Stereospecific Migration

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Enantioselective Synthesis of Spiro Cyclopentane-1,3′-indoles and 2,3,4,9-Tetrahydro-1*H*-carbazoles by Iridium-Catalyzed Allylic Dearomatization and Stereospecific Migration**

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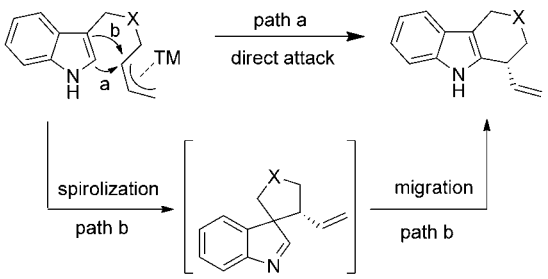
The indole nucleus is embedded in numerous natural products and biologically active compounds, including commercial drugs.[1] Thus, enormous effort has been devoted to the development of efficient synthetic procedures for the direct functionalization of this privileged compound.[2] Recently, indoles were found to be suitable nucleophiles for transition-metal-catalyzed allylic substitution reactions.[3] With an appropriate chiral metal complex, the catalytic allylic alkylation of indoles led to highly enantioenriched indole derivatives. Through an elegant intramolecular design, Bandini and co-workers achieved facile access to polycyclic indoles such as tetrahydro-β-carbolines, tetrahydro-γ-carbolines, and tetrahydro-1*H*-carbazoles.[4] Mechanistically, this intramolecular allylic arylation reaction still requires further investigation. There are two possible pathways: either through a direct arylation reaction (Scheme 1, path a) or a spirolization/migration reaction (path b).



Scheme 1. Possible pathways for the intramolecular allylic alkylation of C2 indoles.

Apart from the Friedel–Crafts-type arylation reaction, indoles can also undergo an allylic dearomatization reaction in the presence of a metal catalyst. Pioneering studies with palladium catalysts have been carried out by the research groups of Tamaru,[5] Trost,[6] and Rawal.[7] Recently, we reported an intramolecular iridium-catalyzed asymmetric allylic dearomatization of indoles, which provides six-membered spiroindolenines in a highly enantioselective manner.[8–10] When a five-membered ring formation was attempted, alkylation at the C2 position of the indole occurred, as was observed by Bandini and co-workers.[4a] Intrigued by the five-membered spiroindolenine products and the mechanism associated with the intramolecular C2 indole alkylation, we recently explored the iridium-catalyzed intramolecular asymmetric allylic dearomatization of indoles to form spiro cyclopentane-1,3′-indoles. Interestingly, with an acid catalyst, we found that stereospecific migration of spiro cyclopentane-1,3′-indoles can lead to enantioenriched 2,3,4,9-tetrahydro-1*H*-carbazoles. To our knowledge, this type of stereospecific migration of indolenines has not been reported, and provides direct evidence for the spirolization–migration pathway of intramolecular C2 indole alkylation. Herein, we report our preliminary results.

We began our studies by testing carbon-tethered substrate **1a** with an iridium catalyst system derived from $[\{Ir(cod)Cl\}_2]$ and phosphoramidite ligand $\mathbf{L_1}$ (Table 1).[11] Reaction of **1a** in the presence of 2 mol% of $[\{Ir(cod)Cl\}_2]$, 4 mol% of $\mathbf{L_1}$, and 2.0 equiv of Cs_2CO_3, in THF for 2 h gave the five-membered spiroindolenine product **2a** in 12:1 d.r., 94% *ee*, and more than 95% yield (Table 1, entry 1). Screening of phosphoramidite ligands (Table 1, entries 1–7) led to the identification of ligand $\mathbf{L_1}$ as the best one, in terms of d.r. value (Table 1, entry 1). Substituted phosphoramidite ligands $\mathbf{L_2}$, $\mathbf{L_3}$, and $\mathbf{L_4}$ could catalyze the reaction in elevated *ee*, but with decreased diastereomeric ratio. The 2-methyl-1,2,3,4-tetrahydroquinoline-derived phosphoramidite ligands $\mathbf{L_6}$, previously found to be the best ligand for the formation of six-membered spiroindolenines, and $\mathbf{L_7}$ are not effective for this type of substrate (Table 1, entries 6 and 7). Systematically screening solvents and bases showed that reaction in dioxane with Cs_2CO_3 gave optimal results (>95% yield, 16:1 d.r., and 99% *ee*; Table 1, entry 8; for details, see the Supporting Information). Reaction in the absence of base led to comparable selectivity, but a decreased rate.

