Synthesis, structure and catalytic activity of a bimacrocylic NHC palladium allyl complex ☆

Ole Winkelmann [a], Christian Näther [b], Ulrich Lüning [a],*

[a] *Otto-Diels-Institut für Organische Chemie, Christian-Albrechts-Universität zu Kiel, Olshausenstr. 40, D-24098 Kiel, Germany*
[b] *Institut für Anorganische Chemie, Christian-Albrechts-Universität zu Kiel, Olshausenstr. 40, D-24098 Kiel, Germany*

A R T I C L E   I N F O

A B S T R A C T

The preparation of a bimacrocyclic NHC palladium allyl complex **4** is described. The complex was obtained by transmetalation with allyl palladium chloride dimer from the NHC silver complex **2** in 85% yield. Complex **4** was fully characterized by spectroscopic methods and by single-crystal X-ray analysis. In a preliminary catalytic study, complex **4** showed high activity in the Suzuki–Miyaura cross-coupling of unactivated aryl chlorides and bromides with 1-naphthalene-boronic acid at low catalyst loading. Good results were also obtained in the Mizoroki–Heck reaction of aryl bromides with styrene, but a decrease in yield was observed when aryl chlorides were used.

© 2008 Elsevier B.V. All rights reserved.

1. Introduction

N-Heterocyclic carbenes (NHCs) have received great attention since the isolation of a crystalline carbene in 1991 by Arduengo [1] and they are nowadays frequently used in either metalfree organocatalysis [2] or as beneficial ligands in organometallic chemistry [3]. As ligands, the nucleophilic NHCs are strong two-electron σ-donors, displaying similar properties as trialkylphosphines [4], and both species are successfully used in palladium catalyzed cross-coupling reactions [5]. In most cases of phosphine-containing catalytic systems, phosphines are used as free ligands in conjunction with a palladium source. In an analogous fashion, catalytically active NHC palladium complexes can be formed *in situ* from a palladium source and an azolium salt as the NHC precursor [6], but recently also a number of well-defined, air- and moisture-stable NHC-bearing palladium complexes with excellent catalytic activities have been reported [7]. In our continuing investigation of the catalytic properties of bimacrocyclic NHCs [8], accessible from the respective azolium precursors [9], we explored the accessibility of bimacrocyclic NHC palladium complexes and their catalytic activity in cross-coupling reactions.

2. Results and discussion

2.1. Synthesis and characterization of palladium complex **4**
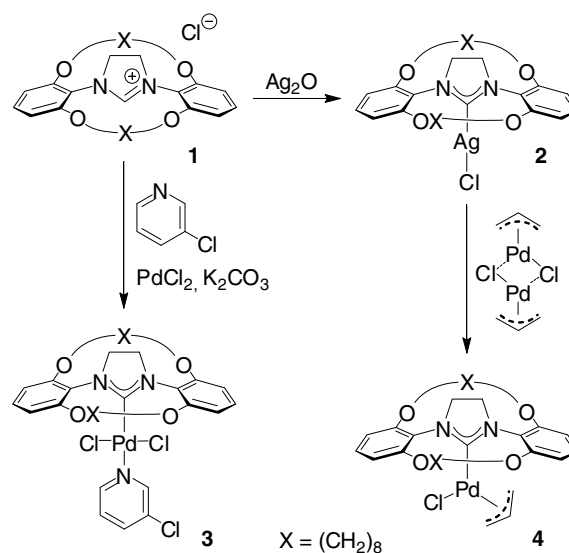
We have recently reported [8] the synthesis of a number of NHC metal complexes derived from the concave bimacrocyclic

---

imidazolinium salt **1**. In contrast to other transition metal complexes, palladium complex **3** was only obtained in poor yield via the free carbene, and **3** was not accessible by transmetalation from silver complex **2** [8]. The use of NHC silver complexes as carbene transfer reagents is a popular method for the synthesis of NHC metal complexes by transmetalation, avoiding the handling of the sensitive free carbenes [10]. However, Nolan and coworkers have reported the synthesis of catalytically active NHC palladium complexes by reaction of the free carbenes with allyl palladium chloride dimer [7e]. We were delighted to find that in an analogous fashion the reaction of silver complex **2** with allyl palladium chloride dimer led to the smooth formation of NHC palladium complex **4** in 85% yield.

