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Isocyanide insertion into Au-H bonds: first gold iminoformyl complexes†

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Accepted 00th January 20xxJulio Fernandez-Cestau,^{a,b*} Luca Rocchigiani,^a Anna Pintus,^{a,c} Raquel J. Rama,^{a,d} Peter H. M. Budzelaar^{e*} and Manfred Bochmann^{a*}

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Isocyanides insert into gold(III)-hydrogen bonds to give the first examples of gold iminoformyl complexes. The reaction is initiated by catalytic amounts of radicals; DFT calculations indicate that this is an equilibrium reaction driven forward by isocyanide in sufficient excess to trap the Au(II) intermediate.

The ability of isocyanides to insert into M-C, M-X and C-H bonds is well documented¹ and widely exploited in synthetic applications.² By contrast, examples of isocyanide insertion reactions into M-H bonds are scarce and largely restricted to early transition metals, where they form η^2 -bonded iminoformyls, either as stable products or as intermediates in more complex reaction sequences. Notable examples are the reactions of isocyanides with hydrido complexes of zirconium³ and tantalum,⁴ which lead to η^2 -iminoformyls or their follow-on products. By contrast, ruthenium hydrido silane complexes were found to react with xyINC under insertion into a Si-H rather than Ru-H bond (xyl = 2,6-Me₂C₆H₃).⁵ There are only very few reports of η^1 -coordinate iminoformyl ligands, such as the reaction of [OsCl(CO)₂(PPh₃)₂(CHSM)]⁺ with methylamine which generates OsCl(CH=NMe)(CO)₂(PPh₃)₂, and the reaction of *trans*-[PtH(CNR)₂]Cl (R = *p*-tolyl; L = PEt₃, PMe₂Ph) in non-polar solvents to give *trans*-PtCl(CHNR)L₂, most probably via an associative process involving 5-coordinate intermediates.^{6,7} However, there was no crystallographic confirmation of the iminoformyl products. The very bulky 2,6-dimesitylphenylisocyanide was recently shown to insert into a Co-H bond to give a product where one of the mesityl

substituents coordinates to the metal to form an η^6 -bonded chelate.⁸

No such reactions are known for gold. Gold complexes have become a major research focus in recent years,⁹ and their reaction mechanisms are being explored in an effort to gain insight into their behaviour as catalysts.¹⁰⁻¹² Of particular interest in this context are insertion reactions of unsaturated substrates such as alkenes, alkynes, CO and isocyanides, which are commonplace for most transition metal compounds and play a key role in catalytic reactions from hydrogenations and carbonylations to polymerisations¹³ but remain little explored for gold, and particularly for gold(III).

In contrast to most other transition metal alkyls and hydrides, Au-H and Au-C bonds have proved to be remarkably resistant to insertion reactions. The first examples of ethylene insertions into Au-C¹⁴ and Au-O bonds^{15,16} have only recently been discovered. The gold(I) hydride (NHC)AuH undergoes a formal *trans*-insertion with dimethylacetylene dicarboxylate (DMAD) to give the corresponding *Z*-vinyl gold complex, by an unknown mechanism.¹⁷ The same stereochemical outcome was observed during the thermal decomposition of the pincer complex (C[^]C[^]N)Au(O₂CH) in the presence of DMAD,¹⁸ and the reaction of (C[^]C[^]N)AuH (H *trans* to phenyl) with DMAD (C[^]C[^]N = 2-aryl-6-pyridylaryl dianion).¹⁹ By contrast, another pincer complex, (C[^]N[^]C)AuH (H *trans* to pyridine) reacts with a wide range of terminal and internal alkynes R¹C≡CR² with almost complete stereo- and regioselectivity to give *trans*-Au-vinyl products, by a binuclear outer-sphere mechanism involving Au(II) radicals (C[^]N[^]C = 2,6-diphenylpyridine dianion).²⁰ The same radical-induced mechanism enabled the 1,2-hydroauration of terminal alkenes.²¹ Whereas the insertion of CO into Au-O bonds of gold(III) methoxides proceeds readily to give stable Au-COOMe products,²² to the best of our knowledge there are no reports to-date of CO or isocyanide insertions into Au-H or Au-C bonds. We report here the first examples of gold η^1 -iminoformyl complexes generated by the insertion of isocyanides into Au(III)-H bonds.

