Asymmetric Auto-Tandem Catalysis

DOI: 10.1002/ange.201300485

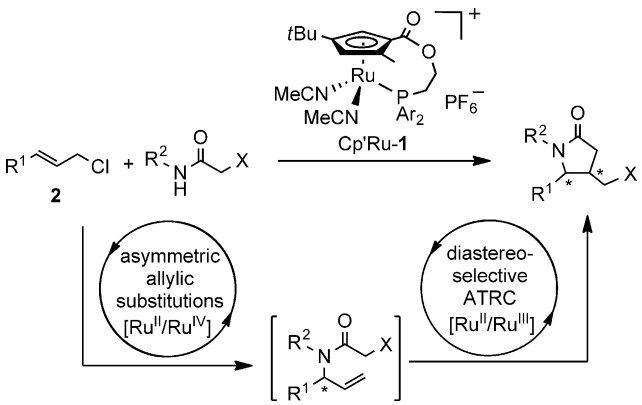
Asymmetric Auto-Tandem Catalysis with a Planar-Chiral Ruthenium Complex: Sequential Allylic Amidation and Atom-Transfer Radical Cyclization**

Naoya Kanbayashi, Kazuhiro Takenaka, Taka-aki Okamura, and Kiyotaka Onitsuka**

The efficient synthesis of complex molecules with multiple stereogenic centers is a challenging task in synthetic organic chemistry. One-pot reactions have received considerable attention for the improvement of reaction efficiency, because they can avoid time-consuming workups and the often formidable isolation of intermediary products.[1] A representative example is domino catalysis, in which two or more mechanistically similar reactions proceed in only one operation.[1,2] Another method, auto-tandem catalysis is also an ideal and eco-friendly synthetic process, which involves two or more mechanistically distinct reactions promoted by only a single catalyst.[3] Despite numerous examples of domino catalysis, there are limited numbers of reports on auto-tandem catalysis,[4] this is probably due to the difficulty of optimizing the reaction conditions.

We have shown that planar-chiral cyclopentadienylruthenium (Cp′Ru) complex **1** is a proficient catalyst for asymmetric allylic substitutions.[5,6] Recently, we succeeded in the development of regio- and enantioselective reactions of monosubstituted allylic halides with oxygen nucleophiles, which produced enantiomerically enriched branched allylic ethers, esters, and alcohols in good yields.[7] These products possess a reactive terminal olefin, which can be potentially applied in a further transformation.[7d,8] As the catalytic activity of **1** is preserved, even at the end of the allylic substitution,[7b] and ruthenium complexes show various desirable oxidation states for catalytic behavior,[9] we conceived an extension of our system to auto-tandem asymmetric catalysis. As a candidate for the transformation of a terminal olefin on a branched allylic compound, we focused on the atom-transfer radical cyclization (ATRC) because half-sandwiched Ru complexes similar to **1** are known to promote this reaction.[10] ATRC is an atom-economical method for the formation of cyclic compounds, which proceeds under mild conditions and exhibits broad functional group tolerance. Hence, it was hypothesized that complex **1** could realize an asymmetric auto-tandem catalysis consisting of allylic substitution and ATRC.

To test this theory, we envisioned the facile synthesis of optically active γ-lactams, an important structural motif found in a variety of biologically active molecules.[11] Nagashima and co-workers reported that ATRC reaction of branched allylic amides using a Ru catalyst proceeded diastereoselectively,[12,13] with the configuration at the new stereogenic carbon controlled by the stereochemistry of the substrate. The preparation of optically active allylic amides by **1**-catalyzed enantioselective allylic amidation would therefore provide γ-lactams with multiple stereogenic centers in a pure form through **1**-catalyzed ATRC (Scheme 1). Herein, we report



Scheme 1. Synthesis of enantiomerically enriched γ-lactams through auto-tandem asymmetric catalysis using **1**.

a sequential regio-, enantio-, and diastereoselective reaction of allylic chlorides with amide derivatives promoted by a single catalyst, **1**, and involving completely different reaction mechanisms. To the best of our knowledge, this is a novel example of asymmetric auto-tandem catalysis.

