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Organogold(III) complexes containing chelating bis(amidate) ligands: Synthesis, characterisation and biological activity

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Abstract

Reactions of cycloaurated gold(III) dichloride complexes, with 1,2-$C_6H_4(NHCOMe)_2$ and silver(I) oxide, or with $C_2H_4(NHSO_2Tol)_2$ (Tol = *p*-tolyl) or 1,2-$C_6H_4(NHSO_2Tol)_2$ and trimethylamine, give a series of new auracyclic complexes containing the Au–NR–CH_2CH_2–NR (R = SO_2Tol) and Au–NR–C_6H_4–NR (R = COMe or SO_2Tol) five-membered ring systems. An X-ray structure determination on (2-bp)Au{N(COMe)C_6H_4N(COMe)} (2-bp = cycloaurated 2-benzylpyridine) shows the presence of puckered metallacyclic rings, with both acetyl substituents positioned below the Au(III) coordination plane. The complex (2-bp)Au{N(COMe)C_6H_4N(COMe)} undergoes ring cleavage in the presence of halide and water, to give the complex (2-bp)Au{N(COMe)C_6H_4NH(COMe)}Cl, which was characterised crystallographically, and shown to contain a monodentate amidate ligand. Biological activity studies of the new auracyclic complexes are also reported, against P388 murine leukaemia cells and a range of bacteria and fungi, with a number of complexes showing high activity.

Keywords: Gold complexes; Metallacylic complexes; Crystal structures; Electrospray mass spectrometry; Anti-tumour activity

1. Introduction

The chemistry of cyclometallated gold(III) complexes has been attracting recent interest [1], in part due to the isoelectronic nature of this metal centre with platinum(II), and the thoroughly established anticancer activity of the latter [2–7]. Since gold(III) is considerably more labile than platinum(II) [8,9], we have been investigating the synthesis and biological activity of cycloaurated complexes that also contain a chelating ligand, and have found that certain systems, notably thiosalicylate **1** [10,11] and catecholate **2** [12] derivatives show promising anticancer activity. To date, little is known about the chemistry of cycloaurated complexes that also contain ancillary amidate ligands, with the only Au(III) cyclometallated species containing a chelating bis(amidate) ligand being the ureylene complexes **3**, and an insertion product thereof with PhNCO [13]. In this contribution we report the synthesis and characterisation of some auracyclic derivatives containing the phenylenediamide and ethylenediamide moieties, with the nitrogen atoms bearing electron-withdrawing COMe or SO_2Tol (Tol = *p*-tolyl) groups. Although they are formally similar to the catecholate complexes **2**, the presence of a (variable) group on the amide nitrogen introduces the possibility of tuning the physical (e.g. solubility) and chemical properties of the ligands. Isoelectronic platinum(II) complexes containing such ligands have been well described, and many have been tested for anticancer activity [14,15]. Complexes containing chelating sulfonamide ligands have attracted much interest; there is a vast literature on the application of chiral metal–sulfonamide complexes as catalysts for organic transformations such as asymmetric hydrogenation (Ru) [16], amination [17] and alkylation [18] (Ti), Diels–Alder [19] and [2+2] cycloaddition [20] (Al), Claisen rearrangements (B) [21], and the synthesis of aryl glycines (Mg) [22]. Tungsten Schrock-type complexes, containing

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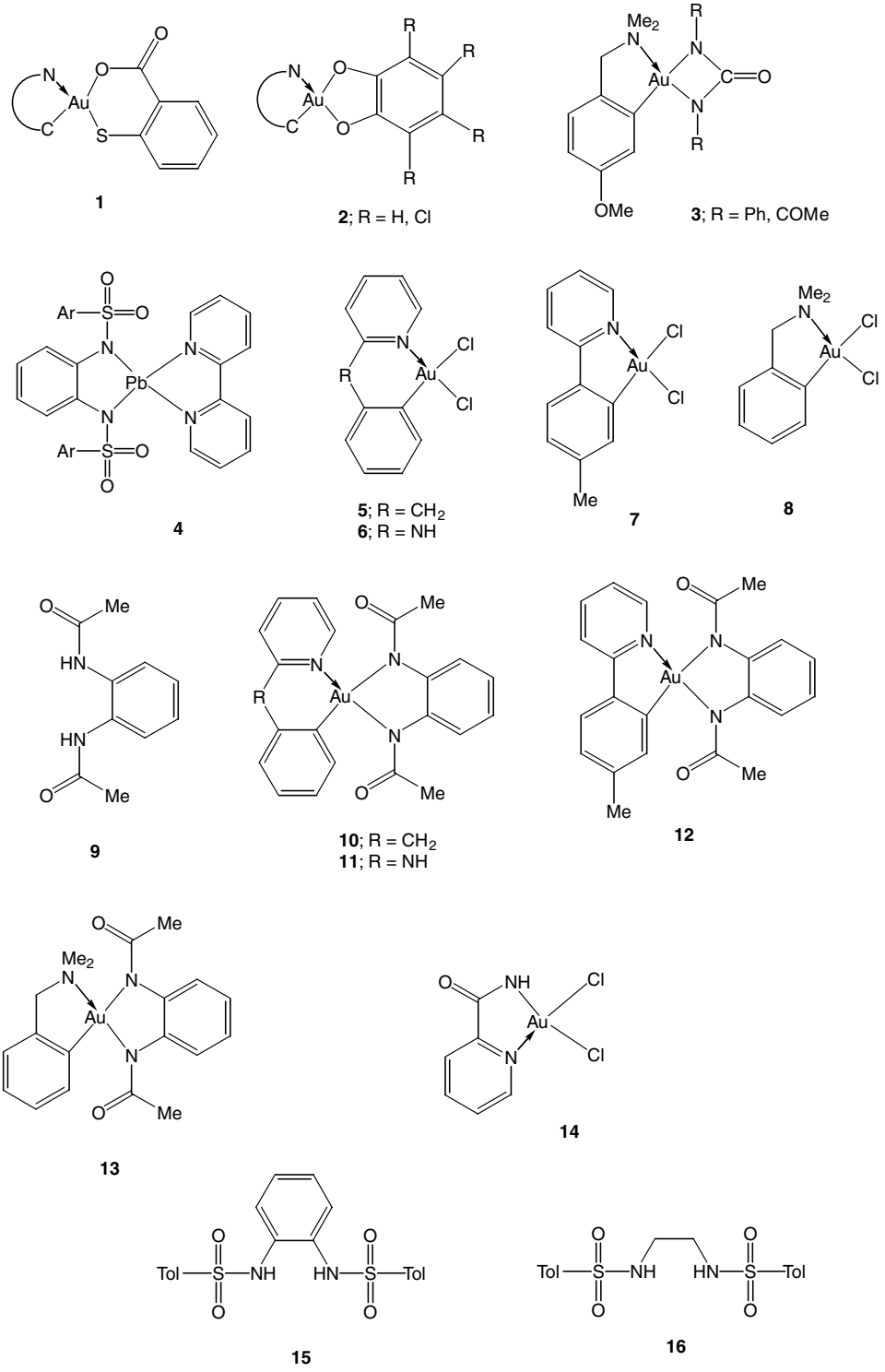
a W–N sulfonamide bond to increase the stability of the complex, have been developed to cleave hydrazine to ammonia [23]. Bis(sulfonamides) have also been explored as ligands for the extraction of lead(II) from aqueous to organic solutions via synergistic ion-exchange mechanisms with 2,2′-bipyridine, giving species such as **4** [24]; incorporation of the dansyl group gives derivatives that allow sensing of lead ions by fluorescence quenching [25].

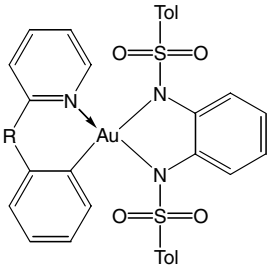
2. Results and discussion

2.1. Synthesis and characterisation of auracyclic amidate complexes

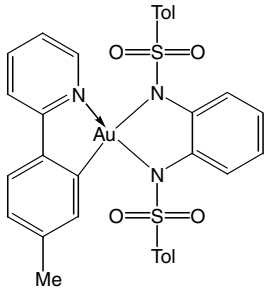
The reaction of the cycloaurated gold(III) dihalide starting materials (2-bp)$AuCl_2$ (**5**), (2-anp)$AuCl_2$ (**6**), (tolpy)-$AuCl_2$ (**7**) and (damp)$AuCl_2$ (**8**) with 1,2-diacetamidobenzene



(**9**) and silver(I) oxide in refluxing dichloromethane gave the auracyclic products **10**–**13**, in moderate yields as pale yellow to yellow solids. The reaction time of 24 h was notably longer than the 2 h previously required for similar gold(III) ureylene systems [13] synthesised by the same method. When the same gold(III) dihalide starting materials, together with the cycloaurated picolinamide complex **14** was reacted with the sulfonamide ligand **15** or **16** in refluxing methanol with excess trimethylamine, the auracyclic complexes **17**–**25** were readily isolated in good yields, by precipitation with water. This suggests that the more strongly electron-withdrawing sulfonamide group facilitates proton removal from the amide nitrogen, and stabilises the Au–N bond. Reaction times were considerably less than those required for analogous platinum compounds [15]. The attempted synthesis of diacetamidobenzene complexes using trimethylamine in refluxing methanol was unsuccessful.



17; R = CH_2
18; R = NH



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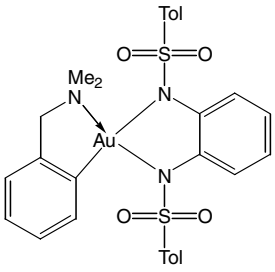

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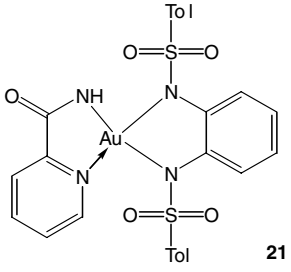

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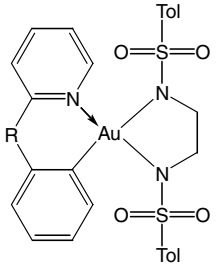
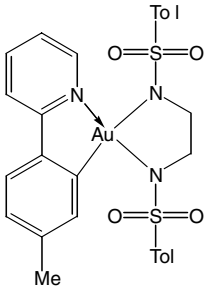


22; R = CH_2
23; R = NH



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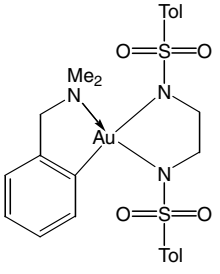

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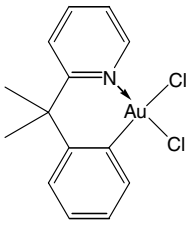

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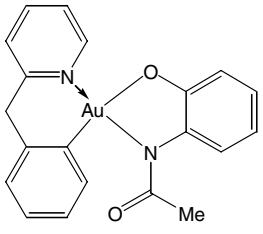

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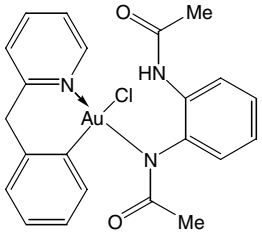

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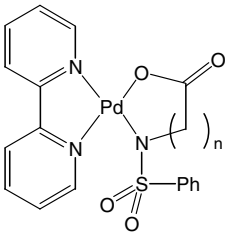


29, n=2
30, n=1

^{1}H, ^{13}C and DEPT135 NMR spectra were acquired for all compounds with the exception of the anilinopyridine complexes **11**, **18** and **23** which were too insoluble in common deuterated solvents [$CDCl_3$, D_2O and $(CD_3)_2SO$] to acquire satisfactory spectra. The low solubility of complexes containing this ligand has been noted previously [1,12]. Due to the complex overlapping of signals in the aromatic regions of the ^{1}H spectra, full NMR assignments were not made, however, integration of the aromatic region was used to ascertain that the expected number of signals were present, and hence as an indication of sample purity. Compounds **10**, **17** and **22** containing the benzylpyridyl ligand displayed the characteristic AB doublet of doublets due to the two methylene protons having different chemical environments in a puckered six-membered ring; Fuchita et al. have previously discussed the ring inversion process in the Au–benzylpyridyl system [26]. The pattern indicates that there is no inversion (at 30 °C, on the NMR timescale) between the two boat conformations. The compounds containing the damp ligand (**13**, **20** and **25**) contained two singlets corresponding to the *N*-methyl and -methylene protons. This was as expected, as all three compounds contain a plane of symmetry through the Au co-ordination plane.

