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Smooth C(alkyl)–H bond activation in rhodium complexes comprising abnormal carbene ligands

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Rhodation of trimethylene-bridged diimidazolium salts induces the intramolecular activation of an alkane-type C–H bond and yields mono- and dimetallic complexes containing a formally monoanionic C,C,C-tridentate dicarbene ligand bound to each rhodium centre. Mechanistic investigation of the Calkyl–H bond activation revealed a significant rate enhancement when the carbene ligands are bound to the rhodium centre via C4 (instantaneous activation) as compared to C2-bound carbene homologues (activation incomplete after 2 days). The slow C–H activation in normal C2-bound carbene complexes allowed intermediates to be isolated and suggests a critical role of acetate in mediating the bond activation process. Computational modelling supported by spectroscopic analyses indicate that halide dissociation as well as formation of the agostic intermediate is substantially favoured with C4-bound carbens. It is these processes that discriminate the C4- and C2-bound systems rather than the subsequent C–H bond activation, where the computed barriers are very similar in each case. The tridentate dicarbene ligand undergoes selective H/D exchange at the C5 position of the C4-bound carbene exclusively. A mechanism has been proposed for this process, which is based on the electronic separation of the abnormal carbene ligand into a cationic N–C–N amidinium unit and a metalla-allyl type M–C–C fragment.

Introduction

The selective activation of inert bonds, in particular C–H bonds in alkanes and related compounds, has significant implications in many different areas of chemistry.1 Foremost, mild routes to Calkyl–H bond activation provide access to unprecedented retrosynthetic opportunities in organic synthesis2 and yield highly desirable processes for a more efficient fossil fuel utilisation.3 Although promising advances have been made in homogeneous transition metal-mediated activation of unfunctionalised C–H bonds,4 drawbacks persist such as the limited substrate scope, or the harsh reaction conditions required to achieve substantial turnover frequencies, and industrial processes are relatively rare.5 Two major pathways have been put forward for Calkyl–H bond activation,4b,4i,6 and they involve either (complex-assisted) σ-bond metathesis7 or oxidative additions.8 The former is perhaps most prominently illustrated with Hartwig’s rhodium(III) catalyst for mild and selective alkane borylation.9 Most other alkane activation catalysts operate, however, along the oxidative addition route and include the insertion of a metal centre into the C–H bond.4 Recent calculations have suggested that the metal centre for oxidative addition may be either nucleophilic, electrophilic, or amphiphilic.10 A further variation is amphiphilic metal-ligand assisted (AMLA) Calkyl–H bond activation involving chelating bases, and this is thought to be widely operative in synthesis.11

A conceivable approach to develop new systems for (catalytic) Calkyl–H bond activation thus consists of using electron-rich transition metals that are bound by strong electron donor ligands, thus providing a high level of nucleophilicity to promote C–H oxidative addition. Ligands derived from N-heterocyclic carbens (NHCs) may be particularly useful spectator ligands for such application, as NHCs entail high σ-basicity and low π-acidity paired with a rather covalent bonding to the metal centre.12 Late transition metals comprising NHC ligands have indeed been reported to activate unreactive bonds.13 Further enhancement of the donor ability imparted by the NHC ligand may be achieved upon changing the ligand coordination. Substantially stronger donor properties were noted for NHCs bound via C4 rather than C2,14 often referred to as abnormal bonding.15 In this coordination mode, the metal-bound carbon experiences a lower σ-withdrawing effect due to the presence of only one nitrogen atom in the σ position. Indeed, abnormally bound carbene complexes have shown intriguing catalytic activity in bond activation processes, surpassing in many instances that of normal carbene analogues.16 Within this context, we recently communicated the smooth intramolecular activation of an alkane-type C–H bond in a rhodium complex featuring abnormally bound NHC ligands.17 Upon expanding on these studies we have identified key parameters that govern the C–H bond activation step. Bond activation in these abnormal carbene complexes presumably is a chelate-assisted process, thus disclosing an additional feature of this particular ligand.

Results and Discussion

C–H bond activation in C2-substituted diimidazolium salts

Reaction of the trimethylene-linked diimidazolium salts 1 with hydrated RhCl3 in the presence of NaOAc yielded the
tridentate dicarbene complexes 2, and after column chromatography the dimetallic complexes 3 (Scheme 1). Formation of 2 implies a triple C-H bond activation process including activation of the alkyl C-H bond in the linker in addition to the expected\(^{18}\) heterocyclic C-H bond activation. The activation of the linker occurred under relatively mild conditions, i.e. in moist MeCN at 82 °C and in an aerobic atmosphere. Variation of the substituents within the heterocycle (aryl \(\text{vs}\) alkyl group at C2 and N1, bulky i-Pr \(\text{vs}\) linear alkyl groups at N1) did not have a significant effect on the bond activation process and the ligand consistently adopted a tridentate bonding mode. No intermediate was detected when stopping the reaction at low conversion. Hence the aliphatic C-H bond activation is a general process, provided the rhodium centre is bound by abnormal carbene ligands. An abnormal bonding mode is enforced in 1a-d by protection of the imidazolium C2 position.

