Half-Sandwich Complexes of Iridium and Ruthenium Containing Cysteine-Derived Ligands†

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The dimers [{(η^n-ring)MCl}$_2$(μ-Cl)$_2$] ((η^n-ring)M = (η^5-C_5Me_5)Ir, (η^6-*p*-MeC_6H_4*i*Pr)Ru) react with the modified cysteines *S*-benzyl-*L*-cysteine (**HL1**) or *S*-benzyl-α-methyl-*L*-cysteine (**HL2**) rendering cationic complexes of formula [(η^n-ring)MCl(κ^2*N*,*S*-**HL**)]Cl (**1**, **2**) in good yield. Addition of $NaHCO_3$ to complexes **1** and **2** gave equilibrium mixtures of neutral [(η^n-ring)MCl(κ^2*N*,*O*-**L**)] (**3**, **4**) and cationic [(η^n-ring)M(κ^3*N*,*O*,*S*-**L**)]Cl (**6Cl**, **7Cl**) complexes. Similar mixtures were obtained in one-pot reaction by successive addition of the modified cysteine and $NaHCO_3$ to the above formulated dimers. Addition of the *N*-Boc substituted cysteine derivative *S*-benzyl-*N*-Boc-*L*-cysteine (**HL3**) and $NaHCO_3$ to the dimers [{(η^n-ring)MCl}$_2$(μ-Cl)$_2$] affords the neutral compounds [(η^n-ring)MCl(κ^2*O*,*S*-**L3**)] ((η^n-ring)M = (η^5-C_5Me_5)Ir (**5a**), (η^6-*p*-MeC_6H_4*i*Pr)Ru (**5b**)). Complexes of formula [(η^n-ring)MCl(κ^3*N*,*O*,*S*-**L**)][SbF_6] (**6Sb**-**8Sb**), in which the cysteine derivative acts as tridentate chelate ligand, can be prepared by adding one equivalent of $AgSbF_6$ to solutions of compounds **5** or to mixtures of complexes **3**/**6Cl** and **4**/**7Cl**. The amide proton of compounds **8aSb** and **8bSb** can be removed by addition of $NaHCO_3$ affording the neutral complexes [(η^n-ring)M(κ^3*N*,*O*,*S*-**L3**$_{-H}$)] ((η^n-ring)M = (η^5-C_5Me_5)Ir (**9a**), (η^6-*p*-MeC_6H_4*i*Pr)Ru (**9b**)). Complexes **9a** and **9b** can also be prepared by reacting the dimers [{(η^n-ring)MCl}$_2$(μ-Cl)$_2$] with **HL3** and two equivalents of $NaHCO_3$. The absolute configuration of the complexes has been established by spectroscopic and diffractometric means including the crystal structure determination of (R_{Ir},R_C,R_S)-[(η^5-C_5Me_5)Ir(κ^3*N*,*O*,*S*-**L1**)][SbF_6] (**6aSb**). The

thermodynamic parameters associated to the epimerization at sulphur that undergoes the iridium compound [(η^5-C_5Me_5)Ir(κ^3*N,O,S*-**L3**$_{-H}$)] (**9a**) have been determined through variable temperature ^{1}H NMR studies.

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Introduction

The coordination chemistry of α-amino acids towards transition-metal ions has been extensively studied[1] mostly due to the extremely important role that the resulting compounds play in a wide variety of biological processes.[2] This biological activity is often closely related to the nature of the metallic species. Changes in the nuclearity or structure of the complexes can strongly modify their biological properties but also small variations in the ligands or in their coordination modes may be enough to dramatically alter reactivities.[3]

Sulphur-containing α-amino acids play a key role in living systems.[4] For example, cysteine, methionine and glutathione appear to be crucial in the biological chemistry of platinum anticancer agents[5] and silver (I) acetylmethioninates showed effective antimicrobial activities against two Gram-negative bacteria and two yeasts.[6]

Cysteine exhibits a wide variety of coordination modes to transition metals including monodentate, bidentate or tridentate chelate as well as bidentate chelate and bridge at the same time, among others. Although the biological activity of the derived complexes depends on both the product distribution and rates of interconversion, the factors that govern these features are far for being understood.[7]

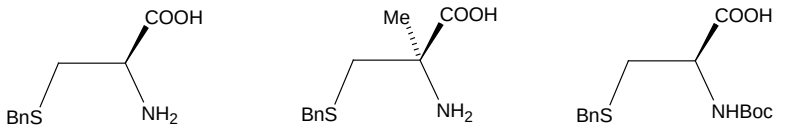
On the other hand, cyclopentadienyl-iridium(III) and arene-ruthenium(II) complexes, containing a wide range of ligands, have shown important biological activity as potent anticancer agents both in vivo and in vitro.[8,9] For example, half-sandwich iridium(III) complexes containing 2-phenylpyridine ligands bind strongly nucleobase 9EtG indicating that DNA could be a target for these complexes[8b] and half-sandwich ruthenium (II) complexes containing diaminohexopyranosides as ligands have shown in vitro antiproliferative activity against different cancer cells.[9e]

In the present paper, we study the coordination chemistry of the cysteine-derived ligands *S*-benzyl-*L*-cysteine (**HL1**), *S*-benzyl-*α*-methyl-*L*-cysteine (**HL2**) and *S*-benzyl-*N*-Boc-*L*-cysteine (**HL3**) towards (η^5-C_5Me_5)Ir and (η^6-*p*-MeC_6H_4*i*Pr)Ru moieties. Special attention is paid to the different coordination modes that the modified cysteines display and to the stereochemistry of the resulting complexes.

Results and discussion

Synthesis of the metallic compounds.

The synthetic routes developed for the preparation of the new compounds are depicted in Scheme 1. The dimers [{(η^n-ring)MCl}$_2$(μ-Cl)$_2$] ((η^n-ring)M = (η^5-C_5Me_5)Ir,[10] (η^6-*p*-MeC_6H_4*i*Pr)Ru)[11] react with the modified cysteines *S*-benzyl-*L*-cysteine (**HL1**) or *S*-benzyl-α-methyl-*L*-cysteine (**HL2**) (Chart 1) rendering cationic complexes of formula [(η^n-ring)MCl(κ^2*N,S*-**HL**)]Cl (**1**, **2**) in good yield. However, the addition of the *N*-Boc substituted cysteine derivative *S*-benzyl-*N*-Boc-*L*-cysteine (**HL3**) to solutions of the dimers gave intractable mixtures of unidentified species together with unreacted starting materials.



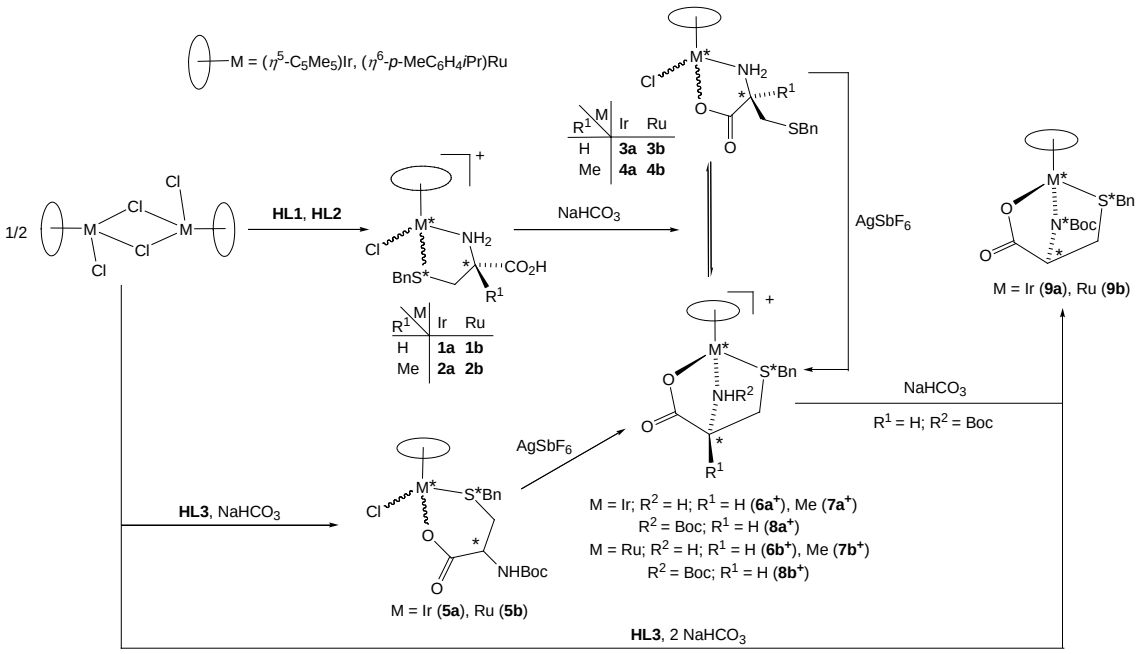
S-Benzyl-*L*-cysteine **HL1** | *S*-Benzyl-α-methyl-*L*-cysteine **HL2** | *S*-Benzyl-*N*-Boc-*L*-cysteine **HL3**

Chart 1. Modified cysteines

Addition of $NaHCO_3$ to complexes **1** and **2** gave equilibrium mixtures of neutral [(η^n-ring)MCl(κ^2*N,O*-**L**)] (**3**, **4**) and cationic [(η^n-ring)M(κ^3*N,O,S*-**L**)]Cl (**6Cl**, **7Cl**) complexes. Similar mixtures were obtained in one-pot reaction by successive addition of the corresponding cysteine-derived ligand and $NaHCO_3$ to the above formulated dimers.

The *N*-Boc protected ligand **HL3** also behaves differently in basic medium. Thus, when **HL3** and $NaHCO_3$ were added to the dimers [{(η^n-ring)MCl}$_2$(μ-Cl)$_2$], the neutral compounds [(η^n-ring)MCl(κ^2*O,S*-**L3**)] ((η^n-ring)M = (η^5-C_5Me_5)Ir (**5a**), (η^6-*p*-MeC_6H_4*i*Pr)Ru (**5b**)), in which the amino carboxylate shows a κ^2*O,S* coordination

mode, were isolated. However, nitrogen coordination can be forced by removing the chloride with subsequent generation of a vacant site. Thus, addition of one equivalent of $AgSbF_6$ to complexes **5** gave rise to the cationic complexes [(η^n-ring)M(κ^3*N,O,S*-**L3**)][SbF_6] ((η^n-ring)M = (η^5-C_5Me_5)Ir (**8aSb**), (η^6-*p*-MeC_6H_4*i*Pr)Ru (**8bSb**)) in which, along with the sulphur and the oxygen, the nitrogen atom is also coordinated to the metal. The **L1** and **L2** containing cationic analogues [(η^n-ring)M(κ^3*N,O,S*-**L**)][SbF_6] ((η^n-ring)M = (η^5-C_5Me_5)Ir, **L** = **L1** (**6aSb**), **L2** (**7aSb**); η^n-ring = (η^6-*p*-MeC_6H_4*i*Pr)Ru **L** = **L1** (**6bSb**), **L2** (**7bSb**)) were isolated by adding one equivalent of $AgSbF_6$ to mixtures of **3** and **6Cl** or **4** and **7Cl**.



Scheme 1. Preparative routes for complexes **1**-**9**

Finally, the amide proton of compounds **8aSb** and **8bSb** can be removed by addition of $NaHCO_3$ affording the neutral complexes **9a** and **9b**, respectively. Alternatively, complexes **9** can also be prepared by reacting the dimers [{(η^n-ring)MCl}$_2$(μ-Cl)$_2$] with **HL3** and two equivalents of $NaHCO_3$.

All these preparative routes are essentially similar to those recently reported for the (η^5-C_5Me_5)Rh analogues.[12]

Molecular structure of the complex (R_{Ir},R_C,R_S)-[(η^5-C_5Me_5)Ir(κ^3*N,O,S*-L1)][SbF_6] (6aSb).

Single crystals of the complex were grown by slow diffusion of diethyl ether into dry methanolic solutions of the compound and the solid state molecular structure was determined by X-ray diffraction. A molecular representation of the cation is depicted in Figure 1 and selected geometrical parameters are listed in Table 1. The structural features found in **6aSb** are similar to those recently reported for the rhodium analogue [(η^5-C_5Me_5)Rh(κ^3*N,O,S*-**L1**)][SbF_6].[12] Complex **6aSb** exhibits the common "three-legged piano-stool" geometry, with three *fac* positions occupied by an η^5-C_5Me_5 group and the three remaining coordination sites held by the *S*-benzyl-*L*-cysteine which adopts a κ^3*N,O,S* coordination mode. According to the ligand priority sequence,[13] the absolute configuration is R_{Ir},R_C,S_S.

