Enantioselective hydrogenation of alkenes and imines by a gold catalyst

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A new neutral dimeric gold(I) complex bearing the 1,2-bis[(2*R*,5*R*)-2,5-dimethylphospholanebenzene] [(*R*,*R*)-Me-Duphos] ligand has been synthesized which catalyzes the asymmetric hydrogenation of alkenes and imines under mild reaction conditions.

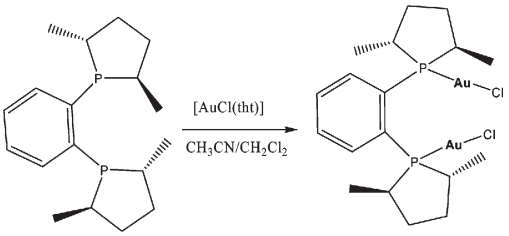
The use of gold compounds in homogeneous and heterogeneous catalytic organic reactions has been undervalued for many years due to the preconceived idea that gold is chemically inert. However, recent reports have changed this assessment and gold salts in small amounts are known to display high catalytic activity.[1] Indeed, Au(III) can act as a Lewis acid catalyst for a large variety of reactions.[2,3] In the case of solid gold catalysts, it has been reported that small clusters of gold are active and selective catalysts for oxidation, water gas shift, and some C–C bond forming reactions, probably due to the presence of cationic gold species.[4–12]

In the case of homogeneous catalysis,[13–16] gold, in the form of soft, carbophilic efficient Lewis acid catalysts, is able to activate C–C multiple bonds for the formation of C–C, C–O, C–N and C–S bonds.[17,18] However, asymmetric catalysis with gold is still scarce, the paradigmatic case being the asymmetric aldol condensation developed by Ito *et al.*[19] in which the addition of an isocyanoacetate to an aldehyde produces the corresponding *trans* isomer as the major and the *cis* isomer as the minor product, the former in an enantiomeric excess of ~96%. In this case, cationic gold and a chiral diphosphanylferrocene ligand was used as catalyst.[19]

In the case of gold hydrogenation catalysts we have not found any examples of asymmetric catalysis in our literature survey. Nevertheless, a patent was filed[20] in which complexes of tris(*m*-sulfophenyl) phosphate with numerous metals, including gold, were prepared and the use claimed for hydrogenations, water gas shift, hydroformylations, oxidations, carbon–carbon cross linking and hydroamination reactions. Interestingly, none of the catalytic examples was carried out with gold.[18]

Here we have synthesized a new dimeric gold(I) complex with the [(*R*,*R*)-Me-Duphos] ligand that is able to catalyze the enantioselective hydrogenation of alkenes and imines at 4 bar H_2 pressure, and room temperature.

The complex {$(AuCl)_2$[(*R*,*R*)-Me-Duphos]} (Scheme 1) was readily prepared by reacting the diphosphine with two equivalents of [AuCl(tht)] (tht = tetrahydrothiophene) in a mixture of acetonitrile–dichloromethane (2:1). More specifically, two equivalents of [AuCl(tht)] (104 mg, 0.32 mmol) were added to a solution of [(*R*,*R*)-Me-Duphos] (50 mg, 0.16 mmol) in 10 ml CH_3CN–CH_2Cl_2 (2:1). The resulting solution was stirred at room temperature under N_2 atmosphere for 2 hours, and then



Scheme 1

concentrated to dryness. A mixture of CH_2Cl_2–diethyl ether (1:15, *ca.*, 15 cc) was added to the residue and the resulting suspension was filtered. The resulting pale yellow solid (86 mg, 70%) was dried; mp: 221 °C (dec.). $[\alpha]_D^{25} = -254$ (*C* = 0.1, CH_2Cl_2). $C_{18}H_{28}Cl_2P_2Au_2$ (771): calcd. C: 28.0; H: 3.7; Au: 51.1; found C: 45.20; H: 5.03; Au: 32.09%. IR (KBr, cm^{-1}): ν = 329 (Au–Cl). UV-vis (λ, nm): 307 (CH_2Cl_2); 396, 356, 263 (solid). ^{1}H-NMR (MeOD, ppm): δ = 0.99 (6H, CH_3); 1.14 (6H, CH_3); 1.23–1.29 (2H, m, CH_2); 1.45–1.50 (1H, m, CH_2); 1.50–1.80 (1H, m, CH_2); 2.18–2.60 (6H, m, CH_2, CH); 3.37–3.85 (2H, m, CH); 7.51–7.89 (4H, Ph). ^{13}C-NMR (MeOD, ppm): δ = 18.2, 17.0 (CH_3); 20.0 (CH_2); 31.0, 30.0 (CH_3); 36.8 (CH); 41.2 (CH); 131.1–134.5 (Ph). ^{31}P-NMR (CD_2Cl_2, ppm) δ = 44.2 (s). EM (*m*/*z*): 736 ($[M]^+ - Cl$).

