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Catalytic Asymmetric Synthesis of 2,5-Naphthylpyrrolidine

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Abstract: A novel, straightforward fully catalytic asymmetric synthesis of chiral 2,5-naphthylpyrrolidine based upon an iridium-catalyzed double allylic amination with ammonia has been developed. The products are available in high yields and enantioselectivities.

Key words: asymmetric catalysis, enantioselectivity, heterocycles, transition metals, amination

Chiral 2,5-disubstituted pyrrolidines **1** are versatile chiral compounds that have been used for a large variety of asymmetric transformations (Figure 1). For example, they have been employed as chiral C_2 -symmetric auxiliaries¹ for the asymmetric synthesis of α -amino acids through α -alkylation of glycine derivatives² or stereoselective iodolactonization.³ Furthermore, derivatives of 2,5-chiral pyrrolidines have been shown to act as stereodirecting auxiliaries in asymmetric Wittig rearrangements.⁴ In catalytic asymmetric transformations, these compounds have been used as chiral ligands for the asymmetric addition of diethylzinc to aldehydes⁵ or in palladium-catalyzed allylic alkylation reactions.⁶ More recently, chiral 2,5-disubstituted pyrrolidines have been shown to be efficient organocatalysts for a variety of asymmetric transformations such as Michael additions⁷ and α -halogenation of aldehydes and ketones.⁸

Figure 1 Chiral 2,5-disubstituted pyrrolidines

Phosphoramidite ligands^{9,10} prepared from chiral 2,5-disubstituted pyrrolidines were reported to give high enantioselectivities in asymmetric palladium-catalyzed [3+2] trimethylenemethane cycloadditions.^{11–13} This methodology represents an elegant route towards cyclic compounds, including heterocycles.^{12,13} Not until the introduction of 2,5-arylpyrrolidine-derived phosphoramidites such as **L1** (Figure 2), could these transformations be rendered enantioselective. These ligands thus create a unique chiral environment around a catalytically active metal center upon coordination.¹³ It was this ability that

Figure 2 Phosphoramidite ligand with 2,5-(2-naphthyl)pyrrolidine moiety

prompted us to investigate this class of ligands for transition-metal catalyzed reactions.

Although a few synthetic routes towards chiral 2,5-arylpyrrolidines are known,^{14–16} they do not include the preparation of sterically demanding naphthyl-substituted pyrrolidines **1**. A report employing asymmetric borane reduction of 1,4-diketones specifically highlights the elusiveness of these substrates in undergoing reduction.¹⁵

Approaches based upon the enantioselective deprotonation/arylation of Boc-protected pyrrolidines utilizing organolithium reagents and naturally occurring (–)-sparteine have been disclosed.^{16,17} However, the use of a stoichiometric reagent renders this method expensive and not attractive in terms of atom economy. Moreover, only one enantiomer of the products is available through this approach; a drawback when chiral ligands derived from chiral pyrrolidines are employed in the synthesis of complex target molecules where a particular stereoisomer is desirable.

An elegant catalytic enantioselective synthesis of chiral 2,5-naphthylpyrrolidines based on the reduction of 1,4-diketones with chiral cobalt–salen complexes was reported.¹⁸ Unfortunately, in our hands, these results were not reproducible for the naphthyl-substituted products. Another handicap of this method is the tedious and expensive synthesis of the chiral salen ligands.

Herein, we present a new, catalytic enantioselective synthesis of chiral 2,5-arylpyrrolidines **1** utilizing a catalytic enantioselective allylic amination with iridacycles **8** as the key step (Scheme 1). An important feature of this methodology is the fact that both enantiomers of phosphoramidite ligands^{10,19,20} **L2** for the chiral iridium/phosphoramidite

complex²⁰ **8** are readily available and consequently both enantiomers of the products are accessible.

