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Molecular Recognition Utilizing Complexes with NH,NR-Stabilized Carbene Ligands

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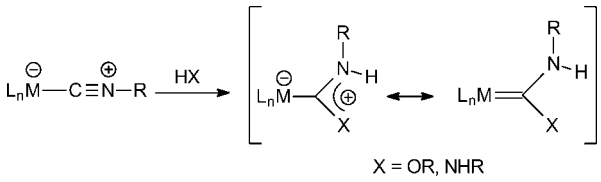
Tungsten complex [W(NHC)(CO)$_5$] (**1**) (NHC=NH,N-ethyl-substituted benzimidazolin-2-ylidene ligand) was prepared by transmetallation of lithiated 1-ethylbenzimidazole with the pentacarbonyltungsten complex fragment. The hydrogen-bonding ability of the carbene-NH group to substrates with carbonyl groups was investigated by NMR titration. Structural analogues to **1** with a catalytically active rhodium center show a distinct substrate-selective hydrogenation behaviour.

Introduction

Complexes with NR,NR-substituted N-heterocyclic carbene ligands are important catalysts for various transformations. However, much less is known about complexes with NH,NR-substituted carbene ligands, which thus have been disregarded for catalytic applications.[1] We became interested in complexes with NH,NR-substituted carbene ligands because the NH function could act as a hydrogen-bonding donor. In a catalytically active complex bearing an NH,NR-functionalized carbene ligand this could lead to recognition and temporary binding of a substrate with a hydrogen-bonding acceptor moiety like carbonyl compounds. We report here a new one-pot synthesis of a tungsten complex with an NH,NR-stabilized carbene ligand and the observation of hydrogen bonding between the carbene-NH group and carbonyl compounds in solution.

Aminocarbenes with an NH group are obtained, when protic nucleophiles like alcohols or primary or secondary amines attack a coordinated isocyanide ligand (Scheme 1). Unintentionally and most likely unrecognized, this method was first applied as early as 1915 when Tschugajeff and Skanawy-Grigorjewa treated tetrakis(methyl isocyanide)-platinum(II) with hydrazine and isolated a red salt[2] which was very likely the first carbene complex to be synthesized in pure form, predating Fischer's seminal carbene synthesis from carbonylmetal compounds[3] by 49 years. Tschugajeff's red salt was unambiguously established as a carbene complex in 1970[4] and a number of derivatives, partially forming higher associates through hydrogen bonds, have been described recently.[5]



Scheme 1. Nucleophilic attack of a proton base HX at a coordinated isocyanide ligand.

The use of β-functionalized isocyanides, which contain both the isocyanide und the nucleophile in the same molecule, gives access to complexes with N-heterocyclic carbenes through an intramolecular 1,2-addition across the C≡N triple bond (Scheme 2). This method has been used for the preparation of a large number of complexes with NH,O-[6] and NH,NH-heterocyclic carbenes derived from aliphatic[7] and aromatic[8] isocyanides. The NH,NH-stabilized carbene ligands in **A** are easily and stepwise alkylated to give the *N*-alkyl derivatives **B** and **C** by reaction with a base and an alkyl halide.[7,8] However, the preparation of the β-functionalized isocyanides is tedious as are alternative methods for the preparation of complexes with NH,NR-stabilized carbene ligands like the metalla Ugi reaction[9] and others.[10]

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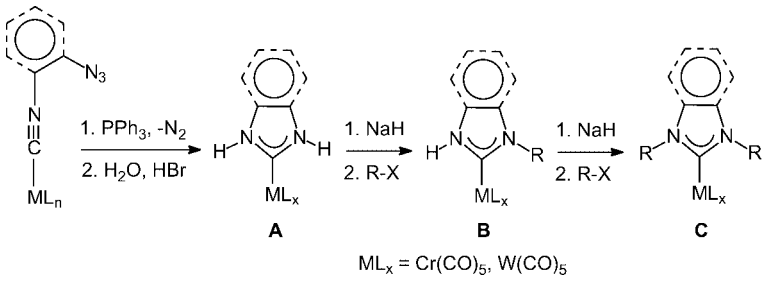


Scheme 2. Template-controlled cyclization of β-functionalized isocyanides.

