Gold Catalysis

Simple Gold-Catalyzed Synthesis of Benzofulvenes—gem-Diaurated Species as "Instant Dual-Activation" Precatalysts**

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In the field of homogeneous transition-metal chemistry, gold plays a major role in the discovery of new reactions.^[1] Most of the transformations are based on the *electrophilic* activation of a multiple bond. The decrease of electron density upon π coordination of a carbophilic gold center allows nucleophilic attack. Now, in independent and parallel work the group of Zhang and our team have discovered a different reactivity which was so far unprecedented in the field of gold chemistry.^[2] Initial activation of an alkyne by σ coordination to gold increases the *nucleophilicity* of the β -carbon atom of this alkyne. This first alkyne combines with a second alkyne, which is activated by π coordination, and highly reactive gold vinylidene intermediates are formed by this dual σ/π activation. The Zhang group's publication^[2b] on the synthesis of benzofulvenes now prompts us to publish our additional findings on that specific reaction.

Since alkyl-substituted alkynes are readily available, a new fascinating reaction pathway was opened for the gold vinylidene intermediates. The first two elementary steps of this reaction are identical to the previous reactions,^[2a,c] which seem to be general for this new sector of gold catalysis. Herein we report on the use of tertiary alkyl groups, the isolation of *gem*-diaurated species which prove to be ideal precatalysts for this type of transformation, the dynamics of the equilibrium involving these diaurated species, and the catalyst transfer in the context of a detailed mechanistic discussion.

We investigated several diyne systems **1** with a terminal alkynyl group and a *tert*-alkyl-substituted alkynyl group as potential substrates for the gold(I)-catalyzed intermolecular arene addition.^[2a] A new reaction was observed, the clean formation of a benzofulvene derivative, a class of compounds that usually is not easily available.^[3] No incorporation of the solvent benzene was observed. To optimize the reaction, we performed reactions of substrate **1a** (Table 1) with different gold catalysts and different counterions (see the Supporting

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[⁺] Crystallographic investigation

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Information); the well-established catalyst [(IPr)AuCl],^[4] in combination with $AgNTf_2$ gave the best results.

To evaluate the substrate scope, a small library of substrates was transformed to the corresponding products under the optimized conditions (Table 1). One advantage of substrates **1** is their easy two-step synthesis (Sonogashira reaction, Seyferth–Gilbert homologation) from commercially available 2-bromobenzaldehydes. With our test substrate **1a**,







[a] Only 2 mol % [(IPr)AuNTf₂], 30 h.

no problems occurred during column chromatography and the yield of isolated 2a was in the range of the yield determined by gas chromatography (Table 1, entry 1). Similar reactivity was observed for benzodioxole derivative 1b (Table 1, entry 2). Reduced yields were observed for substrates 1c and 1d with electron-donating substituents in meta and para position, respectively, relative to the terminal alkynyl group (Table 1, entries 3 and 4). The reason for this is most probably the instability of the products under the reaction conditions. Consistent with this observation, in substrates 1e, 1f, and 1g electronically neutral (Table 1, entry 5) and electron-withdrawing substituents (entries 6 and 7) led to a stabilization of the products; the yields were good to excellent. In the case of the dimethoxy-substituted product 2a, crystals suitable for X-ray crystal structure analysis could be obtained.^[5] The results unambiguously prove the presence of the benzofulvene core. Changing the tert-butyl group at the nonterminal alkyne to isopropyl led to a drop in yield, but still benzofulvene derivative 2h could be isolated in 30% yield (Table 1, entry 8). A cyclopentyl substituent was also tolerated (Table 1, entry 9). In this case, in addition to the expected product 2i, minor amounts of constitutional isomer 3a were isolated. The unambiguous structural assignment of **3a** was possible by an X-ray crystal structure analysis.^[5] The sensitive triene substructure likely arises from a cyclization that is initiated by attack of the nonterminal alkyne onto the terminal triple bond. Unfortunately, the cyclohexyl-substituted substrate delivered a product that was unstable during the workup and isolation; hence only traces of triene 3b could be obtained.

