

Asymmetric *N*-Allylation of Indoles Through the Iridium-Catalyzed Allylic Alkylation/Oxidation of Indolines**

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The synthesis of enantiopure indole derivatives is of significant importance because optically active indole moieties are a common occurrence in bioactive natural products and pharmaceuticals.^[1] To this end, enormous efforts have been devoted to the development of catalytic asymmetric reactions of indoles in the past decade.^[2] It has been well documented that the C3-position of an indole is the most reactive one among the three positions (N1, C2, C3) under the conditions of the Friedel–Crafts reaction.^[3] Recently, the enantioselective C2 alkylation of indoles was realized through variations of the Pictet–Spengler reaction,^[4] alkylation of 2-indolyl trifluoroborate salts,^[5] and alkylation/oxidation of 4,7-dihydroindoles.^[6] However, the enantioselective *N*-substitution^[7] of indoles has rarely been explored due to the weak acidity of the N–H group, despite the fact that the products are privileged structural motifs in natural alkaloids and biologically active compounds (Figure 1).^[8]

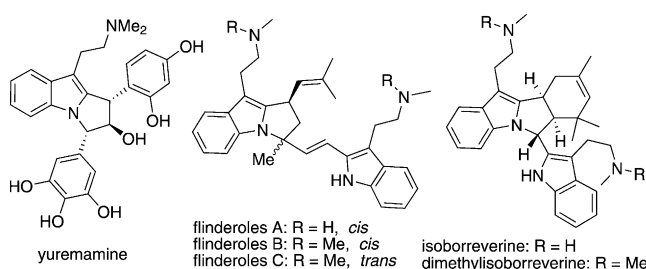
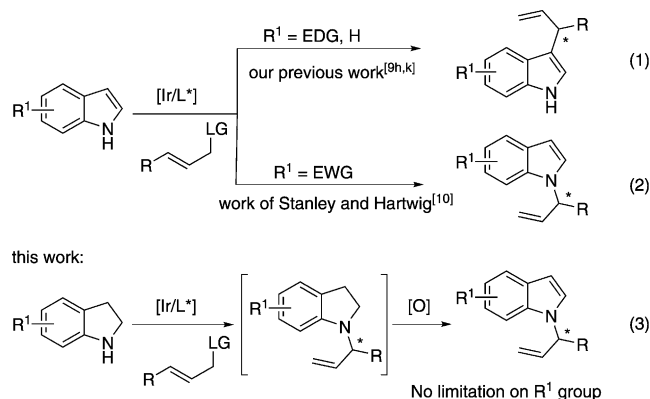


Figure 1. Biologically active *N*-allylated indole derivatives.

In the last decade, the transition-metal-catalyzed allylic alkylation reaction has proven suitable for direct functionalization of indoles at the C3 position [Scheme 1, Eq. (1)].^[9] Recent work by Stanley and Hartwig^[10] elegantly realized the enantioselective N1 allylic alkylation of indoles with an iridium catalyst [Scheme 1, Eq. (2)].^[11] Their reaction fea-



Scheme 1. The synthesis of allylindoles by Ir-catalyzed allylic substitution reactions. EDG = electron donating group, EWG = electron withdrawing group, L* = chiral ligand, LG = leaving group.

tures the introduction of electron-withdrawing groups on the indole ring or substituent at the C3-position, which limits the scope of indole substrates. Herein, we report a general synthesis of *N*-allylindoles through a one-pot reaction involving an iridium-catalyzed allylic alkylation^[11] of indolines followed by oxidation^[12] [Scheme 1, Eq. (3)]. Notably, indolines are commercially available and can also be easily prepared by the reduction of indoles, which allows access to a broad range of enantioenriched *N*-allylindoles in excellent enantioselectivity without the limitation on substituents found in previous work.