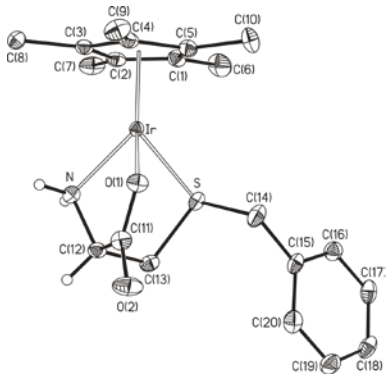


Figure 1. Molecular representation of the cation of **6aSb**

Table 1. Selected bond distances (Å) and angles (º) for **6aSb**

Ir-S	2.3646(9)	S-Ir-O(1)	85.32(7)
Ir-N	2.137(3)	S-Ir-Ct[a]	131.03(4)
Ir-O(1)	2.114(2)	N-Ir-O(1)	75.28(11)
Ir-Ct[a]	1.7812(1)	N-Ir-Ct[a]	134.91(8)
S-Ir-N	81.40(8)	O(1)-Ir-Ct[a]	128.79(6)

[a] Ct represents the centroid of the η^5-C_5Me_5 ring

The tridentate coordination of *S*-benzyl-*L*-cysteine leads to the formation of two five-membered, Ir-O-C-C-N and Ir-S-C-C-N, and one six-membered Ir-S-C-C-C-O metallacycles. Ring puckering parameters (q = 0.558(3), Φ = 155.2(3)°; q = 0.632(3), φ = -41.1(3)°; q = 1.240(2), φ = -170.0(1)°; θ = 100.7(1)°; respectively)[14] are characteristic of $^5E/T_1$, E_5 and $B_{4,1}$ conformations. The adopted conformations in the metallacycles minimize the steric impediments between the bulkiest fragments, with the C_5Me_5 and benzyl groups occupying pseudoequatorial and pseudoaxial positions, respectively, in the six-membered ring.

Comparison of the structure of **6aSb** with that of the isolated *S*-benzyl-*L*-cysteine, whose crystal structure exhibits two independent molecules,[15] revealed the lengthening of S-C(13) (**6aSb**: 1.832(4) Å, **HL1**: 1.810(3) and 1.805(4) Å) and O(1)-C(11) bonds (1.292(4) Å, **HL1**: 1.268(4) and 1.258(4) Å), due to the coordination of sulphur and oxygen atom to the metal. However, the N-C(12) bond is less affected (**6aSb**: 1.478(4) Å, **HL1**: 1.486(4) and 1.496(4) Å).

Protons of the NH_2 fragment of the cysteine derivative are involved in strong N-H···O hydrogen bonds and weak N-H···π interactions with carboxylate and benzyl groups of neighbouring molecules, stabilizing the solid state structure (See ESI†).

Characterization of the metallic compounds

The new complexes were characterized by analytical and spectroscopic means (see Experimental section). Assignment of the NMR signals was verified by two dimensional homonuclear and heteronuclear correlations. The IR spectra showed strong ν(C=O) absorptions in the 1610-1730 cm^{-1} range (carboxylate) and around 1760 cm^{-1} (Boc).[16] The SbF_6 derivatives present a strong band around 650 cm^{-1} attributed to this

anion. The ^{1}H NMR data are consistent with the presence of the C_5Me_5 and cysteine-derived ligands in a 1:1 molar ratio, in all cases.

Regarding the stereochemistry of the new complexes, in all of them, the metal is a stereogenic centre and, therefore, two stereoisomers, epimers at the metal, can be obtained. The *R* at carbon enantiomer of the cysteine-derived ligands was employed and we estimate that, due to the soft reaction conditions employed, no changes in the configuration at this carbon occur in the course of the reactions. Therefore, we assume that the configuration of the carbon of the modified cysteine is *R* in all complexes. Notably, in complexes bearing κ^3*N,O,S* coordinated cysteine derivatives, the *R* configuration at carbon forces the metal to exclusively adopt the *R* configuration.[12] On the other hand, when the sulphur coordinates to the metal (compounds **1**, **2**, **5-9**) two isomers with opposite configuration at sulphur could be formed. Additionally, in compounds **8** and **9**, the nitrogen is also a stereogenic centre with two possible configurations.

Complexes with κ^2N,S coordination mode. No base has been added in the preparative reaction of complexes **1** and **2**. A broad peak in the ^{1}H NMR, centred at around 9.5 ppm (complexes **1**) or at around 6 ppm (complexes **2**),[17] indicates that the proton of the carboxylic group was not dissociated. Consistently, the IR spectra present a very broad absorption centred at around 2950 cm^{-1} (ν(OH)) and the carboxylic ν(C=O) band appears in the 1715-1729 cm^{-1} range, 60-100 cm^{-1} shifted to greater energies than that of compounds **3-9** in which the carboxylic group is deprotonated (see Experimental section).

At room temperature, the NMR spectra of compounds **1a**,**b** and **2a** show two sharp sets of signals, in 92/8 (**1a**), 80/20 (**1b**) and 91/9 (**2a**) molar ratio, attributed to the S_M,R_C and R_M,R_C diastereomers. However, for complex **2b** three sets of resonance signals, in

64/27/9 molar ratio, were registered. We assume that in complexes **1** and **2** the sulphur is coordinated to the metal and, therefore, it is a stereogenic centre. For complexes **1a**,**b** and **2a**, either only one epimer at sulphur is obtained or both epimers quickly exchange in solution. However, for complex **2b**, probably the two epimers at sulphur either of the S_M,R_C or of the R_M,R_C isomer were observed.

Variable temperature proton NMR experiments, in the 298-213 K range, show an apparent broadening of the resonance signals in all cases but no splitting of the signals was observed even at the lowest temperature recorded and NOESY spectra were not informative about the stereochemistry of the compounds.

However, the circular dichroism (CD) spectra of the mixtures present a positive Cotton effect centred at around 340 nm for the iridium complexes and at around 360 nm for the ruthenium analogues. As we will comment later, the positive sign of this maximum is associated to an *S* configuration at the metal centre and, therefore, the configuration of the major isomer of complexes **1** and **2** would be S_M,R_C.

Table 2. Chemical shift of the C_5Me_5 protons in the iridium complexes

κ^2-coordination		κ^3-coordination	
	$\delta(C_5Me_5)$		$\delta(C_5Me_5)$
1a	1.66, 1.73	**6aCl**	1.87
2a	1.64, 1.67	**7aCl**	1.88
3a	1.60, 1.67	**6aSb**	1.92
4a	1.55, 1.58	**7aSb**	1.84
5a	1.43, 1.66, 1.60, 1.71	**8aSb**	1.84
		9a	1.93

The value of the C_5Me_5 protons chemical shift in complexes **1a** and **2a**, 1.64-1.73 ppm, is characteristic of a bidentate chelate coordination of the cysteine-derived ligands (Table 2). The carbon resonance of the methylene group bonded to the stereogenic carbon of the cysteine derivative (CH_2C^*) appears at 36.76-38.83 ppm for the complexes with the **HL1** ligand (**1a**,**b**) and at 38.71-45.27 ppm for the complexes with

the modified cysteine **HL2** (**2a**,**b**). These values were characteristic for the methylene group when it is engaged in a metallacyle ring (Table 3).

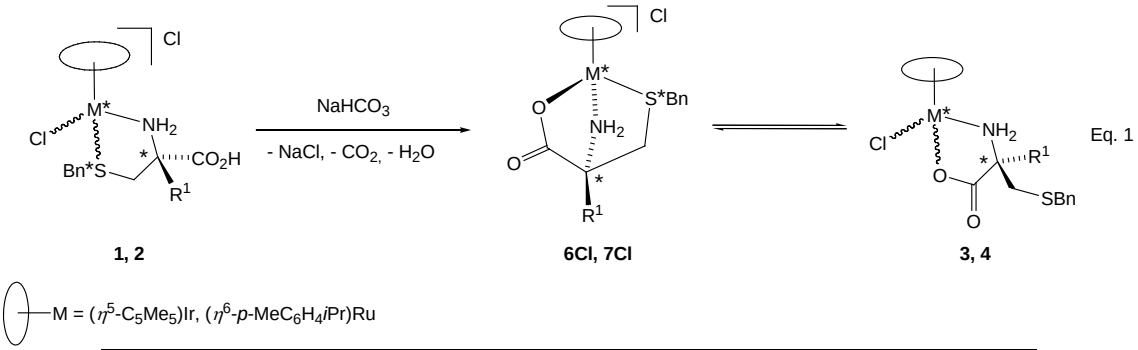
Table 3. Chemical shift of the methylene carbon CH_2C^* and number of metallacycles in which the CH_2C^* group is engaged

Ir		HL1	HL2	HL3	Number of Metallacycles
	1a	36.76, 38.83	--	--	1
	2a	--	38.71, 40.51	--	1
	3a	40.66, 41.05	--	--	0
	4a	--	45.89, 46.22	--	0
	5a			34.67, 37.56, 35.02, 37.03	1
	6aCl	32.24	--	--	2
	6aSb	31.37	--	--	2
	7aCl	--	36.47	--	2
	7aSb	--	35.84	--	2
	8aSb	--	--	28.13	2
	9a	--	--	32.00	2
Ru	**1b**	37.67, 38.38	--	--	1
	2b	--	39.91, 44,35, 45.27	--	1
	3b	45.60	--	--	0
	5b	--	--	33.48, 33.48, 35.69	1
	6bCl	32.80	--	--	2
	7bCl	--	37.70, 36.75	--	2
	6bSb	31.05	--	--	2
	7bSb	--	35.98	--	2
	8bSb	--	--	31.81	2
	9b	--	--	32.57, 33.44	2

*Reaction of complexes **1** and **2** with $NaHCO_3$.* The carboxylic group of compounds **1** and **2** can be deprotonated with $NaHCO_3$. Formally, the resulting carboxylate group displaces the chloride from the coordination sphere of the metal giving rise to the κ^3N,O,S coordinated cationic complexes **6Cl** and **7Cl**. These complexes are in equilibrium with the corresponding κ^2N,O neutral compounds **3** and **4** in which the chloride replaces the coordinated SBn arm in complexes **6Cl** and **7Cl** (Eq. 1). In the Table of Eq. 1, the relative amounts of neutral and cationic complexes, the isomeric composition and configuration of the obtained mixtures, in chloroform, are shown.

For the iridium complexes, NMR measurements at room temperature indicate that the two epimers at the metal of the κ^2N,O complexes **3a** and **4a** were present in 90/10 and 89/11 molar ratio, respectively. Under the same conditions, only the R_{Ir},R_C isomer

of the cationic complexes **6aCl** and **7aCl** was detected. If present, the epimers at the sulphur were not resolved even at 193 K.



1, 2 **6Cl, 7Cl** **3, 4**

M = (η^5-C_5Me_5)Ir, (η^6-*p*-MeC_6H_4*i*Pr)Ru

M	R^1	Compounds, Composition and Configuration	
Ir	H	**3a** (91 %) S_{Ir},R_C (90 %) / R_{Ir},R_C (10 %)	**6aCl** (9 %) R_{Ir},R_C
Ru	H	**3b** (4 %) S_{Ru},R_C	**6bCl** (96 %) R_{Ru},R_C,S_S (96 %) / R_{Ru},R_C,R_S (4 %)
Ir	Me	**4a** (54 %) S_{Ir},R_C (89 %) / R_{Ir},R_C (11 %)	**7aCl** (46 %) R_{Ir},R_C
Ru	Me	**4b** Not detected	**7bCl** (100 %) R_{Ru},R_C,S_S (96 %) / R_{Ru},R_C,R_S (4 %)

Solvent: $CDCl_3$

For the ruthenium complexes, a small amount of a single epimer at the metal of **3b** (4 %) was present in $CDCl_3$, at room temperature. The amount of the other metal epimer should be negligible. For the methylated cysteine-derived ligand **HL2**, the presence of the corresponding bidentate chelate complex **4b** can be excluded because the composition of the mixture, that depends on the solvent (see below), does not change significantly in CD_3OD. Under the same conditions, the two epimers at sulphur were observed for the cationic tripodal complexes **6bCl** and **7bCl** in 96/4 molar ratio in both cases. Most probably, the *S* at sulphur diastereomer, for which less steric hindrance between the C_5Me_5 and Bn groups is expected, was the most abundant isomer.

In acetone, the CD spectrum of the **3a**/**6aCl** mixtures showed a positive Cotton effect centred at 344 nm. However, negative maxima at 334 and 332 nm were recorded

for **3b**/**6bCl** mixtures and **7bCl**, respectively. As free α-amino acids do not show Cotton effects above 230 nm,[18] this absorption was tentatively assigned to transitions associated to the metal. On the other hand, the major isomer of the iridium complex **4a** shows a NOESY relationship between one of the CH_2Ph methylene protons and the C_5Me_5 protons indicating that the configuration at iridium is *S*. Taking into account all these observations, we propose the S_{Ir} configuration to the major epimer of the complex **3a**.

As it can be seen in the Table of Equation 1, the composition of the mixtures strongly depends on the metal, the cysteine derivative and the solvent employed. Thus, the amount of cationic compound is greater for the ruthenium complexes than for the corresponding iridium ones, the equilibrium is shifted to the left when the methylated cysteine-derived ligand **HL2** (R^1 = Me) replaces cysteine derivative **HL1** (R^1 = H) and, as expected, the relative concentration of the cationic chlorides **6Cl** and **7Cl** is higher in methanol than in chloroform.

