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Synthesis and Catalytic Application of Homoleptic Bis(triazol-5-ylidene)-Silver Complexes

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Abstract. Treatment of 1,2,3-triazolium salts with equimolar amounts of silver oxide (in presence of potassium hexafluorophosphate) generates a series of bis-triazol-5-ylidene silver(I) complexes with the general formula $[(MIC)_2Ag]PF_6$ (MIC = triazol-5-ylidene). The new biscarbenic species have been fully characterized including FT-IR and NMR spectroscopies, melting points, and elemental analysis. The catalytic performance of the silver(I) complexes in the solvent free KA^2 (ketone-alkyne-amine) coupling for the generation of propargylic amines and the A^3 coupling (aldehyde, amine, alkyne) is investigated.

Resumen. El tratamiento de sales de 1,2,3-triazolio con cantidades equimolares de óxido de plata (en presencia de hexafluorofosfato de potasio), genera una serie de complejos de plata soportados por bis(triazol-5-ilidenos) con formula general $[(MIC)_2Ag]PF_6$ (MIC = triazol-5-ilideno). Los nuevos complejos de plata(I) han sido completamente caracterizados mediante espectroscopías de FT-IR y RMN, así como puntos de fusión y análisis elementales. El potencial catalítico de los biscarbenos de plata en el acoplamiento KA^2 (cetona, aldehído, alquino) para la generación de aminas propargílicas así como el acoplamiento A^3 (aldehído, amina, alquino), es investigado.

Introduction

For over two decades, the chemistry of N-heterocyclic carbene (NHC) silver complexes has attracted considerable attention owing to their straightforward synthesis, and its coordination to many different carbene architectures which usually delivers air and moisture-stable species.[1] Indeed, a variety of silver precursors can be employed for the synthesis of the respective NHC complexes including silver oxide,[2] acetate,[3] carbonate,[4] triflate,[5] and perfluoroisobutanoate.[6] With the use of the popular imidazolium salts as precursors, a large variety of NHC-silver complexes have been described in the literature including mono-NHC Ag^I species of the formula (NHC)AgX (X = halides) and cationic bis(NHC)Ag complexes of the type $[(NHC)_2Ag]Y$ where Y is a non-coordinating anion such as NO_3^-, OTf, BF_4^- and PF_6^-.[7]

Although the most common application of NHC-silver complexes is related to their use as transfer agents in transmetallation reactions,[8] the low silver toxicity in humans has motivated its exploration in the biology and medicine fields, with particular attention in antimicrobial and anticancer applications.[9] Additionally, it has been found that NHC-silver complexes are capable of activating various π-basic sites such as alkynes, allenes[10] or isocyanates [11] while, their use in carboxylative cyclizations has also been recently reported.[12]

After Carbtree´s discovery in 2001,[13] a new subclass of NHC ligands with reduced heteroatom stabilization, namely mesoionic carbenes (MICs), have attracted a great deal of attention owing to their arguable enhanced sigma-donor properties compared to classical NHCs.[14] In particular 1,2,3-triazol-5-ylidenes have become highly popular as their mesoionic character improves their ability for stabilizing different oxidation states.[15] Their triazolium salt precursors can be readily prepared via copper(I) catalyzed "click" cycloaddition of alkynes and azides followed by an alkylation step.[16] Additionally, the facile modification of the substituents at the N1-, N3- and C4- positions of the heterocycle, permits the tuning of electronic and steric properties of the resulting triazol-5-ylidenes and their metal complexes.

With the previously mentioned relevance of NHC-silver complexes in coordination chemistry, catalysis and medicine, the design and preparation of analogue bis(carbene) derivatives supported by mesoionic triazol-5-ylidenes is clearly interesting as they could offer new alternatives for more reactive species with good potential for catalytic applications.

In the present work and in line with our research line focused on MIC-derived metal complexes, we report the synthesis of a new series of bis(triazol-5-ylidene) silver complexes with the general formula $[(MIC)_2Ag]PF_6$ (**4a-c**). The new biscarbenic species have been properly characterized via FT-IR and NMR spectroscopies, melting points, and elemental analysis. Details of the synthetic procedures, structural characterization, and catalytic optimization in the A^3 (aldehyde, amine, alkyne) and KA^2 (ketone, alkyne, amine) couplings will be described.

