Carbocations as secondary coordination sphere Z-type ligands – Anion-induced Au(I)/Au(III) oxidation and impact on reactivity

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ABSTRACT: Controlling the reactivity of transition metals by secondary coordination sphere effects is an active area of investigation with potential benefits in the area of molecular catalysis. Here we describe our efforts towards the design of phosphine-based ligands featuring an electrophilic carbocationic moiety positioned to enter the secondary coordination sphere of the phosphine-bound metal atom. Using simple synthetic protocols, we have been able to obtain and fully characterize the complexes $[(o\text{-Ph}_2\text{P}(\text{C}_6\text{H}_4)\text{Acr})\text{AuCl}]^+$ (**[3]**⁺, Acr = 9-*N*-methylacridinium) and $[(o\text{-Ph}_2\text{P}(\text{C}_6\text{H}_4)\text{Xan})\text{AuCl}]^+$ (**[4]**⁺, Xan = 9-xanthylum). While only weak interactions occur between the gold atom and the methylium centers of these complexes, the more Lewis acidic **[4]**⁺ readily reacts with chloride to afford a trivalent phosphine gold dichloride derivative (**7**) in which the metal atom is covalently bound to the former methylium center. This anion-induced Au(I)/Au(III) oxidation is accompanied by a conversion of the Lewis acidic methylium center in **[4]**⁺ into an X-type ligand in **7**. This transformation leads us to conclude that the methylium center acts as a latent Z-type ligand poised to increase the Lewis acidity of the gold center, a notion supported by the carbophilic reactivity of these complexes.

A new paradigm has emerged in catalysis whereby the positioning of an electron-deficient moiety proximal to late transition metals has led to remarkable changes in catalytic activity for a number of reactions.¹⁻³ This area of chemistry has seen its most notable advances in the chemistry of transition metal complexes bearing boron-containing Lewis acidic Z-type ligands.⁴⁻⁸ The boron atoms of such ligands may directly interact with the catalytic center leading to substantial benefits in catalysis. This point is illustrated by the properties of tris(phosphino)borane iron complexes (**I**) and their ability to promote the reduction of dinitrogen into ammonia (Figure 1).⁹ Given the multiple redox states adopted by the dinuclear core during catalysis, the Fe→B interaction provides a conduit through which accumulation of electron density at the iron center can be partly dissipated. This buffering effect and the adaptive nature of the Lewis acid-metal interaction are not unique to boron and have been invoked in complexes involving other types of σ -accepting ligands.¹⁰⁻¹¹ In ambiphilic boron-containing ligands, the boron atom can enhance the electrophilic properties of an adjacent late transition metal by drawing electron density through a direct M→B interaction. For example, gold complexes of type (**II**) display enhanced carbophilic reactivity as demonstrated by their ability to promote enyne cyclization reactions.¹² Cases also exist where the boron atom does not directly interact with the metal but instead acts in concert with the adjacent transition metal towards activation of a small molecule. Examples of such complexes include the nickel complex **III** that activates dihydrogen and promotes the hydrogenation of styrene.¹³ Based on the isolobal relationship that connects boranes and methylium cations, one would predict that the positive attributes displayed by boron in these ambiphilic ligand systems may also apply to the chemistry of methylium-based systems (Figure 1).

Motivated by this possibility, we have thus decided to reengage in carbocation chemistry¹⁴⁻¹⁶ and explore the synthesis and properties of methylium-based analogs of ambiphilic boron-containing ligands, a class of compound that remains remarkably absent from the literature. In this paper, we describe the initial results that we have obtained while pursuing this idea. In particular, we describe the methylium analogs of known L/Z ambiphilic monophosphinoborane ligands,¹⁷ their coordination to gold fragments and their impact on metal-centered reactivity. Our original efforts toward the synthesis of such species focused on cations such

as $[o\text{-Ph}_2\text{P}(\text{C}_6\text{H}_4)\text{CPh}_2]^+.$ ¹⁸ We found that this formulation actually existed as four-membered phosphonium species as a result of an intramolecular cyclization resulting from nucleophilic attack of the methylium carbon atom by the phosphino group.

Figure 1. Selected examples of Z-type ligand scaffolds. General phosphino-methylium scaffolds investigated herein.