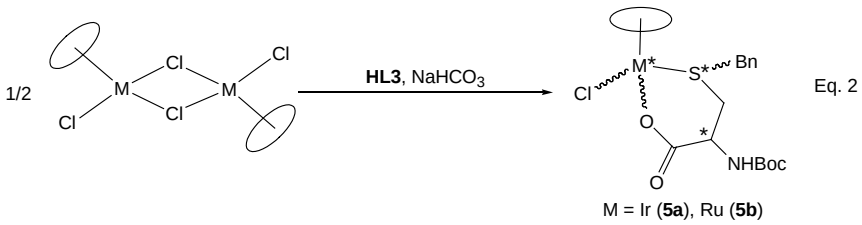
Thus, for example, while a **3a/6aCl** molar ratio of 91/9 was measured in chloroform for iridium complexes, for the ruthenium analogues only a 4 % of **3b** was measured in the mixture with **6bCl**. As complex **4b** was not detected in chloroform, we assume that, in this solvent, the equilibrium of a mixture of the methylated cysteine derivative ruthenium complexes **4b** and **7bCl** is completely shifted to the left (Eq. 1). Regarding the solvents, for mixtures **3a**/**6aCl** and **4a**/**7aCl** molar ratios of 91/9 and 54/46 were measured in chloroform; these ratios decrease to 39/61 and 16/84, respectively, in a polar solvent such as methanol.

In the iridium compounds, the C_5Me_5 proton resonance was affected by the coordination mode. While in the tripodal compounds **6aCl** and **7aCl** this signal appears near of 1.90 ppm, in the bidentate chelate complexes **3a** and **4a** these protons resonate at

about 1.60 ppm, a value comparable to those measured for the also bidentate chelate complexes **1a** and **2a** (Table 2).

The chemical shift of the CH_2C^* methylene carbon is strongly affected by the coordination mode. Thus, while in the κ^3*N,O,S* complexes **6aCl** and **6bCl**, in which this group is included in the M-O-C-C-N and M-S-C-C-N metallacycles, it appears at about 32.5 ppm, in the κ^2*N,O* compounds **3** and **4a**, in which this methylene group is pendant, it resonates from 40.66 to 46.22 ppm (Table 3). An intermediate value of the chemical sift was encountered when this methylene is included only in one metallacycle, as it is the case of compounds **1** and **2** (Table 3).

*Reactions with **HL3** in basic medium.* Complexes **5a** and **5b** were prepared by reacting the dimers $[\{(\eta^n\text{-ring})MCl\}_2(\mu\text{-}Cl)_2]$ with **HL3** in the presence of one equivalent of $NaHCO_3$.



Eq. 2

In these complexes, the metal, the asymmetric carbon of the cysteine derivative and the sulphur atom are stereogenic centres. As the configuration at the carbon is fixed, four diastereomers are possible. In fact, the four isomers were isolated for the iridium complex **5a**, in 62/21/9/8 molar ratio, and three isomers in 64/27/9 molar ratio were obtained for the ruthenium complex **5b**.

The ν(CO) frequency, 1630 and 1622 cm^{-1} for **5a** and **5b**, respectively, suggests a monodentate coordination for the carboxylate group. The values of the chemical shift of the C_5Me_5 protons in **5a**, 1.43-1.71 ppm, indicated a bidentate chelate coordination for the amino carboxylate ligand (Table 2). The CH_2C^* methylene carbon is deshielded

with respect to the analogue methylene carbon in the corresponding tripodal complexes **8aSb** and **8bSb** (Table 3).

All these spectroscopic data pointed to a $\kappa^2 O,S$ coordination mode for the amino carboxylate in complexes **5**. Most probably, coordination of the nitrogen is inhibited sterically, by the presence of the bulky Boc substituent, as well as electronically, by delocalization of the nitrogen electron pair by conjugation to the CO double bond.

A NOE enhancement was observed in the C_5Me_5 protons of the major isomer of the iridium complex **5a** when the *pro-R* proton of the CH_2C^* group was irradiated. This NOE relationship suggests that the configuration at the iridium in this isomer is *S*.

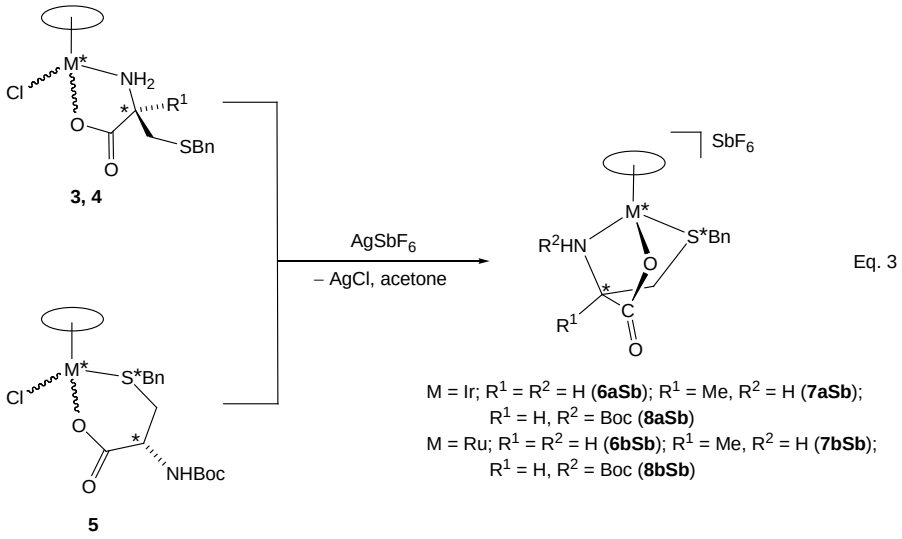
No relevant changes have been observed in the NMR spectra of the complexes from 298 to 193 K.

*Chloride abstraction in complexes **3**-**5***. Addition of $AgSbF_6$ to solutions of mixtures of **3** and **6Cl** or **4** and **7Cl** or pure **5** afforded the cationic complexes **6Sb**-**8Sb** in which the cysteine-based ligand featured a $\kappa^3 N,O,S$ coordination mode (Scheme 1, Eq. 3). The iridium complex **8aSb** was alternatively prepared by reacting $[\{(\eta^5\text{-}C_5Me_5)IrCl\}_2(\mu\text{-}Cl)_2]$ with 4 equivalents of $AgSbF_6$ and subsequent addition of **HL3** in the presence of $NaHCO_3$.

Compounds **6Sb** and **7Sb** contain three stereogenic centres: the metal, the asymmetric carbon of the cysteine derivative and the sulphur atom. As stated above, in half-sandwich bearing $\kappa^3 N,O,S$ coordinated (*R*)-cysteine derivatives, the only possible configuration for the metal is *R*. Therefore, two diastereomers, epimers at sulphur, namely R_M,R_C,R_S and R_M,R_C,S_S, could be obtained.[19]

In the temperature range 298-193 K, the NMR spectra of the iridium complexes **6aSb** and **7aSb** consisted of only one set of resonance signals. Therefore, either the

sulphur only adopts one configuration or both epimers at sulphur quickly exchange even at 193 K. The configuration at sulphur of solid **6aSb**, determined by diffractometric methods, is *S* (see above). However, for their ruthenium counterparts **6bSb** and **7bSb**, the NMR spectra revealed that, in solution, the two epimers at sulphur R_M,R_C,S_S and R_M,R_C,R_S were present. From steric grounds we propose that the less abundant isomer (5 % in **6bSb** and less than 3 % in **7bSb**) was the *R* at sulphur diastereomer.



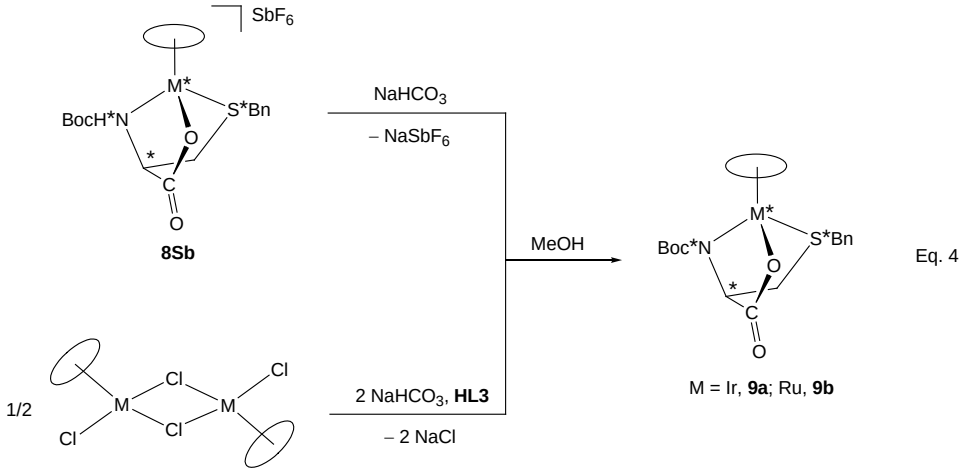
Eq. 3

Again, the NBoc containing compounds **8aSb** and **8bSb** behaved differently. In spite of the nitrogen also being a stereocentre, only one stereoisomer was obtained. Furthermore, in solution, hydrolysis of the Boc moiety renders small amounts of **6aSb** (about 8 %) and of **6bSb** (about 10 %), respectively. Additionally, about 18 % of other compound has been detected by NMR. Probably, this compound is the solvated complex in which a solvent molecule occupies the vacant site resulting from the decoordination of the NBoc arm of the cysteine derivative in **8aSb**. In fact, after addition of MeCN (30 equiv.) to a dichloromethane solution of the mixture, the percentage of this compound increases from 18 to 25 %.

The chemical shift of the C_5Me_5 protons in the iridium compounds **6aSb**-**8aSb** (1.84-1.92 ppm, Table 2) indicated a κ^3*N,O,S* coordination for the cysteine-derived

ligands and the strong shielding measured for the CH_2C^* methylene carbon in complexes **6** and **7** with respect to **3** and **4a** (more than 8 ppm, Table 3) was attributed to the inclusion of this carbon into the M-N-C-C-S and M-O-C-C-C-S metallacycles.

*Deprotonation of complexes **8***. Treatment of the complexes **8aSb** and **8bSb** with $NaHCO_3$ afforded the corresponding neutral deprotonated compounds **9a** and **9b**. These complexes can also be prepared treating the dimers $[\{(\eta^n\text{-ring})MCl\}_2(\mu\text{-Cl})_2]$ with **HL3** in the presence of 2 equiv. of $NaHCO_3$ (Eq. 4).



Eq. 4

At 298 K, the proton and carbon NMR spectra of complex **9a** consist of only one set of sharp peaks but two sets of peaks in 68/32 molar ratio were observed for **9b**, at the same temperature.

The CD spectrum of complex **9a** presents a negative maximum centred at 352 nm assigned to an *R* configuration at the metal.

The chemical shift of the C_5Me_5 protons in **9a** (1.93 ppm) and that of the CH_2C^* methylene carbon in both compounds (32.00 ppm, **9a** and 32.57 and 33.44 ppm, **9b**) strongly suggest that, in the reaction, the κ^3N,O,S coordination mode has been retained and that, therefore, the configuration at both metal and cysteine-derived ligand carbon is *R*. However, the nitrogen and the sulphur atoms are also stereogenic centres and, as only

one or two isomers were detected at 298 K, most probably the complexes undergo equilibrating processes in solution at this temperature. At this respect, the recently reported crystal structure of the rhodium analogue[12] [(η^5-C_5Me_5)Rh(κ^3*N*,*O*,*S*-**L3**$_{-H}$)] reveals that the nitrogen adopts an almost planar geometry and DFT calculations showed a very low energy transition state for the epimerization process at this atom. Probably, a consequence of the planarization is the shift of ca. 5 ppm to low field of the resonance of the asymmetric carbon, C*, adjacent to the nitrogen, with respect to that of the related protonated complex [(η^5-C_5Me_5)Rh(κ^3*N*,*O*,*S*-**L3**]$^+$.[12] In fact, a similar deshielding was observed for this carbon in complexes **9a** ($\Delta\delta$ = 4.6 ppm) and **9b** ($\Delta\delta$ = 6.6 ppm). Hence, we argue that also in complexes **9** inversion at nitrogen is low energy-demanding and that the observed isomers for **9b** are the two epimers at sulphur which, in turn, can be also observed for the iridium complex, by lowering temperature.[19]

To verify this issue, a variable temperature NMR study, in the range 298-183K, was undertaken for complex **9a**. The singlet attributed to the *t*Bu substituent of the Boc, which resonates at 1.39 ppm at 298 K, was taken as reference. On cooling, this singlet broadens out, coalesces at about 264 K and splits into two differently populated signals (85/15 ratio) below 238 K. The low temperature limiting spectrum was achieved at 193 K. The process obeys a first-order rate law, with derived activation parameters at 293 K of $\Delta H^{\#} = -0.55 \pm 0.03$ kcal·mol^{-1}, $\Delta S^{\#} = -44.3 \pm 6.0$ cal·mol^{-1}·K^{-1} and $\Delta G^{\#} = 12.4 \pm 2.3$ kcal·mol^{-1} (see ESI†). These values are very similar to those recently reported for the rhodium analogue. In particular, the relatively high negative value measured for $\Delta S^{\neq}$ indicate that the epimerisation at sulphur could take place through an associative mechanism identical to that calculated for the rhodium analogue: de-coordination of sulphur, coordination of a solvent molecule, turning around the C-S bond, de-coordination of the solvent molecule and re-coordination of sulphur.[12]

In summary, while the R_{Ir},R_C,S_S and R_{Ir},R_C,R_S diastereomers of complex **9a** were quickly exchanging at 298 K, the corresponding isomers of complex **9b** can be separately observed at this temperature. These data suggest again that epimerization at sulphur is more energy-demanding in the ruthenium complex. For steric grounds, in both cases, the most abundant isomer would be the *S* at sulphur epimer (see above).

