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Synthesis and structures of gold and copper carbene intermediates in catalytic amination of alkynes

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Metal carbenes are often proposed as reactive intermediates in the late transition metal-catalysed transformations of alkynes. Owing to their high reactivity, however, isolation and structural characterization of metal carbene intermediates in these transformations has remained unknown. Herein, we report the isolation of two acyclic gold and copper carbene intermediates in either Au(I)- or Cu(I)-catalysed cyclization of *N*-alkynyl formamides through five-*exo*-dig cyclization. X-ray diffraction, ¹³C NMR spectra data and computational analyses provide evidence for the formation of a gold carbene intermediate with a carbocation-like electronic character. Using the intrinsic bond orbital (IBO) approach, we also evaluate the π -stabilizing effects of organic substituents at the carbene carbon atom in the gold carbene intermediate. Another rare six-membered copper carbene complex is also obtained through 6-*endo*-dig cyclization. These metal carbenes have proven reactive toward oxidation. The metal-promoted cyclization of *N*-alkynyl formamide provides a facile approach to synthesize metal carbene species.

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Late transition metal carbenes are widely proposed as active intermediate in many catalytic reactions^{1–5}, and the most common metal carbenes are those prepared by decomposition of an appropriate diazo compound (Fig. 1a)^{3–5}. The addition of nucleophilic agents to alkynes catalysed by late transition metals are of profound significance due to their high selectivity and mild conditions and has been investigated extensively for the synthesis of a variety of heterocycles and complex molecules^{6–8}. Metal carbenes, in many cases converted from vinyl metal species, are often proposed as key intermediate in these transformations^{9,10}. In the past 15 years, the transition-metal-catalysed cycloisomerization of ene-yne-ketones has been well established, and provides a safe, effective and practical alternative to the diazo decomposition route for metal carbene generation^{11–23}. In the transformations, the metal π -activated alkyne is attacked by the carbonyl oxygen through 5-*exo*-dig cyclization to generate zwitterionic vinyl metal intermediate **A** that could be transformed into its resonance structure, metal (2-furyl)carbene intermediate **B** (Fig. 1b, M = Cu^{19,22}, Au^{18,23}, Rh^{13,15}, Zn^{17,18} and Pd^{20,21}). Metal carbene **B** subsequently undergoes a variety of transformations, such as oxidation, C-H insertion, cyclopropanation and heteroatom (N, O, Si, S)-H insertion reaction^{11–23}. Recently, the groups of Zhang¹⁸ and Jiang¹⁹ reported that both Au(I) and Cu(I) (2-furyl)carbenes (**B** with M = Au(I) or Cu(I)) can undergo carbene oxidation to give 2-acylfurans (Fig. 1b). Like **B**, both Cu(I)-stabilized indazolylcarbene **C** reported by Haley group^{24–26} and Au(I) imidazopyridinylcarbene **D** reported by Cao group²⁷ can also trap molecular oxygen to generate the corresponding 3-acylindazole or 3-acylimidazo-pyridine product, respectively. Owing to their high reactivity, however, isolation and structural characterization of late transition metal carbene intermediates in catalytic transformation of alkynes has remained unknown; information regarding the property of the metal carbene intermediates is limited to *in situ* NMR study and computational analysis^{28,29}. Structurally characterized copper

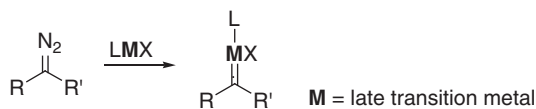
carbenes have been prepared only by either decomposition of the diazo precursors with various copper sources^{30–33} or carbene transfer from chromium complex³⁴. On the other hand, several groups have successfully isolated a variety of structurally characterized gold carbenes^{35–45}, but there remains an ongoing debate on the extent of the electronic character of gold carbenes as either carbene-like with a strong gold-to-carbon π -backbonding or carbocation-like with a weak π -backbonding^{46–55}. Therefore, structurally characterized copper and gold carbenes, especially those involved in catalytic transformations, are highly desired for a clear understanding of the nature of gold carbenes and their essential role in the catalytic cycle.

As part of our long-standing interest in the design and synthesis of *N*-heterocyclic carbenes (NHCs) and abnormal NHC for catalysis, we previously reported the isolation of a rare vinyl silver species through 6-*endo*-dig cyclization of a formamidine with a σ,π -silver-activated terminal alkyne⁵⁶. Herein, we first report the isolation and characterization of gold and copper carbene intermediates, **E'** (M = Au(I) or Cu(I)), in either Au(I) or Cu(I)-catalysed cyclization oxidation of formamidines with an internal alkyne through 5-*exo*-dig cyclization (Fig. 1c). In the presence of base, Cu(I)-promoted amination of a formamidine with a terminal alkyne leads to form a 6-membered copper carbene through 6-*endo*-dig cyclization. The carbene oxidation reaction of these metal carbene species are directly observed. The detailed structural and spectroscopic studies and computational analysis outline the nature of the gold and copper carbenes.

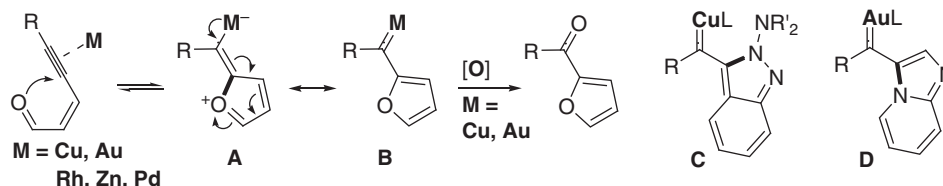
Results

Isolation of active copper carbene intermediates. First, phenyl-substituted formamidine **1** was initially examined in the amination cyclization (Fig. 2a). In the presence of a stoichiometric amount of IPrCuOTf (IPr = 2,6-bis(diisopropyl-phenyl)imidazol-2-ylidene), **1** underwent 5-*exo*-dig cyclization to form

a Known late transition metal carbenes



b Proposed late transition metal carbenes



c This work: Isolable gold and copper carbene intermediates

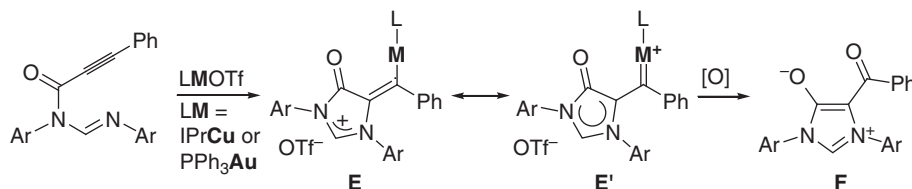


Figure 1 | Selected metal carbene species involved in late transition metal-mediated transformations. (a) Late transition metal carbenes generated by decomposition of the diazo precursors. (b) Proposed late transition metal carbenes in catalytic cycloisomerization of alkynes. (c) Gold and copper carbene intermediates isolated in gold- and copper-catalysed cyclization of *N*-alkynyl formamidines.

