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Diamino Carbenes

Synthesis of Bioactive *N*-Acyclic Gold(I) and Gold(III) Diamino Carbenes with Different Ancillary Ligands

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Dedicated to Professor Cristian Silvestru on the occasion of his 65th birthday.

Abstract: A series of gold(I) and gold(III) *N*-acyclic diamino carbene (ADC) complexes with different ancillary ligands have been synthesized. The chloride carbene derivatives [Au{C(NHR)(NHCH$_2$py)}Cl] (R = Cy, R = naphthyl, R = xylyl) have been obtained by reaction of 2-picolylamine with the corresponding [AuCl(CNR)]. The gold(I) thiolate derivatives [Au{C(NHR)(NHCH$_2$py)}(Spy)] were prepared by reaction of the chlorido complexes with 2-mercaptopyridine (2-HSpy) in presence of potassium carbonate. The phosphane derivative [Au(pyCH$_2$NH$_2$)(PPh$_3$)](OTf) was obtained by reaction of freshly prepared [Au(OTf)(PPh$_3$)] with 2-picolylamine. The phosphane-carbene complexes [Au{C(NHR)(NHCH$_2$py}(PPh$_3$)](OTf) were obtained from the reaction of picolylamino species with the isocyanide. The gold(III) derivative *cis*-[Au(C$_6$F$_5$)$_2$(pyCH$_2$NH$_2$)](ClO$_4$) was obtained by the reaction of 2-picolylamine with freshly [Au(C$_6$F$_5$)$_2$(Et$_2$O)$_2$](ClO$_4$). The reaction of the former with CNCy led to complex *cis*-[Au(C$_6$F$_5$)$_2${C(NHCy)(NHCH$_2$py)}]ClO$_4$ by a nucleophilic attack of the isocyanide to the amine ligand, thus producing a bidentate C,N acyclic carbene ligand. Cytotoxic studies against the tumor human cell lines Jurkat (T-cell leukaemia), MiaPaca2 (pancreatic carcinoma), A549 (lung carcinoma) and MDA-MB-231 (breast carcinoma) showed moderate to good cytotoxic activity for some of the complexes.

Introduction

Isocyanides are an important class of compounds widely used as building blocks in organic chemistry. They can react with both electrophiles and nucleophiles. Coordination of isocyanides to a metal center greatly enhances their electrophilic character. Isocyanide gold(I) derivatives show in general an important electrophilic character through the carbon atom of the isocyanide group. It permits the synthesis of acyclic diamino carbene complexes by reaction with amines. In general, the coordination of the isocyanide group to metals facilitates the addition of nucleophiles to the carbon atom of the isocyanides.[1] The gold(I) acyclic diamine carbene complexes (ADCs) are showing interesting properties, especially in catalysis, as reflects the high volume of papers published about that in the last years.[2] These acyclic carbenes are good σ-*donor* ligands with attractive conformational flexibility and a wide N-$C_{carbene}$–N angle that enhances their catalytic possibilities.[1,2ab,3] On the other hand, the related *N*-heterocyclic gold(I) carbenes (NHCs) have been thoroughly investigated in medicine, especially as antitumor agents showing several of them promising activity.[4] In contrast, as far as we are aware, only some scarcely examples of the antitumor activity has been reported about acyclic gold(I) and gold(III) carbene derivatives.[5] The search in cancer therapy of new alternatives to platinum-based drugs, which present serious side effects and generation of resistance,[6] has conducted to the chemical community to find new metallic drugs with different biological behavior and different biological targets to the platinum chemotherapeutics. Among them, gold derivatives are now thoroughly investigated, especially after the discovery of the great activity of *auranofin* against rheumatoid arthritis.[7] Taking into account all these facts, and the great stability of ADC gold derivatives it is surprising that this type of complexes has been until now neglected in the literature. Additionally, the presence of different ancillary ligands such as phosphanes or thiolates may greatly enhance antitumor activity. This is in agreement with the existence of many complexes bearing phosphane and/or thiolate groups as auxiliary ligands, as particular examples of the wide group of gold complexes with antitumor activity.[8]

With this idea in mind, we have synthesized a series of neutral or cationic acyclic diamino carbene gold(I) and gold(III) derivatives. Chloride, thiolate or triphenylphosphane ligands complete the expected di-coordinated linear geometry around the gold metal atom in the final complexes. Two pentafluorophenyl groups and a new bidentate C,N *N*-acyclic diamino carbene ligand, complete the square-planar geometry in the gold(III) derivative. The in vitro antitumor activity of some of them has been tested against the tumor human cell lines Jurkat (T-cell leukaemia), MiaPaca2 (pancreatic carcinoma), A549 (lung carci-

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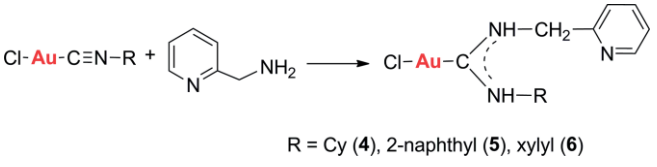
noma) and MDA-MB- 231 (breast carcinoma) and compared the results with those of cisplatin.

Results and Discussion

Synthesis and Characterization

All the complexes synthesized are air- and moisture-stable white solids. They have been characterized by means of IR, NMR spectroscopy and mass spectrometry. Assignments of the ^{1}H NMR and ^{13}C NMR signals were made on the basis of 2D ^{1}H COSY and HSQC spectra. Complete spectroscopic information of the complexes has been collected in the Experimental Section.

The isocyanide complexes [AuCl(CNR)] (R = Cy (**1**), 2-naphthyl (**2**) or xylyl (xylyl = 2,6-dimethylphenyl) (**3**), previously synthesized,[9] were prepared by the reaction of [AuCltht] (tht = tetrahydrothiophene)[10] and an equimolecular amount of the corresponding isocyanide CNR. Spectroscopic information of complexes **1–3** is collected in the Experimental Section. The reaction of [AuCl(CNR)] (**1–3**) (R = cyclohexyl (Cy), 2-naphthyl, xylyl) with equimolecular amounts of 2-picolylamine gives complexes **4**–**6**, respectively. The nucleophilic addition of the amine to the carbon center of the isocyanide group produces the formation of the corresponding mononuclear gold(I) acyclic diamino carbenes (Scheme 1).



Scheme 1. Synthesis of chloro-gold(I) ADC complexes **4–6**.

The IR spectra of complexes **4–6** show the characteristic ν(Au–Cl) vibration of a gold(I) atom coordinated to a chloride ligand at 321, 324 or 308 cm^{-1}, respectively, remarkably lower than those present in the chloride gold(I) isocyanide starting materials infrared spectra, in which these signals appear at ca. 350 cm^{-1} (see experimental section). This is in good accordance with the stronger σ *electron donor* properties of carbene than isocyanide ligand. In the ESI$^+$ mass spectra the fragments [M – Cl]$^+$ appear at m/z (%) = 414 (100) (**4**), 458(100) (**5**), 436(100) (**6**).

One characteristic of these *N*-acyclic carbene derivatives is the presence in their solutions at room temperature of conformational isomers or rotamers. It is a consequence of the electronic delocalization along with the C-N bonds of the carbene group, that hinder the rotation around these bonds at room temperature, unless in the NMR time scale (Figure 1).[2g,11]

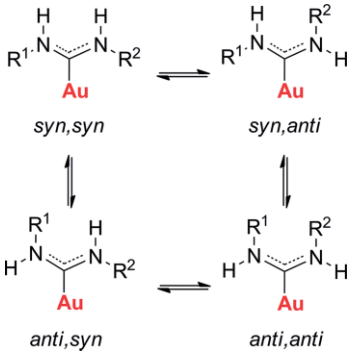
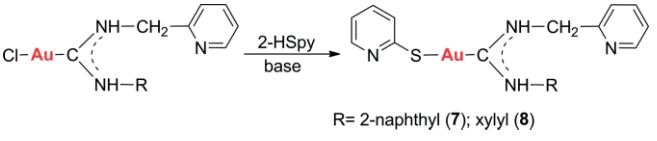


Figure 1. Different structural conformations for ADCs.