To disfavor phosphonium ion formation, we have now decided to pursue the introduction of methylium units where the carbocation is substantially stabilized as in the case of acridinium and xanthylum derivatives.¹⁹⁻²⁰ Toward this end, 1-lithio-2-diphenylphosphino-phenylene was quenched with *N*-methyl acridone or xanthone leading to the formation of the phosphinocarbinols **1** and **2**, respectively (Scheme 1).²¹ Subsequently, the acridinium gold(I) chloride derivative **[3][BF₄]** was generated *via* the sequential addition of (t_ht)AuCl to the carbinol **1** in a 1:1 molar ratio followed by aromatization to the acridinium cation by addition of 1 equiv. of HBF₄. This method afforded the target monocation as an air stable yellow/green solid in 97% yield. The analogous reaction was carried out with the xanthene precursor **2**, generating the xanthylum product **[4][BF₄]** as an orange solid in equally good yield of 93% (Scheme 1). This transformation could be easily tracked using multinuclear NMR spectroscopy for example; the presence of the carbinol proton is diagnostic in the ¹H NMR spectrum giving a resonance at $\delta = 2.24$ ppm for **1** and 2.49 ppm for **2** which disappears upon dehydration. Another prominent resonance that aids in identification is the *N*-methyl protons of **1** which appear at $\delta = 3.64$ ppm which, upon treatment with HBF₄, undergo a down-field shift to $\delta = 4.90$ ppm, concomitant with the aromatization of the acridine backbone. Additionally, the ³¹P NMR signals undergo a shift from $\delta \sim -19$ ppm for both carbinol precursors **1** and **2**, to $\delta = 22.4$ and 25.8 ppm for **[3][BF₄]** and **[4][BF₄]**, respectively.

Scheme 1. Synthetic overview of carbinols **1** and **2** and monocations **[3][BF₄]** and **[4][BF₄]**. Isolated yields shown.

Crystals of **[3][BF₄]** and **[4][BF₄]** suitable for single-crystal X-ray diffraction could be grown by vapor diffusion (Figure 2). The metrics for the solid-state structures of **[3][BF₄]** and **[4][BF₄]** are similar in terms of the eclipsing of the P(1)-Au(1)-Cl(1) motif with the C(6)-C(14)-C(15) plane showing an Au(1)-P(1)-C(14)-C(15) dihedral angle of only 10.0(9)° for **[3][BF₄]** and 1.36(18)° for **[4][BF₄]**. Furthermore, a relatively short interatomic distance is noted between the gold atom and the methylium center of 3.168(9) Å in **[3][BF₄]** and 3.131(3) Å for

[4][BF₄], indicating the possibility of a weak interaction ($\Sigma_{VDW}(Au-C) = 3.36 \text{ \AA}$). In order to probe this interaction, an atoms-in-molecules (AIM)²² analysis was implemented of the geometry optimized structures of [3]⁺ and [4]⁺.

Figure 2. Solid-state structure of [3][BF₄] (left) and [4][BF₄] (right). BF₄ counterions and hydrogen atoms omitted for clarity. Thermal ellipsoids drawn at 50% probability. Result of atoms-in-molecules calculation showing gold-methyl bond path with bond critical points (bottom).

This analysis reveals that a bond path is indeed present between the methylum center and the gold atom with electron density $\rho(r)$ of $1.4 \times 10^{-2} \text{ e/bohr}^3$ and $1.5 \times 10^{-2} \text{ e/bohr}^3$ at the localized bond critical points (BCP) for [3]⁺ and [4]⁺ respectively (Figure 2). The low BCP $\rho(r)$ values suggest that these contacts are rather weak. This conclusion is supported by the results of Natural Bond Orbital calculations that show only weak donor-acceptor bonding between the gold atom and the adjacent acridinium or xanthylum units which act as weakly interacting secondary coordination sphere ligands.²³⁻²⁶

