Angewandte
Communications

International Edition: DOI: 10.1002/anie.201503593
German Edition: DOI: 10.1002/ange.201503593

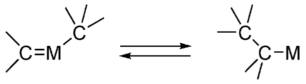
# Reversible α-Hydrogen and α-Alkyl Elimination in PC($sp^3$)P Pincer Complexes of Iridium**

*Klara J. Jonasson, Alexey V. Polukeev, Rocío Marcos, Mårten S. G. Ahlquist, and Ola F. Wendt**

**Abstract:** *Despite significant progress in recent years, the cleavage of unstrained C($sp^3$)–C($sp^3$) bonds remains challenging. A C–C coupling and cleavage reaction in a PC($sp^3$)P iridium pincer complex is mechanistically studied; the reaction proceeds via the formation of a carbene intermediate and can be described as a competition between α-hydrogen and α-alkyl elimination; the latter process was observed experimentally and is an unusual way of C($sp^3$)–C($sp^3$) bond scission, which has previously not been studied in detail. Mechanistic details that are based upon kinetic studies, activation parameters, and DFT calculations are also discussed. A full characterization of a C–C agostic intermediate is presented.*

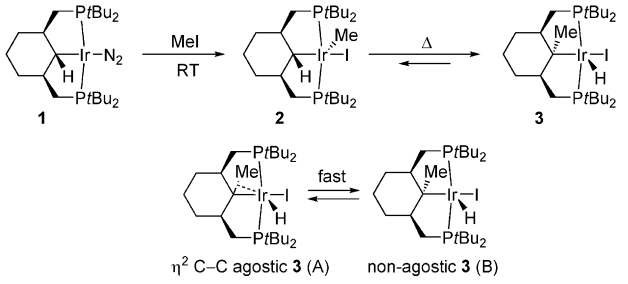
Carbon–carbon single bonds are ubiquitous in chemistry, but they are so unreactive that one rarely considers using them as functional groups. Three fundamental processes are typically used for C–C bond cleavage, namely oxidative addition, β-carbon elimination, and retro-allylation.[1] Of those, only the second one is currently applicable to unactivated C($sp^3$)–C($sp^3$) bonds, with a few examples reported.[1a,b] Therefore, new reactivity patterns that involve such bonds are highly desired.

Previously, we reported a unique, reversible dehydrogenative cross-coupling reaction between up to four unactivated C($sp^3$)–H bonds to give an olefin moiety.[2] We were able to show that the key step responsible for C–C bond formation and cleavage is the formation of a carbene complex through double C–H activation; this intermediate is responsible for C–C bond formation and cleavage by migratory insertion or deinsertion of the carbene moiety into an Ir–C bond (Scheme 1). Although the forward reaction in Scheme 1 has numerous precedents for various metals,[3,4] the only detailed kinetic study was reported over three decades ago for niobocene derivatives.[5] Moreover, and to the best of our knowledge, the reverse reaction, namely the deinsertion of a carbene from a C($sp^3$)–C($sp^3$) bond (or, in other words, the α-elimination of an alkyl group), has previously never been reported for unstrained substrates; the corresponding α-elimination of hydrogen, however, is well known.[6] Given the screened and inaccessible nature of C($sp^3$)–C($sp^3$) bonds, α-alkyl eliminations, especially when combined with the C–H activation activity of iridium pincer complexes, may hold some promise towards their cleavage. Furthermore, whereas cross-coupling reactions are common for first- and second-row transition metals, for third-row metals, such reactions are scarce,[7] not the least because of the more difficult C–C reductive elimination. Specifically, C($sp^3$)–C($sp^3$) reductive elimination is rare for Ir;[8] therefore, coupling through alternative reaction pathways as shown in Scheme 1 is potentially interesting. This prompted us to carry out a mechanistic investigation of the C–C bond-forming/cleaving step. Herein, we present a kinetic study of the reversible 1,2-methyl migration in complex [(PCyP)Ir(Me)I] (**2**) to give [(PCyMeP)Ir(H)I] (**3**) (Scheme 2). Furthermore, a DFT calculation of the mechanism is presented.



*Scheme 1.* C–C bond formation and cleavage through insertion/deinsertion of a carbene into an M–C bond.

