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Perspective

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1,2,3-Triazolium-Derived Mesoionic Carbene Ligands Bearing Chiral Sulfur-Based Moieties: Synthesis, Catalytic Properties, and Their Role in Chirality Transfer

Miguel A. Sierra*,† and María C. de la Torre*,‡

†Dpto. de Química Orgánica, Facultad de Química, and Centro de Innovación en Química Avanzada (ORFEO-CINQA), Universidad Complutense, 28040 Madrid, Spain

‡Instituto de Química Orgánica General, and Centro de Innovación en Química Avanzada (ORFEO-CINQA), Consejo Superior de Investigaciones Científicas (CSIC), Juan de la Cierva 3, 28006 Madrid, Spain

ABSTRACT: 1,2,3-Triazole-derived mesoionic carbenes (MICs) having a chiral sulfur functional group at the C5 position are easily available through a CuAAC between chiral alkynyl sulfoxides and different azides. The MICs form complexes with several metals (Au, Ag, Ir, Rh, and Ru) that are enantiomerically pure. Moreover, enantiomerically pure MIC sulfinilimines are obtained from the corresponding sulfoxide retaining the chirality. Through this article, the participation of sulfoxide moieties in different catalytic and chirality transfer processes, as well as in discovering mechanistically new processes will be shown. The role of the sulfur chiral moiety in catalytic cycloisomerization and cycloisomerization−dimerization processes using Au−MIC catalysts is dual. The sulfur functional group either stabilizes intermediates in the catalytic cycle, allowing for the reaction to occur or significantly increases the selectivity of the cyclization processes. 1,2,3-Triazole MICs having chiral sulfoxides at C5 are extremely efficient in preparing chiral at the metal complexes by C−H insertion processes. The chiral at the metal half-sandwich complexes, having the enantiopure sulfur chiral group unaltered, experiences different reactions with complete retention of the configuration. Finally, mechanistically new processes, like the desulfinilation of 1,2,3-triazolium salts in Ag−MIC complexes have been uncovered. These still-nascent classes of compounds will offer opportunities for the discovery of novel catalytic applications and to study new mechanistically sound processes.

1. INTRODUCTION

The preparation of stable carbenes I in 1988 by Bertrand[1] and the subsequent report by Arduengo describing the synthesis of the first stable *N*-heterocyclic carbenes (NHCs) II (Figure 1)[2]

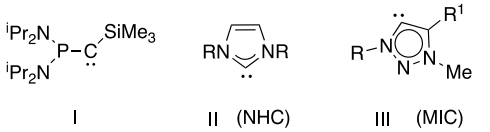
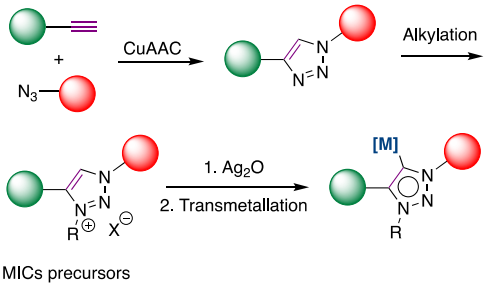


Figure 1. Three examples of stable carbenes.

in 1991 opened up an entirely new research field. Stable carbenes[3] have found extensive application in fields as diverse as organocatalysis,[4] medicinal,[5] or materials chemistry.[6] However, it is in their use as ligands for transition metals that these species are important.[7] In fact, their availability and the possibilities of modification of the structure including steric electronic properties of the carbene ligands allow the modulation of the electronic properties of the metal center. This fact is essential in the efficient use of transition metal complexes having carbene ligands in catalysis.

In this regard, Albretch[8] introduced 1,2,3-triazolilylidene carbenes III as a new type of mesoionic carbene (MIC) in 2008. Since precursor heterocycles for these MICs are prepared through the efficient and regioselective Cu(I)-catalyzed Huisgen cycloaddition (CuAAC) between a terminal alkyne and an azide,[9] these ligands can be prepared almost "a la carte" to fulfill specific electronic and steric properties (Scheme 1). The CuAAC allows for the placement in the 1,2,3-triazole

Scheme 1. Synthesis of Metal-Stabilized 1,2,3-Triazolilyliden Carbenes



ring of a large number of functional groups that can be introduced in the core of the heterocycle through the terminal alkyne, the azide, or both. The MIC ligand is coordinated to different transition metals using several procedures. The most frequent method uses the coordination to silver to form the corresponding Ag−MIC followed by transmetalation. Therefore, the last 10 years have witnessed an explosive outgrowth in

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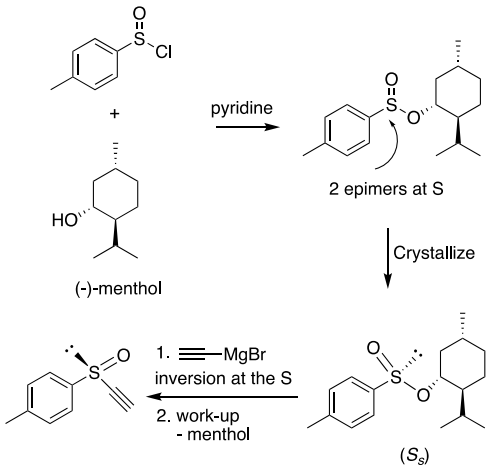
the preparation of new structural types of MICs and their use as ligands in transition-metal-mediated catalysis.[10]

In spite of the fact that sulfoxides are the alternative choice when considering the scarce chiral functional groups based on elements different from the chiral-carbon groups,[11] its incorporation in a 1,2,3-triazolylidene MIC following a CuAAC reaction was unknown at the beginning of our work in this field. The precursors of these heterocycles, namely the enantiopure ethynyl sulfoxides are easy to make through the Andersen method, which involves the reaction between acetylenic Grignard reagents and enantiopure menthyl sulfinate (Scheme 2).[12] Nevertheless, placing an enantiomerically pure

Scheme 2. Andersen's Synthesis of Enantiopure Ethynyl Sulfoxides



sulfoxide moiety in a 1,2,3-triazolylidene carbene requires several problems to be addressed. The main concern was the configurational stability of the sulfoxide center in the conditions required to synthetize the heterocycle. Other problems may arise from the compatibility of the sulfoxide moiety with the strong alkylating agents required to obtain the 1,2,3-triazolylidene precursor,[13] and finally the coordinating nature of the sulfoxide moiety may compete with the emerging carbene during the coordination of such ligands to the metal.

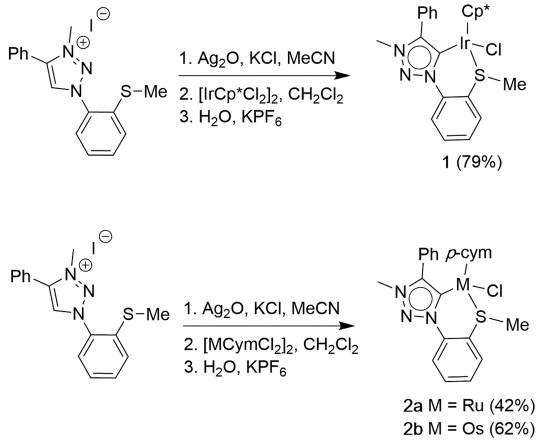
This perspective will present the solution of these problems, the extension of this approach to triazole containing sulfoximines, the scarce examples of triazolylidene carbenes containing sulfur-based chiral (enantiopure or racemic) functional groups, and their emerging applications in catalysis.