Formation of either the monometallic complexes 2 or the dimetallic complexes 3 was dependent on the coordination ability of the solvent. Purification of the complexes by column chromatography using CH\(_2\)Cl\(_2\) and acetonitrile as eluents gave the dimetallic species 3, whereas addition of MeCN afforded the monometallic complexes 2 exclusively. All monomeric complexes displayed two sets of \(^1\)H NMR signals in solution (CD\(_2\)CN), which have been attributed to two isomers featuring the iodide ligand \(\text{trans}\) to the alkyl ligand and \(\text{trans}\) to one of the carbene ligands, respectively. Generally, the signals appear in approximate 2:1 ratio, which indicates a statistical distribution of the iodide ligand over all three available positions, and thus a similar \(\text{trans}\) influence of the abnormal carbene and alkyl ligands. In all complexes but 2b, the major isomer of 2 revealed significant broadening of the carbene resonances both in the \(^1\)H and \(^{13}\)C NMR spectra, while in the minor species, the trimethylene resonances were broad. This behaviour was assigned to fluxional coordination of the iodide ligand, either \(\text{trans}\) to one of the carbene ligands (major isomer) or \(\text{trans}\) to the alkyl ligand (minor isomer). In complex 2b the ratio is inverted (1:1:2) with the major species featuring a well-resolved carbene resonance at \(\delta_C\) 146 (\(^1J_{\text{Rh-C}}\) = 46 Hz), while the minor species, attributed to the isomer with a mutual \(\text{cis}\) arrangement of iodide and alkyl ligands, displays broad carbene signals and a sharp doublet for the rhodium-bound alkyl carbon (\(\delta_C\) 34.0, \(^1J_{\text{Rh-C}}\) = 28.5 Hz). For the dimeric complexes 3, two major sets of signals in approximately 2:1 ratio were identified by NMR spectroscopy. These sets were tentatively assigned to \(\text{syn}\) and an \(\text{anti}\) eclipsed conformations of the two tridentate ligands. The protons of the trimethylene linker and likewise the NCH\(_2\) protons of the butyl wingtip groups in 3a and 3d are diastereotopic, in line with a hindered rotation about the Rh–C bonds.\(^{19}\)

The dimeric structure of 3b was unambiguously confirmed by an X-ray diffraction analysis of a single crystal that was grown after exchange of the non-coordinating anion from \(\text{PF}_6^-\) to \(\text{Cl}^-\). The molecular structure is almost \(C_{3v}\)-symmetric (Fig. 1). The \(C_{\text{carbene}}\)-Rh–\(C_{\text{carbene}}\) bite angles of the two crystallographically independent sites are slightly different (85.6(7)° and 89.7(8)° respectively), which suggests some steric flexibility of the chelate. As reported previously for 3c,\(^{11}\) the Rh–\(C_{\text{carbene}}\) bonds are substantially shorter than the Rh–\(C_{\text{alkyl}}\) bonds (average 1.94(3) Å vs 2.074(1) Å), yet the Rh–I bonds are all similar (average Rh–I 2.80(2) Å). These data suggest similar \(\text{trans}\) influences of alkyl and carbene ligands, in line with the statistical mixture of isomers found in solution (see above).

**Normal and mixed normal-abnormal dicarbene complexes**

In order to evaluate effects that are critical for inducing the smooth \(\text{C}_{\text{alkyl}}\)-H bond activation observed during the formation of 2 and 3, rhodation of ligand precursor 1e was investigated in more detail (Scheme 2). In this precursor, the imidazolium C2-positions are not protected and hence available for metal coordination via the normal carbene coordination mode. Upon exposure of 1e to identical conditions as the imidazolium salts 1a-d, i.e. hydrated RhCl\(_3\) and NaOAc in refluxing MeCN, a mixture of products...
was obtained after 16 h (Scheme 2). Complex 5 was isolated from this mixture in 21% yield after column chromatography. This complex features a bidentate coordinated ligand with both carbenes in the normal bonding mode; a close analogue was previously reported by Peris and coworkers.\textsuperscript{19a}

Careful analysis of the reaction mixture before chromatographic separation revealed, in addition to 5, also the presence of the tridentate biscarbone complexes 4 and 6, both resulting from C\textsubscript{aryl}–H bond activation. In complex 4 the tridentate ligand features an abnormally and a normally bound carbene, whereas in complex 6 both carbenes are in the normal bonding mode. All three complexes were isolated by fractional crystallisation and were fully characterised by X-ray crystallography and NMR spectroscopy.

Complexes 4, 5b, and 6 all crystallised as monomers with the rhodium centre in a slightly distorted octahedral environment (Fig. 2). Like in complex 3, the Rh–C\textsubscript{carbene} bonds in complexes 4 and 6 are significantly shorter than the Rh–C\textsubscript{alkyl} bonds. The normal carbene ligand in 4 is trans to a MeCN ligand and is closer to the rhodium centre (Rh–C\textsubscript{7} 1.962(3) Å) than the abnormal carbene ligand (Rh–C\textsubscript{1} 1.995(3) Å). Longer Rh–C\textsubscript{carbene} bonds were also noted for the all-normal carbene complex 6 (Rh–C\textsubscript{carbene} 1.995(8) and 1.988(8) Å), where the carbenes are positioned trans to iodide, which has a stronger trans influence than MeCN.\textsuperscript{20}

The dicarbene bite angle in complex 5b is unusually large, C1–Rh1–C7 is 98.9(4)°,\textsuperscript{19,21} and the dihedral angle between the imidazolylidene rings and the metal xy coordination plane (defined by C1, Rh1, and C7) is much smaller (20.8–29.0°) than in the tridentate complex 4, where the heterocycles are positioned nearly perpendicularly (dihedral angle between 80.9° and 84.6°). The conformational flexibility of the ligand imparted by the flexible trimethylene linker is further illustrated by the synrotatory twisted arrangement of the imidazolylidene rings, thus avoiding steric congestion and yielding a propeller-like arrangement rather than the generally observed V-shaped conformation.\textsuperscript{19} Steric considerations may also account for the mutual trans arrangement of the iodide and one carbene ligand in complexes 4 and 6.