In the crystal structure of **4** (see Fig. 1), the asymmetric unit contains two crystallographically independent molecules. Selected bond lengths are given in Table 1. The structure of the NHC ligand in palladium complex **4** is similar to that in complex **3** [8], with the two phenyl substituents oriented almost perpendicular to the heterocycle, and the torsion angles C1–N1–C4–C5 and C1–N2–C23–C22 are 81.42(1)° and 70.89(1)°, respectively. The η^3 coordination of the allyl moiety to the palladium center is comparable to that reported for the respective complex using the SIPr NHC ligand   (SIPr = 1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene) [7e]. The angles C1–Pd1–C32, C1–Pd1–C34 and C34–Pd1–Cl1 are 92.95(10)°, 161.34(10)° and 93.67(9)° in **4**, respectively, C1–Pd1–Cl1 is 104.4(6)° and C32–Pd1–C34 is 68.72(12)°. The internal angle of the heterocycle N1–C1–N2 is 108.03(18)°.

The ^{13}C resonance for the carbene carbon atom of **4** was observed at 211.4 ppm which is significantly more downfield than in palladium complex **3** (183.5 ppm) [8]. A comparison of related palladium complexes with the SIPr NHC ligand shows a very similar trend: the carbene carbon atom resonates at 215.4 ppm when SIPr is incorporated into an allyl palladium complex [7e], but in the 3-chloro-pyridine containing complex this resonance is observed at 184.9 ppm [11]. This drastic difference in chemical shifts ($\Delta\delta$ is 30.5 ppm for SIPr and 27.9 ppm for our bimacrocyclic NHC ligand) must be due to a different electronic situation at the palladium center, caused by the varying ancillary ligands. However,
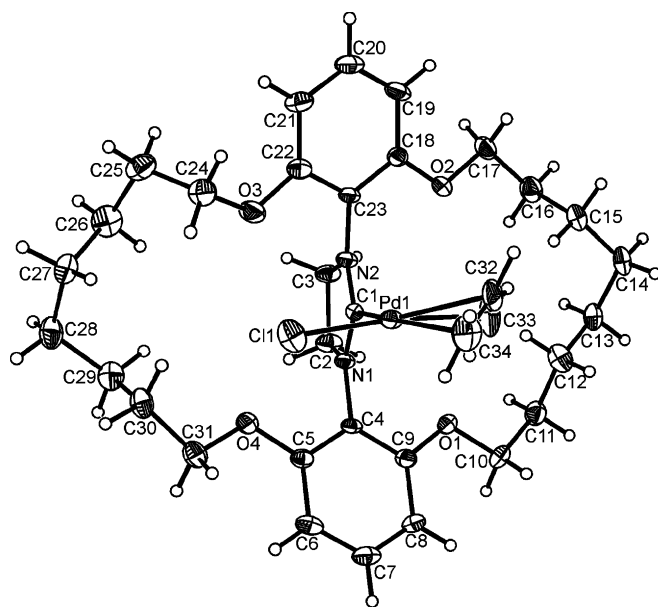
Table 1
Selected bond lengths (Å) for palladium complex **4**

	Pd1[a]	Pd2[a]
Pd–C1/C41	2.045(2)	2.038(2)
Pd–C32/C72	2.105(3)	2.102(3)
Pd–C33/C73	2.142(3)	2.131(3)
Pd–C34/C74	2.211(2)	2.233(2)
Pd–Cl1/Cl2	2.3875(6)	2.3674(6)

[a] Pd1 and Pd2 belong to the respective crystallographically independent complexes.

both kinds of precatalysts are believed to result in the same monoligated NHC–Pd[0]-species as the active catalyst [3a]. A detailed reaction pathway for catalyst activation has been proposed for NHC palladium allyl complexes [7e].

