_2Cl_2 (1 mL) then Et_2O was added (3.75 mL) and the solution was allowed to stand overnight in a closed vial. The resulting precipitate was filtered and vacuum dried (50 ºC, 5 h) to yield the desired complex as a white solid (46mg, 79% yield). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.16 (s, 2H), 3.94 (s, 6H), 3.93 (s, 3H); ^{19}F NMR (376 MHz, CD_2Cl_2)

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

δ -127.5 (br s, 6F), -140.0 (br s, 3F), -156.50 (br s, 6F); ^{31}P NMR (162 MHz, CD_2Cl_2) δ -37.1 (br s, 1P); ESI-MS calcd. for $C_{28}H_{11}AuF_{15}NO_3P^+$ [M-SbF_6]: 922.0; found: 921.8; anal. calcd. for $C_{28}H_{11}AuF_{21}NO_3PSb$: C, 29.04; H, 0.96; N, 1.21; found: C, 28.96; H, 1.01; N, 1.38.

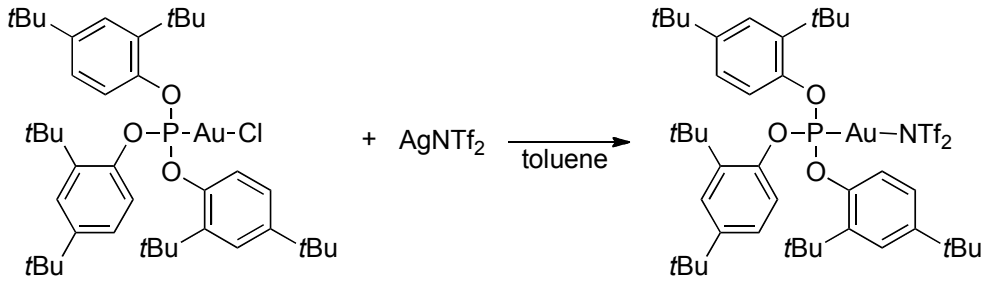
(Tris(2,4-di-*tert*-butylphenyl)phosphite)(2,4,6-trimethoxybenzonitrile)gold(I) hexafluoroantimonate (7c)



A solution of $AgSbF_6$ (70.2 mg, 0.200 mmol) in CH_2Cl_2 (2 mL) was added over a solution of gold (I) chloro(tris(2,4-di-*tert*-butylphenyl)phosphite) (176 mg, 0.200 mmol) and 2,4,6-trimethoxybenzonitrile (38.7 mg, 0.2 mmol) in dry CH_2Cl_2 (2 mL). A white precipitate appeared immediately. After stirring for 5 min, the mixture was filtered (double Teflon filter), evaporated and vacuum dried. (60 ºC, 2 h). The cationic complex was obtained as a light purple solid which contained solvated CH_2Cl_2 (complex : CH_2Cl_2 = 1 : 1) (239 mg, 88%). ^{1}H{^{31}P} NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 2.5 Hz, 3H), 7.35 (d, J = 8.6 Hz, 3H), 7.21 (dd, J = 8.6, 2.5 Hz, 3H), 6.18 (s, 2H), 5.30 (s, 2H), 3.95 (s, 3H), 3.93 (s, 6H), 1.47 (s, 27 H), 1.31 (s, 27 H); ^{13}C NMR (PENDANT, 101 MHz, $CDCl_3$) δ 169.92 (C), 166.24 (C), 149.39 (C), 147.06 (d, J = 6.6 Hz, C), 139.38 (d, J = 7.2 Hz, C), 126.10 (CH), 124.65 (CH), 121.37 (C), 119.03 (d, J = 8.4 Hz, CH), 91.63 (CH), 77.23 (C), 56.99 (CH_3), 56.83 (CH_3), 35.29 (C), 34.91 (C), 31.46 (CH_3), 30.72 (CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 91.8 (s, 1P); MS ESI Calcd for $C_{52}H_{74}AuNO_6P$ (M-SbF_6): 1036.5, found: 1036.1; Anal. calcd. for $C_{52.5}H_{75}AuClF_6NO_6PSb$ (M+0.5CH_2Cl_2): C, 47.94; H, 5.75; N, 1.06; found: C, 47.95; H, 5.62; N, 1.25.

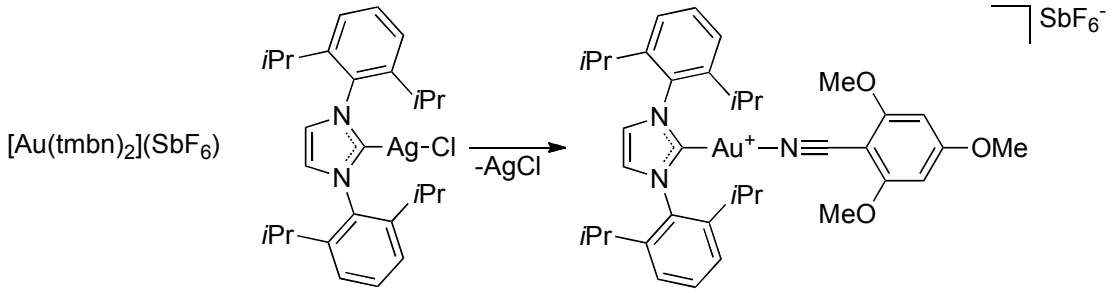
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

(Tris(2,4-di-*tert*-butylphenyl)phosphite)(bis(trifluoromethane)sulfonimidato)gold(I) (7d)



A solution of $AgNTf_2$ (40 mg, 0.10 mmol) in C_6H_6 (1 mL)/CH_2Cl_2 (1 mL) was added over a solution of the phosphite gold complex (88 mg, 0.10 mmol) in CH_2Cl_2 (1 mL). The mixture was stirred for 15 min then it was filtered through Celite and vacuum dried to yield a colorles oil. This oil didn't yield any precipitate from CH_2Cl_2/MeOH and it could not be crystallized from toluene. It slowly turned into a grey solid after 1 week under ambient conditions (95 mg, 85%). $^1H\{^{31}P\}$ NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 2.5 Hz, 3H), 7.36 (d, J = 8.6 Hz, 3H), 7.17 (dd, J = 8.6, 2.5 Hz, 3H), 1.42 (s, 27H), 1.30 (s, 27H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 95.6 (s, 1P); ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.7 (s, 6F); Anal. calcd. for $C_{44}H_{63}AuF_6NO_7PS_2$: C, 47.02; H, 5.65; N, 1.25; S, 5.71; found C, 47.20; H, 5.66; N, 1.14; S, 5.61. MALDI (pyrene-CH_2Cl_2) m/z$^+$ = 1046.5 [M-NTf_2+pyrene+H]$^+$

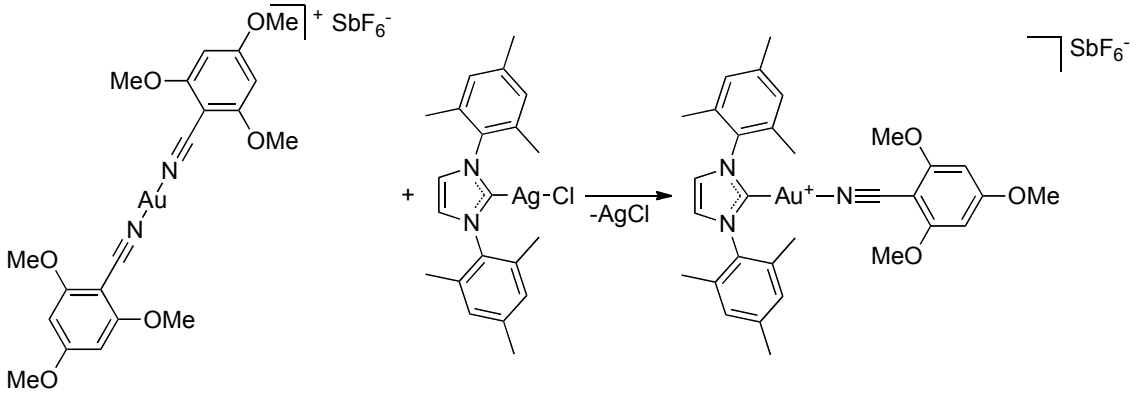
[1,3-Bis(2,6-diisopropyl-phenyl)imidazol-2-ylidene](2,4,6-trimethoxybenzonitrile)gold(I) hexafluoroantimonate (8c)



A solution of IPrAgCl (82 mg, 0.15 mmol) in CH_2Cl_2 (1.5 mL + 0.5 mL rinsing) was added over a solution of $[Au(tmbn)_2](SbF_6)$ (123 mg, 0.15 mmol) in CH_2Cl_2 (3 mL) then the mixture was stirred for 5 min. The resulting AgCl was filtered off (through 2 HPLC Teflon filters) then the mixture was evaporated to dryness. Precipitation from $CHCl_3$ (3 mL) /Et_2O (6 mL) yielded the desired complex as white crystals which were filtered and vacuum dried at 50 ºC for 4 h (130 mg, 86% yield). ^1H NMR (400 MHz,

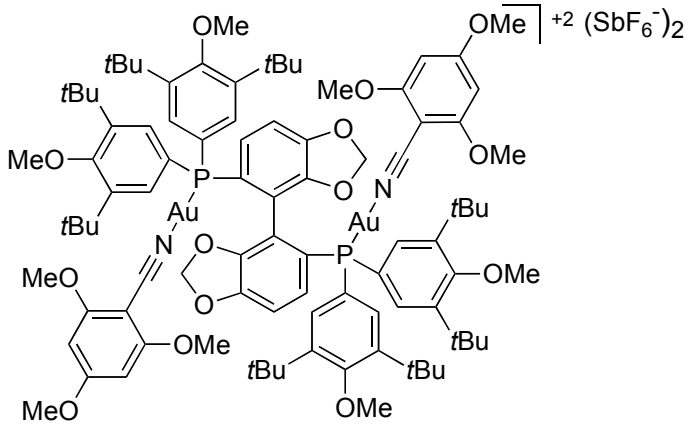
$CDCl_3$) δ 7.59 (t, J = 7.8 Hz, 2H), 7.40 (s, 2H), 7.36 (d, J = 7.8 Hz, 4H), 6.08 (s, 2H), 3.89 (s, 3H), 3.83 (s, 6H), 2.51 (septuplet, J = 6.8 Hz, 4H), 1.32 (d, J = 6.8 Hz, 12H), 1.27 (d, J = 6.8 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.26 (C), 167.06 (C), 165.76 (C), 145.80 (C), 133.38 (C), 131.39 (CH), 124.99 (CH), 124.66 (CH), 119.07 (C), 91.25 (CH), 78.10 (C), 56.75 (CH_3), 56.62 (CH_3), 29.02 (CH), 24.71 (CH_3), 24.15 (CH_3); ESI-MS calcd for $C_{37}H_{47}AuN_3O_3^+$ $[M\text{-}SbF_6]^+$: 778.3; found: 778.2; anal. calcd. for $C_{37}H_{47}AuF_6N_3O_3Sb$: C, 43.80; H, 4.67; N, 4.14; found: C, 43.95; H, 4.61; N, 4.28.