Further studies focused on the isolation of the reaction intermediates. We prepared gold acetylide **4**. In a first experiment **4** was subjected to *catalytic* amounts of activated catalyst. A clean conversion was indicated by thin-layer chromatography, but purification on silica delivered the fairly unstable compound **5** in only 40% yield (Scheme 1). Nevertheless, single crystals suitable for X-ray structure analysis could be grown with extremely careful handling.^[5] The structure analysis proves the formation of the vinyl monogold complex **5** (Figure 1). The gold center is directly bound to the alkene double bond, which is derived from the nonterminal *tert*-butyl-substituted alkyne. Despite the steric bulk of the *tert*-butyl substituent of the substrate, coordination of the gold



Scheme 1. Synthesis of the vinyl monogold compound **5**. IPr = 1,3-bis (diisopropylphenyl)imidazolylidene.



Figure 1. X-ray crystal structure of **5** (thermal ellipsoids at 50% probability).

catalyst at the β -carbon atom of the alkyne must still be possible.

A second reaction was conducted with gold acetylide **4** and *stoichiometric* amounts of the activated catalyst in dichloromethane (Scheme 2). Even at room temperature an immediate conversion of the starting material took place and



Scheme 2. Synthesis of the IPr/IPr-gem-diaurated compound 6.

precipitation of a crystalline solid was observed upon the addition of hexane. X-ray crystal structure analysis^[5] proved the formation of a gem-diaurated species (Figure 2). In this compound the two metal atoms are situated at the same position of the benzofulvene core as the single gold atom in compound 5. There are several examples in the literature of gem-diaurated species that are prepared by the reaction of monogold organometallic compounds and stoichiometric amounts of a cationic gold complex.^[6] Therefore it is reasonable that compound 6 is derived from monogold complex 5 (which itself forms in a previous gold-catalyzed cyclization reaction). The relevance of the gem-diaurated compounds in gold-catalyzed reactions so far is unclear.^[7] Besides our findings with arene–diyne substrates,^[2a,c] only one other example for the formation of a gem-diaurated species out of a catalysis reaction has been reported (derived from an allene precursor).^[8]





Figure 2. X-ray crystal structure of **6** (thermal ellipsoids at 50% probability).

To determine whether the formation of compound **6** is only a dead end for the reaction and responsible for catalyst consumption, *catalytic* amounts of **6** were added to diyne **1e** in the absence of any additional catalyst, co-catalyst, or activator (Scheme 3). Under the normal reaction conditions a 2.5 mol% loading of **6** not only resulted in complete conversion of the starting material but the reaction was even



Scheme 3. Threefold acceleration of the formation of benzofulvene **2e** through the use of 2.5 mol% of the *gem*-diaurated compound **6**.

three times faster than with our usual catalyst system (2 h instead of 6 h)! This observation provides significant insights into the catalytic cycle and the interesting question of catalyst transfer. Starting from the normal catalyst [LAu⁺X⁻], the formation of the gold acetylide is slow,^[9] and only after some time are the gold acetylide and free [LAu⁺X⁻] present in a ratio that is suitable for significant reaction rates. This leads to a prolonged reaction time and increases the likelihood of undesired side reactions. Compound **6**, on the other hand, is in direct equilibrium (Scheme 4) with two species needed for the catalytic conversion, the cationic catalyst (necessary for π activation of the starting material) and the vinyl monogold compound **5** (which directly delivers the σ -activated gold acetylide by the crucial catalyst-transfer step of the catalytic cycle). Providing both species in a well-defined 1:1 ratio



Scheme 4. Equilibrium between the gem-diaurated compound 6 and the vinyl monogold compound 5 as well as the activated gold catalyst.

makes complexes of type **6** ideal instant dual-activation precatalysts, not needing any additives as activators (unlike the system in Ref. [2b]). In an experiment with **1e** and 5 mol% of **4** indeed no conversion was observed; however, when 10 mol% of HNTf₂ was added to generate [(IPr)AuNTf₂] from **4** by protodeauration, conversion to **2e** was immediately detected (72% yield of isolated product).

Thus, shifting the equilibrium depicted in Scheme 4 towards the right side (by means of bulky ligands and/or elevated temperatures) is crucial not only for this reaction but also for other gold-catalyzed processes in which *gem*-diaurated compounds are involved.