2.2. Catalytic activity of palladium complex **4**

NHC palladium complexes are known to catalyze a number of cross-coupling reactions [3,7]. We decided to investigate the reactivity of complex **4** in Mizoroki–Heck and Suzuki–Miyaura cross-coupling reactions. Complex **3** was not tested in respective reactions due to the small amount of **3** obtained in its synthesis [8]. While the use of aryl chlorides as coupling partners is nowadays established in the latter case [7a,7b,7c,7e], the Mizoroki–Heck olefination of unactivated aryl chlorides is not trivial and mainly bromides and activated chlorides are successfully used in the reaction [7c,12]. The results obtained with catalyst **4** are summarized in Table 2. The olefinations were performed in tetrabutylammonium bromide as an ionic liquid at 140 °C (16 h reaction time), following a protocol by Beller and coworkers [12c]. Using 1 mol% of catalyst **4**, good results were obtained in the reaction of activated and electronically neutral aryl bromides with styrene, and also hindered 2-bromo-toluene afforded 72% of the coupling product. Unfortunately, a decrease in yield was observed when analogous aryl chlorides were used as the coupling partners (Table 2, entries 1 and 2). While activated 4-chloro-acetophenone still afforded 37% of the desired product, only 10% yield of stilbene was obtained with chlorobenzene. The low yields are due to incomplete conversion and could not be raised significantly with higher catalyst loadings (Table 2, entry 1).

In contrast to the low conversion of aryl chlorides observed with catalyst **4** in the olefinations, high yields were obtained in the reaction of aryl chlorides with 1-naphthalene-boronic acid at low catalyst loading in short reaction times (0.2 mol% **4**, 2 h at 60 °C). As we are currently working on an axially chiral modification of the bimacroclic NHC ligand [9b], we were interested in the ability of complex **4** to produce axially chiral biaryls (however, in racemic form). 1,1′-Binaphthyl (Table 2, entry 8) could be produced in 91% yield with 1-bromo-naphthalene, but due to its low barrier of racemization [13] it might not be an appropriate candidate for asymmetric catalysis. When 1-bromo-2-methoxy-naphthalene was reacted with 1-naphthalene-boronic acid, only 21% yield of the desired product was obtained (Table 2, entry 9), along with unreacted bromide and 1,1′-binaphthyl (68%, based on boronic acid), resulting from the homocoupling of the boronic acid. A suppression of this side-reaction might be possible [14], but no efforts were taken yet to improve this yield.

3. Conclusion

The accessibility of the NHC palladium complex **4** by transmetalation from silver complex **2** is a great improvement compared to the synthesis of palladium complex **3** that could only be obtained in poor yield [8]. In the Suzuki–Miyaura cross-coupling reaction of aryl chlorides, the activity of the bimacrocyclic complex **4** is

Fig. 1. Crystal structure of palladium complex **4** with displacement ellipsoids drawn at the 50% probability level. Only one of the two crystallographically independent molecules is represented. The carbon atom C33 of the allyl moiety is disordered in two positions and only the atom of higher occupancy is shown for clarity.

Table 2
Catalytic activity of complex **4** in Mizoroki–Heck[a] and Suzuki–Miyaura[b] cross-coupling reactions

Entry	Substrates		Product	Yield[c]
1				X = Br: 86% X = Cl: 37% (43%)[d]
2				X = Br: 73/% X = Cl: 10%
3				72%
4				79%
5				83%
6				91%
7				92%
8				91%
9				21%

[a] Conditions: Palladium complex **4** (10 μmol), aryl halide (1 mmol), styrene (1.5 mmol), NaOAc (1.2 mmol), KOtBu (0.09 mmol), 16 h at 140 °C in tetrabutylammonium bromide (2 g).
[b] Conditions: Palladium complex **4** (2 μmol), aryl halide (1 mmol), boronic acid (1.2 mmol), KOtBu (1.4 mmol), 2 h at 60 °C in 2-propanol (2 mL).
[c] Isolated yield.
[d] 20 μmol of palladium complex **4**.

comparable to related non-macrocyclic NHC palladium allyl complexes [7e], but the formation of a tri-*ortho*-substituted biaryl proved to be difficult with catalyst **4** in this preliminary study. In the Mizoroki–Heck reaction, high yields of the desired coupling products were obtained with aryl bromides, while a decrease in yield was observed with the use of analogous aryl chlorides. As the catalytic activity of complex **4** in cross-coupling reactions shows promise, we are currently focusing on a chiral version of the bimacrocyclic NHC ligand for respective asymmetric reactions [9b].