The iridium-catalyzed allylic amination^{20,21} is a valuable method to efficiently synthesize chiral amines with high optical purity. After the identification of phosphoramidite-derived iridacycles as active catalyst species,²² efforts have been directed to achieve the allylic amination with a variety of nucleophiles, including ammonia.²³ In the latter case, though, double allylic amination was a frequently observed side reaction. We anticipated that a double allylic amination on methyl (*E*)-3-(naphthalen-2-yl)allyl carbonate (**2**) (Scheme 1) could be exploited as a key step for the synthesis of target **4**.

Our synthetic route starts from the carbonate **2**, which was synthesized in good yield by cross-metathesis of 2-vinyl-

naphthalene (**5**) and (*Z*)-4-[methoxycarbonyloxy]but-2-enyl methyl carbonate (**6**) with Hoveyda–Grubbs second-generation catalyst (Scheme 2). To our delight, the allylic amination of **2** employing 6 mol% iridacycle **8**^{22,23} led to dinaphthylallylamine **3** in excellent yields, diastereo- as well as enantioselectivities (95%, 99% ee). The reaction conditions are notably mild, that is, room temperature (Scheme 2). Moreover, ammonia as the nitrogen source is cheap, atom-economic and does not require any further protection group transformations.

The subsequent ring-closing metathesis of **3** was initially examined with molybdenum-based catalysts, since they were reported to exert catalytic activity with unprotected secondary amines.²⁴ In our case however, no turnover was observed, which we attribute to the steric constraints of **3**.

Scheme 1 Asymmetric iridium-catalyzed double allylic amination of **2**

Scheme 2 Asymmetric iridium-catalyzed double allylic amination with ammonia as key step and ring-closing metathesis

Scheme 3 Metal-free reduction of pyrroline 7

Ring-closing metathesis based upon ruthenium catalysts is hampered by the potential donor abilities of the nitrogen in **3**, so we decided to convert **3** to the corresponding HBr salt²⁵ to conceal this functionality. Employing elevated temperatures and 4 mol% **HG II** catalyst, chiral pyrroline **7** was obtained in 79% yield (Scheme 2). Noteworthy is the fact that the corresponding HCl salt of **3** led to decomposition of the starting material. With other Grubbs or Hoveyda–Grubbs (first- or second-generation) catalysts **7** was obtained in lower yields.

The subsequent reduction of the olefin in pyrroline **7** was first attempted by homogenous rhodium-catalyzed hydrogenation, but here also, the unprotected amine suppressed any turnover. The hydrogenation of the HBr salt of **7** was unfruitful as well. Since heterogeneous hydrogenation with palladium on solid supports is known to racemize allylic amines,²⁶ we refrained from applying this methodology to our synthesis. In our institute, a metal-free reduction of olefins based on catalytic formation of diimide **10** from cheap and readily available hydrazine with riboflavin catalyst **9** and molecular oxygen has been developed.²⁷ This method, unobjectionable towards racemization or epimerization, was applied as final step in our synthesis of chiral 2,5-dinaphthylpyrrolidine **4** (Scheme 3). The optimized conditions comprise slow addition of both the riboflavin catalyst **9** and hydrazine hydrate, which gave the desired product in 81% yield without loss of enantioselectivity. The chiral 2,5-substituted pyrrolidine **4** could subsequently be converted into the corresponding phosphoramidite **L1**.¹³

In summary, we have developed a new, concise catalytic asymmetric synthetic route towards chiral 2,5-diarylpyrrolidines. The key step of this synthetic route is a double asymmetric allylic amination with ammonia catalyzed by an iridium/phosphoramidite complex. All steps are high yielding and both enantiomers of the product are available through this novel pathway. We used this new catalytic

route to synthesize the corresponding pyrrolidine-based phosphoramidite ligand **L1**. Studies towards the broadening of the scope of this reaction and the application of the final product as an organocatalyst are currently underway.

