UNIVERSIDAD COMPLUTENSE DE MADRID
FACULTAD DE CIENCIAS QUÍMICAS
Departamento de Química Orgánica I

TESIS DOCTORAL

Nuevos complejos metálicos de carbenos mesoiónicos

New mesoionic carbene metal complexes

MEMORIA PARA OPTAR AL GRADO DE DOCTOR

PRESENTADA POR

María Frutos Pastor

Directores

María del Carmen de la Torre Egido
Miguel Ángel Sierra Rodríguez

Madrid, 2017

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NEW MESOIONIC CARBENE METAL COMPLEXES

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CSIC
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Memoria que para optar al grado de
DOCTORA EN CIENCIAS QUÍMICAS
presenta
María Frutos Pastor

MADRID, 2016

Dña. María del Carmen de la Torre Egido, Investigadora Científica del Consejo Superior de Investigaciones Científicas, **D. Miguel Ángel Sierra Rodríguez**, Catedrático de Química Orgánica de la Facultad de Ciencias Químicas de la Universidad Complutense de Madrid,

CERTIFICAN:

Que la presente Memoria titulada **"NUEVOS COMPLEJOS METÁLICOS DE CARBENOS MESOIÓNICOS"** se ha realizado bajo su dirección en el Departamento de Síntesis, Estructura y Propiedades de Compuestos Orgánicos del Instituto de Química Orgánica General del Consejo Superior de Investigaciones Científicas y en el Departamento de Química Orgánica de la Facultad de Ciencias Químicas de la Universidad Complutense de Madrid, por la Licenciada en Ciencias Químicas **María Frutos Pastor**, y autorizan su presentación para ser calificada como Tesis Doctoral.

Y para que conste firmo el presente certificado en Madrid a 1 de Septiembre de 2016.

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El trabajo recogido en esta Memoria se ha realizado en el Departamento de Síntesis, Estructura y Propiedades de Compuestos Orgánicos del Instituto de Química Orgánica General del Consejo Superior de Investigaciones Científicas y en el Departamento de Química Orgánica de la Facultad de Ciencias Químicas de la Universidad Complutense de Madrid. La financiación que ha permitido llevarlo a cabo procede del Ministerio de Ciencia e Innovación (CTQ2010-20714-CO-02-BQU), del Ministerio de Economía y Competitividad (CTQ2013-46459-C2-01-P, CTQ2013-46459-C2-02-P), MEC-Consolider-Ingenio (2010-CSD2007-00006, CTQ2014 51912-REDC) y la Comunidad Autónoma de Madrid (CAM-S2009/PPQ-1634). Asimismo, agradezco al Ministerio de Ciencia e Innovación por la concesión de una Beca FPI (BES-2011-047329).

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A mi tía Ana

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ABREVIATIONS AND ACRONYMS

Anh	Anhydrous
BBN	Borabicyclo[3.3.1]nonane
Boc	*tert*-Butyloxycarbonyl
Bpy	Bipyridyl
br d	Broad doublet
br s	Broad singlet
^{t}BuLi	*tert*-Butyllithium
^{t}BuOK	Potassium *tert*-butoxide
c	Concentration (g/100 cm^3)
Cat.	Catalyst
CuAAC	Cu(I)-catalysed alkyne-azide cycloaddition
cod	Cyclooctadiene
Cp	Cyclopentadienyl
Cp*	Pentamethylcyclopentadienyl
cym	Cymene
d	Doublet
dd	Doublet of doublets
ddd	Doublet of doublet of doublets
ddt	Doublet of doublet of triplets

DFT	Density functional theory
DiPP	Diisopropylphenyl
dm	Doublet of multiplets
DMA	N,N-dimethylacetamide
DMF	*N,N*-dimethylformamide
DMSO	Dimethyl sulfoxide
dq	Doublet of quadruplets
dt	Doublet of triplets
ee	Enantiomeric excess
EtOAc	Ethyl acetate
h	Heptuplet
HMBC	Heteronuclear multiple-bond correlation spectroscopy
HPLC	High performance liquid chromatography
HRMS (ESI)	High resolution Mass spectrometry electrospray ionization
HRMS (IE)	High resolution Mass spectrometry electronic impact
IR	Infrared
J	Constant coupling
LiHMDS	Lithium bis(trimethylsilyl)amide
m	Multiplet
M	Metal
mcpba	3-Chloroperbenzoic acid

MeOTf	Methyl trifluoromethanesulfonate
Mes	Mesityl
MIC	Mesoionic carbene
m.p.	Melting point
MS	Molecular sieves
mw	Microwaves
NaBArF	Sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate
NaHMDS	Sodium bis(trimethylsilyl)amide
NHC	*N*-heterocyclic carbene
NMR	Nuclear magnetic resonance
NMO	4-methylmorpholine *N*-oxide
N.O.E.	Overhauser nuclear effect
NTs	N-tosyl
Nu	Nucleophile
ORTEP	Oak ridge thermal ellipsoid plot
OTf	Trifluoromethanesulfonate
PIDA	(Diacetoxyiodo)benzene
ppm	Parts per million
ppy	Phenylpyridine
q	Quadruplet
RCM	Ring closing metathesis

RCOM	Ring closing olefin metathesis
ROMP	Ring opening metathesis polymerization
rt	Room temperature
s	Singlet
t	Triplet
TBAF	Tetrabutylammonium fluoride
TBTA	Tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine
TLC	Thin Layer Chromatography
TMEDA	*N*,*N*,*N*′,*N*′-tetramethylethylenediamine
TMS	Trimethylsilyl
TMSCl	Trimethylsilyl chloride
TMSOTf	Trimethylsilyl trifluoromethanesulfonate
td	Triplet of doublets
THF	Tetrahydrofuran
Tol	3-methylphenyl
TOF	Turnover frequencies
TON	Turnover number
Trz	Triazole
Xyl	Dimethylphenyl

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CHAPTER I

Introduction and objectives

I.1 INTRODUCTION

I.1.1 Stable carbenes

Carbenes are neutral compounds with a divalent carbon that has six valence electrons. Their incomplete octet electron makes these species highly reactive and unstable.[1] They have been considered as transient intermediates in organic transformations, making their isolation and characterisation a major challenge.

Carbenes can present linear or bent geometries. Linear carbenes have an sp hybridized carbenic centre displaying two nonbonding p orbitals degenerated in energy (p_x and p_y) (Figure I.1). On the other hand, bent carbenes are based in an sp^2-carbene carbon atom. In this case, the p_y orbital remains almost unchanged in terms of energy (and it is usually named as p_π), while p_x is stabilised because of its partial s character. This orbital is also known as σ orbital.

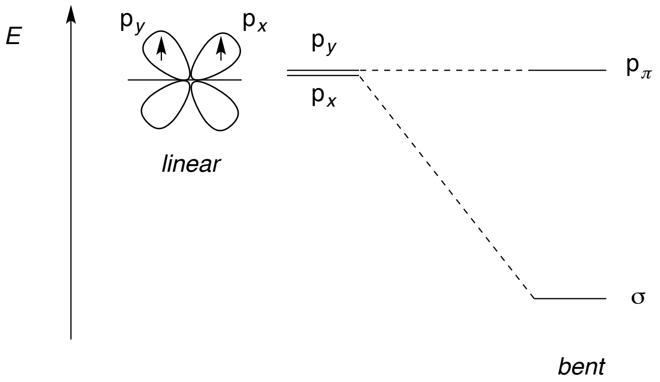

Figure I.1: Orbitals and geometries of carbenes

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[1] For a review on stable carbenes see: D. Bourissou, O. Guerret, F. P. Gabbaï, G. Bertrand, *Chem. Rev.* **2000**, *100*, 39.

[2] A. Herrmann, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2162.

Carbenes can exist in four different electronic configurations. The nonbonding electrons can occupy both σ and p_π orbitals with a parallel spin orientation. This situation is known as a triplet ground state ($^3B_1$). This class of carbene displays a linear geometry. In the case of the singlet state, the electron pair would be oriented in an antiparallel mode. One of the possible configurations would imply the filling of the same orbital leading to two different $^1A_1$ states (σ^2 is in general more stable than the corresponding $p_\pi{}^2$). There is an additional electronic configuration, an excited singlet state $^1B_1$, in which the two electrons are placed in two different orbitals with their spins oriented in an antiparallel manner (Figure I.2).[2] Due to the vacant orbital, singlet carbenes are ambiphilic while triplet carbenes are considered as diradicals.

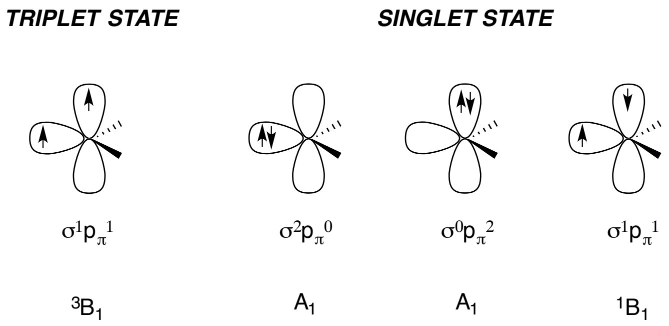

Figure I.2: Electronic configurations of carbenes

The stability and other properties of carbenes are dictated by the multiplicity of the ground state, which will be determined by the difference in energy between σ and p_π orbitals. Values lower than 1.5 eV favour the triplet ground state over the singlet one. On the contrary, differences higher than 2.0 eV would stabilise the singlet state.[3] Steric and electronic effects can modulate this energetic gap: carbenes possessing σ-electron withdrawing substituents have a σ orbital decreased in energy while the energy of the p_π orbital remains essentially unchanged. This situation would stabilise the singlet state. Conversely, substituents with σ electron donating properties decrease the gap between both orbitals, stabilising the triplet ground state.

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[2] A. Herrmann, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2162.

[3] a) R. Hoffmann, *J. Am. Chem. Soc.* **1968**, *90*, 1475; b) R. Hoffmann, G. D. Zeiss, G. W. Van Dine, *J. Am. Chem. Soc.* **1968**, *90*, 1485.

Conjugative effects are determinant in the geometry and stabilisation of singlet carbenes (Figure I.3):

- X substituents (F, Cl, Br, I, NR_2, PR_2, OR, SR, SR_3): they provide π electrons from their filled p orbital to the empty p orbital of the carbene atom. They present a bent geometry. The energy gap becomes larger because the energy of the vacant p_π orbital increases due to its interaction with the lone pair of the substituents. Meanwhile, σ orbital remains unaltered.

- Z substituents (Li, BR_2, BeH_2, SiR_3): stabilisation occurs by donation from the filled p orbital of the carbene centre to the empty p orbitals of the substituents. These carbenes are predicted to be lineal.

- C substituents: they are carbon atoms that are part of a conjugated system.

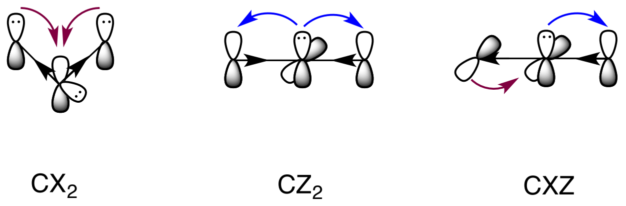
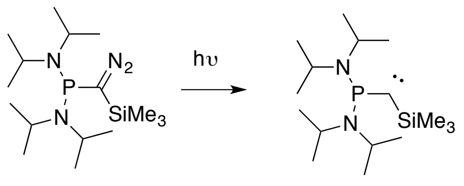


Figure I.3: Structure of substituted carbenes

Bertrand reported the first free carbene stable at room temperature (Scheme I.1).[4] Irradiation of diazocompound **I.1** furnished free carbene **I.2**, which is a good example of the combination of X and C substituents in the same carbene centre. The stability of carbene **I.2** was favoured by electronic interactions with silicon and phosphorous substituents placed in adjacent positions to the carbene carbon, leading to nearly linear compounds.



I.1 **I.2**

Scheme I.1: Synthesis of stable carbene **I.2**

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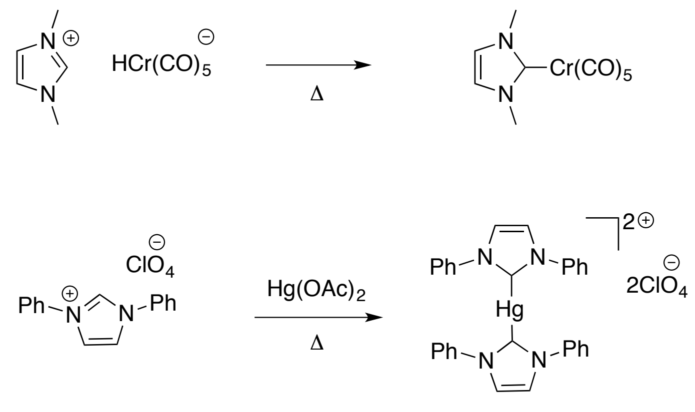
[4] A. Igau, H. Grutzmacher, A. Baceiredo, G. Bertrand, *J. Am. Chem. Soc.* **1988**, *110*, 6463.

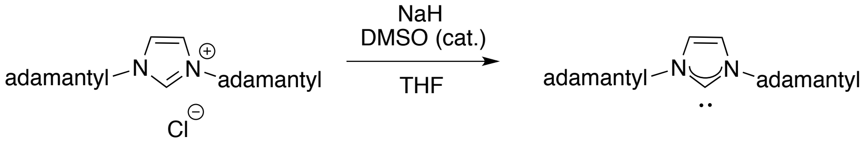
I.1.2 *N*-Heterocyclic carbenes

A milestone in the chemistry of free carbenes was achieved in the early 1990s by Arduengo,[5] who isolated a free *N*-heterocyclic carbene (NHC) for the first time.[6] This work was inspired by the earlier discoveries of Wanzlick[7] and Öfele,[8] who metallated a series of imidazolium salts to form the corresponding stable Cr and Hg complexes (Scheme I.2).



Scheme I.2: First examples of metal *N*-heterocyclic carbenes isolated by Wanzlick and Öfele

In his work, Arduengo resolved the crystalline structure of an imidazolylidene for the first time (Scheme I.3). Deprotonation of the chloride salt **I.3** with NaH as a base, afforded the free carbene **I.4**.



I.3 **I.4** (96%)

Scheme I.3: First example of a free *N*-heterocyclic carbene

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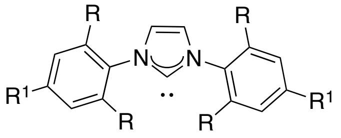
[5] A. J. Arduengo, R. L. Harlow, M. Kline, *J. Am. Chem. Soc.* **1991**, *3*, 361.

[6] For general reviews on heterocyclic carbenes see: a) F. E. Hahn, M. C. Jahnke, *Angew. Chem. Int. Ed.* **2008**, *47*, 3122; b) M. N. Hopkinson, C. Ritcher, M. Schedler, F. Glorius, *Nature* **2014**, *510*, 485.

[7] H.-W. Wanzlick, H.-J. Schönherr, *Angew. Chem. Int. Ed. Engl.* **1968**, *7*, 141.

[8] K. Öfele, *J. Organomet. Chem.* **1968**, *12*, P42.

Stability of this free carbene was thought to emanate from the presence of the two sterically demanding adamantyl groups flanking the carbene carbon that would be the responsible of the kinetic stabilisation of these species, disfavouring the dimerization process. However, subsequent work in which the adamantly groups were replaced by less hindered substituents (Figure I.4, compounds **I.5a**–**c**)[9] demonstrates that not only sterical but also electronic factors play a role in the stabilisation of the free carbene.



I.5a (84%), R= Me, R^1= Me
I.5b (45%), R= H, R^1= Me
I.5c (43%), R= H, R^1= Cl

Figure I.4: Free NHCs

Theoretical studies performed by Heinemann and Thiel[10] proposed that the singlet-triplet gap is also a key factor in the stability of NHCs. As stated above, the geometry and the presence of π systems in neighbouring positions to the carbene carbon influence this singlet-triplet gap.[11] Nitrogen atoms stabilise the carbenic nucleus due to their electron-withdrawing character and their ability to donate their lone electron pair to the empty p orbital of the sp^2 hybridized carbene atom.

The nature of the NHC–M bond

The fact that NHCs are both σ- and π- donors rules the nature of the binding between the metal and the NHC. In fact, there are three different contributions of the NHC's orbitals to the NHC–M bond (Figure I.5):[12]

a) σ bonding from the lone ion pair of the carbene into a d orbital of the metal.

b) π donation from the p orbitals of the carbene to the d orbitals of the metal.

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[9] A. J. Arduengo, H. V. Rasika Dias, R. L. Harlow, M. Kline, *J. Am. Chem. Soc.* **1992**, *114*, 5530.
[10] C. Heinemann, W. Thiel, *Chem. Phys. Lett.* **1994**, *217*, 11.
[11] R. Gleiter, R. Hoffmann, *J. Am. Chem. Soc.* **1968**, *90*, 5457.
[12] H. Jacobsen, A. Correa, A. Poater, C. Costabile, L. Cavallo, *Coord. Chem. Rev.* **2009**, *253*, 687.

c) π backbonding donation between the metal and the π system of the NHC.

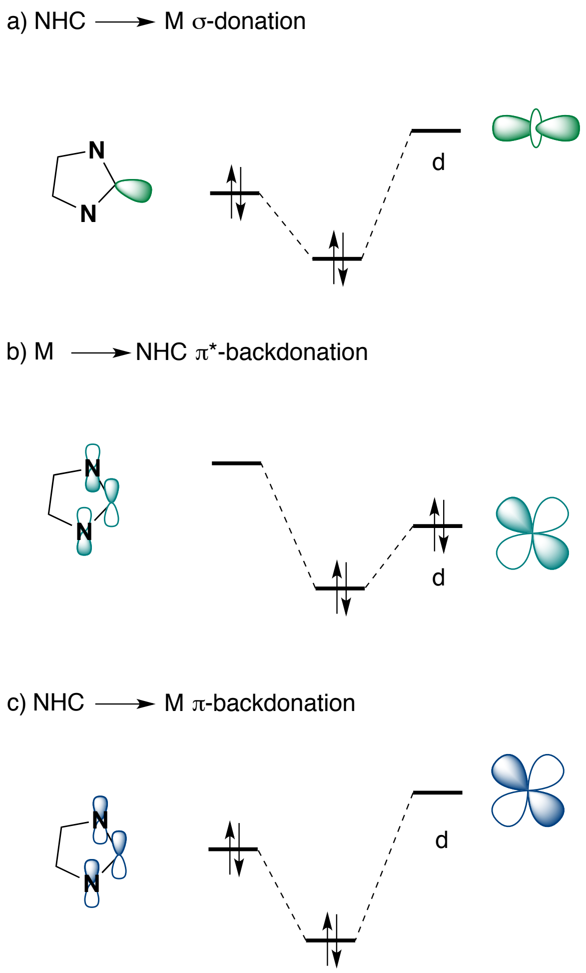
This implies that interactions between the metal and the carbene centre would depend not only on the structure and properties of the NHC but also on the electronic arrangement of the metal.

NHCs present some special properties that confer these species a key role in organometallic chemistry:

a) High covalent contribution of the metal–carbene bond.

b) Strong donor ability.

c) Easy electronic and steric tunability.



a) NHC ⟶ M σ-donation

b) M ⟶ NHC π*-backdonation

c) NHC ⟶ M π-backdonation

Figure I.5: Orbitals diagrams for the NHC-metal bonding

These unique properties are responsible for the astonishing role played by NHCs during the past decade in organometallic chemistry.[13] Thus, they are present in a large number of novel catalytic systems in homogenous[14, 15, 16, 17, 18, 19] and heterogeneous catalysis.[20] They are also powerful ligands for transition metals[21] and f-block species.[22] Some silver, gold and copper carbenes present medical applications[23] because of their antimicrobial[24] and antitumoral activities,[25] and they can also be part of new organometallic materials.[26] It is also important to highlight their role as powerful organocatalysts.[27]

The features of NHCs place these species as competitors with phosphines and cyclopentadienlys as ligands in catalysis.[28] Changes on the structure of phosphines substituents would lead to simultaneous modifications of their steric and electronic

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[13] For reviews on the role of NHC in organometallic chemistry see*:* a) W. A. Herrmann, *Angew. Chem. Int. Ed.* **2002**, *41*, 1290; b) W. A Herrmann, T. Weskamp, V. P. W. Böhm, *Adv. Organomet. Chem*. **2001**, *48*, 1; c) C. M. Crudden, D. P. Allen, *Coord. Chem. Rev.* **2004**, 2247; d) P. de Frémont, N. Marion, S. P. Nolan, *Coord. Chem. Rev.* **2009**, *253*, 862.

[14] For a review on catalysis of gold NHC see: S. P. Nolan, *Acc. Chem. Rev.* **2011**, *44*, 91*.*

[15] For a review on catalysis of copper NHC see: a) J. D. Egbert, C. S. J. Cazin, S. P. Nolan, *Catal. Sci. Technol.* **2013**, *3*, 912; b) F. Lazreg, F. Nahra, C. S. J. Cazin, *Coord. Chem. Rev.* **2015**, *293-294*, 48.

[16] For a review on catalysis of iron NHC see: D. Bézier, J.-B. Sortais, C. Darcel, *Adv. Synth, Catal.* **2013**, *355*, 19.

[17] For a review on catalysis of niquel NHC see: A. P. Prakasham, P. Ghosh, *Inorganic Chimica Acta,* **2015**, *431,* 61.

[18] For a review on asymmetric catalysis of chiral metal NHC see: F. Wang, L.-J. Liu, W. Wang, S. Li, M. Shi, *Coord. Chem. Rev.* **2012**, *256,* 804.

[19] For a review on catalysis of NHC in aqueous media see: H. D. Velazquez, F. Verpoort, *Chem. Soc. Rev.* **2012**, *41*, 7032.

[20] K. V. S. Ranganath, S. Onitsuka, A. K. Kumar, J. Inanaga, *Catal. Sci. Technol.* **2013**, *3*, 2161.

[21] S. Díez-González, N. Marion, S. P. Nolan*, Chem. Rev.* **2009**, *109*, 3612.

[22] P. L. Arnold, I. J. Casely, *Chem. Rev.* **2009**, *109*, 3599.

[23] a) K. M. Hindi, M. J. Panzner, C. A. Tessier, C. L. Cannon, W. J. Youngs, *Chem. Rev.* **2009**, *109*, 3859; b) F. Lazreg, C. S. J. Cazin, *N*-Heterocyclic carbenes: effective tools for organometallic synthesis. **2014** Willey-VCH; c) L. Oehninger, R. Rubbiani, I. Ott, *Dalton Trans.* **2013**, *42*, 3269.

[24] a) A. Kascatan-Nebioglu, M. J. Panzner, C. A. Tessier, C. L. Cannon, W. J. Youngs, *Coord. Chem. Rev.* **2007**, *251*, 884; b) M. Patra, G. Gasser, N. Metzler-Nolte, *Dalton Trans.* **2012**, *41*, 6350.

[25] a) A. Gautier, F. Cisnetti, *Metallomics* **2012**, *4*, 23; b) F. Cisnetti, A. Gautier, *Angew. Chem. Int. Ed.* **2013**, *52*, 11976; c) W. Liu, R. Gust, *Chem. Soc. Rev.* **2013**, *42*, 755.

[26] L. Mercs, M. Albrecht, *Chem. Soc. Rev.* **2010**, *39*, 1903.

[27] a) D. Nders, O. Niemeier, A. Henseler, *Chem. Rev.* **2007**, *107*, 5606; b) A. Grossmann, D. Enders, *Angew. Chem. Int. Ed.* **2012**, *51*, 314; c) M. Fèvre, J. Pinaud, Y. Gnanou, J. Vignolle, D. Taton, *Chem. Soc. Rev.* **2013**, *42*, 2142.

[28] R. H. Crabtree, *J. Organomet. Chem.* **2005**, *690*, 5451.

properties. In contrast, in the case of NHCs, these features could be tuned separately: changes in the nature of the substituents would affect the steric properties while changes in the nature of the heterocyclic scaffolds would be translated into different electronic features. With the aim of finding new donor abilities of NHCs, efforts have been focused in developing new systems having modified cyclic cores.[29] For example, NHCs containing up to six-, seven- and eight-membered rings have been reported;[30] while nitrogen atoms have been displaced to remote positions from the carbene carbon in order to increase their donor ability. [31]

Classification of NHCs

Carbenes can be classified into three main groups: classic carbenes are those having the carbene carbon flanked by two heteroatoms; remote, lacking any heteroatom in the adjacent positions of the carbene carbon; and abnormal, when only one α position to the carbene centre is occupied by a heteroatom (Figure I.6).

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[29] For a review on electronic and steric properties in NHCs see: a) T. Dröge, F. Glorius, *Angew. Chem. Int. Ed.* **2010**, *49*, 6940; b) D. J. Nelson, S. P. Nolan, *Chem. Soc. Rev.* **2013**, *46*, 6723.

[30] a) C. C. Scarborough, M. J. W. Grady, I. A. Guzei, B. A. Gandhi, E. E. Bunel, S. S. Stahl, *Angew. Chem. Int. Ed.* **2005**, *44*, 5269; b) T. W. Hudnall, J. P. Moerdyk, C. W. Bielawski, *Chem. Commun.* **2010**, *46*, 4288; c) M. J. Page, W. Y. Lu, R. C. Poulten, E. Carter, A. G. Algarra, B. M. Kariuki, S. A. Macgregor, M. F. Mahon, K. J. Cavell, D. M. Murphy, M. K. Whittlesey, *Chem. Eur. J.* **2013**, *19*, 2158; d) M. Mayr, K. Wurst, K.-H. Ongania, M. R. Buchmeiser, *Chem. Eur. J.* **2004**, *10*, 1256; e) C. C. Scarborough, I. A. Guzei, S. S. Stahl, *Dalton Trans.* **2009**, 2284; f) A. Binobaid, M. Iglesias, D. J. Beetstra, B. Kariuki, A. Dervisi, I. A. Fallis, K. J. Cavell, *Dalton Trans.* **2009**, 7099; g) J. J. Dunsford, D. S. Tromp, K. J. Cavell, C. J. Elsevier, B. M. Kariuki, *Dalton Trans.* **2013**, *42*, 7318; h) M. Iglesias, D. J. Beetstra, B. Kariuki, K. J. Cavell, A. Dervisi, I. A. Fallis, *Eur. J. Inorg. Chem.* **2009**, 1913; i) M. Iglesias, D. J. Beetstra, K. J. Cavell, A. Dervisi, I. A. Fallis, B. Kariuki, R. W. Harrington, W. Clegg, P. N. Horton, S. J. Coles, M. B. Hursthouse, *Eur. J. Inorg. Chem.* **2010**, 1604; j) A. Binobaid, M. Iglesias, D. Beetstra, A. Dervisi, I. Fallis, K. J. Cavell, *Eur. J. Inorg. Chem.* **2010**, 5426; k) V. César, N. Lugan, G. Lavigne, *J. Am. Chem. Soc.* **2008**, *130*, 11286; l) T. W. Hudnall, C. W. Bielawski, *J. Am. Chem. Soc.* **2009**, *131*, 16039; m) C. C. Scarborough, B. V. Popp, I. A. Guzei, S. S. Stahl, *J. Organomet. Chem.* **2005**, *690*, 6143; n) K. Verlinden, C. Ganter, *J. Organomet. Chem.* **2014**, *750*, 23; o) M. Iglesias, D. J. Beetstra, J. C. Knight, L.-L. Ooi, A. Stasch, S. Coles, L. Male, M. B. Hursthouse, K. J. Cavell, A. Dervisi, I. A. Fallis, *Organometallics* **2008**, *27*, 3279; p) W. Y. Lu, K. J. Cavell, J. S. Wixey, B. Kariuki, *Organometallics* **2011**, *30*, 5649; q) A. Makhloufi, W. Frank, C. Ganter, *Organometallics* **2012**, *31*, 2001; r) N. Philips, T. Dodson, R. Tirfoin, J. I. Bates, S. Aldridge, *Chem. Eur. J.* **2014**, *20*, 16721.

[31] a) P. L. Arnold, S. Pearson, *Coord. Chem. Rev.* **2007**, *251*, 596; b) R. H. Crabtree, *Coord. Chem. Rev.* **2013**, *257*, 755.

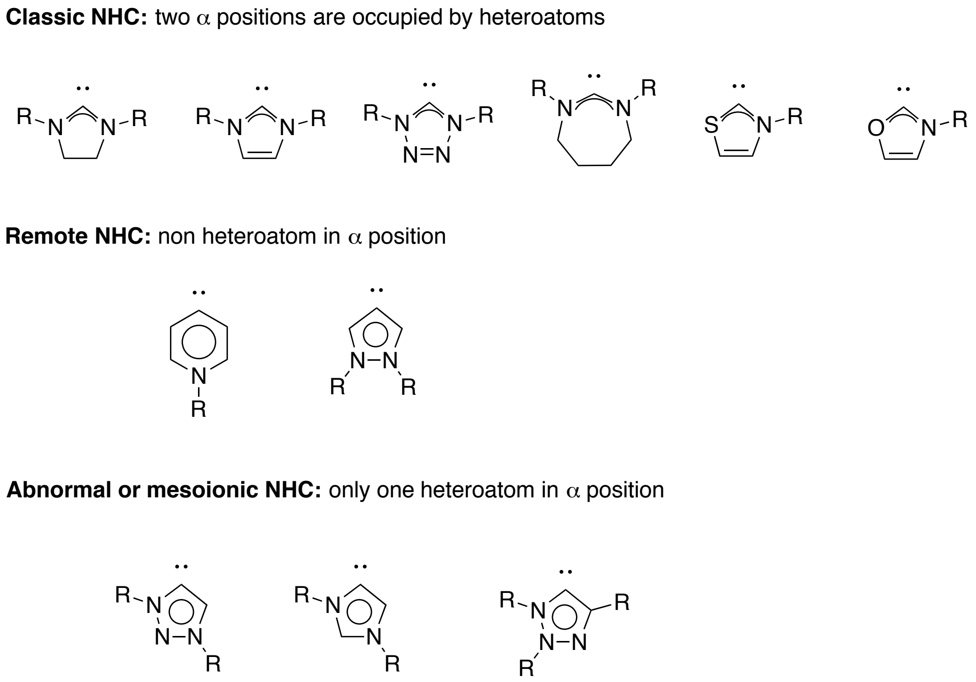
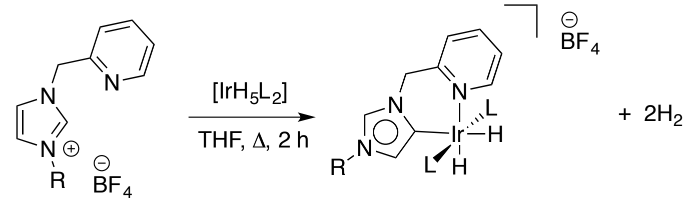


Figure I.6: Classification of NHCs

The term abnormal carbene was coined by Crabtree.[32] When the imidazolium salt **I.6** reacts with $IrH_5(PPh_3)_2$ in refluxing THF for 2 h, the chelating carbene **I.7** is formed, with the iridium centre surprisingly bonding the *abnormal* *C*5 position instead of coordinating to the expected *C*2 position (Scheme I.4).



I.6

I.7a, R= ^{i}Pr, L= PPh_3
I.7b (68%), R= ^{n}Bu, L= PPh_3

Scheme I.4: First examples of *abnormal* carbenes

Following the report by Crabtree, Bertrand named these classes of compounds as mesoionic (MIC), because no canonical resonance structures of the free carbene can be drawn without separation of charges.[33]

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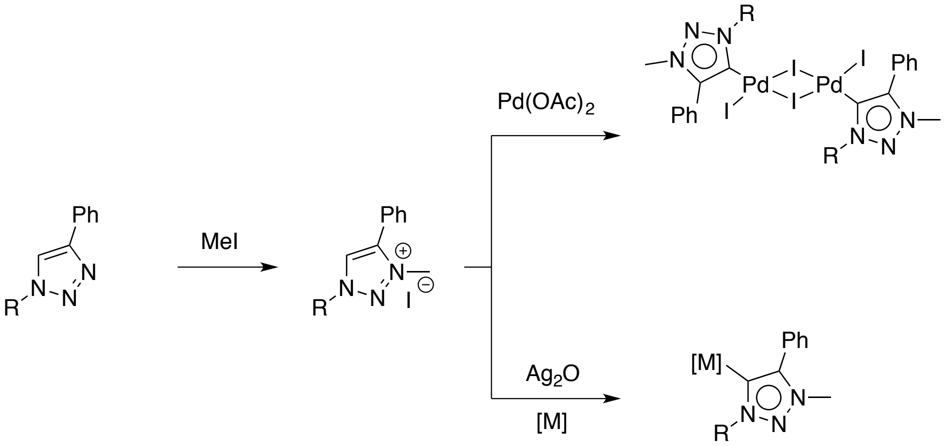
[32] S. Gründemann, A. Kovacevic, M. Albrecht, J. W. Faller, R. H. Crabtree, *Chem. Commun.* **2001**, 2274.

[33] G. Guisado-Barrios, J. Bouffard, B. Donnadieu, G. Bertrand, *Angew. Chem. Int. Ed.* **2010**, *49*, 4759.

1,2,3-Triazolylidenes

1,2,3-Triazolylidenes are among this new class of abnormal or mesoionic NHCs.[34] One of the reasons of the growing attention that these carbenes have recently drawn is the fact that they derive from 1,2,3-triazoles, which are readily available through the highly efficient and regioselective Cu(I)-catalysed Huisgen alkyne-azide cycloaddition (CuAAC).[35] A large number of functional groups with different electronic and steric properties are compatible with this CuAAC due to the mild reaction conditions of this transformation. This allows not only for diversification of their structures but also for a high tunability of the electronic properties of carbenes, which is not always easy to achieve in other NHC families.[36] These features could be transferred to the coordinating metal centre to seek for new applications. The tunability could be achieved by introducing different groups in the heterocyclic core through the terminal alkyne, the azide or both.

The first example of a metal 1,2,3-triazolylidene complex was reported by Albrecht,[37] who employed the CuAAC reaction to synthetize 1,2,3-triazoles that were later methylated by MeI.



Scheme I.5: Synthetic approach of first 1,2,3-triazolylidene complexes

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[34] For recent reviews on 1,2,3-triazolylidenes see: a) J. D. Crowley, A-L. Lee, K. J. Kilpin, *Aust. J. Chem.* **2011**, *64*, 1118; b) K. F. Donnelly, A. Petronilho, M. Albrecht, *Chem. Commun.* **2013**, *49*, 1145.

[35] a) C. W. Tornøe, C. Christensen, M. Meldal, *J. Org. Chem.* **2002**, *67*, 3057; b) V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2002**, *41*, 2596.

[36] F. Cisnetti, C. Gibard, A. Gautier, *J. Organomet. Chem.* **2015**, *782*, 22.

[37] P. Mathew, A. Neels, M. Albrecht, *J. Am. Chem. Soc.* **2008**, *130*, 13534.

Once the triazolium salts were formed, the corresponding transition metal complexes were synthetized through two different approaches (Scheme I.5): direct metallation or Ag-transmetallation protocol that will be discussed later.

Synthesis of metal 1,2,3-triazolylidenes complexes

There are different protocols for the synthesis of metal 1,2,3-triazolylidene complexes. All synthetic approaches share triazolium salts as common precursors for the formation of these complexes. These triazolium salts are usually formed by alkylation of 1,2,3-triazoles.

Transmetallation from Ag-NHCs

The most versatile methodology for the synthesis of 1,2,3-triazolylidene consists of the formation of the Ag-NHC intermediates followed by transmetallation with the suitable metal source. Different Ag(I) salts (Ag_2CO_3,[38] $AgCH_3CO_2$,[39] $AgCF_3CO_2$[40], $AgCF_3SO_3$[41]) can act simultaneously as a base to remove the proton from the triazolium salt and as the metal source, forming the silver carbene. The real breakthrough took place when Ag_2O was employed as a base[42] allowing to perform the synthesis of the M-MIC in air. In addition, the range of solvents compatible with the formation of the silver carbene was wider than with other reagents. Finally, different functional groups are compatible with this procedure due to the tolerance of Ag_2O towards other hydrogen atoms of the heterocyclic salt.[43]

As it has been previously discussed, the deprotonation of 1,2,3-triazolium salts by Ag_2O was performed for the first time by Albrecht.[37] Transmetallation from silver

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[38] A. A. D. Tulloch, A. A. Danopoulos, S. Winston, S. Kleinhenz, G. Eastham, *J. Chem. Soc., Dalton Trans.* **2000**, 4499.

[39] O. Guerret, S. Solé, H. Gornitzka, M. Teichert, G. Trinquier, G. Bertrand, *J. Am. Chem. Soc.* **1997**, *119*, 6668.

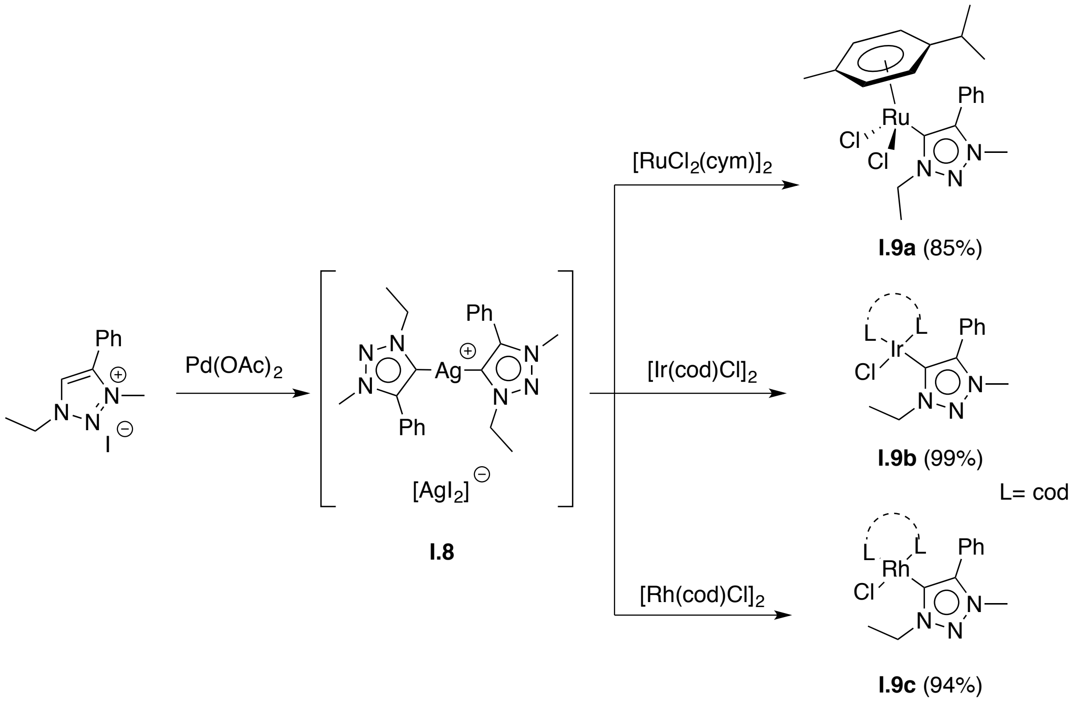
[40] N. Imlinger, M. Mayr, D. Wang, K. Wurst, M. R. Buchmeiser, *Adv. Synth. Catal.* **2004**, *346*, 1836.

[41] A. Schmidt, T. Habeck, *Lett. Org. Chem.* **2005**, *2*, 37.

[42] H. M. J. Wang, I. J. B. Lin, *Organometallics* **1998**, *17*, 972.

[43] I. J. B. Lin, C. S. Vasam, *Coord. Chem. Rev.* **2007**, *251*, 642.

carbene **I.8** was achieved using different Ru, Rh and Ir sources yielding the corresponding carbene complexes (Scheme I.6). In addition, silver triazolylidene **I.8** could be fully characterised by NMR techniques. Mass spectroscopy measurements showed a main peak at *m/z* = 481.2, which was consistent with a bis(carbene) structure.



Scheme I.6: Synthesis of Pd, Ir and Rh 1,2,3-triazolylidenes through the Ag_2O-protocol

With the aim of gaining some insight into the donor properties of the M-MIC, the Ir complex **I.10b** was prepared in order to measure the CO stretching vibrations by IR spectroscopy since it is known that a lineal correlation between $\upsilon_{\text{average}}$(CO) and the Tolman electronic parameter (TEP) exists.[44,45,46]

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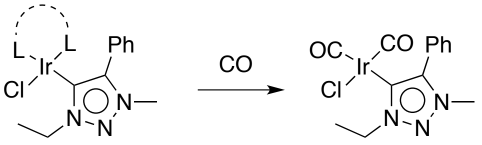
[44] The Tolman electronic parameter (TEP), named after Chadwick A. Tolman, is a measure of the electron donating or withdrawing ability of a ligand. It is determined by measuring the infrared-stretching frequency of the A_1 C–O vibrational mode of a complex, $LM(CO)_n$, where L is the ligand being studied.

[45] C. A. Tolman, *Chem. Rev.* **1977**, *77*, 313.

[46] a) A. R. Chianese, X. Li, M. C. Janzen, J. W. Faller, R. H. Crabtree, *Organometallics* **2003**, *22*, 1663; b) R. Dorta, E. D. Stevens, N. M. Scott, C. Costabile, L. Cavallo, C. D. Hoff, S. P. Nolan, *J. Am. Chem. Soc.* **2005**, *127*, 2485; c) R. A. Kelly, H. Clavier, S. Giudice, N. M. Scott, E. D. Stevens, J. Bordner, I. Samardjiev, C. D. Hoff. L. Cavallo, S.P. Nolan, *Organometallics* **2008**, *27*, 202.



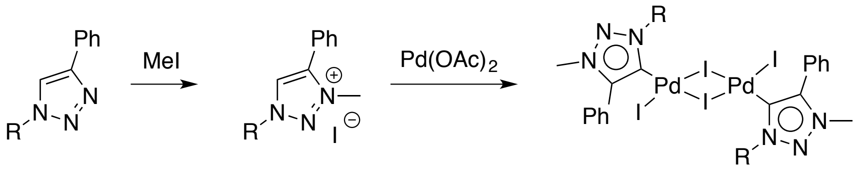
I.9b, L= cod **I.10b** (94%)

Scheme I.7: Replacement of cod ligand by CO

In fact, the more electron-donating the NHC is, the more electron-rich the metal becomes. Then, the π-backbonding from the metal to the carbonyl groups increases, making the bond order of the M–CO higher and the infrared stretching frequencies lower. Comparison of this parameter allowed to conclude that the donor properties of the iridium triazolylidene carbene are similar to those of the normal imidazolylidenes, but still higher than those of other abnormal carbenes.

Direct metallation

Albrecht reported the direct reaction of salts **I.11a**–**b** with Pd(OAc)$_2$ in DMSO at 120 °C to yield the dinuclear mono(carbene) complexes **I.12a**–**b** as major products (Scheme I.8).[37] Neither silver salts nor bases were used in these reactions.



R= Et, Bn

I.11a (95%), R= Et
I.11b (98%), R= Bn

I.12a (42%), R= Et
I.12b (39%), R= Bn

Scheme I.8: Synthesis of palladium 1,2,3-triazolylidene by direct metallation

Bertrand reported an approach to Cu(I)-1,2,3-triazolylidene complex **I.13** also based in direct metallation of the triazolium salt **I.14** in absence of bases (Scheme I.9).[47]

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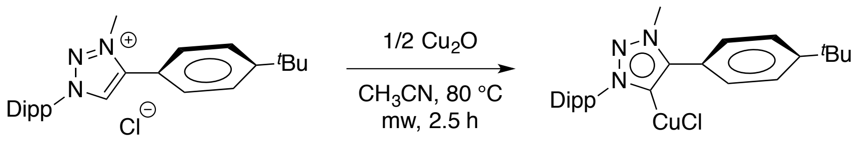
[47] Y. D. Bidal, M. Lesieur, M. Melaimi, F. Nahra, D. B. Cordes, K. S. Athukorala Arachchige, A. M. Z. Slawin, G. Bertrand, C. S. J. Cazin, *Adv. Synth. Catal.* **2015**, *357*, 3155.



I.14 **I.13** (95%)

Scheme I.9: Synthesis of copper triazolylidenes by direct metallation

Thus, the reaction of the salt **I.14** with Cu_2O in refluxing acetonitrile using microwave radiation gave the corresponding carbene **I.13** in 95% yield. This approach represents an efficient alternative for the preparation of copper carbenes.[48] Nevertheless this methodology requires triazolium chloride salts that are not always readily accessible, albeit they can be obtained from the tetrafluoroborate salts using an ionic exchange column.

Another synthetic approach to afford metal-1,2,3-triazolylidene complexes by direct metallation was reported by Albrecht.[49] In this work, series of Ni 1,2,3-triazolylidenes were prepared by direct metallation of triazolium salts **I.15** with $NiCp_2$. Interestingly, a relation was found between the nature of the counteranion of the triazolium salts, the times of reaction and the products obtained (Scheme I.10). Thus, chloride salt **I.15a** was totally converted into a 1:1 mixture of mono and bis(carbenes) **I.16a** and **I.17a** after 20 h. By contrast, reaction of iodine analogous gave a mixture of the demethylated triazole (84% of yield)[33,50] together with 14% of unaltered starting material. When metallation reactions were carried out with triazolium salts having less coordinating anions like OTf^- and BF_4^-, a demethylation process took part yielding the starting triazole **I.18a** quantitatively. The demethylation process can be largely suppressed through the addition of NEt_4Cl as a source of chlorides forming bis(carbene) **I.17a** as the major product. In these cases, formation of the mono(carbene) **1.16a** is observed at the beginning of the reaction, suggesting that this mono(carbene) species is the precursor of the bis(carbene) **I.17a**. As a proof of the

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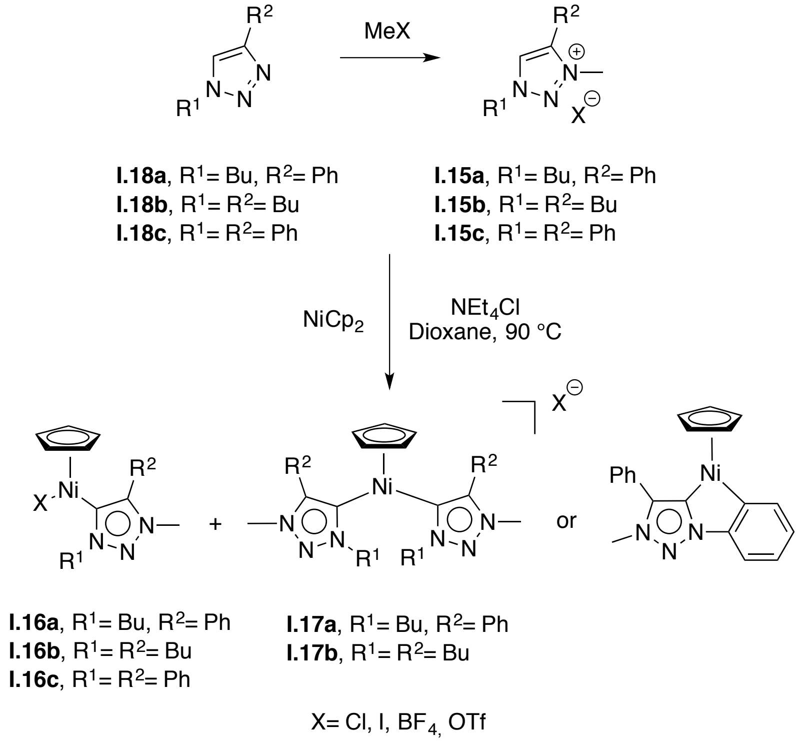
[48] a) G. Venkatachalam, M. Heckenroth, A. Neels, M. Albrecht, *Helv. Chim. Acta*, **2009**, *92*, 1034; b) M. R. L. Furst, C. S. J. Cazin, *Chem. Commun.* **2010**, *46*, 6924; c) B. Landers, O. Navarro, *Eur. J. Inorg. Chem.* **2012**, 2980; d) J. Al Thagfi, G. G. Lavoie, *Organometallics* **2012**, *31*, 7351; e) A. C. Badaj, G. G. Lavoie, *Organometallics* **2012**, *31*, 1103; f) E. K. Bullough, M. A. Little, C. E. Willians, *Organometallics* **2013**, *32*, 570; g) J. Mormul, M. Steimann, U. Nagel, *Eur. J. Inorg. Chem.* **2014**, 1389.

[49] Y. Wei, A. Petronilho, H. Mueller-Bunz, M. Albrecht, *Organometallics* **2014**, *33*, 5834.

lability of the Ni–C$_{trz}$ bond, mono(carbenes) **I.16** were heated under vacuum for 24 h yielding bis(carbenes) **I.17** together with NiCp$_2$ (Scheme I.10).



I.18a, R^1= Bu, R^2= Ph
I.18b, R^1= R^2= Bu
I.18c, R^1= R^2= Ph

I.15a, R^1= Bu, R^2= Ph
I.15b, R^1= R^2= Bu
I.15c, R^1= R^2= Ph

I.16a, R^1= Bu, R^2= Ph
I.16b, R^1= R^2= Bu
I.16c, R^1= R^2= Ph

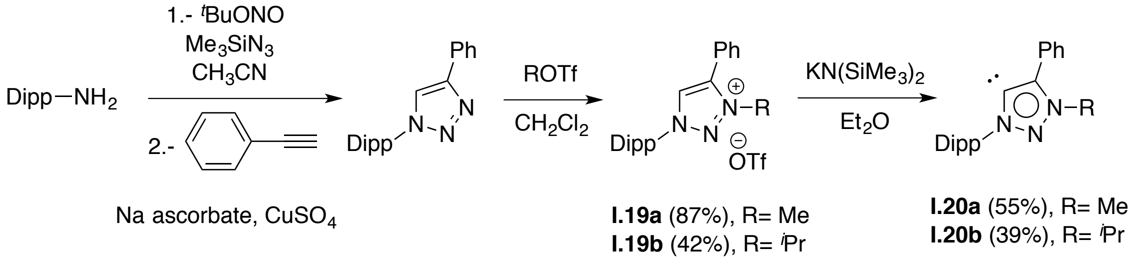
I.17a, R^1= Bu, R^2= Ph
I.17b, R^1= R^2= Bu

X= Cl, I, BF_4, OTf

Scheme I.10: Synthesis of Ni 1,2,3-triazolylidenes by direct metallation

Coordination of the free carbene

Bertrand reported the first example of the synthesis of free 1*H*-1,2,3-triazol-5-ylidenes by deprotonation of the precursor triazolium salts **I.19a–b** using KN(SiMe$_3$)$_2$ as a base (Scheme I.11).[33]

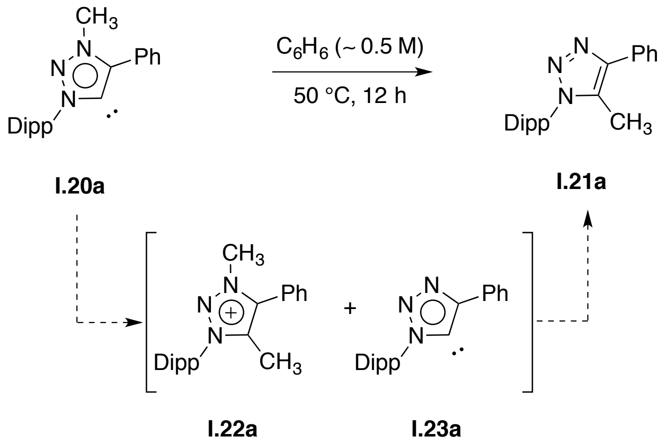


I.19a (87%), R= Me
I.19b (42%), R= ^{i}Pr

I.20a (55%), R= Me
I.20b (39%), R= ^{i}Pr

Scheme I.11: Synthesis of free 1,2,3-triazolylidenes

In the solid state and under exclusion of air and moisture, the free triazolylidene **I.20a** remained stable for several days at –30 °C or for some hours at room temperature. Nevertheless, when this carbene was heated at 50 °C in benzene for 12 h, it decomposed giving triazole **I.21a**. These decomposition pathways are the result of the nucleophilic attack of the lone pair of the carbene to the methyl group of a second molecule of the free carbene affording **I.22a** and **I.23a**. Reaction of these two intermediates would lead to triazole **I.21a** (Scheme I.12). On the other hand, an analogous carbene **I.20b** bearing a more sterically hindered and less electrophilic isopropyl group in *N*3 was found to be more stable against this decomposition mechanism.



Scheme I.12: Free NHC decomposition pathway

Several attempts to metallate the free triazolylidene with different metal sources were fruitless, probably as a consequence of the instability of these carbenes. In order to increase their stability, 1,5-diarylated-1,2,3-triazolylidenes were prepared.[50] In this case, preparation of the *N*3-arylated salts was not possible through the direct arylation of the triazole. Therefore, the *N*3-diarylated triazoles **I.24a**–**d** were synthetized through a 1,3-dipolar cycloaddition between 1,3-diaza-2-azoniaallene salts and alkynes.[51] Compounds **I.24a**–**d** were deprotonated using ^{t}BuOK yielding the

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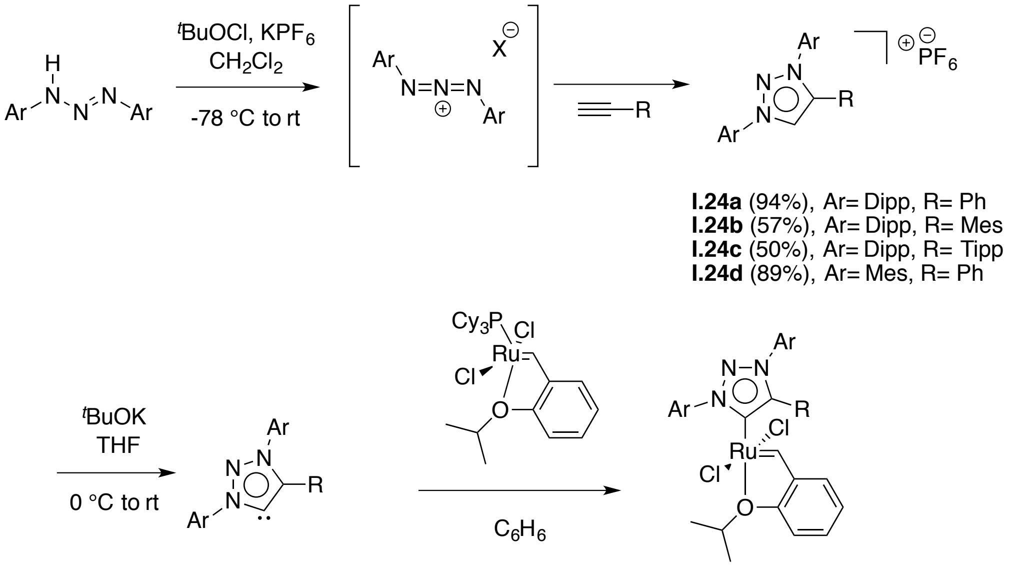
[50] J. Bouffard, B. K. Keitz, R. Tonner, G. Guisado-Barrios, G. Frenking, R. H. Grubbs, G. Bertrand, *Organometallics* **2011**, *30*, 2617.

[51] a) W. Wirschun, M. Winkler, K. Lutz, J. C. Jochims, *J. Chem. Soc., Perkin Trans. 1*, **1998**, 1755; b) W. Wirschun, *Prakt. Chem.* **1998**, *340*, 300; c) N. Al-Masoudi, N. A. Hassan, Y. A. Al-Soud, P. Schmidt, A. E.-D. M. Gaafar, M. Weng, S. Marino, A. Schoch, A. Amer, J. C. Jochims, *J. Chem. Soc., Perkin Trans. 1*, **1998**, 947.

corresponding free carbenes **I.25a–d**. These triazolylidenes were more robust than their *N*3-alkylated precursors and they could be stored at room temperature under inert atmosphere without decomposition. Then, reactions of the free carbenes with ruthenium salts led to the ensuing metal complexes **I.26a–d** (Scheme I.13).



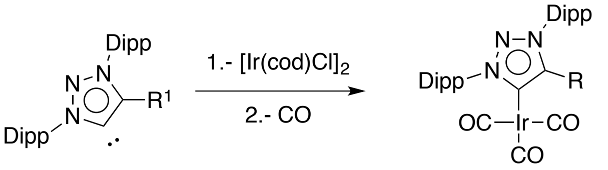
I.24a (94%), Ar= Dipp, R= Ph
I.24b (57%), Ar= Dipp, R= Mes
I.24c (50%), Ar= Dipp, R= Tipp
I.24d (89%), Ar= Mes, R= Ph

I.25a (90%), Ar= Dipp, R= Ph
I.25b (77%), Ar= Dipp, R= Mes
I.25c (>99%), Ar= Dipp, R= Tipp
I.25d (98%), Ar= Mes, R= Ph

I.26a (49%), Ar= Dipp, R= Ph
I.26b (21%), Ar= Dipp, R= Mes
I.26c (50%), Ar= Dipp, R= Tipp
I.26d (17%), Ar= Mes, R= Ph

Scheme I.13: Synthetic route for the synthesis of 1,3-diarylated triazolylidenes

When free triazolylidenes **I.25c–d** were reacted with [Ir(cod)Cl]$_2$, Ir complexes **I.27a–b** were obtained.



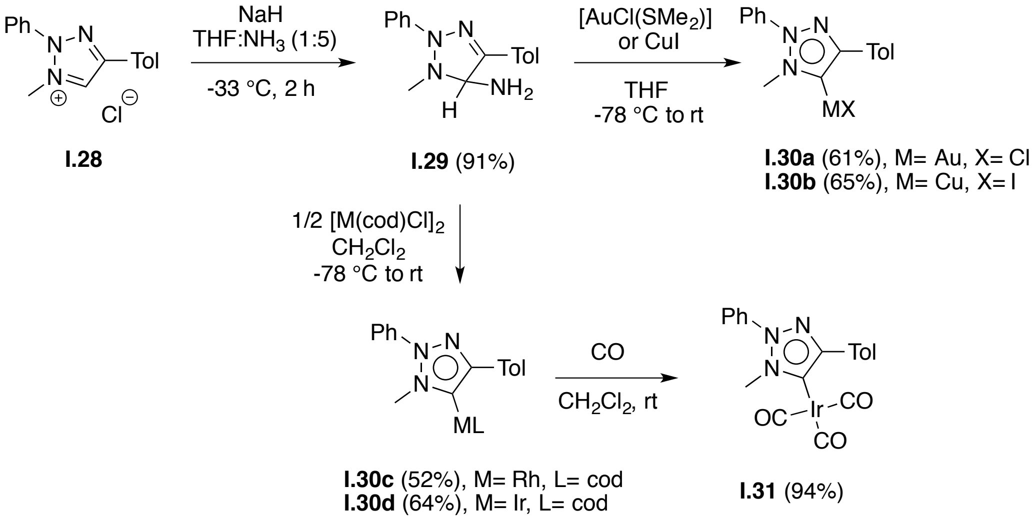
I.25c (88%), R= Dipp
I.25d (83%), R= OEt

I.27a (64%), R= Dipp
I.27b (80%), R= OEt

Scheme I.14: Synthesis of iridium complexes from free triazolylidenes

Additional methods

Kühn developed an alternative route for the preparation of metal-1,2,3-triazolylidene complexes.[52] 1,2,3-triazolium **I.28** having a 1,2,4 substitution pattern was prepared through a ring closing between *N*-phenyl-*p*-tolylcarbohydrazonoyl chloride and methyl isocyanide.[53] The reaction of the salt **I.28** with NaH in a mixture of ammonia and THF yields the ammonia adduct **I.29**. When **I.29** reacts with [M(cod)Cl]$_2$, [AuCl(SMe$_2$)] or CuCl at –78 °C, the corresponding triazolylidene complexes **I.30a**–**d** were formed, proving the ability of adduct **I.29** as carbene precursor (Scheme I.15). The authors also studied the donor strength of the new normal triazolylidene ligand by carbonylation of the iridium complex **I.30d** leading to formation of **I.31**. The measurements of the CO stretching vibrations concluded that the donor ability of this carbene is comparable to mesoionic 1,2,3-triazolylidenes and other normal carbenes, but lower than other families of abnormal NHCs.



Scheme I.15: Synthesis of 1,2,4-substituted triazolylidenes

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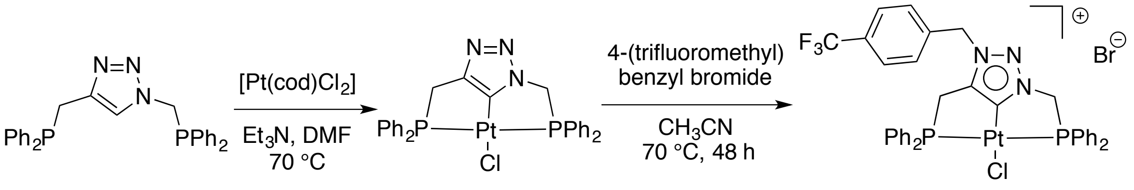
[52] L.-A. Schaper, K. Öfele, R. Kadyrov, B. Bechlars, M. Drees, M. Cokoja, W. A. Herrmann, F. E. Kühn, *Chem. Commun.* **2012**, *48*, 3857.

[53] a) D. Moderhack, M. Lorke, *Heterocycles*, **1987**, *26*, 1751; b) D. Moderhack, A. Daoud, *J. Heterocycl. Chem.* **2003**, *40*, 625; c) D. Moderhack, *Liebigs Ann. Chem.* **1989**, 1271.

An additional methodology to access to M-MIC complexes consists in the post-modification of a preformed MIC metal complex.[54] Thus, reaction of the triazole derivative **I.32**[55] with [Pt(cod)Cl$_2$] in the presence of Et$_3$N as the base, gave the platinum complex **I.33**[56] that was selectively *N*3 methylated in refluxing CH$_3$CN (Scheme I.16) to yield the corresponding mesoionic carbene **I.34**. An analogous approach was also used for the synthesis of a palladium triazolylidene complex.[57] The latter complex showed equal *N*1–*N*2 and *N*2–*N*3 bonds, which confirmed its mesoionic character.



I.32 **I.33** (100%) **I.34** (73%)

Scheme I.16: Synthesis of palladium pincer triazolylidenes by postmodification

Applications of metal mesoionic carbene complexes

Up to date, the use of metal 1,2,3-triazolylidene complexes is mainly straitened to the field of catalysis, although novel applications in different fields of chemistry are being developed.

Catalysis

Palladium complexes

Sankararaman published the first example of a catalytic reaction using Pd 1,2,3-triazolylidene **I.35** as the catalyst in the Suzuki coupling of substituted benzenes to form biaryl derivatives in good yields (Scheme I.17).[58]

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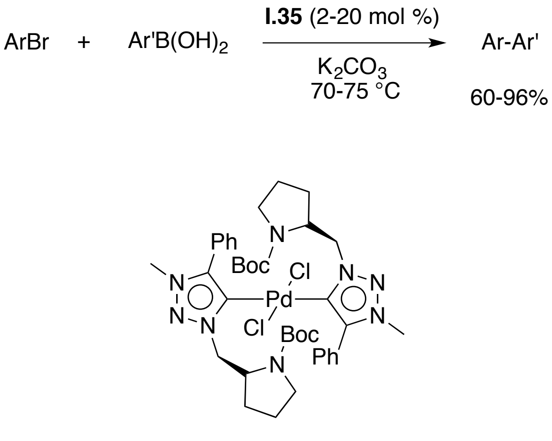
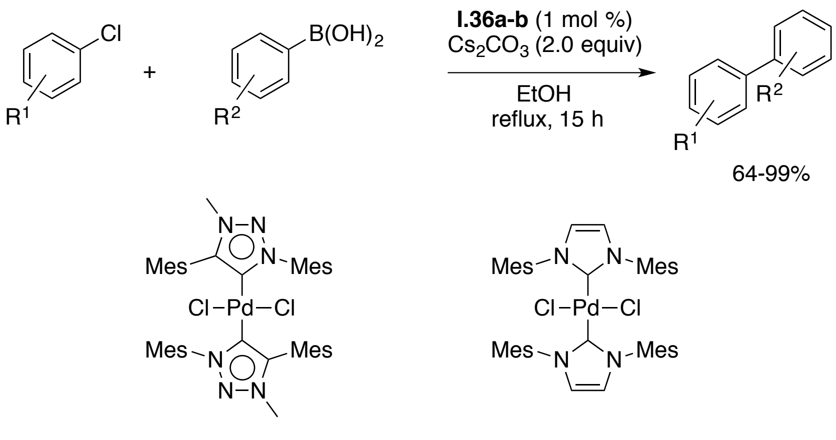
[54] E. M. Schuster, M. Botoshansky, M. Gandelman, *Dalton Trans.* **2011**, *40*, 8764.
[55] E. M. Schuster, M. Botoshansky, M. Gandelman, *Angew. Chem. Int. Ed.* **2008**, *47*, 4555.
[56] E. M. Schuster, M. Botoshansky, M. Gandelman, *Organometallics* **2009**, *28*, 7001.
[57] E. M. Schuster, G. Nisnevich, M. Botoshansky, M. Gandelman, *Organometallics* **2009**, *28*, 5025.
[58] T. Karthikeyan, S. Sankararaman, *Tetrahedron Lett.* **2009**, *50*, 5834.



I.35 (67%)

Scheme I.17: Palladium complex **I.35** catalysed Suzuki coupling

Fukuzawa synthetized the palladium 1,4-dimesytil-1,2,3-triazolylidene complex **I.36a**, which effectively catalysed the Suzuki coupling between different aryl chlorides and boronic acids.[59] In addition, they compared the catalytic activity of the triazolylidene **I.36a** against the analogous imidazolylidene **I.36b**, showing that the mesoinic complex was more efficient in the coupling of 4-chloroanisole with phenylboronic acid (99% against 60%) than the NHC-derivative **I.36b** (Scheme I.18).



I.36a (98%) **I.36b**

Scheme I.18: Palladium complexes **I.36a**–**b** catalysed Suzuki coupling

Complex **I.36a** can also catalyse Heck reaction between bromobenzene and *tert*-butyl acrylate forming the coupling product in nearly quantitative yields (Scheme I.19).

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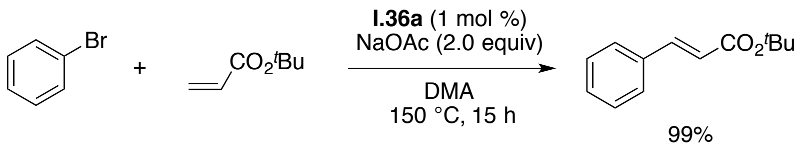
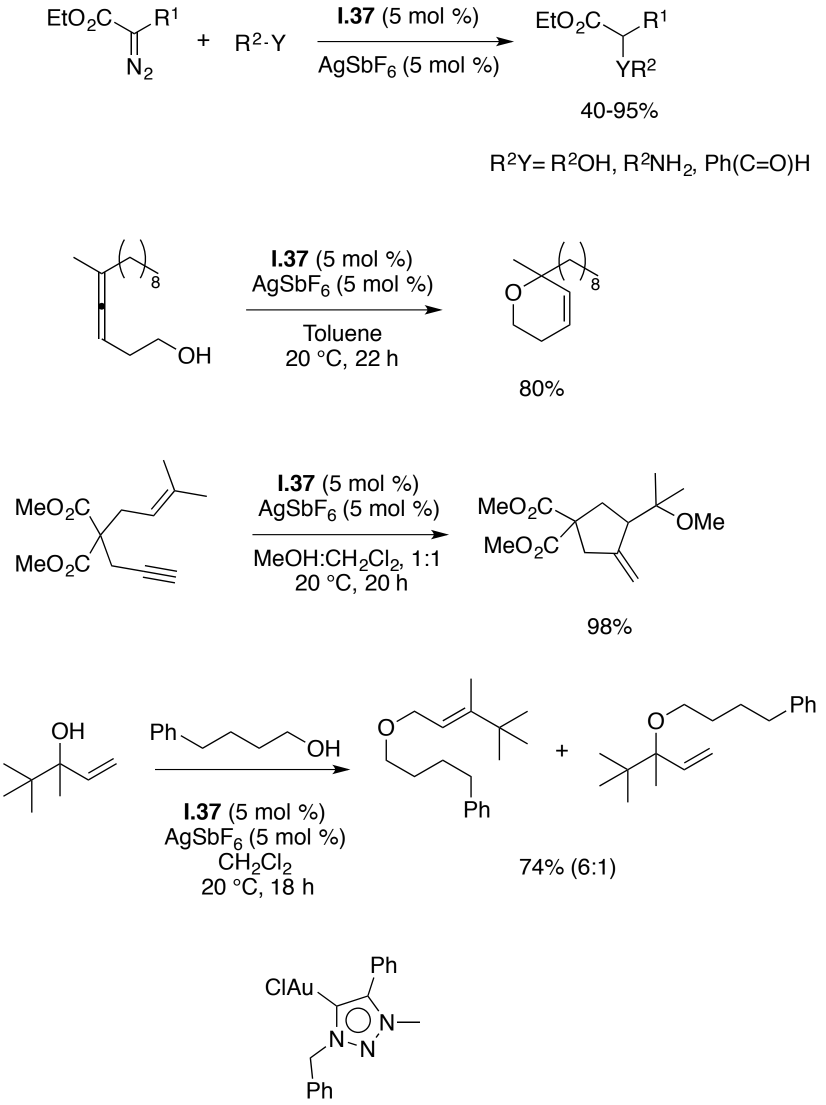
[59] T. Nakamura, K. Ogata, S. Fukuzawa, *Chem. Lett.* **2010**, *39*, 920.



Scheme I.19: Heck reaction catalysed by **I.36a**

Gold complexes

Crowley tested the gold complex **I.37** in the carbene transfer reaction from diazo compunds into O–H, N–H and C–H bonds employing $AgSbF_6$ to form the Au cationic species.[60]



I.37 (82%)

Scheme I.20: Catalytic transformations performed by Au-MIC **I.37**

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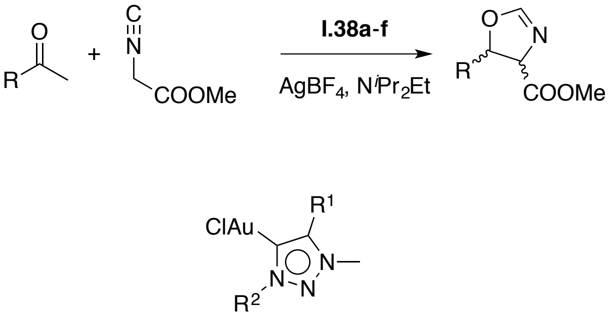
[60] K. J. Kilpin, U. S. D. Paul, A.-L. Lee, J. D. Crowley, *Chem. Commun.* **2011**, *47*, 328.

The pre-catalyst **I.37** could also effectively catalyse the hydroalkoxylation of allenes, the cyclizations of enynes and allylic etherifications[61] (Scheme I.20).

Albrecht reported the aldol condensation of isocyanides and carbonyl compounds to afford oxazolines in the presence of gold carbenes **I.38a–f**.[62] The triazolylidene dissociation from the gold complex was the crucial step in the catalyst activation. This dissociation process would render a ligand-less metal centre, which is the active species. Addition of $AgBF_4$ accelerates the process because of its twofold role, as halide scavenger and as transfer mediator (Scheme I.21).



I.38a (60%), R^1= Mes, R^2= Mes
I.38b (80%),R^1= 3,4,5-$(MeO)_3$-C_6H_2, R^2= 4-(MeO)-C_6H_4
I.38c (70%), R^1= Ph, R^2= Ph
I.38d (45%), R^1= ^{t}Bu
I.38e (77%), R^1= adamantyl, R^2= Ph
I.38f (65%), R^1= adamantyl, R^2= ^{t}Bu

Scheme I.21: Gold 1,2,3-triazolylidenes catalysed the formation of oxazolines

Iridium complexes

Ir-MIC complexes were tested in water oxidation reactions.[63] Metallation of the 4-pyridyl-1,2,3-triazolium salt **I.39** gave two different isomers.

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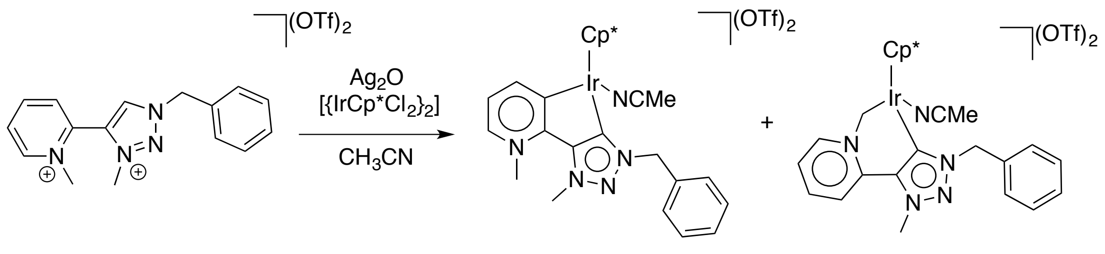
[61] J. R. Wright, P. C. Young, N. T. Lucas, A.-L. Lee, J. D. Crowley, *Organometallics* **2013**, *32*, 7065.

[62] D. Canseco-Gonzalez, A. Petronilho, H. Mueller-Bunz, K. Ohmatsu, T. Ooi, M. Albrecht, *J. Am. Chem. Soc.* **2013**, *135*, 13193.

[63] R. Lalrempuia, N. D. McDaniel, H. Müller-Bunz, S. Bernhard, M. Albrecht, *Angew. Chem. Int. Ed.* **2010**, *49*, 9765.



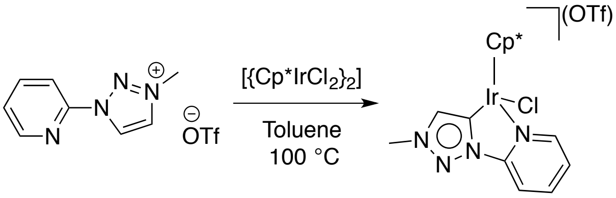
I.39 **I.40** (12%) **I.41** (35%)

Scheme I.22: Synthesis of iridium carbenes **I.40** and **I.41**

Iridium complex **I.40** presented one abnormally bounded carbene and one MIC in their structure while iridium MIC **I.41** showed an ylide-binding mode of the pyridinium centre in addition to the mesoinic bound carbene (Scheme I.22).

Quantitative analysis revealed that both complexes could generate O_2 from water in the presence of $(NH_4)_2Ce(NO_3)_6$ (CAN). The initial TOF were comparable to those of the benchmark iridium catalyst $[Ir(ppy)_2(OH)_2]OTf$ and increased after the initiation period. After 5 days, the TON of complex **I.40** was nearly 10000, which represents one of the largest numbers of TON reported to date. The electronic flexibility of 1,2,3-triazolylidene would be behind these stunning results: while normal carbenes could only stabilise low oxidation states, the zwitterionic nature of the 1,2,3-triazolylidene could also stabilise higher oxidation states. This redox-flexibility is one of the key features that must be present in catalytic complexes for water oxidation since the transfer of four electrons is required in the formation of oxygen from water.

In a later paper, the same group reported the synthesis and catalytic applications of new iridium complexes.[64] In this case, the pyridyl group in the triazolium salt **I.42** was not methylated, thus only one iridium carbene (**I.43**) was formed (Scheme I.23).



I.42 **I.43** (67%)

Scheme I.23: Synthesis of Ir-MIC **I.43**

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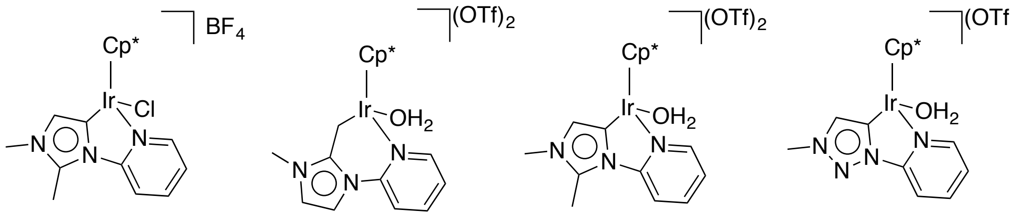
[64] A. Petronilho, J. A. Woods, H. Mueller-Bunz, S. Bernhard, M. Albrecht, *Chem. Eur. J.* **2014**, *20*, 15775.

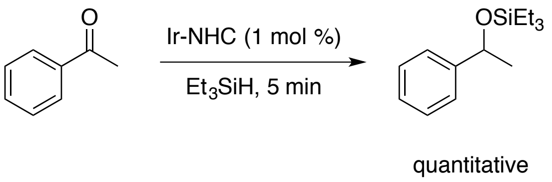
Complex **I.43** was also tested in water oxidation reactions, and its catalytic behaviour was compared with their imidazolylidene analogous **I.44**, the latter showing a higher catalytic activity. The reason could be traced to the higher donor strength of the imidazolylidenes compared to 1,2,3-triazolylidenes that may be the responsible for an easier stabilisation of higher oxidation states in the metal centre.



I.44 (85%) **I.45a** (49%) **I.45b** (82%) **I.45c** (59%)

Figure I.7: Iridium *N*-heterocyclic carbenes **I.44** and **I.45a**-**c**

These complexes were also tested in the catalytic hydrosilylation of acetophenone. Species with chloride ligands were not active, suggesting that the presence of labile solvent ligands is crucial in its catalytic behaviour. When reaction was performed by iridium complexes **I.45a**–**c**, hydrosilylation ended in 5 min (Scheme I.24).



Scheme I.24: Catalytic transformation of acetophenone performed by Ir-NHCs

Sarkar reported the synthesis of iridium and ruthenium complexes **I.46a**–**b** with a bidentate ligand bearing 1,2,3-triazolylidene acting as a chelating agent for the metal (Scheme I.25).[65]

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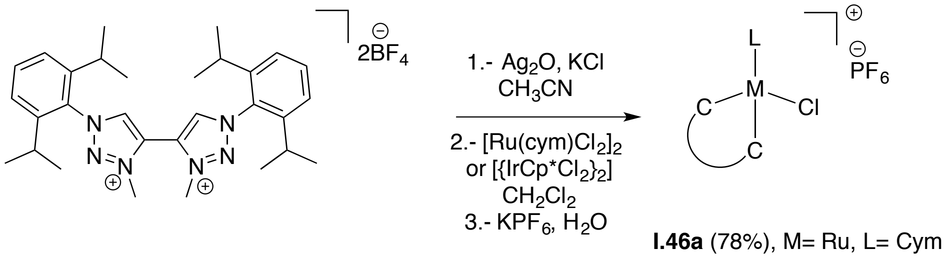
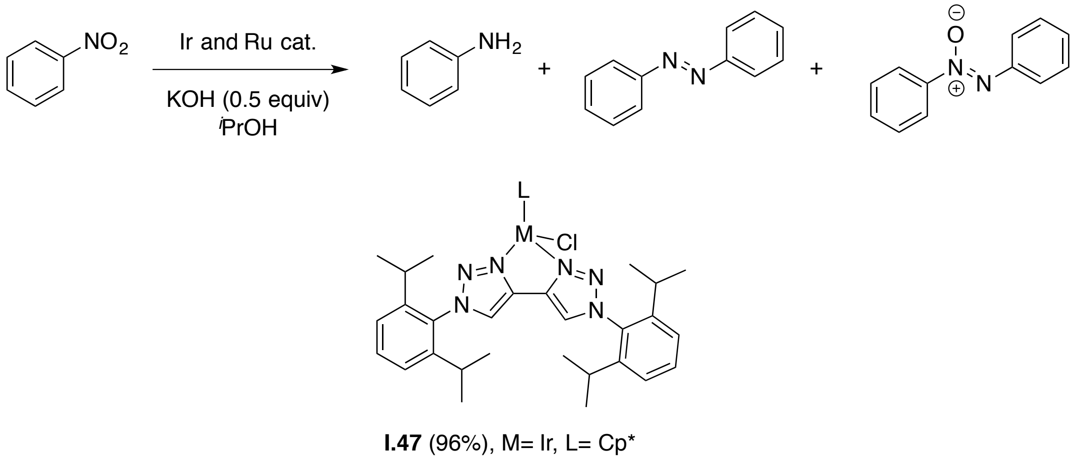
[65] S. Hohloch, L. Suntrup, B. Sarkar, *Organometallics* **2013**, *32*, 7376.



I.46a (78%), M= Ru, L= Cym
I.46b (84%), M= Ir, L= Cp*

Scheme I.25: Synthesis of chelating iridium and rhodium triazolylidenes

The catalytic activity of these new complexes was studied in the transfer hydrogenation of nitrobenzene (Scheme I.26). Their behaviour was compared to the performance displayed by analogous Ir and Ru complexes lacking carbenes as ligands. Iridium complex **I.47** was the best catalyst for converting nitrobenzene in azobenzene. On the other hand, Ru complex **I.48** was the best catalyst to afford aniline from nitrobenzene.

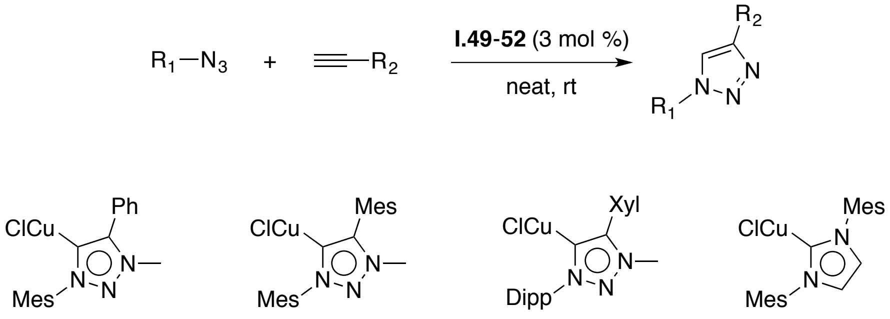


I.47 (96%), M= Ir, L= Cp*
I.48 (84%), M= Ru, L= *p*-cym

Scheme I.26: Catalytic hydrogenation of nitrobenzene

Copper complexes

Fukuzawa reported the synthesis of some copper carbene complexes **I.49**, **I.50** and **I.51** that were tested in the cycloaddition between benzyl azide and phenylacetylene (Scheme I.27).[66] **I.52** was also tested to compare the catalytic activity between classical and mesoionic carbenes.



I.49 (82%) **I.50** (84%) **I.51** (74%) **I.52**

Scheme I.27: CuAAC reaction catalysed by copper complexes **I.49–I.52**

When copper carbenes **I.49–52** were employed as catalysts in the benchmark CuAAC reaction between benzyl azide and phenylacetylene, triazolylidene **I.49** resulted to be the best catalyst, leading to complete conversions within 30 min. With carbene **I.50** as catalyst, 100% of conversion was reached after 90 min. This carbene performed the reaction faster than the analogous imidazolylidene **I.52** where complete conversion was achieved after 5 h. Catalyst **I.49** was tested in the reactions of azides with different alkynes. Aromatic, electron-rich, electron-poor, sterically demanding and functionalized alkynes would lead the corresponding *click* products with good yields and short reaction times.

More recently Bertrand studied the catalytic behaviour of a set of mesoionic Cu carbene complexes **I.53–55** in the CuAAC reaction (Scheme I.28).[47] The activity of these complexes was compared to the classic Cu imidazolylidene **I.52**. Once again, mesoionic carbene **I.55** was more active than its imidazolylidene counterpart in the CuAAC. In addition, this catalyst was compatible with a broad range of functionalities in the starting materials including nitro, nitrile, ether, carbonyl, alcohol, amine and cyano groups.

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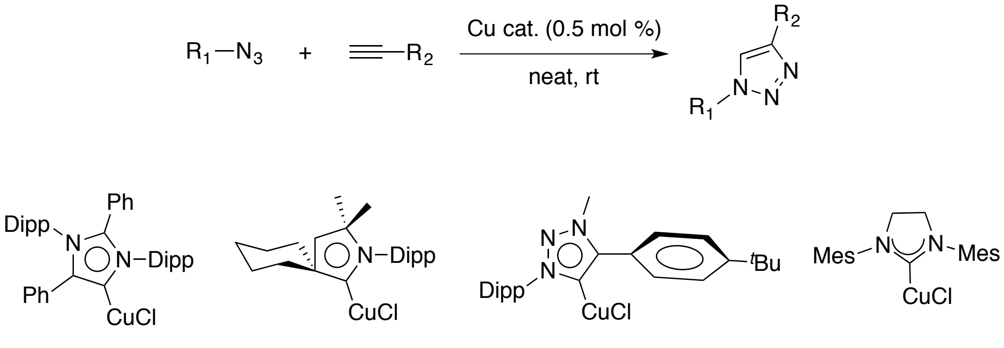
[66] T. Nakamura, T. Terashima, K. Ogata, S. Fukuzawa, *Org. Lett.* **2011**, *13*, 620.

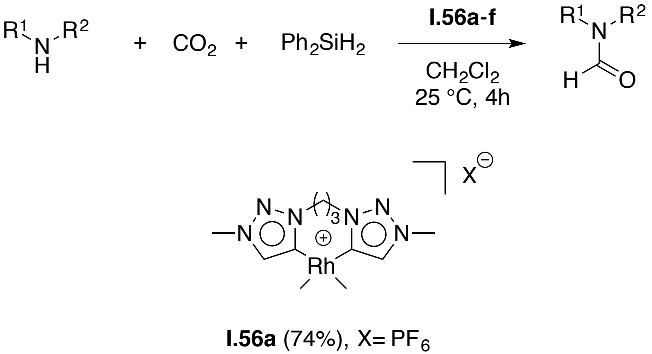


I.53 (98%) **I.54** (75%) **I.55** (95%) **I.52**

Scheme I.28: CuAAC reaction catalysed by Cu-NHCs **I.53–I.55**

Rhodium complexes

Kobayashi reported the first example of formylation of amines with carbon dioxide catalysed by a rhodium 1,2,3-triazolylidene complex. [67] Chelating bis(triazolylidene) complexes **I.56a–f** facilitated the reduction of CO_2 due to the strong electron donating nature of these mesoionic ligands. These complexes were more active than their classic NHC analogues, which were unreactive under these reaction conditions (Scheme I.29).



I.56a (74%), X= PF_6
I.56b (66%), X=SbF_6
I.56c (65%), X= OTf
I.56d (55%), X= NTf_2
I.56e (80%), X= BPh_4
I.56f (63%), X= BArF

Scheme I.29: Rhodium complexes catalysed formylation of CO_2

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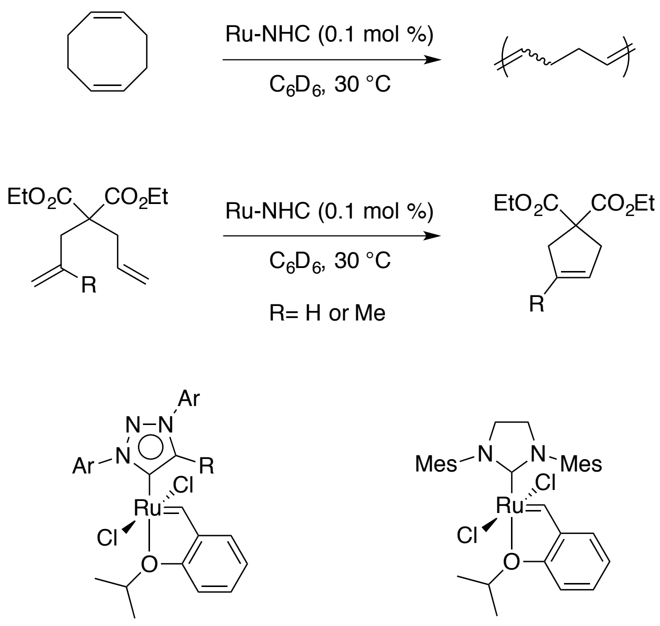
[67] T. V. Q. Nguyen, W.-J. Yoo, S. Kobayashi, *Angew. Chem. Int. Ed.* **2015**, *54*, 9209.

Ruthenium complexes

Bertrand[50] reported the use of free triazolylidenes **I.25a**–**b**,**d** to replace the phosphine ligand in the Hoveyda-Grubbs catalyst.[68] The new ruthenium complexes **I.26a**–**b**,**d** were tested as catalysts in the ring opening methathesis (ROM) of cyclic olefins and in the ring-closing olefin methatesis (RCOM).



I.26a, Ar= Dipp, R= Ph
I.26b, Ar= Dipp, R= Mes
I.26d, Ar= Mes, R= Ph

I.57

Scheme I.30: ROM and RCOM reactions catalysed by Ru complexes

They encountered a dependence between the nature of the MIC substituents and the rates of initiation and resistance to deactivation of the catalysts. In addition, some of these new complexes could rival the traditional NHC ruthenium catalyst for olefin methatesis **I.57** (Scheme I.30).[69]

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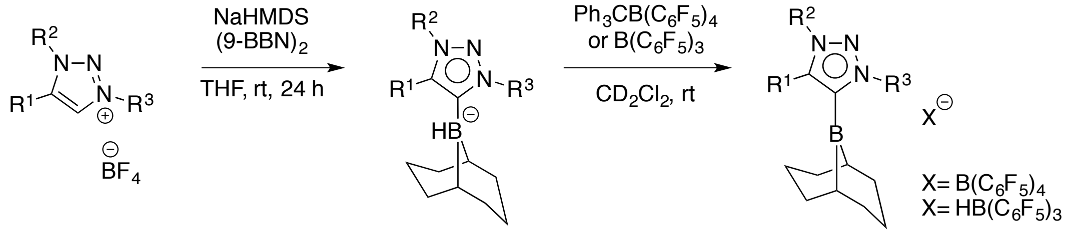
[68] a) S. T. Nguyen, L. K. Johnson, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1992**, *114*, 3974; b) J. S. Kingsbury, J. P. A. Harrity, P. J. Bonitatebus, A. H. Hoveyda, *J. Am. Chem. Soc.* **1999**, *121*, 791.

[69] M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 953.

Boron complexes

Recently, Crudden reported examples of 1,2,3-triazolylidene borenium ions having unprecedented catalytic activity in the hydrogenation of imines and *N*-heterocycles at atmospheric pressure.[70] These complexes could carry out this reaction at room temperature. The synthesis of the boron carbenes was performed by deprotonation of the triazolium salts **I.58a**–**e** with NaHMDS in the presence of 9-borabicyclo(3.3.1)nonane to yield carbenes **I.59a**–**e** at room temperature. Hydride abstraction by $Ph_3CB(C_6F_5)_4$ afforded the borenium ions **I.60a**–**e** (Scheme I.31).



I.58a, R^1= R^2= R^3= Ph
I.58b, R^1= H, R^2= R^3= Ph
I.58c, R^1= H, R^2= R^3= *p*Anisyl
I.58d, R^1= H, R^2= Me, R^3= Ph
I.58e, R^1= H, R^2= Dipp, R^3= Ph

I.59a (86%)
I.59b (86%)
I.59c (91%)
I.59d (42%)
I.59e (57%)

I.60a
I.60b
I.60c
I.60d
I.60e

Scheme I.31: Synthesis of B-NHCs

Moreover, they developed a strategy where borenium ions **I.60a**–**e** were not necessary to be isolated to perform the catalytic studies. These active species could be generated *in situ* in the catalytic process from their precursors **I.59a**–**e**. Comparison of the activity between the mesoionic borenium ions and analogous imidazolylidene demonstrates the higher activity of the former over the latter. They also evidence the selectivity of the catalyst in the reduction of different *N*-heterocyclic cores where no traces of over-reduction products were observed (Scheme I.32).

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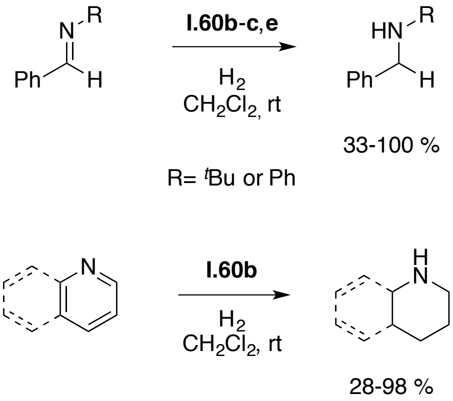
[70] P. Eisenberger, B. P. Bestvater, E. C. Keske, C. M. Crudden, *Angew. Chem. Int. Ed.* **2015**, *54*, 2467.



Scheme I.32: Hydrogenation reactions catalysed by B-NHCs

Other applications

Recently, the application field of M–MIC complexes has been extended to their role as antitumoral drugs,[71] as enzymes mimetic[72] and as photosensitizers.[73]

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[71] K. J. Kilpin, S. Crot, T. Riedel, J. A. Kitchen, P. J. Dyson, *Dalton Trans.* **2014**, *43*, 1443.

[72] R. Lalrempuia, H. Müller-Bunz, M. Albrecht, *Angew. Chem. Int. Ed.* **2011**, *50*, 9969.

[73] a) B. Schulze, D. Escudero, C. Friebe, R. Siebert, H. Görls, U. Köhn, E. Altuntas, A. Baumgaertel, M. D. Hager, A. Winter, B. Dietzek, J. Popp, L. González, U. S. Schubert, *Chem. Eur. J.* **2011**, *17*, 5494; b) V. Leigh, W. Ghattas, R. Lalrempuia, H. Müller-Bunz, M. T. Pryce, M. Albrecht, *Inorg. Chem.* **2013**, *52*, 5395; c) S. Sinn, B. Schulze, C. Friebe, D. G. Brown, M. Jäger, E. Altuntaş, J. Kübel, O. Guntner, C. P. Berlinguette, B. Dietzek, U. S. Schubert, *Inorg. Chem.* **2014**, *53*, 2083; d) Y. Liu, K. S. Kjær, L. A. Fredin, P. Chábera, T. Harlang, S. E. Canton, S. Lidin, J. Zhang, R. Lomoth, K.-E. Bergquist, P. Persson, K. Wärnmark, V. Sundström, *Chem. Eur. J.* **2015**, *21*, 3628.

I.2 OBJECTIVES

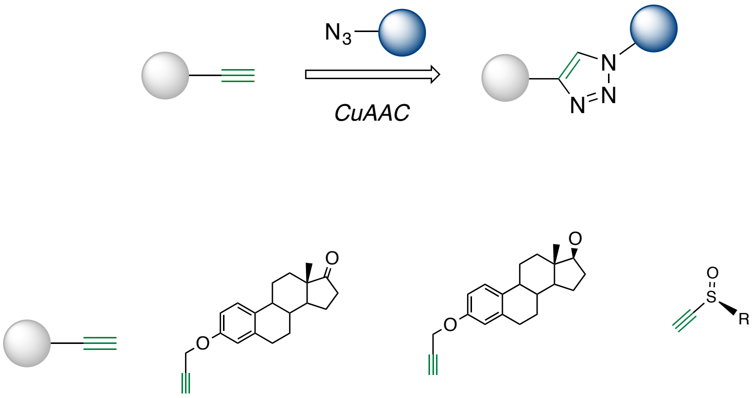
Based on the above introduction the general objectives of this work are:

1.- Synthesis of new M-MIC complexes based on 1,2,3-triazolylidenes. These new metallic carbenes could be separated into two different groups:

- Bioorganometallic derivatives formed by mesoionic carbenes and steroidic derivatives (estrone and estradiol).
- Metallic 1,2,3-triazolylidene complexes bearing enantiomerically pure sulfoxide group in the *C*4 position of the heterocyclic core.

