Available online at www.sciencedirect.com
SCIENCE DIRECT®
Inorganica Chimica Acta 357 (2004) 1969–1974
Inorganica Chimica Acta
www.elsevier.com/locate/ica

Note

Activation and deactivation of a carbene containing non-classical ruthenium hydride complex in catalytic processes involving C–H bond cleavage

Pascal Buskens, Daniela Giunta, Walter Leitner *

Institut für Technische und Makromolekulare Chemie, Technische Chemie und Petrolchemie, Rheinisch-Westfälische Technische Hochschule Aachen, Worringer Weg 1, D-52074 Aachen, Germany

Received 5 November 2003; accepted 18 January 2004

Dedicated to Prof. Dr. Helmut Werner on the occasion of his 70th birthday

Abstract

The carbene-containing non-classical ruthenium hydride complex $[(PCy_3)Ru(H)_2(H_2)_2(IMes)]$ **1** (IMes = 1,3-Bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene) is an active catalyst for H/D exchange in aromatic ketones. It is also capable of combining sp^2 C–H bond activation with C–C bond formation. Comparing the chemo- and regio-selectivities of the H/D exchange process and the C–C bond formation clearly indicates that different intermediates are involved in the two processes. High pressure NMR studies provide strong evidence that the key intermediate for the C–C coupling reaction is analogous to that for other ruthenium catalysts reported previously. Catalytic turnover is limited by the instability of this intermediate in the presence of the olefinic coupling partner.

Keywords: C–H bond activation; H/D exchange; C–C coupling; Ruthenium complexes; Dihydrogen complexes

1. Introduction

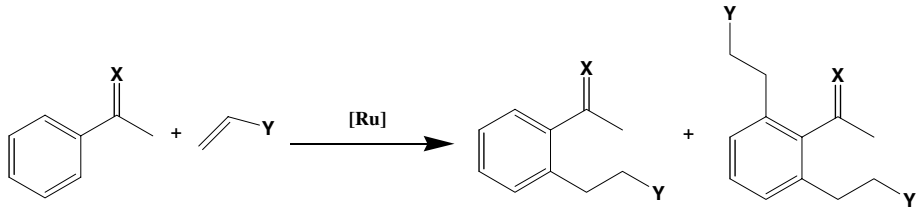
Aromatic compounds are readily available from petrochemical feedstock and constitute a major class of intermediates in the fine chemical and life science industries [1]. Indeed, aromatic structures are ubiquitous in final products such as agrochemicals, fragrances and pharmaceuticals. The direct transformation of aromatic C–H bonds into C–C or C-heteroatom bonds would open sustainable pathways for the transformation of cheap substrates into high value products. However, the combination of C–H bond cleavage and C–C bond formation in one catalytic cycle is still a challenge for organometallic chemistry [2,3]. A major breakthrough in this field was achieved by Murai and coworkers in 1993. They described the ruthenium-catalyzed coupling of aromatic substrates with unsaturated compounds such as olefins (Scheme 1) [4]. The Murai coupling represents an ideal atom economic transformation offering a waste-free and green alternative to conventional aromatic functionalization such as Friedel–Crafts chemistry [5].

Key steps of this reaction are the cleavage of the sp^2 C–H bond in *ortho*-position to a C=X (X = O or NR) anchoring group and subsequent insertion of the unsaturated coupling partner into the resulting metal–carbon bond. Recent experimental and theoretical investigations indicate, however, that the most energy demanding steps are those at the end of the catalytic cycle, liberating the product and regenerating the active species [6].

