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Facile syntheses of four-membered aurathietane dioxide [Au–CHR-SO_2-CHR] ring systems, and the first isonitrile insertion reaction into a gold(III)–carbon bond

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Abstract

Cyclometallated gold(III) complexes derived from 2-benzylpyridine, 2-anilinopyridine [$AuCl_2(C_5H_4N\text{-}X\text{-}C_6H_4)$] [X = CH_2 (2-bp) or NH (2-anp)] or 2-*p*-tolylpyridine (tolpy) [$AuCl_2(C_5H_4NC_6H_3CH_3)$] react with the sulfones $RCH_2SO_2CH_2R$ (R = CN or COPh) in hot methanol with added trimethylamine base to give new aurathietanedioxide complexes containing the Au($CHRSO_2CHR$) four-membered ring system. The previously reported cyclo-aurated dimethylbenzylamine (MeO-damp) complex [Au{$CH(COPh)SO_2CH(COPh)$}-($Me_2NCH_2C_6H_3OMe$)] was also synthesised by this method, and found to exist as a mixture of major (*trans*) and minor (*cis*) isomers with respect to the orientation of the COPh substituents across the four-membered ring. The reaction of one complex with ^{t}BuNC in refluxing dichloromethane results in insertion of the isonitrile into the Au–C bond *trans* to the phenyl ring, followed by proton transfer. An X-ray crystal structure determination on this product was carried out.

Keywords: Gold; Metallacyclic complexes; Sulfones; Isonitrile; Insertion reaction

1. Introduction

Complexes containing the metallathietane-3,3-dioxide ring system **1** are rare in the literature. Platinum(II), palladium(II) and nickel(II) complexes have been known for some time [1,2], and insertion reactions with alkyl isonitriles have been studied for some of these complexes [3]. Recently, we have been carrying out studies into metallacyclic complexes of gold(III) [4,5]. Gold(III) is isoelectronic (d^8) with platinum(II), and is expected to show similar chemistry. Reaction of the gold(III) dichloride complex **2** with $PhCOCH_2SO_2CH_2COPh$ and Ag_2O in refluxing dichloromethane gave the first example of an aurathietane-3,3-dioxide complex **3** [6]. In this paper, we report a convenient synthetic route to a range of new aurathietane-3,3-dioxide complexes, which uses trimethylamine as the base. Using this methodology, products can be easily isolated in high yields and purities. We also report that a gold(III) complex, like its platinum(II) counterparts, undergoes isonitrile insertion into a metal–carbon bond.

2. Results and discussion

Reaction of the gold(III) complex **2** with an excess of diphenacylsulfone ($PhCOCH_2SO_2CH_2COPh$) and excess trimethylamine base in refluxing methanol gave the previously reported [6] aurathietane dioxide complex **3** as a white solid in good yield. The complex is only slightly soluble in the methanol solvent used, and is isolated in an analytically pure state directly from the reaction mixture. Previously, this complex has been synthesised by the use of silver(I) oxide as the base [6], but in our hands, this reagent often leads to the formation of products which are apparently contaminated with traces of gold-containing impurities and/or silver salts, as they are often more

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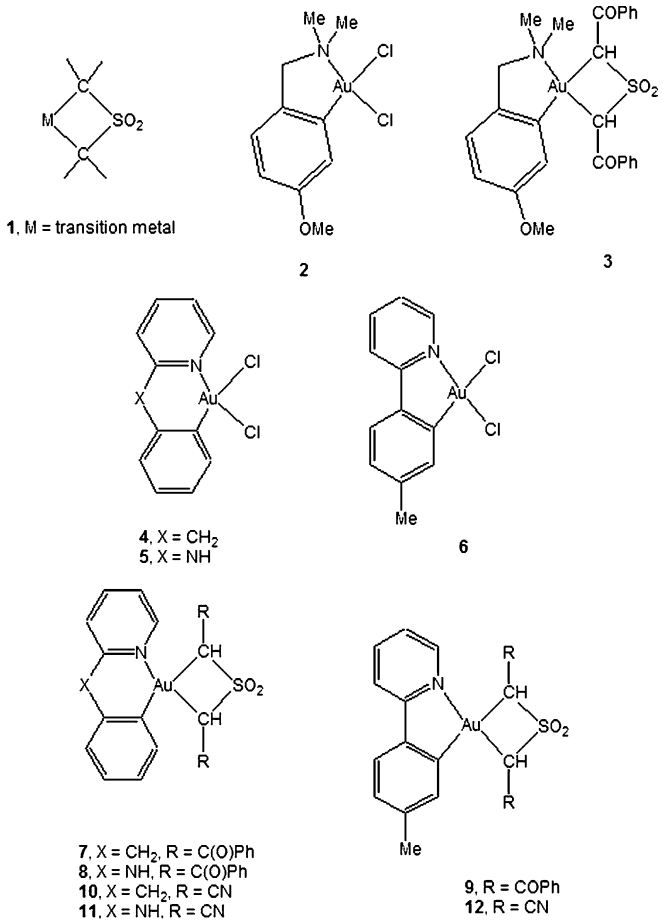
coloured, and light-sensitive, than the same product prepared by the use of a tertiary amine as the base. We therefore prefer the use of a tertiary amine base for the synthesis of such metallacycles, wherever it is successful.



