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Article

Antiproliferative Activity of Gold(I) Alkyne Complexes Containing Water-Soluble Phosphane Ligands

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A series of mono-, di-, and trinuclear organometallic alkynyl phosphane gold(I) complexes containing the stable and water-soluble PTA and DAPTA ligands have been synthesized and characterized. The solid-state structure of one of these compounds was also established by X-ray crystallography. Luminiscence was observed for most of these Au(I) alkynyl derivatives in the solid state. The cytotoxicity of the complexes was evaluated on A2780 ovarian cancer cells and on their cisplatin-resistant cell line A2780cisR; the compounds showed an activity in the low μM range, being markedly more active than cisplatin in the A2780cisR cell line. The intracellular distribution of some representative compounds was determined using epifluorescence microscopy. The presented results are discussed in relation to the putative mechanism of action of this family of gold-based cytotoxic agents.

Introduction

Cisplatin (*cis*-diaminodichloroplatinum(II)) is one of the most widely employed anticancer drugs used to treat, but not restricted to, testicular, ovarian, head and neck, and bladder cancers.[1] However, its use is severely hindered by side effects and the frequent occurrence of resistance to the treatment. These drawbacks are among the reasons for the research efforts to identify other metal complexes for cancer treatment. In this context, gold complexes have been extensively studied due to the clinically established antiarthritic properties of Au(I) thiolates, such as sodium aurothiomalate (Myocrisin), aurothioglucose (Solganol), and [(1-thio-β-D-glucopyranose-2,3,4,6-tetraaceta-to-S)(triethylphosphane)gold] (auranofin) (Chart 1).[2] Cytotoxicity profiles rivalling those of cisplatin have been observed for auranofin and related thiolate gold phosphane and gold phosphane derivatives.[3] Additionally, it has been shown that gold(I) complexes inhibit mitochondrial functions and stimulate the release of cytochrome *c*, which induces apoptosis.[4] Very recently, organometallic gold(I) derivatives with N-heterocyclic carbene ligands, which exhibit comparable binding properties to phosphane ligands, have been described as potential antitumor agents that selectively target the mitochondria of cancer cells.[5]

Alkynyl Au(I) derivatives with phosphane ligands have been extensively studied,[6] with a focus on their luminescent properties,[7] nonlinear optical properties,[8] and supramolecular chemistry.[9] In contrast, biological studies of metal acetylide compounds are extremely scarce. Platinum arylacetylides, with the formula $[Pt(terpy)(C{\equiv}C\text{-}Ar)]^+$ (terpy = terpyridine ligand, C≡C-Ar = glycosylated acetylides and arylacetylide ligands),[10] were shown to be more cytotoxic than the related complex $[Pt(terpy)Cl]^+$ and about 100 times more cytotoxic than cisplatin. Gold(I) diethynylfluorene derivatives have been studied for their antitumor activity against human carcinoma cells both *in vitro* and *in vivo*.[11] These compounds display a higher cytotoxicity than cisplatin, and no evidence of necrosis was found from autopsies of mice vital organs.

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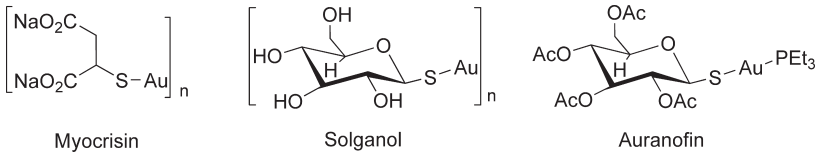
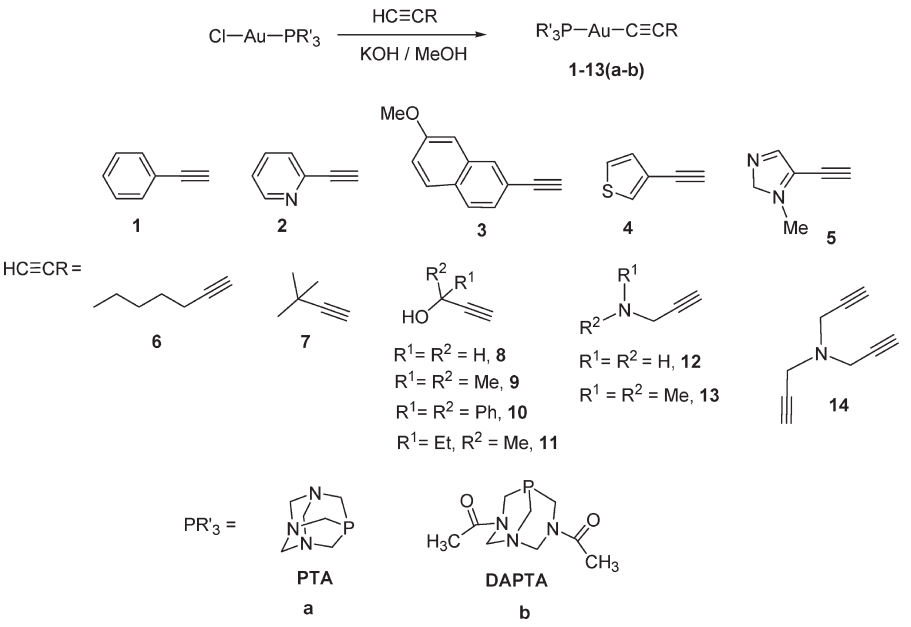
Chart 1



Scheme 1. Synthesis of Mononuclear Alkynyl Gold(I) Derivatives and a Trinuclear Derivative



In the past few years, metallic derivatives with the water-soluble phosphane PTA (1,3,5-triaza-7-phosphaadamantane) have been shown to possess anticancer properties,[12] the arene-ruthenium(II) complexes, named RAPTA, being studied *in vitro* and *in vivo*.[13,14] In most of these cases, the PTA ligand provides a degree of water solubility that could facilitate drug administration and transport in the body. In previous papers,[15] we have described gold(I) derivatives with PTA and the diacetylated derivative DAPTA (3,7-diacetyl-1,3,7-triaza-5-phosphabicyclo-[3.3.1]nonane), exploring the anticancer activity of the corresponding thiolate complexes against human cancer cells.[15a,c] Some of them exhibited excellent *in vitro* anticancer activity against human ovarian carcinoma cells, with the ability to overcome the resistance to cisplatin, possibly by inhibiting the seleno-enzyme thioredoxinereductase (TrxR).[15a]

Within this frame, we have developed new organometallic alkynyl phosphane gold(I) complexes with the PTA and DAPTA co-ligands. Herein, we describe the synthesis and characterization of mononuclear and dinuclear alkynyl Au-(I) derivatives and the cytotoxic properties of some of them against the human ovarian carcinoma cell lines sensitive (A2780) and resistant (A2780cisR) to cisplatin.

Results and Discussion

The mononuclear phosphane Au(I) acetylides **1**−**7** were prepared by treatment of [AuCl(PR′$_3$)] (PR′$_3$ corresponding to the water-soluble phosphanes PTA and DAPTA) with terminal acetylenes in the presence of a base (KOH in methanol) (Scheme 1). The $^{31}P\{^1H\}$ NMR spectra of **1**−**7** display singlet resonances at ca. −50 ppm in the case of the PTA ligand and around −20 ppm for the DAPTA derivatives, in accordance with P-donor ligand coordination. Their ^1H NMR spectra show, apart from the corresponding signals of the alkyne fragment, a singlet resonance and an AB system due to the NCH_2P and NCH_2N groups in the PTA complexes. The presence of a singlet instead of a doublet for the NCH_2P group has been observed in other metallic derivatives.[16] The displacement of this singlet is dependent on the alkyne substituents, being downfield shifted in the