[1,3-Bis(2,4,6-trimethyl-phenyl)imidazol-2-ylidene](2,4,6-trimethoxybenzonitrile)gold(I) hexafluoroantimonate (9c)



A solution of IMesAgCl (27 mg, 60 μmol) in CH_2Cl_2 (0.6 mL) was added over a solution of $[Au(tmbn)_2](SbF_6)$ (49 mg, 60 μmol) in CH_2Cl_2 (1.2 mL). After shaking for 5 min, the mixture was filtered through a Teflon HPLC filter, then Et_2O (7.2 mL) was added and the mixture was allowed to stand overnight. $[(IMes)Au(tmbn)](SbF_6)$ was obtained as colorless needles which were separated by decantation, washed with Et_2O (3x1.2 mL) and vacuum dried (39 mg, 70%).

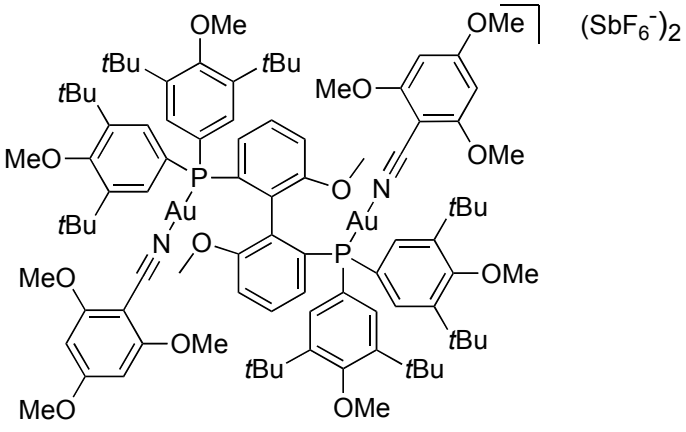
$[Au_2((R)\text{-DTBM-SEGPHOS})(tmbn)_2](SbF_6)_2$ (80)



UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

A solution of (R)-DTBM-SEGPHOS (35.4 mg, 30 μmol) in CH_2Cl_2 (0.3 mL), was added dropwise with shaking over a solution of $[Au(tmbn)_2](SbF_6)$ (49 mg, 60 μmol) in CH_2Cl_2 (1.2 mL) then Et_2O (commercial grade, 6 mL) was added and the turbid mixture was allowed to stand overnight in a capped vial. The resulting small colorless needles were filtered and vacuum dried (50 ºC, overnight) (52 mg, 71% yield). X-ray quality crystals were obtained by slow counter diffusion of Et_2O into a solution of the complex in CH_2Cl_2. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.36 (d, J = 14.9 Hz, 4H), 7.31 (d, J = 14.8 Hz, 4H), 7.07 (dd, J = 8.1, 1.6 Hz, 2H), 6.97 (dd, J = 12.1, 8.1 Hz, 2H), 6.14 (s, 4H), 5.77 (d, J = 1.3 Hz, 2H), 4.75 (d, J = 1.3 Hz, 2H), 3.92 (s, 6H), 3.86 (s, 12H), 3.74 (s, 6H), 3.51 (s, 6H), 1.35 (s, 36H), 1.30 (s, 36H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 170.05 (C), 166.24 (C), 164.44 (C), 164.25 (C), 152.01 (C), 149.91 (d, J = 14.2 Hz, C), 146.20 (d, J = 13.1 Hz, C), 146.08 (d, J = 12.9 Hz, C), 133.98 (d, J = 16.5 Hz, CH), 133.42 (d, J = 16.9 Hz, CH), 131.32 (d, J = 7.4 Hz, CH), 120.80 (d, J = 42.8 Hz, C), 120.23 (d, J = 42.1 Hz, C), 119.58 (d, J = 72.8 Hz, C), 119.66-119.56 (m, C), 117.89-117.70 (m, C), 109.95 (d, J = 12.5 Hz, CH), 103.01 (CH_2), 91.80 (CH), 77.86 (C), 65.36 (CH_3), 64.93 (CH_3), 57.18 (CH_3), 57.02 (CH_3), 36.47 (C), 36.38 (C), 31.87 (CH_3), 31.81 (CH_3); ^{31}P NMR (162 MHz, CD_2Cl_2) δ 23.1 (s, 2P); ESI-MS calcd for $C_{94}H_{122}Au_2F_6N_2O_{14}P_2Sb^+$ $[M\text{-}SbF_6]^+$: 2195.7, found: 2195.5. Anal. calcd. for: $C_{94}H_{122}Au_2F_{12}N_2O_{14}P_2Sb_2$: C, 46.44; H, 5.06; N, 1.15; found: C, 46.31; H, 4.93; N, 1.31.

$[Au_2$((*R*)-DTBM-MeO-BIPHEP)$(tmbn)_2](SbF_6)_2$ (81)

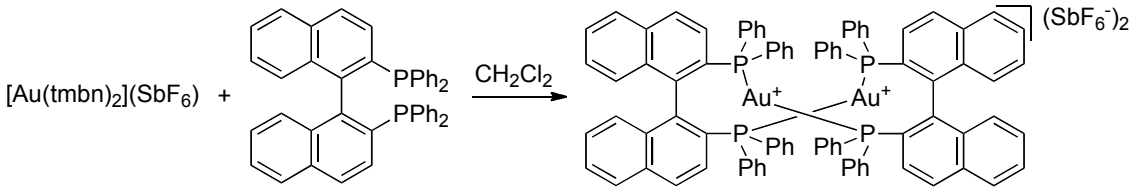


A solution of (R)-DTBM-MeO-BIPHEP (58 mg, 50 μmol) in CH_2Cl_2 (0.5 mL) was added with shaking over a solution of $[Au(tmbn)_2](SbF_6)$ (82 mg, 0.10 mmol) in CH_2Cl_2 (2 mL) then Et_2O (10 mL) and was added. After 24 h the mixture was homogenized by sonication and a small amount of solid $[Au(tmbn)_2](SbF_6)$ (<0.1 mg)

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

was added then the mixture was allowed to stand for 24 h. The resulting small needles were separated by decantation, washed with Et_2O (2x1 mL) and vacuum dried at 50 ºC, overnight (78 mg, 65% yield). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.66 (td, J = 8.1, 2.9 Hz, 2H), 7.36 (d, J = 14.7 Hz, 4H), 7.18 (d, J = 14.6 Hz, 4H), 7.13 (d, J = 8.5 Hz, 2H), 7.04 (dd, J = 11.2, 7.7 Hz, 2H), 6.14 (s, 4H), 3.93 (s, 6H), 3.86 (s, 12H), 3.75 (s, 6H), 3.52 (s, 6H), 2.85 (s, 6H), 1.38 (s, 36H), 1.29 (s, 36H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 169.97 (br s, C), 166.23 (br s, C), 164.12 (d, J = 3.0 Hz, C), 163.66 (d, J = 2.9 Hz, C), 160.01 (d, J = 12.7 Hz, C), 146.33 (d, J = 12.7 Hz, C), 146.06 (d, J = 12.3 Hz, C), 133.31 (d, J = 15.9 Hz, CH), 133.01 (d, J = 15.4 Hz, CH), 131.06 (d, J = 11.9 Hz, CH), 129.95-129.73 (m, C), 128.08 (d, J = 68.1 Hz, C), 127.15 (d, J = 6.3 Hz, CH), 121.92 (d, J = 70.1 Hz, C), 120.10 (d, J = 72.8 Hz, C), 118.94 (C), 115.24 (d, J = 1.9 Hz, CH), 91.75 (CH), 77.90 (br s, C), 65.30 (CH_3), 64.86 (CH_3), 57.10 (CH_3), 56.97 (CH_3), 54.77 (CH_3), 36.54 (C), 36.34 (C), 31.95 (CH_3); ^{31}P NMR (162 MHz, CD_2Cl_2) δ 20.8 (s, 2P); ESI-MS calcd. for $C_{94}H_{126}Au_2F_6N_2O_{12}P_2Sb^+$ $[M\text{-}SbF_6]^+$: 2167.7, found: 2167.4; anal. calcd. for $C_{94}H_{126}Au_2F_{12}N_2O_{12}P_2Sb_2$: C, 46.98; H, 5.28; N, 1.17; found: C, 46.79; H, 5.06; N, 1.33.

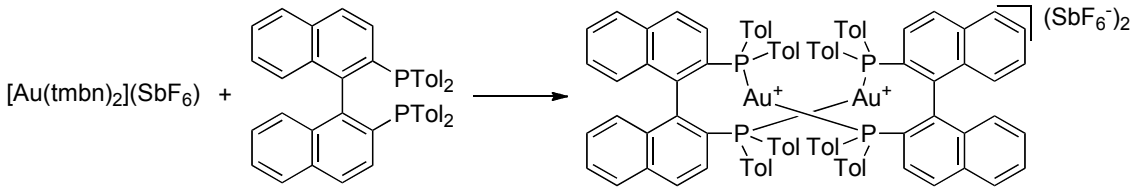
$[Au_2((S)\text{-BINAP})_2](SbF_6)_2$ (82)



A solution of (S)-BINAP (62 mg, 0.10 mmol) in CH_2Cl_2 (0.5 mL) was added over a stirred solution of $[Au(tmbn)_2](SbF_6)$ (82 mg, 0.10 mmol) in CH_2Cl_2 (2 mL) then the mixture was evaporated to dryness. Precipitation from CH_2Cl_2 (1 mL) / $CHCl_3$ (1 mL) / Et_2O (1 mL) resulted in a white solid which was filtered and vacuum dried at 65 ºC overnight (96 mg, 90%). X-ray quality crystals were obtained by slow evaporation of a solution of the complex in CH_2Cl_2 / $CHCl_3$ = 1 : 1. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.81 (t, J = 7.3 Hz, 4H), 7.69 (d, J = 8.2 Hz, 4H), 7.62-7.51 (m, 20H), 7.43 (t, J = 7.5 Hz, 4H), 7.16 (t, J = 7.3 Hz, 4H), 7.11 (dt, J = 8.9, 5.1 Hz, 4H), 6.94-6.80 (m, 20H), 6.37 (d, J = 8.6 Hz, 4H); ^{31}P NMR (162 MHz, CD_2Cl_2) δ 44.3 (s, 4P); MALDI-MS calcd. for. $C_{88}H_{64}Au_2F_6P_4Sb^+$ $[M\text{-}SbF_6]^+$: 1875.2, found: 1875.5; anal. calcd. for $C_{88}H_{64}Au_2F_{12}P_4Sb_2$: C, 50.07; H, 3.06; found: C, 50.00; H, 3.03.