In the ^{1}H NMR spectra of complexes **4** and **5**, three and two isomers, respectively, could be identified. The relative ratio of the isomers, **4** (1:0.6:0.2) or **5** (1:0.8), could be quantified with the protons of the CH_2 of the 2-picolylamine group, which appear in a clear region of the spectra. In the ^{1}H NMR spectrum of complex **6,** a major isomer was identified with only a small amount of a second one (Figure 2).

Complexes **7**–**8** (Scheme 2) were synthesized by the reaction between the carbene (**5**, **6**) gold(I) chloride and the thiol 2-mercaptopyridine (2-HSpy) in the presence of potassium carbonate. Infrared spectra of complexes show, among others, one band corresponding to the Au–S vibration at ca. 400 cm^{-1} and the absorptions from NH at ca. 3200 cm^{-1} and 3000 cm^{-1}. In the ESI$^+$ mass spectra the fragments [M + H]$^+$ appear at m/z = 569 (100 %) (**7**), 547 (2 %) (**8**) and [M – py]$^+$ at 463 (100 %) (**8**). The ^{1}H NMR of the ADC derivatives **7** and **8** appeared as a mixture of two and three rotamers, respectively. Integration of



Scheme 2. Synthesis of thiolate-gold(I) ADC complexes **7–8**.

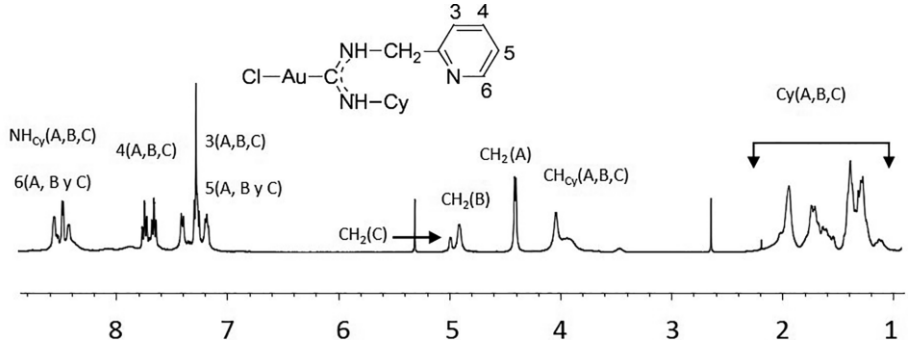
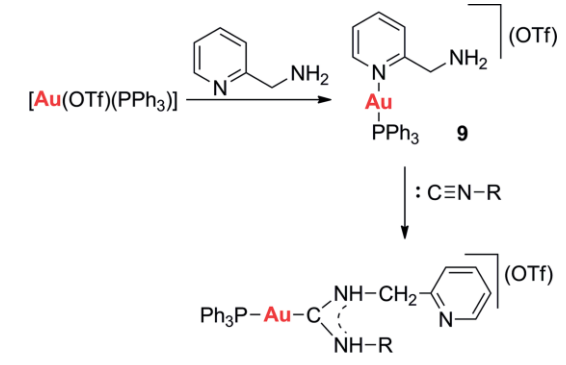


Figure 2. ^{1}H NMR spectrum of complex **4**.

the signals of CH_2 protons gave a relative ratio of isomers of 1:0.7 for **7** and 1:0.2:0.3 for **8**.

With the aim to prepare gold(I) derivatives with carbene and phosphane ligands, we synthesized the precursor complex **9** bearing a phosphane and a pyridylamine ligands (Scheme 3). It has a nucleophilic NH_2 group capable of reacting with isocyanide groups to lead P–Au-$C_{acyclic\text{-}carbene}$ complexes. Complex **9** was synthesized by the reaction of an equimolar amount of 2-picolylamine and freshly prepared [Au(OTf)(PPh_3)]. The coordination through the pyridine nitrogen to the gold atom is proposed. The IR spectrum shows a band corresponding to the amine NH_2 group at 3205 cm^{-1} and the absorptions arising from the trifluoromethanesulfonate anion at 1279, 1251, 1223, 1148 and 1027 cm^{-1}. In the ESI^+ mass spectra the fragment $[M - OTf]^+$ appears at m/z = 567 (100 %). The ^1H NMR spectrum shows the resonances for the 2-picolylamine ligand and the phenyl rings in the appropriate ratio. The $^{31}P\{^1H\}$ NMR spectrum is one singlet at 30.9 ppm.



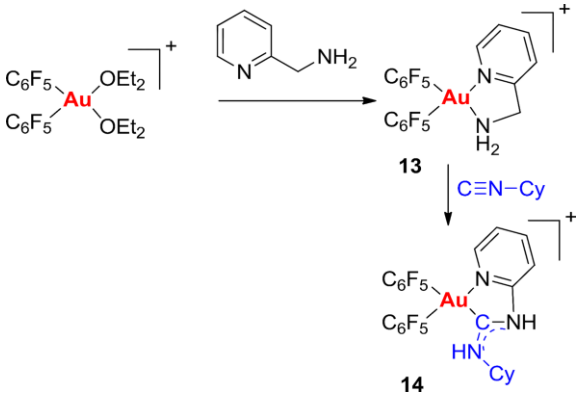
R = Cy (**10**), 2-naphthyl (**11**), xylyl (**12**)

Scheme 3. Synthesis of phosphane-gold(I) ADC complexes **10–12**.

Three carbene triphenylphosphane gold(I) derivatives were synthesized by the reaction of complex **9** with the equimolecular amount of the corresponding isocyanide group CNR (R = Cy (**10**), 2-naphthyl (**11**), xylyl (**12**)) (Scheme 3). Infrared spectra of the complexes display, among others signals, two bands at ca. 3250 and 3050 cm^{-1} corresponding to the NH groups of the carbene N-C-N core. The ESI^+ spectra show the cation molecular peak $[M - OTf]^+$ at m/z = 676 (100 %) (**10**), 720 (100 %) (**11**), 698 (100 %) (**12**).

Two rotamers were identified in the ^1H NMR spectrum of each complex. Again, the relative ratio of isomers in each derivative could be assessed with the CH_2 signals which appear as a doublet by coupling with the NH proton, 1:0.7 (**10**), 1:0.6 (**11**), 1:0.9 (**12**). The $^{31}P\{^1H\}$ NMR spectra of complexes **10** and **12** present a unique broad resonance corresponding to the phosphorus of triphenylphosphane at 40 and 40.5 ppm, respectively; complex **11** showed two thin signals at 39.5 and 39.0 ppm that may be attributed to the rotamers. In all the cases, the chemical shift is higher than that of the starting material, showing the stronger σ *donor* capability of the carbene ligand than 2-picolylamine.

Moreover, two gold(III) derivatives **13** and **14** have been synthesized (Scheme 4). Complex **13** was obtained by the reaction of $[Au(C_6F_5)_2(OEt_2)_2]ClO_4$, prepared in situ, with an equimolecular amount of 2-picolylamine (Scheme 4). The reaction of complex **13**, *cis*-$[Au(C_6F_5)_2$(2-picolylamine)$]ClO_4$, with an equimolecular amount of the isocyanide CNCy gave compound **14** with a bidentate C^N acyclic diamino carbene ligand. IR spectra of the complexes show the absorptions corresponding to the pentafluorophenyl groups at around 1500, 960, 815 and 795 cm^{-1} and those of the ClO_4^- anion at around 1060 and 620 cm^{-1}. Two different pentafluorophenyl groups, with free rotation in the ring, can be identified in the ^{19}F NMR spectra of **13** and **14**. The ^1H NMR spectrum of complex **14** displays the absorptions for the 2-picolylamine and the cyclohexyl groups in an appropriate ratio. The ESI^+ spectra show the cation molecular peak $[M - ClO_4]^+$ at m/z = 639 (100 %) (**13**), 748 (100 %) (**14**).