In the same manner, reactions of the readily prepared gold(III) dichloride complexes **4**–**6** with an excess of $PhCOCH_2SO_2CH_2COPh$ and aqueous trimethylamine in refluxing methanol resulted in the formation of precipitates of the aurathietane-3,3-dioxide complexes **7**–**9**. Reactions of **4**–**6** with the cyano-substituted sulfone $NCCH_2SO_2CH_2CN$ and Me_3N gave the corresponding derivatives **10**–**12**. All complexes were isolated in good yields by filtration and washing with cold methanol, and were analytically pure without recourse to further purification. The colourless benzylpyridyl complex **7** is moderately soluble in dichloromethane, DMSO and pyridine, while the cyano derivative **10** is much less soluble; the tolylpyridyl complex **9** is only slightly soluble. The pale yellow anilinopyridyl complexes **8** and **11** are effectively insoluble in all common organic solvents tested.

The positive ion electrospray ionisation (ESI) mass spectrum of the benzoyl substituted aurathietane dioxide complexes **7**–**9** gave various adduct ions, with the $[M + H]^+$ ion always the most intense. Adduct ions with Na^+ and pyridinium (pyH^+) ions (formed from the pyridine used in an attempt to dissolve the complexes for ESI MS analysis) were also observed. The relative intensities of the $[M + Na]^+$ ions varied depending on the solvent quality and instrument cleanliness; for example, on some occasions the $[M + Na]^+$ ion for **7** dominated the spectrum whereas on other occasions it was a relatively low intensity ion. The cyano-substituted complex **10** showed rather different behaviour, with the $[M + pyH]^+$ ion (m/z 588) and $[M + Na]^+$ (m/z 531) the most intense peaks in the spectrum. Complex **11** had a very low solubility, even in pyridine, such that it was difficult to obtain strong ion signals, but the $[M + Na]^+$ ion was the most intense for this compound.

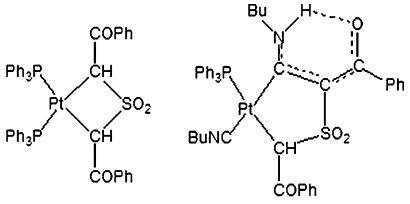
We have investigated the behaviour of one of these complexes (**7**) towards cone voltage-induced fragmentation, where it shows appreciable stability. Thus, the spectrum at a cone voltage of 200 V (the maximum for the instrument used) has no observed fragment ions. Gold(III) complexes with two ring systems typically show this extremely high stability [4].

3. NMR spectroscopic characterisation

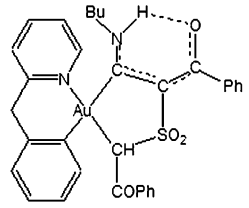
Detailed NMR spectroscopic characterisation of complex **3** has been previously reported [6]. The ^1H NMR spectrum of the sample of **3** reported herein (prepared by the tertiary amine method) showed a major product species with identical NMR spectroscopic properties to those previously reported, together with an additional set of signals with approximately 10% relative intensity. With minor differences, discussed below, the number and types of resonances is consistent with the presence of an isomer of this complex. A previous X-ray structure determination on **3** revealed it to have a *trans* disposition of COPh substituents across the four-membered ring [6] and this is also the isomer previously observed in platinum(II) analogues [1,2]. The minor component is therefore tentatively assigned as the *cis* isomer, with the COPh substituents in a *syn* arrangement with respect to the four-membered ring. Close inspection of the previously reported ^1H NMR data for the structurally characterised *trans* isomer also reveals a very small trace of the *cis* isomer in this sample [6]. The *cis* isomer of **3** shows ring CH protons at ca. δ 5.4 and 4.8, which are shielded relative to values of δ 5.68 and 5.11 in the *trans* isomer. Importantly, while the AuCH protons of the major *trans* isomer appear as singlets, those of the minor *cis* isomer appear as doublets. This arises as a result of $^4J(HH)$ coupling. The NCH_2 protons of the *cis* isomer also appear as an AB doublet of doublets, but the chemical shift difference between them is rather smaller than for the *trans* isomer. Inspection of the crystal structure of the *trans* complex **13** suggests that a *cis* isomer would have the two *cis* protons in a distorted 'W' configuration, in which long range coupling constants are well known to be favoured. Linking of two protons by alternative bond chains is also known to optimise long-range couplings [7]. Heating a 1,2-dichloroethane solution of **3** did not effect any change in the isomer ratio, suggesting that they are formed in the

synthesis process, and no interconversion occurs once formed.

