# Gold(I) Complexes of 1-Diphenylarsino-2-diphenylphosphinoethane (dadpe): Solution Studies, *X*-Ray Crystal Structures, and Cytotoxicity of $[(AuCl)_2dadpe]\cdot 0.5dma$ (dma = dimethylacetamide) and $[Au(dadpe)_2]Cl\cdot 2H_2O$†

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The complexes $[(AuCl)_2dadpe]$ (**1**) and $[Au(dadpe)_2]Cl$ (**2**) where dadpe is $Ph_2PCH_2CH_2AsPh_2$ have been prepared and characterized by n.m.r. spectroscopy ($^{31}P$-{$^1H$}, $^1H$, and $^{13}C$-{$^1H$}) and by *X*-ray crystallography. $^{31}P$-{$^1H$} N.m.r. spectroscopy shows that complex (**1**) is converted into (**2**) on titration with dadpe in $CDCl_3$ at a Au : dadpe ratio of 1 : 2. At higher ratios there is exchange between complex (**2**) and the excess of ligand. Such rapid ligand exchange is also indicated by the $^1H$ n.m.r. data. Crystals of (**1**) are monoclinic, space group *Cc* with $a$ = 19.385(3), $b$ = 11.011(2), $c$ = 27.260(1) Å, β = 96.40(1)°, and $Z$ = 8. The ligand co-ordinates two AuCl chains with intermolecular Au · · · Au contact of 3.21 Å. The P and As atoms are disordered and there appears to be conformational flexibility about the ethane bridge. Crystals of (**2**) are monoclinic, space group $P2_1/n$, $a$ = 10.192(1), $b$ = 21.797(7), $c$ = 21.683(10) Å, β = 94.14(3)°, and $Z$ = 4 and contain bis chelated $Au^I$ in a distorted-tetrahedral environment; again the P and As atoms are disordered. Complexes (**1**) and (**2**) are significantly more toxic towards L1210, WS, and V.79 cells *in vitro* than is the free ligand, dadpe, and are comparable to $[Au(dppe)_2]Cl$ in their toxicity towards WS and V.79 cell lines.

The bidentate phosphine ligand, dppe, $Ph_2PCH_2CH_2PPh_2$, has cytotoxic and antitumour activity[1,2] and its potency is increased when co-ordinated to $Au^I$. Compounds of the type $[(AuL)_2dppe]$ (L = thiosugar, selenosugar, or Cl) are active against i.p. P388 leukaemia and a range of other tumours *in vivo*.[3] In plasma, the complex $[(AuL)_2dppe]$ (L = thioglucose) containing linear two-co-ordinate $Au^I$ is readily converted into a tetrahedral 1:2 Au:dppe complex.[4] This complex, $[Au(dppe)_2]Cl$, has significant cytotoxic potency *in vitro*, and activity against a wide spectrum of tumours *in vivo*.[5]

The mechanism of action of this four-co-ordinate diphosphine complex differs from that of cisplatin *cis*-$[PtCl_2(NH_3)_2]$ in that the major lesion responsible for cytotoxicity appears to involve DNA–protein cross-links.[6] Further evidence for this difference is provided by the synergistic action of cisplatin and $[Au(dppe)_2]Cl$ against P388 leukaemia and by the retention of activity of $[Au(dppe)_2]Cl$ against a platinum-resistant cell line.[5]

Related dppe complexes of $Ag^I$ (ref. 7) and $Cu^I$ (ref. 8) also show activity and since, like $[Au(dppe)_2]Cl$, these are kinetically labile, it appears that the metal is acting as a delivery system for the reactive dppe ligand. The lipophilic cation $[Au(dppe)_2]^+$ is also a potent uncoupler of oxidative phosphorylation in mitochondria and can increase the permeability of the inner mitochondrial membrane towards protons and other metal cations.[9] Such reactions may be responsible for some of the undesirable side-effects (*e.g.* cardiotoxicity)[10] observed with this complex.

In order to provide a deeper understanding of the mechanism of action of this novel class of antineoplastic agent, we have now studied gold(I) complexes of the related ligand dadpe, $Ph_2PCH_2CH_2AsPh_2$. Arsines are weaker donors than phosphines[11] and it is of interest to determine whether tetrahedral species can still be formed and to examine their lability in solution.

## Results and Discussion

*Preparation of the Complexes* $[(AuCl)_2dadpe]\cdot 0.5dma$ *and* $[Au(dadpe)_2]Cl\cdot 2H_2O$.—The complex $[(AuCl)_2dadpe]$ (**1**) was prepared by a method similar to that described previously for $[(AuCl)_2dppe]$;[12] namely by dropwise addition of 0.5 mol equivalent of an acetone solution of dadpe (1-diphenylarsino-2-diphenylphosphinoethane) to an aqueous acetone solution of $Na[AuCl_4]\cdot 0.5H_2O$, which had been reduced to $Au^I$ *in situ* by addition of thiodiglycol (2,2′-thiodiethanol). The resultant white precipitate was recrystallized from $CHCl_3$; white crystals suitable for *X*-ray analysis were grown from dimethylacetamide (dma). Complex (**1**) has been previously prepared from $HAuCl_4$ and thiodiglycol[2] and has also been made[13] *in situ* in $CH_2Cl_2$ from 2 equivalents of $[AuCl(SC_4H_8)]$ and 1 equivalent of ligand.

Preparations of the four-co-ordinate complex $[Au(dadpe)_2]Cl\cdot 2H_2O$ was carried out in a similar manner to that previously reported[14] for $[Au(dppe)_2]Cl$, *i.e.* by dropwise addition of 0.5 mol equivalent of an ice-cooled gold(I) solution (prepared *in situ* from $Na[AuCl_4]\cdot 0.5H_2O$ and thiodiglycol in aqueous acetone) to an acetone solution of dadpe. A white solid was isolated from the reaction which was recrystallized from aqueous acetone as white crystals suitable for *X*-ray analysis.

*Characterization of* $[(AuCl)_2dadpe]\cdot 0.5dma$ (**1**) *and* $[Au(dadpe)_2]Cl\cdot 2H_2O$ (**2**).—*X-Ray crystallography.* Complex

† μ-(1-Diphenylarsino-2-diphenylphosphinoethane)-bis[chlorogold(I)]–dimethylacetamide(1/0.5) and bis(1-diphenylarsino-2-diphenylphosphinoethane)gold(I) chloride dihydrate.

*Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1990, Issue 1, pp. xix—xxii.

**Table 1.** Final positional parameters ($\times 10^4$) for the non-hydrogen atoms of molecule 1 of $[(AuCl)_2dadpe]\cdot 0.5dma$ (**1**) with estimated standard deviations (e.s.d.s) in parentheses

| Atom | *x* | *y* | *z* | Atom | *x* | *y* | *z* |
|---|---|---|---|---|---|---|---|
| Au(1) | 10 000(0) | 1 803(1) | 10 000(0) | C(13B) | 10 280(20) | −3 418(25) | 10 115(10) |
| Au(4) | 9 519(1) | 378(1) | 7 820(0) | C(14B) | 9 982(17) | −3 289(26) | 10 526(9) |
| [As,P(1)] | 10 603(2) | 183(3) | 9 752(1) | C(15B) | 9 909(16) | −2 206(27) | 10 729(10) |
| [As,P(4)] | 10 641(2) | 816(3) | 8 122(1) | C(16B) | 10 099(14) | −1 162(24) | 10 497(10) |
| Cl(1) | 9 463(4) | 3 408(7) | 10 291(4) | C(41A) | 10 997(12) | 2 217(21) | 7 828(9) |
| Cl(4) | 8 408(4) | 47(9) | 7 538(3) | C(42A) | 11 472(15) | 3 003(24) | 8 070(8) |
| C(1E) | 10 527(11) | −56(22) | 9 076(9) | C(43A) | 11 748(16) | 3 930(27) | 7 861(11) |
| C(4E) | 10 763(12) | 1 023(23) | 8 812(9) | C(44A) | 11 541(15) | 4 130(23) | 7 553(11) |
| C(11A) | 11 559(12) | 246(22) | 9 925(10) | C(45A) | 11 105(18) | 3 369(31) | 7 110(11) |
| C(12A) | 11 842(13) | 1 081(25) | 10 256(9) | C(46A) | 10 769(17) | 2 436(27) | 7 361(31) |
| C(13A) | 12 963(14) | 1 095(32) | 10 444(11) | C(41B) | 11 302(13) | −406(20) | 8 033(8) |
| C(14A) | 12 963(14) | 247(34) | 10 216(13) | C(42B) | 11 983(13) | −296(27) | 8 229(11) |
| C(15A) | 12 719(14) | −550(27) | 9 890(12) | C(43B) | 12 440(17) | −1 234(39) | 8 161(14) |
| C(16A) | 12 041(14) | −557(27) | 9 737(10) | C(44B) | 12 218(21) | −2 253(28) | 7 882(13) |
| C(11B) | 10 381(15) | −1 252(24) | 10 049(10) | C(45B) | 11 572(18) | −2 386(29) | 7 679(7) |
| C(12B) | 10 448(20) | −2 418(25) | 9 857(13) | C(46B) | 11 134(15) | −1 417(25) | 7 781(8) |