2. SYNTHESIS

Hybrid ligands composed of classic NHCs and sulphur-based functional groups have been repeatedly investigated.[14] Placing hemilabile functional groups based on sulphur into a 1,2,3-triazolylylidene heterocyclic system is straight due to the versatility of the CuAAC process, where the sulphur functional group may be introduced either through the azide, the alkyne, or both. Following this approach, several 1,2,3-triazolylylidenes having aliphatic thioether moieties at the C4 of the triazole core were prepared.[15] Metalation (Pd, Rh, Au) of these compounds showed no coordination of the pendant thioether to the metal center. The synthesis of thioether functionalized ligands 1-[2-(methylthio)phenyl]-4-phenyl-1*H*-1,2,3-triazole and 3-methyl-1-[2-(methylthio)phenyl]-4-phenyl-1*H*-1,2,3-triazol-5-ylidene) has been also reported.[16]

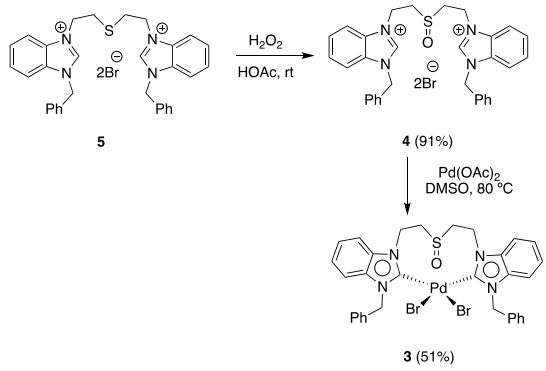
Sarkar reported in 2014 the first heteroleptic ligand formed by an aromatic thioether and one 1,2,3-triazolilylidene MIC.[17] Thus, Ir complex **1**, and Ru and Os-complexes **2** were prepared from the corresponding 1,2,3-triazolium salts using the sequence Ag-complexation−transmetalation on the C5-position of the heterocycle, with the concomitant coordination of the arylthioether group. This route provided the desired complexes in high yields (Scheme 3).

Scheme 3. Synthesis of Complexes Having 1,2,3-Triazolilydenes with Aromatic Thioether MICs as Ligands



Contrary to sulphide-containing NHCs,[14] the NHCs having sulfoxide functional groups have been much less studied. The first example of a metal−NHC complex having a sulfoxide was the CSC-pincer compound **3** reported by Huyhn.[18] This NHC-pincer ligand has the sulfoxide group as a bridge of two dibenzimidazolium salts. The synthetic approach to ligand **4** involved the oxidation of the sulphide group of compound **5** using H_2O_2. Subsequent reaction with $Pd(OAc)_2$ in dimethyl sulfoxide at 80 °C afforded the pincer complex **3**. It should be noted that the sulphoxide group of **3** did not coordinate the Pd-center (X-ray) (Scheme 4).

Scheme 4. Synthesis of Pseudo Pincer 3



Cardenas reported[19] the synthesis of Pd-imidazolilylidenes having a sulfoxide moiety in a chain attached to N3. Thus, alkylation of imidazoles **6** with racemic bromosulphoxide **7** under microwave irradiation conditions (MW) formed imidazolium salts **8** that were coordinated to Pd using Ag_2O in MeCN to form complexes **9** (Scheme 5). The structure of complexes $[\mathbf{9a}NCMe]^+$ and $(\mathbf{9d})_2$ were unambiguously

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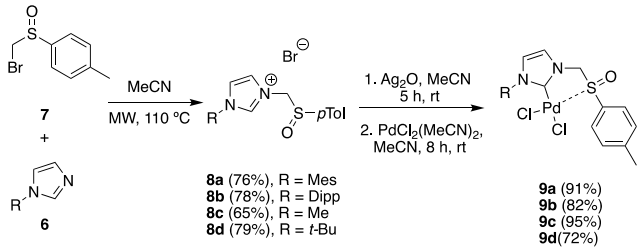
Scheme 5. Synthesis of Palladium Sulfinyl Imidazolilydenes

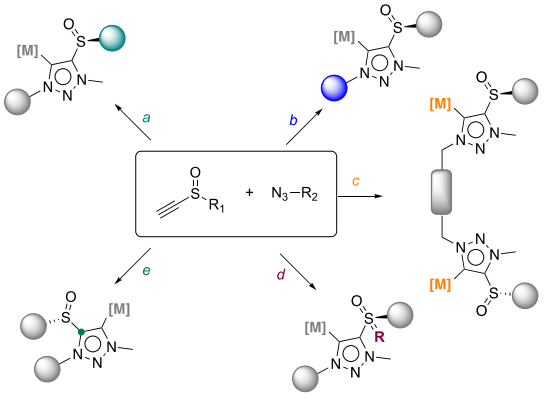


Dipp = 2,6-diisopropylphenyl

determined by X-ray diffraction. The Pd complex [**9a**NCMe]$^+$ has a nondistorted square-planar geometry with a distance between Pd and S atoms of 3.34(2) Å, which is lower than the sum of van der Waals radii, suggesting a weak interaction between both centers, while the sulfoxide moiety of the dimeric complex (**9d**)$_2$ shows no interaction between the sulfoxide group and the metal center.

It should be noted that in the examples above, the sulfoxide moiety is racemic. At the beginning of our work, procedures to prepare enantiomerically pure 1,2,3-triazolilylidene ligands having chiral sulfoxide moieties were unknown. We devised a methodology suitable to access different enantiomerically pure 1,2,3-triazolilyliden-ligands having in mind the possibility of introducing diversity[20] in the prepared molecules. Within this scheme, considering that the reagents have to be easily available and that the reaction to be used to build the heterocyclic ring will be the CuAAC between one alkynylsulfoxide and one azide, the following structural variants in the reagents can be taken into account (Scheme 6):

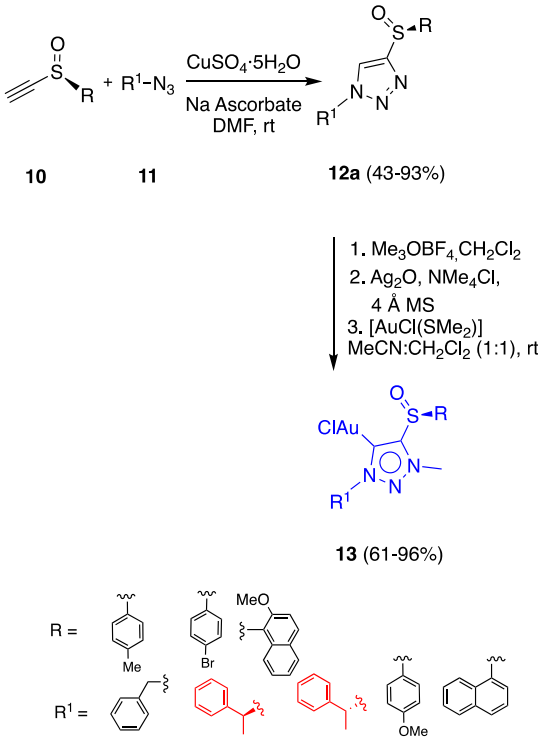
Scheme 6. Structural Diversity in the Synthesis of Enantiopure Sulfinyl 1,2,3-Triazolilydenes



- The nature of the ethynyl sulfoxide (a).
- The azide (b).
- The nuclearity (c).
- Post-functionalization of the sulfoxide (ca transformation in sulfoximines) (d).
- Change on the catalytic system to effect the AAC (translated into the regiochemistry of the AAC) (e).

