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Peptide Coupling between Amino Acids and the Carboxylic Acid of a Functionalized Chlorido-gold(I)-phosphane

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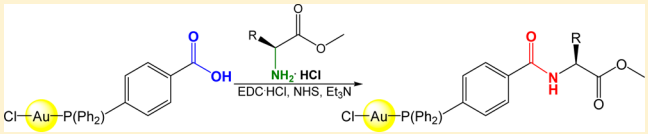
Supporting Information

ABSTRACT: We have developed a protocol for the direct coupling between methyl ester protected amino acids and the chlorido-gold(I)-phosphane (*p*-HOOC(C_6H_4)PPh_2)AuCl. By applying the EDC·HCl/NHS strategy (EDC·HCl = *N*-ethyl-*N*′-(3-(dimethylamino)propyl)carbodiimide hydrochloride, NHS = *N*-hydroxysuccinimide), the methyl esters of L-phenylalanine, glycine, L-leucine, L-alanine, and L-methionine are coupled with the carboxylic acid of the gold complex in moderate to good yields (62−88%). All amino acid tagged gold complexes were characterized by ^{1}H and ^{13}C NMR spectroscopy and high-resolution mass spectrometry. As corroborated by measurement of the angle of optical rotation, no racemization occurred during the reaction. The molecular structure of the leucine derivative was determined by single-crystal X-ray diffraction. In the course of developing an efficient coupling protocol, the acyl chlorides (*p*-Cl(O)C(C_6H_4)PPh_2)AuX (X = Cl, Br) were also prepared and characterized.



INTRODUCTION

In recent years, the number of reports on pharmaceutically active gold complexes has increased significantly.[1−9] Usually, gold(I) complexes of the form L−Au−Y with a neutral ligand L (phosphane, N-heterocyclic carbene (NHC)) and an anionic ligand (halide, thiolate) are investigated. The classical example is auranofin, which was introduced in 1982 as an antirheumatic agent[10,11] and which contains triethylphosphane and a thiosugar as ligands. In addition to this well-established application in the treatment of rheumatism, gold compounds—among them also gold(III) compounds—were also tested for their efficacy against cancer, HIV, and malaria. The exact mechanism is not always well understood, but usually an interaction between the thiophilic gold atom and a sulfur-containing protein is postulated and has in some cases been verified.[12−27]

It is widely recognized that one of the main issues in the development of pharmaceutically active agents is targeting the drug to the site of action. Several strategies have been investigated; a promising approach is to tag the active molecule with a transport or recognition moiety, for instance, a peptide including a recognition sequence. Peptides are particularly interesting because they constitute an attractive class of bioactive and biocompatible ligands. Studies of the incorporation of gold complexes into a peptide sequence usually describe the complexation of the gold atom by the thiol function of cysteine or by the thiol group of a nonnatural (amino) acid. Most studies used presynthesized peptides as ligands.[24,28−31] To the best of our knowledge, there is only one publication which describes direct peptide coupling of an amino acid with a functionalized gold complex. Gimeno et al. prepared Ph_3P−Au−SR (R = nicotinic acid thiolate) and coupled the carboxylate of the thiolate ligand with several amino acids using PyBOP/DIPEA as coupling agents (PyBOP = benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate, DIPEA = diisopropylethylamine).[32]

Hence, it is of interest to develop further robust protocols for the coupling of an amino acid or a peptide sequence to a metal(-organic) complex. Peptide coupling (i.e., peptide synthesis) is a process that has been optimized continuously over the past decades and is thus characterized by extremely high yields under very mild conditions. Numerous very efficient coupling reagents are known.[33−36] They are commonly used to activate the carboxylic acid by converting the OH group into a leaving group and to prevent loss of the chiral information via racemization. The first step in functionalizing metal(-organic) complexes via a peptide coupling reaction is finding suitable coupling reagents which are compatible with the metal complex moiety in terms of reactivity, solubility, and efficiency. Stability of the metal complex under reaction conditions is also critical.

We decided to develop an efficient coupling reaction between RPh_2P−Au−Cl (R = −C_6H_4COOH) and various amino acids. We chose the carboxylic acid tagged phosphane for several reasons: (i) In recent studies, phosphane−gold complexes of the form R_3P−Au−Cl proved to be pharmaceuti-

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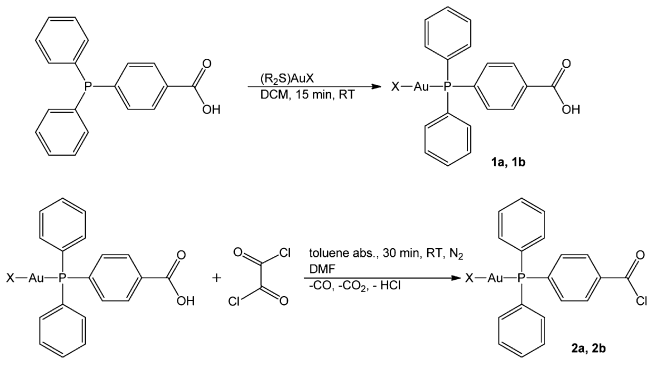
cally active;[7,16,37] under physiological conditions, the chloride is replaced with a thiol group of a protein. A comparable behavior is also observed for complexes of the form $R_3P-Au-SR'$. This means that the phosphane ligand is bound more strongly to the gold atom than the chloride or thiolate ligand.[11,15] (ii) For further modification of the peptide-tagged phosphane−gold−chloride complex, the chloride ligand can be easily exchanged for another anionic ligand such as thiolate and alkynyl. (iii) Since the FMOC (FMOC = 9-fluorenylmethoxycarbonyl) protection route is a commonly used method for peptide synthesis, the peptide is synthesized in the N-terminal direction and offers a free terminal amino group after deprotection. Hence, the complex can be used to terminate the synthesis of a peptide, which yields a gold complex tagged with the peptide of choice. (iv) The strategy could be transferred to other (natural) products, polymers, or surfaces which contain an amino group. The gold complex presented here as well as related gold complexes with different substituent patterns therefore offers the potential to function as a platform for synthesizing a variety of gold compounds.

RESULTS AND DISCUSSION

Strategy 1. Our first approach was to activate the carboxylic acid function of the free phosphane ligand in the form of its acyl chloride and to synthesize the gold complex in the next step. However, the reaction of the tertiary phosphane 4-(diphenylphosphino)benzoic acid with thionyl chloride led not only to the formation of the desired acyl chloride but also to several byproducts, such as phosphane oxide, as confirmed by ^{31}P NMR spectroscopy. A recently published detailed study of the reaction of triphenylphosphane with thionyl chloride revealed the formation of phosphane oxide and sulfide.[38] Hence, to avoid side-product formation, we prepared first the gold(I) complex **1a** by the reaction of 4-(diphenylphosphino)-benzoic acid with a gold(I) precursor of the form $(R_2S)AuCl$ (R_2S = Me_2S, C_4H_8S; Scheme 1). The air-stable gold(I) complex also exhibits good thermal stability (decomposition at ∼205−213 °C).[39] Nevertheless, we tried to avoid harsh reaction conditions to prevent decomposition of the gold(I) complex and used oxalyl chloride instead of thionyl chloride to introduce the acyl chloride functionality, because the reaction takes place at ambient temperatures. Under an atmosphere of nitrogen with a catalytic amount of DMF, the reaction gives chlorido[4-(diphenylphosphino)benzoyl chloride]gold(I), **2a**, in good yields.[40] The analogue bromido complexes **1b** and **2b** can be prepared by using bromido(tetrahydrothiophene)gold-(I) as a gold(I) precursor. Interestingly, we could not detect extensive ligand scrambling upon reaction of the bromido complex with oxalyl chloride. The bromide remained bonded to the gold atom. Nevertheless, we used the chlorido complex in the following coupling reactions to avoid the possible formation of mixed halide compounds.