To test the generality of the reaction, various allyl carbonates were subjected to the above optimized reaction conditions (2 mol% of $[\{Ir(cod)Cl\}_2]$, 4 mol% of $\mathbf{L_1}$, and 2.0 equiv of Cs_2CO_3, in dioxane). In some cases, the imine functionality of the indolenine products caused purification difficulties. Therefore, upon completion of the dearomatization reaction, the concentrated reaction mixture was subjected to a $NaBH_3CN$ reduction, affording the corresponding

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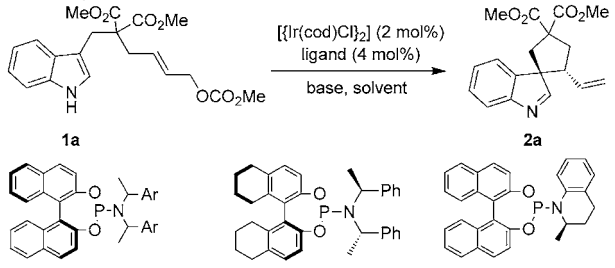
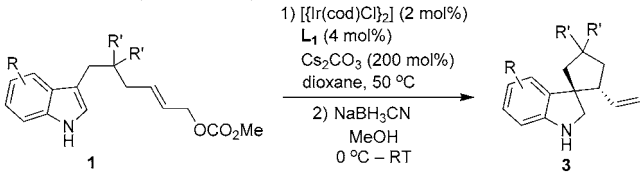
Table 1: Optimization of reaction conditions.[a]



Entry	Ligand	Solvent	Base	Temp [°C]	*t* [h]	Yield [%][b]	d.r.[c]	*ee* [%][d]
1	L_1	THF	Cs_2CO_3	50	2	>95	12:1	94
2	L_2	THF	Cs_2CO_3	50	2	>95	8:1	97
3	L_3	THF	Cs_2CO_3	50	2	>95	4:1	96
4	L_4	THF	Cs_2CO_3	50	12	62[e]	7:1	96
5	L_5	THF	Cs_2CO_3	50	12	21[e]	4:1	58
6	L_6	THF	Cs_2CO_3	50	12	trace	–	–
7	L_7	THF	Cs_2CO_3	50	12	trace	–	–
8	L_1	dioxane	Cs_2CO_3	50	2	>95	16:1	99

[a] Reaction conditions: **1a** (0.2 mmol) and base (0.4 mmol) in solvent (2.0 mL). [b] Yield of isolated product. [c] Determined by ^{1}H NMR spectroscopy of the crude reaction mixture. [d] Determined by HPLC analysis. [e] Conversion determined by ^{1}H NMR spectroscopy.

Table 2: The asymmetric allylic dearomatization reaction.



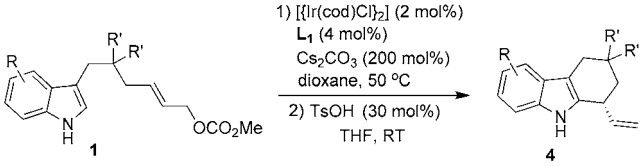
Entry	1	R	R′	3	d.r.[a]	Yield [%][b]	*ee* [%][c]
1	**1a**	H	CO_2Me	**3a**	16:1	93	98
2	**1b**	5-MeO	CO_2Me	**3b**	14:1	91	95
3	**1c**	6-BnO	CO_2Me	**3c**	10:1	89	92
4	**1d**	4-Me	CO_2Me	**3d**	5:1	78[d]	99
5	**1e**	5-Br	CO_2Me	**3e**	13:1	92	96
6	**1f**	7-Br	CO_2Me	**3f**	11:1	90	97
7	**1g**	5-F	CO_2Me	**3g**	12:1	92	97
8	**1h**	H	CO_2Et	**3h**	11:1	93	97
9	**1i**	H	CO_2tBu	**3i**	12:1	95	96
10	**1j**	H	H	**3j**	4.5:1	71/11	92/87
11	**1k**	5-MeO	H	**3k**	2.3:1	60/23	92/86
12	**1l**	4-Me	H	**3l**	1.5:1	45/32	92/72
13	**1m**	5-Br	H	**3m**	1:1	42/40	89/82
14[e]	**1n**	2-Me	CO_2Me	**2n**	15:1	96	97
15[e]	**1o**	2-Ph	CO_2Me	**2o**	13:1	94	97

