Tricarbonylrhenium(I) Complexes with Tridentate Schiff Bases

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Introduction

Schiff bases are flexible and easily tunable ligand systems and form stable complexes with almost all transition metal ions. Consequently, their complexes found applications in many fields such as catalysis, magnetocochemistry or as model compounds in bioinorganic chemistry.[1–4] In the latter research area, Schiff bases and related ligand systems have not only been used as mimics for metalloenzymes, but also as metal-based pharmaceuticals. An illustrative example is the myocardial imaging agent 99mTc-furifosmin, a technetium(III) complex with the tetradentate Schiff base 4,4′-[(1E,1′E)-ethane-1,2-diylbis (azanylylidene)]bis(methanylylidene)]bis(2,2,5,5-tetramethyl-2,5-dihydrofuran-3-ol) (H₂Tmf₃en),[7] which has also been found suitable for the imaging of glioma and multidrug-resistant tumors.[8,9]

Such a behavior makes the structurally analogous rhenium complexes of this type interesting for cancer treatment. Rhenium possesses two β-emitting isotopes, which can be used for nuclear medical therapy: 186Re and 188Re.[9,10] The latter one can be obtained for clinical use from a so-called 186W/188Re nuclide generator, which makes it readily available at the clinical site.[11,12] Very recently, Re(V) and Re(III) complexes with the Schiff base H₂tmf₃en have been synthesized and structurally characterized.[13]

Potentially tridentate Schiff bases become interesting, since they can match the available coordination positions of the [M(CO)₃]+ cores (M = Re, Tc) and, thus, provide a maximum of stability for the corresponding complexes.[14–27] Such a stability, preferably accompanied by a kinetic inertness, is a fundamental requirement for use of corresponding tricarbonyl complexes in nuclear medical applications.

We have prepared a small series of Schiff bases from 2-(diphenylphosphino)benzaldehyde, salicylaldehyde, 2-amino-phenol and 2-((diphenylphosphino)phenyl)methylamine and reacted with (NEt₃)₂[Re(CO)₃Br] in methanol. Deprotonation and the formation of neutral [Re(CO)₃(L)] complexes with tridentate coordination of the Schiff bases has been obtained for the salicylidene derivatives, while the potential P,N,P ligand L₃ forms [Re(CO)₃Br(L₃)] with the Schiff base in a bidentate bonding mode. The formation of a cationic [Re(CO)₃(L₃)]⁺ complex with tripodal coordination of the organic ligand could be achieved by the addition of Ag(PF₆)₂ to the reaction mixture. The obtained rhenium(I) complexes were studied spectroscopically and by X-ray diffraction.

Figure 1. Schiff bases used in this study.
Results and Discussion

\((\text{NET}_4)_2[\text{Re(CO)}_3\text{Br}]_3\) is a suitable starting material to mimic reactions of \((\text{NET}_4)_2[\text{\textsuperscript{99}Tc(CO)}_3\text{Cl}]_3\) and the nuclear medically relevant cations \([\text{M(CO)}_3(\text{H}_2\text{O})_3]^+\) (M = \textsuperscript{99m}Tc or \textsuperscript{188}Re). Reactions of \((\text{NET}_4)_2[\text{Re(CO)}_3\text{Br}]_3\) with the Schiff bases \(\text{HL}^1\) or \(\text{HL}^2\) in methanol give yellow to orange-red solids of the composition \([\text{Re(CO)}_3\text{L}]\) (Scheme 1). The organic ligands undergo deprotonation without the addition of a supporting base and coordinate in a tripodal fashion. The products can be recrystallized from methanol and are readily soluble in organic solvents such as CHCl\(_3\) or CH\(_2\)Cl\(_2\). Their IR spectra show each three \(\nu\text{CO}\) bands in the range between 1878 and 2016 cm\(^{-1}\). Their positions at lower wavenumbers than in non-coordinated carbon monoxide (2143 cm\(^{-1}\)) confirm the \(\pi\)-back donation, which is commonly observed for electron-rich metal ions such as the \(d^6\) system of the present study. The presence of three IR-active modes is typical for facial tricarbonyl complexes with a low-symmetric coordination sphere. The \(^1H\) and \(^{13}C\) NMR spectra of the products are unexceptional and the \(^{31}P\) spectra show resonances at 31.7 ppm ([Re(CO)\(_3\)(L\(_1\)]) and 37.1 ppm [Re(CO)\(_3\)(L\(_2\))]), which is in the expected range for coordinated phosphines.