Scheme 4. Synthesis of gold(III) complexes **13–14**.

Crystal Structural Discussion

The molecular structures of complexes **4**, **6** and **10** (Figure 3) have been confirmed by X-ray diffraction.

Gold(I) complexes **4**, **6** and **10** crystallize in the monoclinic (*C*2/*c*), orthorhombic (Ibca) and monoclinic ($P2_1/n$) systems, respectively. One of the *syn,anti*-diastereomer, in which steric influence of the *N*-substituents is low, crystallizes in all the complexes. Gold(I) atoms are in the almost linear geometry expected for gold(I) derivatives, defined by the $C_{carbene}$ and the chloride (**4**, **6**) or the P of the triphenylphosphane (**10**). The chloride, **4** and **6**, derivatives show aurophilic interactions with Au···Au distances of 3.4085 (7) Å and 3.3631 (6) Å, respectively. Besides, dimers form chains through classical H bonds between the NH amide groups and the pyridine nitrogen atom of different molecules (Figure 4). In **4** the N(2)–H(2)···N(3) [x + 1/2, –y + 2, z] distance is 2.254 Å with an angle of 148.24° and in **6** the N(1)–H(1)···N(3) [–x + 1, –y + 2, –z] distance is 2.149 Å with an angle of 160.02°. Similar intermolecular interactions were found in the related gold(I) carbene derivative [AuCl{C(NEt_2)(NH_2Py-2)}][12] obtained from 2-pyridilisocyanide derivative. There are not aurophilic interactions in complex **10**, probably because of the bulkiness of the PPh_3 group prevents the short distances between the gold atoms. However, the molecules are associated in dimers through H bonds between one NH amide group and the pyridine nitrogen atom of the neighbouring molecule (N(1)–H(1)···N(3) [–x + 1, –y, –z + 1] distance of 2.056 Å, angle of 163.6°).

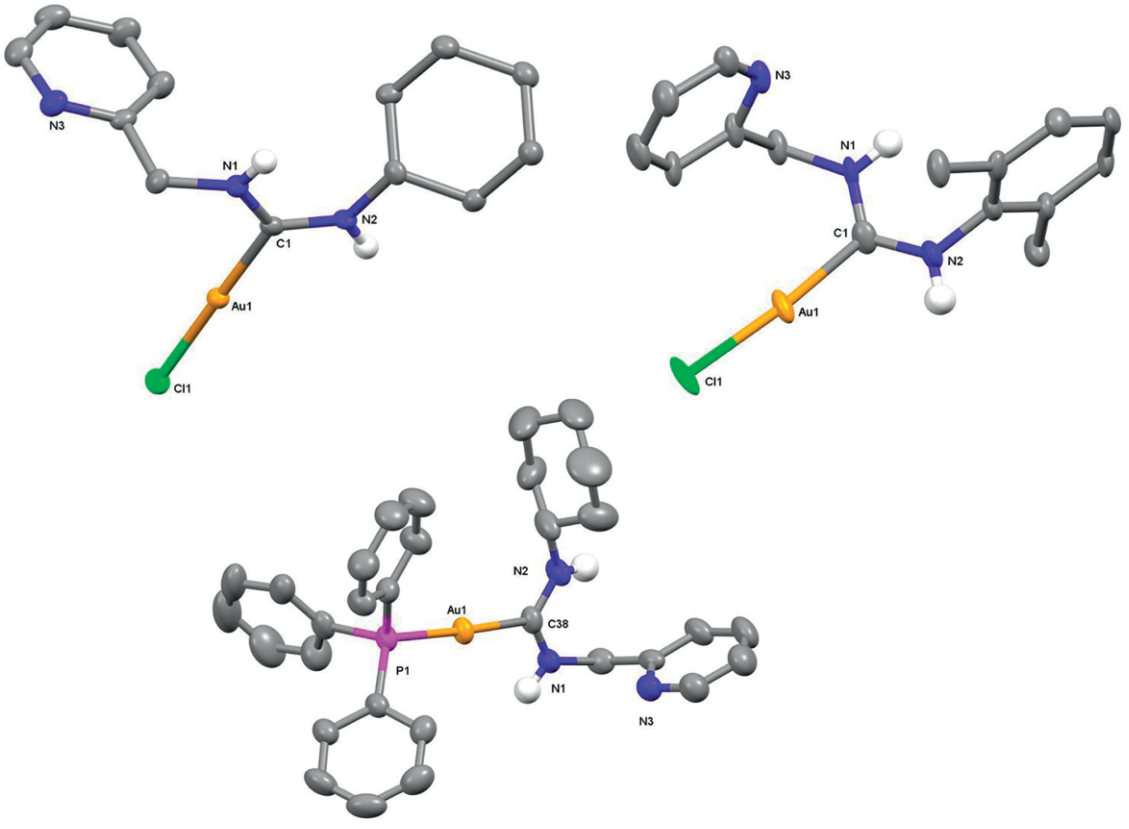


Figure 3. Molecular crystal structures of **4**, **6** and **10** (50 % thermal ellipsoids); H atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: **4**: Au(1)–C(1) 2.005(4); Au(1)–Cl(1) 2.307(1); C(1)–Au(1)–Cl(1) 179.2(1). **6**: Au(1)–C(1) 2.019(6); Au(1)–Cl(1) 2.305(2); C(1)–Au(1)–Cl(1) 173.0(2). **10**: Au(1)–C(38) 2.060(4); Au(1)–P(1) 2.288(1); C(38)–Au(1)–P(1) 177.3(1).

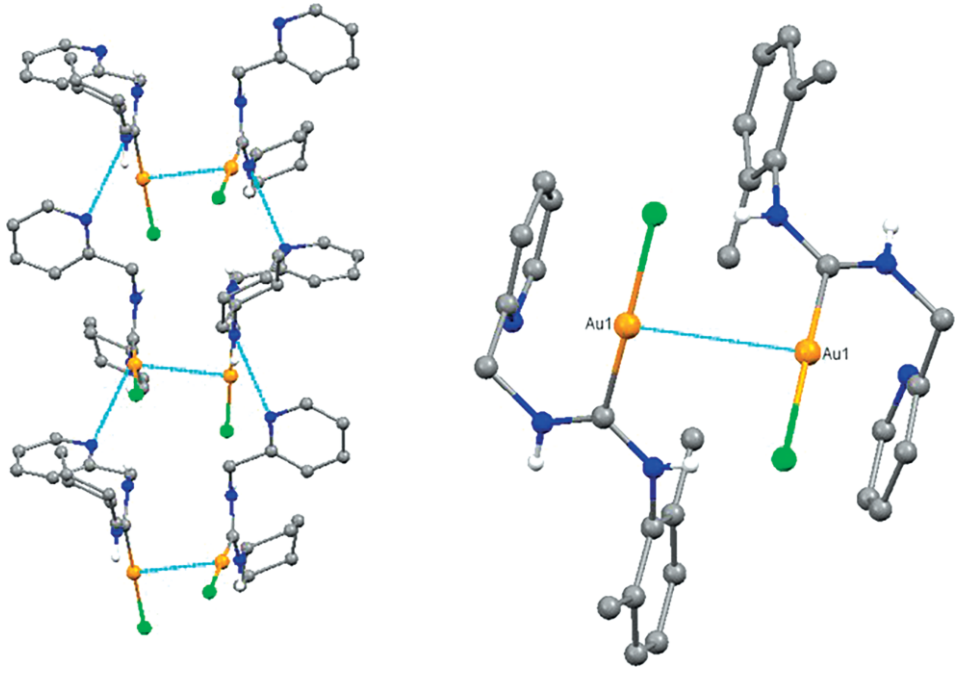


Figure 4. Examples of secondary bonds in **4** and **6**: Chain polymer in **4** through aurophilic interactions and hydrogen bonding; formation of dimers in complex **6** through aurophilic contacts.