[a] Determined by ^{1}H NMR spectroscopy of the crude spiroindolenine intermediate. [b] Yield of isolated product; for entries 10–13, the yield of the minor diastereomer is shown after the slash. [c] Determined by HPLC analysis; for entries 10–13, the *ee* of the minor diastereomer is shown after the slash. [d] Yield of the major diastereoisomer. [e] Without $NaBH_3CN$ reduction.

indolines as stable compounds. The results are summarized in Table 2. Reaction of various dimethyl malonate linked substrates bearing either an electron-donating group (5-MeO, 6-BnO, 4-Me; Table 2, entries 2–4) or an electron-withdrawing group (5-Br, 7-Br, 5-F; Table 2, entries 5–7) on the indole core all led to the corresponding indoline products in excellent yield, d.r., and *ee* (78–92% yield, 5:1–14:1 d.r., 92–99% *ee*). Substrates bearing either an ethyl or *tert*-butyl ester group on the tether were well tolerated (Table 2, entries 8 and 9). The stereochemistry of the products was determined by a single-crystal X-ray analysis of the HCl salt of enantiopure **3f**. The reaction proceeded smoothly for methylene-tethered substrates with different electronic properties (Table 2, entries 10–13), affording the five-membered spiroindoline products in good yield and *ee*, but with decreased diastereomeric ratios. Notably, when 2-methyl and 2-phenyl indolyl allyl carbonates were used, spiroindolenine products were obtained as stable compounds in excellent yield and selectivity (Table 2, entries 14 and 15).

The formation of five-membered spiroindolenines encouraged us to examine whether they could be transformed to the C2 indole alkylation product, namely 2,3,4,9-tetrahydro-1*H*-carbazoles. If this were the case, we would also be interested in knowing whether or not the process is stereospecific. With five-membered spiroindolenine **2a** in hand, we tested it with a variety of acids. With a catalytic amount of TsOH (30 mol%), spiroindoline **2a** was smoothly isomerized to the tetrahydrocarbazole **4a** in almost quantitative yield. Fortunately, the *ee* value of **2a** was well preserved during the migration process. In a one-pot procedure, including asymmetric allylic dearomatization and treatment with TsOH, various indolyl allyl carbonates were tested to determine the generality of the reaction. As summarized in Table 3, the reaction proceeded well in all cases, affording the corresponding tetrahydrocarbazoles in good to excellent yield and *ee* (Table 3, entries 1–13). The absolute configuration of the tetrahydrocarbazole products was assigned by an X-ray

Table 3: Allylic dearomatization and stereospecific migration.