Experimental

General considerations

Commercially available reagents and solvents were used as received. 1,2,3-Triazolium salts **3a-c** were prepared according to the literature procedure.[17-19] Synthesis of all metal complexes was performed under an atmosphere of dry argon using standard Schlenk techniques. Solvents were dried by standard methods and distilled under nitrogen. Column chromatography was performed on silica gel (Merck, 230-700 mesh). Melting points were determined on a Fisher-Johns apparatus and are uncorrected. NMR spectra were obtained with a Bruker Ascend (400 MHz) spectrometer. The deuterated solvent used was $CDCl_3$; chemical shifts (δ) are quoted in ppm and coupling constants in Hz; to indicate the multiplicity of the signals of ^1H NMR spectra, the following abbreviations have been used: (s) singlet, (d) doublet, (t) triplet, (at) apparent triplet, (m) multiplet, (dd) double doublet, (bs) broad signal. Elemental analyses were obtained with a Thermo Finnegan CHNSO-1112 apparatus and a Perkin Elmer Series II CHNS/O 2400 instruments. FT-IR spectra were recorded on a Bruker Alpha spectrometer using the attenuated total reflectance (ATR) method. The absorbance peaks are reported in reciprocal centimeters (cm^{-1}).

General procedure for the synthesis of silver complexes 1-3

In a Schlenk flask purged with argon were added the appropriate 1,2,3-triazolium salt (1.0 eq), Ag_2O (1.1 eq), KPF_6 (1.0 eq) and they were dissolved in 5 mL of DCM. The mixture was stirred for 24 h. After cannula filtration, the solvent was reduced to 2/3 of the original volume and hexane was added until a precipitate was formed. The solid was filtered and dried under vacuum and washed with copious amounts of diethyl ether to obtain the pure products.

Complex 4a. According to general method, the title product was obtained as a white powder starting from salt **3a** (50 mg, 0.112 mmol), Ag_2O (0.026 g, 0.113 mmol) and KPF_6 (0.025 g, 0.136 mmol) with an isolated yield of 95 % (0.106 mmol). M.p. = 197-198 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.53-7.44 (m, 4H, *H*Ar), 7.43-7.32 (m, 8H, *H*Ar), 7.22-7.13 (m, 4H, *H*Ar), 4.19 (s, 6H, C*H_3*N), 2.09 (sept, 4H, C*H*(CH_3)_2), 1.08 (d, 12H, CH(C*H_3*)_2), 0.84 (d, 12H, CH(C*H_3*)_2). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 169.4 (d, C-Ag, $J1(^{13}C,^{109}Ag)$ = 192.9 Hz, $J1(^{13}C,^{107}Ag)$ = 166.5 Hz), 148.9 (d, C-Ag), 144.92, 135.58, 131.14, 130.16, 129.93, 129.70, 129.52, 129.24, 126.50, 124.64, 124.21, 124.00, 37.76, 28.34, 24.05, 23.94. ^{19}F-NMR (376 MHz, $CDCl_3$) δ = -73.80 (d, *J* = 711.9 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ = -144.37 (septet, *J* = 712.2 Hz). Anal. calcd for $C_{42}H_{50}AgF_6N_6P$ (891.7364 g/mol): C,56.57, H, 5.65, N,9.42; Found C, 56.18, H, 5.92, N, 9.80.

Complex 4b. According to general method, the title product was obtained as a white-beige powder starting from salt **3b** (50 mg, 0.139 mmol), Ag_2O (0.036 g, 0.153 mmol), and KPF_6 (0.032 g, 0.174 mmol) with an isolated yield of 96 % (0.133 mmol). M.p. = 109-110 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.78-7.73 (m, 4H, *H*Ar), 7.55-7.50 (m, 4H, *H*Ar), 7.50-7.38 (m, 8H, HAr), 7.36-7.29 (m, 4H, HAr), 4.17 (s, 6H, C*H_3*N). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 149.4, 139.8, 130.4, 129.6, 129.6, 129.3, 127.2, 123.4, 37.8. ^{19}F-NMR (376 MHz, $CDCl_3$) δ (ppm): -73.74 (d, *J* = 711.9 Hz). ^{31}P-NMR (162 MHz, $CDCl_3$) δ = -144.40 (septet, *J* = 712.2 Hz). Anal. calcd for $C_{30}H_{26}AgF_6N_6P$ (723.4124 g/mol): C,49.81, H, 3.62, N, 11.62; Found C, 50.02, H, 3.78, N, 11.34.

