VIP Homogeneous Catalysis

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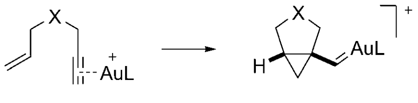
Elementary Steps of Gold Catalysis: NMR Spectroscopy Reveals the Highly Cationic Character of a "Gold Carbenoid"**

*Günter Seidel, Richard Mynott, and Alois Fürstner**

The impressive advances in homogeneous gold and platinum catalysis during the last decade stand in marked contrast to the lack of secured knowledge about the nature of the reactive intermediates involved.[1] Based on empirical knowledge and numerous computational studies, it has become common practice to invoke metal carbenes in the various transformations effected by such carbophilic catalysts. This is illustrated, for example, by the rich and diverse chemistry of 1,6-enynes, which is usually traced back to intermediates of type **2** (Scheme 1).[2]

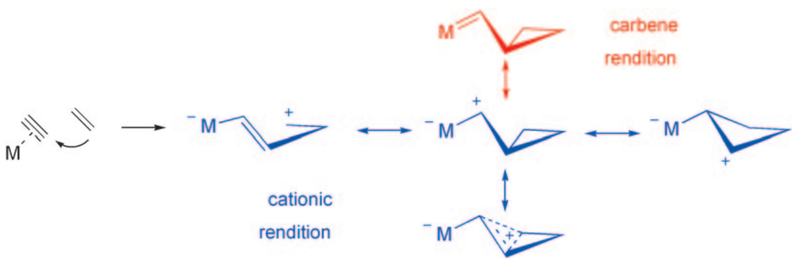
However, this convention may not be an accurate description of the true nature of the reactive organogold species.[3] The vastly different size of the frontier orbitals of gold and carbon might preclude significant back-donation from the metal to the ligand, rendering a dipolar bonding situation more likely than a carbon–metal "double bond".



1 **2**

Scheme 1. The commonly postulated formation of a "gold carbene" as the first step of enyne cycloisomerization.

One may object, however, that these forms are nothing but the canonical extremes of the very same intermediate, thus rendering any further elaboration pointless (Scheme 2). Nevertheless, a growing body of evidence in the recent literature seems to indicate that the situation is more complicated. Our group has studied a series of gold-catalyzed transformations that strikingly resemble the logic of cationic polycyclization reactions (Stork–Eschenmoser paradigm) but cannot be easily explained in terms of regular carbenes.[4]



Scheme 2. Attack of an alkene on an alkyne, catalyzed by a carbophilic Lewis acid, generates a reactive intermediate that can be described in terms of either cationic or carbenoid resonance extremes.

These data suggest that the conceivable cationic and carbene extremes make very different contributions to the actual character of the reactive intermediates. Further investigations have since emphasized the intervention of highly charged, cation-like species in gold catalysis.[5–8]

As **2** and congeners had eluded all attempts at direct characterization, we sought to generate a "gold carbene" by an independent route, to investigate the actual bonding situation.[9–12] To achieve this, recourse was taken to the rearrangement of the 3,3-disubstituted cyclopropenes **3a–d** (see below), which is known to constitute an excellent entry into metal carbene chemistry in general.[13] Building on the pioneering studies of Binger et al.,[14] this transformation allowed the synthesis of a host of well-defined carbene complexes of transition metals as different as Ti, Co, Zr, Ru, Ta, W, Re, and Os.[14–16] Most notably, it opened the very first route to the now-classical Grubbs ruthenium carbene catalysts [$(R_3P)_2Cl_2Ru{=}CH{-}CH{=}CPh_2$] (R = Ph, Cy (cyclohexyl)) for olefin metathesis.[16]

