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**Preliminary communication**

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# Enantioselective synthesis: catalysis of the aldol reaction by neutral gold(I)-chiral ferrocenylphosphine complexes. Crystal structure of the complex $[\{(\eta^5\text{-}C_5H_4PPh_2)(\eta^5\text{-}C_5H_3(PPh_2)CH(Me)N(Me)CH_2CH_2NMe_2)Fe\}_2(AuCl)_3]\cdot Et_2O$

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## Abstract

The chiral aminoferrocenylphosphine $[(\eta^5\text{-}C_5H_4PPh_2)(\eta^5\text{-}C_5H_3(PPh_2)CH(CH_3)\text{-}N(CH_3)CH_2CH_2N(CH_3)_2)Fe]$ (**1**) reacts with $(H_3C)_2SAuCl$ to give neutral gold(I) complexes that are active catalysts for the enantioselective coupling of isocyanoacetate esters with aldehydes, forming dihydrooxazoles. The structure of the trimeric complex $[(\text{rac-}\mathbf{1})_2(AuCl)_3]\cdot Et_2O$ has been determined by X-ray diffraction.

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In 1986 Hayashi and Ito [1] reported an elegant and very efficient synthesis of optically active dihydrooxazoles **6** involving a gold(I)-catalyzed coupling of isocyanoacetate esters with aldehydes in the presence of chiral ferrocenylphosphine ligands of type **1**. As the gold(I) catalyst precursor they used exclusively the cationic complex **2** (see Scheme 1).

As part of an extensive study of this reaction [2], we decided to explore the applicability of the more readily available neutral complex $(H_3C)_2S{-}Au{-}Cl$ (**3**) as a starting material for the in situ formation of the catalyst. No detailed information of the behavior of this type of gold(I)-catalyst in solution and/or about the effect of ancillary ligands on their structure and selectivity has been reported. Furthermore no gold(I) complex containing chiral ferrocenylphosphine ligands of type **1** has previously been structurally characterized. We report here the first X-ray diffraction study of a gold(I) complex containing such chiral ligands [3].

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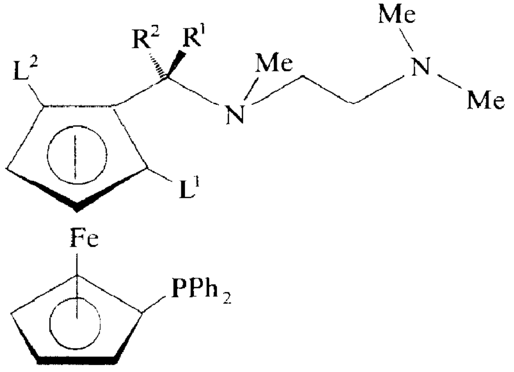


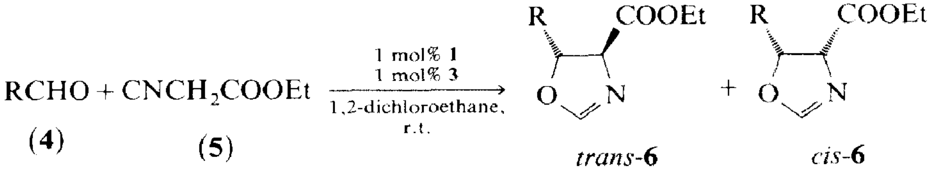
$[Au(CN\text{-cyclo-}C_6H_{11})_2]BF_4$

(**2**)

$(H_3C)_2SAuCl$

(**3**)

((*R*,*S*)-**1**: $R^1$ = Me; $R^2$ = H; $L^1$ = $PPh_2$; $L^2$ = H;
(*S*,*R*)-**1**: $R^1$ = H; $R^2$ = Me; $L^1$ = H; $L^2$ = $PPh_2$)



Scheme 1

An equimolar mixture of **1** and **3** in $CH_2Cl_2$ or 1,2-dichloroethane forms a catalytically active species. Its activity is comparable to that of the cationic counterpart, but its diastereo- and enantio-selectivity are not as good as those reported for the original system. The previously described change in the stereoselectivity induced by the presence of heteroatoms in the substrate aldehyde [2c] was also observed with our neutral catalyst. Selected results obtained with the neutral complex are given in Table 1. Interestingly, the absolute configuration of the *trans*-dihydrooxazole produced in the reaction of benzaldehyde with ethyl isocyanoacetate catalyzed by the neutral complex is the same as that produced with the cationic gold(I) complex as catalyst and by use of the same enantiomer of **1**. The same absolute configuration was also found for the major *trans*-enantiomer formed

Table 1

Distribution of diastereoisomers in the catalytic formation of dihydrooxazoles from selected aldehydes, according to the equation given in Scheme 1 [a]

| R | *trans*-**6** | | *cis*-**6** | | Total yield (%) |
|---|---|---|---|---|---|
| | % | % e.e. | % | % e.e. | |
| Phenyl | 89 | 82 | 11 | 3 | 92 |
| 3-Furyl | 85 | 79 | 15 | 0 | 80 |
| 2-Furyl | 76 | 25 | 24 | 74 | 65 |
| 3-Pyridinyl | 93 | 58 | 7 | 13 | 73 |
| 2-Pyridinyl | 73 | 0 | 27 | 47 | 62 |

[a] For a general procedure and determination of optical purities, see ref. 2b. All reactions were carried out with (*R*,*S*)-**1**.