Routes (a) and (b) shown in Scheme 6 were tested by synthetizing enantiopure 1,2,3-triazole-containing sulfoxide moieties by the reaction of alkynylsulfoxides **10** and azides **11**. Examples shown in Scheme 7 demonstrate that the synthesis of triazoles **12** is compatible with alkyl and aryl azides as well as with differently substituted sulfoxides. Especially

Scheme 7. Synthesis of Gold Sulfinyl 1,2,3-Triazolilydenes



relevant in these experiments was the preparation of triazoles containing an additional chiral center. One single enantiomer was obtained in both cases confirming that the stereochemistry of both centers was maintained during the cycloaddition process.[21] Methylation of triazoles **12** occurred uneventfully in the presence of Me_3OBF_4, and the gold complexes **13** were prepared through the corresponding silver carbene complexes as intermediates (Ag_2O, NMe_4Cl) and subsequent transmetalation with [$AuCl(Me_2S)$]. Yields were high in most cases. Complexes **13** were characterized by X-ray diffraction. Interestingly, complex **13** (R = Me, R^1 = (−)-α-phenylethyl) shows, in the solid state, a gold(I)−gold(I) distance of 3.223 Å that reflects unsupported strong aurophilic interactions. The two C−Au−Cl units involved in the interaction show a crossed arrangement with a C−Au−Au−C torsion angle of 66.5°.

The subsequent transformation of triazoles **12** into sulfoximines **15** (route d in Scheme 5) was affected by the chemoselective oxidation with *m*-CPBA to form the corresponding sulfonyl triazole **14** and subsequent imination[22] with PhI=NTs/Cu(OTf)$_2$ to form the racemic sulfoximine **15** in an excellent yield (a in Scheme 8).[23] Enantiopure sulfoximines **15** were prepared avoiding the oxidation step by the reaction of triazole sulfoxides **12** and PhI=NTs/Cu(OTf)$_2$. Subsequent methylation yielded the enantiopure salts **16** (b in Scheme 8).[24]

An alternate route to 1,2,3-sulfoximidoyl-substituted triazoles was reported by Bolm using a Huisgen 1,3-dipolar cycloaddition between organoazides and sulfoximidoyl alkynes **17** (Scheme 9).[25] In these cases, the sulfoximidoyl alkynes were prepared by copper-catalyzed imination of the corresponding sulfoxides with PhI=NTs. The cycloaddition reaction was regioselective favoring the depicted product, although variable amounts of the regioisomeric triazoles were formed. Compounds **18** were not used in metal complexation. A related procedure to prepare fully substituted 1,2,3-triazolyl-

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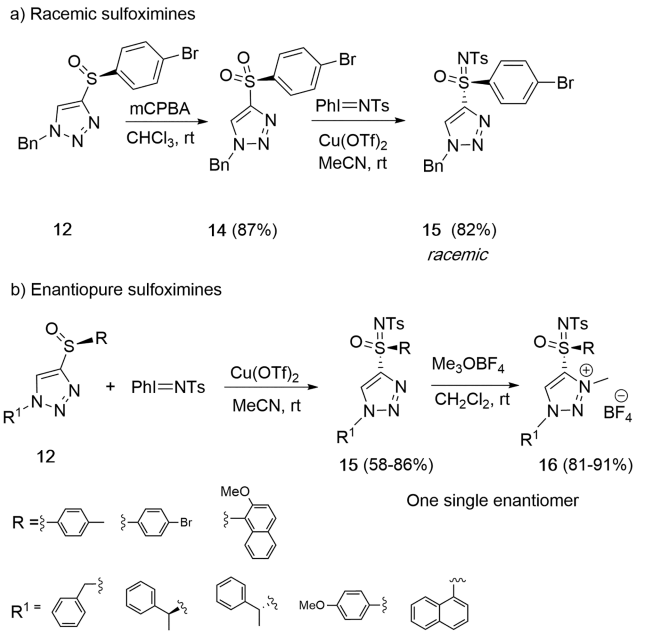
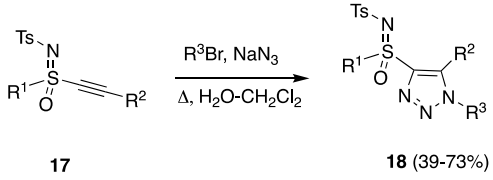
Scheme 8. Synthesis of 1,2,3-Sulfonyl- and 1,2,3-Sulfoximidoyl-Substituted Triazoles



Scheme 9. Bolm's Synthesis of 1,2,3-Sulfoximidoyl-Substituted Triazoles



R^1 = *p*-Tol, Me, Ph
R^2 = Bu, CH_2OMe, Ph
R^3 = 4-NO_2Bn, 4-MeOBn, $Ph(CH_2)_2$, 2-NaphthCH_2, Bn

5-sulfoximines by Cu(I)-catalyzed three component coupling of sulfoximines, alkynes, and azides has been reported recently.[26]

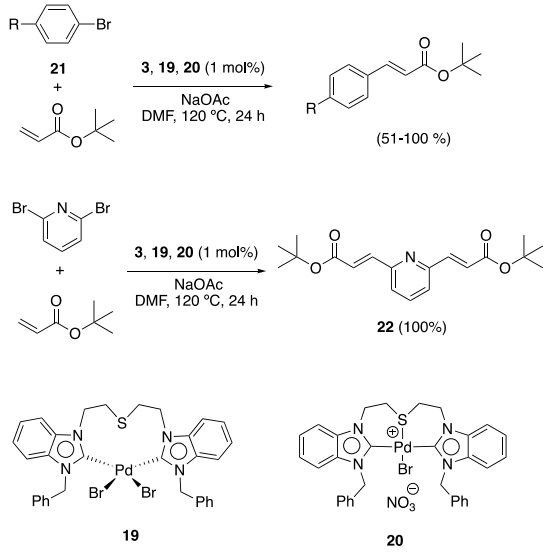
3. CATALYSIS

The metal complexes derived from 1,2,3-MICs containing sulfoxide or sufoximidoyl moieties have been used in different catalytic processes. Thus complexes **3** (Scheme 4), **19**, and **20** were good catalysts for the Heck reaction (Scheme 10).[18] Essentially, the reactions of bromoaryl derivatives **21** and *t*-Bu-acrylate gave the expected products with the above catalysts. Double adducts **22** were obtained when 2,6-dibromopiridine was used. What is interesting is that both the coordinated cationic sulfide **20** and the uncoordinated sulfide **19** behave identically to the uncoordinated sulfoxide catalyst **3**, which indicates that the sulfur-derived moiety is not participating in the catalytic process (Scheme 10).