The ^{1}H NMR spectra of the benzylpyridyl and tolylpyridyl complexes (**7** and **9**, respectively) also show the presence of major and minor isomers. For example, in complex **9**, Au–CH resonances for the major isomer (presumably *trans*) occur at δ 5.74 and 5.21, while those for the minor isomer occur at ca. δ 5.6 and 4.9. The CH_2 protons of both isomers of **7** are also inequivalent, and appear as two AB doublets showing geminal ^3J(HH) coupling of 14.7 Hz. The Au–CH protons are somewhat deshielded relative to the corresponding protons in the analogous platinum–triphenylphosphine complex **13** (δ 4.86), and this can be attributed to the higher oxidation state and electronegativity of gold(III) compared to platinum(II). Complex **12** was too insoluble to enable NMR spectroscopic characterisation to be carried out, and indeed even characterisation of this complex by ESI MS was not possible due to its low solubility.



13 14



15

4. Insertion reactions of aurathietane dioxide complexes

Previous studies on platinathietane dioxide complexes have demonstrated a facile reaction with alkylisonitriles, whereupon insertion of an RNC molecule into a Pt–C bond, followed by proton transfer, led to complexes of the type **14**, in which a phosphine ligand has been substituted by an RNC [3]. We thus wished to explore the analogous insertion chemistry with the corresponding gold(III) system. As far as we are aware, there has only been one report in the literature of isonitrile insertion into a gold–carbon bond, involving insertion of RNC (R = 2,6-dimethylphenyl) into the Au–C bond of the gold(I) complex $Ph_3PAuCH_2C(O)Ph$, giving $Ph_3PAuC(=NR)CH_2C(O)Ph$ [8].

Reaction of **7** with an excess of *t*-butylisonitrile in refluxing dichloromethane for 10 min gave (on precipitation with petroleum spirits) a pale yellow solid (**15**), for which the positive-ion ESI mass spectrum showed addition of a *t*-butylisonitrile moiety to the parent metallacycle. In contrast, no reaction was observed between **7** and either norbornene, CO, or CS_2 after standing in dichloromethane for 5 days at room temperature, when monitored by ESI mass spectrometry. In order to fully characterise the isonitrile insertion product, a single-crystal X-ray diffraction study was carried out.

The molecular structure of **15** is shown in Fig. 1, while selected bond lengths and angles are given in Table 1. Complex **7** has undergone an insertion reaction into the Au–C bond *trans* to the cycloaurated phenyl ring, to give the product **15**. This is the isomer that would be expected on the basis of the higher *trans* influence of the aryl group, which labilises the *trans* Au–C bond. The insertion of the isonitrile into the Au–C bond is followed by a transfer of H from C(2) to N(1) giving rise to a hydrogen-bonded six-membered ring which is planar to within ±0.02 Å. This feature is analogous to the behaviour observed previously in the platinum(II) complex **14** [3]. The sums of the bond angles around the carbon atoms C(2) and C(1) are 359.12° and 360.03°, respectively, consistent with planar sp^2 hybridisation at these carbons. However, the metallacyclic bond angle C(1)–C(2)–S(1) [112.10(19)°] is somewhat smaller than the other two bond angles. The hydrogen is strongly bonded to N(1) [N(1)–H(1) 0.79 Å] and weakly hydrogen-bonded to O(3) [O(3)···H(1) 1.88 Å]. The C(4)–O(3) [1.245(3)], C(2)–C(4) [1.426(4)], C(1)–C(2) [1.415(3)] and C(1)–N(1) [1.315(3)] bond distances (Å) in the hydrogen-bonded ring compare reasonably with corresponding values of 1.246(17), 1.446(19), 1.396(16) and 1.333(17) Å in the related platinum complex **14**, though the poorer precision in the platinum structure makes a detailed comparison difficult [3]. Shorter C(5)–O(4) [1.208(3) Å] and longer C(3)–C(5) [1.511(4) Å] bond distances in the CH(COPh) unit indicate the presence of substantial delocalisation of the C–O, C–C and C–N bonds in the hydrogen-bonded ring. The C(2)–S(1) and C(3)–S(1) bond distances

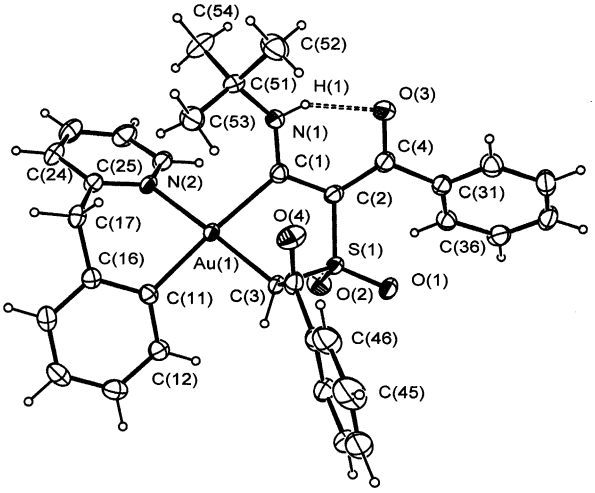


Fig. 1. X-ray molecular structure of the *t*-butylisonitrile insertion product **15**, showing the atom numbering scheme.