3a R, R = -O(CH$_2$)$_3$O-
b R = OMe
c R = Me
d R = Ph

[(R$_3$P)Au][NTf$_2$]
4a R = Ph
b R = Me
c R = Cy

However, all attempts to generate a defined organogold species on treatment of **3c** or **3d**[17] with [$(Ph_3P)Au]^+$ $[NTf_2]^-$ (**4a**, NTf$_2$ = bis(trifluoromethylsulfonyl)imide)[18] in rigorously dried CD_2Cl_2 at −78 °C under Ar resulted only in very rapid oligomerization.[19,20] Therefore, we turned our attention to the acetal derivatives **3a** and **3b**,[21] in the hope that the oxygen substituents might help to stabilize the reactive intermediates. In fact, addition of the gold complex **4a** to a slight excess of **3a** in CD_2Cl_2 at −78 °C instantaneously afforded a yellow solution containing one major new product

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[*] Ing. G. Seidel, Dr. R. Mynott, Prof. A. Fürstner
Max-Planck-Institut für Kohlenforschung
45470 Mülheim/Ruhr (Germany)
Fax: (+49) 208-306-2994
E-mail: fuerstner@kofo.mpg.de

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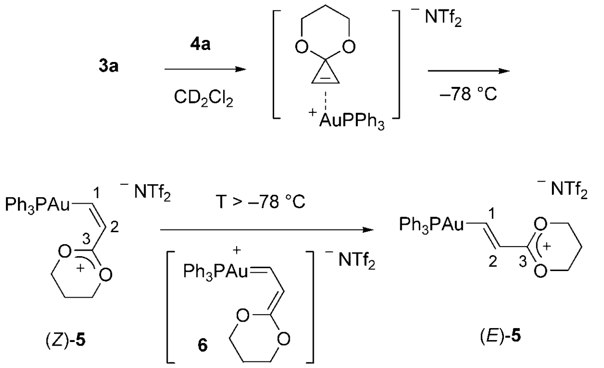
with very characteristic spectroscopic properties (Scheme 3, Table 1, and Figure 1).[22]

The chemical shift of C1 at $\delta = 214.6$ ppm does not allow us to draw any firm conclusions about the bonding situation in this organogold species because electrophilic carbenes and cationic centers are both strongly deshielded. Much more indicative is the observation that the two -O-CH_2- groups of the ketal ring give rise to just one signal in both the ^1H and the ^{13}C NMR spectra, suggesting there is rapid rotation about the C2–C3 bond on the NMR timescale, even at −78 °C. Whereas this finding is incompatible with the putative gold carbene structure **6**, it is consistent with the presence of an oxocarbenium cation of type **5** (Scheme 3).[23] The chemical shift of C3 also falls into the expected range of a cationic center stabilized by two oxygen substituents.[24] Moreover, the analysis of the pertinent coupling constants reveals the *Z*-olefin character of the C1–C2 bond (Table 1).



Scheme 3. Gold-induced rearrangement of cyclopropenone ketal **3a**.

Table 1: Selected NMR spectroscopic data of the isomeric organogold species (*E*)-**5** and (*Z*)-**5**.[22] Chemical shift values are given in ppm, coupling constants are given in Hz.

	(*Z*)-**5**	(*E*)-**5**
δ_{H1}	9.19	9.71
δ_{H2}	6.85	6.51
δ_{C1}	214.6	212.9
δ_{C2}	127.8	127.1
δ_{C3}	178.0	172.9
$J_{H1,H2}$	13.9	19.1
$J_{H1,C3}$	17.5	10.3
$J_{P,C3}$	4.6	11.2
$J_{P,H2}$	13.9	6.5

On carefully raising the temperature, the solution gradually changed color from yellow to dark red. NMR spectroscopy shows that (*Z*)-**5** rearranges over the course of several hours to a new compound, featuring the distinctive spectroscopic fingerprint of the corresponding *E* isomer (*E*)-**5** (Figure 1). Even in solutions in which both gold species are present, their NMR spectroscopic signals are not significantly broadened by mutual exchange, thus confirming the high barrier to interconversion. This key observation, together with the characteristic *J*-coupling pattern, unequivocally shows that it is the C1–C2 rather than the C2–C3 bond in each geometrical isomer that has a very high degree of double-bond character. The contribution of the "carbene" resonance from **6** to the ground-state structure of the organogold species formed from **3a** and **4a** is therefore marginal. Interestingly, the alternating bond orders in **5** stand in contrast to the computed structure of the gold "carbene" **7**, for which the C1–C2 and the C2–C3 bonds were proposed to be of almost equal length (Figure 2).[25]