The weakness of the Au→C interactions in the structures of [3][BF₄] and [4][BF₄] is consistent with the observation of the ¹³C NMR signals at $\delta = 159.7$ and 173.8 ppm corresponding to the methylum centers respectively. These structural and spectroscopic findings indicate that the methylum center present in these complexes are uncompromised and thus potentially poised for engaging a Lewis basic partner. Intrigued by this possibility, we decided to interrogate the complexes with a simple Lewis base, a chloride anion. As a prelude to these studies, we first studied the interaction of *N*-methyl-phenyl-acridinium [5]⁺ and phenyl-xanthylum [6]⁺ with chloride anions. UV-vis. titration experiments carried out by addition of TBACl to solutions of the cation (10^{-4} M) in CH₂Cl₂ indicate that chloride anion binding by [6]⁺ is essentially quantitative upon addition of 1 equivalent, even under dilute conditions ($K > 5 \times 10^6 \text{ M}^{-1}$) (Scheme 2). By contrast, [5]⁺ shows no affinity for chloride anions under dilute conditions. The same conclusion is reached when the reaction is studied by ¹H NMR spectroscopy at $8.3 \times 10^{-2} \text{ M}$ concentrations of the cation. Under these conditions, the acridinium derivative does not interact with chloride while the xanthylum derivative is quantitatively neutralized. We also tested the interaction of Ph₃PAuCl with chloride and confirmed by ³¹P NMR the absence of any changes.

Scheme 2. Quenching of methylium center by chloride with experimental rate constant

With this reactivity baseline established, we moved to studying the behavior of the gold(I) complexes upon addition of chloride, using UV-vis spectroscopy. While the spectrum of **[3][BF₄]** remained unchanged, addition of chloride to the more Lewis acidic xanthylum derivative **[4][BF₄]** led to the formation of a new species, referred to as **7**, characterized by a strong absorption band centered at 328 and 432 nm. The appearance of this atypical feature prompted us to also study the reaction by NMR spectroscopy. Addition of 1 equiv. of TBACl gave rise to a new broad singlet resonance in the ³¹P NMR at $\delta = 58.3$ ppm which resolved upon cooling to -30 °C to a much sharper singlet centered at $\delta = 60.2$ ppm. Furthermore, the resonance of the methylium center was no longer present in the ¹³C NMR spectrum with a quaternary carbon being observed at $\delta = 77.7$ ppm.²⁷ Formation of **7** is also observed when the carbinol precursor (**2**) is combined with (tht)AuCl and ethereal HCl simultaneously.

Scheme 3. Oxidative addition of gold upon chloride coordination. Yield shown from alternative synthesis using HCl.

Figure 3. (Left) Solid-state structure of **7**. Thermal ellipsoids drawn at 50% probability. Hydrogen atoms omitted for clarity. (Center) NBO depictions of the LUMO, HOMO and HOMO-1 orbitals. Isosurface value = 0.04. (Right) UV-vis. spectrum where solid trace = experimental, dashed trace = simulated.

We reasoned that the changes observed upon combining **[4][BF₄]** with chloride could be the results of chloride addition either to the methylium center or to the gold center. An optimization of the structure of the product resulting from addition of chloride to the gold center followed by a TD-DFT simulation of the UV-vis spectrum provided initial evidence for the nature of this complex. Indeed, the TD-DFT simulation afforded two

