Asymmetric Hydrogenation

Asymmetric Hydrogenation of Disubstituted Furans**

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Dedicated to the MPI für Kohlenforschung on the occasion of its centenary

Abstract: *An enantioselective hydrogenation of disubstituted furans has been developed by using a chiral ruthenium catalyst with N-heterocyclic carbene ligands. This reaction converts furans into valuable enantioenriched disubstituted tetrahydrofurans.*

During the past few decades the asymmetric hydrogenation of heterocyclic aromatic compounds has received increasing interest among synthetic organic chemists.[1] As a consequence of its straightforwardness and excellent atom economy, hydrogenation constitutes a highly attractive method for obtaining enantioenriched organic compounds. Moreover, the asymmetric hydrogenation of aromatic or heteroaromatic compounds gives rapid access to saturated or partially saturated cyclic systems of great importance in biology.[2] When combined with well-established methods for the functionalization of aromatic or heteroaromatic feedstocks, asymmetric hydrogenation constitutes an elegant method for the preparation of enantioenriched densely functionalized cyclic compounds.

However, the asymmetric hydrogenation of aromatic systems is inherently challenging in terms of reactivity (dearomatization) and selectivity (shape and face recognition). In recent years, several impressive homogeneous catalyst systems have been developed which enabled the asymmetric hydrogenation of various heterocycles. Since 1987 efficient methods have been described for quinolines,[3] isoquinolines,[4] quinoxalines,[5] pyridines,[6] indoles/pyrroles,[7] phenanthrolines,[8] (benzo)thiophenes,[9] benzofurans,[10] and carbocycles.[11] In contrast, however, the asymmetric hydrogenation of furans has been notably less explored,[10b,12] despite the importance of tetrahydrofurans as pharmaceut-

icals, agrochemicals, and materials. A pioneering study by Takaya and co-workers in 1995 resulted in the first asymmetric homogeneous hydrogenation of 2-methylfuran.[12a] An enantioselectivity of 50% *ee* was achieved by utilizing a Ru-binap catalyst system. Other significant examples were reported by the Pfaltz research group, who successfully hydrogenated two monosubstituted furans with up to 93% *ee*.[10b] Disubstituted furans have been even less explored, with the sole example in the literature to date being reported by Albert and co-workers (Scheme 1).[12c]
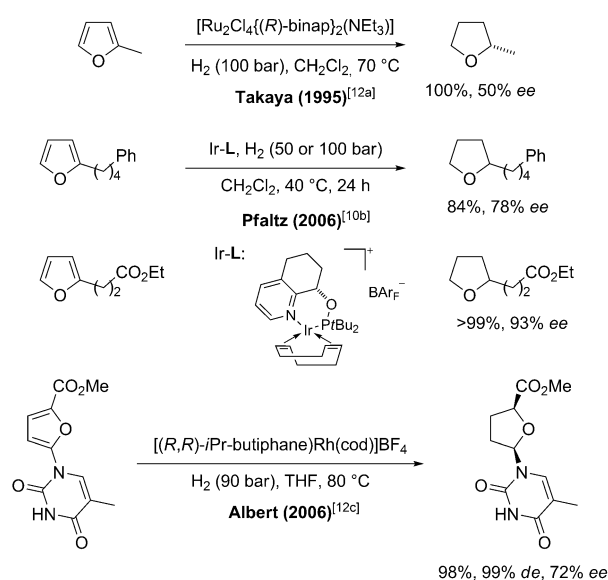
Scheme 1. Rare examples of the asymmetric hydrogenation of furans. $BAr_F^- = [B[3,5-(CF_3)_2C_6H_3]_4]^-$, cod = cycloocta-1,5-dienyl.

Recently, we reported a novel asymmetric hydrogenation catalyst consisting of a Ru^{II} complex bearing the chiral N-heterocyclic carbene ligand SINpEt (see Table 1). This catalyst exhibited excellent activity and high selectivity in the asymmetric hydrogenation of a range of heterocyclic compounds: quinoxalines,[11b] benzofurans,[10c,d] benzothio-phenes,[9c] thiophenes,[9c] flavones,[13] and indolizines.[14] Encouraged by these results we sought to investigate whether challenging furan substrates could also be reduced asymmetrically using this privileged catalytic system.