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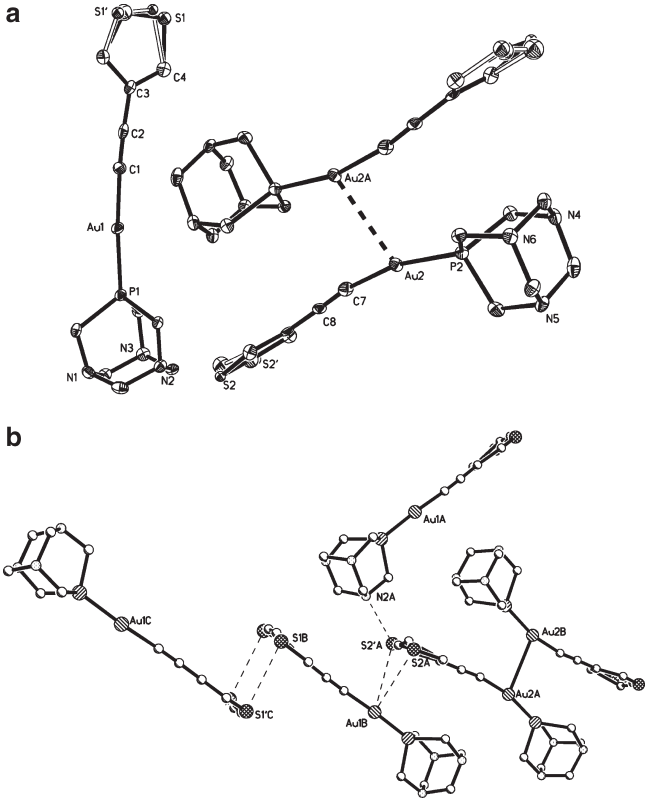

Figure 1. (a) Molecular structure of [Au(C≡C-3-SC_4H_3)(PTA)] (**4a**). Selected bond lengths [Å] and angles [deg], #1 $-x$, $-y+1$, $-z+2$: Au(1)−C(1) 1.997(6), Au(1)−P(1) 2.2580(17), Au(2)−C(7) 2.004(6), Au(2)−P(2) 2.2650(17), Au(2)−Au(2)#1 3,1389(9) C(1)−C(2) 1.212(8), C(7)−C(8) 1.202(8), C(1)−Au(1)−P(1) 175.55(19), C(7)−Au(2)−P(2) 167.13(19), C(7)−Au(2)−Au(2)#1 82.42(18), P(2)−Au(2)−Au(2)#1 110.27(5). H atoms are omitted for clarity. (b) View of the packing in the unit cell of complex **4a**.

cases of the aryl radicals. Only in the case of [Au(C≡CPh)-(PTA)] (**1a**) can the resonances of the alkyne units be observed in the ^{13}C NMR spectrum: two singlets centered at 63.8 ppm for Au*C*≡C and at 82.7 ppm for AuC≡*C*. Lower solubilities of the other alkynyl derivatives in $CDCl_3$ prevented the detection of these resonances. Nevertheless, the IR spectra of **1**−**7** exhibit a characteristic absorption band for the C≡C unit at ca. 2100 cm^{-1}, which is hardly influenced by the substituent on the acetylene unit.

Coordination of the alkyne unit to the gold(I) center was confirmed by X-ray diffraction analysis of [Au(C≡C-3-SC_4H_3)(PTA)] (**4a**). The structure (Figure 1) consists of two independent molecules in the unit cell, one of them associated with a third unit related by symmetry in a nearly parallel rearrangement (torsion angle of 173.23°) with a head-to-tail disposition and with a Au···Au distance of 3.1389(9) Å. This short interaction is in the range observed for aurophilic bonds between two gold(I) centers.[17] Both independent molecules display a typical linear geometry around the metal, although, in the case of the associated molecule, the presence of Au−Au interactions gives a smaller P−Au−C angle (P1−Au1−C1 = 175.55(19)° and P2−Au2−C7 = 167.13(19)°). The Au−C (Au1−C1 = 1.997(6) Å and Au2−C7 = 2.004(6) Å) and Au−P (Au1−P1 = 2.2580(17) Å and Au2−P2 = 2.2650(17) Å) bond lenghts and the C−C distances in the alkyne unit (C1−C2 = 1.212(8) Å and C7−C8 = 1.202(8) Å) are similar to those found in the unique alkyne Au derivative with PTA described in the literature.[16a] Similar Au−C and Au−P bond lengths have been observed in related alkynyl phosphane gold(I) derivatives, for example in [Au(C≡C-Ph)(PMe_3)],[18] [Au(C≡CC(Et)(Me)(OH)(PMe_3)],[19] and [(PPh_3)Au(C≡C)($C_6H_2S_2$)(C≡C)Au(PPh_3)].[20] Disorder was observed in the thiophene moiety in both molecules in the form of a 2-fold rotation of the group about its longitudinal axis. The principal effect of the disorder is to generate cogeneric S,C sites for both termini.

The packing of the molecules (Figure 1b) is dominated by short Au···S (3.569 Å) and S···N (3.322 Å) interactions between isolated and associated molecules and additional S···S interactions of 3.413 Å between the isolated molecules.

Deprotonation of the alkyne with a propargyl alcohol substituent by KOH probably gives an equilibrium between the alkoxide ($^-$OCRR′C≡CH) and the acetylide (HOCRR′C≡C$^-$) anions, the latter being displaced by the former because of its lower pK_a.[21] However the affinity of Au(I), a soft acid, toward C displaces the equilibrium to give the corresponding acetylides **8**−**11**. The PTA derivatives **8a**−**11a** have been described previously.[16a] Compounds **8b**−**11b**, with the DAPTA ligand, display a singlet in the $^{31}P\{^1H\}$ NMR as in the previous derivatives (**1**−**7**) and a similar pattern in the ^1H NMR with the characteristic signals of the DAPTA ligand. Their IR spectra display, apart from the band due to the C≡C stretch at ca. 2100 cm^{-1}, a very broad band at ca. 3400 cm^{-1} due to the O−H stretch.

These alkyne derivatives (**8**−**11**) are all soluble in water, with higher solubility for the DAPTA complexes, with the most soluble derivative being [Au(C≡CC(CH_2CH_3)(CH_3)-(OH))(DAPTA)] (**11b**), with a value of $s_{25°}$ = 15 mg/mL. Complexes **1**−**7** are essentially insoluble in water, except **5a** ($s_{25°}$ = 1.3 mg/mL) and **5b** ($s_{25°}$ = 2.5 mg/mL), but soluble in DMSO and partially soluble in alcohol/water mixtures. The presence of the OH groups in the propargyl alcohol derivatives clearly enhances the water solubility. Thus, reaction of the propargyl amines $R^1R^2NCH_2C{\equiv}CH$ in basic media with [AuCl(PR′$_3$)] (PR′$_3$ = PTA and DAPTA) gave the corresponding alkynyl derivatives (**12**, **13**) with similar solubilities to those of the other propargyl alcohol compounds. Notably, water solubility is markedly reduced when more than one Au-PR′$_3$ unit is added to the propargyl amine, as in the trinuclear complexes N[Au(C≡CCH_2)(PR′$_3$)]$_3$ (PR′$_3$ = PTA, **14a**, and DAPTA, **14b**).

Dinuclear alkynyl Au(I) compounds were prepared starting from the bis-alkynes depicted in Scheme 2. Complexes **15**−**17** exhibit similar spectroscopic properties to the mononuclear derivatives, with one signal in $^{31}P\{^1H\}$ NMR at ca. −50 ppm for the PTA complexes and in the range −20 to −25 ppm for the DAPTA systems, and also display very low solubility in water.

Luminiscence was observed for most of these alkynyl derivatives in the solid state at room temperature (Table 1

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Scheme 2. Synthesis of Dinuclear Alkynyl Gold(I) Derivatives

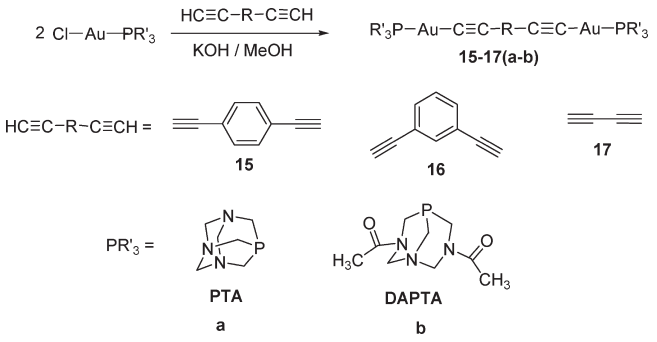

Table 1. Excitation and Emission Data in the Solid State at Room Temperature

complex	λ_{exc}/nm	λ_{emis}/nm	complex	λ_{exc}/nm	λ_{emis}/nm
1a	387	499	**9a**	372	496
1b	411	534	**9b**	372	498
2a	420	510	**10a**	382	502
2b	426	541	**10b**	370	487
4a	365	467	**11a**	380	504
4a	370	488	**11b**	374	488
2a	412	525	**14a**	384	486
2b	398	513	**14b**	370	495
6a	356	473	**15a**	422	645
6b	369	498	**15b**	486	657
7a	370	486	**16a**	423	540
7b	382	490	**16b**	428	555
8a	380	491	**17a**	410	542
8b	364, 411	481	**17b**	416	553

and Figure 2). The excitation maxima are in the range 356−428 nm in the majority of the complexes, except for the dinuclear species $[Au_2\{(C{\equiv}C)_2\text{-}1,4\text{-}C_6H_4\}(DAPTA)_2]$ (**15b**), which displays an excitation at 486 nm and a shorter range for the propargyl compunds **8**−**11** (360−380 nm). The emission maxima are between 486 and 555 nm, although a red-shifted emission is observed for complexes $[Au_2\{(C{\equiv}C)_2\text{-}1,4\text{-}C_6H_4\}(PTA)_2]$ (**15a**) (645 nm) and $[Au_2\{(C{\equiv}C)_2\text{-}1,4\text{-}C_6H_4\}(DAPTA)_2]$ (**15b**) (657 nm).