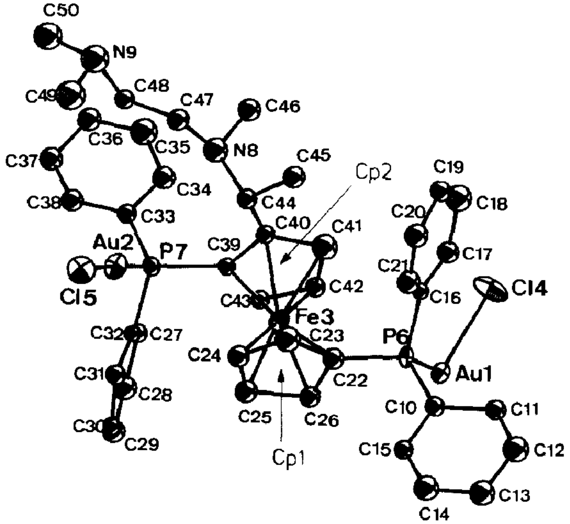


Fig. 1. ORTEP-view [8] of complex 7 showing one of the two symmetry related units and the atom numbering scheme; thermal ellipsoids are at the 20% probability level. Relevant bonding parameters: Au(1)–Cl(4) 2.52(3), Au(1)–P(6) 2.31(2), Au(2)–Cl(5) 2.28(2) and Au(2)–P(7) 2.20(2) Å; P(6)–Au(1)–P(6′) 134(2), P(6)–Au(1)–Cl(4) 113(2) and P(7)–Au(2)–Cl(5) 177(2).

in the reaction with the heteroaldehydes. These results suggest that there is a similar transition state structure in the stereoselective step in the presence of neutral and cationic gold(I) complexes.

From a benzene solution containing equimolar amounts of racemic **1** and **3** [4*], a microcrystalline complex of the composition [(*rac*-**1**)AuCl] was readily isolated by evaporation of the solvent in vacuo. In an attempt to recrystallize this material by slow diffusion of diethyl ether into a benzene solution at 4° C, we observed the formation of orange platelets in about 30% yield. These showed a different composition from that of starting material and analyzed as $[(rac\text{-}\mathbf{1})_2(AuCl)_3] \cdot Et_2O$ (**7**). We undertook an X-ray diffraction study and this confirmed its trimeric structure [5*]. Figure 1 shows the atom numbering scheme and relevant bonding parameters. The overall geometry of the complex is shown in Fig. 2. The solvate ether molecule was found to be highly disordered and could not be accurately located.

The complex consists of two identical (homochiral) [AuCl(**1**)]-moieties joined together by the third AuCl fragment, the Au–Cl bond of the latter being aligned with a crystallographic $C_2$-symmetry axis. The bis(diphenylphosphino)ferrocenyl moiety adopts an *anti*-conformation, the torsion angle $P(6)\text{–}Cp(1)_{Centroid}\text{–}Cp(2)_{Centroid}\text{–}P(7)$ being 178° thus minimizing the steric interaction between the phenyl rings. The two cyclopentadienyl rings are not perfectly coplanar, forming an angle of 5°. The methyl substituent on the stereogenic center of the diamino side chain lies slightly above the plane defined by the Cp(2)-ring (torsion angle C(39)–C(40)–C(44)–C(45) 170(5)°). This is qualitatively consistent with the results of conformational studies of the free ligand in solution [6]. The two symmetry-equivalent gold atoms are coordinated to the "upper" diphenylphosphino sub-

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* Reference number with asterisk indicates a note in the list of references.