Conclusions

Cysteine derivatives **HL1**, **HL2** and **HL3** display a variety of coordination modes towards (η^5-C_5Me_5)Ir and (η^6-*p*-MeC_6H_4*i*Pr)Ru moieties. Examples of neutral κ^2*N,S*, monoanionic κ^2*N,O*, κ^2*S,O* and κ^3*N,O,S*, as well as, dianionic κ^3*N,O,S* have been shown. The metal, the asymmetric carbon of the cysteine derivative and, in some instances, the sulphur and the nitrogen atoms are stereogenic centres. In most cases, the absolute configuration of the complexes has been determined, in solution, by NMR and CD spectrocopies and for **6aSb**, in the solid state by diffractometric methods. In the iridium complexes, the chemical shift of the C_5Me_5 protons discriminates between κ^2 and κ^3 coordination modes. The chemical shift of the CH_2C^* methylene carbon is a useful diagnostic for the inclusion of this group into metallacycles. In complexes in which the cysteine-based ligand is κ^3 coordinated, the metal adopts exclusively the same configuration than the carbon of the cysteine derivative with the subsequent reduction of the number of possible isomers. The configuration at sulphur is governed by the steric hindrance between the C_5Me_5 and benzyl substituents within the formed metallacycles and epimerization at sulphur is less energy-demanding for the iridium complexes than for the ruthenium analogues. Finally, in the iridium complex **9a**, the thermodynamic parameters for the epimerization at sulphur have been determined by variable temperature proton NMR measurements.

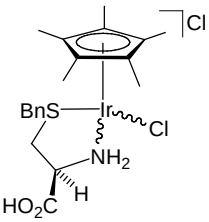
Experimental section

General information

General Comments. All preparations have been carried out under argon. All solvents were treated in a PS-400-6 Innovative Technologies Solvent Purification System (SPS) and degassed prior to use. Infrared spectra were recorded on Perkin-Elmer Spectrum-100 (ATR mode) FT-IR spectrometer. Carbon, hydrogen, nitrogen and sulphur analyses were performed using a Perkin-Elmer 240 B microanalyzer. ^{1}H and ^{13}C spectra were recorded on a Bruker AV-300 (300.13 MHz), a Bruker AV-400 (400.16 MHz) or a Bruker AV-500 (500.13 MHz) spectrometers. In both, ^{1}H NMR and ^{13}C NMR measurements the chemical shifts are expressed in ppm downfield from $SiMe_4$. *J* values are given in Hz. COSY, NOESY, HSQC, HMQC and HMBC ^{1}H-X (X = ^{1}H, ^{13}C) correlation spectra were obtained using standard procedures. CD spectra were determined in acetone (ca. 5×10^{-4} mol L^{-1} solutions) in a 1 cm path length cell by using a JASCO J-810 spectropolarimeter. Cysteine derivatives **HL1** and **HL3** are commercially available from Acros and Aldrich, respectively. Cysteine-based ligand **HL2** was prepared as reported in ref. 12.

Preparation of the complexes [(η^5-C_5Me_5)IrCl(κ^2*N,S*-HL)]Cl, (HL = HL1 (1a), HL2 (2a) and [(η^6-*p*-MeC_6H_4*i*Pr)RuCl(κ^2*N,S*-HL)]Cl, (HL = HL1 (1b), HL2 (2b)). At room temperature, to a suspension of the corresponding dimer [{(η^n-ring)MCl}$_2$(μ-Cl)$_2$] (0.16 mmol), in 10 mL of CH_3OH, 0.32 mmol of the corresponding cysteine derivative were added. The resulting yellow solution was stirred for 1 h and then was filtered to remove any insoluble material. The solution was concentrated under reduced pressure to ca. 1 mL. The slow addition of Et_2O led to the precipitation of a yellow solid which was washed with Et_2O (3 × 5 mL) and vacuum-dried.

[(η^5-C_5Me_5)IrCl(κ^2*N,S*-HL1)]Cl (1a). Yield: 74 %. Diastereomeric ratio: 92/8. Anal. calcd for $C_{20}H_{28}Cl_2IrNO_2S$, %: C, 39.4; H, 4.6; N, 2.3; S, 5.3. Found, %: C, 39.4; H, 4.8; N, 2.2; S, 5.3. IR (solid, cm^{-1}): *ν*(OH) 2916 (vbr), *ν*(C=O) 1724 (s). CD (acetone, 5.1×10^{-4} M, 298 K): λ, nm, (Δε): 341 (+ 4.34).

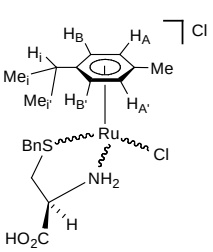


S_{Ir},R_C diastereomer (92 %). *^{1}H NMR (500.13 MHz, CD_2Cl_2, 298 K, ppm):* *δ* 10.6 - 8.9 (vbr, 1H, OH), 7.68 - 7.20 (2 × m, 5H, H_{Ar}), 6.80 (pt, *J* = 9.7 Hz, 1H, NH), 4.98 (d, *J* = 8.9 Hz, 1H, NH), 4.78 (AB system, J_{AB} = 11.1 Hz, 2H, CH_2Ph), 4.22 (m, 1H, C^*H), 3.57 (ABXX' system, J_{AB} = 13.3, J_{AX} = 10.9, $J_{AX'}$ = 3.1 Hz, 2H, CH_2C^*), 1.66 (s, 15H, C_5Me_5). *$^{13}C\{^1H\}$ NMR (125.8 MHz, CD_2Cl_2, 298 K, ppm):* *δ* 170.11 (C=O), 133.49, 130.85, 128.75, 128.46 (C_{Ar}), 91.27 (C_5Me_5), 60.37 (C^*), 38.48 (CH_2Ph), 36.76 (CH_2C^*), 8.46 (C_5Me_5).

R_{Ir},R_C diastereomer (8 %). *^{1}H NMR (500.13 MHz, CD_2Cl_2, 298 K, ppm):* *δ* 7.68 - 7.20 (2 × m, 5H, H_{Ar}), 4.51 (d, J_{AB} = 11.8 Hz, 1H, CH_2Ph), 4.20 (1H, CH_2Ph), 3.76 (m, 1H, C^*H), 3.41 (m, 1H, CH_2C^*), 2.72 (pt, 11.9 Hz, 1H, CH_2C^*), 1.73 (s, 15H, C_5Me_5). *$^{13}C\{^1H\}$ NMR (125.8 MHz, CD_2Cl_2, 298 K, ppm):* *δ* 170.44 (C=O), 133.23, 130.46, 128.95, 128.44 (C_{Ar}), 91.61 (C_5Me_5), 61.01 (C^*), 39.68 (CH_2Ph), 38.83 (CH_2C^*), 8.84 (C_5Me_5).

[(η^6-*p*-MeC_6H_4*i*Pr)RuCl(κ^2*N,S*-HL1)]Cl (1b). Yield: 85 %. Diastereomeric ratio: 80/20. Anal. calcd for $C_{20}H_{27}Cl_2NO_2RuS$, %: C, 44.9; H, 5.5; N, 2.6; S, 6.0. Found, %: C, 45.2; H, 5.8; N, 2.6; S, 6.1. IR (solid, cm^{-1}): *ν*(OH) 2963 (vbr), *ν*(C=O) 1721 (s). CD (acetone, 5.0×10^{-4} M, 298 K): λ, nm, (Δε): 358 (+ 2.49).

S_{Ru},R_C diastereomer (80 %). *^{1}H NMR (500.13 MHz, CD_2Cl_2, 298 K, ppm):* *δ* 10.0 - 8.2 (vbr, 1H, OH), 7.76 - 7.22 (m, 5H, H_{Ar}), 7.14 (brs, 1H, NH), 5.97, 5.65, 5.34, 4.97 (4 × d, *J* = 5.6 Hz, 4H, H_A, H_B, $H_{A'}$, $H_{B'}$), 4.39 (AB system, J_{AB} = 11.2 Hz, 2H, CH_2Ph), 4.15 (m, 1H, C^*H), 4.08 (br, 1H, NH), 2.53 (ABXX' system, J_{AB} = 12.7, J_{AX} = 7.3, $J_{AX'}$ = 4.5

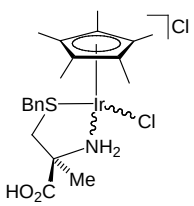


Hz, 2H, CH_2C^*), 2.87 (sept, J = 6.7 Hz, 1H, H_i), 1.99 (s, 3H, Me), 1.28 (d, J = 6.7 Hz, 6H, Me_i, $Me_{i'}$). *$^{13}C\{^1H\}$ NMR (125.8 MHz, CD_2Cl_2, 298 K, ppm):* δ 169.81 (C=O), 134.02, 130.59, 128.77, 128.68 (C_{Ar}), 110.91, 98.76 ($C_{p\text{-cymene}}$), 84.83, 84.61, 84.05, 83.64 (CH_A, CH_B, $CH_{A'}$, $CH_{B'}$), 57.70 (C^*), 37.86 (CH_2Ph), 37.67 (CH_2C^*), 30.82 (CH_i), 22.69, 21.30 (Me_i, $Me_{i'}$), 17.54 (Me).

R_{Ru},R_C diastereomer (20 %). *^1H NMR (500.13 MHz, CD_2Cl_2, 298 K, ppm):* δ 10.0 - 8.2 (vbr, 1H, OH), 8.15 (brs, 1H, NH), 7.76 - 7.22 (m, 5H, H_{Ar}), 5.64, 5.48, 5.42, 5.01 (4 × d, J = 5.6 Hz, 4H, H_A, H_B, $H_{A'}$, $H_{B'}$), 4.32 (AB system, J_{AB} = 10.9 Hz, 2H, CH_2Ph), 3.54 (m, 1H, C^*H), 2.72 (sept, J = 6.8 Hz, 1H, H_i), 3.32 (ABXX' system, J_{AB} = 13.6, J_{AX} = 11.5, $J_{AX'}$ = 10.2 Hz, 2H, CH_2C^*), 2.03 (s, 3H, Me), 1.24 (d, J = 7.0 Hz, 3H, Me_i), 1.21 (d, J = 6.9 Hz, 3H, $Me_{i'}$). *$^{13}C\{^1H\}$ NMR (125.8 MHz, CD_2Cl_2, 298 K, ppm):* δ 170.24 (C=O), 133.95, 130.61, 129.00, 128.84 (6C, C_{Ar}), 108.31, 100.81 (2C, $C_{p\text{-cymene}}$), 84.50, 84.14, 84.01, 83.56 (CH_A, CH_B, $CH_{A'}$, $CH_{B'}$), 59.38 (C^*), 39.22 (CH_2Ph), 38.38 (CH_2C^*), 30.63 (CH_i), 21.83, 21.79 (Me_i, $Me_{i'}$), 18.07 (Me).

[(η^5-C_5Me_5)IrCl(κ^2*N,S*-HL2)]Cl (2a). Yield: 85 %. Diastereomeric ratio: 91/9. Anal.[20] calcd for $C_{21}H_{30}Cl_2IrNO_2S\cdot H_2O$, %: C, 39.3; H, 5.0; N, 2.2; S, 5.0. Found, %: C, 39.1; H, 5.0; N, 2.2; S, 5.0. IR (solid, cm^{-1}): ν(OH) 2973 (vbr), ν(C=O) 1715 (s). CD (acetone, 5.1 × 10^{-4} M, 298 K): λ, nm, (Δε): 335 (+ 1.28).

S_{Ir},R_C diastereomer (91 %). *^1H NMR (500.13 MHz, $CDCl_3$, 298 K, ppm):* δ 7.55 - 7.33 (2 × m, 5H, H_{Ar}), 6.20-5.30 (vbr, 1H, OH), 4.51 (AB system, J = 11.7 Hz, 2H, CH_2Ph),

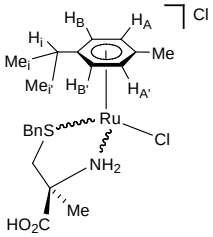


3.56 (AB system, J = 10.8 Hz, 2H, CH_2C^*), 2.00 (brs, 3H, C^*Me), 1.64 (s, 15H, C_5Me_5). *$^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$, 298 K, ppm):* δ 169.82 (C=O), 132.70, 130.58, 129.05, 128.95 (C_{Ar}), 91.87 (C_5Me_5), 67.75 (C^*), 44.90 (CH_2Ph), 38.71 (CH_2C^*), 24.99 (C^*Me), 8.84 (C_5Me_5).

R_{Ir},R_C diastereomer (9 %). *^{1}H NMR (500.13 MHz, $CDCl_3$, 298 K, ppm): δ* 7.55 - 7.33 (2 × m, 5H, H_{Ar}), 4.62 (AB system, J = 11.5 Hz, 2H, CH_2Ph), 3.62 (AB system, J = 11.3 Hz, 2H, CH_2C^*), 1.93 (brs, 3H, C^*Me), 1.67 (s, 15H, C_5Me_5). *$^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$, 298 K, ppm):* 130.63, 129.21, 129.00 (C_{Ar}), 92.20 (C_5Me_5), 67.64 (C^*), 45.23 (CH_2Ph), 40.51 (CH_2C^*), 25.50 (C^*Me), 9.07 (C_5Me_5).

