

Synthesis of Functionalized Hydrazines: Facile Homogeneous (N-Heterocyclic Carbene)-Palladium(0)-Catalyzed Diboration and Silaboration of Azobenzenes

Melvyn B. Ansell,^a George E. Kostakis,^a Holger Braunschweig,^{b,c,*} Oscar Navarro,^{a,d,*} and John Spencer^{a,*}

^a Department of Chemistry, University of Sussex, Brighton, BN1 9QJ, U.K.
E-mail: j.spencer@sussex.ac.uk


^b Institut für Anorganische Chemie, Julius-Maximilians-Universität Würzburg, Am Hubland, 97074 Würzburg, Germany

^c Institute for Sustainable Chemistry & Catalysis with Boron, Julius-Maximilians-Universität Würzburg, Am Hubland, 97074 Würzburg, Germany
E-mail: h.braunschweig@uni-wuerzburg.de

^d Division of Biomaterials and Biomechanics, Department of Restorative Dentistry, School of Dentistry, Oregon Health & Science University, 2730 SW Moody Ave., Portland, Oregon 97239, USA
E-mail: navarrof@ohsu.edu

Received: October 8, 2016; Revised: October 13, 2016; Published online: November 9, 2016

 Supporting information for this article can be found under: <http://dx.doi.org/10.1002/adsc.201601106>.

 ©2016 The Authors. Published by Wiley-VCH Verlag GmbH & Co. KGaA. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

Abstract: The bis(N-heterocyclic carbene)(diphenylacetylene)palladium complex [Pd(ITMe)₂(PhC≡CPh)] (ITMe = 1,3,4,5-tetramethylimidazol-2-ylidene) acts as a highly active pre-catalyst in the diboration and silaboration of azobenzenes to synthesize a series of novel functionalized hydrazines. The reactions proceed using commercially available diboranes and silaboranes under mild reaction conditions.

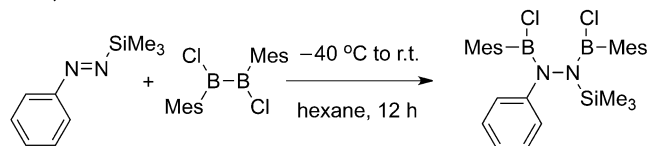
Keywords: azobenzenes; diboration; N-heterocyclic carbenes; palladium; silaboration

The transition metal-catalyzed diboration (B-B) and silaboration (Si-B) reactions of carbon-based unsaturated species such as alkynes,^[1] alkenes,^[2] and 1,3-dienes,^[3] represent some of the most valuable and widely studied organic transformations in the literature. Nevertheless, the translation of this chemistry to other element-based unsaturated bonds remains a considerable challenge. In particular, the diboration and silaboration of N=N (azo) bonds harnesses the potential for the synthesis of highly functionalized hydrazines as precursors to, for instance, polymeric materi-

als,^[4] DNA modifiers,^[5] and glycosidase inhibitors.^[6] Despite this potential, such element-element additions to azo moieties are extremely rare. There are only three reported isolated examples of azo diborations to yield the corresponding 1,2-bis(boryl)hydrazines. These require the use of either an extremely reactive B–B bond in the form of azadiboriridenes,^[7] dichlorodiboranes,^[8] or a highly strained B–B bond as in [2]borametallarenophanes (Scheme 1).^[9] Recently, however, a combined computational and experimental article from Li and co-workers showed that the diboration of N=N bonds using a commercially available and air-stable tetraalkoxydiboron reagent such as bis(pinacolato)diboron is feasible.^[10] To the best of our knowledge there are no examples in the literature of N=N silaborations.

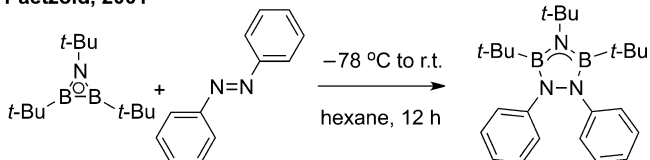
We have described the synthesis of the complex [Pd(ITMe)₂(PhC≡CPh)] (**1**),^[11] which showed high catalytic reactivity in the regio- and stereoselective diboration^[12] and silaboration of alkynes.^[13] We pondered whether **1** could catalyze these element-element additions across N=N bonds. Herein, we report the use of **1** as a very active pre-catalyst in the diboration and silaboration of azobenzenes. The products represent the first isolated examples of 1,2-bis(boryl)hydrazines and 1-silyl-2-borylhydrazines, starting from commercially available diboranes and silaboranes, respectively.