Subjecting the known[9] terminal dinitrogen iridium(I) complex **1** to methyl iodide resulted in full conversion into compound **2** within hours (Scheme 2). The complex displayed a triplet at $\delta = 2.15$ ppm in the $^1$H NMR spectrum and a triplet at $\delta = -27.8$ ppm in the $^{13}$C{$^1$H} NMR spectrum, which correspond to the Ir–$CH_3$ moiety, in analogy with the previously reported aromatic counterpart.[8d] The presence of a characteristic broadened triplet at $\delta = 1.95$ ppm, which corresponds to the α-proton of the cyclohexyl ring, is indicative of a coordinated PCP motif. The molecular



*Scheme 2.* Synthesis of **2** and subsequent transformation into compound **3**.

---

[*] Dr. K. J. Jonasson,[+] Dr. A. V. Polukeev,[+] Prof. O. F. Wendt
Centre for Analysis and Synthesis
Department of Chemistry, Lund University
PO Box 124, 22100 Lund (Sweden)
E-mail: ola.wendt@chem.lu.se

Dr. R. Marcos, Prof. M. S. G. Ahlquist
Division of Theoretical Chemistry & Biology
School of Biotechnology, KTH Royal Institute of Technology
10691 Stockholm (Sweden)

[+] These authors contributed equally to this work.

[**] Financial support from the Swedish Research Council, the Knut and Alice Wallenberg Foundation, and the Crafoord Foundation is gratefully acknowledged. Computational resources have been provided by the National Supercomputer Centre in Linköping, Sweden.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201503593.

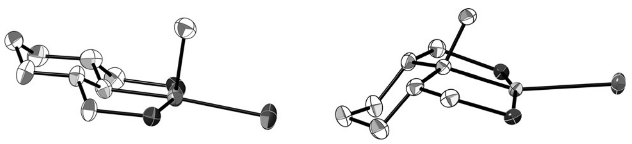


*Figure 1.* Side views of complexes **2** (left) and **3** (right), displaying the PCyP carbon atom coordinated to the metal center in an axial position in complex **3**. Hydrogen atoms and substituents on the phosphorus atoms are omitted for clarity.

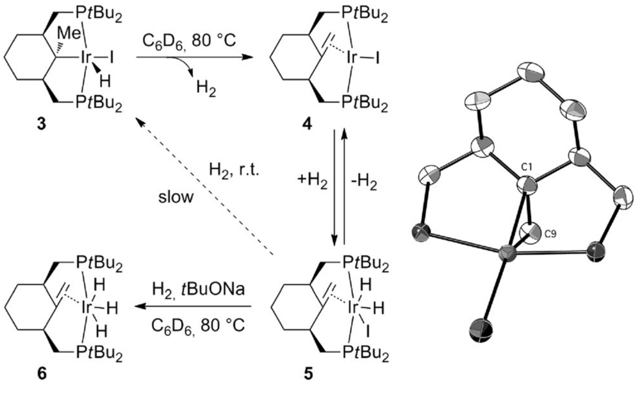
structure of compound **2** is given in Figure 1. Complex **2** adopts a distorted square-pyramidal geometry around the iridium center with the methyl ligand in an apical position with an *anti* relationship to the α-hydrogen atom.

