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Desulfinylation of Ag(I) Sulfinyl Mesoionic Carbenes: Preparation of *C*-Unsubstituted Au(I)−1,2,3-Triazole Carbene Complexes

María Frutos,[†,‖] Manuel A. Ortuño,[‡,‖,⊗] Agustí Lledos,[‡,‖] Alma Viso,[†,‖] Roberto Fernández de la Pradilla,[†,‖] María C. de la Torre,[*,†,‖] Miguel A. Sierra,[*,§,‖] Heinz Gornitzka,[⊥,#] and Catherine Hemmert[⊥,#]

[†]Instituto de Química Orgánica General, Consejo Superior de Investigaciones Científicas (CSIC), Juan de la Cierva 3, 28006 Madrid, Spain

[‡]Departament de Química, Universitat Autònoma de Barcelona, 08193 Cerdanyola del Vallès, Spain

[§]Departmento de Química Orgánica I, Facultad de Química, Universidad Complutense, 28040 Madrid, Spain

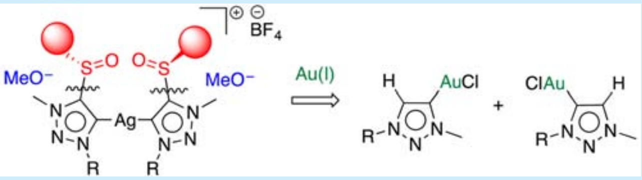
[‖]Centro de Innovación en Química Avanzada (ORFEO−CINQA), Universidad Complutense, 28040 Madrid, Spain

[⊥]CNRS, LCC (Laboratoire de Chimie de Coordination), 205 route de Narbonne, BP 44099, ToulouseF-31077 Cedex 4, France

[#]Université de Toulouse, UPS, INPT, Toulouse F-31077 Cedex 4, France

S *Supporting Information*

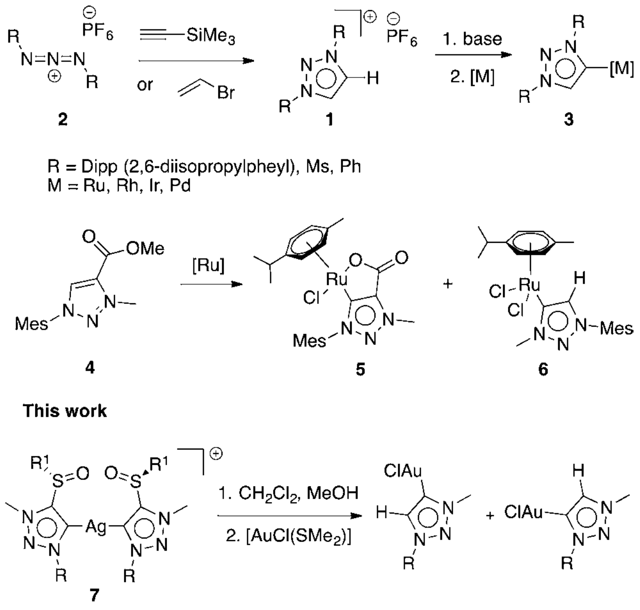
ABSTRACT: New and well-characterized Ag−bis(1,2,3-triazolylidene) complexes having enantiopure (*S*)-sulfoxides upon sequential treatment with alcohols and Au(I) form separable mixtures of regioisomeric *C*-unsubstituted Au−1,2,3-triazolylidene complexes. Mechanistic studies and DFT calculations support a desulfinylation process for in situ generated free triazolylidene salts.



While the number of 1,2,3-triazolylidene metal complexes (M−MIC, MIC = mesoionic carbene) and their use as catalysts and in the building of 3D-metal frameworks increase every day,[1] the synthesis of *C*-unsubstituted M−MIC is not obvious. Bertrand reported the preparation of series of *C*-unsubstituted triazolium salts **1** using the 1,3-dipolar cycloaddition between 1,3-diaza-2-azoniallene salts **2** and (trimethylsilyl)acetylene or vinyl bromide (Scheme 1).[2] From symmetric salts **1** different metal carbene complexes **3** were prepared. Recently, Albrecht[3] reported the partial decarbonylation of 1,2,3-triazoles having a methoxycarbonyl group attached to C-4, **4**, upon methylation (MeOTf) and metalation. The mixture of the chelated Ru−MIC **5** and the *C*-unsubstituted Ru−MIC **6** was obtained. Subsequent reports[4] described the similar formation of *C*-unsusbtituted triazolium salts by either decarboxylation or acetone removal of triazolium salts during different metalation processes.