Solvent molecule positional parameters ($\times 10^3$)

| Atom | *x* | *y* | *z* | Atom | *x* | *y* | *z* |
|---|---|---|---|---|---|---|---|
| O(1) | 402(2) | −99(3) | 650(1) | C(2) | 390(2) | −161(4) | 725(1) |
| C(1) | 418(2) | −72(3) | 693(1) | C(3) | 465(2) | 110(4) | 669(2) |
| N(1) | 445(2) | 24(3) | 704(1) | C(4) | 458(2) | 42(4) | 756(2) |

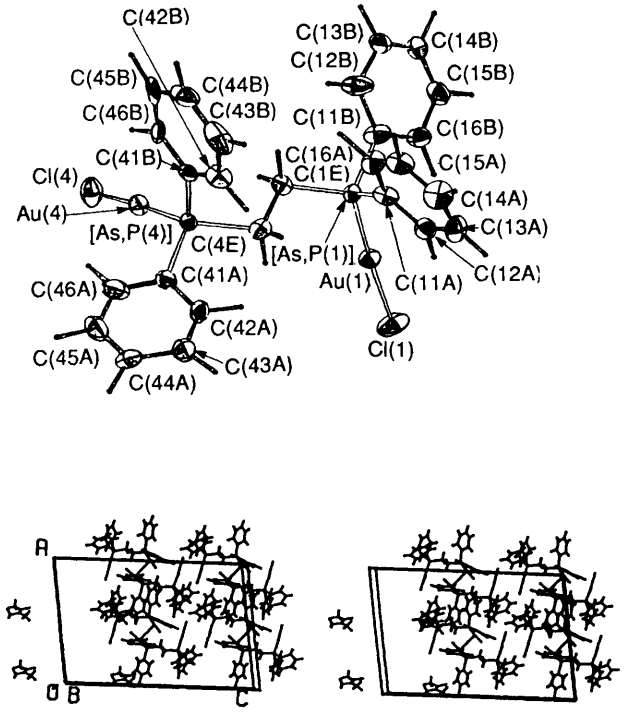



**Figure 1.** (*a*) *X*-Ray structure of $[(AuCl)_2dadpe]\cdot 0.5dma$ (**1**) showing the numbering scheme. (*b*) Crystal packing diagram for (**1**)

(**1**) was crystallized as a dimethylacetamide solvate. By *X*-ray crystallography it was shown to have two virtually linear gold(I) units bridged by a dadpe ligand with minor deviations of the As, P–Au–Cl angles from the theoretical 180° (175—177°) (Tables 1 and 2). Figure 1 shows the molecular geometry with thermal ellipsoids [15] and the crystal packings. The P and As atoms in the ligand were found to be disordered and the structure was solved by using averaged atomic scattering factors for As and P in each of the four co-ordination sites. The thermal parameter for the Au atom is large ($B_{eq}$ = 3.80 Å$^2$) for a heavy atom and this seems to be due to the disordering. There are two independent molecules, 1 and 2, in the crystal structure which are related by a pseudo-inversion centre at (0.935, 0.0, 0.705). The Au$^I$ · · · Au$^I$ bond distance between molecules 1 and 2 is 3.21 Å which is outside the typical range of Au–Au bond distances reported (2.76—3.04 Å),[16] but is less than the van der Waals contacts of 3.4 Å;[17] thus there is a significant interaction between the two metal centres. Short Au · · · Au contacts, both inter- and intramolecular, are quite common in gold(I) chemistry, *e.g.* in the bridged phosphine complex *cis*-$[(AuCl)_2dppen]$ [dppen is *cis*-1,2-bis(diphenylphosphino)ethene][18] there are intramolecular Au · · · Au contacts of 3.05(1) Å. Intermolecular contacts in $[(AuCl)_2dppp]$ [dppp is 1,3-bis(diphenylphosphino)propane] of 3.316 Å between adjacent molecules related by the *b* glide[19] mean that the structure may be considered as being composed of polymeric chains. For *trans*-$[(AuCl)_2dppen]$ it has been proposed[20] that the overall structure, which contains Au · · · Au intermolecular contacts of 3.043(1) Å, is also stabilized by the formation of polymeric chains. The dppe analogue of (**1**), $[(AuCl)_2dppe]$, was found to crystallize in two pseudo-polymorphs,[21,22] I and II, and in both of these there are short intermolecular Au · · · Au contacts of the order of 3.2 Å, giving a dimeric structure as in (**1**).

The dadpe moiety adopts a slightly different conformation from that of the dppe analogue[22] as may be seen by a comparison of the torsion angles about the $C_b$–E–Au–Cl bonds in both complexes, Table 3 ($C_b$ corresponds to the methylene group of the ligand; E is As,P in the case of the dadpe complex, and P in the dppe case). The difference in the torsion angles between molecules 1 and 2 in the crystal structure of (**1**) suggests that the complex can adopt different conformations about the Au–(As,P) bond, *i.e.* it is flexible, the flexibility arising from free rotation about the ethane bridge. Similar non-rigidity is observed in the case of the dppe analogue,[22] the two pseudo-polymorphs differing most in their relative conformation about the Au–P bond, Table 3.

Since the crystal possesses a pseudo-inversion centre it was not possible to determine the absolute configuration. Even the solvent molecule which does not possess an inversion centre

**Table 2.** Selected bond lengths (Å) and angles (°) for non-hydrogen atoms of $[(AuCl)_2dadpe]$ (**1**) with e.s.d.s in parentheses

| Molecule 1 | | Molecule 2 | |
|---|---|---|---|
| Au(1)–[As,P(1)] | 2.276(4) | Au(2)–[As,P(2)] | 2.252(4) |
| Au(1)–Cl(1) | 2.240(10) | Au(2)–Cl(2) | 2.300(10) |
| Au(4)–[As,P(4)] | 2.290(4) | Au(3)–[As,P(3)] | 2.227(3) |
| Au(4)–Cl(4) | 2.235(9) | Au(3)–Cl(3) | 2.316(9) |
| [As,P(1)]–C(1E) | 1.85(2) | [As,P(2)]–C(2E) | 1.92(2) |
| [As,P(1)]–C(11A) | 1.86(3) | [As,P(2)]–C(21A) | 1.89(3) |
| [As,P(1)]–C(11B) | 1.85(3) | [As,P(2)]–C(21B) | 1.90(3) |
| [As,P(4)]–C(4E) | 1.88(3) | [As,P(3)]–C(3E) | 1.86(2) |
| [As,P(4)]–C(41A) | 1.90(2) | [As,P(3)]–C(31A) | 1.88(3) |
| [As,P(4)]–C(41B) | 1.89(3) | [As,P(3)]–C(31B) | 1.84(3) |

| Molecule 1 | |
|---|---|
| [As,P(1)]–Au(1)–Cl(1) | 175.9(3) |
| [As,P(4)]–Au(4)–Cl(4) | 177.0(3) |
| Au(1)–[As,P(1)]–C(1E) | 114.9(8) |
| Au(4)–[As,P(4)]–C(4E) | 113.1(8) |
| Au(1)–[As,P(1)]–C(11A) | 115.2(8) |
| Au(1)–[As,P(1)]–C(11B) | 112.8(9) |
| Au(4)–[As,P(4)]–C(41A) | 113.2(7) |
| Au(4)–[As,P(4)]–C(41B) | 115.7(8) |

| Molecule 2 | |
|---|---|
| [As,P(2)]–Au(2)–Cl(2) | 175.1(3) |
| [As,P(3)]–Au(3)–Cl(3) | 175.4(2) |
| Au(2)–[As,P(2)]–C(2E) | 116.5(8) |
| Au(3)–[As,P(3)]–C(3E) | 110.6(7) |
| Au(2)–[As,P(2)]–C(21A) | 112.4(9) |
| Au(2)–[As,P(2)]–C(21B) | 110.3(8) |
| Au(3)–[As,P(3)]–C(31A) | 116.2(9) |
| Au(3)–[As,P(3)]–C(31B) | 108(1) |