Complex **14** crystallizes in the triclinic $P\bar{1}$ space group with one molecule by asymmetric unit (Figure 5). The gold(III) atom displays a distorted square-planar geometry. The angles around the gold(III) atom range from 87.2 to 93.2, the lowest corre-

sponds to the C27–Au1–N1 angle of the chelating C,N ligand. The mean deviation from the plane formed by the four donor atoms (C1, C11, N1, and C27) of the gold center is 0.0641 Å. The Au–$C_{pentafluorophenyl}$ bond lengths are 2.057 and 2.015 Å. The longest length is *trans* to the Au–$C_{carbene}$, which is in agreement with a higher *trans* influence of the carbene ligand than the nitrogen one. A boat conformation is adopted by the six-membered AuC_4N chelate ring as have been observed in the related gold(III) derivatives collected in reference 5a. There are intra- and intermolecular $NH_{amide}\cdots O_{anion}$ interactions that can be considered as classical hydrogens bonds, the strongest being N(2)–H(3)··· O2 [x-1, y, z] of 2.145 Å with an angle of 156.3° and N3–H2···O1 of 2.264 Å with an angle of 155.8°.

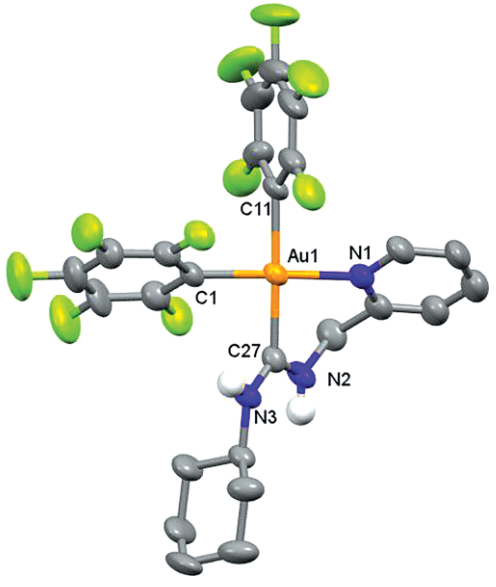


Figure 5. Molecular crystal structure of the cation of **14** (50 % thermal ellipsoids); H atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: Au(1)–C(1) 2.015(6); Au(1)–C(11) 2.057(6); Au(1)–C(27) 2.059(6); Au(1)–N(1) 2.089(5); C(11)–Au(1)–C(1) 88.9(3); C(1)–Au(1)–C(27) 90.5(2); C(11)–Au(1)–N(1) 93.2(2); C(27)–Au(1)–N(1) 87.2(2).

Cytotoxic Studies

The in vitro cytotoxic activity of metal complexes **1**, **4–7**, **9**, **10**, **13**, **14** has been studied. Compounds **1**, **4–7** and **9** were tested against three different human tumor cell lines: Jurkat (T-cell leukaemia), MiaPaca2 (pancreatic carcinoma) and A549 (lung carcinoma), **10** and **13** against A549 and the human breast cancer cell line MDA-MB-231, and the gold(III) carbene **14** against the MDA-MB-231 cell line. Cytotoxicity values of cisplatin (chemotherapeutic platinum clinically employed) are used for comparison purposes (Table 1 and Table 2).

The tested compounds are not soluble in water, but they are soluble in DMSO and in the DMSO/water mixtures used in the tests, which contain a small amount of DMSO. We did not observe any precipitation of the complexes or metallic gold while performing the test. Their colorless [D_6]DMSO solutions are very stable at room temperature, as shown in the ^{1}H NMR spectra in which the signals remain the same for weeks. Cells were exposed to different concentrations of each compound for a total of 24 h. Using the colorimetric MTT viability assay,[14] (MTT = 3-(4,5-dimethyl-thiazol-2-yl)-2,5-diphenyltetrazolium bromide), the IC_{50} values (final concentration < 0.5 % DMSO) were calculated from dose–response curves obtained by non-linear regression analysis. IC_{50} values are concentrations of a drug required to inhibit tumor cell proliferation by 50 %, compared to the control cells treated with DMSO alone.

Table 1. IC_{50} (μM) (24 h) of complexes against Jurkat, MiaPaca2 and A549.

Compound	Jurkat	MiaPaca2	A549
Cisplatin[a]	10.8 ± 1.2	114.2 ± 9.1	76.5 ± 7.4
(1)	0.61 ± 0.2	5.56 ± 0.5	22.22 ± 1.1
(4)	>25	>25	>25
(5)	>25	>25	>25
(6)	>25	>25	>25
(7)	20.96 ± 1.2	>25	9.85 ± 0.8
(9)	4.29 ± 0.7	5.30 ± 0.6	13.63 ± 1.3
(10)	nt	nt	13.81 ± 0.4
(13)	nt	nt	>25

[a] Cisplatin was dissolved in H_2O, see ref.[13] nt: not tested.

Table 2. IC_{50} (μM) (24 h) of complexes MDA-MB-231.

Compounds	MDA-MB-231
Cisplatin[a]	131.2 ± 18
(10)	8.8 ± 1.6
(13)	>25
(14)	16.0 ± 5.4

[a] Cisplatin was dissolved in H_2O, see ref.[13].

As can be seen in Table 1, the starting derivative **1** is very active against the Jurkat and the MiaPaca cell lines but the carbene chloride complexes **4**, **5** and **6**, with values of IC_{50} >25, have not significant activity against the cell lines studied. Bertrand et al.[5b] have reported the low antiproliferative activity against the A549 and MCF-7 cell lines of a series of neutral chloride acyclic-carbene complexes. In our work, the substitution of chloride in **5** by 2-thiolpyridine (**7**) provided higher cytotoxicity against Jurkat and A-549 cell lines.

The antiproliferative activity of the phosphane derivatives **9**, against Jurkat, MiaPaca2, and A549, and **10**, against A549 and MDA-MB-231, has also been measured (Table 2). Both are highly effective against the cell lines tested (IC_{50} values range between 4.29 and 13.81 μM, notably lower than those found for cisplatin). Complex **13** showed no significant activity against A549 and MDA-MB-231 while the carbene gold(III) derivative **14** showed good activity against the MDA-MB-231 cell line with an IC_{50} value of 16.0 μM.

In summary, while isocyanide gold(I) **1** showed high activity against Jurkat and MiaPaca cell lines and moderate against A-549, the chloride carbene derivatives **4**, **5** and **6**, with values of IC_{50} >25, are not significantly actives against the cell lines studied. Substitution of chloride by 2-thiolpyridine (**7**) provided higher cytotoxicity against Jurkat and A549 cell lines and the phosphane derivatives **9** and **10** were highly effective against the cell lines tested. The carbene gold(III) derivative **14** showed significant activity against the MDA-MB-231 cell line.

Conclusions

A series of new gold(I) acyclic diamino gold(I) carbene compounds with various ancillary ligands such as chloride [Au{C(NHR)(NHCH$_2$py)}Cl], thiolate [Au{C(NHR)(NHCH$_2$py)}(Spy)] or triphenylphosphane [Au{C(NHR)(NHCH$_2$py}(PPh$_3$)](OTf) have been synthesized. Different conformational isomers, in solution at room temperature, were observed for the gold(I) carbene derivatives. Moreover, two gold(III) derivatives, *cis*-[Au(C$_6$F$_5$)$_2$-(2-picolylamine)]ClO$_4$, and the bidentate N,C carbene species, *cis*-[Au(C$_6$F$_5$)$_2${C(NHCy)(NHCH$_2$py)}]ClO$_4$, have been obtained. IC$_{50}$ values of the starting material [AuCl(CNCy)], and the complexes in the tumor human cell lines Jurkat (T-cell leukaemia), MiaPaca2 (pancreatic carcinoma), A549 (lung carcinoma) and MDA-MB- 231 (breast carcinoma) were determined. The starting material [AuCl(CNCy)] **1**, the thiolate complex **7**, the phosphane derivatives **9** and **10** and the gold(III) carbene derivative **14** showed moderate to high activities against the cell lines tested.