During our work directed toward the synthesis of new M−MICs having either natural product[5] or enantiopure (*S*)-sulfoxide subtituents[6] attached to the C-4 of the triazole ring, we found the unprecedented desulfinylation reaction of silver mesoionic carbene complexes **7** leading to *C*-unsubstituted 1,2,3-triazolylidene ligands.[7] The scarcity of approaches to this class of ligands prompted us to study the scope and mechanism of these processes.

Scheme 1



Silver−MIC **7aa** was prepared in 89% yield by reacting triazolium salt **8aa** with Ag_2O in the presence of NMe_4Cl in a mixture of CH_3CN/CH_2Cl_2 (1:10). Salt **8aa** was obtained by CuAAC (copper-catalyzed azide−alkyne cycloaddition) between alkynyl sulfoxide **9a** and azide **10a** followed by methylation of the resulting triazole **11aa** with Me_3OBF_4 at

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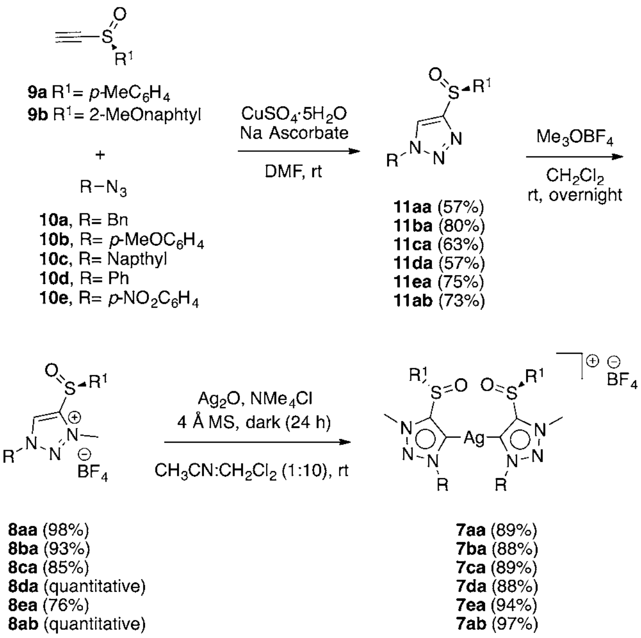
room temperature (Scheme 2). Silver carbene **7aa** was fully characterized by NMR and HRMS. Additional Ag—MICs **7ba—ea** and **7ab** were prepared following an analogous approach from the corresponding azides. Yields were excellent in all cases ranging from 88 to 97%. Complexes **7ba—ea** and **7ab** were stable, and they were fully characterized by spectroscopic and spectrometric media.

Scheme 2



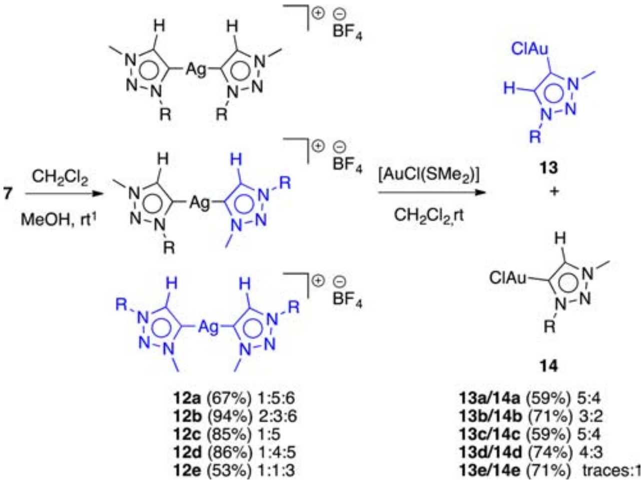
MeOH was added to a solution of the complex in CH_2Cl_2 during manipulation of the silver carbene **7aa**. Surprisingly, in the ^{1}H NMR spectrum of the crude mixture, the symmetry of the Ag—MIC **7aa** was lost as it could clearly be seen by the presence of three signals for the benzylic methylene group and another set of three signals corresponding to the methyl group bonded to N-3.

