Cationic rhenium complexes ligated with N-heterocyclic carbenes – an overview

Claudia Hille and Fritz E. Kühn*

This review provides an overview of the currently known cationic rhenium NHC complexes. Synthesis, structures and properties are described. The title compounds are potential candidates for both catalytic and medical applications. Besides the variety of ancillary ligands, which are in some cases easily substituted, functionalization can be carried out in the side chain or at the backbone of the carbene ligand as well as in the case of biscarbene ligands – at the bridging moiety. Cationic Re NHC complexes are promising precursors for radiopharmaceuticals and diagnostics – not only because of the possibility to radiolabel the metal (steps in this direction have been made and described already) – but rather the opportunity to link the complexes to biomolecules via the different possibilities provided by the ligands. The development of OLEDs based on luminescent Re(I) carbene complexes renders another potential application.

1. Introduction

In recent years several overview articles and reviews concerning the metal rhenium and NHCS – including their applications in catalysis and radiochemistry – as well as group 7 metal–NHC complexes have been published.3

The profound interest in this research area is due to the fact that rhenium is cheaper than most of the noble metals which are commonly used in catalysis, and it can bear a variety of different ligand systems18 and has two isotopes, which can be easily produced – even directly in hospitals – which are therefore suitable for radiotherapeutic purposes.2 Rhenium further provides an almost unrivalled variety of oxidation states that are accessible under “non-exotic” reaction conditions.3

1.1 Pharmaceuticals

The reactor-produced radionuclide 186Re with a half-life of 89.2 h and moderate emission energy (Eγ max/average = 1.1/0.36 MeV; Eγ = 137 keV) can be received in analogy to 188Re (Eγ max/average = 2.1/0.8 MeV; Eγ = 155 keV), which is produced by using a 188W/188Re generator system in the form of Na[188ReO4].2

Although both isotopes can be transferred to cancer tissue and can be identified by single photon emission computed tomography imaging, 186Re features a more convenient half-life time (t1/2 = 16.9 h).1d,2c,4

The application of radioactive rhenium complexes is variegated – not only for treatment of cancer (bone, liver, ovarian, breast etc.) but also for inflammable joint diseases (e.g. arthritis).5 For nuclear medicine therapies like radiation synovectomy 186/188Re sulfur colloids have been applied and 188Re–tin colloids are already in clinical trials.5c,6c 188Re-HEDP therapy for bone pain palliation proved to be effective5a and Lipiodol with radiolabelled rhenium is in clinical trials for the metabolic radiotherapy of heptacellular carcinoma.2d,f For this most common type of liver cancer several complexes with a 186/188-rehenuim(IV) oxo scaffold are known.2b–k The design of radio labeled antibodies with rhenium is popular with respect to radio immunotherapy.5a,5m,9 In cases, where rhenium oxo cores as the chelate site – for instance 188Re-MAG3-HBP is expected to be a useful radiopharmaceutical for the palliation of metastatic bone pain5a or 186/188Re-(CO)3·A7 showed high uptake in tumor-bearing mice.5p Besides the conventional cancer therapy, Re(i)(CO)3 derivatives showing anticancer activity are promising candidates as organometallic therapeutic and diagnostic agents.7

1.2 Catalysis

Although rhenium complexes are known in different oxidation states (−II to +VI) and with a variety of ligand systems, particularly rhenium oxo and carbonyl complexes are established in catalysis.1b,8 Besides the oxygen atom transfer reaction – for instance deoxygenation reactions as well as dehydrogenation or deoxydehydration reactions can be catalyzed by Re(V) complexes,9a–d rhenium carbonyl complexes can act as catalysts in quite a number of different reactions e.g. hydroarlyations, transfer-hydrogenation reactions and formation of carbon-
carbon or carbon–heteroatom bonds, which were summarized by Kuninobu and Takai in 2011.\textsuperscript{11,42\textdagger}