Complex 4c. According to general method, the title product was obtained as a beige powder starting from salt **3c** (100 mg, 0.196 mmol), Ag_2O (0.046 g, 0.198 mmol), and KPF_6 (0.044 g, 0.237 mmol) with an isolated yield of 98 % (0.192 mmol). M.p. = 144-145 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.46-7.38 (m, 2H, *H*Ar), 7.30-7.22 (m, 8H, *H*Ar), 7.00 (s, 4H, *H*Ar), 6.99 (s, 4H, *H*Ar), 2.45 (s, 6H, CH_3Ar), 2.34 (s, 6H, CH_3Ar), 1.94 (s, 12H, C*H_3*Ar), 1.93 (s, 12H, C*H_3*Ar). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 168.4 (d, C-Ag, $J^1(^{13}C,^{109}Ag)$ = 191.1 Hz, $J^1(^{13}C,^{107}Ag)$ = 165.5 Hz), 149.8, 149.7, 141.8, 140.5, 136.3, 134.2, 133.7, 131.0, 130.2, 129.9, 129.4, 129.0, 128.1, 128.0, 126.7, 21.3, 21.2, 17.4, 17.3. ^{19}F-NMR (376 MHz, $CDCl_3$) δ = -73.90 (d, J = 711.9 Hz). ^{31}P-NMR (162 MHz, $CDCl_3$) δ = -144.38 (septet, J = 712.2 Hz). Anal. calcd for $C_{52}H_{54}AgF_6N_6P$ (1015.8784 g/mol): C, 61.48, H, 5.36, N, 8.27; Found C, 61.77, H, 5.12, N, 8.49.

General procedure for the A³ coupling reaction

Under argon, a teflon seal screw-cap pressure tube was charged with the proper aldehyde (0.1 mmol), the amine substrate (0.11 mmol) and the alkyne (0.11 mmol). After the subsequent addition of the catalyst (2.5 mol%), the final reaction mixture was stirred at 90 °C for 8 h. After reaching room temperature, ethyl acetate was added (2×10 mL) and the mixture was stirred for 10 min. The mixture was filtered through a short silica gel plug, concentrated under vacuum and the crude materials were purified by column chromatography (silica gel) with a proper mixture of ethyl acetate/petroleum ether as eluent. The purified products were identified by ^{1}H-NMR spectroscopy and they are consistent with the literature data.
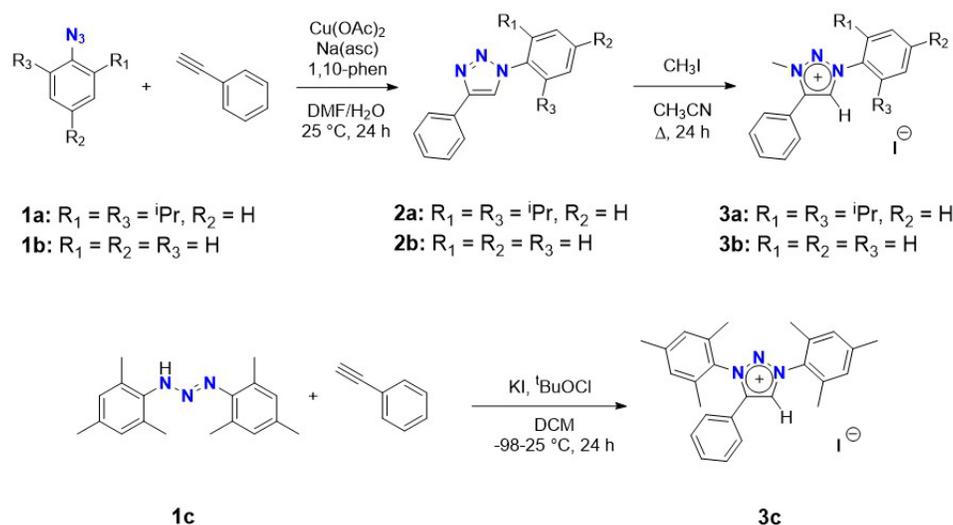
General procedure for the KA² coupling reaction