Starting materials were purchased from Acros, Sigma-Aldrich or Strem and were used as received unless stated otherwise. All solvents were reagent grade and, if necessary, dried, and distilled prior to use. Toluene was distilled over Na; THF and Et₂O were distilled over Na/benzophenone. Column chromatography was performed on silica gel (Silicycle SiliFlash P60, 230–400 mesh). TLC was performed on silica gel 60/Kieselguhr F254. ¹H and ¹³C NMR spectra were recorded on a Varian Gemini 200, a Varian VXR300 (299.97 MHz for ¹H, 75.48 MHz for ¹³C) or a Varian AMX400 (399.93 MHz for ¹H, 100.59 MHz for ¹³C) spectrometer. Chemical shifts are reported in δ values (ppm) relative to the solvent peak²⁸ [CHCl_3 , δ = 7.26 (¹H), 77.0 (¹³C)]. Mass spectra (HRMS) were performed on a Orbitrap system from Thermo Scientific. HPLC analysis was performed on a Shimadzu HPLC system equipped with two LC-10AD vp solvent delivery systems, a DGU-14 A degasser, a SIL-10AD vp auto injector, an SPD-M10 A vp diode array detector, a CTO-10 A vp column oven, and an SCL-10A vp system controller by using the columns indicated for each compound separately. All glassware were flame-dried prior to use unless noted otherwise. The dicarbonate **6** was synthesized from but-2-ene-1,4-diol according to literature²⁹ and (*S*)-(-)-(1,1'-binaphthalene-2,2'-dioxy)chlorophosphine was synthesized as reported.³⁰ Iridacycle **8**^{22,23} and riboflavin **9**²⁷ were synthesized according to literature.

Methyl (*E*)-3-(Naphthalen-2-yl)allyl Carbonate (**2**)³¹

2-Vinylnaphthalene (**5**; 0.154 g, 1 mmol, 1 equiv) was dissolved in CH_2Cl_2 (10 mL) at r.t. and the dicarbonate **6** (0.409 g, 2 mmol, 2 equiv) was added. Then, a solution of Hoveyda–Grubbs second-generation catalyst (0.031 g, 0.05 mmol, 5 mol%) in CH_2Cl_2 (0.5 mL) was added and the reaction mixture was refluxed for 16 h. After cooling, all volatiles were removed in vacuo to give a brown-green solid. This was purified by column chromatography (SiO_2 , pentane–EtOAc, 20:1) to give **2** as a white powder (0.218 g, 0.9 mmol, 90%); R_f = 0.8 (pentane–EtOAc, 10:1).

¹H NMR (200 MHz, CDCl_3): δ = 7.90–7.72 (m, 4 H), 7.60 (m, 1 H), 7.48 (m, 2 H), 6.86 (d, J = 15.9 Hz, 1 H), 6.43 (dt, J = 15.8, 6.4 Hz, 1 H), 4.86 (dd, J = 6.4, 1.2 Hz, 2 H), 3.85–3.82 (s, 2 H).

^{13}C NMR (50 MHz, CDCl_3): δ = 155.66, 134.85, 133.44, 133.42, 133.20, 128.28, 128.05, 127.64, 127.01, 126.33, 126.15, 123.41, 122.70, 68.46, 54.85.

HRMS-ESI+: m/z [$\text{M} - \text{OCO}_2\text{Me}$] $^+$ calcd for $\text{C}_{13}\text{H}_{11}$: 167.0861; found: 167.0853.

(S)-Bis[(S)-1-(naphthalen-2-yl)allyl]amine (3)

In a glove box, methyl (*E*)-3-(naphthalen-2-yl)allyl carbonate (2; 0.242 g, 1 mmol, 1 equiv) and **8** (0.083 g, 0.060 mmol, 6 mol%) were introduced into a flame-dried Schlenk tube. After sealing, the tube was taken out of the glove box, flushed with N_2 and a 2.0 molar solution of ammonia in EtOH (1.5 mL) was added. Then, anhyd THF was added dropwise until all of the starting material had dissolved (~0.8 mL). The yellow mixture was stirred at r.t. for 16 h. After full conversion had been reached, as checked by TLC, all volatiles were removed in vacuo and the resulting yellow oil was purified by flash chromatography (SiO_2 , pentane–EtOAc, 40:1 + 1% Et_3N) to yield **3** (0.166 g, 0.475 mmol, 95%) as a colorless oil; R_f = 0.85 (pentane–EtOAc, 10:1); $[\alpha]_{\text{D}}^{20}$ –104.6 (c = 1.02, CHCl_3).