The complex was obtained as pale yellow solid. The composition was confirmed by elemental analysis and mass spectrometry (ESI-MS). The ESI spectrum (MeOH–H_2O) shows a peak at *m*/*z* = 736 which corresponds to the loss of one chloride ligand. The FT IR spectrum shows a strong band at 329 cm^{-1}, assigned to the ν(Au–Cl) vibration. The electronic absorption spectrum in the 200–800 nm range, was obtained using 10^{-3}–10^{-5} CH_2Cl_2 solutions and solid samples. The complex shows a band maximum in the UV region at 307 nm (in CH_2Cl_2) and bands at 396, 356, and 263 for solid samples. The diamagnetic gold complex has been characterized by ^{1}H, ^{13}C and ^{31}P NMR spectroscopy. The NMR spectra are consistent with the proposed structure (Fig. 1). All

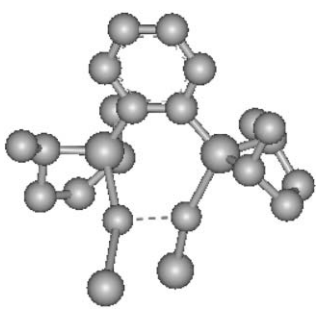


Fig. 1 Proposed structure for {$(AuCl)_2$[(*R*,*R*)-Me-Duphos]}.

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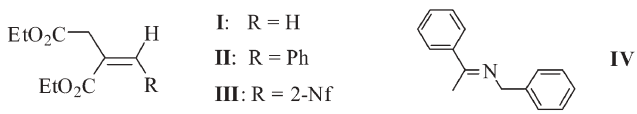
assignments are based on several correlations in the 2D spectra. In the aromatic regions of the ^{1}H NMR spectrum, the signals appears at 7.51–7.89 ppm, the signals due to aliphatic rings of the 2,5-dialkylphospholane moieties appear as a slightly high field shifted multiplet due to the coordination with Au, in positions close to those for the free phosphine. In the ^{13}C NMR spectrum all the resonances were shifted as compared to the uncoordinated ligand, in agreement with metallation of the ligand and coordination of the metal atom *via* the P atom. The ^{31}P NMR spectrum in CD_2Cl_2 shows a singlet signal at 44.2 ppm (δ = 2.9 ppm for the free ligand in C_6D_6) that indicates a symmetric geometry for the P atoms in accordance with the proposed structure (Fig. 1).

A model for complex {$(AuCl)_2$[(*R*,*R*)-Me-Duphos)]} shows an aurophilic, Au···Au, interaction (Fig. 1). This interaction forces the Au coordination environments which deviates the P–Au–Cl angles a little from linearity. The P–Au–Cl fragments are almost perpendicular to each other.

The rich photochemistry exhibited by many Au(I) complexes and the potential applications derived therefrom, has triggered numerous studies focused on clarifying the relationships between the structures and the optical properties of the compounds.[21] In this context, dinuclear Au(I) complexes with bridging diphosphines of variable length have been extensively studied.[22] In our case, the freshly prepared chiral gold Au-[(*R*,*R*)-Me-Duphos] complex was studied for asymmetric hydrogenation of diethyl itaconate (**I**), diethyl 2-benzylidenesuccinate (**II**), diethyl 2-naphthylidenesuccinate (**III**) and *anti*-*N*-benzyl(1-phenylethylidene)imine (**IV**) (Scheme 2) and the results were compared with those obtained with the Pt- and Ir-[(*R*,*R*)-Me-Duphos] complexes {$PtCl_2$[(*R*,*R*)-Me-Duphos]} and {(Ir[cod][(*R*,*R*)-Me-Duphos])PF_6} (Table 1). The reactions were carried out in a 100 ml autoclave at 20 °C and 45 °C for **I**, **II**, **IV**, and **III** respectively, under 4 bar of H_2 with a 1:1000 metal to substrate molar ratio, and ethanol as solvent. The evolution of the reaction was followed by GC, and the enantiomeric excess was measured by HPLC using a chiral column chiralcel OD at 214 nm for substrate **I** and 254 nm for **II**, **III** and **IV**. It can be seen in Fig. 2 that the catalyst is efficient in terms of conversions under mild conditions and, except for diethyl itaconate, the activity of the gold catalyst (TOF) was similar to those of Pt and Ir (see Table 1).

The TOFs were calculated from the initial rates, as moles of reactant transformed per mole of complex per hour, and the results are given in Table 1. It can be seen that, except for the less bulky diethyl itaconate, the activity of the gold catalyst is only slightly lower than the corresponding Pt or Ir catalysts.