Upon heating a toluene solution of **2** to 60 °C, the color turned from burgundy red to pale pink/orange within several hours. The reaction went to approximately 90 % completion, and the single product formed was characterized as complex **3**; it is the result of a 1,2-methyl migration from the metal to the metalated PCyP carbon atom with simultaneous α-hydride elimination. The chemical shifts of the hydride ($\delta = -28.4$ ppm, t, $J_{PH} = 13.0$ Hz) and the methyl group ($\delta = -1.02$ ppm, m) are strongly temperature-dependent ($\Delta\delta \approx 9$ ppm for Ir−H between −90 and +110 °C), suggesting the presence of a rapid equilibrium between two distinct structures in solution. By treating the data as two compounds in a temperature-dependent equilibrium (see the Supporting Information for details), the limiting chemical shifts were obtained. Compound A was found to displays peaks at $\delta = -23.18 \pm 0.03$ (Ir−H) and $-2.08 \pm 0.01$ ppm (Ir−$CH_3$); for compound B, the values are $\delta = -38.6 \pm 0.2$ (Ir−H) and $0.94 \pm 0.05$ ppm (Ir−$CH_3$). These findings suggest the presence of an equilibrium between an agostic and a non-agostic compound, and the values are in good agreement with literature data for related structures. Thus, an Ir hydride *trans* to a vacant site typically appears around $\delta = -40$ ppm ($\delta = -38.6$ ppm for B), whereas an Ir hydride *trans* to a weak-field ligand resonates near $\delta = -20$ ppm ($\delta = -23.18$ ppm for A). The average $^1J_{CH}$ value of 122.6 Hz for the methyl group (determined using $^{13}CH_3I$) does not change with temperature, and **3** is better described as an $\eta^2$ C−C or $\eta^3$ C−C−H rather than an $\eta^2$ C−H structure (calculations favor the $\eta^3$ C−C−H one, see below).[11] Further support for this hypothesis comes from the $^1J_{C,C}$ coupling. The quaternary α-carbon atom and the Ir−$CH_3$ moiety are observed at $\delta = 53.9$ and 5.0 ppm in the $^{13}C\{^1H\}$ NMR spectrum, and limiting chemical shifts for Ir−$^{13}CH_3$ are $\delta = -7.2 \pm 0.2$ and $29.4 \pm 0.3$ ppm. The observed $^1J_{C,C}$ coupling constant between Ir−$^{13}CH_3$ and the α-carbon atom is $31 \pm 1$ Hz; assuming $^1J_{C,C} = 35$ Hz for the non-agostic compound[11] and using the ratio between isomers calculated from the limiting chemical shifts, a coupling constant of $27 \pm 2$ Hz is obtained for the agostic complex. The agostic bond thus appears to be relatively weak, which is further supported by thermochemical data, according to which the formation of the agostic bond is accompanied by $\Delta H° = -2.71 \pm 0.04$ kcal mol$^{-1}$ and $\Delta S° = -8.0 \pm 0.2$ cal mol$^{-1}$K$^{-1}$, values that were tentatively explained by hindered rotation of the methyl group in the agostic structure. Optimizing an agostic structure using the B3LYP functional with or without D3 correction led back to the original non-agostic structure. However, the potential was found to be very flat around the minimum. Furthermore, prior studies have shown that functionals using the LYP correlation functional underestimate agostic interactions.[12] We therefore tried PBE and PBE-D3 for the geometry optimization, and with both, we located two distinct minima. With PB3-D3, we calculated the difference in electronic energy to be 1.5 kcal mol$^{-1}$ in favor of the non-agostic complex. We would like to note that the formation of the agostic complex is accompanied by an increase in the C-Ir-H angle, from 80.2° to 114.9°, which indicates that the methyl group is interacting with the antibonding Ir−H σ* orbital. Geometries are shown in the Supporting Information, Figure S11.

The structure of **3** was confirmed by X-ray diffraction analysis,[13] and the structure is given in Figure 1. Complex **3** has a square-pyramidal geometry around the iridium center with the hydride ligand in an axial position, *anti* to the methyl group. The distance between the methyl substituent and the metal (Ir1−C9) in compound **3** is 2.449 Å, clearly indicating an interaction. This interaction gives rise to bond angles around the α-carbon atom that strongly deviate from the ideal tetrahedral geometry. The C1−C9 bond is only slightly elongated (1.553(4) Å) compared to typical C($sp^3$)−C($sp^3$) single-bond lengths (ca. 1.54 Å). Complex **3** further displayed an unusual all-*cis* metal coordination with the PCP carbon atoms in axial positions, resulting in a tilt of the cyclohexyl ring with respect to the coordination plane (Figure 1).

Keeping a $C_6D_6$ solution of complex **3** at 80 °C for several days gave rise to a new $^{31}P$ NMR shift at 55.5 ppm, coinciding with the consumption of the starting material as confirmed by the disappearance of the peak at 68.6 ppm. The new product formed is the alkene complex **4** (Scheme 3), which is the result of a β-elimination.[14] The molecular structure of compound **4** is also shown in Scheme 3. The complex adopts a distorted square-planar geometry around the iridium center, and the C1–C9 distance of 1.438(15) Å is in agreement with an olefin complex.[2] The cyclohexyl backbone maintains its chair conformation and the ring tilt as observed in **3**.