Complexes **9a−d** were used as catalysts in the acetoxylation reaction of toluene-promoted (diacetoxyiodo)benzene as the oxidant in AcOH/H_2O mixtures. The yields in acetoxylated toluene derivatives ranged from acceptable to good (Scheme 11).[19]

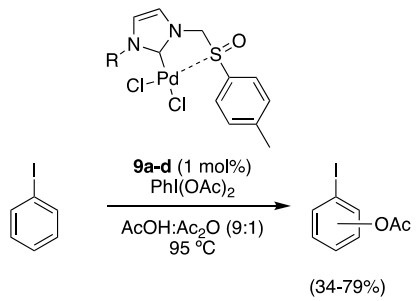
Enantiomerically pure Au−MIC **13** were tested in the cycloisomerization of 1,6-enynes **23**. While these complexes

Scheme 10. Sulfur-Containing Palladium Benzimidazolilylidenes as Catalysts in the Heck Reaction



were very efficient in the formation of cyclic products **24** and **25**, it soon became evident that sulfoxide moieties were required for the cycloisomerization to occur. Thus, Au−MICs **27** lacking the sulfur functional group did not promote the cycloisomerization of enyne **23a**, while the analogous product **13a** having the sulfoxide moiety instead of the benzyl group formed exclusively the cyclized product **24** in essentially quantitative yields. Moreover, while the sulfoxide moiety is essential for the activity of the catalyst, the bulkiness of the substituent at nitrogen determines the 5-exo versus 6-endo ratio of cyclized products (Scheme 12). The bulkier the substituent at nitrogen, the higher is the selectivity favoring the 5-exo cyclization product. For example, catalyst **13b** formed a 1:1.4 mixture of compounds **24** and **25** while the analogous reaction with catalyst **13a** formed exclusively compound **24** in essentially quantitative yields.

Scheme 11. Sulfinyl Palladium-Imidazolilylidenes as Catalysts



The proposed catalytic cycle[21] to explain these observations involve an initial formation of gold carbene complexes **A** and **B** by reaction of the terminal alkyne and the catalyst (internal alkynes do not react under these conditions). This is the standard mechanism for Au-promoted carbocyclizations,[27] and at this stage the sulfoxide moiety should be a spectator. The 5-exo versus 6-endo cyclization selectivity should be related to the bulkiness of the carbon linked to N1. Since intermediate **C** is much more crowded than **D**, the bulkier *α*-phenylethyl moiety of complex **13a** should favor the formation of **A** leading

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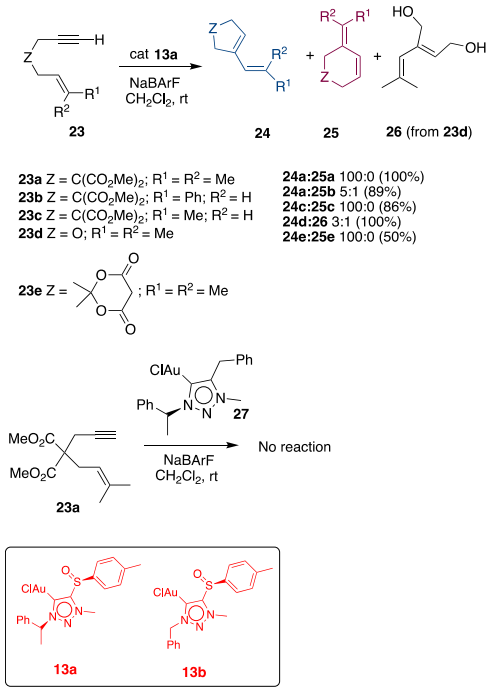
exclusively to the 5-*exo* product **24** (Scheme 12). On the other hand, the benzyl moiety of complex **13b** is less sterically

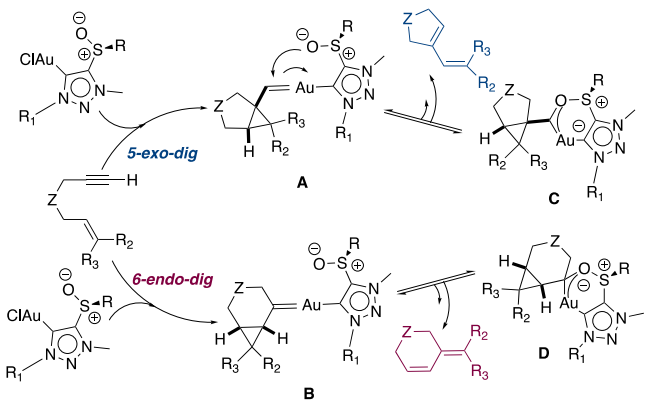
Scheme 12. Enantiopure Gold–MICs as Catalysts in 1,6-Enyne Cycloisomerizations



demanding, leading to mixtures of two regioisomers. This mechanistic hypothesis is congruent with the results obtained and gives the apparent ancillary moiety (the sulfoxide group) a key role unprecedented in the literature. In fact, the lack of catalytic activity observed for **27** (Scheme 12) indicated a clear involvement of the sulfoxide oxygen to stabilize Au–carbene intermediates, very probably by the interaction of either the sulfur lone pair or oxygen with carbene carbon or the gold center.[28] This interaction stabilizes intermediates **A** and **B** and allows the reaction to proceed (Scheme 13).

These results show that the sulfoxide group of the enantiopure MICs **13** has a role in the catalytic cycles in contrast with the results reported by other authors. In fact, no differences in the catalytic activity were reported for

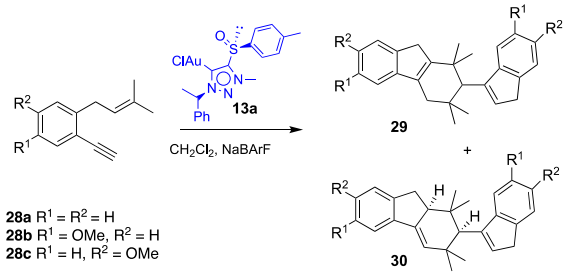
Scheme 13. Mechanistic Hypothesis for the Au-Catalyzed Carbocyclization of Enynes Promoted by Catalysts 13



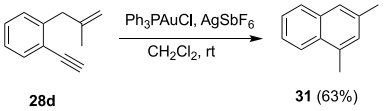
isostructural catalysts having a sulfide, a coordinated sulfide, or non-coordinated sulfoxide functional groups.[18]

The catalytic activity of Au–MICs **13** was also tested in the cycloisomerization of enynes tethered to an aromatic ring.[29] The reaction of enynes **28** with catalyst **13a** in the presence of NaBArF yielded mixtures of compounds **29** and **30** differing in the position of one double bond. These compounds are formed through a cyclization dimerization cascade in excellent yields. The ratio **29**:**30** is temperature-dependent. Compounds **29** are the thermodynamic products and are formed at rt, while compounds **30** are the kinetic products and are formed at low temperatures. Compound **30** converts to the thermodynamic **29** on heating at rt in the presence of catalyst **13a**. Again, the use of a simple Au-catalyst like $Ph_3PAuCl/AgSbF_6$ formed a different product, namely naphthalene **31** (Scheme 14).

