Rhodium-mediated activation of an alkane-type C–H bond †

Anneke Krüger,a Antonia Neelsb and Martin Albrecht*a

Received (in XXX, XXX) Xth XXXXXXXXX 200X, Accepted Xth XXXXXXXXX 200X
First published on the web Xth XXXXXXXXX 200X
DOI: 10.1039/b000000x

Abnormal C4-bonding of N-heterocyclic carbenes effectively modulates the electron density at rhodium and allows for the selective cleavage of an unactivated C(sp3)–H bond, whereas no such intramolecular C–H bond breaking is observed when the carbene binds normally through the C2 carbon.

The functionalization of unactivated C–H bonds, especially in alkanes, constitutes one of the most challenging areas of catalysis and has major implications in various areas such as in organic (retro)synthesis or in utilizing fossil fuel feedstocks with greater efficiency.1,2 The absence of electronically active substituents in alkane substrates renders the C(sp3)–H bond particularly inert. Functionalization of alkanes has been achieved under heterogeneous conditions, though the required high temperatures are economically unattractive and typically preclude selective product formation.3 Consequently, strong donor ligands tend to facilitate metal-mediated C–H bond activation. In search for strong donors, N-heterocyclic carbenes have emerged as a class of formally neutral ligands that are significantly more basic than the strongest trialkylphosphine donors, and indeed, modifications on Shilov’s system using NHC ligands have successfully been accomplished.4 More recently, abnormal variations of NHCs have shown to substantially enhance the ligand donor properties,5 thus representing an attractive scaffold for metal-catalyzed functionalization of unactivated bonds.6 Here, we report on the successful application of this strategy for rhodium-mediated intramolecular activation of an alkane-type C–H bond. Such bond activation requires the abnormal bonding of the NHC ligand and was not observed in analogous normally bound NHC complexes, thus providing further evidence for the unique impact of abnormal carbene ligands.1,1

The reaction of propylene-linked diimidazolium salts 1 and RhCl3 in the presence of NaOAc induced multiple C–H bond activation (Scheme 1).7 After anion metathesis using KI and subsequent column chromatography (SiO2, CH2Cl2/acetone), the cyclometalated rhodium(III) complexes 3 comprising a facially C,C,C-tridentate coordinating ligand were obtained in good yields (3a 59%, 3b 71%) While C4 bonding of the NHC ligand has been expected from previous studies on methylene-linked dicarbene ligands,8 activation of the CnHn–H bond in the propylene linker is unprecedented and remarkable, given the mild (MeCN, 80 °C) and aerobic reaction conditions.

A crystal structure of 3a confirmed the C–H bond activation (Figure 1, Table 1).† The two rhodium centers are crystallographically symmetry-related through a mirror plane and reside in a slightly distorted octahedral environment comprising the C,C,C-tridentate dicarbene ligand and three μ3-bridging iodide ligands. The Rh–CnHC bond lengths are 1.968(17) Å and 1.957(17) Å and hence similar to the rhodium-carbene bond lengths in analogous bidentate NHC complexes (1.98 – 2.04 Å).12,13 Yet they are significantly shorter than the Rh–CnHS bond (2.066(12) Å).

The dimeric structure of the tridentate complex can easily be cleaved in solution with a coordinating solvent such as acetonitrile, thus quantitatively affording the monomeric complexes 2 (Scheme 1). This monomeric complex is also

**Table 1.** Selected bond lengths (Å) for 2a and 3a.

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The cyclometalated rhodium(III) complexes have been expected from previous studies on methylene.

Common to the most successful systems is the underlying mechanism, which involves oxidative addition of the C–H bond to an electron-rich transition center.7 Consequently, strong donor ligands tend to facilitate metal-mediated C–H bond activation. In search for strong donors, N-heterocyclic carbenes have emerged as a class of formally neutral ligands that are significantly more basic than the strongest trialkylphosphine donors, and indeed, modifications on Shilov’s system using NHC ligands have successfully been accomplished.4 More recently, abnormal variations of NHCs have shown to substantially enhance the ligand donor properties,5 thus representing an attractive scaffold for metal-catalyzed functionalization of unactivated bonds.6 Here, we report on the successful application of this strategy for rhodium-mediated intramolecular activation of an alkane-type C–H bond. Such bond activation requires the abnormal bonding of the NHC ligand and was not observed in analogous normally bound NHC complexes, thus providing further evidence for the unique impact of abnormal carbene ligands.1,1