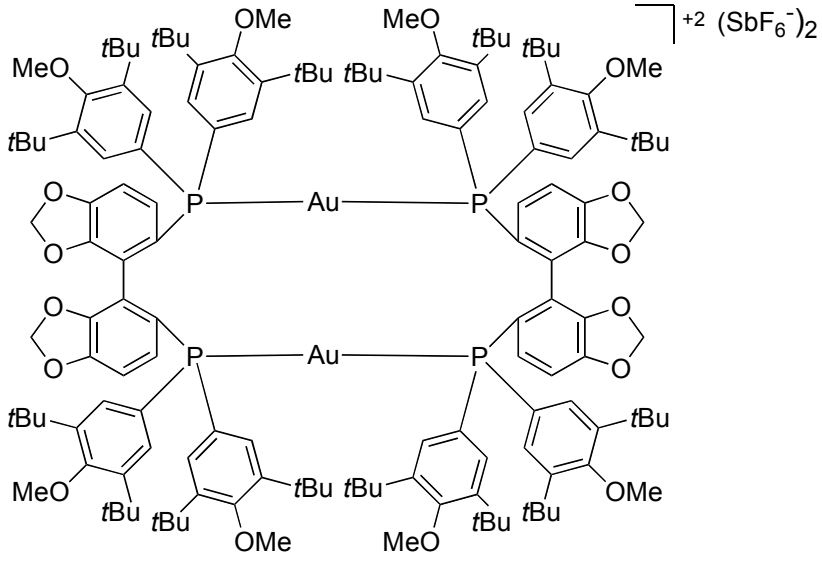
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

$[Au_2((R)\text{-TolBINAP})_2](SbF_6)_2$ (83)



A solution of (R)-TolBINAP (68 mg, 0.1 mmol) in CH_2Cl_2 (2.5 mL) was added over a stirred solution of $[Au(tmbn)_2](SbF_6)$ (82 mg, 0.1 mmol) in CH_2Cl_2 (2.5 mL) then hexane was added (5 mL) and the resulting mixture was applied directly over a slurry packed silica gel column (2x15 cm) and purified by flash chromatography (hexane/CH_2Cl_2/MeCN = 3 : 7 : 1 to 0 : 4 : 1). The desired complex was obtained as a pale yellow solid (97 mg, 87%). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.63 (d, J = 8.1 Hz, 4H), 7.52-7.47 (m, 12H), 7.42 (ddd, J = 8.2, 6.9, 1.0 Hz, 4H), 7.33 (d, J = 7.9 Hz, 8H), 7.04 (dt, J = 8.8, 5.2 Hz, 4H), 6.87 (ddd, J = 8.6, 6.9, 1.2 Hz, 4H), 6.76-6.70 (m, 8H), 6.59 (d, J = 7.8 Hz, 8H), 6.32 (d, J = 8.6, 4H), 2.58 (s, 12H), 2.16 (s, 12H); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 144.56 (C), 143.63 (C), 141.69 (C), 134.81 (CH), 134.28 (CH), 134.09 (C), 133.86 (C), 131.27 (CH), 130.39 (CH), 129.70 (CH), 129.34 (CH), 128.43 (CH), 128.35 (CH), 128.11 (CH), 126.99 (CH), 126.73 (m, C), 125.76 (m, C), 122.56 (m, C), 21.79 (CH_3), 21.35 (CH_3); ^{31}P NMR (162 MHz, CD_2Cl_2) δ 43.0 (s, 4P); MALDI (dctb/CH_2Cl_2) m/z$^+$ 1986.2 [M-SbF_6], 1537.2 [TolBINAP$Au_4(H_2O)_4$-H], 1285.2 [TolBINAPAu_3O], 875.2 [M/2-SbF_6], 467.5 [dctb$AuH_2(H_2O)$]; Anal. calcd. for $C_{96}H_{80}Au_2F_{12}P_4Sb_2$: C, 51.87; H, 3.63; found: C, 51.86; H, 3.77.

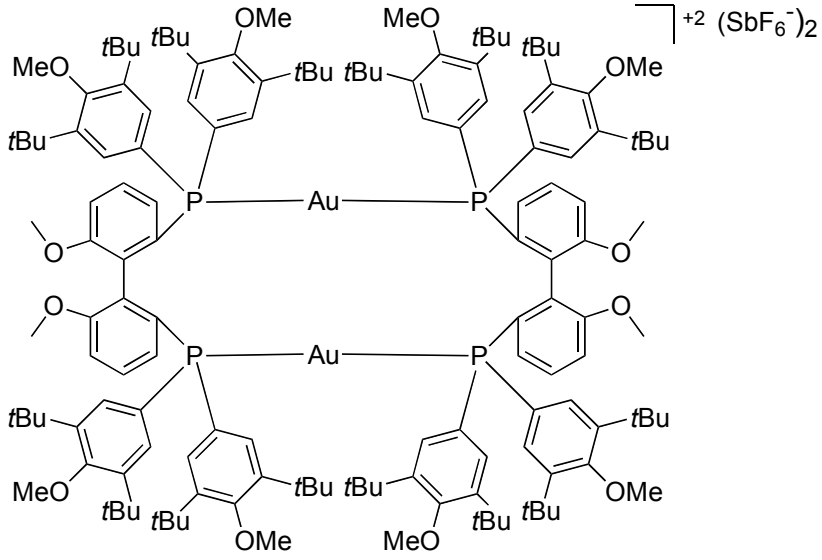
$[Au_2((R)\text{-DTBM-SEGPHOS})_2](SbF_6)_2$ (84)



UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

A solution of $[Au(tmbn)_2](SbF_6)$ (82 mg, 0.10 mmol) in CH_2Cl_2 (2.0 mL) was added dropwise with shaking over a solution of (R)-DTBM-SEGPHOS (118 mg, 0.10 mmol) in CH_2Cl_2 (0.5 mL), then Et_2O (commercial grade, 10 mL) was added and the mixture was allowed to settle overnight in a capped vial. The resulting white powder was filtered and vacuum dried (50 ºC, overnight) (49 mg, 30% yield). X-ray quality crystals were obtained by slow counter diffusion of Et_2O into a solution of the complex in CH_2Cl_2. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.25 (dd, J = 18.1, 2.1 Hz, 2H), 7.91 (dd, J = 15.5, 2.2 Hz, 2H), 7.56 (dd, J = 17.8, 8.1 Hz, 2H), 7.49 (dd, J = 9.2, 2.1 Hz, 2H), 7.35 (dd, J = 15.3, 2.2 Hz, 2H), 7.26 (dd, J = 17.0, 2.1 Hz, 2H), 7.11 (dd, J = 9.9, 2.2 Hz, 2H), 7.01 (dd, J = 8.0, 0.9 Hz, 2H), 6.66-6.61 (m, 4H), 6.44 (dd, J = 11.1, 2.2 Hz, 2H), 6.22 (dd, J = 13.5, 2.2 Hz, 2H), 5.89 (s, 2H), 5.83 (s, 2H), 5.73 (d, J = 1.2 Hz, 2H), 4.84 (d, J = 1.2 Hz, 2H), 3.76 (s, 6H), 3.71 (s, 6H), 3.69 (s, 6H), 3.61 (s, 6H), 1.34 (s, 18H), 1.34 (s, 18H), 1.31 (s, 18H), 1.24 (s, 18H), 1.06 (s, 18H), 1.04 (s, 18H), 0.95 (s, 18H), 0.65 (s, 18H); ^{31}P NMR (162 MHz, CD_2Cl_2) δ 48.5 (apparent dt, J = 318, 4 Hz, 2P), 41.8 (apparent dt, J = 318, 4 Hz, 2P); MALDI-MS calcd for $C_{148}H_{200}Au_2F_6O_{16}P_4Sb^+$ $[M\text{-}SbF_6]^+$: 2988.2; found: 2988.2; Anal. calcd. for $(C_{74}H_{100}AuF_6O_8P_2Sb)_2$: C, 55.13; H, 6.25; found: C, 55.05; H, 6.05.

$[Au_2((R)$-DTBM-MeO-BIPHEP$)_2](SbF_6)_2$ (85)

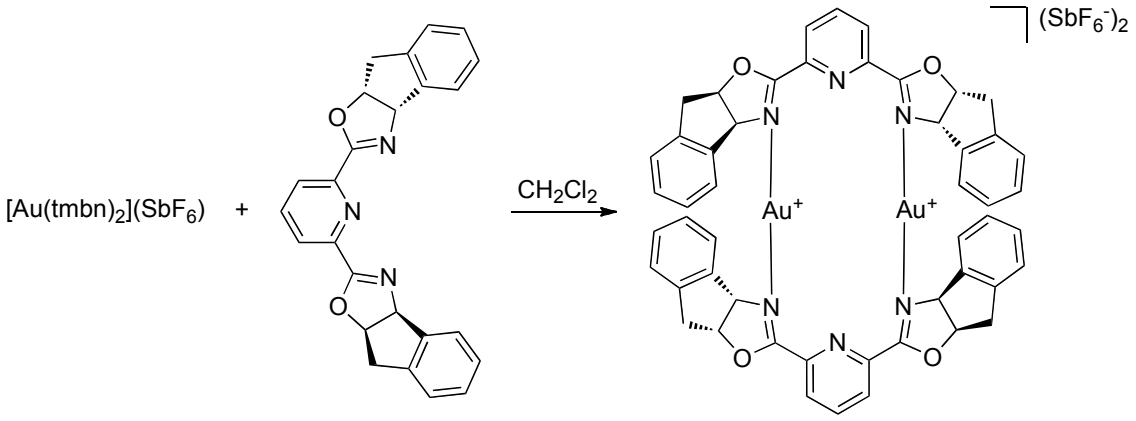


A solution of (R)-DTBM-MeO-BIPHEP (35 mg, 30 μmol) in CH_2Cl_2 (0.3 mL) was added with shaking over a solution of $[Au(tmbn)_2](SbF_6)$ (25 mg, 30 μmol) in CH_2Cl_2 (0.6 mL) then Et_2O (4.5 mL) was added. The mixture was allowed to stand overnight and the resulting small needles were separated by decatation, washed with Et_2O (2x0.9

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

mL) and vacuum dried at 50 ºC, overnight (37 mg, 78% yield). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.25 (dd, J = 17.8, 2.1 Hz, 2H), 7.85-7.77 (m, 4H), 7.62-7.56 (m, 4H), 7.29 (dd, J = 15.2, 2.2 Hz, 2H), 7.16 (td, J = 8.1, 2.8 Hz, 2H), 7.10 (dd, J = 17.1, 2.0, 2H), 7.02 (dd, J = 9.7, 2.1 Hz, 2H), 6.75-6.66 (m, 6H), 6.28 (dd, J = 10.8, 2.2 Hz, 2H), 6.15 (dd, J = 13.2, 2.2 Hz, 2H), 3.74 (s, 6H), 3.73 (s, 6H), 3.65 (s, 6H), 3.65 (s, 6H), 3.58 (s, 6H), 3.28 (s, 6H), 1.36 (s, 18H), 1.34 (s, 18H), 1.29 (s, 18H), 1.21 (s, 18H), 1.04 (s, 18H), 1.00 (s, 18H), 0.93 (s, 18H), 0.57 (s, 18H); ^{31}P NMR (162 MHz, CD_2Cl_2) δ 48.3-46.3 (AA'BB' system, J_{AB} = 312 Hz, 2P), 42.9-40.9 (AA'BB' system, J_{AB} = 312 Hz, 2P); MALDI-MS calcd. for $C_{148}H_{208}Au_2F_6O_{12}P_4Sb^+$ [M-SbF_6]: 2932.3; found: 2932.2; anal. calcd. for $(C_{74}H_{104}AuF_6O_6P_2Sb)_2$: C, 56.10; H, 6.62; found: C, 56.08; H, 6.40.