Under argon, a teflon seal screw-cap pressure tube was charged with the catalyst (3 mol%) and the amine substrate (0.1 mmol) and the resulting mixture was stirred for 5 min. The alkyne (0.1 mmol) and the ketone (0.1 mmol) substrates were subsequently added, and the final reaction mixture was stirred at 100 °C for 6 h. After reaching room temperature, ethyl acetate was added (2×5 mL) and the mixture was stirred for 15 min. The mixture was filtered through a short silica gel plug, concentrated under vacuum and the crude materials were purified by column chromatography (silica gel) with a proper mixture of ethyl acetate/petroleum ether as eluent. The purified products were identified by ^{1}H-NMR spectroscopy and they are consistent with the literature data.
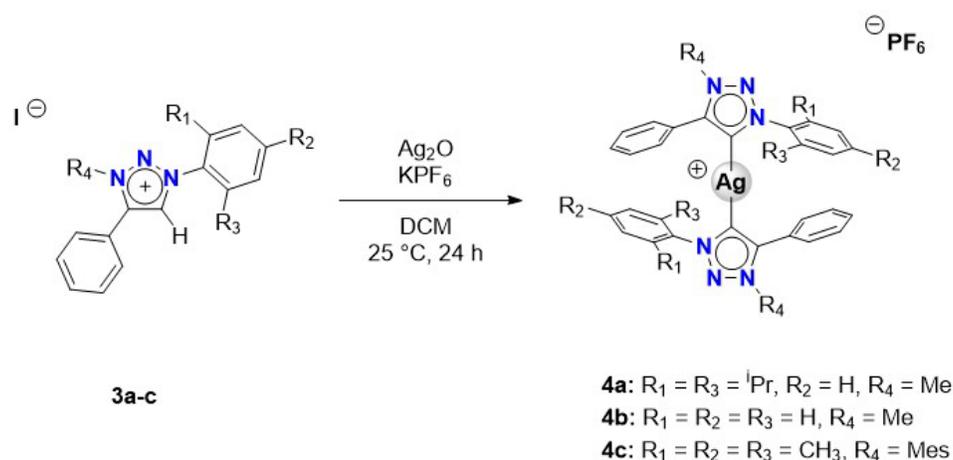
Results and discussion

Synthesis and characterization

Synthesis of the 1,2,3-triazolium salts **3a-c** was carried out using slightly modified reported literature procedures.[17-19] For instance, the copper(I) catalyzed cycloaddition between azides and terminal alkynes (CuAAC) followed by N-alkylation provides salts **3a** and **3b** in good yields. For the preparation of salt **3c**, the oxidative cycloaddition between the 1,2-diaza-2-azoniaallene salt **1c** with phenylacetylene delivers the cationic derivative in a single step (Scheme 1). With salts **3a-c** available, we then proceeded to their treatment with equimolar amounts of silver oxide in presence of potassium hexafluorophosphate using dichloromethane as solvent. After a simple work up and purification, the desired bis(triazol-5-ylidene) silver complexes **4a-c** were obtained in excellent yields as white or beige air stable solids (Scheme 2).

1a: R$_1$ = R$_3$ = ^{i}Pr, R$_2$ = H
1b: R$_1$ = R$_2$ = R$_3$ = H

2a: R$_1$ = R$_3$ = ^{i}Pr, R$_2$ = H
2b: R$_1$ = R$_2$ = R$_3$ = H

3a: R$_1$ = R$_3$ = ^{i}Pr, R$_2$ = H
3b: R$_1$ = R$_2$ = R$_3$ = H

Scheme 1. Synthesis of 1,2,3-triazolium salts **3a-c**.

3a-c

4a: R$_1$ = R$_3$ = ^{i}Pr, R$_2$ = H, R$_4$ = Me
4b: R$_1$ = R$_2$ = R$_3$ = H, R$_4$ = Me
4c: R$_1$ = R$_2$ = R$_3$ = CH$_3$, R$_4$ = Mes

Scheme 2. Synthesis of silver complexes **4a-c**.

Identification of the new bis(MIC) silver complexes was initially assessed by ^{1}H NMR spectroscopy, where the acidic triazolium C5-H proton was no longer observable (above 9 ppm), indicating the formation of the carbenic species. In general, and as expected from the symmetry of the silver complexes, the ^{1}H-NMR spectra from **4a-c** display a single set of resonances including a singlet around 4.2 ppm for the N-methyl groups in **4a** and **4b**. The methyl and CH groups from the isopropyl moiety in **4a** are resolved as two pair of doublets (at 0.84 and 1.08 ppm) and a septuplet (2.09 ppm), respectively. For all complexes **4a-c**, the aromatic area displays the classical three set of multiplets for the phenyl groups (in the range 7.13-7.78 ppm) while the mesitylene CH groups in complex **4c** (singlet peaks), are located around 7.0 ppm.

More revealing is the ^{13}C-NMR spectroscopy where a new low field signal located at 192.9 and 191.1 ppm is assigned to the (MIC)Ag bond for complexes **4a** and **4c**, respectively. The (MIC)$_2$Ag signals are depicted as two doublet signals with an observable coupling between carbon and silver of $J^1(^{13}C,^{109}Ag) = 192.9$ Hz and $J^1(^{13}C,^{107}Ag) = 166.5$ Hz for complex **4a**, and $J^1(^{13}C, ^{109}Ag) = 191.1$ Hz and $J^1(^{13}C, ^{107}Ag) = 165.5$ Hz for complex **4c**. In case of complex **4b**, the carbenic peak could not be observed likely due the to slow relaxation time and low concentration phenomena which has been observed in analogue bis(NHC)-silver complexes reported in the literature.[20] The cationic structure of the homoleptic biscarbene complexes was also established with elemental analysis and complementary ^{31}P-NMR (septep signal around – 144 ppm) and ^{19}F-NMR (doublet around -74 ppm) spectroscopy.