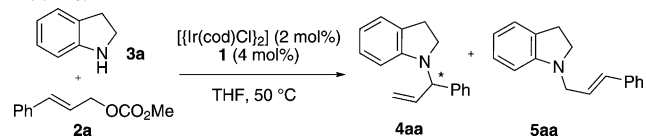
With a catalyst derived from $[\text{Ir}(\text{cod})\text{Cl}]_2/\mathbf{1a}$,^[13b] (cod = cyclooctadiene) indoline **3a** smoothly reacted with carbonate **2a**, affording the alkylation product **4aa** in 82% yield and 95% *ee* (Table 1, entry 1).^[13] Different chiral ligands (Figure 2) were next examined, and the results are summarized in Table 1. Phosphoramidite ligand **1b**, containing an *ortho*-methoxy substituent on the aryl group of the amine moiety, developed by Alexakis and Polet,^[14] led to the formation of product **4aa** in a higher yield and *ee* (90% yield, 99% *ee*, entry 2), while ligand **1c** afforded the product in a decreased yield (entry 3). The catalyst derived from **1d**, which is the diastereoisomer of **1a**, could catalyze the reaction, but gave lower selectivities (**4aa/5aa** 87:13, 84% *ee*; entry 4). This result indicates that there is a match of chiralities within **1a**. The use of either ligand **1e** or **1f** resulted in reduced yields and moderate enantioselectivity (entries 5 and 6). Ligands **1g**, **1h**, **1i**, and **1j** were also suitable for this reaction, but gave slightly poorer ratios of branched to linear products (entries 7–10). Ligands **1k** and **1l**^[13g,o] resulted in lower yields, enantioselectivity, and regioselectivity (entries 11 and 12). Fortunately, with the catalyst derived

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Table 1: Screening of chiral ligands for the Ir-catalyzed allylic alkylation of indoline.



Entry ^[a]	Ligand	t [h]	4 aa/5 aa ^[b]	Yield [%] ^[c]	ee [%] ^[d]
1	1 a	17	95:5	82	95
2	1 b	17	95:5	90	99
3	1 c	17	96:4	74	95
4	1 d	24	87:13	93	84
5	1 e	36	99:1	24	88
6	1 f	36	87:13	27	71
7 ^[e]	1 g	36	77:23	70	89
8	1 h	6	78:22	93	90
9	1 i	2	80:20	92	87
10	1 j	36	83:17	61	97
11 ^[e]	1 k	36	57:43	49	−15
12 ^[e]	1 l	36	67:33	50	43
13 ^[f]	1 b	6	97:3	95	99

[a] **3 a**/**2 a**/[{Ir(cod)Cl}₂]/ligand, 1.5:1.0:0.02:0.04; **2 a** (0.25 mmol) was used in THF (2.5 mL) at 50 °C. [b] Determined by ¹H NMR of the crude reaction mixture. [c] Yields of isolated **4 aa** and **5 aa**. [d] The ee of **4 aa** was determined by HPLC analysis (Chiralcel OD-H). [e] Yield determined by ¹H NMR spectroscopy. [f] [{Ir(dbcot)Cl}₂] was used. Cod = cyclooctadiene, dbcot = dibenzo[a,e]cyclooctatetraene.

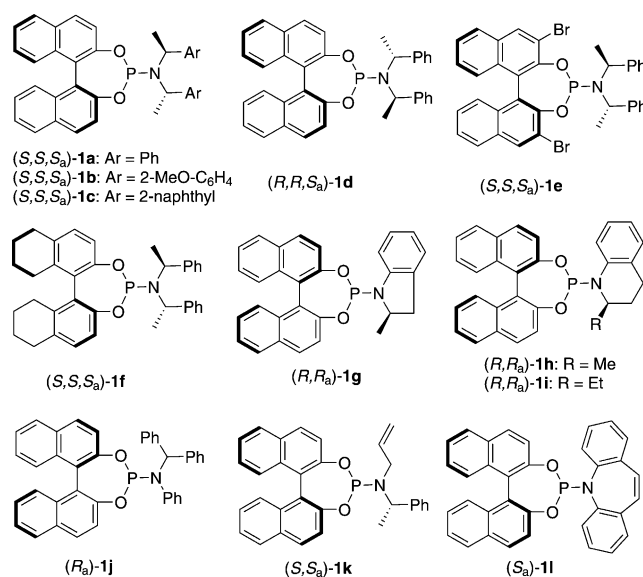


Figure 2. Chiral ligands **1 a–l**.

from [{Ir(dbcot)Cl}₂]/**1 b** (dbcot = dibenzo[a,e]cyclooctatetraene), developed in the Helmchen group,^[13h,15] the allylic alkylation reaction proceeded in 95% yield and 99% ee (entry 13). Various temperatures, substrate concentrations, and solvents, including CH₂Cl₂, dioxane, Et₂O, and toluene, were found to be well tolerated.^[16] Taking multiple factors into consideration, the optimal reaction conditions were determined to be: [{Ir(dbcot)Cl}₂]/**1 b** as catalyst in THF at 50 °C.