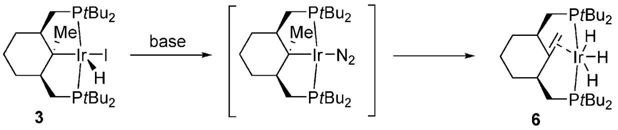
Complex **4** was further treated with an excess of $H_2$ to probe for reversibility and regeneration of **3**, but this resulted in a pronounced color change from orange to colorless and



*Scheme 3.* Synthesis of **4** and reversible hydrogenation to compound **5**. In the molecular structure of **4**, hydrogen atoms and *tert*-butyl groups are omitted for clarity. The Ir–C distances are 2.163(9) and 2.11(1) Å.

a previously unobserved $^{31}$P NMR singlet peak at 41.1 ppm, which corresponded to the sole product in solution. This compound appeared to be dihydride **5** (Scheme 3). The hydride signals were very broad at room temperature, but at −50 °C, two triplets with well-resolved P,H couplings were observed at $\delta = -8.86$ (t, $J_{P,H} = 12.0$ Hz) and −18.69 ppm (t, $J_{P,H} = 13.0$ Hz). Concentration of a solution of **5** in vacuo led to a clean transformation back to **4**. Keeping **5** under a $H_2$ atmosphere resulted in the slow formation of complex **3**. Hydrogen iodide can be removed from **5** using *t*BuONa to give trihydride **6**, which, unlike **5**, does not tend to lose a $H_2$ molecule.

Attempts to synthesize a dinitrogen complex (analogous to **1**) from **3** were unsuccessful (Scheme 4). The reaction with *t*BuONa slowly produced a number of unidentified compounds, which were converted into **6** after evaporation of the solvent, and the reaction with *t*BuLi similarly produced **6**. It is likely that the presence of a labile $N_2$ ligand makes β-elimination facile; a related $N_2$-triggered elimination in a Rh complex was reported by Milstein and co-workers.[15]