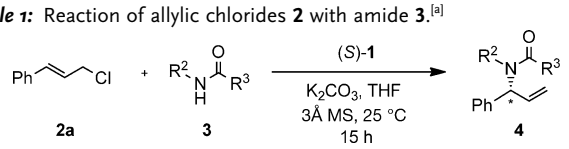
To accomplish the asymmetric auto-tandem catalysis, we initially examined the enantioselective allylic amidation[13–15] of cinnamyl chloride (**2a**) using (*S*)-**1** (Ar = 3,5-$Me_2C_6H_3$) as the catalyst. After optimization of the conditions in the reaction of trifluoroacetoamide (**3a**), we observed the formation of desired branched allylic amide **4a** with high regio- and enantioselectivity. Thus, treatment of **2a** and **3a** with (*S*)-**1** (1 mol%) in the presence of K_2CO_3 and 3 Å molecular

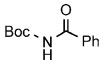
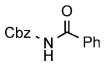
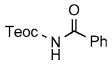
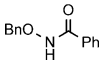
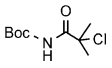
[*] N. Kanbayashi, Dr. T. Okamura, Prof. K. Onitsuka
Department of Macromolecular Science
Graduate School of Science, Osaka University
Machikaneyama 1-1, Toyonaka
Osaka 560-0043 (Japan)
E-mail: tokamura@chem.sci.osaka-u.ac.jp
onitsuka@chem.sci.osaka-u.ac.jp
Dr. K. Takenaka
The Institute of Scientific and Industrial Research (ISIR)
Osaka University, Mihogaoka, Ibaraki, Osaka 567-0047 (Japan)

[**] This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology (Japan), and partly by the Sumitomo Foundation and a JSPS Research Fellowship.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201300485.

Table 1: Reaction of allylic chlorides **2** with amide **3**.[a]



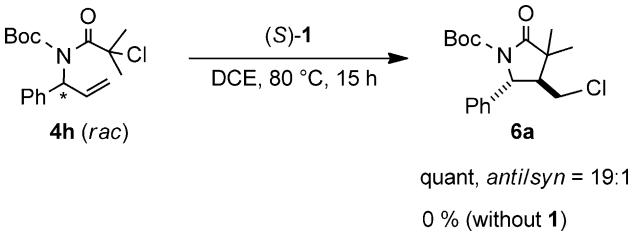
Entry	3		Yield [%][b,c]	*ee* [%][d]
1		(**3a**)	80 (**4a**)	98 (*R*)[f]
2		(**3b**)	0 (**4b**)	–
3		(**3c**)	99 (**4c**)	96
4		(**3d**)	90 (**4d**)	96
5		(**3e**)	99 (**4e**)	96
6[e]		(**3f**)	99 (**4f**)	95 (*R*)[f]
7		(**3g**)	99 (**4g**)	96 (*R*)[f]
8		(**3h**)	96 (**4h**)	98

[a] Reaction conditions: (*S*)-**1** (5 μmol), **2** (0.60 mmol), **3** (0.50 mmol), K_2CO_3 (0.6 mmol), THF (2.0 mL), 25 °C, 15 h. [b] Yield of isolated product. [c] In each case, the branched product was selectively formed (branched/linear > 20:1). [d] Determined by HPLC analysis on a chiral stationary phase. [e] $KHCO_3$ was used instead of K_2CO_3. [f] Absolute configuration determined by comparison of the specific rotation with literature values.