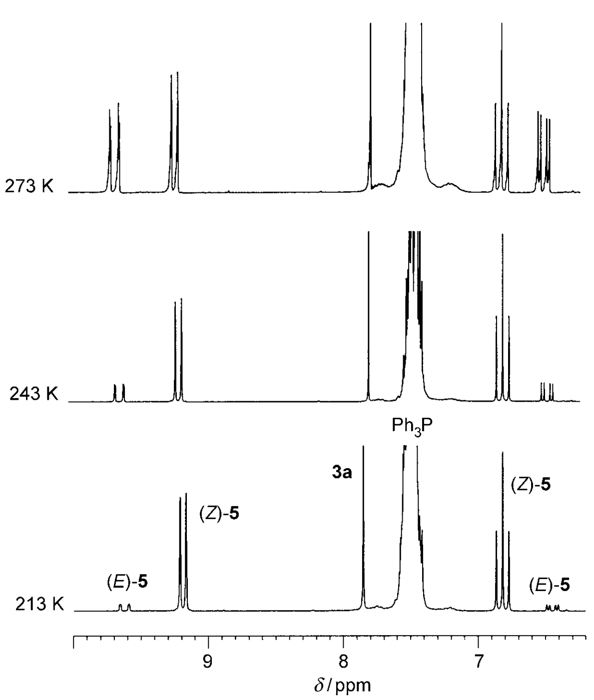


Figure 1. ^1H NMR spectroscopy reveals the slow rearrangement of (*Z*)-**5** into (*E*)-**5** upon raising the temperature of the solution in CD_2Cl_2; for the assignments, see Table 1.

Next, we attempted to push the system toward the carbene extreme by carrying out the rearrangement of **3a** with the precursor complexes **4b** and **4c** bearing much more electron-donating trialkylphosphine ligands. However, the spectra of the resulting organogold derivatives **8** and **9** (Figure 2) once again showed the characteristic signature pattern for oxocarbenium cation species.[22] A noteworthy difference, however, is that the corresponding *E* isomers now predominated even at −80 °C [(*E*)-**8**/(*Z*)-**8** = 96:4; (*E*)-**9**/(*Z*)-**9** = 83:17].[26]

The use of 3,3-dimethoxycyclopropene **3b** instead of the cyclic ketal **3a** afforded the isomeric gold intermediates **10**, which are exceptionally sensitive and noticeably decompose at temperatures below −20 °C. In contrast to **5**, there were two methoxy signals in the ^1H and ^{13}C NMR spectra at −80 °C that rapidly became broader on raising the temperature. For **10b**, which bears the electron-donating Me_3P ligand, the barrier to rotation about the C2–C3 bond was estimated from the line broadening to be (46 ± 1) kJ mol^{-1}. No accurate value can be given for the corresponding barrier in the complexes **5** because there is no evidence for such line broadening through restricted rotation at −80 °C. Assuming that the difference between the chemical shifts of the -O-CH_2 groups is much the

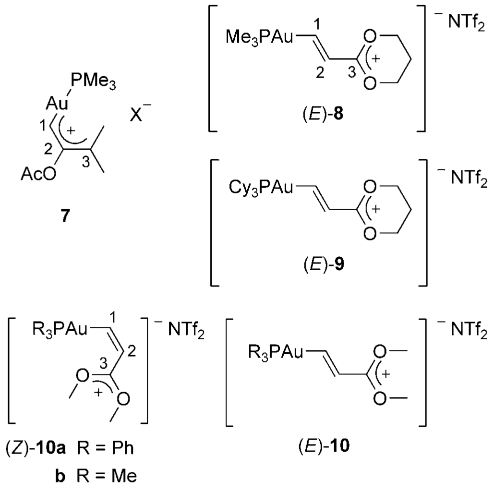


Figure 2. Whereas the C1–C2 and C2–C3 bonds of **7** were computed to be of almost equal length,[25] our NMR spectroscopic data indicate that the ground-state structures of **8**–**10**, prepared by gold-induced rearrangement of **3a** or **3b**, respectively, must have alternating bond lengths. Ac = acetyl.

same as between the methoxy signals in **10**, this suggests that the barrier cannot be more than about 30 kJ mol^{-1}.