To test our hypothesis for the synthesis of *N*-allylated indoles, 1.5 equivalents of 2,6-dichloro-3,5-dicyano-*p*-benzoquinone (DDQ) were added to the reaction mixture upon completion of the Ir-catalyzed allylic amination. After stirring for 30 min, the *N*-allylated indoles were obtained in good yields without loss of enantiomeric purity.

Under the optimal reaction conditions, the one-pot allylic alkylation/oxidation reaction was investigated with a wide range of indolines and allyl carbonates. As summarized in Table 2, the method was general for both indolines and allyl carbonates. Aryl allyl carbonates **2 b–e**, with either an electron-donating group (4-Me, 4-OMe) or an electron-withdrawing group (4-Br, 3-CF₃) on the phenyl ring, all gave their corresponding indole products in excellent yields with 96–98% ee (Table 2, entries 2–5). The reaction of 2-thienyl allyl carbonate **2 g** led to **6 ag** in 84% yield and 99% ee (entry 15). Aliphatic allyl carbonates **2 h** and **2 i** were both well tolerated and gave their desired products in slightly lower regioselectivity and enantioselectivity (**6 ah**, **6/7** 90:10, 92% ee, and **6 ai**, **6/7** 91:9, 82% ee; entries 16 and 17). As for the nucleophiles, indolines having different substitution patterns (4-Me, 5-OMe, 6-Br) worked well to afford the products in 81–92% yields with 96–99% ee (entries 6–8, 11). Notably, the 2-methyl and 3-methyl indolines were also suitable substrates, leading to excellent enantioselectivity (entries 9, 10, and 12). The enantiopure bromo-containing product **6 da** was easily obtained after recrystallization from *n*-hexane/isopropanol. An X-ray crystallographic analysis to determine the absolute configuration of the enantiopure product revealed it to be (*S*)-**6 da**.^[17]

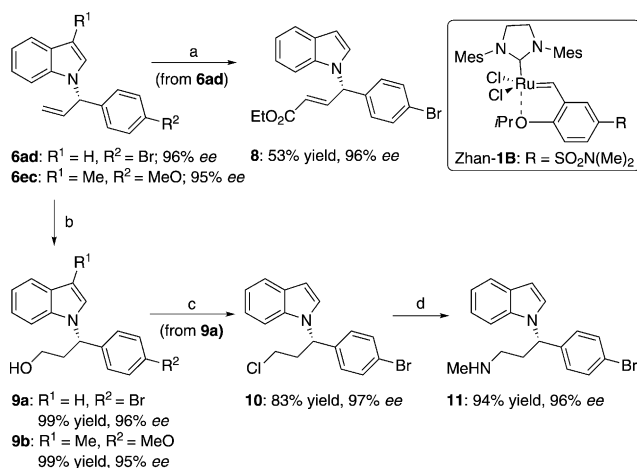
As depicted in Scheme 2, several diverse transformations were carried out to further test the utility of the current methodology. Allylindole **6 ad** was readily converted into α,β-unsaturated ester **8** in 53% yield through an olefin cross-metathesis reaction. Primary alcohols **9 a** and **9 b** were obtained in quantitative yields through hydroboration of terminal alkenes with 9-borabicyclo[3.3.1]nonane (9-BBN) followed by oxidation. A monoamine reuptake inhibitor analogue,^[8c] 3-(1*H*-indol-1-yl)-3-arylpropan-1-amine (**11**), was synthesized in 78% yield over two straightforward steps.

Reactions with 3,4,5-trimethoxyphenyl allyl carbonate were carried out on a gram scale to smoothly afford **6 gf** and **6 hf** in 94 and 98% ee, respectively (Table 2, entries 13 and 14). Both of these products are potentially valuable synthons of yuremamine, a new phytoindole recently isolated from the stem bark of *Mimosa hostilis*.^[18] The diastereoisomer of methyluremamine **15** was synthesized as shown in Scheme 3. Compound **6 hf** was converted into a diol with a 3:1 d.r. through a dihydroxylation reaction. Protection/deprotection of the diols afforded product **12** in 68% yield (three steps). Oxidation of **12** with Dess–Martin periodinane and subsequent treatment with (2,4-dimethoxyphenyl)lithium gave **13**, which was treated with an excess of trifluoroacetic acid (TFA), a process which required a carefully controlled reaction time.^[19] The resulting cascade sequence, featuring cation generation, stereoselective cyclization, and deprotection, afforded dihydropyrrolo[1,2-*a*]indole **14** in 57% yield after 2 h. The relative stereochemistry of compound **14** was confirmed by X-ray diffraction analysis.^[17] Compound **15** was