Experimental Section

Solvents were used as received without purification or drying. The starting material [AuClTht] (tht = tetrahydrothiophene) was prepared according to published procedures.[10] [Au(OTf)(PPh$_3$)] was obtained by reaction of [AuCl(PPh$_3$)][15] with Ag(OTf) in dichloromethane and used "in situ". The starting material [Au(C$_6$F$_5$)$_2$(OEt$_2$)$_2$]ClO$_4$ was prepared by published procedures.[16] All other reagents were commercially available and used without further purification. ^{1}H, ^{13}C{^{1}H}, ^{19}F, and ^{31}P{^{1}H}, including 2D experiments, were recorded at room temperature on a Bruker Avance 400 or a Bruker ARX 300 spectrometers. Chemical shifts (δ, ppm) were reported relative to the solvent peaks in the ^{1}H, ^{13}C spectra or external 85 % H$_3$PO$_4$ or CFCl$_3$ in ^{31}P or ^{19}F spectra.

Caution: perchlorate salts with organic cations might be explosive.

General procedure of the synthesis of the complexes [AuCl(CNR)] (R = Cy (1), R = naphthyl (2), R = xylyl (3)).

A mixture of [AuCl(tht)] (0.6412 g, 2 mmol), and CNCy (0.2183 g, 2 mmol, ρ = 0.878 g mL^{-1}) or CN-naphthyl (0.3064 g, 2 mmol) or CN-xylyl (0.2624 g, 2 mmol) in dichloromethane (20 mL) was stirred at room temperature for 2 h. The volume was reduced to ca 5 mL and addition of *n*-hexane afforded **1–3** as white solids, which were finally filtered.

Complex 1. Yield: 0.5172 g, 76 %. IR (cm^{-1}): (C≡N) 2255; (Au–Cl) 354. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 3.89 (m, 1H, CHCy), 2.00 (m, 2H, Cy), 1.78 (m, 4H, Cy), 1.47 (m, 4H, Cy) ppm. ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ: 133.8 (t, 1C, $^1J_{C,N}$ = 24.7 Hz, C≡N), 55.1 (m, 1C, CHCy), 31.7 (s, 2C, Cy), 24.7 (s, 1C, Cy), 22.7 (s, 2C, Cy) ppm.

Complex 2. Yield: 0.7020 g, 91 %. IR (cm^{-1}): (C≡N) 2229; (Au–Cl) 345. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 8.10 (m, 1H), 7.97 (d, 1H, J_{H-H} = 8.8 Hz), 7.92 (m, 2H), 7.67 (m, 2H), 7.52 (dd, 1H, J_{H-H} = 8.8 Hz, J_{H-H} = 2.1 Hz) ppm. ^{13}C{^{1}H} NMR (101 MHz, (CD$_3$)$_2$CO) δ: 164.1 (s, 1C, C≡N), 131.3 (s, 1C), 129.9 (s, 1C), 129.3 (s, 1C), 129.1 (s, 1C), 128.9 (s, 1C), 123.8 (s, 1C) ppm. MS(ESI$^+$): [M – Cl]$^+$ m/z =351 (67 %).

Complex 3. Yield: 0.5208 g, 72 %. IR (cm^{-1}): (C≡N) 2213; (Au–Cl) 352. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.35 (t, 1H, $^3J_{H-H}$ = 7.7 Hz, 4-H); 7.17 (d, 2H, $^3J_{H-H}$ = 7.6 Hz, 3-H); 2.45 (s, 6H, CH$_3$) ppm. ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ: 131.2 (s, 1C, 4-C), 128.7 (s, 2C, 3-C, 3-C), 18.9 (s, 2C, CH$_3$) ppm. MS(ESI$^+$): [M – Cl]$^+$ m/z = 329 (4 %).

General procedure of the synthesis of the complexes [Au{C(NHR)(NHCH$_2$py)}Cl] (R = Cy, (4), R = naphthyl (5), R = xylyl (6))

A mixture of 2-picolylamine (0.0357 g, 0.33 mmol, ρ = 1.049 g mL^{-1}) and [AuCl(CNR)] (R = Cy: 0.1025 g, 0.3 mmol; naphthyl: 0.1157 g, 0.3 mmol; xylyl: 0.1091 g, 0.3 mmol) in dichloromethane (20 mL) was stirred at room temperature for 24 h. The volume was reduced to ca 5 mL and addition of *n*-hexane afforded **4–6** as white solids, which were finally filtered.

Complex 4. Yield: 0.0516 g, 38 %. IR (cm^{-1}): (NH) 3208, 3045; (C=N) 1566; (Au–Cl) 321. ^{1}H NMR (400 MHz, CDCl$_3$), three rotamers A, B, C, relative ratio 1:0.6:0.2, δ: 8.46 (A, B and C) (m, 6H, 6-H, NHCy), 7.68 (A, B and C) (m, 3H, 4-H), 7.28 (A, B and C) (m, 9H, 3-H, 5-H, NH$_{picolylamine}$), 4.96 (C) (m, 2H, CH$_2$), 4.89 (B) (m, 2H, CH$_2$), 4.37 (A) (d, 2H, $^3J_{H-H}$ = 5.6 Hz, CH$_2$), 4.00 and 3.44 (A, B and C) (m, 3H, CHCy), 1.91 (A, B and C) (m, 6H, Cy), 1.68 (A, B and C) (m, 9H, Cy), 1.30 (A, B and C) (m, 15H, Cy) ppm. ^{13}C{^{1}H}-NMR (101 MHz, CDCl$_3$) δ: 148.3 (s, C), 139.1 (s, C), 138.1 (s, C), 123.3 (s, C), 58.8 (s, CHCy), 49.3 (s, CH$_2$), 33.8 (s, CH$_2$Cy), 25.2 (s, CH$_2$Cy), 25.1 (s, CH$_2$Cy), 24.5 (s, CH$_2$Cy), 24.3 (s, CH$_2$Cy) ppm. MS(ESI$^+$): [M – Cl]$^+$ m/z = 414 (100 %); [M + H]$^+$ m/z = 450 (42 %).

Complex 5. Yield: 0.1017 g, 69 %. IR (cm^{-1}): (NH) 3211, 3046; (C=N) 1559, (Au–Cl) 324. ^{1}H NMR (400 MHz, CDCl$_3$), two rotamers A, B, relative ratio 1:0.8, δ: 11.38 (A) (bs, 1H, NH$_{naphthyl}$), 8.63 (A) (m, 1H, 6-H), 8.53 (B) (bs, 1H, NH$_{naphthyl}$), 8.37 (B) (m, 1H, 6-H), 8.28 (B) (bs, 1H, NH$_{picolylamine}$), 8.11 (A) (bs, 1H, NH$_{picolylamine}$), 8.07 (m, 2H), 7.93–7.28 (m, 17H), 7.18 (B) (m, 1H, 5-H), 5.01 (A) (m, 2H, CH$_2$), 4.60 (B) (d, 2H, $^3J_{H-H}$ = 5.7 Hz, CH$_2$) ppm. ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ: 155.4 and 154.9 (2s, 2C), 149.2 (B) (s, 1C), 148.5 (A) (s, 1C), 138.5 and 137.2 (A and B) (2s, 2C), 138.3 and 137.6 (A and B) (2s, 2C), 133.8 and 132.6 (A and B) (2s, 2C), 133.5 and 131.9 (A and B) (2s, 2C), 130.7 (s), 129.3 (s); 129.2 (s), 128.0 (s), 127.9 (s); 127.4 (s), 127.1 (s), 126.8 (s), 126.0 (s, C), 125.8 (s), 124.3 (s), 123.7 (s), 123.2 (s), 123.0 (s), 122.1 (s), 121.8 (s), 120.0 (s), 119.4 (s), 53.9 (A) (s, 1C, CH$_2$), 50.4 (B) (s, 1C, CH$_2$) ppm. MS(ESI$^+$): [M – Cl]$^+$ m/z = 458 (100 %); [M + H]$^+$ m/z = 494 (9 %).