Alkynyl gold(I) phosphane derivatives frequently display lumiscence at room temperature, which is associated with intraligand electronic transitions, gold-centered transitions, Au−P to alkyne transitions, or even Au−Au bond to alkyne transitions, with the Au-PR_3 unit able to enhance the emission from the triplet states of C≡CR luminomophores.[22] Emission values (see Table 1) are dependent on the nature of the phosphane ligand and on the substituents of the alkyne ligand in most cases. The presence of phenyl groups, with more extensive electron delocalization, on the alkyne ligand produces a red-shift in the emission values, being more pronounced in the case of the dinuclear derivatives (**15**−**17**).

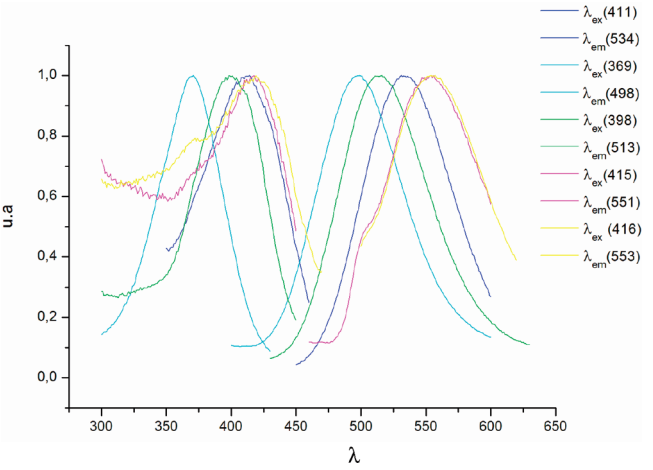

Figure 2. Excitation and emission spectra of **1b** (dark blue), **2a** (green), 7**b** (blue), **16b** (yellow), and **17b** (pink).

This effect might be attributed to a $\pi{\rightarrow}\pi^*$(C≡C) or σ(Au−P)$\rightarrow\pi^*$(C≡C) transition, as reported for similar Au(I) alkynyl phosphane derivatives.[22c,k] In **4a** the origin of the emission may also be tentatively attributed to aurophilic interactions, since its X-ray analysis displays short Au···Au interactions of 3.1389(9) Å.

Biological Evaluation. The cytotoxic properties of some of the alkynyl derivatives were analyzed *in vitro* against the cisplatin sensitive (A2780) and cisplatin-resistant (A2780cisR) human ovarian cancer cells. The mononuclear complexes [Au(C≡CPh)(DAPTA)] (**1b**), $[Au(C{\equiv}C\text{-}3\text{-}SC_4H_3)(PR_3)]$ (**4a**,**b**), and $[Au(C{\equiv}CCH_2OH)(PR_3)]$ (**8a**,**b**) and the trinuclear derivative with the propargyl amine $N[Au(C{\equiv}CCH_2)(PR_3)]_3$ (**14a**,**b**) (PR_3 = PTA and DAPTA) were evaluated in comparison to cisplatin and auranofin. All the complexes display moderate to high cytotoxicities, with IC_{50} values ranging from 0.8 to 14 μM. Notably, **1b** is more potent than cisplatin in both cell lines, with IC_{50} values more than 20-fold lower for the resistant cell line. These values are similar to those observed for auranofin.[23] These data suggest that **1b** can overcome the resistance to cisplatin and support the hypothesis of a different mechanism of action of the gold(I) complexes with respect to cisplatin.[2b,4b,24]

It has been shown that phosphane Au(I) thiolates, such as auranofin, are more cytotoxic than gold thiolates and their chloride analogues,[25] indicating the importance of the presence of both thiolate and phosphane ligands for the observed pharmacological effects. With the complexes described herein the thiolate unit has been replaced by an alkyne ligand while maintaining the Au-phosphane fragment. Although the exact mechanism of Au(I) phosphane-induced cytotoxicity is unclear, several lines of evidence point to the involvement of mitochondria.[4b] The high affinity of Au(I) for S- and Se-donor ligands suggests that proteins, including enzymes and transport proteins, might be possible targets. Studies of gold(I) complexes such as auranofin and myochrysine indicate that ligand displacement reactions between

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Table 2. IC_{50} Values of 1, 4, 8, and 14 against Ovarian Carcinoma Cell Lines Sensitive (A2780/S) or Resistant (A2780/R) to Cisplatin Compared with Cisplatin and Auranofin

	IC_{50} (μM)	
	A2780	A2780cisR
[Au(C≡CPh)(DAPTA)] (**1b**)	1.2 ± 0.4	2.8 ± 0.4
[Au(C≡C-3-SC_4H_3)(PTA)] (**4a**)	1.0 ± 0.3	4.5 ± 2.1
[Au(C≡C-3-SC_4H_3)(DAPTA)] (**4b**)	0.8 ± 0.1	6.7 ± 1.8
[Au(C≡CCH_2OH)(PTA)] (**8a**)	10.1 ± 0.3	11.2 ± 1.1
[Au(C≡CCH_2OH)(DAPTA)] (**8b**)	38 ± 2.1	11.0 ± 1.9
N[Au(C≡CCH_2)(PTA)]$_3$ (**14a**)	3.3 ± 0.2	10.7 ± 1.1
N[Au(C≡CCH_2)(DAPTA)]$_3$ (**14b**)	1.1 ± 0.2	14.7 ± 1.3
cisplatin	4.3 ± 0.5	18.2 ± 1
auranofin	1.25 ± 0.5	1.5 ± 0.5

cysteine residues and the thiol bound to the gold center take place on binding.[26] For the compounds reported herein, the thiolate unit has been replaced by an alkyne ligand, while maintaining the Au-phosphane fragment. The alkyne ligand bonded to the gold center probably undergoes the same substitution reaction with cysteines. In addition, the phosphane PTA would play a similar role to PEt_3 in auranofin, since the nucleophilicity of PTA is comparable to other trialkylphosphanes.[27] In keeping with the possibility of protein targets of these compounds, no significant interactions were observed with plasmid pBR322 DNA after incubation at 37 °C with **4b**, **8a**, and **8b** and compared to cisplatin[28] (see Supporting Information). The lack of reactivity with DNA is comparable to that observed for auranofin.[29]

Some of the cytotoxic compounds show luminescence, and this property was used to determine their intracellular distribution using epifluorescence microscopy. Related studies of N-hetereocyclic carbene Au(I) complexes[30] and the antiarthritic drug myocrisin[31] provided evidence of intracelular gold localization in the lysosomes rather than in the mitocondria. Complexes **4a**, **14a**, and **14b** were incubated with the A2780 cells for 6 h at 37 °C, and the images recorded (Figure 3) reveal luminescence throughout the entire cell, indicating that the alkynyl derivatives enter the cells. However, the relatively low level of the fluorescence observed prevented the subcellular compartments where the complexes accumulate from being identified. Nevertheless, the images show that the complexes are efficiently and rapidly taken up by the cancer cells.

To conclude, the gold(I) alkynyl complexes described herein, containing the stable and water-soluble PTA and DAPTA ligands, behave *in vitro* in a similar way to clinically used phosphane Au(I) thiolates. Replacement of the thiolate by the alkynyl ligand appears to lead to a similar biological function at the molecular level, although further experiments are required to confirm this hypothesis. The use of PTA and DAPTA appears to be particularly advantageous, over the triethylphosphane ligand present in auranofin, since the latter ligand is unstable and toxic. The compounds studied were shown to enter cells, and since they do not damage DNA, they probably exert their *in vitro* antiproliferative effect via interactions with critical proteins/enzymes in keeping with other gold complexes.