Complexes **4a-c** revealed in their FT-IR spectra a specific ν(C=N) band between 1317-1322 cm^{-1}. The observed downshift compared to the former triazolium salts (1550-1560 cm^{-1}) is consistent with analogue NHC-based silver complexes[20, 25] and is related to the presence of the electropositive silver atom which attracts the electron density, weakening the C=N bond of the heterocyclic scaffold.

Catalytic applications

Propargyl amines are highly valuable synthons for the preparation of nitrogen-containing heterocycles with application in several fields including catalysis, pharmaceuticals and agrochemicals.[21] Ever since the discovery that metals could catalyze the A^3 (aldehyde, amine, alkyne) coupling, investigation related to the synthetic strategies for the generation of propargyl amines and related heterocycles, is under constant development. Up to now, a variety of catalytic systems based on transition metals including rhodium, iridium, iron, magnesium and zinc centers have shown good performance in the A^3 process.[22] Regarding group 11, although gold and copper are the most employed catalysts for this transformation, silver feature several advantages including greener and cheaper access, lower catalyst loadings, and shorter reaction times.[23]

With the seminal work of Li on the use of AgI as an efficient catalyst for the A^3 process, several studies have described the catalytic application of this metal center in various presentations including salts, nanoparticles, metal-organic frameworks or discrete organometallic complexes.[24] In case of the organometallic derivatives, the use of (NHC)-Ag^I complexes in the A^3 coupling have attracted high attention owing to their relatively simple preparation, air stability, and their good catalytic performance under relative mild conditions.[25]

With complexes **4a-c** in hand and with the premise that the high electrophilic nature of these cationic triazol-5-ylidene silver complexes would favor efficient coordination of the alkyne on the catalyst and subsequent formation of the silver alkynide, we envisioned studying the efficiency of these species as catalysts for the A^3 (aldehyde, amine, alkyne) and the KA^2 (ketone, amine, alkyne) couplings for the formation of propargylic amines.

As initial investigation, we carried out the solvent free coupling of benzaldehyde, piperidine and phenylacetylene (A^3 process) employing 3 mol% of catalyst loading at 100 °C for 8 h. As observed in Table 1, complexes **4a** and **4c** demonstrated good performance delivering conversions of 95 and 99 %, respectively. In case of complex **4b** which bears two phenyl moieties at the heterocycle, maximum of 77 % conversion was reached. Decrease of the catalyst loading to 2 mol% resulted in an important detriment of the catalytic performance of complexes **4a** and **4b** (conversions of 90 and 70 %, respectively) whilst, the conversion under complex **4c** resulted unaffected (entry 6). Additional optimization trials unveil complex **4c** as the best of the series generating the coupling product in 97 % with loads of 1 mol%, at 80 °C and 6 h of reaction (entry 13).

Table 1. Optimization of the A^3 reaction under catalytic **4a-c**.
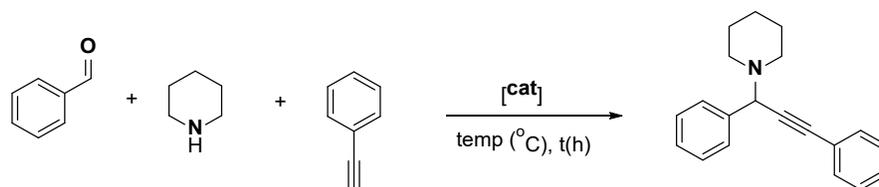
| Entry	Cat: (mol %)	Temp (°C)	Time (h)	Yield (%)^a
1	**4a** : 3.0	100	8	95
2	**4b** : 3.0	100	8	77
3	**4c** : 3.0	100	8	99
4	**4a** : 2.0	100	8	90
5	**4b** : 2.0	100	8	70
6	**4c** : 2.0	100	8	99
7	**4a** : 1.0	100	8	89
8	**4b** : 1.0	100	8	64
9	**4a** : 1.0	90	8	86
10	**4c** : 1.0	90	8	98
11	**4c** : 1.0	80	8	97
12	**4c** : 1.0	70	8	92
13	**4c** : 1.0	80	6	97
14	**4c** : 1.0	80	4	91
15	**4c** : 0.5	80	6	85

Reaction conditions: benzaldehyde (0.1 mmol), piperidine (0.11 mmol), phenylacetylene (0.12 mmol), catalyst (3 mol%). ^{a}Isolated yields as the average of two runs.