The synthetic methodology to prepare both groups of carbenes will be analogous, and will consists of the following steps:

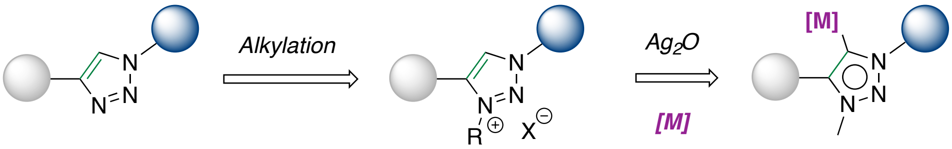
- Preparation of a 1,2,3-triazole precursor through the straightforward and regioselective cycloaddition reaction between alkynes and azides catalysed by Cu(I).



Scheme I.33: General approach for the synthesis of 1,2,3-triazoles

In the case of the ligand derived from steroids, the natural product will be introduced through the alkyne. For sulphur based triazole ligands the enantiopure sulfoxide will be also introduced in the heterocycle through the alkyne.

- Methylation and silver mediated transmetallation to form the desired M-MIC complexes.



Scheme I.34: Functionalization of triazole cores for the obtainement of 1,2,3-triazolylidenes

2.- Study of the reactivity of M-MIC having enantiopure sulphur functionalities, specifically the desulfinylation reaction to prepare unsubstituted at the triazole carbons MIC-M (M= Ag, Au) complexes.

3.- Study of sulfoxide containing Au-MIC complexes as catalysts in the cycloisomerization of enynes. Determination of the key role of the sulfoxide moiety in the activity of these catalysts.

CHAPTER II

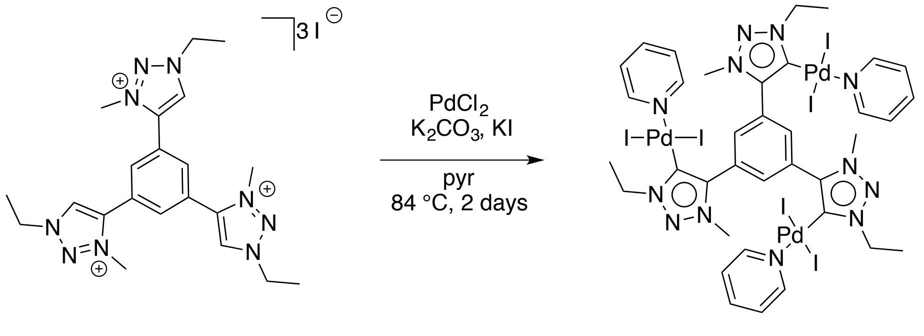
Synthesis of polymetallic mesoionic carbenes supported by steroid derivatives

II.1 INTRODUCTION

II.1.1 Polymetallic 1,2,3-triazolylidene complexes

The large amount of multimetallic complexes bearing classic NHCs,[74] has been crucial for the important number of supramolecular entities displaying NHC in their backbones. They can be part of a great number of structures including squares, triangles, cylinders and metallic polymers. However, analogous supramolecular assemblies featuring mesoionic carbenes are still scarce. This can probably be due to the fact that polymetallic MICs are still very uncommon.

Sarkar reported the first example of a palladium 1,2,3-triazolylidene complex having three metallic nuclei in its structure.[75] Reaction of triazolium salt **II.1** with $PdCl_2$ in pyridine and K_2CO_3 as a base afforded the trinuclear complex **II.2** in 61% yield (Scheme II.1).



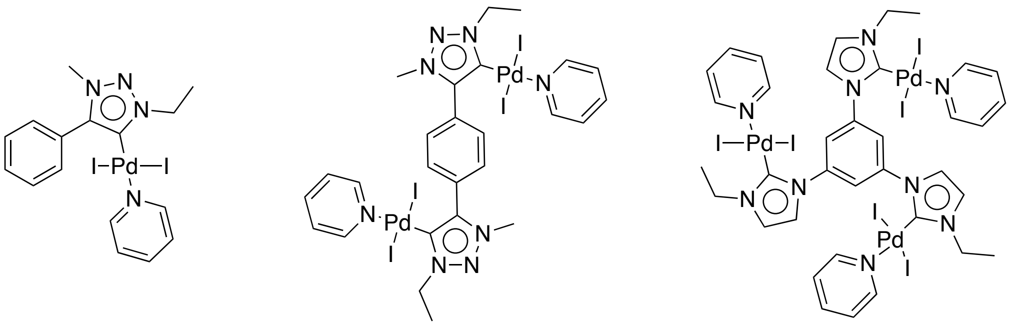
II.1 **II.2** (61%)

Scheme II.1: Synthesis of trimetallic palladium complex **II.2**

---

[74] J. A. Mata, M. Poyatos, E. Peris, *Coord. Chem. Rev.* **2007**, *251*, 841.
[75] R. Maity, M. van der Meer, B. Sarkar, *Dalt. Trans.* **2015**, *44*, 46.

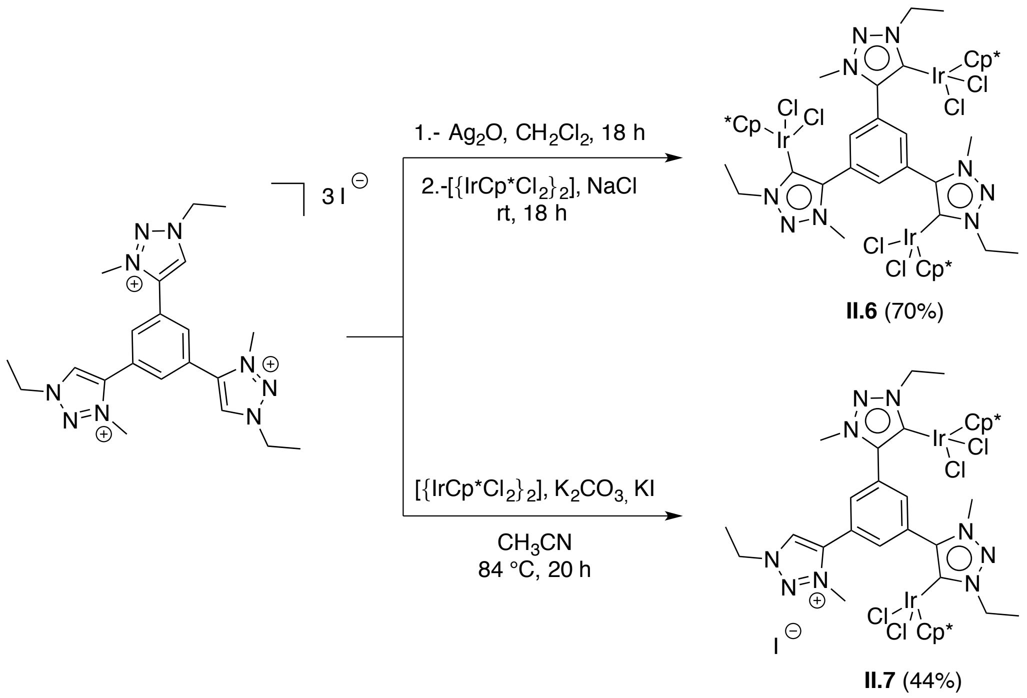
In the study, authors investigated the different electrochemical behaviour of the mono- and dinuclear palladium mesoionic complexes **II.3** and **II.4**, respectively, together with the trimetallic analogous **II.5**, bearing three imidazolylidenes nuclei instead of triazolylidenes. The presence of more than one reduction peaks for these multimetallic complexes **II.2** and **II.4** suggests a stepwise reduction of the Pd centres. These data pointed out a strong electrochemical coupling among the metallic centres. Nevertheless, this metallic connectivity is not observed for the analogous trimetallic imidazolylidene complex **II.5**.



II.3 **II.4** **II.5**

Figure II.1: Pd complexes measured in cyclic voltamperometry

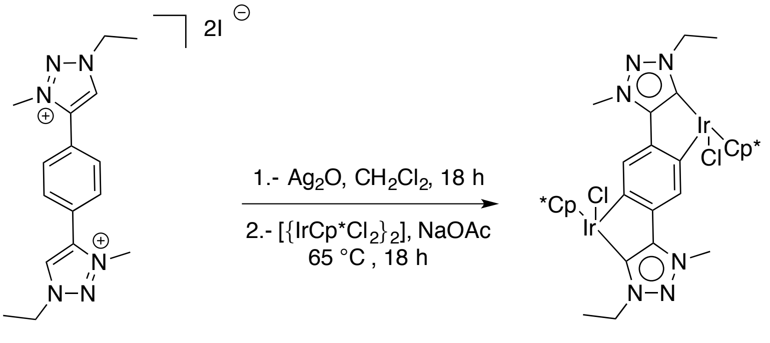
The same group reported analogous multimetallic iridium complexes **II.6** and **II.7**.



Scheme II.2: Synthesis of multimetallic iridium carbenes

When the tris(triazolium) salt was treated with Ag_2O followed by transmetallation using [{IrCp*Cl_2}$_2$], trimetallic complex **II.6** was obtained (Scheme II.2).[76] On the other hand, the use of K_2CO_3 as a base yielded the bimetallic complex **II.7** where the third triazolium core remained unreacted.

No orthometallated products were observed in the formation of complexes **II.6** and **II.7**, contrary to the C–H activated phenyl backbone of polymetallic carbenes **II.8**, previously reported by the same group (Scheme II.3).[77] Steric factors would probably be behind the inertia towards orthometallation of complexes **II.6** and **II.7**.



II.8 (69%)

Scheme II.3: Orthometallated iridium 1,2,3-triazolylidene **II.8**

Another synthetic approach for the generation of polymetallic complexes bearing MICs uses alkynylmetal derivatives.[78] The use of a ferrocene group in a metallo-ligand backbone has been widely employed in organometallic chemistry to obtain heterobimetallic NHC complexes.[79] Sarkar reported the first example of a combination of a ferrocene unit with a gold MIC complex (Scheme II.4).[80] Reaction between ((trimethylsilyl)ethynyl)ferrocene **II.9** and different azides in the presence of catalytic amounts of Cu(I) furnished the corresponding ferrocenyl-triazoles **II.10a**–**b**. After methylation with Meerwein's salt, the heterometallic gold-iron complexes **II.11a**–**b** were obtained through the Ag_2O-transmetallation protocol from the triazolium salts **II.12a**–**b** (Scheme II.4).

---

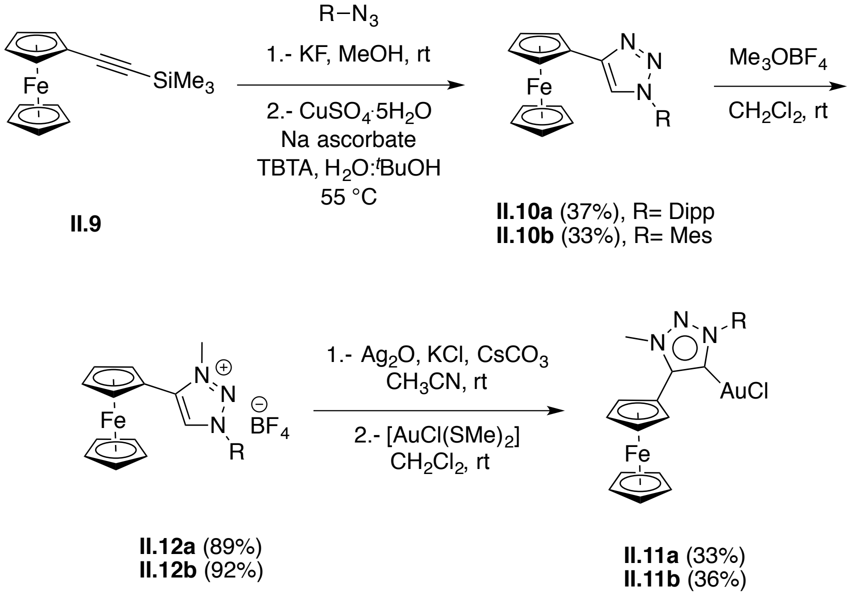
[76] R. Maity, M. van der Meer, S. Hohloch, B. Sarkar, *Organometallics* **2015**, *34*, 3090.

[77] R. Maity, S. Hohloch, C.-Y. Su, M. van der Meer, B. Sarkar, *Chem. Eur. J.* **2014**, *20*, 9952.

[78] G. Kumar, R. Gupta, *Chem. Soc. Rev.* **2013**, *42*, 9403.

[79] a) M. Süβner, H. Plenio, *Angew. Chem. Int. Ed.* **2005**, *44*, 6885; b) N. Debono, A. Labande, E. Manoury, J.-C. Daran, R. Poli, *Organometallics* **2010**, *29*, 1879; c) K. Arumugam, C. D. VarnadoS. Sproules, V. M. Lynch, C. W. Bielawski, *Chem. Eur. J.* **2013**, *19*, 10866.

[80] L. Hettmanczyk, S. Manck, C. Hoyer, S. Hohloch, B. Sarkar, *Chem. Commun.* **2015**, *51*, 10949.



Scheme II.4: Synthesis of ferrocenyl gold 1,2,3-triazolylidene

A bimetallic hybrid containing a palladium imidazolylidene and a rhodium mesoinic carbene was reported by Cowie (Scheme II.5).[81] The synthetic approach consists firstly in preparing the imidazolium salt **II.13** having a propargylic pending arm. This alkyne reacted next with an azide to form triazole **II.14**. Methylation of the heterocycle led the dicationic imidazolium-triazolium hybrid ligand **II.15**. Reaction with $Pd(OAc)_2$ in the presence of KI selectively metallated the more acidic imidazolium moiety yielding **II.16**. Addition of half equivalent of $[\{Rh(\mu\text{-}OMe)(cod)\}_2]$ in boiling acetonitrile and in the presence of KI afforded the desired unsymmetrical heterobimetallic complex **II.17**. This heterodimetallic complex is a promising catalyst to effect tandem processes in which the two different metals play differentiated roles in the catalytic process.

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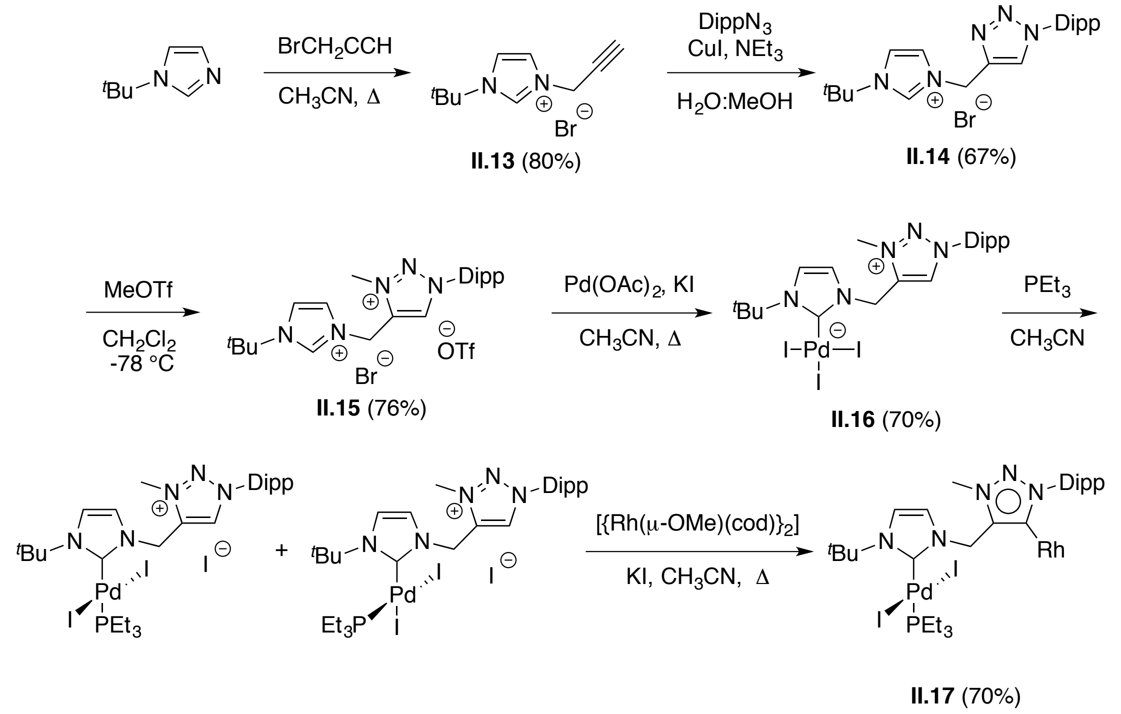
[81] M. T. Zamora, M. J. Ferguson, R. McDonald, M. Cowie, *Organometallics* **2012**, *31*, 5463.



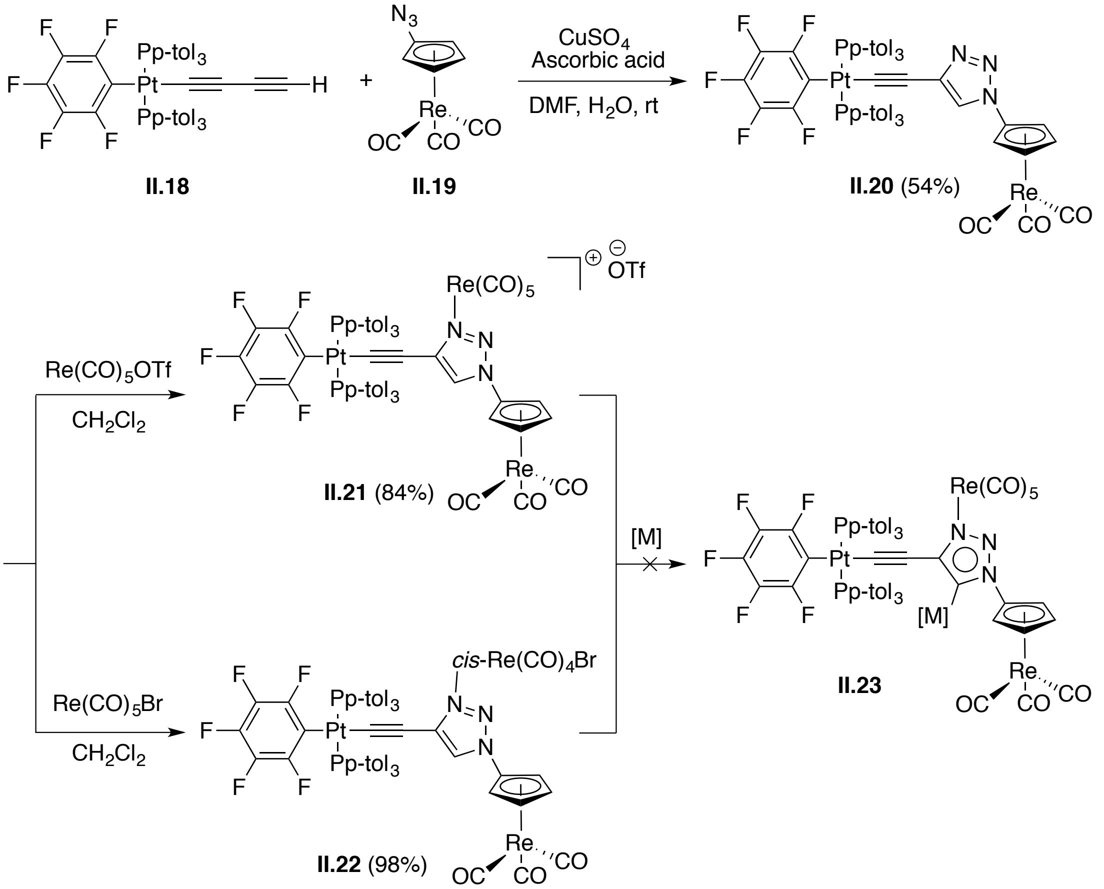
Scheme II.5: Synthetic route of heterobimetallic complex **II.17**

Due to the flexibility of the Cu(I)-catalysed cycloaddition between azides and alkynes, a new methodology for the synthesis of multimetallic–MIC complexes can be achieved by placing the metallic moiety through the azide, the alkyne or both.[82] Gladysz and co-workers developed a methodology for the synthesis of trimetallic triazoles (Scheme II.6).[83] Reaction of [*trans*-(C_6F_5)(*p*-$tol_3P)_2Pt(C{\equiv}C)_2H$] **II.18** and the rhenium cyclopentadienyl azide **II.19** in the presence of catalytic amounts of Cu(I) gave the heterobimetallic triazole **II.20**. Introduction of the third metallic fragment was achieved by reaction of bimetallic triazole **II.20** with $Re(CO)_5OTf$ in CH_2Cl_2 for 5 days (affording **II.21**) or by the less electrophilic rhenium bromide $Re(CO)_5Br$ trough 10-days reaction (yielding **II.22**). Unfortunately, all attempts to introduce of a fourth metal moiety in order to synthetize a mesoionic carbene **II.23** failed.

---

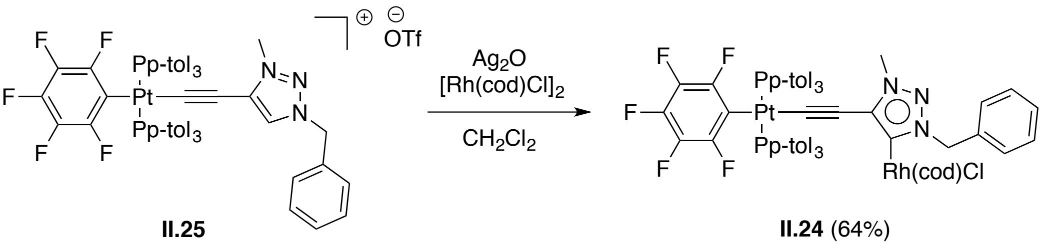
[82] L. Casarrubios, M. C. de la Torre, M. A. Sierra, *Chem. Eur. J.* **2013**, *19*, 3534.

[83] M. C. Clough, P. D. Zeits, N. Bhuvanesh, J. A. Gladysz, *Organometallics* **2012**, *31*, 5231.



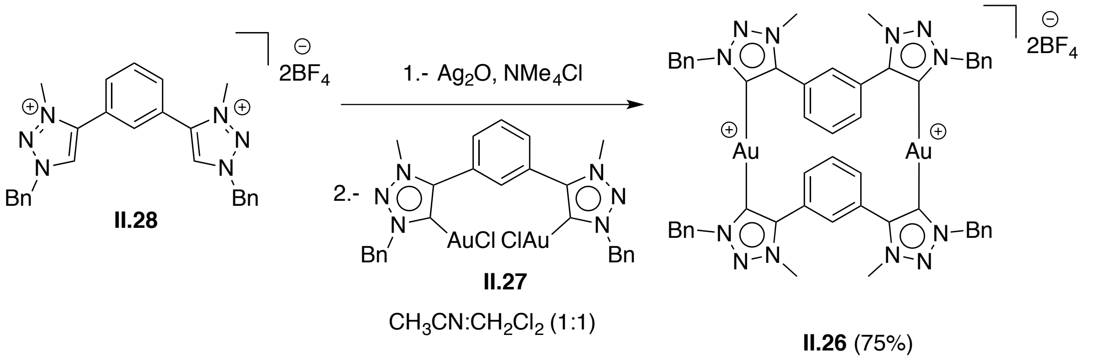
Scheme II.6: Synthesis of trimetallic triazoles

Nevertheless, heterobimetallic 1,2,3-triazolylidene carbene **II.24** was prepared through reaction of triazolium **II.25** with Ag_2O and later transmetallation with $[Rh(cod)Cl]_2$ (Scheme II.7). Authors reasoned that the less acidic nature of H5 in the trimetallic triazolium salts **II.21** and **II.22** inhibit the formation of the desired **II.23** complex.



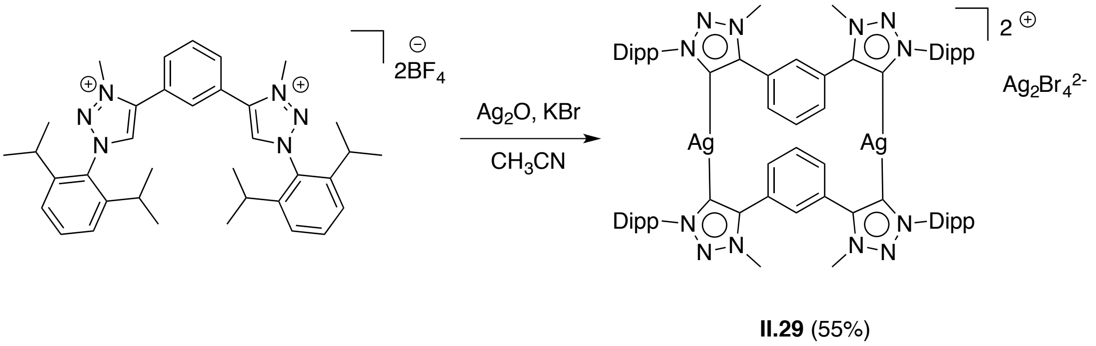
Scheme II.7: Synthesis of heterobimetallic triazolylidenes complex **II.24**

Crowley reported the synthesis of a gold metallomacrocycle **II.26** through the self-assembly of the dinuclear mesoionic carbene **II.27**.[60] Treatment of **II.28** with 1.00 equiv of the *in situ* generated disilver triazolylidene complex afforded the metallomacrocycle **II.26** in one-pot process (Scheme II.8).



Scheme II.8: Synthesis of gold macrocycle **II.26**

Crudden reported the X-ray structure of an analogous silver macrocyclic carbene **II.29** (Scheme II.9).[84] The two ligands interconnected through a silver atom were almost parallel to each other. No π interactions between the bridging phenyl groups were observed.



Scheme II.9: Synthesis of silver triazolylidene macrocycle **II.29**

The structure of the copper macrocycles **II.30a–c** was determined by Sarkar (Scheme II.10).[85] In this case, the distance between the two copper centres made them ideal for the investigation of potential cooperative effects. When these macrocycles were used in the cycloaddition between benzyl azide and phenyl acetylene they performed a greater activity compared to analogous mononuclear 1,2,3-triazolylidene complexes. These results agree with the recent mechanistic studies carried by Fokin where the involvement of two copper centres in the active site of the reaction is proposed.[86]

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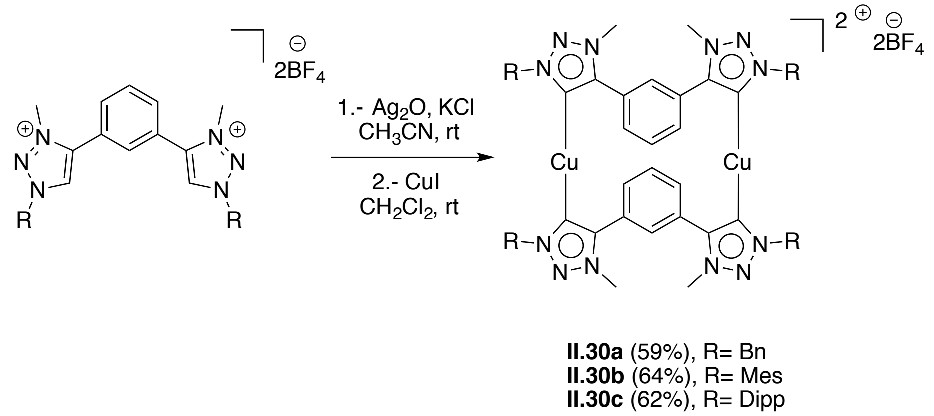
[84] E. C. Keske, O. V. Zenkina, R. Wang, C. M. Crudden, *Organometallics* **2012**, *31*, 456.

[85] S. Hohloch, L. Suntrup, B. Sarkar, *Inorg. Chem. Front.* **2016**, *3*, 67.

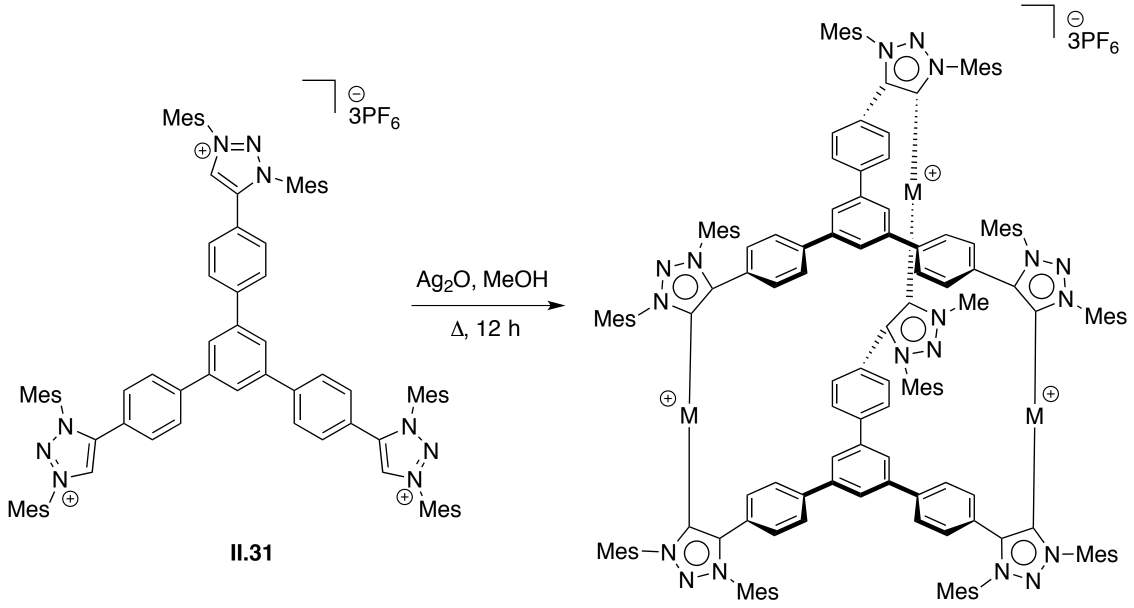
[86] B. T. Worrell, J. A. Malik, V. V. Fokin, *Science* **2013**, *340*, 457.



II.30a (59%), R= Bn
II.30b (64%), R= Mes
II.30c (62%), R= Dipp

Scheme II.10: Synthesis of triazolylidene macrocycles **II.30a–c**

Peris reported the synthesis of supramolecular cages based on silver and gold triazolylidenes (Scheme II.11).[87] Reaction of the 1,3,5-triphenylbenzene-bridged tris(triazolium) salt **II.31** with 1.50 equiv of Ag_2O in MeOH at 60 °C yielded the trimetallic silver mesoionic complex **II.32a**. The ^1H NMR spectrum showed the high symmetry of this sandwich-like structure with the silver atoms between the two trimeric triazole ligands. Subsequent reaction of the silver complex **II.32a** with $[AuCl(SMe_2)]$ afforded the analogous trimetallic gold complex **II.32b**.



II.32a (42%)
M= Ag

$\xrightarrow[\text{CH}_3\text{CN, rt, 5 days}]{[\text{Au}]}$ **II.32b** (58%)
M= Au

Scheme II.11: Synthesis of silver and gold cages

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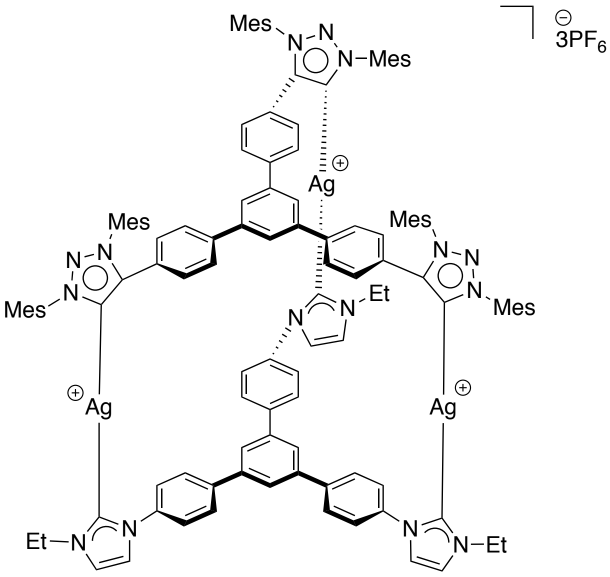
[87] C. Mejuto, G. Guisado-Barrios, D. Gusev, E. Peris, *Chem. Commun.* **2015**, *51*, 13914.

These authors also achieved the formation, for the first time, of a silver metallo-macrocyclic complex **II.33** featuring both tris(NHC) and tris(MIC) ligands (Figure II.2). Reaction of equimolar ammounts of both ligands with 3 equiv of Ag_2O in MeOH at 60 °C led macrocycle **II.33** after 12 h. DFT calculations carried out with the mononuclear analogous, reveal that under equilibrium conditions, the mixed carbene complex is predicted to be the main compound.



II.33 (43%)

Figure II.2: Metallo-macrocycle **II.33**

II.1.2 Metal-steroid derivatives

Interest on steroids containing transition metals has steadily grown since the original report from Tsutsui in the early 60s describing the preparation of the acetylergosterol iron tricarbonyl complex **II.34**, [88] prepared by reaction of acetylergosterol with triiron dodecarbonyl in refluxing benzene (Scheme II.12).

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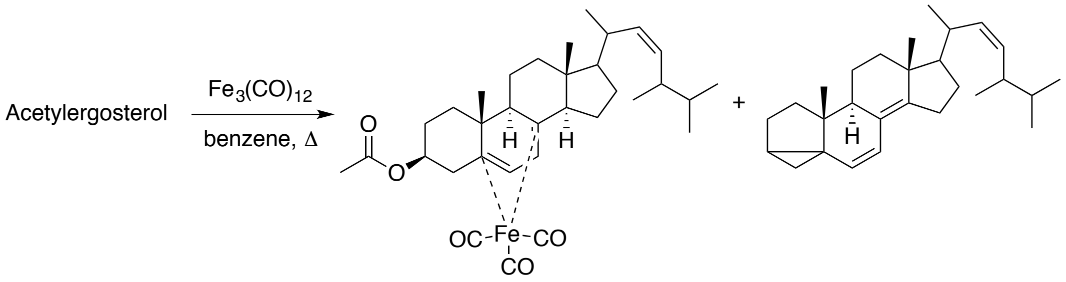
[88] A. Nakamura, M. Tsutsui, *J. Med. Chem.* **1963**, *6*, 796.

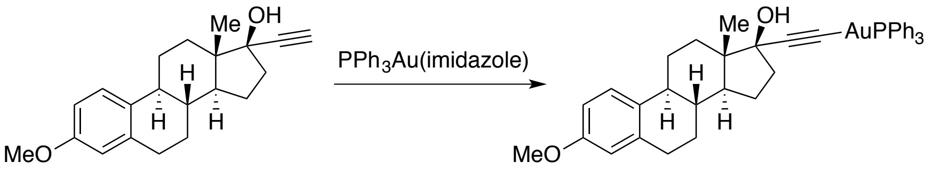


II.34 (17%)

Scheme II.12: Synthesis of the first metal-steroid complex

Although this first example of a metallated natural product was achieved in 1963, it was not until the late 1970s when the idea of using this class of organometallic derivatives for biological applications was developed.[89] Nowadays, steroid-functionalized metal complexes are used in different applications ranging from medicinal and biological fields to metalloenzymes or as intermediates in the transformation of steroids.

Several gold-steroid complexes have been described usually having a structure of Au-ethynylestrone. Bonati reported the first example of a gold ethynyl steroid complex.[90] PPh_3Au(imidazole) was basic enough to deprotonate mestranol yielding the corresponding gold complex **II.35** (Scheme II.13).



II.35

Scheme II.13: Synthesis of mestranol gold complex **II.35**

Inspired by this work, Stockland reported the synthesis of a series of ethynyl estradiol and mestranol based gold species.[91]

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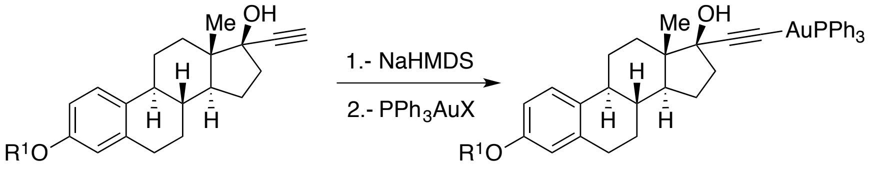
[89] F. Le Bideau, S. Dagorne, *Chem. Rev.* **2013**, *113*, 7793.

[90] F. Bonati, A. Burini, B. R. Pietroni, E. Giorgini, B. Bovio, *J. Organomet. Chem.* **1988**, *344*, 119.

[91] R. A. Stockland, M. C. Kohler, I. A. Guzei, M. E. Kastner, J. A. Bawiec, D. C. Labaree, R. B. Hochberg, *Organometallics* **2006**, *25*, 2475.

These organometallic compounds were prepared by deprotonation of the ethynyl moiety with NaHMDS and followed by reaction with different Ph_3PAuX salts (Scheme II.14).[92] To the best of our knowledge, no biological data about the activity of such complexes is known.



Mestranol (R^1= Me)
Ethynyl estradiol (R^1= H)

Scheme II.14: Synthesis of gold steroid derivatives

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[92] J. Carrasco, J. J. Criado, R. I. R. Macías, J. L. Manzano, J. J. G. Marín, M. Medarde, E. Rodríguez, *Inorg. Biochem.* **2001**, *84*, 287.

II.2 OBJECTIVES

In this context, it is surprising that steroid derivatives containing 1,2,3-triazolylidene ligands and one or more metals have not been reported yet. Previous work in our laboratories has resulted in different approaches to prepare steroid, diterpene, alkaloid and in general natural products derived structures containing the 1,2,3-triazole moiety.[93] Therefore, alkylation of the triazole and subsequent treatment with Ag_2O and a metal source should lead to the corresponding 1,2,3-triazolylidene complex. Moreover, since steroid derivatives containing up to four 1,2,3-triazole nuclei are easily available following our reported methodologies, in principle up to tetrametallic carbenes derivatives can be accessed.

Thus, the objectives of this first chapter are:

- Synthesis of a new family of 1,2,3-triazoles based in a series of natural products and the corresponding metal 1,2,3-triazolylidene complexes.

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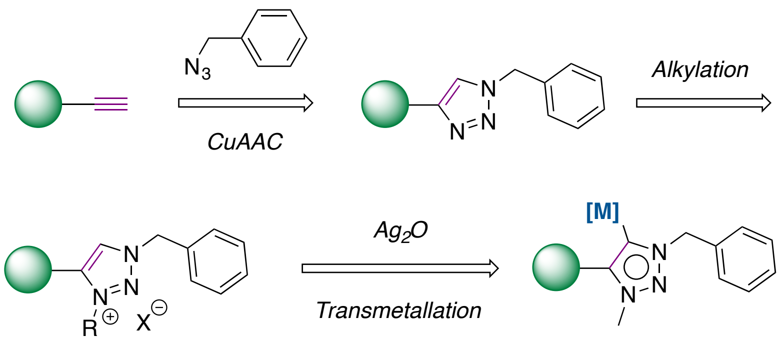
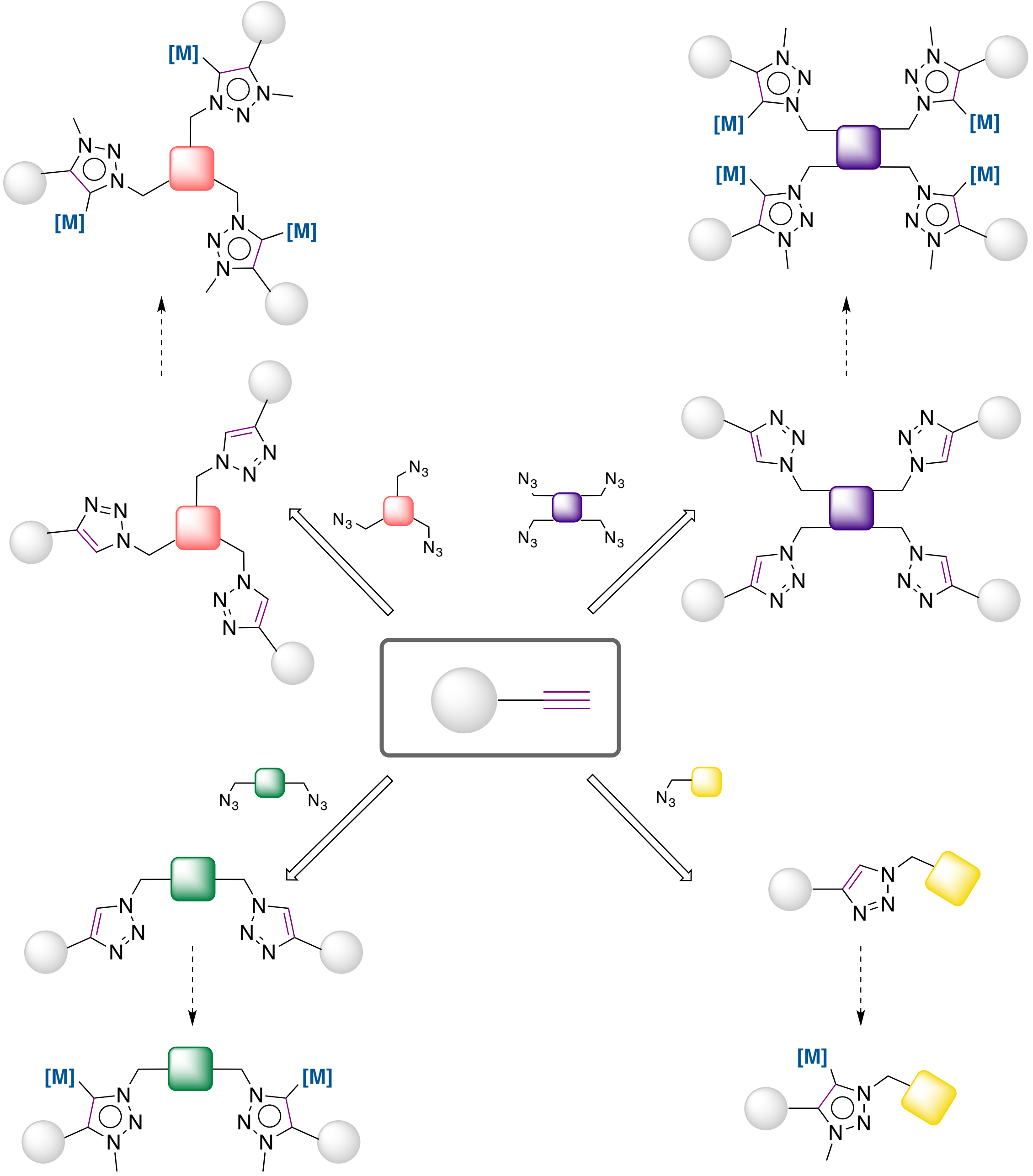
[93] a) P. Ramírez-López, M. C. de la Torre, H. E. Montenegro, M. Asenjo, M. A. Sierra, *Org. Lett*. **2008**, *10*, 3555; b) H. E. Montenegro, P. Ramírez-López, M. C. de la Torre, M. Asenjo, M. A. Sierra, *Chem. Eur. J*. **2010**, *16*, 3798; c) M. C. de la Torre, M. Asenjo, P. Ramírez-López, M. A. Sierra, *Eur. J. Org. Chem.* **2015**, 1054.



Scheme II.15: Synthetic approach for monometallic 1,2,3-triazolylidene complexes

- Preparation of silver and gold multimetallic MIC based on estrone (dimers, trimers, tetramers).

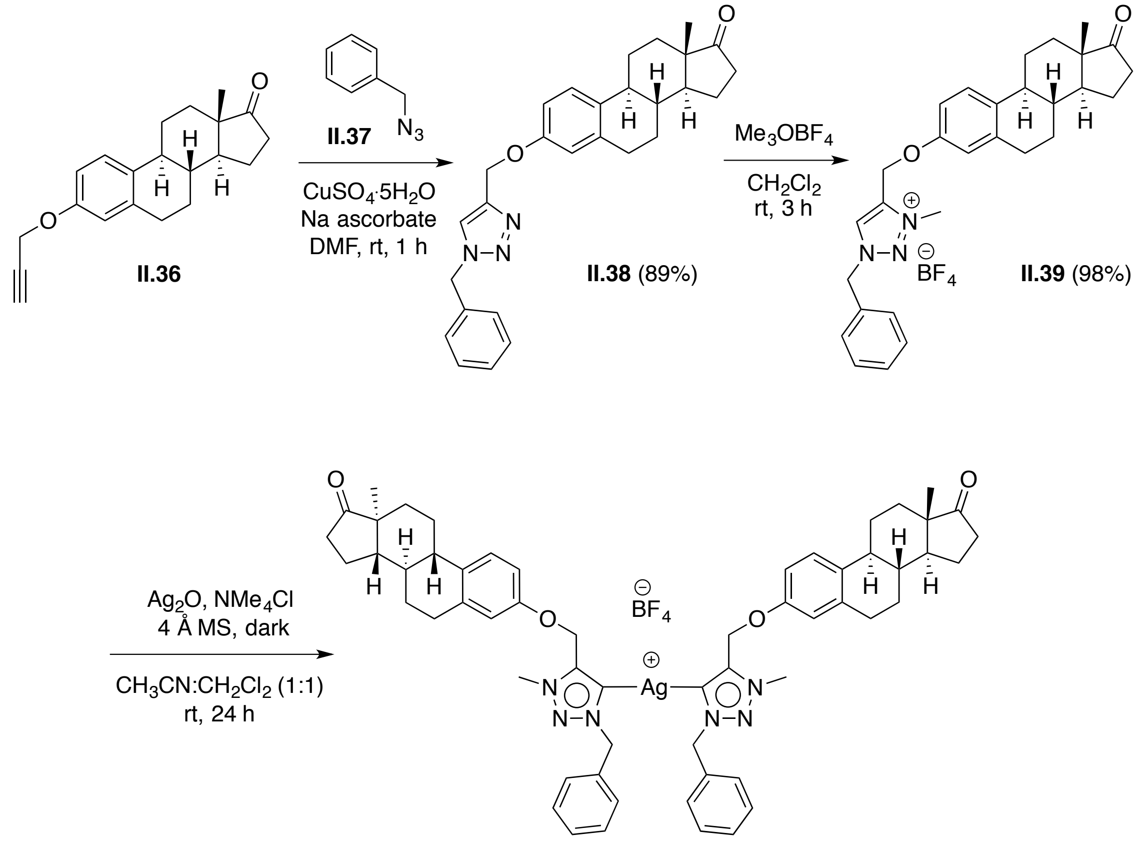


Scheme II.16: Synthetic approach for polymetallic 1,2,3-triazolylidene complexes

- This synthetic approach would represent a new family of uncommon poly-MICs. It would also represent a new methodology to obtain metallo-hybrids of steroids.

II.3 RESULTS AND DISCUSSION

To demonstrate the viability of preparing steroid based silver and gold carbene complexes, the alkynyl derivative of estrone **II.36** was reacted with benzyl azide **II.37** forming the triazole derivative **II.38** in 89% yield. Methylation (Me_3OBF_4) occurred uneventfully in nearly quantitative yield at the *N*3 of the triazole nucleus. The resulting salt **II.39** was submitted to treatment with Ag_2O in the presence of NMe_4Cl in a mixture of CH_3CN:CH_2Cl_2 (1:1) forming the silver bis(carbene) **II.40** in 98% yield.



II.40 (98%)

Scheme II.17: Synthesis of silver carbene **II.40**

Compound **II.40** was unstable but it could be characterised by ^{1}H NMR, ^{13}C NMR and HRMS means. Silver carbene formation was evidenced by the disappearance of the triazolium CH signal in the ^{1}H NMR spectra (**II.39**: δ_H = 8.63 ppm) and the appearance of a low field shifted signal in the ^{13}C NMR (**II.39**: δ_C = 129.5 ppm; **II.40**: δ_C = 166.5 ppm).

HRMS obtained under ESI conditions yields a peak at m/z = 1019.4216, which corresponds to the proposed molecular formula $[C_{58}H_{66}N_6O_4Ag]^+$. Besides, the isotopic composition of the molecular peak matches the theoretical one (calculated M^+= 1019.4191). Therefore, the silver bis(carbene) **II.40** must be formed by two estrone-derived triazolylidene fragments $[(trz_2)Ag]$ rather than the mono(carbene) structure AgX(trz) (Figure II.3).[38]

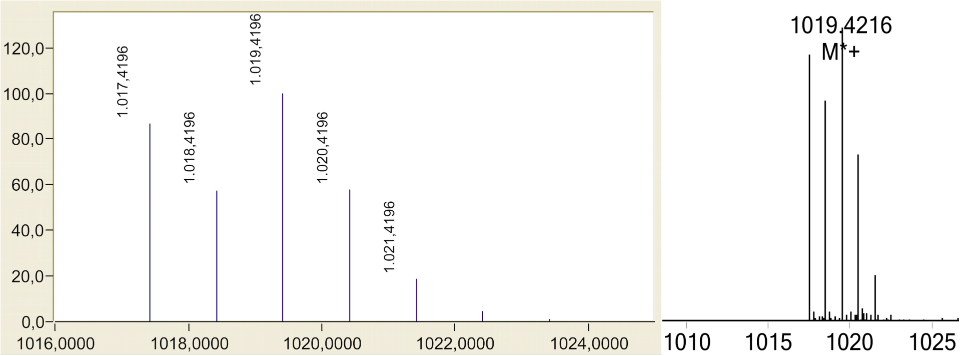
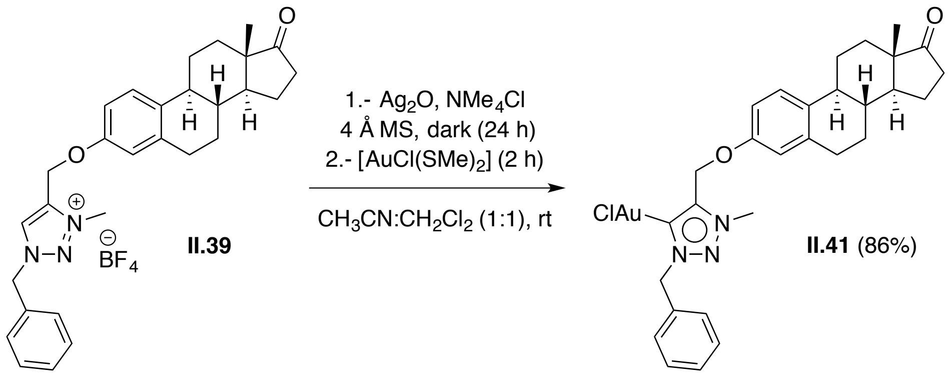


Figure II.3: Theoretical (left) and experimental (right) HRMS spectra of complex **II.40**

The stable gold mono(carbene) **II.41** was obtained in a one-pot reaction without isolation of the intermediate silver carbene **II.40** by reacting salt **II.39** with 0.75 equiv of Ag_2O in the presence of 1.50 equiv of NMe_4Cl and 4 Å molecular sieves, in a mixture of CH_3CN:CH_2Cl_2 (1:1) with air exclusion, followed by treatment with 1.00 equiv of $[AuCl(SMe)_2]$. Compound **II.41** was obtained in 86% isolated yield (Scheme II.18). The structure of compound **II.41** was established by spectroscopic means. Its ^{1}H and ^{13}C NMR spectra show signals attributable to the estrone and benzylic fragments. The NMR spectra of complex **II.41** were almost identical to the silver carbene **II.40**, being the major difference the chemical shift of the carbene centre, which appeared high field shifted with respect to silver carbene ($\Delta\delta$ = + 6.7 ppm).



Scheme II.18: Synthesis of gold monocarbene **II.41**

In addition the HRMS spectrum of **II.41** shows a molecular peak at *m*/*z* = 688.1832 ([M+H]$^+$), accounting for the molecular formula $C_{29}H_{32}N_3O_2AuCl$, which is in accordance with the proposed structure.

It is important to note that all the reactions that composed this synthetic approach, from the triazole to the metallic carbene, can be easily followed by NMR analysis (^{1}H NMR and ^{13}C NMR). As it can be observed in Figure II.4, the signal of the *H*5 of the heterocyclic core is of great diagnostic value. When 1,2,3-triazole is formed, a singlet used to appear at δ_H around 7.50 ppm. When this core is selectively methylated in *N*3, this proton resonates downfield shifted around 1.00 ppm compared to its precursor. Finally, the absence of this singlet confirmed the coordination of the carbenic centre to the metal.

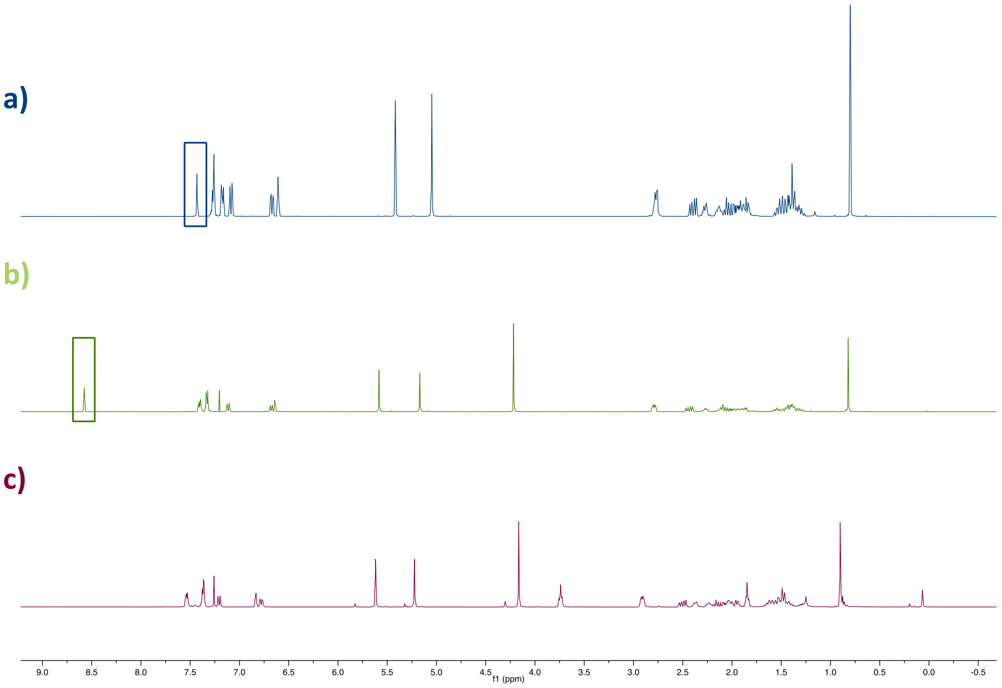


Figure II.4: ^{1}H NMR spectra of **II.38**, **II.39** and **II.41**

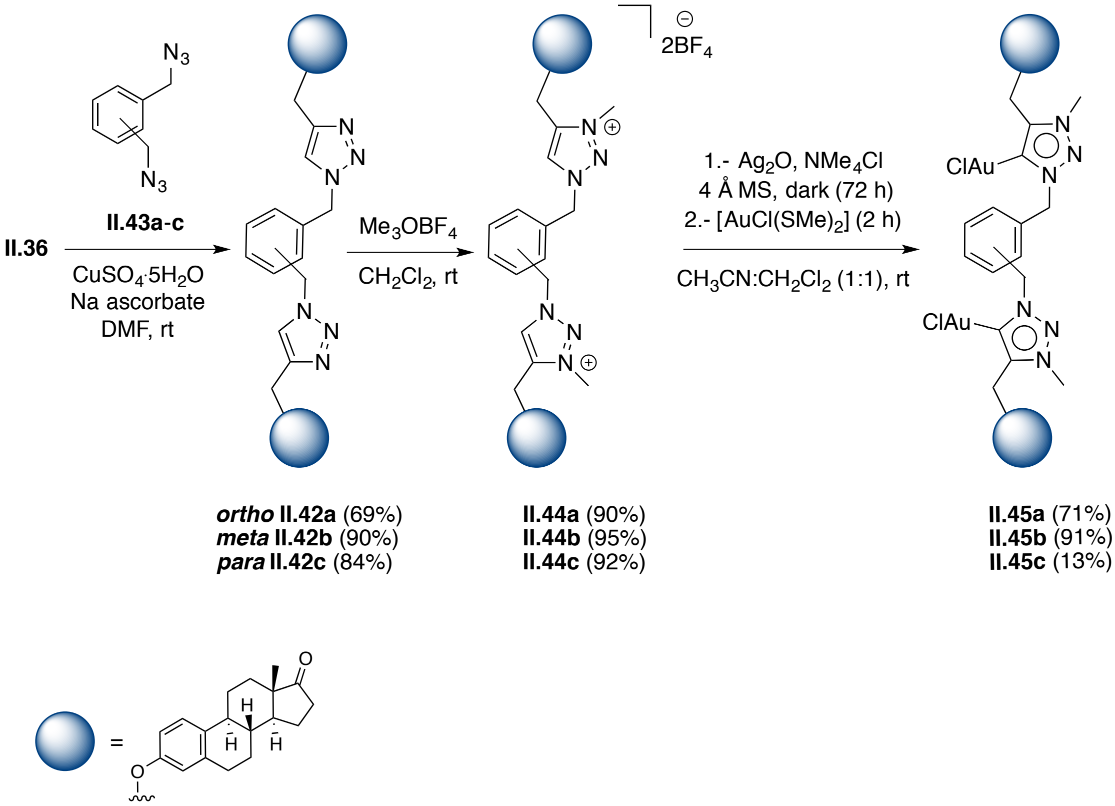
The study of ^{13}C NMR also showed significant differences in the shift of *C*5 in each product of the steps that conform the synthesis of the metallic carbene as it is summarized in Table II.1.

Table II.1: Chemical shift for *H*5 and *C*5.

Entry	Compound	δ_{H5}	δ_{C5}
1	**II.38**	7.43	122.6
2	**II.39**	8.63	129.5
3	**II.41**	-	159.8

[a] NMR performed in $CDCl_3$

The synthesis of polymetallic complexes using estrone based derivatives was addressed next. Thus, bis(steroids) **II.42a**, **II.42b** and **II.42c** tethered by *ortho-*, *meta-* and *para-* phenyl bis(triazole) bridges were prepared by reaction between the propargylated estrone derivative **II.36** and the corresponding bis(azides) **II.43a–c** under the same CuAAC conditions previously described. Triazoles **II.42a–c** were subsequently dimethylated (Me_3OBF_4) in essentially quantitative yields (Scheme II.19).



Scheme II.19: Synthesis of dimetallic gold 1,2,3-triazolylidene complexes **II.45a–c**

The dimethylated salts (**II.44a**–**c**) were reacted with Ag_2O (1.50 equiv) in the presence of 3.00 equiv of NMe_4Cl in a mixture of CH_3CN:CH_2Cl_2 (1:1). The putative silver carbene complexes were treated with 2.00 equiv of [AuCl(SMe_2)], forming the corresponding gold bis(carbenes) **II.45a**–**c** in 71%, 63% and 13% yields of isolated product, respectively. It is worth noting the decrease in terms of yields of the *p*-tethered bimetallic carbene **II.45c** compared to those of the *o*- and *m*- substituted.

Compound **II.45c** rapidly decomposes in solution and in the chromatographic column to form a purple solid (this behaviour has been preliminarily attributed to the formation of gold nanoparticles). This was also observed for the *o*- and *m*- substituted isomers but in a much lower extent than in the case of the *p*- substituted gold triazolylidene complex. Reasons for this anomaly are still unknown.

The structures of the gold carbenes **II.45a**–**c** were established according to their NMR and MS spectra. ^1H and ^{13}C NMR showed signals attributable to half of the molecule, which is a consequence of their C_2 symmetry. In addition to the characteristic signals of the steroid fragments, signals for the aromatic joint were observed. As in the case of the simple gold mono(carbene) **II.41**, with the exception of those of the ketone group, carbene carbon atoms are the most deshielded, appearing around δ_C = 160.0 ppm. Finally, for the three isomers, the HRMS spectra showed peaks corresponding to the fragmentation of one Cl–Au bond (Figure II.5).

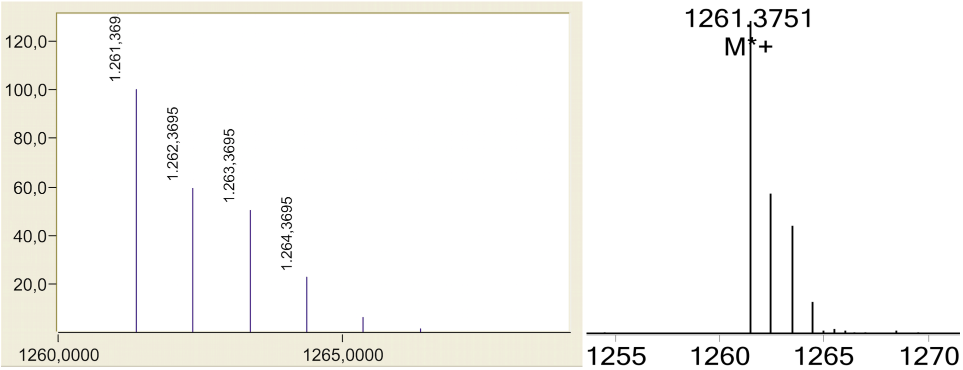


Figure II.5: Theoretical (left) and experimental (right) HRMS spectra of complex **II.45a**

In addition, a double charged peak was observed in the case *o*- substituted gold carbene **II.45a** at *m*/*z* = 613.1979 as the result of the fragmentation of the two Cl–Au bonds. Therefore HRMS analysis provides a molecular formula of $C_{52}H_{62}N_6O_4Au_2Cl_2$ for the three isomers and supports the proposed structures **II.45a**, **II.45b** and **II.45c** for these compounds.

Once these series of gold 1,2,3-triazolylidene complexes with estrone moieties in their structure were accomplished, the synthesis of estradiol-derived gold complexes was performed next.

In this case, the reaction of *O*-propargylated estradiol **II.46** with the *o*- bridged bis(azide) yielded the bis(triazole) derivative **II.47**.[94] Methylation with Meerwein's salt resulted in an alkylation of the triazole cores together with the hydroxy groups. The use of equimolar amounts of Me_3OBF_4, decrease of the temperature of reaction to 0 °C or the use of milder methylating agents as MeOTf failed in affording exclusive methylation in the triazole core over alcohols. Therefore, protection of the hydroxyl groups prior to methylation was carried out reacting triazole **II.47** with Et_3N as a base and TMSCl as protecting group.

The persylilated product **II.48** was then methylated with Me_3OBF_4 in CH_2Cl_2. After a quenching with methanol, pH of the reaction media was measured revealing an acidic value, probably due to the formation of traces of HBF_4 after the addition of methanol. The acidic pH cleaved the O–TMS bonds yielding the triazolium salt **II.49** with the hydroxyl groups deprotected. Formation of the gold 1,2,3-triazolylidene complex was carried out following the Ag protocol with subsequent transmetallation. Thus, the gold estradiol-based 1,2,3-triazolylidene **II.50** was obtained in 88% yield (Scheme II.20).

The structure proposed was unambiguously confirmed by ^{1}H, ^{13}C and HRMS experiments. The ^{1}H spectrum did not show any signal at δ_H = 9.05 ppm as a result of the new Au–$C_{carbene}$ bond formed. As in the bridged estrone-derived gold complexes, the ^{13}C NMR spectrum showed a down fielded signal at δ_C = 160.1 ppm corresponding to the carbene centre. Again, ^{1}H and ^{13}C NMR spectra were in agreement with a C_2 symmetry of the final product.

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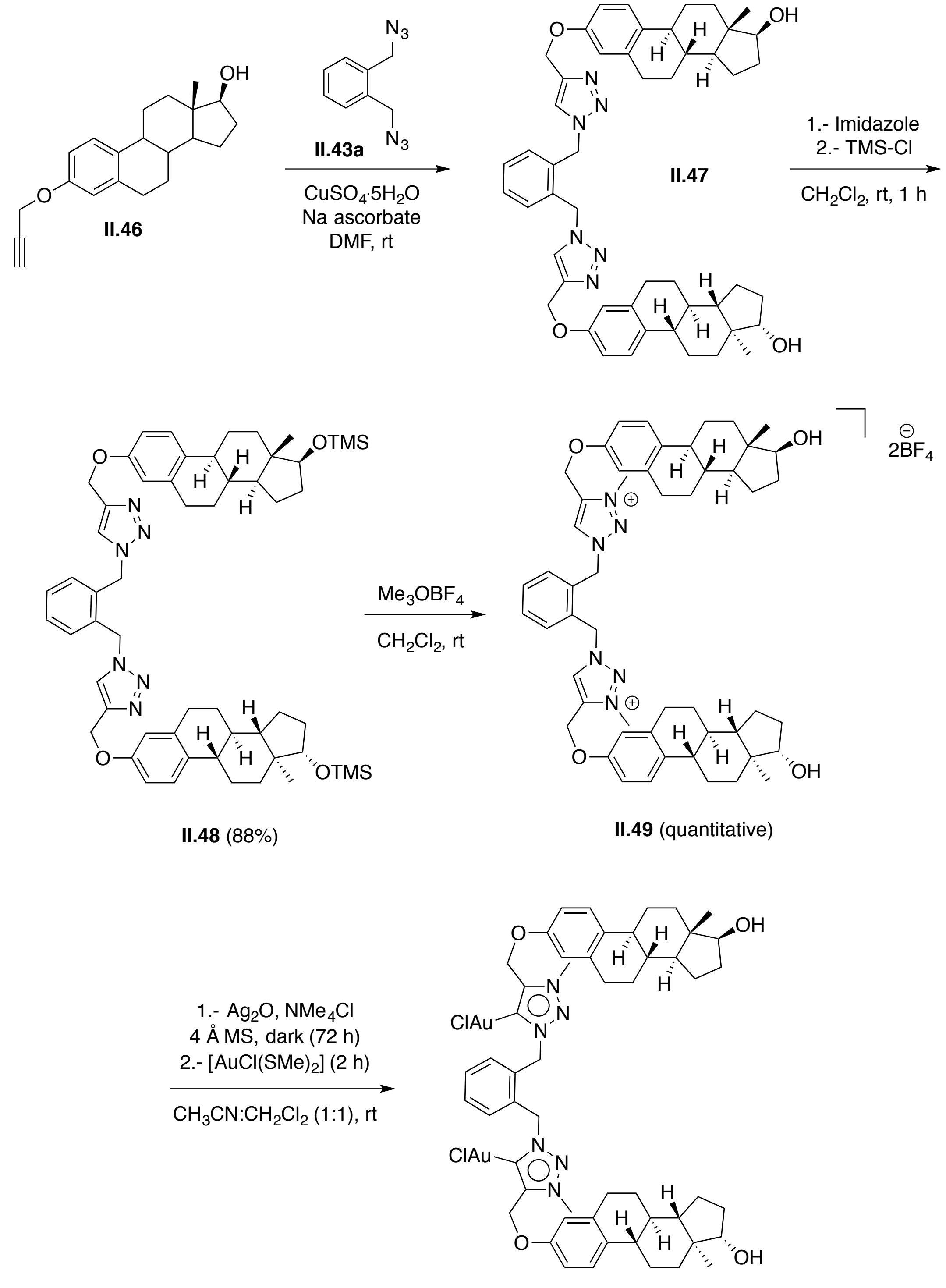
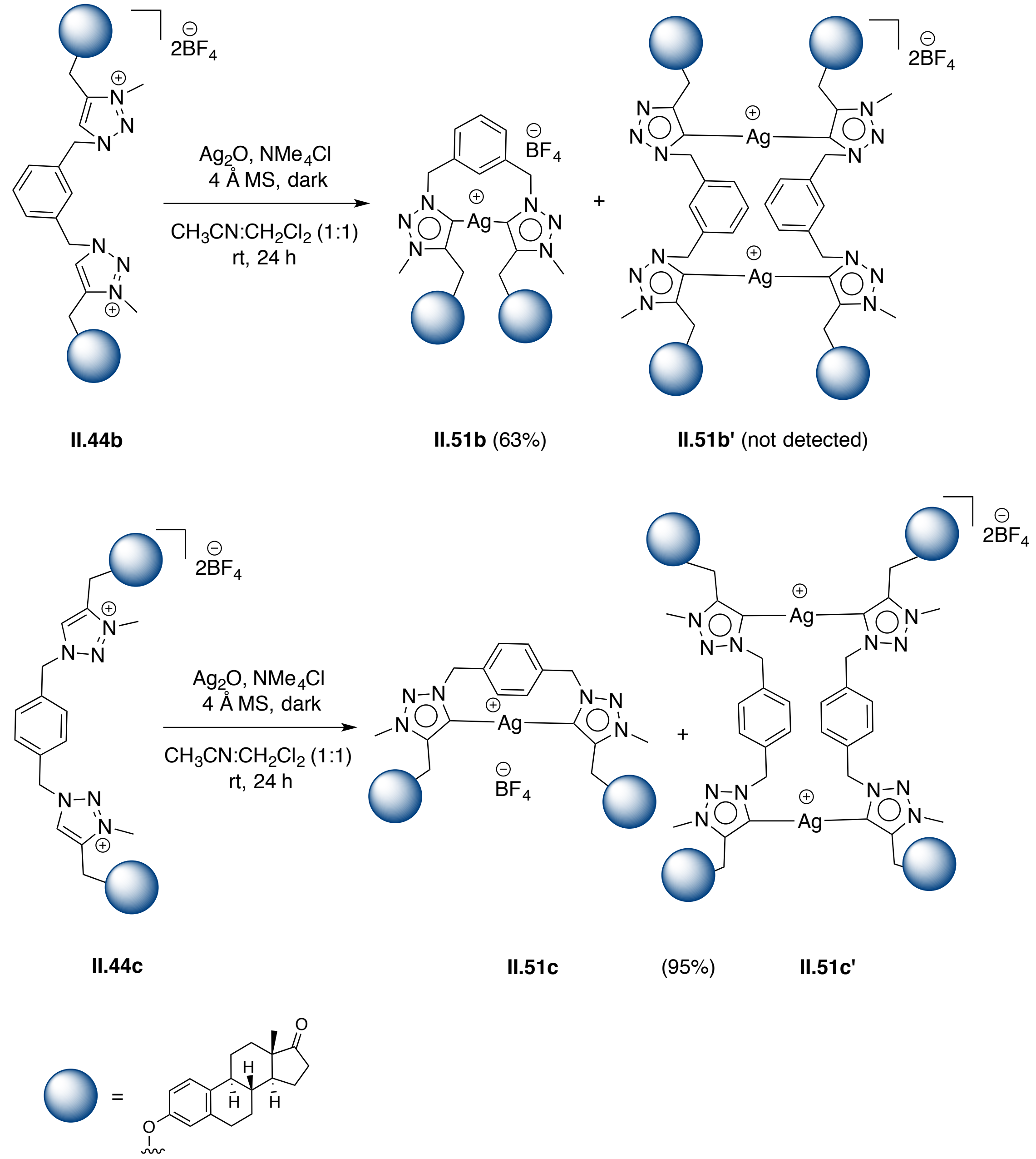
[94] P. Ramírez-López, M. C. de la Torre, M. Asenjo, J. Ramírez-Castellanos, J. M. González-Calbet, A. Rodríguez-Gimeno, C. Ramírez de Arellano, M. A. Sierra, *Chem. Commun.* **2011**, *47*, 10281.



II.50 (88%)

Scheme II.20: Synthesis of estradiol based gold carbene **II.50**

Once the synthesis of gold bimetallic carbene complexes was performed, we pursued the isolation and characterisation of the intermediate silver carbene complexes. Being aware of the instability of such complexes *o-, m-* and *p-* bridged bis(triazole) derivatives **II.44a–c** were reacted in the dark with Ag_2O (1.50 equiv) in the presence of 3.00 equiv of NMe_4Cl and 4 Å molecular sieves in a mixture of $CH_3CN:CH_2Cl_2$ (1:1), with exclusion of air. The corresponding silver carbene complexes **II.51a–c** were isolated in 46%, 63% and 95% yields, respectively. Interestingly, except for the *ortho* derivative **II.51a**, which was unstable,[95] carbenes **II.51b** and **II.51c** were stable enough for full spectroscopic characterisation (Scheme II.21).



II.44b **II.51b** (63%) **II.51b'** (not detected)

II.44c **II.51c** (95%) **II.51c'**

Scheme II.21: Possible Ag-MICs complexes

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[95] For silver carbene **II.51a** only ^1H NMR could be obtained.

^{1}H NMR spectra of the silver carbenes were devoid of signals attributable to any triazolium proton (**II.44b**: δ_H = 8.55 ppm; **II.44c**: δ_H = 9.08 ppm), and the ^{13}C NMR showed a new signal (**II.51b**: δ_C = 165.2 ppm; **II.51c**: δ_C = 165.9 ppm) identifiable to the carbene carbon, instead of the upfielded signal due to the CH carbon of the triazolium precursor (**II.44b**: δ_C = 130.1 ppm; **II.44c**: δ_C = 129.6 ppm).

With respect to the coordination of the Ag(I) carbenes, HRMS of **II.51b** showed a main fragment at *m/z* = 941.3720 [M–BF$_4^-$]$^+$, which is consistent for a monometallic charged silver complex incorporating one molecule of bis(triazole), as represented by formula **II.51b** (Figure II.6).

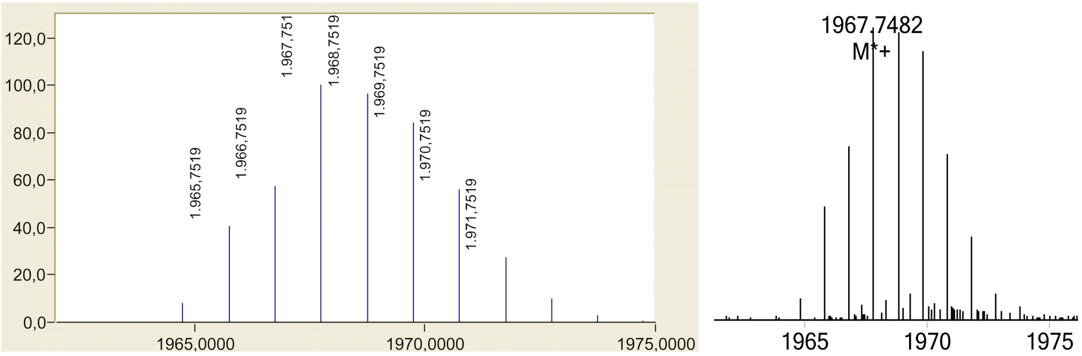

Figure II.6: Theoretical (left) and experimental (right) HRMS spectra of complex **II.51b**

On the contrary, HRMS of the carbene **II.51c** showed two peaks in accordance with the existence of two species. One of them fits with the charged bimetallic carbene represented by structure **II.51c'**, since one peak at *m/z* = 1965.7491 [M–BF$_4^-$]$^+$, accounting for the molecular formula [$C_{104}H_{120}N_{12}O_8Ag_2BF_4$]$^+$ was detected (M$^+$ calculated = 1965.7472). In addition, a double charged peak appeared at *m/z* = 940.3802 [M–2BF$_4^-$]$^{2+}$, corresponding to the radical ion with molecular formula [$C_{104}H_{120}N_{12}O_8 Ag_2$]$^{2+}$. Interestingly, one additional cluster of peaks appeared at *m/z* = 941.3000, which can be attributed to the single charged silver bis(carbene) species [$C_{52}H_{60}N_6O_4Ag$]$^+$ having the structure represented by **II.51c** (Scheme II.21).[96]

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[96] Crudden has reported the preparation of dinuclear silver mesoionic carbenes analogous to **II.51b'** and **II.51c'** containing two bis(triazole) ligands directly attached to the benzene ring in a meta disposition (see reference 84). The absence of the methylene group favours the exclusive formation of the symmetric dimeric structure having C–Ag–C bonds of 173.9(3). Obviously, the formation of structures referable to **II.51b** or **II.51c** is highly unfavourable due to constraints imposed by the rigidity of the spacer. See a) E. C. Keske, O. V. Zenkina, R. Wang, R. C. M.

The isotopical distribution for peaks obtained in the ESI-HRMS spectrum for molecular cluster of the *meta* regioisomer **II.51b** was decesive to establish the ratio of **II.51c** [(trz)Ag]$^+$ and **II.51c'** [(trz)$_2$Ag$_2$]$^{2+}$. A series of simulated molecular clusters for different mixtures of **II.51c**:**II.51c'** were obtained. As it can be clearly seen in Figure II.7, when the ratio between **II.51c**:**II.51c'** is 3:2, the simulated molecular cluster perfectly matches with the experimental spectrum within a minimal error range.

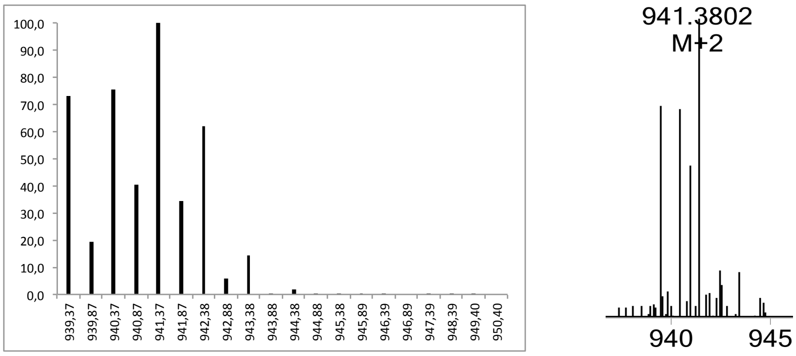

Figure II.7: Experimental (left) and theoretical (right) isotopical distribution of peaks [(steroid)Ag]$^+$:[(steroid)$_2$Ag$_2$] of **II.51c**:**II.51c'** (3:2).

Computational calculations (DFT) were carried out to gain some insight into the formation and the structure of the silver complexes **II.51**. Calculations were performed using the actual monosilver **II.51b** and bis(silver) complexes **II.51b'** without simplifications in the steroidic ligand framework. It may look easier to form a dimeric dimetallic carbene like **II.51b'** than the apparently distorted monometallic complex **II.51b**.[96] However, as it can be seen in Figure II.8, the monometallic carbene **II.51b** shows a nearly linear arrangement for the triazole–Ag–triazole array (C–Ag–C = 173.57 °),[96] while complex **II.51b'** shows a slightly distorted array with respect to **II.51b** for one triazole–Ag–triazole arrangement (C–Ag–C = 169.75 °). In addition, the disposition in the first triazole moiety imposes a bent geometry for the second triazole–Ag–

Crudden, *Organometallics* **2012**, *31*, 456. For examples on the preparation of silver-based cage-like Arduengo carbene complexes, see: b) F. Dominique, H. Gornitzka, C. Hemmert, *J. Organomet. Chem*. **2008**, *693*, 579; c) D. B. Qin, X. S. Zeng, Q. S. Li, F. B. Xu, H. B. Song, Z. Z. Zhang, *Chem. Commun.* **2007**, 147; d) A. Rit, T. Pape, A. Hepp, F. E. Hahn, *Organometallics* **2011**, *30*, 334; e) A. Rit, T. Pape, F. E. Hahn, *J. Am. Chem. Soc.* **2010**, *132*, 4572; f) C. Segarra, G. Guisado-Barrios, F. E. Hahn, E. Peris, *Organometallics* **2014**, *33*, 5077; g) N. Sinha, F. Roelfes, A. Hepp, C. Mejuto, E. Peris, F. E. Hahn, *Organometallics* **2014**, *33*, 6898.

triazole array (C–Ag–C = 151.78 °), which undoubtedly decreases the overall stability of the silver-steroid tetramer **II.51b'**.[97]

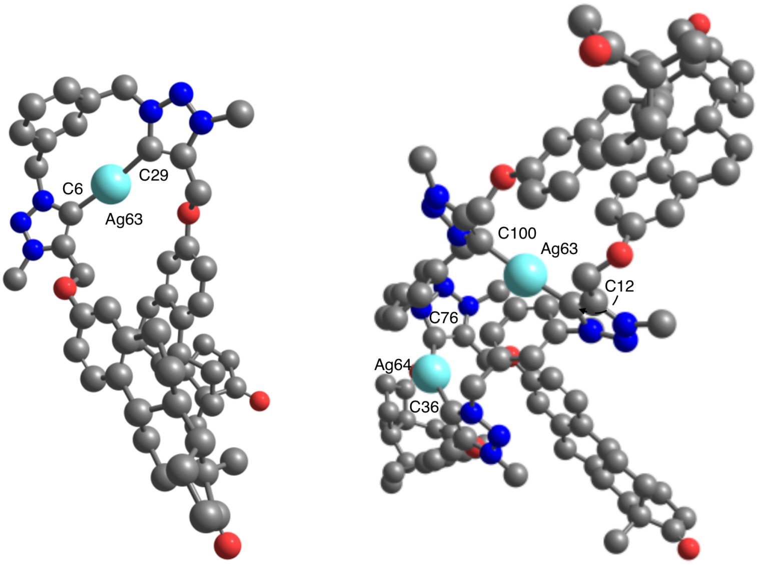

Figure II.8: Computed structures of **II.51b** and **II.51b'**. Selected angles: (**II.51b**) C6–Ag63–C29 = 173.57 °; (**II.51'**) C100–Ag63–C12 = 169.75 °; C76–Ag64–C36 = 151.78 °

An analogous DFT computational study carried out in the gold complex **II.45a**, now having an *ortho*-disposition, shows a conventional structure in which each carbene is acting as a ligand of the Au(I) nuclei.

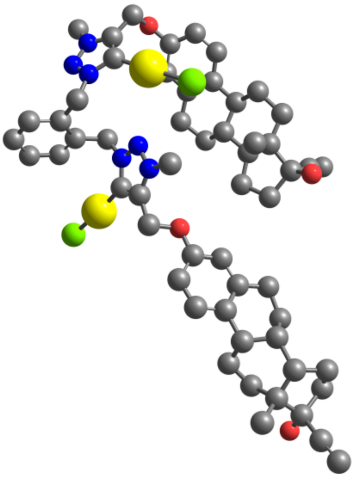

Figure II.9: Computed structure of **II.41a**

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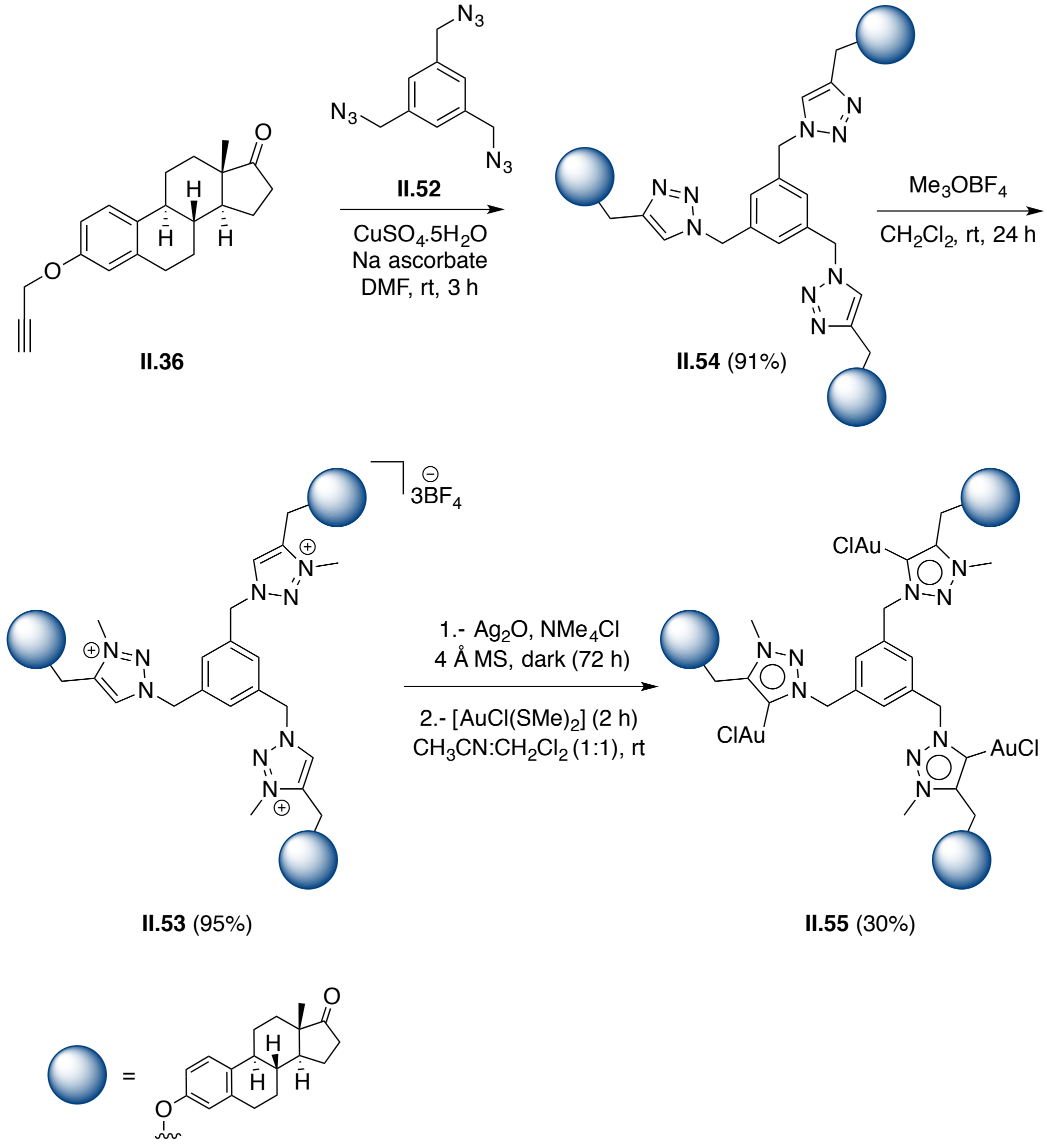
[97] We attempted to compute the structure of a modified compound **II.51b'** having both C–Ag–C angles frozen to 169.75 °. We were unable to obtain a minimum-energy point for this molecular arrangement. However, after eliminating one of the two restrictions the resulting molecule easily converges to **II.51b'**. Therefore, we believe that the bending of the second silver angle is required to obtain a molecule having a structure like **II.51b'**, and this bending is the responsible for the instability of **II.51b'** compared to **II.51b**.

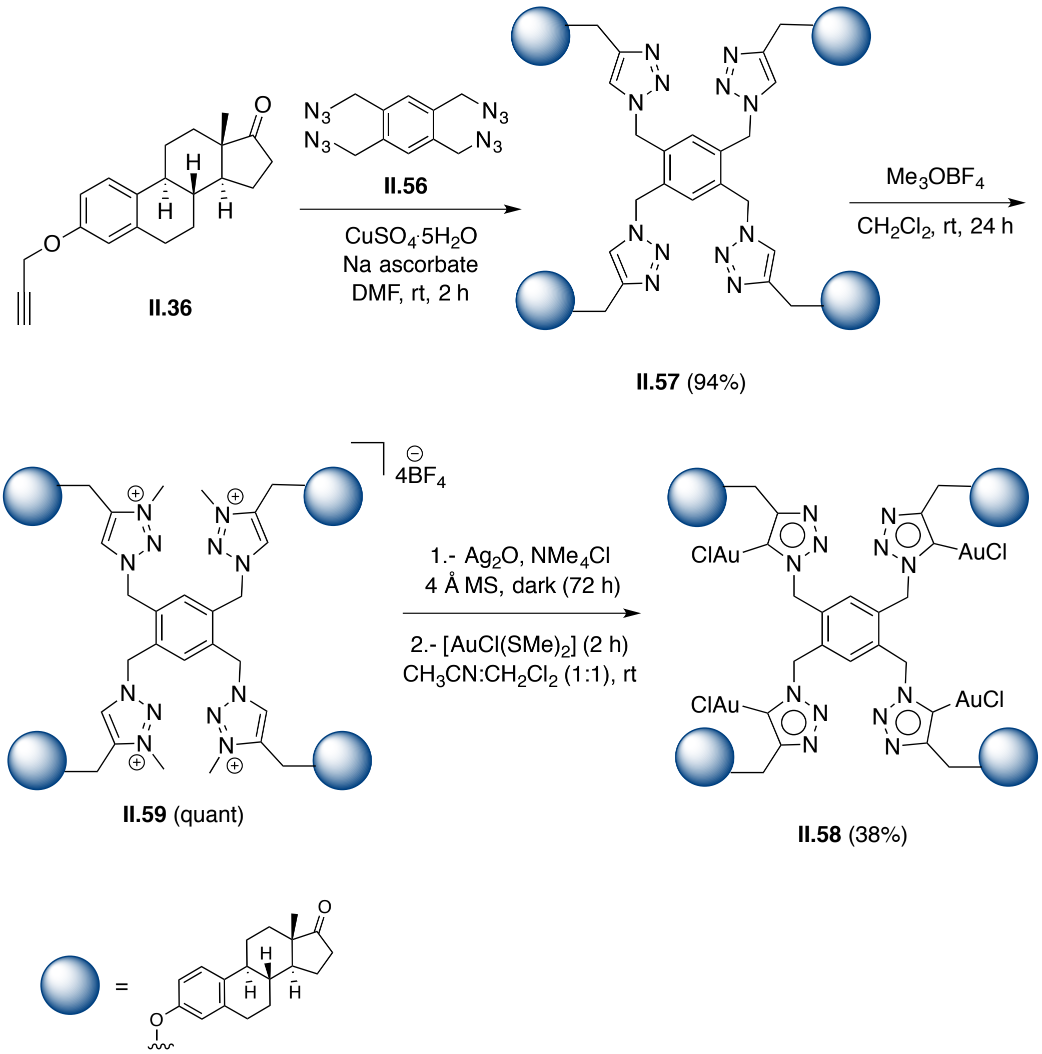
The methodology developed above was tested next for C_3-symmetric tris(triazole) and C_2-symmetric tetra(triazole) estrone derivatives.



Scheme II.21: The preparation of C_3-symmetric tris(triazole) estrone derivatives

Methylated tris(triazole) **II.53** was prepared from triazole **II.54** by alkylation under the usual conditions (to complete the reaction 24 h were needed), and submitted to the sequence Ag_2O, NMe_4Cl in a mixture of $CH_3CN:CH_2Cl_2$ (1:1) followed by transmetallation with [AuCl(SMe$_2$)] (3 equiv). The Au(I) tris(carbene) complex **II.55** was obtained in 30% yield (Scheme II.22).

The C_2 tetra(triazole) **II.57** yielded the corresponding tetrametallic gold carbene **I.58** following the Ag_2O protocol (Scheme II.23). Methylation of **II.57** (using Meerwein's salt as alkylating reagent) yielded **II.59** quantitatively, albeit longer reaction times were needed. Submission of **II.59** to Ag_2O, NMe_4Cl in a mixture of $CH_3CN:CH_2Cl_2$ (1:1) followed by transmetallation with $[AuCl(SMe_2)]$ (4 equiv) afforded **II.58** in 38% yield (Scheme II.23).



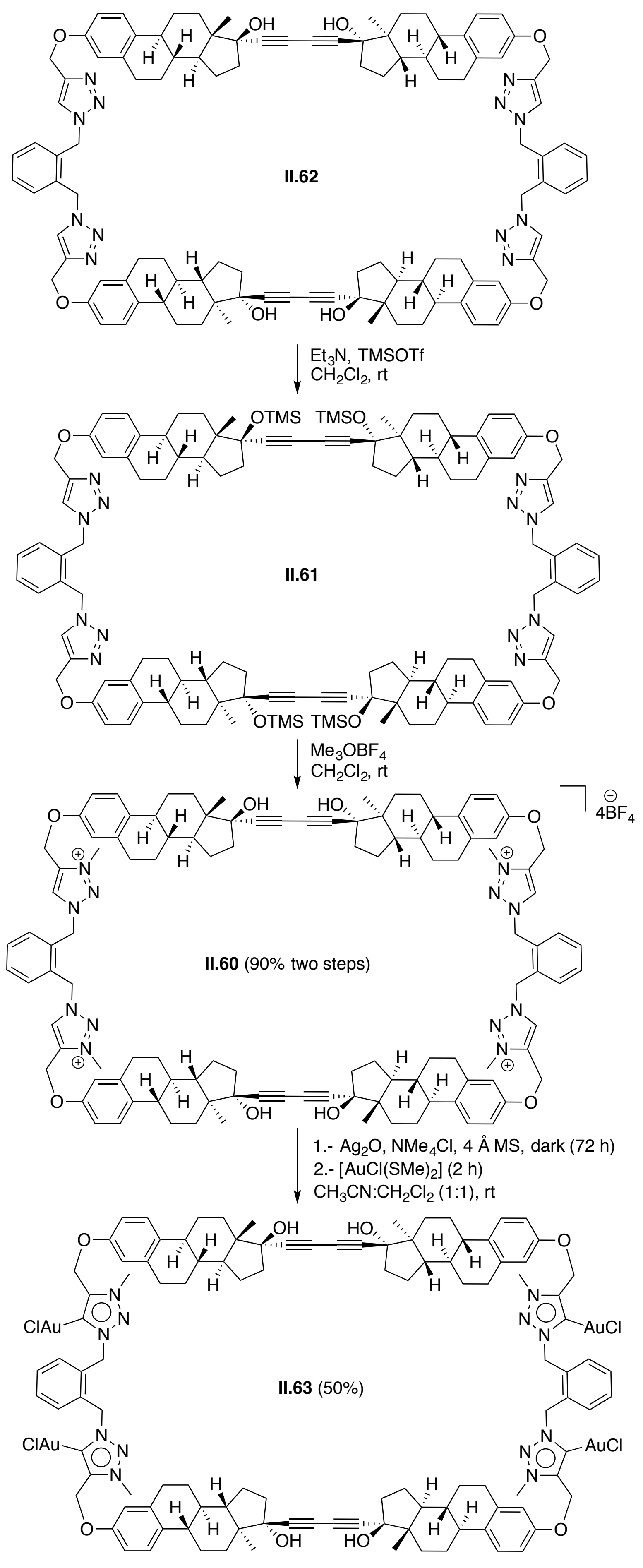
Scheme II.22: Preparation of C_2-symmetric tetra(triazole) estrone derivatives

It is worthy to note that crude products of the reactions for carbenes **II.55** and **II.58** show clean ^1H NMR spectra attributable to the presence of single products. However, extensive decomposition (with the formation of black material, probably due to colloidal gold) was observed during column chromatography. ^1H and ^{13}C NMR spectra were in accordance with the proposed structures.

In addition, the HRMS spectra showed peaks for the positively charged radicals corresponding to the molecular formulas $[C_{75}H_{87}N_9O_6Au_3Cl_2]^+$ and $[C_{98}H_{114}N_{12}O_8Au_4Cl_3]^+$ for the tri- and tetrametallic carbenes **II.55** and **II.58**, respectively. The experimental molecular clusters of the ESI-mass spectra were congruent with the theoretical isotopical distribution.