With respect to asymmetric synthesis we can see that in the case of the gold complex enantioselective hydrogenation is achieved, and the ee increases with increasing steric hindrance of the reactant. The bulkiest substrate **III** gives the larger ee of the three metal complexes, and it is remarkable that the 95% ee was obtained with gold. This observation opens the possibility for



Scheme 2

Table 1 Turnover rates[a] and ees for the M-Duphos catalyzed hydrogenation reaction[b]

	Au		Pt		Ir	
Substrate	TOF	ee (%)[c]	TOF	ee (%)[c]	TOF	ee (%)[c]
I	3942	20	10188	3	8088	1
II	906	80	926	90	1110	26
III	214[d]	95	250	93	325	68
IV	1005	75	1365	15	1118	15

[a] TOF: mmol substrate per mmol catalyst per h; conditions: 4 atm, 20 °C. [b] Substrate:catalyst ratio 1000:1. [c] Determined by HPLC using a chiral column chiralcel OD at 214 nm (**I**) and 254 nm (**II**, **III**, **IV**). [d] Experiment at 45 °C, 4 atm H_2.

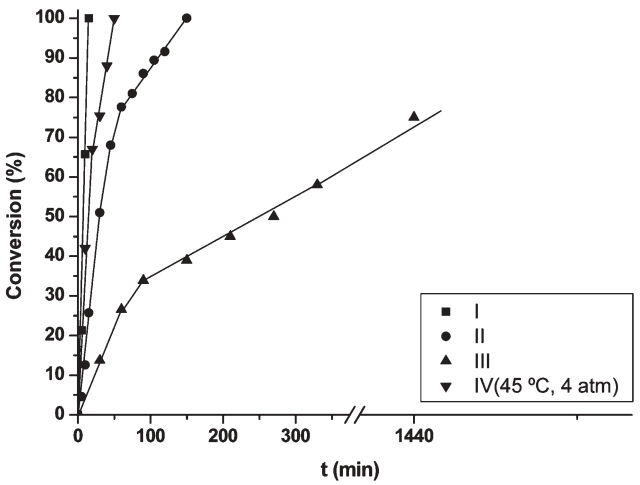
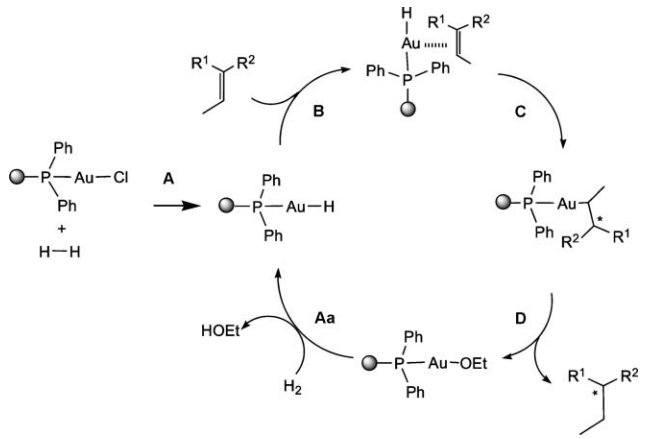


Fig. 2 Kinetic curves for the hydrogenation of substrates **I** (■), **II** (●), **III** (▲) and **IV** (▼), at 20 °C and 4 bar H_2 for **I**, **II**, **IV**, and 45 °C and 4 bar H_2 for **III**, with {$(AuCl)_2$[(*R*,*R*)-Me-Duphos)]}.

achieving high ee with less bulky substrates on gold complexes, by means of ligand modifications.

As a tentative mechanism through which the gold complex may operate, we propose a hydrogen activation based on the heterolytic hydrogen splitting promoted by the electron rich Au-complex bearing heteroatoms (Cl). This should stabilize H^+ in a similar way as has been proposed for Pd-salen[23] and Pd-Schiff base[24] complexes. This mechanism would be different from the oxidative addition of H_2 generally accepted for Rh- and Ir-complexes that can form very stable octahedral dihydride complexes, which are less favored in the case of Au. Then, the reaction could start (Scheme 3) by the addition of H_2 to the catalyst, to give a hydride complex, **A**, that involves a hydride ion transfer to the gold, replacing the chloride ion. In the second step, the alkene forms a π-complex, **B**, with the gold and simultaneous hydride ion transfer from gold to alkene occurs. The last step involves the transfer of a proton to the substrate, leading to the separation of the hydrogenated product and the regeneration of the catalyst.

In conclusion, a new neutral dimeric gold (I) complex has been synthesized. On the basis of spectroscopic characterization, a structure model has been proposed. This complex gives good catalytic activities and selectivities which are comparable with those of the Pt and Ir complexes derived from the same ligand [(*R*,*R*)-Me-Duphos]. The gold complex can perform the asymmetric hydrogenation of olefins and imines. The ee increases the



Scheme 3 Tentative reaction mechanism for the asymmetric hydrogenation of olefins on {$(AuCl)_2$[(*R*,*R*)-Me-Duphos]} complex.

bulkier the substrate, and 95% ee could be achieved in one of the cases

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