Even though complexes 4 and 6 have a related tridentate ligand, only complex 6 contains a formally neutral rhodium centre while complex 4 is monocationic. The stabilisation of a formally cationic rhodium centre in 4 may be a direct consequence of the larger mesoionic character of the C4-bound imidazolylidene ligand as compared to the normal analogue in 6,\textsuperscript{22} thus illustrating the stronger donor power of the abnormal carbene.\textsuperscript{14,23} Bond length analysis in the heterocycles suggests a vinyl-type bonding of the C4-bound carbene ligand in 4, including remote charge stabilisation by

\begin{table}[h]
\centering
\caption{Selected bond lengths and angles for complexes 4, 5b, and 6}
\begin{tabular}{|c|c|c|c|}
\hline
Complex & 4 & 5 & 6 \\
\hline
Rh1–C1 & 1.995(3) & 1.978(10) & 1.995(8) \\
Rh1–C7 & 1.962(3) & 1.970(8) & 1.988(8) \\
Rh1–C5 & 2.071(3) & --- & 2.063(8) \\
C1–Rh1–C7 & 85.07(11) & 98.9(4) & 91.5(3) \\
C1–Rh1–C5 & 82.81(11) & --- & 80.6(3) \\
C5–Rh1–C7 & 81.59(11) & --- & 81.7(3) \\
\hline
\end{tabular}
\end{table}

\textsuperscript{25} Bond lengths in Å, bond angles in deg.

\begin{align}
\text{Scheme 2 Metallation of 1e. Reagents and conditions: RhCl}_3, \text{NaOAc, MeCN (reflux), then KI (for 4, 5a, and 6) or KBr (for 5b).}\end{align}
the cationic amidinium fragment.

In solution, complex 4 displays a complicated $^1$H NMR signal pattern that simplifies upon heating to 60 °C. At this elevated temperature, the inequivalence of the carbene bonding modes is reflected by the presence of four singlet resonances for the imidazolium protons. The two butyl groups resonate as two disparate sets of signals both in the $^1$H and $^{13}$C NMR spectra. Similarly, the NCH$_2$ protons of the trimethylene linker appear as two distinct sets of AB doublets, one at δ$_H$ 4.38 and 3.83 ($^{3}$J$_{HH}$ = 13.0 Hz) and the other at δ$_H$ 4.32 and 3.67 ($^{3}$J$_{HH}$ = 12.0 Hz). The proton attached to the rhodium-bound carbon is very broad due to the coupling to four inequivalent protons and to the rhodium centre.

At room temperature, the presence of three different species were identified to be present from the split of the lowest field singlet into three resonances between 8.4 and 8.2 ppm in approximate 1:4:6 ratio. The presence of three species may be rationalised with rigid iodide coordination at room temperature, either trans to the alkyl group or to either of the two different carbene ligands and may thus reflect the different trans influence of normally and abnormally bound NHC ligands and the alkyl ligand, respectively.

The NMR spectrum of complex 5b displays a single set of signals for the imidazolylidene ligands (δ$_H$ 7.61 and 7.41, $^{2}$J$_{HH}$ = 2.5 Hz), indicating C$_s$-type symmetry in solution. All N-bound CH$_2$ protons are diastereotopic and resonate as four sets of multiplets due to the rigid conformation of the metallacycle on the NMR time scale even at elevated temperatures (up to 60 °C). Obviously, the crystallographically deduced C$_s$ symmetry is not preserved in solution and swinging about the C$_{carbene}$–Rh bond is fluxional.

A similar C$_s$ symmetric conformation was deduced for complex 6 at 70 °C. The aromatic signals of the tridentate ligand are shifted to higher field as compared to the bidentate ligand in 5b and appear at δ$_H$ 7.15 and 7.03. The C$_s$ symmetry supposedly arises from dissociation of one iodide ligand and fluxional coordination of the second iodide in the formally cationic system (see complex 2 above). Upon lowering the temperature, the structure becomes unsymmetrical and at −10 °C the imidazolium protons resonate as four doublets at δ$_H$ 7.23, 7.08, 7.07 and 6.97 ($^{3}$J$_{HH}$ = 1.9 Hz). In line with the observed behaviour of complexes 2 and 4, iodide coordination at lower temperature is surmised to be rigid on the NMR time scale, thus producing an asymmetric cationic complex with the iodide presumably cis to the alkyl ligand.

Mechanistic studies

Based on the characteristic $^1$H NMR signals, it was possible to identify and quantify complexes 4, 5, and 6 also in composite mixtures. Since kinetic studies through in situ measurements were hampered by the inhomogeneity of the reaction mixture, the progress of the reaction was monitored through $^1$H NMR measurement of samples taken at regular intervals. A typical plot of the relative concentrations of 4, 5, and 6 during the first 12 h of the reaction is shown in Fig. 3. In addition to these three complexes, the reaction mixture was composed of the diimidazolium salt 1e and presumably some monocarbene species, which could not be confidently identified and quantified in the product mixture.

Analysis of the reaction mixture composition allowed key factors to be identified that govern the formation of the different cyclometalated products. Thus, initial production of complex 4 is relatively fast and essentially complete after 2 h. No mono- or bidentate intermediate comprising a C4-bound carbene was observed and the concentration of the tridentate complex did not change any further, even though the reaction mixture contained residual monocarbene species (see below). Only after heating for several days, a slow decrease of the concentration of 4 was observed. This decrease was attributed to complex decomposition, hence revealing a limited long-term stability of this complex at elevated temperatures.