NHC complexes with almost every metal in the periodic table are known as homogeneous as well as heterogeneous catalysts.\textsuperscript{9} In addition to the “classical” catalysis in organic solvents the field of catalysis in aqueous media or water became more interesting in the past few years.\textsuperscript{15,16} However, only two groups have reported on rhenium carbene complexes as catalysts so far.\textsuperscript{11} Rhenium(i) hydride complexes \textbf{1x} catalyze the dehydro coupling of \textit{Me}_2\textit{NH·BH}_3 and ammonia borane \textit{NH}_3·\textit{BH}_3 as well as the transfer hydrogenation of several olefins, where \textit{Me}_2\textit{NH·BH}_3 donates hydrogen to produce the corresponding alkanes.\textsuperscript{11a} Liu \textit{et al}. tested the catalytic activity of several rhenium carbonyl complexes in the insertion reaction of terminal alkynes into β keto esters. Complexes 2, 3 and [(NHC)\textit{Re}((CO)\textsubscript{9})] (NHC = 1,3-bis(hydro)-4,5-dihydroimidazol-2-ylidene) are able to catalyze the formation of ethyl(2\textit{E})-2-methyl-5-oxo-3-phenyl-2-hexenoate but need the support of photoirradiation and show only moderate activities (Fig. 1).\textsuperscript{11b}

Although the metal rhenium is known since 1925, significant amounts were accessible only since the 1950s.\textsuperscript{12} Synthesis routes of a broad variety of rhenium complexes are well established since then and some general reviews were published, this review focuses on the synthesis and properties of cationic rhenium NHC complexes – particularly with regard to their potential application in medicine.

\section{Cationic rhenium mono-NHC complexes}

\subsection{Re(i) complexes bearing saturated mono-NHC ligands}

The \textit{Re}(CO\textsubscript{3}) fragment, which can be found in the majority of cationic \textit{Re}(i) NHC complexes, has attracted attention concerning luminescence for potential application in light emitting diodes (LEDs), organic light emitting diodes (OLEDs) and biological labelling markers.\textsuperscript{10,13}

The first cationic \textit{Re}(i) NHC complexes were isolated by Che and coworkers.\textsuperscript{14} These compounds contain bidentate diimine or phosphine ligands and could be obtained by the reaction of the corresponding diimines (L\textsubscript{1}, L\textsubscript{2}) or chelating phosphines (L\textsubscript{3}) with the literature known complex 4.\textsuperscript{15} All complexes (5–7) are assumed to display a pseudo-octahedral geometry, although only the molecular structures of 5c, 5e and 7 have been determined by X-ray analysis. Based on molecular orbital calculations and photophysical studies it is found out that changing the electron-donating/accepting ability of the bidentate diimine ligand via modification of the electron-withdrawing character of the \textit{R} group leads to reasonable emission lifetimes, quantum yields and well defined redox potentials. The metal to ligand charge transfer (MLCT) excited stage energy is strongly influenced by the \textit{R} group of complexes 5 and can only be altered by changing the polarity of the solvent at room temperature. However a change to intra-ligand (IL) charge transfer occurs at 77 K in the case of the Phphen ligand. At this temperature all complexes were found to be emitting, nevertheless only complexes 5 and 6 maintained this behaviour at room temperature.\textsuperscript{14}

Related to complex 5c, bipyridine NHC \textit{Re}(i) complexes bearing mesityl substituted ligands could be isolated by the same group.\textsuperscript{16} In order to achieve substitution with bipyridine, addition of a silver salt has been necessary. Liu \textit{et al}. ascribe this to the steric bulkiness of the ligands, which may exacerbate the replacement of the CO ligands. Both the saturated and unsaturated compounds 9a and 9b have been characterized by NMR, IR and mass spectrometry, but no crystal structures are reported (Schemes 1 and 2).\textsuperscript{16}

A cationic macrocycle substituted \textit{Re}(i) complex with a coordinated PCC ligand was achieved via template (controlled) synthesis in 2007.\textsuperscript{17} Starting from \textit{Re}(i) template 2a and a fluorinated diphosphate 1,2-bis(di(o-fluorophenyl)phosphine)-

\begin{figure}
\centering
\includegraphics[width=\textwidth]{fig1.png}
\caption{Re(i) hydride (1x)\textsuperscript{11a} and carbonyl (2, 3).\textsuperscript{11b}}
\end{figure}
benzene) a bidentate phosphine complex 10a could be formed selectively in acetonitrile. Efforts to carry out this synthesis according to the literature-known conditions with similar diphosphine resulted in mixtures of complexes 10a, 11 and 12. This formation of mixtures was ascribed to the simultaneously activation of NH and CF, respectively the insolubility of the products in solvents of low polarity (Scheme 3).18