[Au_2((Indapybox)$_2$](SbF_6)$_2$ (86)

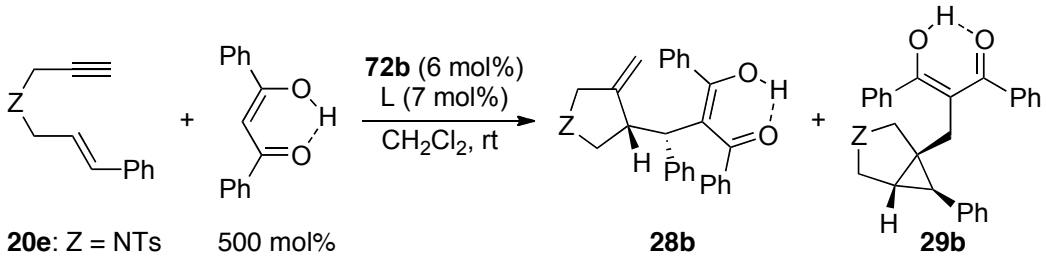


A solution of pyridine derivative (79 mg, 0.20 mmol) in CH_2Cl_2 (4 mL) was added over a solution of [Au(tmbn)$_2$](SbF_6) (164 mg, 0.200 mmol) in CH_2Cl_2 (4 mL) then Et_2O (12 mL) was added. A grey precipitate was obtained which was filtered and vacuum dried (50 ºC) (128 mg, 74%). X-ray quality crystals were obtained by slow diffusion of Et_2O into a solution of the complex in CH_2Cl_2.

^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.44 (s, 6H), 7.30 (t, J = 7.4 Hz, 4H), 7.12 (d, J = 7.6 Hz, 4H), 6.88 (d, J = 7.6 Hz, 4H), 6.81 (t, J = 7.4 Hz, 4H), 5.92 (ddd, J = 9.0, 7.7, 1.9 Hz, 4H), 5.70 (d, J = 9.0 Hz, 4H), 3.44 (dd, J = 18.5, 7.7 Hz, 4H), 3.12 (d, J = 18.7 Hz, 4H); ^{13}C NMR (100 MHz, CD_2Cl_2, PENDANT) δ 167.20 (C), 143.65 (C), 141.26 (CH), 139.43 (C), 137.32 (C), 129.84 (CH), 129.41 (CH), 127.62 (CH), 127.26 (CH), 124.72 (CH), 86.60 (CH), 76.89 (CH), 38.83 (CH_2); MALDI (pyrene-CH_2Cl_2) m/z^{+} 1415.0 [M-(SbF_6)]$^{+}$, 1180.1 [M-2(SbF_6)]$^{+}$, 1022.1 [M-2Au-(SbF_6)]$^{+}$, 983.2 [M-Au-2(SbF_6)]$^{+}$, 822.0 [M-2Au-2(SbF_6)+2(H_2O)]$^{+}$, 793.2 [M/2-(SbF_6)+pyrene+H]$^{+}$, 603.1 [AuH_2(pyrene)$_2$]$^{+}$,

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

590.1 $[M/2-(SbF_6)]^+$; Anal. calcd. for $(C_{25}H_{19}AuF_6N_3O_2Sb)_2$: C, 36.35; H, 2.32; N, 5.09; found: C, 36.25; H, 2.37; N, 4.82.



20e: Z = NTs 500 mol% **28b** **29b**

General procedure for the trapping of enyne with dibenzoylmethane[61]

To a solution of $[Au(tmbn)_2](SbF_6)$ (9.8 mg, 12 μmol) and additive in CH_2Cl_2 (0.3 mL) a solution of the ligand (14 μmol) in CH_2Cl_2 (0.3 mL) was added then the resulting mixture was added to a solution of enyne **20e** (65 mg, 0.20 mmol) and dibenzoylmethane (224 mg, 1.00 mmol) in CH_2Cl_2 (1.4 mL). The reaction mixture was stirred at room temperature for the time indicated in Table. The mixture was filtered trough silica gel which was further eluted with CH_2Cl_2 several times.

Determination of the yield by NMR: a precisely weighed quantity of internal standard (1,3,5 trimethoxybenzene or BHT) was added to the CH_2Cl_2 solution and a sample of the homogeneous mixture was evaporated and analyzed by H NMR ($CDCl_3$). Compounds **28b**, **29b**,[62] **87**,[20a] **88**,[51] and **89**[133] were previously described

Isolated yield: The CH_2Cl_2 solution was concentrated over Florisil and purified by flash chromatography chromatography (hexane/EtOAc = 5:1, 3x15 cm silica) to give a mixture of products **A** and **B** as a white solid. Ratios and yield in the table. When te mixture contained traces of contaminants (dibenzoylmethane, CH_2Cl_2, EtOAc, C_{OH}), the purity of the cyclized compound was determined by H NMR and the yield was corrected accordingly.

20. (a) Nevado, C.; Charruault, L.; Michelet, V.; Nieto-Oberhuber, C.; Muñoz, M. P.; Mendez, M.; Rager, M.; Genet, J.; Echavarren, A. M. *Eur. J. Org. Chem*. **2003**, *4*, 706-713.

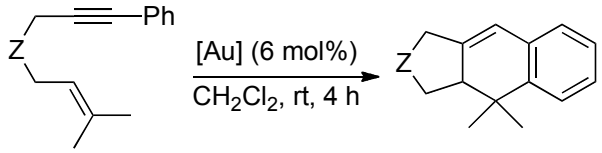
51. Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jimenez-Nuñez, E.; Nevado, C.; Herrero-Gómez, Elena; Raducan, M.; Echavarren, A. M. *Chem. Eur. J*. **2006**, *12*, 1677-1693.

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

62. Amijs, C. H. M.; Ferrer, C.; Echavarren, A. M. Chem. Commun. 2007, 698-700.

133. 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.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



20d: Z = $C(COOMe)_2$ **25**

General procedure for the enantioselective Au-catalyzed [4+2] cyclization of arylenines[23]

In situ preparation of the gold catalyst: a solution of the phosphine (4 mol%) in CH_2Cl_2 (0.4 mL) was added dropwise with shaking over a solution of $[Au(tmbn)_2](SbF_6)$ (14.4 mg, 7 mol%) in CH_2Cl_2 (0.4 mL) then solid $[Ag(NCMe)_2](SbF_6)$ (7.5 mg, 7 mol%) was added. The enyne **20d** (79 mg, 0.25 mmol) was dissolved in a solution of the gold catalyst (6 mol%) in CH_2Cl_2 (0.8 mL) and the mixture was stirred at room temperature for the time indicated in the table. The mixture was filtered over a small pad of silica (pipette) which was washed with CH_2Cl_2 (5x). The resulting solution was concentrated over Florisil (250 mg) and purified by flash chromatography (hexane/EtOAc = 20 : 1, 3x15 cm silica). The ^1H NMR spectrum of compound **25** was in concordance with the bibliography.[23] Enantiomeric excesses were determined using a CHIRALPAK ® IA column (4.6 mmΦx250mmL; eluent: hexane/iPrOH = 95 : 5; flow: 0.7 mL/min; sample concentration: 1.5 mg/mL; injection volume: 2 μL). The chromatograms were recorded at 220 nm and 270 nm and the average ee value is reported.

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

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

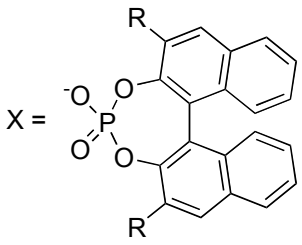
Chiral phosphate counteranions in Au(I) catalysis

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Introduction

In 2007, Toste and coworkers showed that upon activation with chiral silver phosphate salts AgX, achiral complexes [AuCl(L)] could induce enantioselectivity in the intramolecular addition of alcohols and sulfonamides to allenes.[134] The in situ formation of gold(I) complexes [AuX(L)] was postulated, but these complexes were not isolated or characterized. Two years later similar complexes were proposed in the intramolecular hydroamination of alkynes[135,136] in the presence of [AuMe(L)] complexes and phosphoric acids HX. Gold(I) complexes with chiral phosphate counteranions are likely to be the catalysts for the enantioselective synthesis of pyrazolidines, isoxazolidines and tetrahydrooxazines.[137]



Recently, $[(AuX)_2L]$ complexes (L = bidentate phosphine) were isolated as part of a methodology for the chiral resolution of $[(AuCl)_2L]$ complexes.[138] However, the authors did not to report their activity in catalysis.

134. Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science* **2007**, *317*, 496-499.

135. Aikawa, K.; Kojima, M.; Mikami, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 6073-6077.

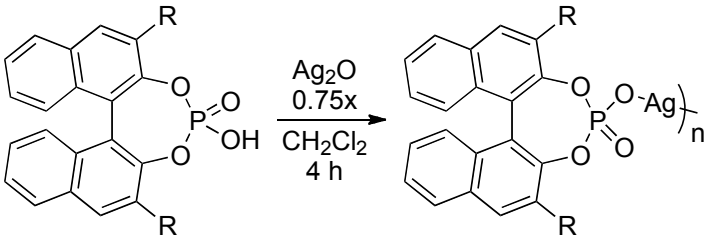
136. Liu, X.-Y.; Che, C.-M. Org. Lett. **2009**, *11*, 4204-4207.