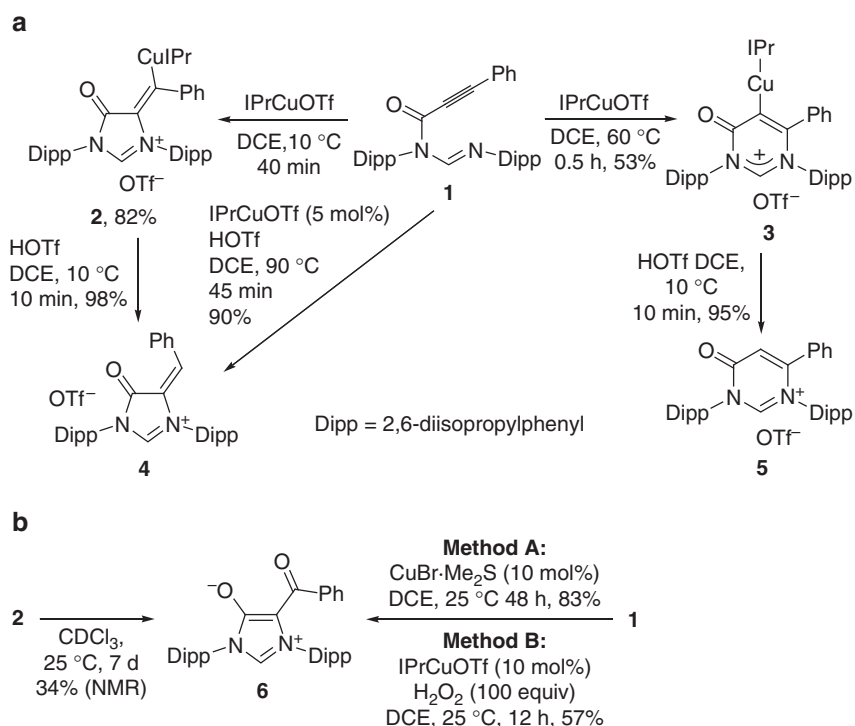


Figure 2 | Cu-mediated cyclization of *N*-alkynyl formamide. (a) Cu-promoted amidinium formation of *N*-alkynyl formamide **1**. **(b)** Cu-catalysed cyclization oxidation of *N*-alkynyl formamide **1** and transformation of copper intermediate **2** into compound **6**.

a 5-membered vinylcopper species **2** at 10 °C in 82% yield, while raising the reaction temperature to 60 °C resulted in 6-endo-dig cyclization to afford a 6-membered vinylcopper species **3** in 53% isolated yield. Hydrolysis of either **2** or **3** with HOTf gave the corresponding cyclic formamidinium salt **4** or **5**, respectively. In the presence of a catalytic amount of IPrCuOTf and one equivalent of trifluoromethanesulfonic acid (HOTf), the cyclization of the protonated formamide **1** was required at elevated temperature to achieve a good yield (90%), forming a 5-membered product **4**. The structures of **4** and **5** were confirmed by X-ray diffraction analysis (see Supplementary Figs 26 and 27).

The Cu-mediated cyclization of formamide **1** seems to be kinetic versus thermodynamic control reaction. However, attempt to form **3** by heating **2** failed. Vinylcopper species **2** has proven stable only in the solid state at room temperature, and is quite sensitive to oxidation in solution. The formation of a zwitterionic compound **6** was observed from the CDCl₃ solution of **2** on standing 1 week (Fig. 2b). Compound **6** represents a zwitterionic precursor for a kind of hybrid ambidentate NHC ligand decorating the classical imidazol-2-ylidene with an acetylacetonato unit⁵⁷. Further investigation showed **6** can also be directly obtained via cyclization of **1** using a catalytic amount of IPrCuOTf and H₂O₂ as oxidant at 25 °C in 57% isolated yield. When using CuBr·Me₂S (10 mol%) as catalyst, **6** could be formed in air with a considerable yield (83%). The structure of **6** was confirmed by X-ray crystallography (Fig. 3a), showing it contains a conjugated backbone of alternating single and double bonds of type O1–C2 = C3–C16 = O2 as evidenced by comparison of bond distances within the acac backbone.

The transformation of either vinylcopper species **2** or alkynyl formamide **1** into **6** is reminiscent of the observation of the carbene oxidation products of both copper (2-furyl)carbene **B** (M = Cu)¹⁹ and copper pyrazolylcarbene **C**^{24–26} in the Cu-catalysed cyclization of alkynes (Fig. 1b). Based on the observations, the transformation of **2** into **6** would be better

described as a copper carbene oxidation reaction (Fig. 2b). The ¹³C NMR analysis of **2** exhibits one signal for the carbene carbon at $\delta = 211.4$ p.p.m., which is similar to the imidophosphamidato copper α -carbonyl carbene signal at $\delta = 219.0$ p.p.m.³², upfield of that for the diketiminato copper carbene ($\delta = 253.1$ p.p.m.)³¹, and fall into the approximate range of 200–400 p.p.m. established for the very deshielded terminal carbene complexes⁵⁸. It is more deshielded than the carbene signal of IPr moiety in **2** at 181.9 p.p.m. The observation verifies the presence of an electrophilic carbene in **2**. Vinylcopper **3** is quite stable in solvent and substantially inert to oxidation. The **3** is colourless, and copper carbene **2** is purple. Similarly, both imidophosphamidato copper α -carbonyl carbenes^{30,32} and diketiminato copper carbene complexes³¹ are all violet or purple. It indicates that the presence of a β -carbonyl in **2** is crucial for generating a copper carbene intermediate.

After massive attempts to isolate single crystals of **2** failed, we managed to obtain a single crystal of its IPr⁺ counterpart copper carbene **7** suitable for X-ray diffraction analysis (Figs 3b and 4a). Copper carbene **7** was prepared as a wine red solid from the cyclization of **1** in the presence of one equivalent of IPr⁺CuNTf₂, which could also catalyse the transformation of **1** into **6**. The direct oxidation of **7** to form **6** was also observed in an oxygen atmosphere. In complex **7**, the C–O bond distance of 1.207(7) Å is characteristic for a C=O double bond. The imidazol-4-one ring in **7** is essentially planar, indicating charge delocalization. The observation suggests the imidazol-4-one ring in **7** could be regarded as a mesoionic imidazolium-4-olate (Fig. 4b). The related mesoionic compounds have been known for several decades, and a similar 1,2,3-triazolium-4-olate compound **G** was reported by Albrecht and co-workers⁵⁹. Therefore, copper complex **7** could be described as a copper carbene complex **7'** bearing a mesoionic imidazolium-4-olate ring. The Cu1–C1 bond (1.924(6) Å) in **7** is similar to that (1.882(3) Å) for a three-coordinate cationic copper carbene

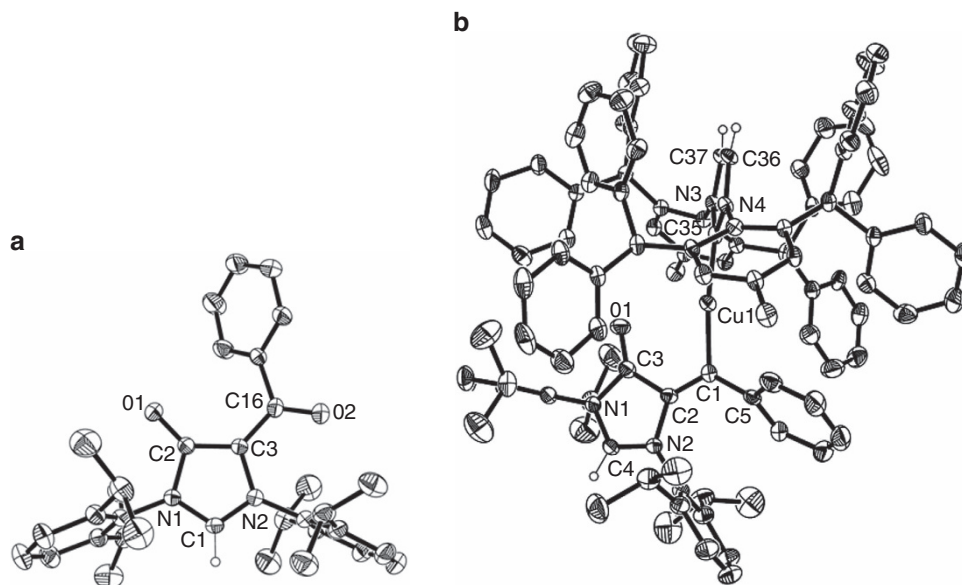


Figure 3 | Molecular structure of 6 and 7. (a) Molecular structure of **6** with 20% probability. H atoms in aryl rings have been omitted for clarity. (b) Molecular structure of **7** · CH₂Cl₂ with 20% probability. The counterion (NTf₂⁻) and CH₂Cl₂ in **7** and H atoms in aryl rings have been omitted for clarity.