HPLC: ee was determined by HPLC analysis, Chiralpak AD (*n*-heptane–*i*-PrOH, 95:5, 215 nm), t_{R} = *S,S*-enantiomer: 4.05 min, *R,R*-enantiomer: 4.67 min. The enantiomeric excess was obtained by comparison of both the pure enantiomers as well as a mixture of both enantiomers of **3**.

^1H NMR (200 MHz, CDCl_3): δ = 7.97–7.81 (m, 6 H), 7.77 (s, 2 H), 7.62–7.40 (m, 6 H), 6.26–5.90 (m, 2 H), 5.33 (t, J = 1.4 Hz, 1 H), 5.28–5.21 (m, 2 H), 5.20–5.15 (m, 1 H), 4.41 (d, J = 6.6 Hz, 2 H), 3.86 (br s, 1 H).

^{13}C NMR (50 MHz, CDCl_3): δ = 140.80, 140.01, 133.45, 132.85, 128.29, 127.81, 127.63, 126.13, 125.98, 125.64, 125.61, 115.23, 62.28.

HRMS-ESI+: m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{26}\text{H}_{24}\text{N}$: 350.1909; found: 350.1901.

(2*S*,5*S*)-2,5-Di(naphthalen-2-yl)-2,5-dihydro-1*H*-pyrrole (7)

(*S*)-Bis[(*S*)-1-(naphthalen-2-yl)allyl]amine (**3**; 0.330 g, 0.944 mmol, 1 equiv) was dissolved in EtOAc (10 mL) at r.t. and HBr solution (32% in AcOH, 5 mL) was added. After stirring for 5 min, all volatiles were removed in vacuo and the yellow oil was dried under vacuum for 16 h to yield a pale yellow solid. This was dissolved in degassed 1,2-dichloroethane (DCE, 5 mL) and subsequently a solution of Hoveyda–Grubbs second-generation catalyst (0.024 g, 0.038 mmol, 2 mol%) in DCE (1 mL) was added. This mixture was heated to reflux for 6 h. Then, an additional 2 mol% of catalyst in DCE (1 mL) was added and the mixture was refluxed for 16 h. The turnover of the reaction was checked by ^1H NMR spectroscopy (samples were washed with 2 N aq KOH and extracted with CH_2Cl_2). After cooling, the mixture was filtered and the resulting brown solid was washed with acetone (3 $\times$ 10 mL) to yield the HBr salt of the desired product **7** as an off-white solid after drying. The resulting organic phase was washed with 2 N aq KOH solution (3 $\times$ 10 mL). After re-extraction of the aqueous layers with CH_2Cl_2 (10 mL), the combined organic phases were dried (Na_2SO_4) and all volatiles were removed in vacuo to yield a dark green solid. This was purified by column chromatography (SiO_2 , pentane–EtOAc, 20:1 + 1% Et_3N) to yield **7** (0.240 g, 0.746 mmol, 79%) as a white powder (combined yield from column chromatography and filtration); R_f = 0.5 (pentane–EtOAc, 10:1); $[\alpha]_{\text{D}}^{20}$ –521.25 (c = 1.01, CHCl_3).

HPLC: ee was determined by HPLC analysis, Chiralcel OD-H (*n*-heptane–*i*-PrOH, 95.5:0.5, 210 nm), t_{R} = *S,S*-enantiomer: 9.47 min, *R,R*-enantiomer: 10.29 min. The enantiomeric excess was obtained by comparison of both the pure enantiomers as well as a mixture of both enantiomers of **7**.

^1H NMR (400 MHz, CDCl_3): δ = 7.90–7.80 (m, 8 H), 7.54 (m, 2 H), 7.52–7.42 (m, 4 H), 6.11 (m, 2 H), 5.56 (m, 2 H), 2.44 (br s, 1 H).