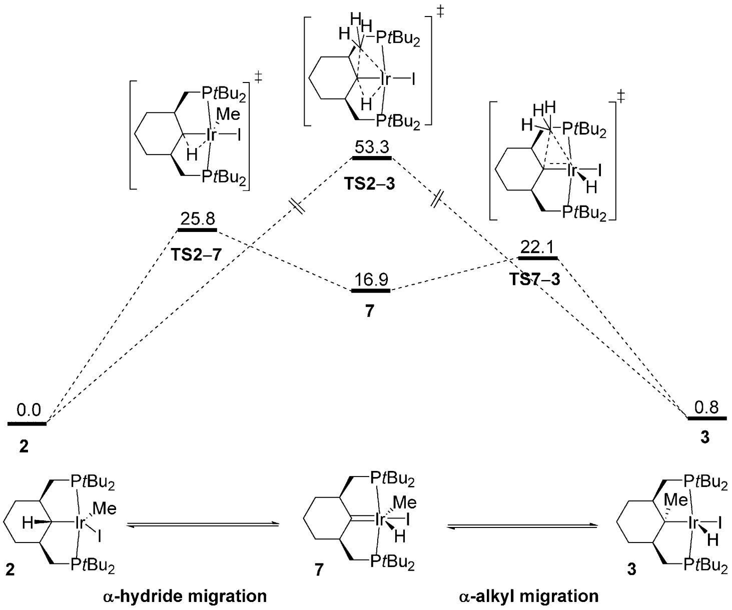


***Scheme 4.*** Attempted synthesis of a dinitrogen complex from **3**.

The reversible conversion of **2** into **3** could be conveniently studied by $^1$H NMR spectroscopy, by monitoring the decrease in the intensity of the methyl proton signal of **2** ($\delta = 2.15$ ppm) and the concomitant increase in the methyl proton signal in **3** ($\delta = -1.02$ ppm) as a function of time. Fitting the standard equation for a reversible first-order process to this data gave rate and equilibrium constants at different temperatures, and these were fitted to the Eyring and van't Hoff equations to obtain activation and reaction enthalpies and entropies. The transformation of **2** into **3** is an almost thermoneutral entropy-driven process ($K_{313} = 6.8$, $\Delta H° = 0.3 \pm 0.3$ kcal mol$^{-1}$, $\Delta S° = 5.0 \pm 0.8$ cal mol$^{-1}$K$^{-1}$). During the course of the reaction, Ir−C and C−H bonds are broken, and Ir−H as well as C−C bonds are formed; given that the Ir−H bond is approximately 20 kcal mol$^{-1}$ stronger than the Ir−C bond[16] and the C−H bond is about 15 kcal mol$^{-1}$ stronger than the C−C bond, one could expect the reaction to be exothermic by approximately 5 kcal mol$^{-1}$. However, in complex **2**, Ir occupies an equatorial position of the cyclohexyl ring, whereas in complex **3**, the unfavorable axial position is metalated. The axial isomer is destabilized by approximately 5 kcal mol$^{-1}$ (according to DFT calculations, see the Supporting Information) compared to the equatorial one, likely owing to increased repulsive interactions within a bulky ligand. With the inclusion of this destabilization energy, the observed $\Delta H°$ value is in good agreement with the one expected from bond-dissociation enthalpy data. The rate constants at 313 K are $k_1 = 4.32 \times 10^{-5}$ s$^{-1}$ and $k_{-1} = 6.33 \times 10^{-6}$ s$^{-1}$, and the activation parameters are $\Delta H_1^{\ddagger} = 22.0 \pm 0.4$ kcal mol$^{-1}$, $\Delta S_1^{\ddagger} = -8.7 \pm 1.3$ cal mol$^{-1}$K$^{-1}$, $\Delta H_{-1}^{\ddagger} = 21.5 \pm 0.1$ kcal mol$^{-1}$, and $\Delta S_{-1}^{\ddagger} = -13.7 \pm 0.3$ cal mol$^{-1}$K$^{-1}$.

In line with our previous studies,[2] DFT calculations showed that the isomerization of **2** to **3** begins with an α-elimination of a hydrogen atom to give Ir carbene **7**, followed by migratory insertion of the carbene moiety into the Ir−C bond (Scheme 5). Other possible mechanisms are prohibitively high in energy. The iridium(I) complex resulting from C−C reductive elimination could not be located. Instead, reductive elimination and oxidative addition of the C−H bond in the α-position are concerted with an activation energy of 53.3 kcal mol$^{-1}$ (**TS2–3**), which indicates that this path is essentially impossible (see the Supporting Information for more details).

The computed energies are in very good agreement with the experimental results, the main difference being that **3** is approximately 1 kcal mol$^{-1}$ higher in energy than **2** whereas the experimental result indicates vice versa. The barrier for the forward reaction, which is calculated to be associated with α-elimination of a hydrogen atom, is significantly higher than previously reported for related systems. Therefore, free energy barriers for α-hydrogen elimination in [N$_3$N]W(cyclopentyl)[17] and in cationic Cp*Ir cyclometalated phosphine complexes[18] are approximately 10–12 kcal mol$^{-1}$. In these systems, the alkyl and carbene species are of similar stability whereas the carbene complex **7** is 16.9 kcal mol$^{-1}$ higher in energy than **2**, which probably raises the barrier for elimination. On the other hand, the barrier for insertion of the carbene into the Ir−Me or Ir−H bonds was found to be low for **7**, with calculated barriers of less than 10 kcal mol$^{-1}$. Previously, Bercaw and Threlkel had found a barrier of approximately 24 kcal mol$^{-1}$ (mainly enthalpic) for the insertion of a zirconoxy carbene into niobocene alkyl bonds.[5] In a reaction somewhat related to that of **7**, Fryzuk et al. showed that the adduct of MeI and (PNP)Ir=C=CH$_2$ undergoes isomer-



***Scheme 5.*** Calculated free energy profile for the conversion of complex **2** into complex **3**. The relative Gibbs free energies are given in kcal mol$^{-1}$ at 60 °C.

ization above 0 °C likely through a 1,2-shift of the methyl group.[19] This reaction is irreversible, which is in agreement with experimental[3,4] and computational[20] data on many other systems where the insertion of a carbene into M–C bonds is facile.