Nöth, 1995

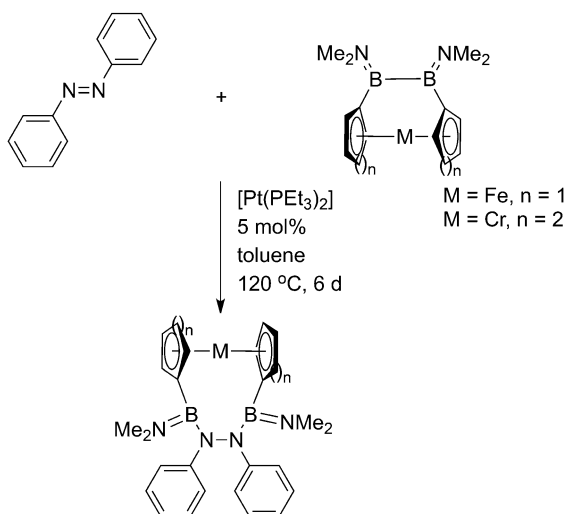


Mes = 2,4,6-trimethylphenyl

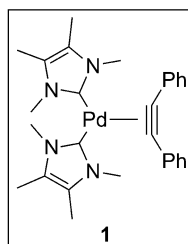
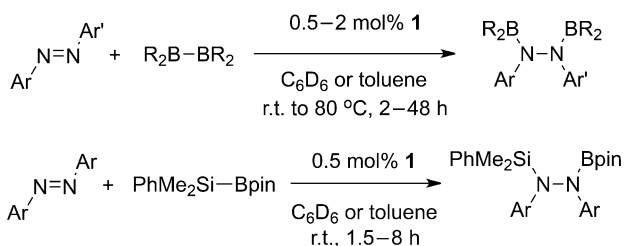
Paetzold, 2001



Braunschweig, 2008



This work

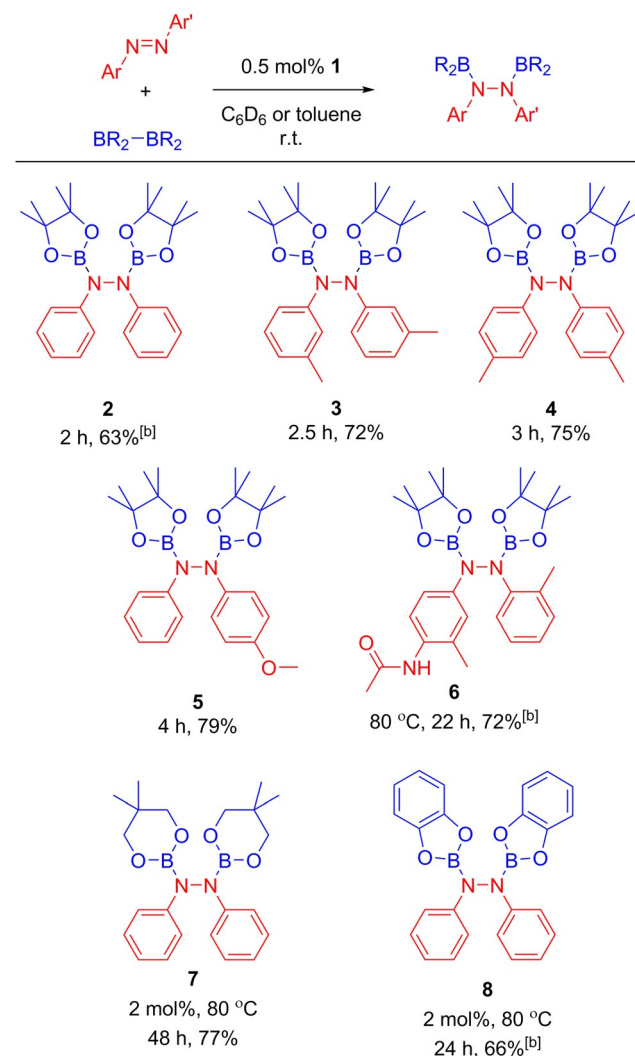


Scheme 1. Element-element additions to N=N bonds.

