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Well-Defined Dinuclear Gold Complexes for Preorganization-Induced Selective Dual Gold Catalysis

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Abstract: The synthesis, reactivity, and potential of well-defined dinuclear gold complexes as precursors for dual gold catalysis are explored. Using the preorganizing abilities of the ditopic PNHPPPr ligand, dinuclear Au1–Au2 complexes 1 and mixed-valent Au1III–Au2II complex 2 provide access to structurally characterized chlorido-bridged cationic species 3 and 4 upon halide abstraction. For 2, this transformation involves unprecedented two-electron oxidation of the redox-active ligand, generating a highly rigidified environment for the Au1 center. Facile reaction with phenylacetylene affords the α,π-activated phenylacetylide complex 5. When applied in the dual gold heterocycleaddition of a urea-functionalized alkyne, well-defined precatalyst 3 provides high regioselectivities for the anti-Markovnikov product, even at low catalyst loadings, and outperforms common mononuclear Au1 systems. This proof-of-concept demonstrates the benefit of preorganization of two gold centers to enforce selective non-classical α,π-activation with bifunctional substrates.

Gold catalysis has flourished over the past 15 years, enabling a wide range of transformations.1 More recently, dual gold catalysis has been developed successfully.[2] Whereas “traditional” mono-gold catalysis relies on π-activation of a substrate by a cationic Au1 center, dual gold catalysis typically involves both σ- and π-activation (of one or two functionalities, such as C=O bonds) by two gold centers. The prevailing strategy utilizes mononuclear Au1 complexes to induce dual-gold heterocycleaddition of a urea-functionalized alkyne, with Cu1 and Ag1 providing high regioselectivities for the anti-Markovnikov product, even at low catalyst loadings, and outperforms common mononuclear Au1 systems. This proof-of-concept demonstrates the benefit of preorganization of two gold centers to enforce selective non-classical α,π-activation with bifunctional substrates.

The synthesis, coordination chemistry and catalytic applications of dinuclear Au1 complexes are well-developed.[4–5] The proximity of both gold centers has occasionally been credited to enhance reactivity.[6] However, to the best of our knowledge the competence of well-defined dinuclear σ,π-alkynide complexes in dual gold catalysis has never been reported, despite the potential benefits of two preorganized gold centers with respect to chemoselectivity and activity for this type of reaction. Additionally, facile access to dinuclear mixed-valent gold complexes might be an interesting target in the context of cascade and Au1/Au2 cooperative catalysis.[7]

The ditopic tridentate ligand PNHPPPr ligand L1 (Scheme 1) displays versatile coordination chemistry with respect to a wide range of transition metals,8 including Cu1 and Ag1.9 Strikingly, no single complex of gold with this type of ditopic framework is known to date. Furthermore, chemistry related to the redox-active nature10 of L1 has been well-established in nickel, manganese, and thienium complexes,11 but ligand redox-activity with Group 11 metals is limited to one example with Cu1, leading to dimerization of a para-position of the L backbone.12 New avenues for gold coordination chemistry and catalysis may become accessible by developing strategies to preorganize and stabilize multiple gold centers on suitable ligand platforms and to selectively bind and activate bifunctional substrates. To address these challenges, we herein 1) uncover the versatile coordination chemistry of gold using the redox-active ditopic PNHPPPr ligand, 2) disclose the interesting ligand and metal-based reactivity of (mixed-valent) dinuclear species, and 3) establish well-defined pre-catalyst systems ideally suited for α,π-activation of alkenes and demonstrate their use in highly selective dual gold catalysis.
The straightforward reaction of \( \text{PN}^{\text{III}}\text{P} \) with \( \text{AuCl(SMe}_2 \) in a 1:2 ratio provides white solid \( 1 \) \((^{31}\text{P} \text{NMR: } \delta = 40.9 \text{ ppm})\) with a \( ^1\text{H} \text{NMR} \) spectrum suggestive of a \( C_2 \) symmetric species (Scheme 2). Single crystal X-ray diffraction analysis reveals an intramolecular \( \text{Au}^{1}-\text{Au}^{2} \) distance of 3.23791(17) Å, which suggests an aurophilic \( d^{8}-d^{10} \) interaction\(^{13}\) in the solid state (Figure 1). Reaction of \( 1 \) with one equivalent of dichloro-\( \lambda^5 \)-(iodanyl)benzene (PhICl\(_2 \)) in \( \text{CH}_2\text{Cl}_2 \) instantaneously generates a dark purple solution that shows two signals in the \( ^{31}\text{P} \text{NMR} \) spectrum at \( \delta = 44.3 \) (P2) and 105.3 ppm (P1). The strongly downfield shifted signal for P1 supports coordination to a \( \text{Au}^{1} \) center by site-selective two-electron \( \text{Au}^{1} \) oxidation with formation of \( \text{Au}^{1}-\text{Au}^{3} \) derivative \( 2 \). Mass spectrometry supports an overall \( \text{Au}_2\text{Cl}_3(\text{L}) \) configuration. The \( ^1\text{H} \text{NMR} \) spectrum contains one strongly upfield shifted aromatic signal at \( \delta = 5.90 \) ppm but no \(-\text{NH}\) signal could be identified. X-ray structure determination confirms the sole formation of species \( 2 \), with the central deprotonated amido nitrogen coordinating to the square-planar \( \text{Au}^{11} \) center (Figure 1).