The simultaneous formation of methyl *p*-tolylsulfinate was unambiguously confirmed by isolation, washing the crude reaction mixture with pentane, and spectroscopic characterization. ^{1}H NMR analysis of the solid product revealed the presence of the triazole moiety by the appearance of a set of three signals for the methylene group in a 1:5:6 proportion. Moreover, the ^{13}C NMR spectrum of the solid clearly showed three signals for the carbon center of the NCH_3 and another three signals for the NCH_2 groups. Furthermore, analysis of the *g*HMBC experiment unambiguously confirmed the formation of three different $Ag-(MIC)_2$ complexes **12a** (see the Supporting Information).

With these results in hand, we can conclude that the presence of MeOH in the solution of silver—MIC **7aa** resulted in the removal of the sulfinyl functionality as methyl *p*-tolylsulfinate. The elimination of the sulfur moiety was accompanied by a partial rearrangement of the Ag atom, yielding a mixture of "naked" carbenes **12a** (Scheme 3).

Due to the difficulty of separation of the three silver carbenes **12a**, transmetalation of this mixture with $[AuCl(SMe_2)]$ was next addressed. Reaction of a solution of silver carbenes **12a** in CH_2Cl_2 with 2.00 equiv of $[AuCl(SMe_2)]$ at room temperature afforded a mixture of the two regioisomeric MIC—AuCl complexes **13a/14a** in a 98% combined yield and in a 5:4 ratio (Scheme 3). Separation of both complexes was achieved by chromatography on SiO_2. The C-4 regioisomer **13a** was the most apolar, and it was totally characterized by ^{1}H and ^{13}C NMR and HRMS techniques. On the other hand, the second regioisomer **14a** was also characterized by ^{1}H and ^{13}C NMR and NOE techniques together with HRMS analysis.

Scheme 3[a]



[a]The formation of sulfinate esters is ommited (see text).

To study the scope of the reaction, methanolysis of different silver carbenes **7ba—ea** and **7ba** was carried out. In all cases, the new mixture of silver complexes **12b—e** was transmetalated with $[AuCl(SMe_2)]$ to form the mixture of regioisomeric Au complexes **13b—e/14b—e** (Scheme 3).[8] The *C*-unsubstituted silver carbenes **12a—e** were formed in good yields. The desulfinylation reaction was compatible with electron-donor groups (**7ba**), electron-withdrawing groups (**7ea**), as well as naphthyl moieties (**7ca**) attached to the aromatic ring of the former azide. In addition, the presence of the more sterically demanding 2-MeO-naphtyl substituent at the sulfur atom (**7ab**) requires higher temperatures (50 °C) and longer reaction time (2 h) for the desulfinylation to take place. In all cases, the ratio of Ag complexes **12** did not match the ratio of Au—carbene complexes **13/14**. This suggests a dynamic equilibrium in solution between complexes **12** that translates to a variable C4/C5 (**13/14**) gold carbene ratio. Finally, the nature of regioisomeric compounds **13/14** was confirmed by X-ray diffraction studies carried out in crystals grown from complexes **13d** and **14d** (Figure 1).

With these results in hand, different experiments were carried out to disentangle the reaction pathway. Silver carbene **15** (Scheme 4) having a sulfone attached to C-4 was prepared from the triazole **16** following the methodology used in this work in 94% yield.[9] In this case, the Ag—MIC **15** also showed a bis(carbene) structure as could be confirmed by HRMS analysis, with a main fragment at *m/z* = 763.1136 that corresponds to the cationic part of the complex **15**. Reaction of silver carbene **15** with MeOH in CH_2Cl_2 at room temperature or in boiling CH_2Cl_2 did not produce (TLC) any transformation. Therefore, it was clear that the presence of an additional oxygen atom prevented the loss of the sulfur fragment.