sieves (3 Å MS) at 25 °C in THF afforded **4a** in 80 % yield with 98 % *ee* (Table 1, entry 1). However, benzamide (**3b**) did not react at all under otherwise identical conditions (entry 2). These observations implied the crucial role of the acidity of the amide NH group in this catalysis. Amides **3c**–**f**, protected with *tert*-butoxycarbonyl (Boc), carboxybenzyl (Cbz), trimethylsilylethoxycarbonyl (Teoc), or benzyloxy (BnO) groups, could be used as nucleophiles to produce the corresponding allylic amides **4c**–**f** in excellent yields with high enantioselectivities (entries 3–6). Moreover, reaction with phthalimide (**3g**), which is known as an ammonia equivalent, also proceeded smoothly to give **4g** quantitatively (entry 7). The substrate α-chloroamide (**3h**) was also applicable to this reaction without any loss in yield or enantioselectivity; amide **4h**, which bears a terminal olefin and chloroalkyl group, was obtained in 96 % yield with 98 % *ee* (entry 8).

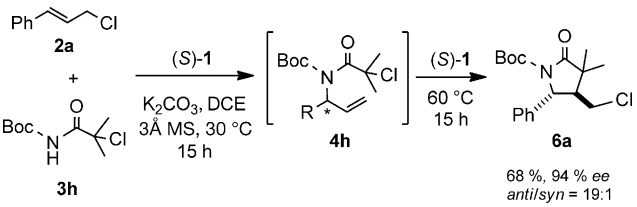
To realize asymmetric auto-tandem catalysis, we next investigated the catalytic activity of **1** in ATRC. When racemic **4h** was heated at 80 °C in 1,2-dichloroethane (DCE) with **1** (1 mol %) for 15 h, ATRC took place to give γ-lactam **6a** diastereoselectively and in quantitative yield (Scheme 2). No reaction was observed without the use of **1**, which strongly indicates that complex **1** indeed worked as a catalyst in this ATRC.

As Cp′Ru complex **1** turned out to be an effective catalyst in both the allylic amidation and ATRC, we applied it in the asymmetric auto-tandem catalysis. To our delight, when the



Scheme 2. Atom-transfer radical cyclization catalyzed by Cp′Ru complex **1**.

reaction mixture was warmed to 60 °C after the asymmetric allylic amidation reaction of **2a** with α-chloroamide **3h**, the ATRC reaction proceeded successively. The target γ-lactam **6a** was obtained in 68 % yield with 94 % *ee* and 19:1 d.r., with the *anti* diastereomer predominantly formed (Scheme 3).

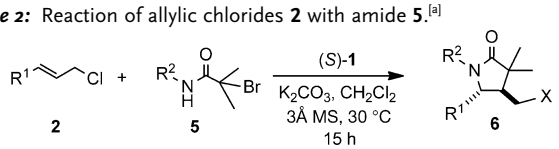


Scheme 3. Asymmetric auto-tandem catalysis.

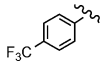
Subsequently, we examined a more reactive substrate for ATRC, α-bromoamide **5**, in an effort to simplify this auto-tandem catalysis. The auto-tandem reaction of **2a** with α-bromoamide **5a** was found to take place at 30 °C, leading to the diastereo- and enantioselective formation of γ-lactam **6b** (*anti*/*syn* = 19:1, *anti* isomer formed with 92 % *ee*) along with ca. 20 % of the chloride analogue **6a** in 99 % combined yield (Table 2, entry 1).[16] Upon recrystallization, the diastereo- and enantiopurities of product **6b** were improved to > 20/1 d.r. and > 99 % *ee*. The substrate scope of this auto-tandem reaction is summarized in Table 2. In each case, the desired γ-lactam was obtained quantitatively as an inseparable mixture of the bromide and the chloride forms, and with high diastereo- and enantioselectivities. The α-bromoamide substrate **5b**, which bears a Cbz protecting group, produced optically active γ-lactam **6c**, whose absolute configuration was unequivocally determined to be (*R*,*R*) by X-ray crystallographic analysis of an enantiomerically pure sample.[17] Various allylic chlorides were applicable to the auto-tandem catalysis, aryl-substituted γ-lactams **6d**–**f**, as well as alkyl-substituted **6g** were obtained with high diastereo- and enantioselectivities (entries 3–6).