[(η^6-*p*-MeC$_6$H$_4$*i*Pr)RuCl(κ^2*N,S*-HL2)]Cl (2b). Yield: 70 %. Isomeric ratio: 64/27/9. Anal.[20] calcd for $C_{21}H_{29}Cl_2NO_2RuS\cdot 3H_2O$, %: C, 43.1; H, 6.0; N, 2.4; S, 5.5. Found, %: C, 43.4; H, 6.4; N, 2.3; S, 5.5. IR (solid, cm^{-1}): *ν*(OH) 2961 (vbr), *ν*(C=O) 1729 (s). CD (acetone, 5.5×10^{-4} M, 298 K): λ, nm, (Δε): 362 (+ 0.63).

Isomer **A**, 64 %. *^{1}H NMR (500.13 MHz, CD_3OD, 298 K, ppm): δ* 7.58 - 7.40 (m, 5H, H_{Ar}), 5.76, 5.40, 5.37, 4.46 (4 × d, J = 5.9 Hz, 4H, H_A, H_B, $H_{A'}$, $H_{B'}$), 4.30 (AB system, J_{AB} = 11.0 Hz, 2H, CH_2Ph), 3.16 (AB system, J_{AB} = 11.8 Hz, 2H, CH_2C^*), 2.87 (sept, J = 6.9 Hz 1H, H_i), 1.91 (s, 3H, Me), 1.67 (s, 3H, C^*Me), 1.30, 1.28 (2 × brs, 6H, Me_i, $Me_{i'}$). *$^{13}C\{^1H\}$ NMR (125.8 MHz, CD_3OD, 298 K, ppm): δ* 173.86 (C=O), 135.43, 131.77, 130.38, 130.13 (C_{Ar}), 112.46, 99.90 ($C_{p\text{-cymene}}$), 87.78, 84.96, 84.29, 83.10 (CH_A, CH_B, $CH_{A'}$, $CH_{B'}$), 64.82 (C^*), 45.27 (CH_2C^*), 39.78 (CH_2Ph), 32.08 (CH_i), 26.18 (C^*Me), 23.67, 20.89 (Me_i, $Me_{i'}$), 18.84 (Me).



Isomer **B**, 27 %. *^{1}H NMR (500.13 MHz, CD_3OD, 298 K, ppm): δ* 7.58 - 7.40 (m, 5H, H_{Ar}), 5.63, 5.34, 5.20, 4.56 (4 × d, J = 6.3 Hz, 4H, H_A, H_B, $H_{A'}$, $H_{B'}$), 4.34 (AB system, J_{AB} = 11.0 Hz, 2H, CH_2Ph), 3.38 (AB system, J_{AB} = 11.4 Hz, 2H, CH_2C^*), 2.79 (sept, J = 6.8 Hz, 1H, H_i), 1.84 (s, 3H, Me), 1.44 (s, 3H, C^*Me), 1.26, 1.25 (2 × brs, 6H, Me_i, $Me_{i'}$). *$^{13}C\{^1H\}$ NMR (125.8 MHz, CD_3OD, 298 K, ppm): δ* 134.84, 131.74, 130.33, 130.06 (C_{Ar}), 113.34, 98.68 ($C_{p\text{-cymene}}$), 85.89, 85.78, 85.39, 82.87 (CH_A, CH_B, $CH_{A'}$,

$CH_{B'}$), 65.53 (C^*), 44.35 (CH_2C^*), 39.91 (CH_2Ph), 32.51 (CH_i), 23.39, 21.31 (Me_i, $Me_{i'}$), 17.61 (Me).

Isomer **C**, 9 %. *^{1}H NMR (500.13 MHz, CD_3OD, 298 K, ppm):* δ 7.58 - 7.40 (m, 5H, H_{Ar}), 4.02 (AB system, J_{AB} = 11.9 Hz, 2H, CH_2Ph), 2.66 (sept, J = 6.8 Hz, 1H, H_i), 1.25, 1.24 (2 × brs, 6H, Me_i, $Me_{i'}$). *$^{13}C\{^1H\}$ NMR (125.8 MHz, CD_3OD, 298 K, ppm):* δ 136.21, 131.80, 131.51, 130.21 (C_{Ar}), 100.97 ($C_{p\text{-cymene}}$), 85.87, 84.80, 84.08, 823.10 (CH_A, CH_B, $CH_{A'}$, $CH_{B'}$), 42.61 (CH_2Ph), 39.91 (CH_2C^*), 32.01 (CH_i), 22.98, 22.34 (Me_i, $Me_{i'}$), 18.22 (Me).

Preparation of the complexes [(η^5-C_5Me_5)IrCl(κ^2*N,O*-L)] (L = L1 (3a), L2 (4a), L3 (5a)), [(η^5-C_5Me_5)Ir(κ^3*N,O,S*-L)]Cl (L = L1 (6aCl), L2 (7aCl)) and [(η^6-*p*-MeC_6H_4*i*Pr)RuCl(κ^2*N,O*-L)], (L = L1 (3b), L2 (4b), L3 (5b)) [(η^6-*p*-MeC_6H_4*i*Pr)RuCl(κ^3*N,O,S*-L)]Cl (L = L1 (6bCl), L2 (7bCl)). At room temperature, to a suspension of the corresponding dimer [{(η^n-ring)MCl}$_2$(μ-Cl)$_2$] (0,32 mmol), in 10 mL of MeOH, 0.64 mmol of the corresponding cysteine-derived ligand, **HL1** or **HL2**, were added. The resulting yellow (Ir) or orange (Ru) solution was stirred for 15 min and then 64.7 mg (0.77 mmol) of $NaHCO_3$ were added. The suspension was vigorously stirred for 2 h and then concentrated in vacuum until dryness. The residue was extracted with CH_2Cl_2 (4 × 5 mL) and the resulting solution was concentrated under reduced pressure to *ca*. 3 mL. The slow addition of *n*-hexane led to the precipitation of a yellow solid which was washed with *n*-hexane (4 × 5 mL) and vacuum-dried. The solid was spectroscopically characterized as a mixture of **3** and **6Cl** (**HL1**) or **4** and **7Cl** (**HL2**) compounds. With the ligand **HL3**, pure complexes **5** were obtained. Yield: **3a** + **6aCl**, 74 %; **3b** + **6bCl**, 74%; **4a** + **7aCl**, 56 %; **7bCl**, 65 %.

3a + **6aCl**, Anal.[20] calcd for $C_{20}H_{27}ClIrNO_2S \cdot 2H_2O$, %: C, 39.4; H, 5.1; N, 2.3; S, 5.3. Found, %: C, 39.5; H, 5.3; N 2.5; S 5.6. IR (solid, cm^{-1}): *ν*(C=O) 1611(s). CD (acetone, 3.8×10^{-4} M, 298 K): λ, nm, (Δε): 344 (+ 2.81).

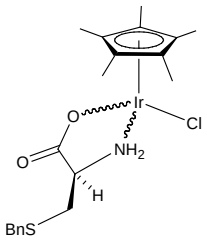
3b + **6bCl**, Anal.[20] calcd for $C_{20}H_{26}ClNO_2RuS \cdot 2H_2O$, %: C, 46.4; H, 5.8; N, 2.7; S, 6.2. Found, %: C, 46.8; H, 5.8; N, 2.9; S, 6.5. IR (solid, cm^{-1}): *ν*(C=O) 1653 (s). CD (acetone, 5.0×10^{-4} M, 298 K): λ, nm, (Δε): 334 (−0.60).

4a + **7aCl**, Anal.[20] calcd for $C_{21}H_{29}ClIrNO_2S \cdot 3H_2O$, %: C, 39.3; H, 5.4; N, 2.2; S, 5.0. Found, %: C, 39.1; H, 5.2; N, 2.2; S, 4.6. IR (solid, cm^{-1}): *ν*(C=O) 1653 (s).

7bCl, Anal.[20] calcd for $C_{21}H_{28}ClNO_2RuS \cdot 3H_2O$, %: C, 45.9; H, 6.2; N, 2.6; S, 5.8. Found, %: C, 45.6; H, 5.8; N, 2.7; S, 5.8. IR (solid, cm^{-1}): *ν*(C=O) 1642 (s). CD (acetone, 5.1×10^{-4} M, 298 K): λ, nm, (Δε): 332 (−1.34).

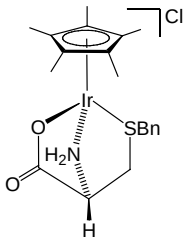
[(η^5-C_5Me_5)IrCl(k^2*N,O*-L1)] (3a). Yield: 67 %. Isomeric ratio: 90/10.

S_{Ir},R_C diastereomer (90 %). *^{1}H NMR (300.13 MHz, $CDCl_3$, 298 K, ppm):* *δ* 7.70 - 7.12 (2 × m, 5H, H_{Ar}), 6.35 (br, 1H, NH), 4.66 (AB system, J_{AB} = 11.2 Hz, 2H, CH_2Ph), 4.45 (br, 1H, NH), 3.87 (brs, 1H, C^*H), 3.59, 2.82 (2 × br, 2H, CH_2C^*), 1.60 (brs, 15H, C_5Me_5). *$^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$, 298 K, ppm):* *δ* 179.48 (C=O), 133.58, 130.77, 128.69, 128.42 (C_{Ar}), 90.99 (C_5Me_5), 61.40 (C^*), 40.66 (CH_2C^*), 37.40 (CH_2Ph), 8.45 (C_5Me_5).



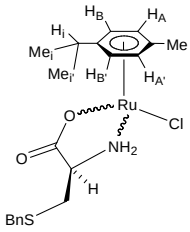
R_{Ir},R_C diastereomer (10 %). *^{1}H NMR (300.13 MHz, $CDCl_3$, 298 K, ppm):* *δ* 3.92 (d, *J* = 12.8 Hz, 1H, CH_2Ph), 3.87 (1H, C^*H), 3.70 (1H, CH_2Ph), 3.54 (1H, CH_2C^*), 2.55 (pt, *J* = 12.3 Hz, 1H, CH_2C^*), 1.67 (brs, 15H, C_5Me_5). *$^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$, 298 K, ppm):* *δ* 91.04 (C_5Me_5), 61.40 (C^*), 41.05 (CH_2C^*), 39.40 (CH_2Ph), 8.80 (C_5Me_5).

[(η^5-C_5Me_5)Ir(κ^3*N,O,S*-L1)]Cl (6aCl). Yield: 7 %.



R_{Ir},R_C diastereomer. *^{1}H NMR (300.13 MHz, $CDCl_3$, 298 K, ppm):* δ 4.42 (brd, J = 12.4 Hz, 1H, CH_2Ph), 4.29 (brs, 1H, C^*H), 4.06 (brd, J = 12.4 Hz, 1H, CH_2Ph), 3.54 (1H, CH_2C^*), 2.32 (d, J = 13.3 Hz, 1H, CH_2C^*), 1.87 (brs, 15H, C_5Me_5). *$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$, 298 K, ppm):* δ 89.04 (C_5Me_5), 60.69 (C^*), 38.26 (CH_2Ph), 32.24 (CH_2C^*), 9.25 (C_5Me_5).

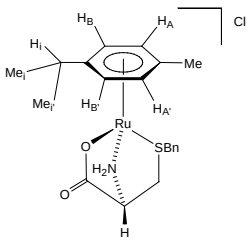
[(η^6-*p*-MeC$_6$H$_4$*i*Pr)RuCl(k^2*N*,*O*-L1)] (3b). Yield: 3 %.



^{1}H NMR (500.13 MHz, $CDCl_3$, 250 K, ppm): δ 5.05, 4.57 (2 × brs, 2H, CH_2C^*), 4.31, 3.85 (2 × brs, 2H, CH_2Ph), 1.85 (s, 3H, Me). *$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$, 250 K, ppm):* δ 45.60 (CH_2C^*), 38.08 (CH_2Ph), 17.91 (Me).

[(η^6-*p*-MeC$_6$H$_4$*i*Pr)Ru(κ^3*N*,*O*,*S*-L1)]Cl (6bCl). Yield: 71 %. Isomeric ratio: 96/4.

R_{Ru},R_C,S_S diastereomer (96 %). *^{1}H NMR (500.13 MHz, $CDCl_3$, 250 K, ppm):* δ 7.55 - 7.35 (m, 5H, H_{Ar}), 6.83 (br, 1H, NH), 6.73 (br, 1H, NH), 5.50, 5.38, 5.33, 4.98 (4 × s, 4H, H_A, H_B, $H_{A'}$, $H_{B'}$), 3.96 (AB system, J_{AB} = 11.1 Hz, 2H, CH_2Ph), 3.93 (brs, 1H, C^*H), 3.36 (AB system, J_{AB} = 13.1 Hz, 2H, CH_2C^*), 2.70 (br, 1H, H_i), 2.11 (s, 3H, Me), 1.25, 1.23 (2 × d, J = 7.2 Hz, 6H, Me_i, $Me_{i'}$).

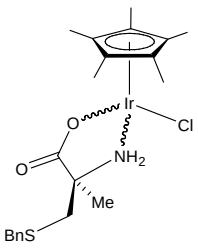


$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$, 250 K, ppm): δ 178.45 (C=O), 133.64, 130.46, 129.36, 129.15 (C_{Ar}), 107.37, 96.99 ($C_{p\text{-cymene}}$), 84.72, 83.27, 82.86, 81.57 (CH_A, CH_B, $CH_{A'}$, $CH_{B'}$), 58.89 (C^*), 41.04 (CH_2Ph), 32.80 (CH_2C^*), 31.26 (CH_i), 22.61, 22.42 (Me_i, $Me_{i'}$), 18.44 (Me).