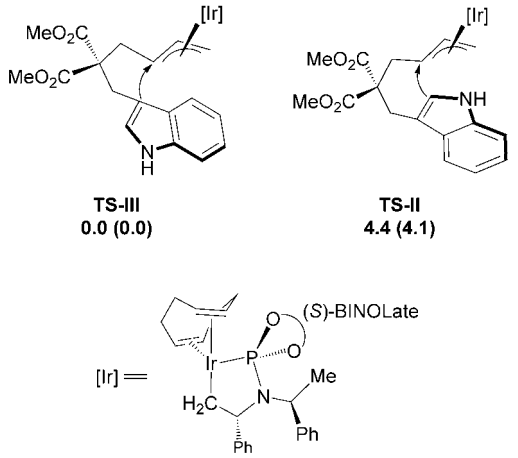


Entry	1	R	R′	4	yield [%][a]	*ee* [%][b]
1	**1a**	H	CO_2Me	**4a**	92	97
2	**1b**	5-MeO	CO_2Me	**4b**	92	94
3	**1c**	6-BnO	CO_2Me	**4c**	85	95
4	**1d**	4-Me	CO_2Me	**4d**	80	96
5	**1e**	5-Br	CO_2Me	**4e**	94	93
6	**1f**	7-Br	CO_2Me	**4f**	88	99
7	**1g**	5-F	CO_2Me	**4g**	90	96
8	**1h**	H	CO_2Et	**4h**	92	97
9	**1i**	H	CO_2tBu	**4i**	90	95
10	**1j**	H	H	**4j**	82	90
11	**1k**	5-MeO	H	**4k**	72	90
12	**1l**	4-Me	H	**4l**	78	91
13	**1m**	5-Br	H	**4m**	70	88

[a] Yield of isolated product. [b] Determined by HPLC analysis.

analysis of enantiopure **4 f**, which was found to be consistent with that of the spiroindoline products.

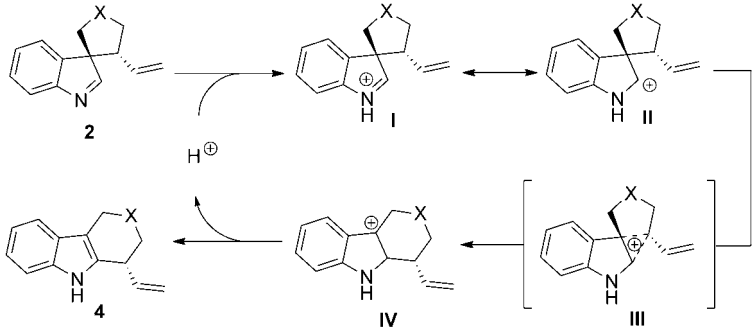
To understand the origin of the selective formation of the five-membered ring during the dearomatization process, a DFT calculation was carried out.[12] The results were in good accord with the experimental observations. As shown in Scheme 2, the transition states for the nucleophilic attack of



Scheme 2. Representation and relative energies of **TS-III** and **TS-II**. ΔG_{sol} and ΔE_{sol} (the latter shown in parentheses), are given in kcal mol^{-1}. Calculated at the M06-2X/SDD/6-31G(d,p) level of theory (solvent = 1,4-dioxane).

the C3 and C2 positions of the indole ring to the iridium–allylic moiety (**TS-III** and **TS-II**) were determined. The energetic barrier of **TS-II** is 4.4 kcal mol^{-1} higher than that of **TS-III**, indicating that C3 attack is the favored process. There are two reasons that might account for the energetic difference between these transition states. The C3 position of the indole structure, although substituted, still exhibits stronger nucleophilicity than the C2 position in this case. Furthermore, the C3 attack makes the indole substrate adopt a more suitable conformation in **TS-III**, avoiding steric congestion with one phenyl group of $\mathbf{L_1}$, as shown in **TS-II**.

Based on the above data, we propose the following mechanism for the TsOH-catalyzed stereospecific migration. As depicted in Scheme 3, the protonation of indolenine leads to intermediate **I** or **II**. Intermediate **II** most likely undergoes migration through a three-center two-electron pathway to generate intermediate **IV**, which further eliminates a proton to yield tetrahydrocarbazole product **4**. Although the non-classical carbocation **III** might account for the stereospecific migration, further study is needed.



Scheme 3. Possible mechanism for the stereospecific migration of spiro cyclopentane-1,3′-indoles.

In summary, we have developed a highly enantioselective synthesis of spiro cyclopentane-1,3′-indoles through an iridium-catalyzed asymmetric allylic dearomatization reaction. The spiro cyclopentane-1,3′-indoles, in the presence of a catalytic amount of TsOH, underwent stereospecific migration to provide 2,3,4,9-tetrahydro-1*H*-carbazoles. This novel stereospecific migration of indolenines to tetrahydro-1*H*-carbazoles provides direct mechanistic evidence for the intramolecular Friedel–Crafts-type C2 indole alkylation reaction. Further investigation into the mechanism of the migration process and applications of this method are currently underway in our laboratory.