The role of the alcohol was next addressed. A solution of Ag—MIC **7aa** in $CDCl_3$ stayed unaltered for 1 week in solution

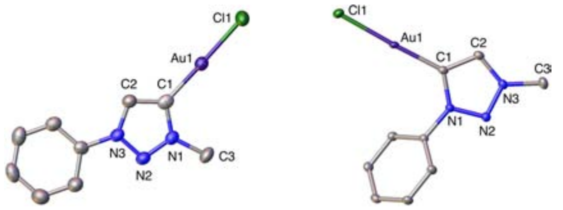
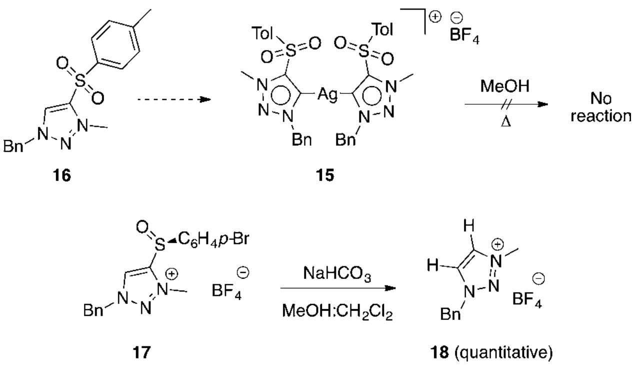


Figure 1. ORTEP representation of gold carbene **13d**. Selected bond lengths (Å) and angles (deg): Au1−Cl1 2.2792(13), Au1−C1 1.962(5), C1−N1 1.375(6), N1−N2 1.332(5), N2−N3 1.317(5), N3−C2 1.353(6), C2−C1 1.369(7), C1−Au1−Cl1 178.586(4). ORTEP representation of gold carbene **14d**. Selected bond lengths (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.

(NMR). This confirmed the stability of the S(O)−C4 bond in the Ag−MIC **7aa** in solution in the absence of MeOH. Different alcohols were next tested. Desulfinylation reaction proceeded at room temperature when EtOH and ^{i}PrOH were added over a solution of **7aa** in CH_2Cl_2. In the case of EtOH, the corresponding sulfinate was generated instantaneously, while the reaction of **7aa** with ^{i}PrOH required longer times. The ^{1}H NMR spectrum of the crude mixture showed the formation of ethyl and isopropyl sulfinates. Reaction of **7aa** with ^{t}BuOH at room temperature or by heating at 50 °C for 1 h resulted in the recovery of unaltered starting material.

On the other hand, to determine whether the desulfinylation reaction occurs in the complexed Ag−MIC or in a free decoordinated triazolylidene ligand, triazolium salt **17** was reacted in CH_2Cl_2/MeOH and filtered through a $NaHCO_3$ pad. *C*-Unsubstituted triazolium salt **18** was now detected upon inspection of the ^{1}H NMR of the crude reaction mixture and isolated in quantitative yield (Scheme 4).

Scheme 4



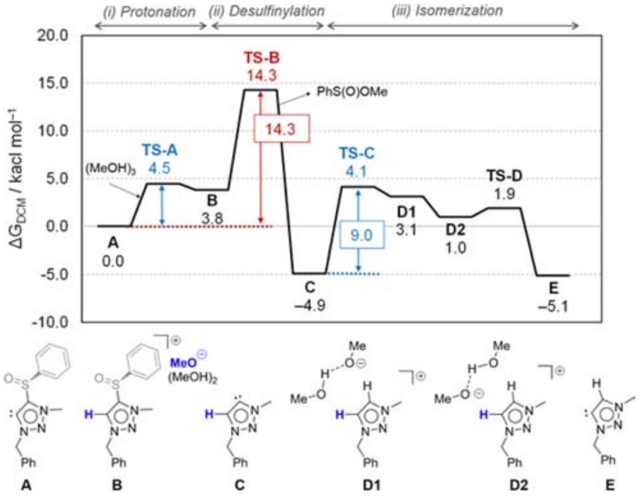
Deuteration experiments were next carried out. Thus, complex **7ba** was dissolved in $CDCl_3$ and drops of CD_3OD were added to the solution. A ^{1}H NMR spectrum showed that the desulfinylation process occurred since three sets of signals for the methyl group appeared. Comparison of the values of the integrals of the new H substituents of the triazole core of complexes **12b** to the spectrum registered when reaction was performed in nondeuterated solvents showed clearly that deuteration has occurred in H4 and H5 of complexes **12b**. Therefore, we could affirm that the heterocycle is protonated by MeOH, and these experiments confirm a primary protonation upon decoordination and a second protonation event upon desulfinylation. These protonations accounts for the observed fully (C4 and C5) deuterated Ag-MICs.