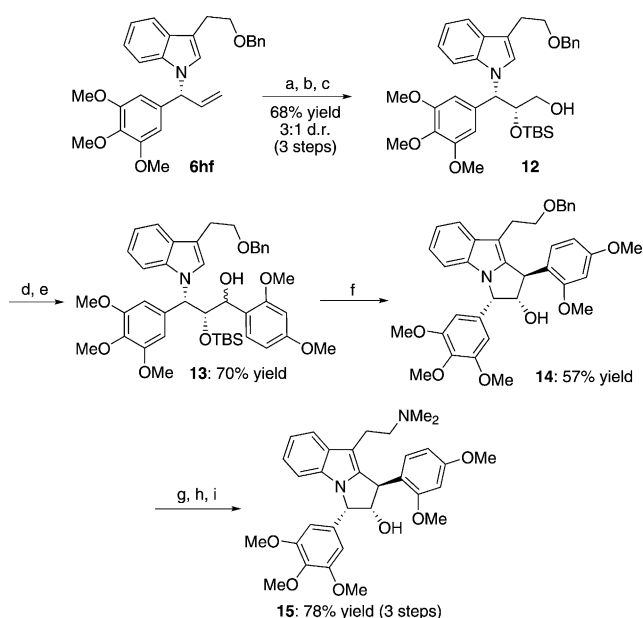
Table 2: Substrate scope.

Entry ^[a]	Product	<i>t</i> [h]	6/7 ^[b]	Yield [%] ^[c]	ee [%] ^[d]
1	6aa : Ar = Ph	6	97:3	88	98
2	6ab : Ar = 4-MeC ₆ H ₄	6	98:2	85	98
3	6ac : Ar = 4-MeOC ₆ H ₄	6	> 99:1	88	98
4	6ad : Ar = 4-BrC ₆ H ₄	12	> 99:1	92	96
5	6ae : Ar = 3-CF ₃ C ₆ H ₄	6	97:3	87	97
6	6ba : R ¹ = 4-Me	10	96:4	82	98
7	6ca : R ¹ = 5-OMe	4	98:2	92	96
8	6da : R ¹ = 6-Br	12	> 99:1	88	96
9 ^[e]	6ea : R ¹ = 3-Me	8	> 99:1	82	92
10 ^[e]	6fa : R ¹ = 2-Me	12	97:3	76	97
11	6dd	11	97:3	81	99
12 ^[e]	6ec	8	> 99:1	86	95
13 ^[e,f]	6gf : R = NMe ₂	8	> 99:1	77	94
14 ^[e,f]	6hf : R = OBn	10	> 99:1	85	98
15	6ag : R ² = 2-thienyl	20	97:3	84	99
16	6ah : R ² = <i>n</i> -propyl	18	90:10	76	92
17	6ai : R ² = Me	5	91:9	81	82

[a] **3a**/**2a**/[[Ir(dbcot)Cl]₂]/**1b**, 1.1–1.5:1:0.02:0.04; **2a** (0.25 mmol) in THF (2.5 mL) at 50 °C for the indicated time. DDQ was then added and the reaction was stirred at RT for another 30 min. [b] Determined by ¹H NMR spectroscopy of the crude reaction mixture. [c] Yield of isolated product. [d] The ee of **6** was determined by HPLC analysis. [e] The DDQ oxidation takes 2 h. [f] Gram scale at RT with [[Ir(cod)Cl]₂]/(*R,R*,*R_a*)-**1a**. Cod = cyclooctadiene, dbcot = dibenzo[*a,e*]cyclooctatetraene, DDQ = 2,6-dichloro-3,5-dicyano-*p*-benzoquinone.



Scheme 2. Transformations of products. Reaction conditions: a) Zhan-**1B** (5 mol %), CH₂=CHCO₂Et, CH₂Cl₂, reflux, 24 h; b) 9-BBN, THF, –78 °C–RT, 8 h, then NaOH (3 M), H₂O₂ (30%), RT, 6 h; c) PPh₃, CCl₄, CH₂Cl₂, reflux, 24 h; d) MeNH₂, EtOH, 90 °C, sealed tube, 6 h. 9-BBN = 9-borabicyclo[3.3.1]nonane, Mes = 2,4,6-Me₃C₆H₂.