dominant vertical excitations at 340 and 420 nm which satisfactorily coincided with those experimentally observed at 328 and 432 nm. Both absorptions, which have ligand to metal charge transfer character, involve the xanthene-based HOMO and HOMO-1 as the ligand based orbitals, respectively. For both transitions, the metal-based orbital, which is the LUMO of the complex, has $d_{x^2-y^2}$ character as expected in the case of d^8 electronic configuration (Figure 3). X-ray diffraction confirmed coordination of the added chloride to the gold center, in concert with the formation of a covalent bond between the gold atom and the former methylium center (Scheme 3). Indeed the structure of **7** displays a square planar gold atom with the cis-angles about gold comprised between $86.142(6)^\circ$ and $92.851(6)^\circ$. The two Au-Cl bonds have similar lengths ($2.3746(2)$ Å for Au(1)-Cl(1) and $2.3943(3)$ Å for Au(1)-Cl(2)) and the Au(1)-C(6) bond of $2.135(6)$ Å is in line with a covalent bond between an sp^3 carbon and gold atom.²⁷ This structural assay indicates that the arrested $Au \rightarrow C_{\text{methylium}}$ coordination seen in **[4][BF₄]** may be bolstered by the addition of a chloride anion to the gold atom to spur electron density to flow from gold to the methylium center. In other words, coordination of an extra chloride anion enhances the metallobasic character of the gold atom, promoting its coordination to the Lewis acidic methylium center. The result is a net anion-induced oxidation of the gold center which transitions from a d^{10} electronic configuration in **[4][BF₄]** into a d^8 electronic configuration in **7**. The anion induced oxidation of the gold center in complex **[4][BF₄]** bears a parallel with the susceptibility of aurates towards oxidation as documented in the seminal work of Kochi.²⁸ The reaction of **[4]⁺** with chloride could be viewed as providing a snapshot of a hypothetical, SN_1 -like, C_{sp^3} -X bond activation reaction where halide dissociation from the carbon electrophile would have occurred first. Such a pathway has not been proposed for the insertion of gold(I) fragments into C_{sp^3} -X bonds which are generally assumed to occur via an SN_2 mechanism,²⁹⁻³² as typically seen in late transition metal chemistry.³³ The structure of the L/Z ligand in **[4][BF₄]** and its rigidity are certainly conducive of the formation of a d^8 gold center, an attribute that has been exploited to promote C_{sp^2} -X bond activation by gold using structurally related L_2 -type ligands.^{29, 34-35} Finally, we will note that the carbon ligand also changes from Z-type in **[4][BF₄]** to X-type in **7**. As a result, **7** resembles complexes obtained by intramolecular oxidative insertion of gold(I) halide moieties into C-X bonds.³⁶ A parallel must also be drawn with a series of recently reported Pd(II) and Rh(I) complexes featuring *o*-phosphino-triarylmethyl ligands.³⁷

The conversion of **[4]⁺** into **7** is the result of a chloride push – methylium pull effect. We reasoned that the pull exerted by the methylium center could also be assessed by probing the electrophilic reactivity of the gold center. Following up on this idea, we selected the cyclization of propargyl amide as a reporter reaction,³⁸ specifically using the *p*-fluoro derivative **8** which contains a convenient NMR handle. Using a 2 mol% catalyst loading, cyclization of **8** progressed swiftly at 60 °C in CH_2Cl_2 in the case of **[4][BF₄]** which proved to be markedly more active than **[3][BF₄]**, in line with the higher Lewis acidity of the xanthylum unit (Scheme 4).

Scheme 4. Cyclization of 4-fluoro-N-(prop-2-yn-1-yl)benzamide (**8**). In situ conversion measured by ^{19}F NMR spectroscopy of the ratio between starting material **8** and product **9**. Yields given as isolated yields.

As the reaction progresses, ^{19}F NMR monitoring shows the disappearance of the resonance at $\delta = -109$ ppm and the appearance of a new peak at $\delta = -107$ ppm for the cyclized product **9**. Of note is the overwhelming selectivity for the *exo*-alkene dihydrooxazole product **9** over the oxazoline tautomer which is in contrast to other gold(I) catalysts which show inverse selectivity or show a mixture in various ratios.³⁹⁻⁴⁰ Interestingly, no conversion was observed when Ph_3PAuCl was used in the presence or in the absence of either **[5]** $[\text{BF}_4]$ or **[6]** $[\text{BF}_4]$. These results underscore the importance of having the Lewis acidic carbocationic unit integrated within the same molecular platform, leading us to propose that substrate activation by **[3]** $[\text{BF}_4]$ and **[4]** $[\text{BF}_4]$ is the result of transient substrate coordination to the gold center as per the working model presented in Scheme 4.

The synthesis and characterization of the cationic complexes **[3]** $^+$ and **[4]** $^+$ reported herein allow us to introduce the use of triarylmethyl cations as secondary coordination sphere ligands. In the absence of a base, the methyl cation center of these complexes acts as a latent Z-type ligand poised to increase the Lewis acidity of the gold center, should a Lewis base become available. This possibility is illustrated by the reaction of **[4]** $^+$ with chloride which results in the formation of the trivalent gold derivative **7**. This anion-induced oxidation is also accompanied by a conversion of the methyl cation Z-type ligand in **[4]** $^+$ into an X-type ligand in **7**. Finally, the methyl cation secondary-coordination sphere ligand also influences the carbophilic reactivity of the gold center as illustrated by the activity of **[4]** $^+$ as a catalyst for the cyclization of propargyl amide **8**.

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