The 1,2-diacetamidobenzene derivatives **10**–**13** showed strong stretches in the C=O region (1603–1630 cm^{-1}), at a lower wavenumber than the ν(C=O) in the free ligand **9** (1668 cm^{-1}). The sulfonamide derivatives **17**–**25** showed the expected strong peaks in the S=O stretching regions of the spectra, i.e. ~1160 cm^{-1} (symmetric) and ~1350 cm^{-1} (asymmetric) [27]. Upon co-ordination of the sulfonamide ligands to the gold(III) centre, the band due to NH stretching (3222 cm^{-1} and 3289 cm^{-1} for the free phenylenediamide and ethylenediamide ligands **15** and **16**, respectively) was lost, confirming that the ligands bind in the deprotonated form.

The auracyclic complexes have also been characterised by electrospray ionisation mass spectrometry (ESI-MS). At low cone voltages (20 V) complexes **10**–**13** all showed strong ions due to either $[M+H]^+$ or $[M+Na]^+$ (from adventitious Na^+ ions) with much less intense $[2M+H]^+$ and $[2M+Na]^+$ species. Increasing the cone voltage (40–60 V) produced fragmentation and the loss of $COCH_2$, possibly as ketene (Scheme 1, shown for (2-bp)Au{N(COMe)C_6H_4N(COMe)} (**10**)) as observed with the free ligand [28]. The ESI-MS behaviour of these complexes in the presence of added alkali metal halides is described later.

At low cone voltages (20 V) the sulfonamide complexes **17**–**25** showed ions assigned as $[M+Me_3NH]^+$ (presumably from the Me_3N used in synthesis, although not present in ^{1}H NMR) along with less intense $[M+Na]^+$ and $[M+H]^+$ adducts. Addition of NaCl as an ionisation aid produced much cleaner spectra, dominated by $[M+Na]^+$ ions. Aggregate ions $[2M+Na]^+$ and $[3M+Na]^+$ were also present at lower intensities. At higher cone voltages the Me_3NH^+ adduct disappeared and fragmentation of the parent ion by successive loss of *p*-toluenesulfonyl moieties was observed, as shown for complex **17** in Fig. 1. Oxidation produced radical cations, as proposed in Scheme 2. Confirmation of these ions was achieved using a Bruker Daltonics MicrOTOF high-resolution mass spectrometer; data are summarised in Table 1, and show excellent agreement between observed

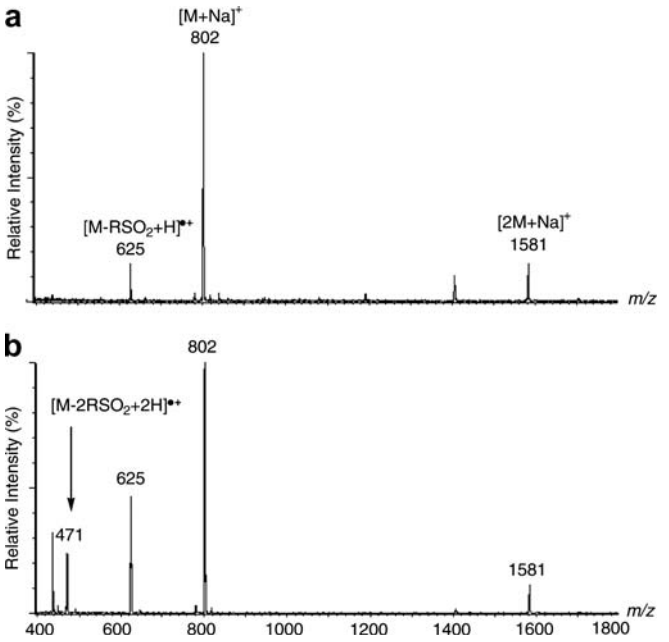
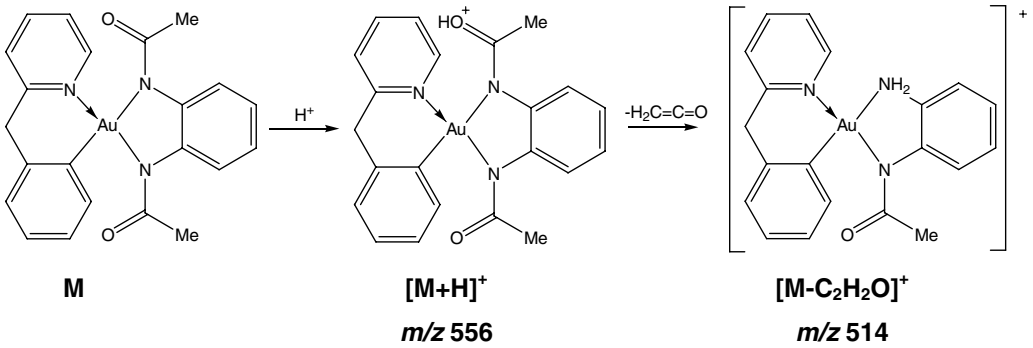
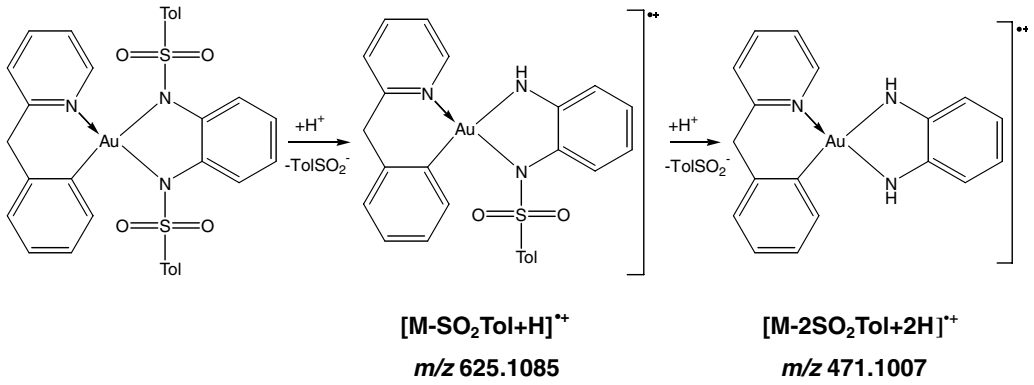


Fig. 1. ESI-MS Spectra of (2-bp)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**17**) (=M) in MeOH, recorded at cone voltages of: (a) 20 V; (b) 80 V, showing successive losses of *p*-toluenesulfonyl moieties, and the formation of radical cation fragment ions.



Scheme 1. Postulated ESMS fragmentation scheme for the compound (2-bp)Au{N(COMe)C_6H_4N(COMe)} (**10**) (=M).



Scheme 2. Postulated ESMS fragmentation and oxidation scheme for the compound (2-bp)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**17**) (=M).

Table 1
Comparison between calculated and observed accurate masses[a] of ions observed in the ESI mass spectrum of (2-bp)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**17**) (=M)

Ion	Formula	Observed *m/z*	Calculated *m/z*	σ[b]
$[M+Na]^+$	$C_{32}H_{28}N_3O_4S_2AuNa$	802.1087	802.1079	0.01
$[2M+Na]^+$	$C_{64}H_{56}N_3O_8S_4Au_2Na$	1581.2205	1581.2266	0.03
$[M-SO_2Tol+H]^{\bullet+}$	$C_{25}H_{22}N_3O_2SAu$	625.1085	625.1093	0.17
$[M-2SO_2Tol+2H]^{\bullet+}$	$C_{18}H_{16}N_3Au$	471.1007	471.1004	0.01

[a] Obtained using a Bruker Daltonics MicrOTOF mass spectrometer.
[b] A combined value for the standard deviation of masses and the intensities of all peaks in the isotopic envelope, compared to the calculated values.

and calculated accurate masses for the major observed ions. To determine if the added hydrogen originates from the solvent, spectra were obtained in CD_3OD solution; the ions at *m/z* 625 and 471 produced isotope patterns containing peaks respectively 1 or 2 mass units heavier which were tentatively assigned as the deuterium adducts (hence protonation from the solvent). However, due to the overlapping nature of the isotope patterns (from species containing hydrogen or deuterium) precise assignment was difficult.

It is well established that the metal electrospray capillary can act as an electrochemical cell allowing neutral molecules to be oxidised (when in positive ion mode); oxidation of the analyte is promoted by a low mobile phase flow rate, which increases the time the compound has to diffuse to the surface of the capillary [29,30]. Decreasing the rate of injection of **17** into the mass spectrometer, in the absence of added NaCl ionisation aid, resulted in the appearance of a small peak at *m/z* 779 (corresponding to the radical cation $[M]^{\bullet+}$ [M = (2-bp)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**17**)]), in addition to the $[M+H]^+$ ion at *m/z* 780, indicating that the parent metallacycle could also be oxidised. The same effect has been seen previously with analogous Pt(II) compounds [15] and oxidation of coordinated phenylenediamine ligands is well documented [31,32]. As expected, this was not seen for the gold–sulfonamide derivatives containing the ethylene backbone.