Complex 6. Yield: 0.1085 g, 77 %. IR (cm^{-1}): (NH) 3234, 3007; (C=N) 1539; (Au–Cl) 308. In the explanation of the NMR spectra H and C atoms of xylyl group that were identified have been noted as X'. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 8.38 (m, 1H, 6-H), 7.67 (td, 1H, $^3J_{H-H}$ = 7.6 Hz, J_{H-H} = 1.7 Hz, 4-H), 7.48 (bs, 1H, NH$_{xylyl}$), 7.34 (d, 1H, $^3J_{H-H}$ = 7.8 Hz, 3-H), 7.26 (m, 1H, 4'-H), 7.16 (m, 4H, 5-H, 3'-H, 3'-H, NH$_{picolylamine}$), 4.96 (d, 2H, $^3J_{H-H}$ =5.3 Hz, CH$_2$), 2.22 (s, 6H, CH$_3$) ppm. ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ: 190.6 (s, 1C, C=N), 155.4 (s, 1C), 149.3 (s, 1C, 6-C), 137.2 (s, 1C, 4-C), 136.2 (s, 1C), 132.6 (s, 1C), 129.6 (s, 1C), 129.4 (s, 2C, 3'-C, 3'-C), 128.7 (s, 1C, 4'-C), 123.0 (s, 1C, 5-C), 122.1 (s, 1C, 3-C), 53.9 (s, 1C, CH$_2$), 18.4 (s, 2C, CH$_3$) ppm. MS(ESI$^+$): [M – Cl]$^+$ m/z = 436 (100 %); [M + H]$^+$ m/z = 472 (16 %).

Synthesis of [Au{C(NHR)(NHCH$_2$py)}(Spy)] (R = naphthyl (7), R = xylyl (8))

To a suspension of K$_2$CO$_3$ (0.0456 g, 0.33 mmol) and 2-HSpy (0.0334 g, 0.3 mmol) in 20 mL of dichloromethane were added [Au{C(NHnaphthyl)(NHCH$_2$py)}Cl] (**5**) (0.1481 g, 0.3 mmol) or [Au{C(NHxylyl)(NHCH$_2$py)}Cl] (**6**) (0.1415 g, 0.3 mmol) and the mixture was stirred for 3 h. The suspension was filtered to remove the KCl formed. Concentration of the solution to approximately 5 mL and addition of hexane gave complexes **7** or **8** as white solids.

Complex 7. Yield: 0.0544 g, 32 %. IR (cm^{-1}): (NH) 3195, 3008; (C=N) 1572; (Au–S) 401. ^{1}H NMR (400 MHz, (CD$_3$)$_2$CO), two rotamers A, B, relative ratio 1:0.7, δ: 11.09 (B) (bs, 1H, NH$_{naphthyl}$), 10.37 (A) (bs, 1H,NH$_{naphthyl}$), 8.98 (A) (bs, 1H, NH), 8.51 (B) (bs, 1H, NH), 8.76 (m,

1H), 8.59 (m, 2H), 8.32 (m, 2H), 7.93 (m, 12H), 7.56 (m, 6H), 7.23 (m, 4H), 6.67 (m, 2H), 5.28 (A) (m, 2H, CH_2), 4.85 (B) (m, 2H, CH_2) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $(CD_3)_2CO$) δ: 170.7 (s, 1C, C=N), 150.0 (s), 138.9 (s), 129.7 (s), 128.6 (s), 127.5 (s), 126.4 (s), 124.0 (s), 123.5 (s), 122.7 (s), 121.0 (s), 120.4 (s), 117.7 (s), 55.21 (A) (s, 1C, CH_2), 49.9 (B) (s, 1C, CH_2) ppm. MS(ESI$^+$): $[M + H]^+$ m/z = 569 (100 %).

Complex 8. Yield: 0.0738 g, 45 %. IR (cm^{-1}): (NH) 3186; (C=N) 1572; (Au–S) 402. H and C atoms of xylyl and 2-thiolpyridine groups have been noted as X′ and X″, respectively. ^1H NMR (400 MHz, $CDCl_3$), three rotamers A, B, C, relative ratio 1:0.2:0.1, δ: 9.76 (B) (bs, 1H, NH_{xylyl}), 9.55 (C) (bs, 1H, NH_{xylyl}), 9.32 (A) (bs, 1H, NH_{xylyl}), 8.45 (B) (m, 1H, 6-H), 8.45 (C) (m, 1H, 4-H), 8.42 (C) (m, 1H, 6-H), 8.40 (A) (m, 1H, 6-H), 8.10 (A, B and C) (m, 3H, 6″-H), 7.68 (B) (m, 1H, 4-H), 7.63 (A) (td, 1H, $^3J_{H\text{-}H}$ = 7.7 Hz, $J_{H\text{-}H}$ = 1.8 Hz, 4-H), 7.55 (B) (m, 1H, 3-H), 7.50 (B and C) (bs, 2H, NH), 7.41 (A) (m, 1H, 3-H), 7.37 (C) (m, 1H, 3-H), 7.20–7.05 (A, B and C) (m, 18H, 5-H, 3′-H, 3′-H, 4′-H, 3″-H, 4″-H), 6.92 (A) (t, 1H, $^3J_{H\text{-}H}$ = 5.5 Hz, NH), 6.77 (A, B and C) (m, 3H, 5″-H), 5.11 (C) (d, 2H, $J_{H\text{-}H}$ = 5.7 Hz, CH_2), 4.97 (A) (d, 2H, $J_{H\text{-}H}$ = 5.7 Hz, CH_2), 4.58 (B) (d, 2H, $J_{H\text{-}H}$ = 6.1 Hz, CH_2), 2.27 (C) (s, 6H, CH_3), 2.18 (A) (s, 6H, CH_3), 2.11 (B) (s, 6H, CH_3) ppm. MS(ESI$^+$): [M – py] m/z = 463 (100 %); $[M + H]^+$ m/z = 547 (2 %).

Synthesis de [Au(pyCH$_2$NH$_2$)(PPh$_3$)](OTf) (9)

A solution of [Au(OTf)(PPh_3)] (0.1277 g, 0.2 mmol) prepared in situ and 2-picolylamine (0.0216 g, 0.2 mmol, ρ = 1.049 g mL^{-1}) was stirred in dichloromethane (20 mL) for 2 h at room temperature. The volume was reduced to 5 mL, and addition of hexane afforded compound **9** as a white solid.

Complex 9. Yield: 0.1318 g, 92 %. IR (cm^{-1}): (NH_2) 3205; CF_3SO_3: 1279, 1251, 1223; 1148, 1027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$), δ: 8.44 (m, 1H, 6-H), 7.71 (td, 1H, $^3J_{H\text{-}H}$ = 7.7 Hz, $^4J_{H\text{-}H}$ = 1.8 Hz, 4-H), 7.49 (m, 15H, PPh_3), 7.37 (d, 1H, $^3J_{H\text{-}H}$ = 7.7 Hz, 3-H), 7.23 (m, 1H, 5-H), 4.97 (m, 2H, NH_2), 4.49 (m, 2H, CH_2) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ: 30.9 (s, 1P, PPh_3) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$) δ: –78.1 (s, 3F, CF_3SO_3) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 149.3 (s, 1C, 6-C), 139.0 (s, 1C, 4-C), 134.3 (d, 6C, $^3Jc\text{-}p$ = 13.6 Hz, C_{ortho}, PPh_3), 132.4 (d, 3C, $^5Jc\text{-}p$ = 2.5 Hz, C_{para}, PPh_3), 129.6 (d, 6C, $^4Jc\text{-}p$ = 12.0 Hz, C_{meta}, PPh_3), 128.0 (d, 3C, $^1Jc\text{-}p$ = 63.3 Hz, C_{ipso}, PPh_3), 123.3, 123.3 (2s, 2C, 3-C, 5-C), 49.23 (s, 1C, CH_2) ppm. MS(ESI$^+$): $[M – OTf]^+$ m/z = 567 (100 %).