The viability of the diboration of azobenzenes was assessed by combining, under an inert atmosphere and at room temperature, azobenzene (PhN=NPh), bis(pinacolato)diboron (B_2pin_2) and catalytic quanti-

ties of **1** in C_6D_6 in order to monitor the reaction progress by 1H NMR spectroscopy. The optimization of the reaction parameters resulted in 100% conversion to 1,2-diphenyl-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hydrazine (**2**) after 2 h, using as little as 0.5 mol% of **1** (Table 1).

The reaction also proceeded in toluene under the same conditions on a larger scale. After several recrystallizations from hexanes, **2** was isolated as an air- and moisture-sensitive white powder in 63% yield. Single crystals of **2** were isolated from a saturated hexane solution at -30 °C and the resulting X-ray analysis is depicted in Figure 1. The crystalline structure of **2** was solved in the $P2_12_12_1$ space group with one of the Bpin functionalities displaying a degree of dynamic disorder. A notable feature of this molecular structure is the length of the N–N bond [1.419(4) Å]

Table 1. Diboration of azobenzenes.^[a]

^[a] B_2R_4 : 1–1.5 equiv. (see the Supporting Information for details).

^[b] Yields from scaled-up reactions in toluene.

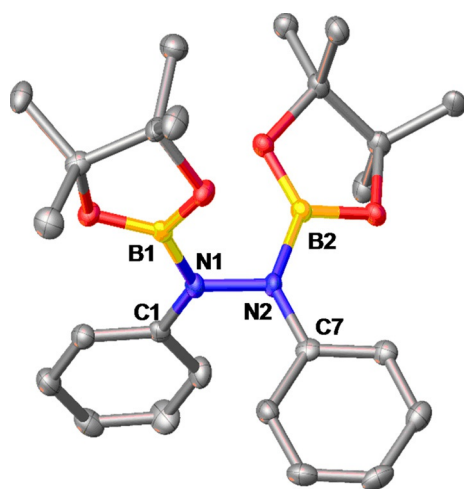


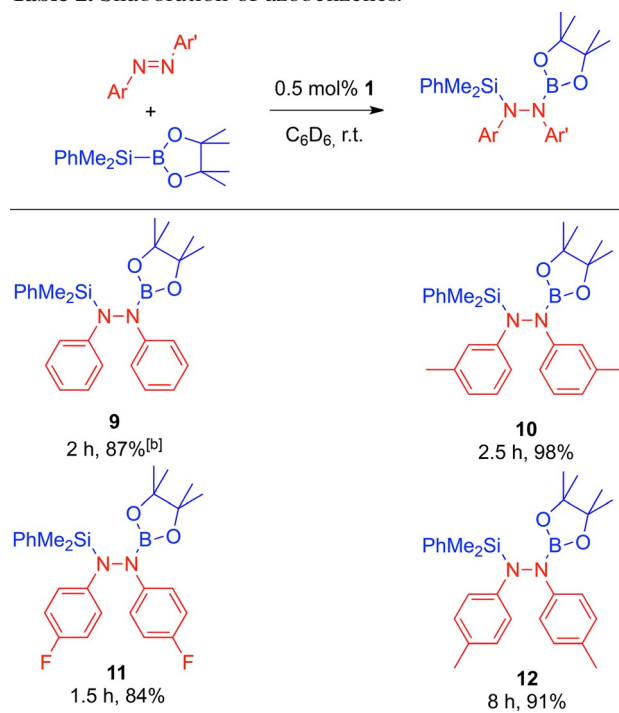
Figure 1. Molecular structure of **2** with thermal ellipsoids at 50% probability level. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: N1–N2: 1.419(4), N1–B1: 1.433(4), N2–B2: 1.410(14), C1–N1–B1: 128.1(3), N2–N1–C1: 116.2(2), N2–N1–B1: 115.2(2), C7–N2–N1: 116.1(2), B2–N2–N1: 115.5(6), B2–N2–C7: 128.4(6), O1–B1–N1: 124.6(3), O1–B1–O2: 114.3(3), O2–B1–N1: 121.3(3), O13–B2–N2: 119.4(12), O13–B2–O14: 113.0(9), O14–B2–N2: 127.6(9).