Finally, the preparation of a giant macrocycle containing four gold carbene ligands was attempted. Thus compound **II.60** was prepared by methylation of the per-*O*-silylated derivative **II.61**, since the direct methylation of **II.62** produced the concomitant but not quantitative methylation of the hydroxy groups. Compound **II.61** was accessed from **II.62** by reaction with Et_3N and TMSOTf as protective reagent (quantitative yield). Methylation of **II.61** using the Meerwein's salt proportionates the tetramethylated tetrazolium salt **II.60**. As previously described for the estradiol derivative, acidic media cleavaged the O–TMS bonds, yielding the tetramethylated triazolium salt with the four alcohol groups free. The yield of this reaction was 90% from **II.62**. Again, submission of macrocycle **II.60** to Ag_2O/NMe_4Cl followed by transmetallation with $[AuCl(SMe_2)]$ yielded the tetracarbenic macrocycle **II.63** as a white solid in a considerable 50% yield upon purification by flash chromatography (Scheme II.24).

The structure of **II.63** was confirmed by spectroscopic means. The ^1H and ^{13}C NMR spectra showed a single set of signals for the estrone and the aromatic fragments as a result of the symmetry of the macrocycle. In addition, the presence of the gold carbene moieties is demonstrated by the absence of signals corresponding to the triazolium protons (**II.60**: $\delta_H = 8.84$ ppm) and the presence of a down field shifted signal in the ^{13}C NMR spectrum at $\delta_C = 159.1$ ppm.[19]



Scheme II.23: Synthesis of polymetallic gold carbene **II.63** supported by a macrocyclic structure

In addition, a peak at *m/z* = 2657.7465 was detected in the HRMS spectra, which is consistent with the molecular formula $[C_{112}H_{124}N_{12}O_8Au_4Cl_3]^+$ (calculated M^+ = 2657.7393). Therefore, the tetrametallic structure represented by **II.63** was assigned to the macrocyclic tetrametallic carbene. To the best of our knowledge this is the first macrocyclic structure based on natural products containing a polymetallic carbene feature.[98]

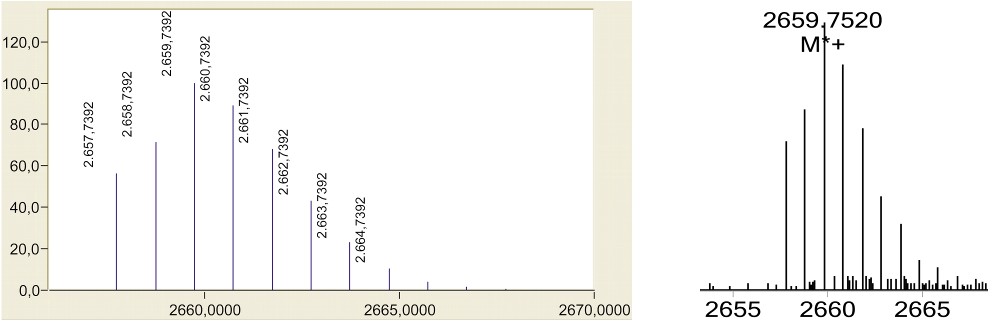


Figure II.10: Theoretical (left) and experimental (right) HRMS spectra of complex **II.63**

Once the methodology to obtain M-steroid derived (M= Ag, Au) mono- and polymetallic 1,2,3-triazolylidene carbenes, containing up to four metals in their structures and having different geometries was established, their role as catalysts of several model reactions was tested. It is well established that Au-NHCs catalyse the transfer of the carbene moiety of diazo compounds to a nucleophile, avoiding the formation of the homocoupling products.[99] Therefore, we tested gold carbene **II.41** in the reactions of ethylphenyldiazoacetate and alcohols. Thus, ethyl phenyldiazoacetate (1 equiv) was reacted with excess of MeOH (10 equiv) in the presence of 1 mol % (related to the ester) of gold-carbene **II.41** and 1 mol % of $AgSbF_6$.[100] The reaction occurs instantaneously yielding quantitatively ethyl α-methoxyphenylacetate.[101]

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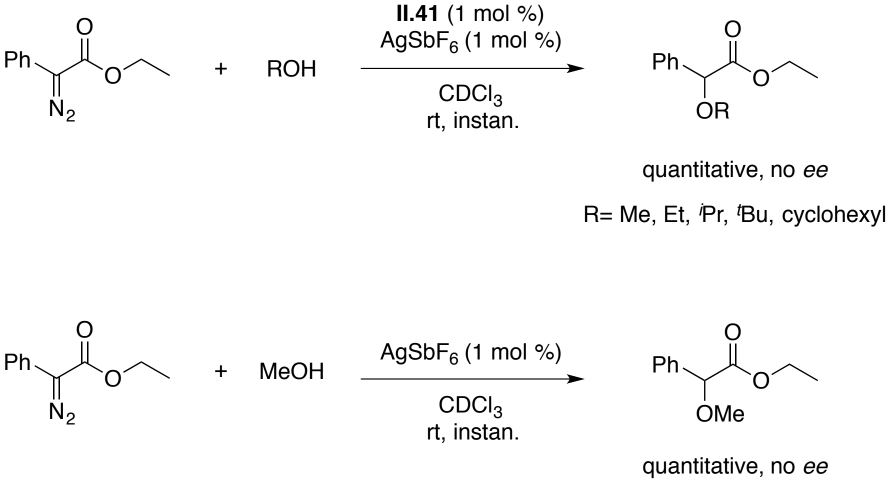
[98] We have previously reported the synthesis of macrocycles having pendant pentacarbonyl M(0)carbene moieties (M = Cr, W). M. P. López-Alberca, M. J. Mancheño, I. Fernández, M. Gómez-Gallego, M. A. Sierra, C. Hemmert, H. Gornizka, *Eur. J. Inorg. Chem.* **2011**, 842.

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

[100] These conditions ensure the formation of a cationic gold carbene complex as the active catalyst. See: D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*, 3351.

[101] The ^1H NMR of the α-alkoxy-α-phenylacetates matches the literature data: a) H. Tomioka, H. Okuno, Y. Izawa. *J. Chem. Soc., Perkin Trans. 2,* **1980**, 1636. b) W. Brouillette, G. L. Grunewald, *J. Med. Chem.* **1984**, *27*, 202.

Unfortunately, HPLC analysis using a chiral column shows no *ee* in the product.[102] Similar results were obtained when ethanol, isopropanol, *tert*-butanol and cyclohexanol were used (Scheme II.25).



Scheme II.24: Studies of reactivity

The reaction of ethyl phenyldiazoacetate and MeOH (10 equiv) in the conditions used above but in the absence of the gold carbene **II.41**, also occurs instantaneously (Scheme II.25). Therefore, 1 mol % of $AgSbF_6$ per mol of diazoester efficiently catalyses these reactions. This strong catalytic activity may be behind the absence of enantioselection observed in the presence of gold carbene **II.41.**[103] Interestingly, silver carbenes do not show any catalytic activity.

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[102] Crude reactions were analysed by HPLC using an OD-H or an OJ-H column chromatography.

[103] Gold carbenes **II.41**, **II.45a**, **II.45b**, and **II.58** (5 mol %) in the absence of Ag(I) salts also catalyse the transfer ethylphenyldiazoacetate to methanol in a 50% of conversion after 5 days of reaction at rt. Again, no *ee* was obtained under these conditions.

II.4 CONCLUSIONS

- A new class of bio-organometallic derivatives based on estrone and estradiol has been synthetized. This represents, to the best of our knowledge, the first example of a steroid nucleus containing M-MIC complexes (M= Ag, Au).

- The methodology developed allowed to obtain complexes having up to four triazole cores. Upon functionalization of the heterocyclic motifs, multimetallic MICs having up to four gold nuclei were prepared.

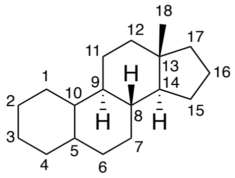
- Steroid derived silver-MIC complexes have been isolated and characterised. In the case of compounds bearing two triazole moieties, it is remarkable that the nuclearity of the final products is dictated by the structure of the starting triazolium salt. Thus, silver-MICs derived from the *m*-substituted salts are composed by one metallic atom linked to the two carbenes centres of the molecule. However, in the case of the *p*-substituted salts, two different complexes are formed. In addition to the monometallic compound, a macrocyclic silver-MIC containing two molecules of the precursor salt, linked by two silver atoms, is obtained.

- DFT calculations carried out to study the structure of these metallic derivatives showed that the formation of the bimetallic compound is not favoured in the case of the *meta* regioisomer because this arrangement would produce structures having bent angles of 169.75 ° and 151.78 ° between the silver atom and the two carbenic centres bounded to the metal.

II.5 EXPERIMENTAL SECTION

Azides,[104] 3-*O*-Propargylestrone **II.36**,[93a] 3-*O*-propargylestradiol **II.46**,[94] and macrocycle **II.62**[93a] were synthesized by using an experimental procedure previously described. Azides are potentially explosive materials, they must be prepared and handled behind safety screens, and protected from light, shock and heat.

The compounds herein described have been numbered as estrene derivatives:



General procedure for the synthesis of 1,2,3-triazoles

A mixture of organic azide (1.00 or 1.20 equiv), alkyne (1.00, 2.20, 3.30 or 4.40 equiv), sodium (L)-ascorbate (0.20, 0.40, 0.60 or 0.80 equiv) and $CuSO_4{\cdot}5H_2O$ (0.10, 0.20, 0.30 or 0.40 equiv) in DMF was stirred under Ar at rt until completion of the reaction (TLC analysis). The reaction was quenched with water at 0 °C and allowed to reach rt. The mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with water (twice) and once with brine. The organic layer was dried over $MgSO_4$, filtered and the solvent was removed under vacuum to afford the corresponding reaction products, which were purified through a short pad of SiO_2.

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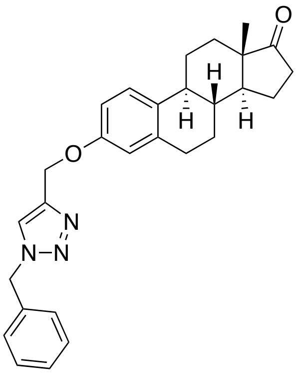
[104] S. G. Alvarez, M. T. Alvarez, *Synthesis* **1997**, 413.

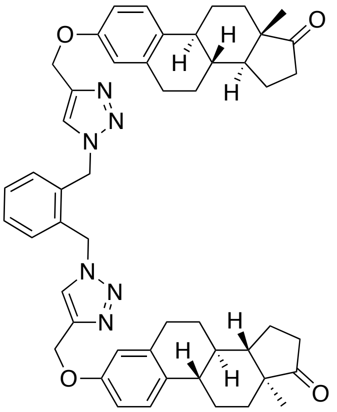
Synthesis of compound II.38



Following the general procedure a mixture of benzyl azide **II.37** (307 mg, 2.31 mmol, 1.50 equiv), alkyne **II.36** (474 mg, 1.54 mmol, 1.00 equiv), sodium (L)-ascorbate (61 mg, 0.31 mmol, 0.20 equiv) and $CuSO_4{\cdot}5H_2O$ (38 mg, 0.15 mmol, 0.10 equiv) in DMF (25 mL) was stirred under Ar at rt for 1 h. The resulting residue was purified (SiO_2, Hex/EtOAc 4:1 to 3:7) to yield **II.38** as a white solid (604 mg, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 1H, $N_3C{=}CH$), 7.28 (m, 3H, Ar), 7.17 (m, 2H, Ar), 7.09 (d, J = 8.6 Hz, 1H, H-1), 6.67 (dd, J = 8.6 Hz, 2.8 Hz, 1H, H-2), 6.61 (d, J = 2.8 Hz, 1H, H-4), 5.42 (s, 2H, NCH_2), 5.05 (s, 2H, OCH_2), 2.78 (m, 2H, CH_2, H-6), 2.38 (dd, J = 18.7 Hz, 8.6 Hz, 1H), 2.26 (m, 1H), 1.99 (m, 5H), 1.42 (m, 6H), 0.80 (s, 3H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 221.0 (C=O, C-17), 156.3 (C, C-3), 144.9 (C, $N_3C{=}CH$), 137.9 (C, C-5), 134.6 (C, Ar), 132.7 (C, C-10), 129.2 (2CH, Ar), 128.9 (CH, Ar), 128.2 (2CH, Ar), 126.5 (CH, C-1), 122.6 (CH, $N_3C{=}CH$), 114.8 (CH, C-4), 112.4 (CH, C-2), 62.2 (OCH_2), 54.3 (NCH_2), 50.4 (CH, C-14), 48.1 (C, C-13), 44.0 (CH, C-9), 38.3 (CH, C-8), 35.9 (CH_2, C-16), 31.6 (CH_2, C-12), 29.7 (CH_2, C-6), 26.6 (CH_2, C-7), 25.9 (CH_2, C-11), 21.6 (CH_2, C-15), 13.9 (CH_3, C-18). **IR (KBr) ν_{max}** 3437, 2923, 1737, 1605, 1500, 1460, 1500, 1460, 1234, 1055, 733. **$[\alpha]_D^{25}$** + 103.8 (c 0.3, $CHCl_3$). **HRMS (ESI)** m/z calculated for $C_{28}H_{32}N_3O_2$: 442.2489 $[M+H]^+$, found: 441.2490. **m.p.** 163–165 °C.

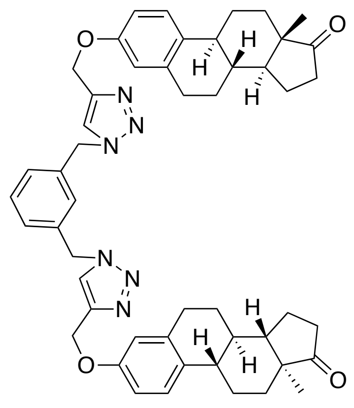
Synthesis of compound II.42a



Following the general procedure a mixture of bis(azide) **II.43a** (164 mg, 0.88 mmol, 1.00 equiv), alkyne **II.36** (542 mg, 1.76 mmol, 2.20 equiv), sodium (L)-ascorbate (70 mg, 0.35 mmol, 0.40 equiv) and $CuSO_4{\cdot}5H_2O$ (44 mg, 0.18 mmol, 0.20 equiv) in DMF (25 mL) was stirred under Ar at rt for 2 h 30. The resulting residue was purified (SiO_2, Hex/EtOAc 1:1 to 1:9) to yield **II.42a** as a white solid (489 mg, 69%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 2H, $N_3C{=}CH$), 7.39 (m, 2H, Ar), 7.26 (m, 2H, Ar), 7.18 (d, *J* = 8.6 Hz, 2H, H-1), 6.76 (dd, *J* = 8.6 Hz, 2.6 Hz, 2H, H-2), 6.70 (d, *J* = 2.6 Hz, 2H, H-4), 5.63 (s, 4H, NCH_2), 5.13 (s, 4H, OCH_2), 2.87 (m, 4H, CH_2, H-6), 2.50 (dd, *J* = 18.8 Hz, 8.6 Hz, 2H), 2.37 (m, 2H), 2.08 (m, 10H), 1.51 (m, 12H), 0.89 (s, 6H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 221.0 (2C=O, C-17), 156.2 (2C, C-3), 145.0 (2C, $N_3C{=}CH$), 138.0 (2C, C-5), 133.3 (2C, Ar), 132.8 (2C, C-10), 130.6 (2CH, Ar), 129.9 (2CH, Ar), 126.5 (2CH, C-1), 123.0 (2CH, $N_3C{=}CH$), 114.8 (2CH, C-4), 112.4 (2CH, C-2), 62.0 ($2OCH_2$), 51.4 ($2NCH_2$), 50.4 (2CH, C-14), 48.1 (2C, C-13), 44.0 (2CH, C-9), 38.4 (2CH, C-8), 35.9 ($2CH_2$, C-16), 31.6 ($2CH_2$, C-12), 29.7 ($2CH_2$, C-6), 26.6 ($2CH_2$, C-7), 26.0 ($2CH_2$, C-11), 21.7 ($2CH_2$, C-15), 13.9 ($2CH_3$, C-18). **IR (KBr) ν_{max}** 3436, 2928, 1736, 1608, 1498, 1454, 1253, 1232, 1052, 753. **$[\alpha]_D^{25}$** + 111.8 (*c* 0.7, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{50}H_{57}N_6O_4$: 805.4436 $[M+H]^+$, found: 805.4462. **m.p.** 125–128 °C.

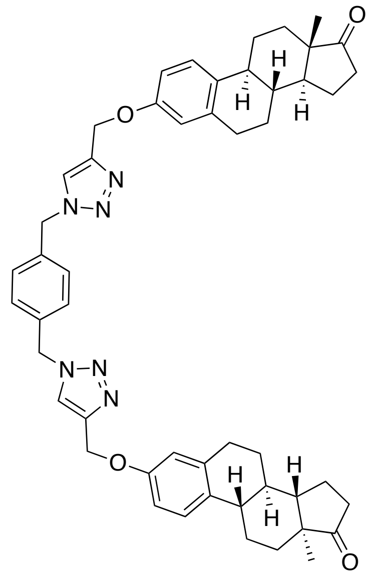
Synthesis of compound II.42b



Following the general procedure a mixture of bis(azide) **II.43b** (174 mg, 0.92 mmol, 1.50 equiv), alkyne **II.36** (627 mg, 2.03 mmol, 2.20 equiv), sodium (L)-ascorbate (73 mg, 0.37 mmol, 0.40 equiv) and $CuSO_4{\cdot}5H_2O$ (44 mg, 0.18 mmol, 0.20 equiv) in DMF (25 mL) was stirred under Ar at rt for 4 h. The resulting residue was purified (SiO_2, Hex/EtOAc 1:1 to 3:7) to yield **II.42b** as a white solid (665 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 2H, $N_3C{=}CH$), 7.37 (t, J = 8.1 Hz, 1H, Ar), 7.25 (m, 3H, Ar), 7.18 (d, J = 8.6 Hz, 2H, H-1), 6.76 (dd, J = 8.6 Hz, 2.8 Hz, 2H, H-2), 6.70 (d, J = 2.8 Hz, 2H, H-4), 5.50 (s, 4H, NCH_2), 5.15 (s, 4H, OCH_2), 2.87 (m, 4H, CH_2, H-6), 2.49 (dd, J = 18.7 Hz, 8.6 Hz, 2H), 2.36 (m, 2H), 2.07 (m, 10H), 1.51 (m, 12H), 0.89 (s, 6H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 221.0 (2C=O, C-17), 156.3 (2C, C-3), 145.0 (2C, $N_3C{=}CH$), 138.0 (2C, C-5), 135.7 (2C, Ar), 132.8 (2C, C-10), 130.1 (CH, Ar), 128.4 (2CH, Ar), 127.6 (CH, Ar), 126.5 (2CH, C-1), 122.8 (2CH, $N_3C{=}CH$), 114.8 (2CH, C-4), 112.4 (2CH, C-2), 62.1 ($2OCH_2$), 53.8 ($2NCH_2$), 50.4 (2CH, C-14), 48.1 (2C, C-13), 44.0 (2CH, C-9), 38.4 (2CH, C-8), 35.9 ($2CH_2$, C-16), 31.6 ($2CH_2$, C-12), 29.7 ($2CH_2$, C-6), 26.6 ($2CH_2$, C-7), 26.0 ($2CH_2$, C-11), 21.7 ($2CH_2$, C-15), 13.9 ($2CH_3$, C-18). **IR (KBr) ν_{max}** 3436, 2928, 1736, 1608, 1498, 1234, 1050. **$[\alpha]_D^{25}$** + 108.7 (c 0.4, $CHCl_3$). **HRMS (ESI)** m/z calculated for $C_{50}H_{57}N_6O_4$: 805.4436 $[M+H]^+$, found: 805.4460. **m.p.** 108–112 °C.

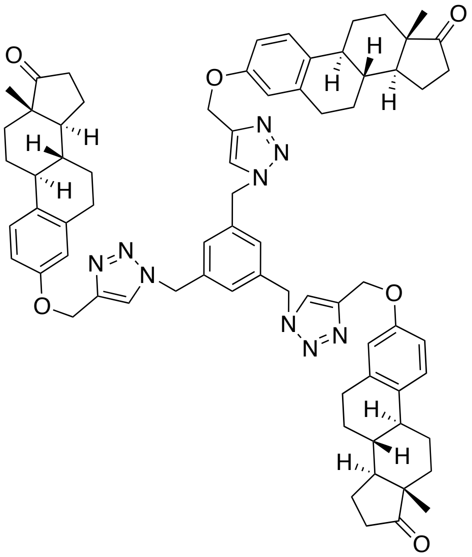
Synthesis of compound II.42c



Following the general procedure a mixture of bis(azide) **II.43c** (194 mg, 1.03 mmol, 1.00 equiv), alkyne **II.36** (700 mg, 2.27 mmol, 2.20 equiv), sodium (L)-ascorbate (82 mg, 0.41 mmol, 0.40 equiv) and $CuSO_4{\cdot}5H_2O$ (51 mg, 0.21 mmol, 0.20 equiv) in DMF (32 mL) was stirred under Ar at rt for 3 h. The resulting residue was purified (SiO_2, $MeOH/CH_2Cl_2$ 2%) to yield **II.42c** as a white solid (700 mg, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (s, 2H, $N_3C{=}CH$), 7.28 (s, 4H, Ar), 7.17 (d, J = 8.4 Hz, 2H, H-1), 6.75 (dd, J = 8.4 Hz, 2.7 Hz, 2H, H-2), 6.68 (d, J = 2.7 Hz, 2H, H-4), 5.50 (s, 4H, NCH_2), 5.13 (s, 4H, OCH_2), 2.86 (m, 4H, CH_2, H-6), 2.47 (dd, J = 18.7 Hz, 8.5 Hz, 2H), 2.35 (m, 2H), 2.06 (m, 10H), 1.50 (m, 12H), 0.88 (s, 6H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 221.0 (2C=O, C-17), 156.3 (2C, C-3), 145.1 (2C, $N_3C{=}CH$), 138.0 (2C, C-5), 135.3 (2C, Ar), 132.8 (2C, C-10), 128.9 (4CH, Ar), 126.5 (2CH, C-1), 122.7 (2CH, $N_3C{=}CH$), 114.8 (2CH, C-4), 112.4 (2CH, C-2), 62.1 ($2OCH_2$), 53.8 ($2NCH_2$), 50.4 (2CH, C-14), 48.1 (2C, C-13), 44.0 (2CH, C-9), 38.4 (2CH, C-8), 35.9 ($2CH_2$, C-16), 31.6 ($2CH_2$, C-12), 29.7 ($2CH_2$, C-6), 26.6 ($2CH_2$, C-7), 26.0 ($2CH_2$, C-11), 21.7 ($2CH_2$, C-15), 13.9 ($2CH_3$, C-18). **IR (KBr)** $\boldsymbol{\nu}_{\mathbf{max}}$ 3436, 2925, 1736, 1605, 1500, 1230, 1053, 817. $[\alpha]_D^{25}$ + 96.3 (c 0.3, $CHCl_3$). **HRMS (ESI)** m/z calculated for $C_{50}H_{57}N_6O_4$: 805.4436 $[M+H]^+$, found: 805.4436. **m.p.** 215–218 °C.

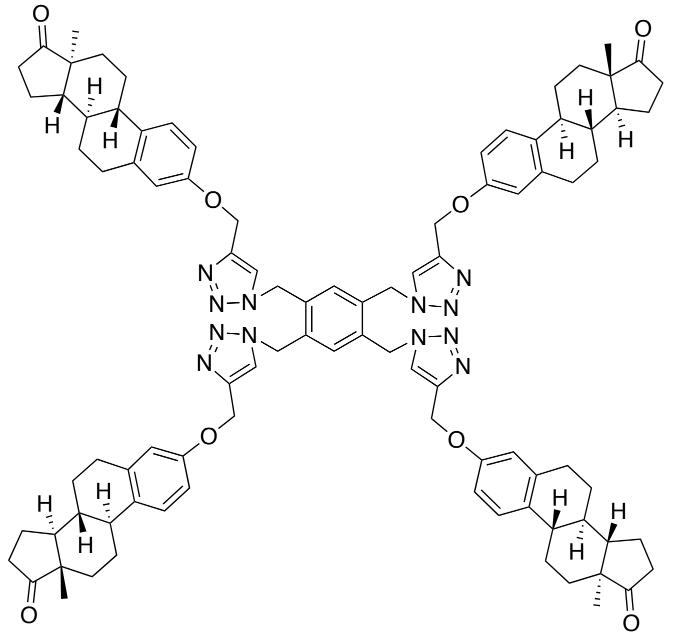
Synthesis of compound II.54



Following the general procedure a mixture of tris(azide) **II.52** (179 mg, 0.74 mmol, 1.00 equiv), alkyne **II.36** (749 mg, 2.43 mmol, 3.30 equiv), sodium (L)-ascorbate (87 mg, 0.44 mmol, 0.60 equiv) and $CuSO_4 \cdot 5H_2O$ (55 mg, 0.22 mmol, 0.30 equiv) in DMF (30 mL) was stirred under Ar at rt for 3 h. The resulting residue was purified (SiO_2, MeOH/CH_2Cl_2 2%) to yield **II.54** as a white solid (790 mg, 91%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 3H, $N_3C{=}CH$), 7.18 (d, *J* = 2.8 Hz, 3H, H-1), 7.14 (s, 3H, Ar), 6.76 (dd, *J* = 8.6 Hz, 2.8 Hz, 3H, H-2), 6.70 (d, *J* = 2.8 Hz, 3H, H-4), 5.46 (s, 6H, NCH_2), 5.14 (s, 6H, OCH_2), 2.87 (m, 6H, H-6), 2.49 (dd, *J* = 18.8 Hz, 8.6 Hz, 3H), 2.36 (m, 3H), 2.07 (m, 15H), 1.51 (m, 18H), 0.89 (s, 9H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 221.0 (3C=O, C-17), 156.2 (3C, C-3), 145.2 (3C, $N_3C{=}CH$), 138.0 (3C, C-5), 136.9 (3C, Ar), 132.9 (3C, C-10), 127.7 (3CH, Ar), 126.5 (3CH, C-1), 123.0 (3CH, $N_3C{=}CH$), 114.8 (3CH, C-4), 112.3 (3CH, C-2), 62.0 ($3OCH_2$), 53.4 ($3NCH_2$), 50.4 (3CH, C-14), 48.1 (3C, C-13), 44.0 (3CH, C-9), 38.4 (3CH, C-8), 35.9 ($3CH_2$, C-16), 31.6 ($3CH_2$, C-12), 29.7 ($3CH_2$, C-6), 26.6 ($3CH_2$, C-7), 26.0 ($3CH_2$, C-11), 21.7 ($3CH_2$, C-15), 13.9 ($3CH_3$, C-18). **IR (KBr)** ν_{max} 3445, 2928, 1736, 1608, 1498, 1454, 1253, 1232, 1052, 1007, 817, 752. $[\alpha]_D^{25}$ + 75.7 (*c* 0.6, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{72}H_{82}N_9O_6$: 1168.6383 $[M+H]^+$, found: 1168.6337. **m.p.** 148–150 °C.

Synthesis of compound II.57

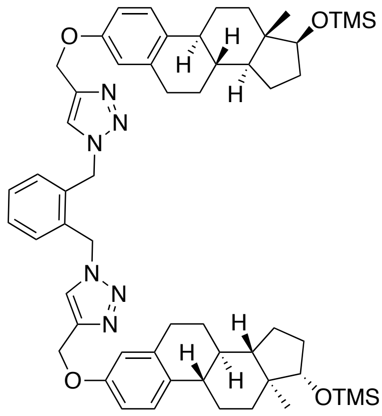


Following the general procedure a mixture of tetra(azide) **II.56** (110 mg, 0.37 mmol, 1.00 equiv), alkyne **II.36** (500 mg, 1.62 mmol, 4.40 equiv), sodium (L)-ascorbate (58 mg, 0.30 mmol, 0.80 equiv) and $CuSO_4{\cdot}5H_2O$ (37 mg, 0.15 mmol, 0.40 equiv) in DMF (23 mL) was stirred under Ar at rt for 2 h. The resulting residue was purified (SiO_2, $MeOH/CH_2Cl_2$ 4%) to yield **II.57** as a white solid (534 mg, 94%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 4H, $N_3C{=}CH$), 7.16 (d, *J* = 8.6 Hz, 4H, H-1), 7.13 (s, 2H, Ar), 6.74 (dd, *J* = 8.6 Hz, 2.7 Hz, 4H, H-2), 6.69 (br s, 4H, H-4), 5.58 (s, 8H, NCH_2), 5.10 (s, 8H, OCH_2), 2.85 (m, 8H, H-6), 2.49 (dd, *J* = 18.8 Hz, 8.6 Hz, 4H), 2.35 (m, 4H), 2.06 (m, 20H), 1.49 (m, 24H), 0.88 (s, 12H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 220.9 (4C=O, C-17), 156.2 (4C, C-3), 145.2 (4C, $N_3C{=}CH$), 138.1 (4C, C-5), 135.0 (4C, Ar), 132.9 (4C, C-10), 132.4 (2CH, Ar), 126.5 (4CH, C-1), 123.4 (4CH, $N_3C{=}CH$), 114.8 (4CH, C-4), 112.4 (4CH, C-2), 61.9 ($4OCH_2$), 50.7 ($4NCH_2$), 50.5 (4CH, C-14), 48.1 (4C, C-13), 44.0 (4CH, C-9), 38.4 (4CH, C-8), 35.9 ($4CH_2$, C-16), 31.7 ($4CH_2$, C-12), 29.7 ($4CH_2$, C-6), 26.6 ($4CH_2$, C-7), 26.0 ($4CH_2$, C-11), 21.7 ($4CH_2$, C-15), 14.0 ($4CH_3$, C-18). **IR (KBr) ν_{max}** 3436, 2927, 1737, 1608, 1575, 1498, 1454, 1232, 1157, 1053, 816, 752. **$[\alpha]_D^{25}$** + 126.5 (*c* 0.6,

$CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{94}H_{107}N_{12}O_8$: 1532.8361 $[M+H]^+$, found: 1532.8307. **m.p.** 163–165 °C.

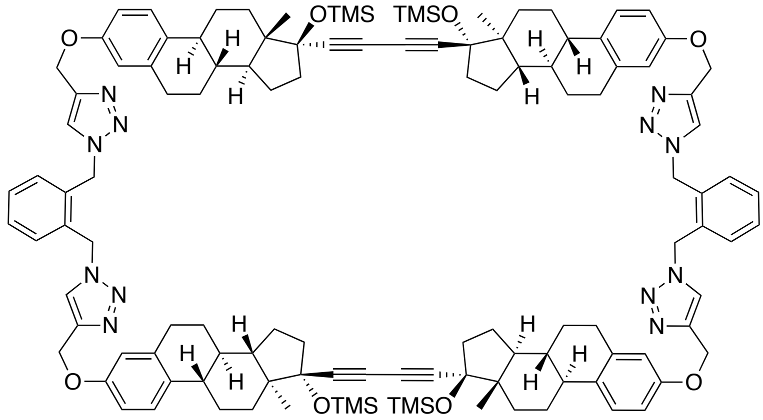
Synthesis of compound II.48



Following the general procedure triazole **II.47** (1074 mg, 1.33 mmol, 1.00 equiv) was dissolved in anhydrous CH_2Cl_2 (110 mL). Imidazole (542 mg, 7.96 mmol, 6.00 equiv) was added followed by the addition of TMSCl (505 μL, 3.98 mmol, 3.00 equiv). The reaction was stirred at rt for one hour. The mixture was quenched with water and extracted three times with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered and the solvent was removed under vacuum to afford the corresponding reaction product **II.48** as a white solid without further purification required (1115 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 2H, $N_3C{=}CH$), 7.27 (m, 2H, Ar), 7.15 (m, 2H, Ar), 7.07 (d, J = 8.6 Hz, 2H, H-1), 6.63 (dd, J = 8.6, 2.3 Hz, 2H, H-2), 6.57 (br s, 2H, H-4), 5.50 (s, 4H, NCH_2), 5.01 (s, 4H, OCH_2), 3.53 (t, J = 8.3 Hz, H-17), 2.71 (m, 4H), 2.16 (m, 2H), 2.05 (m, 2H), 1.80 (m, 6H), 1.55 (m, 2H), 1.22 (m, 16H), 0.64 (s, 6H, H-18), 0.00 (s, 18H, TMS). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.1 (2C, C-3), 145.2 (2C, $N_3C{=}CH$), 138.3 (2C, C-5), 133.6 (2C, Ar), 133.3 (2C, C-10), 130.6 (2CH, Ar), 129.9 (2CH, Ar), 126.5 (2CH, C-1), 122.9 (2CH, $N_3C{=}CH$), 114.8 (2CH, C-4), 112.3 (2CH, C-2), 81.8 (2CH, C-17), 62.1 ($2OCH_2$), 51.4 ($2NCH_2$), 49.9 (2CH, C-14), 44.2 (2CH, C-9), 43.4 (2C, C-13), 38.9 (2CH, C-8), 37.1 ($2CH_2$, C-12), 31.0 ($2CH_2$, C-16) 29.9 ($2CH_2$, C-6), 27.3 ($2CH_2$, C-7), 26.5 ($2CH_2$, C-11), 23.3 ($2CH_2$, C-15), 11.4 ($2CH_3$, C-18), 0.3 ($3CH_3$, TMS). **IR (KBr) ν_{max}** 3429, 2954, 2927, 1609, 1499, 1250, 1139, 1095, 895, 841. **$[\alpha]_D^{25}$** + 15.9 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{56}H_{77}N_6O_4Si_2$: 953.5539 $[M+H]^+$, found: 953.5546. **m.p.** 123–126 °C.

Synthesis of compound II.61



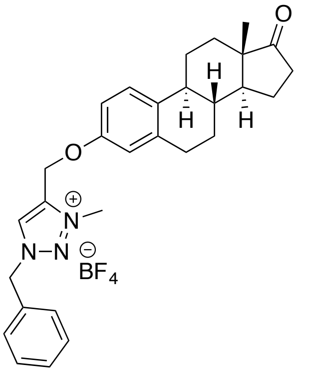
To a solution of the macrocycle **II.62** (151 mg, 0.09 mmol, 1.00 equiv) in CH_2Cl_2 (25 mL) under Ar, triethylamine was added (97μL, 0.70 mmol, 8.00 equiv). The reaction was stirred for 15 min. Trimethylsilane triflate was then added (97μL, 0.52 mmol, 6.00 equiv) drop by drop. The mixture was stirred at rt for 1 h until the reaction was complete (TLC analysis). The solvent was removed under vacuum. **II.61** was obtained as a white solid. (The product was isolated after the methylation process. A sample of **II.61** was taken for its characterisation).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (m, 4H, Ar), 7.23 (m, 4H, Ar), 7.16 (s, 4H, $N_3C{=}CH$), 6.99 (d, *J* = 8.8 Hz, 4H, H-1), 6.59 (dd, *J* = 8.8 Hz, 2.8 Hz, 4H, H-2), 6.46 (d, *J* = 2.8, 4H, H-4), 5.57 (d, *J* = 4.2 Hz, 8H, NCH_2), 5.15 (s, 8H, OCH_2), 2.66 (m, 8H), 2.26 (m, 8H), 2.06 (m, 4H), 1.93 (m, 4H), 1.72 (m, 16H), 1.29 (m, 20H), 0.80 (s, 12H, H-18), 0.18 (s, 36H, OTMS). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.4 (4C, C-3), 145.5 (4C, $N_3C{=}CH$), 137.9 (4C, C-5), 133.1 (4C, Ar), 132.8 (4C, C-10), 130.6 (4CH, Ar), 130.0 (4CH, Ar), 126.2 (4CH, C-1), 122.7 (4CH, $N_3C{=}CH$), 115.4 (4CH, C-4), 112.2 (4CH, C-2), 85.0 (4C, *C*≡C), 81.3 (4C, C-17), 71.2 (4C, C≡*C*), 61.9 ($4OCH_2$), 51.3 ($4NCH_2$), 49.3 (4CH, C-14), 48.9 (4C, C-13), 44.3 (4CH, C-9), 40.0 (4CH, C-8), 39.4 ($4CH_2$, C-16), 33.2 ($4CH_2$, C-12), 29.9 ($4CH_2$, C-6), 27.4 ($4CH_2$, C-7), 26.5 ($4CH_2$, C-11), 23.2 ($4CH_2$, C-15), 13.1 ($4CH_3$, C-18), 1.8 ($12CH_3$, OTMS). **IR (KBr)** ν_{max} 3435, 2929, 1610, 1499, 1455, 1250, 1140, 1109, 1088, 892, 842, 754. $[\alpha]_D^{25}$ + 87.7 (*c* 0.6, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{120}H_{149}N_{12}O_8Si_4$: 1999.0720 $[M+H]^+$, found: 1999.0735. **m.p.** decomposes before melting.

General procedure for the synthesis of triazolium salts

Triazole (1.00 equiv) and Meerwein's salt (1.30 equiv per triazole) were stirred under Ar at rt in CH_2Cl_2 until the reaction was completed (^1H NMR analysis). The reaction was quenched with methanol and filtered through a short pad of $NaHCO_3$. The solvent was removed under vacuum to afford the corresponding reaction product without further purification.

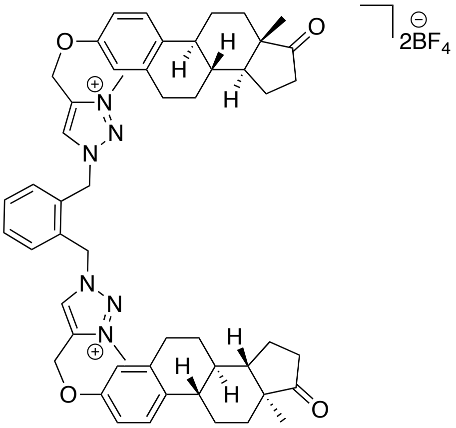
Synthesis of compound II.39



Following the general procedure a mixture of **II.38** (340 mg, 1.13 mmol, 1.00 equiv) and Me_3OBF_4 (218 mg, 1.47 mmol, 1.30 equiv) in CH_2Cl_2 (70 mL) was stirred under Ar at rt for 3 h. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **II.39** as a white solid (605 mg, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H, $N_3C=CH$), 7.46 (m, 2H, Ar), 7.38 (m, 3H, Ar), 7.17 (d, *J* = 8.6 Hz, 1H, H-1), 6.74 (dd, *J* = 8.6 Hz, 2.7 Hz, 1H, H-2), 6.70 (d, *J* = 2.7 Hz, 1H, H-4), 5.64 (s, 2H, NCH_2), 5.23 (s, 2H, OCH_2), 4.27 (s, 3H, NCH_3), 2.85 (m, 2H, CH_2, H-6), 2.49 (dd, *J* = 18.9 Hz, 8.6 Hz, 1H), 2.33 (m, 1H), 2.01 (m, 5H), 1.49 (m, 6H), 0.88 (s, 3H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 220.9 (C=O, C-17), 154.9 (C, C-3), 140.1 (C, N_3C=CH), 138.6 (C, C-5), 134.1 (C, Ar), 131.3 (C, C-10), 130.0 (2CH, Ar), 129.9 (CH, Ar), 129.6 (2CH, Ar), 129.5 (2CH, N_3C=CH), 126.9 (CH, C-1), 114.7 (CH, C-4), 112.3 (CH, C-2), 57.9 (OCH_2), 57.6 (NCH_2), 50.5 (CH, C-14), 48.0 (C, C-13), 44.0 (CH, C-9), 38.7 (CH, C-8), 38.3 (NCH_3), 35.9 (CH_2, C-16), 31.6 (CH_2, C-12), 29.6 (CH_2, C-6), 26.5 (CH_2, C-7), 25.9 (CH_2, C-11), 21.7 (CH_2, C-15), 13.9 (CH_3, C-18). **IR (KBr) ν_{max}** 3436, 2930, 1735, 1610, 1498, 1456, 1084, 1063, 710. **$[\alpha]_D^{25}$** + 87.9 (*c* 0.5, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{29}H_{34}N_3O_2$: 456.2646 $[M–BF_4^-]^+$, found: 456.2648. **m.p.** 119–122 °C.

Synthesis of compound II.44a

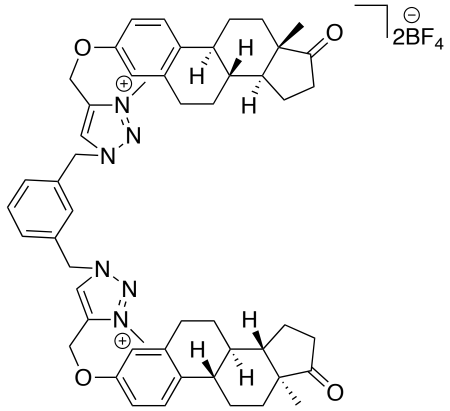


Following the general procedure a mixture of **II.42a** (90 mg, 0.11 mmol, 1.00 equiv) and Me_3OBF_4 (43 mg, 0.29 mmol, 2.60 equiv) in CH_2Cl_2 (14 mL) was stirred under Ar at rt for 19 h. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **II.44a** as a white solid (103 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 2H, N_3C=CH), 7.41 (s, 4H, Ar), 7.16 (d, *J* = 8.5 Hz, 2H, H-1), 6.72 (d, *J* = 8.5 Hz, 2H, H-2), 6.68 (br s, 2H, H-4), 5.84 (s, 4H, NCH_2), 5.18 (s, 4H, OCH_2), 4.19 (s, 6H, NCH_3), 2.84 (m, 4H, H-6), 2.49 (dd, *J* = 18.8 Hz, 8.7 Hz, 2H), 2.31 (m, 2H), 2.04 (m, 10H), 1.48 (m, 12H), 0.87 (s, 6H, CH_3). **^{13}C NMR** (100 MHz,

$CDCl_3$) δ 220.9 (2C=O, C-17), 155.0 (2C, C-3), 140.3 (2C, N_3C=CH), 138.6 (2C, C-5), 134.2 (2C, Ar), 131.9 (2C, C-10), 131.1 (2CH, Ar), 130.8 (2CH, Ar), 130.2 (2CH, N_3C=CH), 126.9 (2CH, C-1), 114.8 (2CH, C-4), 112.3 (2CH, C-2), 57.9 ($2OCH_2$), 54.3 ($2NCH_2$), 50.5 (2CH, C-14), 48.0 (2C, C-13), 44.0 (2CH, C-9), 38.9 ($2NCH_3$), 38.3 (2CH, C-8), 36.0 ($2CH_2$, C-16), 31.6 ($2CH_2$, C-12), 29.6 ($2CH_2$, C-6), 26.5 ($2CH_2$, C-7), 26.0 ($2CH_2$, C-11), 21.7 ($2CH_2$, C-15), 14.0 ($2CH_3$, C-18). **IR (KBr) ν_{max}** 3436, 2928, 1735, 1609, 1498, 1454, 1233, 1083, 1058, 750. **$[\alpha]_D^{25}$** + 91.5 (*c* 0.3, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{52}H_{62}BF_4N_6O_4$: 921.4865 $[M–BF_4^-]^+$, found: 921.4915 and for $C_{52}H_{62}N_6O_4$: 417.2411 $[M–2BF_4^-]^{2+}$, found: 417.2401. **m.p.** 140–142 °C.

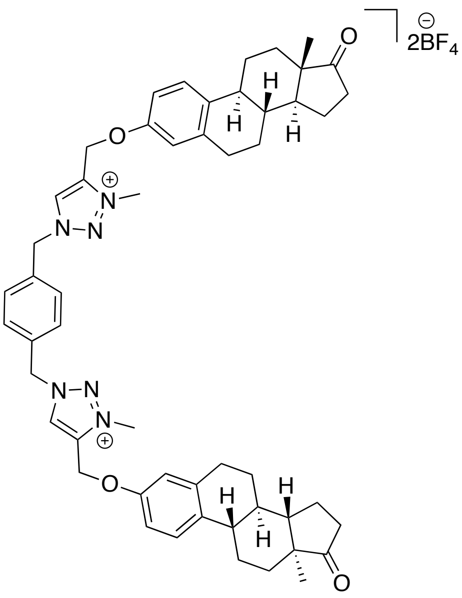
Synthesis of compound II.44b



Following the general procedure a mixture of **II.42b** (90 mg, 0.11 mmol, 1.00 equiv) and Me_3OBF_4 (43 mg, 0.29 mmol, 2.60 equiv) in CH_2Cl_2 (14 mL) was stirred under Ar at rt for 1 h. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **II.44b** as a white solid (105 mg, 95%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 2H, N_3C=CH), 7.42 (s, 4H, Ar), 7.15 (d, *J* = 8.7 Hz, 2H, H-1), 6.72 (dd, *J* = 8.7 Hz, 2.7 Hz, 2H, H-2), 6.68 (d, *J* = 2.7 Hz, 2H, H-4), 5.64 (s, 4H, NCH_2), 5.20 (s, 4H, OCH_2), 4.23 (s, 6H, NCH_3), 2.84 (m, 4H, H-6), 2.49 (dd, *J* = 18.6 Hz, 8.7 Hz, 2H), 2.30 (m, 2H), 2.17 (m, 10H), 1.47 (m, 12H), 0.86 (s, 6H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 221.2 (2C=O, C-17), 154.9 (2C, C-3), 140.3 (2C, N_3C=CH), 138.6 (2C, C-5), 134.0 (2C, Ar), 132.8 (2C, C-10), 130.5 (2CH, Ar), 130.3 (CH, Ar), 130.1 (2CH, N_3C=CH), 129.5 (CH, Ar), 126.9 (2CH, C-1), 114.8 (2CH, C-4), 112.2 (2CH, C-2), 57.6 ($2OCH_2$), 56.8 ($2NCH_2$), 50.4 (2CH, C-14), 48.1 (2C, C-13), 44.0 (2CH, C-9), 38.7 ($2NCH_3$), 38.3 (2CH, C-8), 36.0 ($2CH_2$, C-16), 31.6 ($2CH_2$, C-12), 29.6 ($2CH_2$, C-6), 26.5 ($2CH_2$, C-7), 25.9 ($2CH_2$, C-11), 21.7 ($2CH_2$, C-15), 13.9 ($2CH_3$, C-18). **IR (KBr)** $\boldsymbol{\nu}_{\mathbf{max}}$ 3435, 2929, 1735, 1609, 1498, 1454, 1234, 1083, 1057, 756. $[\alpha]_D^{25}$ + 69.8 (*c* 0.3, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{52}H_{62}BF_4N_6O_4$: 921.4865 $[M–BF_4^-]^+$, found: 921.4895 and for $C_{52}H_{62}N_6O_4$: 417.2411 $[M–2BF_4^-]^{2+}$, found: 417.2449. **m.p.** 124–127 °C.

Synthesis of compound II.44c

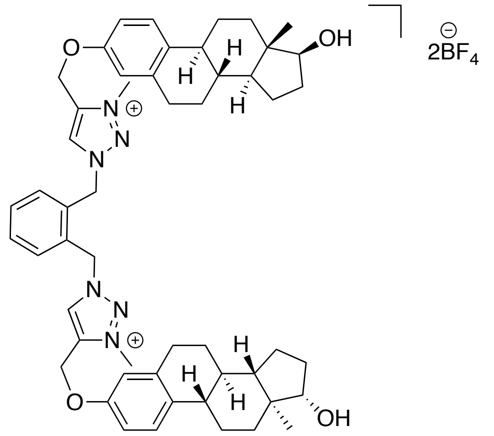


Following the general procedure a mixture of **II.42c** (375 mg, 0.47 mmol, 1.00 equiv) and Me_3OBF_4 (179 mg, 1.21 mmol, 2.60 equiv) in CH_2Cl_2 (60 mL) was stirred under Ar at rt for 19 h. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **II.44c** as a white solid (437 mg, 92%).

^{1}H NMR (500 MHz, DMSO-*d*$_6$) *δ* 9.08 (s, 2H, N_3C=CH), 7.57 (s, 4H, Ar), 7.26 (d, *J* = 8.6 Hz, 2H, H-1), 6.87 (dd, *J* = 8.6 Hz, 2.5 Hz, 2H, H-2), 6.83 (d, *J* = 2.5 Hz, 2H, H-4), 5.92 (s, 4H, NCH_2), 5.39 (s, 4H, OCH_2), 4.29 (s, 6H, NCH_3), 2.86 (m, 4H, H-6), 2.45 (dd, *J* =

18.8 Hz, 8.4 Hz, 2H), 2.36 (m, 2H), 2.21 (m, 2H), 2.08 (m, 2H), 1.97 (m, 4H), 1.78 (m, 2H), 1.48 (m, 12H), 0.83 (s, 6H, H-18). **^{13}C NMR** (125 MHz, DMSO-*d*$_6$) *δ* 219.6 (2C=O, C-17), 155.0 (2C, C-3), 140.1 (2C, N_3C=CH), 137.9 (2C, C-5), 133.9 (2C, Ar), 133.4 (2C, C-10), 129.8 (4CH, Ar), 129.6 (2CH, N_3C=CH), 126.5 (CH, C-1), 114.6 (2CH, C-4), 112.4 (2CH, C-2), 58.2 (2OCH$_2$), 55.7 (2NCH$_2$), 49.5 (2CH, C-14), 47.3 (2C, C-13), 43.4 (2CH, C-9), 38.4 (2NCH$_3$), 37.8 (2CH, C-8), 35.4 (2CH$_2$, C-16), 31.3 (2CH$_2$, C-12), 29.2 (2CH$_2$, C-6), 26.0 (2CH$_2$, C-7), 25.5 (2CH$_2$, C-11), 21.1 (2CH$_2$, C-15), 13.5 (2CH$_3$, C-18). **IR (KBr) ν_{max}** 3436, 2931, 1736, 1609, 1498, 1455, 1233, 1083, 1059, 821. **$[\alpha]_D^{25}$** + 97.6 (*c* 0.2, CH_3CN). **HRMS (ESI)** *m/z* calculated for $C_{52}H_{62}BF_4N_6O_4$: 921.4865 $[M–BF_4^-]^+$, found: 921.4899. **m.p.** 155–157 °C.

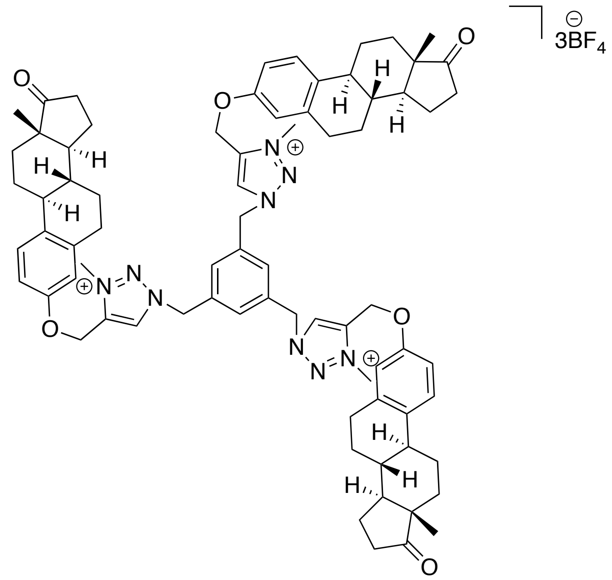
Synthesis of compound II.49



Following the general procedure a mixture of **II.48** (300 mg, 0.31 mmol, 1.00 equiv) and Me_3OBF_4 (102 mg, 0.69 mmol, 2.20 equiv) in CH_2Cl_2 (22 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **II.49** as a white solid (319 mg, quantitative).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 9.05 (s, 2H, N_3C=CH), 7.53 (m, 4H, Ar), 7.24 (d, *J* = 8.6 Hz, 2H, H-1), 6.84 (br d, *J* = 8.6, 2H, H-2), 6.79 (br s, 2H, H-4), 6.09 (s, 4H, NCH$_2$), 5.40 (s, 4H, OCH$_2$), 4.50 (d, *J* = 4.7 Hz, 2H, OH), 4.28 (s, 6H, NCH$_3$), 3.53 (q, *J* = 8.4 Hz, H-17), 2.79 (br s, 4H), 2.29 (m, 2H), 2.12 (t, *J* = 8.8 Hz, 2H), 1.87 (m, 6H), 1.59 (m, 2H), 1.26 (m, 16H), 0.67 (s, 6H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.8 (2C, C-3), 140.1 (2C, $N_3C=CH$), 137.9 (2C, C-5), 133.9 (2C, Ar), 131.8 (2C, C-10), 130.8 (2CH, Ar), 130.3 (2CH, Ar), 130.1 (2CH, $N_3C=CH$), 126.5 (2CH, C-1), 114.5 (2CH, C-4), 112.3 (2CH, C-2), 80.0 (2CH, C-17), 58.1 ($2OCH_2$), 53.2 ($2NCH_2$), 49.5 (2CH, C-14), 43.5 (2CH, C-9), 42.8 (2C, C-13), 38.5 ($2NCH_3$), 38.4 (2CH, C-8), 36.5 ($2CH_2$, C-16), 29.9 ($2CH_2$, C-12) 29.2 ($2CH_2$, C-6), 26.7 ($2CH_2$, C-7), 26.0 ($2CH_2$, C-11), 22.8 ($2CH_2$, C-15), 11.2 ($2CH_3$, C-18). **IR (KBr) ν_{max}** 3429, 2927, 1608, 1498, 1234, 1083. **$[\alpha]_D^{25}$** + 24.9 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{56}H_{66}BF_4N_6O_4$: 925.5178 $[M–BF_4^-]^+$, found: 925.5223 and for $C_{56}H_{66}N_6O_4$: 419.2567 $[M–2BF_4^-]^{2+}$, found: 419.2583. **m.p.** 113–116 °C.

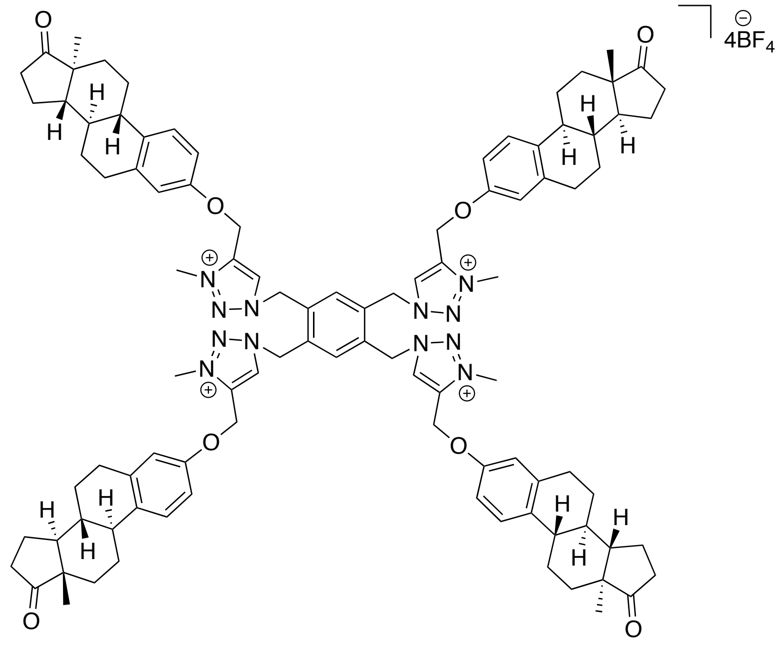
Synthesis of compound II.53



Following the general procedure a mixture of **II.54** (300 mg, 0.26 mmol, 1.00 equiv) and Me_3OBF_4 (148 mg, 1.00 mmol, 3.90 equiv) in CH_2Cl_2 (66 mL) was stirred under Ar at rt for 24 h. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **II.53** as a white solid (363 mg, 95%).

^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.07 (s, 3H, $N_3C=CH$), 7.67 (s, 3H, Ar), 7.25 (d, *J* = 8.5 Hz, 3H, H-1), 6.86 (dd, *J* = 8.5 Hz, 2.8 Hz, 3H, H-2), 6.82 (d, *J* = 2.8 Hz, 3H, H-4), 5.92 (s, 6H, NCH_2), 5.41 (s, 6H, NCH_2), 4.30 (s, 9H, OCH_3), 2.85 (m, 6H, H-6), 2.42 (m, 6H), 2.21 (m, 3H), 2.08 (m, 3H), 1.95 (m, 6H), 1.77 (m, 3H), 1.54 (m, 9H), 1.38 (m, 9H), 0.83 (s, 9H, H-18). **^{13}C NMR** (100 MHz, DMSO-*d_6*) *δ* 219.6 (3C=O, C-17), 155.0 (3C, C-3), 140.1 (3C, N_3C=CH), 137.9 (3C, C-5), 134.4 (3C, Ar), 133.4 (3C, C-10), 130.4 (3CH, Ar), 130.0 (3CH, C-1), 126.5 (3CH, N_3C=CH), 114.5 (3CH, C-4), 112.4 (3CH, C-2), 58.2 ($3OCH_2$), 55.5 ($3NCH_2$), 49.5 (3CH, C-14), 47.3 (3C, C-13), 43.4 (3CH, C-9), 38.5 ($3NCH_3$), 37.8 (3CH, C-8), 35.4 ($3CH_2$, C-16), 31.3 ($3CH_2$, C-12), 29.2 ($3CH_2$, C-6), 25.9 ($3CH_2$, C-7), 25.5 ($3CH_2$, C-11), 21.1 ($3CH_2$, C-15), 13.5 ($3CH_3$, C-18). **IR (KBr) ν_{max}** 3435, 2926, 1736, 1610, 1498, 1454, 1234, 1083, 1057, 819. **$[\alpha]_D^{25}$** + 65.1 (*c* 0.6, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{75}H_{90}B_2F_8N_9O_6$: 1386.7089 $[M–BF_4^-]^+$, found: 1386.6978; for $C_{75}H_{90}BF_4N_9O_6$: 649.8522 $[M–2BF_4^-]^{2+}$, found: 649.8586 and for $C_{75}H_{90}N_9O_6$: 404.2333 $[M–3BF_4^-]^{3+}$, found: 404.2321. **m.p.** 160–163 °C.

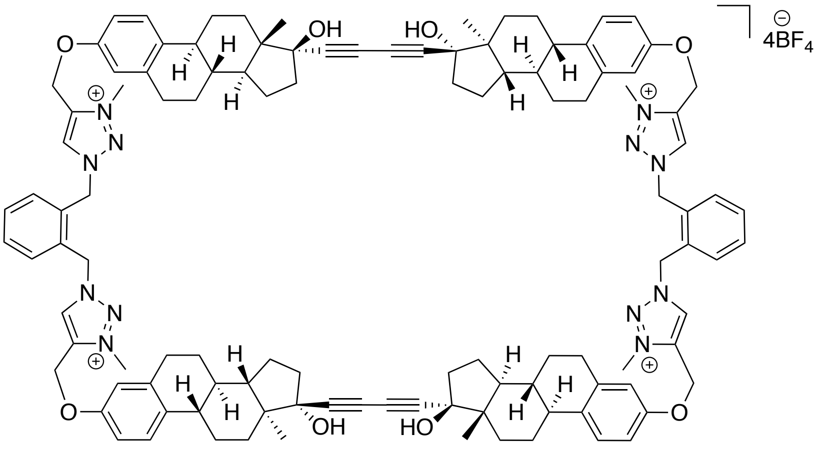
Synthesis of compound II.59



Following the general procedure a mixture of **II.57** (320 mg, 0.21 mmol, 1.00 equiv) and Me_3OBF_4 (161 mg, 1.09 mmol, 5.20 equiv) in CH_2Cl_2 (53 mL) was stirred under Ar at rt for 24 h. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **II.59** as a white solid (436 mg, quantitative).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.05 (s, 4H, N_3C=CH), 7.72 (s, 2H, Ar), 7.26 (d, *J* = 8.6 Hz, 4H, H-1), 6.85 (br d, *J* = 8.5 Hz, 4H, H-2), 6.81 (br s, 4H, H-4), 6.09 (s, 8H, NCH_2), 5.41 (s, 8H, OCH_2), 4.27 (s, 12H, NCH_3), 2.84 (m, 8H, H-6), 2.40 (m, 8H), 2.20 (m, 4H), 2.08 (m, 4H), 1.96 (m, 8H), 1.75 (m, 4H), 1.50 (m, 24H), 0.83 (s, 12H, H-18). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 219.6 (4C=O, C-17), 155.0 (4C, C-3), 140.1 (4C, N_3C=CH), 138.0 (4C, C-5), 133.9 (2CH, Ar), 133.8 (4C, Ar), 133.5 (4C, C-10), 130.3 (4CH, C-1), 126.6 (4CH, N_3C=CH), 114.5 (4CH, C-4), 112.4 (4CH, C-2), 58.2 (4OCH_2), 52.8 (4NCH_2), 49.5 (4CH, C-14), 47.3 (4C, C-13), 43.5 (4CH, C-9), 38.6 (4NCH_3), 37.8 (4CH, C-8), 35.4 (4CH_2, C-16), 31.3 (4CH_2, C-12), 29.2 (4CH_2, C-6), 26.0 (4CH_2, C-7), 25.5 (4CH_2, C-11), 21.2 (4CH_2, C-15), 13.5 (4CH_3, C-18). **IR (KBr) ν_{max}** 3435, 2929, 1735, 1609, 1498, 1454, 1234, 1083, 1059, 846. **$[\alpha]_D^{25}$** + 108.6 (*c* 0.5, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{98}H_{118}B_3F_{12}N_{12}O_8$: 1850.9330 $[M-BF_4^-]^+$, found: 1850.9630. **m.p.** decomposes before melting.

Synthesis of compound II.60



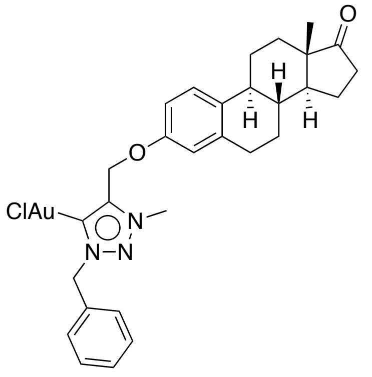
Following the general procedure a mixture of **II.61** (362 mg, 0.18 mmol, 1.00 equiv) and Me_3OBF_4 (139 mg, 0.94 mmol, 5.20 equiv) in CH_2Cl_2 (40 mL) was stirred under Ar at rt until completion of the reaction (5h 30). The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum and the residue was precipitated in a mixture of $CHCl_3$ and methanol to remove the triethylammonium salt formed in the previous step. **II.60** is obtained as a white solid (210 mg, 90% two steps).

^{1}H NMR (400 MHz, DMSO-*d*$_6$) *δ* 8.84 (s, 4H, $N_3C{=}CH$), 7.51 (m, 4H, Ar), 7.41 (m, 4H, Ar), 7.08 (d, *J* = 8.6 Hz, 4H, H-1), 6.75 (dd, *J* = 8.6 Hz, 2.7 Hz, 4H, H-2), 6.70 (d, *J* = 2.7 Hz, 4H, H-4), 6.03 (s, 8H, NCH_2), 5.59 (s, 4H, OH), 5.46 (s, 8H, OCH_2), 4.28 (s, 12H, NCH_3), 2.72 (m, 8H), 2.30 (m, 4H), 2.12 (m, 4H), 1.82 (m, 25H), 1.55 (m, 5H), 1.32 (m, 14H), 0.77 (s, 12H, H-18). **^{13}C NMR** (100 MHz, DMSO-*d*$_6$) *δ* 153.9 (4C, C-3), 140.3 (4C, $N_3C{=}CH$), 137.7 (4C, C-5), 133.2 (4C, Ar), 131.7 (4C, C-10), 130.7 (4CH, Ar), 130.2 (4CH, Ar), 129.8 (4CH, $N_3C{=}CH$), 126.4 (4CH, C-1), 115.0 (4CH, C-4), 112.3 (4CH, C-2), 85.1 (4C, *C*≡C), 78.8 (4C, C-17), 68.7 (4C, C≡*C*), 57.7 ($4OCH_2$), 53.3 ($4NCH_2$), 49.6 (4CH, C-14), 47.7 (4C, C-13), 45.8 (4CH, C-9), 43.8 (4CH, C-8), 38.8 ($4NCH_3$), 38.5 ($4CH_2$, C-16), 33.0 ($4CH_2$, C-12), 29.2 ($4CH_2$, C-6), 26.9 ($4CH_2$, C-7), 26.0 ($4CH_2$, C-11), 22.4 ($4CH_2$, C-15), 12.8 ($4CH_3$, C-18). **IR (KBr) *ν*$_{max}$** 3436, 2932, 1610, 1498, 1455, 1256, 1083, 1031, 819. **$[\alpha]_D^{25}$** + 83.7 (*c* 0.5, MeOH). **HRMS (ESI)** *m/z* calculated for $C_{112}H_{128}B_3F_{12}N_{12}O_8$: 2029.0114 $[M{-}BF_4^-]^+$, found: 2028.9998. **m.p.** 184–187 °C.

General procedure for the synthesis of gold carbenes

In a Schlenk tube charged with 4 Å molecular sieves, a mixture of triazolium salt (1.00 equiv), NMe_4Cl (1.50 equiv per triazole) and Ag_2O (0.75 equiv per triazole) was stirred at rt in the dark in $CH_3CN:CH_2Cl_2$ (1:1) until the formation of the silver carbene (^{1}H NMR analysis). The $[AuCl(SMe_2)]$ (1.00 equiv per triazole) was added and the reaction was stirred at rt until the reaction was completed (^{1}H NMR analysis). The reaction was filtered through a pad of Celite and the solvent was removed under vacuum to afford the corresponding reaction products, which were purified through a short pad of SiO_2.

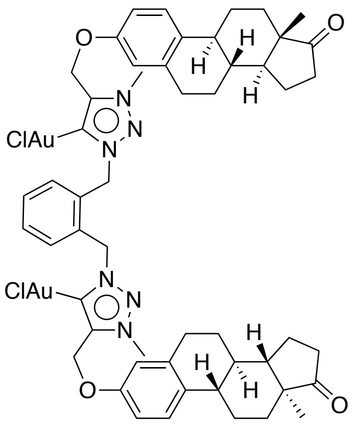
Synthesis of compound II.41



Following the general procedure a mixture of **II.39** (270 mg, 0.50 mmol, 1.00 equiv), NMe_4Cl (82 mg, 0.75 mmol, 1.50 equiv) and Ag_2O (86 mg, 0.37 mmol, 0.75 equiv) in $CH_3CN:CH_2Cl_2$ (26 mL) was stirred under Ar at rt for 18 h. $[AuCl(SMe_2)]$ (146 mg, 0.50 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, Hex/EtOAc 4:6) to yield **II.40** as a white solid (296 mg, 86%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.54 (m, 2H, Ar), 7.37 (m, 3H, Ar), 7.21 (d, *J* = 8.5 Hz, 1H, H-1), 6.84 (d, *J* = 2.8 Hz, 1H, H-4), 6.78 (dd, *J* = 8.5 Hz, 2.8 Hz, 1H, H-2), 5.62 (s, 2H, NCH_2), 5.23 (s, 2H, OCH_2), 4.17 (s, 3H, NCH_3), 2.91 (m, 2H, H-6), 2.50 (dd, *J* = 18.3 Hz, 8.3 Hz, 1H), 2.38 (m, 1H), 2.09 (m, 5H), 1.47 (m, 6H), 0.91 (s, 3H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 221.0 (C=O, C-17), 159.8 (C, $N_3C{=}\mathit{C}Au$), 154.9 (C, C-3), 142.5 (C, $N_3\mathit{C}{=}CAu$), 138.6 (C, C-5), 133.9 (C, Ar), 133.4 (C, C-10), 129.4 (CH, Ar), 129.2 (2CH, Ar), 129.1 (2CH, Ar), 126.9 (CH, C-1), 114.7 (CH, C-4), 112.7 (CH, C-2), 59.7 (OCH_2), 59.1 (NCH_2), 50.5 (CH, C-14), 48.1 (C, C-13), 44.1 (CH, C-9), 38.4 (NCH_3), 37.8 (CH, C-8), 36.0 (CH_2, C-16), 31.7 (CH_2, C-12), 29.8 (CH_2, C-6), 26.6 (CH_2, C-7), 26.0 (CH_2, C-11), 21.7 (CH_2, C-15), 14.0 (CH_3, C-18). **IR (KBr) ν_{max}** 3436, 2927, 1733, 1607, 1497, 1454, 1230, 1157, 1055, 1026, 750, 708. **$[\alpha]_D^{25}$** + 58.6 (*c* 0.2, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{29}H_{34}AuClN_3O_2$: 688.2000 $[M+H]^+$, found 688.1832; for $C_{29}H_{37}AuClN_4O_2$: 705.2265 $[M+NH_4]^+$, found: 705.2298 and for $C_{29}H_{33}AuClN_3NaO_2$: 710.1819 $[M+Na]^+$, found: 710.1859. **m.p.** decomposes before melting.

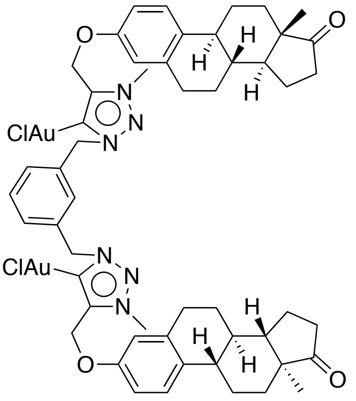
Synthesis of compound II.45a



Following the general procedure a mixture of **II.44a** (35 mg, 0.03 mmol, 1.00 equiv), NMe_4Cl (11 mg, 0.10 mmol, 3.00 equiv) and Ag_2O (12 mg, 0.05 mmol, 1.50 equiv) in CH_3CN:CH_2Cl_2 (8 mL) was stirred under Ar at rt for 3 days. [AuCl(SMe_2)] (20 mg, 0.07 mmol, 2.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, MeOH/CH_2Cl_2 1%) to yield **II.45a** as a white solid (33 mg, 71%).

^{1}**H NMR** (500 MHz, $CDCl_3$) *δ* 7.43 (s, 4H, Ar), 7.21 (d, *J* = 8.6 Hz, 2H, H-1), 6.83 (d, *J* = 2.7 Hz, 2H, H-4), 6.79 (dd, *J* = 8.6 Hz, 2.8 Hz, 2H, H-2), 5.85 (s, 4H, NCH_2), 5.26 (s, 4H, OCH_2), 4.23 (s, 6H, NCH_3), 2.91 (m, 4H, H-6), 2.50 (dd, *J* = 18.8 Hz, 8.6 Hz, 2H), 2.37 (m, 2H), 2.24 (m, 2H), 2.06 (m, 10 H), 1.53 (m, 12H), 0.91 (s, 6H, H-18). ^{13}**C NMR** (125 MHz, $CDCl_3$) *δ* 220.8 (2C=O, C-17), 160.1 (2C, $N_3C{=}\mathit{C}Au$), 154.9 (2C, C-3), 142.8 (2C, $N_3\mathit{C}{=}CAu$), 138.4 (2C, C-5), 133.7 (2C, Ar), 131.9 (2C, C-10), 131.2 (2CH, Ar), 130.1 (2CH, Ar), 126.7 (2CH, C-1), 114.6 (2CH, C-4), 112.6 (2CH, C-2), 59.8 (2OCH_2), 56.1 (2NCH_2), 50.4 (2CH, C-14), 48.0 (2C, C-13), 44.0 (2CH, C-9), 38.2 (NCH_3), 38.0 (2CH, C-8), 35.8 (2CH_2, C-16), 31.5 (2CH_2, C-12), 29.6 (2CH_2, C-6), 26.4 (2CH_2, C-7), 25.9 (2CH_2, C-11), 21.6 (2CH_2, C-15), 13.8 (2CH_3, C-18). **IR (KBr)** $\boldsymbol{\nu}_{\mathbf{max}}$ 3436, 2926, 1736, 1611, 1496, 1453, 1230, 1163, 1056, 1026, 751. $[\alpha]_D^{25}$ + 62.9 (*c* 0.2, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{52}H_{60}Au_2Cl N_6O_4$: 1261.3690 $[M–Cl^-]^+$, found: 1261.3751 and for $C_{52}H_{60}Au_2N_6O_4$: 613.1998 $[M–2Cl^-]^{2+}$, found: 613.1979. **m.p.** decomposes before melting.

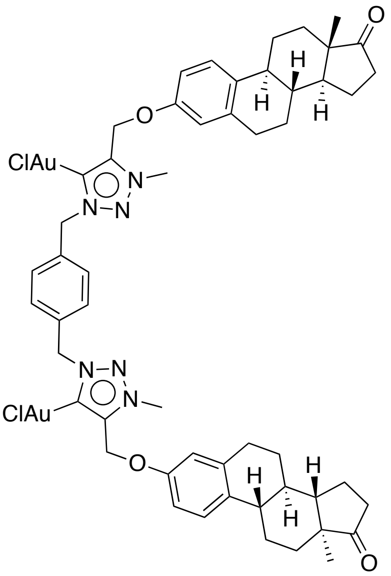
Synthesis of compound II.45b



Following the general procedure a mixture of **II.44b** (235 mg, 0.23 mmol, 1.00 equiv), NMe_4Cl (76 mg, 0.69 mmol, 3.00 equiv) and Ag_2O (81 mg, 0.35 mmol, 1.50 equiv) in $CH_3CN:CH_2Cl_2$ (50 mL) was stirred under Ar at rt for 3 days. [AuCl(SMe_2)] (135 mg, 0.46 mmol, 2.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, $CHCl_3$) to yield **II.45b** as a white solid (273 mg, 91%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 1H, Ar), 7.40 (m, 3H, Ar), 7.22 (d, J = 8.51 Hz, 2H, H-1), 6.87 (br s, 2H, H-4), 6.83 (br d, J = 2.8 Hz, H-2), 5.56 (s, 2H, NCH_2), 5.41 (s, 2H, OCH_2), 4.24 (s, 6H, NCH_3), 2.92 (m, 4H, H-6), 2.50 (dd, J = 18.9 Hz, 8.6 Hz, 2H), 2.38 (m, 2H), 2.09 (m, 10 H), 1.46 (m, 12H), 0.91 (s, 6H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 221.0 (2C=O, C-17), 159.9 (2C, $N_3C{=}\mathit{C}Au$), 155.3 (2C, C-3), 143.3 (2C, $N_3\mathit{C}{=}CAu$), 138.4 (2C, C-5), 134.9 (2C, Ar), 133.6 (2C, C-10), 129.7 (CH, Ar), 128.2 (2CH, Ar), 126.8 (2CH, C-1), 126.0 (CH, Ar), 114.9 (2CH, C-4), 112.7 (2CH, C-2), 60.0 ($2OCH_2$), 57.7 ($2NCH_2$), 50.5 (2CH, C-14), 48.1 (2C, C-13), 44.1 (2CH, C-9), 38.4 (NCH_3), 38.1 (2CH, C-8), 36.0 ($2CH_2$, C-16), 31.7 ($2CH_2$, C-12), 29.8 ($2CH_2$, C-6), 26.6 ($2CH_2$, C-7), 26.0 ($2CH_2$, C-11), 21.7 ($2CH_2$, C-15), 14.0 ($2CH_3$, C-18). **IR (KBr) ν_{max}** 3436, 2925, 1736, 1609, 1496, 1452, 1232, 1085, 753. **$[\alpha]_D^{25}$** + 37.1 (c 0.3, $CHCl_3$). **HRMS (ESI)** m/z calculated for $C_{52}H_{60}Au_2Cl$ N_6O_4: 1261.3690 $[M{-}Cl^-]^+$, found: 1261.3727. **m.p.** decomposes before melting.

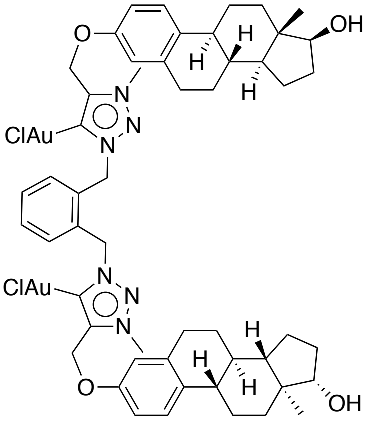
Synthesis of compound II.45c



Following the general procedure a mixture of **II.44c** (35 mg, 0.03 mmol, 1.00 equiv), NMe_4Cl (11 mg, 0.10 mmol, 3.00 equiv) and Ag_2O (12 mg, 0.05 mmol, 1.50 equiv) in $CH_3CN:CH_2Cl_2$ (8 mL) was stirred under Ar at rt for 3 days. [AuCl(SMe_2)] (20 mg, 0.07 mmol, 2.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, $CHCl_3$) to yield **II.45c** as a white solid (6 mg, 13%).

^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.54 (s, 4H, Ar), 7.22 (d, *J* = 8.6 Hz, 2H, H-1), 6.83 (d, *J* = 2.6 Hz, 2H, H-4), 6.79 (dd, *J* = 8.5 Hz, 2H, H-2), 5.59 (s, 4H, NCH_2), 5.21 (s, 4H, OCH_2), 4.21 (s, 6H, NCH_3), 2.92 (m, 4H, H-6), 2.15 (dd, *J* = 18.8 Hz, 8.6 Hz, 2H), 2.36 (m, 2H), 2.11 (m, 10H), 1.57 (m, 12H), 0.91 (s, 6H, H-18). **^{13}C NMR** (125 MHz, $CDCl_3$) *δ* 220.8 (2C=O, C-17), 159.4 (2C, $N_3C{=}\mathit{C}Au$), 154.8 (2C, C-3), 142.6 (2C, $N_3\mathit{C}{=}CAu$), 138.4 (2C, C-5), 134.4 (2C, Ar), 133.8 (2C, C-10), 129.6 (4CH, Ar), 126.8 (2CH, C-1), 114.5 (2CH, C-4), 112.5 (2CH, C-2), 59.6 ($2OCH_2$), 58.2 ($2NCH_2$), 50.4 (2CH, C-14), 48.0 (2C, C-13), 43.9 (2CH, C-9), 38.2 (NCH_3), 37.8 (2CH, C-8), 35.8 ($2CH_2$, C-16), 31.5 ($2CH_2$, C-12), 29.7 ($2CH_2$, C-6), 26.4 ($2CH_2$, C-7), 25.9 ($2CH_2$, C-11), 21.6 ($2CH_2$, C-15), 13.8 ($2CH_3$, C-18). **HRMS (ESI)** *m/z* calculated for $C_{52}H_{60}Au_2Cl\ N_6O_4$: 1261.3690 $[M–Cl^−]^+$, found: 1261.3747. **m.p.** decomposes before melting.

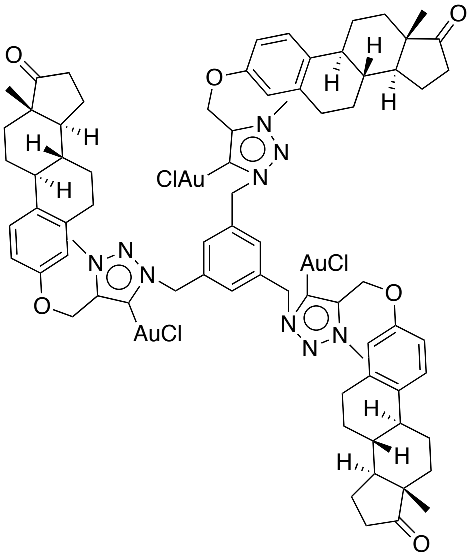
Synthesis of compound II.50



Following the general procedure a mixture of **II.49** (200 mg, 0.20 mmol, 1.00 equiv), NMe_4Cl (65 mg, 0.59 mmol, 3.00 equiv) and Ag_2O (69 mg, 0.30 mmol, 1.50 equiv) in $CH_3CN:CH_2Cl_2$ (44 mL) was stirred under Ar at rt for 3 days. $[AuCl(SMe_2)]$ (116 mg, 0.39 mmol, 2.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, $MeOH/CH_2Cl_2$ 2%) to yield **II.50** as a white solid (217 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.43 (br s, 4H, Ar), 7.20 (d, *J* = 8.9 Hz, 2H, H-1), 6.78 (br d, *J* = 8.6 Hz, 4H, H-2 and H-4), 5.85 (s, 4H, NCH_2), 5.24 (s, 4H, OCH_2), 4.22 (s, 6H, NCH_3), 3.73 (t, *J* = 8.4 Hz, 2H, H-17), 2.83 (m, 4H), 2.29 (br d, *J* = 12.3 Hz, 2H), 2.13 (m, 4H), 1.91 (m, 4H), 1.70 (m, 2H), 1.60 (br s, 2H), 1.34 (m, 12H), 0.77 (s, 6H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 160.1 (2C, $N_3C{=}C$Au), 154.9 (2C, C-3), 143.0 (2C, $N_3C{=}CH$), 138.7 (2C, C-5), 134.5 (2C, Ar), 132.1 (2C, C-10), 131.4 (2CH, Ar), 130.3 (2CH, Ar), 126.8 (2CH, C-1), (2CH, Ar), 114.8 (2CH, C-4), 112.4 (2CH, C-2), 82.0 (2CH, C-17), 59.9 ($2OCH_2$), 56.2 ($2NCH_2$), 50.2 (2CH, C-14), 44.1 (2CH, C-9), 43.4 (2C, C-13), 38.9 ($2NCH_3$), 38.2 (2CH, C-8), 36.8 ($2CH_2$, C-12), 30.7 ($2CH_2$, C-16), 29.9 ($2CH_2$, C-6), 27.3 ($2CH_2$, C-7), 26.4 ($2CH_2$, C-11), 23.3 ($2CH_2$, C-15), 11.2 ($2CH_3$, C-18). **IR (KBr) ν_{max}** 3454, 2923, 1607, 1496, 1454, 1250, 1232, 1156, 1053, 1022, 754. **$[\alpha]_D^{25}$** + 31.8 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{52}H_{64}Au_2ClN_6O_4$: 1265.4003 $[M{-}Cl^-]^+$, found: 1265.3973. **m.p.** decomposes before melting.

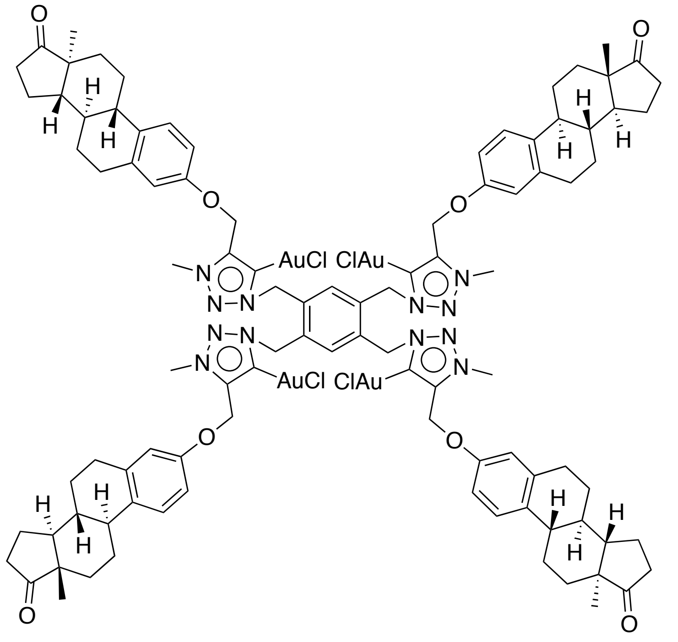
Synthesis of compound II.55



Following the general procedure a mixture of **II.53** (70 mg, 0.05 mmol, 1.00 equiv), NMe_4Cl (23 mg, 0.21 mmol, 4.50 equiv) and Ag_2O (25 mg, 0.11 mmol, 2.25 equiv) in $CH_3CN:CH_2Cl_2$ (48 mL) was stirred under Ar at rt for 3 days. [AuCl(SMe_2)] (42 mg, 0.14 mmol, 3.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, Hex/EtOAc, 1:9) to yield **II.55** as a white solid (27 mg, 30%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (s, 3H, Ar), 7.21 (d, J = 8.5 Hz, 3H, H-1), 6.82 (m, 6H, H-2 and H-4), 5.57 (s, 6H, NCH_2), 5.30 (s, 6H, OCH_2), 4.25 (s, 9H, NCH_3), 2.92 (m, 6H, H-6), 2.50 (dd, J = 18.9 Hz, 8.5 Hz, 3H), 2.37 (m, 3H), 2.09 (m, 15H), 1.53 (m, 18H), 0.90 (s, 9H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 221.0 (3C=O, C-17), 159.4 (3C, $N_3C=C$Au), 155.2 (3C, C-3), 143.2 (3C, N_3C=CAu), 138.4 (3C, C-5), 135.6 (3C, Ar), 133.7 (3C, C-10), 128.9 (3CH, Ar), 126.8 (3CH, C-1), 114.8 (3CH, C-4), 112.7 (3CH, C-2), 59.9 (3OCH_2), 57.7 (3NCH_2), 50.5 (3CH, C-14), 48.1 (3C, C-13), 44.1 (3CH, C-9), 38.4 (3NCH_3), 38.2 (3CH, C-8), 36.0 (3CH_2, C-16), 31.7 (3CH_2, C-12), 29.8 (3CH_2, C-6), 26.6 (3CH_2, C-7), 26.0 (3CH_2, C-11), 21.7 (3CH_2, C-15), 14.0 (3CH_3, C-18). **IR (KBr) ν_{max}** 3437, 2924, 1737, 1608, 1496, 1453, 1261, 1158, 1085, 1054, 1027, 804. **$[\alpha]_D^{25}$** + 51.1 (c 0.6, $CHCl_3$). **HRMS (ESI)** m/z calculated for $C_{75}H_{87}Au_3Cl_2N_9O_6$: 1870.5147 $[M-Cl^-]^+$, found: 1870.5140. **m.p.** decomposes before melting.

Synthesis of compound II.58

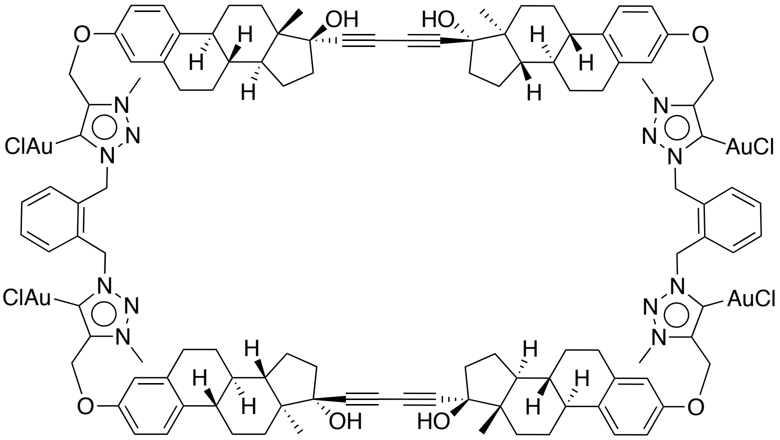


Following the general procedure a mixture of **II.59** (200 mg, 0.10 mmol, 1.00 equiv), NMe_4Cl (68 mg, 0.62 mmol, 6.00 equiv) and Ag_2O (72 mg, 0.31 mmol, 3.00 equiv) in CH_3CN:CH_2Cl_2 (23 mL) was stirred under Ar at rt for 3 days. [AuCl(SMe_2)] (183 mg, 0.62 mmol, 6.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, MeOH/CH_2Cl_2 0.5%) to yield **II.58** as a white solid (96 mg, 38%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 2H, Ar), 7.21 (d, *J* = 8.3 Hz, 4H, H-1), 6.82 (m, 8H, H-2 and H-4), 5.82 (s, 8H, NCH_2), 5.33 (s, 8H, OCH_2), 4.27 (s, 12H, NCH_3), 2.92 (m, 8H, H-6), 2.51 (dd, *J* = 18.8 Hz, 8.6 Hz, 4H), 2.38 (m, 4H), 2.09 (m, 20H), 1.53 (m, 24H), 0.90 (s, 12H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 220.9 (4C=O, C-17), 159.9 (4C, N_3C=*C*Au), 155.2 (4C, C-3), 143.5 (4C, N_3*C*=CAu), 138.5 (4C, C-5), 133.8 (4C, Ar), 133.5 (4C, C-10), 131.4 (2CH, Ar), 126.8 (4CH, C-1), 114.9 (4CH, C-4), 112.7 (4CH, C-2), 60.0 (4OCH_2), 54.4 (4NCH_2), 50.5 (4CH, C-14), 48.1 (4C, C-13), 44.1 (4CH, C-9), 38.4 (4NCH_3 and 4CH, C-8), 36.0 (4CH_2, C-16), 31.7 (4CH_2, C-12), 29.8 (4CH_2, C-6), 26.6 (4CH_2, C-7), 26.1 (4CH_2, C-11), 21.7 (4CH_2, C-15), 14.0 (4CH_3, C-18). **IR (KBr) ν_{max}** 3447, 2927, 1736, 1607, 1577, 1607, 1496, 1453, 1231, 1161, 1084, 1055, 1026, 1007, 842. **[α]$_D$** + 41.6 (*c*

0.3, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{98}H_{114}Au_4Cl_3N_{12}O_8$: 2481.6612 $[M{-}Cl^{-}]^+$, found: 2481.6749. **m.p.** decomposes before melting.

Synthesis of compound II.63



Following the general procedure a mixture of **II.60** (100 mg, 0.05 mmol, 1.00 equiv), NMe_4Cl (31 mg, 0.14 mmol, 6.00 equiv) and Ag_2O (33 mg, 0.14 mmol, 3.00 equiv) in CH_3CN:CH_2Cl_2 (11 mL) was stirred under Ar at rt for 3 days. [AuCl(SMe_2)] (55 mg, 0.19 mmol, 4.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, MeOH/CH_2Cl_2 0.5%) to yield **II.63** as a white solid (63 mg, 50%).

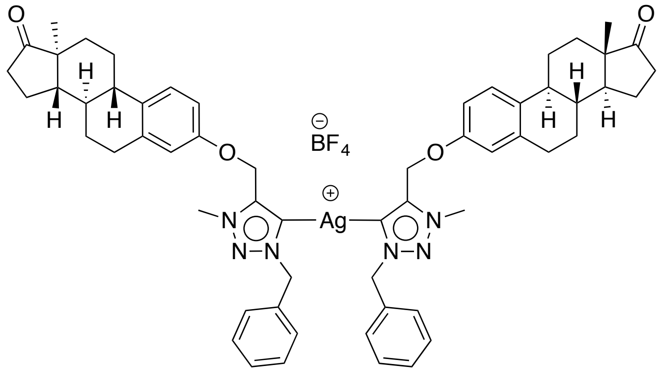
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 8H, Ar), 7.10 (d, *J* = 8.6 Hz, 4H, H-1), 6.80 (dd, *J* = 8.6 Hz, 2.8 Hz, 4H, H-2), 6.75 (d, *J* = 2.8 Hz, 4H, H-4), 5.82 (s, 8H, NCH_2), 5.26 (d, *J* = 14.3 Hz, 4H, OCH_2), 5.22 (d, *J* = 14.3 Hz, 4H, OCH_2), 4.23 (s, 12H, NCH_3), 2.82 (m, 8H), 2.33 (m, 8H), 2.14 (m, 4H), 2.02 (m, 8H), 1.83 (m, 16H), 1.53 (m, 20H), 0.80 (s, 12H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.6 (4C, $N_3C{=}C$Au), 153.1 (4C, C-3), 142.8 (4C, $N_3C{=}C$Au), 138.5 (4C, C-5), 134.3 (4C, Ar), 132.4 (4C, C-10), 131.1 (4CH, Ar), 130.2 (4CH, Ar), 126.7 (4CH, C-1), 116.3 (4CH, C-4), 113.2 (4CH, C-2), 83.7 (4C, $C{\equiv}C$), 80.7 (C-17), 70.3 (4C, $C{\equiv}C$), 59.1 ($4OCH_2$), 55.7 ($4NCH_2$), 50.1 (4CH, C-14), 48.2 (4C, C-13), 43.9 (4CH, C-9), 39.2 (4CH, C-8), 38.9 ($4CH_2$, C-16), 37.9 ($4NCH_3$), 33.2 ($4CH_2$, C-12), 29.9 ($4CH_2$, C-6), 27.3 ($4CH_2$, C-7), 26.3 ($4CH_2$, C-11), 22.9 ($4CH_2$, C-15), 12.9 ($4CH_3$, C-18). **IR**

(KBr) ν_{max} 3435, 2929, 1610, 1455, 1378, 1250, 1140, 1109, 1088, 1047, 842. **HRMS (ESI)** *m/z* calculated for $C_{112}H_{124}Au_4Cl_3N_{12}O_8$: 2657.7387 $[M–Cl^-]^+$, found: 2657.7465. **m.p.** decomposes before melting.

General procedure for the synthesis of silver carbenes

In a Schlenk tube charged with 4 Å molecular sieves a mixture of triazolium salt (1.00 equiv), NMe_4Cl (1.50 equiv per triazole) and Ag_2O (0.75 equiv per triazole) was stirred at rt in the dark in CH_3CN:CH_2Cl_2 (1:1) until the reaction was completed (^1H NMR analysis). The reaction was filtered through a pad of Celite and the solvent was removed under vacuum to afford the corresponding reaction products.

Synthesis of compound II.40



Following the general procedure a mixture of **II.39** (270 mg, 0.50 mmol, 1.00 equiv), NMe_4Cl (82 mg, 0.75 mmol, 1.50 equiv) and Ag_2O (86 mg, 0.37 mmol, 0.75 equiv) in CH_3CN:CH_2Cl_2 (26 mL) was stirred under Ar at rt for 24 h. The reaction was filtered through a pad of Celite and the solvent was removed under vacuum to yield **II.40** as a white solid (272 mg, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 10H, Ar), 7.18 (d, *J* = 8.4 Hz, 2H, H-1), 6.75 (dd, *J* = 8.4 Hz, *J* = 2.9 Hz, 2H, H-2), 6.72 (d, *J* = 8.9 Hz, 2H, H-4), 5.54 (s, 4H, NCH_2), 5.15

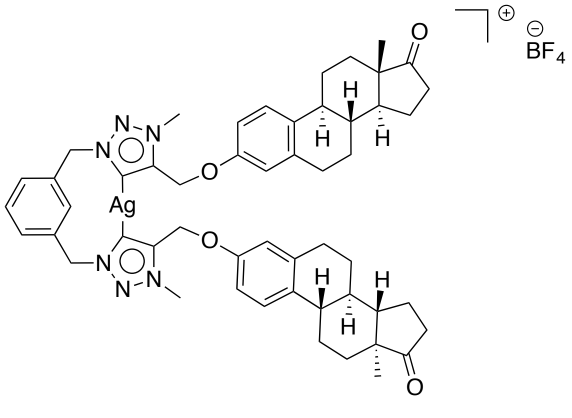
(s, 4H, OCH_2), 4.18 (s, 6H, NCH_3), 2.87 (m, 4H), 2.49 (dd, J = 18.8 Hz, J = 8.4 Hz, 2H), 2.36 (m, 2H), 2.06 (m, 12H), 1.50 (m, 10H), 0.88 (s, 6H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 220.9 (2C=O, C-17), 166.5 (2C, $N_3C{=}C$Ag), 155.2 (2C, C-3), 144.1 (2C, $N_3C{=}C$Ag), 138.4 (2C, C-5), 134.0 (2C, Ar), 133.7 (2C, C-10), 129.2 (5CH, Ar), 128.7 (5CH, Ar), 126.8 (2CH, C-1), 114.8 (2CH, C-4), 112.5 (2CH, C-2), 60.6 ($2OCH_2$), 59.6 ($2NCH_2$), 50.4 (2CH, C-14), 48.0 (2C, C-13), 44.0 (2CH, C-9), 38.3 (2CH, C-8), 37.2 ($2NCH_3$), 35.9 ($2CH_2$, C-16), 31.6 ($2CH_2$, C-12), 29.7 ($2CH_2$, C-6), 26.5 ($2CH_2$, C-7), 25.9 ($2CH_2$, C-11), 21.6 ($2CH_2$, C-15), 13.9 ($2CH_3$, C-18). **IR (KBr) $\nu_{máx}$** 3437, 2927, 1736, 1607, 1497, 1455, 1232, 1055, 819, 721. **$[\alpha]_D^{25}$** + 67.2 (c 0.8, $CHCl_3$). **HRMS (ESI)** m/z calculated for $C_{58}H_{66}AgN_6O_4$: 1019.4200 $[M{-}BF_4^{-}]^{+}$, found: 1019.4216. **m.p.** decomposes before melting.