**Table 3.** Selected torsion angles (°) for (*a*) $[(AuCl)_2dadpe]$ (**1**) and (*b*) $[(AuCl)_2dppe]$ *

| (*a*) Molecule 1 | |
|---|---|
| Cl(1)–Au(1)–[As,P(1)]–C(1E) | −151 |
| Cl(4)–Au(4)–[As,P(4)]–C(4E) | 65 |
| **Molecule 2** | |
| Cl(2)–Au(2)–[As,P(2)]–C(2E) | 151 |
| Cl(3)–Au(3)–[As,P(3)]–C(3E) | 32 |

| (*b*) | Polymorph I | Polymorph II |
|---|---|---|
| Cl(1)–Au(1)–P(1)–C(1) | −18.6 | 50.7 |
| Cl(2)–Au(2)–P(2)–C(2) | 179.6 | 177.2 |

* From ref. 22.

places the centre of the molecule [*i.e.* the midpoint of the C(1)–N(1) bond] close to the quasi-inversion centre. The phenyl rings which are related by this pseudo-symmetry are nearly parallel with the dihedral angles between the average ring planes being 2, 4, and 8°; however one set of rings, C(1*n*A) and C(1*n*B) (*n* = 1—6) (Figure 1) form a dihedral angle of 23°.

Detailed discussion of the bond lengths and angles in complex (**1**) is not possible due to the disordered nature of the P,As atoms, however it can be seen that the co-ordination about each Au atom is approximately linear with (As,P)–Au–Cl angles of 175.9(3) and 177.0(3)° for molecule 1 and 175.1(3) and 175.4(2)° in molecule 2, Table 2. These are comparable to the values observed for the analogous $[(AuCl)_2dppe]$ complex[21] [173.1(2) and 175.4(2)°]. The Au–As,P bond lengths in the two molecules of (**1**) lie in the range 2.227(3)—2.290(4) Å, Table 2,

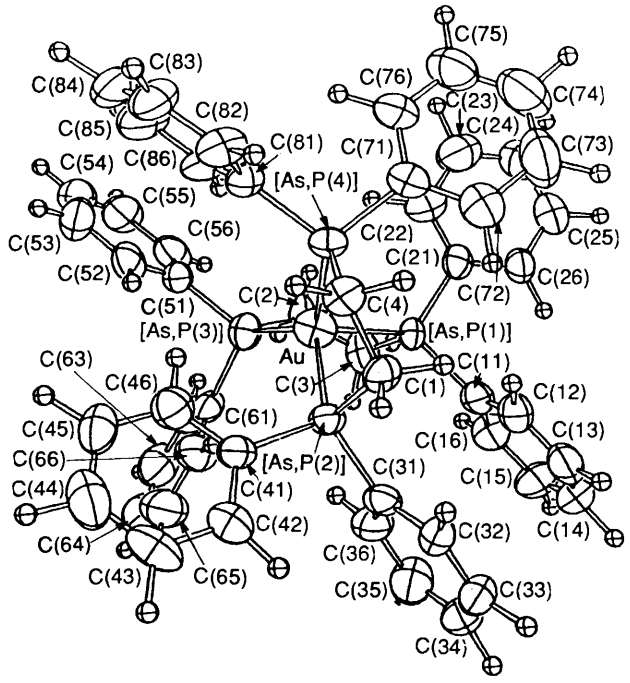



**Figure 2.** *X*-Ray structure of $[Au(dadpe)_2]Cl{\cdot}2H_2O$ (**2**) showing the numbering scheme

which, apart from the Au(3)–As,P(3) distance of 2.227(3) Å, are longer than for the dppe analogue (Au–P range 2.224(3)—2.242(6) Å)[21,22] reflecting the influence of the large As atom. In general Au–P bonds are shorter than Au–As bonds for similar compounds, *e.g.* $[AuCl(PPh_3)]$ (Au–P 2.243 Å)[23] and $[AuBr(AsPh_3)]$ [Au–As 2.342(5) Å],[24] and in the case of the heteronuclear gold cluster $[Au_2Ru_4(\mu_3\text{-}H)(\mu\text{-}H)(\mu\text{-}Ph_2AsCH_2PPh_2)(CO)_{12}]$[13] which contains the ligand $Ph_2AsCH_2PPh_2$ bridging two Au cluster atoms the Au–P and Au–As bond lengths are 2.309(5) and 2.421(4) Å respectively.

In complex (**2**), $[Au(dadpe)_2]Cl{\cdot}2H_2O$, the gold(I) atom is essentially tetrahedral co-ordinating to two P and two As atoms, although only the averaged ligand atoms could be seen in this crystal structure. Figure 2 shows the structure with the thermal ellipsoids[15] and the numbering scheme used, while the positional parameters and selected bond distances and angles are presented in Tables 4 and 5 respectively. The two chelate-forming planes defined by Au–[As,P(1)]–[As,P(3)] and Au–[As,P(2)]–[As,P(4)] are almost perpendicular to each other (89°) as expected for a regular tetrahedron. However, due to chelate formation by the dadpe ligand the 'bite' angles within the rings are reduced {[As,P(1)]–Au–[As,P(3)] 88.09(6); [As,P(2)]–Au–[As,P(4)] 86.82(6)°}. A similar type of co-ordination has been noted previously for the related $[Au(dppe)_2]^+$ cation[12,25] which has 'bite' angles of 87.1(1) and 86.4(1)° for P(1)–Au–P(3) and P(2)–Au–P(4) respectively.[25] In complex (**2**) one of the chelate rings {defined by Au–[As,P(1)]–C(3)–C(2)–[As,P(3)], Figure 2} has a skewboat conformation with the deviation of the carbon atoms from the plane being −0.40 and 0.33 Å. The other chelate ring {defined by Au–[As,P(2)]–C(1)–C(4)–[As,P(4)], Figure 2}, is in the form of an envelope with C(1) displaced by 0.72 Å from the plane and C(4) almost on the plane. As can be seen from Figure 2 three of the four sets of two phenyl rings belonging to different chelate rings are almost parallel to each other with dihedral angles of 10—22° between them. Only one set forms a nearly perpendicular arrangement; that of one of the phenyl groups attached to [As,P(2)] and one of the two attached to [As,P(3)]. In this complex the Au–As,P bond lengths lie in the range

**Table 4.** Final positional parameters ( $\times 10^4$) for the non-hydrogen atoms of $[Au(dadpe)_2]Cl\cdot 2H_2O$ (**2**) with e.s.d.s in parentheses