Scheme 1. Reaction Scheme for Preparation of Gold(I) Complexes[a]



[a] **a**, X = Cl; **b**, X = Br. R_2S = Me_2S, C_4H_8S.

In the ^{31}P NMR spectrum of the free ligand 4-(diphenylphosphino)benzoic acid, a singlet appears at −4.7 ppm which is shifted to 33.2 and 35.2 ppm upon formation of the gold(I) complexes **1a** and **1b**, respectively. Formation of the acyl chlorides has only a slight effect on the ^{31}P NMR resonances (**2a**, 33.1 ppm; **2b**, 35.1 ppm). A distinct high-field shift of the carbonyl carbon can be seen in the ^{13}C NMR: from 170.6 to 167.6 ppm for **1a** and **2a** and from 170.7 to 167.7 ppm for **1b** and **2b**, respectively.

However, the reaction of the corresponding acyl chloride, **2a**, with a primary amine is slow, resulting in low yields of the desired product. Triethylamine (TEA) was used to trap the formed HCl. Coupling reactions with acyl halides are known to be accelerated by catalytic amounts of pyridine or *N*,*N*-dimethyl-4-aminopyridine (DMAP), but coordination of the pyridine to the gold(I) atom might cause the formation of side products. Therefore, we decided to use other noncoordinating and milder coupling reagents for activating the carboxylic acid in order to increase the reaction rate.

Strategy 2. Two coupling agents based on a carbodiimide functionality were tested to develop a protocol for the amide bond formation. Activating carboxylic acids with carbodiimides is one of the most frequently used methods in peptide synthesis. The use of *N*,*N*′-dicyclohexylcarbodiimide (DCC) to accelerate peptide bond formation has been known since 1955.[41] Upon reaction of the carboxylic acid with the carbodiimine R—N═C═N—R, a highly reactive *O*-acylisourea derivative is formed which reacts with an amine $R'NH_2$ to the desired amide RCONHR′. An urea of the form R−N−CO−N−R, for example, dicyclohexyl urea (DHU), is formed as a byproduct. The formation of DHU is, however, also the major disadvantage of using DCC as coupling agent, because traces of DHU often remain in solution and are difficult to remove from the product, even by column chromatography.[33] Alternatives are water-soluble carbodiimides, which also form water-soluble ureas. They can be removed easily upon aqueous workup. For example, *N*-ethyl-*N*′-(3-(dimethylamino)propyl)carbodiimide (EDC) and its hydrochloride salt are frequently used coupling agents (often referred to as "WSC", water-soluble carbodiimide).[33]

A further problem is an undesirable side reaction due to the high reactivity of the *O*-acylisourea derivative: The *O*-acylurea can undergo an irreversible rearrangement (i.e., [O → N] acyl migration) to form an *N*-acylurea derivative. This side reaction not only decreases the yield of the desired peptide significantly, but the *N*-acylurea is also very difficult to remove from the reaction mixture. Its solubilities are very similar to those of the desired products. Of course, the reaction conditions influence the amount of this side product: Formation of the *N*-acylurea is decreased considerably when solvents with low polarity (dichloromethane (DCM), CCl_4, benzene) rather than polar solvents (dimethylformamide (DMF), dimethyl sulfoxide (DMSO), water, acetonitrile (ACN)) are used. Lower reaction temperatures are likewise favorable. Protic additives, such as 1-hydroxybenzotriazole (HOBt) or *N*-hydroxysuccinimide

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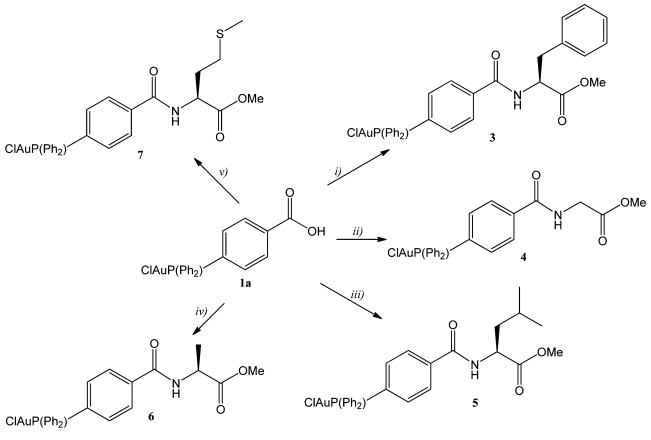
(NHS), suppress the side reaction by formation of an active ester and protonation of the *O*-acylisourea, which inhibits the rearrangement to the *N*-acylurea. Furthermore, the *N*-acylurea derivatives of water-soluble carbodiimides are also water-soluble, which facilitates their removal from the reaction mixture.[34]

For developing a protocol for the amide bond formation, both DCC and EDC·HCl were tested as coupling agents for **1a** and L-phenylalanine methyl ester hydrochloride as primary amine. The reaction was always performed under a nitrogen atmosphere using dry solvents. When DCC was used as coupling agent without any additive, a considerable amount of the corresponding *N*-acylurea derivative was formed. The lower solubility of the *N*-acylurea in methanol compared to the desired amide can be utilized to remove a proportion of the byproduct. However, several washing steps are required to remove most of the *N*-acylurea, each of which lowers the yield. The *N*-acylurea derivative was isolated and characterized by NMR spectroscopy and ESI mass spectrometry (see Experimental Section). With *N*-hydroxysuccinimide as a protic additive, formation of the *N*-acylurea was successfully suppressed. As previously mentioned, full removal of the DHU is challenging. With several precipitation and washing steps, most of the DHU can be removed, but again the yield of the desired amide decreases significantly with each step.

To avoid contamination of the target amide with the urea byproduct, EDC·HCl was chosen as coupling agent because the corresponding urea can be extracted upon aqueous workup. Screening of the reaction conditions revealed that the yields are higher if DCM rather than DMSO is used as solvent. Further, it is advantageous to generate the active ester of the carboxylic acid with *N*-hydroxysuccinimide before the amine is added and basic conditions are set.[34] This avoids the formation of the corresponding *N*-acylurea derivative almost completely. In fact, the *N*-acylurea derivative and the urea byproduct are water-soluble and can be easily removed in the aqueous workup. We tested our protocol with five amino acid methyl esters (Scheme 2). The reactions were carried out under inert conditions. In a general reaction, the carboxylic acid was dissolved in dry DCM, and subsequently EDC·HCl and *N*-hydroxysuccinimide (NHS) were added and completely dissolved. Each reaction mixture was stirred at room temperature for 5−6 h to generate the active ester before the respective amine methyl ester hydrochloride and TEA were added. The reaction mixture was stirred at ambient temperature overnight and then diluted with ethyl acetate and washed with acidic and basic aqueous solutions to remove the remaining starting materials and byproducts. After this procedure, compounds **3**, **4**, and **6** were analytically pure, whereas **5** and **7** had to be purified by column chromatography. The yields ranged from 62 to 88%, which is on average slightly better than the yields reported for the coupling reactions between [Au(SpyCOOH)(PPh_3)] (SpyCOOH = mercaptonicotinic acid) and amino acid methyl esters using the DIPEA/PyBOP strategy.[32]

Scheme 2. Synthesis of Gold Phosphane Amide Derivatives Using EDC·HCl and NHS in DCM[a]



[a](i) L-Phenylalanine methyl ester; (ii) glycine methyl ester; (iii) L-leucine methyl ester; (iv) L-alanine methyl ester; (v) L-methionine methyl ester.