Table 1
Selected bond lengths (Å) and angles (°) for **15**

Au(1)–C(3)	2.017(2)
Au(1)–N(2)	2.086(2)
S(1)–O(2)	1.434(2)
S(1)–C(2)	1.732(3)
O(3)–C(4)	1.245(3)
N(1)–C(1)	1.315(3)
N(2)–C(21)	1.338(3)
C(1)–C(2)	1.415(3)
C(3)–C(5)	1.511(4)
C(5)–C(41)	1.486(4)
C(17)–C(25)	1.492(4)
C(51)–C(54)	1.518(4)
Au(1)–C(11)	2.068(3)
Au(1)–C(1)	2.104(3)
S(1)–O(1)	1.4354(19)
S(1)–C(3)	1.783(3)
O(4)–C(5)	1.208(3)
N(1)–C(51)	1.476(3)
N(2)–C(25)	1.344(3)
C(2)–C(4)	1.426(4)
C(4)–C(31)	1.492(4)
C(16)–C(17)	1.507(4)
C(51)–C(53)	1.507(4)
C(51)–C(52)	1.519(4)
C(3)–Au(1)–C(11)	92.79(10)
C(11)–Au(1)–N(2)	86.24(9)
C(11)–Au(1)–C(1)	174.78(9)
O(2)–S(1)–O(1)	115.94(12)
O(1)–S(1)–C(2)	111.42(12)
O(1)–S(1)–C(3)	107.85(12)
C(1)–N(1)–C(51)	133.3(2)
C(25)–N(2)–Au(1)	121.90(18)
N(1)–C(1)–Au(1)	126.63(19)
C(1)–C(2)–C(4)	124.5(2)
C(4)–C(2)–S(1)	122.52(19)
C(5)–C(3)–Au(1)	114.45(17)
O(3)–C(4)–C(2)	121.0(2)
C(2)–C(4)–C(31)	124.0(2)
O(4)–C(5)–C(3)	120.9(2)
C(12)–C(11)–Au(1)	124.36(19)
C(25)–C(17)–C(16)	111.0(2)
C(3)–Au(1)–N(2)	171.20(10)
C(3)–Au(1)–C(1)	82.71(10)
N(2)–Au(1)–C(1)	98.60(9)
O(2)–S(1)–C(2)	111.81(13)
O(2)–S(1)–C(3)	106.97(12)
C(2)–S(1)–C(3)	101.67(12)
C(21)–N(2)–Au(1)	117.77(17)
N(1)–C(1)–C(2)	117.8(2)
C(2)–C(1)–Au(1)	115.60(18)
C(1)–C(2)–S(1)	112.10(19)
C(5)–C(3)–S(1)	112.36(17)
S(1)–C(3)–Au(1)	104.45(12)
O(3)–C(4)–C(31)	115.1(2)
O(4)–C(5)–C(41)	121.1(3)
C(41)–C(5)–C(3)	117.9(2)
C(16)–C(11)–Au(1)	117.43(18)

[1.732(3) and 1.783(3) Å, respectively] have significantly different lengths, and compare with 1.73(2) and 1.75(2) Å in the four-membered aurathietanedioxide ring system in **3**.

The Au centre is square-planar to within ±0.1 Å, and the cyclometallated ligand is strongly folded so that the dihedral angle between the two rings is 65.3°; this is clearly seen in Fig. 2. The benzoyl group on C(3) has remained fully planar (to ±0.1 Å) while that on C(2) is twisted so that the aromatic plane is at 45.2° to the C(2)–C(4)–O(3)–C(31) plane, precluding conjugation with this group. The five-membered ring Au(1)–C(1)–C(2)–S(1)–C(3) is in an envelope conformation with the Au atom at the apex.

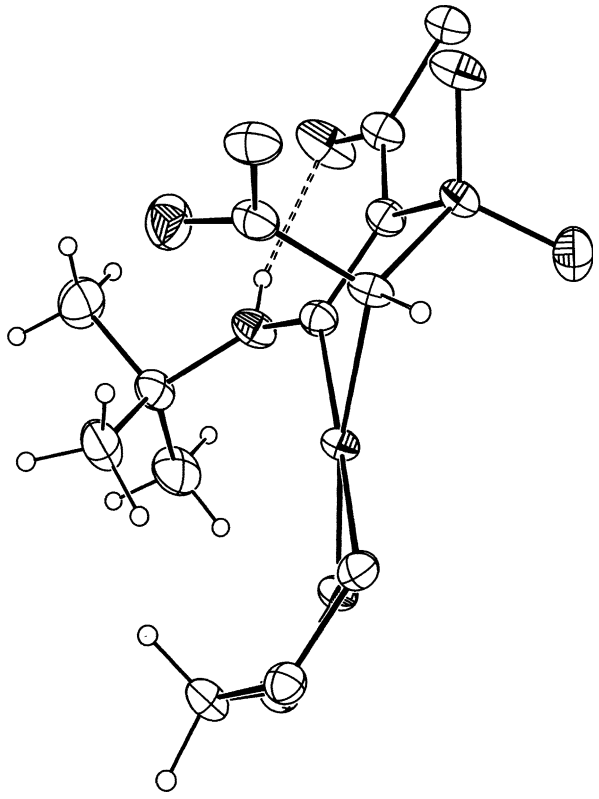


Fig. 2. Side view of the central part of complex **15**, showing the puckering of cyclo-aurated gold-benzylpyridyl ligand, and the five-membered ring formed by isonitrile insertion.