2.2. X-ray crystal structure determination of (2-bp)Au{N(COMe)C_6H_4N(COMe)} (**10**)

The crystal structure of **10** was determined in order to verify that the complex was the predicted auracycle. This was confirmed with the 1,2-diacetamidobenzene ligand coordinated to the gold through the amidate nitrogen donors. Views of the structure are shown in Figs. 2 and 3 along with the atom numbering scheme; selected bond lengths and bond angles are given in Table 2. The geometry around the gold atom is approximately square planar, with slight deviations; no atom deviates from the least-squares plane defined by N(1), N(2), Au(1), N(3) and C(31) by more than 0.0612(12) Å. Due to C(31) having a higher *trans*-influence than N(3) [33], the Au(1)–N(2) bond

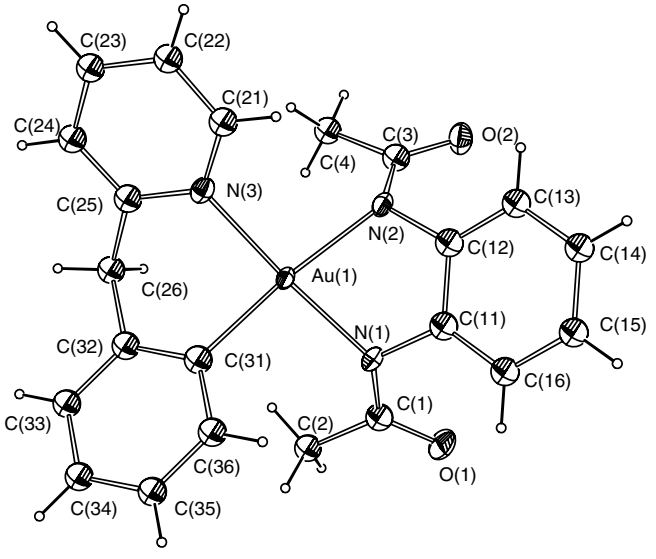


Fig. 2. Perspective view of the X-ray crystal structure of the complex (2-bp)Au{N(COMe)C_6H_4N(COMe)} (**10**), showing the atom labelling scheme. Thermal ellipsoids are shown at the 50% probability level.

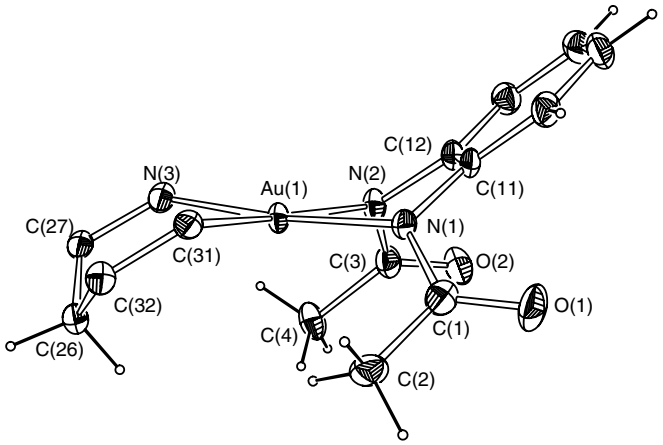


Fig. 3. Side view of the X-ray crystal structure of the complex (2-bp)Au{N(COMe)C_6H_4N(COMe)} (**10**), showing the non-planarity of 1,2-diacetamidobenzene nitrogen atoms and the orientation relative to the benzylpyridine ring system. Thermal ellipsoids are shown at the 50% probability level and atoms completing the benzyl and pyridyl rings have been omitted for clarity.

Table 2
Selected bond lengths (Å) and bond angles (°) (estimated standard deviations in parentheses) for (2-bp)Au{N(COMe)C_6H_4N(COMe)} (**10**)

Bond	Length (Å)	Bond	Angle (°)
Au(1)–N(1)	2.022(3)	N(1)–Au(1)–C(31)	94.76(12)
Au(1)–N(2)	2.089(3)	N(3)–Au(1)–N(2)	97.23(11)
Au(1)–N(3)	2.058(3)	C(31)–Au(1)–N(3)	88.11(12)
Au(1)–C(31)	2.031(3)	N(1)–Au(1)–N(2)	79.61(11)
1,2-Diacetamidobenzene ligand			
N(1)–C(1)	1.366(4)	C(1)–N(1)–C(11)	118.6(3)
N(1)–C(11)	1.435(4)	C(1)–N(1)–Au(1)	129.8(2)
N(2)–C(12)	1.433(4)	C(11)–N(1)–Au(1)	107.3(2)
N(2)–C(3)	1.356(5)	C(3)–N(2)–C(12)	118.0(3)
		C(3)–N(2)–Au(1)	129.1(2)
		C(12)–N(2)–Au(1)	105.9(2)

[2.089(3) Å] *trans* to C(31) is significantly longer than the Au(1)–N(1) bond [2.022(3) Å] *trans* to N(3). The benzylpyridyl moiety has a puckered boat configuration (Fig. 3), as seen with similar gold systems. Both acetyl moieties of the metallacycle are positioned below the Au(III) coordination plane (Fig. 3), in contrast to the uncoordinated ligand where the two acetyl groups are orientated in opposite directions [34]. Due to the puckering of the metallacycle, the aromatic ring of the amidate ligand [C(11)–C(16)] is orientated *trans* to the benzylpyridyl system, possibly to reduce steric interactions between acetyl groups of the acetamidobenzene ligand and the *ortho* ring protons of the benzylpyridyl ligand. The bite angle of the benzylpyridine ligand is 88.11(12)°. This is greater than that observed in compound **26** [35] (85.8°) which has two monodentate chloride ligands attached, but smaller than when a similar *O*,*N*-donor bidentate ligand is coordinated in **27** [89.7(3)°] [12]. The bite angle of the 1,2-diacetamidobenzene ligand is 79.61(11)°, which is less than the idealised 90° of a square-planar complex. This is a general feature of metallacyclic complexes.

The sums of the bond angles around the amidate nitrogens N(1) and N(2) are 355.7° and 353.0°, respectively, indicating a slight deviation from the planarity expected for formally sp^2 hybridised nitrogen atoms. Fully planar sp^2 nitrogen atoms would result in the auracyclic ring [defined by Au(1)–N(1)–C(11)–C(12)–N(2)] being planar, hence the distortion of the amidate nitrogen towards a tetrahedral geometry is most probably to reduce steric interactions. Non-planarity of formally sp^2 nitrogens was first reported in the Re–amide system CpRe(NO)(PPh_3)(NHPh) [36] and has since been observed in similar Pt(II) [15] and Zn [37] sulfonamide compounds along with Pd(II) *N*-sulfonylamino acid complexes [38]. X-ray crystal structures of bis-coordinated sulfonamide complexes of Ru(IV) [39], Os(VI) [40], Cu(II) [32,41,42], Ni(II), Zn(II) and Cd(II) [42] have been reported, however, no comments were offered on the geometry of the coordinating amide nitrogen. Investigation into the geometry around the nitrogen atoms in these structures was conducted using MERCURY [43] and defined as being in a planar environment.

2.3. Synthesis and characterisation of the monodentate amidate complex *28*

Addition of 1 molar equivalent of NaCl to a $CDCl_3$ solution of the auracyclic complex **10** (with monitoring by NMR spectroscopy) resulted in no reaction, but with subsequent addition of 1 molar equivalent of benzoic acid, reaction took place readily giving a new set of signals, subsequently identified as the monodentate complex **28**. Furthermore, this species was also observed in ESI mass spectra of **10**, in the presence of alkali metal halides, added as an ionisation aid. Here, it is significant to note that the electrospray process is known to result in a pH decrease [44,45], so the ESI-MS observations of ring cleavage do parallel those from NMR. Thus, in addition to the expected $[\mathbf{10}+\text{cation}]^+$ and $[2(\mathbf{10})+\text{cation}]^+$ ions (cation = Na or K), an additional ion 36 mass units higher was observed, which by analysis of the isotope pattern, was shown to contain a chloride ion. Fig. 4 shows the spectrum observed for complex **10** upon addition of NaCl. Interestingly, this effect was seen for all the acetamidobenzene metallacycles with the exception of **11**. Addition of small amounts of either Me_4NCl or Me_4NBr to the metallacycle **10** also resulted in cleavage of one Au–amidate bond in the ESI mass spectra.

When (2-bp)$AuCl_2$ (**5**) was reacted with **9** and Ag_2O using a shorter reaction time (2 h) than for the synthesis of the metallacycle **10**, a mixture of the monodentate amidate complex **28** with some metallacyclic complex was obtained. Unambiguous characterisation of **28** was achieved by carrying out a single-crystal X-ray structure determination. The structure of complex **28** is shown in Figs. 5 and 6, along with the atom numbering scheme; selected bond lengths and bond angles are given in Table 3. The structure confirms monodentate coordination of the 1,2-diacetamidobenzene ligand to the Au(III) centre

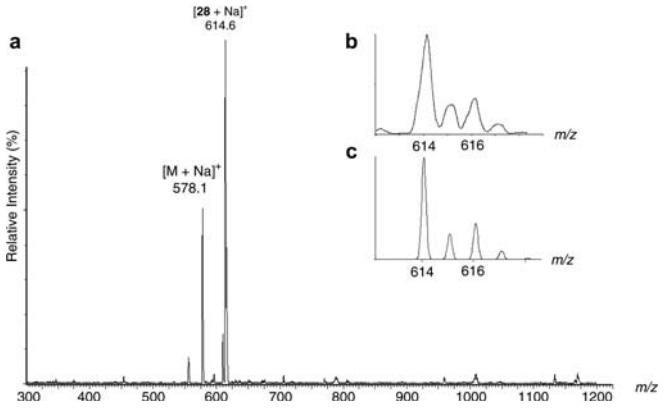


Fig. 4. (a) Positive-ion ESMS spectrum of (2-bp)Au{N(COMe)C_6H_4N-(COMe)} (**10**) (=M) in MeOH, recorded at a cone voltage of 20 V with aqueous NaCl added; (b) and (c) experimental and calculated isotope patterns of *m*/*z* 614 ion, [**28**+Na]$^+$.

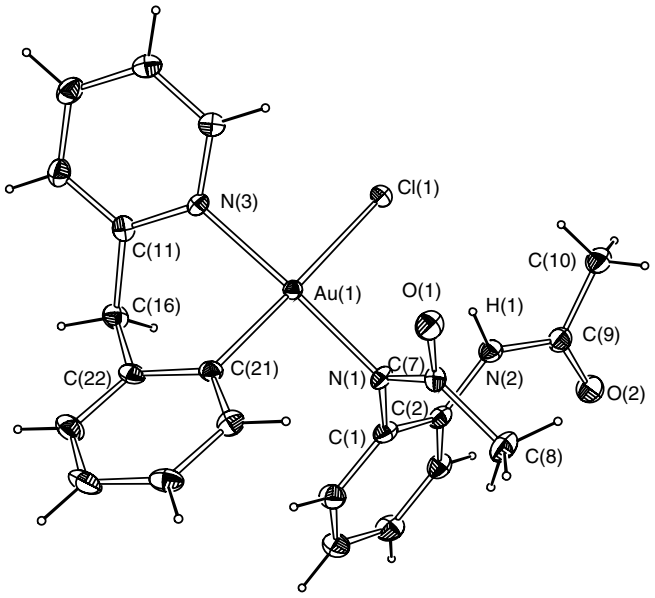


Fig. 5. Perspective view of the X-ray crystal structure of the complex (2-bp)Au{N(COMe)C_6H_4NH(COMe)}Cl (**28**), showing the atom labelling scheme. Thermal ellipsoids are shown at the 50% probability level.