Formation of the bidentate dicarbene species 5 occurred at slightly lower rates than the tridentate complex 4 and preceded the formation of the tridentate complex 6. Only after about 2 h and significant build-up of 5, C$_{alkyl}$–H activation was induced and complex 6 started to appear. The increase of 6 was more pronounced than the apparent consumption of 5, presumably because of continuous formation of this complex from 1e or the corresponding monocarbene species. At extended reaction times (12–24 h), the rates for the formation of 6 and the consumption of 5 became essentially equal, yet low. After 60 h, the 5:6 ratio is about 1:2, indicating that C$_{alkyl}$–H bond activation from 5 is very slow and not complete even after several days, thus sharply contrasting the instantaneous bond activation in the formation of 4.

The data further suggest that formation of 4 and 6 are mutually independent processes and do not result from interconversion of an abnormal carbene bonding mode to a normal one or vice versa. However, complexes 5 and 6 seem to be interconnected. Indeed, separate experiments starting from pure 5 revealed a slow C$_{alkyl}$–H bond activation in the presence of NaOAc in refluxing MeCN, and conversion to 6 occurred over several days. Hence, product selectivity should be biased at an early stage of the reaction, most likely at the initial heterocyclic C–H bond activation process. This model suggests that initial activation of the C4–H in 1e is energetically not much different from C2–H bond activation. The substantially lower acidity of the C4-bound proton may thus be compensated by steric (de)shielding, suggesting the
The proximity of the agostic C–H and C5–H1 bond distances are very similar in the two structures. The strength of these interactions appears to be comparable in the C5–H1 bond and proton transfer step itself, where a correction for MeCN solvation (PCM method).

Figure 4 also shows the relative free energies of the various species implicated in C5 alkyl-H activation seen experimentally for complexes 2 and 4. Perhaps surprisingly, however, the origin of this difference does not lie in the C5 alkyl–H activation step itself, where a slightly lower barrier is actually computed from intermediate A (12.4 kcal mol⁻¹ cf. 13.1 kcal mol⁻¹ from Aab). Instead it is the greater ease of iodide dissociation and rearrangement to form the agostic intermediate, lower by 5.1 kcal mol⁻¹ compared to the experimental structure of 5ab.

Figure 4. Computed geometries with selected distances in angstrom for C–H activation from 5a' and 5a'ab (H atoms, excepting those of the C5 methylene group, are omitted for clarity). Free energies (kcal mol⁻¹) include a correction for MeCN solvation (PCM method).

**Theoretical analyses**

Density functional theory (DFT) calculations employing the BP86 functional have been performed to obtain further insight into how the NHC binding mode affects the C5 alkyl-H bond activation process. Calculations considered the mechanism of C5 alkyl-H bond activation from the key intermediate 5a' (the prime indicating use of the N–Me analogue of complex 5 used experimentally) and its abnormal NHC analogue 5a'ab (E = +1.7 kcal mol⁻¹) and the propeller arrangement of the ligand are correctly reproduced. These features are also apparent in the computed structure of 5a'ab in which the C1–Rh–C7 angle is slightly larger (102.1°) and the Rh−C distances slightly shorter (average 1.98 Å cf. 2.01 Å in 5a'). The remaining Rh−ligand bond distances are very similar in the two structures.

One possible pathway for C5 alkyl-H activation in 5a' and 5a'ab is shown in Figure 4 and involves initial iodide dissociation and rearrangement of the bis-NHC ligand to give intermediates A and Aab. Both these species feature an upright orientation of the carbene rings and greatly reduced bidentate chelate angles (A: 92°; Aab: 86.4°). This arrangement allows the C5–H1 bond to engage in agostic bonding with the Rh centre. The strength of these interactions appears to be comparable in A and Aab, as judged by the similar Rh−H1 and C5−H1 distances (ca. 1.91 Å and 1.14 Å respectively). The proximity of the agostic C–H bond cis to the k²-OAc ligand in A and Aab allows these systems to effect C–H activation via an ambipolar metal-ligand assisted (AMLA) mechanism. This proceeds via TS(A−B)/TS(A−B) and involves dissociation of one Rh−O bond. The free acetate arm becomes available as an intramolecular base to deprotonate the agostic C–H bond. TS(A−B) displays a slightly later geometry with shorter Rh⋯C5 and Rh⋯H1 contacts, somewhat greater C5⋯H1 elongation and a shorter O1⋯H1 distance. These C–H activation transition states states lead to the 5-coordinated metalated intermediates B (E = −0.6 kcal mol⁻¹) and Bab (E = +1.7 kcal mol⁻¹). The structures of these species closely resemble their preceding transition states, with the full formation of the Rh−C5 bond and proton transfer forming a bound acetic acid molecule (see the ESI for full details).
energies of these species, +13.3 kcal/mol and +10.2 kcal/mol respectively, show iodide dissociation is ca. 3 kcal mol\(^{-1}\) easier in the C4-bound NHC system. The subsequent rearrangement is also slightly more facile in this case and contributes to the 5.1 kcal mol\(^{-1}\) overall difference in the formation of A and A\(_{ab}\). This latter component may reflect a greater donation from C4-bound NHC and hence the more effective stabilisation of the agostic intermediate. While this is not particularly apparent in 5a\(^{t}\) and 5a\(_{ab}\), where the Rh–I distances and even the Rh–O distances (\textit{trans} to the NHC ligands) are very similar, the Rh–O distances in A\(_{ab}\) are ca. 0.02 Å longer than in A. Trends in the computed natural charges also suggest greater donation from the NHC upon iodide loss. For 5a\(^{t}\) the computed charge on Rh is +0.367 and is actually less positive than the value of +0.384 in 5a\(_{ab}\). In contrast, for intermediate A the charge on Rh increases to +0.389, whereas in A\(_{ab}\) there is almost no increase in charge on Rh (+0.385). Although these effects are rather subtle they do point to a greater ability of the C4-bound NHC to stabilise the agostic intermediate and that this, together with the enhanced propensity of iodide dissociation, is responsible for promoting the C–H activation reaction in the C4-bound NHC system.\(^{30}\)

