Low symmetry metal complexes: chloro cysteine ethyl ester-*N*,*S* triphenylphosphine palladium(II), a new regioselective hydrocarboxylation catalyst for 2-phenylpropanoic acid, and its crystal structure

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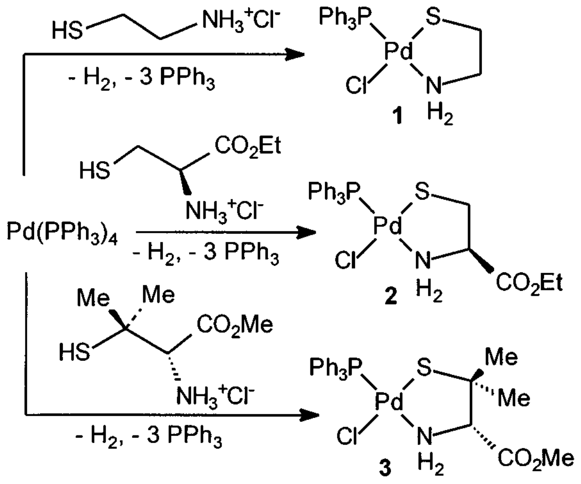
The hydrochlorides of cysteamine, cysteine ethyl ester and penicillamine methyl ester, react with $Pd(PPh_3)_4$ to yield low symmetry complexes of palladium(II) that incorporate the *N*,*S*-aminothiolato ligand and triphenylphosphine; the complex with cysteine ethyl ester, structurally characterized by X-ray diffraction, proved to be an effective catalyst for the hydrocarboxylation of styrene with high selectivity (98%) towards 2-phenylpropanoic acid.

Low symmetry complexes of the transition metals in general, and the platinum group metals in particular, are of interest because of their potential as selective catalysts in homogeneous reactions. Geometric and electronic asymmetry is associated with increased stability of one of the possible key intermediates, which should give rise to improved selectivity. The preferred ligands in many selective catalytic reactions are sophisticated diphosphines. However, these are often even more expensive than the precious metal itself. This report is part of our efforts to evaluate the use of inexpensive, low symmetry ligands from the chiral pool, in structurally well characterised complexes, to promote selective homogeneous catalytic reactions.[1]

Cysteine ligand type containing complexes are not very common,[2] but we have shown that chelate assisted oxidative addition to Pt(0) is a reaction that can introduce acidic hydrogen containing cysteamine and cysteine ethyl ester ligands in the co-ordination sphere of the metal.[3] However, in the case of palladium the expected metal complexes would contain the often-unstable Pd–H bond. In a new approach, we have added an acid to quench the possible palladium hydride in order to obtain stable palladium(II) complexes in one step. The stoichiometric addition of acid has been achieved by the use of the hydrochlorides of the ligands.

The hydrochlorides of cysteamine ($HSCH_2CH_2NH_2{\cdot}HCl$), cysteine ethyl ester [$HSCH_2C^*H(CO_2Et)NH_2{\cdot}HCl$] and also penicillamine methyl ester [$HSCMe_2C^*H(CO_2Me)NH_2{\cdot}HCl$] reacted with $Pd(PPh_3)_4$ to yield the corresponding *N*,*S*-aminothiolato chloro triphenylphosphine complexes in good yield, with displacement of three PPh_3 ligands, oxidation of the metal and evolution of hydrogen (Scheme 1). In this way, complexes **1**–**3** were obtained as stable crystalline solids.† The *cis*-P,S coordination was established by single crystal X-ray analysis. Complex **2** exhibits a very short Pd–S distance of 2.253(2) Å that is effectively equal to the Pd–P distance of 2.254(2) Å, owing to the non-bridging coordination of the sulfur and the low *trans* influence of the chloro ligand.‡[4] Complexes **1**–**3** are stable in solution and do not form sulfur-bridged dimers or polymers, even when exposed to air. In these complexes four very different atoms coordinate the metal, but only when the asymmetric carbon containing cysteine and penicillamine are used, is the symmetry plane of the square planar complex broken and the compounds become optically active. Fig. 1 shows that in the solid state,[5] the ethyl carboxylate substituent in the chelate ring of **2** adopts an axial orientation and the oxygen of the carbonyl group approaches the coordinated nitrogen.§