Experimental Section

General procedure for the iridium-catalyzed enantioselective allylic alkylation: [{Ir(cod)Cl}$_2$] (2.7 mg, 0.004 mmol), phosphoramidite ligand $\mathbf{L_1}$ (4.2 mg, 0.008 mmol), THF (0.5 mL) and *n*-propylamine (0.5 mL) were added to a flame-dried Schlenk tube. The reaction mixture was heated to 50 °C for 30 min and then the volatile solvents were removed under reduced pressure to give a pale yellow solid. Next, allylic carbonate **1** (0.20 mmol, dissolved in 2.0 mL dioxane) and cesium carbonate (130.3 mg, 0.40 mmol) were added. The reaction mixture was heated to 50 °C for 2–5 h. After the reaction was complete (as indicated by TLC), the crude mixture was filtered through celite and washed with EtOAc. The solvents were removed under reduced pressure and the diastereomeric ratio of the crude reaction mixture was determined by ^{1}H NMR spectroscopy. The residue was then purified by silica gel column chromatography (2:1 petroleum ether/EtOAc) to afford the desired product **2**.

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[1] a) *The Chemistry of Heterocyclic Compounds*, *Vol. 25* (Eds.: E. C. Taylor, J. E. Saxton), Wiley-Interscience, New York, **1983**; *The Chemistry of Heterocyclic Compounds*, *Vol. 25*(Eds.: E. C. Taylor, J. E. Saxton), Wiley-Interscience, New York, **1994**; b) R. J. Sundberg, *Indoles*; Academic: New York, **1996**; c) T. Kawasaki, K. Higuchi, *Nat. Prod. Rep.* **2005**, *22*, 761; d) S. E. O'Connor, J. J. Maresh, *Nat. Prod. Rep.* **2006**, *23*, 532; e) N. Saracoglu, *Top. Heterocycl. Chem.* **2007**, *11*, 145 (Bioactive Heterocycles V).

[2] a) G. W. Gribble, *Top. Heterocycl. Chem.* **2010**, *26*, 327 (Heterocyclic Scaffolds II: Reactions and Applications of Indoles); for recent reviews, see: b) S. Cacchi, G. Fabrizi, *Chem. Rev.* **2005**, *105*, 2873; c) M. Bandini, A. Melloni, S. Tommasi, A. Umani-Ronchi, *Synlett* **2005**, 1199; d) M. Bandini, A. Eichholzer, *Angew. Chem.* **2009**, *121*, 9786; *Angew. Chem. Int. Ed.* **2009**, *48*, 9608; e) L. Joucla, L. Djakovitch, *Adv. Synth. Catal.* **2009**, *351*, 673; f) M. Zeng, S.-L. You,

Synlett **2010**, 1289; g) G. Bartoli, G. Bencivenni, R. Dalpozzo, *Chem. Soc. Rev.* **2010**, *39*, 4449; h) S. Cacchi, G. Fabrizi, *Chem. Rev.* **2011**, *111*, PR215.