through an Au–N bond. The geometry around the gold atom is essentially square-planar and the sum of the angles around the gold is 359.95°. No atom deviates from the least-squares plane that is defined by N(1), C(21), N(3), Cl(1) and Au(1) by more than 0.0229(7) Å. H(1) is in a position to form a hydrogen bond with Cl(1) (Fig. 6). The H···Cl and N···Cl distances are 2.48(4) Å and 3.302(2) Å, respectively, and the N···H···Cl angle is 153(3)°. These parameters are comparable to those which have recently been characterised as strong hydrogen bonds in organic compounds [46]. The benzylpyridyl moiety is in the expected puckered boat conformation. The bite angle of the benzylpyridine ligand is 87.41(9)° which is not significantly less than in the metallacyclic species **10**. The plane of the 1,2-diacetamidobenzene ligand [defined by C(1)–

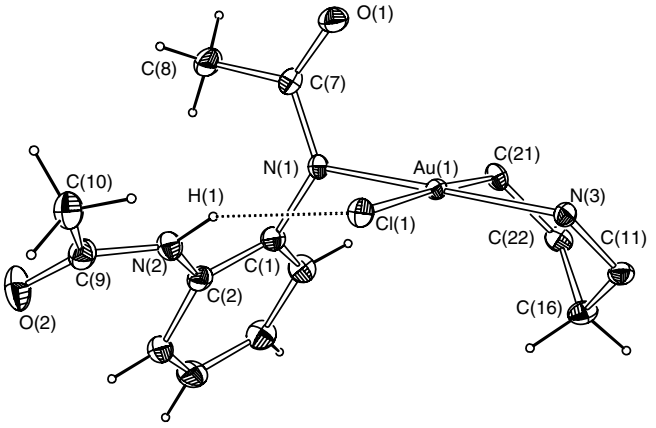


Fig. 6. Side view of the X-ray crystal structure of the complex (2-bp)Au{N(COMe)C_6H_4NH(COMe)}Cl (**28**), showing the puckering of the benzylpyridine ligand, orientation of the 1,2-diacetamidobenzene ligand and the hydrogen bond between H(1) and Cl(1). Thermal ellipsoids are shown at the 50% probability level and atoms completing the benzyl and pyridyl rings have been omitted for clarity.

Table 3
Selected bond lengths (Å) and bond angles (°) (estimated standard deviations in parentheses) for (2-bp)Au{N(COMe)C_6H_4NH(COMe)}Cl (**28**)

Bond	Length (Å)	Bond	Angle (°)
Au(1)–N(3)	2.053(2)	N(1)–Au(1)–C(21)	89.95(9)
Au(1)–C(21)	2.013(3)	C(21)–Au(1)–N(3)	87.41(9)
Au(1)–N(1)	2.014(2)	Cl(1)–Au(1)–N(3)	90.87(6)
Au(1)–Cl(1)	2.3941(6)	N(1)–Au(1)–Cl(1)	91.73(7)
1,2-Diacetamidobenzene ligand			
N(1)–C(1)	1.434(3)	Au(1)–N(1)–C(1)	119.6(2)
N(1)–C(7)	1.353(3)	C(1)–N(1)–C(7)	124.8(2)
N(2)–C(2)	1.410(3)	C(7)–N(1)–Au(1)	115.6(2)
N(2)–C(9)	1.366(4)		

C(6)] is perpendicular to the plane of the gold atom and the two acetyl groups point in opposite directions which differs from that in **10** but not in the free ligand [34].

The geometry around the coordinated nitrogen N(1) is essentially planar, with the sum of the angles adding to 360.03°. This differs from the metallacyclic species where both of the amidate nitrogen atoms show significant deviations from planarity, suggesting that the formation of a five-membered ring forces the nitrogen atoms towards a tetrahedral geometry in an effort to reduce strain on the ring. Digression towards a tetrahedral structure has been reported in Pd(II) complexes where decreasing the ring size from six atoms in **29** to five in **30** resulted in the sum of the bond angles around the sulfonamide nitrogen decreasing from 352.7(8)° to 332.2(3)° [38]. The Au(1)–N(1) bond of 2.014(2) Å in **28** is shorter than the Au(1)–N(2) (2.089 Å) and Au(1)–N(1) (2.022 Å) bonds in the metallacyclic complex **10**. The chlorine atom is in a position *trans* to C(21); this is presumably due to C having a higher *trans* effect than N, making the rate of ligand substitution *trans* to the C higher. The two low *trans* influence ligand atoms, Cl(1) and N(3), are also mutually *cis* due to antisymbiosis

[47]. This effect has been seen in many gold(III) cyclometallated compounds [1] including thiosalicylate [10,11], auralactam [48], and amidophenolate [12] systems, as well as in the interesting structurally characterised thiocyanate complex [LAu(NCS)(SCN)] (L = cycloaurated 2-phenylpyridyl), where the thiocyanate ligand *cis* to the aryl carbon is *S*-bonded, but the other thiocyanate is *N*-bonded [49].

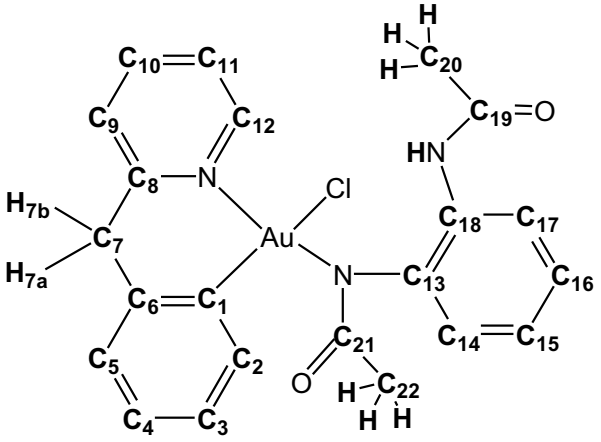
^{1}H NMR of the impure product containing **10** and **28** clearly indicated the presence of two sets of CH_2 AB resonances in the region δ 3.7–4.7 and all other signals showing a less intense partner. Peaks arising from **28** were more poorly resolved, which may be indicative of the auracyclic species **10** being more rigid. The ^{1}H NMR spectrum of **28** was fully assigned using a combination of ^{1}H, ^{13}C, DEPT135, ^{1}H–^{1}H COSY, HSQC, HMBC and 2D-NOESY experiments; data and the NMR atom numbering scheme are summarised in Table 4. A singlet peak at δ 9.43 in the ^{1}H spectrum was assigned to the amide NH proton, which shows no correlation to any other proton or carbon signals in the COSY or HSQC spectra, respectively. It did, however, show a weak correlation in the HMBC spectrum to a carbon in the phenylenediamido aromatic ring.

The ^{1}H–^{1}H COSY spectrum of **28** showed three distinct aromatic ring systems with most protons showing ^3J and ^4J coupling. In conjunction with HSQC and HMBC experiments, the chemical shifts of the ring protons and carbons could be assigned. The 2D-NOESY experiment was used to differentiate between the two acetyl moieties. The methyl protons at δ 2.30 produced a correlation to the amide proton whereas those at δ 1.88 showed correlations to the amide proton and protons in both the phenylenediamine and benzyl rings. The uncoordinated $NHC(O)CH_3$ group is located too far from the phenyl ring of the benzylpyridyl ligand to show an NOE correlation, but the coordinated $NC(O)CH_3$ group, in closer proximity, does show a correlation, placing the coordinated amidate ligand *cis* to the cycloaurated phenyl ring. As expected, the proton at δ 7.60 (H9, Table 4) showed a strong NOE to the proton at δ 7.96 (H10), its neighbour in the pyridyl ring. Inspection of the crystal structure revealed that H9 is closer to the methylene proton in the *pseudo*-equatorial position than in the *pseudo*-axial position. The larger NOE to the proton at δ 3.87 suggests it is the *pseudo*-equatorial proton, leaving the proton at δ 4.26 in the *pseudo*-axial position, assuming that the structure in solution is the same as in the crystalline state. This is to be expected, as the *pseudo*-axial proton is in closer proximity to the gold atom and thus more deshielded.

Two independent samples of **28**, recrystallised from dichloromethane and diethyl ether and dried under vacuum prior to analysis, produced microanalytical data with

Table 4
^{1}H and ^{13}C NMR chemical shift data, and NMR atom numbering scheme of (2-bp)Au{N(COMe)C_6H_4NH(COMe)}Cl (**28**)[a]

Atom	Type	^{13}C	^{1}H	
1	C	131.5		
2	CH	132.9	7.72	d, J = 9.7 Hz
3	CH	128.8	7.23	t, J = 7.2 Hz
4	CH	128.9	7.13	m, overlapping with H5, H16
5	CH	127.9	7.09	m, overlapping with H4, H16
6	C	141.4		
7	CH_2	48.0	3.87 (H_{ax})	d, J = 15 Hz
			4.26 (H_{eq})	d, J = 15 Hz
8	C	157.1		
9	CH	125.9	7.60	d, J = 6.4 Hz
10	CH	142.3	7.96	t, d, J = 7.7, 1.5 Hz
11	CH	124.3	7.49	t, J = 6.3 Hz
12	CH	152.6	9.30	br d, J = 5.3 Hz
13	C	135.7		
14	CH	122.2	8.30	br d, J = 7.9 Hz
15	CH	124.6	6.71	br t, J = 7.1 Hz
16	CH	128.2	7.11	m, overlapping with H4, H5
17	CH	128.7	6.35	br d, J = 7.5 Hz
18	C	136.6		
19	C=O	170.0		
20	CH_3	25.2	2.30	s
21	C=O	173.0		
22	CH_3	22.7	1.88	s
23	NH		9.43	br s



[a] 400 MHz, 300 K in $CDCl_3$. Protons are numbered after the carbon atoms to which they are bonded.

Table 5
Anti-tumour (P388) activities for metallacyclic gold(III) amidate derivatives

Compound	Anti-tumour IC_{50}[a]	
	ng mL^{-1}	μM
(2-bp)Au{N(COMe)C_6H_4N(COMe)} (**10**)	2434	4.38
(2-anp)Au{N(COMe)C_6H_4N(COMe)} (**11**)	3479	6.26
(tolpy)Au{N(COMe)C_6H_4N(COMe)} (**12**)	441	0.80
(damp)Au{N(COMe)C_6H_4N(COMe)} (**13**)	7546	14.47
(2-bp)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**17**)	236	0.30
(2-anp)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**18**)	>62 500	>80.13
(tolpy)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**19**)	41 201	52.89
(damp)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**20**)	4974	6.68
(pic)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**21**)	160	0.22
(2-bp)Au{N(SO_2Tol)C_2H_4N(SO_2Tol)} (**22**)	243	0.33
(2-anp)Au{N(SO_2Tol)C_2H_4N(SO_2Tol)} (**23**)	1156	1.58
(tolpy)Au{N(SO_2Tol)C_2H_4N(SO_2Tol)} (**24**)	3182	4.35
(damp)Au{N(SO_2Tol)C_2H_4N(SO_2Tol)} (**25**)	762	1.09
(TolSO_2)NHC_2H_4NH(SO_2Tol) (**16**)	>25 000	>67.93
Cisplatin	2583	8.15

[a] The concentration of the sample required to reduce the cell growth of the P388 leukaemia cell line (ATCC CCL 46) by 50%.

