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Rationale for the Sluggish Oxidative Addition of Aryl Halides to Au(I)

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The oxidative addition of C6H2-Br or C6H5-Br bonds to gold(I) does not take place even under very favorable intramolecular conditions that could form five- or six-membered gold(III) metallacycles. DFT calculations reveal that, although this process could be feasible thermodynamically, it is kinetically very sluggish.

Gold(I) complexes activate unsaturated substrates in catalytic processes that are characterized by the invariance of the oxidation state of the metal.1 Although it was proposed that the Sonogashira2,3,4,5 and Suzuki coupling could be catalysed by gold,4,6 it seems now clear that at least in some cases the catalytic role is played by either small amounts of palladium contaminants5,8 or by gold nanoparticles,10,11,12,13,14 which probably mediate these couplings by mechanisms very different from those occurring under homogeneous conditions.15,16

Organogold(I) complexes transmetallate with Pd(II), which has been used in their coupling with aryl iodides with palladium catalysts.17,18,19 However, the oxidative addition of aryl halide ArX to a gold(I) complex [AuXL] is a necessary step for a cross-coupling catalysed by this type of d10 complexes is unprecedented. Indeed, an alkynyl gold(I) complex with a pending aryl iodide has been structurally characterized as an stable complex, although it could have undergone intramolecular oxidative addition through a six-membered transition state.20 Complexes [AuMePPh] behave as ordinary S‚2 nucleophiles adding slowly with alkyl iodides, following the expected order of reactivity: CH3I > EtI > i-PrI.21,22,23 Disulphides undergo oxidative addition reactions with gold(I) dithiolate complexes.24 Interestingly, the oxidative addition of a relatively weak Si-Si bond to gold(I) is a very favourable process.25 DFT calculations showed that the oxidative addition of iodobenzene to complex [Au(I)PMe3] has a high activation barrier (31.6 kcal mol−1 in potential energy, likely higher in free energy).10a However, bisphosphine gold clusters [Au2L3] and [Au2L3] react in the gas phase by C-I bond activation.26

We decided to study the oxidative addition of Ar-X bonds to [AuXL] by examining systems of type I in which the metal coordinates the phosphorous ligand of a phosphine or phosphite bearing an ortho-halogenated aryl group (Scheme 1). Under these very favourable conditions, the oxidative addition could occur intramolecularly to form gold(III) metallacycles of type II. We have performed DFT calculations to clarify the origin of the sluggishness, thermodynamic or kinetic, of the oxidative addition of aryl halides to gold(I) complexes.

Scheme 1 Hypothetical intramolecular oxidative addition of C6H5-X bonds to Au(I) to form Au(III) metallacycles II.

Reaction of phosphites (α-IC3H7O)P (1a) and (α-IC3H7H2CH2)3P (1b) with [AuCl(THT)] (THT = tetrahydrothiophene) in CH2Cl2 led to complexes 2a (17%) and 2b (10%) as white solids. Their structures were determined by single crystal X-ray diffraction (Figures 1 and 2).27 These complexes show non-C3-symmetrical structures in the solid state with the phosphite ligands adopting a syn-conformation.28 The Au-P (2.19-2.20 Å) and Au-Cl (2.28 Å) bond distances are similar in both complexes. In the case of complex 1a, two of the α-iodophenyl rings have the C-I bonds pointing towards the Au(I) centre, with a closest Csp2-Au distance of 3.795 Å (Figure 1a). In contrast, in complex 2b the C-I bonds of the three aryl rings are anti oriented with respect to the P-Au-Cl bond (Figure 1b).

The related phosphine complex 4a was obtained in 60% yield by reacting (α-BrC6H5)3P (3) with [AuCl(THT)] in a 1:1 ratio. When the reaction was carried out in a 2:1 ligand to Au(I) ratio, bisphosphine gold(I) complex 5 was isolated in 70% yield. The structures of 4a and 5 were confirmed by X-ray diffraction (Figure 2).27 The Au-P distance in 4a (2.22 Å) is much shorter that those in more crowded complex 5 (2.30 Å). Complex 4a displays an almost C3-symmetrical structure with C6H5(Br)-Au distances between 3.61 and 3.86 Å. We also prepared an...
analogous complex 4b from (2-bromobenzyl)diphenylphosphine. Complex 5 shows a \(D_{3d}\) symmetrical structure with \(C_{3v}\) (Br)-Au distances of 4.1 Å and the six Br atoms in a non-octahedral arrangement around the metal centre (Br-Au distances of 3.7-3.8 Å).