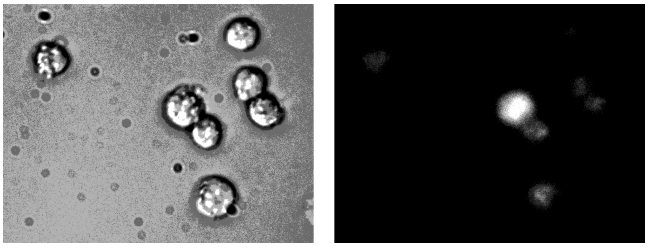

Figure 3. Cellular distribution of **14a** in A2780 cancer cells after 6 h incubation at 37 °C (left, transmitted light; right, **14a** fluorescence).

Experimental Section

General Procedures. NMR spectra were recorded on 400 MHz Varian Inova or Bruker Avance spectrometers. Chemical shifts are quoted relative to external TMS (^{1}H) or 85% H_3PO_4 (^{31}P); coupling constants are reported in Hz. FAB mass spectra were measured on a Micromass Autospec spectrometer in positive ion mode using NBA as matrix. IR spectra were recorded as KBr or polyethylene disks on a Nicolet Impact 410 or JASCO FTIR (far-IR) spectrometer. Steady-state photoluminescence spectra were recorded on a Jobin-Yvon-Horiba fluorolog FL-3-11 spectrometer using band pathways of 3 nm for both excitation and emission. Elemental analyses were obtained using a LECO CHNS-932 microanalyzer. Epifluorecence microscope images were recorded using de Epifluorescence Zeiss Axiovert 200M microscope with filters: Nikon UV-2E/C DAPI (absortion 325−375 nm, emission 435−485 nm). PTA,[32] DAPTA,[33] and [AuCl(PR′$_3$)][15c,34] were prepared according to literature methods.

Preparation of [Au(C≡CR)(PR′$_3$)] Complexes. To a solution of KOH (0.022 g, 0.385 mmol) in MeOH (ca. 10 mL) containing the alkyne (0.308 mmol) was added [AuCl(PR′$_3$)] (PR′$_3$ = PTA, DAPTA) (0.257 mmol). The mixture was stirred for ca. 20 h, and the precipitate was isolated by filtration, washed with methanol and diethyl ether, and dried in air. Using this method the following complexes were prepared:

[Au(C≡CPh)(PTA)] (1a): 73% yield, yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 4.28 (s, 6H, NCH_2P), 4.48, 4.53 (J_{AB} = 13.3 Hz, 6H, NCH_2N), 7.20−7.31 (m, 3H, *m*- and *p*-Ph), 7.43−7.50 (m, 2H, *o*-Ph) ppm. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$, 25 °C): δ −51.5 ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 400 MHz): δ 52.4 (d, 3C, J = 21.6 Hz, NCH_2P), 63.8 (s, 1C, AuC≡C), 73.3 (d, J = 7.8 Hz, 3C, NCH_2N), 82.7 (s, 1C, AuC≡C), 127.30 (s, 2C, *p*-Ph (CPh$_2$OH)), 128.51 (s, 4C, *o*-Ph (CPh$_2$OH)), 132.4 (s, 4C, *m*-Ph (CPh$_2$OH)) ppm. IR (KBr): 2112 cm^{-1} ν(C≡C). FAB-MS: m/z 456 [M]$^+$. Anal. Calcd (%) for $C_{14}H_{17}AuN_3P$ (455.25): C 36.94, H 3.76, N 9.23. Found: C 36.35, H 3.23, N 9.11

[Au(C≡CPh)(DAPTA)] (1b): 79% yield, yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 2.09 (s, 6H, DAPTA-Me), 3.70 (d, J = 16.2 Hz, 1H, NCH_2P), 4.05 (s, 2H, NCH_2P), 4.10 (d, J = 14.3 Hz, 1H, NCH_2N), 4.32 (d, J = 15.6 Hz, 1H, NCH_2P), 4.73 (d, J = 14.3 Hz, 1H, NCH_2N), 4.80 (dd, J = 15.9, 10.1 Hz, 1H,

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NCH_2P), 4.97 (d, J = 14.1 Hz, 1H, NCH_2N), 5.60 (dd, J = 15.7/7.9 Hz, 1H, NCH_2P), 5.78 (d, J = 14.4 Hz, 1H, NCH_2N), 7.17−7.28 (m, 3H, *m*- and *p*-Ph), 7.32−7.41 (m, 2H, *o*-Ph) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −24.9 ppm. IR (KBr): 2106 cm^{-1} ν(C≡C). FAB-MS: m/z 528 $[M]^+$. Anal. Calcd (%) for $C_{17}H_{21}AuN_3O_2P$ (527.31): C 38.72, H 4.01, N 7.97. Found: C 38.95, H 3.65, N 7.39.

[Au(C≡C-2-NC$_5$H$_4$)(PTA)] (2a): 78% yield, pale yellow solid. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 4.44 (m, 12H, PTA), 7.09 (dd, J = 4.8/1.0 Hz, 1H, NC_5H_4 (H^5)), 7.38 (dd, J = 7.8/1.0 Hz, NC_5H_4 (H^3)), 7.55 (dt, J = 7.6/1.5 Hz, 1H, NC_5H_4 (H^4)), 8.50 (d, J = 4.8 Hz, 1H, NC_5H_4 (H^6)) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −51.8 ppm. IR (KBr): 2105 cm^{-1} ν(C≡C). FAB-MS: m/z 457 $[M]^+$. Anal. Calcd (%) for $C_{13}H_{16}AuN_4P$ (456.23): C 34.22, H 3.53, N 12.28. Found: C 34.55, H 3.75, N 12.50.

[Au(C≡C-2-NC$_5$H$_4$)(DAPTA)] (2b): 63% yield, pale yellow solid. ^1H NMR (400 MHz, dmso-d_6, 25 °C): δ 1.96 (s, 6H, DAPTA-Me), 3.72 (d, J = 16.0 Hz, 1H, NCH_2P), 3.97 (s, 2H, NCH_2P), 4.09 (d, J = 15.1 Hz, 1H, NCH_2N), 4.27 (d, J = 15.8 Hz, 1H, NCH_2P), 4.64 (d, J = 14.1 Hz, 1H, NCH_2N), 4.80 (m, 1H, NCH_2P), 4.91 (d, J = 13.9 Hz, 1H, NCH_2N), 5.38 (dd, J = 15.2/7.4 Hz, 1H, NCH_2P). 5.54 (d, J = 14.2 Hz, 1H, NCH_2N), 7.05 (m, 1H, py-H^5), 7.48 (dd, J = 7.9/1.0 Hz, 1H, py-H^3), 7.63 (dt, J = 5.3/1.3 Hz, 1H, py-H^4), 8.21 (d, J = 5.0 Hz, 1H, py-H^6) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, dmso-d_6, 25 °C): δ −19.3 ppm. IR (KBr): 2114 cm^{-1} ν(C≡C). FAB-MS: m/z 529 $[M]^+$. Anal. Calcd (%) for $C_{16}H_{20}AuN_4O_2P$ (528.3): C 36.38, H 3.82, N 10.61. Found: C 36.18, H 3.67, N 10.22.

[Au(C≡C-2-C$_{10}$H$_6$OMe-6)(PTA)] (3a): 79% yield, yellow solid. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 3.48 (s, 3H, OMe), 4.36 (s, 6H, NCH_2P), 4.45, 4.51 (J_{AB} = 13.1 Hz, 6H, NCH_2N), 7.06 (d, J = 2.3 Hz, 1H, $C_{10}H_6$ (H^5), 7.10 (dd, J = 8.8/2.5 Hz, 1H, $C_{11}H_9O$ (H^7)), 7.49 (dd, J = 8.3/1.5 Hz, 1H, $C_{10}H_6$ (H^3)), 7,63 (t, J = 9.1 Hz, 2H, $C_{10}H_6$ (H^4)(H^8), 7.89 (d, J = 2.3 Hz, 1H, $C_{11}H_9O$ (H^1)) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −51.09 ppm. IR (KBr): 2096 cm^{-1} ν(C≡C). FAB-MS: m/z 535 $[M]^+$. Anal. Calcd (%) for $C_{19}H_{21}AuN_3OP$ (535.3): C 42.63, H 3.95, N 7.85. Found: C 42.30, H 3.67, N 7.49.

