chemistry proceedings

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Proceeding Paper

Synthesis of *N*-Heterocyclic Carbene Gold Complexes Using 2,4,6-Trimethylphenyl Sydnone as Model Substrate †

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† Presented at the 26th International Electronic Conference on Synthetic Organic Chemistry, 15–30 November 2022. Available online: https://ecsoc-26.sciforum.net.

Abstract: Two gold(I) complexes have been synthesized by a two-step reaction. The first reaction step was the deprotonation with butyllithium to obtain the corresponding NHC. In a second reaction step the metal precursor was added to afford the corresponding gold complex. At this point, the complex obtained depends on the nature of the metal precursor. A monocarbene complex (sydnone-Au-tht) was obtained using [Au(tht)Cl] as metal precursor and a biscarbene complex (sydnone-Au-imidazolium) was obtained using a gold imidazolium complex as metal precursor instead. The ^{13}C-NMR resonance frequencies of the carbene carbon atom are shifted to higher values from 97.3 to 135.6–139.7 ppm, mono and biscarbene respectively.

Keywords: *N*-heterocyclic carbene; sydnone; Gold(I) complex

Citation: Vita, D.E.; Badajoz, M.A.; Lo Fiego, M.J.; Silbestri, G.F. Synthesis of *N*-Heterocyclic Carbene Gold Complexes Using 2,4,6-Trimethylphenyl Sydnone as Model Substrate. *Chem. Proc.* **2022**, *4*, x. https://doi.org/10.3390/xxxxx

Published: 15 November 2022

1. Introduction

Sydnones (1,2,3-oxadiazolium-5-olates), discovered by Earl and Mackney in 1935 [1], are mesoionic compounds "dipolar five-membered heterocyclic compounds in which both the negative and the positive charge are delocalized, for which a totally covalent structure cannot be written, and which cannot be represented satisfactorily by any one polar structure" according to IUPAC [2]. Their properties like planar aromatic character, relatively small size and variation in electron density around the ring are auspicious to become biologically active scaffolds [3,4]. Unlike other mesoionic compounds, sydnones have the particularity of being very stable and easily synthesized [5]. On the other hand, they can be functionalized at C-4 by hydrogen substitution for different groups (heteroatoms, acyl substituents, metals).

Gold has been used for therapeutic or catalytic purposes for decades [6]. The current concern is to achieve higher stability of the compounds that carry metals, for which the coordination with *N*-heterocyclic carbene (NHC) ligands has been an excellent strategy [7]. Seeking new ligands that could stabilize and modify the complexes properties, sydnones result an interesting option since they are adequate starting materials for NHC generation.

Based on, a series of Au(I)-NHC complexes synthesized by our research group [8] and a report of sydnone imine-Au complexes [9], herein we inform about the synthesis of new gold(I)-NHC complexes from 2,4,6 trimethylsydnone.

2. Materials and Methods

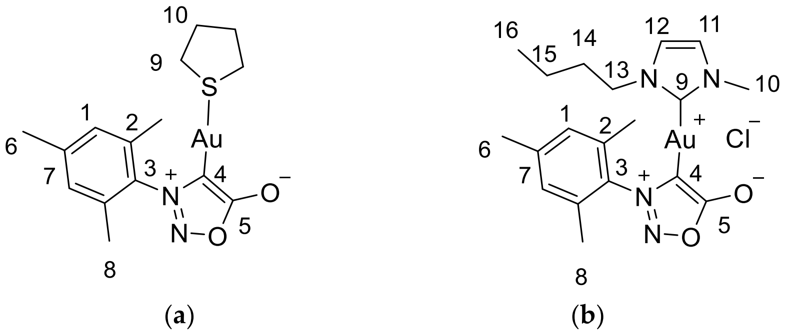
Solvents were distilled, dried and stored according to standard procedures [10]. 2,4,6-trimethylphenyl sydnone [5], butyllithium [11], 1-methyl-3-butyl imidazole-2-ylidene cloro gold(I) [6a] and Au(tht)Cl [12] were prepared according to reported procedures. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker Advance 300 spectrometer. Chemical shifts (δ) are reported in ppm with the residual solvent resonance signal: δ H/C 7.27/77.2 for $CDCl_3$, coupling constants (J) are reported in hertz. Infrared spectra were collected on a FT-IR Spectrometer Nicolet Nexus-470.