As part of our continuing studies towards C–H bond functionalization using ruthenium complexes [7,8], we recently reported the synthesis of and aromatic C–H bond activation with the non-classical ruthenium hydride complex $[(PCy_3)Ru(H)_2(H_2)_2(IMes)]$ **1** (IMes = 1,3-Bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene) [9]. Complex **1** is derived from Chaudret's complex $[(PCy_3)_2Ru(H)_2(H_2)_2]$ **2** [8–10] by substitution of a PCy_3 ligand for a heterocyclic carbene ligand [11]. It is the first

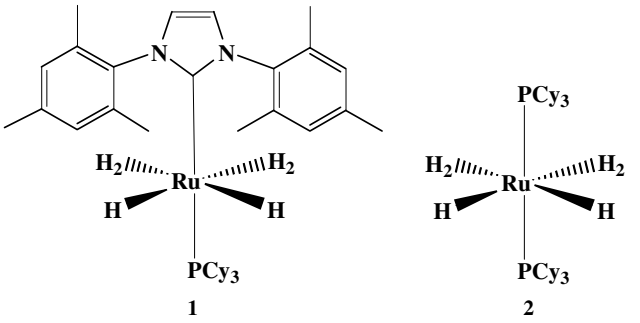
* Corresponding author. Tel.: +49-241-8026480; fax: +49-241-8022177.
E-mail address: leitner@itmc.rwth-aachen.de (W. Leitner).

0020-1693/$ - see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.ica.2004.01.018



Scheme 1. General scheme for the Murai reaction.

structurally characterized example of an organometallic compound containing a strongly basic carbene ligand in the same coordination sphere as the acidic η^2-H_2 moiety [12]. Most notably, complex **1** exhibits a unique reactivity towards aromatic C–H bonds resulting in a remarkably rapid and regio-selective H/D exchange process at room temperature [9].



In the present paper, we report on the catalytic properties of complex **1** for H/D exchange and Murai-type coupling reactions of aromatic ketones with ethylene as the olefinic reaction partner. In particular, we describe the results of multinuclear high-pressure NMR investigations providing insight into the major activation and deactivation processes. These results can help in developing guidelines for the design of future generations of improved catalysts.

2. Experimental

2.1. Safety warning

The use of pressurized gases, especially in delicate equipment for analysis, can be hazardous and must be carried out only with suitable equipment and under appropriate safety precautions.

2.2. General techniques and materials

All experimental work was carried out under argon atmosphere using the Schlenk or dry box technique. Toluene, toluene-d_8, and benzene-d_6 were distilled from sodium benzophenone ketyl under argon atmosphere prior to use. All commercially obtained chemicals were degassed and stored under argon at room temperature. Complex **1** was synthesized according to Giunta et al. [9] starting from Chaudret's complex **2** and 1,3-Bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene. The complex was stored under hydrogen at −30 °C and stock solutions were prepared for catalytic applications.

2.3. Analysis

Routine measurements and high pressure NMR experiments were carried out on a Bruker DPX 300 and AC 300 spectrometer, respectively. The spectrometers operate at frequencies of 299.6 MHz for ^{1}H, 75.3 MHz for ^{13}C and 121.29 MHz for ^{31}P. Chemical shift values δ are given in ppm relative to tetramethylsilane (TMS) using solvent resonances as internal standard for ^{1}H and ^{13}C, and relative to H_3PO_4 as external reference for ^{31}P.

Gas chromatographic (GC) analysis was performed on a HP 19091 S-433 gaschromatograph in combination with a HP 5973 Mass Selective Detector. A HP-5MS (5% phenylmethylsiloxane, capillary 30 m × 250 μm × 0.25 μm) column was used, and helium was applied as carrier gas. The temperature program was: 5 min at 60 °C (starting phase), 12 °C min^{-1} (heating phase), variable time at 300 °C (final phase).

2.4. Catalytic H/D exchange between acetophenone (*3a*) and benzene-d_6

Complex **1** (1.8 mg; 2.6 μmol), benzene-d_6 (0.5 ml) and one drop of cyclohexane as internal standard were introduced in a NMR tube under argon. The solution was kept at room temperature for 24 h and then checked by ^{1}H NMR for quantitative deuteration of **1** to [(IMes-d_6)Ru$(D_2)_2(D)_2(PCy_3)$] (**1′**). Then, **3a** (3.0 mg; 25.7 μmol) was introduced and the solution was analyzed by ^{1}H NMR after 1 and 24 h. Deuterium incorporation in **3a** was quantified by monitoring the decrease of the relevant signal intensities relative to the signal of cyclohexane.