Single crystal X-ray studies on both compounds confirm the tripodal coordination of the deprotonated Schiff bases. Ellipsoid representations of the two structures are given in Figure 2. Table 1 contains selected bond lengths and angles of the neutral complexes.

The rhenium coordination spheres in both complexes are distorted octahedra. Main distortions of the bonding angles are due to restrictions caused by the chelating ligands. Thus, the N1–Re1–P1 angles in both compounds are small with values of 78.1(1) and 79.1(1)°, respectively. But also the N1–Re1–O1 angle in [Re(CO)\(_3\)(L\(_1\))], which belongs to a five-membered chelate ring, is remarkably small (75.0(2)°). The steric stress caused by the tripodal coordination of [L\(_1\)]\(^-\) is also reflected by a lengthening of the rhenium-nitrogen bond compared to the value in [Re(CO)\(_3\)(L\(_2\))], in which two six-membered chelate rings can be established. The imine bonds in the backbones of both ligands remain almost located as can be derived from the corresponding C–N bond lengths of 1.291(7) and 1.262(7) Å.

The ready formation of neutral complexes with tripodal coordinated Schiff bases is most probably supported by the deprotonation of the ligands \(\text{HL}^1\) and \(\text{HL}^2\) during their reactions.

Figure 2. Ellipsoid representations of the molecular structures of a) \([\text{Re(CO)}_3\text{L}^1]^-\) and b) \([\text{Re(CO)}_3\text{L}^2]^-\). Thermal ellipsoids represent 50 per cent probability. Hydrogen atoms have been omitted for clarity.

Scheme 1. Reactions performed and composition of the products.
with (NEt₃)[Re(CO)₂Br₃], since the corresponding reaction with the ligand L₁ results in an only incomplete replacement of the bromido ligands and the formation of the neutral complex [Re(CO)₂Br₃L₁]. Expectedly, also the addition of NEt₃ as a supporting base did not result in the abstraction of the third Br⁻ ligand. The formation of a cationic complex of the composition [Re(CO)₂Br₃]⁺[PF₆]⁻ finally succeeded by the addition of three equivalents of Ag(PF₆) to (NEt₃)[Re(CO)₂Br₃], removal of the formed AgBr and subsequent addition of L₁ (Scheme 1).

Both complexes with L₁ are yellow solids, which are readily soluble in organic solvents such as CH₂Cl₂ or acetonitrile, but insoluble in diethyl ether or hydrocarbons.

The IR spectra of the two L₁ complexes show in their carbonyl region the typical facial splitting pattern as has been found for the compounds with [L₁]⁻ and [L₂]⁻. ³¹P NMR spectroscopy confirms that only one of the phosphorus atoms of L₁ is coordinated in [Re(CO)₂Br₃L₁], since only one of the resonances observed for the uncoordinated Schiff base (−13.1, −15.1 ppm) is markedly shifted upon coordination to 13.3 ppm. This is different to the spectrum of [Re(CO)₃L₂], where the coordination of both phosphorus atoms is indicated by signals at 31.6 and 37.3 ppm.

The spectroscopic findings are in accord with the results of single crystal X-ray structural studies on the complexes. Ellipsoid representations of both complex molecules are shown in Figure 3. Selected bond lengths and angles are summarized in Table 2.

An almost ideal octahedral coordination sphere is found for [Re(CO)₂Br₃L₁], while slightly larger deviations from 90° between neighboring donor atoms are found when L₁ establishes a tripodal coordination mode. This demonstrates a remarkable flexibility of the neutral, potentially tridentate P,N,P ligand, particularly keeping in mind that a located C=N double bond is preserved in the backbone of the ligand after coordination.

Although the described complexes with L₁ are the first P,N,P Schiff base complexes with a tricarbonylrhenium(I) unit, there are some amine complexes with a similar coordination pattern. They found interest for potential pharmaceutical applications,[30–32] but also because of their catalytic activity for hydrogen transfer and methylation reactions.[33–36] Due to their flexibility, such tridentate, pincer-type amine ligands may allow isomerization between the facial and meridional coordination modes and can, thus, activate carbonyl ligands as has been demonstrated for bis[diisopropylphosphino]ethyl]amine and related ligands after the addition of a base.[34,35] Changes between bidentate and tridentate coordination, as observed for the tricarbonyl complexes of L₁, has not been reported for the corresponding amines.