The air and water stable macrocyclic [11]ane-P2CNHC Re(I) complex 12 was obtained via the template controlled ring formation reaction via the isolatable neutral intermediate 13.17,18 Deprotonation of 10a and a S_N2Ar type attack of the deprotonated nitrogen atoms at the C–F bond of the o-fluorenyl diphosphine connects it to the carbene ligand, resulting in a macrocyclic and polydentate NHC complex 12 (Scheme 4).17–19

In addition, cationic Re(i) macrocycles with a mixed NHC/phosphine donor set (14, 15) could be obtained by the same group. Using the same method of template synthesis ethylene bridged diphosphines and NHC ligands could be facially coordinated to the metal. No intermediates have been reported (Scheme 5).20

As a comparatively easy method, to generate carbene complexes of different metals, is known since a couple of years.17 Using functionalized isocyanides, which contain – beside the isocyanide moiety – a nucleophilic part, leads via intramolecular 1,2 addition usually to imidazolidin-2-ylidene.17,21

Hahn and coworkers established a cationic tris-NHC-Re(i) by template controlled cyclization of a β-azido functionalized isocyanide.22 As the metal template they used complex 17,15 which contains besides strong π-acceptor CO-ligands two strong σ-donor NHCs and one bromide ligand, so that the abstraction of the halide followed by attaching 2-azidoethyl isocyanide at the ‘free coordination site’ yields complex 18. IR spectroscopy revealed that the functionalized isocyanide is activated for a nucleophilic attack upon coordination to the rhenium core. As a result the formation of tris(NHC) complex 19 could be achieved by reduction and of the azido function and ensuing intramolecular cyclization (Scheme 6).22

2.2 Re(i) complexes bearing unsaturated mono-NHC-ligands

Formation of cationic agostic and solvent stabilized 16 electron complexes via halide abstraction was achieved by Whittlesey et al.23 By reacting neutral mono-Re NHC precursors (20, 23) with NaBArF salts, complexes 21 and 24 are generated. Attempts to isolate agostic product 21 failed leading to an undefined rhenium carbonyl species and the additionally appearing tetracarbonyl compound [Re(IiPr2Me2)2(CO)4]BArF (22). Directly bubbling of CO into the reaction mixture of 20 and NaBArF leads to selective formation of an 18 electron
complex cis-22. Addition of acetonitrile to the reaction mixture instead of CO results in the formation of [Re(l'Pr₂Me₂)₃(CO)]⁻(MeCN)[BAr₄]F. These observations suggest that even less weakly coordinating ligands are able to displace the agostic interactions in complex 21. As a less electrophilic bis-NHC species 21 is stabilized via the agnostic bond of one NHC, monocarbene complex 24, which contains a less nucleophilic ligand, and binds a less strongly coordinating solvent molecule to become stable. Preparation of this complex is achieved by reacting the neutral triflate rhenium precursor 23 with the sodium salt of the non-coordinating anion BAr₄F in dichloromethane. After halide abstraction subsequent monodentate binding of the solvent takes place, whereas in the presence of CO the carbonylated cationic rhenium complex 25 is formed (Schemes 7 and 8).²³

Another literature known synthetic route to NHC complexes with different metals is the transformation of coordinated imidazoles to NHC ligands.²⁴ Pérez, Riera, López and coworkers described the formation of cationic rhenium(i) carbonyl complexes containing both NHC and N-alkylimidazole ligands as a pseudo-tautomerisation.²⁴ᵃ,ᵇ,ᶜ,ᵈ Starting from a highly stable cationic N-alkylimidazole containing fac-Re[(CO)₃] complex 26, one of the imidazole ligands is deprotonated by a strong base resulting in a stable neutral but not isolable intermediate 27, which features an imidazole-2-yl ligand. The non-substituted nitrogen atom at the NHC of the highly reactive compound 27 can be protonated or methylated easily by electrophiles. Using methyltrifluoromethanesulfonic acid affords the cationic complex 29 and trifluoromethanesulfonic acid leads to 28, which contains a NH–NHC ligand, respectively (Scheme 9).²⁴ᵃ–ｃ

In addition, the group discovered that besides the nature of the imidazole ligands, the ancillary substituents at the metal influence the resulting product.²⁶