Synthesis of compound II.51a

Following the general procedure a mixture of **II.44a** (163 mg, 0.16 mmol, 1.00 equiv), NMe_4Cl (53 mg, 0.49 mmol, 3.00 equiv) and Ag_2O (56 mg, 0.24 mmol, 1.50 equiv) in $CH_3CN:CH_2Cl_2$ (17 mL) was stirred under Ar at rt for 3 days. The reaction was filtered through a pad of Celite and the solvent was removed under vacuum to yield **II.51a** as a white solid (76 mg, 46%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (s, 8H, Ar), 7.21 (d, J = 8.1 Hz, 4H, H-1), 6.66 (m, 8H, H-2 and H-4), 5.77 (s, 8H, NCH_2), 5.21 (s, 8H, OCH_2), 4.22 (s, 12H, NCH_3), 2.90 (m, 8H, H-6), 2.51 (dd, J = 18.3 Hz, 8.4 Hz, 4H), 2.36 (m, 4H), 2.11 (m, 20H), 1.55 (m, 24H), 0.91 (s, 12H, H-18). The compound was unstable and correct MS data could not be registered.

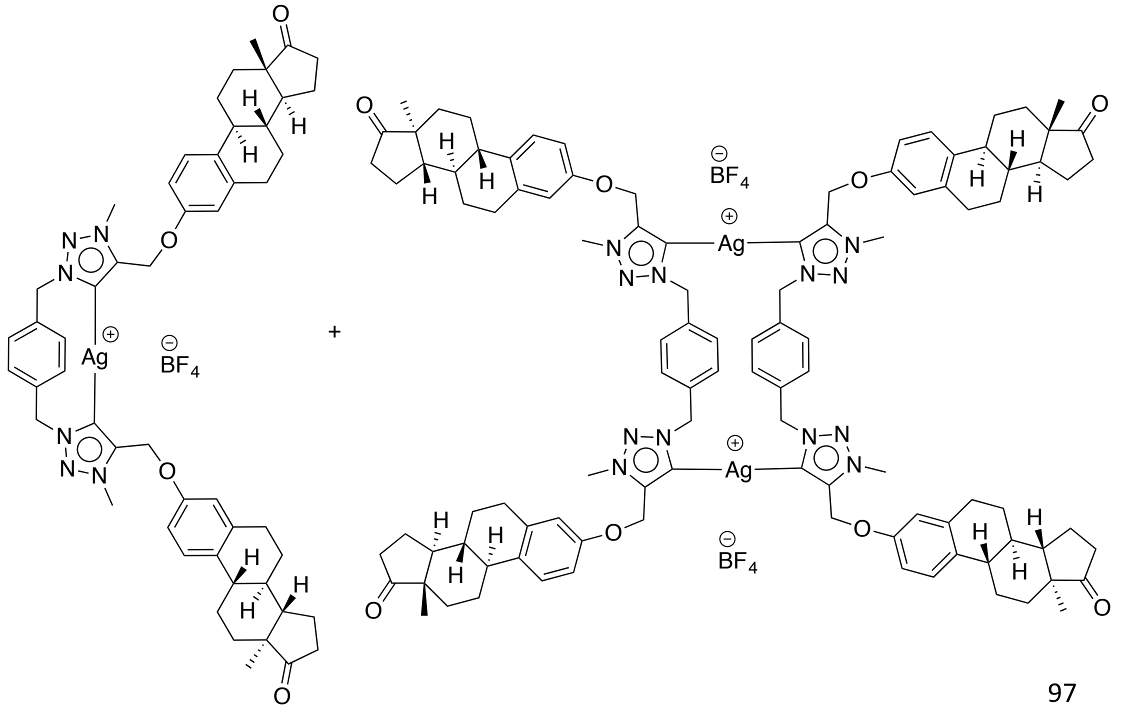
Synthesis of compound II.51b



Following the general procedure a mixture of **II.44b** (250 mg, 0.25 mmol, 1.00 equiv), NMe_4Cl (81 mg, 0.74 mmol, 3.00 equiv) and Ag_2O (86 mg, 0.15 mmol, 1.50 equiv) in CH_3CN:CH_2Cl_2 (55 mL) was stirred under Ar at rt for 3 days. The reaction was filtered through a pad of Celite and the solvent was removed under vacuum to yield **II.51b** as a white solid (163 mg, 63%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (s, 2H, Ar), 7.44 (m, 6H, Ar), 7.20 (d, J = 8.6 Hz, 4H, H-1), 6.77 (m, 8H, H-2 and H-4), 5.54 (s, 8H, NCH_2), 5.28 (s, 8H, OCH_2), 4.22 (s, 12H, NCH_3), 2.87 (m, 8H, H-6), 2.51 (dd, J = 18.4 Hz, 8.2 Hz, 4H), 2.38 (m, 4H), 2.09 (m, 20H), 1.52 (m, 24H), 0.90 (s, 12H, H-18). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 219.7 (4C=O, C-17), 165.1 (4C, $N_3C=C$Ag) 155.3 (4C, C-3), 144.1 (4C, N_3C=CAg), 137.6 (4C, C-5), 135.6 (4C, Ar), 132.8 (4C, C-10), 129.6 (2CH, Ar), 128.6 (6CH, Ar), 126.3 (4CH, C-1), 114.8 (4CH, C-4), 112.6 (4CH, C-2), 60.2 ($4OCH_2$), 57.7 ($4NCH_2$), 49.6 (4CH, C-14), 47.3 (4C, C-13), 43.4 (4CH, C-9), 37.8 ($4NCH_3$), 37.0 (4CH, C-8), 35.4 ($4CH_2$, C-16), 31.4 ($4CH_2$, C-12), 29.2 ($4CH_2$, C-6), 26.0 ($4CH_2$, C-7), 25.5 ($4CH_2$, C-11), 21.2 ($4CH_2$, C-15), 13.5 ($4CH_3$, C-18). **IR (KBr) $\nu_{máx}$** 3445, 2927, 1736, 1607, 1497, 1453, 1311, 1232, 1158, 1055, 818. **$[\alpha]^{25}_{D}$** + 53.2 (c 0.8, $CHCl_3$). **HRMS (ESI)** m/z calculated for $C_{52}H_{60}AgN_6O_4$: 939.3729 $[M-BF_4^-]^+$, found: 941.3720. **m.p.** decomposes before melting.

Synthesis of compounds II.51c and II.51c'



Following the general procedure a mixture of **II.44c** (250 mg, 0.25 mmol, 1.00 equiv), NMe_4Cl (82 mg, 0.75 mmol, 3.00 equiv) and Ag_2O (86 mg, 0.15 mmol, 1.50 equiv) in $CH_3CN:CH_2Cl_2$ (55 mL) was stirred under Ar at rt for 3 days. The reaction was filtered through a pad of Celite and the solvent was removed under vacuum to yield **II.51c** and **II.51c'** as a white solid (243 mg, 95%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.44 (s, 8H, Ar), 7.21 (d, *J* = 8.4 Hz, 4H, H-1), 6.75 (m, 8H, H-2 and H-4), 5.53 (s, 8H, NCH_2), 5.17 (s, 8H, OCH_2), 4.20 (s, 12H, NCH_3), 2.90 (m, 8H, H-6), 2.50 (dd, *J* = 18.7 Hz, 8.6 Hz, 4H), 2.37 (m, 4H), 2.09 (m, 20H), 1.52 (m, 24H), 0.90 (s, 12H, H-18). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 221.0 (4C=O, C-17), 165.9 (4C, $N_3C{=}\mathit{C}Ag$), 155.3 (4C, C-3), 144.3 (4C, $N_3\mathit{C}{=}CAg$), 138.5 (4C, C-5), 135.1 (4C, C-Ar), 133.9 (4C, C-10), 129.9 (8CH, Ar), 126.9 (4CH, C-1), 114.7 (4CH, C-4), 112.6 (4CH, C-2), 60.8 ($4OCH_2$), 59.0 ($4NCH_2$), 50.5 (4CH, C-14), 48.1 (4C, C-13), 44.1 (4CH, C-9), 38.4 ($4NCH_3$), 37.4 (4CH, C-8), 36.0 ($4CH_2$, C-16), 31.7 ($4CH_2$, C-12), 29.8 ($4CH_2$, C-6), 26.6 ($4CH_2$, C-7), 26.0 ($4CH_2$, C-11), 21.7 ($4CH_2$, C-15), 14.0 ($4CH_3$, C-18). **IR (KBr) *ν*$_{\mathbf{máx}}$** 3436, 2928, 1736, 1609, 1492, 1232, 1084, 1054, 949, 759. **HRMS (ESI)** *m*/*z* calculated for $C_{104}H_{120}Ag_2BF_4N_{12}O_8$: 1965.7493 $[M{-}BF_4^-]^+$, found: 1965.7491. **m.p.** decomposes before melting.

General procedure for catalytic studies

Gold carbene (0.002 mmol, 0.01 equiv) and $AgSbF_6$ (0.002 mmol, 0.01 equiv) were dissolved in 1 mL of the $CDCl_3$ under Ar and stirred for 15 min at rt. Alcohol (1.80 mmol, 10 equiv) was added followed by ethylphenyldiazoacetate (0.18 mmol, 1.00 equiv) dissolved in 1 mL of $CDCl_3$. The reaction mixture was stirred at rt.

Computational details

All calculations were carried at the DFT level using the M06 functional[105] with an ultrafine grid[106] as implemented in Gaussian09.[107] This functional accounts for dispersion interactions and performs with good accuracy in transition-metal chemistry.[108] The geometries of compounds **II.51b**, **II.51b'** and **II.41a** were optimized using basis set I (BS-I). With BS-I, the non metal atoms were described with the 6-31G(d,p) basis set,[109] whereas Ag and Au were described with the SDD double-ζ basis set,[110] complemented with a set of f-polarization functions.[111]

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[105] Y. Zhao, D. G. Truhlar, *Theor. Chem. Acc.* **2008**, *120*, 215.

[106] S. E.Wheeler, K. N. Houk, *J. Chem. Theory Comput.* **2010**, *6*, 395.

[107] M. J. Frisch *et al.* Gaussian 09, Revision A.1; Gaussian, Inc., Wallingford, CT, 2009.

[108] a) Y. Zhao, D. G. Truhlar, *Acc. Chem. Res.* **2008**, *41*, 157. b) Y. Zhao, D. G. Truhlar, *Chem. Phys. Lett.* **2011**, *502*, 1.

[109] a) W. J. Hehre, R. Ditchfield, J. A. Pople, *J. Chem. Phys.* **1972**, *56*, 2257. b) M. M. Francl, W. J. Pietro, W. J. Hehre, J. S. Binkley, M. S. Gordon, D. J. DeFrees, J. A. Pople, *J. Chem. Phys.* **1982**, *77*, 3654.

[110] D. Andrae, U. Häußermann, M. Dolg, H. Stoll, H. Preuß, *Theor. Chim. Acta* **1990**, *77*, 123.

[111] A. W. Ehlers, M. Böhme, S. Dapprich, A. Gobbi, A. Höllwarth, V. Jonas, K. F. Köhler, R. Stegmann, A.Veldkamp, G. Frenking, *Chem. Phys. Lett.* **1993**, *208*, 111.

CHAPTER III

Synthesis of metallic mesoionic complexes bearing chiral sulfoxides

III.1 INTRODUCTION

III.1.1 NHCs and chelating ligands

As discussed before, efforts in NHC chemistry are focused on modulating the donor properties of the carbenic centre to find new applications of these compounds in different fields. Modulation could be achieved by increasing the size of the ring or by placing the heteroatoms in positions remote to the carbenic centre. Moreover, positioning functional groups close to the heterocyclic ring could result in carbene ligands having new features and properties. Among others, hybrid ligands composed by classic NHCs and functional groups based on sulphur have been widely investigated.[112] In particular, functionalized transition metal carbene complexes having alylthio or arylthio substitutents have demonstrated good catalytic activity because the coordination of the sulphur to the metal centre is weaker compared to the coordination displayed by NHCs. Thus, coordination with NHCs ligands would stabilise the metal centre, while the tioether may generate the vacant coordination site required for the catalytic process.

The introduction of these hemilabile functional groups based on sulphur is easy to accomplish in the case of 1,2,3-triazolylidene because of the high versatility of the CuAAC process where the new groups could be introduced either through the azide, the alkyne or both.

Recently, Mendoza-Espinosa and colleagues reported the synthesis of a new family of 1,2,3-triazolylidenes *O*- and *S*- functionalized in the *C*4 position of the triazole

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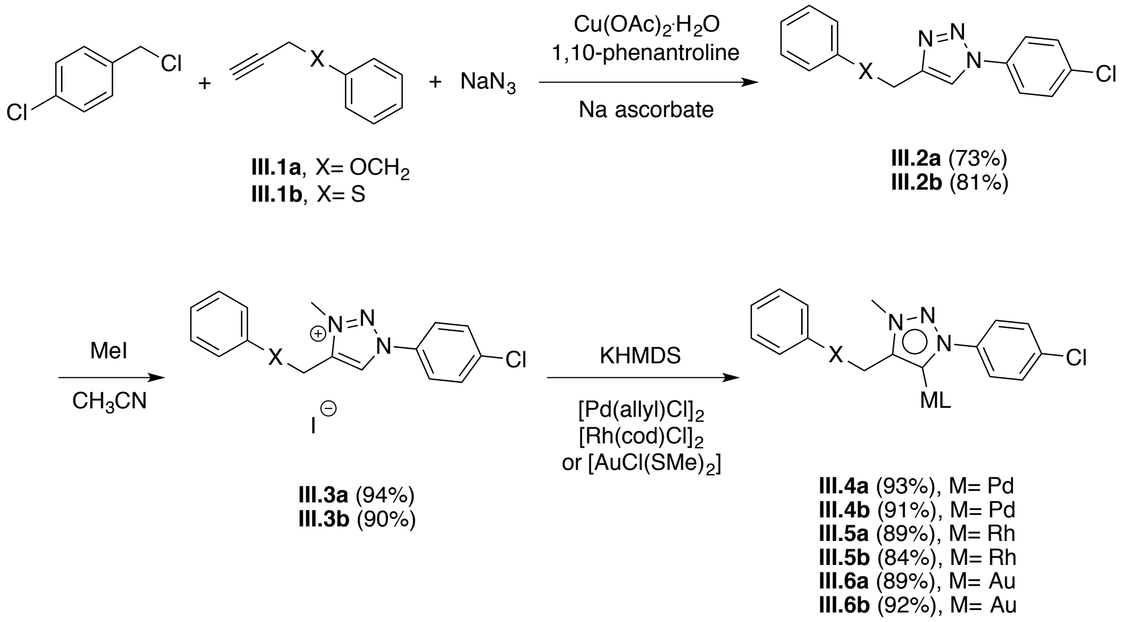
[112] C. Fliedel, P. Braunstein, *J. Organomet. Chem.* **2014**, *751*, 286.

core.[113] Reaction of benzyloxy and thiophenoxy alkynes **III.1a**–**b** with 4-chlorobenzyl chloride, in the presence of sodium azide afforded the respective 1,2,3-triazoles **III.2a**–**b**.[114] Subsequent methylation with methyl iodide as alkylating agent, gave the triazolium salts **III.3a**–**b**. These compounds were deprotonated with KHMDS at –78 °C. The free carbene could not be isolated because it decomposed very fast. However, *in situ* transmetallation with [Pd(allyl)Cl]$_2$, [Rh(cod)Cl]$_2$ or [AuCl(SMe$_2$)] gave the corresponding complexes **III.4**–**6** in high yields (Scheme III.1).



Scheme III.1: Synthesis of monometallic 1,2,3-triazolylidene complexes

Following the same synthetic approach, these authors prepared multinuclear Pd(II), Rh(II) and Au(I) complexes bearing an oxy group in β-position to the *C*4 of the triazole (Scheme II.2).[115] Thus, deprotonation of the bi- and tricationic salts **III.7** and **III.8** with KHMDS, followed by metallation with the corresponding metallic sources

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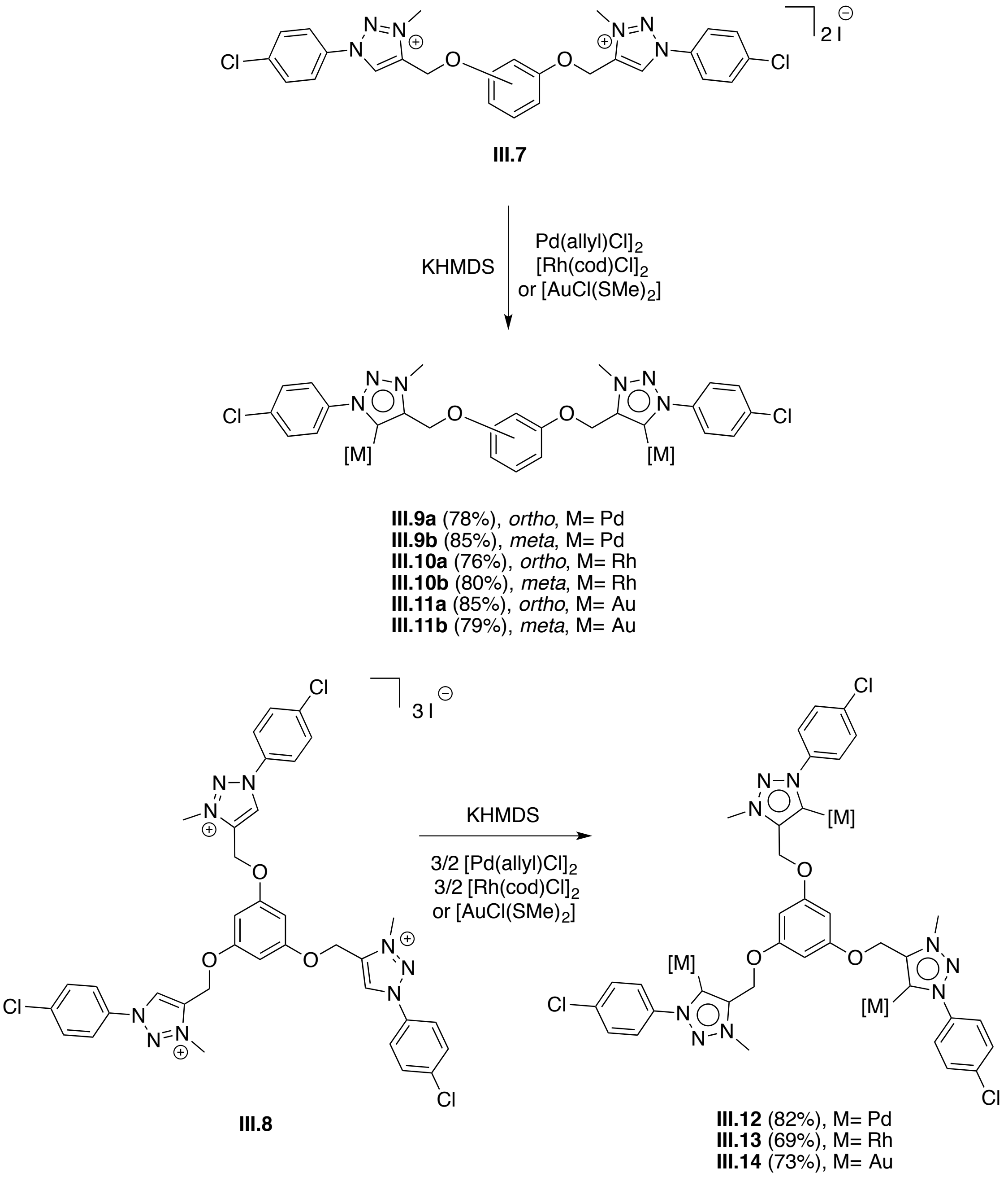
[113] a) D. Mendoza-Espinosa, R. González-Olvera, C. Osornio, G. E. Negrón-Silva, R. Santillan, *New J. Chem.* **2015**, *39*, 1587; b) D. Mendoza-Espinosa, R. González-Olvera, C. Osornio, G. E. Negrón-Silva, A. Álvarez-Hernández, C. I. Bautista-Hernández, O. R. Suárez-Castillo, *J. Organomet. Chem.* **2016**, *803*, 142.

[114] D. Mendoza-Espinosa, G. Negrón-Silva, L. Lomas-Romero, A. Gutiérrez-Carrillo, R. Santillán, *Synth. Commun.* **2014**, *44*, 807.

[115] D. Mendoza-Espinosa, R. González-Olvera, G. E. Negrón-Silva, D. Angeles-Beltrán, O. R. Suárez-Castillo, A. Álvarez-Hernández, R. Santillan, *Organometallics* **2015**, *34*, 4529.

yielded the desired complexes **III.9–14**. Unfortunately, coordination of the S or the O to the metal centre was not observed in any of the examples reported.



III.7

III.9a (78%), *ortho*, M= Pd
III.9b (85%), *meta*, M= Pd
III.10a (76%), *ortho*, M= Rh
III.10b (80%), *meta*, M= Rh
III.11a (85%), *ortho*, M= Au
III.11b (79%), *meta*, M= Au

III.8

III.12 (82%), M= Pd
III.13 (69%), M= Rh
III.14 (73%), M= Au

Scheme III.2: Synthesis of bi- and trimetallic carbenes

The first example of a heteroleptic ligand formed by a thioether and 1,2,3-triazolylidenes was recently reported.[116] Sarkar synthesized a series of Ru(II), Os(II) and Ir(III) complexes with 1,2,3-triazole and triazolylidene ligands bearing a thioether

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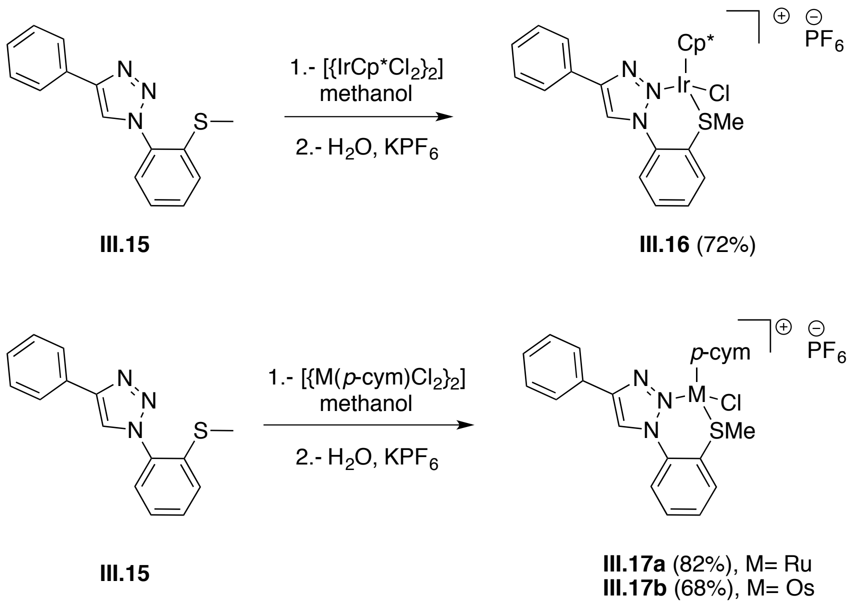
[116] S. Hohloch, L. Hettmanczyck, B. Sarkar, *Eur. J. Inorg. Chem.* **2014**, 3164.

functionality (Scheme III.3). Reaction of the bis-chelating 1,2,3-triazole ligand **III.15** with the dimeric metal salts [{$RuCl_2$(*p*-cymene)}$_2$], [{Os(*p*-cymene)Cl_2}$_2$] and [{$IrCp^*Cl_2$}$_2$], yielded the corresponding complexes **III.16** and **III.17a**–**b**. The structure of **III.16** was confirmed by X-ray diffraction. It revealed that chelating atoms of the ligand were the less basic *N*2 atoms and the S atoms of the thioether function.

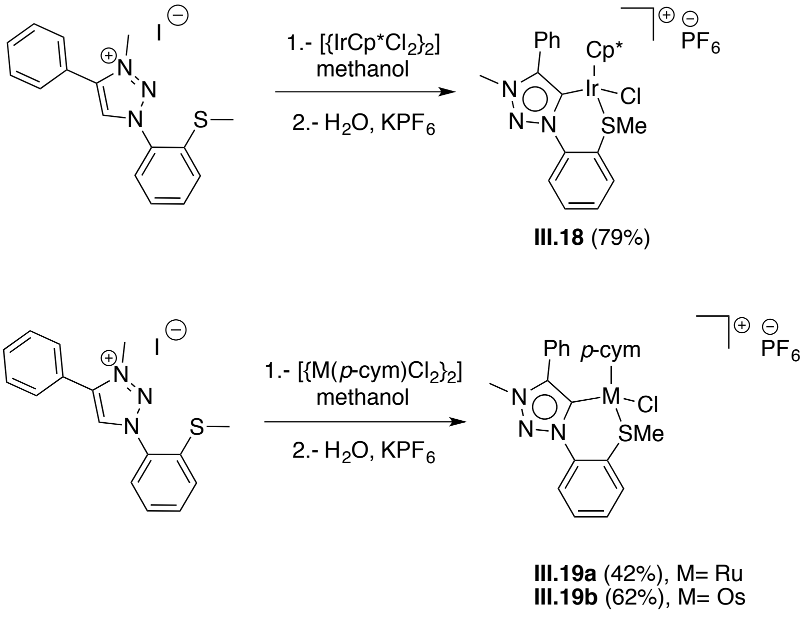


III.15 **III.16** (72%)

III.15 **III.17a** (82%), M= Ru
III.17b (68%), M= Os

Scheme III.3: Synthesis of metallic complexes bearing 1,2,3-triazole as ligands

These authors also achieved the formation of the analogous metal complexes with 1,2,3-triazolylidenes **III.18**–**19** (Scheme III.4).

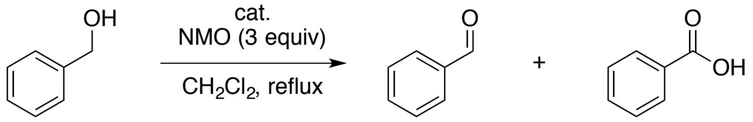


III.18 (79%)

III.19a (42%), M= Ru
III.19b (62%), M= Os

Scheme III.4: Synthesis of metallic complexes bearing 1,2,3-triazolylidene as ligands

Complexes **III.16–19** were tested as catalysts in the oxidation reaction of benzyl alcohol with NMO as sacrificial oxidant. It is remarkable that complexes with 1,2,3-triazole as ligands always show better catalytic activity than their triazolylidenes counterparts (Scheme III.5).



Scheme III.5: Oxidation of benzylic alcohol performed by complexes **III.16–19**

III.1.2 Sulfoxides

Sulfoxide groups are an interesting subclass of sulphur-based ligands.[117] They are among the scarce examples of chiral auxiliaries different from carbon-based groups that can participate in a varied number of asymmetric reactions. These compounds present high configurational stability since the interaction between the S–O bond and other electronegative groups in vicinal positions helps to fix the conformation. In addition, important differences regarding steric and stereoelectronic factors between the different substituents on the sulphur atom can also take part of this type of molecules.

Enantiopure sulfoxides are easily available through different methodologies. There are two main approaches for the synthesis of chiral sulfoxides. The first strategy was reported by Andersen.[118] It consists in the addition of an organometallic reagent to an enantiomerically pure sulfinate ester, which contains a menthyl group as homochiral auxiliary group. This reaction occurs with inversion configuration at the sulphur atom (Scheme III.6).

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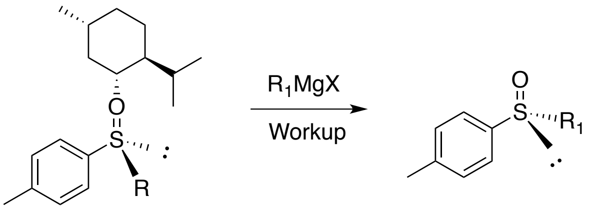
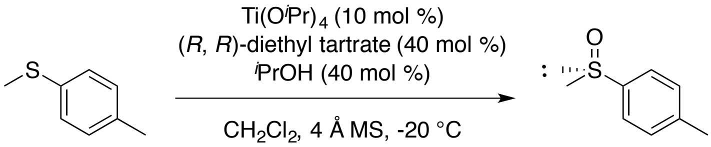
[117] a) M. C. Carreño, G. Hernández-Torres, M. Ribagorda, A. Urbano, *Chem. Commun.* **2009**, 6129; b) B. M. Trost, M. Rao, *Angew. Chem. Int. Ed.* **2015**, *54*, 5026.

[118] K. K. Andersen, *Tetrahedron Lett.* **1962**, *3*, 93.



Scheme III.6: Andersen method for the synthesis of chiral sulfoxides

The alternative methodology consists of the enantioselective oxidation of sulphides to sulfoxides. At the beginning, this process was achieved using chiral oxidants. Nevertheless, to avoid the waste of stoichiometric amount of chiral material, many groups have performed this oxidation using transition metals as catalysts (Scheme III.7).[119] Although this methodology presents some advantages over the Andersen method, the number of substrates compatible with the conditions used is still very narrow.



Scheme III.7: Enantioselective oxidation of sulphides

III.1.3 NHCs containing sulfoxides: A new class of chelating ligands

The number of examples of NHC ligands having sulfoxide groups in their structure is still very limited. To the best of our knowledge, only two examples have been reported to date. The first example of metal-NHC complexes with a sulfoxide was prepared in the group of Huyhn.[120] In this case, they described the synthesis of a CSC type of pincer complex with a sulfoxide moiety acting as a bridge of two dibenzimidazolium salts. The synthetic approach to this novel ligand was achieved by reacting benzimidazole with neat dibromoethane at 85 °C to yield 1-benzyl-3-bromoethylbenzimidazolium bromide **III.20**. Subsequent nucleophilic substitution with

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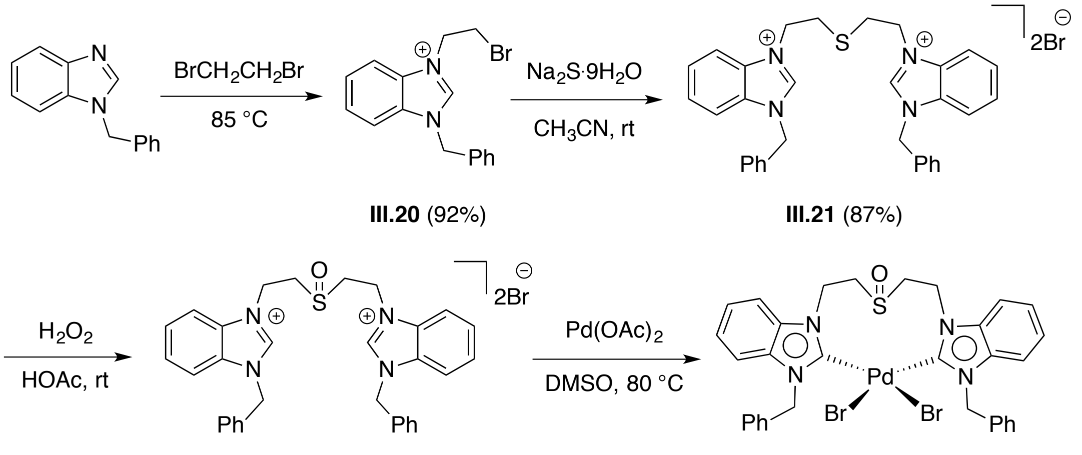
[119] a) F. Di Furia, G. Modena, R. Seraglia, *Synthesis* **1984**, 325; b) J. M. Brunel, H. B. Kagan, *Synlett* **1996**, 404. c) H. Srour, P. Le Maux, S. Chevance, G. Simonneaux, *Coord. Chem. Rev.* **2013**, *257*, 3030.

[120] H. V. Huynh, D. Yuan, Y. Han, *Dalton Trans.* **2009**, 7262.

Na_2S formed the thioether-bridged dibenzimidazolium salt **III.21**. The sulphide group was oxidized to the sulfoxide **III.22** using H_2O_2 and acetic acid. Reaction with $Pd(OAc)_2$ in DMSO at 80 °C overnight afforded the pincer complex **III.23** in 51% yield. X-ray diffraction of the compound featured a square planar geometry of the metal with a *cis*-chelating dicarbene with two bromide ligands filling the remaining coordination sites. It should be noted that the sulfoxide group pointed away from the coordination side (Scheme III.8).

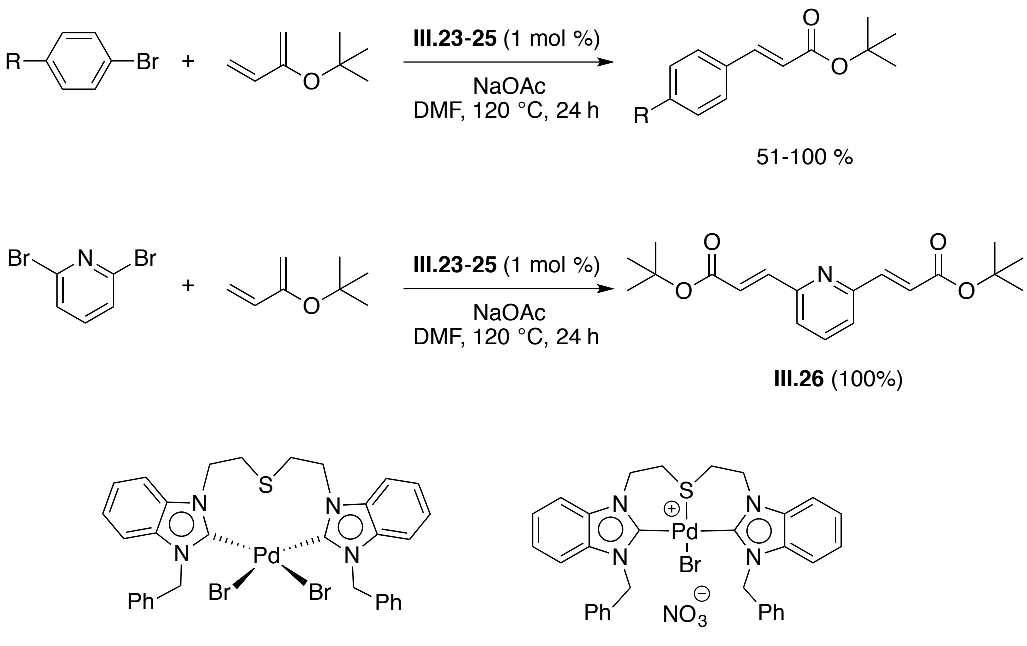


III.20 (92%) **III.21** (87%)

III.22 (91%) **III.23** (51%)

Scheme III.8: Synthesis of pseudo pincer complex **III.23**

This complex together with analogous complexes **III.24** and **III.25** were tested in the Heck reaction of aryl halides and *tert*-butyl acrylate (Scheme III.9).



51-100 %

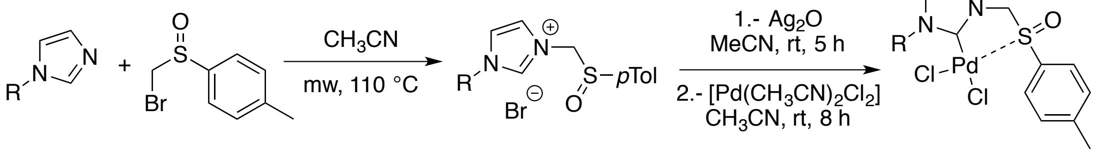
III.26 (100%)

III.24 **III.25**

Scheme III.9: Heck reaction catalysed by palladium complexes **III.23**-**25**

Quantitative yields were obtained with the three in the reactions with 4-bromo-1-nitrobenzene, 4-bromobenzaldehyde, 4-bromoacetonitrile, 4-benzoacetophenone. The doubly-coupled product **III.26** was also obtained when 2,6-bromopyridine was employed as substrate.

Cárdenas reported the synthesis of palladium imidazolylidenes bearing a sulfoxide in *N*3.[121] These complexes were obtained through a nucleophilic substitution of a series of imidazoles with bromomethyl sulfoxide. The corresponding palladium carbenes were obtained using the Ag-transmetallation protocol. Reaction of imidazolium salts **III.27a**–**d** with Ag_2O in CH_3CN and subsequent addition of a palladium salt formed the metal complexes **III.28a**–**d** in good yields (Scheme III.10).



III.27a (76%), R= Mes
III.27b (78%), R= Dipp
III.27c (65%), R= Me
III.27d (79%), R= ^{t}Bu

III.28a (91%)
III.28b (82%)
III.28c (95%)
III.28d (72%)

Scheme III.10: Synthesis of palladium sulfinyl imidazolylidenes

In the case of **III.28a**, the structure was unambiguously confirmed by X-ray diffraction studies. It presented a square-planar geometry with nearly no distortion. The sulfinyl group was orientated in an axial position with respect to the palladium centre. The distance between Pd and S atoms was 3.34(2)Å, which is lower than the sum of the van der Waals radii, suggesting a weak interaction between both centres.

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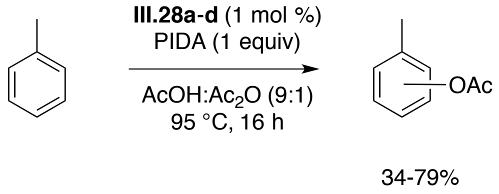
[121] F. Tato, A. García-Domínguez, D. J. Cárdenas, *Organometallics* **2013**, *32*, 7487.

All the complexes were used as catalysts in the acetoxylation reaction of toluene. After catalytic optimizations, they reached a respectable 79% yield when reaction was performed by **III.28d** with a catalytic load of 1 mol % in a mixture of AcOH:Ac_2O 9:1 at 95 °C for 16 h and PIDA acting as oxidant.



Scheme III.11: Pd-NHCs **III.28a**-**d** catalysed acetoxylation of toluene

III.2 OBJECTIVES

The results above show that NHC ligands bearing sulfoxide groups in their structures are built on a preformed imidazolylidene scaffold and the sulfoxide functionalities are always racemic. It is worthy to note that no examples of M-MIC complexes having a chiral sulfoxide were known at the beginning of this work. Based on these premises, the objectives of this chapter are:

- Synthesis and characterisation of a new type of ligands having the 1,2,3-triazole nucleus and enantiomerically pure sulfinyl moieties directly bonded to the *C*4 of the heterocyclic ring. This step will be achieved by the reaction of enantiomerically pure ethynyl sulfoxides with different azides under the catalytic conditions of the CuAAC.

- Formation of 1,2,3-triazolium salts by selective alkylation of the *N*3 of the heterocycle using methylating reagents.

- Synthesis and characterisation of new families of enantiomerically pure MIC complexes (M= Au, Ag, Pd, Cu, Ru) by the successive deprotonation of the triazolium salts with Ag_2O and subsequent transmetallation. The target is to develop a methodology suitable to achieve structural diversity by changing the nature of the different actors that can play a role in this approach (Scheme III.12). We focus on:

a) The change on the nature of the ethynyl sulfoxide (*rute a*).

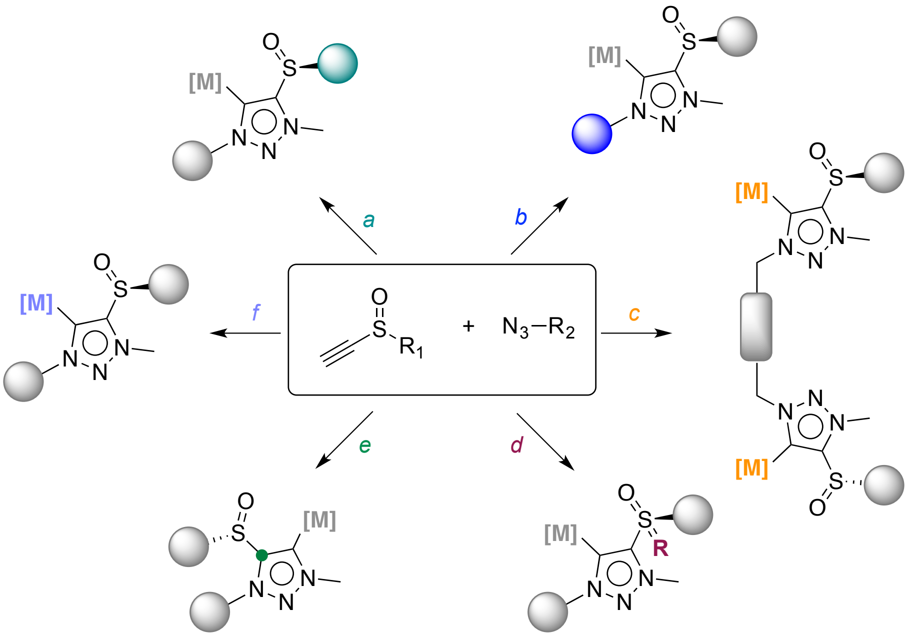
b) Change on the azide (*rute b*).

c) Nuclearity (*rute c*).

d) Post-modification of the sulfoxide moiety (*rute d*).

e) Change on the catalytic system nature in the CuAAC reaction (*rute e*).

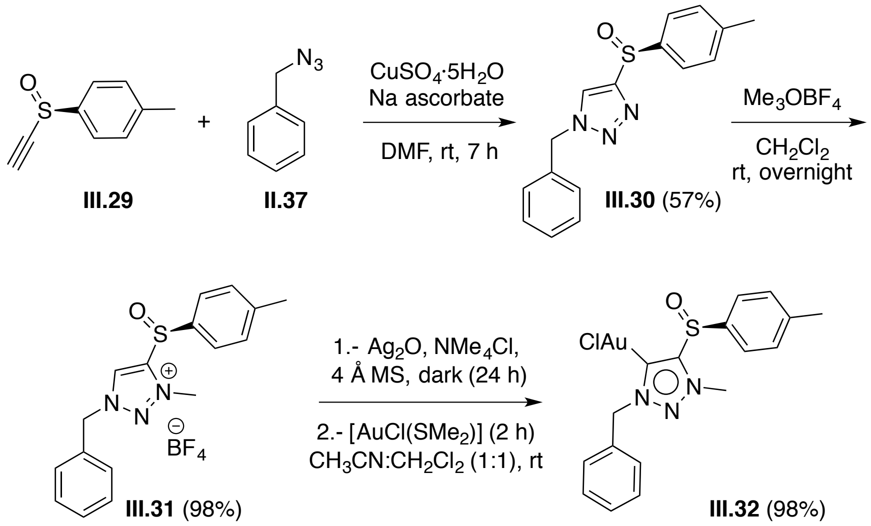
f) Change on the metal source (*rute f*).



Scheme III.12: Structural diversity afforded by the use of sulfoxides derivatives

III.3 RESULTS AND DISCUSSION

The compatibility of CuAACs with the ethynyl sulfoxide moiety in the alkyne was first addressed. Reaction of 1.00 equiv of the alkyne **III.29**[122] with 1.20 equiv of benzyl azide **II.37** in the presence of 0.25 mol % of Na ascorbate and 0.50 mol % of $CuSO_4·5H_2O$ in DMF yielded triazole **III.30** (57%) after 4 h at rt. This compound was characterised by NMR and HRMS. In the ^1H NMR spectrum of triazole **III.30**, the absence of a signal at δ_H = 3.70 ppm that corresponded to the alkyne proton together with the presence of a new singlet at δ_H = 7.62 ppm confirmed the formation of the heterocyclic derivative. In addition, the ^{13}C NMR spectrum showed a signal at δ_C = 123.8 ppm that correspond to the newly formed CH of the triazole core.



Scheme III.13: Synthesis of sulfinyl 1,2,3-triazolylidene **III.32**

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[122] H. Kosugi, M. Kitaoka, K. Tagami, A. Takahashi, H. Uda, *J. Org. Chem.* **1987**, *52*, 1078.

ESI-HRMS analysis of azole **III.30** confirmed the formation of this compound. Thus, a main peak at *m*/*z* = 298.1009 was found that matched with the $[M+H]^+$ ion of the structure proposed in Scheme III.13. These results confirm that the CuAAC is fully compatible with the sulfoxide group.

The following step to access to the desired complexes involves methylation in *N*3 of triazole **III.30**. In this case, the selective alkylation of the heterocyclic nucleus was not obvious *a priori* due to the presence of the sulfoxide group that could also be methylated.[123] Reaction of triazole **III.30** with 1.30 equiv of Me_3OBF_4 in anhydrous CH_2Cl_2 under Ar yielded the triazolium salt **III.31** after stirring at rt overnight. Analysis of the ^1H NMR spectrum of an aliquot of the crude reaction showed a downfield shift in the triazolium proton of 0.86 ppm compared to the triazole proton of **III.30**. Moreover, a new singlet appeared at δ_H = 4.28 that corresponded to the new NCH_3 group. In this spectrum, a minor subproduct (less than 10% by ^1H NMR analysis) could also be observed. However, after quenching the reaction with methanol and filtration of the crude product through a short pad of $NaHCO_3$, this product disappeared. To confirm the nature of this secondary product, the reaction was carried out with 3.00 equiv of the Meerwein's salt. Analysis of the ^1H NMR spectrum of an aliquot of the crude reaction showed again the presence of the signals corresponding to this minority product. The ratio of both products was identical when reaction was performed with 1.30 equiv of the methylating agent. Again, after work up of the crude product, the ^1H NMR spectrum did not show any signals of a secondary product. On the other hand, addition of 1.00 equiv of the alkylating agent also formed the minor product (confirmed by ^1H NMR analysis of an aliquot of the crude reaction). The reaction of the ethynyl sulfoxide **III.29** with 1.30 equiv of Me_3OBF_4 only provoked decomposition of the starting alkyne. Therefore, attempts to identify the minor product were not pursued.

Reaction overnight of the triazolium salt **III.31** with 0.75 equiv of Ag_2O in the presence of 1.50 equiv of NMe_4Cl and 4 Å molecular sieves, in a mixture of anhydrous CH_3CN:CH_2Cl_2 1:1 yielded the intermediate silver carbene. The absence of the triazolium signal in the ^1H NMR spectrum of an aliquot of the crude reaction confirmed

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[123] B. Ronan, H. B. Kagan, *Tetrahedron: Asymmetry* **1991**, *2*, 75.

the coordination of the silver atom to the carbenic centre. Transmetallation was carried out *in situ* by addition of 1.00 equiv of [AuCl(SMe$_2$)] and 2 h of stirring at rt. Gold complex **III.32** was obtained in excellent yields (98%). A complete characterisation of the product was achieved by NMR and HRMS techniques. In the case of the ^{1}H NMR spectrum, it is important to underline the lack of signals corresponding to triazolium protons, which confirmed the formation of the gold triazolylidene **III.32**. ^{13}C NMR spectrum showed a signal at δ_C = 160.7 ppm that was assigned to the C$_{carbenic}$. This shift was in agreement with gold 1,2,3-triazolylidenes previously reported.[60–62] HRMS showed a fragment at *m*/*z* = 508.0756 that matches with the loss of a chloride in the structure proposed. The structure of **III.32** was unambiguously confirmed by X-ray diffraction studies of a single crystal grown by slow diffusion of hexanes over a solution of the gold carbene in EtOAc (Figure III.1).

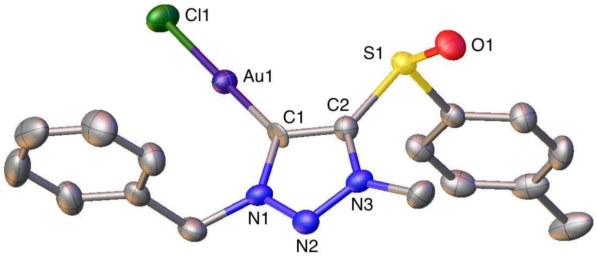
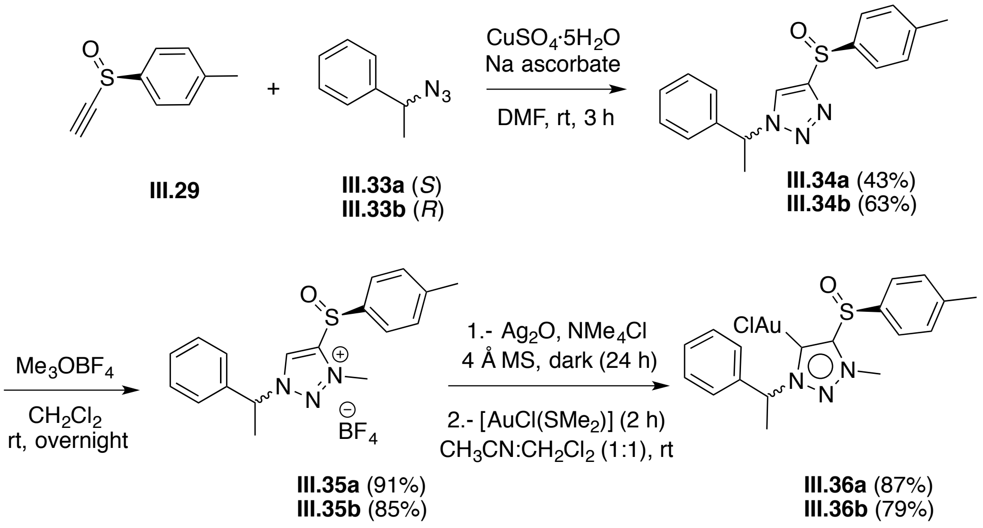


Figure III.1: ORTEP representation of gold carbene **III.32**. Selected bond lengths (Å) and angles (deg): Au1–Cl1 2.272(3), Au1–C1 1.954(10), C1–N1 1.375(10), N1–N2 1.324(7), N2–N3 1.317(7), N3–C2 1.358(7), C2–C1 1.406(11), C2–S1 1.779(5), S1–O1 1.486(4), C1–Au1–Cl1 179.0(4).

This gold complex shows an almost nearly perfect linear geometry with C–Au–Cl angles of 179 °. The distances of the gold atom with C1 (1.954(10) Å) and Cl (2.272(3) Å) are among the range of the ones reported for other Au-NHCs.[60–62]

To confirm that the stereochemical integrity of the sulfoxide group is maintained through the different steps of the synthetic approach to prepare the gold carbene **III.32**, a second chiral motif was introduced in the triazole molecule. Thus, the independent reaction of the enantiopure ethynyl sulfoxide **III.29** with the two enantiomers of α-methylbenzyl azide **III.33a–b** under the CuAAC reaction conditions used above yielded the corresponding diastereoisomers **III.34a** and **III.34b** (Scheme

III.14). Both triazoles were completely characterised by NMR and HRMS studies. Their ^{1}H NMR spectra show signals corresponding to a single diastereoisomer. Specifically, for compound **III.34a** the triazole proton resonates at δ_H = 7.75 ppm while its diastereoisomeric counterpart resonates at δ_H = 7.73 ppm. A single quadruplet was observed for the H atoms bounded to the chiral carbon of the methylbenzyl group: for compound **III.34a**, this signal appeared at δ_H = 5.80 ppm, 0.06 ppm downfield shifted compared to the diastereoisomer **III.34b** (δ_H = 5.74 ppm). The methyl group resonated as a doublet at δ_H = 1.91 ppm. For triazole **III.34b**, this doublet is observed at δ_H = 1.95 ppm. In addition, the ^{13}C NMR spectra also showed a single set of signals as a result of the obtaining of one single diatereoisomer. These results confirmed that the integrity of the chirality of the sulfoxide is maintained during the cycloaddition process. ESI-HRMS of compounds **III.34a**–**b** showed to main peaks at *m*/*z* = 312.1176 and 312.1165 respectively that match with the structure proposed ($[M+H^+]^+$) in Scheme III.14.



Scheme III.14: Synthesis of carbenes **III.36a**–**b**

Triazoles **III.34a**–**b** were methylated under the same conditions described for triazole **III.30** (1.30 equiv of the alkylating agent, in anh CH_2Cl_2, overnight at rt under Ar). The triazolium salts **III.35a**–**b** were obtained in 91 and 85% yield respectively. The structure of these compounds was studied by NMR and HRMS means. The ^{1}H NMR spectra showed again signals attributable to the formation of one single diastereoisomer of the triazolium salt. The most downfield shifted proton at δ_H = 8.48 ppm and 8.43 ppm (for triazolium **III.35a** and **III.35b**) was assigned to the H5 atom. The presence of one quartet (δ_H = 6.08 ppm for **III.35a** and δ_H = 6.04 ppm for **III.35b**) and one doublet (δ_H = 2.02 ppm and δ_H = 2.00 ppm) confirmed the presence of a single product, and thus, the integrity of the configuration of the sulfoxide moiety during the methylation process. In addition, ^{13}C NMR spectra showed signals assigned for only one diastereisomer in each case. ESI-HRMS confirmed the nature of the triazolium salt with the presence of a main peak at *m*/*z* = 326.1308 and 326.1315 respectively that corresponded to the cationic part of the salt depicted in Scheme III.14. Compounds **III.35a**–**b** were deprotonated with 0.75 equiv of Ag_2O in the presence of 1.50 equiv of NMe_4Cl in a mixture of anh CH_3CN:CH_2Cl_2 1:1. After 24 h of reaction at rt, ^{1}H NMR spectra of aliquots revealed the formation of the intermediate silver carbenes that were subsequently transmetallated using 1.00 equiv of [AuCl(SMe_2)]. Carbenes **III.36a**–**b** were obtained in excellent yields (87 and 79%, respectively) and were fully characterised. The signals in ^{1}H NMR spectra confirmed the formation of only one diastereisomer. In the case of carbene **III.36a**, the quartet corresponding to the proton of the quaternary carbon, resonated at δ_H = 6.25 ppm, 0.05 ppm upfield shifted than the diastereoisomeric counterpart **III.36b**. The doublet of the methyl group appeared at δ_H = 1.99 ppm for gold carbene **III.36a** and δ_H = 2.02 ppm for the other carbene **III.36b**. HRMS showed fragments at *m*/*z*= 522.0929 and 522.0899 for **III.36a** and **III.36b** respectively that corresponded to the loss of a chloride ligand in the structures proposed above. The structure of **III.36a**–**b** was confirmed by X-ray diffraction (Figure III.2–3).

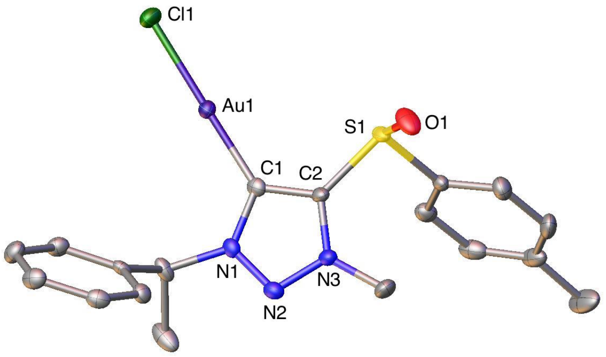


Figure III.2: ORTEP representation of gold carbene **III.36a**. Selected bond lengths (Å) and angles (deg): Au1–Cl1 2.282(1), Au1–C1 1.980(2), C1–N1 1.370(3), N1–N2 1.327(3), N2–N3 1.310(3), N3–C2 1.368(3), C2–C1 1.376(3), C2–S1 1.778(3), S1–O1 1.489(2), C1–Au1–Cl1 176.92(7).

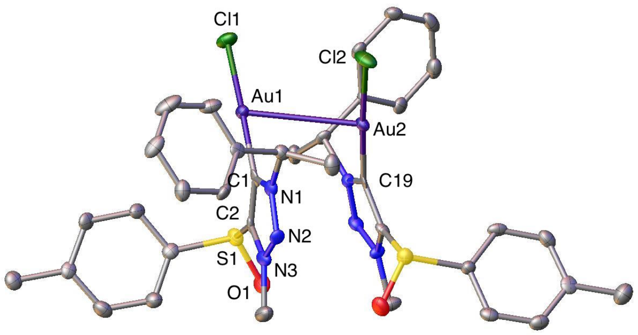


Figure III.3: ORTEP representation of gold carbene **III.36b**. Selected bond lengths (Å) and angles (deg): Au1–Au2 3.223(1), Au1–C1 1.988(11), Au1–Cl1 2.272(3), C1–N1 1.348(14), N1–N2 1.340(11), N2–N3 1.324(13), N3–C2 1.346(14), C2–C1 1.378(14), C2–S1 1.785(12), S1–O1 1.486(8), Au2–Cl2 2.282(3), Au2–C19 1.991(11), C1–Au1–Cl1 175.3(3), C19–Au2–Cl2 176.8(8), C1–Au1–Au2–C19 66.5(4).

The gold cations in **III.36a** and **III.36b** show nearly perfect linear geometries with C–Au–Cl angles between 175 ° and 177 °. All Au–C distances (1.980 to 1.991 Å) and Au–Cl distances (2.272(3) to 2.282(3) Å) lie in the ranges for reported NHC–Au–Cl complexes. A gold(I)–gold(I) distance of 3.223(1) Å in the case of **III.36b** reflects unsupported strong aurophilic interactions in the solid state.[124,125] The two C–Au–Cl units involved in the Au–Au interaction show a crossed arrangement with a C–Au–Au–C torsion angle of 66.5(4) °.

Once the compatibility between the reaction conditions used to prepare carbene complexes and the sterochemical integrity of the sulfoxide group was confirmed, we expanded this methodology to other metal carbenes having different moieties attached to the sulfoxide group and to *N*1.

(*S*)-1-bromo-4-(ethynylsulfinyl)benzene **III.37a** and (*S*)-2-methoxy-1-(ethynylsulfinyl)naphtyle **III.37b** reacted with benzyl azide **II.37** in the presence of catalytic amounts of Cu(I) to form the corresponding triazoles **III.38a**–**b** in good yields.

Methylation with Meerwein's agent yielded the ensuing triazolium salts **III.39a**–**b** that were deprotonated following the conditions previously reported. Transmetallation with [AuCl(SMe$_2$)] resulted in the obtaining of the gold carbenes

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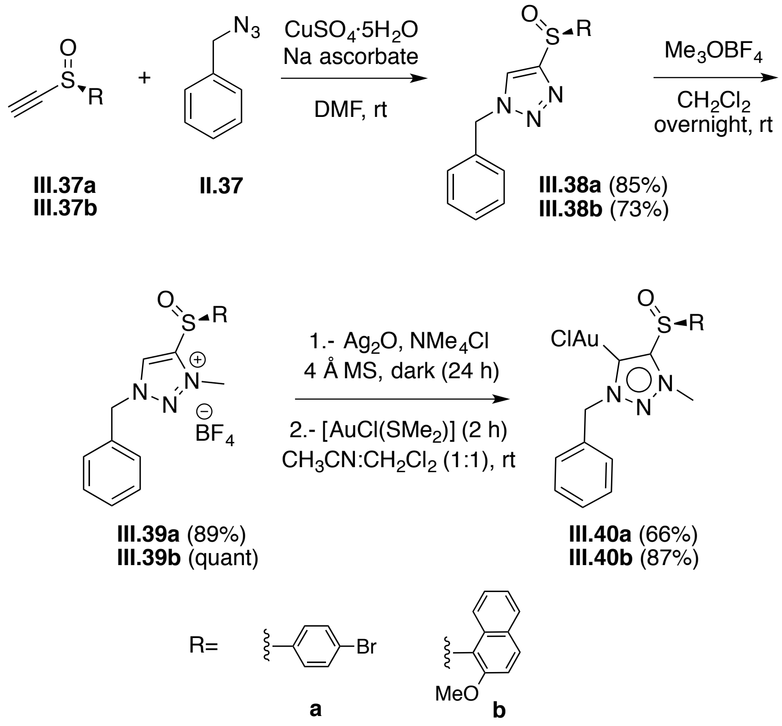
[124] For a review on Au–Au interactions see: H. Schmidbaur, A. Schier, *Chem. Soc. Rev.* **2012**, *41*, 370.

[125] About the role of bimetallic compounds in catalysis see: A. Gómez-Suárez, S. P. Nolan, *Angew. Chem. Int. Ed.* **2012**, *51*, 8156; b) A. S. K. Hashmi, *Acc. Chem. Res.* **2014**, *47*, 864.

III.40a–b. All of these novel compounds were fully characterised by NMR and HRMS. These data were in agreement with the structures proposed in Scheme III.15.



Scheme III.15: Synthesis of carbenes **III.40a–b**

In addition, the structure of the gold triazolylidene **III.40b** was established unambigously by X-ray diffraction studies (Figure III.4).

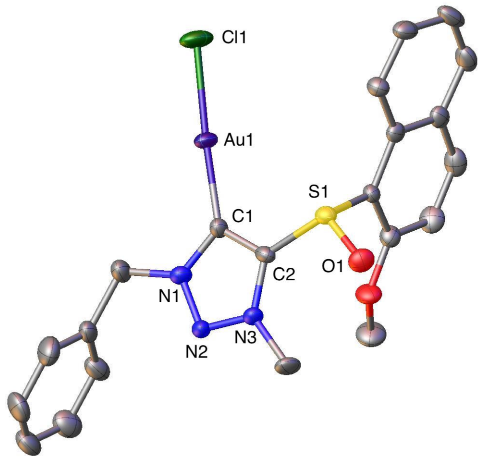
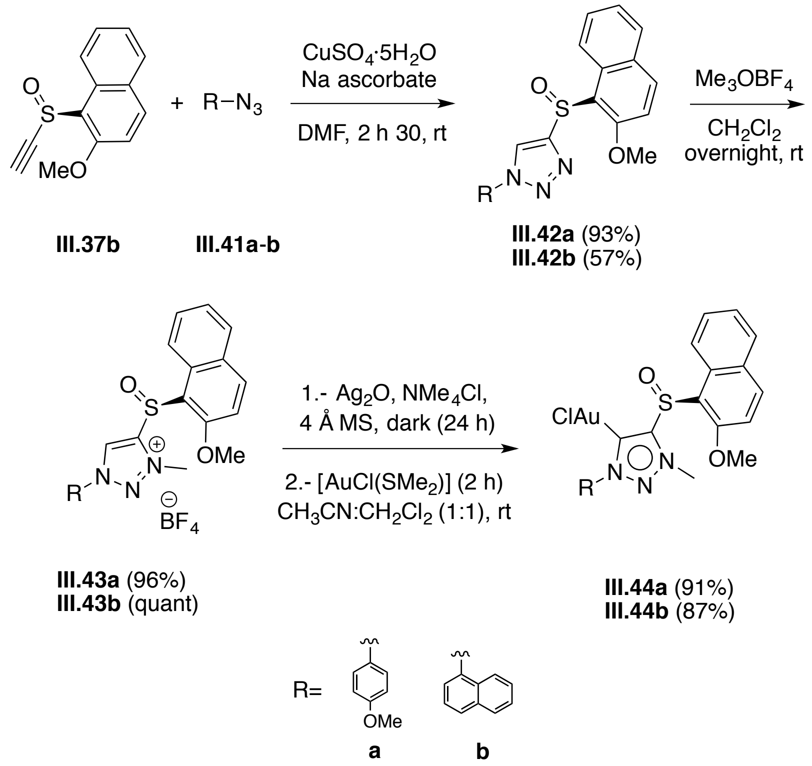


Figure III.4: ORTEP representation of gold carbene **III.40b**. Selected bond lengths (Å) and angles (deg): Au1–Cl1 2.280(2), Au1–C1 1.991(4), C1–N1 1.356(6), N1–N2 1.331(5), N2–N3 1.310(5), N3–C2 1.376(5), C2–C1 1.344(6), C2–S1 1.783(5), S1–O1 1.493(3), C1–Au1–Cl1 176.95(15).

Once this methodology was proved to be compatible with different ethynyl sulfoxides, we studied the variation on the azide using aliphatic and aromatic derivatives. Thus, reaction of 1.00 equiv of alkyne **III.37b** with 1.20 equiv of azides **III.41a–b** in the presence of catalytic amounts of Cu(I) yielded the expected triazoles **III.42a** and **III.42b**. The structures depicted in Scheme III.16 were in agreement with their NMR and HRMS data. Methylation of triazoles **III.42a** and **III.42b** under the conditions previously detailed, afforded the triazolium salts **III.43a** and **III.43b** in excellent yields. These triazolium salts reacted with 0.75 equiv of Ag_2O and in the presence of 1.50 equiv of NMe_4Cl to form the corresponding silver carbenes, that were subsequently transmetallated with 1.00 equiv of $[AuCl(SMe_2)]$ furnishing 1,2,3-triazolylidenes **III.44a** and **III.44b** in excellent yields. The NMR and HRMS data of all of these novel complexes, and their precursors, were in accordance with the structures depicted in Scheme III.16.



Scheme III.16: Synthesis of gold carbenes **III.44a–b**

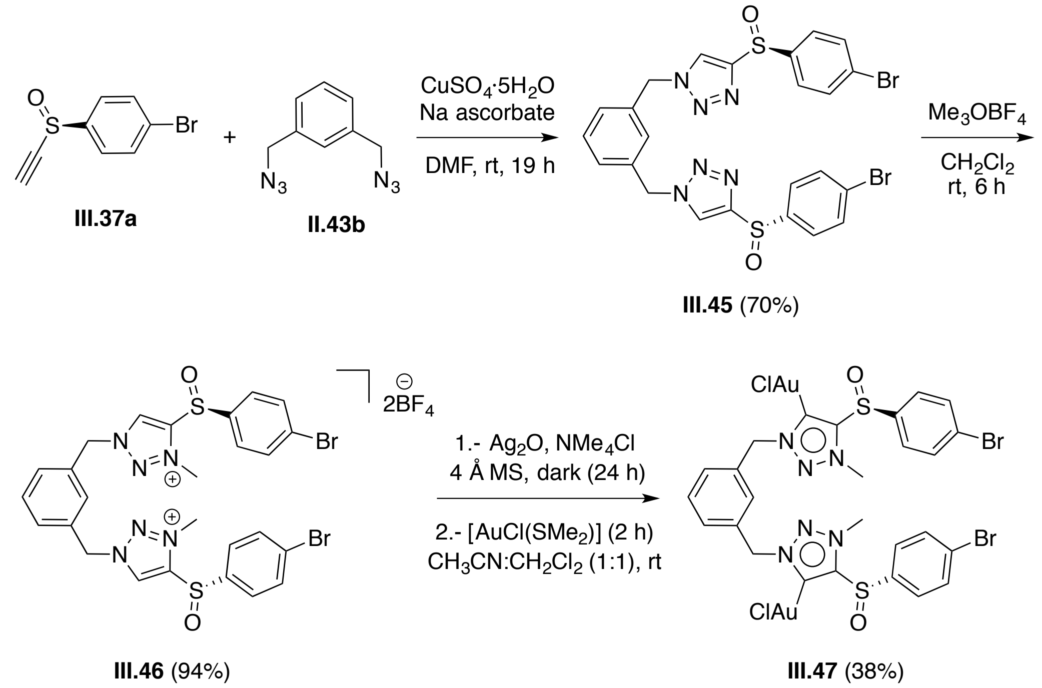
Table III.1 compiles the shifts of the carbene carbon of the Au-MIC complexes synthetized through this work.

Table III.1: Chemical shift of gold 1,2,3-triazolylidenes

Entry	Compound	$\delta_{C\text{-}Au}$[a]
1	**III.32**	160.7
2	**III.36a**	160.2
3	**III.36b**	160.0
4	**III.40a**	160.9
5	**III.40b**	159.0
6	**III.44a**	157.5
7	**III.44b**	162.3

[a] ^{13}C NMR spectra were registered in a 100 MHz in $CDCl_3$ as solvent.

The preparation of multimetallic carbenes was addressed next. Reaction of 2.20 equiv of alkyne **III.29** with 1.00 equiv of bis(azide) **II.43a** and catalytic amounts of Cu(I) led to bis(triazole) **III.45** in a yield of 70% after stirring at rt overnight. The ^{1}H NMR and the ^{13}C NMR spectra showed a set of signals for half of the molecule as a result of the symmetry that this heterocycle presented. Methylation of the bis(triazole) **III.45** was achieved using 3.00 equiv of the Meerwein's salt and stirring for 5 h at rt. The dimethylated nature of compound **III.46** was confirmed by studies of NMR and HRMS data. In the case of the ^{1}H NMR spectrum, it is important to note that signals were again obtained for half of the molecule because of the symmetry of the salt. This symmetry is only possible if methylation occurs in both heterocycles. ESI-HRMS showed two fragments, the first one at *m*/*z* = 762.9798 corresponding to the loss of one BF_4^- anion and a second peak at *m*/*z* = 337.9882 resulting from the loss of two BF_4^- anions. Reaction of the triazolium salt **III.46** with 2.25 equiv of Ag_2O and 4.50 equiv of NMe_4Cl afforded the silver intermediate carbene after 19 h of stirring. Transmetallation with 2.00 equiv of [AuCl(SMe$_2$)] yielded the desired gold carbene **III.47** in a 38% yield (Scheme III.18). This bimetallic carbene was fully characterised by NMR and HRMS. Again, the ^{1}H NMR and ^{13}C NMR spectra showed signals for half of the molecule. No signals attributable to the triazolium proton were observed, confirming the coordination of two gold centres to both carbenic carbons presented in the molecule. In the ^{13}C NMR spectrum, the most downfield shifted signal appeared at δ_C = 161.3 ppm and was assigned to the carbenic centre.



Scheme III.17: Synthesis of bimetallic 1,2,3-triazolylidene complex **III.47**

After setting the scope of the reaction for different alkynes and azides, the modification of the sulfinyl moiety was next pursued. The oxidation of the sulfoxide group to sulfone derivative **III.48** was quantitatively achieved by reacting 1.00 equiv of triazole **III.30** with 2.00 equiv of mcpba in $CHCl_3$ during 1 h at rt.[126] The ^1H NMR spectrum of **III.48** was similar to the sulfinyl triazole **III.30**, except for the shift of the triazole proton. In the case of **III.48**, this proton resonated at δ_H = 8.26 ppm, which is 0.64 ppm more deshielded than sulfoxide **III.30**. In addition, HRMS showed a main fragment at *m*/*z* = 314.0955, which is consistent with a protonated species of the structure proposed in (Scheme III.18). Alkylation of triazole **III.48** with Me_3OBF_4 under the same conditions as previously described, yielded the methylated product **III.49** quantitatively. The formation of the gold carbene **III.50** was achieved following the same methodology discussed above (Scheme III.18). This new complex was characterised by NMR and HRMS means. In the case of the ^1H NMR spectrum, confirmation of the formation of the gold carbene was given by the absence of a triazolium proton as a result of the coordination of the gold centre. On the other hand, a signal at δ_C = 163.4 ppm was assigned to the carbenic carbon. This represents a

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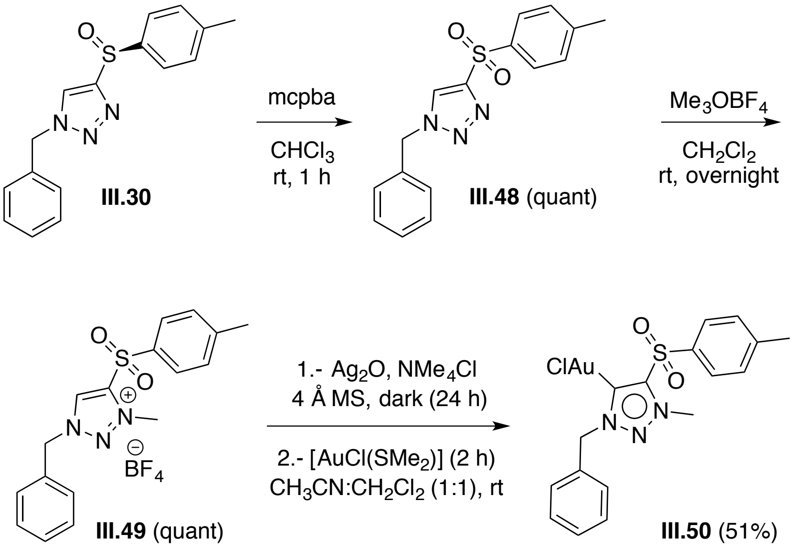
[126] A. Bolje, J. Košmrlj, *Org. Lett.* **2013**, *15*, 5084.

downfield shift of 2.7 ppm compared to the sulfoxide analogous **III.32**. ESI-HRMS showed a peak at m/z = 524.0708 that matches with the structure of **III.50** proposed in Scheme III.18 for the fragment $[M–Cl^-]^+$.



Scheme III.18: Synthesis of gold carbene **III.50**

Formation of sulfoximine **III.51** was attempted next (Scheme III.19). Reaction of triazole **III.30** with 1.90 equiv of PhI=NTs under the presence of catalytic amounts of $Cu(OTf)_2$ gave sulfoximine **III.51** with excellent yields (82%).[127] The formation of this new compound was confirmed by the study of NMR and HRMS data. The ^1H NMR spectrum showed a signal at δ_H = 8.23 ppm for the triazole proton. In addition, a new set of signals for the second *p*-tolyl group presented in the molecule was observed. Methylation of this triazole was performed with 1.50 equiv of Me_3OBF_4 affording triazolium salt **III.52** with excellent yields (89%). **III.53** was obtained after reaction of the triazolium precursor **III.52** with 0.75 equiv of Ag_2O, in the presence of 1.50 equiv NMe_4Cl, followed by transmetallation with 1.00 equiv of $[AuCl(SMe_2)]$. This gold complex was fully characterised (NMR and HRMS data). In the ^1H NMR spectrum, the lack of the triazolium signals confirmed the coordination of the carbenic centre to the gold atom. The ^{13}C NMR spectrum showed a peak at δ_C = 164.2 ppm that was assigned to the $C_{carbenic}$. In this case, the metallic complex **III.53** is again chiral due to the

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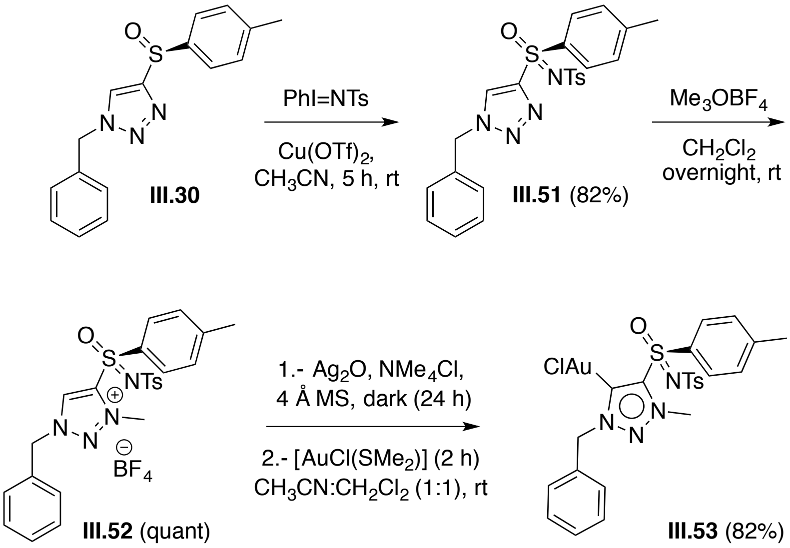
[127] D. Leca, K. Song, M. Amatore, L. Fensterbank, E. Lacôte, M. Malacria, *Chem Eur. J.* **2004**, *10*, 906.

presence of the sulfoximine. The determination of the enantiomeric excess was not pursued in this case.



Scheme III.19: Synthesis of gold carbene **III.53**

With the synthesis of new sulphur-based carbenes secured, the preparation of the regioisomeric complex **III.54** Au(I)-MIC having the sulfoxide in position *C*5 instead of *C*4 was addressed next. To achieve this new complex, 1,5-disubstituted triazole **III.55** must be synthetized firstly. The catalytic role of Ru and Rh salts in the cycloaddition reaction between azides and alkynes is well known.[128,129] The use of these catalysts produces the regioisomeric 1,5-disubstituted-1,2,3-triazoles. Table III.2 summarized the results obtained in the formation of 1,2,3-triazole **III.55** of alkyne **III.29** and benzyl azide **II.37** using different Ru(II) catalysts under different conditions.

Data in Table III.2 show that the use of 1.00 equiv of alkyne **III.29** and 1.50 equiv of benzyl azide **II.37** in the presence of 0.15 equiv of [Cp*RuCl(cod)] produced exclusively the 1,5-regioisomer **III.55** (entry 3).

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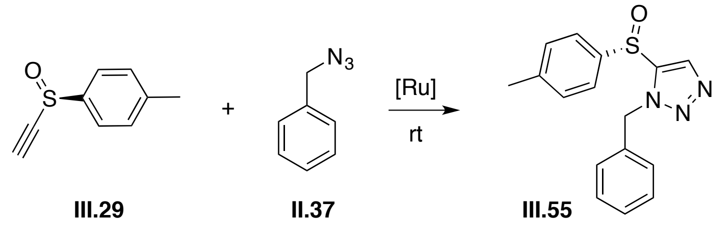
[128] a) L. Zhang, X. Chen, P. Xue, H. H. Y. Sun, I. D. Williams, K. B. Sharpless, V. V. Fokin, G. Jia, *J. Am. Chem. Soc.* **2005**, *127*, 15998; b) L. K. Rasmussen, B. C. Boren, V. V. Fokin, *Org. Lett.* **2007**, *9*, 5337; c) B. C. Boren, S. Narayan, L. K. Rasmussen, L. Zhang, H. Zhao, Z. Lin, G. Jia, V. V. Fokin, *J. Am. Chem. Soc.* **2008**, *130*, 8923.

[129] For an example of Ru-NHC catalysts for the RuAAC reaction see: M. Lamberti, G. C. Fortman, A. Poater, J. Broggi, A. M. Z. Slawin, L. Cavallo, S. P. Nolan, *Organometallics* **2012**, *31*, 756.

Table III.2: Reaction conditions for the synthesis of 1,4 disubstituted 1,2,3-triazol



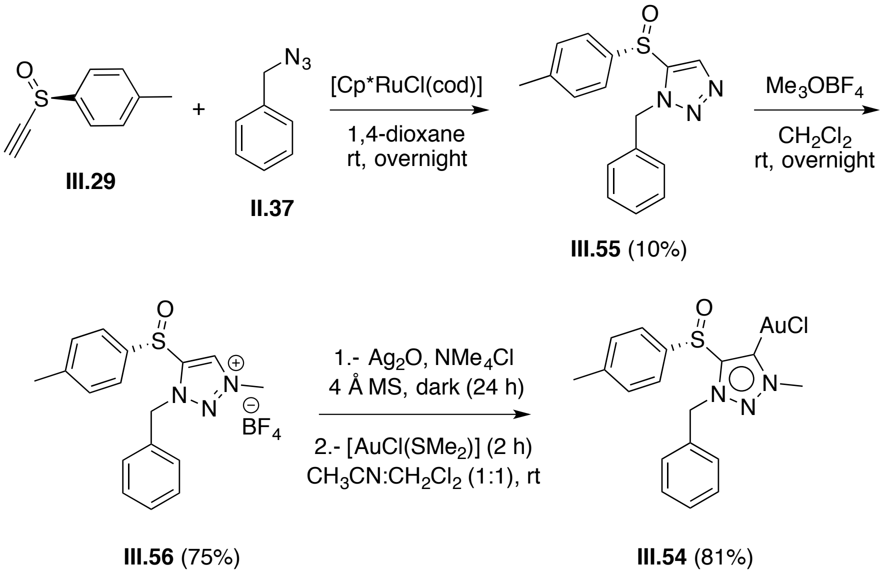
III.29 **II.37** **III.55**

Entry	alk:azi:cat	Catalyst	Solvent	t	Conversion[a]	1,4:1,5
1	1.15:1.00:0.15	[CpRuCl(PPh$_3$)]	CH$_3$CN	2 days	38:62	90:10
2	1.15:1.00:0.15	[CpRuCl(PPh$_3$)]	1,4-Dioxane	2 days	59:41	72:28
3	1.15:1.00:0.15	[Cp*RuCl(cod)]	1,4-Dioxane	4 days	50:50	0:100
4	1.15:1.00:0.15	[Cp*RuCl(cod)]	DMF	3 h	81:19	65:35
5[b]	1.15:1.00:0.10	[Cp*RuCl(cod)]	Toluene	3 h	Traces	-
6	1.00:1.25:0.12	[Cp*RuCl(cod)]	CH$_3$CN	4 days	38:62	73:27
7	1.00:1.20:0.10	[Cp*RuCl(cod)]	THF	4 days	n.r.	-
8[c]	1.15:1.00:0.15	[Cp*RuCl(cod)]	1,4-Dioxane	4 days	24:76	0:100
9	1.83:1.00:0.20	[Cp*RuCl(cod)]	1,4-Dioxane	4 days	28:72	0:100
10	1.00:1.20:0.10	[Cp*RuCl(cod)]	1,4-Dioxane	4 days	29:71	50:50
11	1.00:1.50:0.15	[Cp*RuCl(cod)]	1,4-Dioxane	1 day	21:79	50:50

[a] Conversion is referred to the ratio benzyl azide:triazoles (mixture of 1,4 and 1,5 disubstituted) measured by ^{1}H NMR.
[b] Reaction was performed at reflux.
[c] Alkyne was added in two portions.

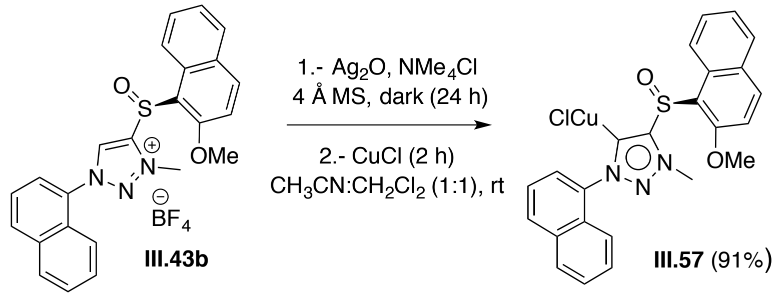
^{1}H NMR spectrum of this compound presented some differences compared to the 1,4-disubstituted regioisomer. For example, the triazole proton in **III.55** resonates at δ_H = 7.47 ppm while in the case of **III.30** this signal is observed at δ_H = 7.62 ppm. In addition the hydrogen atoms of the methylene group are downfield shifted by 0.40 ppm compared to its regioisomer. ESI-HRMS confirmed the structure proposed because of the presence of a peak at *m/z* = 298.1009 that matched with a protonated species of triazole **III.55**.

The selective methylation in *N*3 was carried out with Meerwein's salt as the alkylating agent. The triazolium salt **III.56** was formed exclusively in a 75% yield. ^{1}H NMR spectrum of this compound showed a deshielded signal at δ_H = 8.37 ppm attributable to the triazolium proton, which is 0.10 ppm shifted upfield respect the 1,4 regioisomer **III.31**. HRMS was in agreement with the structure depicted in Scheme III.20. Finally, reaction of **III.56** with Ag$_2$O and NMe$_4$Cl followed by transmetallation with [AuCl(SMe$_2$)] afforded the gold carbene **III.54** in 81% yield. This new gold triazolylidene was characterised by NMR and HRMS means. The lack of the triazolium signal in the ^{1}H NMR spectrum confirmed the coordination between the gold atom and the carbenic centre. Moreover, a signal at $\delta_C = 161.3$ ppm in the ^{13}C NMR spectrum was assigned to the $C_{carbenic}$ atom. Finally, ESI-HRMS showed a peak at $m/z = 561.0776$ corresponding to the structure proposed in Scheme III.20 plus a NH_4^+ cation.



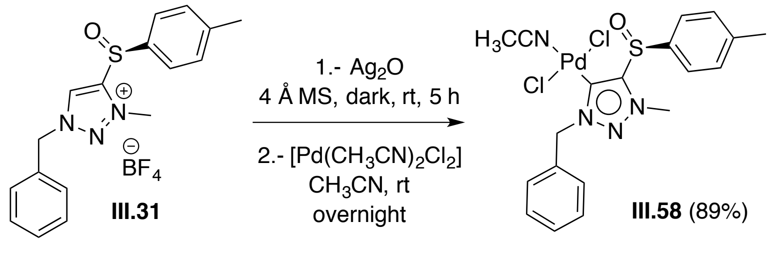
Scheme III.20: Synthesis of gold carbene **III.54**

To demonstrate the versatility of the procedure developed above to prepare M-MIC complexes containing sulphur functional groups on the triazole ring, the synthesis of some Cu and Pd MICs was finally pursued. Thus, Cu-MIC was prepared from triazolium salt **III.43b** following the synthetic procedure described previously. After stirring the heterocyclic salt overnight in the presence of Ag_2O, 1.00 equiv of CuCl was added and the resulting mixture was stirred at rt for two more hours. Cu carbene **III.57** was obtained in 91% yield (Scheme III.21). This new product was characterised by NMR and HRMS techniques. The ^{1}H NMR spectrum confirmed the coordination of carbene to the metallic centre, due to the absence of a triazolium signal at $\delta_H = 9.87$ ppm. The ^{13}C NMR spectrum shows the characteristic signal for the carbene carbon at $\delta_C = 162.6$ ppm. This value is similar to the observed for the analogous gold carbene **III.44b** ($\delta_C = 161.2$ ppm). The ESI-HRMS shows a molecular peak at $m/z = 456.0428$ corresponding to $[M{-}Cl^-]^+$ and confirming the structure **III.57**.



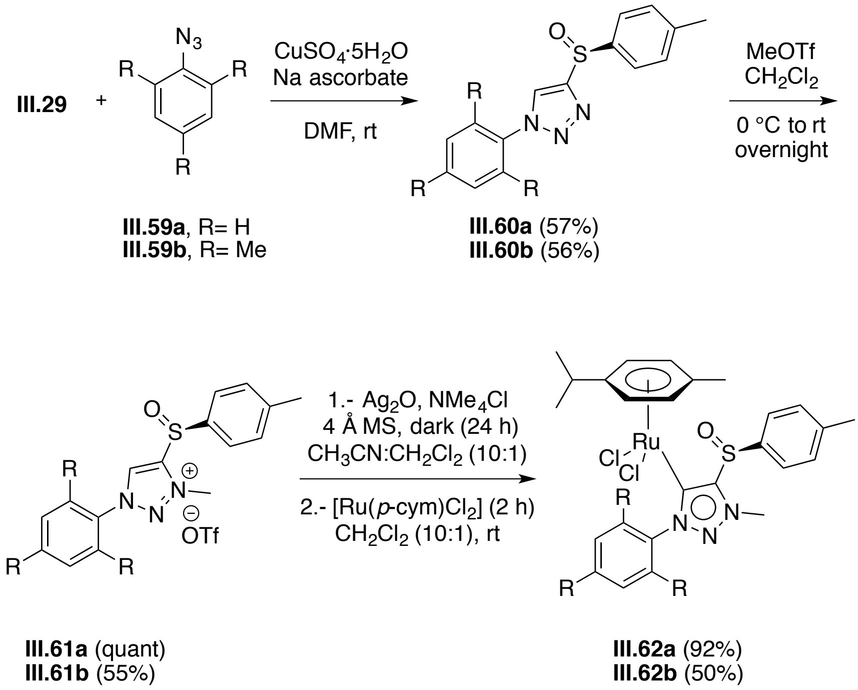
Scheme III.21: Synthesis of copper carbene **III.57**

The synthesis of Pd-MIC **III.58** was effected following a similar methodology. In this case, the triazolium salt **III.31** was dissolved in anh CH_3CN and reacted with Ag_2O at rt for 5 h. After that time, the crude mixture was filtered through a short pad of Celite. $[Pd(CH_3CN)_2Cl_2]$ was then added and reacted overnight. Complex **III.58** was obtained as a red solid and was not further purified (Scheme III.22). Complex **III.58** was fully characterised by NMR and HRMS means. NMR experiments were performed in a coordinating deuterated solvent (d_4-CH_3OH) to avoid the dimerization process of the mononuclear carbene complex.[121] The ^{13}C NMR spectrum of **III.58** showed a signal at δ_C = 139.7 ppm attributable to the $C_{carbenic}$ (HMBC). This signal is considerably downfield shifted compared with other Pd(II)-MIC previously reported.[37,58] ESI-HRMS confirmed the structure proposed in Scheme III.22. Thus, two main clusters containing palladium were obtained. The main peak appered at m/z = 495.0095 and matches with the loss of a chloride anion ($[M–Cl^-]^+$). The second cluster is less intense appearing at m/z = 453.9827 and matching the formula of $[M–Cl^-–CH_3CN]^+$, which confirms the structure proposed.



Scheme III.22: Synthesis of Pd(II)-MIC **III.58**

Ru-MIC complexes were also prepared following an analogous methodology that the one described above (Scheme III.23). Thus, 1.00 equiv of alkyne **III.29** reacted with 1.30 equiv of phenyl azide **III.59a** and mesityl azide **III.59b**[130] in DMF under Ar and in the presence of catalytic amounts of $CuSO_4·5H_2O$ and Na Ascorbate to yield triazoles **III.60a**–**b** in moderate yields (57 and 56% respectively).



Scheme III.23: Synthesis of Ru(II)-MICs **III.62a**–**b**

Triazoles were subsequently methylated using MeOTf as alkylating agent. In this case, 1.00 equiv of **III.60a**–**b** was dissolved in CH_2Cl_2; the solution was cooled at 0 °C and treated with 2.00 equiv of MeOTf. The reaction was left to reach rt and stirred overnight affording the correspondent triazolium salt **III.61a**–**b**. Both triazoles and triazolium salts were completely characterised by NMR and HRMS means.

With the triazolium salts **III.61a**–**b** obtained, the next step was the formation of the Ru(II) 1,2,3-triazolylidene complexes. Thus, 1.00 equiv of the heterocyclic precursors with 1.50 equiv of NMe_4Cl and 0.75 equiv of Ag_2O were stirred in the dark in a mixture of $CH_3CN:CH_2Cl_2$ (1:10) overnight. Once the silver carbene intermediate formed, the crude was filtered through a Celite pad and all the volatiles were removed

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[130] Mesityl azide was employed in order to prevent a C–H activation by the Ru centre: K. F. Donnelly, R. Lalrempuia, H. Müller-Bunz, E. Clot, M. Albrecht, *Organometallics* **2015**, *34*, 858.

under vacuum. In order to avoid competition in the coordination to the metal between the carbene and CH_3CN, the residue was redissolved in non-coordinating CH_2Cl_2 and $[Ru(p\text{-cymene})Cl_2]_2$ was added. The reaction mixture was stirred at rt for two more hours. Ru(II)-MIC **III.62a**–**b** were obtained and fully characterised by NMR and HRMS analysis.

The ^1H NMR spectrum of complex **III.62a** showed four doublets between δ_H = 5.39 and 4.81 ppm corresponding to the aromatic protons of the new *p*-cymene ligand. In addition, a septuplet at δ_H = 2.71 ppm, a singlet at δ_H = 1.97 ppm and two doublets at δ_H = 1.22 and 1.17 ppm were attributable to the functional groups presented in the *p*-cymene ligand. No signals attributable to the triazolium proton were showed in the spectrum. Regarding the ^{13}C NMR spectrum of the complex, it is worthy to note that the carbene carbon resonates at δ_C = 176.3 ppm that was in agreement with other Ru(II)-MIC previously reported in the literature.[131] A main fragment appeared in HRMS at m/z = 568.0762 that corresponded to the loss of a chlorine in the structure depicted in Scheme III.24. The structure of **III.62a** was unambiguously confirmed by X-ray diffraction structure (Figure III.5).

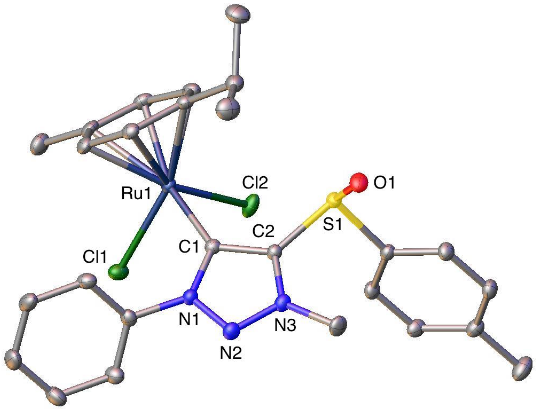

Figure III.5: ORTEP representation of ruthenium carbene **III.62a**. Selected bond lengths (Å) and angles (deg): Ru1–C1 2.0696(15), Ru1–Cl1 2.4103(4), Ru1–Cl2 2.4112(4), Ru–$C_{centroid}$ 1.695(<1), C1–Ru1–Cl1 86.28(4), C1–Ru1–Cl2 84.49(4), C1–N1 1.385(2), N1–N2 1.3383(18), N2–N3 1.3101(18), N3–C2 1.3667(19), C2–C1 1.395(2), C2–S1 1.7800(15), S1–O1 (1.4975(12), Cl1–Ru1–Cl2 87.089(15).

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[131] M. Delgado-Rebollo, D. Canseco-Gonzalez, M. Hollering, H. Mueller-Bunz, M. Albrecht, *Dalton Trans.* **2014**, *43*, 4462.

It exhibits a typical three-legged piano stool geometry with two chlorides ligands and the carbene representing the three legs.

In the case of complex **III.62b** the ^{1}H NMR spectrum also showed four doublets between δ_H = 5.45 and 5.11 ppm corresponding to the four aromatic protons of the *p*-cymene group in addition to the signals attributable to the methyl and isopropyl groups of this ligand. In the ^{13}C NMR, the carbene carbon resonated at δ_C = 174.0 ppm. HRMS confirmed the structure of **III.62b** showing a main peak at *m*/*z* = 610.1260 that corresponded to the loss of a chloride.

It should be noted that none of the compounds prepared in this chapter show coordination between the metal centre and the sulfoxide group.

III.4 CONCLUSIONS

- A new type of chiral sulfinyl 1,2,3-triazolylidenes has been synthetized and fully characterised. The introduction of the enantiopure sulfoxide in the *C*4 position of the triazole moiety was achieved through the CuAAC process where the alkynyl reagent presented the chiral sulfoxide functionality.