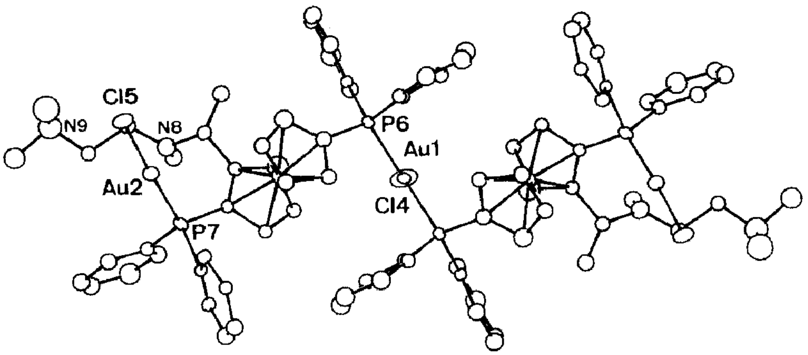

Fig. 2. Overall view of complex 7 projected along the crystallographic $C_2$-axis (Au(1)-Cl(4) bond).

stituent of the ferrocenyl ligand and to the corresponding chlorine atom in a nearly linear fashion. Both "lower" phosphorus atoms are connected to Au(1), which therefore shows a planar trigonal coordination geometry. The bond lengths in the trigonal $P_2AuCl$ and in the linear PAuCl moiety, respectively, are very similar to those in the corresponding triphenylphosphine derivatives, which have been previously characterized by X-ray diffraction [7*]. This observation indicates that the high degree of functionalization of the ferrocenyl ligand does not have any relevant electronic or steric influence on the bonding parameters of the gold atoms. In particular, the nitrogen atoms of the ligand side chain do not show any interaction with the $d^{10}$ centers (the Au(2)-N(8) and Au(2)-N(9) distances being 3.72 and 5.00 Å, respectively). This supports the postulate by Hayashi and Ito [1] that the absence of interaction between the gold and nitrogen atoms in the catalytically active species is a requisite for both activity and high stereoselectivity.

Studies on the structure of 7 and related complexes in solution are in progress.

## References

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3 The crystal structures of Pd$^{II}$-complexes with ($S^*$)-$N$,$N$-dimethyl-1-[($R^*$)-1',2-(bis(diphenylphosphino)-ferrocenyl]ethylamine and 2,2'-bis[1-($N$,$N$-dimethylamino)ethyl]1,1'-bis(diphenylphosphino)-ferrocene were reported by Hayashi et al.: T. Hayashi, M. Kumada, T. Higuchi, and K. Hirotsu, J. Organomet. Chem., 334 (1987) 195; T. Hayashi, A. Yamamoto, M. Hojo, K. Kishi, Y. Ito, E. Nishioka, H. Miura, and K. Yanagi, J. Organomet. Chem., 370 (1989) 129, respectively.

4 All complexes derived from the reaction of **1** and **3**, in ratios from 1/1 to 3/2, show in their $^{31}$P NMR spectra in the temperature range 25 °C to −80 °C two very broad signals (approximate line width 400 to 1000 Hz), at ca. 28 and 37 ppm, respectively. This indicates a highly dynamic behavior for this class of complexes. This contrasts with the observation that the cationic complex $[Au(\mathbf{1})]BF_4$ generates the expected $^{31}$P-AB-pattern ($\delta_A$ 32.0 $\delta_B$ 34.8 ppm in $CDCl_3$, $J_{AB}$ 90 Hz), indicative of bidentate coordination of **1** to the Au-cation. A Togni and S.D. Pastor, unpublished results.

5 Crystal data for 7: $C_{86}H_{98}Au_3Cl_3Fe_2N_4OP_4$, $M = 2136.60$, orthorhombic, centrosymmetrical space group *Pbcn* (No. 60), *a* 12.791, *b* 17.792, *c* 36.966 Å, *V* 8413 Å$^3$, *T* 190 K, $Z = 4$, $D_c$ 1.687 g cm$^{-3}$. Intensity data collection was carried out on a Philips PW 1100 diffractometer with a crystal of approximate dimension 0.45 × 0.31 × 0.08 mm. Mo-$K_\alpha$ X-radiation (λ 0.70926 Å). Of the 6563 unique reflections 2799 were considered observed ($I > 2\sigma(I)$). The structure was solved by heavy atom (Patterson and Fourier) methods and refined by least squares. Final $R = 0.102$. The relatively high *R*-factor is probably due to the high disorder in the diethyl ether solvate molecule. Tables of atomic coordinates, and bond lengths and angles are deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW (Great Britain).

6 A. Togni and S.D. Pastor, J. Org. Chem., in press.

7 [Au($PPh_3$)Cl]: Au–P 2.235(3), Au–Cl 2.279(3) Å; [Au($PPh_3$)$_2$Cl]: Au–P 2.327(4) average, Au–Cl 2.533(4) Å, P–Au–P 135.7(1), P–Au–Cl 109.1(1)°. See: G.A. Bowmaker, J.C. Dyason, P.C. Healy, L.M. Engelhardt, C. Pakawatchai, and A.H. White, J. Chem. Soc. Dalton Trans., (1987) 1089, and ref. cited therein.

8 Program ORTEP II (C.K. Johnson, Oak Ridge Natl. Lab. [Rep.], ORNL (U.S.) 1976 ORNL-5138).