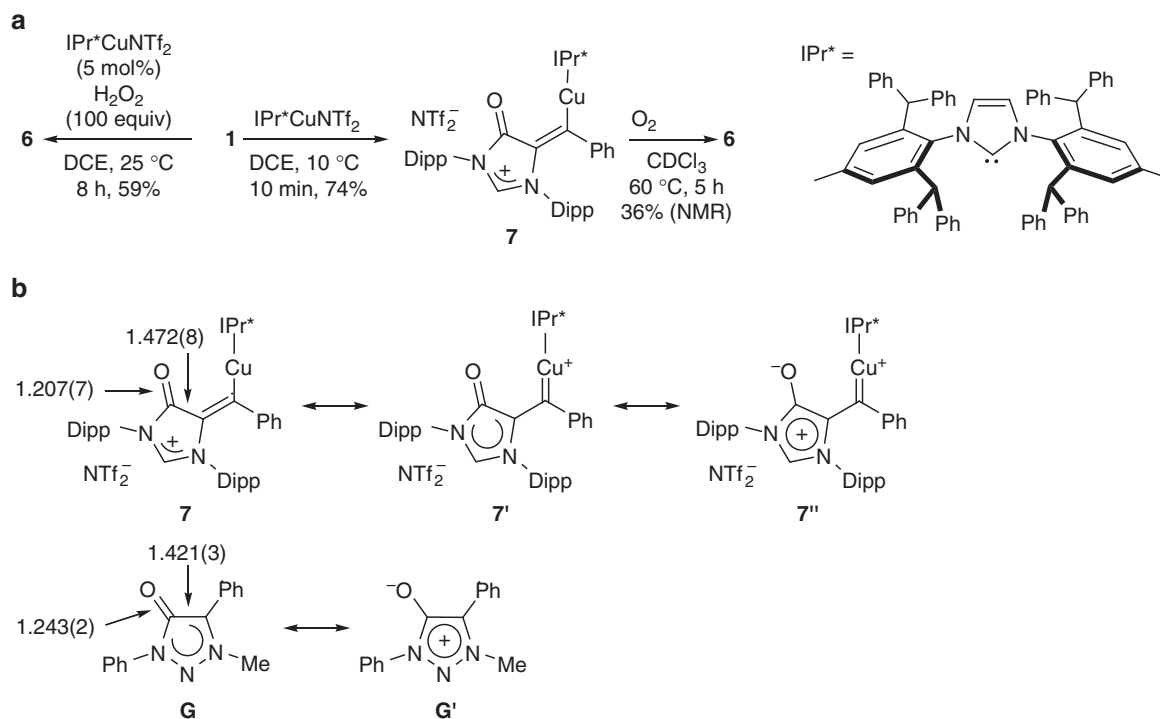


Figure 4 | Formation of compound 6 and copper carbene 7 and related mesoionic compound G. (a) IPr^{*}CuNTf₂-catalysed cyclization oxidation of formamidine **1** and related copper carbene **7**. (b) Copper carbene complex **7** bearing mesoionic imidazolium-4-olate ring and related mesoionic 1,2,3-triazolium-4-olate **G**.

[Cu{=CR¹(OR²)}(MeCN)(OEt₂)]⁺ (R¹ = (*E*)-CH=CH-2-furyl; R² = menthyl)³⁴, and longer than those (1.822–1.834 Å) observed for the copper carbenes obtained from either diphenyldiazomethane or α -carbonyl diazo compounds^{30–33}. The imidazolium-4-olate ring in **7** is nearly co-planar with the carbene centre, and the neighbouring phenyl ring is tilted with a slightly contracted bond (1.470(8) Å) between the carbene centre and the C_{ipso}(Ph) carbon.

Isolation of active gold carbene intermediate. Since gold carbenes are also reactive towards carbene oxidation^{16,27}, we further investigate gold-catalysed cyclization oxidation of **1**. Delightfully, in the presence of a catalytic amount of PPh₃AuOTf (10 mol%) and using H₂O₂ as oxidant, **6** could be obtained in 43% yield (Fig. 5a). Treatment of a stoichiometric amount of PPh₃AuOTf with **1** offered gold carbene **8** as a yellow solid in 60% yield. In the presence of H₂O₂, **8** underwent oxidation to give

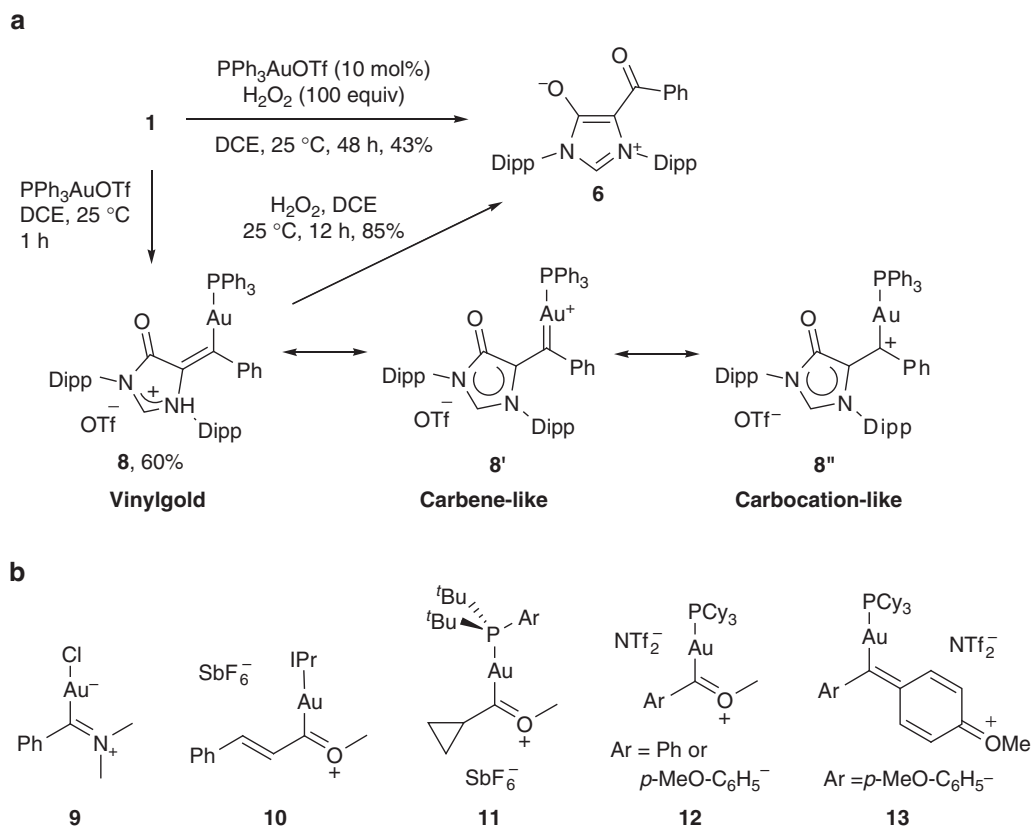


Figure 5 | Preparation of gold carbene **8 and related heteroatom-stabilized gold carbenes **9–13**.** (a) Au-catalysed cyclization oxidation of *N*-alkynyl formamidine **1** and gold carbene intermediate **8**. (b) Heteroatom-stabilized gold carbenes **9–13**.

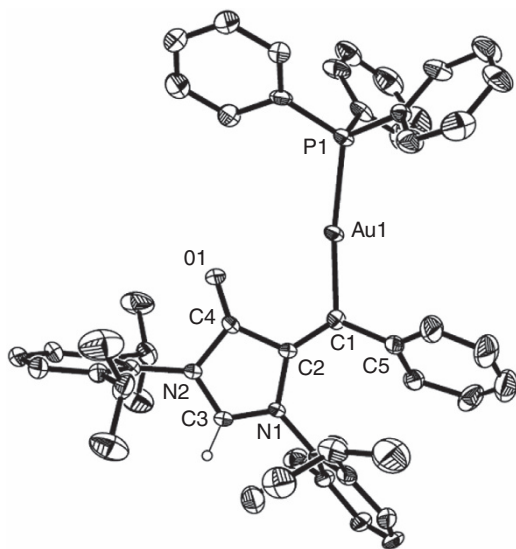


Figure 6 | Molecular structure of **8 with 20% probability.** The counterion (OTf^-) and H atoms in aryl rings have been omitted for clarity.