2.5. Murai-type coupling with ethylene as olefinic substrate

A solution of **1** (10 mg; 0.014 mmol) in toluene (2 ml) was transferred into a stainless-steel autoclave (10 ml

volume) equipped with an inlet valve, pressure gauge and temperature control. The substrate **3a–d**, **5**, or **7** (0.14 mmol) was added and the autoclave was pressurized with ethylene (10 bar). After stirring with a magnetic stir bar for 24 h at room temperature, the reactor was vented. The reaction mixture was filtered through celite before GC analysis. Modifications of this general procedure were applied as appropriate for optimization of the reaction conditions.

2.6. High pressure NMR experiments

Complex **1** (25 mg; 0.036 mmol) was dissolved in toluene-d_8 and acetophenone **3a** (4.3 mg; 0.036 mmol) was added. The mixture was stirred for 5 min at room temperature and transferred via syringe to a high pressure NMR sapphire tube (outer diameter 5 mm) fitted with a titanium pressure head [13]. After recording the spectra under inert gas atmosphere, the tube was pressurized with ethylene (15 bar) and/or hydrogen (1 bar) as appropriate. During pressurization, transport, and mounting of the sample, the tube was kept inside a cylindrical thick-walled poly-carbonate shield that can be fitted on top of the NMR probe head. Experiments with other ratios of **1** to **3a** were carried out in an analogous way.

3. Results and discussion

3.1. Catalytic H/D exchange

First, we investigated the catalytic H/D exchange of **3a** with **1** to ensure that reversible C–H activation occurs also with this relatively electron deficient substrate. Following the published procedure [9], the fully deuterated complex **1′** was generated by dissolving **1** in benzene-d_6. Upon addition of **3a** to this solution, noticeable catalytic H/D exchange occurred already after 1 h and continued over a period of 24 h (Fig. 1).

In the aromatic region, all signal intensities decreased considerably over the course of the exchange process. In contrast to the situation with other aromatic substrates [9], only a moderate regio-selectivity was observed and

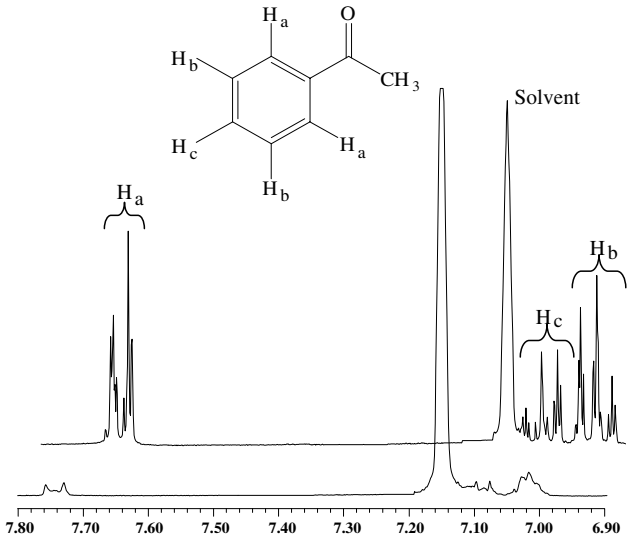
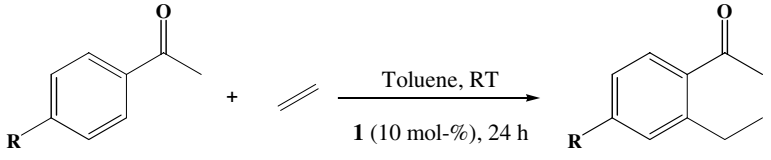


Fig. 1. Aromatic region of the ^{1}H NMR spectra of **3a** dissolved in benzene-d_6 in the presence of a catalytic amount of **1′** demonstrating the deuterium incorporation after 1 h (top trace) and 24 h (bottom trace).