5. Biological activity

In recent years there has been increasing interest in the biological activity (particularly anticancer activity) of gold(III) compounds [9], which are isoelectronic with the well-known platinum(II) counterparts. Because gold(III) is substantially more labile than platinum(II) [10], it could be postulated that the presence of fairly strongly binding ligands to the gold(III) may be required for an active compound. We have therefore tested a selection of the aurathietanedioxide complexes for their in vitro anticancer activity against P388 murine leukemia cells; data are given in Table 2. The isonitrile insertion product **15**, together with the damp derivative **3** both showed good activity, most likely due to the good solubility of these compounds in the solvent mixture used. The solvent itself, a 2:1 mixture of methanol and dichloromethane, showed little activity in the assay. The remaining compounds showed either moderately low or no activity, and no clear trends among the

Table 2
Antitumour (P388 murine leukemia) assay data for a selection of gold complexes

Complex	IC50 (ng mL^{-1})	IC50 (μM)
3	487	0.7
7	1310	2.0
8	4091	6.1
9	>62,500	>93.9
10	30,456	60.1
12	1477	2.9
15	<487	<0.7
Solvent	>12,500	

[a] The concentration of sample in ng mL^{-1} and μM required to reduce the cell growth of the P388 leukemia cell line by 50%.

different types of complexes could be ascertained. It is known from previous studies that damp gold(III) derivatives typically show good anticancer activity and the present study is in concordance with this observation. However, it is noteworthy that the isonitrile insertion product **15** also shows promising anticancer activity, and this suggests that more detailed studies into this type of derivative could prove fruitful.

6. Experimental

General experimental procedures were as reported previously in publications from this laboratory [5,6]. Reactions were carried out in LR grade methanol which was used as supplied, without regard for the exclusion of air or moisture. Electrospray ionisation (ESI) mass spectra were recorded on a VG Platform II instrument, using methanol as the solvent and mobile phase. Samples of the gold complexes were suspended in 2 drops of pyridine, diluted with methanol (total solids content ca. 0.1 mg mL^{-1}) and centrifuged prior to analysis.

The compounds (2-bp)$AuCl_2$ (**4**) [11], (2-anp)$AuCl_2$ (**5**) [12], (tolpy)$AuCl_2$ (**6**) [13], (MeOdamp)$AuCl_2$ (**2**) [14] and $PhCOCH_2SO_2CH_2COPh$ [15] were prepared according to minor modifications of the literature procedures. The sulfone $NCCH_2SO_2CH_2CN$ (Lancaster Synthesis) and aqueous trimethylamine solution (BDH, 25–30%) were used as supplied. The isonitrile ^{t}BuNC was prepared by the literature method [16].

6.1. Synthesis of (MeO-damp)Au{CH(COPh)-SO_2CH(COPh)} (3)

A suspension of complex **2** (200 mg, 0.463 mmol) and $PhCOCH_2SO_2CH_2COPh$ (160 mg, 0.529 mmol) in ethanol (30 mL) with aqueous Me_3N (2 mL) was refluxed for 20 min giving a white suspension and very pale yellow supernatant. After cooling to room temperature the solid was filtered, washed with cold ethanol (5 mL) and dried under vacuum to give **3** as a white solid (180 mg, 59%). Found: C, 47.4; H, 3.9; N, 2.3. $C_{26}H_{26}NAuO_5S$ requires C, 47.2; H, 4.0; N, 2.1%. ESI MS (positive-ion, cone voltage 50 V, MeOH), $[M + H]^+$ (*m/z* 662, 100%), $[M + Na]^+$ (*m/z* 684, 37%), $[M + K]^+$ (*m/z* 700, 68%), $[2M + Na]^+$ (*m/z* 1346, 19%), $[2M + K]^+$ (*m/z* 1361, 17%).