All compounds were fully characterized with NMR spectroscopy and high-resolution (HR) ESI mass spectrometry. The ^{1}H NMR spectra showed resonances of the corresponding amino acid methyl ester and the aromatic protons of the phosphane backbone. The signals in the ^{31}P NMR exhibited only a slight high-field shift compared to those of compound **1a**. In the ^{13}C NMR spectrum, two resonances of carbonyl carbon atoms appeared: one for the carboxylic methyl ester and one for the carboxylic amide. The ^{31}P−^{13}C coupling constants were as expected: For example, the $^1J_{PC}$ coupling constants of the gold complexes were in the range of about 60 Hz. Additionally, two-dimensional heteronuclear single quantum coherence (HSQC) experiments were performed to allocate the ^{13}C NMR resonances of the amino acid residues.

The ^{13}C resonances and the J_{PC} coupling constants of the phosphane moiety were unaffected by the amino acid residues. Exemplary for complex **6**, a high-resolution ^{1}H−^{13}C HSQC experiment with resolved H−H and H−P coupling was recorded to corroborate the assignments of the ^{31}P−^{13}C coupling constants. The spectrum is shown in Figure S2 (Supporting Information) and discussed in the Experimental Section.

ESI mass spectra of the complexes feature m/z peaks for the fragments $[L_2Au]^+$ and $[L_2Au_2Cl]^+$. These fragmentation/aggregation patterns are well established for gold(I) complexes bearing phosphane ligands.[42−44] For the complexes **3**−**7**, exact masses were determined. The protonated molecule peaks $[M + H]^+$ and the ammonium and sodium adducts were detected for all complexes, which confirms the expected composition of the complexes.

In most reported cases, potential loss of chirality takes place at the carboxyl residue undergoing activation. Two major pathways are known, which are both base catalyzed: direct enolization and via oxazolone formation.[33] In our case, since the carboxylic acid does not have any chiral information and, more importantly, does not have any α-H atom, racemization is unlikely. Nevertheless, to ensure that no racemization takes place under the reaction conditions, the angle of optical rotation was measured for complexes **3** and **5**−**7** and for the amino acid methyl ester hydrochlorides used. In chloroform solution, the optical rotation $[\alpha]_D$ values were positive and ranged from +6.0 to +42.1 for **3**, **5**, and **6** and negative for the MetOMe derivative **7** (−6.9). In contrast, in a diluted methanol solution, all complexes gave negative $[\alpha]_D$ values, from −38.8 (PheOMe, **3**) to −4.4 (AlaOMe, **6**) . This underlines the high solvent dependence of the angle of optical rotation. The amino acid methyl ester hydrochlorides featured positive values for $[\alpha]_D$ in a methanolic solution: PheOMe·HCl, +9.1; AlaOMe·HCl, +3.0; LeuOMe·HCl, +11.3; MetOMe·HCl, +18.4.

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STRUCTURAL STUDIES

The structure of **1a** was published 10 years ago. In the crystal, the complex dimerizes via hydrogen bonds of the carboxylic acid, but no aurophilic interactions are present.[45] Single crystals suitable for X-ray diffraction of the homologue bromido complex, **1b**, were obtained from DCM/pentane. Interestingly, it is not isostructural to **1a**: It crystallizes in the orthorhombic space group *Pbca* with two complex molecules and two chloroform molecules in the asymmetric unit (**1a**: triclinic, $P\bar{1}$). The gold atom is coordinated almost linearly by the bromide and the phosphane ligand. The monomers are connected via aurophilic bonding in a "crossed-sword" motif featuring a moderate Au–Au distance of 2.99 Å.[46] Additionally, hydrogen bonds between the carboxylic acid are present, and thus infinite *zigzag* chains of molecules are formed, connected by both aurophilic contacts and hydrogen bonds. The distances between the donor and acceptor oxygen atoms are 2.621 Å for O3···O1 and 2.626 Å for O2···O4 (Figures 1 and 2), which

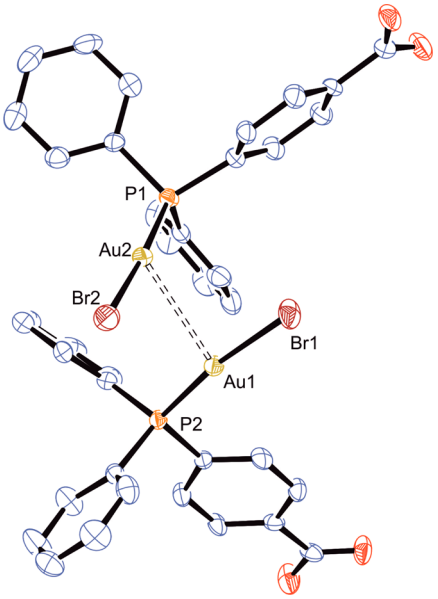

Figure 1. Asymmetric unit of **1b** ($CHCl_3$ molecules and hydrogen atoms omitted for clarity, ellipsoids drawn at the 50% probability level). Selected bond lengths and angles: P1–Au2, 2.2445(18); Au2–Br2, 2.4237(8); P2–Au1, 2.2480(18); Au1–Br1, 2.4191(8); Au1–Au2, 2.990(1); P1–Au2–Br2, 175.60(5); P2–Au1–Br1, 170.80(5).

is well below the sum of the van der Waals radii [r(O) + r(O) = 3.04 Å] and typical for hydrogen bonds. The O–H···O angle is almost linear, with 173.16° for O2–H2···O4 and 170.06° for O1···H3–O3. Further hydrogen bond parameters are given in Table 1. A comparable arrangement was also observed for the (phosphane)gold(I) complexes bearing 4-sulfanylbenzoic acid, where the molecules are aggregated via aurophilic interactions, hydrogen bonding, and/or gold–sulfur interactions.[47]

Single crystals were also obtained for complex **2b**. The compound crystallizes in the monoclinic space group $P2_1/n$ with two molecules of **2b** and one toluene molecule in the asymmetric unit. However, the toluene molecule is highly disordered and no satisfactory atom positions could be found for it. The disordered molecule was treated as a diffuse contribution in the SQUEEZE routine of the PLATON software package.[48] Since the anisotropic refinement was not stable, the structure was refined isotropically. The structure reveals the chemical constitution of the complex, but a discussion of bond lengths and angles is not meaningful (see Figure S1 in the Supporting Information). No aurophilic attractions are present; the smallest gold–gold distance is ~7 Å.

Suitable crystals of the coupling products could be obtained only for complex **5**. The compound crystallizes in the triclinic space group $P1$ with two molecules of **5** and one dichloromethane molecule in the asymmetric unit. The methoxy and isopropyl groups of one of the two complex molecules were found to be disordered. Based on the molecular structure, the α-C atom of the amino acid moiety has an S-configuration, which is in agreement with the configuration of the starting material (Flack parameter 0.009(6)). The coordination of the gold atom deviates from linearity, with angles of 173.45° for the angle Cl1–Au1–P1 and 170.44° for the angle Cl2–Au2–P2, due to Au–Au interactions between two complex molecules, again exhibiting a "crossed-sword" motif. The Au···Au distance amounts to 3.426 Å.[46] Additionally, hydrogen bonds of the form N–H···O between the amide-N and amide-O atoms of neighboring molecules are operative, forming infinite one-dimensional chains which are further interconnected by Au–Au interactions along the z-axis and perpendicular to the "amide chain". Thus, two-dimensional sheets of complex molecules are formed, joined together by the synergistic effect of these noncovalent interactions (Figures 3 and 4). Table 1 summarizes the parameters of the hydrogen bonds.