Although a small amount of the chloride analogue accompanied the major product in this reaction, the mixture was easily transformed into a sole product (**7**) through a reductive dehalogenation reaction. The treatment of optically pure γ-lactam **6b**, whether Br or Cl atoms were present on the side chain, with nBu$_3$SnH and a catalytic amount of 2,2′-azobis(isobutyronitrile) (AIBN) in toluene at 110 °C resulted in the formation of **7** in 88 % yield without racemization (Scheme 4).

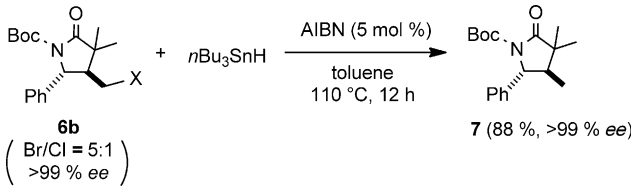
Table 2: Reaction of allylic chlorides **2** with amide **5**.[a]



2 **5** **6**

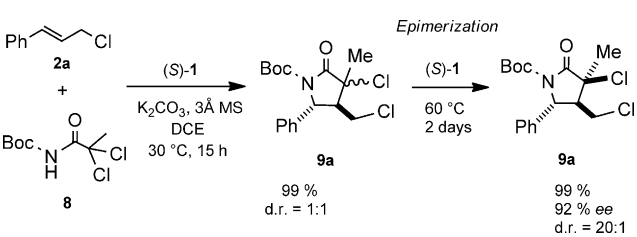
Entry	R^1		R^2	Yield [%][b]	*anti*/*syn*[c]	Br/Cl[d,e]	*ee* [%][f]
1	Ph	(**2a**)	Boc (**5a**)	99 (**6b**) (85)	19:1 (>20:1)	5:1	92 (>99)
2	Ph	(**2a**)	Cbz (**5b**)	99 (**6c**) (93)	19:1 (>20:1)	10:1	93 (>99) (*R*,*R*)[g]
3		(**2b**)	Boc (**5a**)	99 (**6d**) (75)	20:1 (>20:1)	5:1	92 (96)
4		(**2c**)	Boc (**5a**)	94 (**6e**) (68)	20:1 (>20:1)	10:1	94 (96)
5		(**2d**)	Boc (**5a**)	99 (**6f**) (67)	11:1 (>20:1)	10:1	89 (>99)
6		(**2e**)	Cbz (**5b**)	99 (**6g**) (67)[h]	10:1 (>20:1)	>20:1	91

[a] Reaction conditions: (*S*)-**1** (5 μmol), **2** (0.60 mmol), **5** (0.50 mmol), K_2CO_3 (0.60 mmol), CH_2Cl_2 (2.0 mL), 30 °C, 15 h. [b] Determined by ^{1}H NMR spectroscopy, the combined yield of isolated Br and Cl species is given in parentheses. [c] Determined by ^{1}H NMR spectroscopy of the crude product. The d.r. of isolated products is shown in parentheses. [d] Br: X = Br, Cl: X = Cl. [e] Determined by ^{1}H NMR spectroscopy. [f] Determined by HPLC analysis on a chiral stationary phase. The *ee* of isolated products is shown in parentheses. [g] Absolute configuration determined by X-ray crystallographic analysis.



Scheme 4. Reductive dehalogenation of **6b**. Br/Cl refers to the ratio of products where X = Br or Cl.