Table 6
Anti-microbial activities for metallacyclic gold(III) amidate derivatives

Compound	Anti-bacterial[a] and anti-fungal[b] activity[c]					
	Ec	Bs	Pa	Ca	Tm	Cr
(tolpy)Au{N(COMe)C_6H_4N(COMe)} (**12**)	6	11	10	13	14	9
(damp)Au{N(COMe)C_6H_4N(COMe)} (**13**)	10	15	10	10	11	1
(2-bp)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**17**)	–	1	–	–	–	–
(damp)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**20**)	5	10	3	8	13	1
(pic)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**21**)	–	2	1	2	2	–
(2-bp)Au{N(SO_2Tol)C_2H_4N(SO_2Tol)} (**22**)	1	2	1	–	–	–
(damp)Au{N(SO_2Tol)C_2H_4N(SO_2Tol)} (**25**)	8	15	8	10	15	1
(MeCO)NHC_6H_4NH(COMe) (**9**)	–	–	–	–	–	–

[a] Ec = *Escherichia coli*, Bs = *Bacillus subtilis*, Pa = *Pseudomonas aeruginosa*.
[b] Ca = *Candida albicans*, Tm = *Trichophyton mentagrophytes*, Cr = *Cladosporium resinae*.
[c] Inhibition zone as an excess radius (mm) from a 6 mm disc containing 5 μg of sample; – = no activity measured.

carbon, nitrogen and hydrogen compositions lower than expected. The difference in composition does not appear to be due to organic solvents as the ^{1}H NMR spectra lack signals due to dichloromethane or diethyl ether.

2.4. Biological activity

The anti-tumour activity of all compounds was determined against a P388 leukemia cell line, and results are reported in Table 5. The results show no clearly discernible pattern in anti-tumour activity. However, as a group the *N*,*N*′-bis(*p*-toluenesulfonyl)ethylenediamide derivatives appear to have a higher activity, possibly due to greater solubility. IC_{50} values were very comparable to those of catecholate, ureylene and thiosalicylate Au(III) metallacycles. With the exception of complexes **13**, **18** and **19**, all of the gold(III) amidate complexes demonstrated anti-tumour activity that was higher than cisplatin, under the screening conditions. The anti-microbial activities of the damp derivatives, and a selection of other complexes which showed good anti-tumour activity (defined by $IC_{50} < 500$ ng mL^{-1}) was also determined, and are listed in Table 6. The acetamido derivatives **12** and **13** show a broad spectrum activity which appears higher than other derivatives. It is also apparent that a higher anti-cancer activity gives lower anti-microbial activity although the reasons are unclear. Again, anti-microbial activity is probably due to the gold metallacycle as the 1,2-diacetamidobenzene (**9**) ligand itself shows no anti-microbial activity.

3. Conclusions

A series of new gold(III) metallacyclic complexes containing Au–N–C–C–N rings has been synthesised and characterised by NMR, ESI-MS, IR and micro-elemental analysis. Auracycles containing the acetamidobenzene ligand undergo protonolysis to give the monodentate amidate complex; in the case involving the benzylpyridyl ligand this was also synthesised as an intermediate in the Ag_2O-mediated reaction, and characterised by X-ray crystallography. All new auracyclic compounds were assayed in order to assess their anti-tumour activity. Seven of the complexes had an activity higher than cisplatin in the P388 assay, with the more soluble ethylenediamide derivatives showing the best activity. Three of the compounds also show good broad-spectrum anti-microbial activity.

4. Experimental

4.1. General

All reactions were carried out with no efforts at excluding air or light. Solvents were LR grade with the exception of dichloromethane (which was distilled from P_4O_{10}) when used in the workup. The sulfonamides [15] and silver(I) oxide [50] were prepared by the literature methods, the former from *p*-toluenesulfonyl chloride and *o*-phenylenediamine, or ethylenediamine (BDH) as appropriate. 1,2-Diacetamidobenzene was prepared by acetylation of 1,2-diaminobenzene (*o*-phenylenediamine, BDH) using acetic anhydride. Trimethylamine (Eastman, 25% aqueous solution) was used as supplied. The cycloaurated gold(III) complexes (2-bp)$AuCl_2$ (**5**) [35], (2-anp)$AuCl_2$ (**6**) [51], (tolpy)$AuCl_2$ (**7**) [10], (damp)$AuCl_2$ (**8**) [52,53], and (pic)$AuCl_2$ (**14**) [54] were prepared by modified literature methods.

General experimental techniques were as previously described [12]; routine ESI mass spectra were recorded on a VG Platform II instrument, using methanol as the mobile phase. A small quantity of aqueous NaCl solution was often added as an ionisation aid. Confirmation of the formation of oxidised ions was achieved using a Bruker Daltonics MicrOTOF high-resolution mass spectrometer, capable of achieving an accurate *m*/*z* value to ±5 ppm; calibration was achieved using a sodium formate solution. Assignment of mass spectrometric isotope patterns was aided by the ISOTOPE program [55].

4.2. Synthesis of (2-bp)Au{N(COMe)C_6H_4N(COMe)} (*10*)

The complex (2-bp)$AuCl_2$ (**5**) (200 mg, 0.45 mmol), 1,2-diacetamidobenzene (**9**) (88 mg, 0.45 mmol) and silver(I) oxide (400 mg, excess) were added to dichloromethane (30 mL) and refluxed with stirring for 24 h. The resulting

solution was filtered to give a pale yellow solution which was evaporated to give yellow crystals. These were dissolved in dichloromethane (~5 mL) and filtered through an alumina column. Slow addition of diethyl ether to the filtrate resulted in formation of yellow microcrystals which were filtered, washed with water (2 × 10 mL) and diethyl ether (10 mL) and dried under vacuum to give 178 mg (69%) of the product. *Anal.* Calc. for $C_{22}H_{20}N_3O_2Au$: C, 47.6; H, 3.6; N, 7.6. Found: C, 47.8; H, 3.8; N, 7.5%. M.p. 176–178 °C (dec.). IR: ν(C=O) region: 1611 cm^{-1}. ESI-MS: cone voltage 20 V; *m/z* 578 (100%, $[M+Na]^+$), 556 (45%, $[M+H]^+$), 1133 (30% $[2M+Na]^+$). ^1H NMR: δ 1.87 (s, 3H), 2.14 (s, 3H), 4.03 (d, 1H), 4.67 (d, 1H), 6.9–7.2 (m, 6H), 7.38 (t, 1H), 7.48 (d, 1H), 7.68 (d, 1H), 7.95 (t 1H), 8.98 (d, 1H). $^{13}C–\{^1H\}$ NMR: δ 23.0 (CH_3), 27.7 (CH_3), 47.7 (CH_2), 122.1–156.1 (aryl C), 173.5 (C=O), 174.1 (C=O).

4.3. Synthesis of (2-anp)Au{N(COMe)C_6H_4N(COMe)} (**11**)

The complex (2-anp)$AuCl_2$ (**6**) (201 mg, 0.46 mmol), 1,2-diacetamidobenzene (**9**) (89 mg, 0.46 mmol) and silver(I) oxide (400 mg, excess) were added to dichloromethane (30 mL) and refluxed with stirring for 24 h. The solution was filtered, and the filtrate evaporated under reduced pressure to give orange crystals. These were dissolved in dichloromethane (~5 mL) and the solution filtered through a column of neutral alumina. Diethyl ether was slowly added to the filtrate, resulting in the formation of yellow crystals which were filtered, washed with water (2 × 10 mL) and diethyl ether (10 mL) and dried under vacuum to give 142 mg (55%) of the product. *Anal.* Calc. for $C_{21}H_{19}N_4O_2Au$: C, 45.3; H, 3.4; N, 10.1. Found: C, 45.3; H, 3.6; N, 10.0%. M.p. 232–236 °C (dec.). IR: ν(C=O) region: 1604 cm^{-1}. ESI-MS: cone voltage 20 V; *m/z* 579 (100%, $[M+Na]^+$), 1135 (30%, $[2M+Na]^+$). The complex was too insoluble in the common deuterated solvents [$(CD_3)_2SO$, D_2O and $CDCl_3$] to acquire satisfactory NMR spectra.

4.4. Synthesis of (tolpy)Au{N(COMe)C_6H_4N(COMe)} (**12**)

The complex (tolpy)$AuCl_2$ (**7**) (100 mg, 0.23 mmol), 1,2-diacetamidobenzene (**9**) (44 mg, 0.23 mol) and silver(I) oxide (200 mg, excess) were suspended in dichloromethane (30 mL) and refluxed with stirring for 24 h. The resulting mixture was filtered and the filtrate evaporated to give yellow crystals. These were then dissolved in dichloromethane (~5 mL) and the solution filtered through an alumina column to remove remaining silver impurities. Addition of diethyl ether to the filtrate resulted in formation of pale yellow fluffy crystals which were filtered, washed with water (2 × 10 mL) and diethyl ether (2 × 10 mL) and dried under vacuum to give 86 mg (68%) of the product. *Anal.* Calc. for $C_{22}H_{20}N_3O_2Au$: C, 47.6; H, 3.6; N, 7.6. Found: C, 46.3; H, 3.8; N, 7.4%. M.p. 270–273 °C (dec.). IR: ν(C=O) region: 1607 cm^{-1}. ESI-MS: cone voltage 20 V; *m/z* 578 (100%, $[M+Na]^+$), 556 (50%, $[M+H]^+$), 1133 (25%, $[2M+Na]^+$). ^1H NMR: δ 2.23 (s, 3H), 2.36 (s, 3H), 2.44 (s, 3H) 6.9–7.4 (m, 8H), 7.77 (d, 1H), 9.46 (s, 1H). $^{13}C–\{^1H\}$ NMR: δ 14.1 (CH_3), 22.2 (CH_3), 22.4 (CH_3), 119.5–164.8 (aryl C), 173.6 (C=O), 174.7 (C=O).

4.5. Synthesis of (damp)Au{N(COMe)C_6H_4N(COMe)} (**13**)

The complex (damp)$AuCl_2$ (**8**) (100 mg, 0.25 mmol), 1,2-diacetamidobenzene (**9**) (48 mg, 0.25 mol) and silver(I) oxide (200 mg, excess) were suspended in dichloromethane (30 mL) and refluxed for 24 h. The solution was filtered and evaporated to give yellow crystals. These were dissolved in a minimum amount of dichloromethane and slow addition of diethyl ether resulted in the formation of yellow crystals which were filtered, washed with diethyl ether (10 mL) and water (2 × 10 mL) and dried under vacuum to give 64 mg (50%) of the product. *Anal.* Calc. for $C_{19}H_{22}N_3O_2Au \cdot 0.15CH_2Cl_2$: C, 43.1; H, 4.2; N, 7.9. Found: C, 42.3; H, 4.4; N, 7.7%. M.p. 202 °C (dec.). IR: ν(C=O) region: 1612 cm^{-1}. ESI-MS: cone voltage 20 V; *m/z* 544 (100%, $[M+Na]^+$), 522 (78%, $[M+H]^+$), 580 (68%, $[M+HCl+Na]^+$), 1065 (45%, $[2M+Na]^+$), 1101 (38%, $[2M+HCl+Na]^+$), 1043 (25%, $[2M+H]^+$). ^1H NMR: δ 2.15 (s, 3H), 2.23 (s, 3H), 3.39 (s, 6H), 4.21 (s, br, 2H), 5.32 (s, CH_2Cl_2), 6.86–6.89 (m 4H), 6.97–7.00 (m, 2H), 7.05 (m, 2H), 7.17 (m, 2H), 7.60 (d, 1H). $^{13}C–\{^1H\}$ NMR: δ 22.7 (CH_3), 52.6 (NCH_3), 53.4 (CH_2Cl_2), 74.9 (CH_2), 122.2–146.6 (aryl C), 173.5 (C=O), 174.1 (C=O).