| Atom | *x* | *y* | *z* | Atom | *x* | *y* | *z* |
|---|---|---|---|---|---|---|---|
| Au(1) | 1 363(0) | 1 882(0) | 2 360(0) | C(42) | −1 921(13) | 193(6) | 2 141(6) |
| [As,P(1)] | 3 620(1) | 1 840(1) | 2 876(1) | C(43) | −3 002(15) | 53(7) | 1 734(7) |
| [As,P(2)] | 89(2) | 1 001(1) | 2 653(1) | C(44) | −3 532(14) | 474(8) | 1 324(7) |
| [As,P(3)] | 2 335(2) | 2 011(1) | 1 404(1) | C(45) | −2 974(12) | 1 038(6) | 1 294(5) |
| [As,P(4)] | −174(1) | 2 508(1) | 2 892(1) | C(46) | −1 889(12) | 1 180(6) | 1 695(5) |
| Cl(1) | 911(5) | 1 203(2) | 4 953(2) | C(51) | 1 882(11) | 2 619(5) | 834(5) |
| C(1) | −766(10) | 1 297(5) | 3 353(4) | C(52) | 567(12) | 2 720(6) | 680(5) |
| C(2) | 4 139(10) | 2 187(6) | 1 634(5) | C(53) | 179(15) | 3 187(7) | 265(6) |
| C(3) | 4 657(9) | 1 785(6) | 2 155(5) | C(54) | 1 087(17) | 3 525(7) | 1(6) |
| C(4) | −1 359(9) | 1 934(5) | 3 221(5) | C(55) | 2 393(17) | 3 420(6) | 122(6) |
| C(11) | 4 223(10) | 1 171(5) | 3 356(5) | C(56) | 2 822(13) | 2 963(6) | 544(5) |
| C(12) | 3 434(10) | 968(6) | 3 817(5) | C(61) | 2 426(11) | 1 324(5) | 893(5) |
| C(13) | 3 781(13) | 463(6) | 4 172(5) | C(62) | 3 292(13) | 1 303(6) | 427(6) |
| C(14) | 4 936(13) | 152(6) | 4 082(6) | C(63) | 3 264(16) | 806(7) | 32(6) |
| C(15) | 5 712(13) | 336(6) | 3 628(7) | C(64) | 2 360(20) | 330(7) | 80(6) |
| C(16) | 5 375(11) | 846(6) | 3 276(6) | C(65) | 1 534(19) | 356(7) | 554(7) |
| C(21) | 4 349(10) | 2 533(5) | 3 296(4) | C(66) | 1 559(15) | 856(6) | 947(6) |
| C(22) | 3 892(11) | 3 105(6) | 3 120(6) | C(71) | 478(11) | 2 991(5) | 3 551(5) |
| C(23) | 4 420(15) | 3 621(6) | 3 431(7) | C(72) | 1 056(17) | 2 712(7) | 4 077(7) |
| C(24) | 5 396(15) | 3 549(7) | 2 907(7) | C(73) | 1 644(19) | 3 097(9) | 4 542(7) |
| C(25) | 5 830(13) | 2 990(7) | 4 083(6) | C(74) | 1 705(18) | 3 707(7) | 4 468(7) |
| C(26) | 5 341(11) | 2 476(5) | 3 769(5) | C(75) | 1 144(16) | 3 978(6) | 3 951(7) |
| C(31) | 876(10) | 271(5) | 2 924(5) | C(76) | 528(13) | 3 624(6) | 3 504(6) |
| C(32) | 520(10) | −55(5) | 3 444(5) | C(81) | −1 278(10) | 3 053(5) | 2 419(4) |
| C(33) | 1 189(12) | −575(5) | 3 627(5) | C(82) | −2 566(11) | 3 193(5) | 2 544(5) |
| C(34) | 2 214(14) | −787(6) | 3 301(6) | C(83) | −3 293(12) | 3 594(6) | 2 170(6) |
| C(35) | 2 584(13) | −476(7) | 2 798(6) | C(84) | −2 772(14) | 3 863(6) | 1 665(6) |
| C(36) | 1 937(12) | 65(5) | 2 600(6) | C(85) | −1 498(16) | 3 745(7) | 1 560(6) |
| C(41) | −1 370(10) | 766(5) | 2 117(5) | C(86) | −762(12) | 3 334(5) | 1 930(6) |
| Solvent molecules | | | | | | | |
| W(1) | 1 513(11) | −163(6) | 5 441(5) | W(2) | 1 675(14) | 2 363(6) | 5 830(6) |

**Table 5.** Selected bond lengths (Å) and angles (°) for non-hydrogen atoms of $[Au(dadpe)_2]Cl$ (**2**) with e.s.d.s in parentheses

| | | | |
|---|---|---|---|
| Au–[As,P(1)] | 2.485(2) | Au–[As,P(2)] | 2.430(2) |
| Au–[As,P(3)] | 2.377(2) | Au–[As,P(4)] | 2.431(2) |
| [As,P(1)]–C(3) | 1.954(14) | [As,P(2)]–C(1) | 1.917(11) |
| [As,P(1)]–C(11) | 1.868(11) | [As,P(2)]–C(31) | 1.858(11) |
| [As,P(1)]–C(21) | 1.889(11) | [As,P(2)]–C(41) | 1.890(11) |
| [As,P(3)]–C(2) | 1.908(14) | [As,P(4)]–C(4) | 1.913(11) |
| [As,P(3)]–C(51) | 1.848(11) | [As,P(4)]–C(71) | 1.860(11) |
| [As,P(3)]–C(61) | 1.870(12) | [As,P(4)]–C(81) | 1.887(10) |

| | |
|---|---|
| [As,P(1)]–Au–[As,P(2)] | 110.32(6) |
| [As,P(1)]–Au–[As,P(3)] | 88.09(6) |
| [As,P(1)]–Au–[As,P(4)] | 114.49(6) |
| Au–[As,P(1)]–C(3) | 100.29(41) |
| Au–[As,P(1)]–C(11) | 122.45(35) |
| Au–[As,P(1)]–C(21) | 120.43(35) |
| [As,P(2)]–Au–[As,P(3)] | 125.89(6) |
| [As,P(2)]–Au–[As,P(4)] | 86.82(6) |
| [As,P(3)]–Au–[As,P(4)] | 132.11(6) |
| Au–[As,P(2)]–C(1) | 102.89(32) |
| Au–[As,P(2)]–C(31) | 122.21(34) |
| Au–[As,P(2)]–3(41) | 177.68(33) |

* O(W1)–H(W11)···Cl(1), O(W1)···Cl(1) 3.20, H(W11)···Cl(1) 2.30 Å; O(W2)–H(W22)···Cl(1), O(W2)···Cl(1) 3.22, H(W22)···Cl(1) 2.46 Å; O(W1)–H(W11)···Cl(1) 145.8(6), O(W2)–H(W22)···Cl(1) 135.6(8)°, [where O(W1) is the oxygen of water molecule 1, H(W11) the hydrogen of water molecule 1, *etc.*].

2.377(2)—2.485(2) Å, Table 5, *i.e.* apart from the Au–[As,P(3)] bond distance [2.377(2) Å] they are all significantly longer than in the $[Au(dppe)_2]^+$ complex (Au–P range 2.389—2.416 Å)[12] as was the case for the bridged complexes. Two molecules of water are present as solvent of crystallization and they are involved in hydrogen bonding with the $Cl^-$ ion with bond distances of 3.20 and 3.22 Å for O(1)···Cl(1) and O(2)···Cl(1) respectively.* These are comparable to those observed in the structure of the analogous dppe complex, $[Au(dppe)_2]Cl\cdot 2H_2O$, where values of 3.17 and 3.19 Å for Cl···O(1) and Cl···O(2) have been reported.[25]

Similar disorder of the P and As atoms was observed in the case of bis[diethyl(*o*-diethylphosphinophenyl)arsine] metal iodides where the metal is $Cu^I$ or $Au^I$ in which the P and As atoms could not be differentiated owing to an apparently random distribution.[26] The C atoms were not located in these structures and the M–As,P distances are not reported. No such disorder was found in the *X*-ray-determined structure of the cluster $[Au_2Ru_4(\mu_3\text{-}H)(\mu\text{-}H)(\mu\text{-}Ph_2AsCH_2PPh_2)(CO)_{12}]$.[13]

(*b*) $^{31}P\text{-}\{^1H\}$ *N.m.r. spectroscopy.* The 81-MHz $^{31}P\text{-}\{^1H\}$ n.m.r. spectrum of $[(AuCl)_2dadpe]$ (**1**) in $CDCl_3$ showed a peak at δ 32.3 p.p.m., *i.e.* a co-ordination chemical shift $[\delta_{P(complex)} - \delta_{P(ligand)}$; c.c.s.] of 44.95 p.p.m. This is comparable to that of the analogous diphenylphosphinoethane complex $[(AuCl)_2dppe]$ (c.c.s. 44.2 p.p.m.) in the same solvent,[14] indicating that in solution both compounds have similar structures.

The 81-MHz $^{31}P\text{-}\{^1H\}$ n.m.r. spectrum of $[Au(dadpe)_2]Cl$, (**2**), in $CDCl_3$ showed one major resonance at δ 26.18 p.p.m.; c.c.s. 37.9 p.p.m., comparable to that of $[Au(dppe)_2]Cl$ (c.c.s. 35.5 p.p.m.).[14] However, in contrast to $[Au(dppe)_2]Cl$, the resonance is broad ($\Delta\nu_{\frac{1}{2}}$ *ca.* 194 Hz) and spectra of (**2**) show a marked dependence on solvent and concentration, Table 6,

**Table 6.** $^{31}P$-{$^1H$} N.m.r. data for complex (**2**)

| Solvent | Concentration (mmol dm$^{-3}$) | δ (p.p.m.) | $\Delta\nu_{\frac{1}{2}}$ (Hz) |
|---|---|---|---|
| $CDCl_3$ | 18.0 | 24.6 | 155.5 |
| | 4.9* | 26.2 | 194.0 |
| | 2.0 | 29.8 | 77.8 |
| EtOH–$D_2O$ | 18.0 | 31.4 | 116.7 |
| | 6.0 | 31.4 | 68.1 |
| | 2.0 | 31.4 | 68.1 |
| $(CD_3)_2SO$ | 18.0 | 32.0 | 58.0 |
| | 6.0 | 32.0 | 145.8 |
| | 2.0 | 32.0 | 282.0 |
| $(CD_3)_2CO$ | 6.0 | 26.1 | 34.0 |
| | 2.0 | 22.7 | 68.0 |

* After 24 h in solution two resonances were present in the spectrum at δ 28.0 and 33.9 p.p.m. ($\Delta\nu_{\frac{1}{2}}$ 105.3 and 14.2 Hz respectively).