Results and Discussion

We have now found an easy one-pot synthesis leading to complexes with NH,NR-stabilized benzimidazolin-2-ylidenes which avoids the use of functionalized isocyanides. If benzimidazole is deprotonated with *n*BuLi and treated with $[W(CO)_5(THF)]$ followed by protonation, only the complex with an *N*-coordinated benzimidazole was obtained.[11] However, the reaction of 1-ethylbenzimidazole with *n*BuLi in THF yields the lithium 1-ethylbenzimidazolate which reacts exclusively under C2 metallation with freshly prepared $[W(CO)_5(THF)]$ (Scheme 3). Complex **1** was formed by protonation of the initially obtained anionic complex with HCl/Et_2O. The air- and moisture-stable complex **1** was obtained after column chromatography in 69% yield. The method depicted in Scheme 3 constitutes an alternative and time-saving approach to complexes with NH,NR-substituted N-heterocyclic carbene ligands compared to the intramolecular cyclization of coordinated isocyanide ligands followed by *N*-alkylation.

Complex **1** was investigated by ^1H NMR spectroscopy where a broad singlet at δ = 8.65 ppm was observed for the NH proton and by IR spectroscopy showing a strong absorption for the NH stretching mode at $\tilde{\nu}$ = 3422 cm^{-1}. The ^{13}C NMR spectrum shows the resonance for the carbene carbon atom at δ = 191.1 ppm which is a typical value for pentacarbonyltungsten complexes containing a benzannulated N-heterocyclic carbene.[8] The molecular structure of **1** was determined by X-ray diffraction (Figure 1) confirming the connectivity within the complex. Bond lengths and angles in **1** show no unusual features and are within the range observed previously for pentacarbonyltungsten complexes with saturated[7] or benzannulated[9] N-heterocyclic carbene ligands.

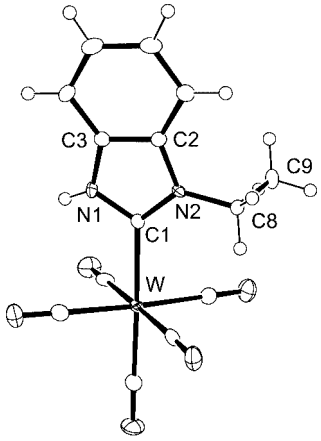
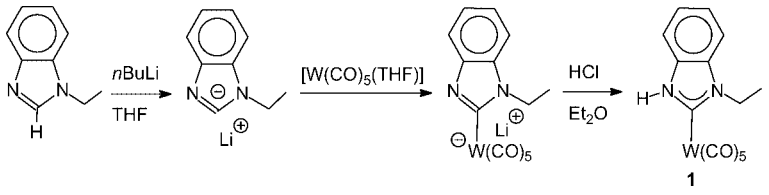


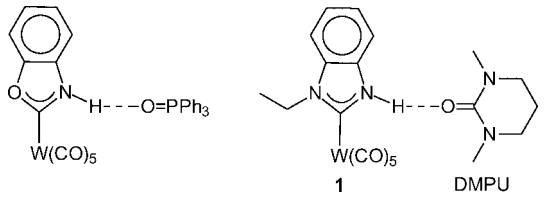
Figure 1. Molecular structure of one of the two independent, essentially identical molecules of **1** in the asymmetric unit. Selected bond lengths [Å] and angles [°] for molecule 1 [molecule 2]: W–C1 2.244(3) [2.242(3)], C1–N1 1.350(4) [1.353(4)], C1–N2 1.351(4) [1.357(4)]; W–C1–N1 123.4(2) [124.2(2)], W–C1–N2 131.1(2) [131.5(2)], N1–C1–N2 105.2(3) [104.2(3)].