4. Experimental

4.1. General

The NHC silver complex **2** [8] and allyl palladium chloride dimer [7b] were prepared according to the literature. ^{1}H and ^{13}C NMR spectra were recorded with Bruker DRX 500 or ARX 300 instruments at room temperature and are referenced to tetramethylsilane. NMR multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, m$_{(c)}$ = multiplet (centered), br = broad

signal. The following abbreviations are used for assignments: Ar = aromatic, Im = imidazolidin. Mass spectra were recorded with a Finnigan MAT 8200 or MAT 8230. IR spectra were recorded with a Perkin–Elmer Paragon 1000 spectrometer. Elemental analyses were carried out with an EuroEA 3000 Elemental Analyzer from Euro Vector.

4.2. Synthesis of η^3-allyl-chloro-(2,11,13,22-tetraoxa-1,12(1,3,2)-dibenzena-23-(1,3)-imidazolidina-bicyclo[10.10.1]-tricosaphane-23^2-ylidene)palladium(II) (**4**)

To a stirred solution of allyl palladium chloride dimer (24 mg, 65 μmol) in dichloromethane (1 mL) was added silver complex **2** (90 mg, 0.14 mmol), dissolved in dichloromethane (5 mL). After stirring for 1 h at room temperature, the mixture was passed through a short pad of silica gel, and the silica gel was rinsed with dichloromethane. The filtrate was concentrated *in vacuo* and the product was precipitated by addition of *n*-pentane. The precipitate was washed with *n*-pentane and dried *in vacuo*. A yellow solid was obtained. Yield: 75 mg (0.11 mmol, 85%).

M.p. 115 °C (decomp.). ^{1}H NMR (500 MHz, CDCl$_3$): δ (ppm) = 7.17 (t, ^3J = 8.4 Hz, 2H, Ar-*H*-4), 6.52 (d, ^3J = 8.4 Hz, 4H, Ar-*H*-3,5), 4.68 (m$_c$, 1H, C*H*$_{allyl}$), 4.14 (m$_c$, 4H, OC*H$_2$*), 4.05–3.90 (m, 8H, OC*H$_2$*, Im-*H*-4,5), 3.67 (d, ^3J = 7.3 Hz, 1H, HC*H*$_{allyl}$), 3.24 (br s, 1H, HC*H*$_{allyl}$), 2.61 (d, ^3J = 13.4 Hz, 1H, HC*H*$_{allyl}$), 1.94 (m$_c$, 4H, C*H$_2$*), 1.80–1.60 (m, 9H, HC*H*$_{allyl}$, C*H$_2$*), 1.55–1.45 (m, 12H, C*H$_2$*). ^{13}C NMR (125 MHz, CDCl$_3$): δ (ppm) = 211.4 (Im-*C*-2), 157.2 (Ar-*C*-2,6), 128.9 (Ar-*C*-4), 118.5 (Ar-*C*-1), 113.9 (*C*H$_{allyl}$), 104.0 (Ar-*C*-3,5), 70.2 (*C*H$_{2\,allyl}$), 68.2 (O*C*H$_2$), 68.0 (O*C*H$_2$), 50.7 (Im-*C*-4,5), 48.7 (*C*H$_{2\,allyl}$), 28.7, 28.5, 26.4, 23.6 (*C*H$_2$). IR (KBr): $\tilde{\nu}$ (cm^{-1}) = 3069, 2934, 2855, 1594, 1503, 1461, 1387, 1297, 1102, 776, 731. Anal. Calc. for C$_{34}$H$_{47}$ClN$_2$O$_4$Pd (689.64): C, 59.22; H, 6.87; N, 4.06. Found: C, 59.42; H, 7.01; N, 4.18%.

4.3. General procedure for Mizoroki–Heck cross-coupling reactions

A flask was charged with styrene (156 mg, 1.50 mmol), tetrabutylammonium bromide (2 g), sodium acetate (99 mg, 1.2 mmol), potassium *tert*-butoxide (10 mg, 89 μmol), palladium complex **4** (7 mg, 0.01 mmol) and the aryl halide (1.0 mmol). The flask was flushed with nitrogen, sealed with a rubber septum and heated to 140 °C for 16 h. After cooling to room temperature, the mixture was triturated in water (10 mL) and extracted with diethyl ether (3 × 15 mL). The organic layer was dried with magnesium sulfate, the solvent was evaporated *in vacuo* and the product was purified by column chromatography on silica gel. The purity and identity of previously described *E*-stilbene [12c], *E*-*p*-acetyl-stilbene [12c], *E*-*o*-methyl-stilbene [12b] and 1-*E*-styryl-naphthalene [15] was confirmed by ^{1}H NMR and mass spectrometric analysis.