[Au(C≡C-2-C$_{10}$H$_6$OMe-6)(DAPTA)] (3b): 82% yield, white solid. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 2.02 (s, 6H, DAPTA-Me), 3.48 (s, 3H, OMe), 3.82 (d, J = 16.1 Hz, 1H, NCH_2P), 3.99 (s, 2H, NCH_2P), 4.03 (d, J = 14.4 Hz, 1H, NCH_2N), 4.17 (d, J = 15.6 Hz, 1H, NCH_2P), 4.31 (d, J = 14.0 Hz, 1H, NCH_2N), 4.51 (dd, J = 15.6/9.7 Hz, 1H, NCH_2P), 4.83 (d, J = 14.0 Hz, 1H, NCH_2N), 5.66 (dd, J = 16.0/7.4 Hz, 1H, NCH_2P), 5.67 (d, J = 14.0 Hz, 1H, NCH_2N), 7.11 (dd, J = 8.8/2.0 Hz, 1H, $C_{10}H_6$ (H^5), 7.18 (s, 1H, $C_{11}H_9O$ (H^7)), 7.64 (d, J = 8.3 Hz, 1H, $C_{10}H_6$ (H^3)) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −22.8 ppm. IR (Nujol): 2095 cm^{-1} ν(C≡C). FAB-MS: m/z 608 $[M]^+$. Anal. Calcd (%) for $C_{22}H_{25}AuN_3O_3P$ (607.39): C 43.50, H 4.15, N 6.92. Found: C 43.29, H 3.95, N 7.01.

[Au(C≡C-3-SC$_4$H$_3$)(PTA)] (4a): 79% yield, white solid. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 4.28 (s, 6H, NCH_2P), 4.43, 4.50 (J_{AB} = 12.9 Hz, 6H, NCH_2N), 6.96 (dd, J = 5.1/1.3 Hz, 1H, SC_4H_3, H^5), 7.38 (dd, J = 2.8/1.1 Hz, 1H, SC_4H_3, H^2), 7.45 (dd, J = 5.1/3.0 Hz, 1H, SC_4H_3, H^4) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −49.06 ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 400 MHz): δ 52.2 (d, 3C, J = 20.3 Hz, NCH_2P), 72.4 (d, J = 7.6 Hz, 3C, NCH_2N), 99.83 (s, 1C, SC_4H_3 (C^3)), 125.78 (s, 2C, SC_4H_3 ((C^2, C^5)), 128.38 (s, 1C, SC_4H_3 (C^4)) ppm. IR (KBr): 2113 cm^{-1} ν(C≡C). FAB-MS: m/z 462 $[M]^+$. Anal. Calcd (%) for $C_{12}H_{15}AuN_3PS$ (461.27): C 31.25, H 3.28, N 9.11. Found: C 31.67, H 3.65, N 9.01.

[Au(C≡C-3-SC$_4$H$_3$)(DAPTA)] (4b): 63% yield, white solid. ^1H NMR (400 MHz, dmso-d_6, 25 °C): δ 2.02 (s, 6H, DAPTA-Me), 3.80 (d, J = 16.1 Hz, 1H, NCH_2P), 3.97 (s, 2H, NCH_2P), 4.03 (d, J = 14.4 Hz, 1H, NCH_2N), 4.17 (d, J = 15.6 Hz, 1H, NCH_2P), 4.30 (d, J = 14.0 Hz, 1H, NCH_2N), 4.52 (d, J = 15.6 Hz, 1H, NCH_2P), 4.82 (d, J = 14.0 Hz, 1H, NCH_2N), 5.46 (dd, J = 16.0/7.4 Hz, 1H, NCH_2P), 5.67 (d, J = 14.0 Hz, 1H, NCH_2N), 7.03 (d, J = 4.8 Hz, 1H, SC_4H_3, H^5), 7.34 (s, 1H, SC_4H_3, H^2), 7.36−7.38 (m, 1H, SC_4H_3, H^4) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, dmso-d_6, 25 °C): δ −19.2 ppm. IR (Nujol): 2095 cm^{-1} ν(C≡C). FAB-MS: m/z 534 $[M]^+$. Anal. Calcd (%) for $C_{15}H_{19}AuN_3O_2PS$ (533.3): C 33.78, H 3.59, N 7.88. Found: C 33.11, H 2.95, N 7.72.

[Au(C≡C-5-C$_3$H$_2$MeN$_2$-1)(PTA)] (5a): 82% yield, white solid. ^1H NMR (400 MHz, dmso-d_6, 25 °C): δ 3.53 (s, 3H, NCH_3), 4.29 (s, 6H, NCH_2P), 4.44, 4.51 (J_{AB} = 13.1 Hz, 3H, NCH_2N), 6.89 (s, 1H, $N_2C_4H_5$ (H^4)), 7.53 (s, 1H, $N_2C_4H_5$ (H^2)) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, dmso-d_6, 25 °C): δ −49.3 ppm. IR (Nujol): 2110 cm^{-1} ν(C≡C). FAB-MS: m/z 460 $[M]^+$. Anal. Calcd (%) for $C_{12}H_{17}AuN_5P$ (459.24): C 31.38, H 3.73, N 15.25. Found: C 31.50, H 3.95, N 15.60.

[Au(C≡C-5-C$_3$H$_2$MeN$_2$-1)(DAPTA)] (5b): 80% yield, white solid. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 1.97 (s, 6H, DAPTA-Me), 3.63 (s, 3H, NCH_3), 4.17 (d, J = 16.1 Hz, 1H, NCH_2P), 4.21 (s, 2H, NCH_2P), 4.52 (d, J = 14.4 Hz, 1H, NCH_2N), 4.61 (d, J = 15.6 Hz, 1H, NCH_2P), 4.90 (s, 1H, NCH_2N), 4.95 (s, 1H, NCH_2P), 5.01 (d, J = 14.0 Hz, 1H, NCH_2N), 5.43 (s, 1H, NCH_2P), 5.53 (d, J = 14.0 Hz, 1H, NCH_2N), 6.99 (s, 1H, $N_2C_4H_5$ (H^2)), 7.49 (s, 1H, $N_2C_4H_5$ (H^4)) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −25.3 ppm. IR (Nujol): 2110 cm^{-1} ν(C≡C). FAB-MS: m/z 532 $[M]^+$. Anal. Calcd (%) for $C_{15}H_{21}AuN_5O_2P$ (531.11): C 33.91, H 3.98, N 13.18. Found: C 33.94, H 3.30, N 13.26.

[Au{C≡C(C$_4$H$_9$)}(PTA)] (6a): 73% yield, white solid. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 0.88 (t, J = 7.1 Hz, 3H, CH_3), 1.42−1.49 (m, 4H, CH_2), 2.29 (t, J = 7.1 Hz, 2H, $CH_2C{\equiv}C$), 4.22 (s, 6H, NCH_2P), 4.50, 4.57 (J_{AB} = 12.9 Hz, 6H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −49.6 ppm. IR (Nujol): 2103 cm^{-1} ν(C≡C). FAB-MS: m/z 436 $[M]^+$. Anal. Calcd (%) for $C_{12}H_{21}AuN_3P$ (435.26): C 33.11, H 4.86, N 9.65. Found: C 33.50, H 4.75, N 9.30.

[Au{C≡C(C$_4$H$_9$)}(DAPTA)] (6b): 62% yield, white solid. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 0.92 (t, J = 7.1 Hz, 3H, CH_3), 1.46−1.49 (m, 4H, CH_2), 2.21 (s, 6H, DAPTA-Me), 2.35 (t, J = 6.7 Hz, 2H, $CH_2C{\equiv}C$), 3.51 (d, J = 16.1 Hz, 1H, NCH_2P), 3.82 (s, 2H, NCH_2P), 4.02 (d, J = 14.4 Hz, 1H, NCH_2N), 4.17 (d, J = 15.6 Hz, 1H, NCH_2P), 4.30 (d, J = 14.0 Hz, 1H, NCH_2N), 4.51 (d, J = 15.6 Hz 1H, NCH_2P), 4.82 (d, J = 14.0 Hz, 1H, NCH_2N), 5.66 (dd, J = 16.0/7.4 Hz, 1H, NCH_2P), 5.82 (d, J = 14.0 Hz, 1H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −21.5 ppm. IR (Nujol): 2096 cm^{-1} ν(C≡C). FAB-MS: m/z 508 $[M]^+$. Anal. Calcd (%) for $C_{15}H_{25}AuN_3O_2P$ (507.32): 35.51, H 4.97, N 8.28. Found: C 35.46, H 4.40, N 8.10.