R_{Ru},R_C,R_S diastereomer (4 %). *^{1}H NMR (500.13 MHz, $CDCl_3$, 250 K, ppm):* δ 4.29, 3.43 (2 × brs, 2H, CH_2Ph), 3.05, 2.49 (2 × brs, 2H, CH_2C^*), 1.99 (s, 3H, Me). *$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$, 250 K, ppm):* δ 38.71 (CH_2Ph), 31.82 (CH_2C^*), 18.44 (Me).

[(η^5-C$_5$Me$_5$)IrCl(k^2*N*,*O*-L2)] (4a). Yield: 30%. Isomeric ratio: 89/11.

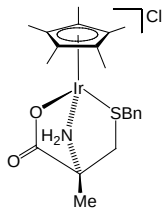
S_{Ir},R_C diastereomer (89 %). *^{1}H NMR (300.13 MHz, $CDCl_3$, 298 K, ppm):* δ 7.65 (br, 1H, NH), 7.40 - 7.29 (m, 5H, H_{Ar}), 5.71 (br, 1H, NH), 4.51 (AB system, J_{AB} = 12.1 Hz, 2H, CH_2Ph), 3.90 (AB system, J_{AB} = 10.8 Hz, 2H, CH_2C^*), 1.78 (s, 3H, C^*Me), 1.55 (s, 15H, C_5Me_5). *$^{13}C\{^1H\}$ NMR (75.47 MHz, $CDCl_3$, 298 K, ppm):* δ 170.98 (C=O), 133.24, 130.76, 128.83, 128.68 (C_{Ar}), 91.17 (C_5Me_5), 68.26 (C^*), 45.89 (CH_2C^*), 38.87 (CH_2Ph), 26.34 (C^*Me), 8.26 (C_5Me_5).



R_{Ir},R_C diastereomer (11 %). *^{1}H NMR (300.13 MHz, $CDCl_3$, 298 K, ppm):* δ 6.47 (br, 1H, NH), 5.87 (br, 1H, NH), 4.65 (d, J = 11.3 Hz, 1H, CH_2Ph), 4.08 (d, J = 11.3 Hz, 1H, CH_2Ph), 3.48 (1H, CH_2C^*), 2.42 (d, J = 10.6 Hz, 1H, CH_2C^*), 1.58 (s, 15H, C_5Me_5). *$^{13}C\{^1H\}$ NMR (75.47 MHz, $CDCl_3$, 298 K, ppm):* δ 91.50 (C_5Me_5), 68.07 (C^*), 46.22 (CH_2C^*), 40.62 (CH_2Ph), 8.49 (C_5Me_5).

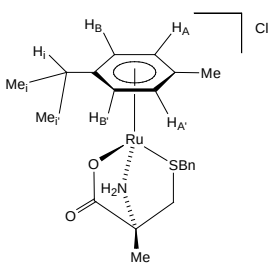
[(η^5-C_5Me_5)Ir(κ^3*N,O,S*-L2)]Cl (7aCl). Yield: 26 %.

R_{Ir},R_C diastereomer. *^{1}H NMR (300.13 MHz, $CDCl_3$, 298 K, ppm):* δ 7.49 - 7.41 (m, 5H, H_{Ar}), 6.36 (br, 1H, NH), 3.93 (AB system, J_{AB} = 11.9 Hz, 2H, CH_2Ph), 3.65 (br, 1H, NH), 3.49 (brd, J = 13.6 Hz, 1H, CH_2C^*), 2.17 (brd, J = 13.6 Hz, 1H, CH_2C^*), 1.88 (s, 15H, C_5Me_5), 1.75 (s, 3H, C^*Me). *$^{13}C\{^1H\}$ NMR (75.47 MHz, $CDCl_3$, 298 K, ppm):* δ 180.38 (C=O), 132.37, 130.30, 129.17, 128.89 (C_{Ar}), 89.05 (C_5Me_5), 66.39 (C^*), 39.31 (CH_2Ph), 36.47 (CH_2C^*), 22.50 (C^*Me), 9.34 (C_5Me_5).



[(η^6-*p*-MeC_6H_4*i*Pr)Ru(κ^3*N,O,S*-L2)]Cl (7bCl). Yield: 65 %. Isomeric ratio: 96/4.

R_{Ru},R_C,S_S diastereomer (96 %). *^{1}H NMR (400.16 MHz, $CDCl_3$, 298 K, ppm):* δ 7.62 (br, 1H, NH), 7.44 - 7.26 (m, 5H, H_{Ar}), 6.63 (br, 1H, NH), 5.51, 5.30, 5.17 (3 × d, J = 4.2 Hz, 4H, H_A, H_B, $H_{A'}$, $H_{B'}$), 3.82 (AB system, J_{AB} = 11.4 Hz, 2H, CH_2Ph), 3.22 (d, J =

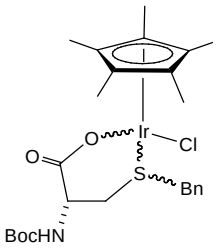


13.6 Hz, 2H, CH_2C^*), 2.71 (m, 1H, H_i), 2.10 (s, 3H, Me), 1.61 (s, 3H, C^*Me), 1.23, 1.16 (2 × d, J = 7.1 Hz, 6H, Me_i, $Me_{i'}$). *$^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 298 K, ppm):* δ 178.67 (C=O), 133.67, 130.43, 129.14, 129.01 (C_{Ar}), 107.22, 97.48 ($C_{p\text{-cymene}}$), 84.87, 83.17, 81.60 (CH_A, CH_B, $CH_{A'}$, $CH_{B'}$), 64.24 (C^*), 41.02 (CH_2Ph), 37.70 (CH_2C^*), 31.14 (CH_i), 23.07 (C^*Me), 22.55, 22.47 (Me_i, $Me_{i'}$), 18.14 (Me).

R_{Ru},R_C,R_S diastereomer (4 %). *^1H NMR (400.16 MHz, $CDCl_3$, 298 K, ppm):* δ 4.51, 2.97 (2 × brs, 2H, CH_2Ph), 2.97, 2.27 (2 × brs, 2H, CH_2C^*). *$^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 298 K, ppm):* δ 41.58 (CH_2Ph), 36.75 (CH_2C^*).

[(η^5-C_5Me_5)IrCl(κ^2*O,S*-L3)] (5a). Yield: 57 %. Diastereomeric ratio: 62/21/9/8. Anal.[20] calcd for $C_{25}H_{35}ClIrNO_4S\cdot 3H_2O$, %: C, 41.2; H, 5.6; N, 1.9; S, 4.4. Found, %: C, 40.7; H, 5.2; N, 2.1; S, 4.8. IR (solid, cm^{-1}): ν(C=O_{Boc}) 1752 (s), ν(C=O) 1630 (s).

Isomer **A**, 62 %. *^1H NMR (500.13 MHz, $CDCl_3$, 298 K, ppm):* δ 7.62 - 7.56, 7.41 - 7.29 (2 × m, 5H, H_{Ar}), 6.15 (br, 1H, NH), 5.05 (AB system, J_{AB} = 12.2 Hz, 2H, CH_2Ph), 4.66



(br, 1H, C^*H), 3.48 (dd, J = 11.8, 1.6 Hz, 1H, CH_2C^*), 2.43 (dd, J = 11.8, 11.5 Hz, 1H, CH_2C^*), 1.45 (brs, 9H, $Me_{t\text{Bu}}$), 1.43 (s, 15H, C_5Me_5). *$^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$, 298 K, ppm):* δ 175.01 (C=O), 155.15 (C=O_{Boc}), 133.96, 131.13, 128.59, 128.19 (C_{Ar}), 89.94 (C_5Me_5), 79.26 ($C_{t\text{Bu}}$), 50.01 (C^*), 37.44 (CH_2Ph), 34.67 (CH_2C^*), 28.44 ($Me_{t\text{Bu}}$), 8.16 (C_5Me_5).

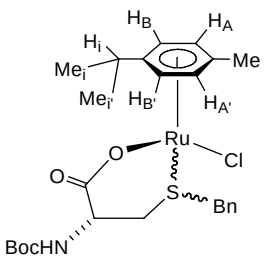
Isomer **B**, 21 %. *^1H NMR (500.13 MHz, $CDCl_3$, 298 K, ppm):* δ 6.08 (br, 1H, NH), 4.86 (d, J = 11.4 Hz, 1H, CH_2Ph), 3.84 (d, J = 11.4 Hz, 1H, CH_2Ph), 3.67 (br, 1H, C^*H), 2.99 (dd, J = 9.9, 4.0 Hz, 1H, CH_2C^*), 2.58 (dd, J = 9.9, 4.0 Hz, 1H, CH_2C^*), 1.66 (s, 15H, C_5Me_5), 1.45 (9H, $Me_{t\text{Bu}}$). *$^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$, 298 K, ppm):* δ 51.65 (C^*), 38.05 (CH_2Ph), 37.56 (CH_2C^*), 8.69 (C_5Me_5).

Isomer **C**, 9 %. *^{1}H NMR (500.13 MHz, $CDCl_3$, 298 K, ppm):* δ 4.62 (m, 1H, CH_2Ph), 4.32 (br, 1H, C^*H), 3.92 (d, J = 12.5 Hz, 1H, CH_2Ph), 3.47 (1H, CH_2C^*), 2.84 (pt, J = 11.2 Hz, 1H, CH_2C^*), 1.60 (s, 15H, C_5Me_5), 1.45 (9H, Me_{tBu}). *$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$, 298 K, ppm):* δ 52.69 (C^*), 35.41 (CH_2Ph), 35.02 (CH_2C^*), 8.49 (C_5Me_5).

Isomer **D**, 8 %. *^{1}H NMR (500.13 MHz, $CDCl_3$, 298 K, ppm):* δ 4.62 (m, 1H, CH_2Ph), 4.08 (1H, CH_2Ph), 3.48 (1H, C^*H), 2.66 (dd, J = 13.0, 4.4 Hz, 1H, CH_2C^*), 2.22 (pt, J = 13.0 Hz, 1H, CH_2C^*), 1.71 (s, 15H, C_5Me_5), 1.45 (9H, Me_{tBu}). *$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$, 298 K, ppm):* δ 50.72 (C^*), 37.44 (CH_2Ph), 37.03 (CH_2C^*), 9.06 (C_5Me_5).

[(η^6-*p*-MeC_6H_4*i*Pr)RuCl(κ^2*O,S*-L3)] (5b). Yield: 79 %. Isomeric ratio: 64/27/9. Anal. calcd for $C_{25}H_{34}ClNO_4RuS$, %: C, 51.6; H, 5.9; N, 2.4; S, 5.5. Found, %: C, 51.8; H, 6.0; N, 2.7; S, 5.7. IR (solid, cm^{-1}): ν(C=O_{Boc}) 1763 (s), 1701 (s), ν(C=O) 1622 (s).

Isomer **A**, 64 %. *^{1}H NMR (500.13 MHz, $CDCl_3$, 298 K, ppm):* δ 7.63 - 7.34 (m, 5H, H_{Ar}), 6.03 (br, 1H, NH), 5.94, 5.37, 5.03, 4.66 (4 × d, J = 5.9 Hz, 4H, H_A, H_B, $H_{A'}$, $H_{B'}$),



4.77 (AB system, J_{AB} = 11.7 Hz, 2H, CH_2Ph), 4.35 (br, 1H, C^*H), 3.17 (dd, J = 11.7, 2.1 Hz, 1H, CH_2C^*), 2.90 (sept, J = 6.7 Hz, 1H, H_i), 2.29 (dd, J = 11.7, 1.6 Hz, 1H, CH_2C^*), 2.04 (s, 3H, Me), 1.41 (s, 9H, Me_{tBu}), 1.25, 1.24 (2 × d, J = 6.9 Hz, 6H, Me_i, $Me_{i'}$). *$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$, 298 K, ppm):* δ 175.62 (C=O), 155.14 (C=O_{Boc}), 134.06, 130.98, 128.54, 128.38 (C_{Ar}), 106.65, 101.28 ($C_{p\text{-cymene}}$), 85.94, 84.63, 83.67, 80.53 (CH_A, CH_B, $CH_{A'}$, $CH_{B'}$), 79.13 (C_{tBu}), 49.58 (brs, C^*), 38.71 (CH_2Ph), 33.48 (brs, CH_2C^*), 30.30 (CH_i), 28.39 (Me_{tBu}), 22.14, 22.04 (Me_i, $Me_{i'}$), 18.01 (Me).

Isomer **B**, 27 %. *^{1}H NMR (500.13 MHz, $CDCl_3$, 298 K, ppm):* δ 5.80 (br, 1H, NH), 4.58 (br, 1H, C^*H), 3.84 (AB system, J_{AB} = 11.6 Hz, 2H, CH_2Ph), 2.58 (br, 1H, H_i), 2.17 (m, 2H, CH_2C^*),1.96 (br, 3H, Me), 1.48 (brs, 9H, Me_{tBu}), 1.18 (br, 6H, Me_i, $Me_{i'}$). *$^{13}C\{^{1}H\}$*

NMR (125.8 MHz, $CDCl_3$, 298 K, ppm): δ 49.58 (C^*), 41.43 (CH_2Ph), 33.48 (brs, CH_2C^*), 30.80 (CH_i), 28.86 (brs, Me_{tBu}).