6 in 85% yield. The carbene carbon of **8** in the $^{13}\text{C}\{^1\text{H}\}$ NMR spectra appears as a doublet at $\delta = 208.6$ p.p.m. ($J_{\text{CP}} = 103.0$ Hz), which is upfield of the carbene carbon resonance of those known gold carbene complexes ($\delta = 225 \sim 321$ p.p.m.)^{35–44}, and downfield of that for IPrAuCl ($\delta = 175.1$ p.p.m.)⁶⁰. The formation of **8** was unequivocally confirmed by X-ray crystallography (Fig. 6). Recently, several groups have reported the isolation of gold carbene complexes **9** (ref. 42), **10** (ref. 41),

11 (ref. 37), **12** (refs 35,36) and **13** (ref. 35), which could be stabilized by π conjugation of the electrodeficient carbene centre with heteroatoms (Fig. 5b). The Au1–C1 bond (2.044(9) Å) in **8** is similar with those found in the gold carbene complexes **12** and **13** (2.039–2.046 Å)^{35,36}, and longer than those in gold carbene complexes **9–11** (2.010–2.032 Å)^{37,41,42} and non-heteroatom- but diaryl-stabilized gold carbene complexes (1.984(4)–2.014(6) Å)^{38,40}. Like **7**, the mesoionic imidazolium-4-olate ring in **8** is nearly co-planar with the carbene centre, which enables efficient π -orbital overlap.

DFT computation and IBO analysis on gold carbene intermediate. Similar to their copper counterparts, structurally characterized gold carbenes have been mainly prepared by either decomposition of the diazo precursors with various gold sources or carbene transfer from chromium complexes^{35–45}. Isolation and structural characterization of gold carbene intermediates generated from the addition of nucleophilic agents to C–C multiple bonds remains very rare. In 2008, the Hammond group⁶¹ reported the spectroscopic detection of a gold carbene/oxonium complex **14** in the gold-mediated cyclization of allenolate and later the Hashmi group⁶² isolated the gold carbene intermediates of type **14** and carried out density functional theory (DFT) calculation to study the bonding properties (Fig. 7). Very recently, Mouries-Mansuy, Fensterbank and colleagues⁶³ isolated and structurally characterized a related gold carbene **15** in the gold-mediated cyclization of pyridyl-allene.

The Au–C bond distance of 1.984(2) Å for **15** with a chloride ligand is shorter than that (2.049(9) Å) for **8**, and is in the low range of those known gold carbenes^{35–45} (Fig. 7). It should be noted that, in contrast to π -acidic phosphine ligand, the π -donating chloride ligand could increase gold-to-carbon

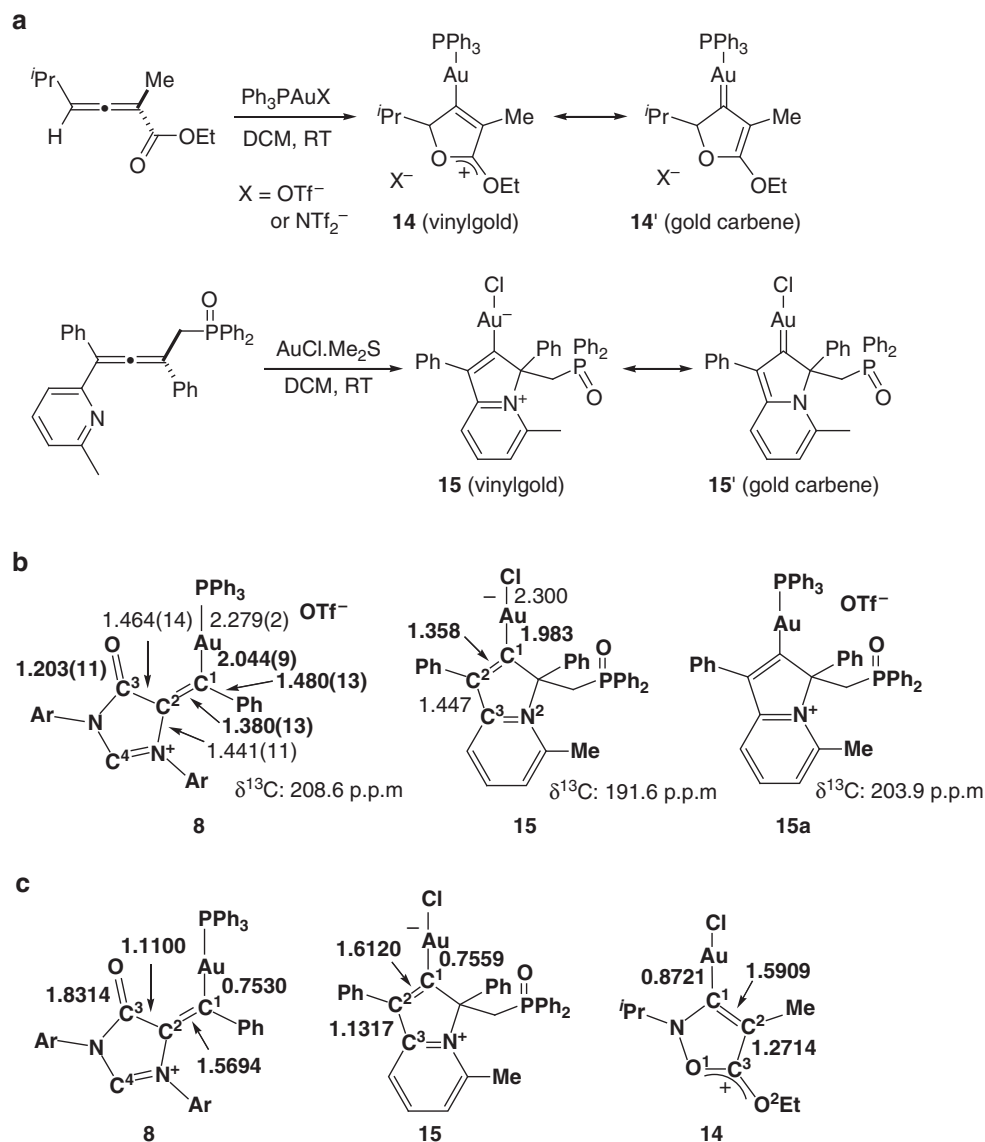


Figure 7 | Known gold carbene complexes 14 and 15 and comparison of them with gold carbene 8. (a) Previously reported gold carbene complexes **14** (top) and **15** (bottom) prepared through gold-mediated cyclization of allenes. **(b)** Comparison of related bond lengths and characteristic NMR spectroscopic data of complex **8** with those of reference complexes **15** and **15a**; see ref. 63. **(c)** Comparison of Mayer bond order of complex **8** with those of reference complexes **14** and **15**; see refs 63 and 62.

π bonding, resulting in a short Au–C bond⁴⁷. The gold carbene signal of a related PPh_3 -ligated gold carbene **15a** in the $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum appears at $\delta = 203.9$ p.p.m.⁶³, which is similar to that for **8**.

Next, we performed DFT calculations to get more insight into the bonding property in **8**. All the DFT calculations were performed using Gaussian 09 suite of program. The TPSS functional with Grimme's D3-BJ correction for van der Waals interaction was utilized in combination with the triple- ζ basis set def2-TZVPP (see Supplementary Methods for more details). The optimized geometry parameters of **8** are in line with the experimental results. Based on the Mayer bond order analysis (Fig. 7), partial single bond for C^2 – C^1 can be formulated in the vinylgold complex **8**. Similar bonding scenario was also observed for the related gold complexes **15** (ref. 63) and **14** (ref. 62).

The intrinsic bond orbital (IBO) analysis is a novel method to analyse chemical bonding. The IBOs mainly depict occupied orbitals in an intuitive way, assigning proportionally the electrons

in the doubly occupied IBOs to the individual atoms and allowing quantitative interpretation of chemical bonding. Quite recently, using DFT and the IBO approach, Hashmi, Kästner and colleagues^{49,50} evaluated the π -stabilizing effects of organic substituents at the carbene carbon atom in several recently isolated and characterized gold carbene complexes, and the observations by the IBO method are consistent with the previously proposed bonding scenario for the gold carbene species. Therefore, we further carried out the IBO approach to study the π -stabilizing effects of organic substituents in gold intermediate **8**.