Synthesis of [Au{C(NHR)(NHCH$_2$py}(PPh$_3$)](OTf) (R = Cy (10), R = naphthyl (11), R = xylyl (12))

A mixture of [Au(pyCH$_2$NH$_2$)(PPh_3)](OTf) (**9**) (0.1433 g, 0.2 mmol) and CNCy (0.0249 g, 0.2 mmol, ρ = 0.878 g mL^{-1}) or CN-naphthyl (0.0306 g, 0.2 mmol) or CN-xylyl (0.0262 g, 0.2 mmol) in dichloromethane (20 mL) was stirred at room temperature for 48 h. The volume was reduced to ca. 5 mL and addition of *n*-hexane afforded **10–12** as white solids, which were finally filtered.

Complex 10. Yield: 0.0760 g, 46 %. IR (cm^{-1}): (NH) 3265, 3055; (C=N) 1570; CF_3SO_3: 1279, 1242, 1222, 1151, 1027. ^1H NMR (400 MHz, $CDCl_3$), two rotamers A, B, relative ratio 1:0.7, δ: 9.04, 8.62 (A and B) (2m, 2H, NHCy), 8.92 (A) (m, 1H, NH), 8.73 (B) (m, 1H, NH), 8.43 (B) (m, 1H, 6-H), 8.36 (A) (m, 1H, 6-H), 7.72 (A, B) (m, 2H, 4-H), 7.65 (B) (m, 1H, 3-H), 7.40 (A) (d, 1H, $^3J_{H\text{-}H}$ = 8.0 Hz, 3-H), 7.50 (A, B) (m, 30H, PPh_3), 7.22 (B) (m, 1H, 5-H), 7.13 (A) (m, 1H, 5-H), 4.84 (A) (d, 2H, $J_{H\text{-}H}$ = 6.1 Hz, CH_2), 4.55 (B) (d, 2H, $J_{H\text{-}H}$ = 5.5 Hz, CH_2), 3.63 (A and B) (m, 2H, CHCy), 2.00–0.88 (m, 20H, CH_2Cy) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ: 40.5 (s, 1P, PPh_3) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$) δ: –78.3 (s, 3F, CF_3SO_3) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 158.5, 155.7 (A, B) (2s, 2C, 2-C), 149.1 (A) (s, 1C, 6-C), 147.8 (B) (s, 1C, 6-C), 138.2, 137.3 (A, B) (2s, 2C, 4-C), 134.2 (d, 6C, $^3Jc\text{-}p$ = 13.2 Hz, C_{ortho}, PPh_3), 132.3 (s, 3C, C_{para}, PPh_3), 129.7 (d, 6C, $^4Jc\text{-}p$ = 10.8 Hz, C_{meta}, PPh_3), 124.9 (B) (s, 1C, 3-C), 123.2 (B) (s, 1C, 5-C), 122.6 (A) (s, 1C, 5-C), 121.9 (A) (s, 1C, 3-C), 59.7, 59.4 (A, B) (2s, 2C, CHCy), 54.2 (A) (s, 1C, CH_2), 49.4 (B) (s, 1C, CH_2), 34.1 (s, CH_2Cy), 25.2 (m, CH_2Cy), 25.0 (s, CH_2Cy), 24.8 (s, CH_2Cy) ppm. MS(ESI$^+$): $[M – OTf]^+$ m/z = 676 (100 %).

Complex 11. Yield: 0.0623 g, 36 %. IR (cm^{-1}): (NH) 3246, 3053; (C=N) 1561; CF_3SO_3: 1276, 1240; 1222; 1151; 1027. ^1H NMR (400 MHz, $CDCl_3$), two rotamers, relative ratio 1:0.6, δ: 11.83 (B) (m, 1H, $NH_{naphthyl}$), 10.85 (A) (m, 1H, $NH_{naphthyl}$), 9.73 (A) (m, 1H, NH), 9.51 (B) (m, 1H, NH), 8.61 (B) (m, 1H, 6-H), 8.39 (A) (m, 1H, 6-H), 8.06 (m, 2H, naphthyl), 7.74, 7.62–7.15 (A, B) (2m, 48H, 3-H, 4-H, 5-H, naphthyl, PPh_3), 5.04 (A) (d, 2H, $J_{H\text{-}H}$ = 6.0 Hz, CH_2), 4.84 (B) (d, 2H, $J_{H\text{-}H}$ = 5.7 Hz, CH_2) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ: 39.5, 39.0 (A, B) (2s, 2P, PPh_3) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$) δ: –78.2 (s, 3F, CF_3SO_3) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$) δ: 157.2, 155.5 (A, B) (2s, 2C, 2-C), 149.3 (A) (s, 1C, 6-C), 148.0 (B) (s, 1C, 6-C), 138.9 (s), 138.6, 137.4 (A, B) (2s, 2C, 4-C), 138.4 (s), 134.1 (m, C_{ortho}, PPh_3), 133.5 (m), 132.1 (m, C_{para}, PPh_3), 131.9 (s, naphthyl), 129.5 (m, C_{meta}, PPh_3), 128.4 (s, naphthyl), 127.9 (s, naphthyl), 127.0 (s, naphthyl), 126.0 (s, naphthyl), 125.1, 122.0 (A, B) (2s, 2C, 3-C), 123.5, 122.7 (A, B) (2s, 2C, 5-C), 123.0 (s, naphthyl), 122.8 (s, naphthyl), 120.6 (s, naphthyl), 118.6 (s, naphthyl), 54.9 (A) (s, 1C, CH_2), 49.9 (B) (s, 1C, CH_2) ppm. MS(ESI$^+$): $[M – OTf]^+$ m/z = 720 (100 %).

Complex 12. Yield: 0.1299 g, 77 %. IR (cm^{-1}): (NH) 3239, 3054; (C=N) 1561; (CF_3SO_3) 1275, 1241, 1222, 1151, 1027. ^1H NMR (400 MHz, $CDCl_3$), H and C atoms of xylyl group has been noted as X′, two rotamers, A, B, relative ratio 1:0.9, δ: 10.40 (A) (bs, 1H, NH_{xylyl}), 9.80 (A) (bs, 1H, NH_{xylyl}), 9.66 (B) (m, 1H, NH), 9.31 (A) (m, 1H, NH), 8.40 (B) (m, 1H, 6-H), 8.46 (A) (m, 1H, 6-H), 7.80, 7.74 (A, B) (2m, 2H, 4-H), 7.74, 7.52–7.02 (A, B) (2m, 39H, 3-H, 5-H, xylyl, PPh_3), 4.93 (A) (d, 2H, $^3J_{H\text{-}H}$ = 5.8 Hz, CH_2), 4.81 (B) (d, 2H, $J_{H\text{-}H}$ = 5.8 Hz, CH_2), 2.30 (s, 3H, CH_3), 2.18 (s, 3H, CH_3) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ: 40.0 (s, 1P, PPh_3) ppm. ^{19}F NMR (282.4 MHz, $CDCl_3$) δ: –78.3 (s, 3F, CF_3SO_3) ppm. $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$) δ: 158.3, 155.8 (A, B) (2s, 2C, 2-C), 149.3 (A) (s, 1C, 6-C), 148.0 (B) (s, 1C, 6-C), 138.6, 138.2 (A, B) (2s), 138.5 (s), 137.3 (s), 137.1, 136.7 (A, B) (2s), 134.1 (bs), 132.1 (bs), 129.5 (bs), 128.5 (s), 128.2 (s), 128.2 (s), 125.1 (s), 123.4 (s), 122.9 (s), 122.7 (s), 121.7 (s), 118.7 (s), 54.1 (A) (s, 1C, CH_2), 49.9 (B) (s, 1C, CH_2), 19.0 (s, 1C, CH_3), 19.0 (s, 1C, CH_3) ppm. MS(ESI$^+$): $[M – OTf]^+$ m/z = 698 (100 %).