Only little is known about the hydrogen-bonding properties of complexes with N-heterocyclic carbenes exhibiting free NH functions. Hydrogen bonding between the NH group of an NH,O-stabilized carbene ligand and triphenylphosphane oxide has been described (Scheme 4).[12] We became interested in the hydrogen-bonding properties of **1**.

^1H NMR techniques allowed a detailed insight into the hydrogen bonding involving the NH proton of the N-heterocyclic carbene. Complex **1** was titrated with the strong hydrogen-bond acceptor DMPU (Scheme 4) as a model for carbonyl compounds in $CDCl_3$ and the reaction was monitored by ^1H NMR spectroscopy (Figure 2). Since **1** involves



Scheme 3. Preparation of **1** by transmetallation of lithium 1-ethylbenzimidazolate.



Scheme 4. Hydrogen bonds involving NH,O- and NH,NR-stabilized cyclic carbene ligands.

both a hydrogen-bond donor (NH) and acceptor (NR_3), self-assembly to supramolecular aggregates seemed possible. Self-aggregation of the carbene complex as well as the formation of higher aggregates could be excluded by dilution experiments. The investigated concentration range covered several orders of magnitude.[13]

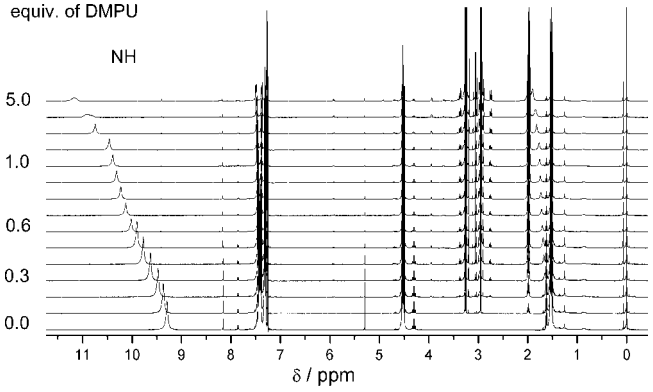


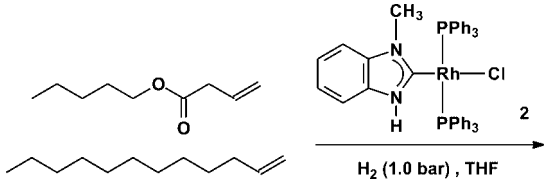
Figure 2. ^{1}H NMR titration of **1** with DMPU (up to 5 equiv.).

The NMR titration was carried out at 27 °C in CD_2Cl_2 and demonstrated a significant downfield shift of the resonance for the NH proton upon addition of DMPU, while the chemical shifts for all other protons remained essentially unchanged. Only broadening of the NH signal was observed after addition of more than 1 equiv. of DMPU (up to 5 equiv.).

The chemical shifts were fitted using standard tools.[14] Multiple experiments revealed a binding constant of about 40 ± 10 M^{-1} for the single hydrogen bond which corresponds to $\Delta G_{ass} = 2.2$ kcal mol^{-1}. Investigations of the secondary interaction using optical spectroscopy failed since the high dilution required does not favour the hydrogen bonding. The hydrogen bonding is supported by chlorinated solvents and THF, whereas protic media like alcohols impede the supramolecular interaction.