[Au(C≡C^{t}Bu)(PTA)] (7a): 77% yield, yellow solid. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 1.24 (s, 9 H, CH_3), 4.15 (s, 6H, NCH_2P), 4.47, 4.55 (J_{AB} = 13.1 Hz, 6H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −48.8 ppm. $^{13}C\{^1H\}$ RMN ($CDCl_3$, 400 MHz): δ 29.07 (s, 1C, CCH_3), 32.44 (s, 3C, CH_3), 51.8 (d, 3C, J = 20.6 Hz, NCH_2P), 72.6 (d, J = 7.6 Hz, 3C, NCH_2N) ppm. IR (Nujol): 2104 cm^{-1} ν(C≡C). FAB-MS: m/z 436 $[M]^+$. Anal. Calcd (%) for $C_{12}H_{21}AuN_3P$ (435.26): C 33.11, H 4.86, N 9.65. Found: C 33.50, H 4.75, N 9.30.

[Au(C≡C^{t}Bu)(DAPTA)] (7b): 82% yield, yellow solid. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 1.30 (s, 9H, CH_3), 2.11 (s, 6H, DAPTA-Me), 3.47 (d, J = 16.1 Hz, 1H, NCH_2P), 3.77 (s, 2H, NCH_2P), 4.06 (d, J = 14.3 Hz, 1H, NCH_2N), 4.10 (s, 1H, NCH_2P), 4.53 (s, 1H, NCH_2N), 4.63 (d, J = 15.9 Hz, 1H, NCH_2P), 4.94 (d, J = 14.3 Hz, 1H, NCH_2N), 5.55 (dd, J = 15.6/7.7 Hz, 1H, NCH_2P), 5.78 (d, J = 14.3 Hz, 1H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −21.3 ppm. IR (Nujol): 2104 cm^{-1} ν(C≡C). FAB-MS: m/z 508 $[M]^+$, 933 [M + (AuDAPTA)]$^+$, 655 $[Au(DAPTA)_2]^+$. Anal. Calcd (%) for $C_{15}H_{25}AuN_3O_2P$ (507.32): C 35.51, H 4.97, N 8.28. Found: C 35.26, H 5.18, N 7.96.

[Au(C≡CCH$_2$OH)(DAPTA)] (8b): 72% yield, white solid. ^1H NMR (400 MHz, D_2O, 25 °C): δ 2.08 (s, 6H, DAPTA-Me), 3.83 (d, J = 15.5 Hz, 1H, NCH_2P), 3.92 (s, 2H, CH_2), 4.19 (s, 2H,

NCH_2P), 4.25 (d, J = 14.1 Hz, 1H, NCH_2N), 4.33 (d, J = 15.6 Hz, 1H, NCH_2P), 4.73 (d, J = 14.1 Hz, 1H, NCH_2N), 4.83 (dd, J = 15.9/10.1 Hz, 1H, NCH_2P), 5.08 (d, J = 14.1 Hz, 1H, NCH_2N), 5.44 (dd, J = 15.7/7.9 Hz, 1H, NCH_2P), 5.59 (d, J = 14.3 Hz, 1H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, D_2O, 25 °C): δ −17.6 ppm. IR (Nujol): 2089 cm^{-1} ν(C≡C). FAB-MS: m/z 482 $[M]^+$, 678 $[M + Au]^+$, 426 $[Au(DAPTA)]^+$, 907 $[M + Au(DAPTA)]^+$. Anal. Calcd (%) for $C_{12}H_{19}AuN_3O_3P$ (481.24): C 29.95, H 3.98, N 8.73. Found: C 30.2, H 4.13, N 8.82.

[Au(C≡CC(CH$_3$)$_2$OH)(DAPTA)] (9b): 70% yield, white solid. ^{1}H NMR (400 MHz, D_2O, 25 °C): δ 1.52 (s, 6H, CH_3), 2.15 (s, 6 H, DAPTA-Me), 3.84 (d, J = 15.3 Hz, 1H, NCH_2P), 4.10 (s, 2H, NCH_2P), 4.32 (d, J = 14.1 Hz, 1H, NCH_2N), 4.40 (d, J = 15.6 Hz, 1H, NCH_2P), 4.83 (d, J = 14.1 Hz, 1H, NCH_2N), 4.95 (dd, J = 15.9/10.1 Hz, 1H, NCH_2P), 5.10 (d, J = 14.2 Hz, 1H, NCH_2N), 5.43 (dd, J = 15.6/7.9 Hz, 1H, NCH_2P), 5.67 (d, J = 14.2 Hz, 1H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, D_2O, 25 °C): δ −17.0 ppm. IR (Nujol): 2090 cm^{-1} ν(C≡C). FAB-MS: m/z 510 $[M]^+$, 836 $[M + Au(DAPTA)]^+$. Anal. Calcd (%) for $C_{14}H_{23}AuN_3O_3P$ (509.29): C 33.02, H 4.55, N 8.25. Found: C 34.01, H 4.68, N 8.58.

[Au(C≡CC(Ph)$_2$OH)(DAPTA)] (10b): 62% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 1.91 (s, 6H, DAPTA-Me), 3.65 (d, J = 15.4 Hz, 1H, NCH_2P), 3.80 (s, 2H, NCH_2P), 4.05 (d, J = 14.1 Hz, 1H, NCH_2N), 4.45 (d, J = 15.6 Hz, 1H, NCH_2P), 4.65 (s, 1H, NCH_2N), 4.80 (s, 1H, NCH_2P), 5.4 (d, J = 14.2 Hz, 1H, NCH_2N), 5.53 (s, 1H, NCH_2P), 5.63 (s, 1H, NCH_2N), 7.17−7.47 (m, 6H, *m*- and *p*-Ph), 7.61−7.73 (m, 2H, *o*-Ph), 7.73−7.92 (m, 2H, *o*-, *m*-, and *p*-PPh) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −23.4 ppm. IR (Nujol): 2115 cm^{-1} ν(C≡C). FAB-MS: m/z 634 $[M]^+$, 545 $[M - OH]^+$, 655 $[Au(DAPTA)_2]^+$, 426 $[Au(DAPTA)]^+$. Anal. Calcd (%) for $C_{24}H_{27}AuN_3O_3P$ (633.43): C 45.51, H 4.30, N 6.63. Found: C 45.08, H 4.01, N 6.82.

[Au(C≡CC(CH$_2$CH$_3$)(CH$_3$)(OH))(DAPTA)] (11b): 85% yield, white solid. ^{1}H NMR (400 MHz, D_2O, 25 °C): δ 1.05 (t, J = 7.2 Hz, 3H, CH_3CH$_2$), 1.47 (s, 3H, CH_3), 1.56−1.71 (m, 2H, CH$_3$-CH_2), 2.12 (s, 6H, DAPTA-Me), 3.85 (d, J = 15.3 Hz, 1H, NCH_2P), 4.05 (s, 2H, NCH_2P), 4.27 (d, J = 14.2 Hz, 1H, NCH_2N), 4.39 (d, J = 15.6 Hz, 1H, NCH_2P), 4.78 (s, 1H, NCH_2N), 4.90 (s, 1H, NCH_2P), 5.15 (d, J = 14.2 Hz, 1H, NCH_2N), 5.45 (s, 1H, NCH_2P), 5.65 (s, 1H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, D_2O, 25 °C): δ −23.2 ppm. IR (Nujol): 2019 cm^{-1} ν(C≡C). FAB-MS: m/z 524 $[M]^+$, 507 $[M - OH]^+$. Anal. Calcd (%) for $C_{15}H_{25}AuN_3O_3P$ (523.32): C 34.43, H 4.82, N 8.03. Found: C 34.92, H 5.02, N 8.53.

[Au(C≡CCH$_2$NH$_2$)(PTA)] (12a): 79% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 2.22 (s, 2H, NH_2), 3.48 (s, 2H, CH_2), 4.36 (s, 6H, CH_2P), 4.40 (J_{AB} = 13.1 Hz, 3H, NCH_2N), 4.50 (J = 13.1 Hz, 6H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −12.5 ppm. IR (ATR): 3284 ν(N−H), 2164 ν(C≡C) cm^{-1}. FAB-MS: m/z 409 $[M]^+$, 763 $[M + AuPTA]^+$. Anal. Calcd (%) for $C_9H_{16}AuN_4P$ (408.19): C 26.48, H 3.95, N 13.73. Found: C 26.80, H 3.75, N 14.20.