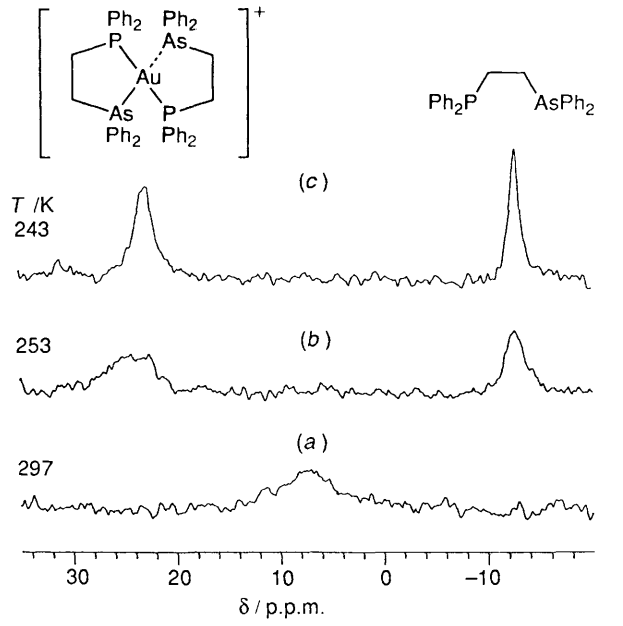



**Figure 3.** 81-MHz $^{31}P$-{$^1H$} n.m.r. spectra of [Au(dadpe)$_2$]Cl·2H$_2$O (**2**) with 2 mol equivalents added dadpe in $CDCl_3$ at various temperatures

indicating that there are dissociation/exchange processes occurring in solution. In the solvents $CDCl_3$ and EtOH–$D_2O$ the resonance is broader at higher concentrations of (**2**) suggesting inter- rather than intra-molecular broadening mechanisms, perhaps involving dimeric bridged species such as [(dadpe)Au(μ-dadpe)$_2$Au(dadpe)], and in $CDCl_3$ may involve ring opening and $Cl^-$ association with $Au^I$. The effect was reversed in $(CD_3)_2SO$ and $(CD_3)_2CO$, the resonance being broader at lower rather than higher concentrations. In these solvents the mechanism of broadening may involve dissociation of the cation–anion pair and possible solvent co-ordination.

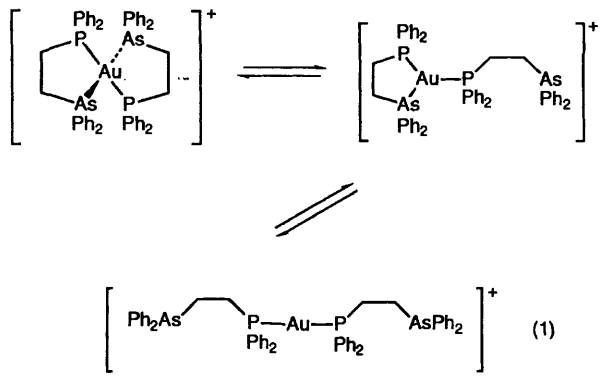
The spectrum of complex (**2**) in $CDCl_3$ was also affected by temperature. At 0 °C the spectrum of a 4.9 mmol dm$^{-3}$ solution showed a shift downfield from δ 26.2 to 31.3 p.p.m. and a broadening of the peak from $\Delta\nu_{\frac{1}{2}}$ = 194 to 331 Hz. On cooling further to −20 °C the peak shifted slightly further downfield to δ 32.65 p.p.m. and sharpened considerably ($\Delta\nu_{\frac{1}{2}}$ = 97 Hz). Equilibria of the type (1) may be involved, the rate of ring opening being slowed down by cooling.

Further evidence for the lability of [Au(dadpe)$_2$]Cl in solution comes from the observation that the addition of 2 mol equivalent of dadpe to a $CDCl_3$ solution of [Au(dadpe)$_2$]Cl

**Table 7.** 400-MHz Proton n.m.r. data for dadpe and complexes (**1**) and (**2**) in $CDCl_3$

| Compound | δ | Assignment |
|---|---|---|
| dadpe | 7.32[a] | $C_6H_5$ |
| | 2.16[a] | $CH_2$–As,P |
| | 2.06[a] | $CH_2$–As,P |
| [(AuCl)$_2$dadpe] | 7.43—7.63[b] | $C_6H_5$ |
| | 2.63[c] | $CH_2$–P,As |
| [Au(dadpe)$_2$]Cl | 7.22—7.53[b] | $C_6H_5$ |
| | 2.59[d] | $CH_2$–As[d] |
| | 2.27[e] | $CH_2$–P[e] |

[a] Multiplet. [b] Series of multiplets over the range quoted. [c] Symmetric multiplet. [d] Quartet, tentative assignment. [e] Quintet, tentative assignment.




caused an upfield shift [from δ 26.2 (c.c.s. 37.9) to 6.4 p.p.m.] with a broadening of the resonance from $\Delta\nu_{\frac{1}{2}}$ = 194 to 331 Hz and an increase in the signal-to-noise ratio. No signal due to free ligand is present, Figure 3(*a*). However, when this solution was cooled to −20 °C two resonances were apparent at δ 24.2 and −12.7 p.p.m. and at −30 °C these sharpened significantly from $\Delta\nu_{\frac{1}{2}}$ = 447 to 175 and 175 to 97 Hz respectively and the downfield signal shifted slightly upfield (from δ 24.2 to 22.7 p.p.m.), Figure 3(*b*) and (*c*). These two signals may be assigned to [Au(dadpe)$_2$]Cl and dadpe respectively. Thus at lower temperatures the rate of exchange between dadpe and [Au(dadpe)$_2$]Cl is slowed considerably. This behaviour is in contrast to that observed with dppe in $CDCl_3$ where tetrahedral [Au(dppe)$_2$]Cl is in relatively slow exchange with free dppe even at ambient temperature and separate signals are observed for each species.[14]

In the titration of dadpe with [(AuCl)$_2$dadpe] in $CDCl_3$ a resonance assignable to (**2**) was observed when a Au:L ratio of 1:2 was reached. At a Au:L ratio of 1:4 only one broad resonance was observed in the room-temperature $^{31}P$-{$^1H$} n.m.r. spectrum; this became two resonances at −30 °C as expected (see above). In contrast, in the titration of dppe with [(AuCl)$_2$dppe] in the same solvent the tetrahedral complex [Au(dppe)$_2$]Cl was formed even at low Au:L ratios,[14] indicating that the tetrahedral dppe complex is more stable.

The addition of dppe to a $CDCl_3$ solution of [Au(dadpe)$_2$]Cl resulted in the formation of the tetrahedral dppe complex, [Au(dppe)$_2$]Cl, even when only 0.5 mol equivalent dppe was added. This suggests that not only are Au–As bonds more kinetically labile than Au–P bonds in these chelate complexes, but also that they are less thermodynamically stable. In accordance with this, the $^{31}P$-{$^1H$} n.m.r. spectrum of [Au(dppe)$_2$]Cl was not changed by addition of dadpe in $CDCl_3$ or $(CD_3)_2SO$. Preferential binding of $Au^I$ to P rather than As

**Table 8.** 100-MHz $^{13}C$-{$^1H$} n.m.r. data for dadpe and complexes (**1**) and (**2**) in $CDCl_3$

| Compound | δ (p.p.m.) Aliphatic | Aromatic | $J$(CP) (Hz) | Assignment |
|---|---|---|---|---|
| dadpe | 24.52 (d) | | 10.35 | $CH_2P$[a] |
| | 23.18 (d) | | 10.35 | $CH_2As$ |
| | | 140.17 | | CAs |
| | | 138.21 (d) | 6.9 | CP |
| | | 132.99 | | $C_{ortho}$(As) |
| | | 132.75 (d) | 12.2 | $C_{ortho}$(P) |
| | | 128.61 | | $C_{para}$(As,P)[b] |
| | | 128.57 | | $C_{meta}$(As) |
| | | 128.44 (d) | 7.0 | $C_{meta}$(P) |
| | | 138.35 | | $C_{para}$(As,P)[b] |
| [$(AuCl)_2$dadpe] | 24.81 | | 35.3 | $CH_2P$ |
| | 23.19 | | 4.3 | $CH_2As$ |
| | | 133.24 | 13.37 | $C_{ortho}$(P) |
| | | 132.66 | | $C_{para}$(As,P)[b] |
| | | 132.56 | | $C_{ortho}$(As) |
| | | 132.03 | | $C_{para}$(As,P)[b] |
| | | 130.02 | | $C_{meta}$(As) |
| | | 129.70 | 12.0 | $C_{meta}$(P) |
| | | 127.81 | | C–As,P[b] |
| | | 127.22 | | C–As,P[b] |
| [Au$(dadpe)_2$]Cl | 26.74 (d) | | 26.3 | $CH_2P$[c] |
| | 23.86 | | | $CH_2As$ |
| | | 137.53 (br) | | *d* |
| | | 132.70 (d) | 13.7 | $C_{ortho}$(P) |
| | | 132.44 | | $C_{ortho}$(As) |
| | | 132.06 | | C–As,P |
| | | 131.67 | | C–As,P |
| | | 131.02 | | $C_{para}$(As,P)[b] |
| | | 129.21 (d) | 12.0 | $C_{meta}$(P) |
| | | 129.04 | | $C_{meta}$(As) |