4.4. General procedure for Suzuki–Miyaura cross-coupling reactions

A flask was charged with potassium *tert*-butoxide (154 mg, 1.37 mmol), boronic acid (1.2 mmol) and palladium complex **4** (1.4 mg, 2.0 μmol). The flask was flushed with nitrogen and sealed with a rubber septum. Via syringe 2-propanol (1 mL) was added and the mixture was stirred at room temperature. After 5 min, the aryl halide (1.0 mmol), dissolved in 2-propanol (1 mL), was injected via syringe and the mixture was heated to 60 °C for 2 h. After cooling to room temperature, water (10 mL) was added to the mixture and it was extracted with dichloromethane (3 × 15 mL). The organic layer was dried with magnesium sulfate, the solvent was evaporated *in vacuo* and the product was purified by column chromatography on silica gel. The purity and identity of previously described 1-phenyl-naphthalene [7b], 1-*o*-tolyl-naphthalene [7a], 1-*p*-tolyl-naphthalene [16], 1,1′-binaphthyl [7b] and 2-methoxy-

Table 3
Crystallographic data for palladium complex **4**

Formula	C$_{34}$H$_{47}$ClN$_2$O$_4$Pd
Formula weight (g/mol)	689.59
Color/habit	yellow/block
Crystal size (mm)	0.13 × 0.11 × 0.09
Crystal system	monoclinic
Space group	$P2_1/c$ (no. 14)
a (Å)	28.5370(15)
b (Å)	9.0128(5)
c (Å)	26.3644(12)
α (°)	90
β (°)	105.489(6)
γ (°)	90
V (Å^3)	6534.6(6)
Z	8
T (K)	170(2)
μ (mm^{-1})	0.689
θ Range (°)	1.94–26.00
Index ranges (h,k,l)	±35, ±11, ±31
Measured reflections	49934
Independent reflections	12515
R_{int}	0.0340
Reflections with [$I > 2\sigma(I)$]	10898
Parameters	762
$R_1wR_2[[I > 2\sigma(I)]^a$	0.0318/0.0841
R_1wR_2 (all data)^a	0.0376/0.0872
GOF (on F^2)^a	1.044
Largest difference in peak and hole (e Å^{-3})	+0.826 and −0.775

^{a} $R_1 = \sum(||F_o| - |F_c||)/\sum|F_o|$; $wR_2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum w(F_o^2)^2]\}^{1/2}$; GOF = $\{\sum[w(F_o^2 - F_c^2)^2]/(n - p)]\}^{1/2}$.

1,1′-binaphthyl [17] was confirmed by ^{1}H NMR and mass spectrometric analysis.

4.5. Single-crystal X-ray structure determination of complex **4**

General: Crystal data and details of the structure determination are given in Table 3. Suitable single crystals were grown by slow diffusion of *n*-pentane into a solution of **4** in chloroform. Data collection was performed using an STOE Imaging Plate Diffraction System (IPDS-1) with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). Structure solutions were performed with direct methods using SHELXS-97. Structure refinements were performed against F^2 with SHELXL-97 [18]. One of the allylic carbon atoms is disordered in two positions and was refined using a split model. All non-hydrogen atoms except the disordered carbon atom of lower occupancy were refined anisotropically. The hydrogen atoms were placed in ideal positions and refined using a riding model. The asymmetric unit contains two crystallographically independent molecules.

5. Supplementary material

CCDC 680552 contains the supplementary crystallographic data for **4**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

References

[1] A.J. Arduengo III, R.L. Harlow, M. Kline, J. Am. Chem. Soc. 113 (1991) 361.
[2] (a) N. Marion, S. Diez-Gonzáles, S.P. Nolan, Angew. Chem., Int. Ed. 46 (2007) 2988;
(b) V. Nair, S. Bindu, V. Sreekumar, Angew. Chem., Int. Ed. 43 (2004) 5130;
(c) D. Enders, T. Balensiefer, Acc. Chem. Res. 37 (2004) 534.
[3] Recent reviews: (a) E.A.B. Kantchev, C.J. O'Brien, M.G. Organ, Angew. Chem., Int. Ed. 46 (2007) 2768;
(b) N.M. Scott, S.P. Nolan, Eur. J. Inorg. Chem. (2005) 1815;
(c) V. César, S. Bellemin-Laponnaz, L.H. Gade, Chem. Soc. Rev. 33 (2004) 619;
(d) W.A. Herrmann, Angew. Chem., Int. Ed. 41 (2002) 1290;

(e) D. Bourissou, O. Guerret, F.P. Gabbai, G. Bertrand, Chem. Rev. 100 (2000) 39;
(f) T. Weskamp, V.P.W. Böhm, W.A. Herrmann, J. Organomet. Chem. 600 (2000) 12.