As depicted in Fig. 8, we identified a strong π -stabilization in **8**, which is mainly achieved through the π system of the imidazolium-4-olate ring attached to C^1 (Fig. 8d). Additionally, small contribution from the phenyl ring attached to C^1 was also identified. The phenyl ring is polarized towards C^1 (Fig. 8b), forming the delocalized π bonding with C^1 . In addition, the IBO of coordinative bond between the lone pair of carbene C^1 and the gold atom was identified (Fig. 8a) since this IBO is

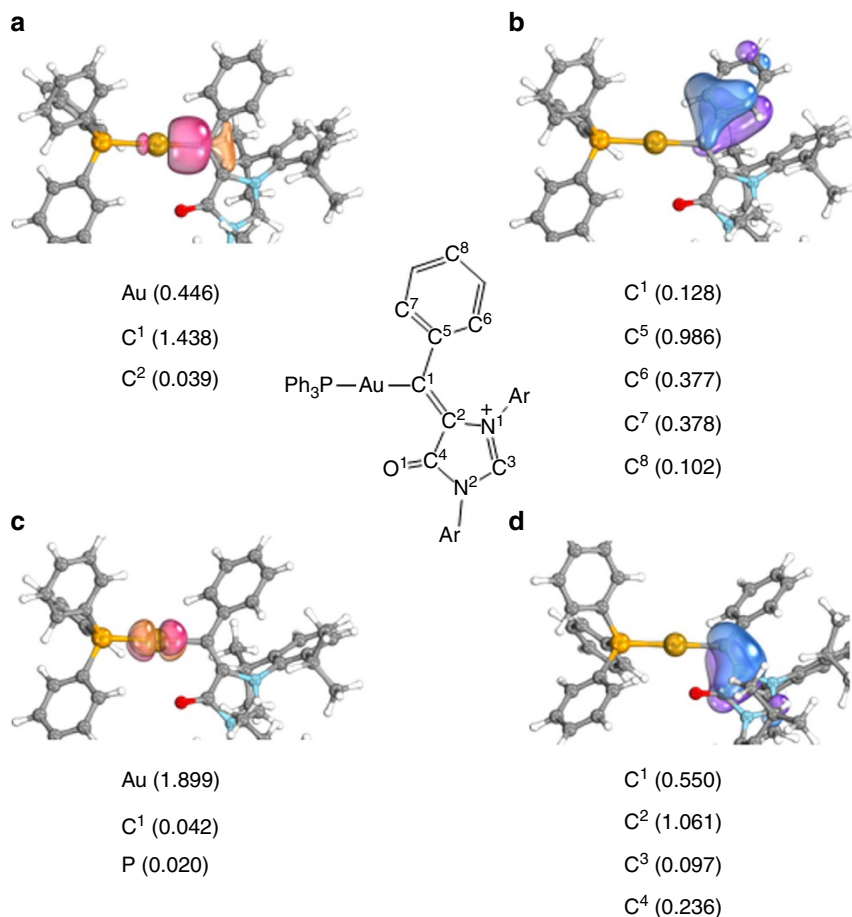


Figure 8 | C¹-stabilizing IBOs of gold complex **8.** Numbers in parentheses indicate the fraction of electrons of the doubly occupied orbital assigned to the individual atoms. **(a)** Coordinative bond between the lone pair electrons of C¹ and Au. **(b)** Delocalized π bond between C¹ and phenyl ring. **(c)** d- π backbond between Au and C¹. **(d)** Delocalized π bond between C¹ and imidazolium-4-olate ring.

mainly located at C¹. The IBO representing the filled d orbital at gold aligned for π backbonding was also identified but it is largely located at gold atom up to 96.8% (Fig. 8c), suggesting little contribution to stabilize carbenic C¹. Therefore, gold carbene intermediate **8** should be better described as gold- and heteroatom-stabilized carbocation **8''** (Fig. 5).

Very recently, we isolated a related vinylgold complex **16** prepared by reacting IPrAuOTf with a formamidine bearing a terminal alkyne moiety⁵⁶, which could undergo protodeauration to afford a bis(hydroxyimidazolium) salt (Supplementary Fig. 22). Different from gold carbene **8**, **16** is quite stable in air, while treatment of **16** with excess H₂O₂ resulted in complex reaction mixtures without clear product identified. We also reported a PPh₃ counterpart of **16**, which is prone to undergo aurophilicity to form a vinyl *gem*-digold species⁶⁴. The observations suggest besides the imidazolium-4-olate ring, a phenyl substituent bonding to the carbenic carbon, is also important to stabilize gold carbene **8**. The differences in reactivity between gold species **8** and **16** may possibly imply the gradation in character from carbene to vinylgold species.

Isolation of six-member copper carbene species. In a stoichiometric AgOTf-promoted cyclization of formamidine **17** bearing a terminal alkyne, we previously revealed that presence of a base can preclude the protonation of imino moiety by HOTf, thus changing cyclization fashion⁵⁶. Moreover, Hashmi *et al.*^{65,66} also reported that addition of a base can slow down the protodemetalation to conserve organometal species.

The observations inspired us to investigate the influence of base in the copper-promoted amidiniumation of **17**. Delightfully, treatment of **17** with CuBr·Me₂S in the presence of N(Pr)₂Et as a base afforded a 6-membered vinylcopper species **18** as a yellow solid in a 6-*endo*-dig cyclization fashion (Fig. 9). Treatment of **18** with AgOTf in the presence of PPh₃ resulted in the formation of a divinylcopper species **19** as a yellow solid, the structure of which was confirmed by X-ray crystallography (Fig. 10). The Cu–C bond (1.870(9) Å) in **19** is shorter than that (1.924(6) Å) for copper carbene **7**. In addition, the Cu–C distance in **19** is shorter than those for IPrCuCl (1.953(8) Å)⁶⁷, and the related (IPr₂Cu)⁺BF₄[−] (1.926(19) Å, 1.938(18) Å)⁶⁸, and similar to those for either mesoionic NHC imidazol-5-ylidene copper complex (1.871(7) Å)⁶⁹, or abnormal NHC triazol-5-ylidene copper complex (1.876(4) Å)⁶⁹. In the ¹³C{¹H} NMR spectra, the carbene carbon resonates at $\delta = 194.5$ p.p.m. for **18** and $\delta = 193.7$ p.p.m. for **19** are similar to the lower range of those established for terminal carbenes ($\delta = 200$ –400 p.p.m.)⁵⁸, and downfield of those for imidazol-5-ylidene copper complex ($\delta = 159.5$ p.p.m.) and triazol-5-ylidene copper complex ($\delta = 166.4$ p.p.m.)⁶⁹. Interestingly, similar to the five-membered copper carbene complex **2**, **18** is also found to be reactive towards oxidation in solution. A zwitterionic oxo-adduct **20** was isolated from the DCE solution of **18** on stirring for 1 day, indicating that vinylcopper species **18** is more like a copper carbene complex **18'**, which also contains a β -carbonyl. Therefore, we speculate that the reason why the six-membered vinylcopper **3** does not react as a copper carbene is largely because of the presence of an

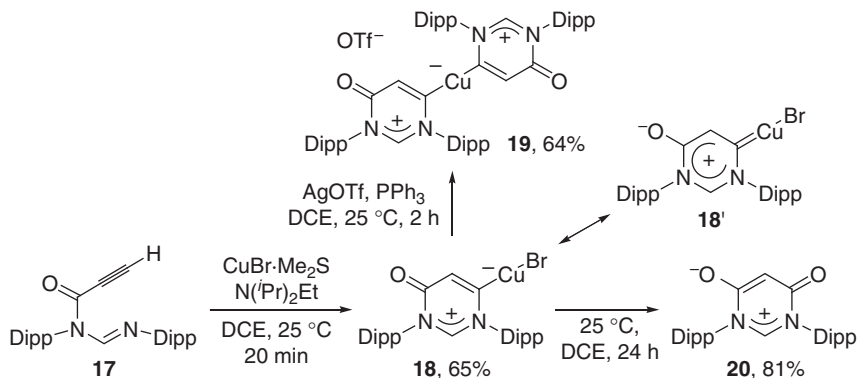


Figure 9 | Cu-activated amidinium of formamidine 17 having a terminal alkyne in the presence of a base. CuBr-mediated cyclization of formamidine 17 in the presence of $N(iPr)_2Et$ as a base afforded a 6-membered vinylcopper species 18, which could be transformed into a divinylcopper species 19. Vinylcopper 18 is prone to undergo carbene oxidation to give a zwitterionic oxo-adduct 20, suggesting that 18 is more like a copper carbene species 18'.