6.2. Synthesis of (2-bp)Au{CH(COPh)SO_2CH(COPh)} (7)

A suspension of complex **4** (250 mg, 0.574 mmol) and $PhCOCH_2SO_2CH_2COPh$ (250 mg, 0.827 mmol) in methanol (30 mL) with aqueous Me_3N (2 mL) was refluxed for 1 h giving a white suspension and very pale yellow supernatant. After cooling to room temperature the solid was filtered, washed with cold methanol (5 mL) and diethyl ether (10 mL) and dried under vacuum to give **7** (330 mg, 86%). M.p. 230–232 °C. Found: C, 50.1; H, 3.3; N, 2.1. $C_{28}H_{22}NAuO_4S$ requires C, 50.5; H, 3.3; N, 2.1%. ESI MS (positive-ion, cone voltage 50 V, MeOH), $[M + H]^+$ (*m/z* 666, 100%), $[M + Na]^+$ (*m/z* 688, 22%), $[M + pyH]^+$ (*m/z* 745, 5%), $[2M + Na]^+$ (*m/z* 1354, 10%). ^{1}H NMR, δ 8.08–6.89 (m, aromatic H), 5.74 (s, Au–CH), 5.34 (s, Au–CH), 4.32 [d, CH_2, ^3J(HH) 14.7] and 4.13 [d, CH_2, ^3J(HH) 14.7].

6.3. Synthesis of (2-anp)Au{CH(COPh)SO_2CH(COPh)} (8)

A suspension of complex **5** (260 mg, 0.596 mmol) and $PhCOCH_2SO_2CH_2COPh$ (230 mg, 0.761 mmol) in methanol (30 mL) with aqueous Me_3N (2.5 mL) was refluxed for 1 h giving a pale yellow suspension. After cooling to room temperature the solid was filtered, washed with cold methanol (5 mL) and diethyl ether (10 mL) and dried under vacuum to give **8** (389 mg, 98%) as a pale yellow solid. M.p. 226–228 °C. Found: C, 48.2; H, 3.1; N, 4.2. $C_{27}H_{21}N_2AuO_4S$ requires C, 48.7; H, 3.2; N, 4.2%. ESI MS (positive-ion, cone voltage 50 V, MeOH), $[M + H]^+$ (*m/z* 667, 100%), $[M + Na]^+$ (*m/z* 689, 22%), $[M + pyH]^+$ (*m/z* 746, 16%), $[2M + Na]^+$ (*m/z* 1355, 5%). ^{1}H NMR, δ 8.25–6.17 (m, aromatic H), 5.51 (s, Au–CH), 4.95 (s, Au–CH).

6.4. Synthesis of (tolpy)Au{CH(COPh)SO_2CH(COPh)} (9)

A suspension of complex **6** (135 mg, 0.310 mmol) and $PhCOCH_2SO_2CH_2COPh$ (140 mg, 0.463 mmol) in methanol (20 mL) with aqueous Me_3N (2 mL) was refluxed for 1 h giving a white suspension. After cooling to room temperature the solid was filtered, washed with cold methanol (5 mL) and diethyl ether (10 mL) and dried under vacuum to give **9** (170 mg, 82%) as a white solid. M.p. decomp. >240 °C. Found: C, 50.5; H, 3.3; N, 2.1. $C_{27}H_{22}NAuO_4S$ requires C, 49.6; H, 3.4; N, 2.1%. ESI MS (positive-ion, cone voltage 50 V, MeOH), $[M + H]^+$ (*m/z* 666, 100%), $[M + Na]^+$ (*m/z* 688, 48%), $[M + pyH]^+$ (*m/z* 745, 5%), $[2M + Na]^+$ (*m/z* 1353, 18%). ^{1}H NMR, δ 8.27–6.89 (m,

aromatic H), 5.78 (s, Au–CH), 5.24 (s, Au–CH), 2.11 (s, CH_3). Minor (*cis*) isomer, δ 5.6, 4.9 (Au–CH), 2.2 (CH_3).

6.5. Synthesis of (2-bp)Au{CH(CN)SO$_2$CH(CN)} (**10**)

A suspension of complex **4** (300 mg, 0.689 mmol) and $NCCH_2SO_2CH_2CN$ (118 mg, 0.819 mmol) in methanol (30 mL) with aqueous Me_3N (2 mL) was refluxed for 40 min to give a white suspension. The mixture was cooled to room temperature, water (10 mL) added, and the product filtered, washed with water (20 mL) and diethyl ether (20 mL) and dried to give 290 mg (83%) of **10** as a white powder. The complex is poorly soluble in chloroform and DMSO. M.p. decomp. >250 °C. Found: C, 37.4; H, 2.1; N, 8.2. $C_{16}H_{12}N_3AuO_2S$ requires C, 37.9; H, 2.4; N, 8.3%. ESI MS (positive-ion, cone voltage 50 V, MeOH), $[M + Na]^+$ (*m*/*z* 531, 97%), $[M + pyH]^+$ (*m*/*z* 588, 100%), $[2M + Na]^+$ (*m*/*z* 1039, 38%), $[2M + pyH]^+$ (*m*/*z* 1096, 10%), $[3M + Na]^+$ (*m*/*z* 1547, 20%), $[3M + pyH]^+$ (*m*/*z* 1604, 5%), $[4M + Na]^+$ (*m*/*z* 2055, 5%).