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surmised to be the initially formed product in the cyclometalation reaction prior to column chromatography. Evidence for the monomeric structure of 2 was provided by X-ray crystallography (Figure 1, Table 1). While most bond lengths and angles of 2 are similar to those of the dimeric complex 3a, the Rh–C\textsubscript{alkyl} bond length is slightly elongated (2.089(8) Å) and the carbene-rhodium-carbene bite angle decreased from 87.5(8)° in 3a to 83.3(3)°. These geometrical changes suggest some flexibility of the tridentate ligand.

Further confirmation of the formed rhodium-alkyl bond was obtained by NMR analyses. Microanalytically pure samples of 2 showed consistently two sets of signals (ca. 2.5:1 ratio). In the major species the resonances of the carbene residue were broad, while ligand broadening comprised predominantly the propylene signals in the minor species. For example, the rhodium-bound alkyl carbon in complex 2a appears in the \(^{13}\)C NMR spectrum as a doublet at 33.7 ppm (\(J_{\text{RhC}} = 28\) Hz; major species) and as a broad signal at \(\delta_c = 39\) (minor species). In contrast, the rhodium-bound carbene resonances were not resolved for the major species, yet they are distinguished as a well-resolved doublet at \(\delta_c = 144.6\) (\(J_{\text{RhC}} = 46\) Hz) in the minor complex.

The nearly statistical distribution of the alkyl ligands in the Rh\textsubscript{3} complex 3 shows two sets of signals in approximate 1:2 ratio, attributed to isomers comprising the alkyl ligands in syn (cf. X-ray of 3a) and anti eclipsed conformation, respectively. All signals are well-resolved, consistent with a rigid dimeric structure.

Obviously, the C–H bond activation process in the propylene linker of 1 benefits from a high degree of intramolecular preoraganization. Related metal-mediated, intramolecular C\textsubscript{alkyl}–H bond cleavage has been demonstrated previously in highly constrained systems. However, in the case reported here, the ligand system would have the flexibility to twist out and to avoid any constrained situation that may promote C–H activation. For example, no C–H bond activation has been detected when normal C\textsubscript{2}-bonding dicarbenes were employed. Thus, reaction of RhCl\textsubscript{3} and the diimidazolium salt 4 under similar reaction conditions as used for 2 gave complex 5 in moderate 21\% yield (Scheme 2). The dicarbene ligand in complex 5 is only bidentate with the propylene bridge folded away from the metal coordination sphere. This configuration is the common motif in propylene-linked dicarbene complexes.

Apparently, only the abnormal bonding mode provides sufficient electron density to the rhodium center for inducing C–H bond activation. While rhodium(I) systems are known to oxidatively add C–H bonds, low oxidation states are less likely involved in the current process due to the absence of reducing agents during C–H bond activation, and owing to the fact that the strongly donating abnormal carbene ligands stabilize high oxidation states. Instead we propose an electrophilic bond activation, which is facilitated by the presence of acetate as ligand to rhodium(III) as well as proton scavenger. Presumably, the bond activation may be further eased by increasing steric constraints in the carbene ligand similar to related phosphine chemistry.

The Rh–C\textsubscript{alkyl} bond in 2 is remarkably stable towards air, moisture, and temperature, presumably due to the rigid tridentate bonding, which minimizes the availability of \(\beta\)-hydrogens for elimination reactions. The complexes also seemed surprisingly stable towards acids. Upon treatment with H\textsubscript{3}PO\textsubscript{4} or HOAc, no changes were observed and complex 2a was recovered quantitatively. When using deuterated phosphoric acid, deuterium exchange of the heterocyclic C5-bound hydrogen atoms occurred instantaneously (2a–\(d_2\), Scheme 3), indicated by the disappearance of the signal at \(\delta_d = 6.78\) in the \(^1\)H NMR spectrum and the appearance of a broad resonance at this frequency in the \(^2\)H NMR spectrum. Further support for the incorporation of two deuterium atoms and formation of 2a–\(d_2\) was provided by HR-MS. With deuterated acetic acid the reaction was slower and required several days for completion. Deuteration of the C5-position may proceed in analogy to the deuteration of free carbenes.