^{13}C NMR (50 MHz, CDCl_3): δ = 141.72, 133.49, 132.91, 132.49, 128.55, 128.36, 127.83, 127.65, 126.64, 126.08, 125.67, 125.32, 125.11, 69.57.

HRMS-ESI+: m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{24}\text{H}_{20}\text{N}$: 322.1596; found: 322.1591.

(2*S*,5*S*)-2,5-Di(naphthalen-2-yl)pyrrolidine (4)¹⁸

(2*S*,5*S*)-2,5-Di(naphthalen-2-yl)-2,5-dihydro-1*H*-pyrrole (**7**; 0.142 g, 0.442 mmol, 1 equiv) (or the corresponding HBr salt) was dissolved in CH_2Cl_2 (10 mL) at r.t., an oxygen atmosphere was applied (balloon) and the reaction mixture was stirred extremely vigorously. Then, via a syringe pump, a solution of riboflavin catalyst **9** (0.180 g) in EtOH (10 mL) and an excess hydrazine hydrate (4.30 mL, 88 mmol) were added over a period of 10 h. The reaction mixture was stirred at r.t. for 16 h and the progress of the reaction was checked by ^1H NMR spectroscopy (samples were washed with H_2O and extracted with CH_2Cl_2). The mixture was washed with H_2O (3 $\times$ 10 mL), the aqueous layers were reextracted with CH_2Cl_2 (10 mL), and the organic layers combined. After drying (Na_2SO_4), all volatiles were removed in vacuo to yield a pale yellow solid. This was purified by column chromatography (SiO_2 , pentane–EtOAc, 20:1 + 1% Et_3N) to yield **4** (0.116 g, 0.358 mmol, 81%) as a white powder; R_f = 0.3 (pentane–EtOAc, 10:1); $[\alpha]_{\text{D}}^{20}$ –127.9 (c = 0.91, CHCl_3).

HPLC: ee was determined by HPLC analysis, Chiralpak AD (*n*-heptane–*i*-PrOH 95:5, 225 nm), t_{R} = *R,R*-enantiomer: 12.33 min, *S,S*-enantiomer: 15.03 min. The enantiomeric excess was obtained by comparison of both the pure enantiomers as well as a mixture of both enantiomers of **4**.

^1H NMR (400 MHz, CDCl_3): δ = 7.94–7.82 (m, 8 H), 7.61 (dd, J = 8.5, 1.7 Hz, 2 H), 7.55–7.42 (m, 4 H), 4.82 (t, J = 6.8 Hz, 2 H), 2.66–2.46 (m, 2 H), 2.39 (br s, 1 H), 2.07 (m, 2 H).

^{13}C NMR (50 MHz, CDCl_3): δ = 143.16, 133.41, 132.63, 128.29, 127.76, 127.60, 126.03, 125.47, 124.99, 124.50, 62.47, 35.53.

HRMS-ESI+: m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{24}\text{H}_{22}\text{N}$: 324.1752; found: 324.1745.

Phosphoramidite Ligand (**L1**)¹³

(2*S*,5*S*)-2,5-Di(naphthalen-2-yl)pyrrolidine (**4**; 0.085 g, 0.263 mmol, 1 equiv), freshly distilled Et_3N (0.183 mL, 1.314 mmol, 5 equiv) and DMAP (3.21 mg, 0.027 mmol, 0.01 equiv) were dissolved in toluene (5 mL) and cooled to 0 $^\circ\text{C}$. To this, a 0.5 molar solution of (*S*)-(–)-(1,1'-binaphthalene-2,2'-dioxo)chlorophosphine (0.631 mL, 0.315 mmol, 1.2 equiv) was added dropwise. The reaction was allowed to warm up to r.t. and stirred for 16 h. Then, all volatiles were removed in vacuo and the residual off-white solid was purified by column chromatography (SiO_2 , pentane–EtOAc, 10:1 + 1% Et_3N) to yield phosphoramidite **L1** (0.100 g, 0.157 mmol, 60%) as a white powder; R_f = 0.9 (pentane–EtOAc, 10:1); $[\alpha]_{\text{D}}^{20}$ –6.2 (c = 0.86, CHCl_3).