Synthesis of *cis*-[Au(C$_6$F$_5$)$_2$(pyCH$_2$NH$_2$)](ClO$_4$) (13)

Di-(2-picolyl)amine (0.0598 g, 0.3 mmol, ρ = 1.107 g mL^{-1}) was added to a freshly prepared solution of $[Au(C_6F_5)_2(OEt_2)_2]ClO_4$ (0.2336 g, 0.3 mmol) in diethyl ether (20 mL), and the mixture was stirred for 1 h. Complex **13** precipitated as a white solid and was filtered off. Yield: 0.124 g (56 %). IR: (NH_2): 3219; (C_6F_5): 1508, 965; (cis-C_6F_5): 818, 807; (ClO_4): 1078, 621 cm^{-1}. ^1H NMR (400 MHz, $(CD_3)_2SO$): δ = 8.42 (td, J_{HH} = 7.6 Hz, J_{HH} = 1.2 Hz, 1H, 4-H), 8.25 (d, J_{HH} = 5.6 Hz, 2H, 6-H), 8.07 (d, J_{HH} = 8Hz, 1H, 3-H), 7.67 (t, J_{HH} = 6.4 Hz, 1H, 5-H), 7.11 (s, 2H, NH_2), 4.99 (s, 2H, CH_2) ppm. ^{19}F NMR (376.5 MHz, $(CD_3)_2SO$): δ = –121.4 (m, "d", $^3Jo\text{-}F$, m-F = 21.2 Hz, 2F, o-F), δ = –122.9 (m, "d", $^3Jo\text{-}F$, m-F = 21.2 Hz, 2F, o-F), –154.6 (m, "q", $^3Jp\text{-}F$, m-F = 22.4 Hz, 2F, p-F),–159.9 (m, 2F, m-F), –161.1 (m, 2F, m-F) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $(CD_3)_2SO$): δ = 165.7 (s, 1C, 2-C), 148.2 (s, 1C, 6-C), 143.3 (s, 1C, 4-C), 125.9 (s, 1C, 5-C), 123.6 (s, 2C, 3-C), 52.1 (s, 1C, CH_2) ppm. MS(ESI$^+$): $[M – ClO_4]^+$ m/z = 639 (100 %).

Synthesis of *cis*-[Au(C$_6$F$_5$)$_2${C(NHCy)(NHCH$_2$py)}]ClO$_4$ (14)

A mixture of CNCy (0.0218 g, 0.2 mmol) and complex **13** (0.0249 g, 0.2 mmol) in a mixture of dichloromethane/acetone (10 mL/5 mL), was stirred at room temperature. After stirring for 48 h, the volume was reduced to 5 mL and addition of *n*-hexane afforded complex

14 as a white solid, which was finally filtered. Yield: 0.139 g (82 %). IR(cm^{-1}): (NH): 3264; (C=N): 1598; (C_6F_5): 1508, 961; (*cis*-C_6F_5): 815, 794; (ClO_4): 1062, 620. ^1H NMR (400 MHz, $CDCl_3$): 8.38 (d, 1H, J_{H-H} = 5.2 Hz, 1H, 6-H), 8.24 (t, 1H, J_{H-H} = 8 Hz, 4-H), 8.08 (d, 1H, J_{HH} = 8 Hz, 3-H), 7.64 (t, 1H, *J*HH = 7.2 Hz, 5-H), 6.14 (d, 1H, J_{HH} = 8 Hz, NHCy), 5.10 (bs, 2H, CH_2), 3.69 (m, 1H, CHCy), 1.1 (m, 10H, Cy). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ = –122.9 (m, 2F, o-F), –151.9 (t, 2F, ^3Jp-F, m-F = 21.2 Hz, p-F), –152.6 (t, 2F, ^3Jp-F, m-F = 20.8 Hz, p-F), –157.7 (m, 2F, m-F), –158.3 (m, 1F, m-F). $^{13}C\{^1H\}$ NMR (101 MHz, $(CD_3)_2SO$): δ = 153.2 (s, 1C, 2-C), δ = 151.6 (s, 1C, 6-C), 143.8 (s, 1C, 4-C), 127.6 (s, 1C, 3-C), 126.7 (s, 1C, 5-C), 53.2 (s, 1C, CHCy), 51.1 (s, 1C, CH_2), 32–22 (5s, 5C, Cy) ppm. $[M - ClO_4]^+$ m/z = 748 (100 %).

Crystal Structure Determinations. Single crystals of complexes were obtained by slow diffusion of hexane into a dichloromethane solution (**4**, **6**, **10**) or chloroform (**14**). Data were registered on a Bruker Smart 1000 CCD diffractometer. The crystals were mounted in inert oil on glass fibers and transferred to the cold gas stream of the diffractometer. Data were collected using monochromated Mo-K_α radiation (λ = 0.71073) in ω-scans. Absorption corrections based on multiple scans were applied with the program SADABS. The structures were solved by direct methods and refined on F^2 using the program SHELXL-2016.[17] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included using a riding model. CCDC numbers 1919426 (**6**), 1919427 (**14**), 1919428 (**10**) and 1919429 (**4**) contains the supplementary crystallographic data. These data can be obtained free of charge by The Cambridge Crystallography Data Center.

CCDC 1919426 (for **6**), 1919427 (for **14**), 1919428 (for **10**), and 1919429 (for **4**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

Cell cultures

Jurkat (leukaemia) and MiaPaca2 (pancreatic carcinoma) cell lines were maintained in RPMI 1640, while A549 (lung carcinoma) were grown in DMEM (Dulbecco's modified Eagle's medium). Both media were supplemented with 5 % fetal bovine serum (FBS), 200 U mL^{-1} penicillin, 100 μg mL^{-1} streptomycin and 2 mM L-glutamine. Medium for A549 cells was also supplemented with 2.2 g L^{-1} Na_2CO_3, 100 μg mL^{-1} piruvate and 5 mL non-essential amino acids (Invitrogen). MDA-MB-231 cells are grown at 37 °C in Leibovitz's L-15 medium supplemented with 2 mM glutamine and 15 % fetal bovine serum (FBS). Cultures were maintained in a humidified atmosphere of 95 % air/ 5 % CO_2 at 37 °C.

Cytotoxicity assays by MTT

The MTT assay was used to determine cell viability as an indicator for cell sensitivity to the complexes. Exponentially growing cells were seeded at a density of approximately 1×10^5 cells per mL (A549, MiaPaca2) or 3×10^5 cells per mL (Jurkat, MDBA-MB-231) in a 96-well flat-bottomed microplate and 24 h later they were incubated for 24 h with the compounds. The complexes were dissolved in DMSO and tested in concentrations ranging from 0.5 to 25 μM and in quadruplicate. Cells were incubated with our compounds for 24 h at 37 °C. 10 μL of MTT (5 mg mL^{-1}) was added and plates were incubated for 1–3 h at 37 °C. Finally, 100 μL per well *i*PrOH (0.05 M HCl) was added. The optical density was measured at 490 nm using a 96-well multiscanner autoreader (ELISA). The IC_{50} was calculated by nonlinear regression analysis using Origin software (Origin Software, Electronic Arts, Redwood City, California, USA).

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Keywords: Cancer · Carbene ligands · Cytotoxicity · Gold

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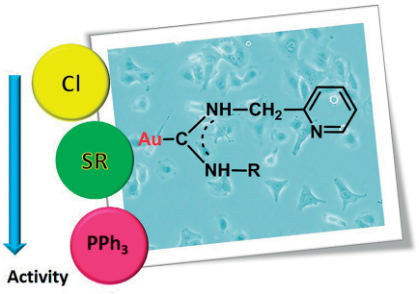
Diamino Carbenes



A series of new gold(I) and gold(III) acyclic diamino gold(I) carbene compounds with various ancillary ligands such as chloride, thiolate and phosphane have been synthesized and their cytotoxic activity tested.

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