- Gold complexes bearing a sulfoxide were enantiopure compounds as was demonstrated by using (*R*)-α-phenylethyl azide and (*S*)-α-phenylethyl azide derivatives **III.33a** and **III.33b**. Diasteromeric mixtures of complexes **III.36a**–**b** were not observed, confirming the integrity of the chiral at sulphur centre during the synthetic pathway.

- This methodology was compatible with the presence of different alkynyl sulfoxides and azides, spreading out the diversity of structures reachable. Moreover, the sulfoxide group could be modified maintining the integrity of the ligand. This postmodification increases the structures of the 1,2,3-triazolylidenes complexes obtained to sulfone and chiral sulfoximine derivatives.

- Our methodology allows to prepare enantiopure Au, Cu, Pd and Ru MIC complexes having an aromatic-SO moiety directly attached either at *C*4 or *C*5 of the triazole ring.

III.5 EXPERIMENTAL SECTION

Alkynes **III.29**, **III.37a**–**b**[122] and azides **III.33a**–**b**[132] were prepared following a procedure previously described:

III.41a–**b** and **III.59a**–**b** were prepared following a modified procedure previously reported:[133]

Amine (16 mmol, 1.00 equiv) was dissolved in THF (20 mL). Ice was then added followed by HCl 37% (3.5 mL). A solution of $NaNO_2$ (24.00 mmol, 1.50 equiv) in H_2O (10 mL) was added to the solution. The reaction was stirred at 0 °C for 15 min. In case of acidic pH of the crude reaction the solution had to be neutralized by $NaHCO_3$. NaN_3 (24 mmol, 1.50 equiv) dissolved in H_2O was added dropwise. The crude mixture was stirred for 1 h. The mixture was extracted with Et_2O three times. The organic layer was washed with HCl 0.1 M (three times), water (three times), dried over $MgSO_4$ and filtered. All the volatiles were removed under vacuum affording the corresponding azide, which was purified through a short pad of SiO_2.

General procedure for the synthesis of 1,2,3-triazoles

A mixture of organic azide (1.20 equiv), alkyne (1.00 equiv), sodium (L)-ascorbate (0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (0.25 equiv) in DMF was stirred under Ar at rt until completion of the reaction (TLC analysis). The reaction was quenched with water

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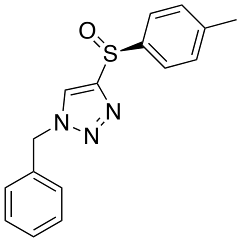
[132] J. R. Suárez, B. Trastoy, M. E. Pérez-Ojeda, R. Marín-Barrios, J. L. Chiara, *Adv. Synth. Catal.* **2010**, *352*, 2515.

[133] I. Wilkening, G. del Signore, C. P. R. Hackenberger, *Chem. Commun.* **2011**, *47*, 349.

at 0 °C and allowed to reach rt. The mixture was extracted with CH_2Cl_2 three times. The organic layer was dried over $MgSO_4$, filtered and the volatiles were removed under vacuum to afford the corresponding reaction products, which were purified through a short pad of SiO_2.

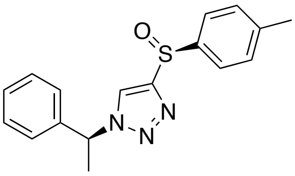
Synthesis of compound III.30



Following the general procedure a mixture of benzyl azide **II.37** (525 mg, 3.95 mmol, 1.20 equiv), alkyne **III.29** (540 mg, 3.29 mmol, 1.00 equiv), sodium (L)-ascorbate (326 mg, 1.60 mmol, 0.50 equiv) and $CuSO_4·5H_2O$ (205 mg, 0.83 mmol, 0.25 equiv) in DMF (72 mL) was stirred under Ar at rt for 4 h. The resulting residue was purified (SiO_2, Hex/EtOAc 6:4) to yield **III.30** as a white solid (557 mg, 57%).

^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.72 (s, 1H, $N_3C{=}CH$), 7.62 (d, J = 8.2 Hz, 2H, Ar *p*-tolyl), 7.37 (m, 3H, Ar), 7.30 (d, J = 8.2 Hz, 2H, Ar *p*-tolyl), 7.25 (m, 2H, Ar), 5.55 (d, J = 14.7 Hz, 1H, NCH_2), 5.54 (d, J = 14.7 Hz, 1H, NCH_2), 2.39 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.5 (C, $N_3C{=}CH$), 142.2 (C, Ar), 140.1 (C, Ar), 133.5 (C, Ar), 130.2 (2CH, Ar), 129.4 (2CH, Ar), 129.3 (CH, Ar), 128.5 (2CH, Ar), 124.8 (2CH), 123.8 (CH, $N_3C{=}CH$), 54.9 (NCH_2), 21.6 (CH_3, *p*-tolyl). **IR (KBr) $\nu_{máx}$** 3435, 3116, 3041, 1496, 1460, 1211, 1105, 1087, 1048, 856, 814, 725, 540. **$[\alpha]_D^{25}$** + 223.0 (*c* 0.6, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{16}H_{16}N_3OS$: 298.1009 $[M+H]^+$, found 298.1009. **m.p.** 132–134 °C.

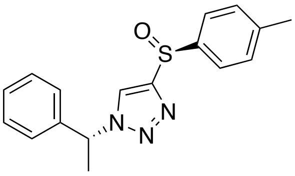
Synthesis of compound III.34a



Following the general procedure a mixture of azide **III.33a** (645 mg, 4.38 mmol, 1.20 equiv), alkyne **III.29** (600 mg, 3.65 mmol, 1.00 equiv), sodium (L)-ascorbate (362 mg, 1.83 mmol, 0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (228 mg, 0.91 mmol, 0.25 equiv) in DMF (80 mL) was stirred under Ar at rt for 3 h 30. The resulting residue was purified (SiO_2, Hex/EtOAc 7:3) to yield **III.34a** as a white solid (491 mg, 43 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H, $N_3C{=}CH$), 7.62 (d, *J* = 8.2 Hz, 2H, Ar *p*-tolyl), 7.29 (m, 7H, 5H Ar and 2H Ar *p*-tolyl), 5.80 (q, *J* = 7.1 Hz, 1H, CH), 2.36 (s, 3H, CH_3 *p*-tolyl), 1.91 (d, *J* = 7.1 Hz, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 152.7 (C, $N_3C{=}CH$), 142.0 (C, Ar), 139.9 (C, Ar), 138.7 (C, Ar), 130.1 (2CH, Ar), 129.2 (2CH, Ar), 129.0 (CH, Ar), 126.7 (2CH, Ar), 124.8 (2CH, Ar), 122.7 (CH, $N_3C{=}CH$), 61.1 (CH), 21.5 (CH_3, *p*-tolyl), 21.3 (CH_3). **IR (KBr) $\nu_{máx}$** 3654, 3103, 1493, 1112, 1084, 1050, 819, 756, 694, 523. **$[\alpha]_D^{25}$** + 127.7 (*c* 0.3, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{17}H_{18}N_3OS$: 312.1165 $[M+H]^+$, found: 312.1176. **m.p.** 149–152 °C.

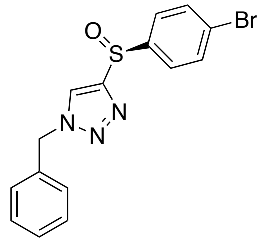
Synthesis of compound III.34b



Following the general procedure a mixture of azide **III.33b** (645 mg, 4.38 mmol, 1.20 equiv), alkyne **III.29** (600 mg, 3.65 mmol, 1.00 equiv), sodium (L)-ascorbate (362 mg, 1.83 mmol, 0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (228 mg, 0.9 mmol, 0.25 equiv) in DMF (80 mL) was stirred under Ar at rt for 3 h. The resulting residue was purified (SiO_2, Hex/EtOAc 7:3) to yield **III.34b** as a white solid (718 mg, 63%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.73 (s, 1H, N_3C=CH), 7.61 (d, *J* = 8.2 Hz, 2H, Ar *p*-tolyl), 7.29 (m, 7H, 5H Ar and 2H Ar *p*-tolyl), 5.74 (q, *J* = 7.1 Hz, 1H, CH), 2.37 (s, 3H, CH_3 *p*-tolyl), 1.95 (d, *J* = 7.1 Hz, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 152.8 (C, N_3C=CH), 142.1 (C, Ar), 140.0 (C, Ar), 138.8 (C, Ar), 130.1 (2CH, Ar), 129.2 (2CH, Ar), 129.0 (CH, Ar), 126.7 (2CH, Ar), 124.8 (2CH, Ar), 122.9 (CH, N_3C=CH), 61.3 (CH), 21.5 (CH_3, *p*-tolyl), 21.3 (CH_3). **IR (KBr)** $\nu_{\text{máx}}$ 3117, 1492, 1450, 1211, 1086, 1055, 809, 755, 695, 552. $[\alpha]_D^{25}$ + 104.5 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{17}H_{18}N_3OS$: 311.1165 $[M+H]^+$, found: 312.1165. **m.p.** 119–121 °C.

Synthesis of compound III.38a

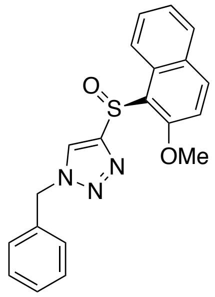


Following the general procedure a mixture of benzyl azide **II.37** (229 mg, 1.72 mmol, 1.30 equiv), alkyne **III.37a** (300 mg, 1.32 mmol, 1.00 equiv), sodium (L)-ascorbate (131 mg, 0.66 mmol, 0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (82 mg, 0.33 mmol, 0.25 equiv) in DMF (11 mL) was stirred under Ar at rt for 3 days. The resulting residue was purified (SiO_2, Hex/EtOAc from 1:1 to 2:8) to yield **III.38a** as a white solid (406 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.74 (s, 1H, N_3C=CH), 7.64 (d, *J* = 8.3 Hz, 4H, *p*-BrC_6H_4), 7.38 (m, 3H, Ar), 7.27 (m, 2H, Ar), 5.56 (d, *J* = 14.7 Hz, 1H, NCH_2), 5.46 (d, *J* = 14.7 Hz, 1H, NCH_2). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 152.7 (C, N_3C=CH), 142.4 (C, Ar), 133.3 (C, Ar), 132.7 (2CH, Ar), 129.5 (2CH, Ar), 129.4 (CH, Ar), 128.6 (2CH, Ar), 126.3 (2CH, Ar), 126.2 (C, Ar), 123.9 (CH, N_3C=CH), 55.0 (NCH_2). **IR (KBr)** $\nu_{\text{máx}}$ 3125, 3065, 2953, 1467, 1384, 12313, 1078, 1046, 1039, 1006, 809, 714, 707. $[\alpha]_D^{25}$ + 208.0 (*c* 0.3, $CHCl_3$).

HRMS (ESI) *m*/*z* calculated for $C_{15}H_{13}BrN_3OS$: 363.9937 $[M+H]^+$, found 363.9941. **m.p.** 129–131 °C.

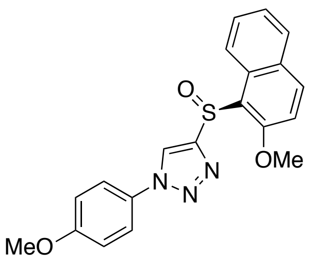
Synthesis of compound III.38b



Following the general procedure a mixture of benzyl azide **II.37** (139 mg, 1.04 mmol, 1.20 equiv), alkyne **III.37b** (200 mg, 0.87 mmol, 1.00 equiv), sodium (L)-ascorbate (34 mg, 0.17 mmol, 0.20 equiv) and $CuSO_4{\cdot}5H_2O$ (21 mg, 0.09 mmol, 0.10 equiv) in DMF (20 mL) was stirred under Ar at rt for 19 h. The resulting residue was purified (SiO_2, Hex/EtOAc 2:8) to yield **III.38b** as a white solid (231 mg, 73 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (dd, *J* = 8.6 Hz, 0.9 Hz, 1H, Ar), 7.96 (d, *J* = 9.0 Hz, 1H, Ar), 7.92 (s, 1H, $N_3C{=}CH$), 7.78 (dt, *J* = 8.4 Hz, 0.4 Hz, 1H, Ar), 7.46 (ddd, *J* = 8.5 Hz, 6.9 Hz, 1.4 Hz, 1H, Ar), 7.36 (m, 4H, Ar), 7.22 (m, 3H, Ar), 5.52 (d, *J* = 14.8 Hz, 1H, NCH_2), 5.47 (d, *J* = 14.8 Hz, 1H, NCH_2), 3.88 (s, 3H, OCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.6 (C, Ar), 151.9 (C, $N_3C{=}CH$), 135.4 (CH, Ar), 134.0 (C, Ar), 132.1 (C, Ar), 129.5 (C, Ar), 129.3 (2CH, Ar), 129.1 (CH, Ar), 128.9 (CH, Ar), 128.2 (3CH, Ar), 124.7 (CH, $N_3C{=}CH$), 124.6 (CH, Ar), 122.9 (CH, Ar), 121.3 (C, Ar), 113.2 (CH, Ar), 57.0 (2-O*C*H_3naph), 54.7 (NCH_2). **IR (KBr)** $\nu_{máx}$ 3435, 3128, 1620, 1594, 1506, 1479, 1336, 1271, 1249, 1150, 1035, 815, 752, 712. $[\alpha]_D^{25}$ + 1.5 (*c* 1.2, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{20}H_{18}N_3O_2S$: 364.1114 $[M+H]^+$, found: 364.1109. **m.p.** 79–82 °C.

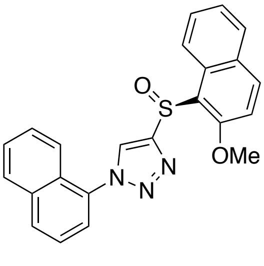
Synthesis of compound III.42a



Following the general procedure a mixture of azide **III.41a** (380 mg, 2.54 mmol, 1.30 equiv), alkyne **III.37b** (450 mg, 1.95 mmol, 1.00 equiv), sodium (L)-ascorbate (194 mg, 0.98 mmol, 0.50 equiv) and $CuSO_4 \cdot 5H_2O$ (122 mg, 0.49 mmol, 0.25 equiv) in DMF (44 mL) was stirred under Ar at rt for 2 h 30. The resulting residue was purified (SiO_2, Hex/EtOAc 3:7) to yield **III.42a** as a white solid (687 mg, 93 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (dd, *J* = 8.6 Hz, 0.9 Hz, 1H, Ar), 8.33 (s, 1H, N_3C=CH), 7.96 (d, *J* = 9.1 Hz, 1H, Ar), 7.77 (dt, *J* = 8.2 Hz, 0.7 Hz, 1H, Ar), 7.55 (d, *J* = 9.0 Hz, 2H, Ar *p*-$OCH_3C_6H_4$), 7.50 (ddt, *J* = 8.5 Hz, 6.9 Hz, 1.4 Hz, 1H, Ar), 7.36 (ddt, *J* = 8.1 Hz, 6.9 Hz, 1.1 Hz, 1H, Ar), 7.25 (d, *J* = 9.1 Hz, 1H, Ar), 6.94 (d, *J* = 9.0 Hz, 2H, Ar *p*-$OCH_3C_6H_4$), 3.97 (s, 3H, 2-OCH_3naph), 3.80 (s, 3H, *p*-$OCH_3C_6H_4$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.2 (C, Ar), 157.4 (C, Ar), 152.0 (C, N_3C=CH), 135.4 (CH, Ar), 132.0 (C, Ar), 129.8 (C, Ar), 129.6 (C, Ar), 128.9 (CH, Ar), 128.3 (CH, Ar), 124.6 (CH, Ar), 123.0 (CH, Ar), 122.7 (CH, N_3C=CH), 122.3 (2CH, Ar), 120.9 (C, Ar), 114.9 (2CH, Ar), 113.2 (CH, Ar), 57.1 (2-O*C*H_3naph), 55.7 (*p*-O*C*$H_3C_6H_4$). **IR (KBr)** $\nu_{máx}$ 3436, 3099, 1618, 1592, 1518, 1272, 1251, 1039, 835, 823, 772. **$[\alpha]_D^{25}$** + 13.2 (*c* 0.7, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{20}H_{18}N_3O_3S$: 380.1063 $[M+H]^+$, found 380.1074; for: $C_{20}H_{17}N_3NaO_3S$: 402.0883 $[M+Na^+]^+$, found: 402.0892. **m.p.** 123–126 °C.

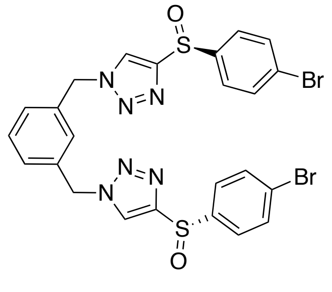
Synthesis of compound III.42b



Following the general procedure a mixture of azide **III.41b** (400 mg, 2.36 mmol, 1.30 equiv), alkyne **III.37b** (419 mg, 1.82 mmol, 1.00 equiv), sodium (L)-ascorbate (180 mg, 0.91 mmol, 0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (114 mg, 0.45 mmol, 0.25 equiv) in DMF (40 mL) was stirred under Ar at rt for 2 h 30. The resulting residue was purified (SiO_2, Hex/EtOAc 3:7) to yield **III.42b** as a white solid (541 mg, 57 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, J = 8.7 Hz, 1H, Ar), 8.33 (s, 1H, $N_3C{=}CH$), 7.99 (m, 2H, Ar), 7.92 (d, J = 8.2 Hz, 1H, Ar), 7.81 (d, J = 8.1 Hz, 1H, Ar), 7.55 (m, 4H, Ar), 7.49 (m, 2H, Ar), 7.41 (ddd, J = 8.1 Hz, 6.9 Hz, 1.1 Hz, 1H, Ar), 7.30 (d, J = 9.1 Hz, 1H, Ar), 4.03 (s, 3H, 2-OCH_3naph). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.6 (C, Ar), 151.7 (C, $N_3C{=}CH$), 135.5 (CH, Ar), 134.1 (C, Ar), 133.0 (C, Ar), 132.1 (C, Ar), 131.0 (CH, Ar), 129.6 (C, Ar), 129.0 (CH, Ar), 128.4 (CH, Ar), 128.3 (CH, Ar), 128.1 (CH, Ar), 127.3 (CH, $N_3C{=}CH$), 127.2 (C, Ar), 125.0 (CH, Ar), 124.7 (CH, Ar), 123.7 (CH, Ar), 123.0 (CH, Ar) 121.9 (CH, Ar) 121.1 (C, Ar), 121.0 (CH, Ar), 113.2 (CH, Ar), 57.2 (2-OCH$_3$naph). **IR (KBr)** $\nu_{máx}$ 3436, 3058, 1620, 1594, 1506, 1468, 1430, 1272, 1251, 1151, 1052, 1027, 802, 772. **$[\alpha]_D^{25}$** + 229.9 (c 0.7, $CHCl_3$). **HRMS (ESI)** m/z calculated for $C_{23}H_{18}N_3O_2S$: 400.1114 $[M+H]^+$, found: 400.1130 and for $C_{23}H_{17}N_3NaO_2S$: 422.0934 $[M+Na^+]^+$, found: 422.0946. **m.p.** 140–143 °C.

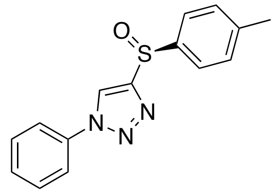
Synthesis of compound III.45



Following the general procedure a mixture of azide **II.43b** (113 mg, 0.60 mmol, 1.00 equiv), alkyne **III.29** (300 mg, 1.32 mmol, 2.20 equiv), sodium (L)-ascorbate (48 mg, 0.24 mmol, 0.40 equiv) and $CuSO_4{\cdot}5H_2O$ (30 mg, 0.12 mmol, 0.20 equiv) in DMF (10 mL) was stirred under Ar at rt for 19 h. The resulting residue was purified (SiO_2, Hex/EtOAc 2:8) to yield **III.45** as a white solid (271 mg, 70 %).

^{1}H NMR (500 MHz, CDCl$_3$) *δ* 7.80 (s, 2H, N$_3$C=CH), 7.66 (d, *J* = 8.8 Hz, 4H, *p*-BrC$_6$H$_4$), 7.63 (d, *J* = 8.8 Hz, 4H, *p*-BrC$_6$H$_4$), 7.42 (m, 2H, Ar), 7.27 (m, 2H, Ar), 5.70 (d, *J* = 15.1 Hz, 2H, NCH$_2$), 5.54 (d, *J* = 15.1 Hz, 2H, NCH$_2$). **^{13}C NMR** (125 MHz, CDCl$_3$) *δ* 153.1 (2C, N$_3$C=CH), 142.2 (2C, Ar), 132.8 (4CH, Ar), 132.5 (2C, Ar), 131.1 (2CH, Ar), 130.7 (2CH, Ar), 126.4 (2C, Ar), 126.3 (4CH, Ar), 124.2 (2CH, N$_3$C=CH), 52.0 (2NCH$_2$). **IR (KBr) ν$_{máx}$** 3437,3 3080, 1569, 1470, 1386, 1083, 1051, 1007, 816, 725, 544, 516. **$[\alpha]_D^{25}$** + 185.9 (*c* 0.8, CHCl$_3$). **HRMS (ESI)** *m/z* calculated for $C_{24}H_{19}Br_2N_6O_2S_2$: 646.9352 $[M+H]^+$, found 646.9383. **m.p.** 175–177 °C.

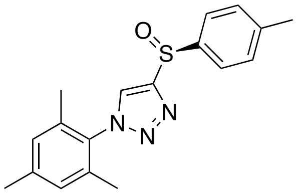
Synthesis of compound III.60a



Following the general procedure a mixture of azide **III.59a** (430 mg, 3.61 mmol, 1.30 equiv), alkyne **III.29** (456 mg, 2.78 mmol, 1.00 equiv), sodium (L)-ascorbate (275 mg, 1.38 mmol, 0.50 equiv) and CuSO$_4$·5H$_2$O (173 mg, 0.69 mmol, 0.25 equiv) in DMF (46 mL) was stirred under Ar at rt for 4 h. The resulting residue was purified (SiO$_2$, Hex/EtOAc 6:4) to yield **III.60a** as a white solid (449 mg, 57%).

^{1}H NMR (400 MHz, CDCl$_3$) *δ* 8.25 (s, 1H, N$_3$C=CH), 7.70 (d, *J* = 8.1 Hz, 2H, Ar *p*-tolyl), 7.67 (m, 2H, Ar), 7.48 (m, 3H, Ar), 7.33 (d, *J* = 8.1 Hz, 2H, Ar *p*-tolyl), 2.39 (s, 3H, CH$_3$ *p*-tolyl). **^{13}C NMR** (100 MHZ, CDCl$_3$) *δ* 154.1 (C, N$_3$C=CH), 142.4 (C, Ar), 140.0 (C, Ar), 136.5 (C, Ar), 130.3 (2CH, Ar), 130.0 (2CH, Ar), 129.6 (CH, Ar), 124.8 (2CH, Ar), 122.1 (CH, N$_3$C=CH), 120.8 (2CH, Ar), 21.6 (CH$_3$, *p*-tolyl). **IR (KBr) ν$_{máx}$** 3119, 1597, 1508, 1237, 1084, 1052, 1038, 811, 759, 686, 549, 511. **$[\alpha]_D^{25}$** + 254.8 (*c* 0.8, CHCl$_3$). **HRMS (ESI)** *m/z* calculated for $C_{15}H_{14}N_3OS$: 284.0852 $[M+H]^+$, found: 284.0859. **m.p.** 116–119 °C.

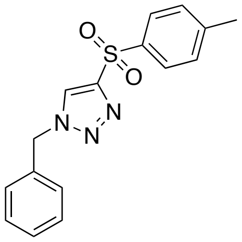
Synthesis of compound III.60b



Following the general procedure a mixture of 2,4,6-trimethylphenylazide **III.59b** (620 mg, 3.85 mmol, 1.30 equiv), alkyne **III.29** (486 mg, 2.96 mmol, 1.00 equiv), sodium (L)-ascorbate (293 mg, 1.48 mmol, 0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (185 mg, 0.74 mmol, 0.25 equiv) in DMF (49 mL) was stirred under Ar at rt for 3 h. The resulting residue was purified (SiO_2, Hex/EtOAc 8:2) to yield **III.60b** as a yellow solid (535 mg, 56%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H, $N_3C{=}CH$), 7.68 (d, J = 8.2 Hz, 2H, Ar *p*-tolyl), 7.33 (d, J = 8.2 Hz, 2H, Ar *p*-tolyl), 6.96 (s, 2H, Ar), 2.40 (s, 3H, CH_3 *p*-tolyl), 2.32 (s, 3H, CH_3), 1.89 (s, 6H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.1 (C, $N_3C{=}CH$), 142.3 (C, Ar), 140.7 (C, Ar), 140.1 (C, Ar), 134.9 (2C, Ar), 132.8 (C, Ar), 130.2 (2CH, Ar), 129.3 (2CH, Ar), 126.1 (CH, $N_3C{=}CH$), 125.0 (2CH, Ar), 21.6 (CH_3), 21.2 ($2CH_3$), 17.4 (CH_3, *p*-tolyl). $[\alpha]_D^{25}$ + 180.5 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{18}H_{19}N_3NaOS$: 348.1160 $[M+Na]^+$, found: 348.1147. **m.p.** 67–70 °C.

Synthesis of compound III.48

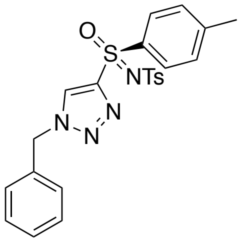


In a bottom flask, triazole **III.30** (90 mg, 0.30 mmol, 1.00 equiv) and mcpba (105 mg, 0.61 mmol, 2.00 equiv) were dissolved in $CHCl_3$ (5 mL) 1 h at rt. The reaction was quenched with $Na_2S_2O_3$ 0.5 M. The crude reaction was extracted twice with CH_2Cl_2.

The organic layers were washed with NaOH 1.0 M and the combined aqueous phases were again extracted three times with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered and the solvent was removed under vacuum to afford the corresponding reaction product **III.48** as a white solid (94 mg, quantitative). No further purifications were needed.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H, N_3C=CH), 8.22 (d, J = 8.1 Hz, 2H, Ar *p*-tolyl), 7.68 (br s, 3H, Ar), 7.61 (d, J = 8.1 Hz, 2H, Ar *p*-tolyl), 7.58 (br s, 2H, Ar), 5.81 (s, 2H, NCH_2), 2.69 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.7 (C, N_3C=CH), 145.2 (C, Ar), 137.1 (C, Ar), 133.1 (C, Ar), 130.1 (2CH, Ar), 129.5 (3CH, Ar), 128.7 (2CH, Ar), 128.2 (2CH, Ar), 125.6 (CH, N_3C=CH), 55.0 (NCH_2), 21.8 (CH_3, *p*-tolyl). **IR (KBr) $\nu_{\text{máx}}$** 2963, 2924, 1769, 1698, 1428, 1324, 1262, 1100, 802, 720, 598. **HRMS (ESI)** *m/z* calculated for $C_{16}H_{16}N_3O_2S$: 314.0958 $[M+H]^+$, found 314.0955. **m.p.** 140–143 °C.

Synthesis of compound III.51

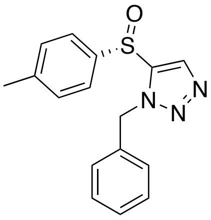


To a suspension of triazole **III.30** (56 mg, 0.19 mmol, 1.00 equiv) in anhydrous CH_3CN (4.5 mL) under Ar, $Cu(OTf)_2$ (17 mg, 0.05 mmol, 0.25 equiv) was added. After 5 min of stirring, PhI=NTs (133 mg, 0.36 mmol, 1.90 equiv) was added to form a greenish solution. After one hour of stirring, a white solid was formed. The reaction was stirred for more 5 h until it was completed. The solvent was removed under vacuum. The resulting residue was purified (SiO_2, CH_2Cl_2/EtOAc, 97:3) to yield **III.51** as a colourless oil (72 mg, 82%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (s, 1H, N_3C=CH), 7.95 (d, J = 8.3 Hz, 2H, Ar *p*-tolyl), 7.80 (d, J = 8.3 Hz, 2H, Ar *p*-tolyl), 7.39 (m, 3H, Ar), 7.30 (m, 4H, Ar), 7.20 (d, J =

8.3 Hz, 2H, Ar *p*-tolyl), 5.54 (d, *J* = 11.6 Hz, 2H, NCH_2), 5.51 (d, *J* = 11.6 Hz, 2H, NCH_2), 2.40 (s, 3H, CH_3 *p*-tolyl), 2.37 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.5 (C, $N_3C{=}CH$), 145.9 (C, Ar), 143.1 (C, Ar), 140.5 (C, Ar), 134.6 (C, Ar), 133.0 (C, Ar), 130.2 (2CH, Ar), 129.6 (2CH, Ar), 129.5 (CH, Ar), 129.4 (2CH, Ar), 128.7 (2CH, Ar), 128.4 (2CH, Ar), 127.4 (CH, $N_3C{=}CH$), 126.8 (2CH, Ar), 55.1 (NCH_2), 21.8 (CH_3, *p*-tolyl), 21.6 (CH_3, *p*-tolyl). **IR (film)** $\nu_{máx}$ 3137, 3063, 1595, 1497, 1456, 1320, 1305, 1247, 1155, 1089, 1070, 1040, 814, 737. **$[\alpha]_D^{25}$** – 19.6 (*c* 0.8, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{23}H_{23}N_4O_3S_2$: 467.1206 $[M+H]^+$, found 467.1196.

Synthesis of compound III.55



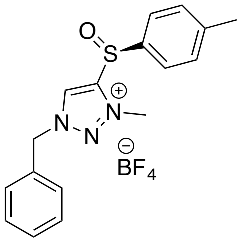
To a mixture of benzyl azide **II.37** (243 mg, 1.83 mmol, 1.50 equiv) and alkyne **III.29** (200 mg, 1.22 mmol, 1.00 equiv) in 1,4-dioxane (6 mL), [Cp*RuCl(cod)] (69 mg, 0.18 mmol, 0.15 equiv) was added and the reaction mixture was stirred under Ar at rt for 4 days. Solvent was removed under vacuum and the resulting residue was analysed by ^{1}H NMR showing a mixture of the two possible regioisomers in a ratio of 1:1. The crude products were separated and purified (SiO_2, Hex/EtOAc 3:7) to yield **III.55** as a white solid (35 mg, 10%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (s, 1H, $N_3C{=}CH$), 7.38 (d, *J* = 8.3 Hz, 2H, Ar *p*-tolyl), 7.29 (m, 3H, Ar), 7.25 (br d, *J* = 8.2 Hz, 2H, Ar *p*-tolyl), 7.20 (m, 2H, Ar), 5.74 (d, *J* = 15.2 Hz, 1H, NCH_2), 5.70 (d, *J* = 15.2 Hz, 1H, NCH_2), 2.39 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.1 (C, Ar), 139.7 ($N_3C{=}CH$), 137.6 (C, Ar), 135.3 (CH, $N_3C{=}CH$), 133.9 (C, Ar), 130.4 (2CH, Ar), 129.0 (2CH, Ar), 128.7 (CH, Ar), 128.1 (2CH, Ar), 125.1 (2CH, Ar), 53.2 (NCH_2), 21.6 (CH_3, *p*-tolyl). **IR (KBr)** $\nu_{máx}$ 3017, 3036, 2930, 1473, 1455, 1267, 1087, 1053, 869, 810, 723. **$[\alpha]_D^{25}$** + 57.5 (*c* 0.4, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{16}H_{16}N_3OS$: 298.1009 $[M+H]^+$, found: 298.1009. **m.p.** 77–79 °C.

General procedure for the synthesis of triazolium salts using Me_3OBF_4 as alkylating agent

Triazole and Meerwein's salt were stirred under Ar at rt in CH_2Cl_2 until complete consumption of the starting material (^1H NMR analysis). The reaction was quenched with methanol and filtered through a short pad of $NaHCO_3$. The solvent was removed under vacuum to afford the corresponding reaction product without further purification. In some cases, the product was washed with a mixture of CH_2Cl_2:pentane to remove starting material traces.

Synthesis of compound III.31

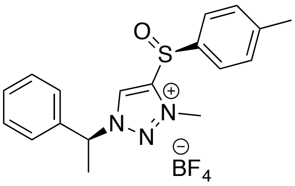


Following the general procedure a mixture of **III.30** (72 mg, 0.24 mmol, 1.00 equiv) and Me_3OBF_4 (47 mg, 0.31 mmol, 1.30 equiv) in CH_2Cl_2 (16 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **III.31** as a white solid (94 mg, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H, $N_3C{=}CH$), 7.72 (d, *J* = 8.3 Hz, 2H, Ar *p*-tolyl), 7.47 (m, 2H, Ar), 7.39 (m, 5H, 3H Ar and 2H Ar *p*-tolyl), 5.74 (d, *J* = 14.4 Hz, 1H, NCH_2), 5.70 (d, *J* = 14.4 Hz, 1H, NCH_2), 4.28 (s, 3H, NCH_3), 2.40 (s, 3H, CH_3 *p*-tolyl). **^{13}C**

NMR (100 MHz, CDCl$_3$) *δ* 145.8 (C, N$_3$C=CH), 145.0 (C, Ar), 134.5 (C, Ar), 131.3 (2CH, Ar), 131.1 (CH, N$_3$C=CH), 130.8 (C, Ar) 130.2 (CH, Ar), 129.9 (2CH, Ar), 129.6 (2CH, Ar), 125.6 (2CH, Ar), 58.4 (NCH$_2$), 39.6 (NCH$_3$), 21.7 (CH$_3$, *p*-tolyl). **IR (KBr) ν$_{\text{máx}}$** 3420, 3147, 2923, 1060, 809, 737. **$[\alpha]_D^{25}$** + 32.4 (*c* 0.2, CHCl$_3$). **HRMS (ESI)** *m/z* calculated for C$_{17}$H$_{18}$N$_3$OS: 312.1165 [M–BF$_4^-$]$^+$, found: 312.1175. **m.p.** 115–118 °C.

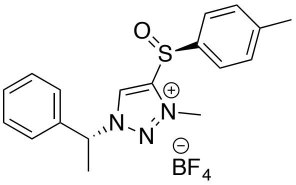
Synthesis of compound III.35a



Following the general procedure a mixture of **III.34a** (350 mg, 1.12 mmol, 1.00 equiv) and Me$_3$OBF$_4$ (216 mg, 1.46 mmol, 1.30 equiv) in CH$_2$Cl$_2$ (35 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of NaHCO$_3$. The solvent was removed under vacuum to yield **III.35a** as a white solid (421 mg, 91%).

^{1}H NMR (400 MHz, CDCl$_3$) *δ* 8.48 (s, 1H, N$_3$C=CH), 7.72 (d, *J* = 8.0 Hz, 2H, Ar *p*-tolyl), 7.39 (m, 7H, 5H Ar and 2H Ar *p*-tolyl), 6.08 (q, *J* = 7.0 Hz, 1H, CH), 4.27 (s, 3H, NCH$_3$), 2.38 (s, 3H, CH$_3$ *p*-tolyl), 2.02 (d, *J* = 7.0 Hz, 3H, CH$_3$). **^{13}C NMR** (100 MHz, CDCl$_3$) *δ* 145.4 (C, N$_3$C=CH), 144.6 (C, Ar), 136.2 (C, Ar), 134.9 (C, Ar), 131.2 (2CH, Ar), 130.3 (CH, N$_3$C=CH), 130.0 (CH, Ar), 129.5 (2CH, Ar), 127.5 (2CH, Ar), 125.5 (2CH, Ar), 66.2 (CH), 39.7 (NCH$_3$), 21.6 (CH$_3$, *p*-tolyl), 20.3 (CH$_3$). **IR (KBr) ν$_{\text{máx}}$** 3434, 3130, 3039, 1594, 1496, 1458, 1058, 814, 732, 705, 521. **$[\alpha]_D^{25}$** + 3.6 (*c* 1.0, CHCl$_3$). **HRMS (ESI)** *m/z* calculated for C$_{18}$H$_{20}$N$_3$OS: 321.1322 [M–BF$_4^-$]$^+$, found: 326.1308. **m.p.** 56–59 °C.

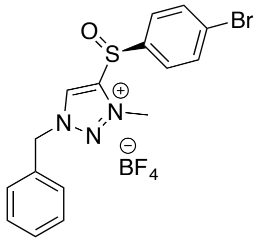
Synthesis of compound III.35b



Following the general procedure a mixture of **III.34b** (274 mg, 0.88 mmol, 1.00 equiv) and Me_3OBF_4 (169 mg, 1.14 mmol, 1.30 equiv) in CH_2Cl_2 (27 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **III.35b** as a white solid (307 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.43 (s, 1H, N_3C=CH), 7.73 (d, *J* = 8.0 Hz, 2H, Ar *p*-tolyl), 7.38 (m, 7H, 5H Ar and 2H Ar *p*-tolyl), 6.04 (q, *J* = 6.8 Hz, 1H, CH), 4.30 (s, 3H, NCH_3), 2.38 (s, 3H, CH_3 *p*-tolyl), 2.00 (d, *J* = 6.8 Hz, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 145.9 (C, N_3C=CH), 144.7 (C, Ar), 136.1 (C, Ar), 134.7 (C, Ar), 131.1 (2CH, Ar), 130.2 (CH, N_3C=CH), 129.9 (CH, Ar), 129.4 (2CH, Ar), 127.5 (2CH, Ar), 125.6 (2CH, Ar), 66.1 (CH), 39.7 (NCH_3), 21.6 (CH_3, *p*-tolyl), 20.4 (CH_3). **IR (KBr)** $\nu_{máx}$ 3427, 3127, 3039, 1594, 1496, 1457, 1249, 1087, 1058, 814, 734, 704, 521. $[\alpha]_D^{25}$ + 146.2 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{18}H_{20}N_3OS$: 321.1322 $[M–BF_4^-]^+$, found: 326.1315. **m.p.** below 30°C.

Synthesis of compound III.39a

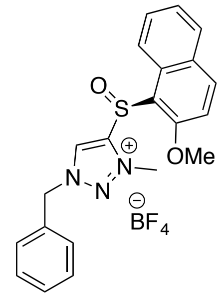


Following the general procedure a mixture of **III.38a** (100 mg, 0.28 mmol, 1.00 equiv) and Me_3OBF_4 (61 mg, 0.41 mmol, 1.50 equiv) in CH_2Cl_2 (17 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol (5 equiv). The solvent was removed under vacuum. The crude product was precipitate in Et_2O to yield **III.39a** as a white solid (114 mg, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.55 (s, 1H, N_3C=CH), 7.75 (s, 4H, Ar *p*-BrC_6H_4), 7.47 (m, 2H, Ar), 7.40 (m, 3H, Ar), 5.75 (d, *J* = 14.5 Hz, 1H, NCH_2), 5.71 (d, *J* = 14.5 Hz, 1H,

NCH_2), 4.31 (s, 3H, NCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.0 (C, N_3C=CH), 137.2 (C, Ar), 133.9 (2CH, Ar), 131.5 (CH, N_3C=CH), 130.6 (C, Ar), 130.3 (CH, Ar), 129.9 (2CH, Ar), 129.7 (2CH, Ar), 128.6 (C, Ar), 127.1 (2CH, Ar), 58.6 (NCH_2), 39.8 (NCH_3). **IR (KBr)** $\nu_{\text{máx}}$ 3430, 3128, 1568, 1499, 1389, 1085, 1065, 822, 738. **$[\alpha]_D^{25}$** - 19.6 (*c* 0.8, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{16}H_{15}BrN_3OS$: 378.0094 $[M–BF_4^-]^+$, found: 378.0097. **m.p.** 136–138 °C.

Synthesis of compound III.39b

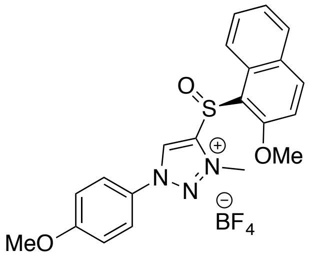


Following the general procedure a mixture of **III.38b** (250 mg, 0.69 mmol, 1.00 equiv) and Me_3OBF_4 (132 mg, 0.89 mmol, 1.30 equiv) in CH_2Cl_2 (22 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **III.39b** as a white solid (321 mg, quantitative).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H, N_3C=CH), 8.48 (dd, *J* = 8.8 Hz, 0.8 Hz, 1H, Ar), 8.06 (d, *J* = 9.1 Hz, 1H, Ar), 7.78 (d, *J* = 8.1 Hz, 1H, Ar), 7.55 (ddd, *J* = 8.5 Hz, 7.0 Hz, 1.4 Hz, 1H, Ar), 7.41 (m, 2H, Ar), 7.36 (ddd, *J* = 8.1 Hz, 6.9 Hz, 1.1 Hz, 1H, Ar), 7.31 (m, 4H, Ar), 5.65 (d, *J* = 14.4 Hz, 1H, NCH_2), 5.61 (d, *J* = 14.4 Hz, 1H, NCH_2), 4.15 (s, 3H, NCH_3), 3.93 (s, 3H, 2-OCH_3naph). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.0 (C, Ar), 146.1 (C, N_3C=CH), 138.4 (CH, Ar), 132.0 (C, Ar), 131.6 (C, Ar), 131.1 (CH, N_3C=CH), 130.3 (CH, Ar), 130.1 (CH, Ar), 130.0 (2CH, Ar), 129.8 (CH, Ar), 129.7 (2CH, Ar), 129.3 (C, Ar), 125.5 (CH, Ar), 121.5 (CH, Ar), 116.3 (C, Ar), 113.6 (CH, Ar), 58.3 (NCH_2), 57.4 (2-O*C*H_3naph), 39.9 (NCH_3). **IR (KBr):** $\nu_{\text{máx}}$ 3435, 3134, 1620, 1593, 1508, 1471, 1278, 1255, 1062, 820,

739. **$[\alpha]_D^{25}$** + 94.5 (*c* 0.2, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{21}H_{20}N_3O_2S$: 378.1271 $[M–BF_4^-]^+$, found: 378.1275. **m.p.** 79–82 °C.

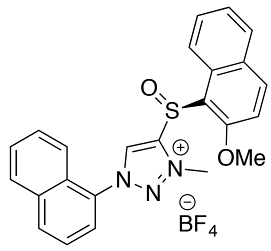
Synthesis of compound III.43a



Following the general procedure a mixture of **III.42a** (300 mg, 0.79 mmol, 1.00 equiv) and Me_3OBF_4 (152 mg, 1.03 mmol, 1.30 equiv) in CH_2Cl_2 (26 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **III.43a** as a white solid (366 mg, 96%).

^{1}H NMR (400 MHz, DMSO-*d*$_6$) *δ* 9.86 (s, 1H, $N_3C=CH$), 8.67 (dd, *J* = 8.4 Hz, 0.8 Hz, 1H, Ar), 8.39 (d, *J* = 9.0 Hz, 1H, Ar), 8.08 (dt, *J* = 8.0 Hz, 1.2 Hz, 1H, Ar), 7.89 (d, *J* = 9.2 Hz, 1H, Ar *p*-$OCH_3C_6H_4$), 7.69 (m, 2H, Ar), 7.54 (ddd, *J* = 8.1 Hz, 6.9 Hz, 1.0 Hz, 1H, Ar), 7.22 (d, *J* = 9.2 Hz, 2H, Ar *p*-$OCH_3C_6H_4$), 4.36 (s, 3H, NCH_3), 4.10 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3). **^{13}C NMR** (125 MHz, DMSO-*d*$_6$) *δ* 161.6 (C, Ar), 158.5 (C, Ar), 145.6 (C, $N_3C=C$), 137.7 (CH, Ar), 130.7 (C, Ar), 129.5 (CH, Ar), 129.2 (C, Ar), 129.0 (CH, Ar), 128.7 (CH, $N_3C=C$), 127.6 (C, Ar), 124.9 (CH, Ar) 123.3 (2CH, Ar), 121.9 (CH, Ar), 116.3 (C, Ar), 115.3 (2CH, Ar), 114.1 (CH, Ar), 57.3 (CH_3, 2-O*C*H_3naph), 56.0 (CH_3, *p*-O*C*$H_3C_6H_4$), 39.5 (NCH_3 overlaped with DMSO-*d*$_6$). **IR (KBr)** **$\nu_{máx}$** 3436, 3120, 1594, 1509, 1470, 1276, 1256, 1183, 1059, 835, 820, 755, 608. **$[\alpha]_D^{25}$** + 273.3 (*c* 0.5, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{21}H_{20}N_3O_3S$: 394.1220 $[M–BF_4^-]^+$, found: 394.1220. **m.p.** 97–100 °C.

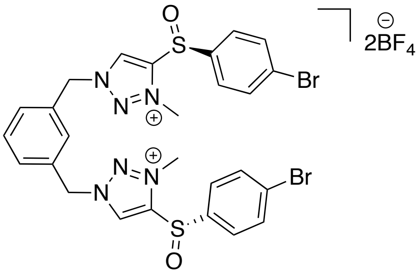
Synthesis of compound III.43b



Following the general procedure a mixture of **III.42b** (400 mg, 1.00 mmol, 1.00 equiv) and Me_3OBF_4 (193 mg, 1.30 mmol, 1.30 equiv) in CH_2Cl_2 (30 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **III.43b** as a white solid (501 mg, quantitative).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.48 (d, *J* = 8.6 Hz, 1H, Ar), 8.33 (s, 1H, N_3C=CH), 8.07 (d, *J* = 9.2 Hz, 1H, Ar), 7.94 (d, *J* = 8.2 Hz, 1H, Ar), 7.83 (m, 2 H, Ar), 7.74 (d, *J* = 8.1 Hz, 1H, Ar), 7.53 (m, 3H, Ar), 7.43 (m, 2H, Ar), 7.32 (m, 2H, Ar), 4.34 (s, 3H, NCH_3), 4.01 (s, 3H, 2-OCH_3naph). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 159.2 (C, Ar), 146.9 (C, N_3C=CH), 138.2 (CH, Ar), 133.8 (C, Ar), 133.0 (CH, Ar), 132.3 (CH, N_3C=CH), 131.6 (C, Ar), 130.6 (C, Ar), 129.7 (CH, Ar), 129.6 (CH, Ar), 129.3 (CH, Ar), 129.1 (C, Ar), 128.7 (CH, Ar), 127.8 (CH, Ar), 126.7 (C, Ar), 125.5 (CH, Ar), 125.2 (CH, Ar), 125.1 (CH, Ar), 121.5 (CH, Ar), 120.5 (CH, Ar), 116.1 (C, Ar), 113.6 (CH, Ar), 57.3 (2-O*C*H_3naph), 40.1 (NCH_3). **IR (KBr)** **$\nu_{máx}$** 3435, 3066, 2950, 1593, 1508, 1470, 1277, 1254, 1059, 806, 772, 651, 461. **$[\alpha]_D^{25}$** + 174.3 (*c* 0.8, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{24}H_{20}N_3O_2S$: 414.1271 $[M–BF_4^-]^+$, found: 414.1281. **m.p.** 109–112 °C.

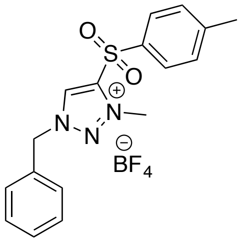
Synthesis of compound III.46



Following the general procedure a mixture of **III.45** (130 mg, 0.20 mmol, 1.00 equiv) and Me_3OBF_4 (89 mg, 0.60 mmol, 3.00 equiv) in CH_2Cl_2 (12 mL) was stirred under Ar at rt for 5h. The reaction was quenched with methanol and the solid residue was washed with Et_2O. The solvent was removed under vacuum to yield **III.46** as a light yellow solid (160 mg, 94%).

^{1}H NMR (400 MHz, Acetone-*d*$_6$) *δ* 9.02 (s, 2H, N_3C=CH), 7.89 (d, *J* = 3.0 Hz, 8H, Ar *p*-BrC_6H_4), 7.61 (m, 2H, Ar), 7.54 (m, 2H, Ar), 6.14 (s, 4H, NCH_2), 4.48 (s, 6H, NCH_3). **^{13}C NMR** (100 MHz, Acetone-*d*$_6$) *δ* 146.6 (2C, N_3C=CH), 139.8 (2C, Ar), 134.2 (4CH, Ar), 132.6 (2CH, Ar), 132.5 (2CH, N_3C=CH), 132.0 (2C, Ar), 131.7 (2CH, Ar), 128.4 (4CH, Ar), 128.2 (2C, Ar), 55.5 (2NCH_2), 40.4 (2NCH_3). **IR (KBr) ν$_{máx}$** 3417, 1618, 1083, 802, 623, 534, 522. **$[\alpha]_D^{25}$** + 62.8 (*c* 0.98, acetone). **HRMS (ESI)** *m/z* calculated for $C_{26}H_{24}BBr_2F_4N_6O_2S_2$: 762.9778 $[M–BF_4^-]^+$, found: 762.9798 and for $C_{26}H_{24}Br_2N_6O_2S_2$: 337.9869 $[M–2BF_4^-]^{+2}$, found: 337.9882. **m.p.** 131–133 °C.

Synthesis of compound III.49

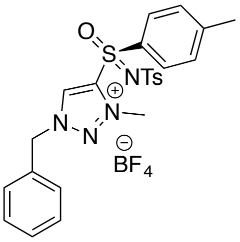


Following the general procedure a mixture of **III.48** (70 mg, 0.22 mmol, 1.00 equiv) and Me_3OBF_4 (43 mg, 0.29 mmol, 1.30 equiv) in CH_2Cl_2 (7 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **III.49** as a white solid (91 mg, quantitative).

^{1}H NMR (400 MHZ, DMSO-*d*$_6$) *δ* 9.82 (s, 1H, N_3C=CH), 8.06 (d, *J* = 8.4 Hz, 2H, Ar *p*-tolyl), 7.60 (d, *J* = 8.4 Hz, 2H, Ar *p*-tolyl), 7.51 (m, 2H, Ar), 7.45 (m, 3H, Ar), 5.85 (s, 2H, NCH_2), 4.37 (s, 3H, NCH_3), 2.46 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHZ, DMSO-*d*$_6$) *δ*

147.8 (C, Ar), 141.1 (C, N_3C=CH), 134.2 (CH, N_3C=CH), 133.7 (C, Ar), 132.0 (C, Ar), 130.9 (2CH, Ar), 129.4 (CH, Ar), 129.3 (2CH, Ar), 129.1 (2CH, Ar), 129.0 (2CH, Ar), 57.1 (NCH_2), 40.2 (NCH_3), 21.3 (CH_3, *p*-tolyl). **IR (KBr) $\nu_{máx}$** 3420, 1594, 1456, 1353, 1169, 1083, 813, 738, 690, 651, 597, 534. **HRMS (ESI)** *m/z* calculated for $C_{17}H_{18}N_3O_2S$: 328.1114 $[M–BF_4^-]^+$, found: 328.1123. **m.p.** 180–183 °C.

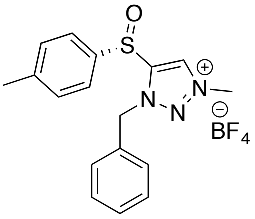
Synthesis of compound III.52



Following the general procedure a mixture of **III.51** (72 mg, 0.15 mmol, 1.00 equiv) and Me_3OBF_4 (34 mg, 0.23 mmol, 1.50 equiv) in CH_2Cl_2 (10 mL) was stirred under Ar at rt for 5h. The reaction was quenched with methanol. The solvent was removed under vacuum. The resulting residue was purified (SiO_2, MeOH/CH_2Cl_2 5%) to yield **III.52** as a colourless oil (78 mg, 89 %).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.72 (s, 1H, N_3C=CH), 8.05 (d, *J* = 8.5 Hz, 2H, Ar *p*-tolyl), 7.76 (d, *J* = 8.5 Hz, 2H, Ar *p*-tolyl), 7.50 (m, 7H, Ar), 7.28 (d, *J* = 8.0 Hz, 2H, Ar *p*-tolyl), 5.87 (d, *J* = 14.5 Hz, 1H, NCH_2), 5.79 (d, *J* = 14.5 Hz, 1H, NCH_2), 4.37 (s, 3H, NCH_3), 2.43 (s, 3H, CH_3 *p*-tolyl), 2.41 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 149.5 (C, Ar), 144.8 (C, Ar), 141.8 (C, N_3C=CH), 138.5 (C Ar), 134.1 (CH, N_3C=CH), 134.0 (C, Ar), 131.6 (2CH, Ar), 130.6 (CH, Ar), 130.1 (2CH, Ar), 129.9 (3CH, Ar), 129.6 (2CH, Ar), 129.3 (CH, Ar), 126.9 (2CH, Ar), 59.1 (NCH_2), 40.5 (NCH_3), 22.1 (CH_3, *p*-tolyl), 21.8 (CH_3, *p*-tolyl). **IR (film) $\nu_{máx}$** 3640, 3125, 2926, 1593, 1458, 1330, 1267, 1159, 1067, 815, 734. **$[\alpha]_D^{25}$** + 117.3 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{24}H_{25}N_4O_3S_2$: 481.1377 $[M–BF_4^-]^+$, found: 481.1368.

Synthesis of compound III.56



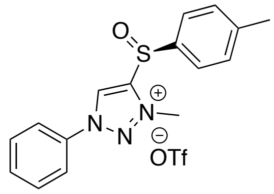
Following the general procedure a mixture of **III.55** (35 mg, 0.12 mmol, 1.00 equiv) and Me_3OBF_4 (23 mg, 0.15 mmol, 1.50 equiv) in CH_2Cl_2 (6 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol. The solvent was removed under vacuum to yield **III.56** as a colourless oil (35 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1 H, N_3C=CH), 7.54 (s, 4H, Ar *p*-tolyl), 7.30 (m, 5H, 3H Ar and 2H Ar *p*-tolyl), 7.21 (m, 2H, Ar), 5.78 (s, 2H, NCH_2), 4.23 (s, 3H, NCH_3), 2.32 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 146.0 (C, N_3C=CH), 144.8 (C, Ar), 135.4 (C, Ar), 132.5 (CH, N_3C=CH), 131.2 (2CH, Ar), 130.5 (C, Ar), 129.9 (CH, Ar), 129.4 (2CH, Ar), 129.1 (2CH, Ar), 125.7 (2CH, Ar), 56.7 (NCH_3), 41.2 (NCH_2), 21.7 (CH_3, *p*-tolyl). **$[\alpha]_D^{25}$** + 144.3 (*c* 1.2, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{17}H_{18}N_3OS$: 312.11706 $[M–BF_4^-]^+$, found: 312.11653.

General procedure for the synthesis of triazolium salts using Me_3OTf as alkylating agent

Triazole (1.00 equiv) was dissolved in CH_2Cl_2. The reaction was cooled at 0 °C. Methyl triflate (2.00 equiv) was added and the reaction was stirred at rt overnight. Volatiles were removed under vacuum to afford the corresponding reaction products without further purification.

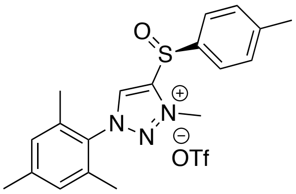
Synthesis of compound III.61a



Following the general procedure a mixture of **III.60a** (300 mg, 1.06 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (24 mL). MeOTf (348 mg, 2.11 mmol, 2.00 equiv) was added at 0 °C and stirred at rt overnight. The solvent was removed under vacuum to yield **III.61a** as a white solid (570 mg, quantitative).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.90 (s, 1H, $N_3C{=}CH$), 7.88 (d, *J* = 8.3 Hz, 2H, Ar p-tolyl), 7.84 (m, 2H), 7.54 (m, 3H), 7.43 (d, *J* = 8.0 Hz, 2H, Ar *p*-tolyl), 4.48 (s, 3H, NCH_3), 2.42 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 147.3 (C, $N_3C{=}CH$), 145.0 (C, Ar), 134.9 (C, Ar), 134.6 (C, Ar), 132.5 (CH, Ar), 131.3 (2CH, Ar), 130.5 (2CH, Ar), 129.2 (CH, $N_3C{=}CH$), 125.8 (2CH, Ar), 122.2 (2CH, Ar), 40.2 (NCH_3), 21.7 (CH_3, *p*-tolyl). **HRMS (ESI)** m/z calculated for $C_{16}H_{16}N_3OS$: 298.1014 $[M{-}OTf^-]^+$, found: 298.1012.

Synthesis of compound III.61b



Following the general procedure a mixture of triazole **III.60b** (535 mg, 1.65 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (46 mL). MeOTf (540 mg, 3.30 mmol, 2.00 equiv) was added at 0 °C and stirred at rt overnight. The solvent was removed under vacuum. The residue was purified (SiO_2, MeOH/CH_2Cl_2 2%) to yield **III.61b** as a white solid (438 mg, 55%).

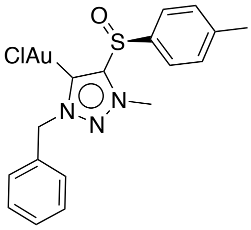
^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.98 (s, 1H, $N_3C{=}CH$), 7.97 (d, *J* = 8.2 Hz, 2H, Ar *p*-

tolyl), 7.46 (d, *J* = 8.2 Hz, 2H, Ar *p*-tolyl), 7.00 (s, 2H, Ar), 4.67 (s, 3H, NCH_3), 2.45 (s, 3H, CH_3 *p*-tolyl), 2.33 (s, 3H, CH_3), 2.02 (s, 6H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.8 (C, N_3C=CH), 144.9 (C, Ar), 143.2 (C, Ar), 135.0 (C, Ar), 134.5 (2C, Ar), 132.0 (CH, N_3C=CH), 131.3 (2CH, Ar), 130.9 (C, Ar), 130.1 (CH, Ar), 125.8 (2CH, Ar), 40.5 (NCH_3) 21.8 (CH_3, *p*-tolyl), 21.3 ($2CH_3$), 17.4 ($2CH_3$). **$[\alpha]_D^{25}$** + 83.7 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{19}H_{22}N_3OS$: 340.1484 $[M–OTf^-]^+$, found: 348.1497.

General procedure for the synthesis of gold carbenes

In a schlenk flask charged with 4 Å molecular sieves, a mixture of triazolium salt (1.00 equiv), NMe_4Cl (1.50 equiv) and Ag_2O (0.75 equiv) was stirred at rt in the dark in $CH_3CN:CH_2Cl_2$ until the formation of the silver carbene (^{1}H NMR analysis). The [AuCl(SMe_2)] (1.00 equiv) was added and the reaction was stirred at rt until completion of the reaction (^{1}H NMR analysis). The reaction was filtered through a pad of Celite and the solvents were removed under vacuum to afford the corresponding reaction products, which were purified through a short pad of SiO_2.

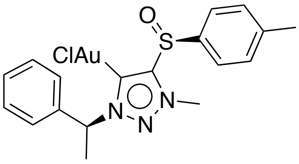
Synthesis of compound III.32



Following the general procedure a mixture of **III.31** (255 mg, 0.64 mmol, 1.00 equiv), NMe_4Cl (105 mg, 0.96 mmol, 1.50 equiv) and Ag_2O (111 mg, 0.48 mmol, 0.75 equiv) in $CH_3CN:CH_2Cl_2$ 1:1 (13 mL) was stirred under Ar at rt for 3 h. [AuCl(SMe_2)] (188 mg, 0.64 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, Hex/EtOAc 3:7) to yield **III.32** as a white solid (243 mg, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.67 (d, *J* = 7.9 Hz, 2H, Ar *p*-tolyl), 7.52 (m, 2H, Ar), 7.37 (m, 5H, 3H Ar and 2H *p*-tolyl), 5.67 (d, *J* = 14 Hz, 1H, NCH_2), 5.61 (d, *J* = 14 Hz, 1H, NCH_2), 4.15 (s, 3H, NCH_3), 2.41 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 160.7 (C, N_3C=*C*Au), 146.8 (C, N_3*C*=CAu), 143.1 (C, Ar), 136.9 (C, Ar), 132.8 (C, Ar), 130.8 (2CH, Ar), 129.7 (CH, Ar), 129.4 (2CH, Ar), 129.2 (2CH, Ar), 124.5 (2CH, Ar), 59.8 (NCH_2), 38.5 (NCH_3), 21.6 (CH_3, *p*-tolyl). **IR (KBr) ν_{máx}** 3436, 3031, 2920, 1491, 1455, 1426, 1321, 1084, 1053, 811, 748, 709, 566. **$[\alpha]_D^{25}$** – 170.8 (*c* 0.5, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{17}H_{17}AuN_3OS$: 508.0752 $[M–Cl^-]^+$, found: 508.0756. **m.p.** decomposes before melting.

Synthesis of compound III.36a

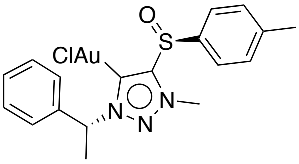


Following the general procedure a mixture of **III.35a** (300 mg, 0.73 mmol, 1.00 equiv), NMe_4Cl (119 mg, 1.09 mmol, 1.50 equiv) and Ag_2O (126 mg, 0.54 mmol, 0.75 equiv) in $CH_3CN:CH_2Cl_2$ 1:10 (35 mL) was stirred under Ar at rt overnight. $[AuCl(SMe_2)]$ (213 mg, 0.73 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, $MeOH/CH_2Cl_2$ 2%) to yield **III.36a** as a white solid (354 mg, 87%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.69 (d, *J* = 8.3 Hz, 2H, Ar *p*-tolyl), 7.48 (m, 2H, Ar), 7.36 (m, 5H, 3H Ar and 2H Ar *p*-tolyl), 6.23 (q, *J* = 7.1 Hz, 1H, CH), 4.14 (s, 3H, NCH_3), 2.42 (s, 3H, CH_3 *p*-tolyl), 1.99 (d, *J* = 7.1 Hz, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 160.2 (C, N_3C=*C*Au), 146.4 (C, N_3*C*=CAu), 143.0 (C, Ar), 137.7 (C, Ar), 136.9 (C, Ar), 130.7 (2CH, Ar), 129.5 (CH, Ar), 129.2 (2CH, Ar), 127.2 (2CH, Ar), 124.5 (2CH, Ar), 66.8 (CH), 38.6 (NCH_3), 21.6 (CH_3, *p*-tolyl), 20.7 (CH_3). **IR (KBr) ν_{máx}** 3032, 2982, 1594, 1492, 1451, 1425, 1381, 1333, 1237, 1083, 1049, 813, 757, 709, 540. **$[\alpha]_D^{25}$** – 246.4 (*c* 1.0, $CHCl_3$).

HRMS (ESI) *m*/*z* calculated for $C_{18}H_{19}AuN_3OS$: 522.0909 $[M–Cl^-]^+$, found: 522.0929. **m.p.** decomposes before melting.

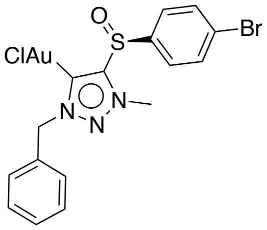
Synthesis of compound III.36b



Following the general procedure a mixture of **III.35b** (206 mg, 0.50 mmol, 1.00 equiv), NMe_4Cl (82 mg, 0.75 mmol, 1.50 equiv) and Ag_2O (87 mg, 0.37 mmol, 0.75 equiv) in $CH_3CN:CH_2Cl_2$ 1:10 (24 mL) was stirred under Ar at rt overnight. $[AuCl(SMe_2)]$ (147 mg, 0.50 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, $MeOH/CH_2Cl_2$ 1%) to yield **III.36b** as a white solid (220 mg, 79 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.6 Hz, 2H, Ar *p*-tolyl), 7.48 (m, 2H, Ar), 7.35 (m, 5H, 3H Ar and 2H Ar *p*-tolyl), 6.28 (q, *J* = 7.1 Hz, 1H, CH), 4.15 (s, 3H, NCH_3), 2.39 (s, 3H, CH_3 *p*-tolyl), 2.02 (d, *J* = 7.1 Hz, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.0 (C, N_3C=*C*Au), 146.5 (C, N_3*C*=CAu), 143.0 (C, Ar), 137.4 (C, Ar), 136.8 (C, Ar), 130.7 (2CH, Ar), 129.5 (CH, Ar), 129.2 (2CH, Ar), 127.5 (2CH, Ar), 124.5 (2CH, Ar), 66.7 (CH), 38.6 (NCH_3), 21.6 (CH_3, *p*-tolyl), 21.0 (CH_3). **IR (KBr)** $\nu_{máx}$ 3032, 2982, 1593, 1491, 1456, 1424, 1381, 1326, 1083, 1052, 809, 754, 709, 562, 542. $[\alpha]_D^{25}$ – 141.8 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{18}H_{19}AuN_3OS$: 522.0909 $[M–Cl^-]^+$, found: 522.0899. **m.p.** decomposes before melting.

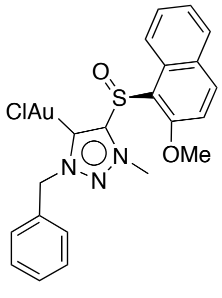
Synthesis of compound III.40a



Following the general procedure a mixture of **III.39a** (70 mg, 0.15 mmol, 1.00 equiv), NMe_4Cl (37 mg, 0.34 mmol, 2.25 equiv) and Ag_2O (39 mg, 0.17 mmol, 1.13 equiv) in CH_3CN:CH_2Cl_2 1:10 (5.5 mL) was stirred under Ar at rt for 3 days. [AuCl(SMe_2)] (45 mg, 0.15 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, hexane:EtAcO 4:6) to yield **III.40a** as a white solid (61 mg, 66 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 4H, Ar *p*-BrC_6H_4), 7.52 (m, 2H, Ar), 7.39 (m, 3H, Ar), 5.68 (d, *J* = 14.0 Hz, 1H, NCH_2), 5.62 (d, *J* = 14.0 Hz, 1H, NCH_2), 4.15 (s, 3H, NCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.9 (C, N_3C=*C*Au), 145.9 (C, N_3*C*=CAu), 139.4 (C, Ar), 133.3 (2CH, Ar), 132.6 (C, Ar), 129.8 (CH, Ar), 129.4 (2CH, Ar), 129.2 (2CH, Ar), 127.1 (C, Ar), 126.1 (2CH, Ar), 60.0 (NCH_2), 38.6 (NCH_3). **IR (KBr)** $\nu_{máx}$ 3436, 3031, 1568, 1496, 1469, 1455, 1385, 1322, 1086, 1054, 1006, 817, 722, 709. **$[\alpha]_D^{25}$** - 19.6 (*c* 0.8, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{16}H_{18}AuBrClN_4OS$: 624.9733 $[M+NH_4]^+$, found 624.9776. **m.p.** decomposes before melting.

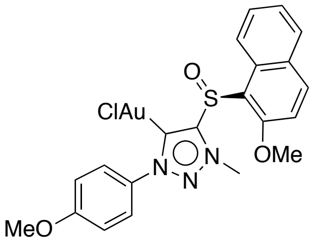
Synthesis of compound III.40b



Following the general procedure a mixture of **III.39b** (250 mg, 0.54 mmol, 1.00 equiv), NMe_4Cl (88 mg, 0.81 mmol, 1.50 equiv) and Ag_2O (93 mg, 0.4 mmol, 0.75 equiv) in CH_3CN:CH_2Cl_2 1:1 (29 mL) was stirred under Ar at rt overnight. [AuCl(SMe_2)] (158 mg, 0.54 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, Hex/EtOAc 3:7) to yield **III.40b** as a white solid (287 mg, 87 %).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.56 (dd, *J* = 8.7 Hz, 0.9 Hz, 1H, Ar), 8.11 (d, *J* = 9.1 Hz, 1H, Ar), 7.84 (d, *J* = 8.1 Hz, 1H, Ar), 7.60 (ddd, *J* = 8.5 Hz, 6.9 Hz, 1.3 Hz, 1H, Ar), 7.44 (ddd, *J* = 8.0 Hz, 6.9 Hz, 1.0 Hz, 1H, Ar), 7.40 (m, 2H, Ar), 7.33 (m, 4H, Ar), 5.50 (d, *J* = 14.1 Hz, 1H, NCH_2), 5.45 (d, *J* = 14.1 Hz, 1H, NCH_2), 4.53 (s, 3H, NCH_3), 4.00 (s, 3H, 2-OCH_3naph). **^{13}C NMR** (100 MHZ, $CDCl_3$) *δ* 159.0 (C, $N_3C{=}\mathit{C}Au$), 158.1 (C, Ar), 146.3 (C, $N_3\mathit{C}{=}CAu$), 137.2 (CH, Ar), 133.1 (C, Ar), 132.0 (C, Ar), 129.5 (C, Ar), 129.4 (CH, Ar), 129.4 (CH, Ar), 129.3 (CH, Ar), 129.1 (2CH, Ar), 128.9 (2CH, Ar), 125.1 (CH, Ar), 122.5 (CH, Ar), 120.7 (C, Ar), 113.1 (CH, Ar), 59.7 (NCH_2), 57.0 (2-$O\mathit{C}H_3$naph), 39.2 (NCH_3). **IR (KBr) $\nu_{máx}$** 3436, 2943, 1619, 1592, 1507, 1430, 1274, 1251, 1057, 814, 747, 708, 650. **$[\alpha]_D^{25}$** – 3.3 (*c* 0.6, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{21}H_{19}AuN_3O_2S$: 574.0858 $[M–Cl^-]^+$, found: 574.0851 $[M–Cl^-]^+$. **m.p.** decomposes before melting.

Synthesis of compound III.44a

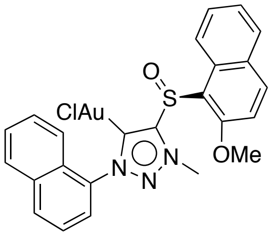


Following the general procedure a mixture of **III.43a** (250 mg, 0.52 mmol, 1.00 equiv), NMe_4Cl (85 mg, 0.78 mmol, 1.50 equiv) and Ag_2O (90 mg, 0.39 mmol, 0.75 equiv) in $CH_3CN:CH_2Cl_2$ 1:1 (29 mL) was stirred under Ar at rt overnight. $[AuCl(SMe_2)]$ (153 mg, 0.52 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, Hex/EtOAc 3:7) to yield **III.44a** as a white solid (297 mg, 91 %).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.69 (dd, *J* = 8.4 Hz, 0.8 Hz, 1H, Ar), 8.13 (d, *J* = 9.2 Hz, 1H, Ar), 7.84 (m, 3H, 1H Ar and 2H *p*-$OCH_3C_6H_4$), 7.66 (ddd, *J* = 8.5 Hz, 7.0 Hz, 1.3 Hz, 1H, Ar), 7.47 (ddd, *J* = 8.0 Hz, 7.0 Hz, 1.0 Hz, 1H, Ar), 7.32 (d, *J* = 9.2 Hz, 1H, Ar), 6.91 (d, *J* = 9.2 Hz, 2H, Ar *p*-$OCH_3C_6H_4$), 4.68 (s, 3H, NCH_3), 4.09 (s, 3H, 2-OCH_3naph), 3.81 (s, 3H, *p*-$OCH_3C_6H_4$). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 161.2 (C, Ar *p*-$OCH_3C_6H_4$), 158.0 (C, Ar 2-

OCH$_3$naph), 157.5 (C, N$_3$C=*C*Au), 146.3 (C, N$_3$*C*=CAu), 137.2 (CH, Ar), 132.1 (C, Ar), 131.8 (C, Ar), 129.5 (CH, Ar), 129.4 (CH, Ar), 129.3 (C, Ar), 125.2 (CH, Ar), 125.1 (2CH, Ar), 122.7 (CH, Ar), 121.1 (C, Ar), 114.6 (2CH, Ar), 113.1 (CH, Ar), 57.1 (2-O*C*H$_3$naph), 55.8 (*p*-O*C*H$_3$C$_6$H$_4$), 39.2 (NCH$_3$). **IR (KBr)** $\nu_{máx}$ 3435, 2936, 2838, 1592, 1509, 1467, 1274, 1253, 1175, 1152, 1065, 835, 809, 741. $[\alpha]_D^{25}$ – 10.0 (*c* 0.5, CHCl$_3$). **HRMS (ESI)** *m/z* calculated for $C_{21}H_{19}AuN_3O_3S$: 590.0807 $[M{-}Cl^-]^+$, found: 590.0808. **m.p.** decomposes before melting.

Synthesis of compound III.44b

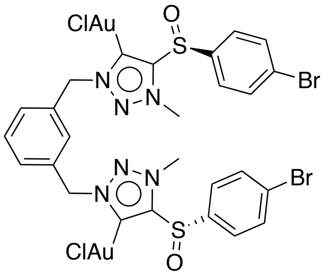


Following the general procedure a mixture of **III.43b** (300 mg, 0.60 mmol, 1.00 equiv), NMe$_4$Cl (98 mg, 0.9 mmol, 1.50 equiv) and Ag$_2$O (104 mg, 0.45 mmol, 0.75 equiv) in CH$_3$CN:CH$_2$Cl$_2$ 1:1 (34 mL) was stirred under Ar at rt overnight. [AuCl(SMe$_2$)] (176 mg, 0.6 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO$_2$, Hex/EtOAc 3:7) to yield **III.44b** as a white solid (339 mg, 87 %).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.68 (d, *J* = 8.6 Hz, 1H, Ar), 8.14 (d, *J* = 9.1 Hz, 1H, Ar), 8.00 (d, *J* = 8.2 Hz, 1H, Ar), 7.90 (d, *J* = 12.2 Hz, 1H, Ar), 7.88 (d, *J* = 12.2 Hz, 1H, Ar), 7.68 (t, *J* = 7.8 Hz, 1H, Ar), 7.60 (d, *J* = 7.4 Hz, 1H, Ar), 7.48 (m, 4H, Ar), 7.35 (d, *J* = 9.2 Hz, 1H, Ar), 7.11 (d, *J* = 8.5 Hz, 1H, Ar), 4.75 (s, 3H, NCH$_3$), 4.14 (s, 3H, 2-OCH$_3$naph). **^{13}C NMR** (100 MHz, CDCl$_3$) δ 162.3 (C, N$_3$C=*C*Au), 158.3 (C, Ar), 146.2 (C, N$_3$*C*=CAu), 137.4 (CH, Ar), 135.3 (C, Ar), 134.1 (C, Ar), 132.1 (C, Ar), 131.8 (CH, Ar), 129.6 (C, Ar), 129.5 (CH, Ar), 129.4 (CH, Ar), 128.6 (CH, Ar), 128.3 (CH, Ar), 128.1 (C, Ar), 127.4 (CH, Ar), 125.1 (CH, Ar), 124.9 (CH, Ar), 124.8 (CH, Ar), 122.5 (CH, Ar) 121.4 (CH, Ar) 121.1 (C, Ar), 113.2 (CH, Ar), 57.1 (2-O*C*H$_3$naph), 39.6 (NCH$_3$). **IR (KBr)** $\nu_{máx}$ 3436, 3056, 2987, 1620, 1592, 1508, 1468, 1274, 1251, 1152, 1059, 804, 770, 750, 655, 551. $[\alpha]_D^{25}$ – 10.6

(*c* 0.5, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{24}H_{19}AuN_3O_2S$: 610.0858 [M–Cl$^-$]$^+$, found: 610.0863. **m.p.** decomposes before melting.

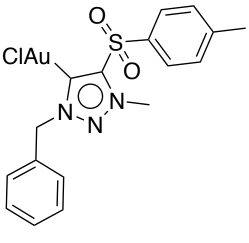
Synthesis of compound III.47



Following the general procedure a mixture of **III.46** (70 mg, 0.08 mmol, 1.00 equiv), NMe_4Cl (39 mg, 0.36 mmol, 4.50 equiv) and Ag_2O (42 mg, 0.18 mmol, 2.25 equiv) in CH_3CN:CH_2Cl_2 1:10 (5.5 mL) was stirred under Ar at rt for 17 h. [AuCl(SMe_2)] (47 mg, 0.16 mmol, 2.00 equiv) was added and the reaction was stirred for three more hours (^{1}H NMR analysis). The resulting residue was purified by vapour difusion recrystallization $CHCl_3$/Hexane to yield **III.47** as a white solid (35 mg, 38%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 8H, Ar *p*-BrC_6H_4), 7.48 (s, 4H, Ar), 5.99 (d, *J* = 14.8 Hz, 2H, NCH_2), 5.92 (d, *J* = 14.8 Hz, 2H, NCH_2), 4.22 (s, 6H, NCH_3). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.3 (2C, $N_3C=C$Au), 146.5 (2C, N_3C=CAu), 139.0 (C, Ar), 133.4 (C, Ar), 131.7 (C, Ar), 130.9 (C, Ar), 127.3 (C, Ar), 126.5 (C, Ar), 56.2 (2NCH_2), 38.8 (2NCH_3). **IR (KBr)** 3436, 1631, 1568, 1470, 1385, 1086, 1065, 1055, 1006, 815, 755, 724, 565, 517. **$[\alpha]_D^{25}$** – 211.7 (*c* 0.39, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{26}H_{22}Au_2Br_2ClN_6O_2S$: 1102.8606 [M–Cl$^-$]$^+$, found: 1102.8654. **m.p.** decomposes before melting.

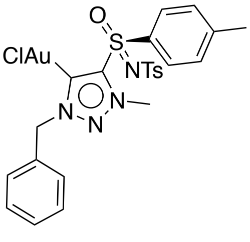
Synthesis of compound III.50



Following the general procedure a mixture of **III.49** (97 mg, 0.23 mmol, 1.00 equiv), NMe_4Cl (38 mg, 0.35 mmol, 1.50 equiv) and Ag_2O (41 mg, 0.18 mmol, 0.75 equiv) in CH_3CN:CH_2Cl_2 1:10 (9 mL) was stirred under Ar at rt overnight. [AuCl(SMe_2)] (69 mg, 0.23 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, MeOH/CH_2Cl_2 2%) to yield **III.50** as a white solid (66 mg, 51%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.3 Hz, 2H, Ar *p*-tolyl), 7.49 (m, 4H, Ar), 7.37 (m, 3H, 1H Ar and 2H *p*-tolyl), 5.60 (s, 2H, NCH_2), 4.47 (s, 3H, NCH_3), 2.52 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.4 (C, $N_3C{=}\mathit{C}Au$), 148.1 (C, Ar), 146.6 (C, $N_3\mathit{C}{=}CAu$), 134.5 (C, Ar), 132.6 (C, Ar), 131.0 (2CH, Ar), 129.8 (CH, Ar), 129.7 (2CH, Ar), 129.3 (2CH, Ar), 129.2 (2CH, Ar), 60.3 (NCH_2), 40.5 (NCH_3), 22.2 (CH_3, *p*-tolyl). **IR (KBr) $\nu_{\text{máx}}$** 3433, 1339, 1160, 1082, 657, 599. **HRMS (ESI)** *m/z* calculated for $C_{17}H_{17}AuN_3O_2S$: 524.0702 $[M{-}Cl^-]^+$, found: 524.0708. **m.p.** decomposes before melting.

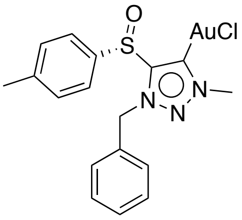
Synthesis of compound III.53



Following the general procedure a mixture of **III.52** (60 mg, 0.11 mmol, 1.00 equiv), NMe_4Cl (17 mg, 0.16 mmol, 1.50 equiv) and Ag_2O (19 mg, 0.08 mmol, 0.75 equiv) in CH_3CN:CH_2Cl_2 1:10 (5.5 mL) was stirred under Ar at rt overnight. [AuCl(SMe_2)] (31 mg, 0.11 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, Hex/EtOAc 1:1) to yield **III.53** as a white solid (57 mg, 75 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.3 Hz, 2H, Ar), 7.64 (d, *J* = 8.2 Hz, 2 H, Ar), 7.42 (m, 7H, Ar), 7.16 (d, *J* = 8.3 Hz, 2H, Ar), 5.59 (d, *J* = 14.0 Hz, 1H, NCH_2), 5.51 (d, *J* = 14.0 Hz, 1H, NCH$_2$), 4.57 (s, 3H, NCH$_3$), 2.46 (s, 3H, CH$_3$ *p*-tolyl), 2.41 (s, 3H, CH$_3$ *p*-tolyl). **^{13}C NMR** (100 MHz, CDCl$_3$) *δ* 164.2 (C, N$_3$C=*C*Au), 148.3 (C, Ar), 144.1 (C, N$_3$*C*=CAu), 143.6 (C, Ar), 138.8 (C, Ar), 132.5 (C, Ar), 132.0 (C, Ar), 130.9 (2CH, Ar), 130.0 (2CH, Ar), 129.8 (2CH, Ar), 129.7 (CH, Ar), 129.3 (2CH, Ar), 129.1 (2CH, Ar), 126.6 (2CH, Ar), 60.2 (NCH$_2$), 41.7 (NCH$_3$), 22.1 (CH$_3$, *p*-tolyl), 21.7 (CH$_3$, *p*-tolyl). **IR (KBr) $\nu_{\text{máx}}$** 3420, 3033, 2923, 1593, 1456, 1322, 1253, 1102, 1156, 1087, 1065, 811, 754. **$[\alpha]_D^{25}$** + 88.8 (*c* 0.3, CHCl$_3$). **HRMS (ESI)** *m/z* calculated for $C_{24}H_{24}AuN_4O_3S_2$: 677.0950 $[M–Cl^-]^+$, found: 677.0958. **m.p.** decomposes before melting.

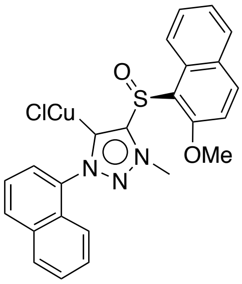
Synthesis of compound III.54



Following the general procedure a mixture of **III.56** (19 mg, 0.05 mmol, 1.00 equiv), NMe$_4$Cl (8 mg, 0.08 mmol, 1.50 equiv) and Ag$_2$O (9 mg, 0.04 mmol, 0.75 equiv) in CH$_3$CN:CH$_2$Cl$_2$ 1:10 (3.3 mL) was stirred under Ar at rt overnight. [AuCl(SMe$_2$)] (15 mg, 0.05 mmol, 1.00 equiv) was added and the reaction was stirred for three more hours. The resulting residue was purified (SiO$_2$, Hex/EtOAc 1:1) to yield **III.54** as a white solid (22 mg, 81 %).

^{1}H NMR (400 MHz, CDCl$_3$) *δ* 7.56 (d, *J* = 8.0 Hz, 2H, Ar *p*-tolyl), 7.34 (m, 3H, Ar), 7.24 (d, *J* = 8.0 Hz, 2H, Ar *p*-tolyl), 7.13 (br d, *J* = 7.3 Hz, 2H, Ar), 5.85 (d, *J* = 14.4 Hz, 1H, NCH$_2$), 5.70 (d, *J* = 14.4 Hz, 1H, NCH$_2$), 4.20 (s, 3H, NCH$_3$), 2.37 (s, 3H, CH$_3$ *p*-tolyl). **^{13}C NMR** (100 MHz, CDCl$_3$) *δ* 161.3 (N$_3$C=*C*Au), 146.8 (N$_3$*C*=CAu), 143.0 (C, Ar), 137.6 (C, Ar), 131.9 (C, Ar), 130.6 (2CH, Ar), 129.4 (CH, Ar), 129.2 (2CH, Ar), 128.7 (2CH, Ar), 124.9 (2CH, Ar), 55.1 (NCH$_2$), 42.9 (NCH$_3$), 21.6 (CH$_3$, *p*-tolyl). **IR (KBr) $\nu_{\text{máx}}$** 3436, 3032, 2922, 1593, 1490, 1469, 1456, 1305, 1180, 1080, 1053, 1006, 815, 750, 708. **$[\alpha]_D^{25}$** – 1.4 (*c* 0.9, CHCl$_3$). **HRMS (ESI)** *m/z* calculated for $C_{17}H_{21}AuClN_4OS$: 561.0785 $[M+NH_4]^+$, found: 561.0776. **m.p.** decomposes before melting.

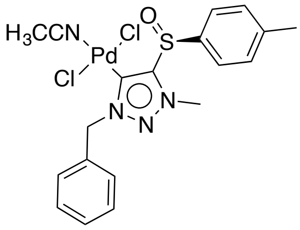
Synthesis of compound III.57



Following the general procedure a mixture of **III.44b** (250 mg, 0.52 mmol, 1.00 equiv), NMe_4Cl (85 mg, 0.78 mmol, 1.50 equiv) and Ag_2O (90 mg, 0.39 mmol, 0.75 equiv) in $CH_3CN:CH_2Cl_2$ 1:10 (29 mL) was stirred under Ar at rt overnight. CuCl (153 mg, 0.52 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, Hex/EtOAc 3:7) to yield **III.57** as a white solid (297 mg, 91 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (dd, *J* = 8.4 Hz, 0.8 Hz, 1H, Ar 2-OCH_3naph), 8.15 (d, *J* = 9.1 Hz, 1H, Ar 2-OCH_3naph), 8.88 (dd, *J* = 8.4 Hz, 0.8 Hz, 1H, Ar 2-OCH_3naph), 7.81 (d, *J* = 9.1 Hz, 2H, Ar *p*-$OCH_3C_6H_4$), 7.58 (ddd, *J* = 8.4 Hz, 7.0 Hz, 1.3 Hz, 1H, Ar 2-OCH_3naph), 7.44 (ddd, *J* = 8.1 Hz, 7.0 Hz, 1.0 Hz, 1H, Ar 2-OCH_3naph), 7.36 (d, *J* = 9.2 Hz, 1H, Ar 2-OCH_3naph), 6.92 (d, *J* = 9.2 Hz, 2H, Ar *p*-$OCH_3C_6H_4$), 4.64 (s, 3H, NCH_3), 4.10 (s, 3H, 2-OCH_3naph), 3.80 (s, 3H, *p*-$OCH_3C_6H_4$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.6 (C, $N_3C{=}\mathit{C}Cu$), 161.1 (C, Ar), 158.1 (C, Ar), 148.8 (C, $N_3\mathit{C}{=}CCu$), 137.3 (CH, Ar), 132.4 (C, Ar), 131.4 (C, Ar), 130.0 (C, Ar), 129.7 (CH, Ar), 129.1 (CH, Ar), 125.0 (CH, Ar), 124.2 (2CH, Ar), 122.8 (CH, Ar), 119.5 (C, Ar), 114.7 (2CH, Ar), 113.3 (CH, Ar), 57.1 (2-$O\mathit{C}H_3$naph), 55.8 (*p*-$O\mathit{C}H_3C_6H_4$), 38.8 (NCH_3). **IR (KBr) $\nu_{máx}$** 2935, 2839, 1592, 1509, 1253, 1056, 833, 814, 741, 612. **$[\alpha]_D^{25}$** + 289.8 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{21}H_{19}CuN_3O_3S$: 456.0438 $[M–Cl^-]^+$, found: 456.0428. **m.p.** decomposes before melting.

Synthesis of compound III.58



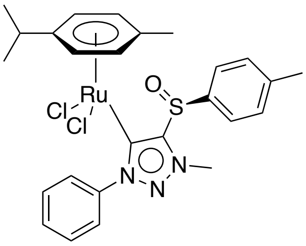
A mixture of **III.31** (80 mg, 0.20 mmol, 1.00 equiv) and Ag_2O (70 mg, 0.30 mmol, 1.50 equiv) in CH_3CN (2 mL) was stirred under Ar at rt for 5 h. The crude reaction was the filtered through a Celite pad. $[Pd(CH_3CN)_2Cl_2]$ (52 mg, 0.20 mmol, 1.00 equiv) was added and the reaction was stirred overnight. The crude mixture was filtered through a Celite pad and the volatiles removed under vacuum. The solid was precipitated in Et_2O to afford **III.58** as an orange solid without further purification required (95 mg, 89 %).

^{1}H NMR (400 MHz, MeOH-*d₄*) *δ* 7.82 (d, *J* = 8.3 Hz, 2H, Ar *p*-tolyl), 7.69 (m, 2H, Ar), 7.41 (d, *J* = 8.3 Hz, 2H, Ar *p*-tolyl), 7.36 (m, 3H, Ar), 6.14 (d, *J* = 14.4 Hz, 1H, NCH_2), 6.03 (d, *J* = 14.4 Hz, 1H, NCH_2), 3.87 (s, 3H, NCH_3), 2.40 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (400 MHz, MeOH-*d₄*) *δ* 144.4 (C, $N_3C{=}CPd$), 143.9 (C, Ar *p*-tolyl-CH_3), 139.7 (C, $N_3C{=}CPd$), 138.3 (C, Ar), 135.0 (C, Ar), 131.5 (2CH, Ar), 130.6 (2CH, Ar), 130.1 (CH, Ar), 129.9 (2CH, Ar), 126.3 (2CH, Ar), 59.8 (NCH_2), 39.2 (NCH_3), 21.4 (CH_3, *p*-tolyl). **IR (KBr)** **$\nu_{máx}$** 3428, 3035, 2934, 2329, 1654, 1595, 1493, 1457, 1439, 1378, 1332, 1084, 1058, 812, 749, 714, 654, 564, 520, 497. **HRMS (ESI)** *m/z* calculated for $C_{19}H_{20}ClN_4OPdS$: 495.0072 $[M–Cl–]^+$, found: 495.0095 and for $C_{17}H_{17}ClN_3OPdS$: 453.9806$[M–Cl^-–CH_3CN]^+$, found: 453.9827. **m.p.** decomposes before melting

General procedure for the synthesis of ruthenium carbenes

Triazolium salt (1.00 equiv), NMe_4Cl (1.50 equiv) and Ag_2O (0.75 equiv) were dissolved in a mixture of CH_3CN:CH_2Cl_2 (1:10) and stirred at rt overnight. The crude was filtered through a pad of Celite and solvents were then removed under vacuum. The resulting residue was redissolved in CH_2Cl_2. [Ru(*p*-cymene)Cl_2]$_2$ (0.45–0.50 equiv) was added and the reaction mixture was stirred at rt for two hours. The crude was filtered through Celite and solvent was removed under vacuum. The resulting residue was purified through a short pad of SiO_2 or washing.

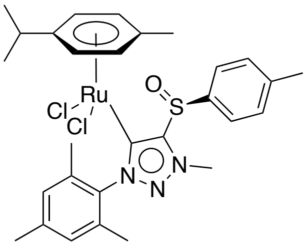
Synthesis of compound III.62a



Following the general procedure a mixture of **III.61a** (489 mg, 1.09 mmol, 1.00 equiv), NMe_4Cl (180 mg, 1.64 mmol, 1.50 equiv) and Ag_2O (190 mg, 0.82 mmol, 0.75 equiv) in CH_3CN:CH_2Cl_2 (50 mL) was stirred under Ar at rt overnight. The crude was filtered through a pad of Celite and solvents were then removed under vacuum. The resulting residue was redissolved in CH_2Cl_2 (25 mL). [Ru(*p*-cymene)Cl_2]$_2$ (300 mg, 0.49 mmol, 0.50 equiv) was added and the reaction mixture was stirred at rt for two more hours. The crude was filtered through Celite and solvent was removed under vacuum. The resulting residue was precipitated with pentanes and washed with a mixture of CH_2Cl_2:Et_2O 2:10 to yield **III.62a** as a dark orange solid (610 mg, 92%).

^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.95 (d, *J* = 8.4 Hz, 2H, Ar *p*-tolyl), 7.84 (m, 2H, Ar), 7.55 (m, 3H, Ar), 7.27 (d, *J* = 8.4 Hz, 2H, Ar *p*-tolyl), 7.01 (s, 2H, Ar), 5.39 (d, *J* = 5.8 Hz, H_{cym}), 5.17 (d, *J* = 6.0 Hz, H_{cym}), 5.12 (d, *J* = 6.8 Hz, H_{cym}), 4.81 (d, *J* = 5.8 Hz, H_{cym}), 3.78 (s, NCH_3), 2.71 (sept, *J* = 6.9 Hz, 1H, C*H*Me_2), 1.97 (s, 3H, $C_{cym}CH_3$), 1.22 (d, *J* = 6.9 Hz, 3H, CHC*H*$_3$), 1.17 (d, *J* = 6.9 Hz, 3H, CHC*H*$_3$). **^{13}C NMR** (125 MHz, $CDCl_3$) *δ* 176.3 (C, N_3C=*C*Ru), 148.9 (C C, N_3*C*=CRu), 141.3 (C, Ar), 139.2 (C, Ar), 138.4 (C, Ar), 130.8 (CH, Ar), 129.8 (2CH, Ar), 128.5 (2CH, Ar), 128.4 (2CH, Ar), 127.1 (2CH, Ar), 106.7 (C, CH*C*$_{cym}$), 98.3 (C, CH_3*C*$_{cym}$), 86.1 (CH, cym), 85.4 (CH, cym), 85.1 (CH, cym), 83.5 (CH, cym), 38.4 (NCH_3), 30.8 (CH, *C*HCMe$_2$), 23.0 (CH_3, CH*C*H$_3$), 22.4 (CH_3, CH*C*H$_3$), 21.4 (CH_3, *p*-tolyl), 18.7 (CH_3, C$_{cym}$C*H*$_3$). **$[\alpha]_D^{25}$** – 192.1 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{26}H_{29}ClN_3ORuS$: 568.0763 $[M–Cl^-]^+$, found: 568.0762.

Synthesis of compound III.62b

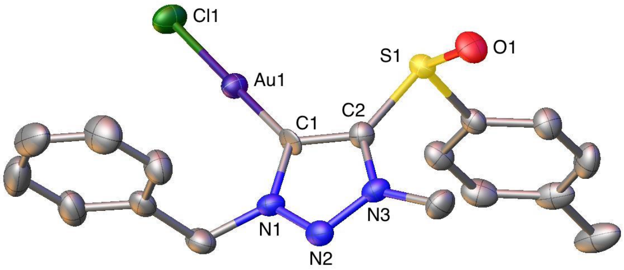


Following the general procedure a mixture of **III.61b** (319 mg, 0.65 mmol, 1.00 equiv), NMe_4Cl (107 mg, 0.98 mmol, 1.50 equiv) and Ag_2O (113 mg, 0.49 mmol, 0.75 equiv) in $CH_3CN:CH_2Cl_2$ (33 mL) was stirred under Ar at rt overnight. The crude was filtered through a pad of Celite and solvents were then removed under vacuum. The resulting residue was redissolved in CH_2Cl_2 (30 mL). [Ru(*p*-cymene)Cl_2]$_2$ (200 mg, 0.33 mmol, 0.50 equiv) was added and the reaction mixture was stirred at rt for two more hours. The crude was filtered through Celite and solvent was removed under vacuum. The resulting residue was purified (SiO_2, MeOH/CH_2Cl_2 10:90) to yield **III.62b** as a dark orange solid (210 mg, 50%).