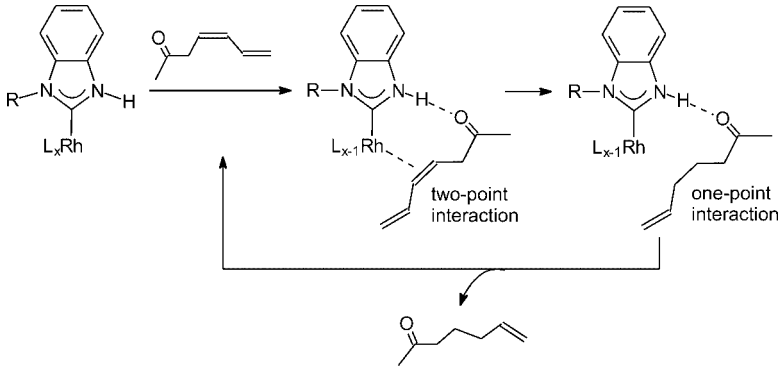
The NH group of an NH,NR-stabilized carbene ligand is able to function as a supramolecular recognition site. Its close proximity to the metal center is unusual. In most described cases the supramolecular host moieties are connected to the metal center by a flexible spacer causing entropic problems.[15] Secondary interactions of the NH group with selected substrates should be suitable to direct metal-mediated conversions. In the rhodium(I)-catalyzed hydrogenation reaction of a suitably carbonyl-functionalized olefin, for example, the substrate will interact initially by multiple contacts while some attractive interactions will disappear after the catalytic transformation at the metal center (Scheme 5), which generates an interesting motif for directed transition metal catalysis.

Preliminary studies of the catalytic properties of the (carbene)rhodium(I) complex **2** (Scheme 6) yielded proof of our concept. Complex **2** is equipped with an NH,NR-stabilized carbene ligand.[16] The use of triphenylphosphane in the preparation of **2**, however, gave a mixture of complexes. Together with complex **2** (major), the complex with an *N*-coordinated methylbenzimidazole ligand (minor) were obtained, which appeared to interconvert in solution.



Scheme 6. Competitive hydrogenation experiment utilizing the substrate selectivity of the NH,NR-stabilized carbene ligand in **2**.

In the hydrogenation of 1-octene the mixture of **2** and its isomer turned out to be catalytically more active than Wilkinson's catalyst. When the mixture was treated in a



Scheme 5. Concept of two-point interaction/recognition of substrates with complexes bearing NH,NR-stabilized N-heterocyclic carbene ligands.

competitive hydrogenation experiment with 1-dodecene and a 3-butenoic acid ester (Figure 3), the substrate with the supramolecular recognition unit is clearly preferred. Up to a conversion of 80% a significant preference for the substrate bearing the supramolecular key was observed. Control experiments with Wilkinson's catalyst clearly eliminate the Lewis acidic properties of rhodium(I) as source for this selectivity since only a very slight preference for the oxygenated substrate was found in this case.

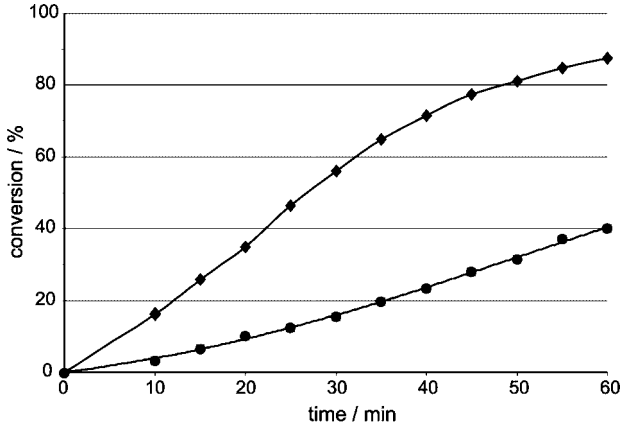


Figure 3. Competitive hydrogenation of 1-dodecene (dots) and a 3-butenoic acid ester (diamonds) using catalyst **2**.

Conclusions

We have described a straightforward one-pot synthesis of complex **1** bearing an N-heterocyclic carbene ligand which exhibits a free NH function. The NH group is able to act as a hydrogen-bond donor. However, hydrogen bonding does not lead to self-aggregation in the case of **1**. The NH group of an NH,NR-stabilized N-heterocyclic carbene ligands can act as a supramolecular key in the vicinity of a catalytically active rhodium center which enabled a substrate-selective hydrogenation. Currently, we are studying complexes with NH,NR-stabilized N-heterocyclic carbene ligands bound to various catalytically active metal centers with the intention of employing the supramolecular recognition of suitable substrates for selective catalytic transformations, e.g. for regioselective C–C coupling reactions.