With the optimal conditions revealed, the preliminary reaction scope for the A^3 coupling (Fig. 1) shows that complex **4c** is capable of producing a variety of propargyl amines featuring substituted phenyl groups and a variety of amines (cyclic and linear) in excellent yields (91-97 %).
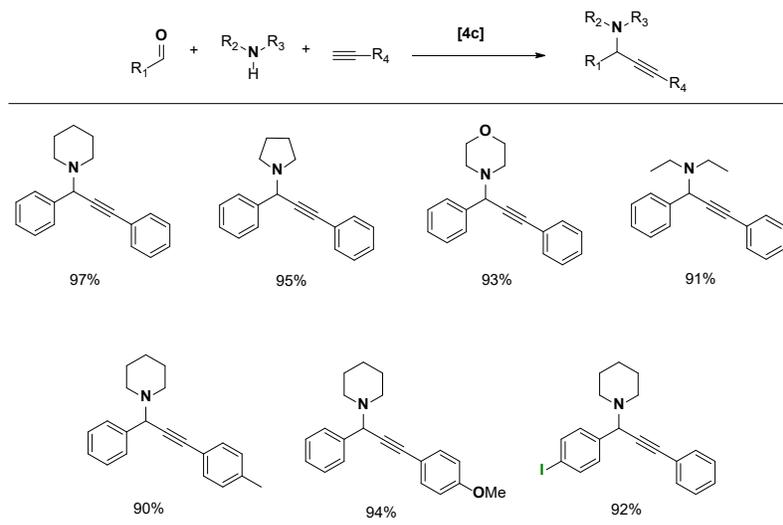
Fig. 1. Scope of the A^3 reaction catalyzed by **4c**. Reaction conditions: aldehyde (0.1 mmol), amine (0.11 mmol), alkyne (0.12 mmol), catalyst (1.0 mol%), 6h at 80ºC. Isolated yields as the average of two runs.
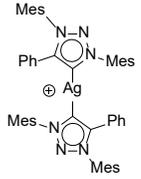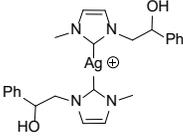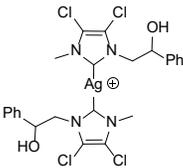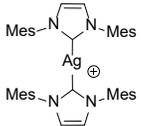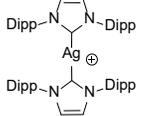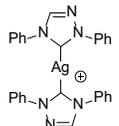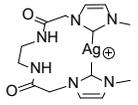
In order to get more insight into the catalytic behavior of complex **4c**, the catalytic profile for the reaction of benzaldehyde, piperidine and phenylacetylene was carried out under the optimized reaction conditions (Table 1, entry 13). As illustrated in Fig. 2, complex **4c** reach conversions higher than 60% after only 3 hours of reaction. The maximum conversion is observed at 6 h (97%) with no further change after time progresses.
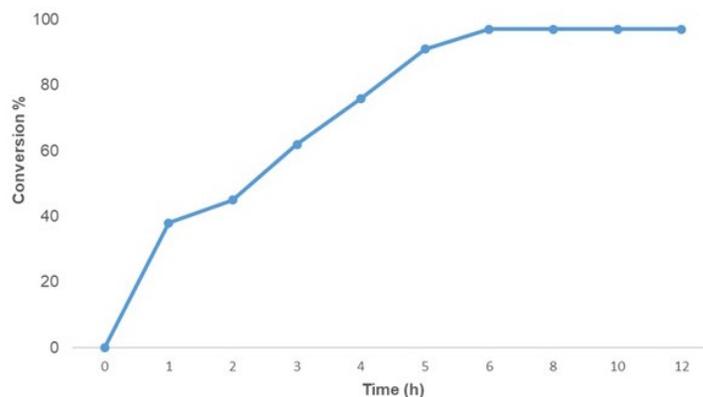
Fig. 2. Performance of complex **4c** in the A^3 coupling of benzaldehyde, piperidine and phenylacetylene under the optimal catalytic conditions.