Starting from [ReOTf]([CO])₃(N-Melm)₃ (30) the triflate ligand was substituted, supported by NaBAr₄ to obtain complex 31a.²⁴⁵ The subsequent change of the coordination mode of one imidazole ligand by deprotonation with KN(SiMe₃)₂ led to the imidazole-2-yl complex 32. From the latter, the cationic Re–NHC complex 33 could be generated via methylation at the non-coordinated nitrogen atom. The influence of the substituent on the phosphane ligand becomes apparent when complexes 31b and 31c, which can be synthesized analogously to complex 31a, were treated under similar conditions as described for complex 31a. In the case of PMe₃ (in complex 31a) a cationic Re(I)–NHC complex 33 is created whereas arylphosphane ligands lead to binuclear Re(I)–Re(I) complexes (35) bearing abnormal NHC ligands obtained via double activation of the N-methylimidazole (Scheme 10).

A methoxycarbene ligand is generated by the formation of a four-membered cycle including one rhenium atom and methylation of the oxygen atom of the cis-carbon-monoxide ligand. The bridging and build-up of the abnormal NHC moiety is achieved via deprotonation of the backbone of the N-methylimidazole and coordination to a second rhenium atom. This leads to a formal intramolecular ligand coupling resulting in an N₃N-bidentate ligand coordinated at rhenium-2. cis/trans-Rhenium complexes featuring N,N-bidentate chelate ligands (36) formed as side products here.²⁷ Various benzoxazol-2-ylidene-substituted Re(i) phenanthroline complexes can be obtained starting from acetonitrile con-
As previously reported, N,O-heterogenocarbene complexes can be built via intramolecular cyclization, if the isocyanide C atom is not deactivated by strong (d → p)π-back-bonding from the metal core.\textsuperscript{14,29} Contrary to similar rhenium complexes published by Hahn \textit{et al.},\textsuperscript{29a} the strong π-accepting carbonyl ligands coordinated to the rhenium precursor support the formation of the reported luminescent rhenium complexes 38, 39 and 43a–c (Scheme 11).

Complex 39, which may be considered as the N-protonated form of the neutral rhenium complex 38 bearing an anionic N-deprotonated carbene ligand, could be generated \textit{via} acidification and subsequent metathesis. This complex as well as the methylated equivalent 40 adopts a distorted octahedral geometry with a facial arrangement of the three carbonyl ligands.

Similar reactions with several phosphines bearing rhenium phenanthroline precursors 41x lead to carbene complexes 43x where both carbonyl ligands are arranged in the \textit{cis} conformation (Scheme 12).\textsuperscript{28} Furthermore, the same group reported – based on their previous work\textsuperscript{28} – in 2014 luminescent N,S-, N,N-, and N,O-NHC rhenium(1) complexes \textit{via} a ligand substitution reaction.\textsuperscript{13b}

Starting from Re(CO)\textsubscript{5}Br (16) \textit{via} a neutral bis(N,O-carbene) rhenium precursor 44 several cationic mono carbene rhenium compounds (45x, 46), could be obtained. X-Ray analysis shows that complex 46 bears two unsymmetrical \textit{cis} carbonyl ligands, one is located \textit{trans} to the carbene ligand, the other, as well as the isocyanide ligand are \textit{trans} to the diimine ligand (Scheme 13).

The opening of one NHC ligand in complex 44 and thus the formation of an isocyanide moiety are favoured by the substitution of the CO ligand, positioned \textit{trans} to the carbene by a diimine, as a consequence of the weakening of the π
(carbene)-π (O) interaction resulting from enhanced π-(rhenium → carbene)-back-donation.

For complexes 45x and 46 an interconversion between the isocyanide and the N,O-heterocyclic carbene form occurs, while complexes 48x and 49 are generated by the conversion of one coordinated isocyanide ligand to a carbene ligand. The formation of only one carbene ligand – even with a large excess of nucleophiles – results from the different reactivities of the coordinated isocyanide ligands in precursor complex 47. While the isocyanide ligand, standing in the trans position to...
the carbonyl ligand is susceptible to the nucleophilic attack, the isocyanide C atom positioned trans to the diimine receives a stronger \(\pi\)-back bonding from the metal and hence is more electron rich, consistent with the observations for complexes 45-x and 46. Reacting complex 50b with concentrated sulfuric acid leads to the distorted octahedral target NHC complex 51 (Scheme 14).13b