The pincer gold(III) hydrides (L^Y)AuH (L^Y = 2,6-(C₆H₃Bu[†])₂-4-Y-pyridine dianion; Y = H, OMe) react with xylyl isocyanide in the

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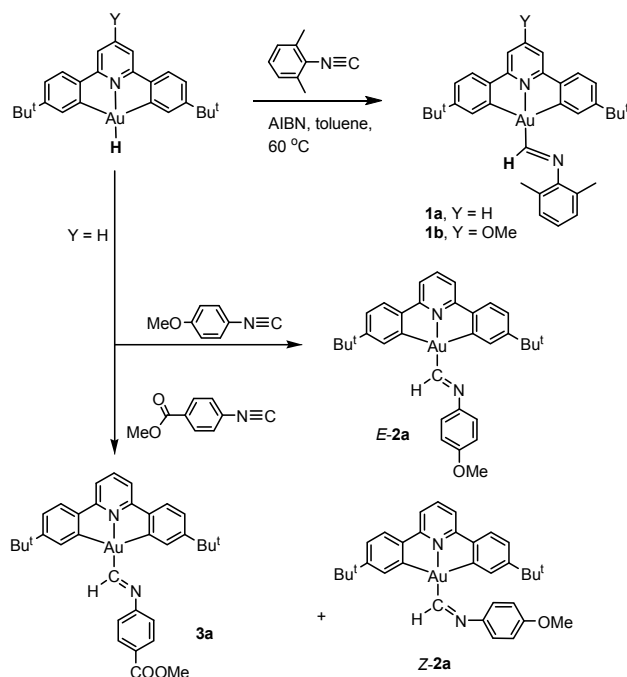
† Dedicated to Professor Ernesto Carmona on the occasion of his 70th birthday.

Electronic Supplementary Information (ESI) available: Synthesis, NMR spectra, X-ray crystallography, computational details. See DOI: 10.1039/x0xx00000x

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presence of a catalytic amount of a radical initiator (azobisisobutyronitrile, AIBN) in toluene at 60 °C to give the iminoformyl complexes (L^Y)AuCH=N(C₆H₃Me₂-2,6) (**1a**, Y = H; **1b**, Y = OMe) as pale-yellow solids. The analogous reactions of (L^H)AuH with *p*-MeOC₆H₄N≡C and *p*-MeOC(O)C₆H₄N≡C gave the insertion products **2a** and **3a**, respectively. Reactions performed in the absence of AIBN only generated small amounts of the insertion product in few cases and the results were irreproducible. Whereas **1a,b** and **3a** exist as single isomers, complex **2a** forms a mixture of *E* and *Z* isomers in an *E/Z* ratio of about 7:1 (Scheme 1). Although isocyanides frequently undergo multiple insertions,^{8,23} there was no evidence for this here, even in the presence of excess isocyanides.



Allowing pentane to diffuse slowly into a solution of **1b** in diethyl ether at -30 °C afforded colourless crystals of the complex suitable for X-ray diffraction. The asymmetric unit contains two independent molecules of the gold complex and three molecules of Et₂O, to give the stoichiometry (L^{OMe})AuCHNxylyl·1.5 Et₂O. The structure of one of the two independent molecules is shown in Fig. 1.