**Reactivity and stability of the complexes**

Both the bidentate and tridentate complexes 2–6 are remarkably stable towards air, moisture and elevated temperatures. Slow decomposition was only noted when heated to 80 °C for extended periods of time (>3 days). The complexes were also seemingly robust when treated with moderately strong acids such as HOAc and H\(_2\)PO\(_4\). However, when treated with deuterated acids such as D\(_3\)PO\(_4\) at RT, complexes 2 and 4 were deuterated at the C5 position to give 2–D\(_2\) and 4–D, respectively (Scheme 3). The deuteration was monitored by \(^1\)H NMR spectroscopy through the disappearance of the C5-bound heterocyclic proton signal (\(\delta_\text{H} \approx 6.78\) for 2e) and was confirmed by the appearance of a resonance at the same frequency in the \(^2\)H NMR spectrum. No such reaction was observed when the carbene was normally bound as in complexes 5 and 6. This reactivity pattern is also illustrated by the exclusive monodeuteration of the mixed abnormal/normal dicarbene complex 4. In this complex, only the C5-bound proton was exchanged in the presence of D\(_3\)PO\(_4\) while the more acidic C2-bound proton was stable and remained unaffected. In line with this observation, the methylene-bridged dicarbene complex 7 underwent H/D exchange under identical reaction conditions and gave 7–D\(_2\) (Scheme 3).

Heterocyclic H/D exchange occurred much slower in complexes 4 and 7 than in 2. After 1h at room temperature, 85% deuteration was observed in 2 as compared to 33% in 4 (7% in 7). Moderate warming to 60 °C accelerated the exchange considerably and reached 72% in 4 after the same reaction time (83% in 7). Mechanistically, the deuterium incorporation may be strongly related to the isotope exchange observed in free normal carbenes,\(^{31}\) and may thus involve transient sp\(^2\)-to-sp\(^3\) rehybridisation at C5. Rehybridisation of heterocyclic carbon atoms in NHC complexes has precedents\(^{32}\) and may be promoted by the abnormal bonding mode of the carbene, in which contributions from mesoionic resonance structures are more pronounced. In such a limiting structure, the ligand may be separated into a vinylic metal-bound C–C fragment and a N–C–N amidinium cation as charge-compensating unit (Scheme 4).\(^{15b}\) When bound to the metal, formally a metalla-allyl anion is formed, which may be reversibly protonated either at the metal centre (reinforcing a vinyl-type ligand bonding as in A) or at the C5 position (producing a C=Rh carbene complex B; Scheme 4).

Alternatively, a 1,3-sigmatropic shift of the metal-bound hydrogen to C5 may allow for accessing intermediate B from A, which upon unselective deprotonation would rationalise the observed H/D exchange at C5. In an attempt to verify this hypothesis, complex 2e was treated with MeOTf (5 equiv.), which should lead to irreversible C–C bond formation at the imidazolylidene C5 position. When following the reaction at room temperature by \(^1\)H NMR using 4,4’-dimethylbiphenyl as internal standard, significant decomposition of the complex was observed after 30 minutes. Presumably, complex degradation was induced by the formation of triflic acid, which may originate from H\(^+\)/CH\(_3\)\(^+\) substitution at C5.\(^{33}\) Independent measurements revealed that the carbene

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complex 2e is indeed instable towards such a strong acid. Performing the reaction in the presence of 1,8-bis(dimethylamino)naphthalene as proton-sponge did not completely prevent decomposition, yet a selective decrease of the signal due to the C5-bound proton to 32% with respect to the other ligand signals was noted, indicating a substantial degree of deprotonation. Although the aliphatic region of the spectrum was rather complicated, a new resonance appearing at δH 2.60 and integrating for three protons was tentatively attributed to the C5-methylated analogue of 2e. These results point to a cooperative mode of action of the complex, involving the metal centre and the abnormal carbene for bond activation.24 Such cooperativity may be key for the smooth C–H activation in complexes containing abnormal carbenes as opposed to analogues with normally bound carbenes only.

Conclusions

The intramolecular Cδimid–H bond activation mediated by rhodium carbene complexes has been investigated by using both C2-alkylated and C2-protonated diimidazolium salt precursors. These studies revealed that the activation of both the second heterocyclic C–H bond and in particular the alkyl C–H bond require less energy and proceed at significantly faster rates when the rhodium centre is ligated by an abnormally bound, strongly electron-donating carbene ligand. Specifically C2-protected diimidazolium salts, where the abnormal binding mode is enforced, undergo smooth Cδimid–H bond activation and yield tridentate complexes at ambient temperatures. Theoretical analyses suggest that the ease of formation of the agnostic precursors to C–H activation discriminates the two systems. This results from a combination of more facile iodide dissociation in the abnormally bound carbene complexes, presumably due to the pronounced mesoionic character of C4-bound imidazolylidenes, and the ensuing stabilisation of agnostic intermediates. Subsequent chelate-assisted C–H bond activation entails similar barriers of ca. 13 kcal/mol in each case.