As the first investigations of luminescence of N-heterocyclic rhenium(I) complexes were reported by Che et al.14 (see before), Ko and coworkers studied the photophysical and electrochemical properties of rhenium diimine complexes bearing N,N-, N,S- and N,O-NHC ligands.13b,28

The knowledge about the influence of the relatively strong \(\pi\)-acceptor ability of almost every modification of or at a ligand (complexes 38–40, 43, 45, 46, 48x–51) can be used for the development of further luminescent NHC complexes for various applications (e.g. photocatalysis of \(\text{CO}_2\) reduction) by tuning the emission properties.13b,28
Scheme 13 Oxazole–Re(I) complexes containing phenol substituted isocyanides.\textsuperscript{13b,28}

Scheme 14 Generation of cationic N,S-, N,N- and N,O-NHC Re(I) diimine complexes.\textsuperscript{13b}
2.3 Unsaturated Re(V) complexes bearing mono-NHC ligands

Various cationic Re(V) complexes with unsaturated mono-NHC ligands have been prepared. Royo, Romão et al. and Abram et al. were the first to obtain cationic Re(V) oxo complexes bearing four unsaturated carbene ligands, by reacting strong Lewis basic NHCs with various rhenium precursors.

Dicaticonic monooxo-complex 53 is the reaction product of \([\text{ReOCl}_3(\text{PPh}_3)_2]\) with an excess of free carbene 52. The triphenylphosphane- and two of the chloride-ligands are displaced by four monocarbene ligands. The green complex 53 is described as moisture-sensitive in solution – traces of water lead to the formation of a dioxo species (see below) – and air-stable for a short time as a solid.

By using the same ligand 52 with different rhenium compounds and reaction conditions, monocationic tetrakis-(carbene)dioxorhenium complexes 54 and 55 can be formed. The brown solid 54 can be generated starting from \([\text{ReO}_2(\text{PPh}_3)_2]\). \([\text{ReO}_2\text{Me}(\text{PhCCPh})]\) yields yellow crystals 55 featuring an approximate \(D_4\) symmetry with perrhenate as an anion and one thf-solvent molecule. Royo, Romão et al. assumed that the formation of complex 55 is caused by adventitious water in the reaction mixture, with some unidentified products additionally found (Scheme 15).

Starting from three different rhenium precursors Abram et al. reported a cationic dioxorhenium(V) complex bearing four carbene ligands, which are methyl-substituted at the backbone.

Depending on the reaction conditions hexafluorophosphate (60b) or perrhenate salts (60a) of the complex could be isolated. Performing the reaction of \([\text{ReOCl}_3(\text{PPh}_3)_2]\) with an excess of the free carbene 56 in air in combination with traces of water in the solvent leads to 60a and \(\text{HLiPr}\) as a side product, whereas the addition of ammonium hexafluorophosphate yields the stable 60b (Scheme 16).

Using the free carbenes 61/65 under the same reaction conditions as applied for the synthesis of compound 60, the monooxo species 62/68 can be isolated as green powders. By solving complexes 62 and 68 in methanol and adding hexafluorophosphate salts in the presence of \(L^\text{Me}\) (61), an exchange of the chloro ligand for a methoxy ligand takes place whereas for \(L^\text{Et}\) (65) crystals of the composition \([\text{ReOCl}(L^\text{Et})_4]\cdot[\text{PF}_6]\cdot2\text{KPF}_6\) (68b) are obtained (Scheme 17).

Another synthetic approach via NHC transfer reagents for compounds considered for radiopharmaceutical applications was shown for 65. By reacting silver tetrafluoroborate with an

Scheme 15  Synthesis of the first cationic Re(v) NHC oxo complexes.
excess of free carbene (56, 63) the corresponding silver(I)NHC complexes could be obtained, which then can be used as transmetallation agents. The known precursors for Re(V) carbene complexes, such as [ReOCl₃(PPh₃)₂] and [NBu₄][ReOCl₄] form the orange-red product 67 with an excess of the silver carbene (66) and addition of (NH₄)(CF₃SO₃) (Scheme 18).30

The dioxo species (60, 64, 67) as well as complexes 62, 63, 66 and 68 feature planar coordination spheres with equatorially bonded NHC ligands.30b–d Although the steric demand of the ligands does not affect the paddle-wheel type ligand arrangement, it influences the stabilities as well as the structures of the complexes depending on the nature of the alkyl substituents at the NHC ligands. Isopropyl substituted imidazoylidene ligands seem to be more basic than the methyl substituted analogues, which signifies a higher nucleophilicity at the carbene C-atom. Consequently dioxo rhenium complexes (60, 64, 67) more stable due to their ability to (better) stabilize the augmented electron density.1k,31