which is, as expected, comparable to the N–N bond in diphenylhydrazines [1.394(7) Å],^[14] and much longer than the N=N bond of azobenzene (1.25 Å).^[15] Each N atom exhibits a distorted trigonal planar geometry [115.2(2)–128.4(6)°; N1, N2: $\Sigma = 360^\circ$]. The B–N bond lengths [1.410(14) Å and 1.433(4) Å] are in agreement with those of other aminoboranes of the form $R_2BNR'_2$,^[9,15,16] and imply partial double bond character.^[17] The distorted trigonal planar geometry surrounding each B atom is indicative of sp^2 hybridization [133.0(9)–127.6(9)°; B1, B2: $\Sigma = 360^\circ$].

The versatility of this catalytic diboration using B_2pin_2 was assessed and this protocol was extended to a series of azobenzenes with a range of functionalities including alkyl, methoxy and amido moieties in the *ortho*, *meta* and *para* positions (Table 1). As with **2**, the syntheses of the novel compounds **3–5** only required 0.5 mol% of **1**, proceeded at room temperature and were completed in 2.5–4 h (Table 1) (see the Supporting Information for the X-ray analysis of **4**). The synthesis of **6** required an increase of temperature (80 °C) and reaction time (22 h) to reach completion. This was attributed to the limited solubility of the azobenzene in C_6D_6 and in toluene. It was also possible to exchange the diboron reagent for other commercially available B–B analogues such as bis(neopentylglycolato)diboron and bis(catecolato)diboron. This resulted in the formation of **7** and **8**, respectively, albeit employing higher catalyst loadings, higher temperatures and longer reaction times than those for their B_2pin_2 counterpart.

We next turned our attention to the catalytic silaboration of azobenzenes. The silaborane of choice was the readily available (dimethylphenyl)silylboronic acid pinacol ester ($PhMe_2SiBpin$). The reaction parameters were optimized using $PhMe_2SiBpin$ and azobenzene as the model substrates. To our delight, [dimethyl(phenyl)silyl]-1,2-diphenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hydrazine (**9**) was synthesized with 100% conversion using 0.5 mol% of **1** at room temperature in 2 h in C_6D_6 or toluene. Interestingly, compound **9** is air- and moisture-stable which simplified purification. On stirring the crude reaction mixture in deionized H_2O overnight, **9** was recovered as a white powder in 87% yield (Table 2). Single crystals of **9** were isolated from slow evaporation of a saturated acetone solution at room temperature. The molecular structure of **9** obtained from X-ray analysis is shown in Figure 2. There are some noteworthy features in this molecular structure, the first was that it was solved in the $P2_1$ space group. The N–N bond length [1.417(4) Å] is comparable to that of **2** [1.419(4) Å] and shorter than that of other silyl-substituted hydrazines (e.g., $Ph_2Si\{NHNH\}SiPh_2$ and $Ph_2Si\{NHNHMe\}_2$) reported in the literature [1.421(5)–1.480(2) Å].^[18] The bonding around each N atom, as with **2**, showed a distorted trigonal planar ge-

Table 2. Silaboration of azobenzenes.^[a]



^[a] $PhMe_2SiBpin$: 1.13–1.36 equiv. (see the Supporting Information for details).

^[b] Isolated yield from scaled-up reactions in toluene. Reaction of 4-methoxyazobenzene with $PhMe_2SiBpin$ gives a mixture of regioisomers (see the Supporting Information).