6.6. Synthesis of (2-anp)Au{CH(CN)SO$_2$CH(CN)} (**11**)

A suspension of complex **5** (400 mg, 0.916 mmol) and $NCCH_2SO_2CH_2CN$ (139 mg, 0.965 mmol) in methanol (30 mL) with aqueous Me_3N (2 mL) was refluxed for 40 min to give a pale yellow suspension. The mixture was cooled to room temperature, and the product filtered, washed with water (20 mL) and diethyl ether (20 mL) and dried to give 385 mg (83%) of pale yellow **11**. The complex is poorly soluble in chloroform and DMSO. M.p. decomp. >50 °C. Found: C, 35.6; H, 2.1; N, 11.0. $C_{15}H_{11}N_4AuO_2S$ requires C, 35.4; H, 2.2; N, 11.0%. ESI MS (positive-ion, cone voltage 50 V, MeOH), $[M + Na]^+$ (*m*/*z* 530, 100%), $[M + K]^+$ (*m*/*z* 546, 40%), $[M + pyH]^+$ (*m*/*z* 587, 35%). The complex was too insoluble for NMR characterisation.

6.7. Synthesis of (tolpy)Au{CH(CN)SO$_2$CH(CN)} (**12**)

A suspension of complex **6** (300 mg, 0.689 mmol) and $NCCH_2SO_2CH_2CN$ (118 mg, 0.919 mmol) in methanol (30 mL) with aqueous Me_3N (2 mL) was refluxed for 20 min to give a white suspension. The mixture was cooled to room temperature, water (10 mL) added, and the product filtered, washed with water (20 mL) and diethyl ether (20 mL) and dried under vacuum to give 330 mg (94%) of **12** as a white powder. M.p. >280 °C. Found: C, 37.7; H, 2.2; N, 8.2. $C_{16}H_{12}N_3AuSO_2$ requires C, 37.9; H, 2.4; N, 8.3%.

6.8. Synthesis of isonitrile insertion complex (**15**)

Complex **7** (100 mg, 0.150 mmol) was dissolved in dichloromethane (20 mL) and *t*-butylisonitrile (3 drops, excess) added. The solution was refluxed for 10 min, and petroleum spirits (70 mL) added to precipitate the product. The solid was filtered off, washed with petroleum spirits (10 mL), and dried under vacuum to give **15** as a pale yellow solid (74 mg, 66%). ESI MS (positive-ion, cone voltage 20 V), $[M + H]^+$ (*m*/*z* 749, 100%). ^{1}H NMR, δ 12.93 (s, NH), 8.72–6.89 (m, aromatic H), 5.66 (s, Au–CH), 4.26 [d, CH_2, ^2J(HH) 14.6], 4.01 [d, CH_2, ^2J(HH) 14.6] and 1.20 (s, ^{t}Bu). Recrystallisation by vapour diffusion of diethyl ether into a dichloromethane solution at room temperature gave colourless crystals of the product. M.p. partial melting 170–190 °C, melting 190–192 °C (decomp.). Found: C, 51.1; H, 4.1; N, 3.6. $C_{33}H_{31}N_2AuSO_4$ requires C, 52.9; H, 4.2; N, 3.7.

6.9. Attempted insertion reactions

Three separate portions of the complex **7** (60 mg) were dissolved in distilled dichloromethane (5 mL), and to the solutions were added norbornene (0.1 g), CS_2 (2 drops), or saturated with CO and sealed. The reaction mixtures were allowed to stand for 5 days, and 1 drop of the reaction mixture diluted with 1 mL of methanol and analysed by ESI MS. In no case was any reaction observed.

6.10. X-ray crystal structure determination on **15**

Colourless crystals were obtained by vapour diffusion of diethyl ether into a dichloromethane solution of the complex at room temperature. Unit cell parameters and intensity data were collected using a Siemens SMART CCD diffractometer, using standard collection procedures, with monochromatic Mo Kα X-rays (0.71073 Å). Corrections for absorption and other effects were carried out with SADABS [17]. All other calculations used the SHELX-97 programs

Table 3
Crystal data, collection and refinement details for the molecular structure determination on **15**

Empirical formula	$C_{33}H_{31}AuN_2O_4S$
Formula weight	748.62
Temperature (K)	165(2)
Crystal system, space group	Monoclinic, $P2_1/c$
Unit cell dimensions	
a (Å)	11.369(3)
b (Å)	15.668(4)
c (Å)	15.643(4)
β (°)	95.410(3)
Volume (Å^3)	2774.0(12)
Z, calculated density (mg m^{-3})	4, 1.793
Absorption coefficient (mm^{-1})	5.422
F(000)	1480
Crystal size	0.77 × 0.35 × 0.25 mm
Theta range for data collection	1.80–26.59°
Reflections collected/unique [R_{int}]	35,206/5730 [0.0280]
Completeness to $\theta = 26.59°$	98.6%
Maximum and minimum transmission	0.3443 and 0.1028
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	5730/0/377
Final *R* indices [$I > 2\sigma(I)$]	$R_1 = 0.0170$, $wR_2 = 0.0406$
R indices (all data)	$R_1 = 0.0198$, $wR_2 = 0.0415$
Largest difference in peak and hole (e Å^{-3})	1.924 and −0.679

[18]. The structure was solved by direct methods and developed and refined routinely. Hydrogen atoms were placed in calculated positions except for H(1) which was located from a penultimate difference map and refined. Crystal data, collection and refinement details are summarised in Table 3.