[4] K. Öfele, W.A. Herrmann, D. Mihalios, M. Elison, E. Herdtweck, W. Scherer, J. Mink, J. Organomet. Chem. 459 (1993) 177.

[5] G.C. Fu, A.F. Littke, Angew. Chem., Int. Ed. 41 (2002) 4176.

[6] C. Zhang, J. Huang, M.L. Trudell, S.P. Nolan, J. Org. Chem. 64 (1999) 3804.

[7] (a) C.J. O'Brien, E.A.B. Kantchev, C. Valente, N. Hadei, G.A. Chass, A. Lough, A.C. Hopkinson, M.G. Organ, Chem. Eur. J. 12 (2006) 4743;
(b) N. Marion, O. Navarro, J. Mei, E.D. Stevens, N.M. Scott, S.P. Nolan, J. Am. Chem. Soc. 128 (2006) 4101;
(c) G.D. Frey, J. Schütz, E. Herdtweck, W.A. Herrmann, Organometallics 24 (2005) 4416;
(d) O. Navarro, R.A. Kelly III, S.P. Nolan, J. Am. Chem. Soc. 125 (2003) 16194;
(e) M.S. Viciu, R.F. Germaneau, O. Navarro-Fernandez, E.D. Stevens, S.P. Nolan, Organometallics 21 (2002) 5470.

[8] O. Winkelmann, C. Näther, U. Lüning, J. Organomet. Chem. 693 (2008) 923.

[9] (a) O. Winkelmann, C. Näther, U. Lüning, Eur. J. Org. Chem. (2007) 981;
(b) O. Winkelmann, D. Linder, J. Lacour, C. Näther, U. Lüning, Eur. J. Org. Chem. (2007) 3687.

[10] I.J.B. Lin, C.S. Vasam, Coord. Chem. Rev. 251 (2007) 642.

[11] No signal was reported in the literature for the carbene carbon atom of the respective NHC palladium complex. Following the synthetic protocol from the literature, the aforementioned complex ("PEPPSI-SIPr") was obtained and the respective resonance could be observed undoubtedly at 184.9 ppm (150 MHz, CDCl$_3$). Except for the missing resonance of the carbene carbon atom, all spectroscopic data are in perfect agreement with our findings: M.G. Organ, M. Abdel-Hadi, S. Avola, N. Hadei, J. Nasielski, C.J. O'Brien, C. Valente, Chem. Eur. J. 13 (2007) 150.

[12] (a) W.A. Herrmann, M. Elison, J. Fischer, C. Köcher, G.R.J. Artus, Angew. Chem., Int. Ed. Engl. 34 (1995) 2371;
(b) C. Yang, S.P. Nolan, Synlett 10 (2001) 1539;
(c) K. Selvakumar, A. Zapf, M. Beller, Org. Lett. 4 (2002) 3031;
(d) G. Zou, W. Huang, Y. Xiao, J. Tang, New. J. Chem. 30 (2006) 803;
(e) C. Wang, Y. Liu, S. Peng, J. Chen, S. Liu, J. Organomet. Chem. 692 (2007) 3976.

[13] A.S. Cooke, M.M. Harris, J. Chem. Soc. (1963) 2365.

[14] W.D. Miller, A.H. Fray, J.T. Quatroche, C.D. Sturgill, Org. Process Res. Dev. 11 (2007) 359.

[15] S.R. Dubbaka, P. Vogel, Chem. Eur. J. 11 (2005) 2633.

[16] C. Cho, H. Yun, K. Park, J. Org. Chem. 68 (2003) 3017.

[17] H. Li, Y. Wu, W. Yan, J. Organomet. Chem. 691 (2006) 5688.

[18] G.M. Sheldrick, SHELXL-97, Universität Göttingen, Göttingen, Germany, 1998.