Scheme 1

Catalytic hydrocarboxylation of olefins is an interesting reaction for the synthesis of the pharmacologically useful 2-arylpropionic acids, provided that a selective catalyst towards the branched acid is used.[6] Complex **2** has been subjected to a preliminary evaluation in the hydrocarboxylation of styrene as a model aryl olefin, with oxalic acid under CO pressure and no added co-catalysts. Complex **2** has been found to be active, and its selectivity in 2-phenylpropanoic acid (2-PP) was very high (Table 1). Hydrogenation was the main side reaction, and it was always under 0.2%. In low conversion conditions (*i.e.*, when the reaction was stopped after 2 h), yields increased steadily with temperature. After 24 h, 75% conversions were reached and selectivities as high as 98% in branched acid (2-PP) were maintained. However, at 100 and 120 °C, lower than expected conversions were observed. This result, together with the fact that after depressurisation of the reactor, palladium black is observed,¶ lead us to believe that the catalytic species suffers degradation under such reaction conditions. The catalytic reaction is faster at higher temperatures, but so is the decomposition of the catalyst.

The 2-phenylpropanoic acid product is racemic in all cases. Considering the fact that the reaction medium is strongly acidic, and that as proposed[7] it is reasonable to think that two free co-ordination sites are needed for this reaction, we are suggesting at this stage structure **A** for the active species. The relatively low bulk of **A** is consistent with branched selectivity. Also, the lack

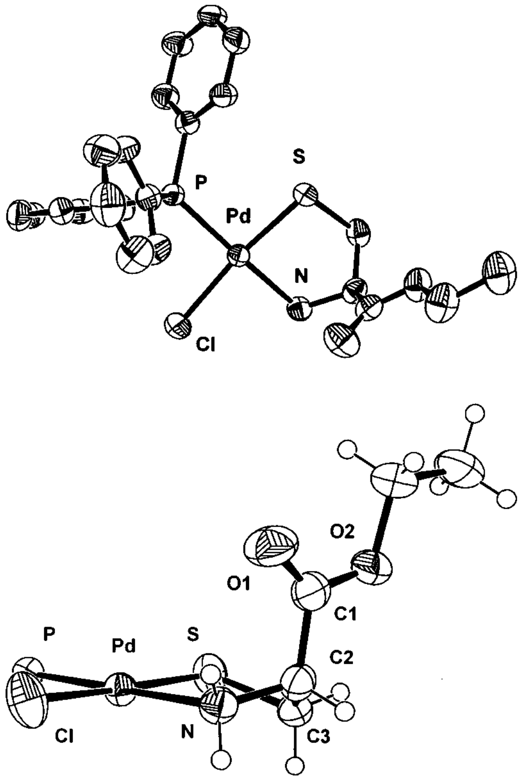


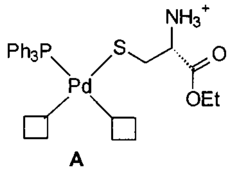
Fig. 1 The above projection of complex **2** includes all non-hydrogen atoms (ORTEP-III, 50% probability). In the nearly eclipsed projection below, the aryl rings have been omitted and the hydrogen atoms have been included, to fully appreciate the axial position of the ethoxycarbonyl group. The C1–C2 bond forms an angle of 84.5(3)° with the coordination plane of the metal and the O1–C1–C2–N torsion angle is 12.1(8)°. Selected distances (Å) and angles (°): Pd–S 2.253(2), Pd–P 2.254(2), Pd–N 2.097(5), Pd–Cl 2.349(2), S–C3 1.826(6), N–C2 1.483(7), C1–C2 1.509(8), C2–C3 1.482(8), C1–O1 1.192(7), C1–O2 1.323(8); S–Pd–P 92.92(6), S–Pd–N 85.7(1), Cl–Pd–P 93.63(6), Cl–Pd–N 87.7(1).