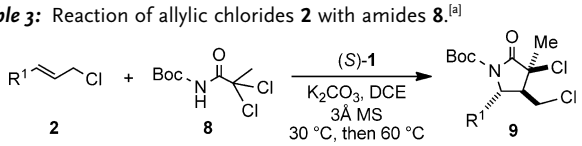
Finally, we examined the reactivity of α-dichloroamide **8** in this asymmetric auto-tandem catalysis, which would produce a γ-lactam with three consecutive stereogenic centers. When the reaction of **8** with **2a** was carried out under conditions similar to those in Table 2, the desired γ-lactam **9a** was obtained quantitatively (Scheme 5). The diastereomeric ratio at the carbon atom adjacent to the carbonyl group, however, was as low as 1:1. We were pleased



Scheme 5. Control of three stereogenic centers in tandem catalysis. Yields shown were determined by ^{1}H NMR spectroscopy.

to find that the epimerization of **9a** occurred at a slightly higher temperature in the presence of **1** to afford the thermodynamically stable diastereomer.[18] Thus, heating of the reaction mixture at 60 °C for 2 days after the auto-tandem catalysis increased the diastereomeric ratio to 20:1. X-ray crystallographic analysis of enantio- and diastereopure **9c** established its relative and absolute configurations.[17] With the favorable conditions for the production of γ-lactam **9** in hand, we conducted the reaction of several cinnamyl chloride derivatives with **8** (Table 3). Although the diastereoselectivity was not so high even after the epimerization, recrystallization of the products furnished γ-lactam **9b–d** with excellent diastereo- and enantiopurities.

Table 3: Reaction of allylic chlorides **2** with amides **8**.[a]



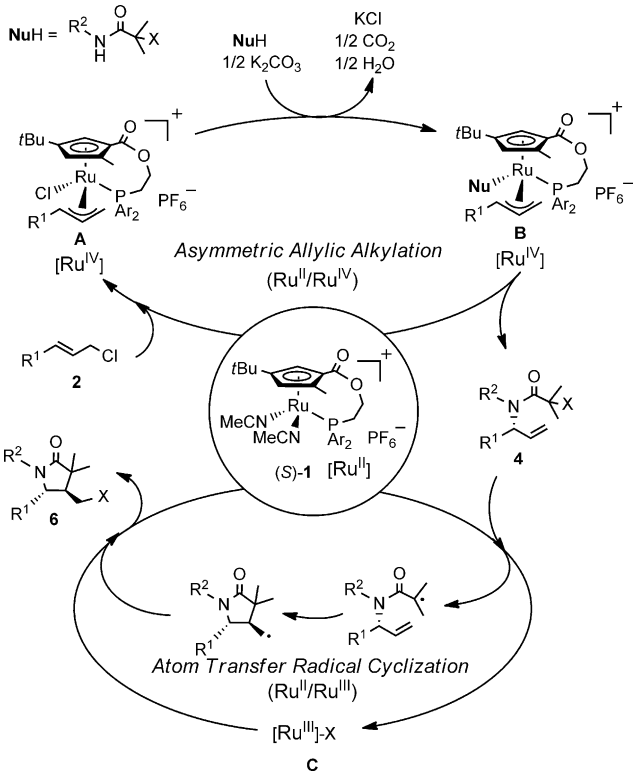
2 **8** **9**

Entry	R^1		Yield [%][b]	d.r.[c]	*ee* [%][d]
1	Ph	(**2a**)	99 (**9a**) (68)	20:1 (>20:1)	92 (99)
2		(**2b**)	99 (**9b**) (54)	6:1 (>20:1)	–[e] (92)
3		(**2c**)	94 (**9c**) (53)	6:1 (>20:1)	92 (>99) (*R*,*R*)[f]
4		(**2d**)	99 (**9d**) (66)	4:1 (>20:1)	91 (>99)

[a] Reaction conditions: (*S*)-**1** (5 μmol), **2** (0.50 mmol), K_2CO_3 (0.60 mmol), 1,2-dichloroethane (2.0 mL), 30 °C, 15 h. [b] Determined by ^{1}H NMR spectroscopy, yield of isolated products is given in parentheses. [c] Diastereomeric ratio at the 3 position determined by ^{1}H NMR spectroscopy of the crude product. The d.r. of isolated products is shown in parentheses. [d] Determined by HPLC analysis on a chiral stationary phase. The *ee* of isolated products is shown in parentheses. [e] Not determined. [f] Absolute configuration determined by X-ray crystallographic analysis.