^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.90 (d, *J* = 8.3 Hz, 2H, Ar *p*-tolyl), 7.27 (d, *J* = 8.3 Hz, 2H, Ar *p*-tolyl), 7.01 (s, 2H, Ar), 5.45 (d, *J* = 6.8 Hz, H$_{cym}$), 5.26 (d, *J* = 6.1 Hz, H$_{cym}$), 5.17 (d, *J* = 5.9 Hz, H$_{cym}$), 5.11 (d, *J* = 6.3 Hz, H$_{cym}$), 3.78 (s, NCH_3), 2.77 (sept, *J* = 6.9 Hz, 1H, $CHMe_2$), 2.38 (s, 3H, CH_3 *p*-tolyl), 2.36 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.04 (s, 3H, CH_3, C$_{cym}$CH$_3$), 1.18 (d, *J* = 6.9 Hz, 3H, CHC*H*$_3$), 0.98 (d, *J* = 6.9 Hz, 3H, CHC*H*$_3$). **^{13}C NMR** (125 MHz, $CDCl_3$) *δ* 174.0 (C, N_3C=*C*Ru), 150.0 (C, N_3C=*C*Ru), 141.0 (C, Ar), 140.9 (C, Ar), 139.4 (C, Ar), 138.5 (C, Ar), 136.0 (C, Ar), 134.1 (C, Ar), 129.8 (2CH, Ar), 129.7 (CH, Ar), 128.2 (CH, Ar), 127.0 (2CH, Ar), 107.3 (C, CH*C*$_{cym}$), 94.1 (C, CH$_3$*C*$_{cym}$) 89.1 (CH, cym), 86.3 (CH, cym), 85.8 (CH, cym), 82.0 (CH, cym), 38.5 (NCH_3), 30.5 (CH, *C*HCMe$_2$), 23.1 (CH_3, CH*C*H$_3$), 21.5 (CH_3, CH*C*H$_3$), 21.4 (CH_3, *p*-tolyl), 21.3 (CH_3), 19.6

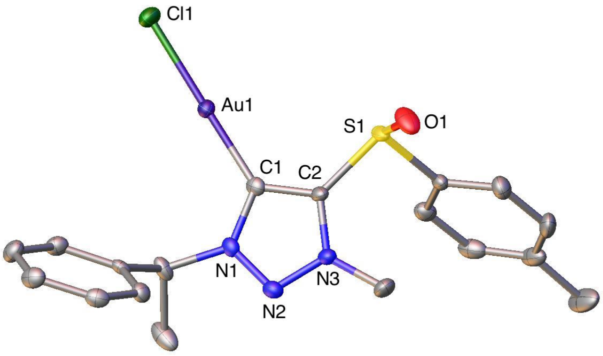
(CH_3), 18.5 (CH_3), 18.3 (CH_3, $C_{cym}CH_3$). **$[\alpha]_D^{25}$** + 51.9 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{29}H_{35}ClN_3ORuS$: 610.1233 $[M–Cl^-]^+$, found: 610.1260.

Crystal data for compound III.32:



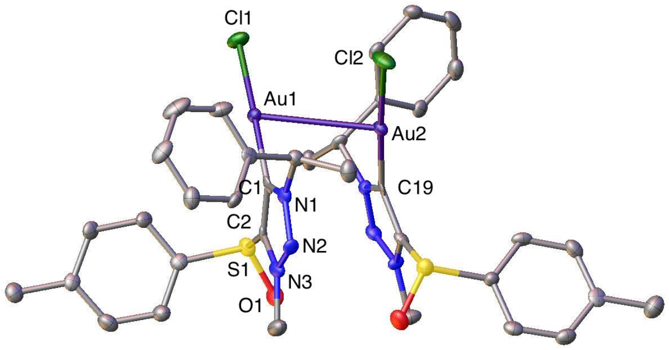
$C_{17}H_{17}AuClN_3OS$, Mr = 543.81, crystal dimensions 0.5 x 0.3 x 0.3 mm^3, triclinic, *P* $\bar{1}$, *a* = 5.087(1) Å, *b* = 7.868(1) Å, *c* = 12.413(1) Å, α = 81.440(3)°, β = 85.701(4)°, γ = 73.075(3)°, cell volume = 469.72(6) $Å^3$, Z = 1, ρ_{calcd} = 1.922 Mg/m^3, μ = 8.092 mm^{-1}, T = 173(2) K, $2\theta_{max}$ = 56.5°, 22411 reflections collected, 3885 independent, R_{int} = 0.0466, R1 = 0.0258 and wR2 = 0.0548 for I > 2σ(I), R1 = 0.0261 and wR2 = 0.0550 for all data, residual electron density = 1.877 eA^{-3}, absolute structure parameter x = –0.013(7).

Crystal data for compound III.36a:



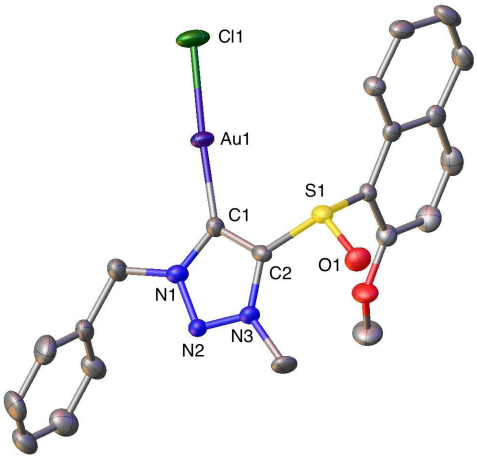
$C_{18}H_{19}AuClN_3OS$, Mr = 557.84, crystal dimensions 0.4 x 0.3 x 0.3 mm^3, orthorhombic, *P*$2_12_12_1$, *a* = 7.5537(2) Å, *b* = 14.1240(5) Å, *c* = 18.0020(6) Å, cell volume = 1920.6(2) Å^3, Z = 4, ρ_{calcd} = 1.929 Mg/m^3, μ = 7.918 mm^{-1}, T = 100(2) K, $2\theta_{max}$ = 56.5°, 19840 reflections collected, 4737 independent, R_{int} = 0.0208, R1 = 0.0104 and wR2 = 0.0240 for I > 2σ(I), R1 = 0.0108 and wR2 = 0.0241 for all data, residual electron density = 0.302 eA^{-3}, absolute structure parameter x = –0.019(2).

Crystal data for compound III.36b:



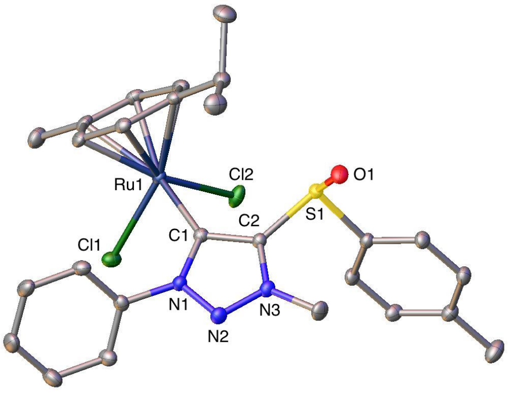
$C_{18}H_{19}AuClN_3OS$, Mr = 557.84, crystal dimensions 0.4 x 0.2 x 0.2 mm^3, orthorhombic, *P*$2_12_12_1$, *a* = 10.9737(4) Å, *b* = 17.4658(7) Å, *c* = 19.9371(7) Å, cell volume = 3821.2(2) Å^3, Z = 8, ρ_{calcd} = 1.939 Mg/m^3, μ = 7.960 mm^{-1}, T = 100(2) K, $2\theta_{max}$ = 55.5°, 39141 reflections collected, 7919 independent, R_{int} = 0.0795, R1 = 0.0498 and wR2 = 0.0607 for I > 2σ(I), R1 = 0.0649 and wR2 = 0.0639 for all data, residual electron density = 3.896 eA^{-3}, absolute structure parameter x = –0.019(6).

Crystal data for compound III.40b:



$C_{21}H_{19}AuClN_3O_2S$, Mr = 609.87, crystal dimensions 0.5 x 0.1 x 0.05 mm, orthorhombic, *P2₁2₁2₁*, *a* = 7.2343(5) Å, *b* = 11.0385(7) Å, *c* = 26.4489(18) Å, cell volume = 2112.1(2) Å^3, Z = 4, ρ_{calcd} = 1.918 Mg/m^3, μ = 7.213 mm^{-1}, T = 173(2) K, $2\theta_{max}$ = 56.5°, 42989 reflections collected, 5159 independent, R_{int} = 0.0788, R1 = 0.0305 and wR2 = 0.0512 for I > 2σ(I), R1 = 0.0470 and wR2 = 0.0549 for all data, residual electron density = 1.449 eA^{-3}, absolute structure parameter x = –0.011(6).

Crystal data for compound III.62a:



$C_{26}H_{29}N_3OSCl_2Ru$, Mr = 603.55, crystal dimensions 0.3 x 0.3 x 0.07 mm^3, monoclinic, *P2₁*, *a* = 8.54976(9) Å, *b* = 13.2349(1) Å, *c* = 11.2256(1) Å, cell volume = 1261.44(2) Å^3, Z = 2, ρ_{calcd} = 1.589 Mg/m^3, μ = 0.941 mm^{-1}, T = 100(2) K, $2\theta_{max}$ = 32.95°, 40417 reflections collected, 8787 independent, R_{int} = 0.0304, R1 = 0.0214 and wR2 = 0.048 for I > 2σ(I), R1 = 0.0224 and wR2 = 0.0487 for all data, residual electron density = 0.191 eA^{-3}, absolute structure parameter x = –0.035(13).

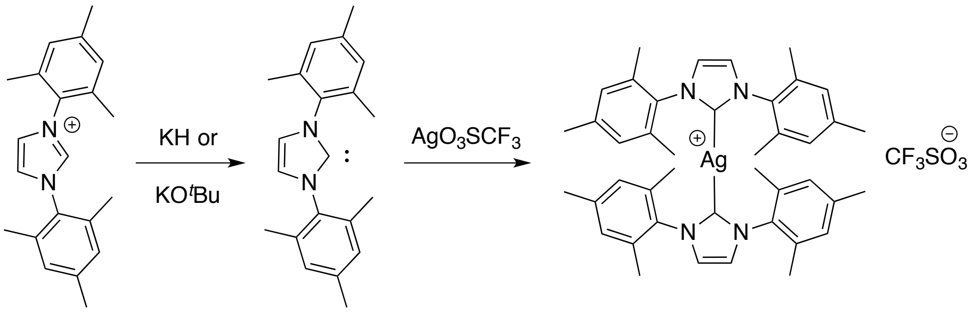
CHAPTER IV

Synthesis of C-unsubstituted MIC complexes

IV.1 INTRODUCTION

IV.1.1 Silver carbenes

Due to the promising activity of silver carbenes as antibiotics and anticancer drugs;[23c,24,25] synthesis, isolation and characterisation of new silver complexes are of great importance. The first silver-NHC complex was synthetized by Arduengo in 1993.[134] The imidazolium salt precursor was deprotonated using KH or KO^{t}Bu as base to form the free carbene **IV.1**, which upon treatment with AgO_3SCF_3 yielded the corresponding silver complex **IV.2** (Scheme IV.1).



IV.1 **IV.2** (80%)

Scheme IV.1: Synthesis of the first silver NHC

The standard procedure to synthesize silver carbenes consists of the use of a basic silver salt to deprotonate the heterocyclic salt followed by the coordination of the silver atom to the carbenic centre. The real breakthrough in the chemistry of silver carbenes took place when Ag_2O was employed as a base because the methodology

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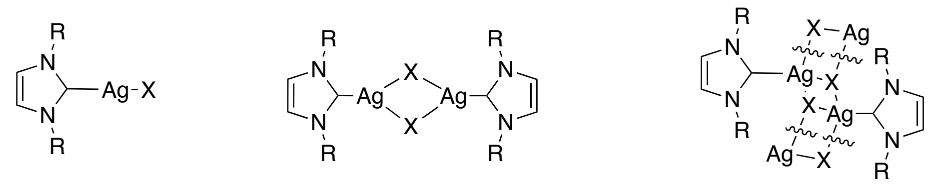
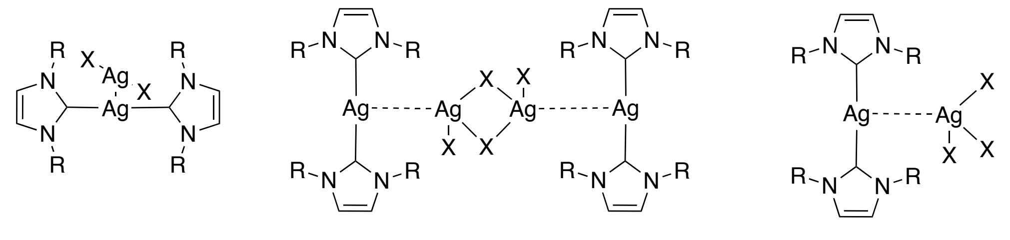
[134] A. J. Arduengo, H. V. R. Dias, J. C. Calabrese, F. Davidson, *Organometallics* **1993**, *12*, 3405.

became simpler and the required reaction conditions were not as strict as with other salts.[42]

Silver complexes can present different structures in the solid state.[135] The factors determining the structure of these complexes are, among others: the ratio of the silver reagent over the precursor salt, the flexibility of the ligand, the bulkiness of the substituents attached to the carbene, and the presence of donor groups (different to NHCs) in the ligand or the temperature of the reaction. For example, heterocyclic salts with non-coordinating anions form bis(carbene) complexes in the solid state. Nonetheless, this situation is more complicated when the nature of the counteranion is coordinating. In this case, silver carbenes can present up to six different structures: coordinating (C-Ag-X), bridging (Ag-Ag-X$_2$), staircase (C-Ag-X$_3$), halogeno counterion of type [AgX$_2$]$^-$[C$_2$-Ag-AgX$_2$], halogeno counterions of type [Ag$_2$X$_4$]$^-$ or Ag-Ag interactions stabilised by three donor groups (Figure IV.1). It is clear that, in the case of carbenes with coordinating anions, X-ray diffraction studies are necessary to confirm their structure in the solid state.



Coordinating C-Ag-X ***Bridging C-Ag-X*** ***Staircase C-Ag-X***



Halogeno counterion [AgX$_2$]C-Ag-AgX$_2$ ***Halogeno counterion [Ag$_2$X$_4$]*** ***Silver interactions-3 donor groups***

Figure IV.1: Structures of silver carbenes and coordinating anions in the solid state

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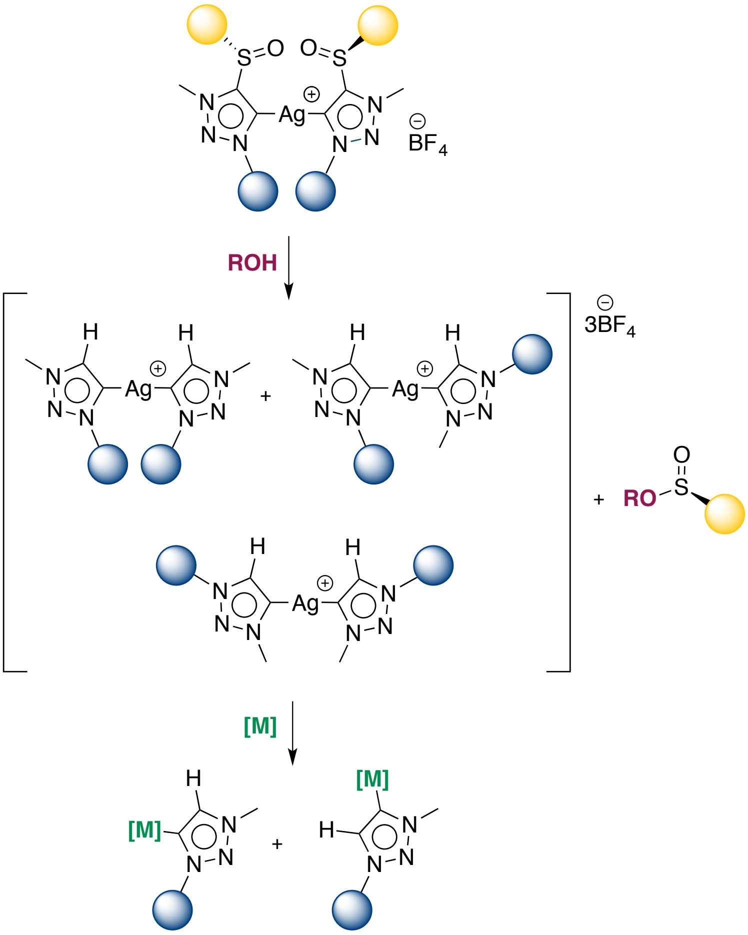
[135] J. C. Garrison, W. J. Youngs, *Chem. Rev.* **2005**, *105*, 3978.

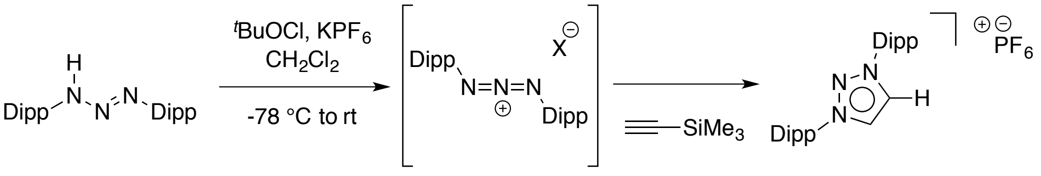
In this chapter, the synthesis of series of silver-MIC having enantiopure sulfinyl groups in *C*4, together with a new, unprecedented, desulfinylation reaction promoted by alcohols is reported. Based on DFT calculations supported by deuteration experiments, this process occurs by a mechanism involving a rearrangement of the sulfinyl moiety, which, to our knowledge, is unreported. Transmetallation to gold yielded the two *C*4 and *C*5 regioisomers of the unsubstituted MIC (Scheme IV.2).



Scheme IV.2: New desulfinylation and rearrangement process

IV.1.2 *C*-unsubstituted 1,2,3-triazolylidenes

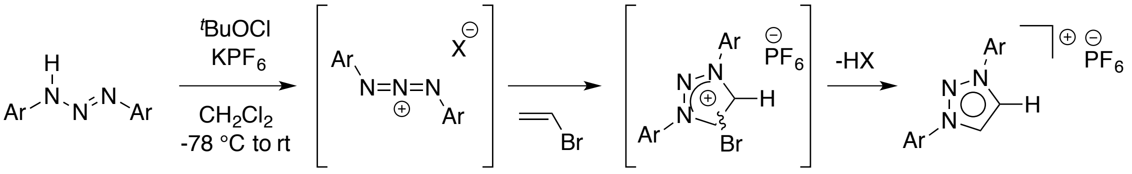
The synthesis of unhindered *C*-unsubstituted triazolylidene complexes is not obvious. Bertrand reported the preparation of series of *C*-unsubstituted triazolium salts through two methodologies.[136] The first one involved the 1,3-dipolar cycloaddition between 1,3-diaza-2-azoniallene salt **IV.3** and ethynyltrimethylsilyl alkynes to yield the triazolium salt **IV.4** (Scheme IV.3).



IV.3 **IV.4** (70%)

Scheme IV.3: Synthesis of H-substituted 1,2,3-triazolium salt **IV.4**

The second approach consisted of the cycloaddition between 1,3-diaza-2-azoniallenes and vinyl halides followed by spontaneous elimination of hydrogen halide. Salts **IV.5a–c** were prepared through this synthetic approach (Scheme IV.4).



IV.5a (65%), Ar= Dipp
IV.5b (91%), Ar= Mes
IV.5c (52%), Ar= Ph

Scheme IV.4: Second synthetic approach for *H*-substituted 1,2,3-triazolium salts

Deprotonation of the salt **IV.4** with KO^{t}Bu yielded the free carbene **IV.6** (Scheme IV.5).[137] Coordination of the unhindered *H*-substituted-1,2,3-triazolylidene **IV.6** with **IV.7** gave the unexpected complex **IV.8**. In the presence of traces of protic acid, protonolysis of Ru was observed giving the starting ruthenium complex **IV.7**. Therefore, carbene **IV.6** was acid labile and it could act as the dissociating ligand of catalysts for metathesis transformations.

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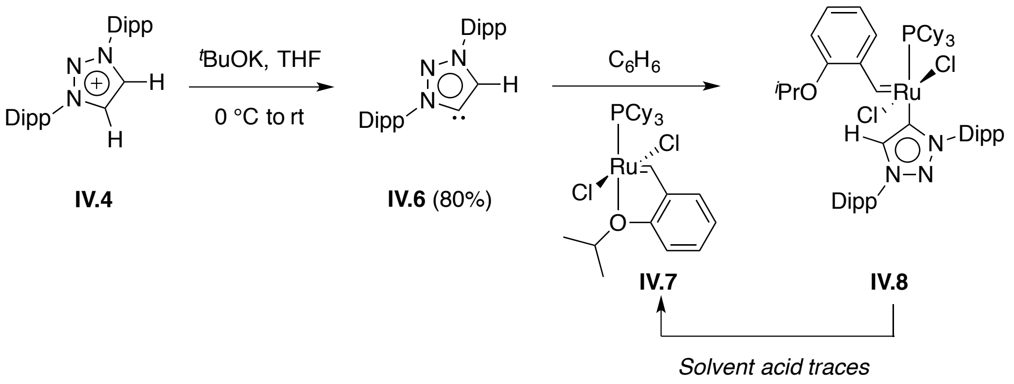
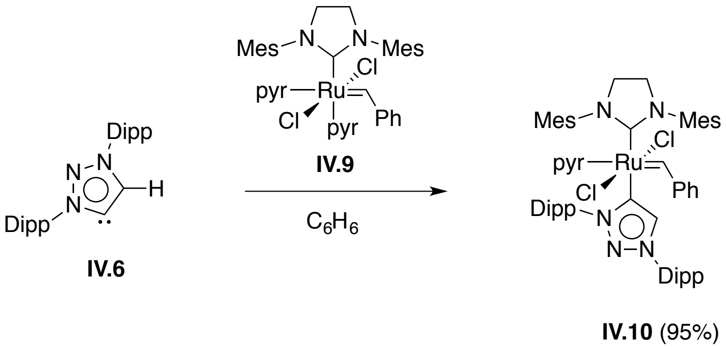
[136] J. Bouffard, B. K. Keitz, R. Tonner, G. Guisado-Barrios, G. Frenking, R. H. Grubbs, G. Bertrand, *Organometallics* **2011**, *30*, 2617.
[137] B. K. Keitz, J. Bouffard, G. Bertrand, R. H. Grubbs, *J. Am. Chem. Soc.* **2011**, *133*, 8498.



Scheme IV.5: Acidic lability of complex **IV.8**

When free triazolylidene **IV.6** was combined with the ruthenium complex **IV.9**, ruthenium 1,2,3-triazolylidene **IV.10** was obtained (Scheme IV.6). This new complex was practically inactive in the ring closing methatesis (RCM) of dimethylmalonate, however, addition of a 1 M solution of HCl in Et_2O accelerated this transformation with full conversion within 20 min at rt. The protonolysis reaction was further investigated demonstrating that this process was the rate-determinant in the RCM. The rate of the catalytic transformation could be enhanced by changes on the nature of either the acid or the solvent.



Scheme IV.6: Synthesis of Ru complex **IV.10**

Taking advantage that these free carbenes with H atoms in *C*4 were stable, Bertrand prepared a series of bimetallic complexes.[138] Deprotonation of the palladium carbene **IV.11** that was synthetized from the free carbene **IV.12**, formed the bimetallic compound **IV.13** (Scheme IV.7).

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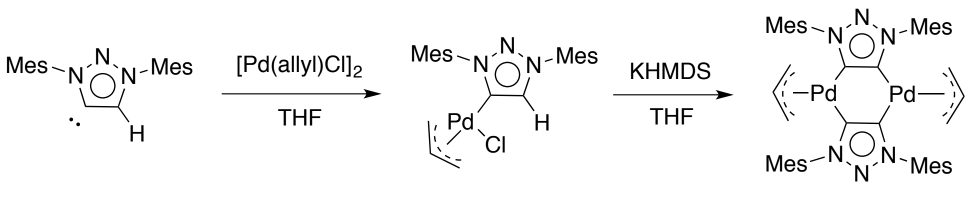
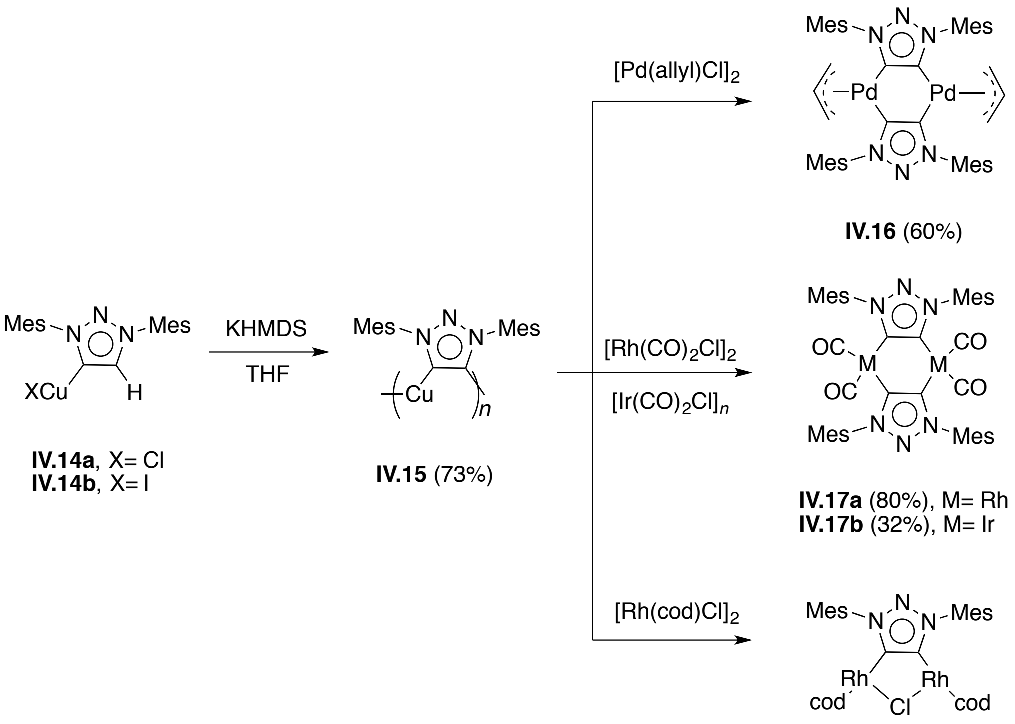
[138] X. Yan, J. Bouffard, G. Guisado-Barrios, B. Donnadieu, G. Bertrand, *Chem. Eur. J.* **2012**, *18*, 14627.



IV.12 **IV.11** (84%) **IV.13** (79%)

Scheme IV.7: Synthesis of bimetallic palladium bis(triazolylidene) **IV.13**

When this approach was employed with the Cu carbenes **IV.14a**–**b**, new complex **IV.15** was obtained. ESI analysis of this compound revealed either its oligomeric or polymeric nature. When copper carbene **IV.15** was transmetallated with different metal sources, discrete bis(carbene) complexes **IV.16**–**18** were obtained (Scheme IV.8).



IV.14a, X= Cl
IV.14b, X= I

IV.15 (73%)

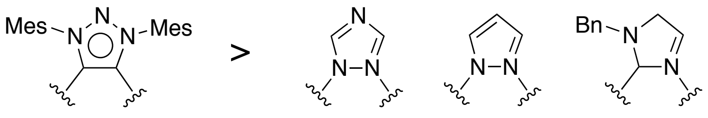
IV.16 (60%)

IV.17a (80%), M= Rh
IV.17b (32%), M= Ir

IV.18 (52%)

Scheme IV.8: Synthesis of bimetallic bis(triazolylidene) complexes

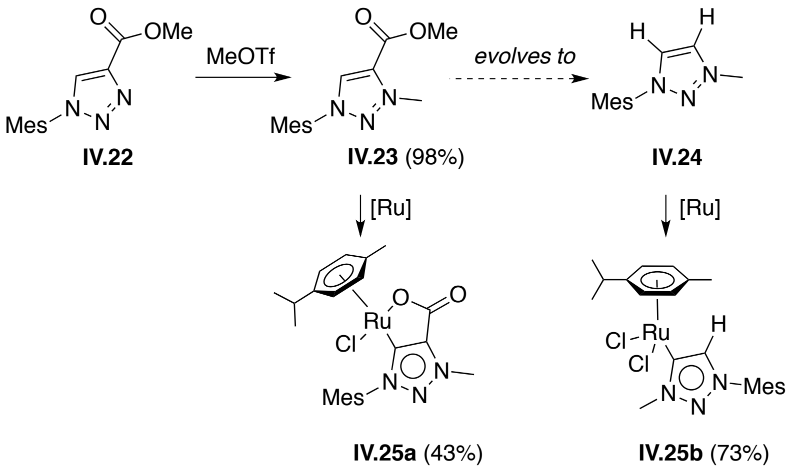
The donor properties of these species were compared by measuring the IR CO stretching frequencies of **IV.17a**. These values were lower than those of the nitrogen-coordinating ligands **IV.19**–**21** in analogous bimetallic Rh complexes confirming the stronger electron donor nature of the triazolylidenes (Figure IV.2).



IV.17a **IV.19** **IV.20** **IV.21**

Figure IV.2: Compared bidentate ligands

Recently, Albrecht prepared a Ru(II) 1,2,3-triazolylidene complex bearing a methylcarboxylate group in *C*4.[131] During the methylation of the triazole precursor with MeOTf as the alkyl source, triazole **IV.22** suffered a partial decarbonylation process to yield a mixture of the desired triazolium salt **IV.23** and the decarbonylated triazolium **IV.24**. When metallation was carried out over the mixture of these two products, the chelated ruthenium complex **IV.25a** was obtained, together with **IV.25b**. Although the triazolium salt **IV.24** presented two possible coordination positions, only *C*5-Ru(II)-MIC was formed, possibly because this position was sterically less demanding than *C*4 having a bulky mesityl group in α position (Scheme IV.9).



Scheme IV.9: Synthesis of ruthenium 1,2,3-triazolylidenes

IV.2 Objectives

Based on these precedents, the objectives of chapter IV are:

- Synthesis and characterisation of new silver bis(1,2,3-triazolylidene) complexes (Ag-MIC) bearing enantiopure (*S*)-sulfoxide subtituents in *C*4.

- Study of an unprecedented desulfinylation reaction that affords two possible MIC-AuL regioisomers having a *C*-unsubstituted triazole core.

- Computational and experimental study of the mechanism of this novel reaction.

IV.3 Results and discussion

Silver-NHC **IV.26** was prepared following analogous conditions to the ones reported in chapter III for the synthesis of M-MIC complexes (M≠ Ag). Triazolium salt **III.31** reacted at rt with 0.75 equiv of Ag_2O, 1.50 equiv of NMe_4Cl in a mixture of CH_3CN:CH_2Cl_2 (1:1) in the presence of 4 Å molecular sieves in the dark. After stirring the reaction overnight, the corresponding silver carbene **IV.26** was formed. ^{1}H NMR spectrum revealed the disappearance of the triazolium proton at δ_H = 8.48 ppm. In addition to the expected signals for the silver compound (see below) a new singlet could be observed at δ_H = 2.00 ppm. This signal points to the formation of $[Ag(CH_3CN)_4]$ complex as a by-product.[139] The formation of this secondary product increased when CH_3CN was used as solvent. When the reaction was performed in CH_2Cl_2, unreacted starting material still remained in the crude reaction after 24 hours. The signal at δ_H = 2.00 ppm was not observed under these conditions. Therefore, the assignation of the new product as $[Ag(CH_3CN)_4]$ was confirmed. It was clear that CH_3CN had to be present in the mixture of solvents to enhance the rate of the reaction, but the amount of this solvent had to be kept to a minimum to reduce the formation of $[Ag(CH_3CN)_4]$. Thus, carrying the reaction in a mixture of CH_3CN:CH_2Cl_2 (1:10) resulted in the exclusively formation of the silver carbene **IV.26** in 89% yield after 24 h of stirring at room temperature in the dark (Scheme IV.10).

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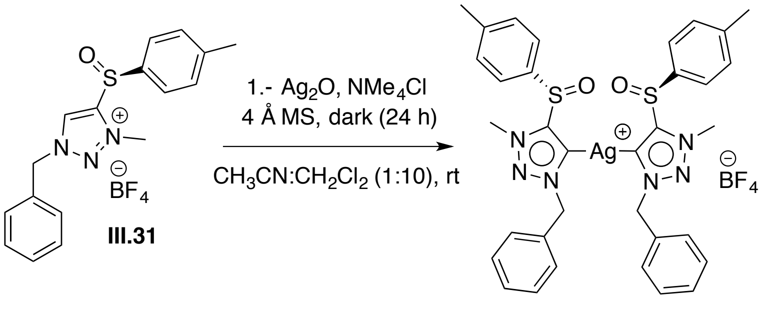
[139] B. Åkermark, A. Vitaglio, *Organometallics* **1985**, *4*, 1275.



IV.26 (89%)

Scheme IV.10: Synthesis of silver bis(triazolylidene) **IV.26**

Silver carbene **IV.26** was fully characterised by NMR and HRMS means. A main fragment was obtained in HRMS at *m/z* = 731.1229 that perfectly matched with the bis(triazolylidene) structure **IV.26** depicted above. ^{1}H NMR spectrum of the complex showed the disappearance of the most deshielded signal of the triazolium ring (δ_H = 8.48 ppm) due to the coordination of the silver atom. In addition, signals were observed for only half of the molecule as a result of the symmetric nature of bis(carbene) **IV.26**. In the ^{13}C NMR spectrum, signals were also obtained for half of the molecule with the most deshielded carbon appearing at δ_C = 149.0 ppm. This signal was assigned to *C*4 of the triazolylidene nucleus based on HMBC studies. In this case, the $C_{carbenic}$ of complex **IV.26** did not resonate in the ^{13}C NMR spectrum. The dynamic behaviour of the silver carbene could be behind the lack of the resonance signal in ^{13}C NMR spectrum (that is common in the ^{13}C NMR spectra of silver carbenes).[135] Additionally, the poor relaxation of the quaternary carbon of the carbenic centre may contribute to the lack of this signal.

In contrast, in the HMBC spectrum of complex **IV.26**, a cross peak between the protons of the methylene group and a region in the ^{13}C NMR spectrum at δ_C = 168.4 ppm lacking any signal is observed (Figure IV.3).

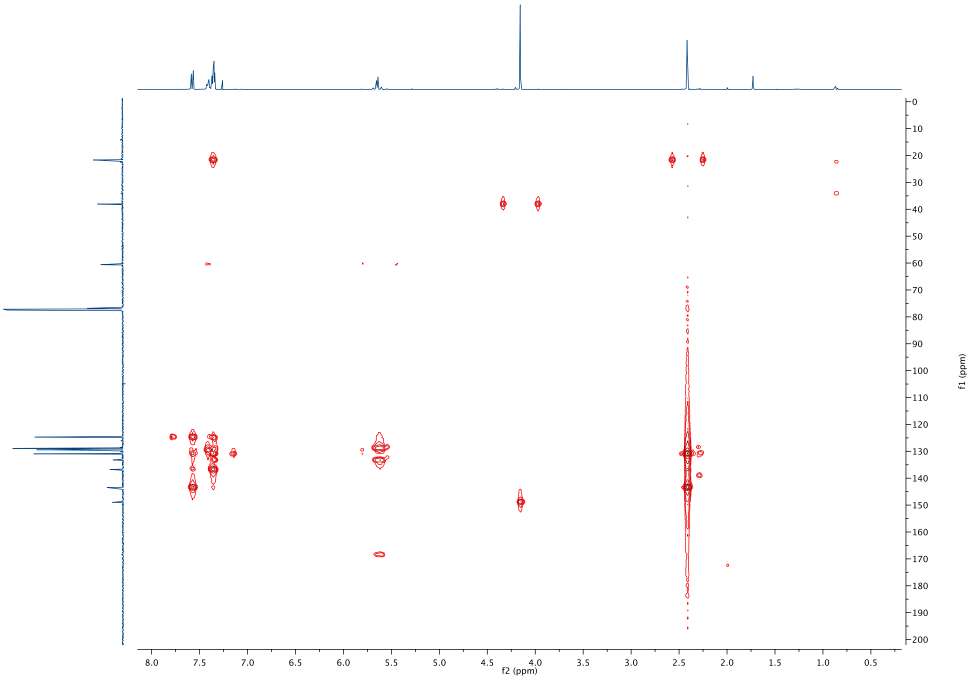


Figure IV.3: HMBC spectrum of silver carbene **IV.26**

The existence of this cross peak confirmed the formation of the desired complex, as it was assigned to the crossing between the methylene protons and the carbene centre. The ^{19}F spectrum showed two peaks at δ_F = 152.97 ppm and 153.02 ppm in a 1:4 ratio as the result of the coupling between the fluorine atom and the two isotopes of the boron of the BF_4^- counteranion.

During manipulation of the silver carbene **IV.26**, when MeOH was added to a solution of the silver complex in CH_2Cl_2, the colour of the solution instantaneously changed from soft to dark brown. After filtering the solution through a Celite pad, and removing the volatiles under vacuum, a ^{1}H NMR spectrum of the solid was registered. Surprisingly, the symmetry of the Ag-NHC **IV.26** was lost as it could clearly be seen by the presence of three signals for the methylene group and another set of three signals corresponding to the methyl group bonded to *N*3. In addition, a new singlet at δ_H = 3.47 ppm was observed. The solid was again precipitated and washed in a mixture of CH_2Cl_2:pentane. The spectroscopic analysis of the mother waters showed signals attributable to the *p*–tolyl group (two doublets at δ_H = 7.59 ppm and 7.34 ppm for the aromatic protons of the molecule; plus a singlet at δ_H = 2.43 ppm for the methyl group). In addition, this ^{1}H NMR spectrum showed the new singlet that appeared at δ_H = 3.47 ppm.

On the other hand, ^{1}H NMR analysis of the solid revealed the presence of the heterocyclic moiety as it could be confirmed by the presence of a set of three signals in the region where the methylene group resonates in a proportion of 1:5:6. In the region of the NCH_3 groups, another set of three signals was observable in the same ratio as for the methylene groups. No signals attributable to the sulfinyl moiety were present in the ^{1}H NMR spectra of the solid. Moreover, ^{13}C NMR spectrum of the solid clearly showed three signals for the carbon centre of the NCH_3 and another three signals for the NCH_2 groups. It is worthy to note, in the HMBC spectrum of the solid, the presence of cross peaks between one of the singlets corresponding to the protons of the methylene group with a ghost signal in the carbon channel at δ_C = 165.1 ppm. Another cross peak was observed involving one of the signals of the methyl group bounded to N3 and a region in the ^{13}C NMR lacking signals at δ_C = 165.8 ppm (Figure IV.5). These two peaks pointed to the presence of at least two different silver carbenes with the metallic centre bounded to different carbon atoms of the triazole core.

To explain the cross peak between the protons of a NCH_3 and the $C_{carbenic}$ it is necessary to invoke a rearrangement process of the silver carbene moiety. In addition, HRMS analysis of the solid gave a main fragment at *m/z* = 453.0938 that perfectly matches with a structure of a silver bis(triazolylidene) complex having H atoms in the two heterocyclic carbons, instead of sulfoxide groups.

With these results in hand, we can conclude that the presence of MeOH in the solution of silver-NHC **IV.26** resulted in the removal of the sulfinyl functionality as the methyl sulfinate **IV.27**. The new singlet that appeared in the ^{1}H NMR of the mother waters at δ_H = 3.47 ppm would be due to the presence of the methyl group of the sulfinate that would originate from the methanol. This attack was accompanied by a transposition of the Ag atom, yielding a mixture of “naked” carbenes **IV.28**.

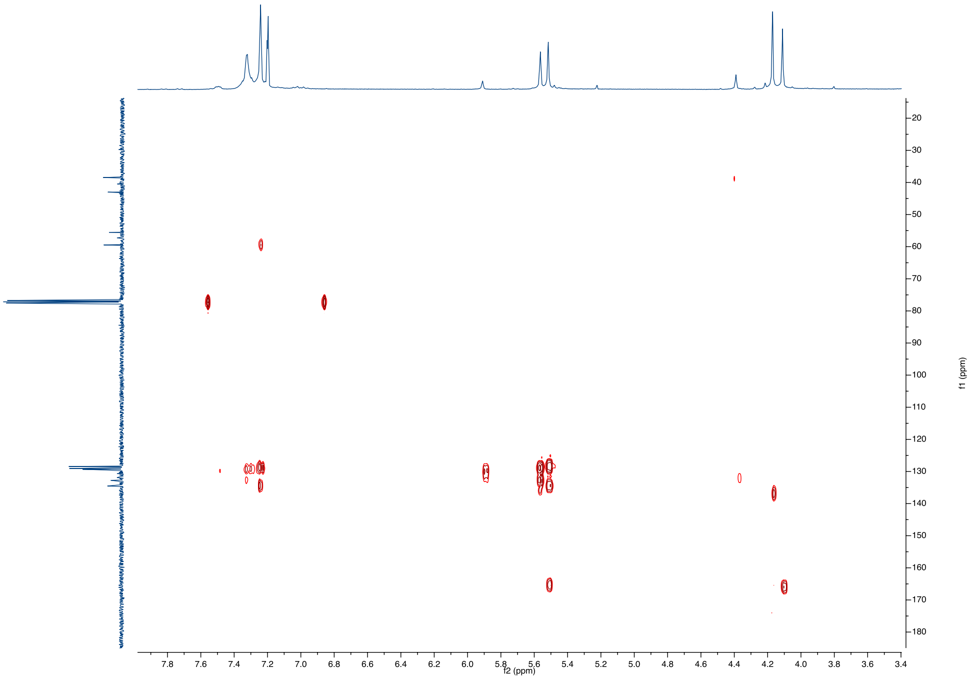
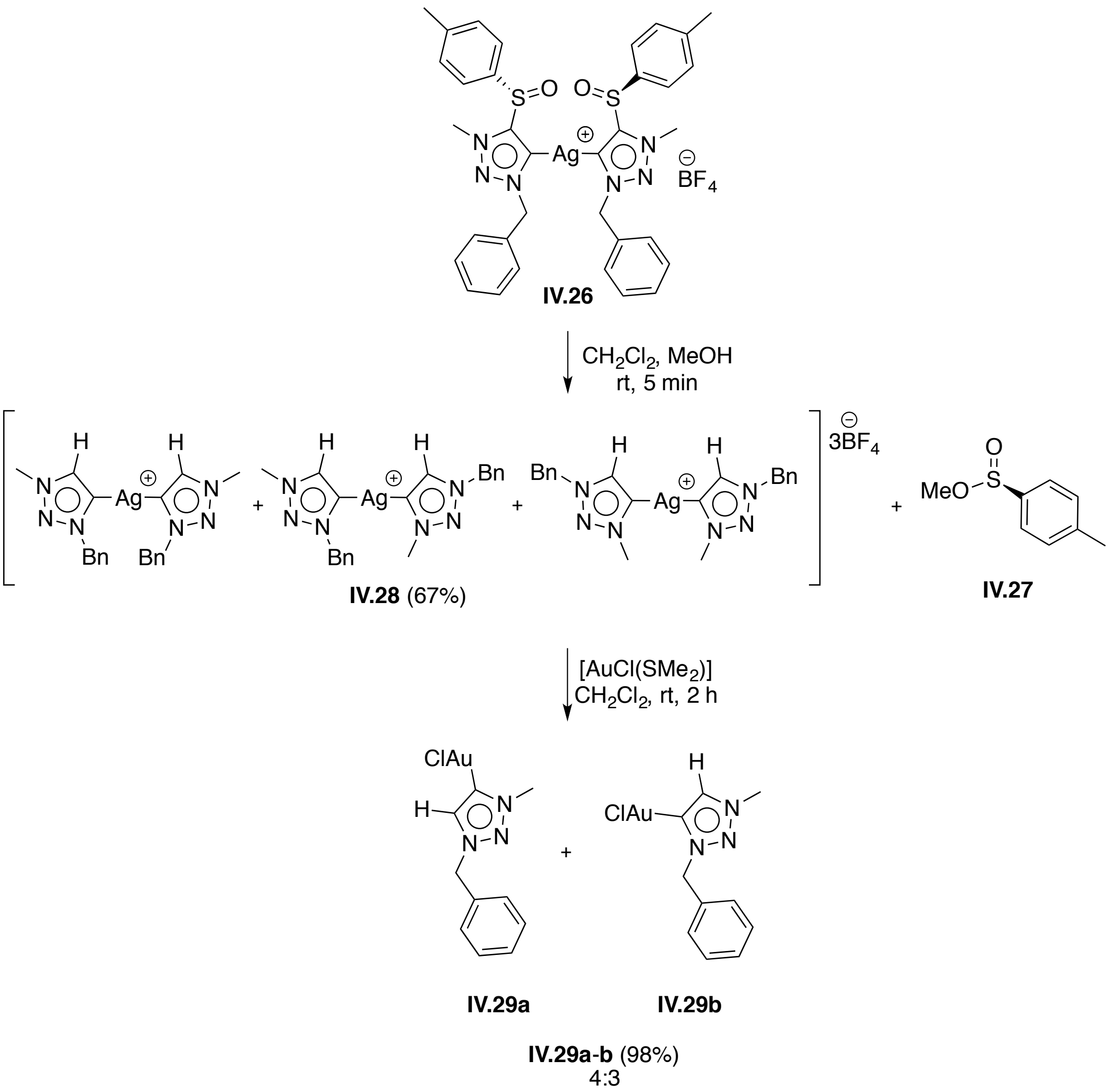


Figure IV.4: HMBC spectrum of silver carbenes **IV.28**

Due to the impossibility of separation of the possible regioisomers of the mixture of silver carbenes **IV.28**, transmetallation of this mixture with [AuCl(SMe$_2$)] was addressed next. Reaction of a solution of silver carbenes **IV.28** in CH_2Cl_2 with 2.00 equiv of [AuCl(SMe$_2$)] at rt for 2 hours afforded a mixture of the two regioisomeric MIC-AuCl complexes **IV.29a–b** in a 98% yield and in a ratio of 3:4 of **IV.29a** over **IV.29b** (Scheme IV.11). Separation of both complexes was achieved through a SiO_2 column purification. The *C*4 regioisomer **IV.29a** was the most apolar. Complex **IV.29a** was totally characterised by ^{1}H, ^{13}C and HRMS techniques. ^{1}H spectrum showed a singlet at δ_H = 7.61 ppm corresponding to the new H5 proton. The ^{13}C NMR spectrum showed a downfield shifted signal at δ_C = 157.4 ppm corresponding to the C–Au centre. HRMS showed a peak at *m*/*z* = 370.0610 that matches with a loss of a chloride from the molecular peak of the structure proposed.



Scheme IV.11: Methanolysis and transmetallation reaction

On the other hand, the second regioisomer **IV.29b** was characterised by ^{1}H and ^{13}C NMR techniques together with HRMS analysis. The ^{1}H spectrum revealed a singlet for the new proton in *C*4 slightly upfield shifted compared to the *C*4 isomer (δ_H = 7.60 ppm). The carbenic centre resonated at δ_C = 158.0 ppm, 0.6 ppm more deshielded than the counterpart **IV.29a**. HRMS also revealed a peak at *m/z* = 370.0595 that corresponds to the structure proposed in Scheme IV.11 after the loss of a chloride.

In order to confirm the structures proposed above, NOE experiments were performed. Irradiation over the protons of NCH_3 group in the gold carbene **IV.29b** provoked an increase in the intensity of the signal of the new CH nucleus in position *C*4 of the heterocycle (Figure IV.5, left image). On the other hand, irradiation over the protons of NCH_3 group in the other regioisomer did not produce any increase in the intensity of the CH protons, thus confirming the structures proposed (Figure IV.6, right image).

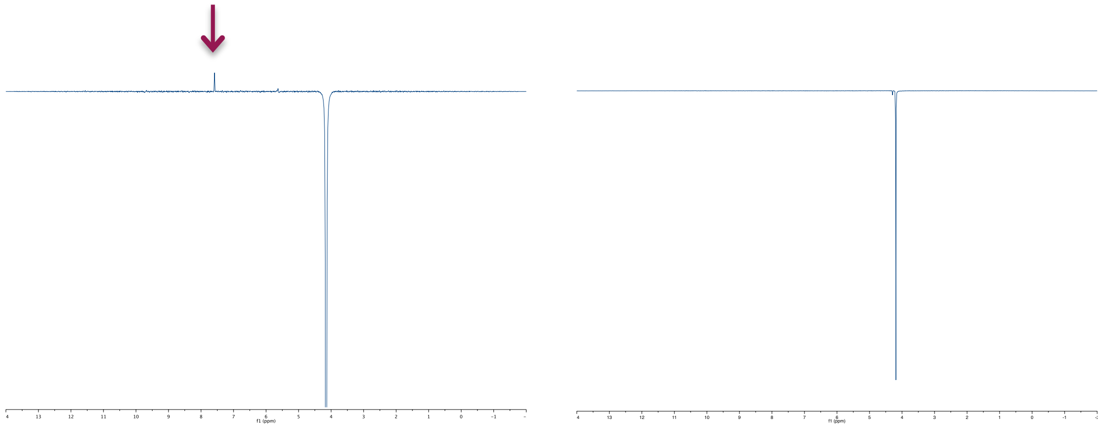
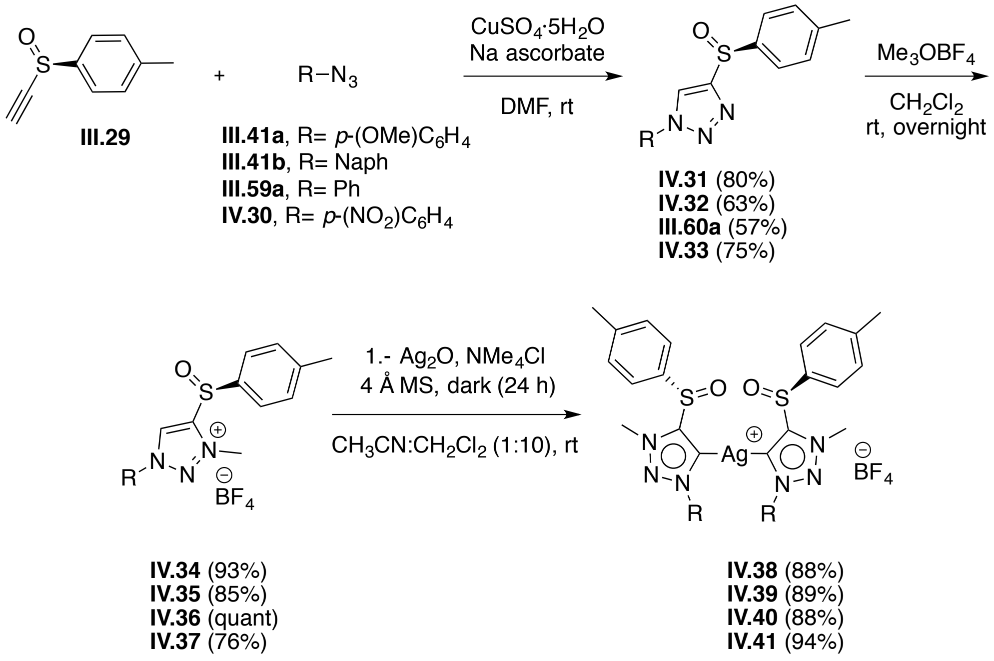


Figure IV.5: NOE experiments of **IV.29b** and **IV.29a**

To study the scope of the reaction over the substrate, the methanolysis of different silver carbenes having different groups attached to *N*1 were tested next. The methodology employed in their synthesis was analogous to the one described for silver 1,2,3-triazolylidene complex **IV.26** (Scheme IV.12). All the intermediates (1,2,3-triazoles and the triazolium salts) as well as the silver complexes, were fully characterised by NMR and HRMS means.



Scheme IV.12: Synthesis of silver carbenes **IV.38**-**41**

Table IV.1: Chemical shifts of silver carbenes and their precursors

Entry	Compound	δ_{H5}	δ_{C5}
1	**IV.31**	8.15	122.2
2	**IV.34**	9.82	129.3
3	**IV.38**	-	-
4	**IV.32**	8.15	126.5
5	**IV.35**	8.08	125.2
6	**IV.39**	-	172.9
7	**III.60a**	8.25	122.1
8	**IV.36**	8.63	128.9
9	**IV.40**	-	-
10	**IV.33**	8.47	122.1
11	**IV.37**	10.05	130.5
12	**IV.41**	-	170.2

^{1}H and ^{13}C NMR spectra were recorded using $CDCl_3$ as solvent except for **IV.34** and **IV.37** where DMSO-d_6 was used as solvent

According to Table IV.1 the formation of the products could be easily confirmed by ^{1}H NMR and ^{13}C NMR experiments. The triazole proton is downfield shifted (0.38 and 1.67 ppm) upon formation of the triazolium salt (Table IV.1, entries 2, 5 and 8). In addition, the *C*5 centre appeared downfield shifted (6.8 and 8.4 ppm) compared to the triazole precursor (Table IV.1, entries 2, 5 and 8).

There is an exception in the case of the triazolium salt **IV.35** (Table IV.1, entry 5). In this example, the proton of the triazolium was not deshielded with respect to its precursor. In fact, the triazolium proton was shielded 0.20 ppm when methylation occurred selectively in *N*3 (Table IV.1, entries 4 and 5). An analogous situation was obtained in the ^{13}C NMR spectrum where the *C*5 of the triazolium salt is 1.3 ppm upfield shifted compared to the triazole precursor. A HMBC ^{1}H-^{15}N experiment was carried out in order to confirm that the methylation happened in this heteroatom and not in the sulfoxide moiety (Figure IV.6).

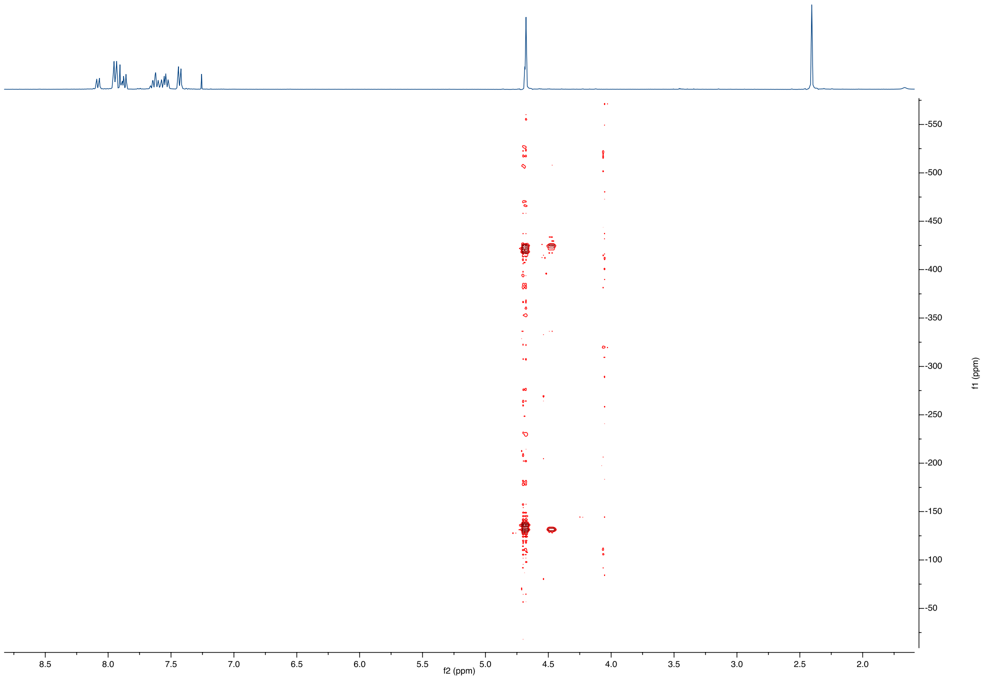


Figure IV.6: HMBC spectrum ^{1}H-^{15}N of triazolium salt **IV.35**

This spectrum showed cross peaks with the protons that corresponded to the new CH_3 group, thus this asserts that the new methyl group was bound to a N centre and not to the sulfoxide moiety as we could suspect. This “anomaly” could be explained as a consequence of the effect of the naphthyl group that can be translated into an unexpected upfield shift of the triazolium proton. Furthermore, structure of the triazolium salt **IV.35** was also confirmed by HRMS, that showed a peak at *m/z* = 348.1165 corresponding to the cationic moiety of the structure proposed.

In the case of the silver complexes, it is worth noting that in both ^{1}H and ^{13}C NMR spectra, a set of signals corresponding to half of the molecule were always obtained. In addition, the lack of a signal for the triazolium proton has a high diagnostic value to confirm the coordination of the carbene to the silver centre. Regarding the ^{13}C NMR spectra, the resonances for the carbene centre were only observed for examples **IV.39** and **IV.41** (Table IV.1, entries 6 and 12). In the case of **IV.41**, this quaternary carbon resonates as a singlet.

However, in the case of silver triazolylidene **IV.39**, this carbenic centre resonated as two doublets at δ_C = 172.9 ppm with a coupling constant of J = 171.9 and 192.8 Hz (Figure IV.7). This resonance is due to the existence of two natural isotopes of the silver element, ^{107}Ag and ^{109}Ag that are present in almost equal abundance (51.839(7)% and 48.161(7)% respectively). Both isotopes are active in NMR with a nuclear spin of ½. So, the carbenic centre must appear as two doublets because of the coupling of the carbenic atom with each of the two isotopes of the silver.

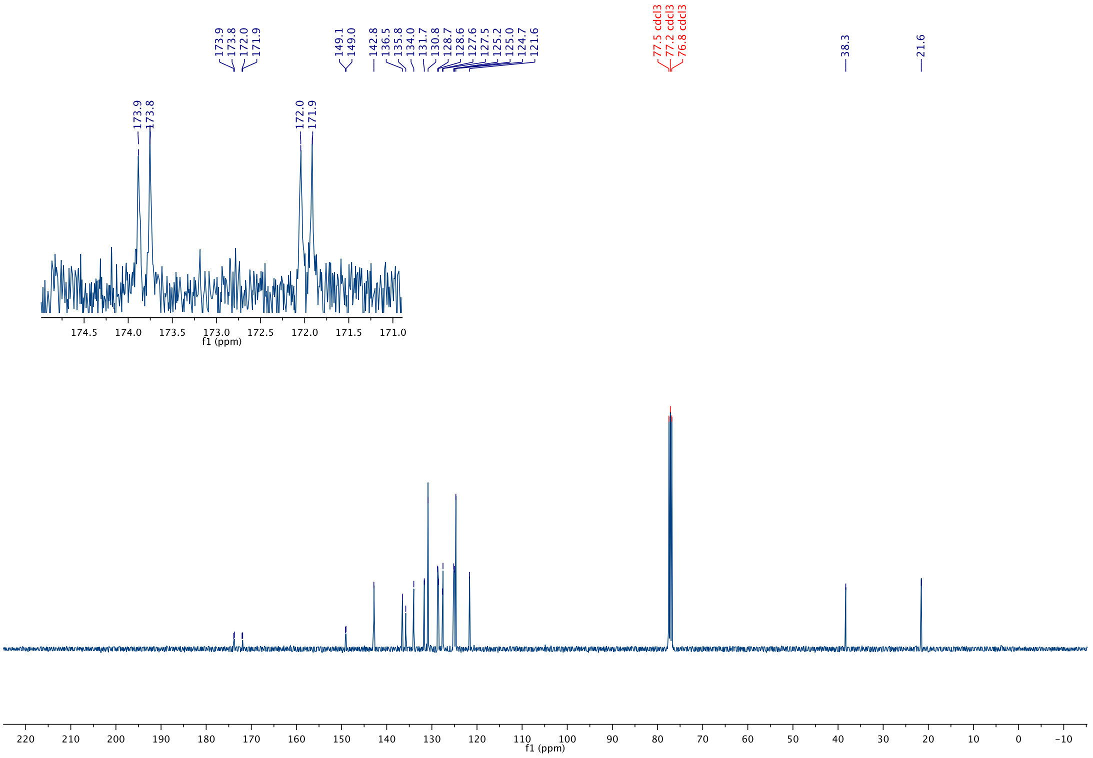


Figure IV.7: ^{13}C NMR of silver complex **IV.39**

Nevertheless, this splitting pattern could only be observed in a few silver carbenes. In other cases, as **IV.39**, $C_{carbene}$ resonates as a sharp or broad singlet. In a significant number of cases, carbene resonances are not observable (in our case, silver complexes **IV.26**, **IV.38** and **IV.40**). It is known that diluted samples of silver complexes give sharper signals than concentrated ones.[140] However, concentration of the sample and the lack of coupling $C_{carbene}$–Ag are independent. Lin and co-workers speculated that the absence of a splitting pattern is due to the fluxional behaviour of silver NHC complexes on the NMR time scale.[141] Thus, silver complexes that are static or have dynamic behaviour that are slow in the NMR time scale, will display $C_{carbene}$–Ag

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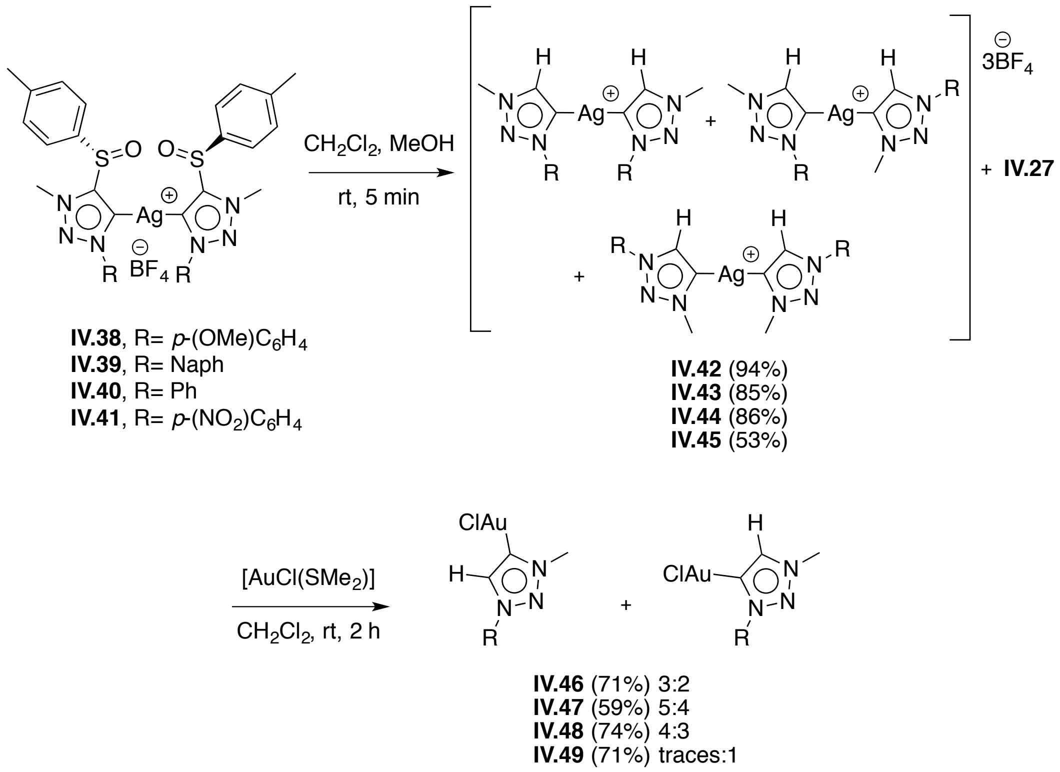
[140] A. A. D. Tulloch, A. A. Danopoulos, S. Winston, S. Kleinhenz, G. Eastham, *J. Chem. Soc., Dalton Trans.* **2002**, *13*, 534.

[141] H. M. J. Wang, I. J. B. Lin, *Organometallics* **1998**, *17*, 972.

couplings. As the dynamic behaviour increases on the NMR time scale, the resonance of the carbene centre will become broader until it could coalescence into a sharp singlet.[135] The coupling constant for the carbene to the ^{107}Ag isotope has a value in the range of 180 to 234 Hz; while the coupling constant for the ^{109}Ag isotope has values between 204 and 270 Hz. The observation of $C_{carbene}$–Ag coupling points to a static conformation for the silver NHC complex relative to the NMR time scale.

Once silver carbenes **IV.38–41** were obtained, reaction with methanol and subsequent transmetallation with [AuCl(SMe_2)] was addressed next (Scheme IV.13).



Scheme IV.13: Methanolysis and transmetallation of silver carbenes

Table IV.2 compiles the results of these two processes, demonstrating that the desulfinylation reaction was compatible with the presence of aromatic groups directly bounded to the heterocycle.

Table IV.2: Yield of the mixture of Ag-NHCs isolated and proportion of gold carbenes regioisomers measured by ^{1}H NMR of the crude product

Entry	Compound	Proportion of Ag-MICs regioisomers	Compound	Proportion of regioisomers *C*4vs*C*5[2]
1	**IV.42**	2:3:6	**IV.46**	3:2
2	**IV.43**	1:5	**IV.47**	5:4
3	**IV.44**	1:4:5	**IV.48**	4:3
4	**IV.45**	1:1:3	**IV.49**	Traces:1

[1] Yield of isolated mixture measured by ^{1}H NMR.
[2] Measured by ^{1}H NMR of the crude product.

The methanolysis is compatible both with electron-donating groups (Table IV.2, entry 2) and electron-withdrawing groups (Table IV.2, entry 3) attached to the aromatic ring of the sulfoxide moiety. In all cases the ratio of *C*4/*C*5 gold carbene complexes did not match the ratio of silver carbene complexes. This suggests a dynamic equilibrium in solution that is translated in a *C*4/*C*5 gold carbene ratio mostly independent on the nitrogen substituents. Thus, while methanolysis of silver carbene **IV.42** showed the presence of three signals in the region of resonance of the NCH_3 groups in a ratio of 2:3:6 (confirmed by the ratio of signals due to the methoxy group), and the transmetallation of this mixture of silver complexes with [AuCl(SMe$_2$)] afforded two gold 1,2,3-triazolylidene regioisomers **IV.46** in a 3:2 ratio and 71% yield, the analogous set of reactions carried out over silver carbene **IV.45** in CH_2Cl_2 formed a mixture of silver carbenes 1:1:3. Characterisation of this mixture could not be effected due to the insolubility that the metallic complex presented. Transmetallation of the solid with [AuCl(SMe$_2$)] in CH_2Cl_2 formed mostly the unrearranged 1,2,3-triazolylidene **IV.49** (71% yield after chromatography column). Traces of the *C*4 regioisomer were seen by TLC analysis of the transmetallation crude reaction, but enough quantity for a complete characterisation of this product could not be obtained.

Finally, the more sterically hindered carbene **IV.39** formed a mixture of silver carbenes in a 1:5 ratio. Transmetallation of the mixture of carbenes **IV.43** with [AuCl(SMe$_2$)] yielded a mixture of regioisomers **IV.47** (59%) in a ratio of 5:4. Therefore, it is clear that the steric differences between a phenyl group and the bulkier naphtyl group are not relevant.

In addition to spectroscopic data, the structures of the regioisomeric complexes **IV.48** were confirmed by X-ray diffraction studies (Figure IV.8–9).

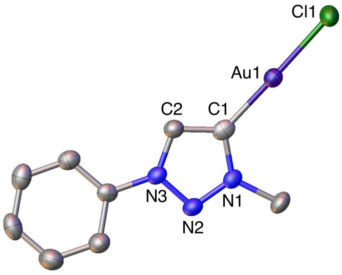


Figure IV.8: ORTEP representation of gold carbene **IV.48a**. Selected bond lengths (Å) and angles (deg): Au1-Cl1 2.2792(13), Au1-C1 1.962(5), C1-N1 1.375(6), N1-N2 1.332(5), N2-N3 1.317(5), N3-C2 1.353(6), C2-C1 1.369(7), C1-Au1-Cl1 178.586(4).

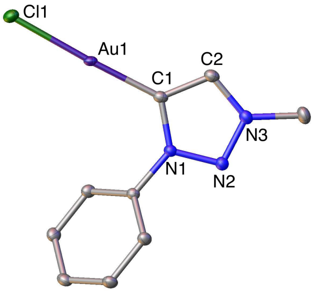
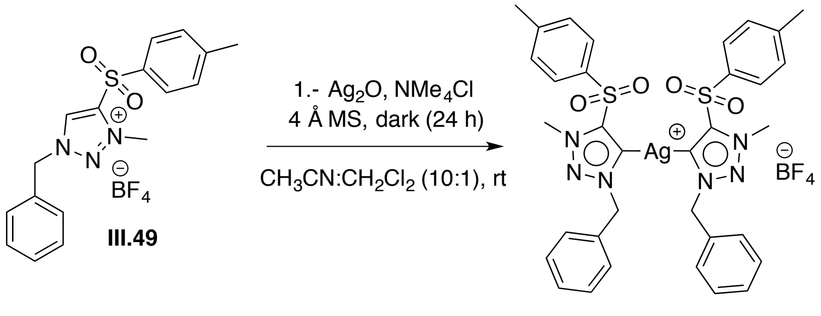


Figure IV.9: ORTEP representation of gold carbene **IV.48b**. Selected bond lengths (Å) and angles (deg): Au1-Cl1 2.2934(4), Au1-C1 1.9816(13), C1-N1 1.3720(16), N1-N2 1.3376(15), N2-N3 1.3121(15), N3-C2 1.3508(18), C2-C1 1.3863(17), C1-Au1-Cl1 177.402.

With these results in hand, we decided to carry out different experiments in order to gain some insights into the mechanism of the reaction. We determined first if the process is limited to the sulfoxide functionality. Silver carbene **IV.50** having a sulfone attached to *C*4 was prepared following the methodology used in this work in 94% yield (Scheme IV.14). In this case, the silver triazolylidene **IV.50** also showed a bis(carbene) structure as it could be confirmed by HRMS analysis, with a main fragment at *m*/*z* = 763.1136 that corresponded to the cationic part of the complex depicted in Scheme IV.14. The ^{1}H NMR spectrum showed signals for half of the molecule as a result of its high degree of symmetry, with the lack of the triazolium proton as a confirmation proof of the carbene formation. Again, a signal for the carbenic centre was not observable in the ^{13}C NMR spectrum of **IV.50**. Unfortunately, in this case the HMBC spectrum did not show any cross-peak attributable to the cross between the protons of the methylene group and the carbenic centre.

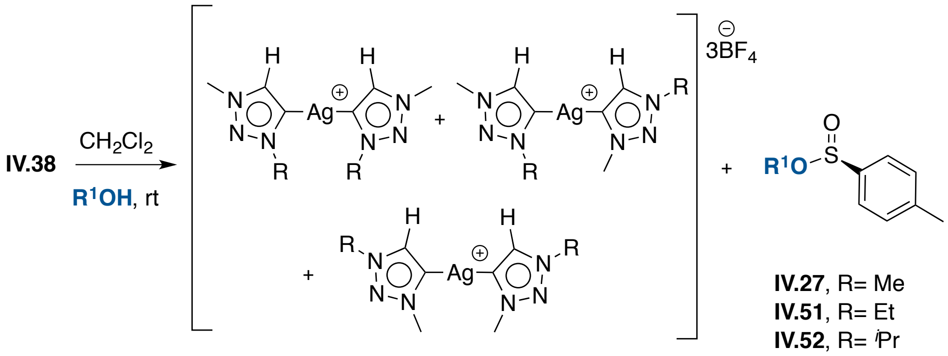


IV.50 (94%)

Scheme IV.14: Synthesis of silver carbene **IV.50** bearing a sulfone in *C*4

Reaction of silver carbene **IV.50** with MeOH in CH_2Cl_2 at rt did not produce any changes in the starting material. The reaction was heated in refluxing CH_2Cl_2 for 2 h 30 but no signs of formation of methyl sulfonate were observed by TLC analysis. So it was clear that the additional oxygen at the sulfone moiety was detrimental for the desulfinylation reaction to occur.

The role of the alcohol was addressed next. Silver carbene **IV.38** was dissolved in $CDCl_3$, staying unaltered for one week in solution. This confirmed the stability of the SO–*C*4 bond in the silver carbene in solution and in the absence of methanol.



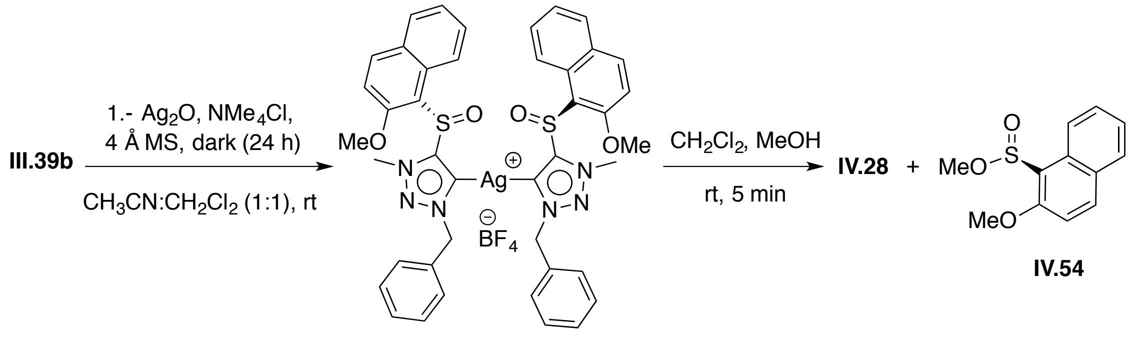
IV.42

Scheme IV.15: Carbene rearrangement performed by different alcohols

Different alcohols were tested next (Scheme IV.15). Desulfinylation reaction proceeded at rt when EtOH and ^{i}PrOH were added over a solution of **IV.38** in CH_2Cl_2. In the case of EtOH, the corresponding sulfinate **IV.51** was generated instantaneously and could be separated washing the reaction mixture with CH_2Cl_2:pentane. Reaction of the silver carbene **IV.38** with ^{i}PrOH, proceeded at rt but not instantaneously. After stirring the mixture of silver carbene and ^{i}PrOH for one hour, the solution became darker, showing the formation of isopropyl sulfinate **IV.52** (^{1}H NMR analysis).

Reaction of silver carbene **IV.38** with ^{t}BuOH at rt did not result in the formation of *tert*-buthylsulfinate either at rt or by heating at 50 °C for 1 h. Finally, silver carbene **IV.38** was reacted with a heterogenous mixture of water and CH_2Cl_2. No reaction was observed and the silver carbene was recovered unaltered.

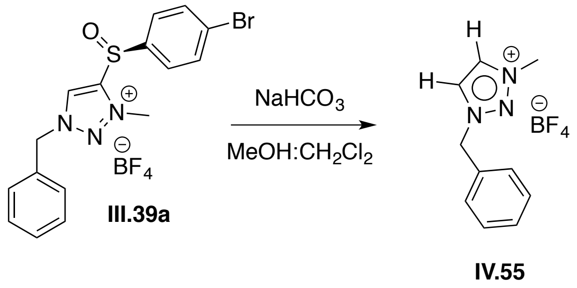
To determine the effect of the moiety attached to the sulfoxide group, silver carbene **IV.53** was synthetized from the triazolium precursor **III.39b** under the usual conditions (Scheme IV.16). When silver carbene **IV.53**, having a 2-methoxynaphty substituted sulfoxide, was dissolved in CH_2Cl_2 and MeOH was added, no changes in the colour of the solution were observed. TLC analysis of the crude reaction revealed the formation of traces of sulfinate **IV.54**. Nevertheless, when reaction was heated at 40 °C for two hours, the colour of the reaction became darker. Filtration of the crude reaction through a Celite pad and removal of the volatiles under vacuum, yielded a brown solid that was again precipitated and washed in a mixture of CH_2Cl_2:pentane. ^1H NMR spectrum of the supernatant confirmed the formation of the methyl 2-methoxynaphthy sulfinate. In addition, the analysis of the solid by ^1H NMR was in agreement with the presence of a mixture of *H*4 and *H*5 disubstituted silver carbenes **IV.28a**–**b**.



IV.53 (97%)

Scheme IV.16: Rearrangement of carbene **IV.51**

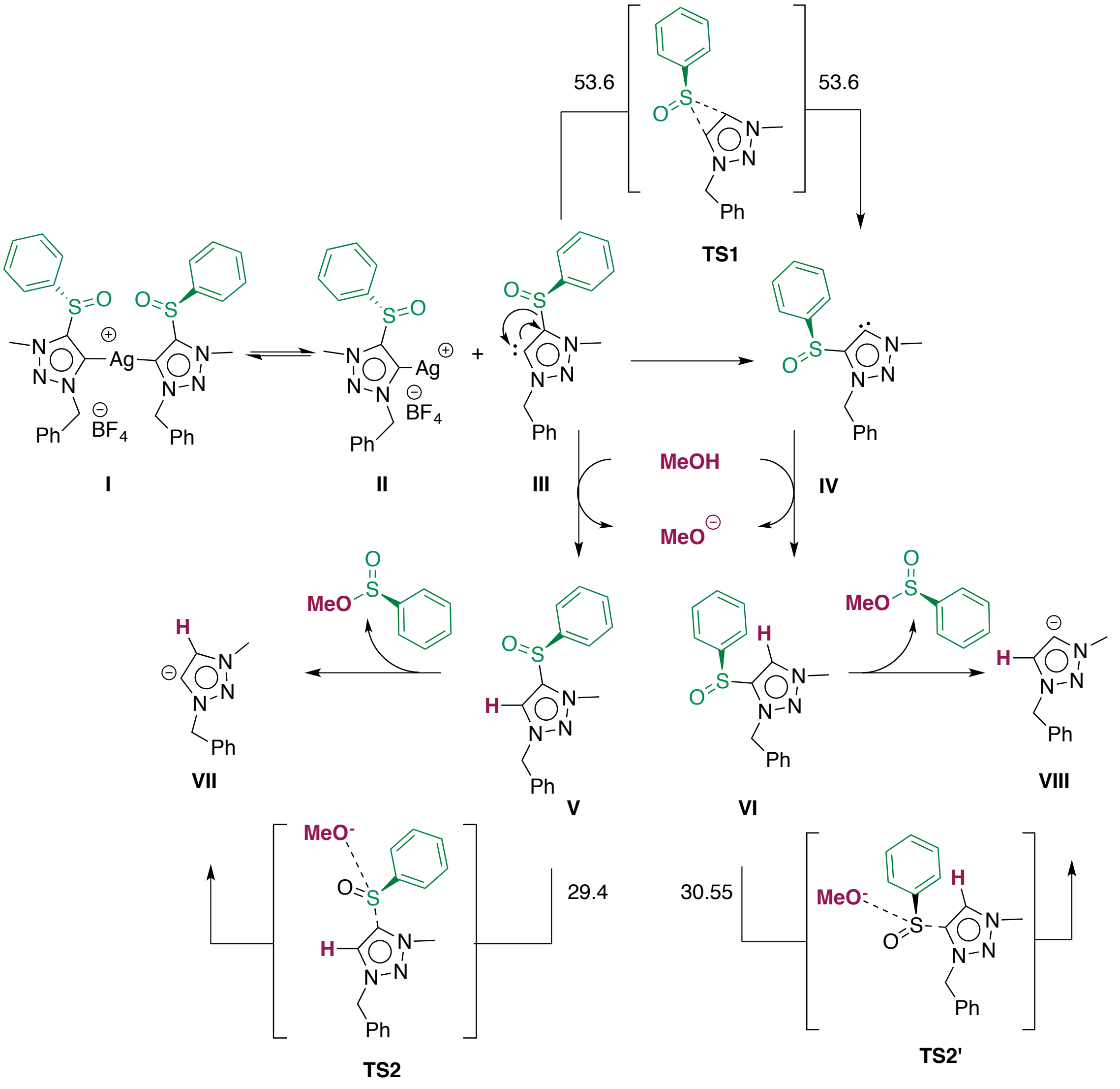
To determine whether the desulfinylation reaction occurs in the complexed silver carbene or in a free de-coordinated triazolylidene ligand, triazolium salt **III.39a** was reacted in CH_2Cl_2/MeOH and filtered through a $NaHCO_3$ pad. This salt was partially dissolved by MeOH. After separation from the resulting reaction mixture, a solid was obtained and analysed by ^1H NMR techniques. The spectrum revealed the formation of triazolium salt **IV.55**. Therefore, we may conclude that at least under the conditions tested, desulfinylation occurred in the free ligand rather than in the silver complex (Scheme IV.17).



Scheme IV.17: Desulfinylation process over a triazolium salt

To cast additional light to the desulfynilation mechanism, deuteration experiments were carried out. Thus, complex **IV.38** was dissolved in $CDCl_3$ and drops of CD_3OD were added to the solution. A ^1H NMR spectrum of the crude product showed that the desulfinylation process occurred, as three sets of signals for the methoxy group appeared (see above). Comparison of the values of the integrals of the new H substituents of the triazole core to the spectrum registered when reaction was performed in non-deuterated solvents, showed clearly that deuteration had occurred in *H4* and *H*5. In addition, when the reaction was performed in non-deuterated solvents a singlet at $\delta_H = 7.98$ ppm appeared in the ^1H NMR spectrum of the solid. This signal was assigned to the new CH proton of the triazolylidene core. This signal is no longer observed when the reaction is carried out in deuterated solvents. Therefore, we could affirm that the heterocycle is protonated from the methanol.

To obtain additional insight into the mechanism, we have studied this catalytic reaction by computational means (DFT). According to our calculations, silver bis(carbene) **I** is in equilibrium with the silver mono(carbene) **II** and the free carbene **III**, which experiences a fast intramolecular rearrangement to a new carbene **IV** through **TS1**. This rearrangement accounts for the formation of the mixed bis(carbene) species during the MeOH reaction (Scheme IV.18). Subsequently, fast protonation of the free carbenes **III** and **IV** liberates MeO^- forming **V** and **VI**. This is essential for the reaction to progress. All attempts to compute a reaction pathway promoting the elimination of methyl sulfonate forming **V** were fruitless. However, the removal of the sulfonate group by MeO^- occurs through **TS2** uneventfully. Evidently, the reaction product **IV** may complex the initial mono(carbene) **II** forming the observed mixed bis(carbenes). Finally, the symmetric fully rearranged silver bis(carbene) would be formed from two rearranged MICs.[142]



ΔG values are given in kcal/mol

Scheme IV.18: Mechanistic proposal supported by DFT calculations

Support for the mechanism in Scheme IV.18 arises from the deuteration experiments. In fact, in the presence of CD_3OD it is expected that protonation of carbenes **III** and **IV** would yield the monodeuterated compounds. However, the necessity of a second protonation event upon desulfinylation account for the fully (*C*4 and *C*5) deuteraded MICs.

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[142] It should be noted that albeit the energies demonstrated in Scheme IV.18 are high for a rt process, the possible participation of more than one molecule or MeOH may decrese this energy barrier.

Moreover, the existence of an equilibrium between the silver bis(carbene) **I** and the free species is demonstrated by the formation of Ag mono(carbene) complex **IV.56** upon crystallization of a solution containing **IV.26**. The X-ray structure of this compound unambiguously confirms the equilibrium between the free species and the double coordinated Ag-MIC (Figure IV.10).

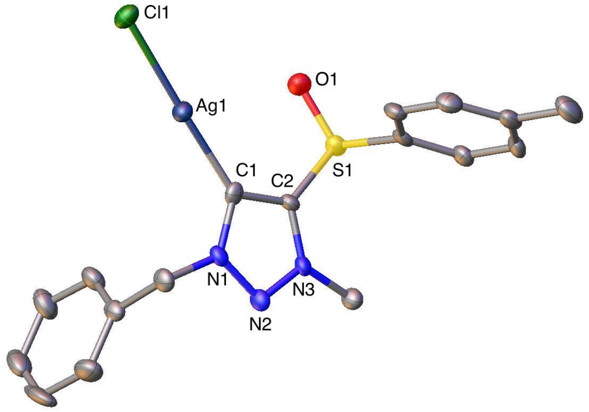
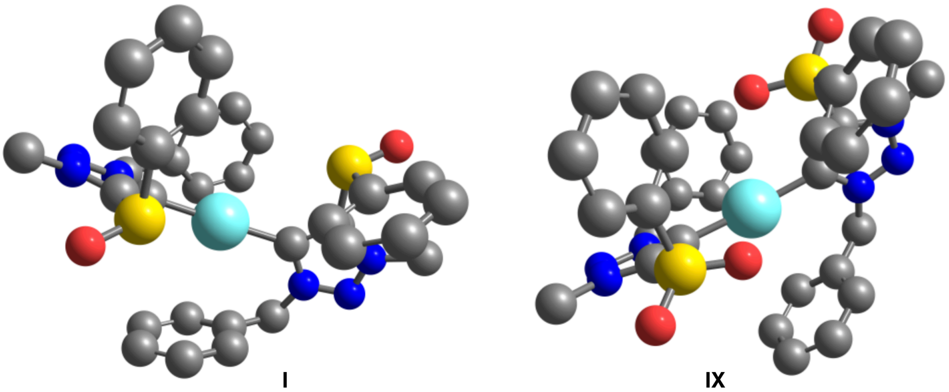


Figure IV.10: ORTEP representation of silver carbene **IV.56**. Selected bond lengths (Å) and angles (deg): Ag1–Cl1 2.064(6), Ag1–C1 2.3408(17), C1–N1 1.362(10), N1–N2 1.334(8), N2–N3 1.314(9), N3–C2 1.346(10), C2–C1 1.385(11), C2–S1 1.797(8), S1–O1 1.480(6), C1–Ag1–Cl1 177.916.

To explain the survival of double coordinated Ag-MIC in a non protic solvent (demonstrated by taking ^{1}H NMR spectra of a solution of complex **IV.38** in $CDCl_3$ at different times), it is necessary to resort to the intrinsically irreversible nature of the protonation of the free carbene. In fact, in the absence of this protonation, no base (alkoxide) is formed, and therefore the equilibrium is completely displaced to the double coordinated Ag-MIC form.

The inertia of sulfone **IV.50** towards alcoholysis should originate by the stabilisation of the silver carbene by the second oxygen atom.

Figure IV.11 shows the optimized structures for sulfoxide **I** and the model sulfone **IX.** Clearly, the interaction of the oxygen of the sulfone and the silver atom is not present in the sulfoxide **I**.



I **IX**

Figure IV.11: Computed structures of **I** and **IX**

IV.4 CONCLUSIONS

- To conclude, the synthesis and characterisation of new silver bis(1,2,3-triazolylidene)complexes (Ag-MIC) bearing enantiopure (*S*)-sulfoxide subtituents in *C*4 has been achieved.

- An unprecedented desulfinylation reaction that affords a mixture of three *C*4-*C*5 unsubstituted silver carbenes (*C*4-*C*4; mixed *C*4-*C*5 and *C*5-*C*5) has been observed by spectroscopic means. The synthesis of the two possible *C*4 and *C*5 MIC-AuL regioisomers having a *C*-unsubstituted triazole core confirms the desulfinylation. These compounds have been structurally characterised by X-ray diffraction. This synthesis of unsubstituted M-MIC is not only unprecedented in the literature but one among the few methods to prepare such compounds.

- Extensive computational and experimental studies, including deuteration experiments and the isolation and X-ray characterisation of MIC-AgCl **IV.56** have allowed to disentangle the mechanism of this novel reaction. Thus, silver bis(MIC) is in equilibrium with the free MIC, which, in the presence of alcohol, experiences a *C*4 to *C*5 rearrangement of the sulfinyl moiety. Protonation of the free carbene followed by alkoxide displacement of the sulfinyl moiety completes the reaction upon a second protonation.

IV.5 EXPERIMENTAL SECTION

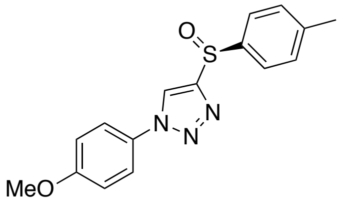
Azide **IV.40** was prepared following a modified procedure previously reported:[133]

Amine (16 mmol, 1.00 equiv) was dissolved in THF (20 mL). Ice was then added followed by HCl 37% (3.5 mL). A solution of $NaNO_2$ (24.00 mmol, 1.50 equiv) in H_2O (10 mL) was added to the solution. The reaction was stirred at 0 °C for 15 min. In case of acidic pH of the crude reaction the solution had to be neutralized by $NaHCO_3$. NaN_3 (24 mmol, 1.50 equiv) dissolved in H_2O was added dropwise. The crude mixture was stirred for 1 h. The mixture was extracted with Et_2O three times. The organic layer was washed with HCl 0.1 M (three times), water (three times), dried over $MgSO_4$ and filtered. All the volatiles were removed under vacuum affording the corresponding azide, which was purified through a short pad of SiO_2.

General procedure for the synthesis of 1,2,3-triazoles

A mixture of organic azide (1.20 equiv), alkyne (1.00 equiv), sodium (L)-ascorbate (0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (0.25 equiv) in DMF was stirred under Ar at rt until completion of the reaction (TLC analysis). The reaction was quenched with water at 0 °C and allowed to reach rt. The mixture was extracted with CH_2Cl_2 three times. The organic layer was dried over $MgSO_4$, filtered and the volatiles were removed under vacuum to afford the corresponding reaction products, which were purified through a short pad of SiO_2.

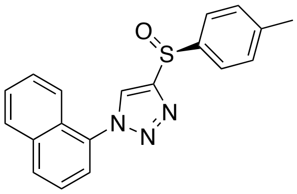
Synthesis of compound IV.31



Following the general procedure a mixture of azide **III.41a** (623 mg, 4.17 mmol, 1.20 equiv), alkyne **III.29** (571 mg, 3.48 mmol, 1.00 equiv), sodium (L)-ascorbate (344 mg, 1.74 mmol, 0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (217 mg, 0.87 mmol, 0.25 equiv) in DMF (76 mL) was stirred under Ar at rt for 2 h. The resulting residue was purified (SiO_2, Hex/EtOAc 6:4) to yield **IV.31** as a white solid (901 mg, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H, $N_3C{=}CH$), 7.69 (d, J = 8.2 Hz, 2H, Ar *p*-tolyl), 7.56 (d, J = 9.0 Hz, 2H, Ar *p*-$OMeC_6H_4$), 7.32 (d, J = 8.2 Hz, 2H, Ar *p*-tolyl), 6.98 (d, J = 9.0 Hz, 2H, Ar *p*-$OMeC_6H_4$), 3.83 (s, OCH_3), 2.38 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.4 (C, Ar), 153.7 (C, $N_3C{=}CH$), 142.0 (C, Ar), 140.0 (C, Ar), 130.2 (2CH, Ar), 129.7 (C, Ar), 124.8 (2CH, Ar), 122.4 (2CH, Ar), 122.2 (CH, $N_3C{=}CH$), 114.9 (2CH, Ar), 55.7 (OCH_3), 21.5 (CH_3, *p*-tolyl). **IR (KBr)** $\nu_{máx}$ 3435, 3124, 1595, 1520, 1312, 1253, 1049, 1039, 826, 810, 631. **$[\alpha]_D^{25}$** + 267.3 (*c* 0.9, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{16}H_{16}N_3O_2S$: 314.0958 $[M+H]^+$, found: 314.0960. **m.p.** 94–97 °C.

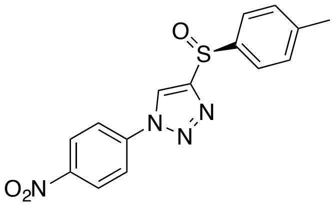
Synthesis of compound IV.32



Following the general procedure a mixture of azide **III.41b** (268 mg, 1.58 mmol, 1.30 equiv), alkyne **III.29** (200 mg, 1.22 mmol, 1.00 equiv), sodium (L)-ascorbate (121 mg, 0.61 mmol, 0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (76 mg, 0.30 mmol, 0.25 equiv) in DMF (27 mL) was stirred under Ar at rt for 3 h. The resulting residue was purified (SiO_2, Hex/EtOAc 6:4) to yield **IV.32** as a white solid (252 mg, 63%).

^{1}H NMR (400 MHz, CDCl$_3$) *δ* 8.15 (s, 1H, N$_3$C=CH), 8.02 (dd, *J* = 7.5 Hz, 2.0 Hz, 1H, Ar naph), 7.95 (br d, *J* = 8.0 Hz, 1H, Ar naph), 7.77 (d, *J* = 8.2 Hz, 2H, Ar *p*-tolyl), 7.55 (m, 5H, Ar), 7.37 (br d, *J* = 8.0 Hz, 0.6 Hz, 2H, Ar *p*-tolyl), 2.42 (s, 3H, CH$_3$ *p*-tolyl); **^{13}C NMR** (100 MHz, CDCl$_3$) *δ* 153.4 (C, N$_3$C=CH), 142.4 (C, Ar), 139.9 (C, Ar), 134.2 (C, Ar), 133.0 (C, Ar), 131.1 (2CH, Ar), 130.3 (2CH, Ar), 128.5 (CH, Ar), 128.3 (CH, Ar), 128.2 (C, Ar), 127.4 (CH, Ar), 126.5 (CH, N$_3$C=CH), 125.0 (CH, Ar), 124.9 (2CH, Ar), 123.8 (CH, Ar), 122.0 (CH, Ar), 21.6 (CH$_3$, *p*-tolyl). **IR (KBr) $\nu_{\text{máx}}$** 3435, 3104, 1490, 1085, 1054, 1033, 814, 796, 768, 521. **$[\alpha]_D^{25}$** + 243.0 (*c* 0.8 CHCl$_3$). **HRMS (ESI)** *m/z* calculated for $C_{19}H_{16}N_3OS$: 334.1009 $[M+H]^+$, found: 334.1006. **m.p.** 97–100 °C.

Preparation of compound IV.33



Following the general procedure a mixture of azide **IV.30** (513 mg, 3.16 mmol, 1.30 equiv), alkyne **III.29** (400 mg, 2.43 mmol, 1.00 equiv), sodium (L)-ascorbate (241 mg, 1.22 mmol, 0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (187 mg, 0.61 mmol, 0.25 equiv) in DMF (40 mL) was stirred under Ar at rt for 2 h 30. The resulting residue was purified (SiO$_2$, Hex/EtOAc 1:1) to yield **IV.33** as a white solid (513 mg, 75%).

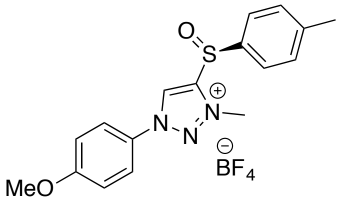
^{1}H NMR (400 MHz, CDCl$_3$) *δ* 8.47 (s, 1H, N$_3$C=CH), 8.41 (d, *J* = 9.1 Hz, 2H, Ar *p*-NO$_2$C$_6$H$_4$), 7.96 (d, *J* = 9.1 Hz, 2H, Ar *p*-NO$_2$C$_6$H$_4$), 7.72 (d, *J* = 8.2 Hz, 2H, Ar *p*-tolyl), 7.36 (d, *J* = 8.2 Hz, 2H, Ar *p*-tolyl), 2.41 (s, 3H, CH$_3$ *p*-tolyl). **^{13}C NMR** (100 MHz, CDCl$_3$) *δ* 155.4 (C, N$_3$C=CH), 147.9 (C, Ar), 142.8 (C, Ar), 140.6 (C, Ar), 139.7 (C, Ar), 130.5 (2CH, Ar), 125.8 (2CH, Ar), 124.9 (2CH, Ar), 122.1 (CH, N$_3$C=CH), 121.0 (2CH, Ar), 21.7 (CH$_3$, *p*-tolyl). **IR (KBr) $\nu_{\text{máx}}$** 3145, 3101, 1598, 1532, 1505, 1344, 1235, 1082, 1055, 1032, 855,

573. **$[\alpha]_D^{25}$** + 252.2 (*c* 0.5 $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{15}H_{13}N_4O_3S$: 329.0703 $[M+H]^+$, found: 329.0710. **m.p.** 209–210 °C.