137. La Londe, R. L.; Wang, Z. J.; Mba, M.; Lackner, A. D.; Toste, F. D. *Angew. Chem. Int. Ed.* **2010**, *49*, 598-601.

138. Aikawa, K.; Kojima, M.; Mikami, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 6073-6077.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Results and discussion



87 R = $SiPh_3$, n = 2, 92% yield
88 R = 2,4,6-*i*$Pr_3C_6H_2$, n > 2, 74% yield

Ag_2O can be successfully used instead of Ag_2CO_3 for the synthesis of chiral phosphate silver complexes. This method is more straightforward than the previously described one[134] because it avoids the use of added water and subsequent aqueous workup. A precipitation step at the end of the process ensured the purity of the resulting complexes.

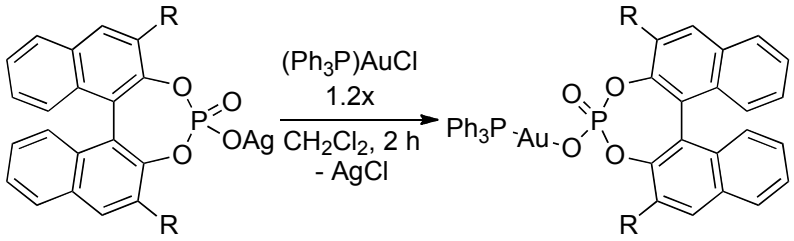
Furthemore, it was observed that in diluted CD_2Cl_2 solutions the ^{31}P NMR spectrum of the previously described silver phosphate[134] (**88**, R = 2,4,6-*i*$Pr_3C_6H_2$) consists of a triplet which becomes a multiplet and then a broad singlet in more concentrated solutions. This indicates the complex is a dimer in diluted solutions and is capable of further aggregation upon concentration.[139] The ^{31}P NMR spectrum of a CD_3CN solution of the same complex consists of a broad singlet at all studied temperatures (238-338 K).

On the other hand, the newly described Ag phosphate (**87** R = $SiPh_3$) has a ^{31}P NMR spectrum consisting of a triplet at all studied concentrations in both CD_2Cl_2 and C_6D_6. This compound is insoluble in CD_3CN, CD_3OH, and DMSO-d_6.

134. Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science* **2007**, *317*, 496-499.

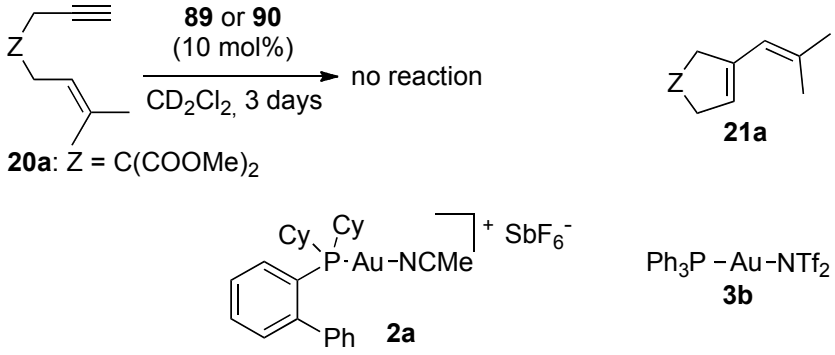
139. See X-ray structure of a similar compound in: Rueping, M.; Koenigs, R. M.; Atodiresei, I. *Chem. Eur. J.* **2010**, *16*, 9350-9365.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011



89 R = $SiPh_3$, 90% yield
90 R = 2,4,6-*i*$Pr_3C_6H_2$, 98% yield

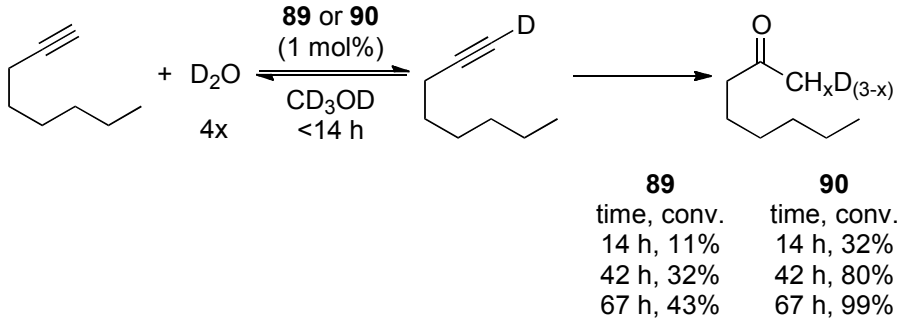
The silver-phosphate complexes were able to abstract the chloride from [AuCl(PPh_3)] (**3**) but due to their high value an excess of **3** was used in order to ensure a full conversion. Although very polar, the resulting gold complexes are robust enough and could be purified by flash chromatography on silica. Interestingly, for both complexes a long range P-P coupling could be observed by ^{31}P NMR.



The Au-phosphate complexes proved catalytically inactive in the cyclization of a highly reactive enyne. After 3 days at room temperature, no reaction was apparent by ^1H NMR. For example 0.01 mol% of neutral complex **3b** completes the transformation of enyne **20a** into **21a** to 30 min.[140] More active cationic catalyst **2a** was shown to achieve the same transformation at temperatures as low as -63 ºC ($t_{1/2}$ = 4.8 h, 2 mol% catalyst **2a**).[21]

21. 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.

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



89	**90**
time, conv.	time, conv.
14 h, 11%	14 h, 32%
42 h, 32%	42 h, 80%
67 h, 43%	67 h, 99%

However, the Au-phosphate complexes showed moderate reactivity in the hydration of 1-octyne.[141] Surprisingly deuterium exchange at the alkyne proton takes place much faster than the hydration itself. In the ^{1}H NMR spectrum of the starting alkyne, the alkyne proton and the neighbouring CH_2 have overlapped signals resulting in a complicated AB_2X_2 system (δ 2.18-2.13, m, 3H). In the first ^{1}H NMR spectrum taken after the addition of the catalyst, this signal simplifies to an AX_2 system (δ 2.15, t, J = 7.0 Hz, 2H).

Finally, conductivity measurements show that **1a** behaves like a weak electrolyte in CH_2Cl_2 (Figure 16). However, under concentrations comparable to the ones employed in catalysis, the molar conductivity of **89** is two orders of magnitude lower than that of **1a** (Figure 17).

According to the X-ray structure of complex **89** (Figure 18) the chiral phosphate behaves as a covalent ligand and not as counteranion. The observed long range coupling ($J_{P\text{-}P}$ = 3.6 Hz) indicates that this strong bonding is maintained in solution.

141. For comparison, 1 mol% of [Au(NTf$_2$)(PPh$_3$)] (**3b**) completes the same hydration (with H_2O in CH_3OH) in 24 h: Leyva, A.; Corma, A. *J. Org. Chem.* **2009**, *74*, 2067-2074.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

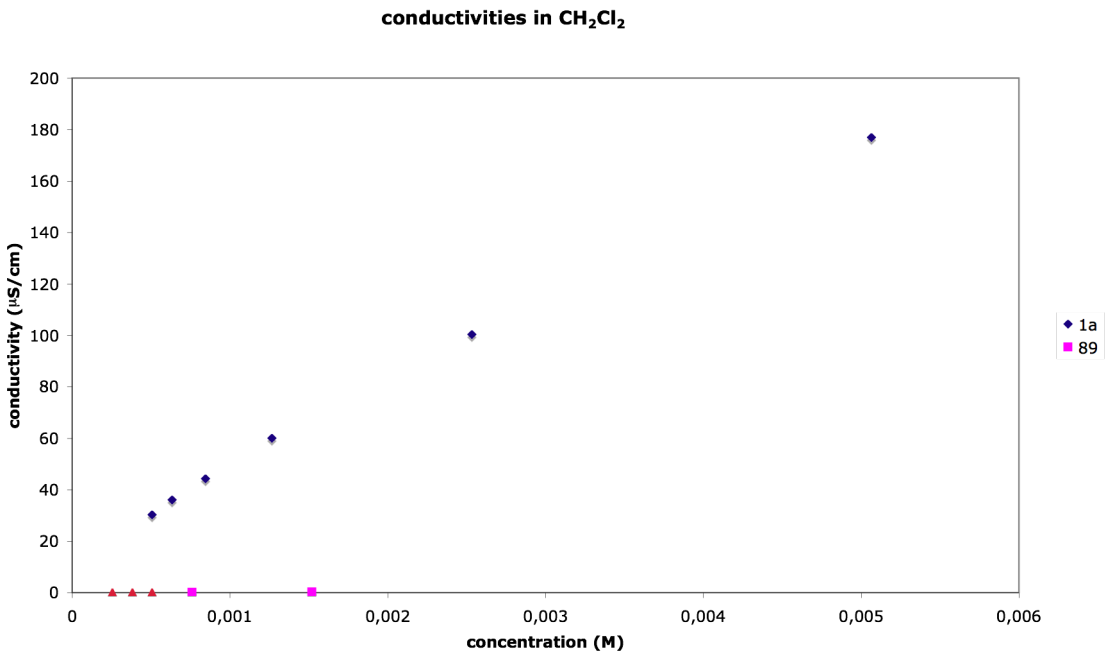


Figure 16. Comparison between the conductivity measurements for CH_2Cl_2 solutions of **1a** and **89**. The red triangles are at the conductivity value of HPLC grade CH_2Cl_2.