the H/D exchange occurred with comparable rate in *ortho*- and *meta*-position (estimated exchange: *ortho*: 20% after 1 h, 90% after 24 h; *meta*: 20% after 1 h, 70% after 24 h). The exchange in *para*-position was slightly slower, with an estimated incorporation of 40% after 24 h. In addition to the H/D exchange at the aromatic core, a rapid H/D exchange in the CH_3 group of **3a** was also observed. After 24 h, only a small set of multiplets indicative of the CH_2D and the CHD_2 groups remained. Thus, the exchange rate of the sp^3 C–H bond in **3a** is in the same range as those of the aromatic sp^2 C–H bonds. This lack of chemo- and regio-selectivity during the H/D exchange process of **3a** is in sharp contrast to the exclusive *ortho*-functionalization observed under Murai-type coupling conditions (vide infra).

3.2. Murai-type couplings

In a first set of experiments, optimum reaction conditions were determined for the coupling of acetophenone **3a** and ethylene to give **4a** as the standard test reaction (Scheme 2). Reactions were performed in



3a, R = H
3b, R = Cl
3c, R = Ph
3d, R = Me

10 bar

4a: 16 %
4b: 13 %
4c: 12 %
4d: 6 %

Scheme 2. Reaction of acetophenone **3a** and its derivatives **3b–d** with ethylene.

Table 1
Optimization of the reaction conditions for the Murai-type coupling of **3a** with ethylene catalyzed by **1** (10 mol%)

Entry	Time [h]	*T* [°C]	*P* [bar]	Solvent	**4a** [%]
1	45	25	30	toluene	16
2	45	25	30	hexane	5
3	24	25	10	toluene	16
4	24	25	5	toluene	12
5	24	25	1.5	toluene	4
6	24	40	10	toluene	15
7	24	70	10	toluene	17

home-built stainless steel high pressure autoclaves using stock solutions of **1**. The mono-substituted derivative **4a** was observed as the only product by GC-MS analysis. Conversion to **4a** was determined by integration of the GC peak of **4a** relative to **3a** (using naphthalene as internal standard) assuming similar response factors. Representative results are summarized in Table 1.

Most reactions were carried out for a standard reaction time of 24 h. Although some formation of **4a** was observed even at low catalyst concentrations, a loading of 10 mol% **1** was found to be the best compromise for conversion and reproducibility. As toluene might interfere with the catalyst cycle through competing C–H activation processes [9], hexane was tested as alternative solvent. However, the saturated hydrocarbon gave consistently lower yields, probably for solubility reasons (Table 1, entry 2). Yields increased with increasing ethylene pressure up to 10 bar, but higher pressures did not result in a further improvement (Table 1 entry 1, 3–5). Notably, the reaction temperature had no significant influence on conversion or selectivity in the range of 25–70 °C, indicating already that the performance of the catalyst is mainly limited by rapid deactivation processes. As a result, only the mono-substituted product is formed with very high selectivity, but yields remain low even under optimized conditions.

Similar results were obtained with *para*-substituted acetophenones **3b–d** under the reaction conditions of entry 3 (Scheme 2). Although double substitution was never observed for substrates **3a–d**, 1-tetralone **5** was alkylated in similar yields under these conditions (Scheme 3). Again, this suggests that catalyst deactivation is turnover limiting.

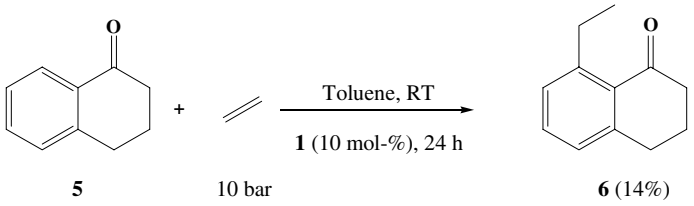
Potential anchoring groups other than keto functions did not promote the coupling process, therefore aromatic imines, amides, or nitriles remained unreactive. Vinylpyridine **7** resulted in 14% formation of the disubstituted olefinic coupling product **8** (Scheme 4), corresponding to three catalytic cycles for the sp^2 C–H cleavage and C–C coupling sequence.