To our surprise, gold acetylide **4** could also be cyclized in the presence of stoichiometric amounts of an activated phosphane complex (Scheme 5). An X-ray crystal structure analysis of the resulting crystals showed the first example of



Scheme 5. Synthesis of the PPh₃/IPr-gem-diaurated compound 7.

a *gem*-diaurated species containing two different ligands at the two gold centers, in this case an N-heterocyclic carbene (NHC) and a phosphane ligand (Figure 3).^[5] Interestingly, only traces of other byproducts were evident in the ¹H and ³¹P NMR spectra and no phosphane/phosphane diaurated species could be detected. To investigate whether a dynamic



Figure 3. X-ray crystal structure of **7** (thermal ellipsoids at 50% probability).

equilibrium exists at room temperature between the monoand digold organometallic compounds, we subjected IPr/IPrgem-diaurated compound **6** to stoichiometric amounts of [(PPh₃)AuNTf₂] (Scheme 6). In perfect agreement with the findings described above, only the phosphane/carbene gemdiaurated species **7** was detected by ¹H and ³¹P NMR spectroscopy (³¹P NMR (CDCl₃): $\delta = 36.7$ ppm, clearly different from [(PPh₃)AuNTf₂] with 30.4 ppm). Apparently, there is a dynamic equilibrium between the digold compound, the monogold compound, and the activated catalyst (as depicted



Scheme 6. Exchange between compound 6 and $[(PPh_3)AuNTf_2]$.

in Scheme 4) even at room temperature in dichloromethane. Interestingly, the mixed phosphane/carbene *gem*-diaurated species **7** is thermodynamically favored.

A comparison of the key structural parameters of compounds **6** and **7** can be obtained from the X-ray crystallographic data.^[10] The Au–Au bond lengths of *gem*-diaurated compounds **6** (282.9 pm) and **7** (284.7 pm) show strong aurophilic interactions.^[11] However, they are slightly weaker than those in other reported diaurated compounds.^[2a,c,12] Remarkably, the Au1–C and the Au2–C bond lengths in both *gem*-diaurated compounds are not equivalent. In the IPr/ IPr compound **6** these are 208.6 pm and 215.0 pm. In IPr/PPh₃ compound **7**, the NHC complex (Au1–C: 209.9 pm) is bonded stronger to the benzofulvene moiety than the phosphane complex is (Au2–C: 216.6 pm).^[13] Noteworthy, the shorter gold–carbon bond of the *gem*-diaurated compounds is only

slightly longer than in the corresponding monogold compound 5. Altogether, auration has only a minor effect on the C-C bond lengths in the benzofulvene moiety. While the length of the C-C single bond to the benzene ring remains almost unchanged (147.4 pm in 2a, 148.2 pm in 5, 151.3 pm in 6, and 148.2 pm in 7), the double bond in the gem-diaurated compounds 6 (138.3 pm) and **7** (137.5 pm) is somewhat longer than in benzofulvene 2a (132.3 pm). In summary, the gem-diaurated species obtained in this study show a bonding mode that can be considered to be a three-center two-electron bond.

The conversion of the deuterium-labeled terminal alkyne [D]-1e was also investigated. A nearly quantitative incorporation of the deuterium in [D]-2e at the former gold position was



Scheme 7. Isotopic-labeling experiment.

detected (Scheme 7), which shows the importance of the catalyst transfer.

Our proposed mechanism for the reaction is summarized in Scheme 8. As in the related reaction pathways,^[2a,c] the formation of a gold acetylide 4 must take place as the first reaction step. One option is simple formation of an acetylide and liberation of the corresponding acid,^[14] the other is the catalyst transfer. Once the acetylide is formed, dual σ / π activation takes place, leading to the fast formation of reactive gold vinylidene II. At this stage, in the case of the alkyl-substituted substrates, instead of the nucleophilic addition of an sp² nucleophile,^[2a] a 1,5-hydride shift to the electrophilic vinylidene carbon takes place. This represents a fascinating C-H activation of an unactivated alkyl group. This leads to cation **III** which is stabilized by the gold atom. (That is the vinylogous case of the well-known discussion of "carbenes or carbocations" in gold chemistry.)^[15] The next step consists of the addition of the vinyl gold double bond onto the cation, followed by elimination of the gold complex. Then the similarities between the reactions recur. A monogold species 5 is formed, which exists in an equilibrium with the





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corresponding *gem*-diaurated species **6**. Finally, catalyst transfer takes place (responsible for the deuterium labeling in the product) and another molecule of the starting material is activated through acetylide formation.

The reaction reported in this contribution offers a significantly simplified entry to the benzofulvene skeleton from simple starting materials. In addition, the role of *gem*diaurated species from gold-catalyzed reactions could be clarified; they are excellent instant dual-activation catalysts for reactions involving σ,π -type dual activation of the substrate. Based on these species, the full catalytic cycle, including the catalyst transfer, is now understood. In our opinion, this general reactivity pattern and this new type of catalyst will trigger the discovery of a series of new reactions.

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