In the presence of mild acids, selective H/D exchange at the abnormally bound carbene heterocycle was observed. This reactivity pattern may be general for C4-bound imidazolylidenes and related ligand systems such as C4-bound 1,2,3-triazolylidenes and may constitute a new pathway for cooperating metal-centred reactivity. Accordingly, these abnormal carbene ligands may act as transient proton acceptors through their mesoionic resonance form, thus transforming the metal-bound carbanion to a formally neutral carbene donor site comprising a remote cationic residue. Preliminary work in our laboratories suggests that this type of metal-ligand cooperativity is general and applicable for the activation of different E–H bonds.

Experimental Section

General comments

The 1,2-disubstituted imidazoles35 and compounds 1e, 2c-d, 5, and 7 were prepared according to previously reported procedures.17,18 All other reagents are commercially available and were used as received. Unless otherwise stated NMR spectra were recorded at 25 °C on Bruker and Varian spectrometers operating at 400, 500 or 600 MHz (1H NMR) and 100, 125 or 150 MHz (13C{1H} NMR), respectively. Chemical shifts (δ in ppm, coupling constants J in Hz) were referenced to residual solvent resonances. Assignments are based on homo- and heteronuclear shift correlation spectroscopy. Elemental analyses were performed by the Microanalytical Laboratory at the Federal Institute of Technology in Zurich, Switzerland and at the University College Dublin, Ireland.

Syntheses of 1a

A solution of 2-phenyl N-n-butyl imidazole (3.47 g, 17.3 mmol) and 1,3-dibromopropane (1.75 g, 8.7 mmol) was stirred in refluxing toluene (20 mL) for 16 h. The formed precipitate was isolated by centrifugation, washed with toluene, and recrystallised from CH2Cl2/Et2O to yield 1a as an off-white solid (3.12 g, 60%). 1H NMR (CD2CN, 500 MHz): δ 7.94 (d, 2H, JHH = 2.5 Hz, HIm), 7.75 (t, 2H, JHH = 7.5 Hz, HAr), 7.66 (t, 4H, JHH = 7.5 Hz, HAr), 7.55 (m, 3H, HAr), 3.97 (t, 4H, JHH = 7.5 Hz, NCH2CH2CH2N), 3.89 (t, 4H, JHH = 7.5 Hz, NCH2CH2CH2N), 2.16 (quintet, 4H, JHH = 7.5 Hz, NCH2CH2CH2N), 1.65 (quintet, 4H, JHH = 7.5 Hz, NCH2CH2CH2N), 1.19 (sextet, 4H, JHH = 7.5 Hz, NCH2CH2CH2N), 0.78 (t, 6H, JHH = 7.5 Hz, NCH2CH2CH2N). 13C(1H) NMR (CD2CN, 125 MHz): δ 145.5 (NCN), 133.7 (Caryl), 131.5 (Caryl), 130.8 (Caryl), 123.3 (Caryl), 123.0 (Caryl), 122.1 (Caryl), 49.4 (NCH2CH2CH2N), 46.3 (NCH2CH2CH2N), 32.3 (NCH2CH2CH2N), 30.9 (NCH2CH2CH2N), 20.0 (NCH2CH2CH2N). HR-MS (ESI): Calc. for C29H32BrN4 (M – Br)–: 521.2280. Found: 521.2280. Anal. calc. for C29H33BrN4 (602.45) × H2O: C, 56.14; H, 6.50; N, 9.03. Found: C, 56.12; H, 6.47; N, 9.00.

Syntheses of 1b

According to the procedure described for 1a, compound 1b was obtained from 2-methyl N-n-butyl imidazole (1.20 g, 6.0 mmol) and 1,3-dibromopropane (0.61 g, 3.0 mmol) as an off-white solid (1.52 g, 73%). 1H NMR (CD2CN, 500 MHz): δ 8.18 (d, 2H, JHH = 2.0 Hz, HIm), 7.36 (d, 2H, JHH = 2.0 Hz, HAr), 7.14 (s, 4H, HAr), 4.55 (t, 4H, JHH = 8.0 Hz, NCH2CH2CH2N), 2.66 (m, 2H, NCH2CH2CH2N), 2.51 (s, 6H, CH2mes), 2.36 (s, 6H, CH2mes), 1.99 (s, 12H, CH2mes), 13.1(1H) NMR (CD2CN, 125 MHz) δ 146.2 (NCN), 142.3 (mes), 136.1 (mes), 131.3 (mes), 130.6 (mes), 123.6 (mes), 123.3 (mes), 46.6 (NCH2CH2CH2N), 30.9 (NCH2CH2CH2N), 21.1 (mes), 17.6 (mes), 10.8 (mes). Anal. calc. for C29H33BrN4 (602.45) × 2 CH2CN: C, 57.90; H, 6.48; N, 12.28. Found: C, 57.92; H, 6.40; N, 12.28.

Spectroscopic data for 2a

The monometallic species 2a was obtained by dissolving complex 3a in MeCN. Two species are distinguishable in the NMR spectra in a 2:1 ratio. Major species: 1H NMR (CD2CN, 500 MHz): δ 7.60 (m, 6H, HAr), 7.42 (d, 4H, JHH = 8.0 Hz, HAr), 7.08 (br, 2H, HIm), 4.22 (m, 2H, NC/HCHC/HN),
3.83 (m, 5H, RhCH + NCH₂CH₂CH₂CH₂), 3.49 (m, 2H, NCH₂CH₂CH₂CH₂), 1.14 (sextet, 4H, J_HH = 7.5 Hz, NCH₂CH₂CH₂CH₂), 0.76 (t, 6H, J_HH = 7.5 Hz, NCH₂CH₂CH₂CH₂).