[3] Selected references for iridium: a) W.-B. Liu, H. He, L.-X. Dai, S.-L. You, *Org. Lett.* **2008**, *10*, 1815; b) W.-B. Liu, H. He, L.-X. Dai, S.-L. You, *Synthesis* **2009**, 2076; c) L. M. Stanley, J. F. Hartwig, *Angew. Chem.* **2009**, *121*, 7981; *Angew. Chem. Int. Ed.* **2009**, *48*, 7841; for palladium: d) B. M. Trost, M. J. Krische, V. Berl, E. M. Grenzer, *Org. Lett.* **2002**, *4*, 2005; e) M. Bandini, A. Melloni, A. Umani-Ronchi, *Org. Lett.* **2004**, *6*, 3199; f) S. Ma, S. Yu, Z. Peng, H. Guo, *J. Org. Chem.* **2006**, *71*, 9865; g) H. Y. Cheung, W.-Y. Yu, F. L. Lam, T. T.-L. Au-Yeung, Z. Zhou, T. H. Chan, A. S. C. Chan, *Org. Lett.* **2007**, *9*, 4295; h) H. Mo, W. Bao, *Adv. Synth. Catal.* **2009**, *351*, 2845; i) B. M. Trost, M. Osipov, G. Dong, *J. Am. Chem. Soc.* **2010**, *132*, 15800; j) T. Hoshi, K. Sasaki, S. Sato, Y. Ishii, T. Suzuki, H. Hagiwara, *Org. Lett.* **2011**, *13*, 932; k) Z. Cao, Y. Liu, Z. Liu, X. Feng, M. Zhuang, H. Du, *Org. Lett.* **2011**, *13*, 2164; for ruthenium: l) A. B. Zaitsev, S. Gruber, P. S. Pregosin, *Chem. Commun.* **2007**, 4692; m) A. B. Zaitsev, S. Gruber, P. A. Plüss, P. S. Pregosin, L. F. Veiros, M. Wörle, *J. Am. Chem. Soc.* **2008**, *130*, 11604; n) S. Gruber, A. B. Zaitsev, M. Wörle, P. S. Pregosin, *Organometallics* **2008**, *27*, 3796; o) S. Gruber, A. B. Zaitsev, M. Wörle, P. S. Pregosin, *Organometallics* **2009**, *28*, 3437; p) B. Sundararaju, M. Achard, B. Demerseman, L. Toupet, G. V. M. Sharma, C. Bruneau, *Angew. Chem.* **2010**, *122*, 2842; *Angew. Chem. Int. Ed.* **2010**, *49*, 2782; q) J. A. van Rijn, M. C. Guijt, D. de Vries, E. Bouwman, E. Drent, *Appl. Organometal. Chem.* **2011**, *25*, 212; for molybdenum: r) A. V. Malkov, S. L. Davis, I. R. Baxendale, W. L. Mitchell, P. Kočovský, *J. Org. Chem.* **1999**, *64*, 2751.

[4] a) M. Bandini, A. Melloni, F. Piccinelli, R. Sinisi, S. Tommasi, A. Umani-Ronchi, *J. Am. Chem. Soc.* **2006**, *128*, 1424; b) M. Bandini, A. Eichholzer, *Angew. Chem.* **2009**, *121*, 9697; *Angew. Chem. Int. Ed.* **2009**, *48*, 9533; c) G. Cera, P. Crispino, M. Monari, M. Bandini, *Chem. Commun.* **2011**, *47*, 7803.

[5] M. Kimura, M. Futamata, R. Mukai, Y. Tamaru, *J. Am. Chem. Soc.* **2005**, *127*, 4592.

[6] B. M. Trost, J. Quancard, *J. Am. Chem. Soc.* **2006**, *128*, 6314.

[7] N. Kagawa, J. P. Malerich, V. H. Rawal, *Org. Lett.* **2008**, *10*, 2381.

[8] Asymmetric allylic dearomatization work from our group: a) Q.-F. Wu, H. He, W.-B. Liu, S.-L. You, *J. Am. Chem. Soc.* **2010**, *132*, 11418; b) Q.-F. Wu, W.-B. Liu, C.-X. Zhuo, Z.-Q. Rong, K.-Y. Ye, S.-L. You, *Angew. Chem.* **2011**, *123*, 4547; *Angew. Chem. Int. Ed.* **2011**, *50*, 4455; c) C.-X. Zhuo, W.-B. Liu, Q.-F. Wu, S.-L. You, *Chem. Sci.* **2012**, *3*, 205.

