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Studies on gold(I) complexes of 1,1′-bis(diphenylphosphino)ferrocene

A Houlton, R.M.G. Roberts, J. Silver
Department of Chemistry and Biological Chemistry, University of Essex, Wivenhoe Park, Colchester, CO4 3SQ (UK)

and R.V. Parish
Department of Chemistry, U.M.I.S.T., Manchester, M60 1QD (UK)

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Abstract

The synthesis and ^{197}Au, ^{57}Fe Mössbauer and ^{31}P NMR spectroscopic data for a series of Au^{I} complexes of 1,1′-bis(diphenylphosphino)ferrocene (fdpp) are reported. Two different Au^{I} coordination geometries are apparent in the solid state, linear and trigonal. There is no evidence in the solid state for a tetrahedral species $[\text{fdpp}_2\text{Au}]^+$, but ^{31}P NMR spectroscopy indicates its existence in solution. Chemical oxidation of the complexes does not yield the expected ferrocenium derivatives. In accord with this, cyclic voltammetry reveals there to be no observable electrochemical processes in the timescales investigated (500–20 mV/s).

Introduction

Organometallic ligands provide a convenient route to the synthesis of heterometallic complexes. Of such ligands ferrocenyl derivatives have been the most widely studied, in particular those employing ferrocenylphosphines [1]. Although a wide range of metal complexes have been synthesised from these ligands, especially 1,1′-bis(diphenylphosphino)ferrocene (fdpp), there have been few studies on gold derivatives [2,3]. This is somewhat surprising in the light of the reported antitumour activity of both gold phosphines [4] and ferrocenium salts [5]. To rectify this omission we decided to investigate these complexes. Our primary interest lay in the preparation of the gold complexes with the aim of synthesising their oxidised (ferrocenium) counterparts. Such complexes should provide examples of multi-functional drugs, i.e. molecules that have more than one mechanism by which they may elicit a biological response.

During this work the structure of one of these complexes, fdpp$(\text{AuCl})_2$ was reported [6]. In this structure the Au atom exhibits linear coordination and fdpp acts as a monodentate ligand to two Au atoms. Also in this report the activity of

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Table 1

^{57}Fe and ^{197}Au Mössbauer spectroscopic data (mm s^{-1}) and solution ^{31}P NMR data (ppm) ($CDCl_3$) for fdpp-Au^{I} complexes

[L : Au]	δ_{Fe}	q.s.$_{Fe}$	δ_{Au}	q.s.$_{Au}$	^{31}P
fdpp	0.52(1)	2.26(1)	–	–	−11.2
[1 : 2]	0.53(1)	2.36(1)	3.91	7.43	28.90
[1 : 1]	0.52(1)	2.31(1)	2.62	7.99	30.06
[2 : 1]	0.51(2)	2.30(2)	2.83	9.05	~ 26(br) [a]

[a] −14.9 and ca. 37 ppm in the solid state spectrum.

this complex against experimental tumours was tested. Compared with that of the structurally analogous [dppe$(AuCl)_2$] (dppe = diphenylphosphinoethane) its activity was poor [6]. This indicated that the ferrocenyl moiety is inactive, in keeping with studies on ferrocene and confirmed the need for oxidation to ferrocenium for anti-tumour activity [5]. We report here the synthesis of three fdpp-Au complexes and their ^{197}Au and ^{57} Mössbauer data together with ^{31}P NMR and electrochemical data.

Results and discussion

Mössbauer and NMR spectroscopic data for fdpp and the complexes prepared are presented in Table 1.