Furthermore nitridorhenium(V) as well as phenyl-imidorhenium(V) complexes with ligands L<sup>Me</sup> (61) and L<sup>Et</sup> (65) were published by the same group.30e–f

They used [ReNCl₂(PR′₂Ph)₃] (R′ = Me, Et) as the rhenium precursor to yield 69a,b as stable solids by application of an excess of the corresponding carbenes (61, 65) in dry solvents. Attempts to generate the analogous isopropyl complex have failed so far. Due to the different steric bulkiness of the NHC ligands, caused by the alkyl side chains, hydrolysis induced by moisture is favoured for [ReNCl(61)₄]Cl (69a); whereas [ReO₂(65)₄][ReO₄] (70) is formed in hot methanol (Scheme 19).30f

Compared to the hydrolysis susceptibility of nitridorhenium carbene complexes (69), using the formally dianionic ligand “PhN<sup>2-</sup>”, isoelectronic with an oxo ligand and thus able to stabilize rhenium in higher oxidation states, leads to “hydrolysis-inert” phenylimidorhenium(V) carbene complex 71.30e

Matching the analogous nitrido complex 69b, the phenylimido ligand is able to generate a conjugated π-system and hence can compensate for the electron density that is donated by the carbene ligands to the rhenium centre. Again, by performing the reaction in dry solvents Abram and coworkers obtained [Re(NPh)X(65)₄]²⁺ (71x; X: Br, Cl), whereas the traces of water in the reaction mixture resulted in the hydroxo derivative (72). Purple crystals of 72c could be obtained via recrystall-
lization in methanol, which is mandatory to get rid of the car-}
benium salt that is formed as a side product. Coordination of
a hydroxo instead of a methoxo ligand can be explained by the
steric shielding of the NHC ligands, which allow less free
space in the trans position to the imido ligand.\textsuperscript{30}

This behaviour was observed before for rhenium oxo complex
\textsuperscript{61}\textsuperscript{30} The fact that only stable phenylimido rhenium complexes with
carbene \textsuperscript{65} can be prepared to date, whereas efforts to generate
analogous complexes with \textsuperscript{56}/\textsuperscript{61} lead to dioxo complexes may
be explained by the matched shielding of the ethyl substituted
carbene caused by its fitting steric demand (Scheme \textsuperscript{20}).\textsuperscript{30c}

3. Cationic rhenium bis-NHC complexes

3.1 Cationic rhenium(i) bis-NHC complexes

Based on the previous work,\textsuperscript{32} Herrmann, Kühn and
coworkers reported the synthesis of chelated NHC cationic
Re(i) carbonyl complexes with weakly coordinating anions
(WCA).\textsuperscript{33}

The uncharged rhenium precursors \textit{fac}-bromotricarbonyl
(NHC)Re(i) (75x) were synthesized by treatment of
[NEt\textsubscript{4}]\textsubscript{2}[ReBr\textsubscript{3}(CO)\textsubscript{3}] with free carbenes (74x), which were
obtained starting from \textit{N} substituted imidazoles (73x) via the
\textit{S}_\textit{N}2 reaction and subsequent deprotonation with a base.\textsuperscript{32}
These stable bis(NHC) complexes (75x) are able to react with
silver WCA salts (AgPF\textsubscript{6}, Ag[Al(OC(CF\textsubscript{3})\textsubscript{3})\textsubscript{4}] in acetonitrile at
room temperature to give the corresponding rhenium(i) bis(NHC)
acetonitrile WCA complexes (76, 77) (Scheme \textsuperscript{21}).

All obtained complexes were characterized by mass spec-
trometry and spectroscopic methods. Interestingly, the vari-
ation of the bridge length and the substituents as well as the
WCA anions did not strongly influence both the yield and the
IR resonances. All the Re(CO)\textsubscript{3} moieties display a distorted C\textsubscript{3v}
local symmetry. This asymmetry results in a degenerate CO
stretching mode, where one of the CO groups differs from the
other two. Though, despite the observed little resonance variance no general trend relating to the influence of the different bridge length could be determined.