A proposed reaction mechanism is shown in Scheme 6. Oxidative addition of **2** to (*S*)-**1** forms key π-allylic intermediate **A**,[7] and triggers this auto-tandem asymmetric catalysis. Subsequent "inside" attack of the amidate by Ru amidate complex **B** gives the initial product, branched allyl amide **4**.[7] The high enantioselectivity and the absolute configuration of the final product can be determined at the allylic amidation stage. The atom transfer reaction between (*S*)-**1** and **4** then furnishes [Ru^{III}]–X intermediate **C** and a tertiary radical species, of which the latter reacts with the terminal olefin in an intramolecular fashion. Finally, the X atom on [Ru^{III}] complex **C** recombines with the resulting primary radical to yield γ-lactam **6**.

In conclusion, we have developed an asymmetric auto-tandem allylic amidation/ATRC reaction, which proceeds in a highly regio-, diastereo-, and enantioselective manner, catalyzed solely by planar-chiral Cp′Ru complex **1**. Optically active γ-lactams are constructed from readily available substrates in one pot. A characteristic redox property of ruthenium complexes may work expediently in different types



Scheme 6. Proposed reaction mechanism of asymmetric auto-tandem catalysis.

of catalyses involving mechanistically distinct allylic substitutions (Ru^{II}/Ru^{IV}) and atom-transfer radical cyclizations (Ru^{II}/Ru^{III}), thus leading to the present asymmetric auto-tandem reaction. The results demonstrate that asymmetric auto-tandem catalysis is an atom-economical and environmentally benign synthetic method for producing useful chiral compounds. Further development of the auto-tandem reaction using other asymmetric allylic substitutions promoted by catalyst **1** is now in progress.

Experimental Section

General procedure: A solution of allylic chloride (0.50 mmol) in THF (2.0 mL) was added to a mixture of K_2CO_3 (0.60 mmol), (*S*)-**1** (5 μmol, 1 mol%), amide (0.60 mmol), and 3 Å MS, and then stirred for 15 h at 30 °C. After dilution with diethyl ether, the reaction mixture was filtered through Celite and the filtrate was concentrated under reduce pressure. The residue was purified by silica gel column chromatography (using a solvent gradient from toluene up to 7:3 Hex/EtOAc) followed by recrystallization from *n*-hexane to give a colorless crystal.

Received: January 19, 2013
Published online: March 28, 2013

Keywords: allylic amidation · asymmetric synthesis · auto-tandem · radical reactions · ruthenium

[1] For reviews, see: a) L. F. Tietze, U. Beifuss, *Angew. Chem.* **1993**, *105*, 137 – 170; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 131 – 163; b) L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115 – 136; c) L. F. Tietze, G. Brasche, K. M. Gericke in *Domino Reactions in Organic Synthesis*, Wiley-VCH, Weinheim, **2006**; d) K. C. Nicolaou, D. J. Edmonds, P. Bulger, *Angew. Chem.* **2006**, *118*, 7292 – 7344; *Angew. Chem. Int. Ed.* **2006**, *45*, 7134 – 7186; e) H. Pellissier, *Adv. Synth. Catal.* **2012**, *354*, 237 – 294.

[2] In this manuscript, the reactions below are classified as domino reactions, because the catalyst conducts two or more mechanistically similar reactions: a) D. Enders, M. Hüttl, C. Grondal, G. Raabe, *Nature* **2006**, *441*, 861 – 863; b) H. Guo, J. Ma, *Angew. Chem.* **2006**, *118*, 362 – 375; *Angew. Chem. Int. Ed.* **2006**, *45*, 354 – 366; c) S. E. Denmark, A. Thorarensen, *Chem. Rev.* **1996**, *96*, 137 – 165.