Minor species: ¹H NMR (CD₂CN, 360 MHz): δ 7.04 (m, 2H, H_mes), 7.02 (m, 2H, H_mes), 4.43 (br, 2H, NCH₂CH₂CH₂CH₂), 4.04 (br, 1H, RhCH), 3.90 (m, 2H, NCH₂CH₂CH₂CH₂), 2.31 (s, 6H, C₆mesCH₃), 1.98 (s, 6H, C₆mesCH₃), 1.75 (s, 6H, C₆mesCH₃).

Minor species: ¹H NMR (CD₂CN, 360 MHz): δ 7.04 (m, 2H, H_mes), 7.02 (m, 2H, H_mes), 4.43 (br, 2H, NCH₂CH₂CH₂CH₂), 4.04 (br, 1H, RhCH), 3.90 (m, 2H, NCH₂CH₂CH₂CH₂), 2.31 (s, 6H, C₆mesCH₃), 1.98 (s, 6H, C₆mesCH₃), 1.75 (s, 6H, C₆mesCH₃).

¹C [¹H] NMR (CD₂CN, 360 MHz): δ 146.0 (J_Rac = 46.2 Hz, C₂mes), 141.2 (s, C₆mes), 136.1 (C₆mes), 132.3 (C₆mes), 130.1 (C₆mes), 120.9 (d, J_Rac = 2.9 Hz, C₂mes), 59.0 (NCH₂CH₂CH₂N), 34.0 (d, J_Rac = 28.5 Hz, RhCH), 21.0 (C₆mesCH₃), 17.4, 17.3, 11.0 (3 × C₆mesCH₃). The C₆mesN signal is not well resolved in the ¹C [¹H] spectrum. The signals of the major and minor species differ by less than 0.3 ppm.

Synthesis of 3b

According to the procedure described for 3a, complex 3b was produced from 1b (277 mg, 0.44 mmol), RhCl₃H₂O (105 mg, 0.4 mmol), NaOAc (263 mg, 3.2 mmol) and KI (266 mg, 1.6 mmol) as a brown solid (189 mg, 74%). Two major sets of signals are distinguishable in the NMR spectra in an approximate 2:1 ratio. ¹H NMR (CD₂Cl₂, 360 MHz): δ 7.05–6.91 (s, 4H, H_mes), 6.65, 6.63, 6.63 (s, 2H, H_mes), 4.67–4.58 (m, 2H, RhCH), 4.58–4.41 (m, 2H, NCH₂CH₂CH₂CH₂), 3.94–3.81 (m, 2H, NCH₂CH₂CH₂CH₂), 2.33, 2.32 (s, 6H, C₆mesCH₃), 2.18 (s, 6H, C₆mesCH₃), 1.99 (s, 6H, C₆mesCH₃), 1.75, 1.72 (s, 6H, C₆mesCH₃). ¹C [¹H] NMR (CD₂Cl₂, 125 MHz): δ 140.6 (NCN), 135.5 (br, C₆mesCH₃), 132.1 (br, C₆mesCH₃), 129.9 (2 × C₆mesCH₃), 121.7 (br, C₆mes), 60.52, 60.17 (2 × NCH₂CH₂CH₂N), 37.7 (d, J_Rac = 32.0, RhCH), 21.4 (C₆mesCH₃), 17.5 (C₆mesCH₃), 10.6 (C₆mesCH₃). The carbon-carbon signal and C₆mesN signals are not well resolved in the ¹C [¹H] spectrum. Anal. calc. for C₆H₉N₅Rh₂ (1592.66) × CH₂Cl₂: C, 40.89; H, 4.23; N, 6.66. Found: C, 40.91; H, 4.30; N, 6.57.

Synthesis of 4

According to the general procedure described for 2a–b, starting from 1f (353 mg, 0.74 mmol), RhCl₃H₂O (194 mg, 0.74 mmol), NaOAc (484 mg, 5.9 mmol) and KI (490 mg, 3.0 mmol). The crude product was purified by column chromatography (SiO₂). Complex 5 was eluted selectively with CH₂Cl₂:acetone (5:2), and a mixture of complexes 4, 5, 6 and some monocarbene species were obtained as a brown solid by increasing the polarity of the mobile phase (CH₂Cl₂:acetone 5:3). Gradient column chromatography followed by fractional crystallisation induced by slow diffusion of Et₂O into a solution of the crude mixture of 4 and 6 in CH₂Cl₂:acetone (1:1) gave two different types of crystals that were manually separated. Complex 4 crystallised as red rods, complex 6 as yellowish needles. ¹H NMR (CD₂CN, 600 MHz, 333 K): δ 8.31, 7.07, 6.91, 6.86 (4 × s, 1H, H_mes), 4.38 (br, 1H, NCH₂CH₂CH₂N), 4.32 (dd, 1H, J_HH = 12.0 Hz, J_HH = 7.7 Hz, NCH₂CH₂CH₂N), 4.21 (br, 3H, RhCH + NCH₂CH₂CH₂CH₂), 3.97 (t, 2H, NCH₂CH₂CH₂CH₂), 3.83 (d, 1H, J_HH = 13.0 Hz, NCH₂CH₂CH₂N), 3.67 (d, 1H, J_HH = 12.0 Hz, NCH₂CH₂CH₂N), 1.80 (m, 2H, NCH₂CH₂CH₂CH₂), 1.75 (quintet, 2H, J_HH = 7.3 Hz, NCH₂CH₂CH₂CH₂), 1.38 (sextet, 2H, J_HH = 6.0 Hz, NCH₂CH₂CH₂CH₂), 1.26 (m, 2H, NCH₂CH₂CH₂CH₂), 0.98, 0.90 (2 × t, 3H, J_HH = 7.4 Hz, NCH₂CH₂CH₂CH₂). ¹C [¹H] NMR (CD₂CN, 150 MHz): δ 132.2, 122.6, 121.6, 119.5 (4 × C₆mes), 60.7, 60.4 (2 ×
NCH₂CH₃N), 49.8, 49.4 (2 × NCH₂CH₂CH₂CH₃), 35.5 (RhCH), 33.7, 33.0 (2 × NCH₂CH₂CH₂CH₃), 20.6, 20.1 (2 × NCH₂CH₂CH₂CH₃), 14.2, 13.7 (2 × NCH₂CH₂CH₂CH₃). The carbene carbon signals are not well resolved in the ¹³C[¹H] spectrum. Anal. calc. for C₂₃H₂₅N₂Rh (726.24): C, 45.7, H, 4.58; N, 11.57. Found: C, 45.76; H, 4.53; N, 11.73.