2.1. General Procedure for Preparation of Gold Complexes

2.1.1. Monocarbene

Under inert atmosphere of N_2 the 2,4,6-trimethylphenyl sydnone was dissolved in anhydrous THF and was cooled to −50 °C. A solution of BuLi in hexane was added. After 30 min, [Au(tht)Cl] was incorporated to the solution. The reaction was warmed up and stirred for 18 h. Then water was added and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were dried over $MgSO_4$ and evaporated. The desired compound was purified by precipitation with hexane from THF.

(3-mesityl-5-oxido-1,2,3-oxadiazol-3-ium-4-yl)-(tetrahydrothiophene)gold(I) (Figure 1a). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.95 (s, 2H, H-1), 3.19 (s, 4H, H-9), 2.33 (s, 3H, H-6), 2.15 (s, 6H, H-8), 2.00 (s, 4H, H-10). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.7 (C-5), 140.2 (C-7), 135.6 (C-4), 134.1 (C-2), 129.0 (C-1), 38.9 (C-9), 30.7 (C-10), 21.3 (C-6), 17.2 (C-8).



(**a**) (**b**)

Figure 1. Numeration in (**a**) monocarbene complex (**b**) biscarbene complex.

2.1.2. Biscarbene

Under inert atm of N_2 the 2,4,6-trimethylphenyl sydnone was dissolved in anhydrous THF and was cooled to −50 °C. A solution of BuLi in hexane was added. After 30 min a solution of imidazolium gold(I) complex in THF was incorporated into the mixture. The reaction was warmed up and stirred for 18 h. Then water was added and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were dried over $MgSO_4$ and evaporated. It was purified by column chromatography.

(3-mesityl-5-oxido-1,2,3-oxadiazol-3-ium-4-yl)-(1-butyl-3-methyl-1,3-dihydro-2H-imidazol-2-ylidene)gold(I) (Figure 1b). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.94–692 (brs, 2H, H-11 H-12), 6.83 (s, J = 1.4 Hz, 2H, H-1), 3.81 (t, J = 7.0 Hz, 2H, H-13), 3.63 (s, 3H, H-10), 2.30 (s, 3H, H-6), 2.18 (s, 6H, H-8), 1.53 (q, J = 7.4 Hz, 2H, H-14), 1.12 (q, J = 7.6 Hz, 2H, H-15), 0.84 (t, J = 7.3 Hz, 3H, H-16). ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.6 (C-9), 179.5 (C-5), 140.1 (C-7), 139.7 (C-4), 136.1 (C-2), 134.2 (C-3), 128.8 (C-1), 121.7 (C-12), 120.5 (C-11), 50.7 (C-13), 37.9 (C-10), 33.2 (C-14), 21.3 (C-6), 19.6 (C-15), 17.2 (C-8), 13.7(C-16).

3. Results and Discussion

In order to obtain the sydnone carbene, several bases were used. NaOAc, K_2CO_3 and $NaHCO_3$ in ethanol at room temperature were tested with negative results. Furthermore, stronger bases, considering that pKa of sydnone is approximately 18 [13], like ^{t}BuONa, $NaNH_2$, LiHMDS, NaHMDS in THF were employed with similar results. However, the last two bases showed promising evidences of carbene formation, like sydnone disappearance (by TLC) and a different pattern of signals in NMR spectra. Unfortunately, despite the efforts made, we could not isolate the desired complex after adding the metal precursor. Additionally, the manipulation and conservation of this bases was extremely difficult because of its sensitivity to water presence. Finally, once complete deprotonation with BuLi was achieved, we studied its coordination to the metal precursor to obtain the desired metal complex.