Scheme 14. Catalyzed Cycloisomerization of Aromatic Enynes



Entry	Compound	Temperature	**29:30** (yield%) [ratio]
1	**28a**	rt	90 [93:7]
2	**28a**	–10 °C	91 [0:100]
3	**28b**	rt	69 [100:0]
4	**28b**	–10 °C	87 [0:100]
5	**28c**	–10 °C	[27:73]
6	**29c+30c**	rt	98% [100:0]



Clearly, the role of the sulfoxide group in determining the nature of the reaction products is decisive. In all cases the obtained products were racemic. Therefore, albeit the sulfoxide group determines the effectiveness of the reaction, it is not able to exercise any enantio-discrimination. It should be noted that the use of stoichiometric amounts of NaBArF in the cycloisomerization–dimerization cascade of enyne **28a** formed quantitatively product **29**. The mechanism of these reactions should be markedly different from the Au-promoted reactions.

The mechanism to explain these findings is depicted in Scheme 15. The initial reaction of the diene system of **32** with Au(I)-catalysis should form the cyclized intermediate **33** through transition state **34**. Deauration of **33** would yield **30** that may form the allylic isomerization product **29** depending on the reaction conditions. It should be noted (see below) that the participation of the sulfoxide moiety in the stabilization of

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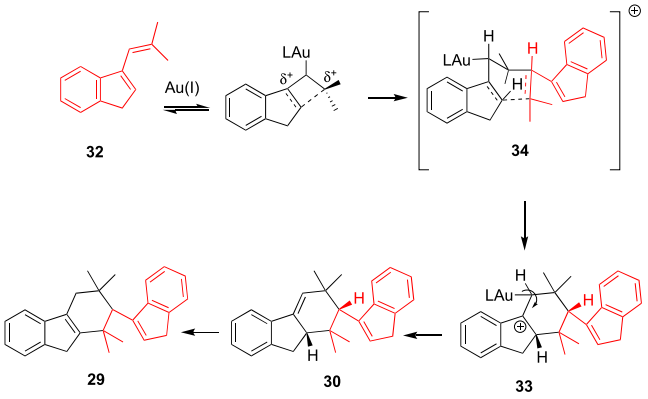
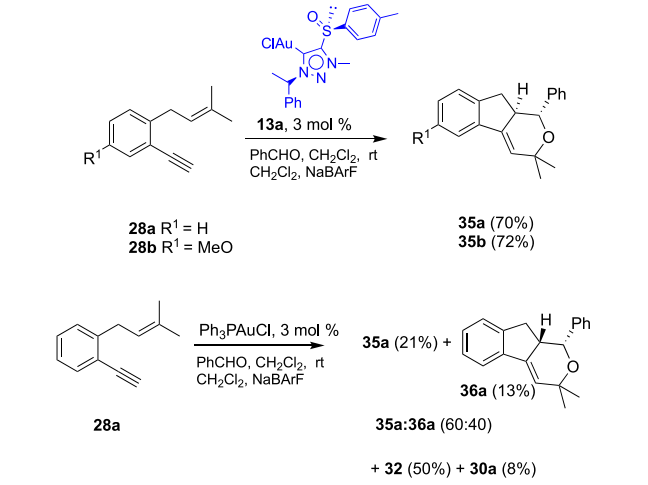
Scheme 15. Mechanistic Hypothesis for the Catalytic Cyclization of Diene 32



intermediates **34** is decisive to determine the nature and the yield of the final products (Scheme 15).

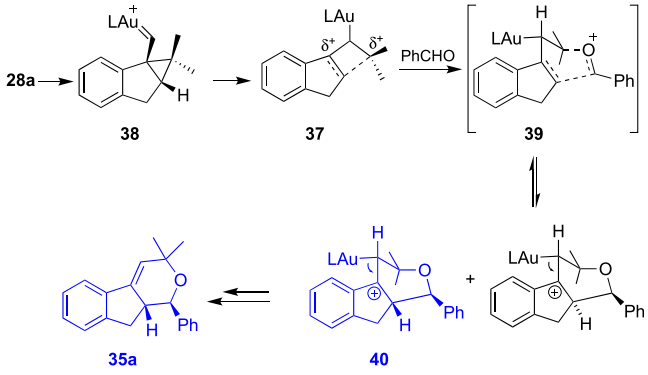
The effect of the sulfoxide group on the MICs in determining the efficiency and selectivity of the cyclization processes is also seen in the reaction of enynes **28a,b**, and benzaldehyde. In fact, catalysts **13a** in the presence of NaBArF formed exclusively compounds **35** as single isomers in excellent yields, while Ph_3PAuCl yielded mixtures of diasteromers **35** and **36** in variable low yields (Scheme 16).

Scheme 16. Influence of the Sulfoxide Group of the MICs in the Selectivity of the Cycloisomerization of Aromatic Tethered Dienes



These differences in selectivity and reactivity were explained by the formation of cationic species **37** through intermediate **38**. This intermediate is trapped by the aldehyde to form Au-species **39** that yielded the final products **35a** and **36a** upon cationic cyclization and deauration. It is clear that the role of the sulfinyl moiety in the stabilization of intermediate **37** is to produce the syn-isomer **35a**. In the absence of this stabilizing factor, both the yields and stereochemistry of the reaction fall dramatically (Scheme 17). This hypothesis requires that the cyclization of **28a** and benzaldehyde through chair-like transition state **39** has to be reversible.[30] Thus, stabilization of the reactive intermediates by the sulfoxide group accounts for the catalytic activity of MIC−Au catalysts **13** against dienes **28** and **32**.

Scheme 17. Mechanistic Hypothesis for the Cyclization of Enyne 28a and Benzaldehyde

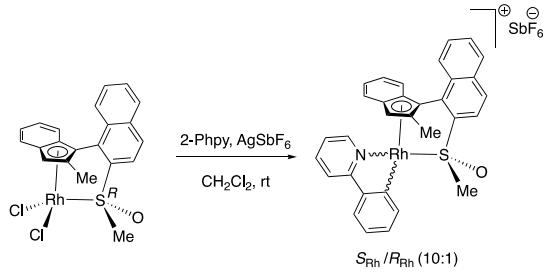


4. CHIRALITY TRANSFER IN ORGANOMETALLIC COMPLEXES

The possibility of affecting the transfer of the chirality residing in the sulfoxide chiral moiety of the MIC ligand to a metal center is especially attractive. Methods to prepare chiral at metal half-sandwich complexes have been extensively developed,[31] including the sequence coordination of the metal to a chiral triazolinylidene and imidazolinylidene carbenes and subsequent diastereoselective C−H insertion,[32] as well as the use of C2-chiral NHCs[33] and sugar-derived NHCs[34] in analogous processes. By contrast, the use of chiral sulfoxide ligands or reagents to achieve the synthesis of chiral at the metal complexes has been scarcely studied.