The C^{^N^A}C)Au moiety shows the familiar square-planar geometry, with angles and distances as expected for this pincer ligand. The identity of the iminoformyl ligand, as opposed to its Au=N=CHR imido isomer, was confirmed on the basis of the ΔMSDA values for the two possible situations. The iminoformyl ligand deviates by 44° from the expected perpendicular orientation relative to the (C^{^N^A}C)Au plane, presumably due to packing forces. The C-N distance is in agreement with a double bond and with 1.24(1) Å is only slightly shorter than comparable C-N distances in zirconium η²-

iminoacyl (1.264(4) Å)^{3a} and tantalum η²-iminoformyl complexes (1.260(6) Å),^{4b} whereas the C-N distance in iminoformyls bridging two tantalum atoms is considerably longer (1.477(5) Å).^{4b} The Au-C27(iminoformyl) distance of 2.005(7) Å is remarkably short for an Au-C single bond; for comparison, Au-C(sp³) and Au-C(sp²) distances ranging from in 2.04 to 2.11 Å have been reported for structurally related (C^{^N^A}C)gold alkyl and aryl complexes.^{13,24,25}

Adding one equivalent of the solid Brønsted acid [H(OEt₂)₂][H₂N{B(C₆F₅)₃}₂] (HAB₂)²⁶ to a solution of **1a** in CD₂Cl₂ affords quantitatively the formimmonium complex [(L^H)Au-(E)-CH=NHxylyl][H₂N{B(C₆F₅)₃}₂] (**4a**) (Scheme 2). The formation of **4a** is indicated by a shift of the -CH=N proton to higher frequency from δ 9.54 to 10.76 ppm and by the appearance of a broadened singlet for N-H at δ 11.56. Although this reaction was carried out initially as a means to aid crystallographic characterisation of an insertion product, attempts to obtain crystals of **4a** suitable for X-ray diffraction proved unsuccessful. Neither protolytic cleavage of Au-C bonds nor H⁺/SMe₂-induced reductive C-C coupling²⁷ were observed.

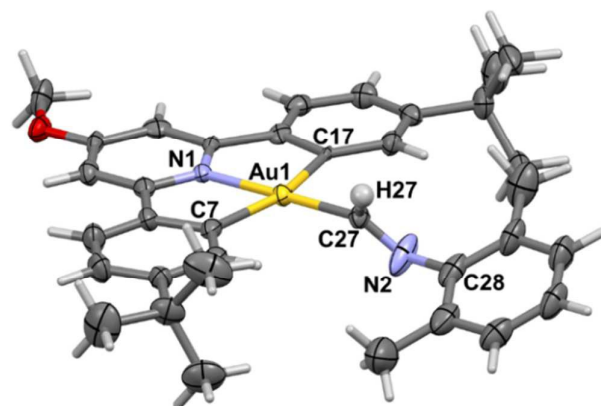
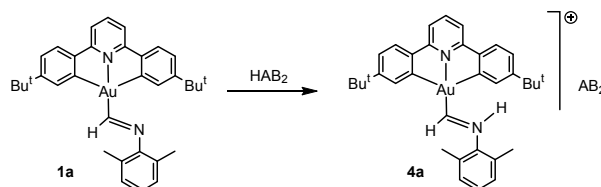


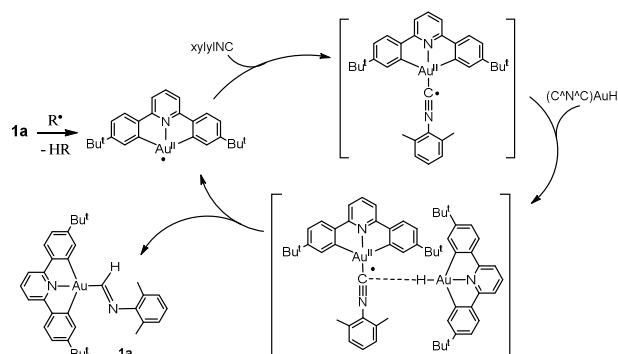
Figure 1. Molecular structure of **1b**, confirming the formation of the *E* isomer. Ellipsoids are drawn at 50% probability. Selected bond distances [Å] and angles [°]: Au1-C7 2.081(9), Au1-N1 2.039(7), Au1-C7 2.08(2), Au1-C27 2.005(7), Au1-C17 2.075(7), C27-N2 1.24(1), C27-H27 0.950, N2-C28 1.44(1), C17-Au1-N1 80.8(3), N1-Au1-C7 80.3(3), C7-Au1-C27 97.5(3), C27-Au1-C17 101.3(3), Au1-C27-N2 126.3(6), Au1-C27-H27 116.8, H27-C27-N2 116.9, C27-N2-C28 120.7(8). Torsion angle N1-Au1-C27-N2 136(7)°; angle between coordination plane of Au1 and the xylyl ring 27.85°.