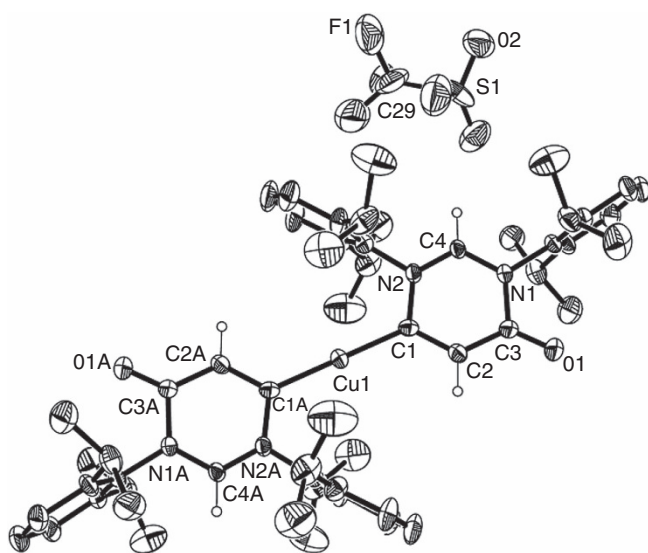


Figure 10 | Molecular structure of 19 with 20% probability. H atoms in aryl rings have been omitted for clarity.

α -carbonyl instead of a β -carbonyl in 2 and 18. Zwitterionic compound 20 is known as a zwitterionic precursor for an amino-acrylamido carbene⁷⁰.

Discussion

We have developed both Au(I)- and Cu(I)-catalysed cyclization oxidation of *N*-propionic formamidines through 5-*exo*-dig cyclization. Key gold and copper carbene intermediates are isolated from the stoichiometric reaction, which were fully characterized. X-ray diffraction analysis and ¹³C NMR spectra data provide evidence for the formation of a gold carbene intermediate with a carbocation-like electronic character. Using DFT and the IBO approach, we evaluated the π -stabilizing effects of organic substituents at the carbene carbon atom in the gold carbene complex 8. In the presence of base, Cu(I)-promoted amidinium of the formamidine with a terminal alkyne leads to form a six-membered copper carbene through 6-*endo*-dig cyclization. The generation of these gold and copper carbene complexes is attributed to the presence of a β -carbonyl group, and their oxidation reactions are directly observed. The metal-promoted cyclization reaction of *N*-alkynyl formamidines

also provides a facile approach to synthesize metal carbene species, and our future efforts are directed at synthesizing other metal species by using the facile method.

Methods

General. Unless otherwise stated, all reactions and manipulations were performed using standard Schlenk techniques. All solvents were purified by distillation using standard methods. Commercially available reagents were used without further purification. NMR spectra were recorded by using a Bruker 400 MHz spectrometer. Chemical shifts are reported in p.p.m. from tetramethylsilane with the solvent resonance as the internal standard (¹H NMR CDCl₃: 7.26 p.p.m.; ¹³C NMR CDCl₃: 77.0 p.p.m.; ¹³C NMR DMSO: 39.43 p.p.m.). Synthetic procedures for compounds 1c, 2–6 and 18–20 are summarized in Supplementary Methods. For NMR analysis and X-ray structures of the compounds in this article, see Supplementary Figs 1–21. For more details, please see also Supplementary Methods.

Synthesis of copper carbene complex 7. The mixture of formamidine 1 (100 mg, 0.20 mmol) and IPr^*CuNTf_2 (205 mg, 0.20 mmol) was stirred in the 1,2-dichloroethane (DCE; 3 ml) at 10 °C for 30 min. All volatiles were removed under vacuum, and the rube product was washed twice with diethyl ether to afford pure 7 as a wine red solid (260 mg, 74%). ¹H NMR (400 MHz, CDCl₃) δ = 9.07 (s, 1H), 7.64 (t, J = 7.9 Hz, 1H), 7.40 (d, J = 7.9 Hz, 2H), 7.17–7.07 (m, 19H), 7.02–6.97 (m, 3H), 6.90–6.84 (m, 14H), 6.76 (d, J = 7.6 Hz, 7H), 6.71 (s, 4H), 6.45 (t, J = 6.8 Hz, 1H), 6.27 (t, J = 7.6 Hz, 2H), 5.80 (d, J = 7.6 Hz, 2H), 5.48 (s, 2H), 5.20 (s, 4H), 2.83–2.76 (m, 2H), 2.74–2.65 (m, 2H), 2.15 (s, 6H), 1.33 (d, J = 6.8 Hz, 6H), 1.27–1.18 (m, 12H), 1.13 (d, J = 6.8 Hz, 3H), 1.05 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ = 215.41, 181.18, 163.28, 151.88, 145.91, 144.13, 143.18, 142.38, 140.81, 140.19, 139.46, 134.48, 131.66, 129.99, 129.55, 129.43, 129.38, 129.18, 128.68, 128.43, 128.06, 126.79, 126.55, 126.24, 124.80, 124.57, 124.41, 124.24, 123.69, 29.79, 29.24, 26.00, 24.60, 23.66, 22.42, 21.99, 21.36; HRMS (MALDI): m/z [M-NTf₂]⁺ calcd. for C₁₀₃H₉₆CuN₄O⁺: 1467.6880; found: 1467.6895.

Synthesis of gold carbene complex 8. The mixture of PPh₃AuCl (99 mg, 0.20 mmol) and silver triflate (51 mg, 0.20 mmol) was stirred in the DCE (1.5 ml) at 25 °C for 15 min, and then the solid components were filtered off and the filtrate was added to the solution of 1 (100 mg, 0.20 mmol) in the DCE (1 ml). After stirring for 1 h at 25 °C, all volatiles were removed under vacuum. The rube product was washed twice with diethyl ether to afford pure 8 as a yellow solid (132 mg, 60%). ¹H NMR (400 MHz, CDCl₃) δ = 10.19 (s, 1H), 7.56–7.47 (m, 10H), 7.46–7.39 (m, 6H), 7.35 (d, J = 7.9 Hz, 3H), 6.96 (d, J = 7.9 Hz, 2H), 6.93–6.83 (m, 5H), 2.84–2.67 (m, 4H), 1.39–1.26 (m, 18H), 1.22 (d, J = 6.8 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ = 208.56 (d, ² J_{C-P} = 103.0 Hz), 162.98, 155.86, 145.75, 144.33, 140.93, 134.16, 131.66, 131.17, 129.60, 129.16, 127.12, 125.70, 125.27, 124.61, 124.21, 121.89, 29.62, 29.22, 25.96, 24.36, 23.62, 21.84; ³¹P NMR (162 MHz, CDCl₃) δ = 39.52; HRMS (MALDI): m/z [M-OTf]⁺ calcd. for C₅₂H₅₅AuN₂O⁺: 951.3718; found: 951.3699.

Data availability. The X-ray crystallographic coordinates for structures reported in this study have been deposited at the Cambridge Crystallographic Data Centre (CCDC), under deposition numbers CCDC 1418063 (4), CCDC 1418064 (5), CCDC 1449714 (6), CCDC 1470533 (7), CCDC 1470532 (8) and CCDC 1449046 (19). These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. All data are available from the authors on reasonable request.