Table 1 Complex **2** as a catalyst in the hydrocarboxylation of styrene. Conversion and selectivity towards 2-phenylpropanoic acid (2-PP) in the reaction of styrene with oxalic acid under CO, at different temperatures over 2 and 24 h[a]

	2 h		24 h	
T/°C	Conversion (%)	Selectivity (%)	Conversion (%)	Selectivity (%)
60	0.6	—	30	98
80	7	98	75	98
100	12	97	68	97
120	16	97	67	96

[a] Conditions: 2 mmol styrene + 2.5 mmol $H_2ox\cdot 2H_2O$ in 10 mL of DME solvent; [styrene]/[**2**] = 50; CO pressure: 30 bar. No oxygen or co-catalysts present.

of chiral induction would be consistent with structure **A**, in which the asymmetric centre is displaced away from the metal. At this point, we rule out complete detachment of the sulfur ligand in the active species, because the activities and selectivities observed with **2** were not those of a simple Pd(II) + PPh_3 system with a phosphine/palladium ratio of unity, which is the ratio in complex **2**.‖ Furthermore, relevant results by Claver, van Koten and coworkers[8] with aryl aminothiolato complexes of palladium, seem to indicate that sulfur ligands promote high branched selectivity.



A

From a purely practical, synthetic point of view complex **2**, which is readily prepared from affordable, easily accessible reagents, catalyses the conversion of styrene to 2-phenylpropanoic acid (98%) by reaction with oxalic acid under CO (30 bar), with a 75% yield at 80 °C in 24 h. Further work on the synthesis, structure and evaluation of this novel class of compounds in catalysis is under way and will be reported in due course.

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Notes and references

† Synthesis of **1**: A solution of $HSCH_2CH_2NH_2\cdot HCl$ (0.52 mmol) in methanol (5 ml) was slowly added to $Pd(PPh_3)_4$ (0.52 mmol) in toluene (20 ml) and stirred under nitrogen at 60 °C for 3 h to afford an orange solution. Concentration of the solution caused precipitation of the product as an orange solid, which was purified by recrystallization in acetone–diethyl ether to yield $[PdCl(SCH_2CH_2NH_2)(PPh_3)]$ **1** as dark orange crystals (65% yield). The same procedure can be used for compounds **2** and **3**. Compounds **1**–**3** gave satisfactory spectral (^1H, ^{31}P and ^{13}C NMR and IR) and analytical data.

‡ *Crystal data* for **2**: $C_{23}H_{25}ClNO_2PPdS$; M = 552.32; orthorhombic, a = 7.929(5), b = 10.330(2), c = 28.769(6) Å, V = 2356(2) $Å^3$; T = 293 K; space group $P2_12_12_1$, Z = 4; μ = 10.8 cm^{-1}; 2069 independent reflections for 277 parameters; $R(F)$ = 0.023 for 1910 reflections with $I > 2\sigma(I)$ and $R_w(F^2)$ = 0.063 for all 2069 reflections; S = 1.129; Flack parameter 0.01(4). CCDC 182/1134. See http://www.rsc.org/suppdata/cc/1999/277/ for crystallographic files in .cif format.

§ The IR stretching frequencies for the CO and NH_2 groups, and the distance between the oxygen and hydrogen atoms O1···H–N of 2.18(4) Å, do not support the existence of hydrogen bonding. The eclipsed conformation could be favoured by an electrostatic interaction between the negatively charged oxygen and a positively charged *quaternary* nitrogen.

¶ Powder X-ray diffraction showed it to be finely divided metal, and not palladium sulfide of any crystallinity. This palladium black does not catalyse the reaction, even when triphenylphosphine is added.

‖ Working in the same conditions as used for **2**, we have found the selectivity of $PdCl_2$ or $PdCl_2(MeCN)_2$ plus 1 equiv. of PPh_3 to be 85–88% in 2-PP, although the second precursor is faster.

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