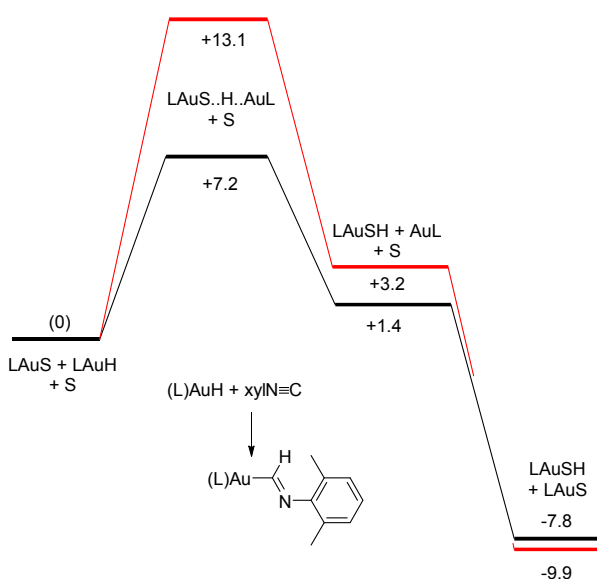
Scheme 2. Iminoformyl protonation

The insertion process is most probably initiated by the abstraction of an H radical by thermally decomposed AIBN, as

previously shown for alkene and alkyne insertions, with the difference that the present reaction constitutes a 1,1- rather than a 1,2-insertion. This mechanism was probed by DFT calculations (Scheme 3). Gibbs free energies were calculated for stationary points on the radical/hydride addition mechanism (optimization Gaussian, B3LYP/def2-SVP, no solvent; final energies Gaussian M06/cc-pVTZ, toluene), relative to the gold(II) radical ($C^{\wedge}N^{\wedge}C$)Au. The ($C^{\wedge}C^{\wedge}N$) ligand, a coordination isomer of ($C^{\wedge}N^{\wedge}C$) which places a strong (C) rather than weak (N) donor *trans* to the inserting ligand, was studied at the same level of theory for comparison. The results are shown in Scheme 4 (see also ESI, Table S3.1).



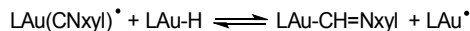
Scheme 3. Proposed radical-initiated isocyanide insertion mechanism



Scheme 4. Free energy profiles for the radical-mediated insertion of xylylisocyanide into Au-H bonds, for ($C^{\wedge}N^{\wedge}C$)AuH (black) and ($C^{\wedge}C^{\wedge}N$)AuH (red); energies in kcal/mol.

Complexation of $ArN\equiv C$ to both ($C^{\wedge}N^{\wedge}C$)Au $^{\bullet}$ and ($C^{\wedge}C^{\wedge}N$)Au $^{\bullet}$ is barrierless. The process starts with gold(III) hydride LAuH, a gold(II) substrate complex LAu-S and the free substrate S. Substrate binding increases in the order $[(C^{\wedge}N^{\wedge}C)Au(CNAr)]^{\bullet} < [(C^{\wedge}C^{\wedge}N)Au(CNAr)]^{\bullet}$. For the $C^{\wedge}N^{\wedge}C$ system, the initial H

transfer step has a low barrier (7.2 kcal/mol) and is slightly endergonic (+1.4 kcal/mol); however, trapping the initially formed Au(II) intermediate LAu $^{\bullet}$ by free substrate makes the overall reaction exergonic (-7.8 kcal/mol). These results indicate that isocyanide insertion will only happen in the presence of excess isocyanide. The equilibrium of the stoichiometric reaction



favours the reactant side and so would not proceed without excess of substrate to trap the LAu product.