Finally, the existence of an equilibrium between the Ag−MIC **7**, the free carbene species, and the corresponding Ag−monocarbenes is demonstrated by the formation of Ag−monocarbene upon crystallization of a solution containing **7aa**. The X-ray structure (see the Supporting Information) of this compound unambiguously confirms the equilibrium between the free carbene species and the doubly coordinated Ag−MIC.

Density functional theory (M06) calculations[10] were performed to fully understand the experimental results and propose a reasonable reaction pathway. Due to the isolation of Ag−monocarbene species (Figure S1) and the desulfinylation of **17** (Scheme 4), we consider that the desulfinylation mechanism of complexes **7** occurs through the free carbene **A** (i.e., the neutral phenyl analogue of **17**). MeOH was modeled as one MeOH solvated by another two explicit MeOH molecules.[11] All values correspond to Gibbs energies in dichloromethane (kcal mol^{-1}).

The proposed reaction mechanism is shown in Scheme 5 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}).[12] Overall, the largest activation energy is 14.3 kcal mol^{-1} (from **A** to **TS-B**), which corresponds to the nucleophilic attack step.

Scheme 5



We now compare the proposed mechanism (Scheme 5) 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 form coordination complex analogues of **12** and **13** as shown in Scheme 3. The exoergic desulfinylation from **B** to **D2** ($\Delta\Delta G$ = −2.8 kcal mol^{-1}) is also in line with the related Ag-free process from **16** to **17** shown in Scheme 4. Finally, the facile carbene isomerization through proton transfer steps is fully compatible with the deuteration data.

To conclude, the synthesis and characterization of new Ag–bis(1,2,3-triazolylidene) complexes having enantiopure (*S*)-sulfoxide substituents in C-4 have been developed. These complexes experience an unprecedented desulfinylation process mediated by primary and secondary (but not tertiary) alcohols to afford, upon transmetalation to Au(I), separable mixtures of the regiosiomeric *C*-unsubstituted Au–1,2,3-triazolylidene complexes. Deuteration and computational studies support a substitution mechanism in the free triazolylidene salt generated in situ by dissociation of the mesoionic ligand. Studies directed toward the control the regioselectivity of the reaction as well as to prepare other "naked" M–MICs are underway in these laboratories.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b03808.

Crystallographic data for compound **13d** (CIF)
Crystallographic data for compound **14d** (CIF)
Crystallographic data for the Ag–monocarbene obtained from **7aa** (CIF)
Experimental procedures and ^{1}H, ^{13}C NMR spectra for all the compounds, X-ray data for compounds **13d**, **14d**, and the Ag–monocarbene obtained from **7aa**, computational details, and Cartesian coordinates for all optimized species (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: mc.delatorre@csic.es.
*E-mail: sierraor@ucm.es.

ORCID

Agustí Lledos: 0000-0001-7909-422X
Miguel A. Sierra: 0000-0002-3360-7795

Present Address

⊗(M.A.O.) Department of Chemistry, Chemical Theory Center and Supercomputing Institute, University of Minnesota, Minneapolis, MN 55455.

Notes

The authors declare no competing financial interest.

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(7) For a comprehensive review in *N*-heterocyclic silver carbene complexes (AgNHC), see: Garrison, J. C.; Youngs, W. J. *Chem. Rev.* **2005**, *105*, 3978.

(8) The methanolysis of complex **7ba** formed methyl 2-methoxy-1-naphtylsulfinate, which was separated and spectroscopically characterized.

(9) Triazole **16** was prepared by oxidation of the sulfoxide derivative **11aa**. See: Bolje, A.; Košmrlj, J. *Org. Lett.* **2013**, *15*, 5084.

(10) DFT calculations were carried out at the M06 level with ultrafine grid as implemented in Gaussian 09. Single-point calculations with triple-ζ basis sets were performed on geometries optimized with double-ζ basis sets in dichloromethane solvent using the SMD model. See the Supporting Information for full computational details.

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(12) **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 dichloromethane solvent.