The Characterization of 2-Thiouracilato(triphenylphosphine)gold(I)

BERNARD F. HOSKINS, LU ZHENRONG

Department of Inorganic Chemistry, University of Melbourne, Parkville, Vic. 3052, Australia

and EDWARD R. T. TIEKINK

Jordan Laboratories, Department of Physical and Inorganic Chemistry, University of Adelaide, S.A. 5001, Australia

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Certain gold(I) coordination compounds have uses in medicinal chemistry; for example, the phosphinegold(I)thioglucose derivative 'auranofin', (1-thio-β-D-glucopyranose 2,3,4,6-tetraacetato-*S*)(triethylphosphine)gold(I), is known to be effective in the treatment of rheumatoid arthritis [1, 2]. Recently, it has been demonstrated that some gold(I) compounds also display anticancer activity [3]. The study of the interaction of gold(I) derivatives with nucleic acid constituents is therefore of interest in order to establish potential cellular binding sites. Nitrogen donor sites have been shown in the crystal structures of $R_3PAu(L)$ (R = Ph, LH = 1-methylthymine [4] and R = Ph [5], Et [6], LH = adenine). It was thought of interest to investigate the gold atom coordination geometry in which the base also contained a sulphur donor atom. The pyrimidine 2-thiouracil, a sulphur-containing analogue of uracil, which occurs naturally in transfer ribonucleic acid [7], was chosen for this investigation. Previous crystallographic studies on metal complexes containing either the neutral or deprotonated 2-thiouracil ligand have shown a diversity of coordination modes. The neutral ligand is known to coordinate as a thione in the Cu(I) complex $Cu(2\text{-}TUH)_2Cl\cdot DMF$ [8]. When deprotonated, 2-thiouracil can bridge two metal centres via the sulphur atom and the deprotonated nitrogen atom (*i.e.* the N(1) atom), as shown in the structure of $[Pt(2\text{-}TU)_2I]_2$ [9]. The remaining example is that found in the organothallium compound $Me_2Tl(2\text{-}TU)$, in which the thallium atom is five-coordinate by virtue of N-, S-coordination of one 2-TU ligand and O-coordination of a symmetry related ligand; this leads to a linear, polymeric structure [10].

Results and Discussion

The infrared spectrum of $Ph_3PAu(2\text{-}TU)$, recorded as a KCl disc on a Perkin-Elmer 683 double-beam spectrophotometer, was measured in the region 4000–250 cm^{-1}. In free 2-thiouracil (2-TUH) a strong absorption at 1702 cm^{-1} is thought to arise from ν(C=O) and similarly a further strong band at 1682 cm^{-1} is assigned to ν(C=O) and ν(C=C) [11]. In the complex, four bands are found in this region at 1682, 1678, 1672 and 1664 cm^{-1}, indicating a shift to lower frequency for ν(C=O) although definitive assignment of the individual bands cannot be made at this stage. It has been shown, however, that shifts of ν(C=O) to lower frequency may not necessarily indicate coordination of the carbonyl group but may reflect the decreased bond order of the C=O bond owing to rearrangement of electron density as a result of deprotonation of the ligand [12]. The thioamide band I (at 1560 cm^{-1} for 2-TUH [11]) is suggested to be more sensitive to coordination that the two low frequency ν(C=S) bands (at 1172 and 1155 cm^{-1}) [11]. In $Ph_3PAu(2\text{-}TU)$ the thioamide band I has been shifted to 1530 cm^{-1} which may be indicative of bonding through the sulphur atom to the metal centre. In order to fully resolve the coordination characteristics of the 2-thiouracil anion in $Ph_3PAu(2\text{-}TU)$, a single-crystal X-ray analysis of the compound was undertaken.

The structure determination confirms the stoichiometry of the compound and reveals the presence of two unique molecules in the crystallographic asymmetric unit; this feature may explain partially the difficulty of interpreting the infrared spectrum for this compound. As shown in Fig. 1, each gold atom exists in the expected linear coordination geometry defined by the P and S atoms of the phosphine and 2-TU ligands respectively. The Au–S bond distances in the two unique molecules (see caption to Fig. 1) are equivalent within experimental error and, similarly, the two Au–P bond lengths are equal. Further, the Au–S and Au–P parameters found in $Ph_3PAu(2\text{-}TU)$ are comparable to those determined in the related dithiolate complexes; *i.e.* 2.338(3) and 2.251(3) Å respectively in $Ph_3PAu(S_2CNEt_2)$ [13] and 2.310(1) and 2.261(1) Å in $Ph_3PAu(S_2COMe)$ [14].