Similarly, more robust complex 4 was recovered unchanged after being heated in toluene solution at 60 °C for several days. Furthermore, bisphosphine gold(I) complex 5 failed to form any gold(III) metallacycle after being heated in DMSO at 100 °C for more than 5 days and was fully recovered without any sign of decomposition.

In order to better understand the reasons for the sluggish reactivity towards oxidative addition of this set of Au(I) complexes, we carried out computational studies (DFT calculations at the M06 level including solvation effects, values reported in text are free energies). The relative energies of all transition states and products are collected in Table 1. A representative transition state, \(2\text{ttts}\), is shown in Figure 3. There is simultaneous formation of the Au-C and Au-Br bonds, with distances of 2.273 and 2.587 Å, respectively. It is thus a concerted transition state that leads to complex [PhAuClBr(PMe\(_3\))] with the phosphine cis to Ph, in contrast to that reported for the oxidative addition of PhI to [Au(PMe\(_3\))I], which leads to trans-[PhAuI\(_2\)(PMe\(_3\))]\(_{10a}\). The alternative S\(_N\)2-like transition states\(^{11}\) with initial departure of a bromide anion were also located in a number of cases but had always higher energies than the concerted ones. The endergonic character of the oxidative addition processes computed in Table 1 is consistent with the facile reductive elimination of R-R from trialkyl [R\(_3\)AuL] complexes.\(^{32}\)

### Table 1. Computed M06 Relative Energies (kcal mol\(^{-1}\)) of transition states and products for oxidative addition.

<table>
<thead>
<tr>
<th>Transition state</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)t (-)</td>
<td>(-)</td>
</tr>
<tr>
<td>(2)t</td>
<td>42.6</td>
</tr>
<tr>
<td>(3)t</td>
<td>47.3</td>
</tr>
<tr>
<td>(4)t</td>
<td>48.5</td>
</tr>
<tr>
<td>(5)t</td>
<td>(-)</td>
</tr>
<tr>
<td>(6)t</td>
<td>23.3</td>
</tr>
</tbody>
</table>

The X-ray structure of 4 was used as a starting point in the geometry optimization of \(1\)tr to avoid time-consuming conformational searches,\(^{35}\) and the same conformation was used in the calculations for \(1\)ttts and \(1\)tp. The associated transition state \(1\)ttts (Figure 3) has a relative free energy of 41.5 kcal mol\(^{-1}\) above the reactant. This is in full agreement with the lack of reactivity under the experimental conditions. The relative free energy of intermediate \(1\)tp, which is only 17.4 kcal mol\(^{-1}\), higher than the starting Au(I) complex \(1\)tr, could be accommodated into a catalytic cycle, but not that of the transition state. This hints to a kinetic rather than thermodynamic origin for the lack of reactivity of Au(I) complexes in oxidative addition processes.

Complexes \(2\)a and \(2\)b did not undergo oxidative addition to form the corresponding metallacycles of type II in CD\(_2\)Cl\(_2\) solution.
Further calculations showed that the more electron depleted the aryl halide was rendered, the lower the barrier for the oxidative addition became. However, even in the most favourable case, 2,4,6-trinitro-bromobenzene, the activation energy is still relatively high (28.0 kcal mol$^{-1}$).

Our joint experimental and computational study demonstrates that linear 2-coordinate di$^{19}$ Au(I) complexes are much less reactive towards oxidative addition than the related Pd(0) complexes. The Au(III) species that would result from the reaction have in most cases reasonable energies, but the barriers to access them are prohibitively high for moderate temperatures.

Oxidative addition is a key step in cross-coupling, and Au(I) will be thus unable to replace Pd(0) in most of these reactions. The sluggishness of the reaction in the Au(I) system seems to be related to its strong preference for coordination 2. This is a specific characteristic of Au(I) that is not shared by Pd(0), and explains why, despite having the same number of valence electrons, these two metals have significantly different reactivity. Our results hint to a possible solution, since the oxidative addition would be much easier when starting from a [LAu(III)] complex. Although this type of mono-coordinated complexes are unknown, complexes [LAu(II)]$^+$ with a very weakly coordinated ligand L$^-$ might undergo the required oxidative addition reaction under sufficiently mild conditions acting as genuine catalysts for cross-coupling reactions of aryl halides.

Work towards achieving this goal is in progress.

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Notes and references