### Table 1. Selected bond lengths (Å) and angles (°) in [Re(CO)₃(L₁)] and [Re(CO)₂(L₂)].

<table>
<thead>
<tr>
<th>Bond</th>
<th>[Re(CO)₃(L₁)]</th>
<th>[Re(CO)₂(L₂)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re1-C10</td>
<td>1.952(7)</td>
<td>1.950(4)</td>
</tr>
<tr>
<td>Re1-C20</td>
<td>1.946(7)</td>
<td>1.958(5)</td>
</tr>
<tr>
<td>Re1-C30</td>
<td>1.920(7)</td>
<td>1.901(6)</td>
</tr>
<tr>
<td>Re1-O1</td>
<td>2.138(4)</td>
<td>2.119(4)</td>
</tr>
<tr>
<td>Re1-N1</td>
<td>2.201(5)</td>
<td>2.168(4)</td>
</tr>
<tr>
<td>Re1-P1</td>
<td>2.433(2)</td>
<td>2.456(1)</td>
</tr>
<tr>
<td>N1-C27</td>
<td>1.291(7)</td>
<td>1.477(7)</td>
</tr>
<tr>
<td>N1-C31/C37</td>
<td>1.431(7)</td>
<td>1.262(7)</td>
</tr>
<tr>
<td>O1-Re1-P1</td>
<td>96.6(1)</td>
<td>88.5(1)</td>
</tr>
<tr>
<td>N1-Re1-P1</td>
<td>78.1(1)</td>
<td>79.1(1)</td>
</tr>
<tr>
<td>N1-C31/C37</td>
<td>122.1(5)</td>
<td>117.5(4)</td>
</tr>
</tbody>
</table>

Figure 3. Ellipsoid representations of the structures of a) [Re(CO)₂Br₃L₁] and b) the complex cation of [Re(CO)₂Br₃L₁][PF₆]. Thermal ellipsoids represent 50 per cent probability. Hydrogen atoms have been omitted for clarity.
Conclusions

In spite of the preservation of located C=N double bonds of the imines during coordination to [Re(CO)₃]⁺ units, the Schiff bases (L¹, L² and L³) can act as tripodal ligands. The formation of a bidentate product has only been observed for the neutral P,N,P ligand L¹. The stability of the products recommends the synthesis of corresponding tricarbonyltcnetunetn(l) complexes as potential radiotherapeutics. Such studies are planned in our laboratory for the future.

Experimental Section

All chemicals in this study were reagent grade and used without further purification. (NEt₄)[Re(CO)₃Br] was prepared from [Re-

\((\text{CO})_3\text{Br}\) and (NEt₄)Br in diglyme.\(^{[15,38]}\) HL¹ was prepared according to a literature procedure.\(^{[39]}\)

Analytical Methods. IR spectra were recorded for KBr pellets on a Shimadzu FTIR spectrometer in the range between 400 and 4000 cm⁻¹. ESI⁺ mass spectra were recorded on an Agilent 6210 ESI-TOF (Agilent Technologies). EI mass spectra were detected on a MAT 711, Varian MAT, Bremen. The energy of the electrons was 80 eV. NMR spectra were recorded in CDCl₃ on a JEOL-400 MHz spectrometer.

X-ray Crystallography. Single crystal X-ray diffraction data were collected on a STOE IPDS II T. Absorption corrections were carried out by integration methods.\(^{[40]}\) Structure solutions and refinements were done with the SHELX program package.\(^{[41,42]}\) Hydrogen atoms were placed at calculated positions and refined by the riding model option of SHELXL. More details are given in Table 3. The visualization of the molecular structures was done using the program DIAMOND 4.2.\(^{[43]}\) CCDC 2033898-2033901 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

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\text{HL}^2 \quad 2-(\text{Diphenylphosphino})\text{phenyl} \text{methylamine} (1.00 \text{ g, 3.55 mmol}) \text{ and 2-hydroxybenzaldehyde (0.38 ml, 3.55 mmol) were dissolved in 10 mL of EtOH. A yellow solid deposited after heating on reflux for 1.5 h and cooling to room temperature. It was recovered by filtration and recrystallized by slow evaporation of a}
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\text{in 10 mL of EtOH. A yellow solid deposited after heating on reflux for 2.5 h}
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\[
\text{and 2-(diphenylphosphino)benzaldehyde (1.00 g, 3.55 mmol) were added. A yellow solid deposited after heating on reflux for 2.5 h and cooling to room temperature. It was isolated by filtration and washed carefully with cold EtOH. Yield: 1.64 g (82 %).}
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C₈H₇NP₂


[43] Diamond – Crystal and Molecular Structure Visualization Crystal Impact, Dr. H. Putz & Dr. K. Brandenburg GbR, Bonn, Germany.

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