Au-197 Mössbauer data

From the ^{197}Au Mössbauer data it is clear that the three complexes fall into two categories, indicating different coordination geometry gold. The [1 : 2] and [1 : 1] complexes have parameters very similar to [AuCl(PPh_3)] and [AuCl$(PPh_3)_2$]: δ = 4.08, 2.35 mm s^{-1}, q.s. = 7.43, 8.22 mm s^{-1} respectively [12]. It is therefore likely that the coordination geometry is analogous, PAuCl (**A**) for the [1 : 2] and P_2AuCl (**B**) for the [1 : 1] complex (see Fig. 1). For the [2 : 1] complex, two structures seem possible, **C** and **D**; a four-coordinate structure with two chelating fdpp ligands can be ruled out because the δ-value would be expected to be very much lower, and the q.s. would be almost zero (c.f. $[Au(pdma)_2]^+$: $\delta = 0.8$, q.s. = 1.1 mm s^{-1}) [10]. Structure **C** involves coordination very similar to that for the [1 : 1] complex, but the Mössbauer parameters are appreciably different. That both parameters are higher suggests P_3Au coordination, but they are rather lower than for $[Au(PPh_3)]^+$ (δ 2.99, q.s. 9.47 mm s^{-1}). However, in structure **D**, one fdpp ligand is chelating, which might well weaken its interaction and lower its contribution to the Mössbauer parameters. Simple geometry indicates that fdpp is unlikely to act as a bidentate ligand to trigonal Au(I) but that tetrahedral co-ordination should be possible. For fdpp bonding in a bidentate manner, at a typical P–Au distance of 2.33 Å, a P–M–P angle of 120° (i.e. trigonal) would need an idealised P ··· P separation of > 4 Å. Such a separation is too large for the ferrocenyl moiety to accommodate. Clearly then, chelation of trigonal Au^{I} involves considerable compromises, and typical parameters would not be expected. Such a structure then contains one fdpp bound in a strained bidentate manner, probably achieved by lengthening (hence weakening) the Au–P bonds, and a second acting as a monodentate ligand (struc-

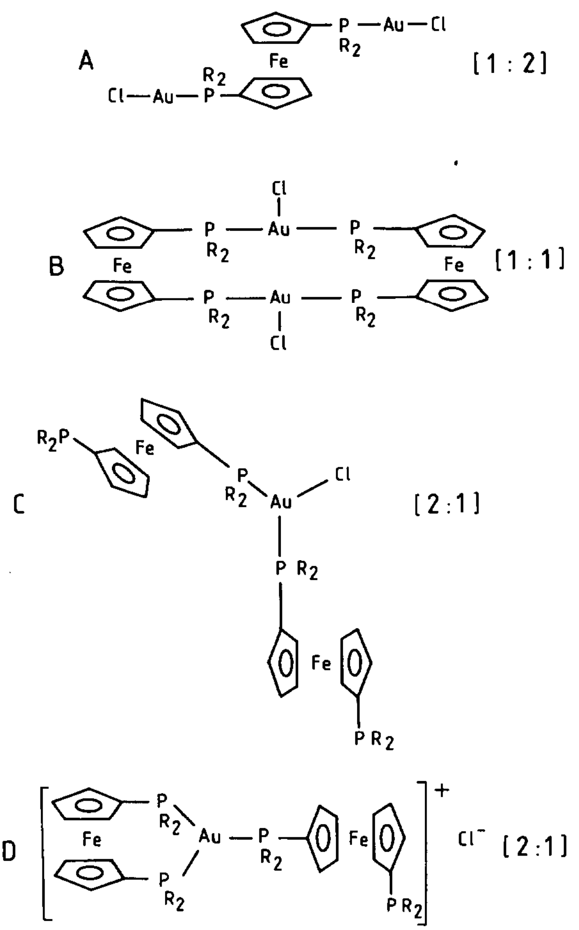

Fig. 1. Structures of compound types A–D.

ture **D**, Fig. 1). This clearly contains two types of phosphorus environment and this was confirmed by solid state ^{31}P NMR spectroscopy. Two resonances were observed, a singlet at −14.9 ppm and a multiplet centred around 37 ppm (w.r.t. external 85% H_3PO_4). The latter signal probably results from P–P through metal coupling [11] of the three P atoms ligated to the Au and overlap of signals from non-equivalent P. It is noteworthy that on the basis of the above calculations a tetrahedral P–Au–P angle of 109° would only need a P···P distance of 3.8 Å which, although long, could be possible.