The \( \text{PNP} \)-ligand backbone in \( 2 \) is severely twisted, with a C6-C1-C7-C8 torsion angle of 76.4(8)°. This distortion relates to the upfield shifted aromatic signal in the \( ^1\text{H} \text{NMR} \) spectrum, which corresponds to the shielded C(6)-H hydrogen that is positioned on top of the second phenyl ring. The intramolecular \( \text{Au}^{1}-\text{Au} \) distance of 4.641 Å excludes an aurophilic \( d^{8}-d^{10} \) interaction. Cyclic voltammetry does not indicate reversible oxidation of the potentially redox-active ligand scaffold in \( 2 \).

A prerequisite for catalysis with a \( \text{AuX(L)} \) precursor (\( X \) is a halide) is the generation of a vacant coordination site by halide abstraction with, for example, \( \text{Ag}^+ \) salts or a suitable Lewis acid. Addition of one equivalent of AgNTf\(_2 \) (or related silver salts or GaCl\(_3 \)); see the Supporting Information) to \( 2 \), which bears multiple chlorido fragments, leads to a mixture of species according to \( ^3\text{P} \text{NMR} \) spectroscopy. However, addition of two equivalents results in rapid decoloration of the reaction solution and generation of a single symmetric product \((^{31}\text{P} \text{NMR: } \delta = 40.4 \text{ ppm})\), suggestive of the presence of only \( \text{Au}^1 \)-phosphine fragments. The \( ^1\text{H} \text{NMR} \) spectrum shows only one methyl signal for the ditolylamine backbone and chemically identical isopropyl groups at phosphorus. Most notably, only two instead of the anticipated three aromatic hydrogen signals are observed, together with a downfield signal at \( \delta = 10.53 \) ppm. This signal integrates for one hydrogen and is attributed to an \(-\text{NH}\) fragment. ESI-MS data suggest that the dinuclear complex, bearing only one chlorido ligand, remains intact during this transformation. The structure of complex \( 3 \) could be elucidated by X-ray structure determination of single crystals grown from CH\(_3\)Cl\(_2\)-pentane (Figure 2).