[Au(C≡CCH$_2$NH$_2$)(DAPTA)] (12b): 82% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 2.08 (s, 6 H, DAPTA-Me), 3.42 (s, 2H, CH_2), 3.83 (d, J = 15.5 Hz, 1H, NCH_2P), 3.92 (s, 2H, CH$_2$), 4.19 (s, 2H, NCH_2P), 4.25 (d, J = 14.1 Hz, 1H, NCH_2N), 4.33 (d, J = 15.6 Hz, 1H, NCH_2P), 4.73 (d, J = 14.1 Hz, 1H, NCH_2N), 4.83 (dd, J = 15.9/10.1 Hz, 1H, NCH_2P), 5.08 (d, J = 14.1 Hz, 1H, NCH_2N), 5.44 (dd, J = 15.7/7.9 Hz, 1H, NCH_2P), 5.59 (d, J = 14.3 Hz, 1H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −10.2 ppm. IR (Nujol): 3359 ν(N−H), 2163 cm^{-1} ν(C≡C). FAB-MS: m/z 482 $[M]^+$, 678 $[M - Au]^+$, 907 $[M - AuDAPTA]^+$, 426 $[AuDAPTA]^+$, 655 $[Au(DAPTA)_2]^+$. Anal. Calcd (%) for $C_{12}H_{20}AuN_4O_2P$ (480.25): C 30.01, H 4.20, N 11.67. Found: C 30.22, H 4.13, N 11.82.

[Au((C≡CC(CH$_2$)(N(CH$_3$)$_2$)(PTA)] (13a): 75% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 2.28 (s, 6H, N(CH_3)$_2$), 3.38 (s, 2H, CH_2), 4.19 (s, 6H, NCH_2P), 4.49, 4.51 (J_{AB} = 13.1 Hz, 6H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −49.5 ppm. IR (KBr): 3207 ν(N−H), 2132 cm^{-1} ν(C≡C). FAB-MS: m/z 437 $[M]^+$, 791 $[M + AuPTA]^+$. Anal. Calcd (%) for $C_{11}H_{20}AuN_4P$ (436.24): C 30.29, H 4.62, N 12.84. Found: C 30.59, H 4.25, N 12.30.

[Au((C≡CC(CH$_2$)(N(CH$_3$)$_2$)(DAPTA)] (13b): 62% yield, white solid. ^{1}H NMR (400 MHz, MeOD, 25 °C): δ 2.12 (s, 6H, DAPTA-Me), 2.30 (s, 6H, N(CH_3)$_2$), 3.85 (d, J = 15.4 Hz, 1H, NCH_2P), 4.05 (s, 2H, NCH_2P), 4.32 (d, J = 14.1 Hz, 1H, NCH_2N), 4.40 (d, J = 15.6 Hz, 1H, NCH_2P), 4.83 (d, J = 14.1 Hz, 1H, NCH_2N), 4.95 (dd, J = 15.9/10.1 Hz, 1H, NCH_2P), 5.10 (d, J = 14.2 Hz, 1H, NCH_2N), 5.43 (dd, J = 15.6/7.9 Hz, 1H, NCH_2P), 5.67 (d, J = 14.2 Hz, 1H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, MeOD, 25 °C): δ −46.0 ppm. IR (Nujol): 3424 ν(N−H), 2100 cm^{-1} ν(C≡C). FAB-MS: m/z 510 $[M]^+$, 936 $[M + AuDAPTA]^+$, 426 $[AuDAPTA]^+$, 655 $[Au(DAPTA)_2]^+$. Anal. Calcd (%) for $C_{14}H_{24}AuN_4O_2P$ (508.31): C 32.91, H 4.76, N 11.02. Found: C 32.90, H 4.67, N 10.58.

N[Au(C≡CCH$_2$)(PTA)]$_3$ (14a): 69% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 3.48 (s, 6H, CH_2), 4.36 (s, 18H, CH_2P), 4.40, 4.50 (J_{AB} = 13.1 Hz, 18H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −50.2 ppm. IR (ATR): 2095 ν(C≡C) cm^{-1}. FAB-MS: m/z 1190 $[M]^+$, 354 $[AuPTA]^+$, 511 $[Au(PTA)_2]^+$. Anal. Calcd (%) for $C_{27}H_{42}Au_3N_{10}P_3$ (1190.51): C 27.24, H 3.56, N 11.77. Found: C 27.59, H 3.35, N 12.00.

N[Au(C≡CCH$_2$)(DAPTA)]$_3$ (14b): 72% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 2.15 (s, 18H, DAPTA-Me), 3.52 (s, 6H, CH_2), 3.85 (d, J = 15.4 Hz, 3H, NCH_2P), 4.10 (s, 6H, NCH_2P), 4.32 (d, J = 14.1 Hz, 3H, NCH_2N), 4.40 (d, J = 15.6 Hz, 3H, NCH_2P), 4.83 (d, J = 14.1 Hz, 3H, NCH_2N), 4.95 (dd, J = 15.9/10.1 Hz, 3H, NCH_2P), 5.10 (d, J = 14.2 Hz, 3H, NCH_2N), 5.43 (dd, J = 15.6/7.9 Hz, 3H, NCH_2P), 5.67 (d, J = 14.2 Hz, 3H, NCH_2N) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −47.0 ppm. IR (ATR): 2117 ν(C≡C) cm^{-1}. FAB-MS: m/z 1422 $[M]^+$, 426 $[AuDAPTA]^+$, 655 $[Au(DAPTA)_2]^+$. Anal. Calcd (%) for $C_{37}H_{56}Au_3N_{10}O_6P_3$ (1406.70): C 29.13, H 3.73, N 10.79. Found: C 29.24, H 3.77, N 9.58.

Preparation of [Au$_2$(C≡CRC≡C)(PR′$_3$)$_2$] Complexes. To a solution of KOH (0.022 g, 0.385 mmol) in MeOH (ca. 10 mL) containing the alkyne (0.308 mmol) was added [AuCl(PR′$_3$)] (PR′$_3$ = PTA, DAPTA) (0.257 mmol). After stirring the mixture for ca. 20 h the precipitate was isolated by filtration, washed with methanol and diethyl ether, and dried in air.

[Au$_2${(C≡C)$_2$-1,4-C$_6$H$_4$)}(PTA)$_2$] (15a): 79% yield, yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 4.14 (s, 12H, NCH_2P), 4.49, 4.58 (J_{AB} = 13.1 Hz, 12H, NCH_2N), 7.17−7.40 (m, 4H, Ph) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −51.9 ppm. IR (Nujol): 2094 cm^{-1} ν(C≡C). FAB-MS: m/z 833 $[M]^+$. Anal. Calcd (%) for $C_{22}H_{28}Au_2N_6P_2$ (832.38): C 31.74, H 3.39, N 10.10. Found: C 31.29, H 3.79, N 10.18.

[Au$_2${(C≡C)$_2$-1,4-C$_6$H$_4$)}(DAPTA)$_2$] (15b): 68% yield, yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 2.11 (s, 12H, DAPTA-Me), 3.15 (d, J = 15.4 Hz, 2H, NCH_2P), 3.49 (s, 2H, NCH_2P), 4.08 (d, J = 13.7 Hz, 2H, NCH_2N), 4.12 (d, J = 15.6 Hz, 2H, NCH_2P), 4.73 (d, J = 14.3 Hz, 2H, NCH_2N), 4.80 (dd, J = 15.9/10.1 Hz, 2H, NCH_2P), 4.97 (d, J = 14.1 Hz, 2H, NCH_2N), 5.60 (dd, J = 15.7/7.9 Hz, 2H, NCH_2P), 5.78 (d, J = 14.4 Hz, 2H, NCH_2N), 7.18−7.29 (m, 3H, *m*- and *p*-Ph), 7.31−7.40 (m, 4H, *Ph*) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 25 °C): δ −21.9 ppm. IR (KBr): 2098 cm^{-1} ν(C≡C). FAB-MS: m/z 977 $[M]^+$. Anal. Calcd (%) for $C_{28}H_{36}Au_2N_6O_4P_2$ (976.50): C 34.44, H 3.72, N 8.61. Found: C 34.09, H 3.69, N 8.18.