The distorted octahedral symmetry is confirmed by X-ray structure analysis for complexes 77a, 77b, 77h and 77i. In comparison with their uncharged Re(I) NHC analogues fairly similar bond distances between the metal and the trans-carbonyl group have been found. However, the steric demand of the acetonitrile ligand, being different from the bromo ligand, influences the position of the bulky mesitylene ligands independent of the length of the bridging moiety in complexes 77h and 77i. The increasing bridge length between the NHC moieties is, however, responsible for a higher torsion angle between the imidazole rings. In the case of a large WCA ligand as a counterion (76a), only a minor change of the bond length compared to the uncharged derivative appears. All attempts to obtain single crystals of the complexes (77c-f) as well as 76b have failed so far, whereas the crystallisation of 76c has led to the first Re(I) NHC CCC pincer complex.

With regard to potential application in catalysis or pharmaceutical chemistry the stability of the Re(I) NHC compounds was examined by temperature dependent NMR experiments. The labile acetonitrile ligand can be easily exchanged by DMSO, changing also the geometry of complex 77h. The compound remains stable up to 93 °C for several minutes. This allows for potential use as a homogeneous transition metal catalyst, for e.g. hydroamination reactions.

Catalytic applications in the hydroamination of 4-pentyn-1-amine as examined by Müller, Yan et al. have failed so far, so that the focus should be laid on other catalytic reactions or on modification of the complex. Replacing one of the strongly

Scheme 19  Formation of cationic Re(V) nitride or oxo complexes due to the reaction conditions.

Scheme 20  Phenylimidorhenium(V) carbene complexes synthesised by Abram and coworkers.
binding NHC ligands – in combination with a WCA – for example pyridine containing Re(I) carbonyl complexes as reported by Stagni, Massi, Brown et al.\(^{35}\) and Yang et al.\(^{36}\) could create efficient catalysts.\(^{37}\)

### 3.2 Cationic rhenium(V) bis-NHC complexes

The group of Hor reported the first Re(V) complexes in which the trans oxo-hydroxo core is stabilized by two chelating N-heterocyclic dicarbene ligands.\(^{30}\) The air and moisture stable complexes \(^{79}\) were obtained via transmetalation from a silver(I) carbene precursor \(^{78}\) with the commercially available complex ReOCl\(_3\)(PPh\(_3\))\(_2\) (\(^{57}\)) in good yields. For \(^{79a/b}\) the characterization of the complexes was carried out via NMR, MS, EA, FTIR and single crystal XRD. All three cationic mononuclear complexes \(^{79}\) occur in an octahedral geometry with the two NHC ligands orthogonal to the trans oxo-rhenium-hydroxo axis. The asymmetric units ([ReO(OH)(LR)\(_2\)]\(^{2+}\) (\(^{79}\)) contain in all cases two disordered anions in the ratios of PF\(_6\)\(^-\):ReO\(_4\)\(^-\) = 0.7:0.3 (\(^{79a}\)); 0.74:0.26 and 0.66:0.34 (\(^{79b}\)); 0.65:0.35 (\(^{79c}\)). The presence of an oxo-rhenium-hydroxo motif is explained as the most likely one. On the one hand the observed length of the rhenium oxo bonds do not fit in the typically literature known range of rhenium oxo bonds in a stable [O=Re=O]\(^{2+}\) rhenium dioxo core with monodentate NHC ligands,\(^{30a,b,d}\) on the other hand the di-hydroxy rhenium motif is excluded due to incongruence regarding charge neutrality and the lower probability of the occurring of a trication (Scheme 22).\(^{10g}\)

Based on this work, the groups of Reiner and Kühn developed a route towards a radiolabeled \(^{188}\)Re N-heterocyclic carbene complex (\(^{188}\)Re-\(^{80}\)).\(^{4}\) The cold trans-dioxobis(1,1'-methylene-bis(3,3'-diisopropylimidazolium-2-ylidene))rhenium(v)-hexa-fluorophosphate (\(^{80}\)) was synthesized following a previously published procedure.\(^{3,30}\) By reacting ReOCl\(_3\)(PPh\(_3\))\(_2\) with one equivalent of the corresponding silver carbene (\(^{78b}\)) and transmetalation via silver carbene (\(^{78b}\)) and purification by HPLC, the \(^{188}\)Re-labeled counterpart (\(^{188}\)Re-\(^{80}\)) can be obtained (Scheme 24).