Scheme 3. Synthesis of a diastereomer of a yurenamine derivative. Reaction conditions: a) 7 mol % of K₂OsO₄·2H₂O, K₃Fe(CN)₆, K₂CO₃, DABCO, *t*BuOH/H₂O, RT, 5 h, 3:1 d.r.; b) TBSOTf, 2,6-lutidine, CH₂Cl₂, 0 °C–RT, 12 h; c) THF/H₂O/TFA (4:1:1), 0 °C–RT, 1 h, 68% yield over three steps; d) DMP, CH₂Cl₂, RT, 30 min; e) THF, 2,4-(MeO)₂-C₆H₃Li, –78 °C–RT, 10 h, 70% yield over two steps; f) TFA (500 mol %), CH₂Cl₂, 0 °C–RT, 3 h, 57% yield; g) Raney-Ni, H₂ (1 atm), MeOH, 50 °C, 12 h; h) TEA, MsCl, CH₂Cl₂, 0 °C, 1 h; i) Me₂NH (2 M in THF), THF, 90 °C, sealed tube, 12 h, 78% yield over three steps. Bn = benzyl, DABCO = 1,4-diazabicyclo[2.2.2]octane, DMP = Dess–Martin periodinane, Ms = methanesulfonyl, OTf = trifluoromethanesulfonyl, TEA = triethylamine, TFA = trifluoroacetic acid.

obtained after removal of the benzyl group,^[20] formation of the primary methanesulfonate, and substitution with dimethylamine in 78% yield over three steps from **14**.

In conclusion, we have developed a general and practical synthesis of enantioenriched *N*-allylindoles by a one-pot strategy involving the Ir-catalyzed asymmetric allylic alkylation and subsequent oxidation of indolines. Starting from readily available indolines and allylic carbonates, various *N*-alkylated indoles were obtained in good yields and with excellent regioselectivity and enantioselectivity. The potential for diverse transformation of the *N*-allylindole products makes this protocol potentially useful in organic synthesis.