3.3. High pressure NMR spectroscopic investigation

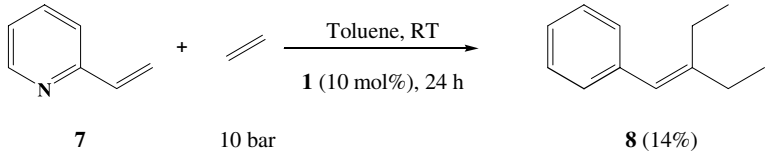
The catalytic properties of complex **1** are in remarkable contrast to those reported earlier for Chaudret's complex **2**. Whereas **1** is highly active for the H/D exchange process with **3a**, it is a poor catalyst for the Murai coupling allowing only a few catalytic turnovers at best. Complex **2** on the other hand shows no measurable activity for H/D exchange on aromatic substrates [9], but can achieve nearly a hundred catalytic cycles for Murai type couplings under optimized conditions [14].

In order to get more insight into the reasons for this discrepancy, we decided to investigate the behavior of **1** under catalytic conditions by high pressure NMR spectroscopy. The key results are summarized in Scheme 5.

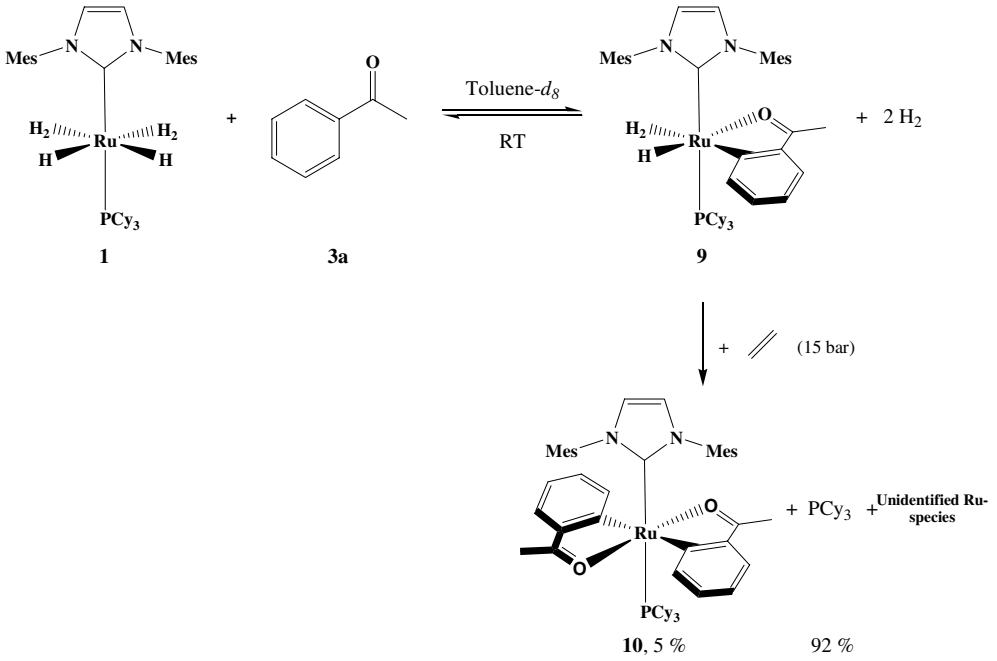
Fortunately, the H/D exchange between **1** and toluene-d_8 was found to proceed slowly enough to allow investigations of the reactivity of **1** by ^1H- and $^{31}P\{^1H\}$-NMR spectroscopy in this solvent at room temperature. Unambiguous assignments of all phosphorous containing complexes were possible on the basis of comparison



Scheme 3. Coupling reaction between 1-tetralone **5** and ethylene.