CONCLUSION

In this Article, we have presented a protocol for the direct coupling between methyl ester protected amino acids and the chlorido-gold(I)-phosphane (p-HOOC(C_6H_4)PPh_2)AuCl. Our first strategy using the acyl chloride (p-Cl(O)C(C_6H_4)PPh_2)-AuCl did not lead to satisfactory coupling rates and was abandoned in favor of the use of established and mild coupling reagents known from peptide coupling chemistry. Use of DDC as coupling reagent resulted in a urea byproduct which was hard to remove, whereas the coupling agent EDC·HCl produced water-soluble urea, which facilitates an efficient aqueous workup. The addition of NHS suppressed the contamination with the N-acylurea gold complex, which is otherwise formed as a side product in a rearrangement reaction of the activated ester. With this method, the methyl esters of L-phenylalanine, glycine, L-leucine, L-alanine, and L-methionine were coupled with the carboxylic acid of the gold complex in moderate to good yields (62–88%). Measurement of the angle of optical rotation showed that no racemization occurred during the reaction. For the leucine derivative the molecular structure was determined by single-crystal X-ray diffraction, which revealed an aggregation of the complexes by both hydrogen and aurophilic bonds, leading to a layer structure in the solid state.

Of course, the reported procedure has a broader synthetic scope and is limited neither to amino acids nor to gold complex **1a**: The amino acids can be replaced by other natural products, polymers, or surfaces which contain an amino group. The protocol should also work for di- or oligopeptides with interesting recognition sequences. Additionally, an application for related gold complexes with different substitution patterns or with different anionic ligands is feasible.

EXPERIMENTAL SECTION

General. All reactions and manipulations of air-sensitive and/or moisture-sensitive compounds were carried out in an atmosphere of

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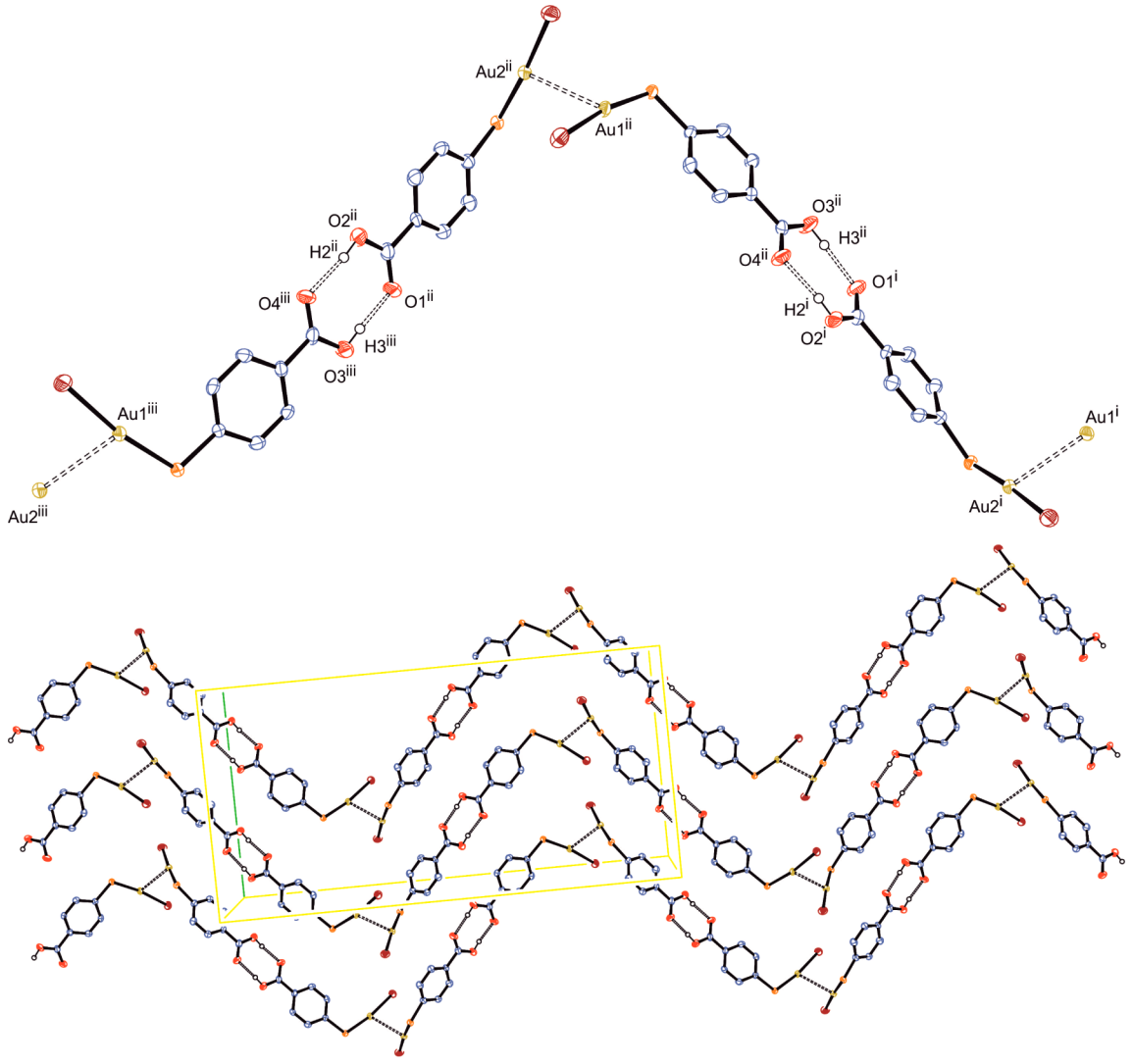

Figure 2. (top) Chains of molecules of **1b** joined by Au−Au interactions and hydrogen bonding between the carboxylic acid groups. (bottom) Unit cell and chains of molecules; unsubstituted phenyl groups and H atoms not involved in hydrogen bonding were omitted for clarity.

Table 1. Hydrogen Bond Parameters in 1b and 5

compd	D−H···A	D−H [Å]	H···A [Å]	D···A [Å]	D−H···A [deg]
1b	O2−H2···O4	0.840	1.790	2.626	173.16
	O3−H3···O1	0.840	1.789	2.621	170.06
5	N1−H1···O4	0.861	2.063	2.899	163.62
	N2−H2a···O1	0.861	1.987	2.818	161.83

dry nitrogen using standard Schlenk techniques. Dichloromethane was dried and distilled over K_2CO_3, and toluene was dried and distilled over Na. Glycine methyl ester hydrochloride, L-alanine methyl ester hydrochloride, L-leucine methyl ester hydrochloride, and L-methionine methyl ester hydrochloride were prepared from the corresponding amino acids and $SOCl_2$ in a microwave-supported reaction according to a published procedure. All analytical data correspond to the literature.[49] The gold(I) precursors (dms)AuCl (dms = Me_2S) and (tht)AuBr (tht = tetrahydrothiophene) were synthesized according to a published procedure from gold, HCl, and DMSO[50] and gold, bromine, and tetrahydrothiophene,[51] respectively. All other solvents and reagents were commercially available and used as received.

NMR spectra were recorded either on a Bruker Digital Avance III (300 MHz) or on a Bruker Digital Avance III (700 MHz) spectrometer, and ^{1}H and ^{13}C shifts are reported in parts per million (ppm) relative to $Si(CH_3)_4$ and were referenced internally with respect to the residual signal of the deuterated solvent. High-resolution mass spectra were obtained using an Agilent 6520 Q-TOF mass spectrometer with an electrospray ionization (ESI) source. All analyses were performed in positive ionization mode. Elemental analyses were carried out at the Institute for Chemical Technology of Organic Materials at Johannes Kepler University Linz. Optical rotations were recorded on a Schmidt & Haensch Polarimeter Model Unipol L-1000. Single-crystal structure analyses of **1b** and **2b** were carried out on a Bruker Smart X2S diffractometer operating with Mo Kα radiation (λ = 0.710 73 Å). Single-crystal analysis of **5** was carried out on a Bruker SMART APEX diffractometer, also operating with Mo Kα radiation (λ = 0.710 73 Å).

Further crystallographic and refinement data can be found in Table 2. The structures were solved by direct methods (SHELXS-97)[52] and refined by full-matrix least squares on F^2 (SHELXL-97).[53] The H atoms were calculated geometrically, and a riding model was applied in the refinement process. CCDC 1006001 and 1006002 contain the supplementary crystallographic data for compounds **1b** and **5**. In **5**, the complex containing the Au2 atom, the carbon atoms of the disordered isopropyl and methyl ester groups were refined isotropically. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk.