[a] Assigned as $CH_2P$ by analogy with the shift of the methylene carbon in dppe (δ 24.4 p.p.m.).[30] [b] Not assigned since there was no C–P coupling apparent in any of the resonances. [c] Assigned as $CH_2P$ since this resonance shows coupling to P. [d] Tentatively assigned to one of the $C_{para}$(As,P), however it is shifted very much downfield.

has been predicted on thermodynamic grounds for trialkyl-substituted ligands.[27] From stability constant measurements, the complex $[Au(PPh_3)_2]^+$ is more stable than the corresponding triphenylarsine compound.[28]

(*c*) *Proton and* $^{13}C$-{$^1H$} *n.m.r. spectroscopy.* To probe further the stabilities of complexes (**1**) and (**2**) in solution, $^1H$ and $^{13}C$-{$^1H$} n.m.r. spectra of dadpe and complexes (**1**) and (**2**) were investigated, Tables 7 and 8 respectively.

In the 400-MHz $^1H$ n.m.r. spectrum of complex (**1**) there is a downfield co-ordination shift for both the $CH_2$ and $C_6H_5$ resonances of *ca.* 0.52 and 0.23 p.p.m. respectively relative to the resonances of free dadpe. Both sets of resonances appear as sharp complex multiplets, the $CH_2$ signals being more symmetrical and less separated than for the free ligand. For complex (**2**), however, two well separated multiplets are observed in the $CH_2$ region at δ 2.59 (q) and 2.27 (qnt) which are broadened showing no further fine structure. Again there are downfield shifts on co-ordination. The $C_6H_5$ resonances are shifted to both high and low field with respect to the free ligand suggesting that the major species in solution is tetrahedral with stacked aromatic rings. However there is a slight broadening of resonances suggesting that dynamic processes are also occurring in solution and this observation supports the $^{31}P$-{$^1H$} data. Addition of 4 mol equivalents of dadpe to a solution of complex (**1**) gave peaks with averaged shifts for (**2**) and dadpe indicative of fast ligand exchange.

The 100-MHz $^{13}C$-{$^1H$} n.m.r. spectra of dadpe and the complexes (**1**) and (**2**), Table 8, are partly assigned on the basis of previously obtained data for $PPh_3$[29] and dppe.[30] There is virtually no change in the shift of the aliphatic carbons on co-ordination of dadpe to $Au^I$ in complex (**1**); for complex (**2**) the resonance assigned to $CH_2P$ is shifted downfield by *ca.* 2 p.p.m. In both cases there is an increase in $^1J$(CP) and a decrease in $^2J$(CP). On co-ordination to $Au^I$ the carbon atoms directly bonded to As and P are shifted upfield [by *ca.* 12 p.p.m. in complex (**1**) and *ca.* 8 p.p.m. in complex (**2**)] and no $^{13}C$–$^{31}P$ coupling is observed. Because of the ambiguity in assignments, Table 8, no attempt was made to investigate dynamic processes further by $^{13}C$ n.m.r. spectroscopy.

*Cytotoxicity of Complexes* (**1**) *and* (**2**) *in vitro.*—The complexes [$(AuCl)_2$dadpe] (**1**) and [Au$(dadpe)_2$]Cl (**2**) together with the free ligand dadpe were tested for cytotoxicity against three cell lines, L1210 (antimetabolite-sensitive leukaemia cells), WS (alkylating-agent-sensitive Walker tumour cells), and V.79 (Chinese hamster lung cells). For comparison, the previously studied compounds dppe and [Au$(dppe)_2$]Cl were also tested against these cell lines. Figure 4(*a*) shows the $IC_{50}$ values for the two ligands ($IC_{50}$ is the concentration of compound required to kill 50% of the cells) while data for the gold(I) complexes are presented in Figure 4(*b*). Comparison of the data for the two ligands, Figure 4(*a*), reveals that dadpe is about six times less toxic towards L1210 cells than is dppe and nearly ten times less toxic to the normal V.79 cells. However both ligands have a comparable lack of toxicity towards WS cells. It has been reported[2] that dadpe has a similar cytotoxicity to dppe towards murine B16 melanoma cells [$IC_{50}$(dadpe) 55, (dppe) 69 μmol $dm^{-3}$]. The mechanism by which phosphines [$P^{III}$] are

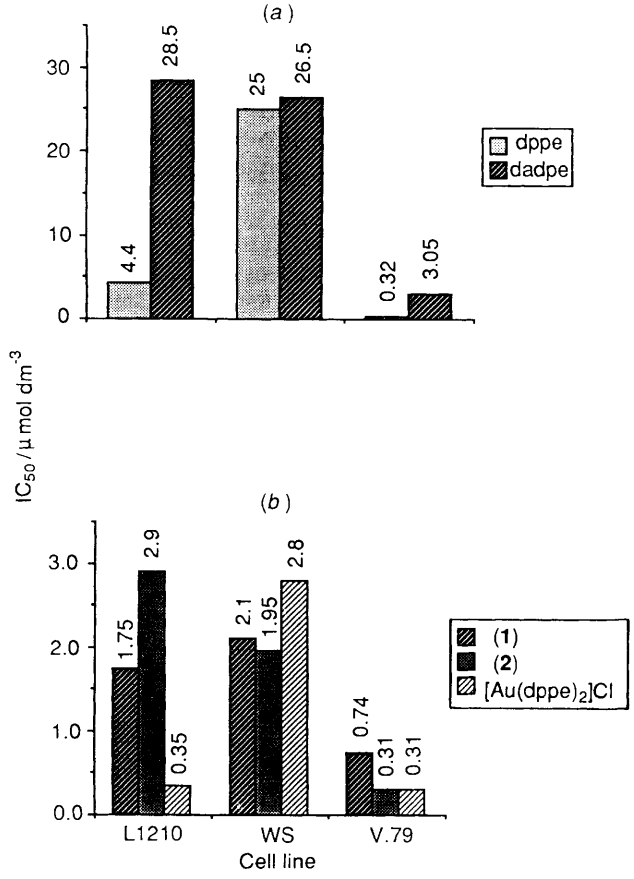



**Figure 4.** *In vitro* cytotoxicity of (*a*) the ligands dadpe and dppe, and (*b*) gold(I) phosphine and phosphinoarsine complexes

detoxicated *in vivo* is *via* oxidation to $P^V$,[1] and it may be that dadpe is more readily oxidized in certain cases than is dppe and thus is rendered less active. Experiments to investigate this are currently underway in our laboratories.

On comparing Figures 4(*a*) and (*b*) it can be seen that complexes (**1**) and (**2**) are more cytotoxic to all three cell lines than is the free ligand. Previous results[2] on the *in vitro* cytotoxicity of complex (**1**) and dadpe towards murine B16 melanoma cells are in agreement with this, showing the complex to be more potent than the free ligand by a factor of 13.8, and similar behaviour was observed for the bis(diphenylarsino)-ethane ligand,[2] $Ph_2AsCH_2CH_2AsPh_2$ (dpae), and its gold(I) complex, $[(AuCl)_2dpae]$ [$IC_{50}$(ligand) > 100, (complex) 7 μmol $dm^{-3}$]. A similar increase in potency of the complex over the free ligand has been observed[1,2] for gold(I) complexes of dppe and it has been suggested that $Au^I$ protects the phosphine ligand from oxidation. The same may be true for dadpe and the bis(arsenic) ligand (dpae). Comparison of the $IC_{50}$ values for complexes (**1**) and (**2**) for the three cell lines, Figure 4(*b*), shows that towards the normal V.79 cell line the tetrahedral complex (**2**) is slightly more toxic than is the bridged complex (**1**); both have comparable activity towards the WS and the L1210 cell lines. Both are more cytotoxic towards the normal V.79 cell line than to either of the tumour cell lines, L1210 or WS. The dppe analogue of (**2**), $[Au(dppe)_2]Cl$, is of equal toxicity towards L1210 cells and V.79 cells and is *ca.* 8 times more potent towards these two cell lines than the WS cells. On comparing the toxicity of complex (**2**) with that of its dppe analogue it can be seen that both complexes have equal activity towards V.79 cells and similar activity towards WS cells. Towards the L1210 cell line the dppe complex is 8 times more toxic. The last result is as might be expected in view of the greater lability of Au–As bonds over Au–P and hence the more facile oxidation and resultant decrease in toxicity of (**2**). However, the data for the other two cell lines, WS and V.79, are perhaps surprising and suggest that the mechanism of toxicity of the complexes differs between cell lines.