[Au$_2${(C≡C)$_2$-1,3-C$_6$H$_4$}(PTA)$_2$] (16a): 69% yield, yellow solid. ^{1}H NMR (400 MHz, dmso-d_6, 25 °C): δ 4.36 (s, 12H, NCH_2P), 4.46, 4.59 (J_{AB} = 13.1 Hz, 12H, NCH_2N), 7.13−7.36 (m, 4H, *m*- and *p*-Ph) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, dmso-d_6, 25 °C): δ −49.3 ppm. IR (Nujol): 2109 cm^{-1} ν(C≡C). FAB-MS: m/z 833 $[M]^+$. Anal. Calcd (%) for $C_{22}H_{28}Au_2N_6P_2$ (832.38): C 31.74, H 3.39, N 10.10. Found: C 31.18, H 3.89, N 10.59.

[Au_2{(C≡C)$_2$-1,3-C_6H_4)}(DAPTA)$_2$] (16b): 69% yield, yellow solid. ^{1}H NMR (400 MHz, dmso-d_6, 25 °C): δ 2.01 (s, 12H, DAPTA-Me), 3.10 (d, J = 15.4 Hz, 2H, NCH_2P), 3.46 (s, 2H, NCH_2P), 4.11 (d, J = 13.7 Hz, 2H, NCH_2N), 4.15 (d, J = 15.6 Hz, 2H, NCH_2P), 4.72 (d, J = 14.3 Hz, 2H, NCH_2N), 4.83 (dd, J = 15.9/10.1 Hz, 2H, NCH_2P), 4.95 (d, J = 14.1 Hz, 2H, NCH_2N), 5.61 (dd, J = 15.7/7.9 Hz, 2H, NCH_2P), 5.78 (d, J = 14.4 Hz, 2H, NCH_2N), 7.03−7.16 (m, 4H, *Ph*) ppm. ^{31}P{^{1}H} NMR (162 MHz, dmso-d_6, 25 °C): δ −19.2 ppm. ^{13}C{^{1}H} RMN (dmso-d_6, 400 MHz): δ 51.9 (d, 3C, J = 20.7 Hz, NCH_2P), 72.8 (d, J = 7.3 Hz, 3C, NCH_2N), 126.20 (s, 2C, C_6H_4 (C^1, C^3)), 129.10 (s, 1C, C_6H_4 (C^5)), 131.60 (s, 2C, C_6H_4 (C^4, C^6)), 136.47 (s, 1C, C_6H_4 (C^2)) ppm. IR (Nujol): 2098 cm^{-1} ν(C≡C). FAB-MS: m/z 977 [M]$^+$. Anal. Calcd (%) for $C_{28}H_{36}Au_2N_6O_4P_2$ (976.50): C 34.44, H 3.72, N 8.61. Found: C 34.64, H 3.70, N 7.98.

[(PTA)AuC≡C-C≡CAu(PTA)] (17a): 82% yield, white solid. ^{1}H NMR (400 MHz, dmso-d_6, 25 °C): δ 4.35 (s, 12H, NCH_2P), 4.48, 4.60 (J_{AB} = 13.1 Hz, 12H, NCH_2N). ^{31}P{^{1}H} NMR (162 MHz, dmso-d_6, 25 °C): δ −47.3 ppm. IR (Nujol): 2081 cm^{-1} ν(C≡C). FAB-MS: m/z 757 [M]$^+$. Anal. Calcd (%) for $C_{16}H_{24}Au_2N_6P_2$ (756.28): C 25.41, H 3.20, N 11.11. Found: C 25.50, H 3.76, N 11.30.

[(PTA)AuC≡C-C≡CAu(DAPTA)] (17b): 87% yield, yellow solid. ^{1}H NMR (400 MHz, dmso-d_6, 25 °C): δ 2.12 (s, 12H, DAPTA-Me), 3.68 (d, J = 15.3 Hz, 2H, NCH_2P), 3.97 (s, 2H, NCH_2P), 4.10 (d, J = 13.7 Hz, 2H, NCH_2N), 4.22 (d, J = 15.6 Hz, 2H, NCH_2P), 4.62 (d, J = 14.3 Hz, 2H, NCH_2N), 4.80 (dd, J = 15.9/10.1 Hz, 2H, NCH_2P), 4.90 (d, J = 14.1 Hz, 2H, NCH_2N), 5.31 (dd, J = 15.7/7.9 Hz, 2H, NCH_2P), 5.50 (d, J = 14.4 Hz, 2H, NCH_2N) ppm. ^{31}P{^{1}H} NMR (162 MHz, dmso-d_6, 25 °C): δ −19.2 ppm. IR (Nujol): 2099 cm^{-1} ν(C≡C). FAB-MS: m/z 901 [M]$^+$. Anal. Calcd (%) for $C_{22}H_{32}Au_2N_6O_4P_2$ (900.41): C 29.35, H 3.58, N 9.33. Found: C 28.89, H 3.70, N 9.98.

Crystallographic Studies. Crystals of **4a** suitable for X-ray diffraction were obtained by slow diffusion of diethyl ether into an ethanolic solution of the compound. The crystal was mounted on a glass fiber with inert oil and centered in a Bruker-Smart CCD diffractometer with graphite-monochromated Mo Kα (λ = 0.7107 Å) radiation for data collection. The diffraction frames were integrated using the SAINT[35] package and corrected for absorption with SADABS.[36] The structure was solved by direct methods using SHELXS.[37] Full-matrix least-squares refinement was carried out using SHELXL[38] minimizing $w(F_o^{2*} - F_c^2)^2$. Hydrogen atoms were included using a riding model. Disorder was observed in the thiophene units of both independent molecules. Restraints were applied to both components of both groups, in an attempt to model the resulting average electron density without losing chemically reasonable geometrical parameters. The complete crystallographic data have been deposited with the Cambridge Crystallographic Data Centre [CCDC 773431]. Principle crystal and refinement data: empirical formula, $C_{24}H_{30}Au_2N_6P_2S_2$; formula weight, 922.53; crystal system and space group, monoclinic, $P_2(1)/n$; a = 6.215-(5) Å, b = 18.705(5) Å, c = 22.755(5) Å, β = 90.069(5)°; volume, 2645(2) Å^3; Z, 4; density (calculated), 2.316 Mg/m^3; absorption coefficient, 11.386 mm^{-1}; theta range for data collection, 1.79° to 28.33°; reflections collected, 17 697; independent reflections, 6320 [R(int) = 0.0491]; $R_1(F^2 > 2\sigma(F^2))$, 0.0354; wR_2(all data), 0.0678; S(all data), 0.939.

Cells and Cell Treatment. Human A2780 and A2780cisR cells were obtained from the European Centre of Cell Cultures (ECACC, Salisbury, UK). All cell culture reagents were obtained from Gibco-BRL (Basel, Switzerland). Cells were grown in RPMI 1640 medium containing 10% fetal calf serum (FCS) and antibiotics. Stock solutions of the complexes (16 mM in DMSO) were diluted in complete medium to the required concentration. DMSO at comparable concentrations did not show any effects on cell cytotoxicity.

Determination of Cytotoxicity. Cells were grown in 96-well cell culture plates (Corning, NY) at a density of ca. 25 × 10^3 cells per well. The culture medium was replaced with fresh medium containing complexes **1b**, **4a/b**, **8a/b**, and **14a/b** at various concentrations with an exposure time of 72 h. Thereafter, the medium was replaced by fresh medium, and cell survival was measured using the MTT test as previously described. Briefly, 3-(4,5-dimethyl-2-thiazoyl)-2,5-diphenyltetrazolium bromide (MTT, Merck) was added at 250 μg/mL, and incubation was continued for 2 h. Then the cell culture supernatants were removed, the cell layer was dissolved in DMSO, and absorbance at 540 nm was measured in a 96-well multiwell plate reader (iEMS Reader MF, Labsystems, Bioconcept, Switzerland) and compared to the values of control cells incubated in the absence of complexes. Experiments were conducted in quadruplicate wells and repeated at least twice.

Fluorescence Microscopy Studies. Cells were grown for 24 h on chambered cover glass slides (Lab-Tek, NUNC) in complete medium at a density of ca. 1 × 10^4 and then exposed to the appropriate compounds at 50% of the IC_{50} concentrations at 37 °C in the dark. Excess complex was removed with PBS, and the cells were fixed with 4% formaldehyde in PBS for 30 min in the dark and rinsed twice with PBS before observation. Cells were mounted in PBS before being observed by fluorescence microscopy using a Zeiss Axiovert 200M microscope equipped with a 40× air immersion objective. Filters used for excitation and detection of DAPI were 345 and 448 nm, respectively. Fluorescence signal intensities were evaluated using MetaMorph software.

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Supporting Information Available: This material is available free of charge via the Internet at http://pubs.acs.org.

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