*Chlorido[4-(diphenylphosphino)benzoic acid]gold(I), **1a**. Preparation of Complex **1a** According to a Modified Procedure.*[39] 4-(Diphenylphosphino)benzoic acid (212 mg, 0.692 mmol) was

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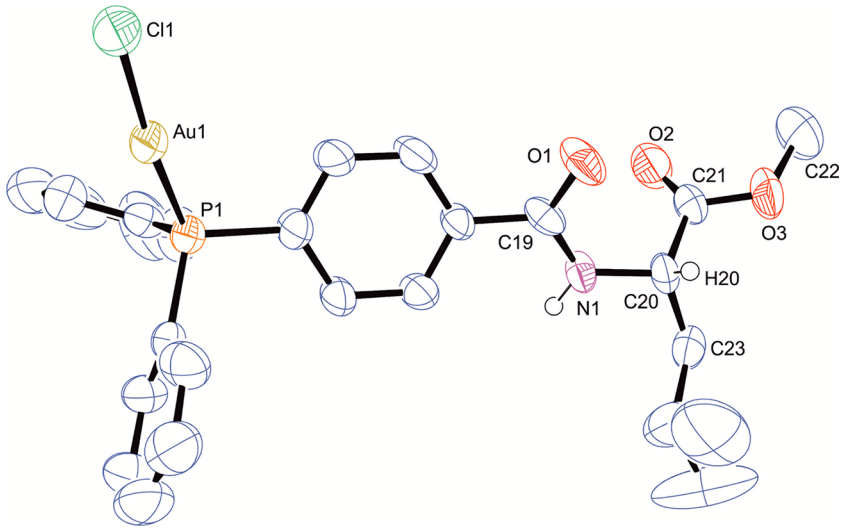

Figure 3. Molecular structure of the complex molecule showing no disorder of the methoxy and isopropyl groups in crystals of **5** (most hydrogen atoms omitted for clarity, ellipsoids drawn at the 50% probability level). Selected bond lengths and angles: P1–Au1, 2.230(2); Au1–Cl1, 2.272(2); C19–N1, 1.341(9); P1–Au1–Cl1, 173.45(9). For the second molecule (not shown): P2–Au2, 2.234(2); Au2–Cl2, 2.286(2); C45–N2, 1.345(8); P2–Au2–Cl2, 170.44(9).

dissolved in 10 mL of dichloromethane (DCM), and (dms)AuCl (204 mg, 0.693 mmol) was added. The reaction mixture was stirred for 15 min at room temperature, resulting in a colorless clear solution. The solvent was partially removed in vacuo, and *n*-pentane was added to precipitate a white solid. Slow gas-phase diffusion of *n*-pentane into a DCM solution gave colorless crystals. Yield: 306 mg (0.57 mmol, 82%).

Complementary NMR Data. ^{1}H NMR (300 MHz, $CDCl_3$, δ [ppm]): 10.77 (s, broad, 1H, O*H*), 8.19–8.16 (m, 2H), 7.66–7.47 (m, 12H). $^{31}P\{^{1}H\}$ NMR (121 MHz, $CDCl_3$, δ [ppm]): 33.2(1). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, δ [ppm]): 170.7, 135.6 (d, $J_{C,P}$ = 59 Hz), 134.4 (d, $J_{C,P}$ = 14 Hz), 134.1 (d, $J_{C,P}$ = 14 Hz), 132.5 (d, $J_{C,P}$ = 3 Hz), 132.5 (d, $J_{C,P}$ = 3 Hz), 130.6 (d, $J_{C,P}$ = 12 Hz), 129.6 (d, $J_{C,P}$ = 12 Hz), 127.8 (d, $J_{C,P}$ = 62 Hz). MS (ESI pos, in MeOH:CH_3OH = 1:1): *m*/*z* 809 $[C_{38}H_{30}O_4P_2Au]^+$, 1041 $[C_{38}H_{30}O_4P_2Au_2Cl]^+$. MS (ESI neg, in MeOH:$CH_3OH$ = 1:1): *m*/*z* 537 $[C_{19}H_{14}O_2PAuCl]^-$. Anal. Calcd for $C_{19}H_{15}O_2PAuCl$ (538.72): C 42.36, H 2.81. Found: C 42.24, H 2.69.

Chlorido[4-(diphenylphosphino)benzoyl chloride]gold(I), ***2a***. Under nitrogen atmosphere, chlorido[4-(diphenylphosphino)benzoic acid]gold(I) (500 mg, 0.93 mmol) was suspended in 100 mL of dry toluene. Oxalyl chloride (150 μL, 1.75 mmol, 1.9 equiv) and 1 drop of DMF were added. The solution was stirred at room temperature for 60 min, causing the reaction mixture to clarify. The solvent was removed in vacuo. The oily residue was dissolved in dry dichloromethane, and dry *n*-pentane was added to precipitate a pale solid, which was filtrated and washed with dry *n*-pentane. Yield: 415 mg (0.74 mmol, 80%). Due to the air and moisture sensitivity of the acyl chloride functionality, no elemental analysis and mass spectrometry could be carried out.

^{1}H NMR (300 MHz, $CDCl_3$, δ [ppm]): 8.17–8.14 (m, 2H), 7.66–7.48 (m, 12H). $^{31}P\{^{1}H\}$ NMR (121 MHz, $CDCl_3$, δ [ppm]): 33.1(2). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, δ [ppm]): 167.8, 137.7 (d, $J_{C,P}$ = 58 Hz), 136.0 (d, $J_{C,P}$ = 3 Hz), 134.4 (d, $J_{C,P}$ = 14 Hz), 134.4 (d, $J_{C,P}$ = 14 Hz), 132.8 (d, $J_{C,P}$ = 3 Hz), 131.5 (d, $J_{C,P}$ = 12 Hz), 129.7 (d, $J_{C,P}$ = 12 Hz), 127.4 (d, $J_{C,P}$ = 63 Hz).

Bromido[4-(diphenylphosphino)benzoic acid]gold(I), ***1b***. 4-(Diphenylphosphino)benzoic acid (50 mg, 0.163 mmol) was dissolved in 5 mL of DCM. (tht)AuBr (60 mg, 0.164 mmol) was added, resulting in a yellow-orange reaction mixture. The mixture was stirred for 15 min at room temperature and filtrated, and *n*-pentane was added to precipitate a pale solid. Slow gas-phase diffusion of *n*-pentane into a chloroform solution gave yellow crystals suitable for X-ray diffraction.

^{1}H NMR (300 MHz, $CDCl_3$, δ [ppm]): 8.17–8.14 (m, 2H), 7.66–7.52 (m, 12H). $^{31}P\{^{1}H\}$ NMR (121 MHz, $CDCl_3$, δ [ppm]): 35.21. $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, δ [ppm]): 170.7, 135.8 (d, $J_{C,P}$ = 58 Hz), 134.4 (d, $J_{C,P}$ = 14 Hz), 134.1 (d, $J_{C,P}$ = 14 Hz), 132.5 (d, $J_{C,P}$ = 3 Hz), 132.3 (d, $J_{C,P}$ = 3 Hz), 130.7 (d, $J_{C,P}$ = 12 Hz), 129.6 (d, $J_{C,P}$ = 12 Hz), 128.0 (d, $J_{C,P}$ = 61 Hz). MS (ESI pos, in MeOH): *m*/*z* 809 $[C_{38}H_{30}O_4P_2Au]^+$, 1087 $[C_{38}H_{30}O_4P_2Au_2Br]^+$. MS (ESI neg, in MeOH): *m*/*z* 581 $[C_{19}H_{14}O_2PAuBr]^-$. Anal. Calcd for $C_{19}H_{15}O_2PAuBr$ (583.17) C 39.13, H 2.59. Found: C 39.01, H 2.47.