Iron-57 Mössbauer data

Recently we have reported an approximately linear correlation between isomer shifts (δ) and quadrupole splittings (q.s.) for the ferrocenyl iron atom in a series of bridged bidentate fdpp-metal complexes [12] (the ferrocenyl groups are bridged due to the bidentate ligation). Moreover, the data appear to fall into well defined domains according to the type of coordination geometry exhibited by the phosphorus bound metal (see Fig. 2). This can be understood by the fact that the ligated

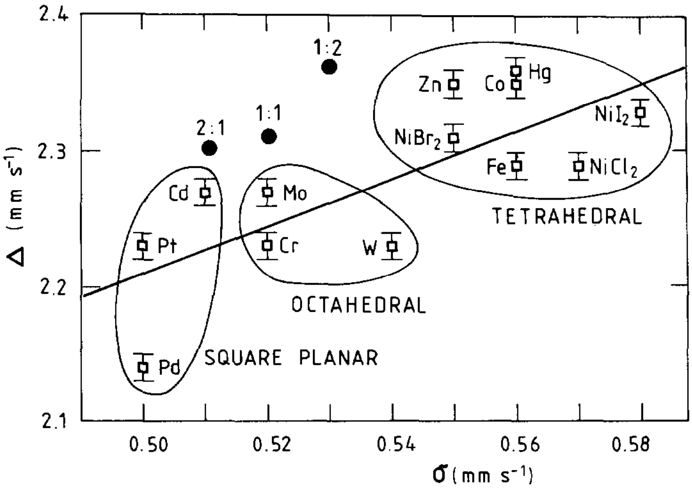

Fig. 2. Plot of isomer shift (δ) (mm s^{-1}) versus quadrupole splitting (Δ) (mm s^{-1}) for fdpp-metal complexes.

metal's coordination geometry causes distortions of the ferrocenyl moiety which in turn influence the hyperfine interactions at the iron centre. The highest δ and q.s. values are those of the tetrahedral complexes with the lowest being the square planar complexes. Octahedral complexes have intermediate values.

When the data for the fdpp-Au complexes are included on the plot (Fig. 2) none of these data fall inside the regions previously established for specific coordination geometries, indicating that Au^1 does not display any of the above mentioned geomtries. The [1 : 2] complex lies furthest from the previous data. The [1 : 1] and [2 : 1] complexes have similar ^{57}Fe Mössbauer parameters and fall in a region close to the previously reported octahedral and square planar complexes. It is not clear why these complexes do not demonstrate the apparently linear correlation observed previously, but it perhaps indicates that too much emphasis should not be placed on this trend, the grouping of the complexes is more important.

Mass spectroscopy

Fast atom bombardment studies showed the presence of a 983 peak in the [1 : 2] and [1 : 1] complexes. This corresponds to the fragment $[fdpp(Au)_2Cl]^+$, and is in keeping with the dimeric nature of the [1 : 1] ratio complex. This peak was absent in the [2 : 1] complex as would be expected. All three complexes showed peaks at 751, corresponding to the $\{fdppAu\}^+$ ion. Despite less than satisfactory elemental analysis for the [2 : 1] complex, unequivocal evidence for the formulation came from the presence of the $\{(fdpp)_2Au\}^+$ molecular ion (mass 1305).

Solution ^{31}P NMR studies

All the complexes have downfield shifts (see Table 1) compared with those of the free ligand, as expected [8]. Both the [1 : 2] and the [1 : 1] complexes gave rise to sharp ^{31}P NMR resonances. The [2 : 1] complex exhibits a broad resonance (~ 26 ppm) at room temperature (Fig. 3C). On cooling this sharpens to reveal one main resonance at ~ 22 ppm and a broader much weaker resonance at ~ 38 ppm (Fig.