Thus for dadpe, the effect of complexation by $Au^I$ is to increase the cytotoxicity towards the three cell lines, though the magnitude of the increase differs between cell lines [by factors of 16, 12.6, and 4.1 for (**1**) and 9.8, 13.6, and 9.8 for (**2**) in the cases of L1210, WS, and V.79 cell lines respectively]. For dppe and $[Au(dppe)_2]Cl$ a similar increase in cytotoxic activity is observed in the case of the L1210 and WS cell lines (by factors of 12.6 and 8.9 respectively). However both the ligand and the complex are of equal toxicity towards the normal V.79 cells. Substitution of one of the P atoms in dppe by As reduces the cytotoxic activity of the ligand towards L1210 and V.79 cells, but has little effect on ligand activity towards WS cells. Use of dadpe rather than dppe as a ligand in the tetrahedral gold(I) complex has little or no effect on the cytotoxicity of the complexes towards V.79 and WS cells, and reduces the activity towards L1210 cells (by a factor of 8). Thus there are a number of factors contributing to the *in vitro* activity of these compounds: replacement of P by As, complexation of the ligand to $Au^I$, and the nature of the cell lines. It must also be noted that each of the cell lines used in these cytotoxicity tests was grown in a slightly different medium and the contact time with the V.79 cell line was longer than those with the other cell lines. Further studies of the metabolism of arsines and phosphines and their metal complexes by various cell types and their interactions with different growth media may help to explain these features.

## Experimental

*Sources of Chemicals.*—1-Diphenylarsino-2-diphenylphosphinoethane (dadpe) was purchased from Strem Chemicals. Sodium tetrachloroaurate was purchased from Johnson Matthey plc, and thiodiglycol from Sigma.

*Physical Measurements.*—$^{13}P$-{$^1H$} N.m.r. spectra were obtained on a Bruker WM200 spectrometer at 81 MHz, using 5- or 15-mm tubes. The shift reference was 85% $H_3PO_4$ (external). Proton n.m.r. spectra were obtained on a Bruker WM400 spectrometer using 5-mm tubes and referenced to $CHCl_3$ at δ 7.25, $^{13}C$-{$^1H$} spectra on either a Bruker WM400 or a Varian 400 spectrometer using 10-mm tubes and referenced to $CDCl_3$ at δ 77.0 p.p.m. Elemental analyses were carried out by the microanalysis service at University College London. Melting points were determined on a Mettler FP800 with an FP82 hot stage. Mass spectra (fast atom bombardment) were recorded using a VG ZAB-SE mass spectrometer (University of London Intercollegiate Research Service, School of Pharmacy).

*Preparations.*—$[(AuCl)_2dadpe]$. The salt $Na[AuCl_4]$·0.5-$H_2O$ (0.67 g, 1.82 mmol) was reduced to $Au^I$ by thiodiglycol (0.231 $cm^3$, 2.31 mmol) in aqueous acetone (2.5:1, 14 $cm^3$). When the solution became colourless, dadpe (0.41 g, 0.93 mmol) in acetone (36 $cm^3$) was added dropwise over 5 min. Immediately the reaction solution became cloudy. After stirring at room temperature for 1.25 h, the white solid product was filtered off, washed with water and acetone, and air-dried. Recrystallization from dimethylacetamide afforded white crystals of $[(AuCl)_2dadpe]$·0.5 dma (0.14 g, 15.8%), m.p. 209 °C (decomp.) (Found: C, 35.35; H, 3.00; N, 0.70. Calc. for $C_{28.5}H_{28}AsAu_2Cl_2N_{0.5}O_{0.5}P$: C, 35.35; H, 3.00; N, 0.75%). $^{31}P$-{$^1H$} N.m.r. (80.96 MHz, $CHCl_3$, 24 °C); δ 31.82 p.p.m.

$[Au(dadpe)_2]Cl$·$2H_2O$. The salt $Na[AuCl_4]$·$0.5H_2O$ (0.60 g, 1.62 mmol) was reduced to $Au^I$ by thiodiglycol (0.162 $cm^3$, 1.62

mmol) in aqueous acetone (2.5:1, 7 $cm^3$). This solution was cooled in ice and added to an acetone (95 $cm^3$) solution of dadpe (1.43 g, 3.2 mmol). The reaction was stirred at room temperature for 2.2 h and then left to stand. On evaporation of most of the solvent a white oily solid was obtained which on recrystallization from aqueous acetone afforded white crystals of $[Au(dadpe)_2]Cl\cdot 2H_2O$ (0.64 g, 35%), m.p. 79.8—81.4 °C (Found: C, 54.40; H, 4.60; P, 5.60. Calc. for $C_{52}H_{52}As_2AuClO_2P_2$: C, 54.15; H, 4.55; P, 5.35%).

*Mass Spectrometry.*—The f.a.b. (fast atom bombardment) mass spectrum of $[Au(dadpe)_2]Cl\cdot 2H_2O$ showed a parent molecular ion (p.m.i.) at $m/z = 1\,081$ corresponding to the formula $[Au(dadpe)_2]^+$.

Mass spectral results for the bridged species $[(AuCl)_2dadpe]$ (**1**) are more complicated. In none of the f.a.b. spectra of unrecrystallized (**1**), crystals of (**1**) from $CHCl_3$ or from dma is the expected p.m.i. of $m/z = 906$ observed but rather a peak at $m/z = 871$ corresponding to $[M - Cl]^+$ indicating that $[Au_2Cl(dadpe)]^+$ is a more stable species. Peaks of higher mass were present in the spectra of all three samples. For both the unrecrystallized sample and that recrystallized from $CHCl_3$ the peak of greatest mass is at $m/z = 1\,545$ corresponding to $[M + Au(dadpe)]$, *i.e.* $[Au_3Cl_2(dadpe)_2]^+$, while there are peaks up to $m/z = 2\,043$ and 2 115 for the sample from dma. The $[M - Cl]^+$ peak at $m/z = 871$ is the base peak in the spectrum of the unrecrystallized sample, however in the spectra of both the other samples the base peak is at $m/z = 307$ assigned as $[Ph_3As + H]^+$, *i.e.* $[M - Au_2Cl_2CH_2CH_2PPh]$. The f.a.b. spectra of the dppe analogue of (**1**), $[(AuCl)_2dppe]$, again showed peaks at $[M - Cl]^+$, $m/z = 827$, instead of the expected $m/z = 862$ in the cases of the unrecrystallized sample, crystals from $CHCl_3$ and from dma. The base peaks for these samples were at $m/z = 138$ $\{[M - 764]\}$, 139 $\{[(M + H) - 764]\}$, and 77 $\{[M - (AuCl)_2Ph_2PCH_2CH_2PPh]$, *i.e.* $[C_6H_5]^+\}$. Only the spectrum of the product recrystallized from dma showed peaks of higher mass than $[M]^+$ at $m/z = 902$ {corresponding to $[(AuCl)_2dppe] + 40$}, and a weak peak at 1 089. Thus in the cases of the bridged dadpe and dppe compounds the solvent from which they are crystallized alters the fragmentation pattern in the mass spectrum.

*Crystal Structure Determination of* $[(AuCl)_2dadpe]\cdot 0.5$ dma (**1**).—*Crystal data.* $C_{28}H_{28.5}AsAu_2Cl_2N_{0.5}O_{0.5}P$ (dimethylacetamide solvate), $M = 950.77$, monoclinic, space group $Cc$, $D_m = 2.18$ g $cm^{-3}$, $Z = 8$, $D_c = 2.184$ g $cm^{-3}$, $a = 19.385(3)$, $b = 11.011(2)$, $c = 27.260(1)$ Å, $\beta = 96.40(1)°$, $U = 5\,782.3(1.8)$ $Å^3$ (by least-squares refinement, $\lambda = 0.710\,69$ Å), $F(000) = 3\,552$, crystal dimensions 0.15 × 0.10 × 0.22 mm, $\mu$(Mo-$K_\alpha$) = 115.14 $cm^{-1}$.