Isomer **C**, 9 %. *^{1}H NMR (500.13 MHz, $CDCl_3$, 298 K, ppm):* δ 7.63 - 7.34 (m, 5H, H_{Ar}), 6.22 (br, 1H, NH), 5.49, 5.17, 4.90, 4.71 (4 × d, J = 5.8 Hz, 4H, H_A, H_B, $H_{A'}$, $H_{B'}$), 4.53 (1H, C^*H), 4.11 (AB system, J_{AB} = 11.3 Hz, 2H, CH_2Ph), 3.22 (d, J = 10.2 Hz, 1H, CH_2C^*), 2.85 (m, 1H, H_i), 2.69 (pt, J = 11.1 Hz, 1H, CH_2C^*), 2.13 (s, 3H, Me), 1.44 (s, 9H, Me_{tBu}), 1.28 (m, 6H, Me_i, $Me_{i'}$). *$^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$, 298 K, ppm):* δ 49.55 (C^*), 40.21 (CH_2Ph), 35.69 (CH_2C^*), 29.78 (CH_i), 28.36 (Me_{tBu}), 18.22 (Me).

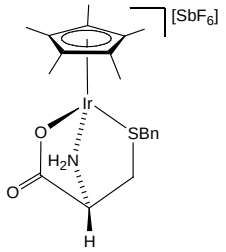
Preparation of the complexes [(η^5-C_5Me_5)Ir(κ^3*N,O,S*-L)][SbF_6] (L = L1 (6aSb), L2 (7aSb), L3 (8aSb)) and [(η^6-*p*-MeC_6H_4*i*Pr)Ru(κ^3*N,O,S*-L)][SbF_6] (L = L1 (6bSb), L2 (7bSb), L3 (8bSb)). To a solution of mixtures of **3** and **6Cl** or **4** and **7Cl** or pure **5** (0.25 mmol) in 10 mL of acetone, 85.9 mg (0.25 mmol) of $AgSbF_6$ were added. After stirring for 1 h, the AgCl formed was filtered off and the solution was concentrated under reduced pressure to *ca.* 3 mL. The slow addition of Et_2O led to the precipitation of a yellow solid which was washed with Et_2O (3 × 5 mL) and vacuum-dried. Yield: **6aSb**, 72 %; **6bSb**, 81 %; **7aSb**, 69 %; **7bSb**, 73 %; **8aSb**, 63 %; **8bSb**, 51 %.

The iridium complex **8aSb** can be alternatively prepared as follows: To a solution of [{(η^5-C_5Me_5)IrCl}$_2$(μ-Cl)$_2$] (120.0 mg, 0.15 mmol) in acetonitrile (20 ml), 207.4 mg (0.60 mmol) of $AgSbF_6$ and 100 mg of 4Å MS were added. The immediate precipitation of a white-grey coloured solid was observed. After stirring at room temperature for 3 h, the light yellow solution was filtered and 93.9 mg (0.30 mmol) of *S*-Bn-*NH*-Boc-*L*-Cys (**7**) and 25.3 mg (0.30 mmol) of $NaHCO_3$ were added. After stirring for 1 h, the solvent was evaporated and the residue extracted in CH_2Cl_2 (4 × 5 ml). The resulting solution was filtered and the filtrate was concentrated to ca 3 ml. The addition of 20 ml of

hexane afforded **8aSb** as a yellow solid which was filtered off and vacuum-dried. Yield 63 %.

[(η^5-C_5Me_5)Ir(κ^3*N,O,S*-L1)][SbF_6] (6aSb). Anal.[20] calcd for $C_{20}H_{27}F_6IrNO_2SSb\cdot 3H_2O$, %: C, 29.0; H, 4.0; N, 1.7; S, 3.9. Found, %: C, 29.1; H, 3.8; N, 1.4; S, 3.7. IR (solid, cm^{-1}): *ν*(C=O) 1654 (s), 1635 (s), *ν*(SbF_6) 650 (s). CD (acetone, 4.4×10^{-4} M, 298 K): λ, nm, (Δε): 335 (−5.22).

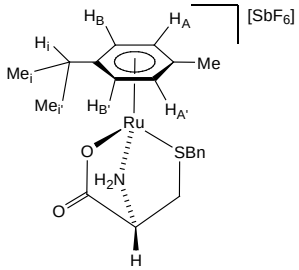
R_{Ir},R_C,S_S diastereomer. *^{1}H NMR (300.13 MHz, acetone-d_6, 298 K, ppm): δ* 7.54 - 7.32 (m, 5H, H_{Ar}), 6.32 (br, 1H, NH), 5.40 (br, 1H, NH), 4.32 (brs, 1H, C^*H), 4.16 (AB



system, J_{AB} = 12.9 Hz, 2H, CH_2Ph), 2.83 (AB part, ABX system, J_{AB} = 14.5 Hz, J_{AX} = 3.7 Hz, 2H, CH_2C^*), 1.92 (s, 15H, C_5Me_5). *$^{13}C\{^1H\}$ NMR (75.47 MHz, acetone-d_6, 298 K, ppm): δ* 177.00 (C=O), 132.95, 130.46, 129.18, 128.89 (C_{Ar}), 89.52 (5C, C_5Me_5), 60.36 (C^*), 39.14 (CH_2Ph), 31.37 (CH_2C^*), 8.25 (C_5Me_5).

[(η^6-*p*-MeC_6H_4*i*Pr)Ru(κ^3*N,O,S*-L1)][SbF_6] (6bSb). Isomeric ratio: 95/5. Anal. calcd for $C_{20}H_{26}F_6NO_2RuSSb$, %: C, 35.3; H, 3.9; N, 2.1; S, 4.7. Found, %: C, 35.7; H, 3.9; N, 2.0; S, 4.7. IR (solid, cm^{-1}): *ν*(C=O) 1658 (s), 1623 (s), *ν*(SbF_6) 653 (s). CD (acetone, 4.9×10^{-4} M, 298 K): λ, nm, (Δε): 334 (−0.75).

R_{Ru},R_C,S_S diastereomer (95 %). *^{1}H NMR (300.13 MHz, acetone-d_6, 298 K, ppm): δ* 7.58 - 7.40 (m, 5H, H_{Ar}), 6.29 (br, 1H, NH), 5.82, 5.79, 5.58 (3 × d, *J* = 5.7 Hz, 4H, H_A, H_B,



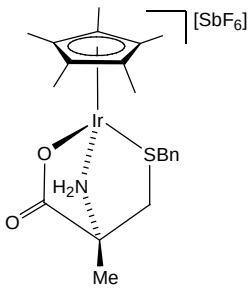
$H_{A'}$, $H_{B'}$), 5.17 (br, 1H, NH), 4.11 (AB system, J_{AB} = 12.0 Hz, 2H, CH_2Ph), 3.85 (brs, 1H, C^*H), 2.78, 2.51 (2 × m, 3H, H_i, ABX system CH_2C^*), 2.17 (s, 3H, Me), 1.31, 1.29 (2 × d, *J* = 4.0 Hz, 6H, Me_i, $Me_{i'}$). *$^{13}C\{^1H\}$ NMR (75.47 MHz, acetone-d_6,*

298 K, ppm): δ 175.81 (C=O), 133.82, 130.42, 129.17, 128.98 (C_{Ar}), 106.28, 99.42 (2C, $C_{p\text{-cymene}}$), 84.11, 83.44, 82.49, 82.17 (CH_A, CH_B, $CH_{A'}$, $CH_{B'}$), 59.18 (C^*), 41.30 (CH_2Ph), 31.05 (CH_2C^*), 31.04 (CH_i), 21.79, 21.46 (Me_i, $Me_{i'}$), 17.32 (Me).

R_{Ru},R_C,R_S diastereomer (5 %). *^{1}H NMR (300.13 MHz, acetone-d_6, 298 K, ppm):* δ 6.06, 5.66, 5.50, 4.88 (4 × brs, 4H, H_A, H_B, $H_{A'}$, $H_{B'}$), 4.37 (d, J = 11.3 Hz, 1H, CH_2Ph), 4.15 (1H, CH_2Ph), 3.85 (1H, C^*H), 1.94 (s, 3H, Me), 1.30 (6H, Me_i, $Me_{i'}$). *$^{13}C\{^1H\}$ NMR (75.47 MHz, acetone-d_6, 298 K, ppm):* δ 59.08 (C^*), 17.22 (Me).

[(η^5-C_5Me_5)Ir(κ^3*N,O,S*-L2)][SbF_6] (7aSb). Anal. calcd for $C_{21}H_{29}F_6IrNO_2SSb$, %: C, 32.0; H, 3.7; N, 1.8; S, 4.1. Found, %: C, 32.4; H, 3.9; N, 1.8; S, 3.8. IR (solid, cm^{-1}): ν(C=O) 1655 (s), 1635 (s), ν(SbF_6) 651 (s). CD (acetone, 5.0×10^{-4} M, 298 K): λ, nm, (Δε): 333 (−4.63).

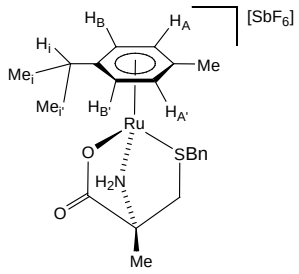
R_{Ir},R_C,S_S diastereomer. *^{1}H NMR (400.16 MHz, acetone-d_6, 298 K, ppm):* δ 7.43 - 7.27 (m, 5H, H_{Ar}), 6.01 (br, 1H, NH), 5.64 (br, 1H, NH), 4.09 (AB system, J_{AB} = 12.9 Hz, 2H, CH_2Ph), 2.66 (AB part, ABX system, J_{AB} = 14.4 Hz, J_{AX} = 2.2 Hz, 2H, CH_2C^*), 1.84 (s, 15H, C_5Me_5), 1.48 (s, 3H, C^*Me). *$^{13}C\{^1H\}$ NMR (100.6 MHz, acetone-d_6, 298 K, ppm):* δ 177.58 (C=O), 132.89, 130.44, 129.17, 128.85 (C_{Ar}), 89.46 (C_5Me_5), 65.82 (C^*), 39.02 (CH_2Ph), 35.84 (CH_2C^*), 22.11 (C^*Me), 8.25 (C_5Me_5).



[(η^6-*p*-MeC_6H_4*i*Pr)Ru(κ^3*N,O,S*-L2)][SbF_6] (7bSb). Isomeric ratio: ≥ 97/3. Anal.[20] calcd for $C_{21}H_{28}F_6NO_2RuSSb \cdot 3H_2O$, %: C, 33.6; H, 4.5; N, 1.9; S, 4.3. Found, %: C, 33.2; H, 4.3; N, 1.5; S, 4.1. IR (solid, cm^{-1}): ν(C=O) 1645 (s), ν(SbF_6) 652 (s). CD (acetone, 4.9×10^{-4} M, 298 K): λ, nm, (Δε): 334 (−1.18).

R_{Ru},R_C,S_S diastereomer (≥ 97 %). *^{1}H NMR (400.16 MHz, acetone-d_6, 298 K, ppm):* δ 7.52 - 7.27 (m, 5H, H_{Ar}), 6.06 (br, 1H, NH), 5.75, 5.58, 5.52, 5.48 (4 × d, J = 5.8 Hz,

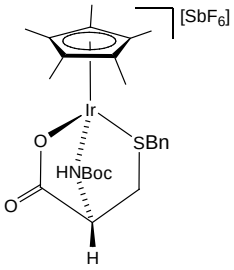
4H, H_A, H_B, $H_{A'}$, $H_{B'}$), 5.34 (br, 1H, NH), 4.02 (AB system, J_{AB} = 12.0 Hz, 2H, CH_2Ph),



2.68 (sept, J = 6.9 Hz, 1H, H_i), 2.53 (AB part, ABX system, J_{AB} = 14.3 Hz, J_{AX} = 2.6 Hz, 2H, CH_2C^*), 2.10 (s, 3H, Me), 1.37 (s, 3H, C^*Me), 1.23 (br, 6H, Me_i, $Me_{i'}$). *$^{13}C\{^1H\}$ NMR (100.6 MHz, acetone-d_6, 298 K, ppm):* δ 176.51 (C=O), 133.79, 130.38, 129.17, 128.96 (C_{Ar}), 105.86, 100.01 ($C_{p\text{-cymene}}$), 84.27, 83.60, 82.85, 81.96 (CH_A, CH_B, $CH_{A'}$, $CH_{B'}$), 64.31 (C^*), 41.24 (CH_2Ph), 35.98 (CH_2C^*), 31.07 (CH_i), 22.43 (C^*Me), 21.93, 21.31 (2C, Me_i, $Me_{i'}$), 17.17 (Me).

[(η^5-C_5Me_5)Ir(κ^3*N,O,S*-L3)][SbF_6] (8aSb). Anal.[20] calcd for $C_{25}H_{35}F_6IrNO_4SSb\cdot H_2O$, %: C, 33.6; H, 4.1; N, 1.6; S, 3.6. Found, %: C, 33.3; H, 4.3; N, 1.9; S, 4.0. IR (solid, cm^{-1}): ν(C=O_{Boc}) 1762 (s), 1698 (s), ν(C=O) 1629 (s), ν(SbF_6) 651 (s). CD (acetone, 5.1 × 10^{-4} M, 298 K): λ, nm, (Δε): 332 (−4.23).