Optically active octahedral Ru-complexes were obtained by reaction of *cis*- or *trans*-$Ru(bpy)_2Cl$, with either (*R*)-(+)- or (*S*)-(−)-methyl *p*-tolyl sulfoxide.[35] An analogous procedure was used to prepare Ru−bis(diimine) sulfoxide complexes,[36] and Ru−trispyridine complexes.[37] The preparation of achiral half-sandwich complexes has been reported for Rh(III)-complexes having an achiral sulfoxide bound to the metal within a naphthylindenyl moiety, which confers planar chirality to the complex.[38] Subsequently, these complexes were resolved and used to prepare the corresponding chiral at the metal complexes by replacing the chloride ligands by a phenylpyridine ligand (Scheme 18).[39]

Scheme 18. Sulfinyl Chiral at the Metal Half-Sandwich Rh(III) complex



MIC ligands containing chiral sulfoxide moieties were used to develop a general method to prepare chiral at the metal half-sandwich complexes (M = Ir, Rh).[24] Triazolium salts **41** were reacted with $[MCl_2Cp^*]_2$ (M = Ir, Rh) to form the corresponding dichloro derivatives **42** using Ag_2O in the presence of NH_4Cl and 4 Å molecular sieves. Treatment of complexes **42** with NaOAc formed the corresponding

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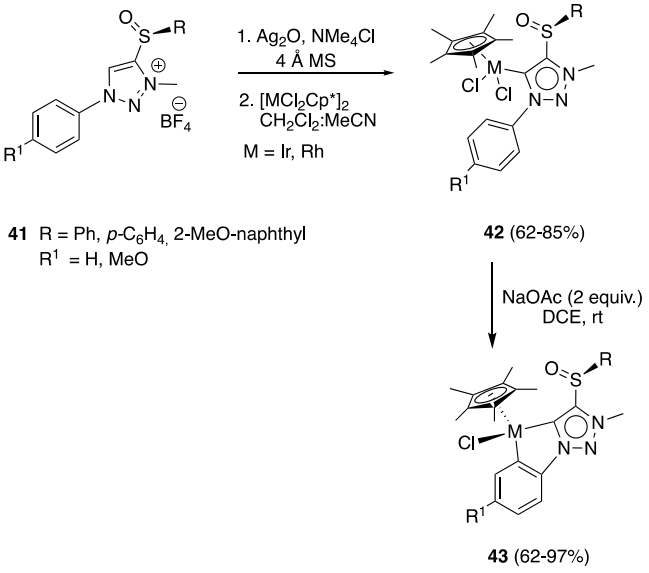
cyclometalated chiral at metal complexes **43** in good yields and as single enantiomers (Scheme 19). It should be noted that the

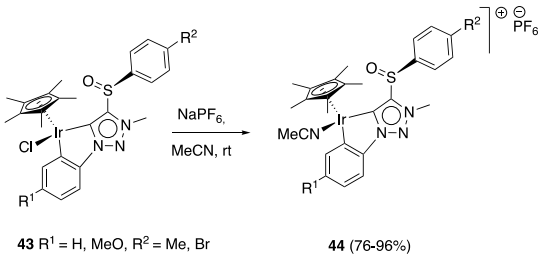
Scheme 19. Synthesis of Enantiopure Chiral at the Metal Half-Sandwich Complexes



sense of the asymmetric induction is independent on the bulkiness of the sulfoxide substituent and on the nature of the metal. Moreover, the use of sulfoximine salts **16** as the elements of asymmetry in the starting MIC precursors also produces excellent levels of asymmetric induction in the formation of complexes analogous to **43** while maintaining good chemical yields.

Enantiopure complexes **43** (M = Ir) can be transformed into cationic complexes **44** by reaction with $NaPF_6$ maintaining the configurational integrity of the metal center (Scheme 20).

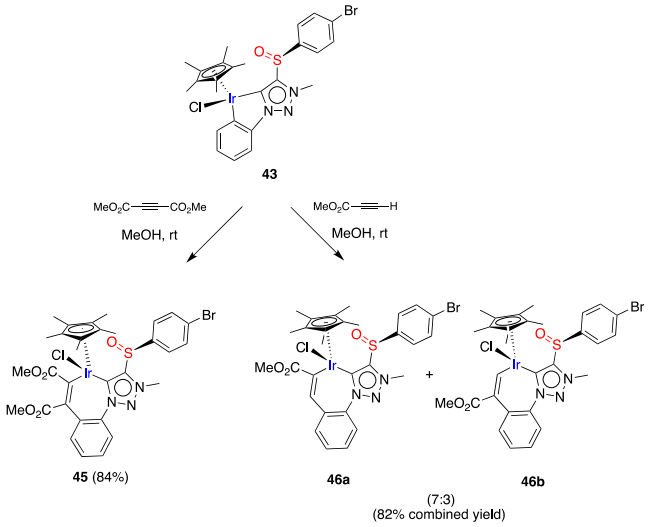
Scheme 20. Cationic Enantiopure Chiral at the Metal Half-Sandwich Complexes



Additionally, the insertion of symmetrical alkynes into the complexes **43** formed the corresponding alkyne-insertion products **45** in excellent yields while maintaining the integrity of the configuration of the metal center. As expected, the insertion of unsymmetrical alkynes (methyl propiolate) produced the mixture of regioisomeric inserted alkynes **46a** and **46b**, with both regioisomers being enantiomerically pure compounds. The configuration at the metal also remains unaltered in this case (Scheme 21).

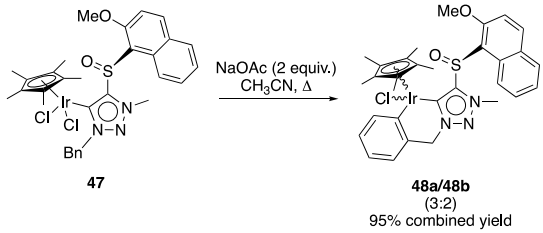
The formation of six-membered metallacycles by C−H activation occurred with a considerable loss of stereoselectivity. Thus, complexes **47** proportionate the corresponding six-membered metallacycles **48** in an excellent chemical yield but

Scheme 21. Insertion of Alkynes Into Complexes 43



with poor estereoselectivity (3:2) (Scheme 22). This is a consequence of the intermediacy of a seven-membered

Scheme 22. Synthesis of Six-Membered Metallacycles



transition state,[40] which places the sulfoxide away from the reactive center. The putative influence of the sulfoxide in the stabilization of reaction intermediates looks clear.