General procedure for the synthesis of triazolium salts

Triazole (1.00 equiv) and Meerwein's salt (1.30 equiv per triazole) were stirred under Ar at rt in CH_2Cl_2 until completion of reaction (^1H NMR analysis). The reaction was quenched with methanol and filtered through a short pad of $NaHCO_3$. The solvent was removed under vacuum to afford the corresponding reaction product without further purification. In some cases, the product was washed with a mixture of CH_2Cl_2:pentane to remove the starting material traces.

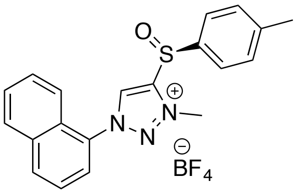
Synthesis of compound IV.34



Following the general procedure a mixture of **IV.31** (112 mg, 0.36 mmol, 1.00 equiv) and Me_3OBF_4 (69 mg, 0.46 mmol, 1.30 equiv) in CH_2Cl_2 (12 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **IV.34** as a white solid (139 mg, 93%).

^{1}H NMR (400 MHz, DMSO-*d*$_6$) *δ* 9.82 (s, 1H, $N_3C=CH$), 7.91 (m, 4H, 2CH Ar *p*-$OMeC_6H_4$ + 2CH *p*-tolyl), 7.54 (d, *J* = 8.1 Hz, 2H, Ar *p*-tolyl), 7.25 (d, *J* = 9.1 Hz, 2H, Ar *p*-$OMeC_6H_4$), 4.37 (s, 3H, NCH_3), 3.87 (s, 3H, OCH_3), 2.43 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, DMSO-*d*$_6$) *δ* 161.7 (C, Ar), 146.4 (C, $N_3C=CH$), 144.0 (C, Ar), 136.5 (C, Ar), 130.8 (2CH, Ar), 129.3 (CH, $N_3C=CH$), 127.7 (C, Ar), 126.2 (2CH, Ar), 123.5 (2CH, Ar), 115.3 (2CH, Ar), 56.0 (OCH_3), 39.6 (NCH_3), 21.1 (CH_3, *p*-tolyl). **IR (KBr)** $\nu_{máx}$ 3436, 3124, 2923, 1607, 1595, 1514, 1260, 1184, 1057, 836, 813, 520. **$[\alpha]_D^{25}$** + 24.6 (*c* 0.5, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{17}H_{18}N_3O_2S$: 328.1114 $[M–BF_4^-]^+$, found: 328.1127. **m.p.** 50–52 °C.

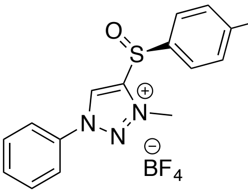
Synthesis of compound IV.35



Following the general procedure a mixture of **IV.32** (430 mg, 1.29 mmol, 1.00 equiv) and Me_3OBF_4 (248 mg, 1.68 mmol, 1.30 equiv) in CH_2Cl_2 (40 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **IV.35** as a white solid (477 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.08 (d, *J* = 8.4 Hz, 1H, Ar naph), 7.95 (m, 5H, Ar *p*-tolyl, N_3C=CH and Ar naph), 7.61 (m, 4 H, Ar naph), 7.43 (d, *J* = 8.0 Hz, 2H, Ar *p*-tolyl), 4.68 (s, 3H, NCH_3), 2.41 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 148.4 (C, N_3C=CH), 145.0 (C, Ar), 134.4 (C, Ar), 133.9 (C, Ar), 133.3 (CH, Ar), 131.8 (C, Ar), 131.2 (2CH, Ar), 130.6 (C, Ar), 129.7 (CH, Ar), 128.8 (CH, Ar), 128.1 (CH, Ar), 126.9 (CH, Ar), 125.9 (2CH, Ar), 125.7 (CH, Ar), 125.2 (CH, N_3C=CH), 120.6 (2CH, Ar), 40.2 (NCH_3), 21.8 (CH_3, *p*-tolyl). **IR (KBr) $\nu_{máx}$** 3436, 3108, 3061, 1059, 807, 772, 519. **$[\alpha]_D^{25}$** + 136.0 (*c* 0.5 $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{20}H_{18}N_3OS$: 348.1165 $[M–BF_4^-]^+$, found: 348.1165. **m.p.** 140–143 °C.

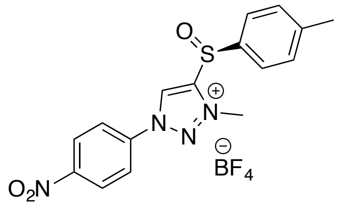
Synthesis of compound IV.36



Following the general procedure a mixture of **III.61a** (91 mg, 0.32 mmol, 1.00 equiv) and Me_3OBF_4 (62 mg, 0.42 mmol, 1.30 equiv) in CH_2Cl_2 (10 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **IV.36** as a white solid (123 mg, quantitative).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H, $N_3C{=}CH$), 7.84 (d, J = 8.2 Hz, 2H, Ar *p*-tolyl), 7.79 (m, 2H, Ar), 7.54 (m, 3H, Ar), 7.42 (d, J = 8.2 Hz, 2H, Ar *p*-tolyl), 4.45 (s, 3H, NCH_3), 2.41 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.1 (C, $N_3C{=}CH$), 144.9 (C, Ar), 135.0 (C, Ar), 134.6 (C, Ar), 132.4 (CH, Ar), 131.3 (2CH, Ar), 130.5 (2CH, Ar), 128.9 (CH, $N_3C{=}CH$), 125.8 (2CH, Ar), 122.3 (2CH, Ar), 40.0 (NCH_3), 21.7 (CH_3, *p*-tolyl). **IR (KBr)** $\nu_{\text{máx}}$ 3414, 3037, 1084, 1062, 817, 772, 521. **$[\alpha]_D^{25}$** + 55.4 (*c* 0.7 $CHCl_3$). **HRMS (ESI)** *m*/*z* calculated for $C_{16}H_{16}N_3OS$: 298.1009 $[M{-}BF_4^-]^+$, found: 298.1018. **m.p.** 110–112 °C.

Synthesis of compound IV.37



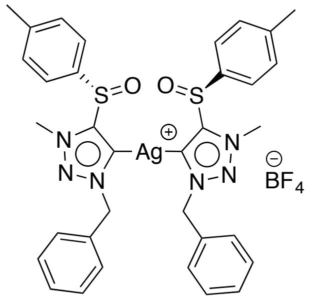
Following the general procedure a mixture of **IV.33** (263 mg, 0.80 mmol, 1.00 equiv) and Me_3OBF_4 (154 mg, 1.04 mmol, 1.30 equiv) in CH_2Cl_2 (25 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **IV.37** as a white solid (210 mg, 76%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.05 (s, 1H, $N_3C{=}CH$), 8.58 (d, J = 9.1 Hz, 2H, Ar *p*-$NO_2C_6H_4$), 8.29 (d, J = 9.1 Hz, 2H, Ar *p*-$NO_2C_6H_4$), 7.91 (d, J = 8.3 Hz, 2H, Ar *p*-tolyl), 7.56 (d, J = 8.3 Hz, 2H, Ar *p*-tolyl), 4.46 (s, 3H, NCH_3), 2.44 (s, 3H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 149.1 (C, Ar), 147.1 (C, $N_3C{=}CH$), 144.1 (C, Ar), 138.6 (C, Ar), 136.3 (C, Ar), 130.8 (2CH, Ar), 130.5 (CH, $N_3C{=}CH$), 126.2 (2CH, Ar), 125.7 (2CH, Ar), 123.3 (2CH, Ar), 40.0 (NCH_3), 21.1 (CH_3, *p*-tolyl). **IR (KBr) $\nu_{máx}$** 3401, 3126, 1536, 1350, 1062, 856, 573. **$[\alpha]_D^{25}$** + 67.5 (*c* 0.2, MeOH/$CHCl_3$ 4:1). **HRMS (ESI)** *m*/*z* calculated for $C_{16}H_{15}N_4O_3S$: 343.0859 $[M–BF_4^-]^+$, found: 343.0861. **m.p.** 209–211 °C.

General procedure for the synthesis of silver carbenes

In a schlenk flask charged with 4 Å molecular sieves, a mixture of triazolium salt (1.00 equiv), NMe_4Cl (1.50 equiv) and Ag_2O (0.75 equiv) was stirred at rt in the dark in CH_3CN:CH_2Cl_2 (1:10) until the formation of the silver carbene (^1H NMR analysis). The reaction was filtered through a pad of Celite and the volatiles were removed under vacuum. The solid was then redissolved in CH_2Cl_2 and filtered again through a pad of Celite to separate the product form NMe_4Cl. The residue was precipitated in a mixture of CH_2Cl_2:pentane to afford the corresponding reaction products.

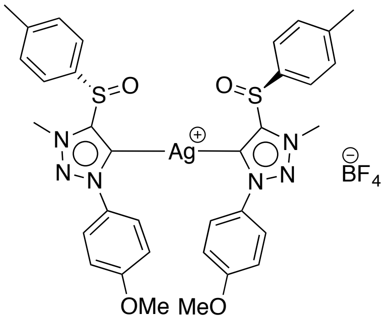
Synthesis of compound IV.26



Following the general procedure a mixture of triazolium salt **III.31** (168 mg, 0.47 mmol, 1.00 equiv), NMe_4Cl (77 mg, 0.70 mmol, 1.50 equiv) and Ag_2O (81 mg, 0.35 mmol, 0.75 equiv) in CH_3CN:CH_2Cl_2 (26 mL) was stirred under Ar at rt overnight until the formation of the silver carbene (^1H NMR analysis). The reaction was filtered through a pad of Celite and the solvent was removed under vacuum. The solid was then redissolved in CH_2Cl_2 and filtered again through a pad of Celite. The residue was precipitated in a mixture of CH_2Cl_2:pentane to afford the corresponding reaction product **IV.26** as a brownish solid (170 mg, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.58 (d, *J* = 8.3 Hz, 4H, Ar *p*-tolyl), 7.21 (m, 4H, Ar), 7.35 (m, 10H, 6H Ar and 4H Ar *p*-tolyl), 5.67 (d, *J* = 14.1 Hz, 2H, NCH_2), 5.62 (d, *J* = 14.1 Hz, 2H, NCH_2), 4.16 (s, 6H, NCH_3), 2.42 (s, 6H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 168.4 (2C, $N_3C=C$Ag, observed in HMBC), 149.0 (2C, N_3C=CAg), 143.5 (2C, Ar), 136.7 (2C, Ar), 133.2 (2C, Ar), 130.9 (4CH, Ar), 129.6 (2CH, Ar), 129.4 (4CH, Ar), 128.9 (4CH, Ar), 124.7 (4CH, Ar), 60.6 ($2NCH_2$), 38.1 ($2NCH_3$), 21.7 ($2CH_3$, *p*-tolyl). **IR (KBr) $\nu_{máx}$** 3440, 3031, 2950, 1492, 1456, 1316, 1083, 1052, 811, 745, 708. **$[\alpha]_D^{25}$** – 40.6 (*c* 0.2, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{34}H_{34}AgN_6O_2S_2$: 731.1228 $[M–BF_4^-]^+$, found: 731.1229. **m.p.** decomposes before melting.

Synthesis of compound IV.38

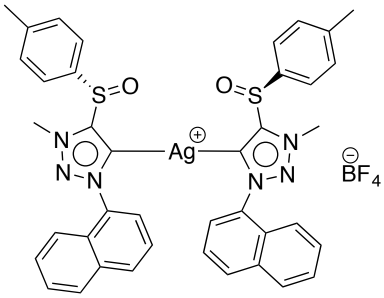


Following the general procedure a mixture of triazolium salt **IV.34** (150 mg, 0.46 mmol, 1.00 equiv), NMe_4Cl (75 mg, 0.69 mmol, 1.50 equiv) and Ag_2O (79 mg, 0.34 mmol, 0.75 equiv) in $CH_3CN:CH_2Cl_2$ (24 mL) was stirred under Ar at rt overnight until the formation of the silver carbene (^{1}H NMR analysis). The reaction was filtered through a pad of Celite and the solvent was removed under vacuum. The solid was then redissolved in CH_2Cl_2 and filtered again through a pad of Celite. The residue was precipitated in a mixture of CH_2Cl_2 to afford the corresponding reaction product **IV.38** as a brownish solid (171 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.80 (d, *J* = 9.0 Hz, 4H, Ar *p*-$OMeC_6H_4$), 7.62 (d, *J* = 8.2 Hz, 4H, Ar *p*-tolyl), 7.33 (d, *J* = 8.2 Hz, 4H, Ar *p*-tolyl), 6.92 (d, *J* = 9.0 Hz, 4H, Ar *p*-

$OMeC_6H_4$), 4.24 (s, 6H, NCH_3), 3.77 (s, 6H, OCH_3), 2.34 (s, 6H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 161.3 (2C, Ar), 149.8 (2C, N_3*C*=CAg), 143.1 (2C, Ar), 137.0 (2C, Ar), 132.6 (2C, Ar), 130.9 (4CH, Ar), 125.0 (4CH, Ar), 124.9 (4CH, Ar), 114.9 (4CH, Ar), 55.8 ($2OCH_3$), 38.2 ($2NCH_3$), 21.5 ($2CH_3$, *p*-tolyl), $C_{carbene}$ not observed. **IR (KBr) $\nu_{máx}$** 3456, 3050, 2957, 2841, 1606, 1512, 1258, 1084, 1055, 837, 813, 738, 612. **$[\alpha]_D^{25}$** – 157.2 (*c* 0.2 $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{34}H_{34}AgN_6O_4S_2$: 763.1127 $[M–BF_4^-]^+$, found: 763.1118. **m.p.** decomposes before melting.

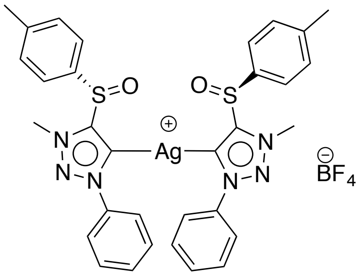
Synthesis of compound IV.39



Following the general procedure a mixture of triazolium salt **IV.35** (186 mg, 0.43 mmol, 1.00 equiv), NMe_4Cl (70 mg, 0.64 mmol, 1.50) and Ag_2O (74 mg, 0.32 mmol, 0.75 equiv) in $CH_3CN:CH_2Cl_2$ (20 mL) was stirred under Ar at rt overnight until the formation of the silver carbene (^{1}H NMR analysis). The reaction was filtered through a pad of Celite and the solvent was removed under vacuum. The solid was then redissolved in CH_2Cl_2 and filtered again through a pad of Celite. The residue was precipitated in a mixture of CH_2Cl_2:pentane to afford the corresponding reaction product **IV.39** as a brownish solid (170 mg, 89 %).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.94 (d, *J* = 8.2 Hz, 2H, Ar naph), 7.86 (d, *J* = 8.1 Hz, 2H, Ar naph), 7.63 (d, *J* = 7.3 Hz, 2H, Ar naph), 7.55 (m, 2H, Ar naph), 7.46 (m, 6H, Ar naph), 7.39 (d, *J* = 8.2 Hz, 4H, Ar *p*-tolyl), 7.29 (d, *J* = 8.2 Hz, 4H, Ar *p*-tolyl) 4.20 (s, 6H, NCH_3), 2.37 (s, 6H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 172.9 (2C, N_3C=*C*Ag), 149.1 (2C, N_3*C*=CAg), 142.8 (2C, Ar), 136.5 (2C, Ar), 135.8 (2C, Ar), 134.0 (2C, Ar), 131.7 (2CH, Ar), 130.8 (4CH, Ar), 128.7 (2CH, Ar), 128.6 (2CH, Ar), 127.6 (2CH, Ar), 127.5 (2C, Ar), 125.2 (2CH, Ar), 125.0 (2CH, Ar), 124.7 (4CH, Ar), 121.6 (2CH, Ar), 38.3 (2NCH$_3$), 21.6 (2CH$_3$, *p*-tolyl). **IR (KBr) ν$_{\text{máx}}$** 3054, 2922, 1598, 1084, 1055, 806, 773. **$[\alpha]_D^{25}$** – 119.3 (*c* 0.8 CHCl$_3$). **HRMS (ESI)** *m/z* calculated for $C_{40}H_{34}AgN_6O_2S_2$: 803.1230 $[M–BF_4^-]^+$, found: 803.1236. **m.p.** decomposes before melting.

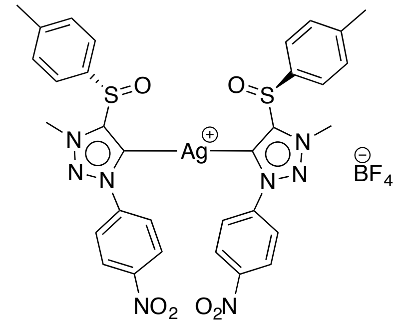
Synthesis of compound IV.40



Following the general procedure a mixture of triazolium salt **IV.36** (153 mg, 0.40 mmol, 1.00 equiv), NMe$_4$Cl (65 mg, 0.59 mmol, 1.50 equiv) and Ag$_2$O (69 mg, 0.30 mmol, 0.75 equiv) in CH$_3$CN:CH$_2$Cl$_2$ (19 mL) was stirred under Ar at rt overnight until the formation of the silver carbene (^{1}H NMR analysis). The reaction was filtered through a pad of Celite and the solvent was removed under vacuum. The solid was then redissolved in CH$_2$Cl$_2$ and filtered again through a pad of Celite. The residue was precipitated in a mixture of CH$_2$Cl$_2$:pentane to afford the corresponding reaction product **IV.40** as a brownish solid (139 mg, 88%).

^{1}H NMR (400 MHz, CDCl$_3$) *δ* 7.83 (m, 4H, Ar), 7.67 (d, *J* = 8.3 Hz, 4H, Ar *p*-tolyl), 7.52 (m, 6H, Ar), 7.39 (d, *J* = 8.3 Hz, 4H, Ar *p*-tolyl), 4.29 (s, 6H, NCH$_3$), 2.42 (s, 2H, CH$_3$ *p*-tolyl). **^{13}C NMR** (100 MHz, CDCl$_3$) *δ* 149.4 (2C, N$_3$*C*=CAg), 143.4 (2C, Ar), 139.2 (2C, Ar), 136.9 (2C, Ar), 131.1 (2CH, Ar), 131.0 (4CH, Ar), 130.0 (4CH, Ar), 124.8 (4CH, Ar), 123.3 (4CH, Ar), 38.3 (2NCH$_3$), 21.7 (2CH$_3$, *p*-tolyl), C$_{\text{carbene}}$ nos observed. **IR (KBr) ν$_{\text{máx}}$** 3467, 3045, 1594, 1493, 1325, 1084, 1054, 813, 766, 687. **$[\alpha]_D^{25}$** – 140.9 (*c* 0.3 CHCl$_3$). **HRMS (ESI)** *m/z* calculated for $C_{32}H_{30}AgN_6O_2S_2$: 703.0915 $[M–BF_4^-]^+$, found: 703.0911. **m.p.** decomposes before melting.

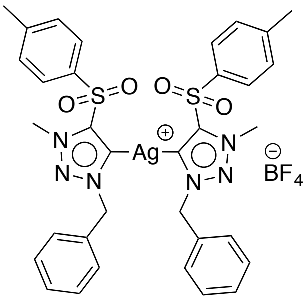
Synthesis of compound IV.41



Following the general procedure a mixture of triazolium salt **IV.37** (107 mg, 0.25 mmol, 1.00 equiv), NMe_4Cl (41mg, 0.38 mmol, 1.50 equiv) and Ag_2O (43 mg, 0.19 mmol, 0.75 equiv) in CH_3CN:CH_2Cl_2 (11 mL) was stirred under Ar at rt overnight until the formation of the silver carbene (^1H NMR analysis). The reaction was filtered through a pad of Celite and the solvent was removed under vacuum. The solid was then redissolved in CH_2Cl_2 and filtered again through a pad of Celite. The residue was precipitated in a mixture of CH_2Cl_2:pentane to afford the corresponding reaction product **IV.41** as a yellow solid (104 mg, 94%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.38 (d, *J* = 9.1 Hz, 4H, Ar *p*-$NO_2C_6H_4$), 8.30 (d, *J* = 9.1 Hz, 4H, Ar *p*-$NO_2C_6H_4$), 7.77 (d, *J* = 8.3 Hz, 4H, Ar *p*-tolyl), 7.38 (d, *J* = 8.3 Hz, 4H, Ar *p*-tolyl), 4.25 (s, 6H, NCH_3), 2.40 (s, 6H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 170.2 (2C, $N_3C{=}\mathit{C}Ag$), 149.7 (2C, $N_3\mathit{C}{=}CAg$), 148.7 (2C, Ar), 143.5 (2C, Ar), 143.4 (2C, Ar), 136.7 (2C, Ar), 131.0 (4CH, Ar), 125.3 (2CH, Ar), 125.0 (4CH, Ar), 124.6 (4CH, Ar), 38.5 ($2NCH_3$), 21.6 ($2CH_3$, *p*-tolyl), $C_{carbene}$ not observed. **IR (KBr)** $\nu_{máx}$ 3435, 3050, 1595, 1530, 1493, 1345, 1081, 1050, 855, 812, 751, 543. $[\alpha]_D^{25}$ – 141.0 (*c* 0.4 $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{32}H_{28}AgN_8O_6S_2$: 793.0617 $[M{-}BF_4^-]^+$, found: 793.0643. **m.p.** decomposes before melting.

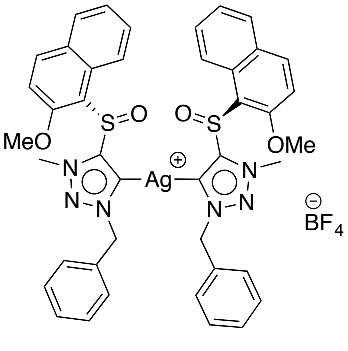
Synthesis of compound IV.50



Following the general procedure a mixture of triazolium salt **III.49** (40 mg, 0.10 mmol, 1.00 equiv), NMe_4Cl (16 mg, 0.14 mmol, 1.50 equiv) and Ag_2O (17 mg, 0.07 mmol, 0.75 equiv) in $CH_3CN:CH_2Cl_2$ (7 mL) was stirred under Ar at rt overnight until the formation of the silver carbene (^{1}H NMR analysis). The reaction was filtered through a pad of Celite and the solvent was removed under vacuum. The solid was then redissolved in CH_2Cl_2 and filtered again through a pad of Celite. The residue was precipitated in a mixture of CH_2Cl_2:pentane to afford the corresponding reaction product **IV.50** as a brownish solid (29 mg, 94%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.96 (d, *J* = 8.4 Hz, 4H, Ar *p*-tolyl), 7.43 (m, 8H, Ar), 7.34 (m, 6H, 2H Ar and 4H Ar *p*-tolyl), 5.67 (s, 4H, NCH_2), 4.39 (s, 6H, NCH_3), 2.47 (s, 6H, CH_3 *p*-tolyl). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 148.2 (2C, Ar) 147.7 (2C, N_3C=CAg), 134.8 (2C, Ar), 133.2 (2C, Ar), 131.1 (4CH, Ar), 129.6 (2CH, Ar), 129.4 (4CH, Ar), 129.1 (6CH, 4CH Ar and 2CH Ar), 129.0 (2CH, Ar), 60.9 ($2NCH_2$) 39.6 ($2NCH_3$), 22.1 ($2CH_3$, *p*-tolyl), $C_{carbene}$ not observed. **IR (KBr) $\nu_{máx}$** 3027, 2955, 2923, 1594, 1337, 1152, 1079, 814, 747, 687, 652, 599, 533. **HRMS (ESI)** *m*/*z* calculated for $C_{34}H_{34}AgN_6O_4S_2$: 763.1136 $[M–BF_4^-]^+$, found: 763.1127. **m.p.** decomposes before melting.

Synthesis of compound IV.53



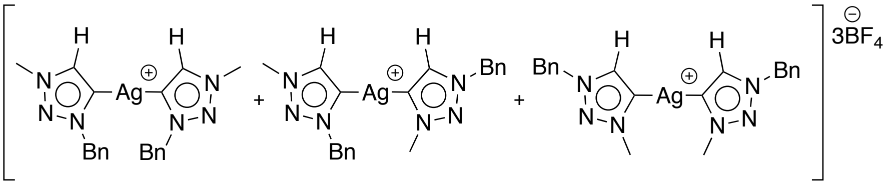
Following the general procedure a mixture of triazolium salt **III.39b** (88 mg, 0.22 mmol, 1.00 equiv), NMe_4Cl (36 mg, 0.33 mmol, 1.50 equiv) and Ag_2O (38 mg, 0.17 mmol, 0.75 equiv) in CH_3CN:CH_2Cl_2 (12 mL) was stirred under Ar at rt overnight until the formation of the silver carbene (^1H NMR analysis). The reaction was filtered through a pad of Celite and the solvent was removed under vacuum. The solid was then redissolved in CH_2Cl_2 and filtered again through a pad of Celite. The residue was precipitated in a mixture of CH_2Cl_2:pentane to afford the corresponding reaction products **IV.53** as a brownish solid (87 mg, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 8.6 Hz, 2H, Ar 2-OCH_3naph), 8.14 (d, *J* = 9.1 Hz, 2H, Ar 2-OCH_3naph), 7.87 (d, *J* = 8.2 Hz, 2H, Ar 2-OCH_3naph), 7.52 (br s, 1H, Ar), 7.42 (t, *J* = 7.5 2H, Ar), 7.30 (m, 6H, Ar), 5.40 (m, 2H, NCH_2), 4.53 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.8 (2C, Ar), 148.6 (2C, N_3C=CAg), 137.3 (2CH, Ar), 133.2 (2C, Ar), 131.3 (2C, Ar), 129.7 (2C, Ar), 129.6 (2CH, Ar) 129.3 (2CH, Ar), 129.2 (4CH, Ar), 129.1 (2CH, Ar), 128.6 (4CH, Ar), 125.0 (2CH, Ar), 122.3 (2CH, Ar), 119.3 (2C, Ar), 113.1 (2CH, Ar), 60.5 (2NCH_2), 57.0 (2OCH_3naph), 38.7 (2NCH_3) $C_{carbene}$ not observed. **IR (KBr)** $\nu_{máx}$ 3435, 1620, 1507, 1275, 1252, 1059, 818, 746. $[\alpha]_D^{25}$ + 51.5 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{42}H_{38}AgN_6O_4S_2$: 863.1442 $[M–BF_4^-]^+$, found: 863.1471. **m.p.** decomposes before melting.

General procedure for the desulfinylation process

In a bottom flask, silver carbene was dissolved in CH_2Cl_2. Alcohol was then added dropwise and the reaction was stirred at rt. Once the sulfinate was formed, volatiles were removed under vacuum. The sulfinate was separated from the carbene mixture washing with CH_2Cl_2:pentane (twice).

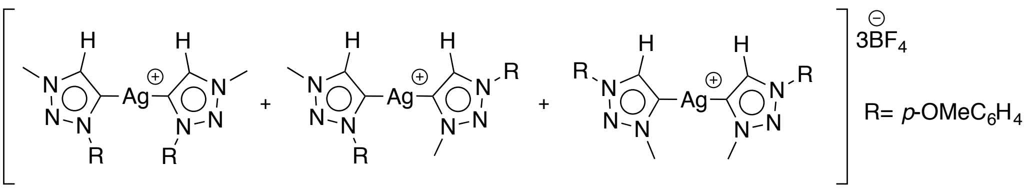
Synthesis of compound IV.28



Following the general procedure silver carbene **IV.26** (81 mg, 0.10 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (1 mL). MeOH was added dropwise. The solution started to become darker instantaneously. After 5 min of stirring at rt, the crude reaction was filtered through a pad of Celite. Volatiles were removed under vaccum yielding a brownish solid. To separate the sulfinate from the solid, the crude mixture was dissolved in the minimum volume of CH_2Cl_2 and precipitated in pentane. The mixture was stirred for 5 min. Solvents were separated from the solid, which was dried under vacuum affording silver carbenes **IV.28** as a brownish solid (36 mg, 67%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, Ar), 5.98 (s, NCH_2), 5.63 (s, NCH_2), 5.58 (s, NCH_2), 4.46 (s, NCH_2), 4.24 (s, NCH_3), 4.18 (s, NCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.0 (C, N_3C=*C*Ag, observed in HMBC), 165.2 (C, N_3C=*C*Ag, observed in HMBC), 134.5 (C), 132.7 (C), 131.9 (C), 130.6 (CH), 129.8 (CH, Ar), 129.5 (CH, Ar), 129.4 (CH, Ar), 129.3 (2CH, Ar), 129.0 (CH, Ar), 128.9 (CH, Ar), 128.8 (2CH, Ar), 128.4 (2CH, Ar), 59.4 (NCH_2), 57.2 (NCH_2), 55.5 (NCH_2), 43.0 (NCH_3), 40.4 (NCH_3), 38.4 (NCH_3). **HRMS (ESI)** *m/z* calculated for $C_{20}H_{22}AgN_6$: 453.0951 $[M{-}BF_4^-]^+$, found: 453.0938. **m.p.** decomposes before melting.

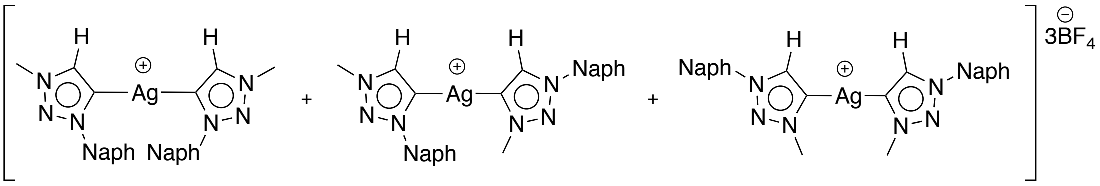
Synthesis of compound IV.42



Following the general procedure silver carbene **IV.38** (115 mg, 0.14 mmol, 1.00 equiv) was dissolved in of CH_2Cl_2 (3 mL). MeOH was added dropwise. The solution started to become darker instantaneously. After 5 min of stirring at rt, the crude reaction was filtered through a pad of Celite. Volatiles were removed under vaccum yielding a brownish solid. To separate the sulfinate from the solid, the crude mixture was dissolved in the minimum volume of CH_2Cl_2 and precipitated in pentane. The mixture was stirred for 5 min. Solvents were separated from the solid, which was dried under vacuum affording silver carbenes **IV.42** as a brownish solid (73 mg, 94%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, Ar), 7.94 (d, J = 9.0 Hz, Ar p-OMeC_6H_4), 7.88 (s, Ar), 7.78 (d, J = 9.0 Hz, Ar p-OMeC_6H_4), 7.64 (d, J = 9.0 Hz, Ar p-OMeC_6H_4), 7.06 (d, J = 9.0 Hz, Ar p-OMeC_6H_4), 6.98 (d, J = 9.0 Hz, Ar p-OMeC_6H_4), 4.57 (s, NCH_3), 4.31 (s, NCH_3), 4.28 (s, NCH_3), 3.88 (s, OCH_3), 3.86 (s, OCH_3), 3.85 (s, OCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.7 (C, N_3C=CAg), 162.2 (C), 161.5 (C), 161.0 (C), 136.6 (CH), 134.1 (CH), 133.2 (CH, Ar), 133.0 (CH, Ar), 129.2 (C, Ar), 128.6 (C, Ar), 124.7 (2CH, Ar), 123.0 (CH, Ar), 122.9 (CH, Ar), 115.6 (CH, Ar), 115.4 (2CH, Ar), 114.8 (2CH, Ar), 56.0 (NCH_2), 55.9 (NCH_2), 55.8 (OCH_3), 43.4 (NCH_3), 40.8 (NCH_3), 38.6 (NCH_3). **HRMS (ESI)** m/z calculated for $C_{20}H_{22}AgN_6O_2$: 485.0850 $[M–BF_4^-]^+$, found: 485.0883. **m.p.** decomposes before melting.

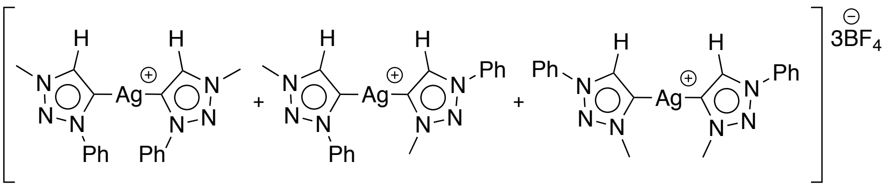
Synthesis of compound IV.43



Following the general procedure silver carbene **IV.39** (164 mg, 0.18 mmol, 1.00 equiv) was dissolved in of CH_2Cl_2 (3 mL). MeOH was added dropwise. The solution started to become darker instantaneously. After 5 min of stirring at rt, the crude reaction was filtered through a pad of Celite. Volatiles were removed under vaccum yielding a brownish solid. To separate the sulfinate from the solid, the crude mixture was dissolved in the minimum volume of CH_2Cl_2 and precipitated in pentane. The mixture was stirred for 5 min. Solvents were separated from the solid, which was dried under vacuum affording silver carbenes **IV.43** as a brownish solid (95 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.91 (s, Ar), 8.60 (s, Ar), 8.10 (m, Ar), 7.91 (m, Ar), 7.59 (m, Ar), 4.58 (s, NCH_3), 4.34 (s, NCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 137.6 (C), 134.2 (C), 134.1 (C, Ar), 134.0 (C, Ar), 132.9 (CH, Ar), 132.8 (C, Ar), 132.6 (CH, Ar), 132.1 (CH, Ar), 131.9 (CH, Ar), 131.0 (CH, Ar), 129.5 (CH, Ar), 128.8 (CH, Ar), 128.7 (CH, Ar), 128.6 (CH, Ar), 128.4 (CH, Ar), 128.1 (CH, Ar), 128.0 (CH, Ar), 127.7 (CH, Ar), 127.6 (H, Ar), 127.3 (CH, Ar), 127.1 (C, Ar), 125.2 (CH, Ar), 125.1 (CH, Ar), 124.1 (CH, Ar), 121.2 (CH, Ar), 120.9 (CH, Ar), 43.2 (NCH_3), 41.1 (NCH_3), 38.8 (NCH_3). **HRMS (EI)** *m/z* calculated for $C_{26}H_{22}AgN_6$: 525.0951 $[M–BF_4^-]^+$, found: 525.0942.

Synthesis of compound IV.44

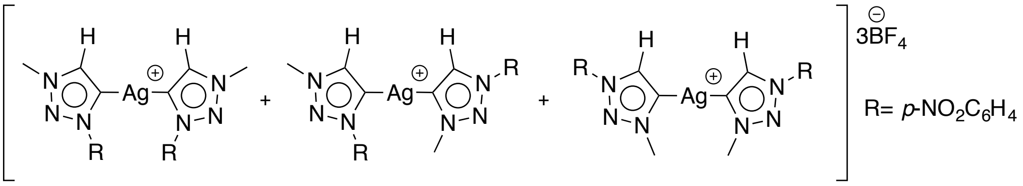


Following the general procedure silver carbene **IV.40** (139 mg, 0.18 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (4 mL). MeOH was added dropwise. The solution started to become darker instataneously. After 5 min of stirring at rt, the crude reaction was filtered through a pad of Celite. Volatiles were removed under vaccum yielding a brownish solid. To separate the sulfinate from the solid, the crude mixture was dissolved in the minimum volume of CH_2Cl_2 and precipitated in pentane. The mixture was stirred for 5 min. Solvents were separated from the solid, which was dried under vacuum affording silver carbenes **IV.44** as a brownish solid (76 mg, 86%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.80 (m, Ar), 7.51 (m, Ar), 4.64 (s, NCH_3), 4.38 (s, NCH_3), 4.37 (s, NCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 167.3 (C, N_3C=*C*Ag, observed in HMBC), 140.0 (C, Ar), 135.4 (C, Ar), 131.8 (CH, Ar), 131.2 (CH, Ar), 130.7 (CH, Ar), 130.5

(CH, Ar), 130.2 (2CH, Ar), 130.0 (CH, Ar), 129.5 (2CH, Ar), 123.2 (2CH, Ar), 121.4 (2CH, Ar), 121.2 (2CH, Ar), 43.4 (NCH_3), 40.9 (NCH_3), 38.8 (NCH_3). **HRMS (ESI)** *m*/*z* calculated for $C_{18}H_{18}AgN_6$: 425.0638 $[M–BF_4^-]^+$, found: 425.0643. **m.p.** decomposes before melting.

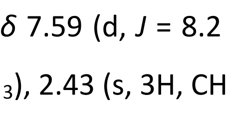
Synthesis of compound IV.45



Following the general procedure silver carbene **IV.41** (94 mg, 0.11 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (6 mL). MeOH was added dropwise. The solution started to become darker instantaneously. After 5 min of stirring at rt, the crude reaction was filtered through a pad of Celite. Volatiles were removed under vaccum yielding a brownish solid. To separate the sulfinate from the solid, the crude mixture was dissolved in the minimum volume of CH_2Cl_2 and precipitated in pentane. The mixture was stirred for 5 min. Solvents were separated from the solid, which was dried under vacuum affording silver carbenes **IV.45** as a brownish solid (34 mg, 53%).

Due to the insolubility and instability of the Ag-MICs **IV.45**, characterisation of the products could not be carried out. Reaction was confirmed to happen through the ^{1}H NMR spectrum analysis of the sulfinate formed.

Synthesis of compound IV.27[143]



^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.59 (d, *J* = 8.2 Hz, 2H, Ar *p*-tolyl), 7.34 (d, *J* = 8.2 Hz, 2H, Ar *p*-tolyl), 3.46 (s, 3H, OCH_3), 2.43 (s, 3H, CH_3 *p*-tolyl).

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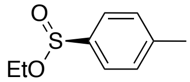
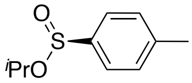
[143] J. L. Ruano, J. Alemán, M. B. Cid, A. Parra, *Org. Lett.* **2005**, *2*, 179.

Synthesis of compound IV.51[144]



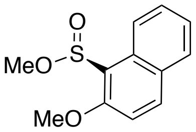
^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.60 (d, *J* = 8.2 Hz, 2H, Ar *p*-tolyl), 7.33 (m, 2H, Ar *p*-tolyl), 4.10 (dq, *J* = 10.0 Hz, 7.1 Hz, 1H, OCH_2CH_3), 3.72 (dq, *J* = 10.0 Hz, 7.1 Hz, 1H, OCH_2CH_3), 2.43 (s, 3H, CH_3 *p*-tolyl), 1.28 (t, *J* = 7.1 Hz, 1H, OCH_2CH_3).

Synthesis of compound IV.52[145]



^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.60 (d, *J* = 8.2 Hz, 2H, Ar *p*-tolyl), 7.33 (d, *J* = 8.2 Hz, 2H, Ar *p*-tolyl), 4.60 (h, *J* = 6.2 Hz, 1H, CH), 2.42 (s, 3H, CH_3 *p*-tolyl), 1.38 (d, *J* = 6.2 Hz, 3H), 1.25 (d, *J* = 6.2 Hz, 3H).

Synthesis of compound IV.54[146]



^{1}H NMR (300 MHZ, $CDCl_3$) δ 9.09 (d, *J* = 8.6 Hz, 1H, Ar), 7.97 (d, *J* = 9.1 Hz, 1H, Ar), 7.80 (d, *J* = 8.6 Hz, 1H, Ar), 7.57 (ddd, *J* = 8.6 Hz, 6.9 Hz, 1.4 Hz, 1H, Ar), 7.42 (ddd, *J* = 8.1 Hz, 6.9 Hz, 1.1 Hz, 1H, Ar), 7.25 (d, *J* = 9.1 Hz, 2H, Ar), 4.01 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3).

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[144] T. Yoshino, S. Imori, H. Togo, *Tetrahedron* **2006**, *62*, 1309.

[145] M. Xia, Z.-C. Chen, *Synth. Commun.* **1997**, *27*, 1321.

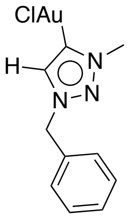
[146] K. H. Bell, *Aust. J. Chem.* **1985**, *38*, 1209.

General procedure for the synthesis of gold carbenes

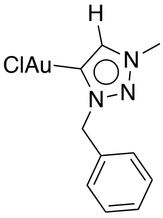
To a solution of Ag-MIC (1.00 equiv) in CH_2Cl_2, [AuCl(SMe_2)] (2.00 equiv) was added**.** The mixture was stirred at rt until the formation of the gold carbenes (TLC analysis). The crude reaction was filtered trough a Celite pad and volatiles were removed under vacuum. Both regioisomers were separated through a chromatography column.

Synthesis of compounds IV.29a–b

Following the general procedure, to a solution of Ag–MIC **IV.28** (36 mg, 0.07 mmol, 1.00 equiv) in CH_2Cl_2 (6 mL), [AuCl(SMe_2)] (39 mg, 0.13 mmol, 2.00 equiv) was added. The mixture was stirred at rt for 2 h. The reaction was filtered through a pad of Celite and the volatiles were removed under vacuum. The two regioisomers **IV.29a**–**b** were obtained as white solids in a mixture of 3:4. They were separated by a short pad of SiO_2 for their characterisation (53 mg, 98%).



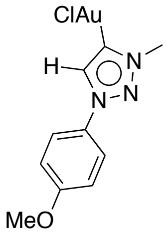
^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.61 (s, 1H, N_3C=CH), 7.43 (m, 3H, Ar), 7.35 (m, 2H, Ar), 5.52 (s, NCH_2), 4.20 (s, 3H, NCH_3). **^{13}C NMR** (125 MHz, $CDCl_3$) *δ* 158.6 (C, AuC=CH), 133.7 (CH, AuC=CH), 131.7 (C, Ar), 130.0 (CH, Ar), 129.7 (2CH, Ar), 128.9 (2CH, Ar), 56.4 (NCH_2), 42.2 (NCH_3). **IR (KBr) $\nu_{\text{máx}}$** 3106, 1497, 1458, 1276, 1094, 725, 694. **HRMS (ESI)** *m/z* calculated for $C_{10}H_{11}AuN_3$: 371.0691 $[M+H]^+$, found: 371.0687. **m.p.** decomposes before melting.



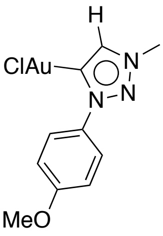
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (s, 1H, $N_3C{=}CH$), 7.21 (m, 2H, Ar), 7.53 (m, 2H, Ar), 7.37 (m, 3H, Ar), 5.64 (s, NCH_2), 4.16 (s, 3H, NCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.0 (C, AuC=CH), 134.9 (CH, AuC=CH), 133.7 (C, Ar), 129.3 (CH, Ar), 129.2 (2CH, Ar), 129.1 (2CH, Ar), 59.2 (NCH_2), 39.0 (NCH_3). **IR (KBr) $\nu_{\text{máx}}$** 3413, 3105, 2320, 1496, 1456, 1431, 1331, 1319, 1160, 1093, 1073, 1040, 1030, 842, 735, 842, 735, 700, 658, 569. **HRMS (ESI)** *m*/*z* calculated for $C_{10}H_{11}AuN_3$: 371.0691 $[M+H]^+$, found: 371.0686. **m.p.** decomposes before melting.

Synthesis of compounds IV.46a–b

Following the general procedure, to a solution of Ag-MIC **IV.42** (64 mg, 0.11 mmol, 1.00 equiv) in CH_2Cl_2 (6 mL), $[AuCl(SMe_2)]$ (66 mg, 0.22 mmol, 2.00 equiv) was added. The mixture was stirred at rt for 2 h. The reaction was filtered through a pad of Celite and the volatiles were removed under vacuum. The two regioisomers **IV.46a**–**b** were obtained as white solids in a mixture of 3:2. They were separated by a short pad of SiO_2 for their characterisation (66 mg, 71%).



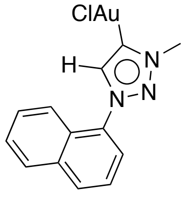
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H, $N_3C{=}CH$), 7.63 (d, *J* = 9.0 Hz, 2H, Ar *p*-$OMeC_6H_4$), 7.08 (d, *J* = 9.0 Hz, 2H, Ar *p*-$OMeC_6H_4$), 4.31 (s, 3H, NCH_3), 3.90 (s, 3H, OCH_3). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.7 (C, Ar), 158.9 (C, $N_3C{=}CAu$), 131.5 (CH, CAu=CH), 128.5 (C, Ar), 122.8 (2CH, Ar), 115.5 (2CH, Ar), 56.0 (OCH_3), 42.4 (NCH_3). **IR (KBr) $\nu_{\text{máx}}$** 3107, 2958, 2924, 2853, 1716, 1641, 1611, 1592, 1519, 1496, 1464, 1378, 1316, 1263, 1214, 1173, 1166, 1099, 1032, 830, 819, 807, 720, 710, 654, 611, 553, 485. **HRMS (ESI)** *m*/*z* calculated for $C_{10}H_{11}AuN_3O$: 386.0562 $[M{-}Cl^-]^+$, found: 386.0562. **m.p.** decomposes before melting.



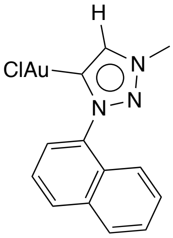
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 9.1 Hz, 2H, Ar p-$OMeC_6H_4$), 7.72 (s, 1H, $N_3C{=}CH$), 7.01 (d, J = 9.1 Hz, 2H, Ar p-$OMeC_6H_4$), 4.27 (s, 3H, NCH_3), 3.88 (s, 3H, OCH_3). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.1 (C, Ar), 157.2 (C, $N_3C{=}CAu$), 135.0 (CH, CAu=CH), 132.1 (C, Ar), 125.4 (2CH, Ar), 114.7 (2CH, Ar), 55.9 (OCH_3), 39.0 (NCH_3). **IR (KBr) $\nu_{\text{máx}}$** 3146, 3117, 3100, 2958, 2924, 2853, 1723, 1606, 1592, 5119, 1463, 1414, 1378. 1333, 1304, 1255, 1171, 1114, 1093, 1059, 1027, 982, 833, 807, 752, 720, 610, 551, 518. **HRMS (ESI)** m/z calculated for $C_{10}H_{11}AuN_3O$: 386.0562 $[M{-}Cl^-]^+$, found: 386.0550. **m.p.** decomposes before melting.

Synthesis of compounds IV.47a–b

Following the general procedure, to a solution of Ag-MIC **IV.43** (223 mg, 0.36 mmol, 1.00 equiv) in CH_2Cl_2 (20 mL), $[AuCl(SMe_2)]$ (215 mg, 0.73 mmol, 2.00 equiv) was added. The mixture was stirred at rt for 2 h. The reaction was filtered through a pad of Celite and the volatiles were removed under vacuum. The two regioisomers **IV.47a–b** were obtained as white solids in a mixture of 5:4. They were separated by a short pad of SiO_2 for their characterisation (188 mg, 59%).



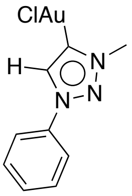
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (m, 1H, Ar napht), 8.03 (m, 1H, Ar napht), 7.91 (s, 1H, $N_3CH{=}CAu$), 7.66 (m, 4H, Ar napht), 7.53 (m, 1H, Ar napht), 4.42 (s, 3H, NCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.6 (C, $N_3CH{=}CAu$), 136.2 (CH, $N_3CH{=}CAu$), 134.3 (C, Ar), 132.5 (CH, Ar), 131.8 (C, Ar), 129.1 (CH, Ar), 128.9 (CH, Ar), 128.0 (CH, Ar), 127.6 (C, Ar), 125.0 (CH, Ar), 124.2 (CH, Ar), 121.1 (CH, Ar), 42.7 (NCH_3). **IR (KBr) ν_{máx}** 3098, 1513, 1411, 1271, 801, 769, 687. **HRMS (ESI)** *m/z* calculated for $C_{13}H_{11}AuN_3$: 406.0613 $[M–Cl^−]^+$, found: 406.0622. **m.p.** decomposes before melting.



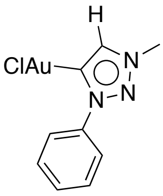
^{1}H NMR (400 MHz, DMSO-*d*$_6$) *δ* 8.49 (s, 1H, N_3CH=CAu), 8.29 (d, *J* = 8.2 Hz, 1H, Ar napht), 8.16 (d, *J* = 8.2 Hz, 1H, Ar napht), 7.89 (br d, *J* = 7.3 Hz, 1H, Ar napht), 7.75 (t, *J* = 7.3 Hz, 1H, Ar napht), 7.69 (ddd, *J* = 8.2 Hz, 6.9 Hz, 1.3 Hz, 1H, Ar napht), 7.64 (td, *J* = 7.6 Hz, 6.9 Hz, 1.3 Hz, 1H, Ar napht), 7.41 (d, *J* = 8.4 Hz, 2H, Ar napht), 4.34 (s, 3H, NCH_3). **^{13}C NMR** (100 MHz, DMSO-*d*$_6$) *δ* 158.6 (C, N_3CH=CAu), 135.5 (CH, N_3CH=CAu), 135.4 (C, Ar), 133.4 (C, Ar), 131.2 (CH, Ar), 128.4 (CH, Ar), 128.2 (CH, Ar), 128.1 (CH, Ar), 127.4 (CH, Ar), 125.4 (C, Ar), 125.3 (CH, Ar), 121.8 (CH, Ar), 39.0 (NCH_3). **IR (KBr) $\nu_{máx}$** 3430, 3114, 2923, 1501, 1330, 1078, 799, 771. **HRMS (ESI)** *m/z* calculated for $C_{13}H_{11}AuN_3$: 406.0613 $[M–Cl^−]^+$, found: 406.0623. **m.p.** decomposes before melting.

Synthesis of compounds IV.48a–b

Following the general procedure, to a solution of Ag-MIC **IV.44** (77 mg, 0.15 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL), [AuCl(SMe_2)] (89 mg, 0.30 mmol, 2.00 equiv) was added. The mixture was stirred at rt for 2 h. The reaction was filtered through a pad of Celite and the volatiles were removed under vacuum. The two regioisomers **IV.48a–b** were obtained as white solids in a mixture of 4:3. They were separated by a short pad of SiO_2 for their characterisation (87 mg, 74%).



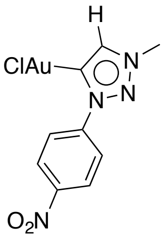
^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.08 (s, 1H, $N_3C{=}CH$), 7.74 (m, 2H, Ar), 7.62 (m, 3H, Ar), 4.34 (s, 3H, NCH_3). **^{13}C NMR** (125 MHz, $CDCl_3$) *δ* 159.2 (C, AuC=CH), 135.4 (C, Ar), 131.7 (CH, CH=CAu), 131.4 (CH, Ar), 130.5 (2CH, Ar), 121.4 (2CH, Ar), 42.6 (NCH_3). **IR (KBr) $\nu_{máx}$** 3435, 3119, 2923, 1595, 1561, 1498, 1464. 1339, 1308, 1262, 1212, 1094, 1032, 982, 820, 760, 732, 682, 669. **HRMS (ESI)** *m*/*z* calculated for $C_7H_9AuN_3$: 356.0457 $[M{-}Cl^-]^+$, found: 356.0499. **m.p.** decomposes before melting.



^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.03 (m, 2H, Ar), 7.81 (s, 1H, $N_3C{=}CH$), 7.54 (m, 3H, Ar), 4.30 (s, 3H, NCH_3). **^{13}C NMR** (125 MHz, $CDCl_3$) *δ* 157.3 (C, AuC=CH), 139.0 (C, Ar), 135.4 (CH, CH=CAu), 130.6 (CH, Ar), 129.7 (2CH, Ar), 124.1 (2CH, Ar), 39.2 (NCH_3). **IR (KBr) $\nu_{máx}$** 3424, 3111, 2922, 1595, 1494, 1456, 1333, 1317, 1261, 1216, 1173, 1072, 1008, 916, 835, 769, 689, 556. **HRMS (ESI)** *m*/*z* calculated for $C_7H_9AuN_3$: 356.0457 $[M{-}Cl^-]^+$, found: 356.0457. **m.p.** decomposes before melting.

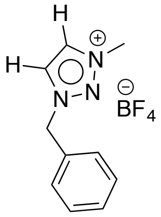
Synthesis of compounds IV.49a–b

Following the general procedure, to a solution of Ag-MIC **IV.45** (34 mg, 0.06 mmol, 1.00 equiv) in CH_2Cl_2 (4 mL), [AuCl(SMe$_2$)] (33 mg, 0.11 mmol, 2.00 equiv) was added. The mixture was stirred at rt for 2 h. The reaction was filtered through a pad of Celite and the volatiles were removed under vacuum. Compound **IV.49b** was obtained together with traces of the regioisomer **IV.49a**, which could not be isolated. **IV.49b** was purified by a short pad of SiO_2 for their characterisation (35 mg, 71%).



^{1}H NMR (400 MHz, DMSO-d_6) δ 8.51 (d, J = 9.0 Hz, 2H, Ar p-$NO_2C_6H_4$), 8.43 (s, 1H, $N_3C=CH$), 8.30 (d, J = 9.0 Hz, 2H, Ar p-$NO_2C_6H_4$), 4.32 (s, 3H, NCH_3). **^{13}C NMR** (125 MHz, DMSO-d_6) δ 155.8 (C, CH=CAu), 148.2 (C, Ar), 143.1 (C, Ar), 136.5 (CH, CAu=CH), 125.7 (2CH, Ar), 125.1 (2CH, Ar), 39.5 (NCH_3, overlaped with deuterated solvent). **IR (KBr) $\nu_{\text{máx}}$** 3435, 3113, 2923, 1612, 1597, 1530, 1494, 1360, 1343, 1316, 1261, 1222, 1173, 1109, 1076, 1025, 1005, 857, 826, 755, 701, 689, 654, 499. **HRMS (ESI)** m/z calculated for $C_9H_8AuN_4O_2$: 401.0307 $[M-Cl^-]^+$, found: 401.0291. **m.p.** decomposes before melting.

Synthesis of compounds IV.55[147]



A mixture of **III.39a** (92 mg, 0.20 mmol, 1.00 equiv) and Me_3OBF_4 (56 mg, 0.38 mmol, 1.50 equiv) in CH_2Cl_2 (20 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol (15 mL) and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum. The crude reaction was redissolved in CH_2Cl_2 and filtered through cotton to remove the $NaHCO_3$ dissolved by MeOH. The volatiles were removed under vacuum. The triazolium salt was separated from the methyl sulfinate washing with pentane. **IV.55** was obtained as a white solid (52 mg, quantitative).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 2H, $N_3CH=CH$), 7.44 (m, 2H, Ar), 7.35 (m, 3H, Ar), 5.68 (s, 2H, NCH_2), 4.26 (s, 3H, NCH_3).

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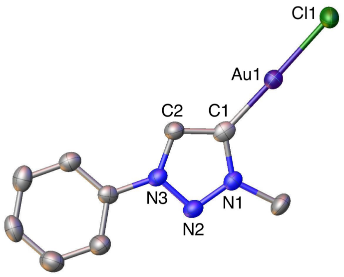
[147] For a complete characterisation of the triazolium salt **IV.55** with iodide as contraion see: a) G. Boche, P. Andrews, K. Harms, M. Marsch, K. S. Rangappa, M. Schimeczek, C. Willeke, *J. Am. Chem. Soc.* **1996**, *118*, 4925; b) Y. Jeong, J.-S. Ryu, *J. Org. Chem.* **2010**, *75*, 4183.

Computational details

All calculations were performed at the DFT level using the M06 functional[105] with an ultrafine integration grid[106] as implemented in Gaussian09.[107] Ag atoms were described using the scalar-relativistic Stuttgart-Dresden SDD pseudopotential[110] and its associated double-ζ basis set complemented with a set of f-polarization functions.[111] The 6-31G** basis set was used for the H, C, N, O and atoms.[109] All structures of the reactants, intermediates, transition states, and products were fully optimized in dichloromethane solvent (ε = 8.93) using the SMD continuum model.[148] Transition states were identified by having one imaginary frequency in the Hessian matrix. It was confirmed that transition states connect with the corresponding intermediates by means of application of the eigenvector corresponding to the imaginary frequency and subsequent optimization of the resulting structures. All energies collected in the text are Gibbs energies in dichloromethane at 298 °K.

Crystal data for compound IV.48a:



$C_9H_9AuClN_3$, Mr = 361.61, crystal dimensions 0.4 x 0.4 x 0.1 mm3, triclinic, P $\bar{1}$, a = 6.5022(3) Å, b = 7.7532(3) Å, c = 11.0346(6) Å, α = 77.138(3)°, β = 82.169(3)°, γ = 83.193(2)°, cell volume = 535.02(4) Å3, Z = 2, ρ_{calcd} = 2.431 Mg/m3, μ = 13.960 mm^{-1}, T = 173(2) K, $2\theta_{max}$ = 61.1°, 17088 reflections collected, 3185 independent, R_{int} = 0.1016,

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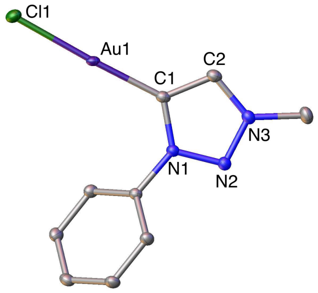
[148] a) S. Miertuš, E. Scrocco, J. Tomasi, *Chem. Phys.* **1981**, *55*,117; b) J. L. Pascual-Ahuir, E. Silla, I. Tuñón, *J. Comput. Chem.***1994**, *15*, 1127; c) V. Barone, M. Cossi, *J. Phys. Chem. A*, **1998**, *102*, 1995.

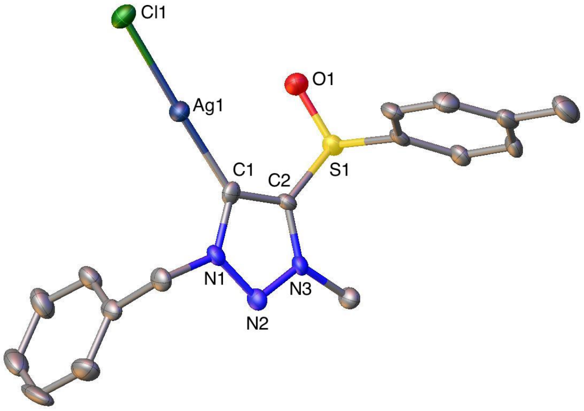
R1 = 0.0356 and wR2 = 0.0488 for I > 2σ(I), R1 = 0.0670 and wR2 = 0.0541 for all data, residual electron density = 1.345 eA^{-3}.

Crystal data for compound IV.48b:



$C_9H_9AuClN_3$, Mr = 391.61, crystal dimensions 0.5 x 0.4 x 0.4 mm^3, monoclinic, *P2$_1$/n*, *a* = 11.668(2) Å, *b* = 7.578(1) Å, *c* = 12.803(2) Å, β = 115.593(4)°, cell volume = 1020.9(2) Å^3, Z = 4, ρ_{calcd} = 2.548 Mg/m^3, μ = 14.633 mm^{-1}, T = 100(2) K, $2\theta_{max}$ = 90.8°, 82542 reflections collected, 8589 independent, R_{int} = 0.0435, R1 = 0.0175 and wR2 = 0.0396 for I > 2σ(I), R1 = 0.0280 and wR2 = 0.0442 for all data, residual electron density = 2.087 eA^{-3}.

Crystal data for compound IV.56[149]



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[149] Silver mono(carbene) **IV.56** could not be isolated in enough quantity for complete characterisation. Only X-ray diffraction and HRMS (ESI) (calculated for $C_{17}H_{17}AgN_3OS$: 418.01378 [M-Cl$^-$]$^+$, found: 418.0145) could be registered.

$C_{17}H_{17}AgClN_3OS$, Mr = 454.71, crystal dimensions 0.5 x 0.1 x 0.05 mm^3, monoclinic, *P2$_1$*, *a* = 10.565(2) Å, *b* = 6.892(1) Å, *c* = 12.256(2) Å, β = 95.573(5)°, cell volume = 888.1(2) Å^3, Z = 2, ρ_{calcd} = 1.700 Mg/m^3, μ = 1.411 mm^{-1}, T = 100(2) K, $2\theta_{max}$ = 55.7°, 12999 reflections collected, 4199 independent, R_{int} = 0.0735, R1 = 0.0500 and wR2 = 0.1114 for I > 2σ(I), R1 = 0.0712 and wR2 = 0.1215 for all data, residual electron density = 1.779 eA^{-3}, absolute structure parameter x = –0.03(4).

CHAPTER V

Cycloisomerization of enynes catalysed by gold mesoionic carbenes

V.1 INTRODUCTION

V.1.1 Cycloisomerization reaction of 1,6-enynes

Since the pioneering work of Teles[150] and Tanaka[151] in the activation of alkynes, gold complexes have emerged as powerful catalysts in a wide range of transformations involving double and triple bonds.[152] In spite of the fact that simple gold salts such as AuCl or $NaAuCl_4$ have been used in several catalytic transformations; gold(I) complexes bearing different ligands can catalyse a wider range of reactions. Gold complexes presenting NHCs as ligands have also been employed for electrophilic activation of alkynes.[153] These complexes are usually of the type [LAuX] where L is the NHC ligand and X is a halide. The catalytic active species are, in general, generated *in situ* using a halide scavenger yielding the cationic gold complex $[NHCAu]^+$ that has not been isolated to date.

Among the large number of examples of reactions catalysed by gold(I), we will focus our work on the cycloisomerization reaction of 1,6-enynes. Since the initial work by Trost,[154] different transition metals have been used in this class of reaction.[155] This

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[150] J. H. Teles, S. Brode, M. Chabanas, *Angew. Chem. Int. Ed.* **1998**, *37*, 1415.

[151] E. Mizushima, K. Sato, T. Hayashi, M. Tanaka, *Angew. Chem. Int. Ed.* **2002**, *41*, 4563.

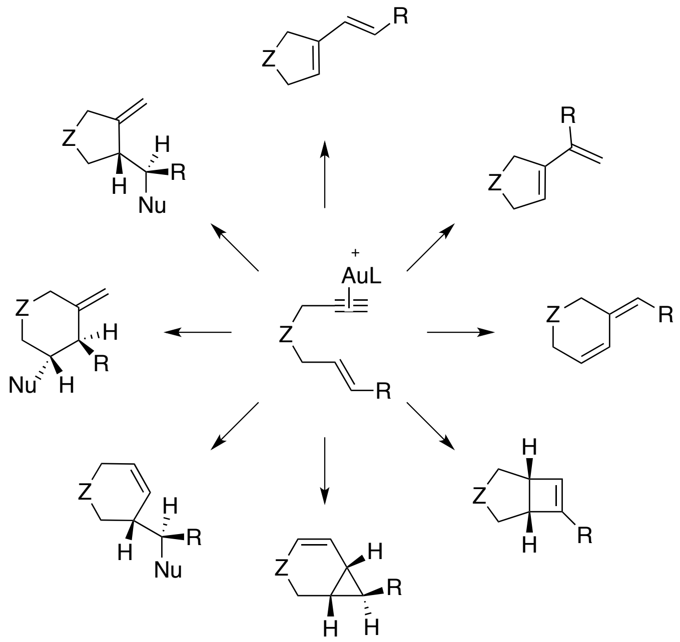
[152] For a review on activation of alkynes by gold(I) see: R. Dorel, A. M. Echavarren, *Chem. Rev.* **2015**, *115*, 9028.

[153] a) S. Gaillard, C. S. J. Cazin, S. P. Nolan, *Acc. Chem. Res.* **2012**, *45*, 778; b) S. P. Nolan, *Acc. Chem. Res.* **2011**, *44*, 91.

[154] B. M. Trost, M. J. Krische, *Synlett*, **1998**, 1.

[155] For reviews on cycloisomerization of 1,*n*-enynes see: a) C. Aubert, O. Buisine, M. Malacria, *Chem. Rev.* **2002**, *102*, 813; b) V. Michelet, P. Y. Toullec, J.-P. Genêt, *Angew. Chem. Int. Ed.* **2008**, *47*, 4268.

skeletal rearrangement is a powerful tool in synthesis because a wide variety of structurally complex cyclic compounds can be obtained in mild conditions (Scheme V.1). Due to the number of isomers that can be formed in these cycloisomerizations, the catalysts employed to promote these reactions should be both efficient and selective.



Scheme V.1: Gold(I)-catalysed the cycloisomerization reaction of enynes

Echavarren demonstrated the increased activity of cationic gold(I) species to catalyse the cycloisomerization of enynes.[156] In his work, the catalytic species was $[Au(PPh_3)]^+$ generated *in situ* using $[AuCl(PPh_3)]$ and $AgSbF_6$ as chloride scavenger. The mechanism of these transformations is well known.[157, 158] Firstly, gold complex coordinates to the alkyne to form a (η^2-alkyne)metal complex **V.1**. Then, the double bond attacks the activated triple bond to form two different metal cyclopropyl carbene

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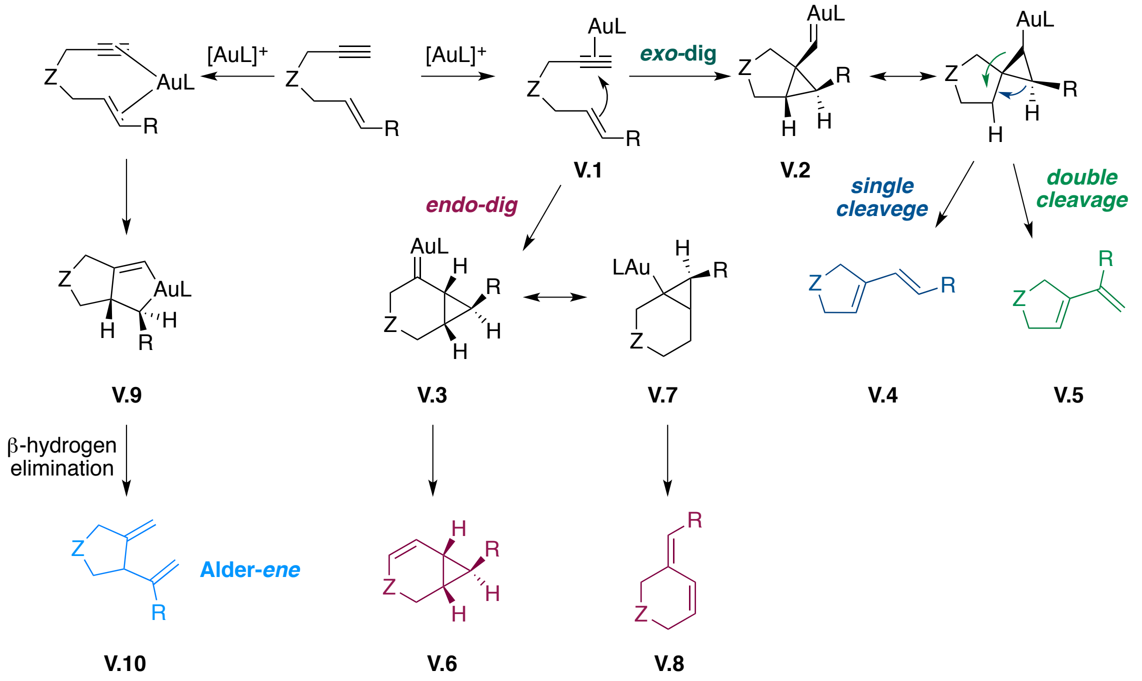
[156] C. Nieto-Oberhuber, M. P. Muñoz, E. Buñuel, C. Nevado, D. J. Cárdenas, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2004**, *43*, 2402.

[157] a) C. Bruneau, *Angew. Chem. Int. Ed.* **2005**, *44*, 2328; b) C. Nieto-Oberhuber, M. P. Muñoz, S. López, E. Jiménez-Núñez, C. Nevado, E. Herrero-Gómez, M. Raducan, A. M. Echavarren, *Chem. Eur. J.* **2006**, *12*, 1677; c) C. Nieto-Oberhuber, S. López, E. Jiménez-Núñez, A. M. Echavarren, *Chem. Eur. J.* **2006**, *12*, 5916; d) G. C. Lloyd-Jones, *Org. Biomol. Chem.* **2003**, *1*, 215.

[158] For a review on mechanism studies of gold-catalysed cycloisomerizations, see: E. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326.

complexes: **V.2** is formed through a *5-exo-dig* attack, while **V.3** is formed after a *6-endo-dig* reaction. In the case of intermediate **V.2**, it can undergo a simple cleavage yielding **V.4** or a double cleavage to form **V.5**. The bicyclic compound **V.6** can be formed from **V.3** after α-insertion and subsequent elimination. Meanwhile, intermediate **V.7** will evolve to compound **V.8**. Theoretical studies have shown that the activation energy is lower for the cyclization that occurs *via* the *exo-dig* pathway. Nevertheless, depending on the nature of the starting enyne a more stable gold carbene intermediate could be generated through *via exo-dig* pathway. In the case that the metal would coordinate the alkyne and the alkene simultaneously, oxidative cyclometallation would yield the intermediate **V.9** that undergoes a β-hydrogen elimination to form Alder-*ene* type products **V.10** (Scheme V.2).



Scheme V.2: Mechanism pathways of the cycloisomerization of 1,6-enynes

V.1.2 NHC-gold complexes as catalysts in cycloisomerization reactions

Gold complexes bearing classic NHCs have been employed as catalysts in several cycloisomerization reactions of enynes.[157b,159]

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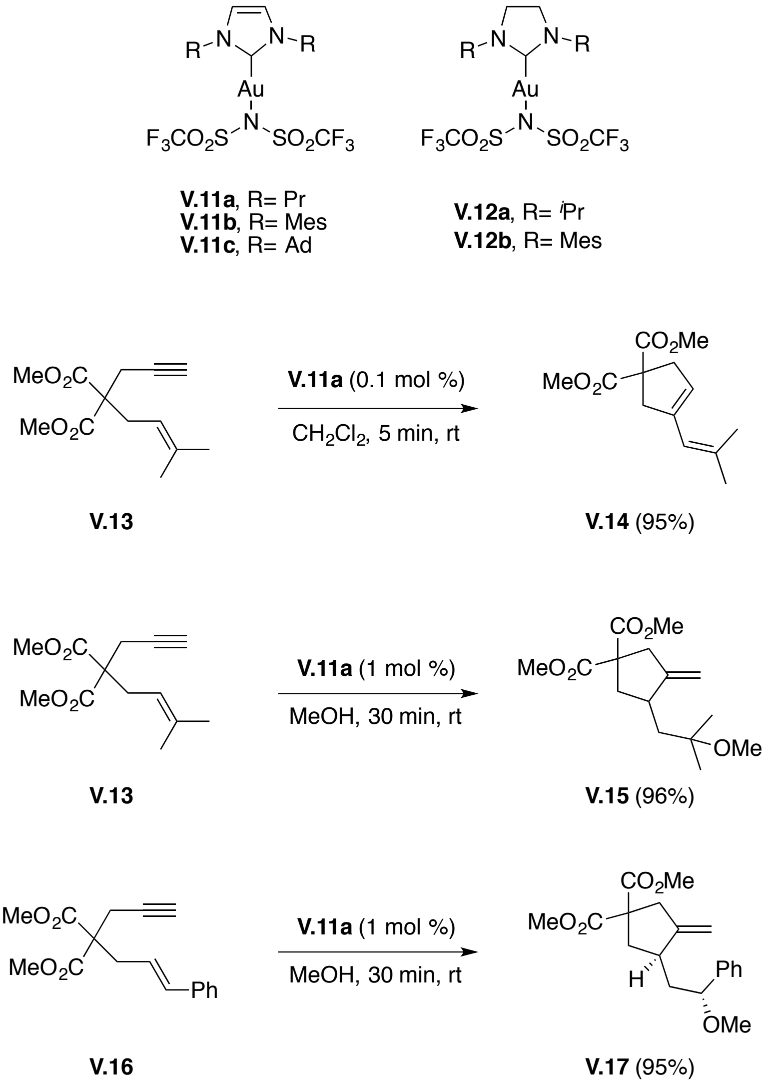
[159] a) S. López, E. Herrero-Gómez, P. Pérez-Galán, C. Nieto-Oberhuber, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2006**, *45*, 6029; b) S. M. Kim, J. H. Park, S. Y. Choi, Y. K. Chung, *Angew. Chem. Int. Ed.* **2007**, *46*, 6172; c) E. Jiménez-Núñez, C. K. Claverie, C. Bour, D. J. Cárdenas, A. M.

Gagosz reported the skeleton rearrangement of enynes catalysed by gold(I) carbenes.[160]



Scheme V.3: Cycloisomerization reactions catalysed by **V.11a**

In this work, they reported the synthesis of gold-NHCs **V.11**-**12** with bis(trifluoromethanesulfonyl)imidate as a weakly coordinating counteranion (Scheme V.3). These complexes were air stable and the use of co-catalysts (as for example silver salts) was not required to form the reactive species. It is worthy to note that the behaviour of silver salts has been demonstrated to be non-innocent in this type of

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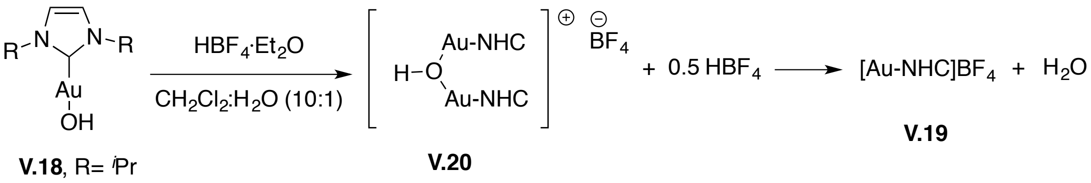
Echavarren, *Chem. Int. Ed.* **2008**, *47*, 7892; d) S. Gaillard, J. Bosson, R. S. Ramón, P. Nun, A. M. Z. Slawin, S. P. Nolan, *Chem. Eur. J.* **2010**, *16*, 13729.

[160] L. Ricard, F. Gagosz, *Organometallics* **2007**, *26*, 4704.

catalytic transformations.[161] Complex **V.11a** was used in the cycloisomerization reaction of enyne **V.13** as well as in the methoxycyclization reaction of enynes **V.13** and **V.16** showing catalytic activities similar or even higher that those previously reported by Echavarren where $AgSbF_6$ was used to generate the active species of gold(I)-NHC complexes.[157b,162]

Nolan also developed a series of gold(I)-NHCs that could be activated without using a silver salt.[159d] Carbene **V.18** could form the active species $[Au(IPr)]^+$ **V.19** by addition of a Brønsted acid ($HBF_4{\cdot}OEt_2$) (Scheme V.4). In addition, **V.19** could also be obtained straightforward from the isolable intermediate **V.20**. Both complexes, **V.18** and **V.20** have been tested in the cycloisomerization and methoxycyclization of enyne **V.13** displaying good activity in terms of conversion and selectivity.



Scheme V.4: Formation of active species **V.13**

More recently, a series of ionic gold complexes **V.21a–c** bearing chloride ligands has been synthetized (Scheme V.5).[163] These new complexes efficiently catalysed the skeleton rearrangement of 1,6-enynes **V.13** and **V.22** to yield the *exo-dig* product without the addition of chloride extractor required.

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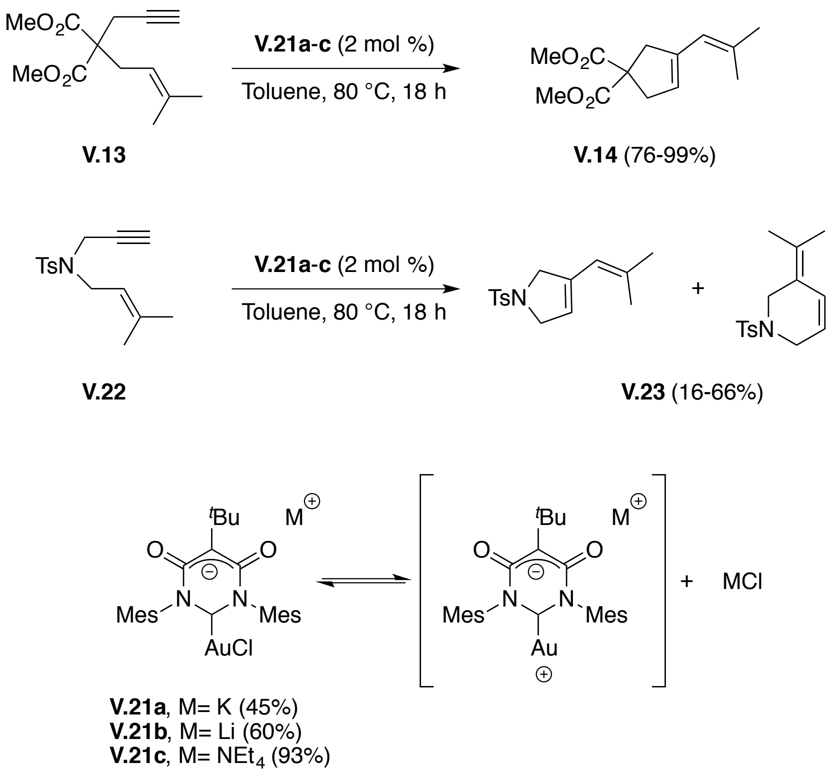
[161] a) C. Nevado, A. M. Echavarren, *Chem. Eur. J.* **2005**, *11*, 3155; b) D. Weber, M. R. Gagné, *Org. Lett.* **2009**, *11*, 4962; c) H. Li, R. A. Widenhoefer, *Org. Lett.* **2009**, *11*, 2671; d) D. Wang, R. Cai, S. Sharma, J. Jirak, S. K. Thummanapelli, N. G. Akhmedov, H. Zhang, X. Liu, J. L. Petersen, X. Shi, *J. Am. Chem. Soc*. **2012**, *134*, 9012; e) A. Homs, I. Escofet, A. M. Echavarren, *Org. Lett.* **2013**, *15*, 5782; f) Y. Zhu, C. S. Day, L. Zhang, K. J. Hauser, A. C. Jones, *Chem. Eur. J.* **2013**, *19*, 12264.

[162] C. Nieto-Oberhuber, S. López, A. M. Echavarren, *J. Am. Chem. Soc.* **2005**, *127*, 6178.

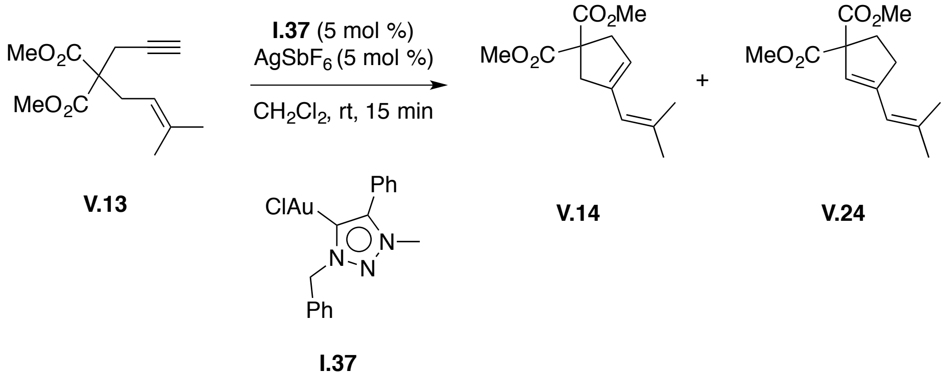
[163] S. Bastin, C. Barthes, N. Lugan, G. Lavigne, V. César, *Eur. J. Inorg. Chem.* **2015**, 2216.



Scheme V.5: Gold complexes **V.21a-c** and their catalytic activity

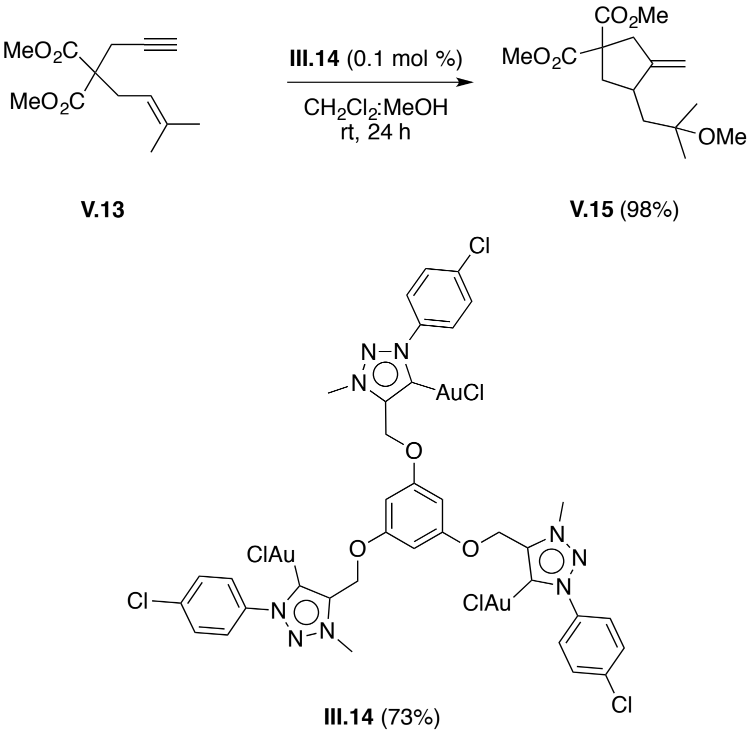
V.1.3 MIC-Gold complexes as catalysts in cycloisomerization reactions

The use of MIC-AuL complexes in the cycloisomerization of enynes has been studied considerably less. The first example of MIC-AuL complexes as catalysts for the cycloisomerization of enynes was reported by Crowley.[60] In this paper, the presence of catalytic amounts of gold carbene **I.37** with $AgSbF_6$ as halide scavenger, produced a mixture of isomers **V.14** and **V.24** (2:1) in 42% yield after 15 min (Scheme V.6).



Scheme V.6: Cyclosiomerisation of enyne **V.13** by gold 1,2,3-triazolylidene **I.37**

Recently, Mendoza employed the Au(I) 1,2,3-triazolylidenes **III.11a**–**b** and **III.14**, already discussed in chapter III, for the methoxycyclization of enyne **V.13**.[115] The highest yield was reached with the trimetallic gold complex **III.14** (Scheme V.7).



V.13

V.15 (98%)

III.14 (73%)

Scheme V.7: Methoxyciclyation of enyne **V.13**

V.2 OBJECTIVES

Based in these precedents, the objectives of this chapter are:

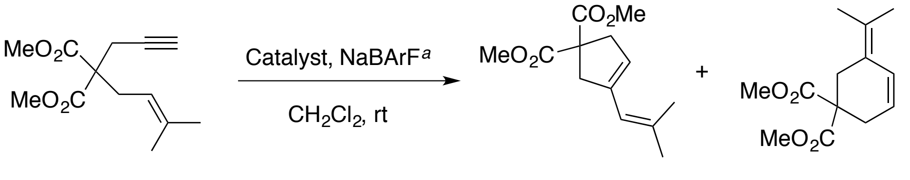
- Study of the catalytic activity of gold(I)-MIC complexes containing enantiopure (*S*)-sulfoxides in the cycloisomerization reaction of enynes.

- Study of the role of the sulphide group in the mechanism of the cycloisomerization.

V.3 RESULTS AND DISCUSSION

The synthesis of enantiopure mesoionic gold carbene complexes having sulfoxide substituents has been described in chapter III. Catalyst **III.32** was chosen, as well as the more sterically hindered at *N*1, **III.36a** and its diastereoisomer **III.36b.** Thus, enyne **V.13** was reacted with catalysts **III.32**, **III.36a**, **III.36b** using 3 mol % of catalyst and in the presence of 3 mol % of NaBArF (Table V.1, entries 1–3). The reaction carried out using catalyst **III.32** afforded a mixture of **V.14** and **V.25** (1:1.4) along with unreacted material after 24 h (22% conversion) (Table V.1, entry 1). Interestingly, catalyst **III.36a** reacted with **V.13** in only five min producing exclusively cyclopentene **V.14** (Table V.1, entry 2). An analogous result was obtained with catalyst **III.36b** (Table 1, entry 3).

Table V.1: Optimization of catalytic conditions for the reaction of enyne **V.13**.



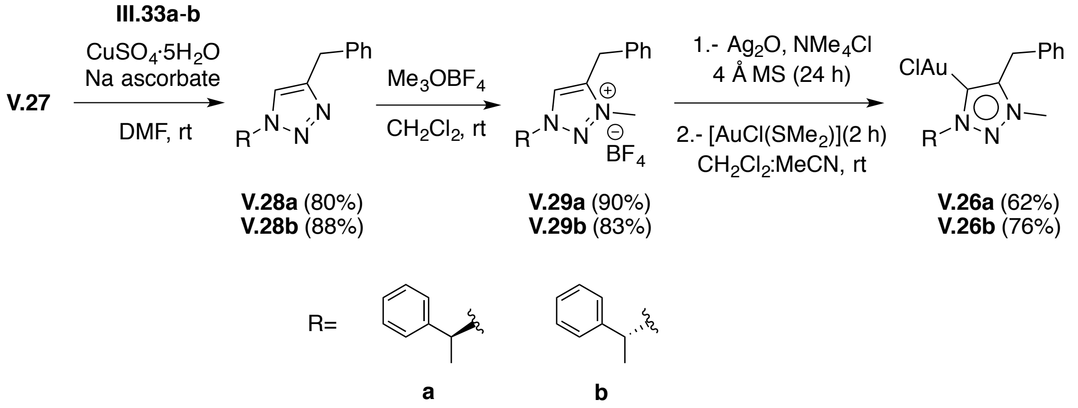
V.13 **V.14** **V.25**

Entry	Catalyst	Catalyst Load	Product	Time	Conversion (%)[a]
1	**III.32**	3 mol %	**V.14**:**V.25** (1:1.4)	24 h	22
2	**III.36a**	3 mol %	**V.14**	5 min	100
3	**III.36b**	3 mol %	**V.14**	1 min	100
4	**III.36a**	1 mol %	**V.14**	60 min	100
5	**III.36b**	1 mol %	**V.14**:**V.25** (1:1)	24 h	91
6	**V.26a**	3 mol %	-	24 h	no reaction
7	**V.26b**	3 mol %	-	24 h	no reaction
8	**V.30**	3 mol %	-	24 h	no reaction
9	-	-	-	24 h	no reaction

[a] Conversion was measured by ^{1}H NMR.

Apparently, catalyst **III.32** having a sulfoxide at *C*4 and a benzyl group attached to *N*1 is neither as efficient as catalysts **III.36a** or **III.36b** in terms of conversion nor in controlling the regioselectivity of the reaction.

To determine the origin of this effect, complexes **V.26a** and **V.26b** lacking the sulfoxide group were prepared from benzylacetylene **V.27** and enantiomerically pure α-methylbenzyl azides **III.33a**–**b**, following a synthetic route similar to those previously described (Scheme V.8).



Scheme V.8: Synthesis of gold complexes **V.26a**-**b**

Complexes **V.26a** and **V.26b** were then used as catalysts in the cycloisomerization of **V.13** (Table 1, entries 6–7). No reaction was observed after 24 hours under identical conditions to those used for **III.32** and **III.36a**–**b**. Clearly, the sulfoxide moiety is required for the reaction, while the presence of both, the sulfoxide and the α-phenylethyl groups in the gold carbene complex, is required to achieve good conversions and complete regioselectivities.

Lower catalyst loads were tested for **III.36a** and **III.36b** (Table V.1, entries 4–5). The use of 1 mol % of **III.36a** promotes the complete conversion of **V.13** to form **V.14** in 1 hour, while 1 mol % **III.36b** produces a partial transformation of the starting material in a mixture of **V.14** and **V.25**.

Since the ability of silver catalysts to promote cycloisomerization reactions is known,[164] enyne **V.13** was reacted using the silver carbene **V.30** obtained from

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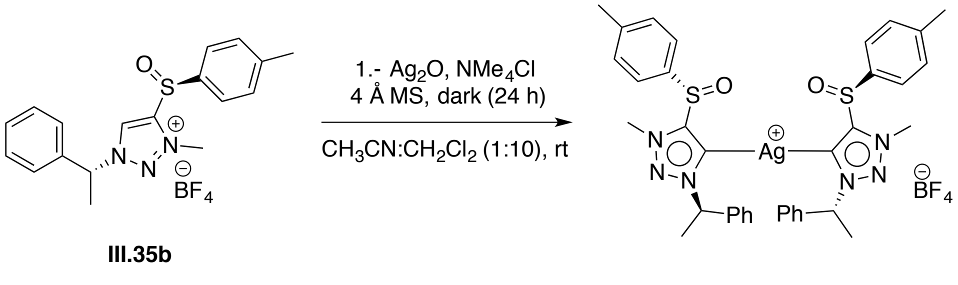
[164] a) G. Fang, X. Bi, *Chem. Soc. Rev.* **2015**, *44*, 8124; b) A. A. Peshkov, A. A. Nechaev, O. P. Pereshivko, J. L. Goeman, J. Van der Eycken, V. A. Peshkov, E. V. Van der Eycken, *Eur. J. Org. Chem.* **2015**, 4190.

triazolium salt **III.35b** under conditions already described (Scheme V.9). No reaction was observed after 24 hours, recovering unaltered enyne **V.13** (Table V.1, entry 8).



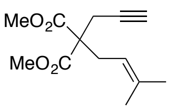
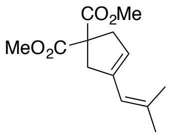
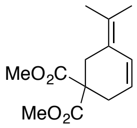
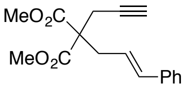
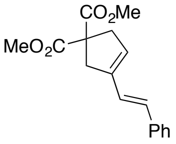
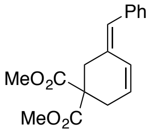
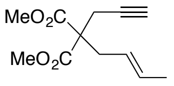
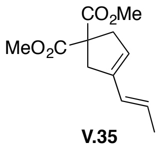
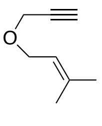
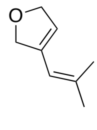
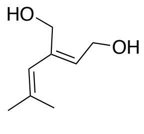
III.35b

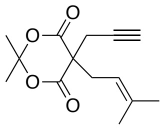
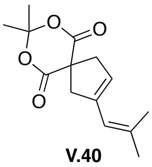
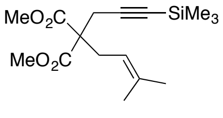
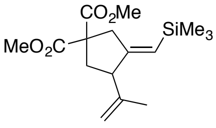
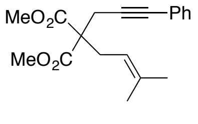
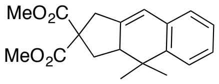
V.30 (95%)

Scheme V.9: Synthesis of silver carbene **V.30**

After determining the optimum catalyst, the effect of the structure of the enyne in the outcome of the reaction was addressed next.

Table V2: Gold carbene **III.36a** catalysed cycloisomerization of enynes.

Entry	Substrate	Products	Time	Yield(%)[a]
1	 **V.13**	 **V.14**  **V.25**	10 min	100 (**V.25** traces)
2	 **V.31**	 **V.33**  **V.34**	60 min	89 (5:1)
3	 **V.32**	 **V.35**	60 min	86[b]
4	 **V.36**	 **V.37**  **V.38**	1 min	100 (3:1)

5	 **V.39**	 **V.40**	180 min	50
6	 **V.41**	 **V.43**	24 h	no reaction
7	 **V.42**	 **V.44**	24 h	no reaction

[a] Isolated product
[b] *E*/*Z* 5:1

Enynes **V.13**, **V.31** and **V.32** having a terminal alkyne and a monosubstituted or disubstituted alkene nicely cyclized to the five-membered derivatives (**V.14**, **V.33**, **V.35**) in high yields (Table V.2, entries 1–3). It is worth noting that compound **V.36** lacking the Thorpe-Ingold effect imposed by the methoxycarbonyl groups in **V.13**, **V.31** and **V.32** formed the five-membered derivative **V.37** together with diol **V.38** arising from the opening of the dihydrofuran ring in a quantitative combined yield (3:1 mixture; Table V.2, entry 4). Meldrum's acid derivative **V.39** formed spirane **V.40** in a considerable 50% yield (Table V.2, entry 5).[165] In contrast, substitution of the terminal acetylenic hydrogen (compounds **V.41** and **V.42**) inhibits the reaction.

Despite the efforts devoted to this cycloisomerization, issues such as the *5-exo/6-endo* selectivity still deserve attention.[166] Remarkably, our results point to a crucial effect of the sulfoxide moiety in determining the activity of the catalyst, while the bulkiness of the *N*-substituent (contributed by the azide) is involved in the *5-exo* vs *6-endo* selectivity. The lack of reactivity of substituted alkyne derivatives **V.41** and **V.42** proves that at least in the first reaction step, formation of gold-carbene complexes

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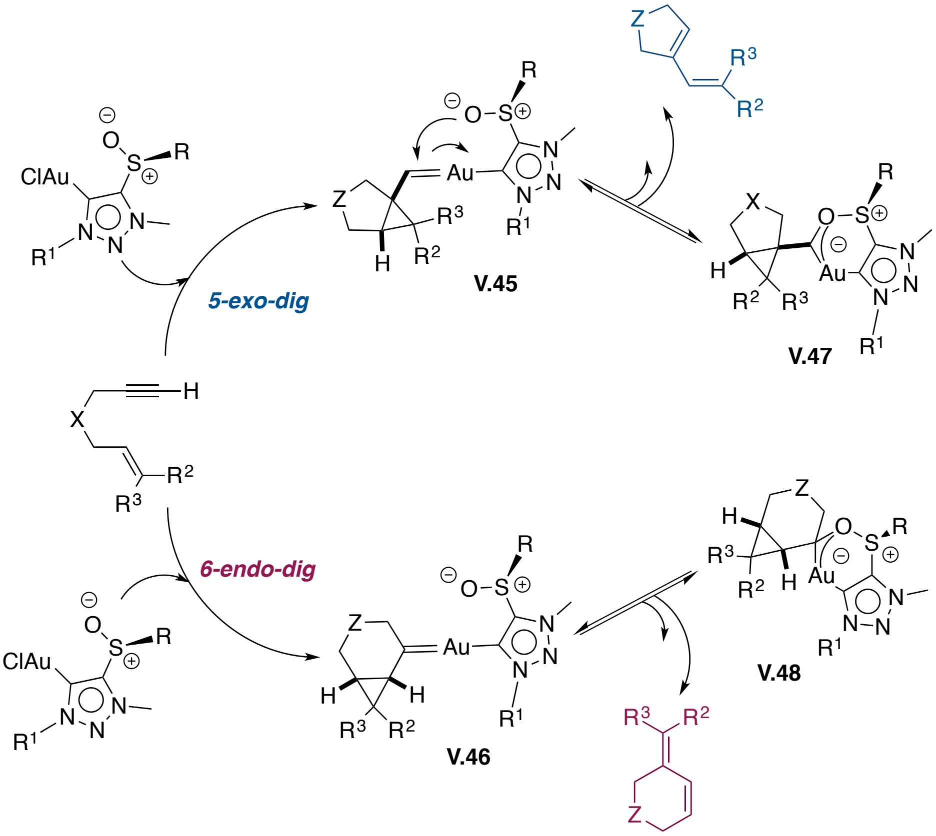
[165] Total conversion could be achieved within 4 h; nevertheless, this implies the formation of a secondary regioisomer.