^1H NMR (400 MHz, CDCl_3): δ = 7.98–7.79 (m, 10 H), 7.56 (m, 5 H), 7.44 (d, J = 8.5 Hz, 2 H), 7.35–7.29 (m, 3 H), 7.25–7.15 (m, 2 H), 7.11 (m, 2 H), 6.60 (d, J = 8.0 Hz, 1 H), 5.87 (d, J = 8.0 Hz, 1 H), 5.39 (d, J = 6.6 Hz, 2 H), 2.54 (m, 2 H), 1.81 (m, 2 H).

^{13}C NMR (50 MHz, CDCl_3): δ = 149.48, 149.04, 143.39, 143.29, 133.43, 132.75, 131.25, 130.19, 129.89, 128.26, 127.99, 127.70, 127.06, 126.94, 126.24, 125.70, 125.41, 125.22, 124.58, 123.98, 121.91, 120.84, 62.86, 33.23.

^{31}P NMR (162 MHz, CDCl_3): δ = 145.98.

HRMS-APCI+: m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{44}\text{H}_{33}\text{NO}_2\text{P}$: 638.2249; found: 638.2245.

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References

- (1) Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581.
- (2) Ikegami, S.; Hayama, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 3403.
- (3) Kitagawa, O.; Hanano, T.; Kikuchi, N.; Taguchi, T. *Tetrahedron Lett.* **1993**, *34*, 2165.
- (4) Uchikawa, M.; Hanamoto, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 4577.
- (5) Shi, M.; Satoh, Y.; Masaki, Y. *J. Chem. Soc., Perkin Trans. I* **1998**, 2547.
- (6) (a) Chen, H. F.; Sweet, J. A.; Lam, K. C.; Rheingold, A. L.; McGrath, D. V. *Tetrahedron: Asymmetry* **2009**, *20*, 1672. (b) Sweet, J. A.; Cavallari, J. M.; Price, W. A.; Ziller, J. W.; McGrath, D. V. *Tetrahedron: Asymmetry* **1997**, *8*, 207.
- (7) Melchiorre, P.; Jørgensen, K. A. *J. Org. Chem.* **2003**, *68*, 4151.
- (8) (a) Bertelsen, S.; Halland, N.; Bachmann, S.; Marigo, M.; Branton, A.; Jørgensen, K. A. *Chem. Commun.* **2005**, 4821. (b) Halland, N.; Branton, A.; Bachmann, S.; Marigo, M.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 4790. (c) Marigo, M.; Bachmann, S.; Halland, N.; Branton, A.; Jørgensen, K. A. *Angew. Chem. Int. Ed.* **2004**, *43*, 5507.
- (9) Feringa, B. L. *Acc. Chem. Res.* **2000**, *33*, 346.
- (10) Teichert, J. F.; Feringa, B. L. *Angew. Chem. Int. Ed.* **2009**, in press; DOI: anie.200904948.
- (11) (a) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1. (b) Trost, B. M.; Stambuli, J. P.; Silverman, S. M.; Schwörer, U. *J. Am. Chem. Soc.* **2006**, *128*, 13328.
- (12) Trost, B. M.; Cramer, N.; Silverman, S. M. *J. Am. Chem. Soc.* **2007**, *129*, 12396.
- (13) Trost, B. M.; Silverman, S. M.; Stambuli, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 12398.
- (14) (a) Davis, F. A.; Song, M. S.; Augustine, A. *J. Org. Chem.* **2006**, *71*, 2779. (b) Pastine, S. J.; Gribkov, D. V.; Sames, D. *J. Am. Chem. Soc.* **2006**, *128*, 14220. (c) Aggarwal, V. K.; Sandrinelli, F.; Charmant, J. P. H. *Tetrahedron: Asymmetry* **2002**, *13*, 87.