Clearly, halide abstraction by AgNTf\(_2 \), related silver salts, or GaCl\(_3 \) induces a highly unusual metal-based reduction of mixed-valent species \( 2 \) to yield \( \text{Au}^{1}-\text{Au}^3 \) species \( 3 \).
Ortho was selected as a proof-of-concept C₄ (featuring the “open” ligand) with one counterion, lattice solvent molecules, and Displacement ellipsoid plot (50% probability level) for the complex, or base), bis(chlorido)-bridged tetranuclear species. Notably, no single example exists of an intramolecular heterocyclization of 1-(ethynylphenyl)urea (85%), in accordance with as elective catalytic competence of this well-defined Au₃ species. Markovnikov addition to generate a six-membered ring (8) involves π-activation by a single gold species, whereas dinuclear π-activation results in anti-Markovnikov addition to give a five-membered ring (7; Scheme 3). Using 2.5 mol% of 3 in DMF at 60°C for five hours leads to full conversion and high regioselectivity for the five-membered indole 7 (85%), in accordance with a selective π-activation mechanism. External base (such as K₂CO₃) inhibits the reactivity, while addition of one equivalent of AgNTf₂ with respect to the catalyst provides slightly higher regioselectivity for 7 (90%); presumably this is due to faster generation of the π-acetylide species. In the absence of additives (Ag⁺ or base), bis(chlorido)-bridged tetranuclear complex 4 displays a similar preference for formation of 7. The high regioselectivity achieved with dinuclear catalysts 3 and 4 is attributed to the ligand-enforced proximity of both Au⁺ centers. Stoichiometric reaction of 3 and 6 shows sole formation of the π-activated substrate by ESI-MS (Supporting Information, Figure S27).

Dilution studies were performed to investigate the effect of decreased catalyst loading on the level of regiocontrol for the conversion of 6 to 7 and 8. The findings clearly validate our hypothesis, as the high regioselectivity for 7 obtained with catalyst 3 is independent of the catalyst concentration (Figure 4). In contrast, dilution experiments with mononuclear AuCl(PBu₃)—reported as the best catalyst to form 7 by π-activation[17]—result in a sharp drop in selectivity. These results demonstrate the benefits of well-defined pre-organization of two gold centers to enforce selective π-activation and to mediate regioselective dual gold catalysis with functionalized alkynes, even at low catalyst loadings.

In summary, we have demonstrated that the redox-active PN₃PP₃ ligand is a suitable framework to preorganize two gold centers for selective π-activation of functionalized alkynes. Halide abstraction from mixed-valent Au⁺–Au³ complex 2 using AgNTf₂ results in highly unusual reactivity

Figure 3. Displacement ellipsoid plot (50% probability level) for the cationic part of 5. The NTf₂ counterion, lattice solvent molecules, and hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Au1–P1 2.2899(10), Au2–P2 2.2676(11), Au1–C15 2.019(5), Au2–Ct(C15-C16) 2.201, C15–C16 1.227(6), Au1–Au2 3.1110(2), P1–Au1-C15 176.81(13), Au1-C15-C16 174.2(4), P2-Au2-Ct(C15-C16) 174.99, C15-C16-C17 170.0(5).
involving two-electron ligand oxidation, generating chlorido-bridged Au-I-Au II species 3 bearing a highly rigidified carbazolyl backbone. Reaction with phenylacetylene enabled the first crystallographically characterized intramolecular dual gold $\alpha,\pi$-acetylide complex (5) supported by a single diphenylphosphine. The well-defined dinuclear Au II complexes are excellent precatalysts for dual gold catalysis involving selective $\alpha,\pi$-activation, inducing high regioselectivity in the gold-catalyzed heterocyclization of urea 6, without the need to add base or silver salts. Dilution experiments show that dinuclear catalyst 3 retains high selectivity at decreased catalyst loadings, unlike mononuclear Au I catalysts typically employed for this reaction. These results illustrate the benefits of preorganization of gold centers to invoke selective substrate activation in dual gold catalysis. The detailed mechanism behind the surprising conversion of 2 into 3 is currently under investigation. This ligand-to-gold two-electron transformation appears to involve several digold intermediates, including the dinuclear “monomer” of complex 4, as well as a unique Au II-Au III species supported by one PNP ligand. [19]

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[14] For the bite angle of the oxygen analogue of L\textsuperscript{1}\textsuperscript{b} and benzofuran derivative, see: M. Kranenburg, Y. E. M. van der Burgt, P. C. J. Kamer, P. W. N. M. van Leeuwen, K. Goubitz, J. Fraanje, Organometallics 1995, 14, 3081–3089.


[19] Because of the anticipated complexity associated with this multistep “cascade” process, which converts 2 into 3, a detailed mechanistic investigation of this transformation is deemed beyond the scope of this study and will be reported elsewhere.

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