**Synthesis of 6.**

**Method A:** According to the procedure described for the synthesis of complex 4.

**Method B:** Complex 5 (80 mg, 0.16 mmol) and NaOAc (107 mg, 1.3 mmol) were stirred together in refluxing acetonitrile (20 mL) for 6 days. Solid KI (224 mg, 1.6 mmol) was added and the reaction mixture refluxed for 2 more days. The product was purified by column chromatography (SiO₂, CH₂Cl₂/acetone first 10:1, then 10:3) and 6 was obtained as a yellow solid (26 mg, 23% yield) after solvent removal. ¹H NMR (CDCl₃, 500 MHz, 334 K): δ 7.15, 7.03 (2 × s, 1H, H₃), 4.56 (br, 1H, RhCH), 4.35 (m, 4H, NCH₂CH₂CH₂H₂N + NCH₂CH₂CH₂CH₃), 4.06 (m, 2H, NCH₂CH₂CH₂CH₃), 3.67 (m, 2H, NCH₂CH₂CH₂CH₃), 1.87, 1.79 (2 × s, 2H, NCH₂CH₂CH₂CH₃), 1.40 (sextet, 4H, 3JHH = 7.4 Hz, NCH₂CH₂CH₂CH₃), 0.98 (t, 6H, 3JHH = 7.3 Hz, NCH₂CH₂CH₂CH₃). ¹³C[¹H] NMR (CDCl₃, 125 MHz): δ 123.0, 122.9, 120.4, 120.2 (4 × C₆H₅), 60.4, 60.1 (2 × NCH₂CH₂CH₂N), 50.1, 49.8 (2 × NCH₂CH₂CH₂CH₃), 36.0 (RhCH), 33.9, 33.3 (2 × NCH₂CH₂CH₂CH₃), 20.6, 20.4 (2 × NCH₂CH₂CH₂CH₃), 14.1 (NCH₂CH₂CH₂CH₃). Carbene carbon signal not resolved. Anal. Calc. for C₁₉H₁₂₂N₂Rh (685.19): C, 33.31; H, 4.41; N, 10.22. Found: C, 33.32; H, 4.14; N, 10.61.

**Structure determination and refinement of 3b, 4, 5b and 6.**

Suitable single crystals were mounted on Stoe Imaging Plate Diffractometer Systems with a two-circle goniometer (3b and 4) or a one-circle φ goniometer (5b), or on a Bruker SMART APEX CCD diffractometer (6). Graphite-monochromators (Mo-Kα radiation, λ = 0.71073 Å) for 3b and 4, a semi-empirical absorption correction was applied using MULscan ABS as implemented in PLATON. An empirical absorption correction was applied for 6 using the SADABS routine, and no absorption correction was applied for 5b. The structures were solved by direct methods using the program SHELXS-97 and refined by full matrix least squares on F² with SHELXL-97. The hydrogen atoms were included in calculated positions and treated as riding atoms using SHELXL-97 default parameters. All non-hydrogen atoms were refined anisotropically.

Crystals of complex 3b contained one half-occupied CH₂Cl₂ per complex molecule. Disorder was found in one methyl substituent and in the PF₆⁻ anion, and more pronounced in the co-crystallised solvent molecules. The SQUEEZE option in PLATON was used to calculate the potential solvent accessible volume (1848 Å³, containing about 385 electrons). Eight hexane molecules (8 × 50 electrons) per unit cell were included in all further calculations. Due to the disorder, the corresponding parts of the ligand were refined as having the same thermal values. Compound 5b crystallised as a racemic twin, therefore the TWIN refinement was applied in SHELXL. For 6, the absolute structure was determined, the final Flack parameter is −0.03(3). Further details on data collection and refinement are summarised in Table S1. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Centre as supplementary publication nos. CCDC 817392–817395. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk].

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4. Electronic Supplementary Information (ESI) available: Crystallographic and computational details and computed structures and energies of all species. See DOI: 10.1039/b000000xc.
Despite experiments were conducted under strictly anhydrous conditions, water as a proton source cannot be fully excluded.


Strongly mesoionic imidazol-4-ylidene N-heterocyclic carbene ligands promote the rhodium-mediated activation of an alkane-type C–H bond and undergo H/D exchange via exclusive C5–H bond activation.