[3] The term "Tandem catalysis" was defined by Fogg and Santos. In this manuscript, we follow their classification. For reviews on tandem catalysis, see: a) D. E. Fogg, E. N. dos Santos, *Coord. Chem. Rev.* **2004**, *248*, 2365 – 2379; b) A. Ajamian, J. L. Gleason, *Angew. Chem.* **2004**, *116*, 3842 – 3848; *Angew. Chem. Int. Ed.* **2004**, *43*, 3754 – 3760; c) J.-C. Wasilke, S. J. Obrey, R. T. Baker, G. C. Bazan, *Chem. Rev.* **2005**, *105*, 1001 – 1020; d) N. Shindoh, Y. Takemoto, K. Takasu, *Chem. Eur. J.* **2009**, *15*, 12168 – 12179; e) J. Zhou, *Chem. Asian J.* **2010**, *5*, 422 – 434.

[4] For selected examples of auto-tandem catalysis, see: a) P. A. Evans, J. E. Robinson, *J. Am. Chem. Soc.* **2001**, *123*, 4609 – 4610; b) B. A. Seigal, C. Fajardo, M. L. Snapper, *J. Am. Chem. Soc.* **2005**, *127*, 16329 – 16332; c) S. Fustero, D. Jiménez, M. Sánchez-Rosellò, C. del Pozo, *J. Am. Chem. Soc.* **2007**, *129*, 6700 – 6701; d) J.-R. Chen, C.-F. Li, X.-L. An, J.-J. Zhang, X.-Y. Zhu, W.-J. Xiao, *Angew. Chem.* **2008**, *120*, 2523 – 2526; *Angew. Chem. Int. Ed.* **2008**, *47*, 2489 – 2492.

[5] a) N. Dodo, Y. Matsushima, M. Uno, K. Onitsuka, S. Takahashi, *J. Chem. Soc. Dalton Trans.* **2000**, 35 – 41; b) Y. Matsushima, N. Komatsuzaki, Y. Ajioka, M. Yamamoto, H. Kikuchi, Y. Takata, N. Dodo, K. Onitsuka, M. Uno, S. Takahashi, *Bull. Chem. Soc. Jpn.* **2001**, *74*, 527 – 537.

[6] a) Y. Matsushima, K. Onitsuka, T. Kondo, T. Mitsudo, S. Takahashi, *J. Am. Chem. Soc.* **2001**, *123*, 10405 – 10406; b) K. Onitsuka, Y. Matsushima, S. Takahashi, *Organometallics* **2005**, *24*, 6472 – 6474.

[7] a) K. Onitsuka, H. Okuda, H. Sasai, *Angew. Chem.* **2008**, *120*, 1476 – 1479; *Angew. Chem. Int. Ed.* **2008**, *47*, 1454 – 1457; b) N. Kanbayashi, K. Onitsuka, *J. Am. Chem. Soc.* **2010**, *132*, 1206 – 1207; c) N. Kanbayashi, K. Onitsuka, *Angew. Chem.* **2011**, *123*, 5303 – 5305; *Angew. Chem. Int. Ed.* **2011**, *50*, 5197 – 5199; d) K. Takii, N. Kanbayashi, K. Onitsuka, *Chem. Commun.* **2012**, *48*, 3872 – 3874.

[8] a) A. Alexakis, C. Croset, *Org. Lett.* **2002**, *4*, 4147 – 4149; b) A. W. van Zijl, W. Szymanski, F. López, A. J. Minnaard, B. L. Feringa, *J. Org. Chem.* **2008**, *73*, 6994 – 7002; c) L. M. Stanley, J. F. Hartwig, *J. Am. Chem. Soc.* **2009**, *131*, 8971 – 8983; d) A. Farwick, J. U. Engelhart, O. Tverskoy, C. Welter, Q. A. Umlauf (née Stang), F. Rominger, W. J. Kerr, G. Helmchen, *Adv. Synth. Catal.* **2011**, *353*, 349; e) M. Gärtner, R. Weihofen, G. Helmchen, *Chem. Eur. J.* **2011**, *17*, 7605 – 7622.

[9] a) T. Naota, H. Takaya, S. Murahashi, *Chem. Rev.* **1998**, *98*, 2599 – 2660; b) B. M. Trost, F. D. Toste, A. B. Pinkerton, *Chem. Rev.* **2001**, *101*, 2067 – 2096.