The stereochemistry of these reactions was determined by a combined circular dichroism (CD)-X-ray study. Circular dichroism has been scarcely used to establish the absolute configuration at the metal center of half-sandwich metal carbene complexes.[34,41] For example, the CD spectra of complexes **43** show one main negative absorption centered around 250 nm. X-ray analysis of complex **43** (R^1 = H, R^2 = Br) established an *S* absolute configuration at the Ir(III) chiral center. Therefore, the negative Cotton effect around 250 nm was correlated to the *S* absolute configuration around the metal center. These results were translated to cationic complexes **44** which showed a negative Cotton effect also around 250 nm. This pointed to a complete retention of the configuration at the metal center upon the formation of the cationic complex by displacement of a chlorine ligand by MeCN. This is due to the participation of the sulfoxide moiety in the S_N1-like mechanism leading to the cationic complexes (Figure 2).[42]

The methodology CD-X-ray diffraction to determine the configurational fate of the metal center during alkyne insertion was also effective. Thus, metallacycle **45** has two weak negative absorptions centered at 232.8 and 204.4 nm, and X-ray diffraction analysis confirmed that the metal center retains its configuration. Again, the retention of the configuration at the metal center can be traced to the participation of the sulfoxide

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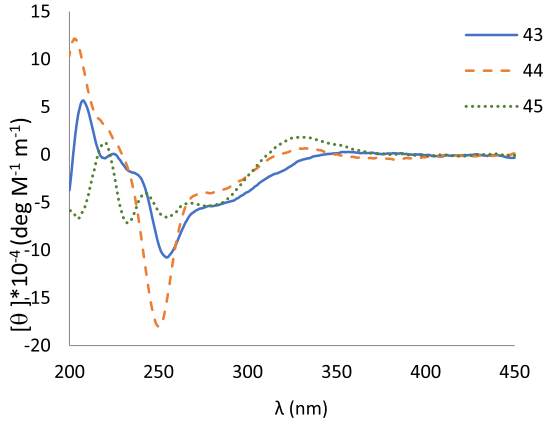


Figure 2. CD-spectra of complexes **43**−**45**.

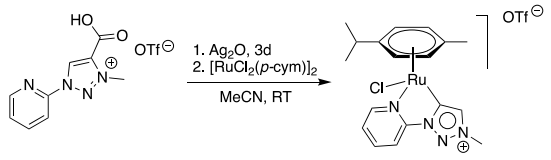
moiety during the dissociative process prior to the coordination of the alkyne (Figure 2).[43]

Clearly, the results above show the crucial participation of the sulfoxide group in the chirality transfer processes, both during the formation of the enantiopure metal center and during the transformation of these enantiopure centers. The combination of CD-X-ray is a powerful methodology to study these processes in the metal center.

5. DESULFINYLATION REACTIONS: NOVEL REACTION PATHWAYS

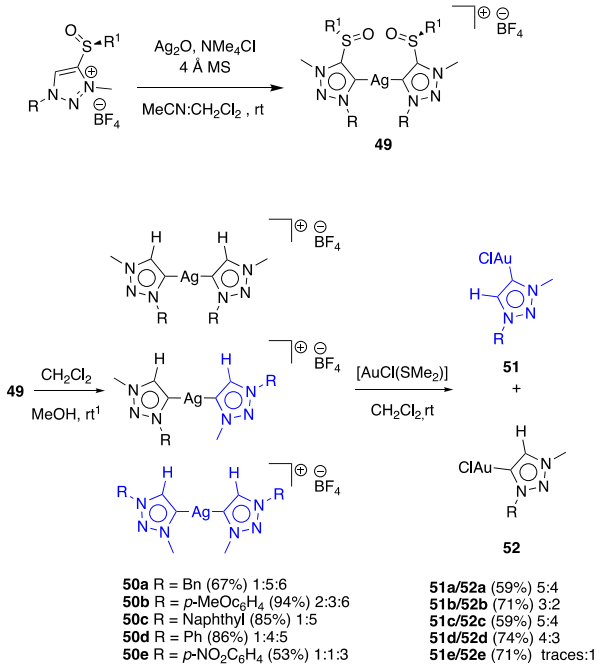
1,2,3-Triazole MICs having sulfoxide moieties are also interesting substrates to study new processes. The lability of some groups attached to the 1,2,3-triazole MICs has been observed by Albrecht.[44] Thus, during the formation of Ru-complexes from 4-methoxycarbonyl-1,2,3-triazolium salts, partial decarboxylation of the ester group in the precursor triazolium salt was detected, which allowed for the preparation of C4-unsubstituted Ru-complexes. Mechanistic studies were not pursued. Subsequent work by these authors[45] resulted in a method to prepare C4-unsubstituted Ru(II) and Au(I) complexes by decarboxylation of the corresponding 4-carboxy-MICs during the coordination process (Scheme 23).

Scheme 23. Decarboxylation of a 1,2,3-Triazolium Salt during a Metalation Process



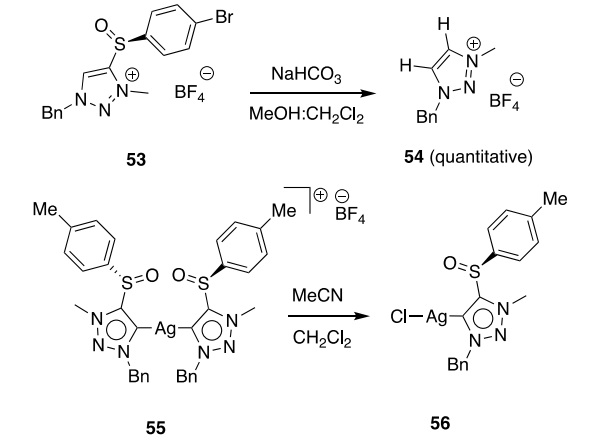
The preparation of silver complexes **49** having two C4-sulfoxide substituted 1,2,3-triazole MICs ligands occurred uneventfully in excellent yields using the standard Ag_2O/Me_4NCl conditions for the metalation of the C5 position of the heterocyclic ring. These complexes were isolated and characterized. However, when complexes **49** were subjected to reaction with MeOH, removal of the sulfinyl group was observed with the concomitant formation of three new Ag(I) complexes **50**, having the C4 position unsubstituted.[46] Regioisomeric Au(I) complexes **51**/**52** were obtained from the mixture of the Ag(I) complexes (Scheme 24). X-ray diffraction of complexes **51d** and **52d** secured the regioisomeric nature of complexes **50**. Additionally, the reaction occurs with other primary and secondary but not tertiary alcohols.

Scheme 24. Silver MIC Carbenes and Their Desulfinilation Reactions



To determine whether the desulfinilation occurred in the silver complexes **49** or in the free triazolium salts formed by dissociation of these silver complexes, the free salt **53** was submitted to treatment with MeOH forming the unsubstituted triazolium salt **54** together with methyl sulfinate (Scheme 25).

Scheme 25. Desulfinylation of Salt 53 and Formation of Ag(I)-Complex 56



The existence of equilibrium between the Ag−MIC **49**, the free carbene species, and the corresponding Ag−monocarbenes was demonstrated by the crystallization of silver monocarbene **56** from a solution of **55**. Moreover, the structure of this silver monocarbene was resolved by X-ray diffraction.