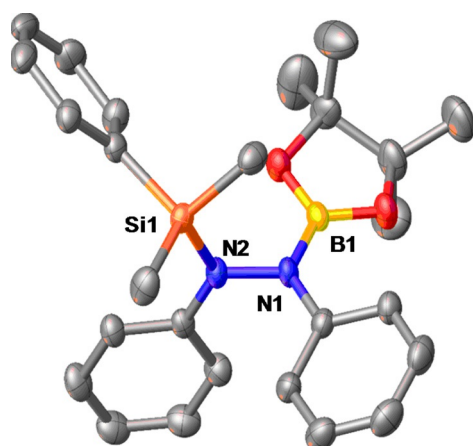
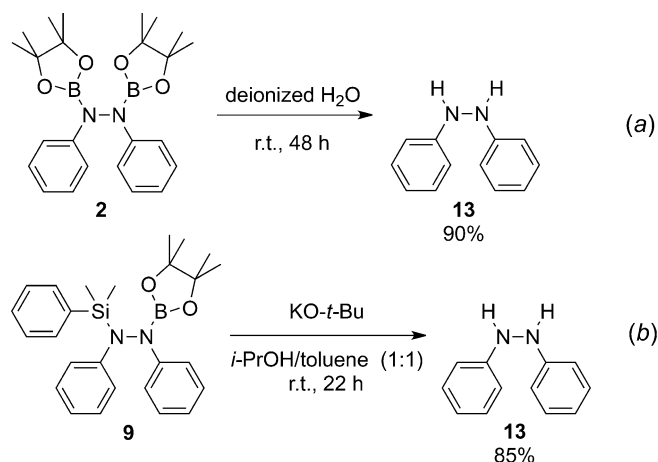


Figure 2. Molecular structure of **9** with thermal ellipsoids at the 50% probability level. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: N1–N2: 1.417(4), N1–B1: 1.438(5), Si1–N2: 1.773(3), N2–N1–C7: 115.8(3), N2–N1–B1: 116.3(3), C7–N1–B1: 127.8(3), N1–N2–Si1: 115.3(2), C6–N2–Si1: 127.9(2), C6–N2–N1: 116.3(3), O2–B1–N1: 123.8(3), O3–B1–O2: 114.6(3), O3–B1–N1: 121.6(3).

ometry [115.3(2)–127.9(2) Å; N1, N2: $\Sigma = 360^\circ$]. The B–N bond length [1.438(5) Å] is in agreement with those of other aminoboranes including **2**. The geometry surrounding the B-atom is distorted trigonal planar [114.6(4)–123.8(3)°; B_p : $\Sigma = 360^\circ$]. The Si–N bond length is longer [1.773(2) Å] than that of other silylamines of the form $R_3SiNR'_2$.^[18,19]

We then investigated the potential of **1** in the silaboration of other azobenzenes. This protocol was expanded to *ortho*-, *meta*- and *para*-substituted symmetrical azobenzenes with alkyl and fluoro groups. The novel compounds **10–12** were synthesized using 0.5 mol% of **1** at room temperature, reaching completion in 1.5 to 8 h (Table 2). Compounds **10–12** were also stable to air and moisture (see the Supporting Information for X-ray analysis of **11**). As expected, the application of this silaboration protocol to unsymmetrical azobenzenes resulted in a mixture of regioisomers (see the Supporting Information).

During our investigations, we found that **2** can undergo hydrolysis upon stirring in degassed deionized H_2O overnight, affording the corresponding 1,2-diphenylhydrazine (**13**, Scheme 2, *a*). This result, albeit accessed through palladium catalysis, supports the proposed mechanism by Li and co-workers, whereby **2** was computationally calculated as an intermediate in the organocatalytic formation of hydrazines from their corresponding azobenzenes.^[10] Interestingly, their reaction conditions proved to be ineffective for the hydrolysis of **9**. Instead, the cleavage of both the Si–N and B–N bonds was achieved using KO-*t*-Bu in a 2-propanol/toluene mixture (Scheme 2, *b*). The cross-coupling potential of the N–B bond in **9** was as-



Scheme 2. Synthesis of hydrazines from 1,2-bis(boryl)hydrazine and 1-silyl-2-borylhydrazine.

sessed, but, initial investigations, using standard reaction conditions, proved unsuccessful.^[20]

We have shown that **1** acts as a highly active pre-catalyst in the diboration and silaboration of azobenzenes using commercially available diboranes and silaboranes, respectively. Novel 1,2-bis(boryl)hydrazines and 1-silyl-2-borylhydrazines were synthesized using low catalyst loadings, mild temperatures and short reaction times.^[21] Investigations into the reactivity potential of this novel set of compounds are ongoing in our laboratories.