The reverse reaction, that is, the transformation of **3** into **7**, is more intriguing, as it corresponds to a unique α-elimination of an alkyl group. We have previously proposed this reaction type to be involved in C(sp$^3$)–C(sp$^3$) bond cleavage in a related system,[2] but it has not been observed for completely unstrained systems thus far, nor have any detailed studies been reported. As the transformation of **2** to **3** is reversible, we were, however, able to obtain kinetic and thermodynamic data for the reaction in both directions. The enthalpic barrier for α-alkyl elimination was found to be comparable to that of α-hydrogen elimination (21.5 vs. 22.0 kcal mol$^{-1}$), and the $\Delta G^{\neq}$ value is only approximately 1 kcal mol$^{-1}$ larger. The DFT calculated barriers are approximately the same. These results suggest that α-alkyl elimination reactions are fully possible for this and related systems from a kinetic point of view, at least when it comes to R$_3$C–M fragments. Thermodynamically, the conversion of **2** into **3** is almost neutral with the equilibrium being slightly shifted towards **3**, the C–C bond-formation product. The comparable barriers for the forward and reverse reaction are surprising at first as concerted reactions are usually more facile for hydrogen compared to carbon atoms, which have more directional orbitals.[21] This means that C–C bond cleavage is expected to be more unfavorable in general, and that one of the driving forces for the current reaction is the transformation of axially metalated **3** into equatorially metalated **2**, which releases some repulsive interactions in the ligand that are worth approximately 5 kcal mol$^{-1}$. Therefore, for C(sp$^3$)–C(sp$^3$) bond cleavage to be successful, an additional driving force is required, for example, some degree of strain in the substrate or subsequent transformations of resulting fragments, as we have previously shown in the hydrogenation example.[2] However, it should be noted that the C–C agostic interaction adds little to the overall energetics as the agostic and non-agostic forms are very close in energy in solution and interconvert very rapidly.

In summary, we have presented a mechanistic investigation of a C–C bond-forming/cleaving process involving an Ir carbene complex that offers an alternative to a reductive-elimination pathway, which is rare for Ir and C(sp$^3$)–C(sp$^3$) bonds. Remarkably, the barrier for C(sp$^3$)–C(sp$^3$) bond cleavage by α-alkyl elimination appears to be fairly low and comparable with the one for α-hydrogen elimination; this finding may assist in the design of novel systems for C–C bond activation.

**Keywords:** density functional calculations · elimination · iridium · kinetics · pincer complexes

**How to cite:** *Angew. Chem. Int. Ed.* **2015**, *54*, 9372–9375
*Angew. Chem.* **2015**, *127*, 9504–9507

---

[1] a) K. Ruhland, *Eur. J. Org. Chem.* **2012**, 2683–2706; b) F. Chen, T. Wang, N. Jiao, *Chem. Rev.* **2014**, *114*, 8613–8661; c) M. Murakami, T. Matsuda, *Chem. Commun.* **2011**, *47*, 1100–1105.

[2] A. V. Polukeev, R. Marcos, M. S. G. Ahlquist, O. F. Wendt, *Chem. Sci.* **2015**, *6*, 2060–2067.

[3] For recent reviews on the insertion of carbenes into M–C bonds in catalytic processes, see: a) Q. Xiao, Y. Zhang, J. Wang, *Acc. Chem. Res.* **2013**, *46*, 236–247; b) Z. Liu, J. Wang, *J. Org. Chem.* **2013**, *78*, 10024–10030; c) N. M. G. Franssen, A. J. C. Walters, J. N. H. Reeka, B. de Bruin, *Catal. Sci. Technol.* **2011**, *1*, 153–165; d) E. Jellema, A. L. Jongerius, J. N. H. Reek, B. de Bruin, *Chem. Soc. Rev.* **2010**, *39*, 1706–1723.