Scheme 4. Coupling reaction between vinylpyridine **7** and ethylene.



Scheme 5. Deactivation pathway of **1** under Murai coupling conditions as observed by high pressure NMR spectroscopy.

of these data to those of the corresponding bis-tricyclohexyl phosphine complexes [14,15]. Only the most characteristic signals are discussed here. Upon treatment of **1** {^{1}H NMR: $\delta = -7.35$ (d, ^2J(P,H) = 8.32 Hz, 6H, Ru–*H*), ^{31}P{^{1}H} NMR: $\delta = 78.1$ (s)} with one equivalent of **3a** a new complex **9** is formed, characterized by a ^{31}P resonance at $\delta = 48.5$ and a broad high field signal at $\delta = -8.65$ in the ^{1}H NMR spectrum. Complex **9** can be assigned to a species where one molecule of **3a** is bound to ruthenium via the C=O group and activated through *ortho*-metallation. Two equivalents of dihydrogen are liberated in this process. The non-activated *ortho*-hydrogen of **3a** gives rise to a very broad signal centered at 8.33 ppm.

The broad signals in the ^{1}H NMR spectrum are indicative of exchange processes occurring at a rate similar to the NMR time scale. Indeed, the formation of **9** occurs in an equilibrium reaction and only 48% of **1** is converted under these conditions according to integration of the ^{31}P{^{1}H} NMR resonances. The reaction is fully reversible and **1** is regenerated quantitatively upon pressurization of the solution with H_2 (1 bar). The equilibrium can be shifted to the right by increasing the **3a**:**1** ratio (**3a**:**1**//**9**:**1**: 1:1//48:52; 2:1//87:13; 100:1//95:5). Even with a large excess of **3a** and long reaction times, no indication for the formation of complexes containing two molecules of **3a** was obtained.

The species present in solution change dramatically upon introduction of the second coupling partner ethylene. Upon pressurization of a 1:1 mixture of **1** and **3a** in toluene-d_8 with 15 bar of ethylene, the bis-acetophenone adduct **10** is the only phosphorous containing complex detectable in solution. However, **10** is observed only in very small amounts (approximately 5% based on **1**), whereas 92% of the phosphine ligand is dissociated from the ruthenium center and present as free PCy_3 in solution. The resulting phosphine-free ruthenium complexes cannot be sufficiently characterized in solution with the techniques employed here. It is noteworthy, however, that no high field ^{1}H NMR signals were detectable under these conditions. This process is irreversible and neither removing ethylene under vacuum nor pressurization with H_2 leads back to a coordination of PCy_3 to the ruthenium center.

The results of the present study demonstrate that carbene-containing non-classical ruthenium hydride complexes such as **1** are capable of combining aromatic C–H bond activation with C–C bond formation. However, comparing the chemo- and regio-selectivities of the H/D exchange process and the C–C bond formation clearly indicates that the two processes do not involve the same intermediates. High pressure NMR studies provide strong evidence that the key intermediate **9** for the Murai reaction is analogous to those reported for other ruthenium catalysts previously [6,14]. This leads to an exclusive functionalization in *ortho*-position to the anchoring keto group. The H/D exchange process, however, shows no comparable regio-selectivity and deuterium incorporation occurs at all aromatic positions with approximately the same rate. Most significantly, this leads to the conclusion that the C–H bond cleavage during the H/D exchange process must involve intermediates other than **9**. At present, we can only speculate on the nature of these intermediates for the H/D

exchange, but η^6-coordination of the aromatic core may provide a plausible hypothesis for further studies [10b].