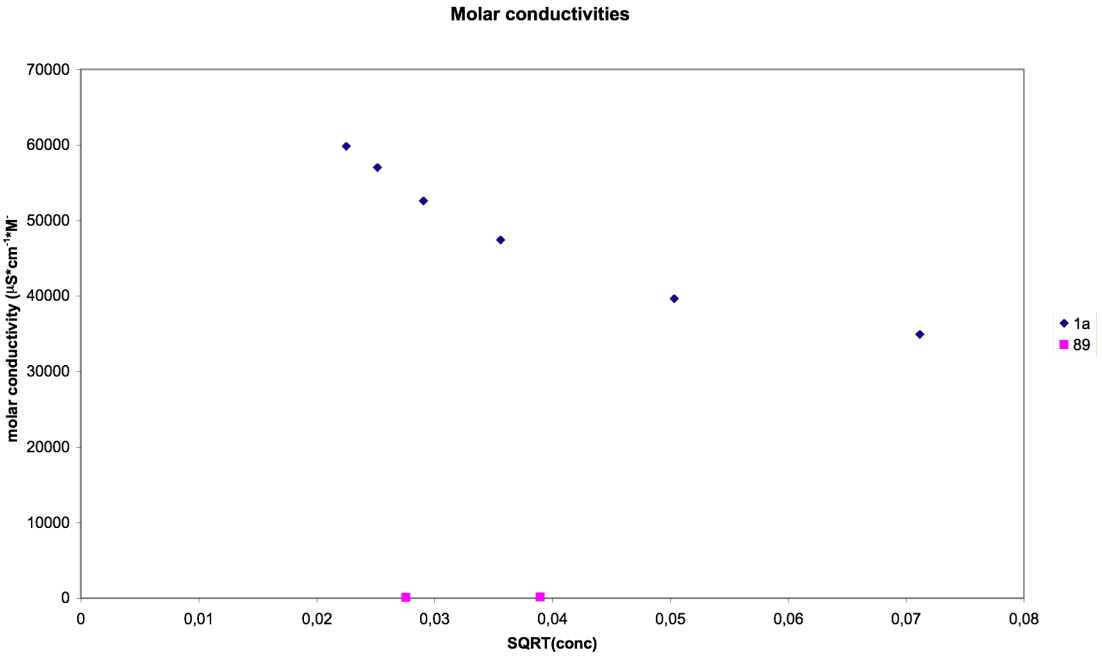


Figure 17. Comparison between the molar conductivities of **1a** and **89** in CH_2Cl_2.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

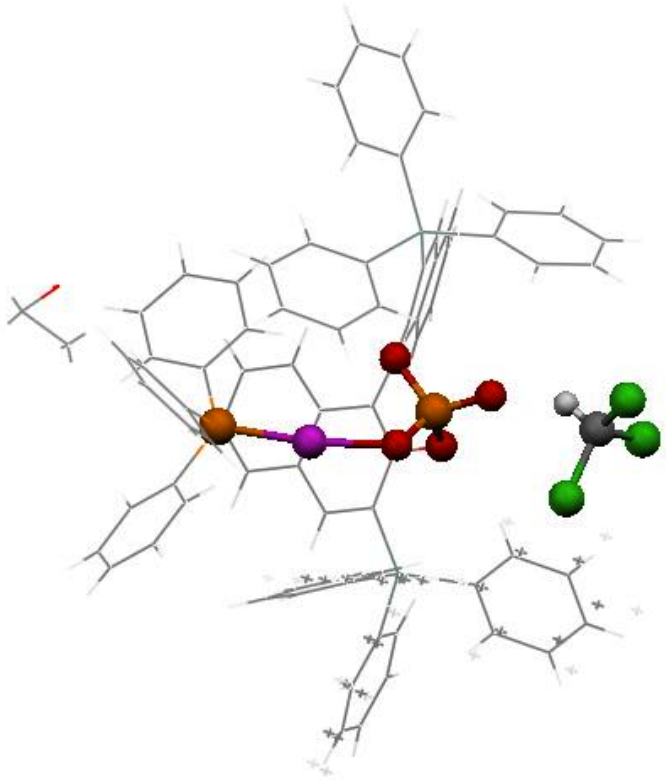


Figure 18. X-ray structure of **89**-$CHCl_3$ solvate; Au, O, P atoms and H-bonded solvent molecule are highlighted; Au-O distance: 2.056.

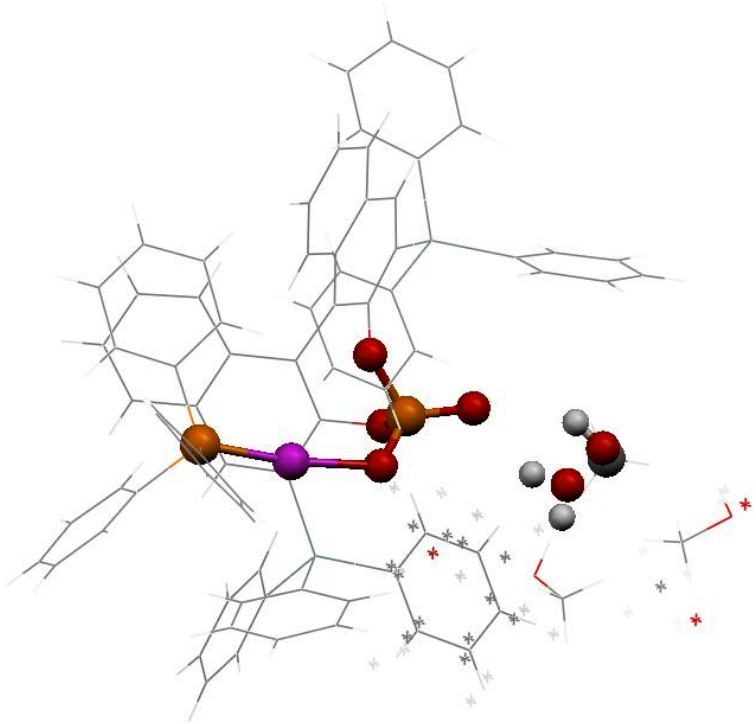
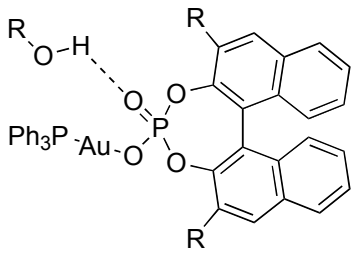


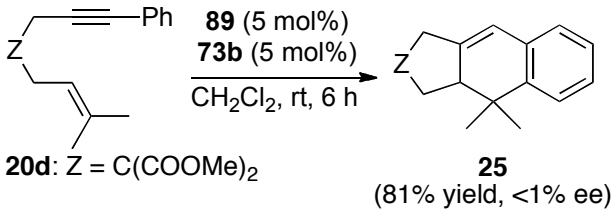
Figure 19. X-ray structure of **89**-MeOH/H_2O solvate; Au, O, P atoms and H-bonded solvent molecules are highlighted; Au-O distance: 2.101.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

We know that the phosphate anion strongly coordinates to the Au centre (^{31}P NMR, X-ray structure). On the other hand the P=O moiety should have a certain basicity. The high polarity of this bond is also probably responsible for the overall polarity (on silica) of these complexes. It is likely that the P=O moiety can act as a H-bond acceptor. The formation of a P=O…H bond with one or multiple H-bond donors could weaken the Au-O bond enough for the attack of the alkyne to be succesfull and a catalytic process to take place. Such an effect is obvious upon analysis of two different X-ray structure of complex **89**. Thus the the Au-O bond is lengthened from 2.056 Å in the **89**-$CHCl_3$ solvate (Figure 18) to 2.101 Å in the **89**-$MeOH/H_2O$ solvate (Figure 19).



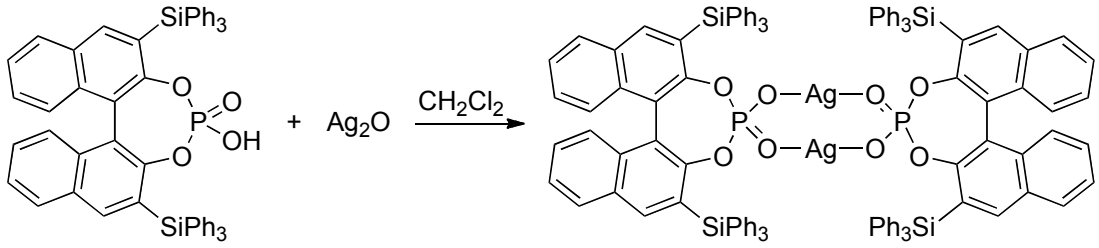
We reasoned that, a Lewis acid such as Ag^+ should act in a similar way, increasing the reactivity of these Au-phosphate complexes. Indeed, activation with the $[Ag(NCMe)_2]^+(SbF_6)^-$ (**73b**) restored the catalytical activity of the system, but with complete loss of enatioselectivity (<1% ee).



UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Experimental part

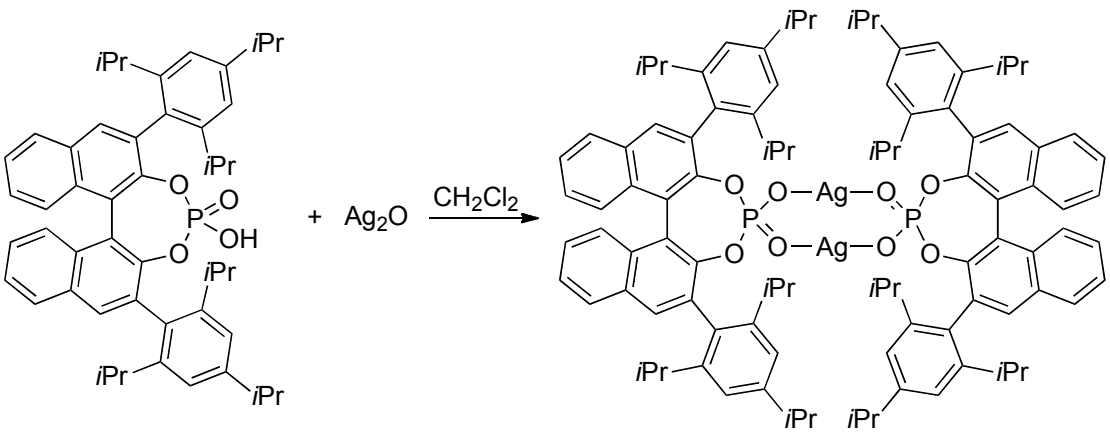
Complex 87



Solid Ag_2O (8.9 mg, 38 μmol) was added over a solution of the $SiPh_3$-BINOL phosphoric acid (44 mg, 51 μmol) in CH_2Cl_2 (1 mL) and the mixture was stirred vigoroulsy at room temperature for 4 h. The mixture was filtered into a tarred vial through a small pad of Celite which was washed with CH_2Cl_2 (4x1 mL). After evaporation of the solvent, the compound was precipitated from CH_2Cl_2 (2 mL)/ MeCN (4 mL) an allowed to stand for 7 h during which time the precipitate became cristalline. Decantation and washing with MeCN (2x0.5 mL) yielded the desired compound as a off-white powder which was vacuum dried (50 ºC, overnight) (46 mg, 92%). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.98 (s, 4H), 7.80 (d, J = 8.2 Hz, 4H), 7.60-7.58 (m, 24H), 7.44 (ddd, J = 8.1, 6.8, 1.2 Hz, 4H), 7.30 (ddd, J = 8.5, 6.7, 1.2 Hz, 4H), 7.25-7.20 (m, 16H), 7.16-7.13 (m, 24H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 152.85 (d, J = 9.3 Hz, C), 142.20 (C), 136.98 (CH), 135.25 (C), 134.72 (C), 130.99 (C), 128.98 (CH), 128.89 (CH), 127.78 (CH), 127.69 (CH), 127.50 (CH), 126.75 (d, J = 3.6 Hz, C), 125.54 (CH), 122.10 (d, J = 2.0 Hz, C); ^{31}P NMR (162 MHz, CD_2Cl_2) δ 12.7 (t, J = 17 Hz, 2P); MALDI-MS calcd. for $C_{112}H_{81}Ag_2O_8P_2Si_4$ $[M+H]^+$: 1943.3, found: 1943.4; other peaks: calcd. for $[M+Ag]^+$: 2051.2, found: 2051.4; calcd. for $[M/2+Ag]^+$: 1079.0, found: 1079.2; calcd. for $[M/2+H]^+$: 973.1, found: 973.2; Anal. Calcd. for $C_{112}H_{82}Ag_2O_9P_2Si_4$ ($M+H_2O$): C, 68.57; H, 4.21; found: C, 68.69; H, 4.01.