*Data collection and processing.* Rigaku AFC5R automated diffractometer, $\omega$—$2\theta$ scanning mode, rotating anode, Mo-$K_\alpha$ radiation; 7 024 independent reflections measured ($1.0 < \theta < 35°$), giving 5 652 with $I \geqslant 1.5\sigma(I)$. Severe absorption effects ($\mu = 115.14$ $cm^{-1}$) were corrected empirically, the minimum and average absorption coefficients being 0.269 and 0.711 respectively.

*Structure analysis and refinement.* Four gold atom positions were located from the Patterson maps. Difference Fourier maps at this stage revealed four chloride atoms and four either arsenic or phosphorus atoms. Least-squares refinements with these heavy atoms and subsequent difference Fourier maps gradually revealed all the phenyl rings. The $R$ factor was 0.092, including all these atoms. However the isotropic thermal parameters ($B_{iso}$) of the atoms co-ordinating to the gold atom were unsatisfactory. Those of the two arsenic atoms were large (5.1 and 4.9 $Å^2$) while those of phosphorus were too small (0.68 and 0.60 $Å^2$). Exchanging the assignment of each pair of atoms merely exchanged the magnitude of the thermal parameters. Crystal-density data together with microanalytical data confirm the presence of two dadpe groups, *i.e.* two P atoms and two As atoms are present. Thus the crystal structure is disordered and in solving the structure an averaged atomic scattering factor for As and P was used for all four ligating atoms. Least-squares refinements with anisotropic thermal parameters for the non-hydrogen atoms reduced the $R$ factor to 0.059, and 0.5 mol dimethylacetamide was revealed in the difference map. Final least-squares refinement carried out anisotropically included all the non-hydrogen atoms, though the solvent molecule was refined isotropically. Hydrogen atoms which were generated assuming an ideal geometry were included in the structure-factor calculations but not refined. The final unweighted $R$ factor was 0.0514 and the final weighted $R$ factor was 0.0619 (weighting scheme: $w = 0.8$ for $|F_o| < 67.30$, 1.0 for $67.3 < |F_o| < 269.0$, and $72\,361/|F_o|^2$ for $|F_o| > 269.0$).

Since the structure obtained was fairly close to that of the space group $C2/c$ and the systematic absences were consistent with this the structure determination was also tried in this centric space group. After shifting the origin of the unit cell to conform to this space group and averaging the two independent molecules in the $Cc$ space group, the structure was refined in the centric space group. However the $R$ factor converged at 0.157. The structure was also solved independently in this space group. All the non-heavy atoms except those of the solvent molecule were revealed after many cycles of refinements and difference Fourier maps, however the $R$ factor never reduced below 0.152 and the phenyl rings were distorted. Also intensity data indicated an acentric structure. Hence the space group of the crystal was confirmed to be $Cc$.

The atomic scattering factors for the non-hydrogen and hydrogen atoms were taken from refs. 31 and 32 respectively. Calculations were performed on a M680H at the University of Tokyo Computer Centre using a program system UNICS III[33] (block-diagonal least-squares refinement) as well as on a micro VAX II using a program system TEXSAN[34] (full-matrix least-squares refinement).

*Crystal Structure Determination of* $[Au(dadpe)_2]Cl\cdot 2H_2O$ (**2**).—*Crystal data.* $C_{52}H_{52}As_2AuClO_2P_2$ (water solvate), $M = 1\,153.14$, monoclinic, space group $P2_1/n$, $a = 10.192(1)$, $b = 21.797(7)$, $c = 21.683(10)$ Å, $\beta = 94.14(3)°$, $U = 4\,804.4(2.8)$ $Å^3$ (by block-diagonal least-squares refinement, $\lambda = 0.710\,69$ Å), $D_m = 1.599$ g $cm^{-3}$, $Z = 4$, $D_c = 1.594$ g $cm^{-3}$, $F(000) = 2\,288$, crystal dimensions 0.1 × 0.33 × 0.25 mm, $\mu$(Mo-$K_\alpha$) = 45.80 $cm^{-1}$.

*Data collection and processing.* Rigaku AFC5R automated diffractometer, $\omega$—$2\theta$ scanning mode, rotating anode Mo-$K_\alpha$ radiation; 19 302 independent reflections measured ($1.0 < \theta < 35°$) giving 5 226 with $I \geqslant 3\sigma(I)$. Crystal decay was observed (12.4%) and the effect was corrected. An empirical absorption correction was applied, the minimum and average transmission factors being 0.438 and 0.779 respectively.

*Structure analysis and refinement.* The position of the Au atom was determined from the Patterson map. Fourier and difference Fourier syntheses with occasional least-squares refinements gradually revealed all the non-hydrogen atoms. Block-diagonal least-squares refinements with isotropic thermal parameters reduced the $R$ factor to 0.23, however, as in the case of (**1**), the isotropic thermal parameters of the ligating P and As atoms were not acceptable. Two atoms assigned as arsenic had slightly larger thermal parameters of 5.04 and 5.64 $Å^2$, while those of the other two, assumed to be phosphorus, were far too small (0.91 and 0.11 $Å^2$). As found for complex (**1**), exchange of the assignments of the atoms merely resulted in an exchange of the $B_{iso}$ values; the first two atoms which this time were assigned

as P had very small thermal parameters. Anisotropic thermal parameters refinement reduced $R$ to 0.165, and the two peaks corresponding to the oxygen atoms of the two waters of hydration were revealed. An empirical absorption correction was applied at this stage. Including the two water molecules and applying anisotropic thermal parameters to all the non-hydrogen atoms, least-squares refinements were carried out, using the absorption-corrected intensity data. The $R$ factor decreased to 0.0950 and twenty hydrogen atoms were revealed in the difference Fourier maps. The rest of the hydrogen atoms were generated assuming an ideal geometry. The abnormal behaviour of the ligating atoms still persisted. The two As atoms had anisotropic thermal parameters ($B_{eq}$) of 5.32 and 5.93 Å$^2$; on the other hand, the two P atoms had $B_{eq}$ values of 1.05 and 0.43 Å$^2$. Exchanging the atom assignments simply exchanged the $B_{eq}$ values, as observed previously for the isotropic refinements before correction for the absorption effect. If all four co-ordinating atoms were assigned as As, the thermal parameters become more equal with $B_{eq}$ values of 4.70, 5.35, 6.68, and 5.07 Å$^2$ and $R$ reduced to 0.0846. However measurement of the crystal density, as well as microanalytical and mass spectral data, establish that the compound contains two As and two P atoms. The presence of P is further confirmed by $^{31}$P n.m.r. data on this batch of crystals, From the difference map excluding the ligating atoms it was not possible to distinguish the atom type from the peak heights. Thus, as in the case of (**1**), the molecules must be disordered in the crystal lattice. Using averaged atomic scattering factors for As and P in the case of all four ligating atoms, least-squares refinements were carried out. The $R$ factor decreased to 0.0625 and the $B_{eq}$ values for the four atoms were 3.4, 3.8, 4.8, and 3.6 Å$^2$. Three out of the four hydrogen atoms of the two water molecules were revealed in the difference Fourier map. After further refinements the structure converged to an unweighted $R$ value of 0.0482. Atomic parameters of hydrogen were not refined. The weighted $R$ factor was 0.0553 (weighting scheme: $w = 0.8$ for $|F_o| < 28.0$, 1.0 for $28.0 < |F_o| < 280.0$, and $78\,400/|F_o|^2$ for $|F_o| > 280.0$).

The atomic scattering factors for the non-hydrogen and hydrogen atoms were taken from refs. 31 and 32 respectively. Programs and computers used were as above.

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom co-ordinates, thermal parameters, and remaining bond lengths and angles.

*Cytotoxicity Assays.*—The ligands and complexes were dissolved in $Me_2SO$ and diluted with water to give a final concentration of 0.5% (v/v) in the growth media. The L1210 cell line was grown in RPMI 1640 medium with 10% added horse serum, while the WS cells were grown in Dulbecco's MEM (minimum essential medium) with 10% added horse serum. The two media also contained L-glutamine, and the antibiotics streptomycin sulphate, neomycin sulphate, and crystapen. Contact with the compounds was for 48 h in both cases. In the case of the V.79 cells the medium used was Eagle's based MEM with 15% added foetal calf serum. The medium also contained L-glutamine and the antibiotics pencillin and streptomycin. Contact with the compounds was for 6 d.

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