4.6. Synthesis of (2-bp)Au{N(SO_2Tol)C_6H_4N(SO_2Tol)} (**17**)

The complex (2-bp)$AuCl_2$ (**5**) (100 mg, 0.229 mmol) and bis(sulfonamide) (**15**) (142 mg, 0.341 mmol) were stirred in refluxing methanol (30 mL). Aqueous trimethylamine (2 mL, excess) was added and the resulting bright orange solution was further refluxed for 15 min. Distilled water (50 mL) was added, resulting in the formation of a milky yellow suspension. This was stirred until cool, filtered, and the product washed with water (2 × 10 mL) and diethyl ether (10 mL) then dried under vacuum to give (88 mg, 49%) of bright yellow solid. *Anal.* Calc. for $C_{32}H_{28}N_3O_4S_2Au$: C, 49.3; H, 3.6; N, 5.4. Found: C, 48.0; H, 3.7; N, 5.5%. M.p. 151–155 °C. IR: ν(SO_2, asym) 1301 cm^{-1}; ν(SO_2, sym) 1145 cm^{-1}. ESI-MS: cone voltage 20 V; *m/z* 802 (100%, $[M+Na]^+$), 1581 (20%, $[2M+Na]^+$). Cone voltage 60 V: *m/z* 802 (100%, $[M+Na]^+$), 625 (20%, $[M-SO_2Tol+H]^{\bullet+}$), 471 (15%, $[M-2SO_2Tol+2H]^{\bullet+}$), 1581 (20%, $[2M+Na]^+$). ^1H NMR: δ 2.33 (s, 3H), 2.39 (s, 3H), 4.08 (d, 1H), 4.77 (d, 1H), 6.8–7.5 (m, 15H), 7.56 (d, 1H), 7.70 (d, 2H), 7.80 (t, 1H), 9.15 (d, 1H). $^{13}C–\{^1H\}$ NMR: δ 21.6 (CH_3), 21.7 (CH_3), 48.1 (CH_2), 121.6–156.8 (aryl C).

4.7. Synthesis of (2-anp)Au{N(SO$_2$Tol)C$_6$H$_4$N(SO$_2$Tol)} (**18**)

The complex (2-anp)AuCl$_2$ (**6**) (100 mg, 0.229 mmol) and bis(sulfonamide) (**15**) (143 mg, 342 mmol) were mixed in refluxing methanol (30 mL). Aqueous trimethylamine (2 mL, excess) was added, resulting in the rapid formation of yellow/brown micro-crystals. The mixture was refluxed for a further 20 min then left to cool and filtered. The yellow solid was washed with water (2 × 10 mL) and diethyl ether (10 mL) and then dried under vacuum to give 150 mg (84%) of product. *Anal*. Calc. for $C_{31}H_{27}N_4O_4S_2Au$: C, 47.7; H, 3.5; N, 7.2. Found: C, 47.5; H, 3.6; N, 7.2%. M.p. 264–265 °C (dec.). IR: ν(SO$_2$, asym) 1284 cm^{-1}, ν(SO$_2$, sym) 1140 cm^{-1}; ν(NH) 3294 cm^{-1}. ESI-MS: cone voltage 20 V; *m*/*z* 803 (100%, [M+Na]$^+$), 1583 (20%, [2M+Na]$^+$). Cone voltage 60 V: *m*/*z* 803 (100%, [M+Na]$^+$), 625 (20%, [M−SO$_2$Tol+H]$^{\cdot+}$), 471 (15%, [M−2SO$_2$Tol+2H]$^{\cdot+}$), 1583 (20%, [2M+Na]$^+$). ^{1}H NMR: δ 2.36 (s, 3H), 2.44 (s, 3H), 6.84 (t, 1H), 6.77 (t, 1H), 6.93–7.25 (m, 6H), 7.36 (d, 1H), 7.55 (d, 1H), 7.63 (d, 2H), 7.80 (t, 1H), 8.02 (d, 2H), 8.87 (d, 1H), 8.76 (s, NH). Due to the insolubility of this compound in common deuterated NMR solvents [(CD$_3$)$_2$SO, D$_2$O, CDCl$_3$], satisfactory ^{13}C NMR spectra could not be acquired.

4.8. Synthesis of (tolpy)Au{N(SO$_2$Tol)C$_6$H$_4$N(SO$_2$Tol)} (**19**)

The complex (tolpy)AuCl$_2$ (**7**) (100 mg, 0.231 mmol) and bis(sulfonamide) (**15**) (144 mg, 0.290 mmol) were mixed in refluxing methanol (30 mL). Aqueous trimethylamine (2 mL, excess) was added, resulting in the rapid deposition of yellow microcrystals. The solution was left to cool, then filtered, washed with water (2 × 10 mL) and diethyl ether (10 mL) then dried under vacuum to give 117 mg (65%) of yellow solid. *Anal*. Calc. for $C_{32}H_{28}N_3O_4S_2Au$: C, 49.3; H, 3.6; N, 5.4. Found: C, 49.5; H, 3.7; N, 5.5%. M.p. 262 °C (dec.). IR: ν(SO$_2$, asym) 1300 cm^{-1}; ν(SO$_2$, sym) 1140 cm^{-1}. ESI-MS: cone voltage 20 V; *m*/*z* 802 (100%, [M+Na]$^+$). Cone voltage 60 V: *m*/*z* 802 (100%, [M+Na]$^+$), 1581 (20%, [2M+Na]$^+$). ^{1}H NMR: δ 2.36 (s, 3H), 2.39 (s, 3H), 2.41 (s, 3H), 6.82 (t, 1H), 6.89 (t, 1H), 7.06 (d 1H), 7.18–7.24 (m, 3H), 7.34 (d, 1H), 7.40 (d, 1H), 7.72 (d, 2H), 7.79–7.81 (m, 3H), 8.00 (t, 1H), 9.31 (d, 1H). ^{13}C–{^{1}H} NMR: δ 21.8 (*C*H$_3$), 21.9 (*C*H$_3$), 23.4 (*C*H$_3$), 120–165 (aryl *C*).

4.9. Synthesis of (damp)Au{N(SO$_2$Tol)C$_6$H$_4$N(SO$_2$Tol)} (**20**)

The complex (damp)AuCl$_2$ (**8**) (75 mg, 0.19 mmol) and bis(sulfonamide) (**15**) (120 mg, 0.28 mmol) were mixed in refluxing methanol (30 mL), resulting in a clear yellow solution. Aqueous trimethylamine (2 mL, excess) was added resulting in a rapid colour change to give an orange solution which was further refluxed for 5 min. Water (75 mL) was added, resulting in the immediate formation of yellow microcrystals. After cooling, the mixture was filtered and the product washed with water (2 × 10 mL) and diethyl ether (10 mL) and dried under vacuum giving 57 mg (41%) of product. *Anal*. Calc. for $C_{29}H_{30}N_3O_4S_2Au$: C, 46.7; H, 4.1; N, 5.6. Found: C, 46.6; H, 3.9; N, 5.7%. M.p. 196–198 °C (dec.). IR: ν(SO$_2$, asym) 1302 cm^{-1}; ν(SO$_2$, sym) 1147 cm^{-1}. ESI-MS: cone voltage 20 V; *m*/*z* 767 (100%, [M+Na]$^+$), 465 (100%, unidentified), 1511 (32%, [2M+Na]$^+$). Cone voltage 60 V: *m*/*z* 767 (100%, [M+Na]$^+$), 591 (32%, [M−SO$_2$Tol+H]$^{\cdot+}$), 1511 (30%, [2M+Na]$^+$). ^{1}H NMR: δ 2.39 (s, 3H), 2.42 (s, 3H), 3.36 (s, 6H), 4.30 (s, 2H), 6.70 (t, 1H), 6.86 (t, 1H), 6.93 (d, 1H), 7.11 (m 2H), 7.2–7.3 (m, 6H), 7.70 (d, 2H), 7.80 (d, 2H), 8.02 (d, 1H). ^{13}C–{^{1}H} NMR: δ 21.5 (*C*H$_3$), 21.5 (*C*H$_3$), 53.2 (N*C*H$_3$), 75.7 (*C*H$_2$), 121.6–144.0 (aryl *C*).

4.10. Synthesis of (pic)Au{N(SO$_2$Tol)C$_6$H$_4$N(SO$_2$Tol)} (**21**)

The complex (pic)AuCl$_2$ (**14**) (75 mg, 0.19 mmol) and bis(sulfonamide) (**15**) (120 mg, 0.28 mmol) were mixed in refluxing methanol (30 mL), resulting in a colour change to give a red solution. Aqueous trimethylamine (2 mL, excess) was added, resulting in the rapid deposition of red/brown microcrystals. The solution was left to cool while stirring and then filtered, washed with water (2 × 10 mL) and diethyl ether (10 mL) then dried under vacuum to give 101 mg (72%) of red solid. *Anal*. Calc. for $C_{26}H_{23}N_4O_5S_2Au$: C, 42.6; H, 3.2; N, 7.7. Found: C, 41.6; H, 3.2; N, 7.4%. M.p. 226 °C. IR: ν(SO$_2$, asym) 1326 cm^{-1}, ν(SO$_2$, sym) 1154 cm^{-1}; ν(NH) 3368 cm^{-1}, ν(C=O) 1658 cm^{-1}. ESI-MS: cone voltage 20 V; *m*/*z* 755 (100%, [M+Na]$^+$), 1487 (30%, [2M+Na]$^+$), 1121 (25%, [3M+2Na]$^{2+}$). Cone voltage 60 V: *m*/*z* 755 (100%, [M+Na]$^+$), 1487 (25%, [2M+Na]$^+$). ^{1}H NMR: δ 2.40 (s, 3H), 2.41 (s, 3H), 6.7–7.5 (m, 8H), 7.60 (d, 2H), 7.71 (d, 2H), 7.95 (t, 1H), 8.17 (d, 1H), 8.36 (t, 1H), 9.61 (d, 1H). ^{13}C–{^{1}H} NMR: δ 21.6 (*C*H$_3$), 21.7 (*C*H$_3$), 118.3–150.0 (aryl C), 170.4 (*C*=O).