The assignment of N(2) to the position *trans* to C(3) was unambiguously indicated by the refinement; interchanging N(2) and C(11) gave a poorer *R* factor and distorted temperature factors.

7. Anticancer screening

Assays were carried out by the Marine Chemistry Group, Department of Chemistry, Canterbury University, New Zealand. Samples were dissolved or suspended in 2:1 methanol–dichloromethane prior to testing; some compounds such as **3** and **15** were freely soluble whereas the others had limited solubility in this (and other) solvents. For these sparingly soluble compounds the observed activity therefore represents a minimum activity, and the true activity is likely to be somewhat higher. Assays were carried out by determining, by means of a twofold dilution series, the concentration of sample in ng mL^{-1} required to reduce the cell growth of the P388 leukemia cell line (ATCC CCL 46) by 50%. The sample of interest was incubated for 72 h with the P388 Murine Leukemia cells. IC_{50} values were determined by measurement of the absorbance values when the yellow dye MTT tetrazolium is reduced by healthy cells to the purple dye MTT formazan.

8. Supplementary information

Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 276066. Copies of this information can be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44 1223 336033; e-mail deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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References

[1] K.W. Chiu, J. Fawcett, W. Henderson, R.D.W. Kemmitt, D.R. Russell, J. Chem. Soc., Dalton Trans. (1987) 733.
[2] W. Henderson, R.D.W. Kemmitt, L.J.S. Prouse, D.R. Russell, J. Chem. Soc., Dalton Trans. (1989) 259.
[3] W. Henderson, R.D.W. Kemmitt, L.J.S. Prouse, D.R. Russell, J. Chem. Soc., Dalton Trans. (1990) 781.
[4] M.B. Dinger, W. Henderson, J. Organomet. Chem. 560 (1998) 233; W. Henderson, B.K. Nicholson, S.J. Faville, D. Fan, J.D. Ranford, J. Organomet. Chem. 631 (2001) 41.
[5] M.B. Dinger, W. Henderson, J. Organomet. Chem. 557 (1998) 231; M.B. Dinger, W. Henderson, B.K. Nicholson, W.T. Robinson, J. Organomet. Chem. 560 (1998) 169;
M.B. Dinger, W. Henderson, J. Organomet. Chem. 577 (1999) 219; W. Henderson, B.K. Nicholson, A.G. Oliver, J. Organomet. Chem. 620 (2001) 182;
C.H.A. Goss, W. Henderson, A.L. Wilkins, C. Evans, J. Organomet. Chem. 679 (2003) 194.
[6] M.B. Dinger, W. Henderson, J. Organomet. Chem. 547 (1997) 243.
[7] W. Kemp, NMR in Chemistry: A Multinuclear Introduction, Macmillan Education Ltd., UK, 1986.
[8] M. Murakami, M. Inouye, M. Suginome, Y. Ito, Bull. Chem. Soc. Jpn. 61 (1988) 3649.
[9] See for example S.P. Fricker, Metal Based Drugs 6 (1999) 291; R.V. Parish, Metal Based Drugs 6 (1999) 271;
E.R.T. Tiekink, Crit. Rev. Oncol/Hematol. 42 (2002) 225.
[10] J.J. Peseck, W.R. Mason, Inorg. Chem. 22 (1983) 2958.
[11] M.A. Cinellu, A. Zucca, S. Stoccoro, G. Minghetti, M. Manassero, M. Sansoni, J. Chem. Soc., Dalton Trans. (1995) 2865.
[12] Y. Fuchita, H. Ieda, A. Kayama, J. Kinoshita-Nagaoka, H. Kawano, S. Kameda, M. Mikuriya, J. Chem. Soc., Dalton Trans. (1998) 4095.
[13] W. Henderson, B.K. Nicholson, S.J. Faville, D. Fan, J.D. Ranford, J. Organomet. Chem. 631 (2001) 41.
[14] P.A. Bonnardel, R.V. Parish, R.G. Pritchard, J. Chem. Soc., Dalton Trans. (1996) 3185.
[15] E. Fromm, J. Flaschen, Liebigs Ann. Chem. 394 (1912) 310.
[16] S.R. Sandler, W. Karo, Organic Functional Group Preparations III, second ed., Academic Pres Inc., San Diego, 1989.
[17] R.H. Blessing, Acta Cryst. A 51 (1995) 33.
[18] G.M. Sheldrick, SHELX-97, Program for the Solution and Refinement of Crystal Structures, University of Göttingen, Germany, 1997.