Experimental Section

General Procedure for the Diboration of Azobenzenes

A mixture of **1** (0.5–2 mol%), azobenzene (1 equiv.) and diboron reagent (1.03–1.33 equiv.) was dissolved in deuterated benzene or toluene and stirred at room temperature or 80°C under an N_2 atmosphere. Upon reaching completion the reaction mixtures were cooled, filtered by cannula and the volatiles were removed under vacuum. The crude materials were purified by multiple recrystallizations in minimum volumes of hexane or hexane/toluene (3:1 or 3:2) at room temperature or –30°C.

General Procedure for the Silaboration of Azobenzenes

A mixture of **1** (0.5 mol%), azobenzene (1 equiv.) and (dimethylphenyl)silyl boronic acid pinacol ester (1.13–1.36 equiv.) was dissolved in deuterated benzene or toluene and stirred at room temperature under an N_2 atmosphere. Upon completion, the volatiles were removed under vacuum, deionized water was added and the precipitated mixture was stirred overnight under ambient conditions. The products were isolated, without further purification, after filtration.

Hydrolysis of **2**

Degassed deionized water (10.0 mL) was added to **2** (32 μ mol). The resulting mixture was stirred at room temperature under an argon atmosphere for 48 h. 1,2-Diphenylhydrazine was isolated after filtration.

Base-Driven Alcoholysis of **9**

Hydrazine **9** (0.06 mmol) and KO-*t*-Bu (0.12 mmol) were dissolved in 2-PrOH/toluene (1:1, 2.0 mL) and stirred for 22 h at room temperature under an N₂ atmosphere. The volatiles were removed under vacuum and 1,2-diphenylhydrazine was extracted with hexane. Clean 1,2-diphenylhydrazine was obtained by recrystallization in hexane at -30°C .

Acknowledgements

The authors wish to thank Dr Iain Day (University of Sussex) for helpful discussions. M. B. A. would like to thank the Royal Society of Chemistry (RSC) for a Research Mobility Grant to visit the Braunschweig laboratory at Julius-Maximilians Universität Würzburg, Germany. M. B. A. is funded as an EPSRC Standard Research Student (DTG) under grant no. EP/L505109/1.