- (15) Aldous, D. J.; Dutton, W. M.; Steel, P. G. *Tetrahedron: Asymmetry* **2000**, *11*, 2455.
- (16) Campos, K. R.; Klapars, A.; Waldman, J. H.; Dormer, P. G.; Chen, C. Y. *J. Am. Chem. Soc.* **2006**, *128*, 3538.
- (17) (a) Beak, P.; Basu, A.; Gallagher, D. J.; Park, Y. S.; Thayumanavan, S. *Acc. Chem. Res.* **1996**, *29*, 552. (b) Beak, P.; Kerrick, S. T.; Wu, S. D.; Chu, J. X. *J. Am. Chem. Soc.* **1994**, *116*, 3231.
- (18) Sato, M.; Gunji, Y.; Ikeno, T.; Yamada, T. *Synthesis* **2004**, 1434.
- (19) (a) Jerphagnon, T.; Pizzuti, M. G.; Minnaard, A. J.; Feringa, B. L. *Chem. Soc. Rev.* **2009**, *38*, 1039. (b) Jerphagnon, T.; Renaud, J. L.; Bruneau, C. *Tetrahedron: Asymmetry* **2004**, *15*, 2101. (c) van den Berg, M.; Feringa, B. L.; Minnaard, A. J. In *Handbook of Homogeneous Hydrogenation*; de Vries, J. G.; Elsevier, C. J., Eds.; Wiley-VCH: Weinheim, **2006**. (d) Harutyunyan, S. R.; den Hartog, T.; Geurts, K.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824. (e) Alexakis, A.; Bäckvall, J. E.; Krause, N.; Pàmies, O.; Diéguez, M. *Chem. Rev.* **2008**, *108*, 2796. (f) Alexakis, A.; Malan, C.; Lea, L.; Tissot-Croset, K.; Polet, D.; Falciola, C. *Chimia* **2006**, *60*, 124. (g) Alexakis, A.; Benhaim, C. *Eur. J. Org. Chem.* **2002**, 3221.
- (20) Helmchen, G.; Dahnz, A.; Dübon, P.; Schelwies, M.; Weihofen, R. *Chem. Commun.* **2007**, 675.
- (21) Defieber, C.; Ariger, M. A.; Moriel, P.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 3139.
- (22) Kiener, C. A.; Shu, C. T.; Incarvito, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 14272.
- (23) Pouy, M. J.; Leitner, A.; Weix, D. J.; Ueno, S.; Hartwig, J. F. *Org. Lett.* **2007**, *9*, 3949.
- (24) Malcolmson, S. J.; Meek, S. J.; Sattely, E. S.; Schrock, R. R.; Hoveyda, A. H. *Nature* **2008**, *456*, 933.
- (25) (a) Weihofen, R.; Tverskoy, E.; Helmchen, G. *Angew. Chem. Int. Ed.* **2006**, *45*, 5546. (b) Binder, J. B.; Blank, J. J.; Raines, R. T. *Org. Lett.* **2007**, *9*, 4885. (c) Jordan, J. P.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **2007**, *46*, 5152.
- (26) (a) Parvulescu, A. N.; Jacobs, P. A.; de Vos, D. *Chem. Eur. J.* **2007**, *13*, 2034. (b) Parvulescu, A.; de Vos, D.; Jacobs, P. *Chem. Commun.* **2005**, 5307.
- (27) Smit, C.; Fraaije, M. W.; Minnaard, A. J. *J. Org. Chem.* **2008**, *73*, 9482.
- (28) Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512.
- (29) Gnam, C.; Franck, G.; Miller, N.; Stork, T.; Brodner, K.; Helmchen, G. *Synthesis* **2008**, 3331.
- (30) Smith, C. R.; Mans, D.; RajanBabu, T. V. *Org. Synth.* **2008**, *85*, 238.
- (31) Stanley, L. M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 8971.