[10] a) F. Simal, L. Wlodarczak, A. Demonceau, A. F. Noels, *Tetrahedron Lett.* **2000**, *41*, 6071 – 6074; b) F. Simal, L. Wlodarczak, A. Demonceau, A. F. Noels, *Eur. J. Org. Chem.* **2001**, 2689 – 2695; c) H. Nagashima, M. Gondo, S. Masuda, H. Kondo, Y. Yamaguchi, K. Matsubara, *Chem. Commun.* **2003**, 442 – 443; d) Y. Motoyama, M. Gondo, S. Masuda, Y. Iwashita, H. Nagashima, *Chem. Lett.* **2004**, *33*, 442 – 443; e) K. Thommes, B. Içli, R. Scopelltiti, K. Severin, *Chem. Eur. J.* **2007**, *13*, 6899 – 6907.

[11] a) A. I. Meyers, I. Snyder, *J. Org. Chem.* **1993**, *58*, 36 – 42; b) A. G. M. Barrett, J. Head, M. L. Smith, N. S. Stock, *J. Org. Chem.* **1999**, *64*, 6005 – 6018; c) C. Milne, A. Powell, J. Jim, M. I. Nakeeb, C. P. Smith, J. Micklefield, *J. Am. Chem. Soc.* **2006**, *128*, 11250 – 11259; d) X. Zhao, D. DiRocco, A. T. Rovis, *J. Am. Chem. Soc.* **2011**, *133*, 12466 – 12469.

[12] a) H. Nagashima, H. Wakamatsu, N. Ozaki, T. Ishii, M. Watanabe, T. Tajima, K. Itoh, *J. Org. Chem.* **1992**, *57*, 1682 – 1689; b) H. Nagashima, N. Ozaki, M. Ishii, K. Seki, M. Washiyama, K. Itoh, *J. Org. Chem.* **1993**, *58*, 464 – 470; c) S. Iwamatsu, K. Matsubara, H. Nagashima, *J. Org. Chem.* **1999**, *64*, 9625 – 9631; d) M. A. Rachita, G. A. Slough, *Tetrahedron Lett.* **1993**, *34*, 6821 – 6824.

[13] a) H. Miyabe, A. Matsumura, K. Moriyama, Y. Takemoto, *Org. Lett.* **2004**, *6*, 4631 – 4634; b) M. Gärtner, M. Jäkel, M. Achaiz, C. Sonnenschein, O. Tverskoy, G. Helmchen, *Org. Lett.* **2011**, *13*, 2810 – 2813.

[14] a) O. M. Singh, H. Han, *J. Am. Chem. Soc.* **2007**, *129*, 774 – 775; b) O. M. Singh, H. Han, *Org. Lett.* **2007**, *9*, 4801 – 4804.

[15] a) R. Weihofen, O. Tverskoy, G. Helmchen, *Angew. Chem.* **2006**, *118*, 5673 – 5676; *Angew. Chem. Int. Ed.* **2006**, *45*, 5546 – 5549; b) M. J. Pouy, A. Leitner, D. J. Weix, S. Ueno, J. F. Hartwig, *Org. Lett.* **2007**, *9*, 3949 – 3952; c) J. F. Teichert, M. Fañanàs-Mastral, B. L. Feringa, *Angew. Chem.* **2011**, *123*, 714 – 717; *Angew. Chem. Int. Ed.* **2011**, *50*, 688 – 691.

[16] This result was confirmed by ^{1}H NMR and mass spectrometry, see the Supporting Information.

[17] Summary of crystal data for **6c** and **9c** is given in the Supporting Information. CCDC 919708 (**6c**) and 919709 (**9c**) 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.

[18] M. Benedetti, L. Forti, F. Ghelfi, U. M. Pagnoni, R. Ronzoni, *Tetrahedron* **1997**, *53*, 14031 – 14042.