References

- [1] a) I. Beletskaya, C. Moberg, *Chem. Rev.* **1999**, *99*, 3435–3462; b) N. Saito, K. Saito, H. Sato, Y. Sato, *Adv. Synth. Catal.* **2013**, *355*, 853–856; c) M. Suginome, H. Nakamura, Y. Ito, *Chem. Commun.* **1996**, 2777–2778; d) T. Ohmura, K. Oshima, M. Suginome, *Chem. Commun.* **2008**, 1416–1418; e) T. Ohmura, K. Oshima, H. Taniguchi, M. Suginome, *J. Am. Chem. Soc.* **2010**, *132*, 12194–12196; f) Q. Cui, D. G. Musaev, K. Morokuma, *Organometallics* **1997**, *16*, 1355–1364; g) R. Barbeyron, E. Benedetti, J. Cossy, J.-J. Vasseur, S. Arseniyadis, M. Smietana, *Tetrahedron* **2014**, *70*, 8431–8452; h) T. B. Marder, N. C. Norman, *Top. Catal.* **1998**, *5*, 63–73.
- [2] a) J. Takaya, N. Iwasawa, *ACS Catal.* **2012**, *2*, 1993–2006; b) M. Oestreich, E. Hartmann, M. Mewald, *Chem. Rev.* **2013**, *113*, 402–441; c) J. Takaya, N. Karai, N. Iwasawa, *J. Am. Chem. Soc.* **2011**, *133*, 12980–12983; d) V. Lillo, E. Mas-Marza, A. M. Segarra, J. J. Carbo, C. Bo, E. Peris, E. Fernández, *Chem. Commun.* **2007**, 3380–3382; e) J. R. Coombs, F. Haeffner, L. T. Kliman, J. P. Morken, *J. Am. Chem. Soc.* **2013**, *135*, 11222–11231.
- [3] a) T. Ohmura, M. Suginome, *Bull. Chem. Soc. Jpn.* **2009**, *82*, 29–49; b) T. Ishiyama, N. Miyaura, *Chem. Rec.* **2004**, *4*, 271–280; c) T. Kliman, S. N. Mlynarski, G. E. Ferris, J. P. Morken, *Angew. Chem.* **2012**, *124*, 536–539; *Angew. Chem. Int. Ed.* **2012**, *51*, 521–524.
- [4] a) A. Costoya, J. Ramos, J. Forcada, *J. Polym. Sci. Part A: Polym. Chem.* **2009**, *47*, 6201–6213; b) A. Staubitz, A. P. Sato, I. Manners, *Angew. Chem.* **2008**, *120*, 6308–6311; *Angew. Chem. Int. Ed.* **2008**, *47*, 6212–6215.
- [5] a) G. Huang, Z. Sun, H. Qin, L. Zhao, Z. Xiong, X. Peng, J. Ou, H. Zou, *Analyst* **2014**, *139*, 2199–2206; b) B. Han, J. F. Stevens, C. S. Maier, *Anal. Chem.* **2007**, *79*, 3342–3354.
- [6] C. Bournaud, D. Robic, M. Bonin, L. Micouin, *J. Org. Chem.* **2005**, *70*, 3316–3317.
- [7] S. Luckert, E. Eversheim, U. Englert, T. Wagner, P. Paetzold, *Z. Anorg. Allg. Chem.* **2001**, *627*, 1815–1823.
- [8] H. Hommer, H. Nöth, H. Sachdev, M. Schmidt, H. Schwenk, *Chem. Ber.* **1995**, *128*, 1187–1194.
- [9] H. Braunschweig, T. Kupfer, *J. Am. Chem. Soc.* **2008**, *130*, 4242–4243.
- [10] G. Wang, H. Zhang, J. Zhao, W. Li, J. Cao, C. Zhu, S. Li, *Angew. Chem.* **2016**, *128*, 6089–6093; *Angew. Chem. Int. Ed.* **2016**, *55*, 5985–5989.
- [11] M. B. Ansell, D. E. Roberts, F. G. N. Cloke, O. Navarro, J. Spencer, *Angew. Chem.* **2015**, *127*, 5670–5674; *Angew. Chem. Int. Ed.* **2015**, *54*, 5578–5582.
- [12] M. B. Ansell, V. H. Menezes da Silva, G. Heerdt, A. A. C. Braga, J. Spencer, O. Navarro, *Catal. Sci. Technol.* **2016**, *6*, 7461–7467.
- [13] M. B. Ansell, J. Spencer, O. Navarro, *ACS Catal.* **2016**, *6*, 2192–2196.
- [14] D. C. Pestana, P. P. Power, *Inorg. Chem.* **1991**, *30*, 528–535.
- [15] A. Mostad, C. Romming, *Acta Chem. Scand.* **1971**, *25*, 3561–3568.
- [16] L. R. Thorne, W. D. Gwinn, *J. Am. Chem. Soc.* **1982**, *104*, 3822–3827.
- [17] S. Berski, Z. Latajka, A. J. Gordon, *New J. Chem.* **2011**, *35*, 89–96.
- [18] a) S. Dielkus, C. Drost, R. Herbst-Irmer, U. Klingebiel, F. Pauer, *Organometallics* **1994**, *13*, 3985–3989; b) J. He, Q. Liu, J. F. Harrod, R. Hynes, *Organometallics* **1994**, *13*, 336–343; c) N. W. Mitzel, H. Schmidbaur, D. W. H. Rankin, B. A. Smart, M. Hofmann, P. von Rague Schleyer, *Inorg. Chem.* **1997**, *36*, 4360–4368.
- [19] a) M. J. Barrow, E. A. V. Ebsworth, *J. Chem. Soc. Dalton Trans.* **1984**, 563–565; b) A. J. Blake, E. A. V. Ebsworth, D. W. H. Rankin, H. E. Robertson, D. E. Smith, A. J. Welch, *J. Chem. Soc. Dalton Trans.* **1986**, 91–95; c) G. P. Clancy, C. S. Clark, G. K. B. Clentsmith, F. G. N. Cloke, P. B. Hitchcock, *J. Chem. Soc. Dalton Trans.* **1999**, 3345–3347.
- [20] I. Maluenda, O. Navarro, *Molecules* **2015**, *20*, 7528–7557.
- [21] CCDC 1501645 (**2**), CCDC 1501646 (**4**), CCDC 1501647 (**9**) and CCDC 1501648 (**11**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.