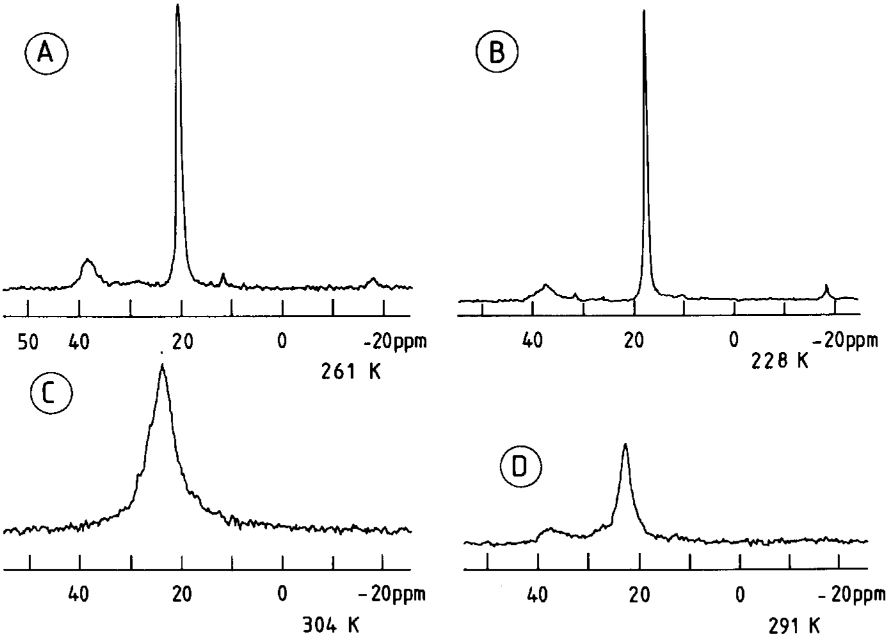

Fig. 3. ^{31}P NMR spectra of [2:1] fdpp:Au complex in $CDCl_3$, at (A) 261 K, (B) 228 K, (C) 304 K, (D) 291 K.

3B). On further cooling below 261 K a small peak at -18.0 ppm corresponding to uncoordinated phosphorus was detected. At 330 K the spectrum sharpened to one resonance at 19.9 ppm. All these changes were fully reversible.

Berners-Price and Sadler have reported the ability of bidentate diphosphines to stabilise four-coordinate Au^I [13]. The species $[Au(dppe)_2]^+$ has been identified to be tetrahedral by X-ray crystallography in its SbF_6^- and Cl^- salts [14,15]. It has been shown to exist in solutions of Au : dppe ratios 1 : 1 at room temperature [13]. ^{31}P NMR shows a resonance at 20.8 ppm corresponding to the $[Au(dppe)_2]^+$ species [13,14]. By analogy, it is reasonable to assume that the main resonance at ~ 22 ppm is due to the $[fdpp_2Au]^+$ species. This is the first reported example of a tetrahedral $[fdpp_2M]^+$ complex, however, as mentioned above the structure does not exist in the solid state. ^{197}Au Mössbauer spectroscopy revealed no evidence for a tetrahedral Au^I site in the solid state, such coordination would exhibit a q.s. value ~ 0 [9]. The two broad resonances, at ~ 38 and ~ -18 ppm correspond to the presence of a small percentage of structure **D** in solution and are comparable to the solid state spectrum.

Electrochemistry

Despite the fact that the ferrocene : ferrocenium redox couple is well established [16], the fdpp-Au complexes did not display any electrochemical activity. Scan rates ranged from 500 mV/s to 0.5 mV/s typically between the voltage range +/− 1.5 V, though exceptionally solutions were scanned between +/− 2.0 V (in dimethylformamide). Either, (1) electron transfer in these complexes is very slow or (2) the complexes are indeed inert to electrochemical oxidation or reduction. Previous studies of fdpp metal complexes have shown electrochemical oxidation to be possible though not fully reversible [17]. We have recently suggested why the isolation of oxidised fdpp complexes may not be possible [18]. However, these Au^{I} complexes would appear to be the first examples of electrochemically inert ferrocenyl derivatives.