The carried out stability tests revealed that indeed the unlabelled rhenium complex (\(^{80}\)) is stable for 24 h at room temperature in a solution of acetonitrile and water, nevertheless undesirable decomposition occurred by testing the \(^{188}\)Re-labeled counterpart (\(^{188}\)Re-\(^{80}\)). Under the applied conditions, starting with water at 37 °C in a pH range from 5 to 8, with phosphate buffered saline solutions (37 °C; pH: 5, 6 & 7) as well as bovine serum, which is reasonably similar to the in vivo environment, the decomposition took place more quickly. The authors ascribe this to the bulkiness of the ligands at the
rhenium centre and to the presence of potentially coordinating anions in the used environmental media.\textsuperscript{4}

In contrast to the similar water stable \textsuperscript{99}Tc NHC complex (dioxobis(1,1′-methylene-bis(3,3′-dimethylimidazolium-2-ylidene))-technecium(\textit{v})) published by Braband and coworkers,\textsuperscript{40} which differs from the metal only by its less bulky methyl substituents, the bulkiness of the isopropyl ligands and the terminal oxo ligands may promote the de-coordination of the NHC ligand as the primary decomposition pathway in aqueous medium instead of reoxidation to free \textsuperscript{188}perrhenate. The rapid decomposition in phosphate buffered saline solutions is due to the higher ionic strength of buffered solutions – especially chloride anions can compete with the carbenes at the rhenium – hence imidazolium salts are generated, that do not have the ability to bind to the metal again. Furthermore, biomacromolecules that are abundant in the fetal bovine serum may facilitate the decomposition of the complex (\textsuperscript{188}Re-\textsuperscript{80}) by undergoing nucleophilic reactions with rhenium. The formed adducts of biomacromolecules with the metal leads to the formation of \textsuperscript{188}ReO\textsubscript{4}\textsuperscript{−}.

Despite the unfitness of this particular complex for use in radiopharmaceutical applications, due to its reduced stability under physiological conditions, a new approach for carrier-free and carrier-added radiolabeled rhenium NHC complexes has been opened.\textsuperscript{4} These investigations done by Reiner and Kühn et al.\textsuperscript{4} illustrate that although several radiopharmaceuticals based on the Re(\textit{I})(CO)\textsubscript{3}-fragment,\textsuperscript{5\textsubscript{o}-\textsubscript{r},41} as well as Re(\textit{V})-complexes\textsuperscript{5\textsubscript{h}-\textsubscript{j},l} are known, only estimations based on steric, kinetic and electronic considerations can be done. Whether Re(\textit{i}) or Re(\textit{v}) in combination with different types of ligands are more stable under physiological relevant conditions can only be figured out by testing these compounds.

4. Conclusion and perspectives

In this review, synthetic routes to cationic rhenium NHC complexes and their properties have been summarized. Since the first cationic Re(\textit{i}) carbene complex was isolated in 1998\textsuperscript{14} a variety of different approaches such as template synthesis or intramolecular cyclization have been reported. Beside the Re(CO)\textsubscript{3} core, bearing varying auxiliary ligands rhenium(\textit{v}) mono- or bis-NHC compounds comprising nitrido, imido and oxo units arouse interest with respect to their potential appli-
cations, particularly in medicine. Apart from the direct coordination of a free NHC moiety to the metal, the synthetic approach via transmetalation of stable silver NHC precursors looks quite promising for future clinical applications. With respect to nuclear medicine, creating diagnostic or therapeutic radiopharmaceuticals for instance can be carried out by radiolabelling of rhenium, or by linking the complexes bearing potential coupling groups (organoimido, alkylamido or alkylcarboxyl) to biomolecules via the N- or C-terminus of peptides. Investigations of high valent Re(v) biscarbene (O, OH) complexes as oxidation catalysts or Re(i) complexes bearing NHCs in hydroamination reactions or as photocatalysts are still ongoing. It also appears to be rather straightforward that in this field further research concerning luminescence, toxicity, air and water stability as well as solubility has to be executed with regard to further development of applications of these complexes.

Acknowledgements

The Margarete Ammon Foundation is acknowledged for a PhD grant to C. H.

Notes and references


41 C. Kluba and T. Mindt, Molecules, 2013, 18, 3206.