Table 2 shows the performance of complex **4c** in the A^3 process (benzaldehyde, piperidine and phenylacetylene) compared with recently reported bis(NHC)-silver-based catalysts. In general, complex **4c** shows better performance in terms of catalyst loading, reaction temperature, and conversion to products compared to homoleptic biscarbene-silver complexes supported on imidazolylidene and 1,2,4-triazolylidene scaffolds.[26,27] Interestingly, complex **4c** display a similar catalytic performance as the registered for the highly active homoleptic chelating NHC silver(I) complex reported by Rycek and cowrokers.[28]

Table 2. Comparison of **4c** with recently reported bis(NHC)-based A^3 coupling catalysts.

Catalyst	mol(%)	Temp (°C)	Time (h)	Conv. (%)	Ref
	1.0	80	6 h	97	This work
	3.0	80	6 h	13	[26]
	3.0	80	6 h	38	[26]
	3.0	110	1 h	55	[27]
	3.0	110	1h	81	[27]
	3.0	110	1h	12	[27]
	1.0	80	5 h	92	[28]

Motivated by the good results obtained in the A^3 process, we decided to tests the potential of complexes **4a-c** in the KA^2 (ketone, alkyne, amine) coupling which usually require of harder conditions for delivering satisfactory results. With the target of optimizing the catalytic conditions, we started our investigation of the KA^2 process with the equimolar treatment of cyclohexanone, pyrrolidine and phenylacetylene as a model reaction. Thus, employing 5 mol% loading of complexes **4a-c** at 110°C under neat conditions (for 8 h), we can observe that once again complexes **4a** and **4c** are the most efficient catalysts with conversions above 95 % (Table 3, entries 1-3).

Table 3. Optimization of the KA^2 reaction under catalytic **4a-c**.
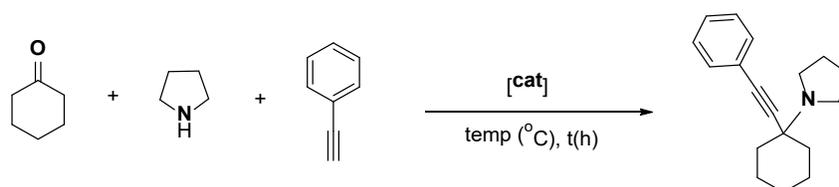
Entry	Cat: (mol %)	Solvent	Temp (°C)	Time (h)	Yield (%)[a]
1	**1** : 5.0	-----	110	8	95
2	**2** : 5.0	-----	110	8	81
3	**3** : 5.0	-----	110	8	99
4	**1** : 3.0	-----	110	8	91
5	**3** : 3.0	-----	110	8	98
6	**1** : 2.0	-----	110	8	66
7	**3** : 2.0	-----	110	8	74
8	**1** : 3.0	-----	100	8	91
9	**3** : 3.0	-----	100	8	98
10	**1** : 3.0	-----	90	8	85
11	**3** : 3.0	-----	90	8	98
12	**3** : 3.0	-----	80	8	91
13	**3** : 3.0	THF	90	8	73
14	**3** : 3.0	MeCN	90	8	58
15	**3** : 3.0	Toluene	90	8	62
16	**3** : 3.0	-----	90	6	87
17	-----	-----	90	8	NR

Reaction conditions: Cyclohexanone (0.1 mmol), pyrrolidine (0.1 mmol), phenylacetylene (0.1 mmol), catalyst (**4a-c**). [a]Isolated yields as the average of two runs.

Further exploration demonstrates that the loading of complex **4c** can be reduced to 3 mol% at 90 °C without significant loss in the conversion (98 %). Under the same conditions, complex **4a** reduced its efficiency to 85 % yield (entry 10). Addition of solvent to the process or temperatures below 90 °C resulted in significant reduction of the yields while, the absence of the catalyst shows only unreacted starting materials (entry 17).

Once the optimal catalytic conditions were set, we proceeded to the investigation of the reaction scope employing a variety of ketones, amines and alkynes. As depicted in Table 4, the KA^2 process under catalytic **4c** works competently with several aromatic alkynes containing electron-donor and electron-withdrawing substituents with yields in the range of 89-98 % (entries 1-4). Additionally, the coupling proved effective using the aliphatic 1-octyne reaching a maximum yield of 92 %.

The coupling was also successful employing linear and cyclic ketones with yields between 90-94 % (entries 6-8) however, the use of acetophenone and 4-chloroacetophenone resulted more challenging with maximum yields of only 77 % (entries 9-10). To complete the reaction scope, several primary and secondary amines were tested observing a best performance with the primary amines (either aromatic or aliphatic) with yields between 80-93 %. In the case of the less reactive secondary amines, the lowest yield was recorded for the N-methylcyclohexyl derivative (72 %).