Experimental Section

Analytical Data for Complex 1: ^{1}H NMR (200.1 MHz, $CDCl_3$): δ = 8.65 (br. s, 1 H, NH), 7.46–7.26 (m, 4 H, Ar-H), 4.52 (q, 2 H, CH_2), 1.50 (t, 3 H, CH_3) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 201.0 (CO_{trans}), 197.6 (CO_{cis}), 191.1 (NCN), 133.9, 132.9, 123.7, 123.3, 110.6, 110.3 (Ar-C), 44.5 (CH_2), 14.9 (CH_3) ppm. IR (KBr): $\tilde{\nu}$ = 3422 (s, NH), 3087–3008 (w, CH aliphatic), 3001–2877 (w, CH aromatic), 2063 (vs, CO), 1910 (vs, CO), 1859 (vs, CO) cm^{-1}. MS (EI): *m/z* (%) = 470 (100) $[M]^+$, 442 (50.0) $[M - CO]^+$, 414 (90.0) $[M - 2\,CO]^+$, 386 (15) $[M - 3\,CO]^+$. $C_{14}H_{10}N_2O_5W$ (470.09): calcd. C 35.77, H 2.14, N 5.96; found C 35.50, H 2.53, N 5.87.

Crystal Data for Complex 1: $C_{14}H_{10}N_2O_5W$, M = 470.09, T = 123(2) K, λ = 0.71073 Å, monoclinic, $P2_1/c$, Z = 8, a = 13.257(2), b = 17.566(2), c = 12.853(2) Å, β = 96.744(3)°, V = 2972.4(7) Å^3, 33820 measured reflections, 8650 unique reflections (R_{int} = 0.0481), R = 0.0279, wR = 0.0567 for 7446 contributing reflections [$I \geq 2\sigma(I)$], refinement against $|F^2|$with anisotropic thermal parameters for all non-hydrogen atoms and hydrogen atoms on calculated positions. CCDC-618744 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk./data/request/cif.

Acknowledgments

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[13] Dilution experiments were performed in CD_2Cl_2. No changes in the ^{1}H NMR chemical shifts were observed in the range of 10^{-5} to 5×10^{-1} M.
[14] Fitting of the data was performed with *SPECFIT*, version 2.12, Spectrum Software Associates, Chapel Hill, NC, USA; H. Gampp, M. Maeder, C. J. Meyer, A. D. Zuberbühler, *Talanta* **1986**, *33*, 943 and references cited therein. The given error is based on the applied method. Multiple determinations gave a good reproducibilty. Prolonged exposure of **1** to ambient conditions lead to some decomposition. Employed conditions: 2×10^{-2} M **1** in CD_2Cl_2 treated with DMPU.

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[16] An analogue of complex **2**, namely [RhCl(PCy_3)$_2$(*N*-methylbenzimidazolin-2-ylidene)], was obtained as an intermediate in the [RhCl(coe)$_2$]-catalyzed arylation of *N*-methylbenzimidazole. This complex could also be obtained from the stoichiometric reaction of *N*-methylbenzimidazole with [RhCl(coe)$_2$] and PCy_3. The mechanism for this reaction is currently unknown. The stoichometric reaction of *N*-methylbenzimidazole with [RhCl(coe)$_2$] and PPh_3 yields complex **2** (major) and its isomer with an *N3*-coordinated *N1*-methylbenzimidazole ligand (minor). See: J. C. Lewis, S. H. Wiedemann, R. G. Bergman, J. A. Ellman, *Org. Lett.* **2004**, *6*, 35–38.

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