4.11. Synthesis of (2-bp)Au{N(SO$_2$Tol)C$_2$H$_4$N(SO$_2$Tol)} (**22**)

The complex (2-bp)AuCl$_2$ (**5**) (100 mg, 0.23 mmol) and bis(sulfonamide) (**16**) (100 mg, 28 mmol) were suspended in refluxing methanol (30 mL). Aqueous trimethylamine (2 mL, excess) was added and the solution further refluxed for 15 min. Water (50 mL) was added which resulted in the deposition of a white precipitate. After cooling to room temperature, the solid was filtered, washed with water (2 × 10 mL) and diethyl ether (10 mL) to give a pale grey solid. This was further purified by dissolving in minimal dichloromethane and filtering through a Pasteur pipette containing florisil. The compound was then isolated by slow addition of diethyl ether, filtered and washed with water (2 × 10 mL) and diethyl ether (10 mL) to give

59 mg (35%) of white microcrystals. *Anal.* Calc. for $C_{28}H_{28}N_3O_4S_2Au$: C, 46.0; H, 3.9; N, 5.8. Found: C, 45.9; H, 4.0; N, 5.8%. M.p. 215–219 °C (dec.). IR: $\nu(SO_2$, asym) 1280 cm^{-1}; $\nu(SO_2$, sym) 1139 cm^{-1}. ESI-MS: cone voltage 20 V; *m/z* 791 (100%, $[M+Me_3NH]^+$), 732 (95%, $[M+H]^+$), 754 (80%, $[M+Na]^+$), 1485 (35%, $[2M+Na]^+$), 1463 (30%, $[2M+H]^+$). Cone voltage 60 V: *m/z* 732 (100%, $[M+H]^+$), 754 (95%, $[M+Na]^+$), 1485 (40%, $[2M+Na]^+$). ^{1}H NMR: δ 2.37 (s, 3H), 2.38 (s, 3H), 3.10 (m, 2H), 3.51 (m, 2H), 4.01 (d, 1H), 4.55 (d, 1H), 6.80 (t, 1H), 7.06–7.33 (m, 9H), 7.42 (t, 1H), 7.63 (d, 1H), 7.75 (d, 2H), 7.94 (t, 1H), 9.16 (d, 1H). ^{13}C–{^{1}H} NMR: δ 21.4 (CH_3), 21.5 (CH_3), 47.9 (CH_2), 51.0 (CH_2), 56.6 (CH_2), 123.2–156.0 (aryl *C*).

4.12. Synthesis of (2-anp)Au{N(SO$_2$Tol)C$_2$H$_4$N-(SO$_2$Tol)} (*23*)

The complex (2-anp)$AuCl_2$ (**6**) (100 mg, 0.23 mmol) and bis(sulfonamide) (**16**) (100 mg, 0.28 mmol) were added to refluxing methanol (30 mL). While stirring, aqueous trimethylamine (2 mL, excess) was added and the solution was refluxed for a further 15 min. Water (50 mL) was added resulting in the formation of a pale yellow precipitate. After cooling, the solid was filtered and washed with water (2 × 10 mL) and diethyl ether (10 mL), and dried under vacuum to give 111 mg (54%) of yellow product. *Anal.* Calc. for $C_{27}H_{27}N_4O_4S_2Au$: C, 44.3; H, 3.7; N, 7.7. Found: C, 44.1; H, 3.8; N, 7.8%. M.p. 244–246 °C (decomp). IR: $\nu(SO_2$, asym) 1276 cm^{-1}, $\nu(SO_2$, sym) 1140 cm^{-1}; ν(NH) 3295 cm^{-1}. ESI-MS: cone voltage 20 V; *m/z* 755 (100%, $[M+Na]^+$), 1487 (20%, $[2M+Na]^+$), 1121 (20%, $[3M+2Na]^{2+}$). Cone voltage 60 V: *m/z* 755 (100%, $[M+Na]^+$), 1487 (25%, $[2M+Na]^+$). ^{1}H NMR: δ 2.44 (s, 6H), 3.29 (m, 2H), 3.62 (m, 2H), 6.69 (t, 1H), 6.76 (t, 1H), 7.03 (m, 2H), 7.22–7.35 (m, 4H), 7.45 (d, 1H), 7.63 (m, 3H), 7.42 (t, 1H), 7.90 (d, 2H), 8.73 (d, 1H), 8.83 (s, NH). Due to the insolubility of this compound in common deuterated NMR solvents [$(CD_3)_2SO$, D_2O, $CDCl_3$], satisfactory ^{13}C NMR spectra could not be acquired.

4.13. Synthesis of (tolpy)Au{N(SO$_2$Tol)C$_2$H$_4$N(SO$_2$Tol)} (*24*)

The complex (tolpy)$AuCl_2$ (**7**) (100 mg, 23 mmol) and bis(sulfonamide) (**16**) (100 mg, 0.23 mmol) were stirred in refluxing methanol (30 mL) and aqueous trimethylamine (2 mL, excess) was added, and the solution refluxed for 5 min. Water (50 mL) was added and the mixture cooled. The resulting pale yellow precipitate was filtered and washed with water (2 × 10 mL) and diethyl ether (10 mL) and dried under vacuum to give 135 mg (80%) of pale yellow microcrystals. *Anal.* Calc. for $C_{28}H_{28}N_3O_4S_2Au$: C, 46.0; H, 3.9; N, 5.8. Found: C, 45.7; H, 3.9; N, 5.8%. M.p. 186–188 °C (dec.). IR: $\nu(SO_2$, asym) 1303 cm^{-1}; $\nu(SO_2$, sym) 1138 cm^{-1}. ESI-MS: cone voltage 20 V; *m/z* 754 (100%, $[M+Na]^+$), 1485 (25%, $[2M+Na]^+$), 791 (20%, $[M+Me_3NH]^+$), 732 (15%, $[M+H]^+$). Cone voltage 60 V: *m/z* 754 (100%, $[M+Na]^+$), 732 (50%, $[M+H]^+$), 1485 (20%, $[2M+Na]^+$). ^{1}H NMR: δ 2.30 (s, 3H), 2.41 (s, 3H), 2.94 (s, 3H), 3.20 (d, 2H), 3.27 (d, 2H), 7.13–7.43 (m, 7H), 7.55 (s 1H), 7.77–7.86 (m, 5H), 8.03 (t, 1H), 9.45 (d, 1H). ^{13}C–{^{1}H} NMR: δ 21.56 (CH_3), 21.74 (2 × CH_3), 51.1 (CH_2), 57.7 (CH_2), 119.6–165.1 (aryl *C*).

4.14. Synthesis of (damp)Au{N(SO$_2$Tol)C$_2$H$_4$N(SO$_2$Tol)} (*25*)

The complex (damp)$AuCl_2$ (**8**) (75 mg, 0.19 mmol) and bis(sulfonamide) (**16**) (83 mg, 0.26 mmol) were mixed in refluxing methanol (30 mL), producing a pale yellow solution. Aqueous trimethylamine (2 mL, excess) was added and the mixture refluxed for 5 min. Water (75 mL) was added, resulting in the deposition of pale yellow microcrystals which were cooled, filtered and washed with water (2 × 10 mL) and diethyl ether (10 mL) and then dried under vacuum to give 115 mg (88%) of **25**. *Anal.* Calc. for $C_{25}H_{30}N_3O_4S_2Au$: C, 43.0; H, 4.3; N, 6.0. Found: C, 42.9; H, 4.3; N, 5.9%. M.p. 184–187 °C (dec.). IR: $\nu(SO_2$, asym) 1276 cm^{-1}; $\nu(SO_2$, sym) 1138 cm^{-1}. ESI-MS: cone voltage 20 V; *m/z* 719 (100%, $[M+Na]^+$), 1415 (35%, $[2M+Na]^+$). Cone voltage 60 V: *m/z* 719 (100%, $[M+Na]^+$), 1415 (30%, $[2M+Na]^+$). ^{1}H NMR: δ 2.40 (s, 6H), 3.13 (m, 2H), 3.18 (m, 2H), 3.40 (s, 6H), 4.34 (s, 2H), 6.97 (t, 1H), 7.12 (d, 1H), 7.17–7.25 (m, 5H), 7.38 (d, 1H), 7.65 (d, 2H), 7.73 (d, 2H). ^{13}C–{^{1}H} NMR: δ 21.5 (CH_3), 21.5 (CH_3), 52.0 (CH_2), 52.5 (NCH_3), 58.1 (CH_2), 77.1 (CH_2), 123.0–147.4 (aryl *C*).

4.15. Synthesis of (2-bp)Au{N(COMe)C$_6$H$_4$NH-(COMe)}Cl (*28*)

The complex (2-bp)$AuCl_2$ (**5**) (200 mg, 0.46 mmol), 1,2-diacetamidobenzene (**9**) (90 mg, 0.46 mmol) and silver(I) oxide (400 mg, excess) were added to dichloromethane (50 mL) and refluxed with stirring for 2 h. The solution was then filtered and the filtrate evaporated to dryness under reduced pressure. The resulting yellow crystals were dissolved in the minimum amount of dichloromethane and filtered through an alumina column. Slow addition of diethyl ether gave a pale yellow precipitate which was subsequently filtered and washed with diethyl ether (10 mL) and water (2 × 10 mL). ^{1}H NMR of the sample showed it to be a mixture of mainly **28** plus the metallacyclic complex **10**. X-ray quality crystals of **28** were grown by vapour diffusion of diethyl ether into a dichloromethane solution of the mixture at room temperature. M.p. 180–182 °C (dec.). *Anal.* Calc. for $C_{22}H_{21}N_3O_2AuCl$: C, 44.6; H, 3.5; N, 7.10. Found: C, 42.1; H, 3.4; N, 6.1%. *Anal.* Calc. for $C_{22}H_{21}N_3O_2AuCl \cdot 2H_2O$: C, 42.1; H, 3.4; N, 6.7%. IR: ν(N–H) 3303 cm^{-1}, ν(C=O) region 1693, 1611 cm^{-1}. ESI-MS: cone voltage 20 V; *m/z* 614

(100%, $[M+H]^+$), 556 (85%, $[M-HCl+Na]^+$), 578 (20%, $[M+Na]^+$).

4.16. Alternative synthesis of **28**

To the metallacyclic complex **10** (16.6 mg, 0.03 mmol) in dichloromethane (5 mL), sodium chloride (1.7 mg, 0.03 mmol) in methanol (2 mL) was added and stirred for 24 h. Benzoic acid (3.6 mg, 0.03 mmol) was then added, resulting immediately in the solution changing from dark to pale yellow. The solution was then filtered, reduced in volume and diethyl ether was added forming a precipitate that was identified as **28** by ^{1}H NMR.

4.17. X-ray crystal structure of (2-bp)Au{N(COMe)-C_6H_4N(COMe)} (**10**)

Yellow needles (m.p. 178 °C (dec.)) were obtained by vapour diffusion of diethyl ether into a dichloromethane solution of the crude product, at room temperature. Intensity data and unit cell dimensions were obtained on a Bruker SMART CCD diffractometer. Crystal size: $0.24 \times 0.10 \times 0.10$ mm, 23 180 total reflections, 3991 unique reflections (R_{int} 0.0378), range: $1.49° < \theta < 26.88°$, empirical absorption correction $T_{max,min}$: 0.518, 0.264. *Crystal data*: $C_{22}H_{20}AuN_3O_2$, M_r 555.38, tetragonal, space group $I4_1/a$. $a = 14.721(3)$ Å, $c = 35.971(1)$ Å, $V = 7795.4(3)$ Å^3, $D_{calc} = 1.893$ g cm^{-3}, $Z = 16$, $F(000) = 4288$, μ(Mo Kα) = 7.6 mm^{-1}.