The full catalytic data indicates that complex **4c** performs slightly better than the homoleptic chelating NHC silver(I) complex reported by the group of Rycek [29] where 2.5 mol% of catalyst loading and a temperature above 110 °C is necessary for optimal conversions. However, complex **3** is still behind the heteroleptic [(NHC]Ag(MIC)]PF$_6$ complex reported by our group[30] where only 1.0 mol% of catalyst loading is required for the coupling reaction. It is worth mentioning that up to now, complex **4c,** the Rycek derivative and [(NHC]Ag(MIC)]PF$_6$, are the only known examples of bis(carbene)-silver(I) complexes successfully applied in the KA^2 process.

Table 4. KA^2 reaction scope under catalytic **4c**.
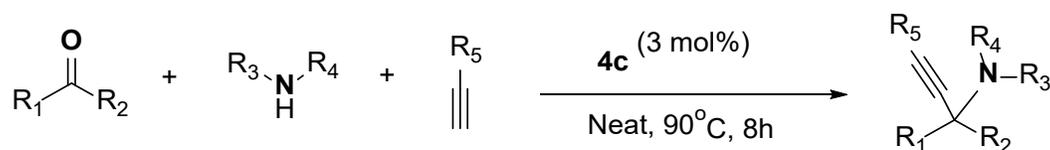
| Entry	Ketone	Amine	Alkyne	Yield(%)*
1				98
2				95
3				94
4				89
5				92
6				94
7				90
8				93
9				71
10				77

11				85
12				82
13				93
14				72
15				90

Reaction conditions: ketone (0.1 mmol), amine (0.1 mmol), alkyne (0.1 mmol), **3** (3 mol%), 90 °C, 8 h. [a]Isolated yields as the average of two runs.

Based on literature reports,[26] a plausible reaction mechanism for the KA^2 process under catalytic **4c** is depicted in Scheme 3. After the initial release of a MIC unit from complex **4c**, the cationic species **I** being highly electrophilic, forms a π-complex with the triple bond of the alkyne (**II**), form which the metal acetylide **III** is generated with the assistance of the amine. Concomitantly, the amine condenses with the carbonyl derivative to generate a ketiminium cation and a water molecule. Subsequently, the nucleophilic metal acetylide attacks the ketiminium cation, forming the propargylamine and regenerating the active catalyst.
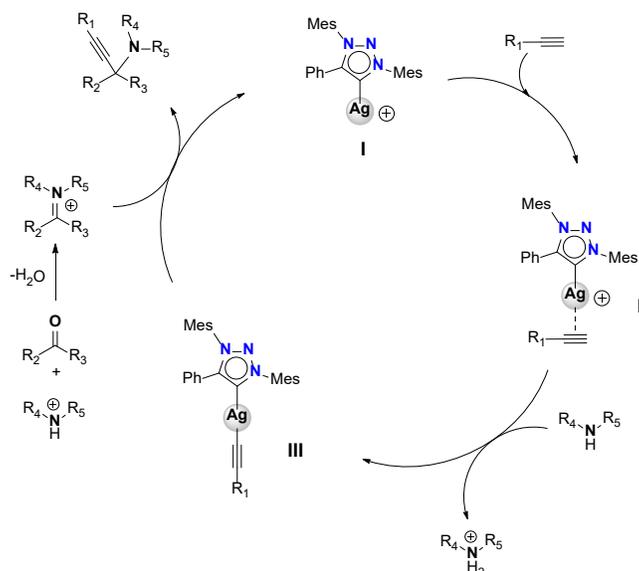
Scheme 3. Proposed catalytic cycle for the KA^2 process catalyzed by complex **4c**.

Conclusions

We have reported the expedient synthesis of a series of air and moisture stable bis(MIC) silver complexes (**4a-c**) with the general formula [(MIC)$_2$Ag]PF$_6$. The bis(triazol-5-ylidene) silver complexes were active in the A^3 coupling of a variety of aldehydes, amines, and alkynes under low catalyst loadings (1 mol%). Furthermore, the silver complexes demonstrated good performance in the KA^2 coupling process under neat

conditions with excellent tolerance to various substitution patterns in the coupling partners (ketones, alkynes and amines). The overall catalytic data indicate that derivative **4c** delivers the best performance of the series in both coupling processes. The superior catalytic capability of **4c** may be related to its enhanced steric protection (provided by three aryl groups in the heterocyclic ring) which results in more stable and long lasting catalytic active species.

Additional exploration on the catalytic applications of complexes **4a-c** is under current development in our research group.

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