Au(tht)Cl is the gold-precursor used to obtain imidazolium gold complexes in our group [8], thus it was added to the sydnone carbene seeking the obtention of the sydnone-Au-Cl complex. However, sydnone-Au-tht was the monocarbene complex obtained instead. The other metal precursor employed was an imidazolium-Au-Cl complex previously synthetized, and this led to the biscarbene complex (sydnone-Au-imidazolium) obtention (Figure 2).

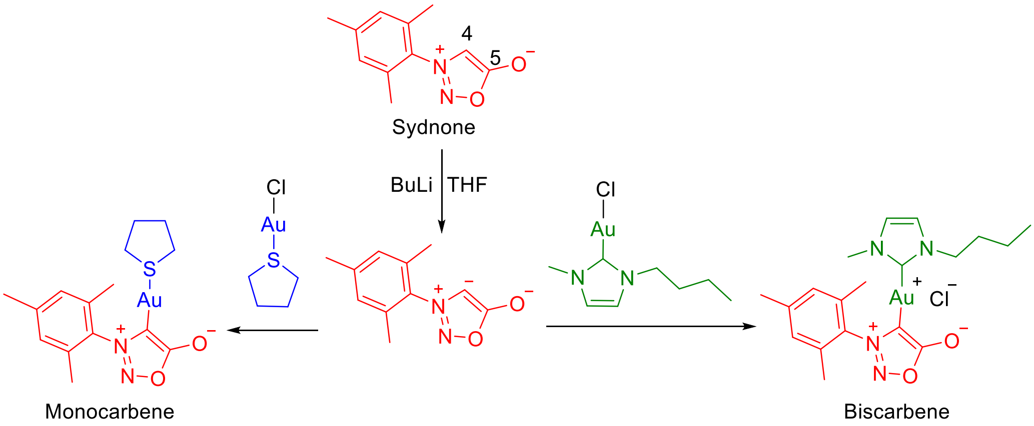


Figure 2. General procedures for preparation of sydnone-gold(I) complexes.

Gold(I) complexes were fully characterized by ^{1}H, ^{13}C, NMR and FT-IR spectroscopy. The ^{1}H NMR data confirmed the metal coordination by the disappearance of the proton signal of the sydnone (singlet at δ 6.34 ppm). Besides, in ^{13}C NMR spectra, some signals were shifted to higher ppm relative to the sydnone substrate. These modifications in complexes spectra are consistent with C-Au bonding. The signals of the ligands from the gold precursors were affected too. Chemical shifts from C-4, C-5, C-9 and C-10 are listed in Table 1.

Table 1. ^{13}C NMR shifts.

Sydnone	Au(tht)Cl	Imidazolium-Au-Cl	Monocarbene	Biscarbene
C-4, 97.3			C-4, 135.6	C-4, 139.7
C-5, 169.4			C-5, 177.7	C-5, 179.5
	C-9, 40.1	C-9, 170.9	C-9, 38.9	C-9, 187.6
	C-9, 30.2		C-10, 30.6	

FT-IR spectra of 2,4,3-trimethylsydnone shows a characteristic band at 1728 cm^{-1} corresponding to carbonyl stretch. This band was modified to 1671 cm^{-1} when bonded to Au(tht) and 1691 cm^{-1} when bonded to Au-imidazolium.

4. Conclusions

Several bases were tested to achieve sydnone deprotonation. Butyllithium was the selected base to effectively deprotonate 2,4,6 trimethylsydnone and then, two metal precursors were used to obtained new NHC-gold(I) complexes. They were purified and fully characterized by NMR and FT-IR spectroscopy. The following next step would be the variation of the sydnone substrate and gold precursors.

Acknowledgments: This work was partially supported by Agencia Nacional de Promoción Científica y Técnica (PICT-2019-2522) and the Universidad Nacional del Sur (PGI 24/Q108), Bahía Blanca, Argentina. CONICET is thanked for a research fellowship to D.E.V.

Conflicts of Interest: The authors declare no conflict of interest.

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