Bromido[4-(diphenylphosphino)benzoyl chloride]gold(I) ***2b***. Under nitrogen atmosphere, bromido[4-(diphenylphosphino)benzoic acid]gold(I) (30 mg, 0.052 mmol) was suspended in 7 mL of dry toluene. Oxalyl chloride (7 μL, 0.082 mmol, 1.6 equiv) and 1 drop of DMF were added. The solution was stirred at room temperature for 30 min, causing the reaction mixture to clarify. The the solvent was removed in vacuo. The oily residue was dissolved in dry toluene, and *n*-pentane was added to precipitate a pale solid, which was filtrated and washed with dry *n*-pentane. Colorless needles suitable for X-ray diffraction were obtained. Due to the air and moisture sensitivity of the acyl chloride functionality, no elemental analysis and mass spectrometry could be carried out.

^{1}H NMR (300 MHz, $CDCl_3$, δ [ppm]): 8.10 (s, 2H), 7.61–7.46 (m, 12H). $^{31}P\{^{1}H\}$ NMR (121 MHz, $CDCl_3$, δ [ppm]): 35.10. $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, δ [ppm]): 167.7, 137.8 (d, $J_{C,P}$ = 56 Hz), 135.9 (d, $J_{C,P}$ = 3 Hz), 134.4 (d, $J_{C,P}$ = 14 Hz), 134.3 (d, $J_{C,P}$ = 14 Hz), 132.7 (d, $J_{C,P}$ = 3 Hz), 131.5 (d, $J_{C,P}$ = 12 Hz), 129.7 (d, $J_{C,P}$ = 12 Hz), 127.5 (d, $J_{C,P}$ = 61 Hz).

General Procedure for the Synthesis of Complexes 3–7. Compound **1a** (100 mg, 0.186 mmol) was dissolved in 5 mL of dry DCM. Then EDC·HCl (1.2 equiv) and *N*-hydroxysuccinimide (1.2 equiv) were added, and the reaction mixture was stirred at ambient temperature for 5 h. The corresponding amino acid methyl ester hydrochloride (1.4 equiv) and triethylamine (4 equiv) were added and stirred overnight at room temperature. The solution was diluted with 80 mL of ethyl acetate and washed with 1 N HCl (2 × 20 mL), water (40 mL), saturated $NaHCO_3$ (2 × 20 mL), and brine (2 × 20 mL). The organic phase was dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was taken up in a small amount of DCM, and *n*-pentane was added to precipitate a white solid. If necessary, the crude product can be purified by column chromatography with a DCM/methanol mixture (6:1) that contains 1% TEA.

[ClAuP(Ph)$_2$(C$_6$H$_4$COPheOMe)], ***(3)***. 87.7 mg (0.16 mmol) of **1a**; 38.8 mg of (0.18 mmol) L-phenylalanine methyl ester hydrochloride. Yield: 98.9 mg (88%) of an off-white solid.

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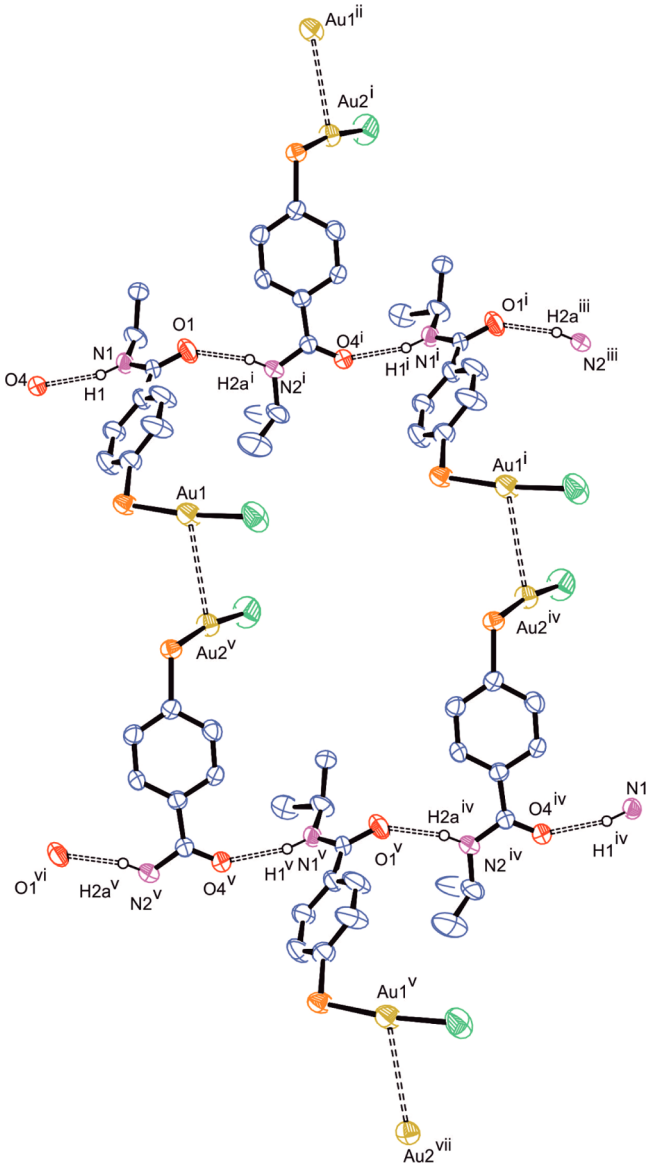

Figure 4. Excerpt from the cell plot of the crystalline phase of compound **5** illustrating the aggregation of the complex molecules by aurophilic interaction (Au1−Au2^{v}, 3.426(1) Å) and hydrogen bonds to form two-dimensional sheets. Nonfunctionalized phenyl groups as well as isopropyl and carboxylate groups of the leucine moiety were omitted for clarity.

^{1}H NMR (300 MHz, $CDCl_3$, δ [ppm]): 7.78−7.75 (m, 2H, aromatic *H*), 7.61−7.47 (m, 12H, aromatic *H*), 7.34−7.28 (m, 3H, aromatic *H* of Phe side chain), 7.15−7.10 (m, 2H, aromatic *H* of Phe side chain), 6.55 (d, 1H, $^{3}J_{HH}$ = 7 Hz, −N*H*), 5.11−5.04 (m, 1H, $C_{\alpha}H$), 3.79 (s, 3H, $-OCH_3$), 3.33 and 3.20 ("ABX", 2H diastereotopic, J_{AB} = 13.8 Hz, $^{3}J_{HH}$ = 6.0 and 5.3 Hz, $C_{\beta}H_2$). ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$, δ [ppm]): 32.85. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, δ [ppm]): 171.9, 165.7, 137.2 (d, J_{PC} = 2.6 Hz), 135.7, 134.4 (d, J_{PC} = 14 Hz), 134.3 (d, J_{PC} = 14 Hz), 133.1 (d, J_{PC} = 60 Hz), 132.4 (d, J_{PC} = 2.5 Hz), 129.5 (d, J_{PC} = 12 Hz), 129.4, 128.9, 128.7, 128.0 (d, J_{PC} = 63 Hz), 127.8 (d, J_{PC} = 12 Hz), 127.5, 127.2, 53.7 (C_{α}), 52.7 ($-OCH_3$), 37.8 (C_{β}). MS (ESI pos, in MeOH:$CHCl_3$ = 1:1): *m*/*z* 664 $[C_{29}H_{26}NO_3PAu]^{+}$, 1131 $[C_{58}H_{52}N_2O_6P_2Au]^{+}$, 1363 $[C_{58}H_{52}N_2O_6P_2Au_2Cl]^{+}$. HRMS (ESI): *m*/*z* calcd for $C_{29}H_{27}NO_3PAuCl$ $[M + H]^{+}$: 700.107 71, found: 700.108 08; calcd for $C_{29}H_{30}N_2O_3PAuCl$ $[M + NH_4]^{+}$: 717.134 26, found: 717.136 40; calcd for $C_{29}H_{26}NO_3PAuClNa$ $[M + Na]^{+}$: 722.089 65, found: 722.090 13. $[\alpha]_D^{21}$: +42.1 (*c* = 1.0 g/L, $CHCl_3$); −38.8 (*c* = 1.3 g/L, CH_3OH).