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- [1] a) J. Bosch, M.-L. Bennasar, *Synlett* **1995**, 587; b) J. A. Joule, K. Mills, *Heterocyclic Chemistry*, 4th ed., Blackwell Science, Oxford, **2000**; c) D. J. Faulkner, *Nat. Prod. Rep.* **2002**, *19*, 1; d) M. Somei, F. Yamada, *Nat. Prod. Rep.* **2004**, *21*, 278; e) S. Agarwal, S. Cammerer, S. Filali, W. Frohner, J. Knoll, M. P. Krah, K. R. Reddy, H.-J. Knolker, *Curr. Org. Chem.* **2005**, *9*, 1601; f) S. E. O'Connor, J. J. Maresh, *Nat. Prod. Rep.* **2006**, *23*, 532; g) A. J. Kochanowska-Karamyan, M. T. Hamann, *Chem. Rev.* **2010**, *110*, 4489.
- [2] For reviews, see: a) M. Bandini, A. Melloni, A. Umani-Ronchi, *Angew. Chem.* **2004**, *116*, 560; *Angew. Chem. Int. Ed.* **2004**, *43*, 550; b) T. B. Poulsen, K. A. Jørgensen, *Chem. Rev.* **2008**, *108*, 2903; c) S.-L. You, Q. Cai, M. Zeng, *Chem. Soc. Rev.* **2009**, *38*, 2190; d) M. Bandini, A. Eichholzer, *Angew. Chem.* **2009**, *121*, 9786; *Angew. Chem. Int. Ed.* **2009**, *48*, 9608; e) M. Zeng, S.-L. You, *Synlett* **2010**, 1289.
- [3] For selected examples of the asymmetric C3 alkylation of indoles, see: a) J. Zhou, Y. Tang, *J. Am. Chem. Soc.* **2002**, *124*, 9030; b) J. F. Austin, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2002**, *124*, 1172; c) D. A. Evans, K. R. Fandrick, H.-J. Song, *J. Am. Chem. Soc.* **2005**, *127*, 8942; d) Y.-Q. Wang, J. Song, R. Hong, H. Li, L. Deng, *J. Am. Chem. Soc.* **2006**, *128*, 8156; e) Y.-X. Jia, J. Zhong, S.-F. Zhu, C.-M. Zhang, Q.-L. Zhou, *Angew. Chem.* **2007**, *119*, 5661; *Angew. Chem. Int. Ed.* **2007**, *46*, 5565; f) Q. Kang, Z.-A. Zhao, S.-L. You, *J. Am. Chem. Soc.* **2007**, *129*, 1484; g) M. Rueping, B. J. Nachtsheim, S. A. Moreth, M. Bolte, *Angew. Chem.* **2008**, *120*, 603; *Angew. Chem. Int. Ed.* **2008**, *47*, 593; h) J. Itoh, K. Fuchibe, T. Akiyama, *Angew. Chem.* **2008**, *120*, 4080; *Angew. Chem. Int. Ed.* **2008**, *47*, 4016; i) P. Bachu, T. Akiyama, *Chem. Commun.* **2010**, 46, 4112.
- [4] For selected examples of asymmetric Pictet–Spengler reactions of indoles, see: a) M. S. Taylor, E. N. Jacobsen, *J. Am. Chem. Soc.* **2004**, *126*, 10558; b) J. Seayad, A. M. Seayad, B. List, *J. Am. Chem. Soc.* **2006**, *128*, 1086; c) M. J. Wanner, R. N. S. van der Haas, K. R. de Cuba, J. H. van Maarseveen, H. Hiemstra, *Angew. Chem.* **2007**, *119*, 7629; *Angew. Chem. Int. Ed.* **2007**, *46*, 7485; d) I. T. Raheem, P. S. Thiara, E. A. Peterson, E. N. Jacobsen, *J. Am. Chem. Soc.* **2007**, *129*, 13404; e) D. J. Mergott, S. J. Zuend, E. N. Jacobsen, *Org. Lett.* **2008**, *10*, 745; f) I. T. Raheem, P. S. Thiara, E. N. Jacobsen, *Org. Lett.* **2008**, *10*, 1577; g) N. V. Sewgobind, M. J. Wanner, S. Ingemann, R. de Gelder, J. H. van Maarseveen, H. Hiemstra, *J. Org. Chem.* **2008**, *73*, 6405.
- [5] S. Lee, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2007**, *129*, 15438.
- [6] a) D. A. Evans, K. R. Fandrick, H.-J. Song, K. A. Scheidt, R. Xu, *J. Am. Chem. Soc.* **2007**, *129*, 10029; b) Q. Kang, X.-J. Zheng, S.-L. You, *Chem. Eur. J.* **2008**, *14*, 3539; c) M. Zeng, Q. Kang, Q.-L. He, S.-L. You, *Adv. Synth. Catal.* **2008**, *350*, 2169; d) Y.-F. Sheng, G.-Q. Li, Q. Kang, A.-J. Zhang, S.-L. You, *Chem. Eur. J.* **2009**, *15*, 3351; e) L. Hong, C. Liu, W. Sun, L. Wang, K. Wong, R. Wang, *Org. Lett.* **2009**, *11*, 2177; f) L. Hong, W. Sun, C. Liu, L. Wang, K. Wong, R. Wang, *Chem. Eur. J.* **2009**, *15*, 11105.