Of particular interest is the mode of coordination of the 2-TU ligand in $Ph_3PAu(2\text{-}TU)$. As seen from Fig. 1, the 2-TU ligand is orientated so that the N(1) atom is directed towards the gold centre. However, the Au···N(1) distance of 3.23 Å (3.13 Å for molecule b) is not indicative of a significant interaction between these atoms when compared to the sum of the van der Waals radii for Au and N of 3.25 Å [15]. It can therefore be concluded that the 2-TU ligand coordinates exclusively via the S atom, in contrast to previous observations [8–10]. The C–S bond distances of 1.722(8) and 1.766(7) Å are longer than the C=S bond distance found in neutral

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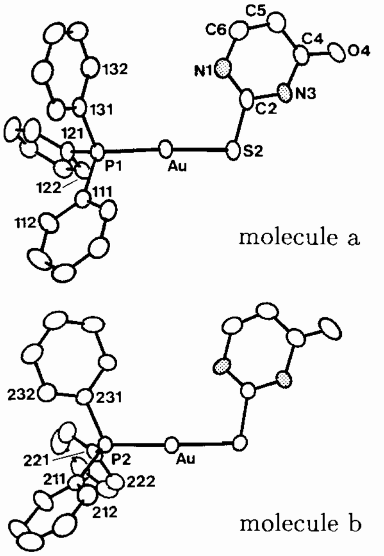

Fig. 1. Molecular structure and numbering scheme employed for Ph_3PAu(2-thiouracil). Selected interactomic parameters (those for molecule a are given first): Au–P 2.248(2), 2.248-(2), Au–S 2.296(2), 2.300(2), S(2)–C(2) 1.722(8), 1.766(7) Å; P–Au–S 175.4(2), 177.0(2)°.

2-thiouracil (1.683(3) Å) which has been shown by X-ray crystallography to exist in the lactam–thione form [16]. These observations suggest that 2-TU is coordinating as a thiolate ligand rather than as a thione.

The differences between the two molecules comprising the asymmetric unit are manifested in a different orientation of phosphine-bound phenyl groups and different intermolecular contacts in the crystal lattice.

Experimental

The complex Ph_3PAu(2-TU) was obtained from the reaction of Ph_3PAuCl (30 mg), 2-thiouracil and NaOH (1:1:1 equimolar ratio) in methanol solution (50 cm^3). After stirring for 0.5 h the clear solution was allowed to stand overnight. The resulting precipitate was recrystallized from acetone yielding well-formed off-white crystals suitable for X-ray diffraction studies. Intensity data were collected on an Enraf-Nonius CAD4F diffractometer fitted with Mo Kα radiation, $\lambda = 0.71069$ Å. A total of 9098 reflections (θ_{max} 25.0°) were measured with the ω–2θ scan technique. The data were corrected for Lorentz and polarization techniques and for absorption [17]. There were 7424 unique reflections and of these 5123 satisfied $I \geqslant 2.0\sigma(I)$.

Crystal data for $C_{22}H_{18}AuN_2OPS$: $M = 586.4$, monoclinic, space group $P2_1/n$; $a = 17.540(2)$, $b = 11.337(1)$, $c = 21.253(4)$ Å; $\beta = 90.87(1)°$, $U = 4226(2)$ Å^3; $D_m = 1.83$, $Z = 8$, $D_c = 1.843$ Mg m^{-3}; $F(000) = 2256$, $\mu = 71.0$ cm^{-1}. The structure was solved by the Patterson technique and refined by a full-matrix least-squares procedure based on F [17]. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were included in the model at their calculated positions. A weighting scheme of the form $w = k/[\sigma^2(F) + 0.001F^2]$ was included and at convergence final values for R, R_w and k were 0.032, 0.033 and 1.09, respectively.

Supplementary Material

Tables of fractional atomic coordinates, thermal parameters, interatomic parameters and structure factor amplitudes are available on request from the authors.

Acknowledgement

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