[ClAuP(Ph)$_2$(C$_6$H$_4$COGlyOMe)], **(4)**. 82.2 mg (0.15 mmol) of **1a**; 23.2 mg (0.18 mmol) of glycine methyl ester hydrochloride. Yield: 78.1 mg (85%) of an off-white solid.

^{1}H NMR (300 MHz, $CDCl_3$, δ [ppm]): 7.90−7.87 (m, 2H, aromatic *H*), 7.61−7.46 (m, 12H, aromatic *H*), 6.86 (t, 1H, $^{3}J_{HH}$ = 5 Hz, −N*H*), 4.24 (d, 2H, $^{3}J_{HH}$ = 5 Hz, $C_{\alpha}H_2$), 3.78 (s, 3H, $-OCH_3$). ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$, δ [ppm]): 32.82. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, δ [ppm]): 170.3, 166.3, 137.0 (d, J_{PC} = 2.5 Hz), 134.4 (d, J_{PC} = 14 Hz), 134.3 (d, J_{PC} = 14 Hz), 133.1 (d, J_{PC} = 60 Hz), 132.5 (d, J_{PC} = 2.5 Hz), 129.6 (d, J_{PC} = 12 Hz), 128.0 (d, J_{PC} = 63 Hz), 127.9 (d, J_{PC} = 12 Hz), 52.7 ($-OCH_3$), 41.9 (C_{α}). MS (ESI pos, in MeOH:$CHCl_3$ = 1:1): *m*/*z* 951 $[C_{44}H_{40}N_2O_6P_2Au]^{+}$, 1183 $[C_{44}H_{40}N_2O_6P_2Au_2Cl]^{+}$. HRMS (ESI): *m*/*z* calcd for $C_{22}H_{21}NO_3PAuCl$ $[M + H]^{+}$: 610.060 76, found: 610.059 42; calcd for $C_{22}H_{24}N_2O_3PAuCl$ $[M + NH_4]^{+}$: 627.087 31, found: 627.085 89; calcd for $C_{22}H_{20}NO_3PAuClNa$ $[M + Na]^{+}$: 632.0427, found: 632.041 84.

[ClAuP(Ph)$_2$(C$_6$H$_4$COLeuMe)], **(5)**. 89.2 mg (0.17 mmol) of **1a**; 43.0 mg (0.24 mmol) of L-leucine methyl ester hydrochloride. The crude product was purified by column chromatography (silica gel, DCM:CH_3OH = 6:1 + 1% TEA). Yield: 72.0 mg (65%) of an off-white solid.

^{1}H NMR (300 MHz, $CDCl_3$, δ [ppm]): 7.87−7.84 (m, 2H, aromatic *H*), 7.59−7.45 (m, 12H, aromatic *H*), 6.70 (d, 1H, $^{3}J_{HH}$ = 8 Hz, −N*H*), 4.87−4.80 (m, 1H, $C_{\alpha}H$), 3.76 (s, 3H, $-OCH_3$), 1.78−1.64 (m, 3H, $C_{\beta}H_2$ and $C_{\gamma}H$), 0.98−0.95 (m, 6H, $C_{\delta}H_3$). ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$, δ [ppm]): 32.78. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, δ [ppm]): 173.6, 165.9, 137.2 (d, J_{PC} = 2.4 Hz), 134.4 (d, J_{PC} = 14 Hz), 134.3 (d, J_{PC} = 14 Hz), 133.0 (d, J_{PC} = 61 Hz), 132.4 (d, J_{PC} = 2.5 Hz), 129.5 (d, J_{PC} = 12 Hz), 128.1 (d, J_{PC} = 63 Hz), 127.8 (d, J_{PC} = 12 Hz), 52.6 ($-OCH_3$), 51.4 (C_{α}), 41.7 (C_{β}), 25.1 (C_{γ}), 22.9 (C_{δ}), 22.1 (C_{δ}). MS (ESI pos, in MeOH:$CHCl_3$ = 1:1): *m*/*z* 1063 $[C_{52}H_{56}N_2O_6P_2Au]^{+}$, 1295 $[C_{52}H_{46}N_2O_6P_2Au_2Cl]^{+}$. HRMS (ESI): *m*/

Table 2. Crystal Data and Data Collection and Structure Refinement Details for Compounds 1b and 5

	1b	5
formula	$C_{40}H_{32}Au_2Br_2Cl_6O_4P_2$	$C_{53}H_{58}Au_2Cl_4N_2O_6P_2$
M_w [g mol^{-1}]	1405.05	1416.69
cryst size [mm]	0.16 × 0.31 × 0.59	0.09 × 0.17 × 0.23
cryst syst	orthorhombic	triclinic
space group	*Pbca*	*P*1
a [Å]	19.3996 (18)	9.0890
b [Å]	15.3683 (12)	9.7690
c [Å]	30.582 (3)	17.2420
α [deg]	90	73.95
β [deg]	90	87.38
γ [deg]	90	72.36
V [Å^3]	9117.7 (14)	1400.9
ρ_{calc} [g cm^{-3}]	2.047	1.679
Z	8	1
μ [mm^{-1}]	8.64	5.53
T [K]	200	298
Θ range [deg]	1.8−24.0	2.3−27.3
reflns collected	76 656	16 211
unique reflns	7 104	12 253
obsd reflns [$I > 2\sigma(I)$]	5 897	10 480
params refined/restraints	505/0	626/7
abs correction	multiscan	multiscan
T_{min}, T_{max}	0.12, 0.34	0.36, 0.64
σ_{fin}(max/min) [e Å^{-3}]	1.46/−1.31	1.77/−0.58
R_1 [$I \geq 2\sigma(I)$]	0.032	0.042
wR_2	0.082	0.092
CCDC no.	1006001	1006002

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z calcd for $C_{26}H_{29}NO_3PAuCl$ $[M + H]^+$: 666.123 36, found: 666.122 58; calcd for $C_{26}H_{32}N_2O_3PAuCl$ $[M + NH_4]^+$: 683.149 91, found: 683.149 77; calcd for $C_{26}H_{28}NO_3PAuClNa$ $[M + Na]^+$: 688.105 31, found: 688.104 30. $[\alpha]_D^{21}$: + 6.0 (*c* = 1.0 g/L, $CHCl_3$); −11.8 (*c* = 0.98 g/L, CH_3OH).

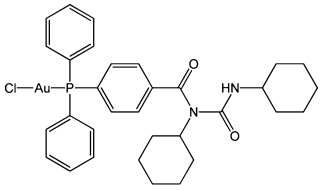
[ClAuP(Ph)$_2$(C$_6$H$_4$COAlaOMe)], **(6)**. 66.1 mg (0.12 mmol) of **1a**; 24.1 mg (0.17 mmol) of L-alanine methyl ester hydrochloride. Yield: 47.4 mg (62%) of an off-white solid.