- [7] a) B. M. Trost, M. J. Krische, V. Berl, E. M. Grenzer, *Org. Lett.* **2002**, *4*, 2005; b) M. Bandini, A. Eichholzer, M. Tragni, A. Umani-Ronchi, *Angew. Chem.* **2008**, *120*, 3282; *Angew. Chem. Int. Ed.* **2008**, *47*, 3238; c) H.-L. Cui, X. Feng, J. Peng, J. Lei, K. Jiang, Y.-C. Chen, *Angew. Chem.* **2009**, *121*, 5847; *Angew. Chem. Int. Ed.* **2009**, *48*, 5737; d) D. Enders, C. Wang, G. Raabe, *Synthesis* **2009**, 4119; e) L. Hong, W. Sun, C. Liu, L. Wang, R. Wang, *Chem. Eur. J.* **2010**, *16*, 440; f) B. M. Trost, M. Osipov, G. Dong, *J. Am. Chem. Soc.* **2010**, *132*, 15800; g) Q. Cai, C. Zheng, S.-L. You, *Angew. Chem.* **2010**, *122*, 8848; *Angew. Chem. Int. Ed.* **2010**, *49*, 8666.
- [8] a) F. Tillequin, M. Koch, M. Bert, T. Sevenet, *J. Nat. Prod.* **1979**, *42*, 92; b) E. O. M. Orlemans, W. Verboom, M. W. Scheltinga, D. N. Reinhoudt, P. Lelieveld, H. H. Fiebig, B. R. Winterhalter, J. A. Double, M. C. Bibby, *J. Med. Chem.* **1989**, *32*, 1612; c) D. Paris, M. Cottin, P. Demonchaux, G. Augert, P. Dupassieux, P. Lenoir, M. J. Peck, D. Jasserand, *J. Med. Chem.* **1995**, *38*, 669; d) P. E. Mahaney, A. T. Vu, C. C. McComas, P. Zhang, L. M. Nogle, W. L. Watts, A. Sarkahian, L. Leventhal, N. R. Sullivan, A. J. Uveges, E. J. Trybulski, *Bioorg. Med. Chem.* **2006**, *14*, 8455; e) L. S. Fernandez, M. S. Buchanan, A. R. Carroll, Y. J. Feng, R. J. Quinn, V. M. Avery, *Org. Lett.* **2009**, *11*, 329; for a review: f) U. Galm, M. H. Hager, S. G. Van Lanen, J. Ju, J. S. Thorson, B. Shen, *Chem. Rev.* **2005**, *105*, 739.
- [9] For the transition-metal-catalyzed allylic alkylation of indoles, see: a) M. Bandini, A. Melloni, A. Umani-Ronchi, *Org. Lett.* **2004**, *6*, 3199; b) M. Bandini, A. Melloni, F. Piccinelli, R. Sinisi, S. Tommasi, A. Umani-Ronchi, *J. Am. Chem. Soc.* **2006**, *128*, 1424; c) S. Ma, S. Yu, Z. Peng, H. Guo, *J. Org. Chem.* **2006**, *71*, 9865; d) B. M. Trost, J. Quancard, *J. Am. Chem. Soc.* **2006**, *128*, 6314; e) 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; f) A. B. Zaitsev, S. Gruber, P. A. Plüss, P. S. Pregosin, L. F. Veiros, M. Wörle, *J. Am. Chem. Soc.* **2008**, *130*, 11604; g) I. Usui, S. Schmidt, M. Keller, B. Breit, *Org. Lett.* **2008**, *10*, 1207; h) W.-B. Liu, H. He, L.-X. Dai, S.-L. You, *Org. Lett.* **2008**, *10*, 1815; i) N. Kagawa, J. P. Malerich, V. H. Rawal, *Org. Lett.* **2008**, *10*, 2381; j) K. Kanao, H. Matsuzawa, Y. Miyake, Y. Nishibayashi, *Synthesis* **2008**, 3869; k) W.-B. Liu, H. He, L.-X. Dai, S.-L. You, *Synthesis* **2009**, 2076; l) K. Onitsuka, C. Kameyama, H. Sasai, *Chem. Lett.* **2009**, *38*, 444; m) Q.-F. Wu, H. He, W.-B. Liu, S.-L. You, *J. Am. Chem. Soc.* **2010**, *132*, 11418; n) M. Bandini, A. Gualandi, M. Monari, A. Romaniello, D. Savoia, M. Tragni, *J. Organomet. Chem.* **2011**, *696*, 338; o) T. Hoshi, K. Sasaki, S. Sato, Y. Ishii, T. Suzuki, H. Hagiwara, *Org. Lett.* **2011**, *13*, 932.
- [10] L. M. Stanley, J. F. Hartwig, *Angew. Chem.* **2009**, *121*, 7981; *Angew. Chem. Int. Ed.* **2009**, *48*, 7841.
- [11] For reviews on Ir-catalyzed allylic substitution reactions, see: a) G. Helmchen, A. Dahnz, P. Dübön, M. Schelwies, R. Weidhofen, *Chem. Commun.* **2007**, 675; b) G. Helmchen in *Iridium complexes in organic synthesis* (Eds.: L. A. Oro, C. Claver), Wiley-VCH, Weinheim, **2009**, p. 211; c) J. F. Hartwig, L. M. Stanley, *Acc. Chem. Res.* **2010**, *43*, 1461; d) G. Helmchen, U. Kazmaier, S. Förster, in *Catalytic Asymmetric Synthesis*, 3rd ed. (Ed.: I. Ojima), Wiley-VCH, New York, **2010**, p. 497; e) J. F. Hartwig, M. J. Pouy, *Top. Organomet. Chem.* **2011**, *34*, 169; f) W.-B. Liu, J.-B. Xia, S.-L. You, *Top. Organomet. Chem.* **2012**, *38*, 155.
- [12] For a recent synthesis of N1-substituted indoles from indolines, see: S. Bayindir, E. Erdogan, H. Kilic, N. Saracoglu, *Synlett* **2010**, 1455, and references therein.
- [13] For selected examples of Ir-catalyzed asymmetric allylic amination reactions, see: a) T. Ohmura, J. F. Hartwig, *J. Am. Chem. Soc.* **2002**, *124*, 15164; b) C. Shu, A. Leitner, J. F. Hartwig, *Angew. Chem.* **2004**, *116*, 4901; *Angew. Chem. Int. Ed.* **2004**, *43*,