The structure was solved using the direct methods option of SHELXS-97 [56]. The gold atom was initially located and then all other non-hydrogen atoms were located (SHELXL-97) by a series of difference maps. The full-matrix least-squares refinement was based upon F_o^2 with all non-hydrogen atoms anisotropic and hydrogen atoms in calculated positions; convergence gave $R_1 = 0.0214$ $[I \geqslant 2\sigma(I)]$, $wR_2 = 0.0427$ (all data), goodness-of-fit = 1.144. A final difference map showed no feature greater than 0.76 e Å^{-3}.

Due to potential *pseudo* symmetry in the molecule it was expected that the benzyl and pyridyl rings could show disorder. This was discounted since N(3) and C(31) were found to be in well-defined positions, based upon the following:

1. In the initial difference map the peak assigned to N(3) was 10 e Å^{-3} whereas for C(31) it was 8.8 e Å^{-3}.
2. When both positions were refined as carbon atoms, the U_{iso} values were 0.02 for the C(31) position and 0.07 for the N(3) (which are very similar to the other N atoms in the molecule when they were treated as carbon atoms).
3. The Au(1)–N(3) distance of 2.058 Å was significantly longer than the Au(1)–C(31) distance of 2.031 Å. The Au(1)–N(2) bond *trans* to C(31) was 2.089 Å, which is longer than the Au(1)–N(1) distance *trans* to N(3) of 2.022 Å. If the molecule had shown disorder presumably these distances would have been similar.
4. When the assignment of C(31) and N(3) was reversed the R factors increased from 0.0214 and 0.0427 to 0.0227 and 0.0466 for R_1 and wR_2, respectively.

4.18. X-ray crystal structure of (2-bp)Au{N(COMe)C_6H_4NH(COMe)}Cl (**28**)

Colourless prisms were obtained by vapour diffusion of diethyl ether into a dichloromethane solution containing the crude product at room temperature. M.p. 180–182 °C (dec.). Intensity data and unit cell dimensions were obtained on a Bruker SMART CCD diffractometer. Crystal size: $0.04 \times 0.32 \times 0.32$ mm, total reflections 11 252, unique reflections 4764 (R_{int} 0.0359), range: $1.73° < \theta < 27.13°$, empirical absorption correction $T_{max,min}$: 0.466, 0.389. *Crystal data*: $C_{22}H_{21}AuClN_3O_2$, M_r 591.83, triclinic, space group $P\bar{1}$. $a = 9.0334(1)$ Å, $b = 10.7766(1)$ Å, $c = 12.3915(1)$ Å, $\alpha = 88.846(1)°$, $\beta = 72.812(1)°$, $\gamma = 72.057(1)°$, $V = 1093.040(18)$ Å^3, $D_{calc} = 1.798$ g cm^{-3}, $Z = 2$, $F(000) = 572$, μ(Mo Kα) = 6.9 mm^{-1}.

The structure was solved by the direct methods option of SHELXS-97 [56], with the gold atom being located. All other non-hydrogen atoms were located by a series of difference maps. Full-matrix least-squares refinement (SHELXL-97) was based upon F_o^2 with all non-hydrogen atoms anisotropic and hydrogen atoms in calculated positions (with the exception of H(1) which was located by a difference map) converged with $R_1 = 0.0170$ $[I \geqslant 2\sigma(I)]$, $wR_2 = 0.0417$ (all data), goodness-of-fit = 1.072. A final difference map showed no feature greater than 0.99 e Å^{-3}. All calculations were carried out by the SHELX-97 suite of programs.

4.19. Biological assays

Details of the biological assays have been published previously [12].

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Appendix A. Supplementary information

Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, CCDC Nos. 602835 (**10**) and 602836 (**28**). Copies of this information can be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk). Supplementary data associated with

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References

[1] W. Henderson, Adv. Organomet. Chem. 54 (2006) 207.
[2] A selection of the significant number of reviews on this topic: S.P. Fricker (Ed.), Metal Compounds in Cancer Chemotherapy, Chapman & Hall, London, 1994.
[3] C.W. Schwietert, J.P. McCue, Coord. Chem. Rev. 184 (1999) 67.
[4] Z. Guo, P.J. Sadler, Angew. Chem., Int. Ed. 38 (1999) 1512.
[5] Z. Guo, P.J. Sadler, Adv. Inorg. Chem. 49 (2000) 183.
[6] E. Wong, C.M. Giandomenico, Chem. Rev. 99 (1999) 2451.
[7] T.W. Hambley, J. Chem. Soc., Dalton Trans. (2001) 2711.
[8] B. Brønnum, H.S. Johansen, L.H. Skibsted, Inorg. Chem. 31 (1992) 3023.
[9] J.J. Pesek, W.R. Mason, Inorg. Chem. 22 (1983) 2958.
[10] W. Henderson, B.K. Nicholson, S.J. Faville, D. Fan, J.D. Ranford, J. Organomet. Chem. 631 (2001) 41.
[11] M.B. Dinger, W. Henderson, J. Organomet. Chem. 560 (1998) 233.
[12] C.H.A. Goss, W. Henderson, A.L. Wilkins, C. Evans, J. Organomet. Chem. 679 (2003) 194.
[13] M.B. Dinger, W. Henderson, J. Organomet. Chem. 557 (1998) 231.
[14] J. Kuduk-Jaworska, Transition Met. Chem. 19 (1994) 296.
[15] C. Evans, W. Henderson, B.K. Nicholson, Inorg. Chim. Acta 314 (2001) 42.
[16] K. Okano, K. Murata, T. Ikariya, Tetrahedron Lett. 41 (2000) 9277.
[17] N. Hazari, P. Mountford, Acc. Chem. Res. 38 (2005) 839.
[18] C. Guo, J. Qiu, X. Zhang, D. Verdugo, M.L. Larter, R. Christie, P. Kenney, P.J. Walsh, Tetrahedron 53 (1997) 4145.
[19] E.J. Corey, M.A. Letavic, J. Am. Chem. Soc. 117 (1995) 9616.
[20] Y. Tamai, H. Yoshiwara, M. Someya, J. Fukumoto, S. Miyano, J. Chem. Soc., Chem. Commun. (1994) 2281.
[21] H. Ito, A. Sato, T. Taguchi, Tetrahedron Lett. 38 (1997) 4815.
[22] D.A. Evans, S.G. Nelson, J. Am. Chem. Soc. 119 (1997) 6452.
[23] S. Cai, R.R. Schrock, Inorg. Chem. 30 (1991) 4105.
[24] K. Kavallieratos, J.M. Rosenberg, J.C. Bryan, Inorg. Chem. 44 (2005) 2573.
[25] K. Kavallieratos, J.M. Rosenberg, W.-Z. Chen, T. Ren, J. Am. Chem. Soc. 127 (2005) 6514.
[26] Y. Fuchita, H. Ieda, Y. Tsunemune, J. Kinoshita-Nagaoka, H. Kawano, J. Chem. Soc., Dalton Trans. (1998) 791.
[27] J.N. Baxter, J. Cymerman-Craig, J.B. Willis, J. Chem. Soc. (1955) 585.
[28] Y.-P. Tu, A.G. Harrison, J. Am. Soc. Mass Spectrom. 9 (1998) 454.
[29] G.J. Van Berkel, F. Zhou, J. Am. Soc. Mass Spectrom. 7 (1996) 157.
[30] G.J. Van Berkel, J.M.E. Quirke, R.A. Tigani, A.S. Dilley, T.R. Covey, Anal. Chem. 70 (1998) 1544.
[31] G.S. Hall, R.H. Soderberg, Inorg. Chem. 7 (1968) 2300.
[32] P.-H. Cheng, H.-Y. Cheng, C.-C. Lin, S.-M. Peng, Inorg. Chim. Acta 169 (1990) 19.
[33] T.G. Appleton, H.C. Clark, L.E. Manzer, Coord. Chem. Rev. 10 (1973) 335.
[34] A. Shivanyuk, K. Rissanen, S.K. Körner, D.M. Rudkevich, J. Rebek Jr., Helv. Chim. Acta 83 (2000) 1778.
[35] M.A. Cinellu, A. Zucca, S. Stoccoro, G. Minghetti, M. Manassero, M. Sansoni, J. Chem. Soc., Dalton Trans. (1995) 2865.
[36] M.A. Dewey, A.M. Arif, J.A. Gladysz, J. Chem. Soc., Chem. Commun. (1991) 712.
[37] S.E. Denmark, S.P. O'Connor, S.R. Wilson, Angew. Chem., Int. Ed. Engl. 37 (1998) 1149.
[38] A.B. Corradi, E. Gozzoli, L. Menabue, M. Saladini, L.P. Battaglia, P. Sgarabotto, J. Chem. Soc., Dalton Trans. (1994) 273.
[39] W.-H. Leung, J.L.C. Chim, H. Hou, T.S.M. Hun, I.D. Williams, W.-T. Wong, Inorg. Chem. 36 (1997) 4432.
[40] W.-H. Leung, E.K.-F. Chow, Polyhedron 12 (1993) 1635.
[41] H.-Y. Cheng, P.-H. Cheng, C.-F. Lee, S.-M. Peng, Inorg. Chim. Acta 181 (1991) 145.
[42] J. Sánchez-Piso, J.A. García-Vázquez, J. Romero, M.L. Durán, A. Sousa-Pedrares, E. Labisbal, O.R. Nascimento, Inorg. Chim. Acta 328 (2002) 111.
[43] MERCURY, version 1.4.1, Cambridge Crystallographic Data Centre, 2005.
[44] H. Wang, G.R. Agnes, Anal. Chem. 71 (1999) 3785.
[45] H. Wang, G.R. Agnes, Anal. Chem. 71 (1999) 4166.
[46] P. Frohberg, G. Drutkowski, C. Wagner, Eur. J. Org. Chem. (2002) 1654.
[47] R.G. Pearson, Inorg. Chem. 12 (1973) 712.
[48] W. Henderson, B.K. Nicholson, A.G. Oliver, J. Organomet. Chem. 620 (2001) 182.
[49] D. Fan, C.-T. Yang, J.D. Ranford, J.J. Vittal, P.F. Lee, Dalton Trans. (2003) 3376.
[50] H.L. Riley, H.B. Baker, J. Chem. Soc. (1926) 2510.
[51] Y. Fuchita, H. Ieda, A. Kayama, J. Kinoshita-Nagaoka, H. Kawano, S. Kameda, M. Mikuriya, J. Chem. Soc., Dalton Trans. (1998) 4095.
[52] P.-A. Bonnardel, R.V. Parish, J. Organomet. Chem. 515 (1996) 221.
[53] J. Vicente, M.T. Chicote, M.D. Bermudez, J. Organomet. Chem. 268 (1984) 191.
[54] D.T. Hill, K. Burns, D.D. Titus, G.R. Girard, W.M. Reiff, L.M. Mascavage, Inorg. Chim. Acta 346 (2003) 1.
[55] L.J. Arnold, J. Chem. Educ. 69 (1992) 811.
[56] G.M. Sheldrick, SHELX Suite of Programs, University of Göttingen, Göttingen, Germany, 1997.