[166] N. Marion, G. Lemière, A. Correa, C. Costabile, R. S. Ramón, X. Moreau, P. de Frémont, R. Dahmane, A. Hours, D. Lesage, J.-C. Tabet, J.-P. Goddard, V. Gandond, L. Cavallo, L. Fensterbank, M. Malacria, S. P. Nolan, *Chem. Eur. J.* **2009**, *15*, 3243.

V.45 (*5-exo* cyclization) and **V.46** (*6-endo* cyclization) should occur through the standard triple-bond coordination by the gold catalyst followed by cyclization (Scheme V.10). The role of the sulfoxide at this point seems to be a mere spectator. However, the inability of catalysts **V.26a–b** to promote the cyclization questions this assertion.

Gold-carbene complexes are prone to react with nucleophiles, therefore involvement of the sulfoxide oxygen to stabilise carbenes **V.45** and **V.46** forming Fischer-like intermediates **V.47** and **V.48** could be crucial for the catalysis to be productive.[167]



Scheme V.10: Mechanistic hypothesis

Evidently, **V.47** and **V.48** will be in equilibrium with the open forms **V.45** and **V.46**, which will evolve to the cyclic products through the well established pathways (Scheme V.10).[156] The *5-exo* vs *6-endo* cyclization selectivity should be related with the bulkiness of the carbon linked to *N*1. Since intermediate **V.47** is much more crowded than **V.48**, the bulkier α-phenylethyl moiety of complexes **III.36a** and **III.36b** should

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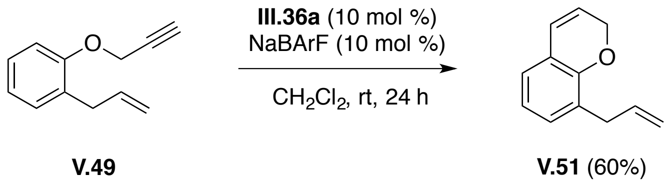
[167] Intermolecular participation of sulfoxides in Au-carbene intermediates has been previously reported: C. A. Witham, P. Mauleón, N. D. Shapiro, B. D. Sherry, F. D. Toste, *J. Am. Chem. Soc.* **2007**, *129*, 5838.

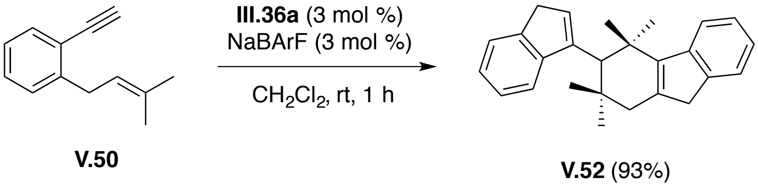
favour formation of **V.45** leading exclusively to the *5-exo* product. On the other hand, the benzyl moiety of complex **III.32** is less sterically demanding, leading to mixtures of two regioisomers. This mechanistic hypothesis is congruent with the results obtained and confers to the apparently ancillary moiety (the sulfoxide group) a key role unprecedented in the literature.

The reactions of enynes **V.49** and **V.50** was tested next. Enyne **V.49** reacted with gold catalyst **III.36a** in a very different way. The reaction was slower than the examples above (60% of conversion is obtained after 24 h of stirring at rt) and requires higher catalytic loads, 10 mol %). Product **V.51** derives from the S_EAr of the enyne on the aromatic ring promoted by the gold catalyst (Scheme V.11).[168]



Scheme V.11: Gold 1,2,3-triazolylidene **III.36a** catalysed C–H activation of **V.49**

Strikingly, reaction of enyne **V.50** with 3 mol % of catalyst **III.36a** afforded the product **V.52** after 1 h of stirring at rt (Scheme V.12). This polycyclic compound was characterised by NMR and EI-MS.



Scheme V.12: Gold 1,2,3-triazolylidene **III.36a** catalysed cycloisomerization of enyne **V.50**

^{1}H NMR showed two mutiplets between δ_H = 7.37 and 7.15 ppm for the eight aromatic protons of the molecule; the proton of the furan ring appears as a singlet at

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[168] For a review on gold-catalysed C–H bond functionalization see: T. C. Boorman, I. Larrosa, *Chem. Soc. Rev.* **2011**, *40*, 1910.

δ_H = 6.34 ppm. The three methylene groups appear as three singlets at δ_H = 3.38, 3.32 and 2.37 ppm. The new CH resonates at δ_H = 3.03 ppm. Finally, the four methyl groups are observed as four singlets between δ_H = 1.23 and 0.84 ppm. In the ^{13}C NMR it is important to note the disappearance of the two signals attributable to the ethynyl moiety at δ_C = 80.9 and 82.5 ppm as the result of the cycloisomerization process. In addition, three signals at δ_C = 39.1, 38.5, and 36.5 ppm are shown, corresponding to the CH_2 groups formed in this novel process. The structure of **V.52** was unambiguously confirmed by X-ray diffraction studies of a single crystal obtained by slow crystallisation in hexanes.

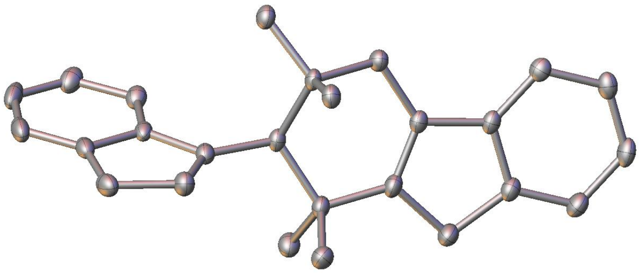
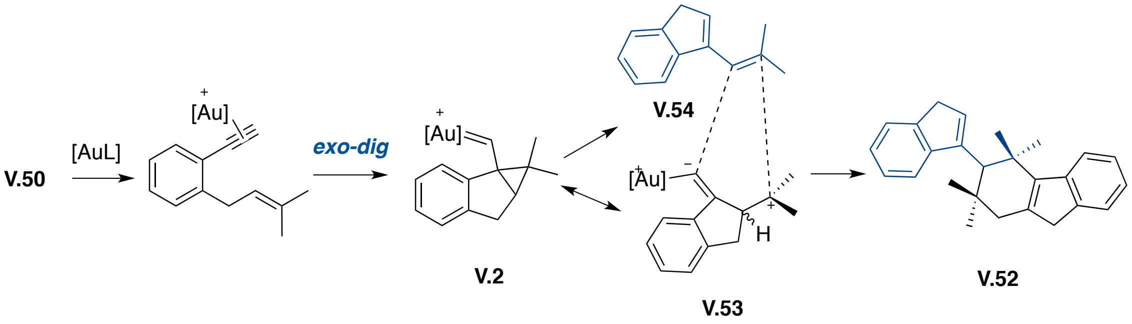


Figure V.1: ORTEP representation of compound **V.52**

Formation of compound **V.52** deserves some explanation. It is known that the intermediate gold carbene complexes **V.2**, formed by reaction of enynes with cationic Au(I), have a 1,3-dipolar nature, and their reaction with nitrones to form seven-membered fused derivatives has been reported.[169]



Scheme V.13: Mechanistic hypothesis of formation of compound **V.52**

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[169] S. A. Gawade, S. Bhunia, R.-S. Liu, *Angew. Chem. Int. Ed.* **2012**, *51*, 7835.

In our case, compound **V.52** may arise from a [4+2] cycloadditon of intermediate **V.53** with the olefin moiety of compound **V.54**, formed *in situ* from the carbene **V.2**.[170] The cycloadduct will isomerise in the reaction media until the obtaining of the observed product **V.52** (Scheme V.13).

Obviously, more experimental and computational work will be needed to corroborate this mechanism. Nevertheless, as a working hypothesis the sequence of reactions depicted in Scheme V.13 opens new reactivity and mechanistic opportunities. This work is now in progress in our laboratories.

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[170] a) T.-M. Teng, A. Das, D. B. Huple, R.-S. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 12565; b) A. M. Sanjuán, A. Martínez, P. García-García, M. A. Fernández-Rodríguez, R. Sanz, *Beilstein J. Org. Chem.* **2013**, *9*, 2242; c) D. B. Huple, S. Ghorpade, R.-S. Liu, *Chem. Eur. J.* **2013**, *19*, 12965.

V.4 CONCLUSIONS

To conclude, the ability of gold complexes **III.36a**–**b** as cycloisomerization catalysts has been studied finding that their catalytic activity is due to the presence of the sulfoxide group that acts in a previously unreported fashion. According to the proposed catalytic cycle, the high degree of *5-exo-dig* selectivity in these processes is attributed to the bulkiness of the substituent at the *N*1-triazole ring. Moreover, the reaction of enynes supported in an aromatic ring produces complete different results, including cyclization of the aromatic ring (which may be considered a C–H activation), and an unreported self-cyclization to form pentacylic derivatives in a process that build three rings and 5 bonds in one single step.

V.5 EXPERIMENTAL SECTION

Enynes **V.13**, **V.31**, **V.32**, **V.39**, **V.41**, **V.42** were prepared from dimethyl malonate following the general methods previously described.[171]

Enyne **V.36** was prepared from 3-methyl-2-buten-1ol following the method described in literature.[172]

Enyne **V.49** was prepared by propargylation of 2-allylphenol following a method previously described.[173]

Enyne **V.50** was synthetized following the procedure previously reported.[169]

The structure of cycloisomerization products **V.14**[174], **V.33**[175], **V.34**[157b], **V.35**[157b], **V.37**[176] were confirmed by ^{1}H NMR according to literature data.

Benzylacetilene **V.27** was obtained from commercial source and used without any purification.

General procedure for the synthesis of 1,2,3-triazoles

A mixture of organic azide (1.20 equiv), alkyne (1.00 equiv), sodium (L)-ascorbate (0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (0.25 equiv) in DMF was stirred under Ar at rt

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[171] O. Buisine, C. Aubert, M. Malacria, *Chem. Eur. J.* **2001**, *7*, 3517.

[172] T. R. Hoye, B. Baire, D. Niu, P. H. Willoughby, B. P. Woods, *Nature* **2012**, *490*, 208.

[173] S. K. Mandal, S. C. Roy, *Tetrahedron*, **2007**, *63*, 11341.

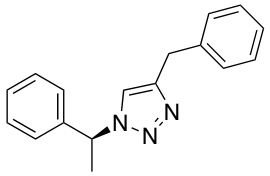
[174] F. Inagaki, C. Matsumoto, Y. Okada, N. Maruyama, C. Mukai, *Angew. Chem. Int. Ed.* **2015**, *54*, 818.

[175] C. Nieto-Oberhuber, M. P. Muñoz, S. López, E. Jiménez-Núñez C. Nevado, E. Herrero-Gómez, M. Raducan, A. M. Echavarren, *Chem. Eur. J.* **2006**, *12*, 1677.

[176] W. M. Hart-Cooper, K. N. Clary, F. D. Toste, R. G. Bergman, K. N. Raymond, *J. Am. Chem. Soc.* **2012**, *134*, 17873.

until completion of the reaction (TLC analysis). The reaction was quenched with water at 0 °C and allowed to reach rt. The mixture was extracted with CH_2Cl_2 three times. The organic layer was dried over $MgSO_4$, filtered and the volatiles were removed under vacuum to afford the corresponding reaction products, which were purified through a short pad of SiO_2.

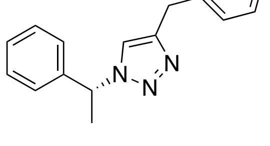
Synthesis of compound V.28a



Following the general procedure a mixture of azide **III.33a** (646 mg, 4.39 mmol, 1.30 equiv), alkyne **V.27** (390 mg, 3.37 mmol, 1.00 equiv), sodium (L)-ascorbate (334 mg, 1.68 mmol, 0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (210 mg, 0.84 mmol, 0.25 equiv) in DMF (50 mL) was stirred under Ar at rt for 3 h. The resulting residue was purified (SiO_2, Hex/EtOAc 6:4) to yield **V.28a** as a white solid (777 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (m, 9H, Ar), 7.09 (s, 1H, $N_3C{=}CH$), 5.73 (q, J = 7.1 Hz, 1H, CH), 4.06 (s, 2H, NCH_2), 1.92 (d, J = 7.1 Hz, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 147.6 (C, $N_3C{=}CH$), 140.2 (C, Ar), 139.2 (C, Ar), 129.0 (2CH, Ar), 128.8 (2CH, Ar), 128.6 (2CH, Ar), 128.5 (CH, Ar), 126.5 (3CH, Ar), 120.2 (CH, $N_3C{=}CH$), 60.2 (CH), 32.4 (NCH_2), 21.4 (CH_3). **IR (KBr) $\nu_{máx}$** 3130, 3028, 1495, 1456, 1449, 1214, 1134, 1046, 727, 699, 534. **$[\alpha]_D^{25}$** + 22.9 (c 1.0, $CHCl_3$). **HRMS (ESI)** m/z calculated for $C_{17}H_{18}N_3$: 264.1495 $[M+H]^+$, found: 264.1495. **m.p.** 80–82 °C.

Preparation of compound V.28b



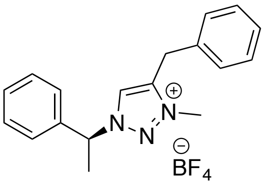
Following the general procedure a mixture of azide **III.33b** (596 mg, 4.05 mmol, 1.20 equiv), alkyne **V.27** (392 mg, 3.37 mmol, 1.00 equiv), sodium (L)-ascorbate (334 mg, 1.68 mmol, 0.50 equiv) and $CuSO_4{\cdot}5H_2O$ (210 mg, 0.84 mmol, 0.25 equiv) in DMF (50 mL) was stirred under Ar at rt for 3 h. The resulting residue was purified (SiO_2, Hex/EtOAc 7:3) to yield **V.28b** as a white solid (718 mg, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (m, 9H, Ar), 7.10 (s, 1H, $N_3C{=}CH$), 5.74 (q, *J* = 7.1 Hz, 1H, CH), 4.07 (s, 2H, NCH_2), 1.93 (d, *J* = 7.1 Hz, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 147.6 (C, $N_3C{=}CH$), 140.2 (C, Ar), 139.2 (C, Ar), 129.0 (2CH, Ar), 128.8 (2CH, Ar), 128.6 (2CH, Ar), 128.5 (CH, Ar), 126.5 (3CH, Ar), 120.3 (CH, $N_3C{=}CH$), 60.2 (CH), 32.4 (NCH_2), 21.4 (CH_3). **IR (KBr) $\nu_{máx}$** 3129, 3029, 1495, 1455, 1446, 1217, 1045, 727, 698. **$[\alpha]_D^{25}$** – 21.2 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{17}H_{18}N_3$: 264.1495 $[M+H]^+$, found: 264.1493. **m.p.** 78–80 °C.

General procedure for the synthesis of triazolium salts

Triazole (1.00 equiv) and Meerwein's salt (1.30 equiv) were stirred under Ar at rt in CH_2Cl_2 until complete consumption of the starting material (^{1}H NMR analysis). The reaction was quenched with methanol and filtered through a short pad of $NaHCO_3$. The solvent was removed under vacuum to afford the corresponding reaction product without further purification. In some cases, the product was washed with a mixture of CH_2Cl_2:pentane to remove starting material traces.

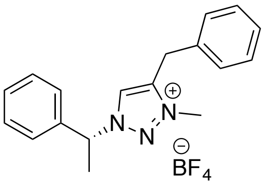
Synthesis of compound V.29a



Following the general procedure a mixture of **V.28a** (643 mg, 2.44 mmol, 1.00 equiv) and Me_3OBF_4 (470 mg, 3.17 mmol, 1.30 equiv) in CH_2Cl_2 (75 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **V.29a** as a white solid (740 mg, 83%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H, $N_3C{=}CH$), 7.39 (m, 5H, Ar), 7.28 (m, 5H, Ar), 5.91 (q, J = 7.0 Hz, 1H, CH), 4.19 (s, 2H, NCH_2), 4.11 (s, 3H, NCH_3), 2.01 (d, J = 7.0 Hz, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.2 (C, $N_3C{=}CH$), 136.7 (C, Ar), 133.2 (C, Ar), 129.9 (CH, Ar), 129.6 (2CH, Ar), 129.5 (2CH, Ar), 129.1 (2CH, Ar), 128.1 (CH, Ar), 127.9 (CH, $N_3C{=}CH$), 127.3 (2CH, Ar), 65.1 (CH), 38.1 (NCH_3), 29.3 (NCH_2), 20.6 (CH_3). **IR (KBr) $\nu_{máx}$** 3430, 3052, 1455, 1083, 749, 702. **$[\alpha]_D^{25}$** + 7.9 (c 1.0, $CHCl_3$). **HRMS (ESI)** m/z calculated for $C_{18}H_{20}N_3$: 278.1652 $[M{-}BF_4^-]^+$, found: 278.1656. **m.p.** 80–82 °C.

Synthesis of compound V.29b

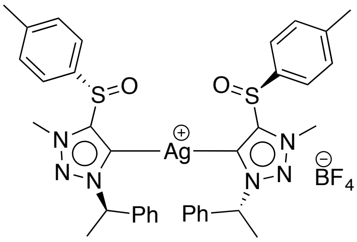


Following the general procedure a mixture of **V.28b** (560 mg, 2.13 mmol, 1.00 equiv) and Me_3OBF_4 (409 mg, 2.76 mmol, 1.30 equiv) in CH_2Cl_2 (65 mL) was stirred under Ar at rt overnight. The reaction was quenched with methanol and filtered through a plug of $NaHCO_3$. The solvent was removed under vacuum to yield **V.29b** as a thick yellowish solid (720 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H, $N_3C{=}CH$), 7.36 (m, 5H, Ar), 7.26 (m, 5H, Ar), 5.91 (q, J = 7.0 Hz, 1H, CH), 4.18 (s, 2H, NCH_2), 4.10 (s, 3H, NCH_3), 1.99 (d, J = 7.0 Hz, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.1 (C, $N_3C{=}CH$), 136.7 (C, Ar), 133.2 (C, Ar), 129.8 (CH, Ar), 129.5 (2CH, Ar), 129.4 (2CH, Ar), 129.1 (2CH, Ar), 128.0 (CH, Ar), 127.8 (CH, $N_3C{=}CH$), 127.2 (2CH, Ar), 64.9 (CH), 38.1 (NCH_3), 29.2 (NCH_2), 20.5 (CH_3). **IR**

(KBr) $\nu_{\text{máx}}$ 3430, 3128, 3034, 1592, 1497, 1455, 1278, 1071, 749, 701, 522. **$[\alpha]_D^{25}$** – 8.0 (*c* 1.0, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{18}H_{20}N_3$: 278.1652 $[M–BF_4^-]^+$, found: 278.1657. **m.p.** 76–79 °C.

Synthesis of compound V.30



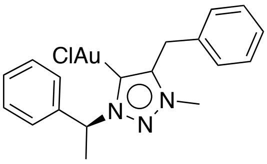
In a schlenk flask charged with 4 Å molecular sieves, a mixture of triazolium salt **III.35b** (166mg, 0.40 mmol, 1.00 equiv), NMe_4Cl (66 mg, 0.60 mmol, 1.50 equiv) and Ag_2O (70 mg, 0.30 mmol, 0.75 equiv) was stirred at rt in the dark in a mixture of CH_3CN:CH_2Cl_2 1:10 (14 mL) until the formation of the silver carbene (^1H NMR analysis). The reaction was filtered through a pad of Celite and the volatiles were removed under vacuum. The solid was then redissolved in CH_2Cl_2 and filtered again through a pad of Celite to separate the product form NMe_4Cl. The residue was precipitated in a mixture of CH_2Cl_2:pentane to afford the corresponding reaction product **V.30** as a yellowish solid (160 mg, 95%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.3 Hz, 4H, Ar *p*-tolyl), 7.35 (m, 14H, 10 Ar and 4H Ar *p*-tolyl), 5.98 (q, *J* = 6.9 Hz, 2H, CH), 4.18 (s, 6H, NCH_3), 2.41 (s, 6H, CH_3 *p*-tolyl), 1.99 (d, *J* = 6.9 Hz, 6H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.8 (2C, N_3C=CAg), 143.5 (2C, Ar), 138.6 (2C, Ar), 136.8 (C, Ar), 130.9 (4CH, Ar), 129.4 (2CH, Ar), 129.3 (4CH, Ar), 127.2 (4CH, Ar), 124.7 (4CH, Ar), 67.2 (2CH), 38.2 ($2NCH_3$), 21.6 ($2CH_3$, *p*-tolyl), 21.4 ($2CH_3$), C_{carbene} not observed. **IR (KBr)** $\nu_{\text{máx}}$ 3436, 1493, 1455, 1316, 1083, 1053, 812, 742, 706. **$[\alpha]_D^{25}$** – 87.7 (c 1.0, $CHCl_3$). **HRMS (ESI)** *m/z* calculated for $C_{36}H_{38}AgN_6O_2S_2$: 759.1542 $[M–BF_4^-]^+$, found: 759.1544. **m.p.** decomposes before melting.

General procedure for the synthesis of gold carbenes

In a schlenk flask charged with 4 Å molecular sieves, a mixture of triazolium salt (1.00 equiv), NMe_4Cl (1.50 equiv) and Ag_2O (0.75 equiv) was stirred at rt in the dark in CH_3CN:CH_2Cl_2 (1:10) until the formation of the silver carbene (^1H NMR analysis). The [AuCl(SMe_2)] (1.00 equiv) was added and the reaction was stirred at rt until completion of the reaction (^1H NMR analysis). The reaction was filtered through a pad of Celite and the solvents were removed under vacuum to afford the corresponding reaction products, which were purified through a short pad of SiO_2.

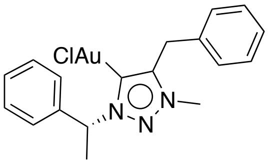
Synthesis of compound V.26a



Following the general procedure a mixture of **V.29a** (200 mg, 0.55 mmol, 1.00 equiv), NMe_4Cl (90 mg, 0.82 mmol, 1.50 equiv) and Ag_2O (95 mg, 0.42 mmol, 0.75 equiv) in CH_3CN:CH_2Cl_2 (33 mL) was stirred under Ar at rt overnight. [AuCl(SMe_2)] (160 mg, 0.55 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO_2, CH_2Cl_2) to yield **V.26a** as a white solid (213 mg, 76 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.2 Hz, 2H, Ar), 7.28 (m, 8H, Ar), 6.26 (q, *J* = 7.2 Hz, 1H, CH), 4.18 (d, *J* = 16.1 Hz, 1H, NCH_2), 4.09 (d, *J* = 16.1 Hz, 1H, NCH_2), 3.86 (s, 3H, NCH_3), 1.99 (d, *J* = 7.2 Hz, 3H, CH_3). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 157.7 (C, N_3C=*C*Au), 145.5 (C, N_3*C*=CAu), 138.5 (C, Ar), 135.1 (C, Ar), 129.2 (2CH, Ar), 129.0 (3CH, Ar), 128.5 (2CH, Ar), 127.6 (CH, Ar), 127.3 (2CH, Ar), 65.4 (CH), 37.3 (NCH_3), 31.3 (NCH_2), 20.9 (CH_3). **IR (KBr) $\nu_{máx}$** 3435, 3028, 1494, 1455, 1321, 1246, 1158, 1094, 1063, 727, 697. **$[\alpha]_D^{25}$** – 66.2 (*c* 1.0 CHCl$_3$). **HRMS (ESI)** *m/z* calculated for $C_{18}H_{19}AuN_3$: 474.1239 $[M–Cl^-]^+$, found: 474.1236. **m.p.** decomposes before melting.

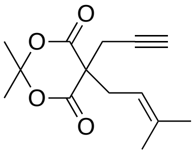
Synthesis of compound V.26b



Following the general procedure a mixture of **V.29b** (200 mg, 0.55 mmol, 1.00 equiv), NMe$_4$Cl (90 mg, 0.82 mmol, 1.50 equiv) and Ag$_2$O (95 mg, 0.42 mmol, 0.75 equiv) in CH$_3$CN:CH$_2$Cl$_2$ (33 mL) was stirred under Ar at rt overnight. [AuCl(SMe$_2$)] (160 mg, 0.55 mmol, 1.00 equiv) was added and the reaction was stirred for two more hours. The resulting residue was purified (SiO$_2$, CH$_2$Cl$_2$) to yield **V.26b** as a white solid (173 mg, 62 %).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.50 (d, *J* = 7.7 Hz, 2H, Ar), 7.28 (m, 8H, Ar), 6.26 (q, *J* = 7.2 Hz, 1H, CH), 4.17 (d, *J* = 16.1 Hz, 1H, NCH$_2$), 4.08 (d, *J* = 16.1 Hz, 1H, NCH$_2$), 3.85 (s, 3H, NCH$_3$), 1.98 (d, *J* = 7.2 Hz, 3H, CH$_3$). **^{13}C NMR** (125 MHz, CDCl$_3$) δ 157.8 (C, N$_3$C=*C*Au), 145.5 (C, N$_3$*C*=CAu), 138.5 (C, Ar), 135.0 (C, Ar), 129.2 (2CH, Ar), 129.1 (CH, Ar), 129.0 (2CH, Ar), 128.6 (2CH, Ar), 127.6 (CH, Ar), 127.3 (2CH, Ar), 65.4 (CH), 37.3 (NCH$_3$), 31.3 (NCH$_2$), 20.9 (CH$_3$). **IR (KBr)** $\nu_{\text{máx}}$ 3435, 3028, 1495, 1455, 1321, 1247, 1063, 727, 697. **$[\alpha]_D^{25}$** + 65.5 (*c* 1.0, CHCl$_3$). **HRMS (ESI)** *m/z* calculated for $C_{18}H_{19}AuN_3$: 474.1239 $[M–Cl^-]^+$, found: 474.1249. **m.p.** decomposes before melting.

Synthesis of compound V.39



2,2-dimethyl-1,3-dioxane-4,6-dione (1451 mg, 10 mmol, 1.00 equiv) was dissolved in 15 mL of anhydrous THF and added over a suspension of NaH (443 mg, 11.07 mmol, 1.10 equiv) in anhydrous THF (6 mL) at 0 °C. The mixture was stirred at rt for 30 min. 3,3-dimethylallyl bromide (1.6 mL, 11.07 mmol, 1.10 equiv) was added at 0 °C. After being stirred at rt overnight, the reaction was quenched with an aqueous solution of HCl 0.1 M to reach an acidic pH. The mixture was extracted with Et_2O (three times) and the combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The solvent was evaporated under vacuum and the residue was purified by a short pad of SiO_2 (Hex/EtOAc 5:1) obtaining a white solid (782 mg, 37%).

The ene-derived (782 mg, 3.68 mmol, 1.00 equiv) were dissolved in anhydrous DMF (5 mL) and added over a suspension of NaH (177 mg, 4.43 mmol, 1.20 equiv) in anhydrous DMF (5 mL of) at 0 °C. The mixture was stirred at rt for 30 min before propargyl bromide (0.40 mL, 3.68 mmol, 1.00 equiv) was added at 0 °C. After being stirred at rt overnight, the reaction was quenched with H_2O. An aqueous solution of HCl 0.1 M was added dropwise to reach an acidic pH. The mixture was extracted with Et_2O (three times) and the combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The solvent was evaporated under vacuum and the residue was purified by a short pad of SiO_2 (Hex/EtOAc 9:1) obtaining **V.39** a white solid (430 mg, 47%).

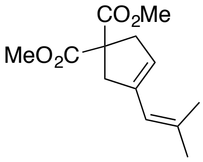
^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.02 (t, *J* = 8.7 Hz, 1H, CH), 2.89 (d, *J* = 2.6 Hz, 2H, CH_2), 2.67 (d, *J* = 8.0 Hz, 2H, CH_2), 2.10 (t, *J* = 2.6 Hz, 1H, CH), 1.78 (s, 3H, CH_3), 1.69 (s, 6H, 2CH_3), 1.59 (s, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 168.3 (2C=O), 139.1 (C), 116.4 (CH), 106.4 (C), 78.9 (C), 72.7 (CH), 54.7 (C), 38.6 (CH_2), 30.7 (CH_3), 29.2 (CH_3), 26.8 (CH_2), 26.0 (CH_3), 17.9 (CH_3). **IR (KBr) $\nu_{máx}$** 3291, 1772, 1725, 1341, 1265, 1104, 1051, 664. **HRMS (ESI)** *m*/*z* calculated for $C_{14}H_{18}NaO_4$: 273.1097 $[M+Na]^+$, found: 273.1094. **m.p.** below 30°C.

General procedure for the cycloisomerization of enynes

Gold carbene **III.36a** (0.01 mmol, 0.03 equiv) and NaBArF (0.01 mmol, 0.03 equiv) were stirred under Ar in anhydrous CH_2Cl_2 (2 mL) for 15 min. A solution of enyne (0.33 mmol, 1.00 equiv) in anhydrous CH_2Cl_2 (2 mL) was added in one portion. The reaction mixture was stirred at rt until completion of the reaction. The crude reaction was filtered through a short pad of Celite and SiO_2. Solvent was removed under pressure. The crude product was purified through a short pad of SiO_2.

Cycloisomerization of enyne V.13

Following the general procedure, gold carbene **III.36a** (6 mg, 0.01 mmol, 0.03 equiv) and NaBArF (9 mg, 0.01 mmol, 0.03 equiv) were dissolved in anhydrous CH_2Cl_2 (2 mL) under Ar for 15 min. Enyne **V.13** (79 mg, 0.33 mmol, 1.00 eq) was added dissolved in anhydrous CH_2Cl_2 (2 mL). After 10 min of stirring at rt, the reaction was filtered through a short pad of Celite and SiO_2. The crude product was purified through a short pad of SiO_2 (hexanes) to obtain **V.14** as colourless oil (79 mg, 100%).

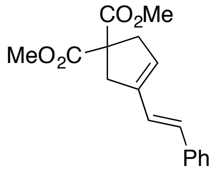


¹H NMR (400 MHz, $CDCl_3$) δ 5.72 (s, 1H), 5.37 (s, 1H), 3.72 (s, 6H), 3.18 (br d, *J* = 1.7 Hz, 2H), 3.03 (s, 2H), 1.81 (s, 3H), 1.77 (s, 3H).

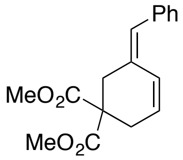
Cycloisomerization of enyne V.31

Following the general procedure, gold carbene **III.36a** (6 mg, 0.01 mmol, 0.03 equiv) and NaBArF (9 mg, 0.01 mmol, 0.03 equiv) were dissolved in anhydrous CH_2Cl_2

(2 mL) under Ar for 15 min. Enyne **V.31** (94 mg, 0.33 mmol, 1.00 eq) was added dissolved in anhydrous CH_2Cl_2 (2 mL). After 1 h of stirring at rt, the reaction was filtered through a short pad of Celite and SiO_2. The crude product was purified through a short pad of SiO_2 (Hex/EtOAc 9:1) to obtain **V.33** and **V.34** as a mixture (5:1) as white solid (84 mg, 89%).



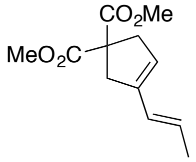
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (m, 5H), 6.82 (d, *J* = 16.2 Hz, 1H), 6.37 (d, *J* = 16.2 Hz, 1H), 5.63 (br s, 1H), 3.70 (s, 6H), 3.20 (s, 2H), 3.09 (s, 2H).



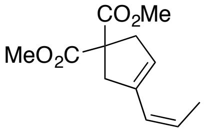
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (m, 5H, overlapped signal), 6.53 (d, *J* = 10.1 Hz, 1H), 6.27 (br s, 1H), 5.80 (m, 1H), 3.66 (s, 6H), 2.89 (br s, 2H), 2.69 (br s, 2H).

Cycloisomerization of enyne V.32

Following the general procedure, gold carbene **III.36a** (6 mg, 0.01 mmol, 0.03 equiv) and NaBArF (9 mg, 0.01 mmol, 0.03 equiv) were dissolved in anhydrous CH_2Cl_2 (2 mL) under Ar for 15 min. Enyne **V.32** (74 mg, 0.33 mmol, 1.00 eq) was added dissolved in anhydrous CH_2Cl_2 (2 mL). After 60 min of stirring at rt, the reaction was filtered through a short pad of Celite and SiO_2. The crude product was purified through a short pad of SiO_2 (Hex/EtOAc 96:4) to obtain **V.35** as yellowish oil in 5:1 *E*/*Z* mixture (64 mg, 86%).



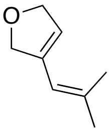
^{1}H NMR (300 MHz, $CDCl_3$) δ 6.18 (br d, J = 15.6 Hz, 1H), 5.60 (dq, J = 15.6 Hz, 6.6 Hz, 1H), 5.40 (br m, 1H), 3.74 (s, 6H), 3.10 (br s, 2H), 3.07 (br s, 2H), 1.77 (br d, J = 6.6 Hz, 3H).



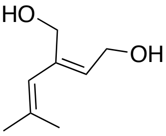
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.93 (dm, J = 11.6 Hz, 1H), 5.50 (m, 2H, overlapped signals), 3.75 (s, 6H), 3.28 (br s, 2H), 3.07 (s, 2H, overlapped signal), 1.83 (d, J = 7.5 Hz, 3H).

Cycloisomerization of enyne V.36

Following the general procedure, gold carbene **III.36a** (14 mg, 0.02 mmol, 1.00 equiv) and NaBArF (21 mg, 0.02 mmol, 0.03 equiv) were dissolved in anhydrous CH_2Cl_2 (2.5 mL) under Ar for 15 min. Enyne **V.36** (100 mg, 0.81 mmol, 1.00 equiv) was added dissolved in anhydrous CH_2Cl_2 (2.5 mL). After 60 min of stirring at rt, the reaction was filtered through a short pad of Celite and SiO_2. The crude product was purified through a short pad of SiO_2 (CH_2Cl_2) to obtain **V.37** and **V.38** as yellow oil in a mixture (3:1) (100 mg, 100%).



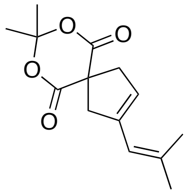
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.52 (d, J = 10.4 Hz, 1H, CH), 5.73 (br d, J = 10.4 Hz, 1H, CH), 4.34 (s, 2H, CH_2), 4.18 (s, 2H, CH_2), 1.76 (s, 3H, CH_3), 1.68 (s, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 127.2 (C), 124.8 (CH), 124.6 (C), 123.3 (C), 66.1 (CH_2), 65.5 (CH_2), 19.7 (CH_3), 19.4 (CH_3).



^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.78 (s, 1H, CH), 5.62 (s, 1H, CH), 4.75 (br s, 2H, CH_2), 4.67 (br s, 2H, CH_2), 1.85 (s, 3H, CH_3), 1.76 (s, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 137.7 (C), 136.9 (C), 122.5 (CH), 117.7 (CH), 76.5 (CH_2), 75.4 (CH_2), 27.2 (CH_3), 20.1 (CH_3). **HRMS (EI)** *m/z* calculated for $C_8H_{14}O_2$: 142.0994 $[M]^+$, found: 142.0835.

Cycloisomerization of enyne V.39

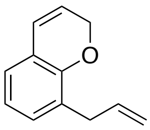
Following the general procedure, gold carbene **III.36a** (4 mg, 0.005 mmol, 0.03 equiv) and NaBArF (5 mg, 0.005 mmol, 0.03 equiv) were dissolved in anhydrous CH_2Cl_2 (1 mL) under Ar for 15 min. Enyne **V.39** (43 mg, 0.17 mmol, 1.00 eq) was added dissolved in anhydrous CH_2Cl_2 (1 mL). After 3 h of stirring at rt, the reaction was filtered through a short pad of Celite and SiO_2. The crude product was purified through a short pad of SiO_2 (Hex/EtOAc 98:2) to obtain **V.40** as white solid (21 mg, 50%).



^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.73 (s, 1H, CH), 5.43 (s, 1H, CH), 3.27 (s, 2H, CH_2), 3.16 (s, 2H, CH_2), 1.82 (s, 3H, CH_3), 1.80 (s, 3H, CH_3), 1.76 (s, 6H, $2CH_3$). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 171.0 (2C=O), 138.7 (C), 137.2 (C), 123.0 (C), 119.6 (CH), 105.0 (C), 51.6 (C), 48.6 (CH_2), 46.5 (CH_2), 29.1 (CH_3), 29.0 (CH_3), 27.4 (CH_3), 20.1 (CH_3). **IR (KBr) $\nu_{\text{máx}}$** 3283, 1765, 1738, 1345, 1269, 1102, 959, 692. **HRMS (ESI)** *m/z* calculated for $C_{14}H_{18}NaO_4$: 273.1097 $[M+Na]^+$, found: 273.1095.

Cycloisomerization of enyne V.49

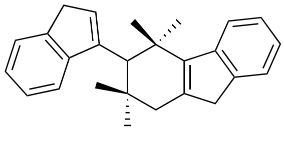
Following the general procedure, gold carbene **III.36a** (18 mg, 0.03 mmol, 0.10 equiv) and NaBArF (29 mg, 0.03 mmol, 0.10 equiv) were dissolved in anhydrous CH_2Cl_2 (2 mL) under Ar for 15 min. Enyne **V.49** (57 mg, 0.33 mmol, 1.00 equiv) was added dissolved in anhydrous CH_2Cl_2 (2 mL). After 3 h of stirring at rt, the reaction was filtered through a short pad of Celite and SiO_2. **V.51** was obtained in a 60% of conversion.



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (br t, J = 7.7 Hz, 1H, Ar), 6.99 (m, 2H, Ar), 6.44 (dt, J = 9.8 Hz, 1.8 Hz, 1H, CH), 6.02 (m, 1H), 5.79 (dt, J = 9.8 Hz, 3.6 Hz, 1H, CH), 5.07 (m, 1.8 Hz, 2H, CH_2), 4.83 (dd, J = 3.6 Hz, 1.8 Hz, 2H, CH_2), 3.36 (d, J = 6.5 Hz, 2H, CH_2). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.7 (C, Ar), 137.0 (CH, Ar), 130.1 (CH, Ar), 127.3 (C, Ar), 125.1 (CH), 124.9 (CH), 122.4 (C, Ar), 121.9 (CH, Ar), 121.0 (CH, Ar), 115.5 (CH_2), 65.6 (CH_2), 33.8 (CH_2).

Cycloisomerization of enyne V.50

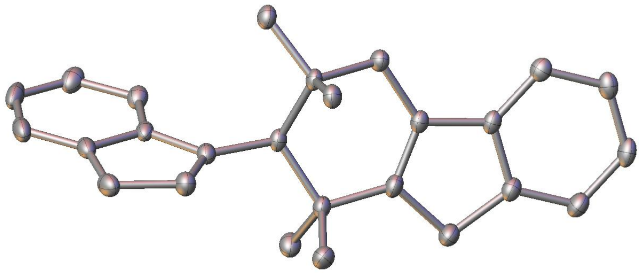
Following the general procedure, gold carbene **III.36a** (6 mg, 0.01 mmol, 0.03 equiv) and NaBArF (9 mg, 0.01 mmol, 0.03 equiv) were dissolved in anhydrous CH_2Cl_2 (2 mL) under Ar for 15 min. Enyne **V.50** (56 mg, 0.33 mmol, 1.00 equiv) was added dissolved in anhydrous CH_2Cl_2 (2 mL). After 1 h of stirring at rt, the reaction was filtered through a short pad of Celite and SiO_2. The crude product was purified through a short pad of SiO_2 (Hex/EtOAc 96:4) to obtain **V.52** as white solid (52 mg, 93%).



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (m, 3H, CH Ar), 7.15 (m, 5H, CH Ar), 6.34 (s, 1H, CH), 3.38 (s, 2H, CH_2), 3.32 (s, 2H, CH_2), 3.02 (s, 1H, CH), 2.37 (br s, 2H, CH_2), 1.23 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 1.01 (s, 3H, CH_3), 0.84 (s, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.9 (C), 148.6 (C), 146.4 (C), 143.3 (C), 143.2 (C), 143.1 (C), 133.4 (C), 130.4 (CH), 126.3 (CH, Ar), 126.1 (CH, Ar), 124.5 (CH, Ar), 124.1 (CH, Ar), 123.7 (CH, Ar), 123.6 (CH, Ar), 119.2 (CH, Ar), 118.1 (CH, Ar), 51.7 (CH), 39.1 (CH_2), 38.5 (CH_2), 37.5 (C), 36.5

(CH_2), 35.1 (C), 32.4 (CH_3), 31.2 (CH_3), 25.2 (CH_3), 24.1 (CH_3). **HRMS (EI)** *m*/*z* calculated for $C_{26}H_{28}$: 340.2186, found: 340.2185.

Crystal data for compound V.52:



$C_{26}H_{28}$, Mr = 340.48, crystal dimensions 0.4 x 0.3 x 0.3 mm^3, monoclinic, $P2_1/c$, *a* = 8.125(1) Å, *b* = 21.014(2) Å, *c* = 11.266(2) Å, β = 99.032(3)°, cell volume = 1899.6(3) Å^3, Z = 4, ρ_{calcd} = 1.191 Mg/m^3, μ = 0.067 mm^{-1}, T = 100(2) K, $2\theta_{max}$ = 52.7°, 31344 reflections collected, 3861 independent, R_{int} = 0.1211, R1 = 0.0496 and wR2 = 0.1002 for I > 2σ(I), R1 = 0.0961 and wR2 = 0.1174 for all data, residual electron density = 0.244eA^{-3}.

CHAPTER VI

General conclusions

The most significant conclusions that could be extracted from this assertion are here summarized:

- Two new classes of metallic mesoionic carbenes derived from 1,2,3-triazoles have been synthetized:

1.- Steroid (estrone and estradiol) derived metallic MIC complexes have been prepared. The approach uses the versatility of this methodology to obtain monometallic and polymetallic complexes. In addition, a tetrametallic derivative embebed in a macrocyclic structure has been isolated and characterised.

2.- Enantiopure MIC-metal complexes having a sulfoxide group in the *C*4 position of the heterocycle have been prepared. The synthetic methodology has allowed us to widen the nature of the sulphur-based triazolylidenes: different azides and alkynes have been employed, in addition to the formation of sulfone and sulfoximines derivatives. Moreover, different metal sources enable the obtaining of different metallic carbenes. Ag, Au, Cu, Pd and Ru complexes are avaibable by this straightforward methodology. In all the cases, the integrity of the sulfoxide group has been demonstrated to be maintained (in a structural and configurational level) along the complete synthetic pathways.

- A new desulfinylation and rearrangement reaction in the triazolylidene nucleus has been discovered. This novel transformation, with no precedent in the literature, represents a new methodology for the synthesis of H-substituted 1,2,3-triazolylidenes and its metallic MIC complexes.

- Experimental and theoretical studies have been carried out in order to establish a mechanistic hypothesis that explains this new reactivity.

- The catalytic activity of *C*4 sulfinyl 1,2,3-triazolylidene gold carbenes has been tested in the cycloisomerization reaction of a series of 1,6-enynes. The sulfoxide group presents an essential role in terms of reactivity while the group bearing the *N*1 position of the heterocyclic core controls the selectivity of the isomerization.

CHAPTER VII

Materials and methods

VII.1 SOLVENTS AND REAGENTS

Unless noted otherwise, all manipulations were carried out under an Ar atmosphere using standard Schlenk techniques. DMF and CH_3CN were dried by passage through solvent purification columns containing activated alumina. CH_2Cl_2 was stored in $CaCl_2$ for 24 h and dried through a distillation with CaH_2. Other solvents were HPLC grade and were used without further purification. Triethylamine and pyridine were distillated over CaH_2. All reagents were obtained from commercial sources and used without further purification, unless noted otherwise. Flash column chromatography was performed using silica gel (Merck, n° 9385, 230–400 mesh).

VII.2 EQUIPMENT

The characterisation of the compounds synthetized in this assertation has been carried out using the following equipment:

- ^1H and ^{13}C NMR spectra were recorded at 300, 400 or 500 MHz (^1H NMR) and at 100 or 125 MHz (^{13}C NMR) using $CDCl_3$ and DMSO-*d₆* as solvents with the residual solvent signal as internal reference ($CDCl_3$, 7.26 and 77.2 ppm) and (DMSO-d_6, 2.50 and 39.5 ppm). The following abbreviations are used to describe peak patterns when appropriate: s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet), and br (broad).

- High-resolution mass spectrometry (HRMS) by the ESI technique was performed with an Agilent 6500 accurate mass apparatus with a Q-TOF analyser.

- IR spectra were recorded on a Perkin-Elmer 681 spectrophotometer.

- Optical rotations were measured on a Jasco P-2000 polarimeter using a sodium lamp.

- Melting points were determined on a Koffler block.

- All data (except for complex **III.62a**) were collected at low temperature using oil-coated shock-cooled crystals on a Bruker-AXS APEX II diffractometer with

MoKa radiation (λ = 0.71073 Å). The structures were solved by direct methods[177] and all non hydrogen atoms were refined anisotropically using the least-squares method on F^2.[178] The absolute structure parameters have been refined using the Flack-method.[179]

- Crystal data was collected for complex **III.62a** using a Rigaku (former Agilent Technologies) Oxford Diffraction SuperNova A diffractometer fitted with an Atlas detector and using monochromated Mo–Kα radiation (0.71073 Å). A complete data set was collected, assuming that the Friedel pairs are not equivalent. All structures were solved by direct methods using SHELXS-97 and refined by full-matrix least squares fitting on F2 for all data using SHELXL-97.[S8] Hydrogen atoms were added at calculated positions and refined by using a riding model. Anisotropic thermal displacement parameters were used for all nonhydrogen atoms.

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VII.3 GENERAL PROCEDURES

VII.3.1 General procedure for the synthesis of 1,2,3-triazoles

A mixture of organic azide, alkyne, sodium (L)-ascorbate and $CuSO_4{\cdot}5H_2O$ in DMF was stirred under Ar at rt until completion of the reaction (TLC analysis). The reaction was quenched with water at 0 °C and allowed to reach rt. The mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with water (twice) and once with brine. The organic layer was dried over $MgSO_4$, filtered and the volatiles were removed under vacuum to afford the corresponding reaction products, which were purified through a short pad of SiO_2.

VII.3.2 General procedure for the synthesis of 1,2,3-triazolium salts

Triazole and Meerwein's salt were stirred under Ar at rt in CH_2Cl_2 until the reaction was completed (^1H NMR analysis). The reaction was quenched with methanol and filtered through a short pad of $NaHCO_3$. The solvent was removed under vacuum to afford the corresponding reaction product without further purification.

VII.3.3 General procedure for the synthesis of silver complexes

In a schlenk flask charged with 4 Å molecular sieves, a mixture of triazolium salt, NMe_4Cl and Ag_2O was stirred at rt in the dark in CH_3CN:CH_2Cl_2 until the formation of the silver carbene (^1H NMR analysis). The reaction was filtered through a pad of Celite and the volatiles were removed under vacuum. The solid was then redissolved in CH_2Cl_2 and filtered again through a pad of Celite to separate the product from NMe_4Cl. The residue was precipitated in a mixture of CH_2Cl_2:pentane to afford the corresponding reaction products.

VII.3.4 General procedure for the synthesis of metallic complexes

In a schlenk flask charged with 4 Å molecular sieves, a mixture of triazolium salt, NMe_4Cl and Ag_2O was stirred at rt in the dark in CH_3CN:CH_2Cl_2 until the formation of the silver carbene (^1H NMR analysis). The metallic source was added and the reaction was stirred at rt until completion of the reaction (^1H NMR analysis). The reaction was filtered through a pad of Celite and the solvents were removed under vacuum to afford the corresponding reaction products.

CHAPTER VIII

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CHAPTER IX

Summaries

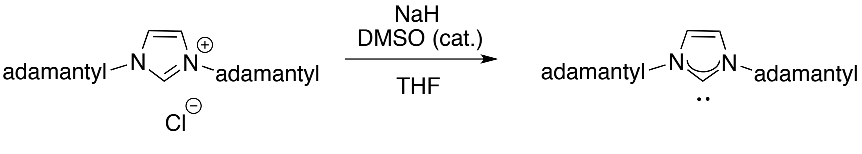
IX.1 SUMMARY

NEW MESOIONIC CARBENE METAL COMPLEXES

Introduction

Carbenes are neutral compounds with a divalent carbon that has six valence electrons. Their incomplete octet electron makes these species highly reactive and unstable. They have been considered as transient intermediates in organic transformations, making their isolation and characterisation a major challenge.

A milestone in the chemistry of carbenes was achieved in the early 1990s by Arduengo. In this work, the crystalline structure of a free carbene was resolved for the first time. It was an imidazolylidene bearing two adamantyl groups binding the nitrogen atoms adjacent to the carbene carbon (Scheme IX.1.1).



I.3 **I.4** (96%)

Scheme IX.1.1: First example of a free N-heterocyclic carbene performed by Arduengo

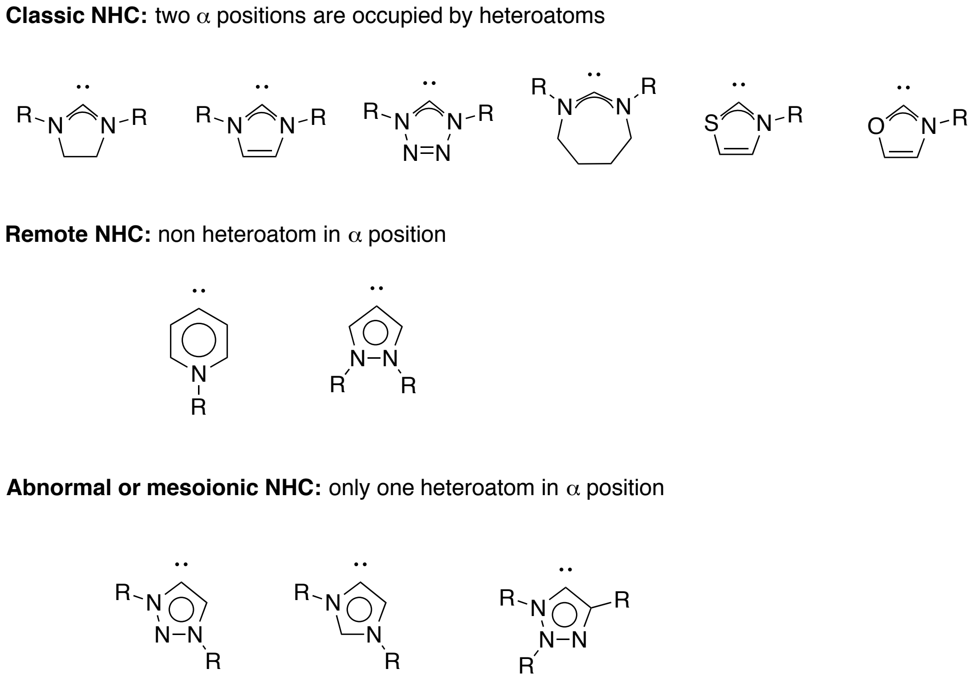
The term *N*-heterocyclic carbenes (NHC) refers to a subclass of carbenes embedded in a cyclic structure with at least one heteroatom. These compounds present some properties that are the responsible of their key role in organometallic chemistry. These properties are:

a) High covalent contribution of the metal–carbene bound.

b) Strong donor ability.

c) Easy electronic and steric tunability.

With the aim of finding new donor abilities of NHCs, efforts have been focused in developing new systems having modified cyclic cores. For example, NHCs containing up to six-, seven- and eight-membered rings have been reported; while nitrogen atoms have been displaced to remote positions from the carbene carbon in order to increase their donor ability. These modifications have yielded to two new groups of *N*-heterocyclic carbenes: remote, when there is not any heteroatom in the adjacent positions of the carbene carbon; or abnormal or mesoionic, when only one α position to the carbene centre is occupied by a heteroatom (Figure IX.1.1).



Classic NHC: two α positions are occupied by heteroatoms

Remote NHC: non heteroatom in α position

Abnormal or mesoionic NHC: only one heteroatom in α position

Figure IX.1.1: Classification of NHCs

1,2,3-Triazolylidenes are among this class of carbenes. One of the reasons of the growing attention that triazolylidenes have recently drawn is the fact that they derive from 1,2,3-triazoles, which are readily available through the highly efficient and regioselective Cu(I)-catalysed Huisgen alkyne-azide cycloaddition (CuAAC).

A large number of functional groups with different electronic and steric properties are compatible due to mild reaction conditions of this transformation. This allows not only for diversification of their structures but also for a high modulation of the electronic properties of the carbene. These features could be transferred to the coordinating metal centre with the aim of seeking for new applications.

Applications of 1,2,3-triazolylidene complexes are mainly straitened to field of catalysis. Nonetheless, these mesoionic carbenes have recently started to extend their applicability to other fields as medicine and photophysics.

Objectives

In this context and considering the precedents, the objectives of this Doctoral Thesis will be:

- Synthesis of new 1,2,3-triazolylidenes metal complexes supported by natural products. Taking advantage of the versatility of the CuAAC process, the use of mono, bis, tris and tetra(azides) will lead to compounds with one, two, three an up to four nuclei of triazoles. The ensuing polymetallic carbenes would be obtained through the functionalization of the heterocyclic.

- Synthesis of a new class of ligands based on 1,2,3-triazoles bearing an enantiomerically pure sulfoxide group in position *C*4 of the heterocyclic ring.

- Functionalization of the triazole nuclei *C*4-substituted for the obtaining of the metallic carbenes.

- Generation of high structural diversity in the new family of functionalized carbenes with sulphur derived groups. This great variety will be addressed by modification of the different actors involved in the distinct steps of the synthetic approach.

- Study of new reactivity of NHCs. A new desulfinylation reaction with no precedents in the literature will be investigated. Different experiments will be performed in order to elucidate a mechanism additionally supported by theoretical studies.

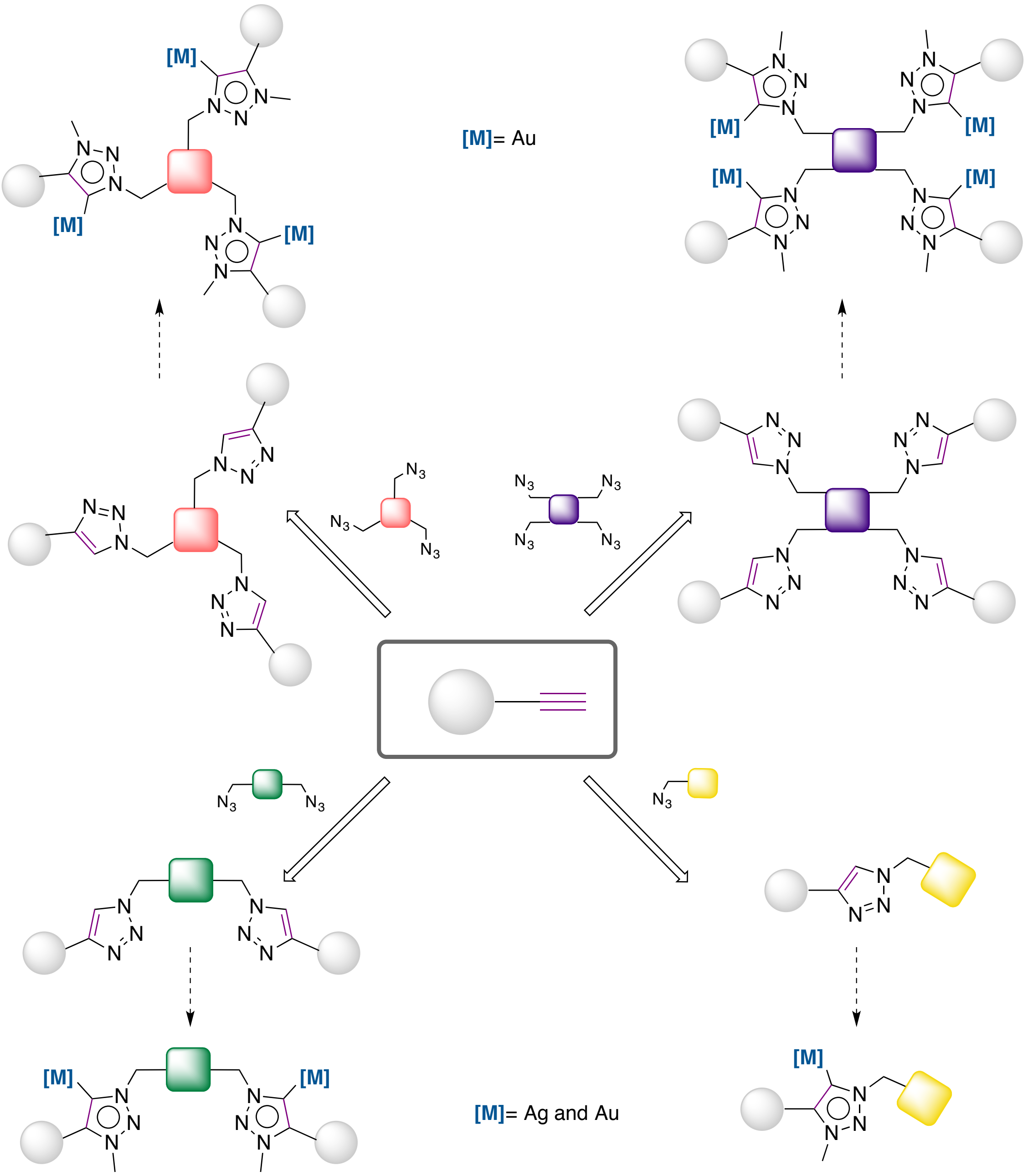
- Study of the catalytic activity of the new NHCs. The catalytic behaviour of these complexes will be evaluated in order to test if the presence of the sulfoxide group could have an effect on the outcome of the catalytic transformation.

Conclusions

1.- A new family of polymetallic 1,2,3-triazolylidenes supported on steroidic nuclei have been synthetized (Scheme IX.1.2). The structure of these new carbenes has been studied through theoretical studies. This is the first example of organometallic hybrids containing NHCs.

2.- A new family of 1,2,3-triazolylidenes metallic complexes with an enantiomerically pure chiral sulfoxide in position *C*4 of the triazole has been obtained. This chiral purity has been demonstrated to be kept among the different steps that composed the synthetic route, from the formation of the triazole until the formation of the carbene.

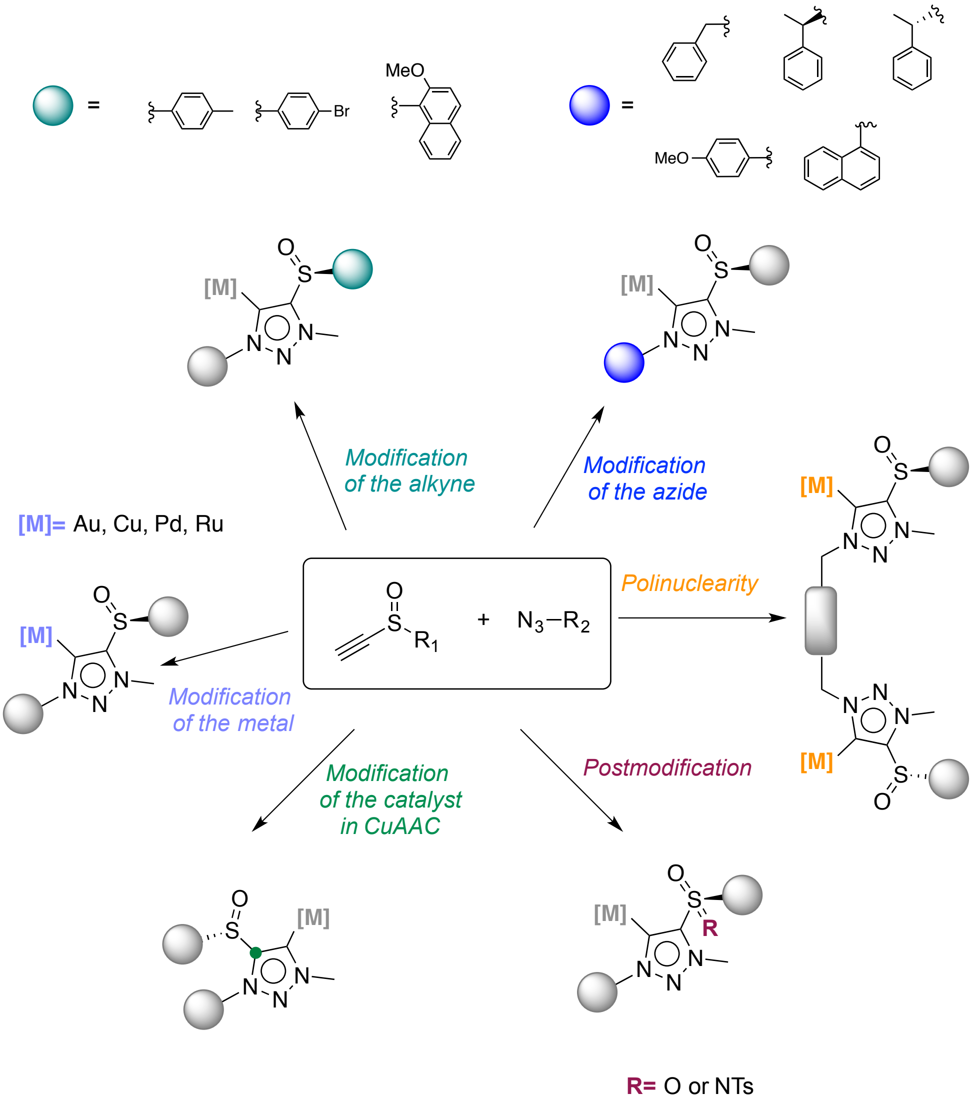
3.- A great structural variety of this new family of NHCs has been achieved changing the nature of the different actors that participate in the synthetic methodology employed (Scheme IX.1.3).



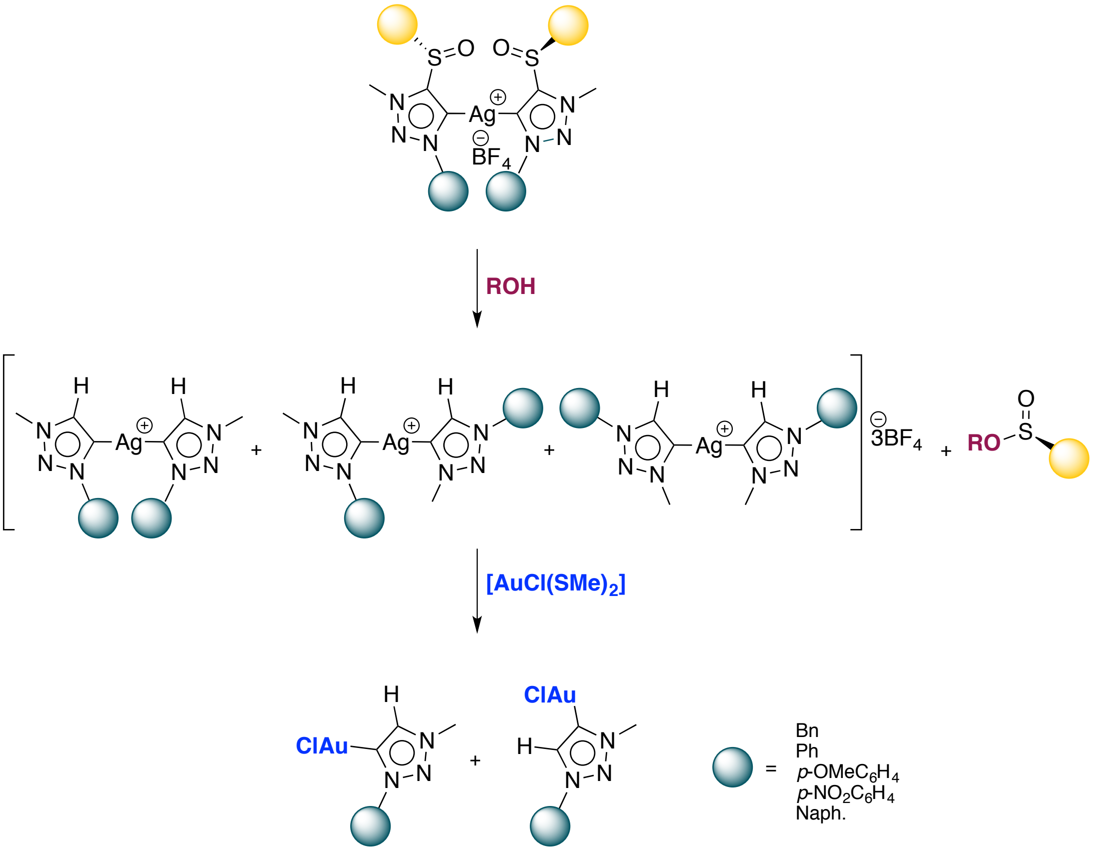
Scheme IX.1.2: Synthesis of polymetallic carbenes supported by esteroidic nuclei

4.- A new methodology for the obtaining of *H*-substituted 1,2,3-triazolylidenes complexes has been developed. This transformation occurs through a novel reaction comprising a desulfinylation process and subsequent transposition of the metal centre. Regioisomeric carbenes in *C*4 and *C*5 are obtained after transmetallation of the silver intermediates (Scheme IX.1.4).

5.- A mechanism of this transformation has been proposed. The hypothetical pathways of the transformation are supported by different experiments and theoretical calculations.



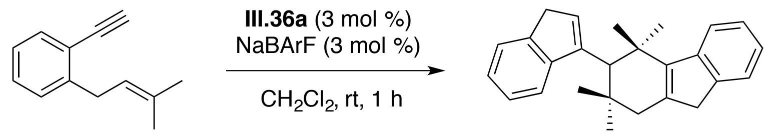
Scheme IX.1.3: Structural diversity of sulphur based MIC complexes



Scheme IX.1.4: New desulfinylation and rearrangement process

6.- The catalytic activity of the new metallic carbenes has been tested. Gold carbenes bearing a sulfoxide in *C*4 have been employed as catalyst in the cycloisomerization of enynes, showing a great activity in terms of efficiency and selectivity. This activity is in contrast to the poor conversions achieved by complexes lacking the sulfinyl moiety. These results prompted that the role of the sulfoxide in these reactions is essential in the outcome of the catalytic transformation by the stabilisation of one of the intermediates.

7.- The cycloaddition reaction of enyne **V.50** catalysed by gold carbene **III.36a** afforded the polycyclic compound **V.52** through an unknown mechanism (Scheme IX.1.5).



V.50

V.52 (93%)

Scheme IX.1.5: Synthesis of compound **V.52**

This result opens a promising way to the synthesis of highly structural complexes in a straighforward and highly efficient way.

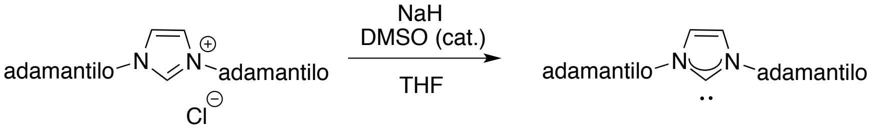
IX.2 RESUMEN

NUEVOS COMPLEJOS METÁLICOS DE CARBENOS MESOIÓNICOS

Introducción

Se denominan carbenos a aquellas especies químicas neutras que poseen un carbono divalente con seis electrones de valencia. Esta configuración electrónica no cumple la regla del octete, haciendo que estas sustancias sean reactivas e inestables. Durante mucho tiempo, los carbenos se han considerado como intermedios en distintas transformaciones orgánicas, y su aislamiento y caracterización es y ha sido un importante desafío.

Arduengo consiguió uno de los grandes hitos en la química de carbenos libres a principio de los años noventa. En este trabajo se resolvió la primera estructura cristalina de un carbeno libre. Se trataba de un anillo de imidazolilideno con un grupo adamantilo unido a cada uno de los átomos de nitrógeno que se encontraban en las posiciones adyacentes al carbono carbénico (Esquema IX.2.1).



I.3 **I.4** (96%)

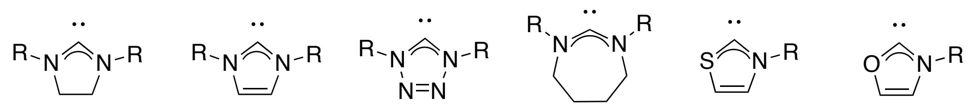
Esquema IX.2.1: Primer ejemplo de carbeno libre de tipo *N*-heterocíclico

Los carbenos de tipo *N*-heterocíclico (NHC) son aquellos que poseen al menos un heteroátomo en su estructura cíclica. Estos compuestos tienen un conjunto de propiedades que son responsables del importante papel que han tenido los NHCs en el campo de la química organometálica durante la pasada década. Estas propiedades se resumen en:

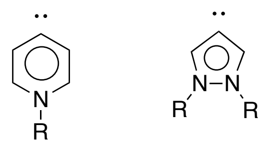
a) Alta contribución covalente en el enlace metal–carbeno.
b) Alta capacidad donadora.
c) Fácil modificación de sus propiedades electrónicas y estéricas.

Entre otras variaciones estructurales, con el objetivo de modificar las capacidades donadoras de los NHCs, se han diseñado nuevos heterociclos conteniendo seis, siete y ocho eslabones en su estructura. Además, los heteroátomos se han desplazado hacia posiciones más alejadas del centro carbénico, aumentando así su carácter donador. Esto ha provocado la aparición de dos nuevos grupos de carbenos de tipo *N*-heterocíclico: los denominados como remotos, cuando el carbono carbénico no tiene heteroátomos en posiciones adyacentes a las del carbono carbénico, y los denominados como anormales o mesoiónicos, cuando únicamente una posición α al centro carbénico está ocupada por un heteroátomo (Figura IX.2.1).

NHC clásico: las dos posiciones α al carbono carbénico están ocupadas por heteroátomos



NHC remoto: no hay heteroátomos en las posiciones α al carbono carbénico



NHC anormal o mesoiónico: solamente hay un heteroátomo en posición α al carbono carbénico

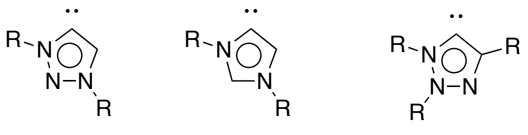


Figura IX.2.1: Clasificación de los NHCs

Los 1,2,3-triazolilidenos se encuentran dentro de este último tipo de carbenos. Una de las razones de su creciente importancia deriva del hecho de que este tipo de carbenos tienen como precursores a los 1,2,3-triazoles, los cuales se sintetizan mediante la reacción de cicloadición altamente eficiente y regioslectiva entre un alquino y una azida catalizada por Cu (CAACu). Un amplio número de grupos funcionales con diferentes propiedades electrónicas y estéricas son compatibles con las condiciones de reacción de esta transformación. Esto permite no solamente la diversificación estructural de una manera sencilla, sino que además pueden modificarse de forma relativamente fácil las propiedades electrónicas del carbeno, las cuales pueden transferirse al metal al que se coordinan.

Las aplicaciones de los carbenos *N*-heterocíclicos derivados de 1,2,3-triazolilidenos se han centrado básicamente en aplicaciones en catálisis, aunque recientemente, se han extendido a otras áreas de estudio como la medicina o la fotofísica.

Objetivos

Teniendo en cuenta los precedentes anteriormente descritos, los objetivos de esta Tesis Doctoral, serán:

- Síntesis de nuevos carbenos *N*-heterocíclicos de tipo 1,2,3-triazolilideno soportados sobre productos naturales. La posterior metalación de estos heterociclos generará los consiguientes carbenos mono-, bi- y polimetálicos.

- Síntesis de nuevos ligandos de 1,2,3-triazol enantioméricamente puros que presentan un grupo sulfinilo en la posición *C*4 del anillo de triazol.

- Funcionalización de los núcleos heterocíclicos sustituidos en *C*4 para la obtención de los correspondientes carbenos metálicos.

- Generación de diversidad estructural en la nueva familia de carbenos funcionalizados con grupos derivados de azufre. Esta variedad se alcanza modificando los distintos actores involucrados en las diferentes etapas de la aproximación sintética.

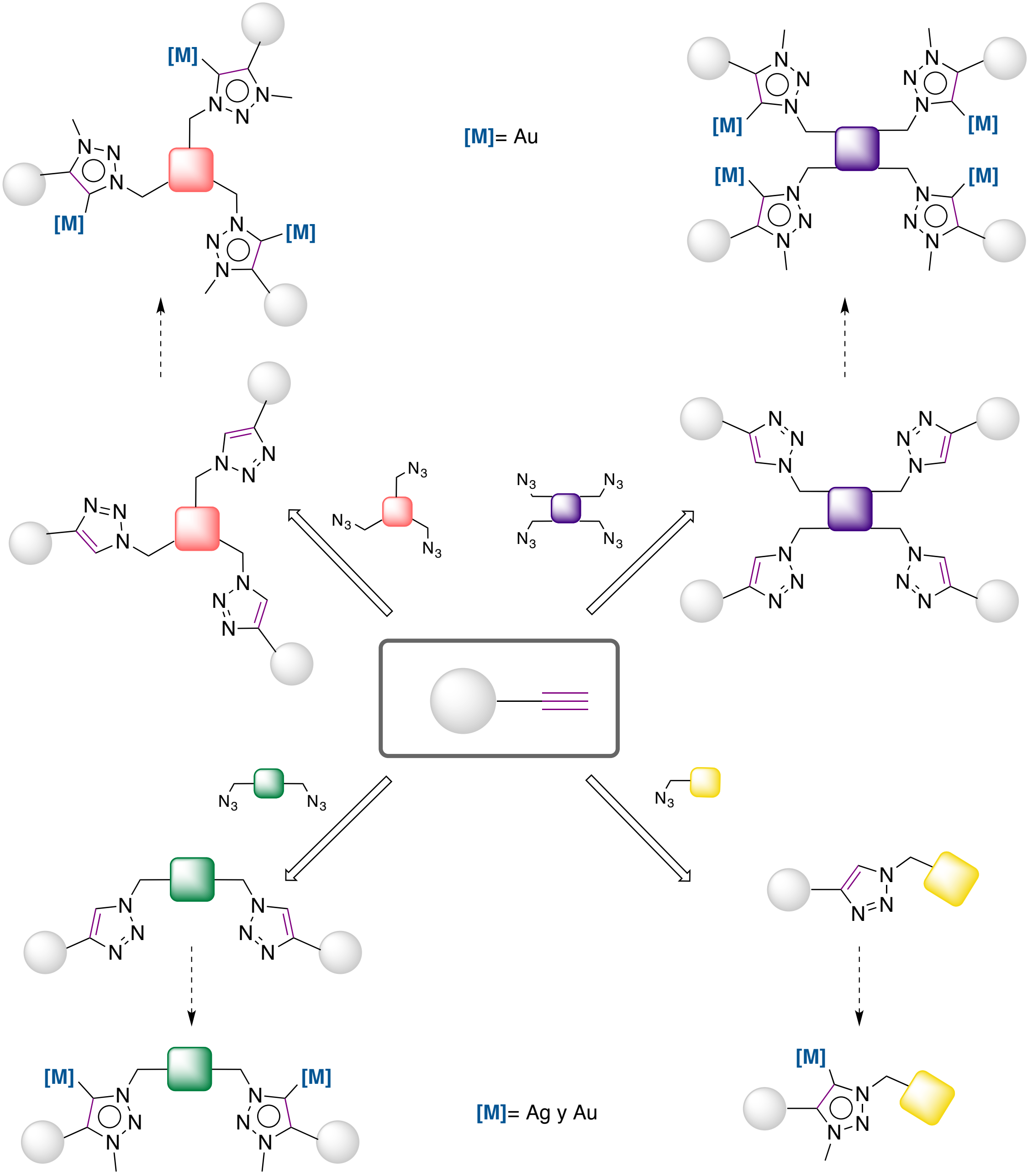
- Estudio de nuevas reactividades de carbenos *N*-heterocíclicos. Se estudiará una nueva reacción de desulfinilación, sin precedentes en la literatura. Se llevarán a cabo distintos experimentos para que, apoyados por cálculos teóricos, se logre elucidar el mecanismo a través del cual transcurre la reacción.

- Estudio de la actividad catalítica de los carbenos *N*-heterocíclicos. Se estudiará la actividad catalítica de estos carbenos con el fin de comprobar si la presencia del sulfóxido puede tener efecto en el transcurso de la transformación que catalice.

Conclusiones y aportaciones fundamentales

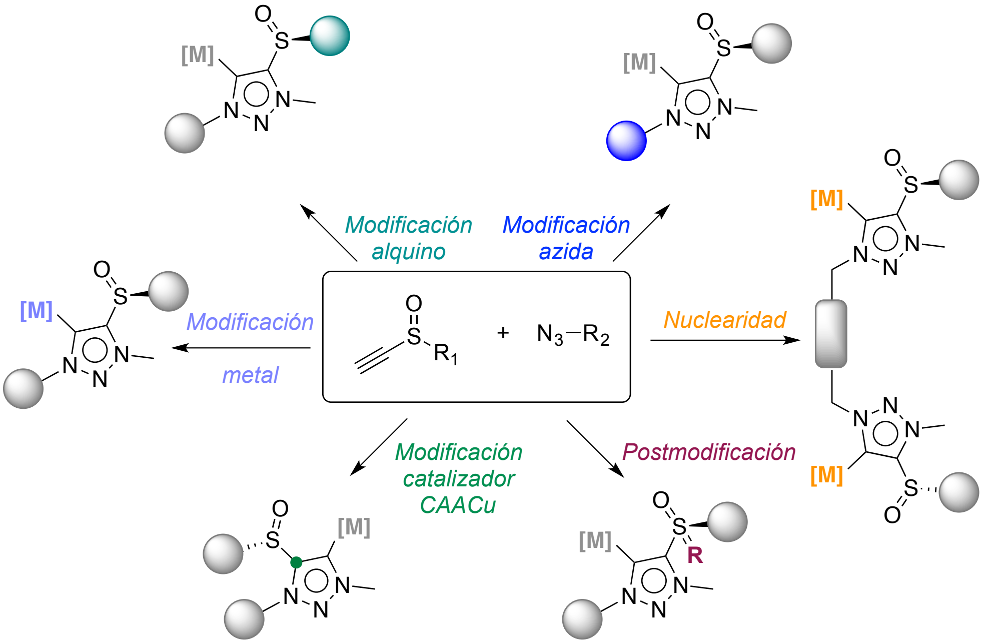
1.- Se ha obtenido una nueva familia de carbenos polimetálicos de Au y Ag de tipo 1,2,3-triazolilideno soportado sobre núcleos de tipo esteroídico (estrona y estradiol). Aprovechando la versatilidad del proceso de CAACu, el empleo de mono-, bis-, tris- y tetra- azidas condujo a compuestos con uno, dos, tres y hasta cuatro núcleos de triazol. La posterior alquilación selectiva en la posición *N*3 del triazol dio lugar a las correspondientes sales de triazolio, precursores de los carbeno metálicos. La estructura de los complejos multimetálicos fue estudiada a través de técnicas de resonancia magnética nuclear, de espectroscopía de alta resolución y de cálculos teóricos. Este es el primer ejemplo de híbridos organometálicos compuestos por carbenos *N*-heterocíclicos (Esquema IX.2.2).

2.- Se ha sintetizado una nueva familia de carbenos metálicos derivados de 1,2,3-triazolilideno conteniendo un resto sulfóxido quiral enantioméricamente puro en *C*4. Se ha comprobado que en todos los pasos de la ruta sintética, desde la obtención de los triazoles hasta la formación del carbeno, la integridad de la configuración del sulfóxido se mantiene inalterada. Esta confirmación se llevó a cabo a través de la introducción de un segundo elemento quiral enantioméricamente puro, la metilbencil azida. La formación de un único diasteromero en estas reacciones confirmó la integridad del resto quiral sulfurado durante el proceso sintético.



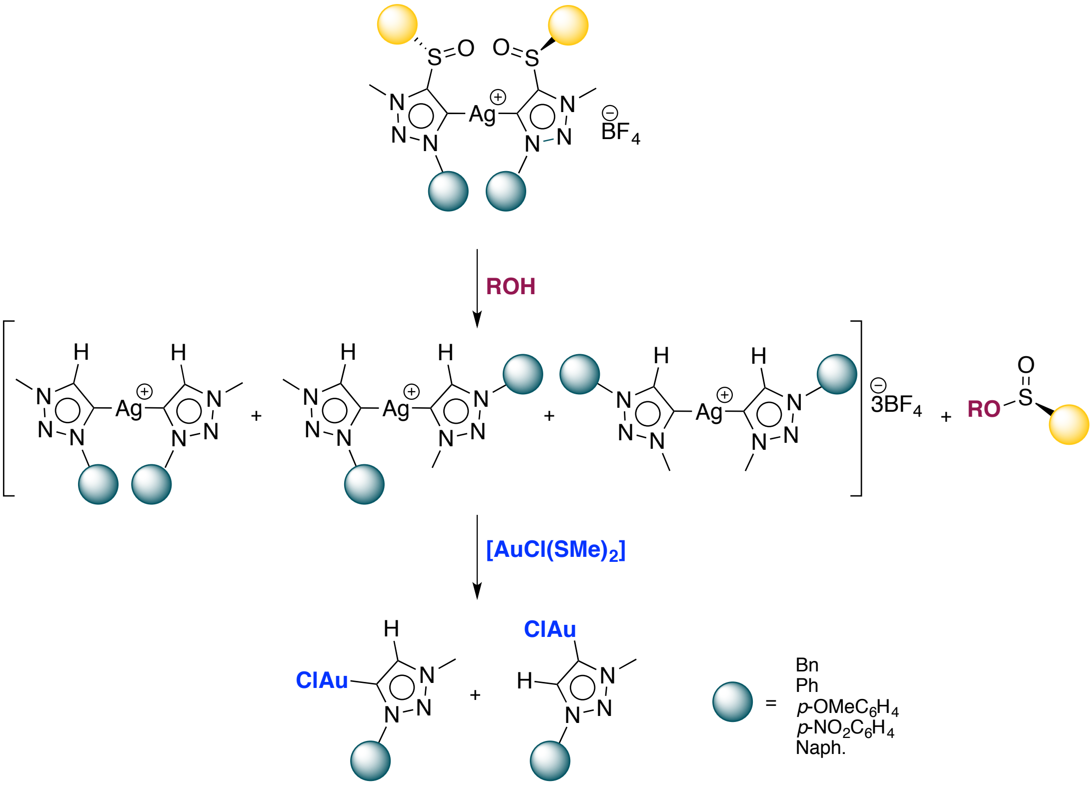
Esquema IX.2.2: Obtención de carbenos mesoiónicos polimetálicos derivados de esteroides

3.- La metodología desarrollada en este trabajo permite la obtención de una variedad estructural dentro de esta nueva familia de carbenos *N*-heterocíclicos modificando la naturaleza de los diferentes agentes que participan en las distintas etapas de la metodología sintética empleada (Esquema IX.2.3).



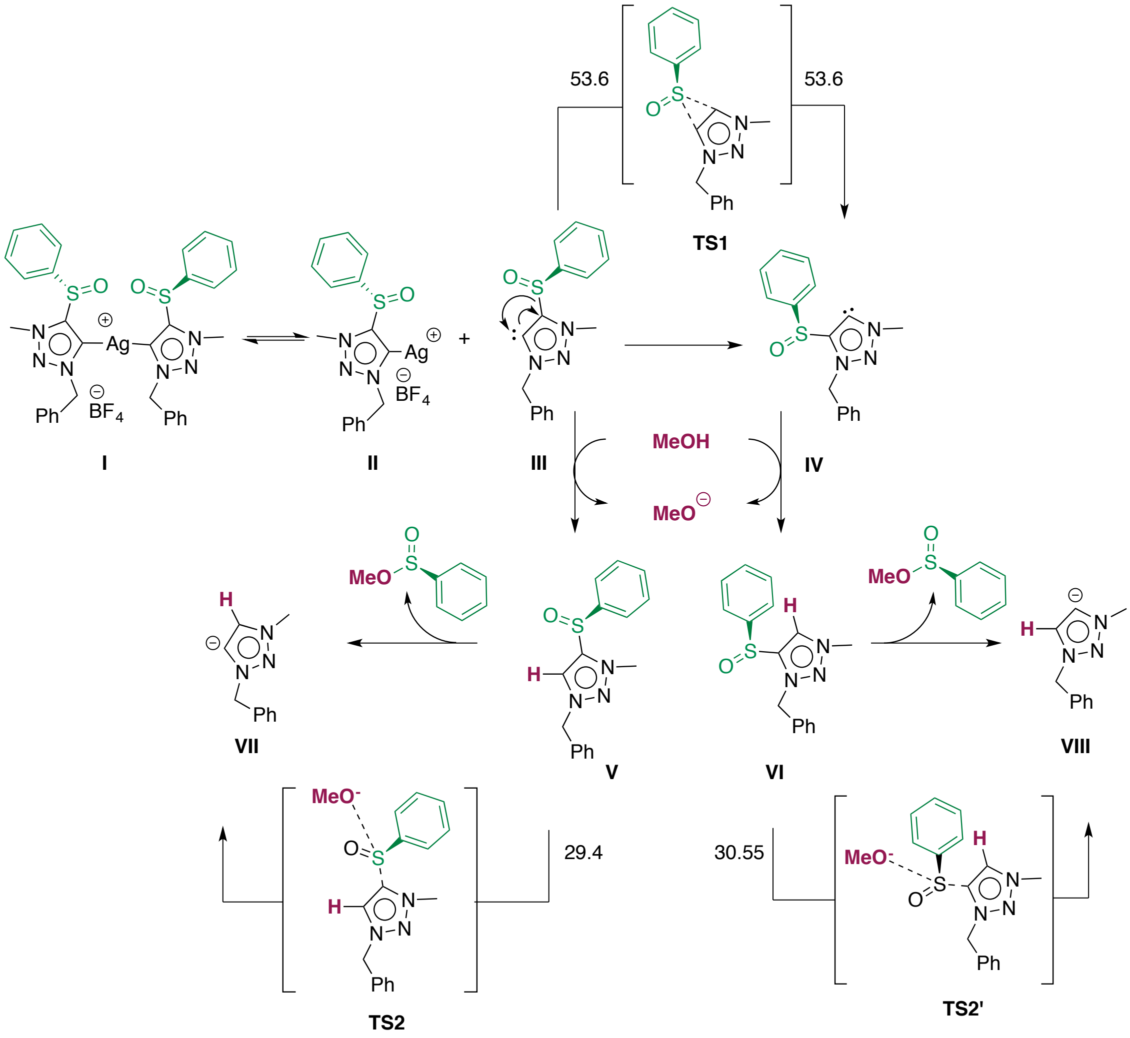
Esquema IX.2.3: Variedad estructural de carbenos mesoiónicos con grupos de azufre

4.- Se ha desarrollado una nueva metodología para la obtención de carbenos metálicos *N*-heterocíclicos sin sustituyentes en *C*4 y *C*5 del anillo del triazol. Este proceso se lleva a cabo a través de una reacción de desulfinilación y posterior transposición de la que no hay precedentes en la literatura. Los carbenos regioisómericos en *C*4 y *C*5 se obtienen tras transmetalación de los intermedios de Ag con una sal de oro (Esquema IX.2.4).



Esquema IX.2.4: Obtención de carbenos mesoiónicos sin sustituyentes sobre los carbonos del anillo de triazol

5.- Se ha propuesto un mecanismo que explica el transcurso de la reacción de desulfinilación el cual se basa en diferentes experimentos, incluyendo reacciones de deuteración así como por cálculos teóricos. Teniendo en cuenta dichos cálculos, el bis(carbeno) de plata **I** se encontraría en equilibrio con el mono(carbeno) **II** el cual experimenta un reordenamiento ultrarrápido al carbeno **IV** a través del estado de transición **TS1**. Estas dos especies se protonarían a través del metanol presente en el medio para dar lugar a las especies **V** y **VI** las cuales, tras la acción del metóxido sobre el grupo sulfóxido generarían el correspondiente sulfinato de metilo y las especies regioisoméricas **VII** y **VIII** a través del estado de transición **TS2** (Esquema IX.2.5).

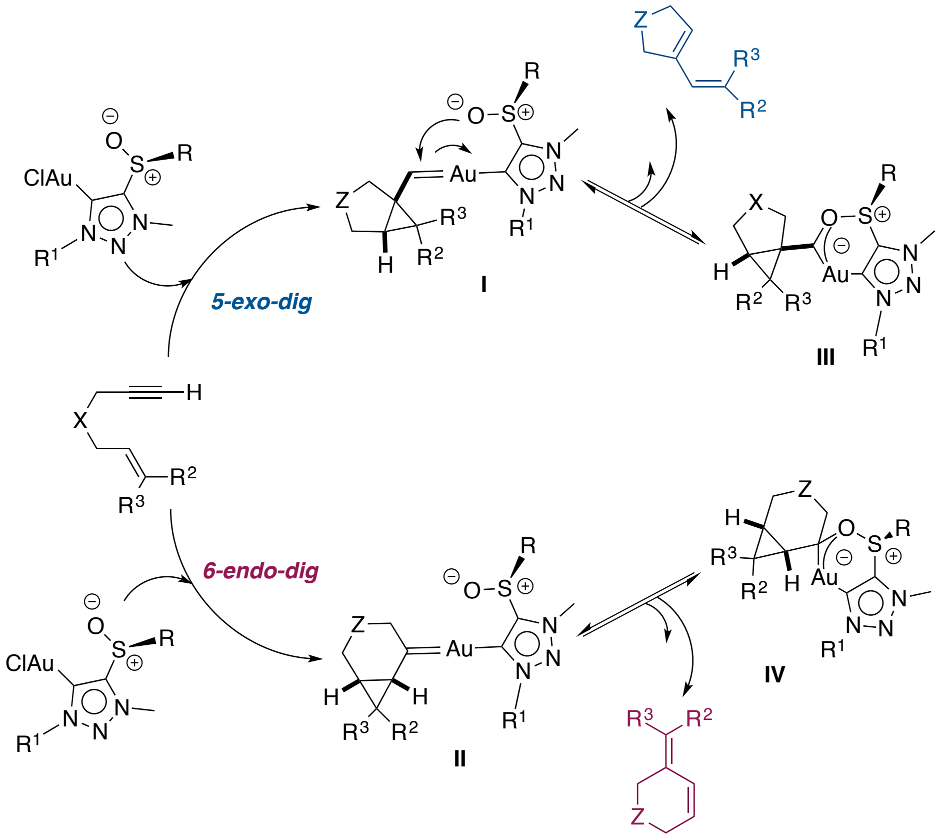


Los valores ΔG vienen dados en kcal/mol

Esquema IX.2.5: Propuesta mecanística para el proceso de reordenamiento y desulfinilación

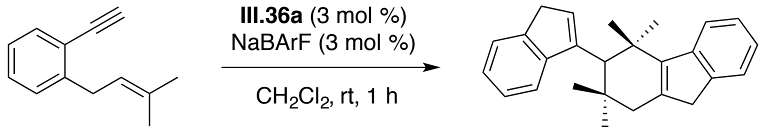
6.- Se ha evaluado la actividad catalítica de los carbenos de oro sintetizados en este trabajo usando la reacción de cicloadición de eninos. El papel del grupo sulfóxido es esencial en términos de reactividad, mientras que la naturaleza del grupo unido a la posición N*1* del heterociclo controla la selectividad del proceso de cicloisomerización. Estos resultados, junto a la inercia de los complejos metálicos frente a eninos sustituidos en el triple enlace, permitió proponer la siguiente hipótesis mecanística (Esquema IX.2.6):

El primer paso de reacción consiste en la formación de los complejos Au-carbeno **I** (ciclación *5-exo*) y **II** (ciclación *6-endo*) a través de la coordinación del catalizador de oro al triple enlace seguida de la ciclación. Los complejos carbénicos de oro son reactivos frente a nucleófilos, por lo que el oxígeno del grupo sulfóxido estaría involucrado en la estabilización de los carbenos **I** y **II** formando los intermedios de tipo Fischer **III** y **IV** los cuales son cruciales para que el proceso catalítico tenga lugar. Estos intermedios estarían en equilibrio con las formas abiertas **I** y **II**, las cuales evolucionarían hacia los productos a través de las distintas etapas de ciclación ya conocidas.



Esquema IX.2.6: Propuesta mecanística para la cicloisomerización de eninos

7.- La reacción de cicloadición sobre el enino **V.50** catalizada por el carbeno de Au **III.36a** dio lugar al compuesto policíclico **V.52** (Esquema IX.2.7).

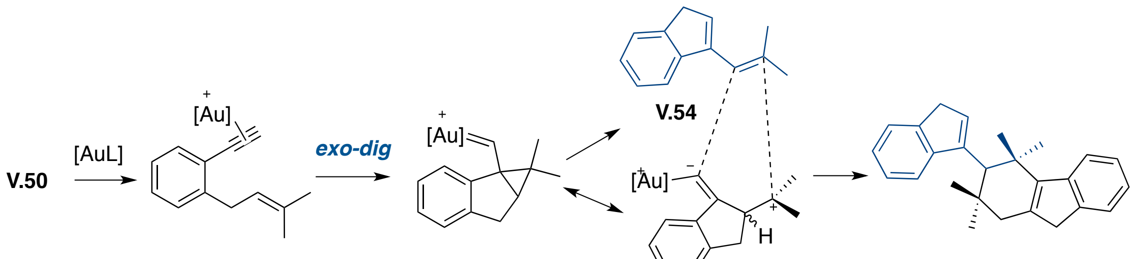


V.50

V.52 (93%)

Esquema IX.2.7: Síntesis del compuesto **V.52**

La formación de este compuesto se explicaría por la reacción del intermedio **V.53** con la olefina derivada del producto de cicloadición **V.54** a través de un proceso [4+2] (Esquema IX.2.8).



V.2

V.53

V.52

Esquema IX.2.8: Propuesta mecanística para la formación de **V.52**

Este resultado abre la puerta a la síntesis de compuestos de elevada complejidad estructural de manera sencilla y altamente eficiente. Tanto la versatilidad del proceso como el mecanismo de formación de estos compuestos se están estudiando en estos momentos.