- 4797; c) K. Tissot-Croset, D. Polet, A. Alexakis, *Angew. Chem.* **2004**, *116*, 2480; *Angew. Chem. Int. Ed.* **2004**, *43*, 2426; d) R. Weihofen, A. Dahnz, O. Tverskoy, G. Helmchen, *Chem. Commun.* **2005**, 3541; e) R. Weihofen, O. Tverskoy, G. Helmchen, *Angew. Chem.* **2006**, *118*, 5673; *Angew. Chem. Int. Ed.* **2006**, *45*, 5546; f) O. V. Singh, H. Han, *J. Am. Chem. Soc.* **2007**, *129*, 774; g) C. Defieber, M. A. Ariger, P. Moriel, E. M. Carreira, *Angew. Chem.* **2007**, *119*, 3200; *Angew. Chem. Int. Ed.* **2007**, *46*, 3139; h) S. Spiess, C. Welter, G. Franck, J.-P. Taquet, G. Helmchen, *Angew. Chem.* **2008**, *120*, 7764; *Angew. Chem. Int. Ed.* **2008**, *47*, 7652; i) L. M. Stanley, J. F. Hartwig, *J. Am. Chem. Soc.* **2009**, *131*, 8971; j) D. J. Weix, D. Markovic, M. Ueda, J. F. Hartwig, *Org. Lett.* **2009**, *11*, 2944; k) M. J. Pouy, L. M. Stanley, J. F. Hartwig, *J. Am. Chem. Soc.* **2009**, *131*, 11312; l) H. He, W.-B. Liu, L.-X. Dai, S.-L. You, *Angew. Chem.* **2010**, *122*, 1538; *Angew. Chem. Int. Ed.* **2010**, *49*, 1496; m) J.-B. Xia, W.-B. Liu, T.-M. Wang, S.-L. You, *Chem. Eur. J.* **2010**, *16*, 6442; n) J. F. Teichert, M. Fañanás-Mastral, B. L. Feringa, *Angew. Chem.* **2011**, *123*, 714; *Angew. Chem. Int. Ed.* **2011**, *50*, 688; o) M. Lafrance, M. Roggen, E. M. Carreira, *Angew. Chem.* **2012**, *124*, 3572; *Angew. Chem. Int. Ed.* **2012**, *51*, 3470; for recent Ir-catalyzed kinetic resolutions with anionic nitrogen, see: p) L. M. Stanley, C. Bai, M. Ueda, J. F. Hartwig, *J. Am. Chem. Soc.* **2010**, *132*, 8918.
- [14] A. Alexakis, D. Polet, *Org. Lett.* **2004**, *6*, 3529.
- [15] For a recent application of $[[\text{Ir}(\text{dbcot})\text{Cl}]_2]$, see: M. Gärtner, S. Mader, K. Seehafer, G. Helmchen, *J. Am. Chem. Soc.* **2011**, *133*, 2072.
- [16] See the Supporting Information for details.
- [17] See the Supporting Information for details on the crystal structures of **6da** and **14**.
- [18] a) J. J. Vepsäläinen, S. Auriola, M. Tukiainen, N. Ropponen, J. C. Callaway, *Planta Med.* **2005**, *71*, 1053; b) M. B. Johansen, M. A. Kerr, *Org. Lett.* **2008**, *10*, 3497.
- [19] Extended reaction times led to the detection of the elimination product.
- [20] Pd/C and Pd(OH)₂/C were found to be ineffective in removing the benzyl group, even under high pressure.