The process involving the alternative $C^{\wedge}C^{\wedge}N$ ligand is similar in principle but has a much higher H transfer barrier (13.1 kcal/mol); this would be commensurate with a much lower reaction rate.

Spin density plots help to explain the different H transfer rates of ($C^{\wedge}N^{\wedge}C$) vs. ($C^{\wedge}C^{\wedge}N$) reactions. In ($C^{\wedge}N^{\wedge}C$)Au $^{\bullet}$ (CNxylyl), the xylyl and pyridine rings are nearly co-planar and the unpaired electron is delocalized over Au, the isonitrile group, and parts of the xylyl and pyridine rings (see ESI, Fig. S3.1); the high concentration on the isonitrile carbon in particular suggests an easy H radical transfer to this carbon. In contrast, in ($C^{\wedge}C^{\wedge}N$)Au $^{\bullet}$ (CNxylyl), the xylyl and pyridine π -systems are almost perpendicular, which leads to a higher concentration of spin density on Au and the pyridine ring it is bound to, and less on the isonitrile carbon, implying that more reorganization would be needed to form the addition product. In either ligand system formation of gold(II) dimers is an energy sink (2 LAu \rightarrow LAu-AuL, $\Delta G_{298K} = -26.8$ and -19.9 kcal/mol for $C^{\wedge}N^{\wedge}C$ and $C^{\wedge}C^{\wedge}N$, respectively).

The computations

The possibility of isocyanide to cyanide isomerisation and formation of an imido product ($C^{\wedge}N^{\wedge}C$)Au-N=CHR was also considered. A control reaction using *p*-MeC₆H₄C \equiv N instead of xylylNC under comparable conditions failed to give a reaction and at elevated temperatures led to the deposition of a gold mirror. This is in agreement with DFT calculations: taking the gold(II) complex LAu(S) as the starting point, nitrile insertion has a large barrier of 15.4 kcal/mol and leads to the addition product and free LAu at 13.6 kcal/mol, i.e. considerable *uphill* from the starting point. Unlike the isocyanide case, coordination of nitrile to LAu(II) is endergonic (by 1.1 kcal/mol) so there is no downhill capture step to compensate for the uphill insertion. As a result, the addition of LAuH to ArCN is considerably endergonic and will not happen to an appreciable extent, regardless of any proposed mechanism. Alternatives, such as direct insertion by RNC addition to (L)AuH can also be ruled out in the basis of their high transition states.

In summary, the first example of an isocyanide insertion into a gold-hydrogen bond has been reported, leading to an η^1 -iminoformyl complex, mediated by Au(II) radicals. Comparison of the energy profiles show that this can be a facile reaction in the presence of excess isocyanide but depends strongly on the *trans*-influence of the pincer ligand system.

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Conflicts of interest

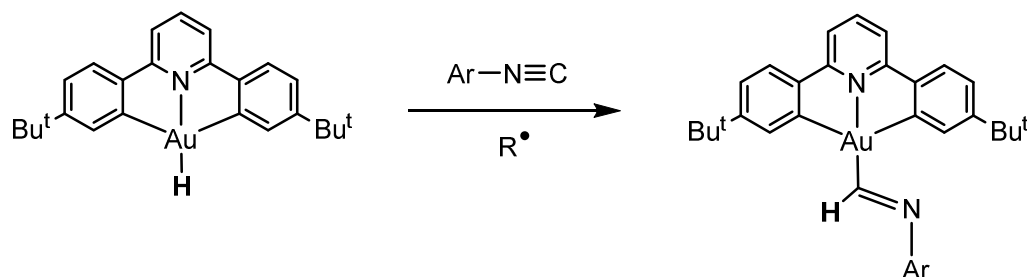
There are no conflicts to declare.

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Graphical Abstract

Isocyanide insertion into Au-H bonds: first gold iminoformyl complexes



The reaction of gold hydrides with isocyanides leads to η^1 -iminoformyl complexes, the first example of an isocyanide insertion in gold chemistry. Key intermediates are gold(II) isocyanide adducts.