References

- Trnka, T. M. & Grubbs, R. H. The development of $L_2X_2Ru=CHR$ olefin metathesis catalysts: an organometallic success story. *Acc. Chem. Res.* **34**, 18–29 (2001).
- Jiménez-Núñez, E. & Echavarren, A. M. Gold-catalyzed cycloisomerizations of enynes: a mechanistic perspective. *Chem. Rev.* **108**, 3326–3350 (2008).
- Doyle, M. P., Duffy, R., Ratnikov, M. & Zhou, L. Catalytic carbene insertion into C-H bonds. *Chem. Rev.* **110**, 704–724 (2010).
- Davies, H. M. L. & Loe, Ø. Intermolecular C-H insertions of donor/acceptor-substituted rhodium carbenoids: a practical solution for catalytic enantioselective C-H activation. *Synthesis* **16**, 2595–2608 (2004).
- Liao, K., Negretti, S., Musaev, D. G., Bacsa, J. & Davies, H. M. L. Site-selective and stereoselective functionalization of unactivated C-H bonds. *Nature* **533**, 230–234 (2016).
- Müller, T. E., Hultsch, K. C., Yus, M., Foubelo, F. & Tada, M. Hydroamination: direct addition of amines to alkenes and alkynes. *Chem. Rev.* **108**, 3795–3892 (2008).
- Huang, L., Arndt, M., Gooßen, K., Heydt, H. & Gooßen, L. J. Late transition metal-catalyzed hydroamination and hydroamidation. *Chem. Rev.* **115**, 2596–2697 (2015).
- Hashmi, A. S. K. & Hutchings, G. J. Gold catalysis. *Angew. Chem. Int. Ed.* **45**, 7896–7936 (2006).
- Zhang, L. A non-diazo approach to α -oxo gold carbenes via gold-catalyzed alkyne oxidation. *Acc. Chem. Res.* **47**, 877–888 (2014).
- Jin, H. *et al.* Gold-catalyzed C-H annulation of anthranils with alkynes: a facile, flexible, and atom-economical synthesis of unprotected 7-acylindoles. *Angew. Chem. Int. Ed.* **55**, 794–797 (2016).
- Ohe, K., Yokoi, T., Miki, K., Nishino, F. & Uemura, S. Chromium- and tungsten-triggered valence isomerism of cis-1-acyl-2-ethynylcyclopropanes via [3,3]sigmatropy of (2-acylcyclopropyl)vinylidene-metal intermediates. *J. Am. Chem. Soc.* **124**, 526–527 (2002).
- Ohe, K., Yokoi, T., Miki, K., Nishino, F. & Uemura, S. Novel approach for catalytic cyclopropanation of alkenes via (2-furyl)carbene complexes from 1-benzoyl-cis-1-buten-3-yne. *J. Am. Chem. Soc.* **124**, 5260–5261 (2002).
- Kato, Y., Miki, K., Nishino, F., Ohe, K. & Uemura, S. Doyle-kirmse reaction of allylic sulfides with diazoalkane-free (2-furyl)carbenoid transfer. *Org. Lett.* **5**, 2619–2621 (2003).
- Miki, K. *et al.* Catalytic cyclopropanation of alkenes via (2-furyl)carbene complexes from 1-benzoyl-cis-1-buten-3-yne with transition metal compounds. *J. Org. Chem.* **69**, 1557–1564 (2004).
- Miki, K., Washitake, Y., Ohe, K. & Uemura, S. Polyaddition and polycondensation reactions of (2-furyl)carbenoid as step-growth polymerization strategies: synthesis of furylcyclopropane- and furfurylidene-containing polymers. *Angew. Chem. Int. Ed.* **43**, 1857–1860 (2004).
- Vicente, R., González, J., Riesgo, L., González, J. & López, L. A. Catalytic generation of zinc carbenes from alkynes: zinc-catalyzed cyclopropanation and Si-H bond insertion reactions. *Angew. Chem. Int. Ed.* **51**, 8063–8067 (2012).
- González, J., González, J., Pérez-Calleja, C., López, L. A. & Vicente, R. Zinc-catalyzed synthesis of functionalized furans and triarylmethanes from enynones and alcohols or azoles: dual X-H bond activation by zinc. *Angew. Chem. Int. Ed.* **52**, 5853–5857 (2013).
- Wang, T. & Zhang, J. Synthesis of 2-acylfurans from 3-(1-alkynyl)-2-alken-1-ones via the oxidation of gold-carbeneintermediates by H_2O_2 . *Dalton Trans.* **39**, 4270–4273 (2010).
- Cao, H. *et al.* Copper-catalyzed C-O bond formation: an efficient one-pot highly regioselective synthesis of furans from (2-furyl)carbene complexes. *Org. Lett.* **15**, 1080–1083 (2013).
- Zhan, H. *et al.* Palladium-catalyzed formation of C=C bonds: a regioselective strategy for the synthesis of 2-vinylfurans by 1,2-H shift of palladium-carbene complexes. *Eur. J. Org. Chem.* **2013**, 2284–2287 (2013).
- Xia, Y. *et al.* Palladium-catalyzed carbene migratory insertion using conjugated enyne-ketones as carbene precursors. *J. Am. Chem. Soc.* **135**, 13502–13511 (2013).
- Hu, F., Xia, Y., Ma, C., Zhang, Y. & Wang, J. Cu(I)-catalyzed cross-coupling of conjugated enyne-ketones and terminal alkynes: synthesis of furan-substituted allenes. *Org. Lett.* **16**, 4082–4085 (2014).
- Ma, J., Jiang, H. & Zhu, S. NHC-AuCl/selectfluor: a highly efficient catalytic system for carbene-transfer reactions. *Org. Lett.* **16**, 4472–4475 (2014).
- Kimball, D. B., Herges, R. & Haley, M. M. Two unusual, competitive mechanisms for (2-ethynylphenyl)triazene cyclization: pseudocoarctate versus pericyclic reactivity. *J. Am. Chem. Soc.* **124**, 1572 (2002).
- Kimball, D. B., Weakley, T. J. R., Herges, R. & Haley, M. M. Deciphering the mechanistic dichotomy in the cyclization of 1-(2-ethynylphenyl)-3,3-dialkyltriazenes: competition between pericyclic and pseudocoarctate pathways. *J. Am. Chem. Soc.* **124**, 13463–13473 (2002).
- Young, B. S., Köhler, F., Herges, R. & Haley, M. M. Phenanthrene-fused azo-ene-yne: synthesis of dibenzo[f,h]cinnoline and dibenzo[e,g]isoindazole derivatives. *J. Org. Chem.* **76**, 8483–8487 (2011).
- Zhan, H. *et al.* Gold-catalyzed synthesis of 3-acylimidazo[1,2-a]pyridines via carbene oxidation. *Adv. Synth. Catal.* **357**, 46–50 (2015).
- Brooner, R. E. M., Brown, T. J. & Widenhoefer, R. A. Direct observation of a cationic gold(I)-bicyclo[3.2.0]hept-1(7)-ene complex generated in the cycloisomerization of a 7-phenyl-1,6-enyne. *Angew. Chem. Int. Ed.* **52**, 6259–6261 (2013).
- Seidel, G., Mynott, R. & Fürstner, A. Elementary steps of gold catalysis: NMR spectroscopy reveals the highly cationic character of a “gold carbenoid”. *Angew. Chem. Int. Ed.* **48**, 2510–2513 (2009).
- Straub, B. F. & Hofmann, P. Copper(I) carbenes: the synthesis of active intermediates in copper-catalyzed cyclopropanation. *Angew. Chem. Int. Ed.* **40**, 1288–1290 (2001).
- Dai, X. & Warren, T. H. Discrete bridging and terminal copper carbenes in copper-catalyzed cyclopropanation. *J. Am. Chem. Soc.* **126**, 10085–10094 (2004).
- Shishkov, I. V., Rominger, F. & Hofmann, P. Remarkably stable copper(I) α -carbonyl carbenes: synthesis, structure, and mechanistic studies of alkene cyclopropanation reactions. *Organometallics* **28**, 1049–1059 (2009).
- Hussong, M. W., Hoffmeister, W. T., Rominger, F. & Straub, B. F. Copper and silver carbene complexes without heteroatom-stabilization: structure, spectroscopy, and relativistic effects. *Angew. Chem. Int. Ed.* **54**, 10331–10335 (2015).
- Barluenga, J. *et al.* Chromium-copper exchange of Fischer carbene complexes: X-ray crystal structure of a $[Cu\{=CR^1(OR^2)\}(MeCN)(Et_2O)]PF_6$ complex. *Angew. Chem. Int. Ed.* **40**, 3392–3394 (2001).
- Seidel, G. & Fürstner, A. Structure of a reactive gold carbenoid. *Angew. Chem. Int. Ed.* **53**, 4807–4811 (2014).
- Seidel, G. *et al.* Gold carbenoids: lessons learnt from a transmetalation approach. *Angew. Chem. Int. Ed.* **53**, 879–882 (2014).
- Brooner, R. E. M. & Widenhoefer, R. A. Experimental evaluation of the electron donor ability of a gold phosphine fragment in a gold carbene complex. *Chem. Commun.* **50**, 2420–2423 (2014).
- Hussong, M. W., Rominger, F., Krämer, P. & Straub, B. F. Isolation of a non-heteroatom-stabilized gold-carbene complex. *Angew. Chem. Int. Ed.* **53**, 9372–9375 (2014).
- Harris, R. J. & Widenhoefer, R. A. Synthesis, structure, and reactivity of a gold carbenoid complex that lacks heteroatom stabilization. *Angew. Chem. Int. Ed.* **53**, 9369–9371 (2014).
- Joost, M. *et al.* Enhanced π -backdonation from gold(I): isolation of original carbonyl and carbene complexes. *Angew. Chem. Int. Ed.* **53**, 14512–14516 (2014).
- Fañanás-Mastral, M. & Aznar, F. Carbene transfer reactions from chromium(0) to gold(I): synthesis and reactivity of new Fischer-type gold(I) alkenyl carbene complexes. *Organometallics* **28**, 666–668 (2009).
- Schubert, U., Ackermann, K. & Aumann, R. Chloro(dimethylamino(phenyl)carbene) gold(I), $AuCl(C_6H_5)N(CH_3)_2$. *Cryst. Struct. Commun.* **11**, 591–594 (1982).
- Ung, G., Soleilhavoup, M. & Bertrand, G. Gold(III)-versus gold(I)-induced cyclization: synthesis of six-membered mesoionic carbene and acyclic (aryl)(heteroaryl) carbene complexes. *Angew. Chem. Int. Ed.* **52**, 758–761 (2013).
- Ung, G. & Bertrand, G. β - and α -Hydride abstraction in gold(I) alkyl complexes. *Angew. Chem. Int. Ed.* **52**, 11388–11391 (2013).
- Werlé, C., Goddard, R. & Fürstner, A. The first crystal structure of a reactive dirhodium carbene complex and a versatile method for the preparation of gold carbenes by rhodium-to-gold transmetalation. *Angew. Chem. Int. Ed.* **54**, 15452–15456 (2015).
- Echavarren, A. M. Gold catalysis: carbene or cation? *Nat. Chem.* **1**, 431–433 (2009).
- Benitez, D. *et al.* A bonding model for gold(I) carbene complexes. *Nat. Chem.* **1**, 482–486 (2009).
- Wang, Y., Muratore, M. E. & Echavarren, A. M. Gold carbene or carbenoid: is there a difference? *Chem. Eur. J.* **21**, 7332–7339 (2015).
- Nunes dos Santos *et al.* The stabilizing effects in gold carbene complexes. *Angew. Chem. Int. Ed.* **54**, 10336–10340 (2015).
- Nunes dos Santos *et al.* Gold(I) vinylidene complexes as reactive intermediates and their tendency to π -backbond. *Chem. Eur. J.* **22**, 2892–2895 (2016).
- Bistoni, G. *et al.* How π back-donation quantitatively controls the CO stretching response in classical and nonclassical metal carbonyl complexes. *Chem. Sci.* **7**, 1174–1184 (2016).
- Harris, R. J. & Widenhoefer, R. A. Gold carbenes, gold-stabilized carbocations, and cationic intermediates relevant to gold-catalysed enyne cycloaddition. *Chem. Soc. Rev.* **45**, 4533–4551 (2016).
- Fürstner, A. & Davies, P. W. Catalytic carbophilic activation: catalysis by platinum and gold π acids. *Angew. Chem. Int. Ed.* **46**, 3410–3449 (2007).
- Fürstner, A., Szillat, H., Gabor, B. & Mynott, R. Platinum- and acid-catalyzed enyne metathesis reactions: mechanistic studies and applications to the