R_{Ir},R_C,S_S diastereomer (82 %). *^1H NMR (500.13 MHz, CD_2Cl_2, 298 K, ppm):* δ 7.52 - 7.31 (m, 5H, H_{Ar}), 5.69 (brs, 1H, NH), 4.43 (brs, 1H, C^*H), 3.96 (brs, 2H, CH_2Ph), 2.90



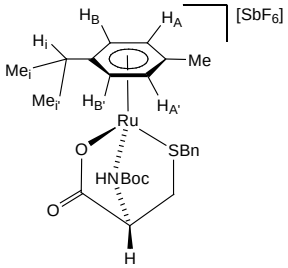
(AB system, J_{AB} = 13.0 Hz, 2H, CH_2C^*), 1.84 (s, 15H, C_5Me_5), 1.61 (s, 9H, $Me_{t\text{Bu}}$). *$^{13}C\{^1H\}$ NMR (125.8 MHz, CD_2Cl_2, 298 K, ppm):* δ 131.88, 130.40, 129.46, 129.30 (4 × brs, C_{Ar}), 90.24 (brs, C_5Me_5), 64.18 (brs, C^*), 39.85 (brs, CH_2Ph), 28.13 (brs, CH_2C^*), 27.72 (brs, $Me_{t\text{Bu}}$), 8.78 (brs, C_5Me_5).

Solvate derivative (18 %). *^1H NMR (500.13 MHz, CD_2Cl_2, 298 K, ppm):* δ 1.49 (brs, 9H, $Me_{t\text{Bu}}$), 1.40 (brs, 15H, C_5Me_5). *$^{13}C\{^1H\}$ NMR (125.8 MHz, CD_2Cl_2, 298 K, ppm):* δ 90.14 (brs, C_5Me_5), 64.18 (brs, C^*), 28.01 (brs, $Me_{t\text{Bu}}$), 7.88 (brs, C_5Me_5).

[(η^6-*p*-MeC_6H_4*i*Pr)Ru(κ^3*N,O,S*-L3)][SbF_6] (8bSb). Anal. calcd for $C_{25}H_{34}F_6NO_4RuSSb$, %: C, 38.4; H, 4.4; N, 1.8; S, 4.1. Found, %: C, 38.6; H, 4.5; N,

2.0; S, 4.4. IR (solid, cm^{-1}): ν(C=O_{Boc}) 1760 (s), ν(C=O) 1637 (s), ν(SbF_6) 653 (s). CD (acetone, 5.0×10^{-4} M, 298 K): λ, nm, (Δε): 401 (−2.93).

R_{Ru},R_C,S_S diastereomer. *^{1}H NMR (400.16 MHz, acetone-d_6, 298 K, ppm)*[a]*: δ* 7.47 (br, 1H, NH), 7.34 - 7.22 (m, 5H, H_{Ar}), 5.27, 5.13, 5.01 (3 × br, 4H, H_A, H_B, $H_{A'}$, $H_{B'}$), 3.84



(AB system, J_{AB} = 11.5 Hz, 2H, CH_2Ph), 3.67 (br, 1H, C^*H), 2.59 (AB system, J_{AB} = 15.2 Hz, 2H, CH_2C^*), 2.49 (m, 1H, H_i), 1.94 (s, 3H, Me), 1.43 (s, 9H, Me_{tBu}) 1.07, 1.05 (2 × d, J = 6.6 Hz, 6H, Me_i, $Me_{i'}$). *$^{13}C\{^1H\}$ NMR (100.6 MHz, acetone-d_6, 298 K, ppm): δ* 177.10 (C=O), 132.92, 130.28, 129.28, 129.12 (6C, C_{Ar}), 107.02, 99.08 (2C, $C_{p\text{-cymene}}$), 84.12, 83.21, 82.26, 81.88 (4C, CH_A, CH_B, $CH_{A'}$, $CH_{B'}$), 58.97 (C^*), 41.51 (CH_2Ph), 31.81 (CH_2C^*), 31.01 (3C, Me_{tBu}), 28.17 (CH_i), 22.17, 21.90 (2C, Me_i, $Me_{i'}$), 17.77 (Me).

Preparation of the complexes [(η^5-C_5Me_5)Ir(κ^3*N,O,S*-L3$_{-H}$)] (9a) and [(η^6-*p*-MeC_6H_4*i*Pr)Ru(κ^3*N,O,S*-L3$_{-H}$)] (9b). At room temperature, to a suspension of the corresponding **8Sb** complex (0.17 mmol), 14.3 mg (0.17 mmol) of $NaHCO_3$ were added. The suspension was vigorously stirred for 3 h and then was concentrated under reduced pressure until dryness. The residue was extracted with CH_2Cl_2 (4 × 5 mL) and the resulting solution was concentrated under reduced pressure to ca. 1 mL. The slow addition of *n*-hexane led to the precipitation of a yellow solid which was washed with *n*-hexane (4 × 5 mL) and vacuum-dried. Yield: 65 % (**9a**), 72 % (**9b**). Alternatively, complexes **9a** and **9b** can be prepared as follows: at 298 K, to a suspension of the corresponding dimer [{(η^n-ring)MCl}$_2$(μ-Cl)$_2$] (0.32 mmol), in 10 mL of MeOH, 201.5 mg (0.64 mmol) of **HL3** were added. The resulting yellow (Ir) or orange (Ru) solution was stirred for 15 min and then 108.7 mg (1.29 mmol) of $NaHCO_3$ were added. The resulting suspension was vigorously stirred for 2 h and then was concentrated under

reduced pressure until dryness. The residue was extracted with CH_2Cl_2 (4 × 5 mL) and the resulting solution was concentrated under reduced pressure to *ca*. 3 mL. The slow addition of *n*-hexane led to the precipitation of a yellow (Ir) or orange (Ru) solid which was washed with *n*-hexane (4 × 5 mL) and vacuum-dried. Yield: 56 % (**9a**), 73 % (**9b**).

[(η^5-C_5Me_5)Ir(κ^3*N,O,S*-L3$_{-H}$)] (9a). Anal.[20] calcd for $C_{25}H_{34}IrNO_4S\cdot H_2O$, %: C, 45.8; H, 5.5; N, 2.1; S, 4.9. Found, %: C, 45.7; H, 5.4; N, 2.2; S, 4.9. IR (solid, cm^{-1}): ν(C=O_{Boc}) 1763 (s), ν(C=O) 1642 (s). CD (acetone, 3.2 × 10^{-4} M, 298 K): λ, nm, (Δε): 352 (−4.01).

R_{Ir},R_C diastereomers. *^{1}H NMR (500.13 MHz, $CDCl_3$, 298 K, ppm):* δ 7.40 - 7.31 (m, 5H, H_{Ar}), 5.07 (br, 1H, C*H), 3.97 (AB system, J_{AB} = 13.4 Hz, 2H, CH_2Ph), 2.14 (dd, *J* = 13.0, 4.5 Hz, 1H, CH_2C^*), 1.96 (dd, *J* = 13.0, 0.8 Hz, 1H, CH_2C^*), 1.93 (s, 15H, C_5Me_5), 1.39 (s, 9H, Me_{tBu}). *^{13}C{^{1}H} NMR (125.8 MHz, $CDCl_3$, 298 K, ppm):* δ 181.22 (C=O), 177.60 (C=O_{Boc}), 133.96, 130.01, 129.07, 128.45 (C_{Ar}), 110.07 (C_5Me_5), 87.94 (C_{tBu}), 68.77 (C*), 39.80 (CH_2Ph), 32.00 (CH_2C^*), 28.69 (Me_{tBu}) 9.40 (C_5Me_5).

[(η^6-*p*-MeC_6H_4*i*Pr)Ru(κ^3*N,O,S*-L3$_{-H}$)] (9b). Isomeric ratio: 68/32. Anal. calcd for $C_{25}H_{33}NO_4RuS\cdot H_2O$, %: C, 53.3; H, 6.2; N, 2.5; S, 5.7. Found, %: C, 53.5; H, 5.8; N, 2.7; S, 5.7. IR (solid, cm^{-1}): ν(C=O) 1623 (s).

R_{Ru},R_C,S_S diastereomer (68 %). *^{1}H NMR (500.13 MHz, $CDCl_3$, 223 K, ppm):* δ 7.57 - 7.34 (m, 5H, H_{Ar}), 5.81, 5.31, 4.75, 3.40 (4 × d, *J* = 5.2 Hz, 4H, H_A, H_B, $H_{A'}$, $H_{B'}$), 4.71 (d, *J* = 4.4 Hz, 1H, C*H), 4.00 (d, *J* = 5.2 Hz, 1H, CH_2Ph), 3.64 - 3.46 (m, 2H, CH_2Ph, H_i), 2.34 - 1.99 (m, 2H, CH_2C^*), 2.18 (s, 3H, Me), 1.51 (brs, 9H, Me_{tBu}) 1.23, 1.18 (2 × d, *J* = 6.8 Hz, 6H, Me_i, $Me_{i'}$). *^{13}C{^{1}H} NMR (125.8 MHz, $CDCl_3$, 223 K, ppm):* δ 180.86 (C=O), 161.30 (C=O_{Boc}), 134.52, 130.50, 129.20, 129.15 (C_{Ar}), 101.73, 98.02 ($C_{p\text{-cymene}}$), 84.24,

83.80, 81.89, 79.38 (CH_A, CH_B, $CH_{A'}$, $CH_{B'}$), 78.04 (C_{tBu}), 65.57 (C^*), 41.23 (CH_2Ph), 32.57 (CH_2C^*), 31.09 (CH_i), 29.13 (Me_{tBu}), 25.06 (Me), 19.65, 18.29 (Me_i, $Me_{i'}$).

R_{Ru},R_C,R_S diastereomer (32 %). *^{1}H NMR (500.13 MHz, $CDCl_3$, 223 K, ppm):* δ 7.57 - 7.34 (m, 5H, H_{Ar}), 6.02, 4.91, 4.87, 3.26 (4 × d, J = 5.2 Hz, 4H, H_A, H_B, $H_{A'}$, $H_{B'}$), 4.80 (d, J = 4.4 Hz, 1H, C^*H), 4.00 (d, J = 5.2 Hz, 1H, CH_2Ph), 3.64 - 3.46 (m, 1H, CH_2Ph), 2.73 (sept, J = 6.7 Hz, 1H, H_i), 2.34 - 1.99 (m, 2H, CH_2C^*), 1.76 (s, 3H, Me), 1.35 (brs, 9H, Me_{tBu}) 0.98 (d, J = 6.3 Hz, 3H, Me_i), 0.89 (d, J = 5.5 Hz, 3H, $Me_{i'}$). *$^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$, 223 K, ppm):* δ 180.62 (C=O), 160.99 ($C{=}O_{Boc}$), 134.67, 130.31, 129.28, 129.15 (C_{Ar}), 106.06, 92.38 ($C_{p\text{-cymene}}$), 86.04, 84.75, 81.10, 77.07 (CH_A, CH_B, $CH_{A'}$, $CH_{B'}$), 77.95 (C_{tBu}), 65.41 (C^*), 40.97 (CH_2Ph), 33.44 (CH_2C^*), 31.06 (CH_i), 28.78 (Me_{tBu}), 24.47 (Me), 20.24, 19.12 (Me_i, $Me_{i'}$).

Crystal Structure Determination of Complex 6aSb

X-Ray diffraction data were collected at 100(2) K with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) using narrow ω rotations (0.3 º) on a Bruker SMART APEX diffractometer. Intensities were integrated and corrected for absorption effects with SAINT-PLUS[21] and SADABS[22] programs. The structure was solved by direct methods with SHEXLS-2013[23] and refined by full-matrix least-squares refinement on F^2 with SHELXL-2014.[24] The absolute configuration was determined on the basis of the previously known internal references, and this assignment was confirmed using the Flack parameter.[25]

*Crystal data for complex **6aSb***: $C_{20}H_{27}F_6IrNO_2SSb$; M = 773.44; yellow prism, 0.140 × 0.161 × 0.240 mm^3; orthorhombic, $P2_12_12_1$; a = 8.6130(4) Å, b = 14.4659(6) Å, c = 19.2824(8) Å; Z = 4; V = 2392.52(18) Å^3; D_c = 2.147 g/cm^3; μ = 6.837 mm^{-1}; min. and max. absorption correction factors 0.293 and 0.422; $2\theta_{max}$ = 57.18º; 34612 collected

reflections, 5816 unique reflections; R_{int} = 0.0202; number of data/restraint/parameters 5816/2/340; final GoF 1.116; R_1 = 0.0137 [5764 reflections, $I > 2\,\sigma(I)$]; *wR2* = 0.337 all data; Flack parameter x = −0.0051(15); largest difference peak 0.908 e·Å^{-3}. Hydrogen atoms (except those of methyl groups) have been included in the model in observed positions and freely refined. Two geometrical restraints in a C-H and an N-H bond lengths have been included in the refinement.

Acknowledgments

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Half-Sandwich Complexes of Iridium and Ruthenium Containing Cysteine-Derived Ligands

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Modified cysteines display five distinct coordination modes towards $(C_5Me_5)Ir$ and (η^6-*p*-MeC_6H_4*i*Pr)Ru moieties. From spectroscopic and crystallographic data, the absolute configuration of the resulting quiral compounds has been established.