^{1}H NMR (300 MHz, $CDCl_3$, δ [ppm]): 7.89−7.85 (m, 2H, aromatic *H*), 7.60−7.44 (m, 12H, aromatic *H*), 6.89 (d, 1H, $^3J_{HH}$ = 7 Hz, −N*H*), 4.77 (quint, 1H, $^3J_{HH}$ = 7 Hz, C$_\alpha$*H*), 3.78 (s, 3H, −OC*H*$_3$), 1.52 (d, 3H, $^3J_{HH}$ = 7 Hz, C$_\beta$*H*$_3$). ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$, δ [ppm]): 32.77. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, δ [ppm]): 173.5, 165.7, 137.2 (d, J_{PC} = 2.4 Hz), 134.4 (d, J_{PC} = 14 Hz), 134.3 (d, J_{PC} = 14 Hz), 132.9 (d, J_{PC} = 60 Hz), 132.4 (d, J_{PC} = 2.6 Hz), 129.5 (d, J_{PC} = 12 Hz), 128.0 (d, J_{PC} = 63 Hz), 127.8 (d, J_{PC} = 12 Hz), 52.8 (−OC*H*$_3$), 48.8 (C$_\alpha$), 18.6 (C$_\beta$). ^{1}H NMR (700 MHz, $CDCl_3$, δ [ppm]): 7.90 (dd, 1H, $H_{A,A'}$, J_{HH} = 8 Hz, J_{HP} = 1.7 Hz), 7.61 (dd, 2H, $H_{B,B'}$, J_{HH} = 8 Hz, J_{HP} = 13 Hz), 7.58 (t, 2H, H_C, J_{HH} = 8 Hz), 7.54 (dd, 4H, $H_{D,D'}$, J_{HH} = 9 Hz, J_{HP} = 13 Hz), 7.51 (dt, 4H, $H_{E,E'}$, J_{HH} = 8 Hz, J_{HP} = 3 Hz). ^{13}C{^{1}H} NMR (175 MHz, $CDCl_3$, δ [ppm]): 173.5, 165.7, 137.3 (d, $^4J_{PC}$ = 2.6 Hz), 134.4 (d, $^2J_{PC}$ = 14 Hz), 134.3 (d, $^2J_{PC}$ = 14 Hz), 133.0 (d, $^1J_{PC}$ = 60 Hz), 132.4 (d, $^4J_{PC}$ = 2.5 Hz), 129.6 (d, J_{PC} = ^{3}12 Hz), 128.1 (d, $^1J_{PC}$ = 62 Hz), 127.8 (d, $^3J_{PC}$ = 12 Hz). MS (ESI pos, in MeOH:$CHCl_3$ = 1:1): *m*/*z* 979 $[C_{46}H_{44}N_2O_6P_2Au]^+$, 1211 $[C_{46}H_{44}N_2O_6P_2Au_2Cl]^+$. HRMS (ESI): *m*/*z* calcd for $C_{23}H_{23}NO_3PAuCl$ $[M + H]^+$: 624.076 41, found: 624.075 67; calcd for $C_{23}H_{26}N_2O_3PAuCl$ $[M + NH_4]^+$: 641.102 96, found: 641.101 69; calcd for $C_{23}H_{22}NO_3PAuClNa$ $[M + Na]^+$: 646.058 35, found: 646.057 47. $[\alpha]_D^{21}$: + 14.7 (*c* = 1.0 g/L, $CHCl_3$); −4.4 (*c* = 0.94 g/L, CH_3OH).

[ClAuP(Ph)$_2$(C$_6$H$_4$COMetOMe)], **(7)**. 64.6 mg (0.12 mmol) of **1a**; 36.0 mg (0.18 mmol) of L-methionine methyl ester hydrochloride. The crude product was purified by column chromatography (silica gel, DCM:CH_3OH = 6:1 + 1% TEA). Yield: 58.8 mg (72%) of an off-white solid.

^{1}H NMR (300 MHz, $CDCl_3$, δ [ppm]): 7.92−7.89 (m, 2H, aromatic *H*), 7.62−7.46 (m, 12H, aromatic *H*), 7.18 (d, 1H, $^3J_{HH}$ = 8 Hz, −N*H*), 4.94−4.88 (m, 1H, C$_\alpha$*H*), 3.80 (s, 3H, −OC*H*$_3$), 2.62−2.57 (m, 2H, C$_\gamma$H), 2.35−2.14 (m, 2H, C$_\beta$*H*$_2$), 2.12 (s, 3H, −SC*H*$_3$). ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$, δ [ppm]): 32.83. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, δ [ppm]): 172.2, 166.0, 137.0 (d, J_{PC} = 2.2 Hz), 134.4 (d, J_{PC} = 14 Hz), 134.3 (d, J_{PC} = 14 Hz), 133.2 (d, J_{PC} = 60 Hz), 132.5 (d, J_{PC} = 2.5 Hz), 129.6 (d, J_{PC} = 12 Hz), 128.1 (d, J_{PC} = 62 Hz), 128.0 (d, J_{PC} = 12 Hz), 52.6 (−OC*H*$_3$), 52.3 (C$_\alpha$), 30.9 (C$_\gamma$), 30.2 (C$_\beta$), 15.5 (−SC*H*$_3$). MS (ESI pos, in MeOH:$CHCl_3$ = 1:1): *m*/*z* 648 $[C_{25}H_{26}NO_3SPAu]^+$, 1099 $[C_{50}H_{52}N_2O_6S_2P_2Au]^+$, 1331 $[C_{50}H_{52}N_2O_6S_2P_2Au_2Cl]^+$. HRMS (ESI): *m*/*z* calcd for $C_{25}H_{27}NO_3SPAuCl$ $[M + H]^+$: 684.079 78, found: 684.080 54; calcd for $C_{25}H_{30}N_2O_3SPAuCl$ $[M + NH_4]^+$: 701.106 33, found: 700.072 65; calcd for $C_{25}H_{26}NO_3SPAuClNa$ $[M + Na]^+$: 706.061 73, found: 706.060 18; calcd for $C_{25}H_{26}NO_3SPAuClK$ $[M + K]^+$: 722.035 66, found: 722.053 44. $[\alpha]_D^{21}$: −6.9 (*c* = 1.0 g/L, $CHCl_3$); −15.6 (*c* = 1.4 g/L, CH_3OH).

Analytical Data of the *N*-Acylurea Byproduct. The complex was formed as a byproduct of the coupling reaction with DCC and



could be isolated upon washing with methanol. ^{1}H NMR (300 MHz, $CDCl_3$, δ [ppm]): 7.63−7.49 (m, 14 H, aromatic *H*), 5.99 (d, broad, *J* = 7 Hz, N*H*), 4.11−4.03 (m, 1H, C*H*), 3.50−3.41 (m, 1H, C*H*), 2.02−1.91 (m, 2H, C*H*$_2$), 1.84−1.78 (m, 4H, C*H*$_2$), 1.63−1.55 (m, 6H, C*H*$_2$), 1.31−1.08 (m, 6H, C*H*$_2$), 0.92−0.82 (m, 2H, C*H*$_2$). ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$, δ [ppm]): 32.96. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, δ [ppm]): 169.5, 153.8, 140.4 (d, $J_{C,P}$ = 2.6 Hz), 134.4 (d, $J_{C,P}$ = 13 Hz), 134.3 (d, $J_{C,P}$ = 14 Hz), 132.5 (d, $J_{C,P}$ = 2.7 Hz), 131.9 (d, $J_{C,P}$ = 61 Hz), 129.6 (d, $J_{C,P}$ = 12 Hz), 128.1 (d, $J_{C,P}$ = 63 Hz), 127.4 (d, $J_{C,P}$ = 12 Hz), 57.4, 49.9, 32.4, 30.8, 26.2, 25.4, 25.3, 24.6. MS (ESI pos, in MeOH:$CHCl_3$ = 1:1): *m*/*z* 1221 $[C_{64}H_{74}O_4N_4P_2Au]^+$, 1453 $[C_{64}H_{74}O_4N_4P_2Au_2Cl]^+$.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Crystallographic data for compounds **1b** and **5**. Molecules of **2b** in the asymmetric unit (isotropically refined); ^{1}H−^{13}C HSQC of compound **6**, displaying H−H and H−P coupling. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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