The different behavior of complexes **1** and **2** as catalysts in the Murai reaction can be explained at least partially on basis of the present investigation. The monoadduct analogous to **9** but resulting from Chaudret's complex and acetophenone is formed quantitatively from a 1:1 mixture of **2** and **3a** [14], demonstrating that the C–H bond cleavage step is shifted completely to the right with the bisphosphine complexes already under stoichiometric conditions. In contrast, complex **1** yields the key intermediate **9** only to a much lesser extent under comparable conditions. At the same time, the catalytic cycle based on **9** is interrupted in the presence of ethylene through formation of **10** and, more predominantly, via rapid and irreversible displacement of PCy_3 from the IMes containing intermediates. The same side reactions have been observed with complex **2** under catalytic conditions and have been suggested as important deactivation pathways [8b,14,15]. They occur considerably slower for the bisphosphine complexes, however, in consistency with the significantly higher turnover number of **2** as compared to **1**.

In summary, non-classical ruthenium hydride complexes remain promising lead structures for the functionalization of aromatic C–H bonds. At present, catalytic turnover is, however, severely limited by the instability of the intermediates under coupling conditions. In case of complex **1**, this appears to result mainly from an increased liability of the ancillary PCy_3 ligand as compared to the corresponding bisphosphine complex **2**. The challenge for future catalyst design results from the balance between flexible exchange of substrates and products with stable coordination of the ancillary ligands.

References

[1] K. Weissermel, H.-J. Arpe, Industrielle Organische Chemie, fifth ed., Wiley-VCH, Weinheim, 1998, p. 343.
[2] J.A. Davies, P.C. Watson, J.F. Liebman, A. Greenberg, Selective Hydrocarbon Activation, VCH, Weinheim, 1990.
[3] (a) A.D. Ryabov, Chem. Rev. 22 (1990) 91;
(b) G. Dyker, Angew. Chem., Int. Ed. 38 (1999) 1698;
(c) V. Ritleng, C. Sirlin, M. Pfeffer, Chem. Rev. 102 (2002) 1731;
(d) Y. Guari, S. Sabo-Etienne, B. Chaudret, Eur. J. Inorg. Chem. (1999) 1047.
[4] S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, Nature 366 (1993) 529.
[5] P.T. Anastas, M.M. Kirchhoff, Acc. Chem. Res. 35 (2002) 686.
[6] (a) F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, S. Murai, Bull. Chem. Soc. Jpn. 68 (1995) 62;
(b) M. Sonoda, F. Kakiuchi, N. Chatani, S. Murai, Bull. Chem. Soc. Jpn. 70 (1997) 3117;
(c) K. Fumitoshi, S. Murai, Acc. Chem. Res. 35 (2002) 826.
[7] C. Six, K. Beck, A. Wegner, W. Leitner, Organometallics 19 (2000) 4639.
[8] (a) S. Busch, W. Leitner, Chem. Commun. (1999) 2305;
(b) S. Busch, W. Leitner, Adv. Synth. Catal. 343 (2) (2001) 192.
[9] D. Giunta, M. Hölscher, C.W. Lehmann, R. Mynott, C. Wirtz, W. Leitner, Adv. Synth. Catal. 345 (2003) 1139.
[10] (a) B. Chaudret, G. Commenges, R. Poilblanc, Chem. Commun. (1983) 641;
(b) B. Chaudret, R. Poilblanc, Organometallics 4 (1985) 1722.
[11] W.A. Herrmann, Angew. Chem., Int. Ed. 41 (2002) 1290.
[12] (a) G.J. Kubas, Metal Dihydrogen and σ-Bond Complexes, Kluver Academic/Plenum Publishers, New York, 2001;
(b) P.J. Jessop, R.H. Morris, Coord. Chem. Rev. 121 (1992) 155;
(c) For the stability of coordinated carbenes in the presence of acidic groups see also A. Füerstner, H. Krause, L. Ackermann, C.W. Lehmann, Chem. Commun. 21 (2001) 2240.
[13] C.J. Elsevier, J. Mol. Catal. 92 (1994) 285.
[14] Y. Guari, S. Sabo-Etienne, B. Chaudret, J. Am. Chem. Soc. 120 (1998) 4228.
[15] S. Busch, Ph.D. Thesis, Max-Planck-Institut für Kohlenforschung, Mülheim an der Ruhr and University of Jena, 2001.