[9] For selected examples of asymmetric dearomatization reactions, see: a) M. Takamura, K. Funabashi, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2000**, *122*, 6327; b) K. Funabashi, H. Ratni, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2001**, *123*, 10784; c) E. Ichikawa, M. Suzuki, K. Yabu, M. Albert, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2004**, *126*, 11808; d) J. F. Austin, S.-G. Kim, C. J. Sinz, W.-J. Xiao, D. W. C. MacMillan, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5482; e) R. P. Reddy, H. M. L. Davies, *J. Am. Chem. Soc.* **2007**, *129*, 10312; f) S. Quideau, G. Lyvinec, M. Marguerit, K. Bathany, A. Ozanne-Beaudenon, T. Buffeteau, D. Cavagnat, A. Chénedé, *Angew. Chem.* **2009**, *121*, 4675; *Angew. Chem. Int. Ed.* **2009**, *48*, 4605; g) J. García-Fortanet, F. Kessler, S. L. Buchwald, *J. Am. Chem. Soc.* **2009**, *131*, 6676; h) S. B. Jones, B. Simmons, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2009**, *131*, 13606; i) Y. Lian, H. M. L. Davies, *J. Am. Chem. Soc.* **2010**, *132*, 440; j) T. Nemoto, Y. Ishige, M. Yoshida, Y. Kohno, M. Kanematsu, Y. Hamada, *Org. Lett.* **2010**, *12*, 5020; k) R. R. Knowles, J. Carpenter, S. B. Blakey, A. Kayano, I. K. Mangion, C. J. Sinz, D. W. C. MacMillan, *Chem. Sci.* **2011**, *2*, 308; l) J. Qi, A. B. Beeler, Q. Zhang, J. A. Porco, Jr., *J. Am. Chem. Soc.* **2010**, *132*, 13642; m) L. M. Repka, J. Ni, S. E. Reisman, *J. Am. Chem. Soc.* **2010**, *132*, 14418; n) S. Rousseaux, J. García-Fortanet, M. A. D. A. Sanchez, S. L. Buchwald, *J. Am. Chem. Soc.* **2011**, *133*, 9282; o) A. Rudolph, P. H. Bos, A. Meetsma, A. J. Minnaard, B. L. Feringa, *Angew. Chem.* **2011**, *123*, 5956; *Angew. Chem. Int. Ed.* **2011**, *50*, 5834; p) O. Lozano, G. Blessley, T. Martinez del Campo, A. L. Thompson, G. T. Giuffredi, M. Bettati, M. Walker, R. Borman, V. Gouverneur, *Angew. Chem.* **2011**, *123*, 8255; *Angew. Chem. Int. Ed.* **2011**, *50*, 8105; for recent examples of the asymmetric reduction of indoles, see: q) D.-S. Wang, Z.-S. Ye, Q.-A. Chen, Y.-G. Zhou, C.-B. Yu, H.-J. Fan, Y. Duan, *J. Am. Chem. Soc.* **2011**, *133*, 8866; r) Y.-C. Xiao, C. Wang, Y. Yao, J. Sun, Y.-C. Chen, *Angew. Chem.* **2011**, *123*, 10849; *Angew. Chem. Int. Ed.* **2011**, *50*, 10661.

[10] For a recent review, see: S. P. Roche, J. A. Porco, Jr., *Angew. Chem.* **2011**, *123*, 4154; *Angew. Chem. Int. Ed.* **2011**, *50*, 4068.

[11] For reviews, see: a) R. Takeuchi, S. Kezuka, *Synthesis* **2006**, 3349; b) G. Helmchen, A. Dahnz, P. Dübon, M. Schelwies, R. Weihofen, *Chem. Commun.* **2007**, 675; c) G. Helmchen in *Iridium Complexes in Organic Synthesis* (Eds.: L. A. Oro, C. Claver), Wiley-VCH, Weinheim, **2009**, pp. 211–250; d) J. F. Hartwig, L. M. Stanley, *Acc. Chem. Res.* **2010**, *43*, 1461; also, for early reports on the catalyst, see: e) T. Ohmura, J. F. Hartwig, *J. Am. Chem. Soc.* **2002**, *124*, 15164; f) C. A. Kiener, C. Shu, C. Incarvito, J. F. Hartwig, *J. Am. Chem. Soc.* **2003**, *125*, 14272.

[12] For details, see the Supporting Information.