Chemical studies

All attempts to chemically oxidise the complexes failed. Yellow chloroform solutions (of the complexes) remained unchanged on addition of mild oxidising agents (e.g. trichloroacetic acid, benzoquinone, silver nitrate) and showed no trace of the characteristic blue/green colour of the ferrocenium ion. With stronger oxidising agents such as $NO^+BF_4^-$, yellow solutions (dichloroethane) turned dark brown. The Mössbauer spectrum of the reaction product of the [1 : 2] complex with $NO^+BF_4^-$ confirmed that no oxidation had occurred, the spectrum being that of fdpp. These results agree with those of Corrain et al. [17] who reported on the instability of the $fdpp^+$ ion. In order to confirm that the $fdpp^+$ ion was a typical ferrocenium species, a sample of $fdppPdCl_2$ was oxidised with a slight excess of $NO^+BF_4^-$ in dichloroethane. The resulting green solid gave a ^{57}Fe Mössbauer spectrum containing two iron sites. One site corresponding to the unoxidised material ($\delta = 0.51(4)$, q.s. = 2.24(8), relative area 27.4%) and a new site ($\delta = 0.55(3)$, q.s. = 0, relative area 72.6%). This reaction then confirms that the $fdpp^+$ ion, in some form at least, exists and displays charateristics typical of ferrocenium ions.

Conclusion

The complexes prepared include the first example of bidentate fdpp in a trigonal co-ordination geometry. However, while fdpp can bind in such a manner to Au^{I}, the evidence suggests that this puts considerable demands on the ligand. The dimeric structure, **B**, represents one way the ligand can avoid this type of co-ordination, rearrangement to the tetrahedral $[(fdpp)_2Au]^+$, as happens in solution, is another. It is interesting that the latter co-ordination is not also found in the solid state.

The lack of electrochemical activity was disappointing, particularly in regard to our initial aims of synthesising potentially multi-functional anti-tumour agents. We are continuing our efforts in this area.

Experimental

Starting materials 1,1′-bis(diphenylphosphino)ferrocene and ammonium tetrachloroaurate were purchased from Aldrich Chemical Co.

The preparations of complexes with ligand to metal ratios fdpp : Au, 1 : 2, 1 : 1 and 2 : 1 were effected by methods analogous to those previously reported [4]. All complexes were isolated as yellow powders. Elemental analysis was performed at the University of Manchester. Analysis: Found: C, 40.8; H, 2.8; Cl, 7.0; Fe, 5.5. $[fdpp(AuCl)_2]$ $C_{34}H_{28}Au_2Cl_2FeP_2$ calc.: C, 40.0; H, 2.7; Cl, 6.7; Fe, 5.5%. Found: C, 51.2; H, 3.6. $[fdppAuCl]_2$ $C_{68}H_{56}Au_2Cl_2Fe_2P_4$ calc.: C, 51.8; H, 3.5%. Repeated analysis of $[(fdpp)_2Au]^+[Cl]^-$ did not yield completely satisfactory results. Typical analysis found: C, 61.6; H, 4.5; Au, 15.2; Cl, 3.3; Fe, 7.8; P, 8.6. $[(fdpp)_2Au]Cl$ $C_{68}H_{56}AuClFe_2P_4$ calc.: C, 60.9; H, 4.2; Au, 14.2; Cl, 2.65; Fe, 8.4; P, 9.3%.

Mössbauer spectra were recorded as described elsewhere [7,8]. Isomer shifts (δ) from ^{57}Fe and ^{197}Au spectra were referred to natural iron at room temperature and gold foil at 4.2 K respectively.

Mass spectra were recorded at the University of Essex and SERC Mass Spectrometry Service Centre, University College Swansea, Swansea.

Solution ^{31}P{H} NMR spectra were obtained on a Bruker WP80 spectrometer. All chemical shifts in ppm relative to 85% H_3PO_4 using the positive downfield convention.

Cyclic voltammetry was carried out using 0.2 *M* solutions of $[NBu_4]^+[BF_4]^-$ in dichloromethane or dimethylformamide as the electrolyte. The working electrodes used were a platinum wire and vitreous carbon, the counter electrode a tungsten wire, and a silver wire pseudo-reference electrode. Measurements were made with an EG and G PAR model 362 scanning potentiostat.

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