The isolation of Ag−monocarbene **56** coupled to the desulfinylation of **53** is coherent with the desulfinylation reaction occurring through the free carbene **A**, analogous to the one derived from **53** (Figure 3). Extensive deuteration

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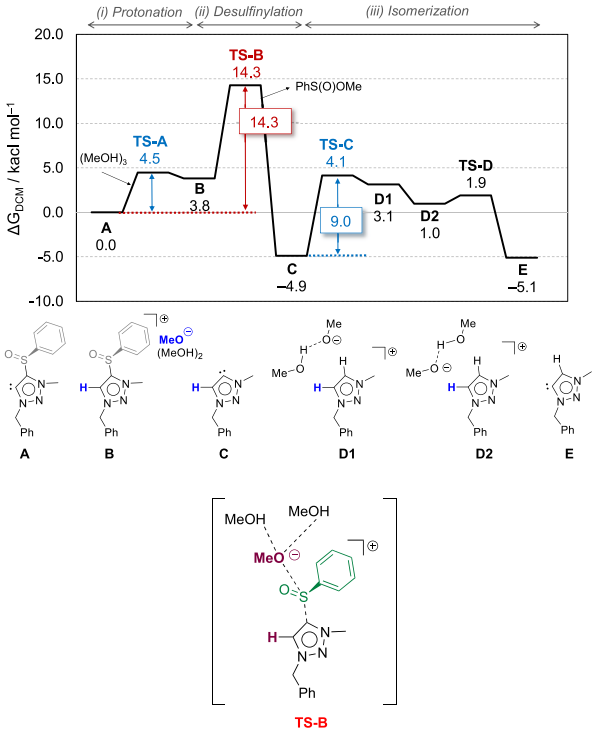

Figure 3. Computed reaction pathway for the desulfinilation reaction in C4-sulfinyl-1,2,3-triazolium salts. All values correspond to Gibbs energies in DCM (dichloromethane) (kcal mol^{-1}). DFT calculations were carried out using the M06 density functional,[48] with an ultrafine grid as implemented in Gaussian 09.[49] Gaussian 09 performs well for main-group chemistry and noncovalent interactions.[50] All intermediates and transition states were fully optimized in DCM solution (ε = 8.93) using the continuum method SMD.[51] The 6-31G** basis set (**BS1**) was used. Final single-point calculations were performed with the 6-311++G** basis set (**BS2**).[52] 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 of the imaginary frequency and subsequent optimization of the resulting structures.

experiments and density functional theory (DFT) calculations allow the proposal of a mechanism for this unprecedented desulfinylation reaction. MeOH was modeled as one MeOH solvated by another two explicit MeOH molecules.[47] The structure of **TS-B** is depicted in Figure 3. In this TS, the MeO$^-$ having two MeOH molecules experiences the nucleophilic attack to the sulfur in a S_N2 type reaction. The participation of two molecules of MeOH proportionates the lower energy TS computed for this rate determining step.

The proposed reaction mechanism is shown in Figure 3 and entails three main steps: (i) protonation of the free carbene, (ii) desulfinylation via nucleophilic attack, and (iii) carbene isomerization. First, the free carbene **A** (zero of energies) is protonated by methanol via **TS-A** (4.5 kcal mol^{-1}) to form the triazolium cation **B** and [MeO$^-$(MeOH)$_2$]. The solvated methoxide performs a nucleophilic attack on the sulfur center via **TS-B** (14.3 kcal mol^{-1}), thus breaking the S−C4 bond. Release of the sulfinate produces carbene **C**, which lacks substituents at the ring carbon atoms. Carbene **C** can then isomerize to **E** via the protonated species **D1** and **D2** involving **TS-C** (4.1 kcal mol^{-1}) and **TS-D** (1.9 kcal mol^{-1}). **D1** and **D2** are computationally less favored than **C** and **E** due to entropic effects and poor stabilization of charged species in the low polar DCM solvent. Overall, the largest activation energy is 14.3 kcal mol^{-1} (from **A** to **TS-B**), which corresponds to the nucleophilic attack step.

This mechanism is consistent with the experimental data. The low activation energy agrees with the mild experimental conditions, and the rate-determining nucleophilic attack explains the slower reaction rates observed with bulkier alcohols. In the presence of strong electrophiles such as [Ag$^+$] and [Au$^+$], the carbenes **C** and **E** would readily react with Au(I) or Ag(I) giving unsubstituted MIC-complexes. The exoergic desulfinylation from **B** to **D2** ($\Delta\Delta G$ = −2.8 kcal mol^{-1}) is also in line with the no participation of Ag in the process. Moreover, the deuteration experiments carried out for these processes show deuterium incorporation in the C3 and C4 positions of the triazole ring, which is consistent with the facile isomerization through proton transfer steps in the species **D1** and **D2**.

6. OUTLOOK

The results presented above show the potential of MICs derived from 1,2,3-triazoles having a chiral sulfur functional group at the C5 position. While for some applications like anion recognition the effect of the sulfur groups is to decrease the electronic density of the triazole ring,[23] the participation of these groups in determining the nature and stereochemistry of the final product is decisive. In catalytic cycloisomerization processes and cycloisomerization−dimerization processes, the role of the sulfoxide moiety is to stabilize intermediates in the catalytic cycle, allowing for the reaction to occur or significantly increasing the selectivity of the cyclization processes. Meanwhile, during chirality transfer processes to the newly formed chiral metal center, the sulfur functional group determines the chirality of this center which is formed in a completely diastereoselective fashion. Moreover, the chiral half-sandwich complexes containing the sulfur chiral group unaltered, experience different reactions with complete retention of the configuration. Finally, mechanistically new processes, like the desulfinilization of 1,2,3-triazolium salts have been uncovered. Clearly, these classes of compounds also offer new opportunities for the discovery and study of new mechanistically relevant reactions. Overall, the sulfur chiral moieties play a pivotal role in these processes. In addition, hypothetically the reversible conversion of the S═O functional group into its reduced and oxidized forms may be possible, which opens up substantial opportunities both in catalysis and in the building of new structures.[53]

The reactions in Scheme 5 show that much remains to be done in this field, including the multinuclear systems, and the synthesis and application of the regioisomeric 1,2,3-triazole MICs having the sulfur chiral group in C4. The catalytic opportunities of these new chiral metal complexes that include the chiral at the metal complexes have been just devised. Again, these new catalysts offer opportunities for asymmetric synthesis to be disclosed during the next few years. Finally, the disentangling of the role of functional groups having more than one mode of coordination to the metal opens up new opportunities for mechanistic studies (both experimental and computational).

AUTHOR INFORMATION

Corresponding Authors

*E-mail: sierraor@ucm.es (M.A.S.).
*E-mail: mc.delatorre@csic.es (M.C.T.).

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ORCID

Miguel A. Sierra: 0000-0002-3360-7795

Notes

The authors declare no competing financial interest.

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