Scheme 3. Deuterium incorporation into 2a.

When complex 2a was heated to 60 °C in the presence of an excess of D\textsubscript{3}PO\textsubscript{4}, D-incorporation at the metal-bound alkyl carbon was observed in addition to H/D exchange at C5, thus affording 2a–\(d_3\). This outcome cannot be rationalized by simple acidolysis of the Rh–C\textsubscript{alkyl} bond. Instead, deuteration of the alkyl carbon may proceed via reversible cleavage of the Rh–C\textsubscript{alkyl} bond and at least one of the Rh–C\textsubscript{carbene} bonds, or via a strained alkyldiene complex. Reversible Rh–C\textsubscript{alkyl} bond making and breaking under acidic conditions suggests that C\textsubscript{alkyl}–H activation is a thermodynamically favored process that possibly occurs already under milder conditions.

No H/D exchange was observed when complex 2 was treated with D\textsubscript{2} (1 bar), even when gently heated to 60 °C. The thermodynamic stability of complex 2 along with the kinetic lability of the Rh–C\textsubscript{alkyl} bond indicates a potential of these complexes for heterolytic bond cleavage across the Rh–C\textsubscript{alkyl} bond. We therefore evaluated the activity of complex 2 in catalytic hydrogenations using cyclooctene as model substrate (Table 2, entries 1–4).


\[
\begin{align*}
\text{Scheme 2. Reagents and conditions: (i), RhCl}_3, \text{NaOAc, MeCN reflux, then KBr.}
\end{align*}
\]
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**Notes and references**

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2 XRD Application Lab, CSEM, Rue Jaquet-Droz 1, CH-2002 Neuchâtel, Switzerland.

3 Electronic Supplementary Information (ESI) available: CCDC 743284, 743285. For experimental and analytical details see DOI: 10.1039/b000000x.

4 Typical experimental procedure: The diimidazolium salt 1a (450 mg, 1.0 mmol), hydrated RhCl₃ (263 mg, 1.0 mmol), and NaOAc (656 mg, 8.0 mmol) were stirred in refluxing acetonitrile (30 mL) for 16 hours. Potassium iodide (664 mg, 4.0 mmol) was added and stirring at reflux was continued for a further hour. The reaction mixture was cooled to room temperature and all volatiles were removed under reduced pressure.

The residue was purified by column chromatography (SO₂Cl₂/CH₂Cl₂/acetonitrile, 5:2); thus affording 3a as a light brown solid (380 mg, 59%). Notably, qualitatively similar results were obtained when salt metathesis was performed with KBr, yielding the bromide analogs of complexes 2 and 3.

Crystal data for 2a: C₂,H₅₈,N₃,Rh = 726.24, orthorhombic, a = 13.2124(12), b = 13.7680(13), c = 15.0238(10) Å, V = 2733.24(24) Å³, T = 173(2) K, space group P2₁₂₁, Z = 4, 1893 total reflections, 4629 unique (R(int) = 0.0593), R₁ = 0.0374, wR₂ = 0.0846 for I > 2σ(I) for 3a: C₃,H₆,N₂,Rh₂ = 1374.44, orthorhombic, a = 15.2889(13), b = 15.9079(13), c = 20.8008(19) Å, V = 5059.18(18) Å³, T = 173(2) K, space group Pna, Z = 4, 36742 total reflections, 5201 unique (R(int) = 0.1149), R₁ = 0.0751, wR₂ = 0.1913 for I > 2σ(I).

§ HR-MS (EI): C₃,H₆,N₂,D₄,(M−1−2MeCN)⁺ requires 519.0414, found 519.0446.


14 No coexistence of the signals was observed up to 70°C.


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Rhodium-mediated intramolecular activation of an electronically unactivated alkane-type C–H bond takes place when the metal center is coordinated by two abnormal carbene ligands, presumably as a direct consequence of the strong donor ability of this class of N-heterocyclic carbenes.