[4] For examples, see: a) P. Jernakoff, N. J. Cooper, *J. Am. Chem. Soc.* **1984**, *106*, 3026–3027; b) M. D. Fryzuk, S. A. Johnson, S. J. Rettig, *J. Am. Chem. Soc.* **2001**, *123*, 1602–1612; c) J. Campos, J. Lopez-Serrano, E. Alvarez, E. Carmona, *J. Am. Chem. Soc.* **2012**, *134*, 7165–7175; d) A. J. C. Walters, O. Troeppner, I. Ivanovic-Burmazovic, C. Tejel, M. P. del Rio, J. N. H. Reek, B. de Bruin, *Angew. Chem. Int. Ed.* **2012**, *51*, 5157–5161; *Angew. Chem.* **2012**, *124*, 5247–5251.

[5] R. S. Threlkel, J. E. Bercaw, *J. Am. Chem. Soc.* **1981**, *103*, 2650–2659.

[6] H. Werner, *Angew. Chem. Int. Ed.* **2010**, *49*, 4714–4728; *Angew. Chem.* **2010**, *122*, 4822–4837.

[7] a) R. Takeuchi, S. Kezuka, *Synthesis* **2006**, 3349–3366; b) S. Pan, T. Shibata, *ACS Catal.* **2013**, *3*, 704–712.

[8] a) E. B. Tjaden, J. M. Stryker, *J. Am. Chem. Soc.* **1990**, *112*, 6420–6422; b) E. Fooladi, T. Graham, M. L. Turner, B. Dalhus, P. M. Maitlis, M. Tilset, *J. Chem. Soc. Dalton Trans.* **2002**, 975–982; c) X. Li, L. N. Appelhans, J. W. Faller, R. H. Crabtree, *Organometallics* **2004**, *23*, 3378–3387; d) R. Ghosh, T. J. Emge, K. Krogh-Jespersen, A. S. Goldman, *J. Am. Chem. Soc.* **2008**, *130*, 11317–11327.

[9] A. Arunachalampillai, D. Olsson, O. F. Wendt, *Dalton Trans.* **2009**, 8626–8630.

[10] For a pioneering procedure of this type, see: R. B. Calvert, J. R. Shapley, *J. Am. Chem. Soc.* **1978**, *100*, 7726–7727.

[11] For a review on agostic C–C bonds, see: M. Etienne, A. S. Weller, *Chem. Soc. Rev.* **2014**, *43*, 242–259.

[12] D. A. Pantazis, J. E. McGrady, F. Maseras, M. Etienne, *J. Chem. Theory Comput.* **2007**, *3*, 1329–1336.

[13] Only the agostic compound seemed to be present in the crystal, unlike for a somewhat related equilibrium between Ir complexes with a BINOR ligand, where both the Ir$^{III}$ σ-complex and the Ir(V) oxidative-addition product co-exist in the solid state; see: A. B. Chaplin, J. C. Green, A. S. Weller, *J. Am. Chem. Soc.* **2011**, *133*, 13162–13168.

[14] For a related β-elimination in an aliphatic Rh pincer complex, see: A. Vigalok, B. Rybtchinski, L. J. W. Shimon, B.-D. Yehoshoa, D. Milstein, *Organometallics* **1999**, *18*, 895–905.

[15] A. Vigalok, H.-B. Kraatz, L. Konstantinovsky, D. Milstein, *Chem. Eur. J.* **1997**, *3*, 253–260.

[16] J. A. Martinho Simões, J. L. Beauchamp, *Chem. Rev.* **1990**, *90*, 629–688.

[17] R. R. Schrock, S. W. Seidel, N. C. Mosch-Zanetti, D. A. Dobbs, K.-Y. Shih, W. M. Davis, *Organometallics* **1997**, *16*, 5195–5208.

[18] J. Campos, E. Carmona, *Organometallics*, **2015**, *34*, 2212–2221.

[19] M. D. Fryzuk, L. Huang, N. T. McManus, P. Paglia, S. J. Reltig, G. S. Whitell, *Organometallics* **1992**, *11*, 2979–2990.

[20] A. J. C. Walters, J. N. H. Reek, B. de Bruin, *ACS Catal.* **2014**, *4*, 1376–1389.

[21] M. E. Thompson, S. M. Baxter, A. R. Bulls, B. J. Burger, M. C. Nolan, B. D. Santarsiero, W. P. Schaefer, J. E. Bercaw, *J. Am. Chem. Soc.* **1987**, *109*, 203–219.

Received: April 20, 2015