- syntheses of streptorubin B and metacycloprodigiosin. *J. Am. Chem. Soc.* **120**, 8305–8314 (1998).
55. Fürstner, A., Stelzer, F. & Szillat, H. Platinum-catalyzed cycloisomerization reactions of enynes. *J. Am. Chem. Soc.* **123**, 11863–11869 (2001).
56. Lv, S. *et al.* Silver-catalyzed amidinium of alkynes: isolation of a silver intermediate, synthesis of enamine amido carbene precursors, and an unprecedented umpolung of propiolamide. *Angew. Chem. Int. Ed.* **54**, 14941–14946 (2015).
57. César, V. *et al.* IMes-acac: hybrid combination of diaminocarbene and acetylacetonato sub-units into a new anionic ambidentate NHC ligand. *Chem. Commun.* **51**, 5271–5274 (2015).
58. Crabtree, R. H. in *The Organometallic Chemistry of the Transition Metals* Ch. 10, 275–308 (John Wiley, 2005).
59. Petronilho, A., Müller-Bunz, H. & Albrecht, M. Mesoionic oxides: facile access from triazolium salts or triazolylidene copper precursors, and catalytic relevance. *Chem. Commun.* **48**, 6499–6501 (2012).
60. Frémont, P., Scott, N. M., Stevens, E. D. & Nolan, S. P. Synthesis and structural characterization of N-heterocyclic carbene gold(I) complexes. *Organometallics* **24**, 2411–2418 (2005).
61. Liu, L.-P., Xu, B., Mashuta, M. S. & Hammond, G. B. Synthesis and structural characterization of stable organogold(I) compounds. Evidence for the mechanism of gold-catalyzed cyclizations. *J. Am. Chem. Soc.* **130**, 17642–17643 (2008).
62. Döpp, R. *et al.* Gold catalysis: hydrolysis of di(alkoxy)carbenium ion intermediates as a sensor for the electronic properties of gold(I) complexes. *Organometallics* **30**, 5894–5903 (2011).
63. Vanitcha, A. *et al.* Synthesis of allenes bearing phosphine oxide groups and investigation of their reactivity toward gold complexes. *Adv. Synth. Catal.* **357**, 2213–2218 (2015).
64. Wang, J., Lv, S., Chen, H., Shi, M. & Zhang, J. Isolation and characterization of gem-diaurated species having two C–Au σ bonds in gold(I)-activated amidinium of alkynes. *Dalton Trans.* **45**, 17091–17094 (2016).
65. Hashmi, A. S. K., Schuster, A. M. & Rominger, F. Gold catalysis: isolation of vinylgold complexes derived from alkynes. *Angew. Chem. Int. Ed.* **48**, 8247–8249 (2009).
66. Hashmi, A. S. K., Ramamurthi, T. D. & Rominger, F. On the trapping of vinylgold intermediates. *Adv. Synth. Catal.* **352**, 971–975 (2010).
67. Kaur, H., Kauer Zinn, F., Stevens, E. D. & Nolan, S. P. (NHC)CuI (NHC = N-heterocyclic carbene) complexes as efficient catalysts for the reduction of carbonyl compounds. *Organometallics* **23**, 1157–1160 (2004).
68. Díez-González, S., Scott, N. M. & Nolan, S. P. Cationic copper(I) complexes as efficient precatalysts for the hydrosilylation of carbonyl compounds. *Organometallics* **25**, 2355–2358 (2006).
69. Bidal, Y. D. *et al.* Copper(I) complexes bearing carbenes beyond classical N-heterocyclic carbenes: synthesis and catalytic activity in ‘click chemistry’. *Adv. Synth. Catal.* **357**, 3155–3161 (2015).
70. Mushinski, R. M., Squires, B. M., Sincerbox, K. A. & Hudnall, T. W. Amino-acrylamido carbenes: modulating carbene reactivity via decoration with an α,β -unsaturated carbonyl moiety. *Organometallics* **31**, 4862–4870 (2012).

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Author contributions

J.W., S.L. and C.Z. performed the synthetic experiments. X.C. performed DFT calculations. J.Z. conceived of metal carbene design and reactivity applications. J.Z., M.S. and S.X. designed the project. J.Z. and J.W. wrote the manuscript.

Additional information

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