To put these results into perspective, the representative data (compiled in Figure 3) show that the "double bond" character innate to C2–C3 of **5** is in the same range as that of the central bond of butadiene or that between the phenyl ring and the carbonyl group of benzaldehyde. The more electron-donating Me_3P ligand in **10b** raises the barrier slightly, yet it is still no higher than that of the sterically hindered single bond of $Cl_3C{-}CCl_3$, smaller than that of methyl acetate as a prototypical ester, and no more than half of that of an amide.[27] A particularly relevant comparison pertains to the Cu^{I} carbene **11** (Figure 3), characterized by Hofmann and Straub.[28] Although this compound is known to be highly electrophilic, the rotational barrier of its C=Cu fragment is nevertheless at least 60 kJ mol^{-1}.[28] These data make unambiguously clear that the ground-state structures of the organogold intermediates described herein must be very close to the cationic resonance extreme, whereas the contribution of the carbene form is marginal.

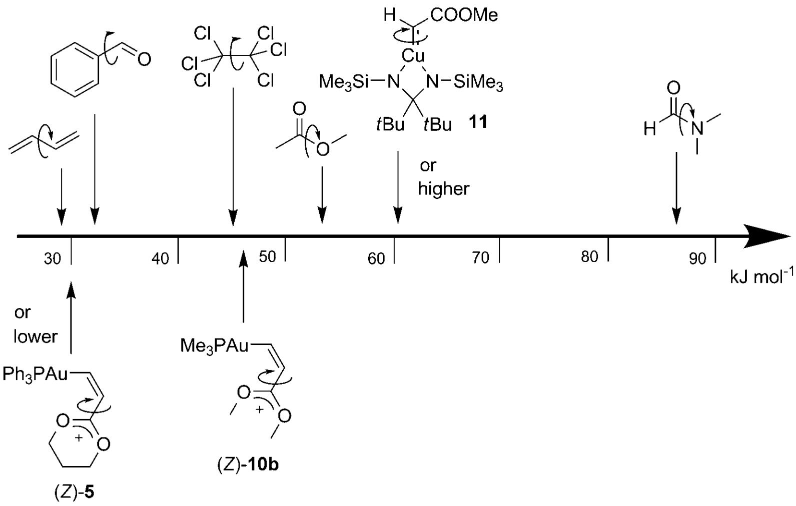


Figure 3. Comparison of the rotational barriers of the organogold species **5** and **10** with those of various reference compounds.[27]

We believe that this result deserves careful consideration in mechanistic discussions of gold catalysis in general,[1] even though one can object that the oxygen substituents in **5** and congeners may not be innocent and could bias the system toward the cationic form. However, the fact that cyclopropenes **3c** and **3d**, which are devoid of such substituents, suffer rapid cationic polymerization contradicts this argument. Moreover, much of the established gold chemistry can be seen as falling into the general categories of Friedel–Crafts reactions, Prins-type processes, and cationic rearrangements.[1,29] Even the widespread formation of cyclopropanes, which is frequently invoked as an indication of the carbene character of the reactive species, is not unambiguous, as cyclopropane formation can also occur in a stepwise, nonconcerted fashion via charged intermediates.[30] Although we pretend by no means that true carbene reactivity cannot surface in gold catalysis,[31] any such claim has to be carefully weighed against the experimental evidence for cationic behavior outlined above. Further investigations on the intermediates of gold catalysis, including studies on the reactivity of **5** and congeners, are underway and will be reported in due course.

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