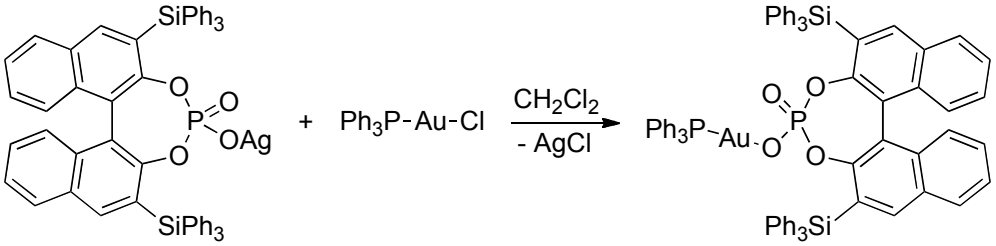
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Complex 88



Solid Ag_2O (21 mg, 91 μmol) was added over a solution of the *i*Pr_3Ph-BINOL phosphoric acid (91 mg, 0.12 mmol) in CH_2Cl_2 (2.4 mL) and the mixture was stirred vigoroulsy at room temperature for 4 h. The mixture was filtered through a small pad of Celite which was washed with CH_2Cl_2 (5x2 mL). After evaporation of the solvent, the compound was precipitated from MeOH (1 mL)/ H_2O (2 mL), filtered and washed with H_2O (2x4 mL). Vacuum drying (50 ºC, overnight) yielded the desired compound as a white powder (77 mg, 74%). ^{1}H NMR (400 MHz, CD_2Cl_2, 5 mg/mL) δ 7.90 (d, J = 8.2 Hz, 4H), 7.83 (s, 4H), 7.46 (ddd, J = 8.1, 6.0, 2.0 Hz, 4H), 7.30-7.25 (m, 8H), 7.05 (s, 4H), 6.97 (s, 4H), 2.82 (septuplet, J = 7.0 Hz, 4H), 2.68-2.61 (m, 8H), 1.21-1.13 (m, 60H), 0.93 (d, J = 6.8 Hz, 12H); ^{31}P NMR (162 MHz, CD_2Cl_2) δ 17.0 (t, J = 11 Hz, 2P). The compound is soluble in CH_2Cl_2, Et_2O, hexane, MeCN, MeOH. ^{1}H and ^{31}P NMR data was in agreement with the literature.[134] Diluted solutions (5 mg/mL) in CD_2Cl_2 showed a triplet which became a multiplet/broad singlet in more concentrated solutions. The ^{31}P NMR spectrum in CD_3CN consisted of a broad singlet in the 238-338 K interval.

Complex 89



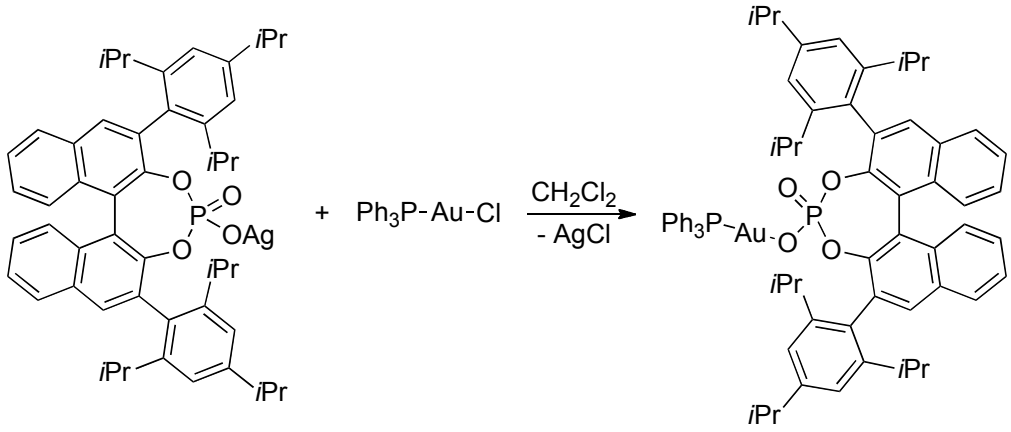
A mixture of Ph_3PAuCl (24 mg, 48 μmol) and **87** (39 mg, 40 μmol monomer) were stirred in CH_2Cl_2 (1.6 mL) for 2 h. The resulting mixture was filtered through a pad of silica (630 mg, pressed between 2 Teflon filters) which was then washed with CH_2Cl_2

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

(3x6.5 mL) and MeCN/CH_2Cl_2 = 4 : 1 (2x6.5 mL). The MeCN containing washings were evaporated and vacuum dried to to yield a white powder (48 mg, 90%). X-ray quality crystals were grown by layering a solution of the complex in CH_2Cl_2 with MeOH or by layering a solution of $CHCl_3$ with EtOH.

$^1H\{^{31}P\}$ NMR (400 MHz, CD_2Cl_2) δ 8.08 (s, 2H), 7.72 (d, J = 8.3 Hz, 2H), 7.68-7.66 (m, 12H), 7.52 (t, J = 7.5 Hz, 3H), 7.37 (t, J = 7.7 Hz, 6H), 7.30 (ddd, J = 8.1, 5.9, 2.1 Hz, 2H), 7.24-7.20 (m, 18H), 7.14-7.10 (m, 10H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 153.54 (d, J = 9.7 Hz, C), 141.67 (CH), 137.30 (CH), 135.12 (C), 134.58 (C), 134.46 (d, J = 13.5 Hz, CH), 132.36 (d, J = 2.7 Hz, CH), 130.63 (d, J = 1.0 Hz, C), 129.65 (CH), 129.43 (d, J = 12.1 Hz, CH), 128.74 (CH), 128.43 (d, J = 66.1 Hz, C), 127.94 (CH), 127.23 (CH), 127.11 (d, J = 3.1 Hz, C), 127.01 (CH), 125.07 (CH), 122.45 (d, J = 2.2 Hz, C); ^{31}P NMR (162 MHz, CD_2Cl_2) δ 29.8 (d, J = 3.6 Hz, 1P), 8.2 (d, J = 3.6 Hz, 1P); MALDI MS m/z: 1782.3 (calcd for $[M + Au(PPh_3)]^+$: 1782.3), 1417.1, 1409.1, 1322.3 (calcd for $[M]^+$: 1322.3), 1260.1, 1245.2, 1066.1, 721.1, 645.1; HRMS calcd. for $C_{74}H_{55}AuO_4P_2Si_2^+$ $[M]^+$: 1322.2774, found: 1322.2784; anal. calcd. for: $C_{148}H_{116}Au_2O_{11}P_4Si_4$ (2M + $3H_2O$): C, 65.82; H, 4.33; found: C, 65.78; H, 4.30.

Complex 90

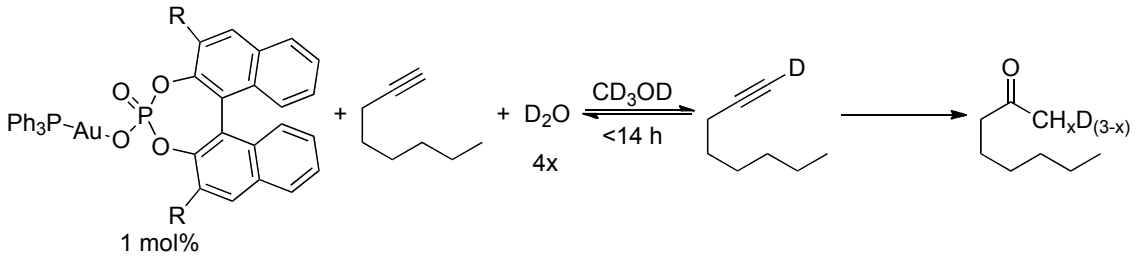


A mixture of Ph_3PAuCl (21 mg, 42 μmol) and **88** (30 mg, 35 μmol monomer) were stirred in CH_2Cl_2 (1.4 mL) for 2 h. The resulting mixture was applied over a pad of silica (1 g, pressed between 2 Teflon filters, dry packed using CH_2Cl_2) and separated by flash chromatography (CH_2Cl_2 to MeCN). After vacuum drying (65 ºC, 4 h), the desired complex was otained as a white powder (42 mg, 98%).

$^1H\{^{31}P\}$ NMR (400 MHz, CD_2Cl_2) δ 7.84 (d, J = 8.2 Hz, 2H), 7.79 (s, 2H), 7.52-7.47 (m, 3H), 7.39-7.35 (m, 8H), 7.24-7.12 (m, 12H), 7.03 (d, J = 1.6 Hz, 2H), 2.96 (br m,

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

2H), 2.88 (septuplet, J = 7.0 Hz, 2H), 2.67 (septuplet, J = 6.8 Hz, 2H), 1.27-1.24 (m, 18H), 1.17 (d, J = 6.8 Hz, 6H), 1.01 (d, J = 6.8 Hz, 6H), 0.88 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 148.61 (C), 148.24 (br s, C), 148.04 (d, J = 9.2 Hz, C), 147.65 (br s, C), 134.35 (d, J = 13.6 Hz, CH), 133.13 (br s, C), 132.85 (C), 132.50 (CH), 132.35 (d, J = 2.7 Hz, CH), 130.98 (C), 129.49 (d, J = 12.1 Hz, CH), 128.43 (CH), 128.36 (d, J = 66.6 Hz, C), 127.42 (CH), 126.18 (CH), 125.34 (CH), 122.78 (d, J = 2.0 Hz, C), 121.66 (CH), 120.61 (CH), 34.61 (CH), 31.68 (br s, CH), 31.29 (CH), 26.61 (CH_3), 24.97 (CH_3), 24.28 (CH_3), 24.13 (CH_3), 24.04 (br s, CH_3), 23.58 (br s, CH_3); ^{31}P NMR (202 MHz, CD_2Cl_2, -40 ºC) δ 29.8 (d, J = 2.6 Hz, 1P), 10.1 (d, J = 2.6 Hz, 1P); HRMS calcd for $C_{68}H_{71}AuO_4P_2^+$ $[M]^+$: 1210.4488, found: 1210.4419; MALDI MS m/z: 1669.5 (calcd for $[M + Au(PPh_3)]^+$: 1669.5), 1417.2, 1409.1, 1227.2, 1210.4 (calcd for $[M]^+$: 1210.4), 1168.3, 1067.1, 1034.2, 721.1, 710.2; anal. calcd. for: $C_{68}H_{71}AuO_4P_2$: C, 67.43; H, 5.91; found: C, 67.56; H, 5.99.



General procedure for the hydration of 1-octyne

The gold phosphate complex (5 μmol) was dissolved in CD_3OD (0.5 mL) then 1-octyne (75 μL, 0.50 mmol) and D_2O (36 μL, 2.0 mmol) were added. The reaction was followed by ^{1}H and ^{31}P NMR. After 14 h deuteration of the alkyne proton was observed. Conversions were determined by ^{1}H NMR at 14 h, 42 h and 67 h.

R = $SiPh_3$: Additional CD_2Cl_2 (0.25 mL) was added in order to achieve solubilization of the gold complex. Partial evaporation of the CD_2Cl_2 caused some precipitation of the catalyst.

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

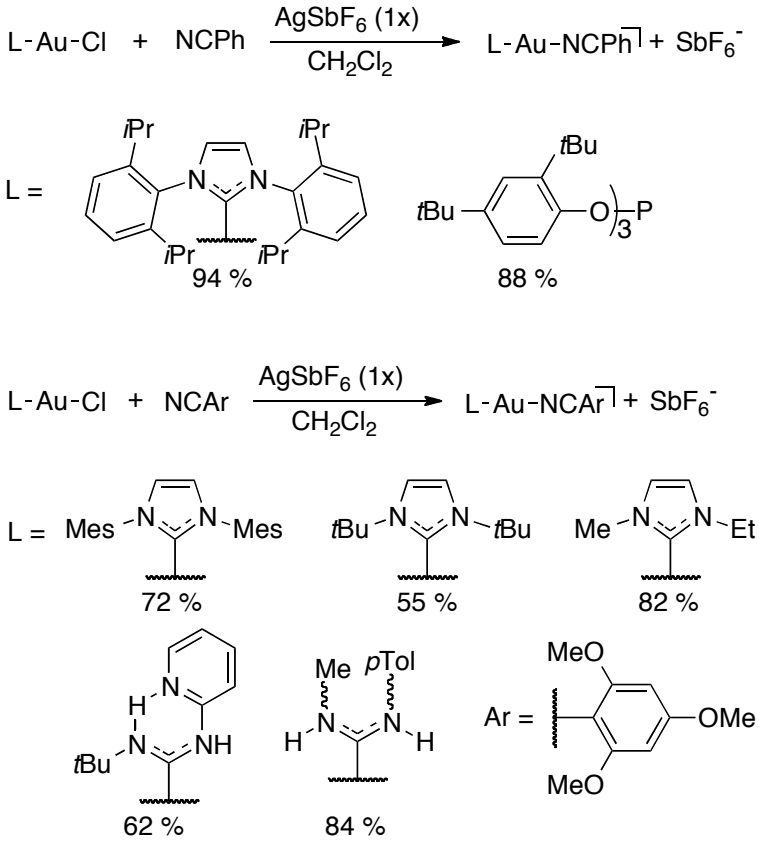
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Conclusions

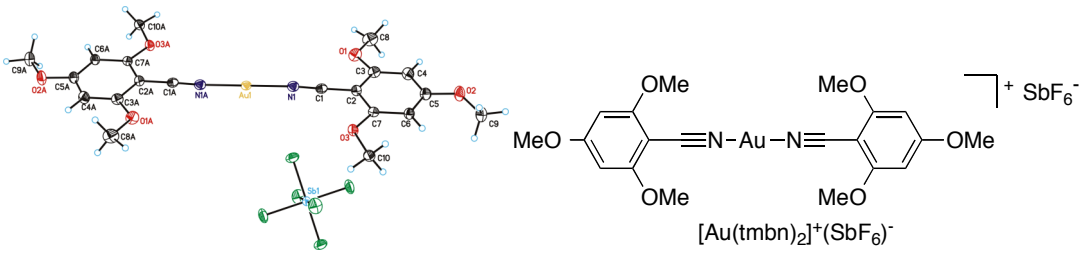
UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

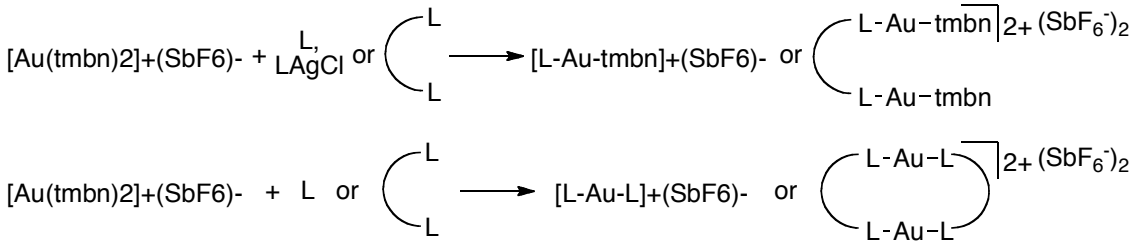
- Employing electron rich aromatic nitriles as labile ligands allowed the isolation of cationic gold(I) complexes as crystalline solids that are stable under ambient conditions yet catalytically active.



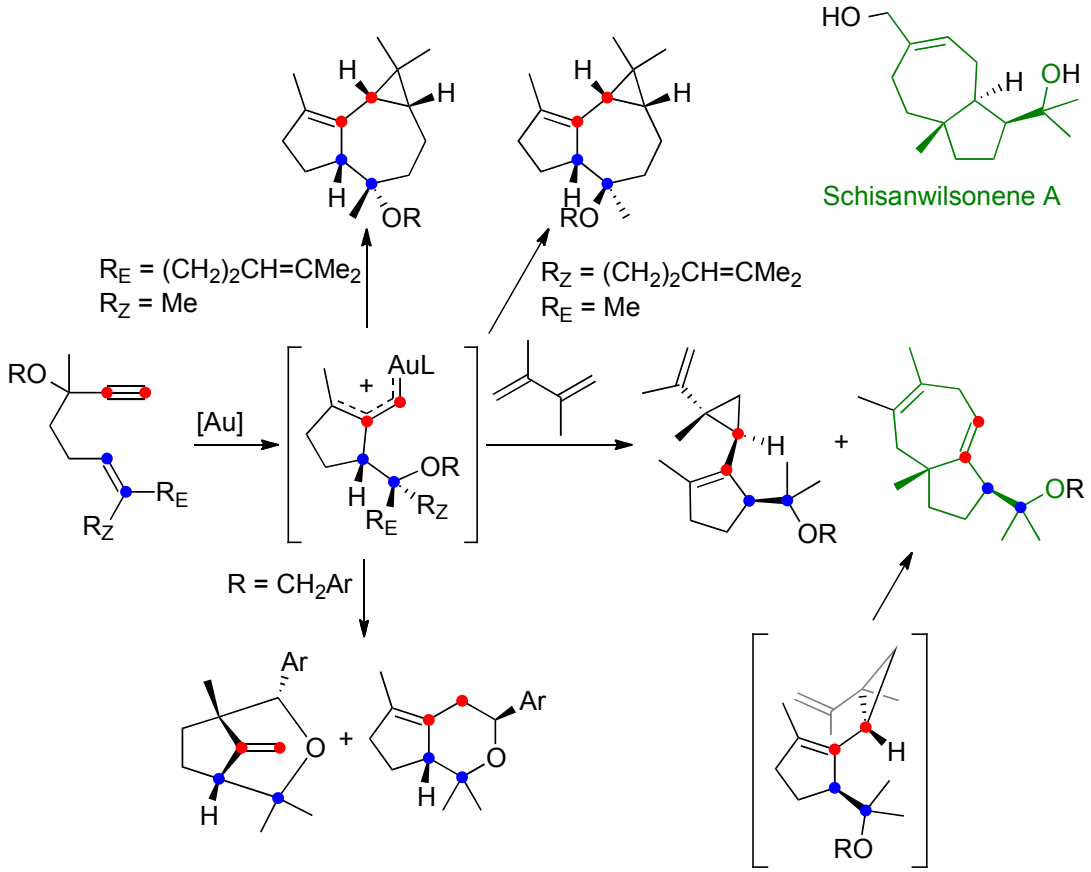
- Dinitrile complex $[Au(tmbn)_2]^+(SbF_6)^-$ is an air stable compound and a valuable starting material for the preparation of gold(I) complexes. Clean susbstitution of either one or both of the labile ligands was observed by NMR. The complexes formed in this way were used *in situ* to replicate the results observed in previously described reactions of 1,6-enynes.



UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

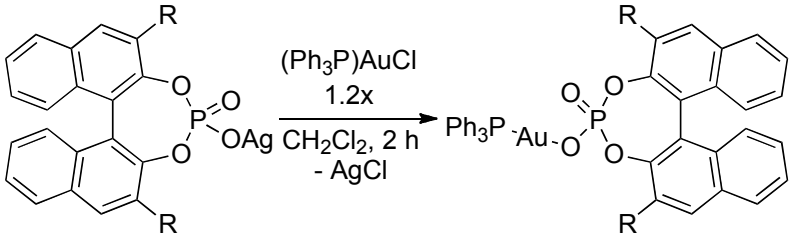


- Upon activation with Au(I) cationic catalysts, 1,6-enynes with propargyl alcohols and ethers undergo stereospecific intramolecular 1,5-migration via allyl-gold cations. These intermediates were trapped inter- or intramolecularly with alkenes and benzyl ethers. Several pathways towards the total synthesis of schinsanwilsonenes A-C were investigated.

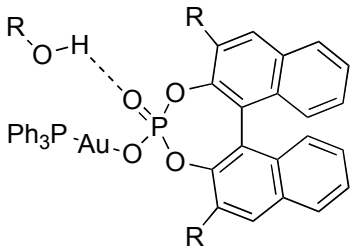


UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

- Gold(I) complexes containing chiral phosphates as ligands were isolated and characterized and a rationale for their catalytic activity was proposed.



89 R = $SiPh_3$, 90% yield
90 R = 2,4,6-*i*$Pr_3C_6H_2$, 98% yield



UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

UNIVERSITAT ROVIRA I VIRGILI
NEW GOLD (I) ALKYNOPHILIC CATALYSTS
Mihai Raducan
ISBN:978-84-694-0315-0/DL: T-196-2011

Annexes

CD containing cif files for compounds **36e**, **46e**, **50**, **69b**, **72b**, **73a**, **73b**, **74**, **80**, **82**, **86**, **89** and the articles published by the author during the course of his Thesis.