In our initial experiments the hydrogenation was conducted on the easily accessible disubstituted furan 2-(4-fluorophenyl)-5-methylfuran (**1a**), which was treated with the active ruthenium precatalyst (preformed from [Ru(cod)(2-

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methylallyl)$_2$], SINpEt·HBF$_4$, and KOtBu) in *n*-hexane under 65 bar H$_2$ pressure at 40°C. Pleasingly, the corresponding tetrahydrofuran **2a** was delivered as a 4:1 diastereomeric mixture (*cis/trans*) in 60% conversion with an e.r. value of 85:15.[15] An extensive screening of the reaction parameters was carried out to optimize the yield and enantioselectivity (see the Supporting Information for more details). In analogy with our previous studies, an evaluation of different chiral NHC ligands confirmed the remarkable efficiency of the SINpEt ligand. The other tested ligands resulted in a dramatic decrease in the e.r. value or the yield.

The effect of changing the solvent, H$_2$ pressure, and temperature was then investigated. In each case the hydrogenation was a very clean process, with no side reactions or decomposition of the starting material being detected. The conversion, however, was highly sensitive towards the reaction medium. For example, THF, which chemically resembles the product, resulted in only a trace amount of a nearly racemic product **2a**, even at an elevated temperature of 60°C (Table 1, entry 1). The use of CH$_2$Cl$_2$, a very popular solvent

Table 1: Optimization study.
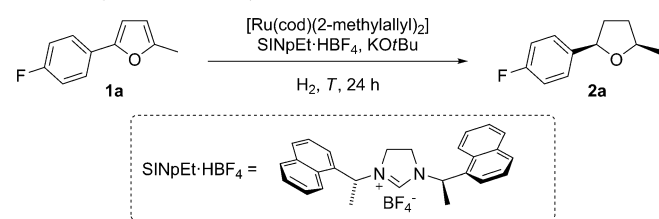
Entry[a]	Solvent	Conv. [%][b]	d.r.[c]	e.r.[d]
1[e,f]	THF	11	n.d.	54:46
2[e,g]	CH$_2$Cl$_2$	0	–	–
3[e,g]	DME	37	3.2:1	89:11
4[e,g]	PhCF$_3$	40	3:1	87:13
5[e,g]	PhCH$_3$	48	3.7:1	86:14
6[e,g]	*n*-hexane	60	4:1	85:15
7[e,g]	*t*-amylOH	66	4.2:1	87:13
8[g,h]	*n*-hexane	90	4.1:1	85:15
9[g,h]	*t*-amylOH	75	4.1:1	87:13
10[g,h]	*t*-amylOH/*n*-hexane (1:1)	80	4.2:1	87:13
11[h,i]	*t*-amylOH/*n*-hexane (1:1)	99 (84%)	4.5:1	88.5:11.5

[a] General conditions: [Ru(cod)(2-methylallyl)$_2$] (0.015 mmol), SINpEt·HBF$_4$ (0.032 mmol), and KOtBu (0.045 mmol) were stirred at 70°C in *n*-hexane (1 mL) overnight, after which the solvent was exchanged for the indicated one (except for entries 7 and 9). The resulting mixture was then added to **1a** (0.30 mmol) and hydrogenated under the shown conditions for 24 h. [b] Determined by ^{1}H NMR spectroscopy; yield of isolated product in parentheses. [c] Determined by ^{1}H NMR spectroscopy; n.d. = not determined. [d] e.r. value for the *cis* product; determined by HPLC on a chiral stationary phase. [e] At 65 bar. [f] At 60°C. [g] At 40°C. [h] At 130 bar. [i] At 25°C. DME = 1,2-dimethoxyethane.

in numerous Ir-catalyzed asymmetric hydrogenations, also returned only starting material (entry 2). More promising results emerged when DME, PhCF$_3$, or toluene were employed as solvents (entries 3–5). Quite surprisingly, the tertiary alcohol *t*-amylOH was a suitable alternative to *n*-hexane, and resulted in a slight increase in conversion as well as the diastereo- and enantioselectivity (entry 7). A more dramatic increase in conversion was achieved upon elevating the pressure of H$_2$ to 130 bar (entry 9). Under this pressure and using a 1:1 (v/v) mixture of *t*-amylOH and *n*-hexane as solvent, the conversion into **2a** was 80%, with no erosion of the e.r. value (entry 10). To our surprise, full conversion could be obtained under these conditions upon lowering the temperature to 25°C (entry 11).

A range of 2,5-disubstituted furans were hydrogenated to their corresponding products under these conditions (Scheme 2). Changing from an electron-withdrawing fluorine atom to an electron-donating OMe group gave rise to product
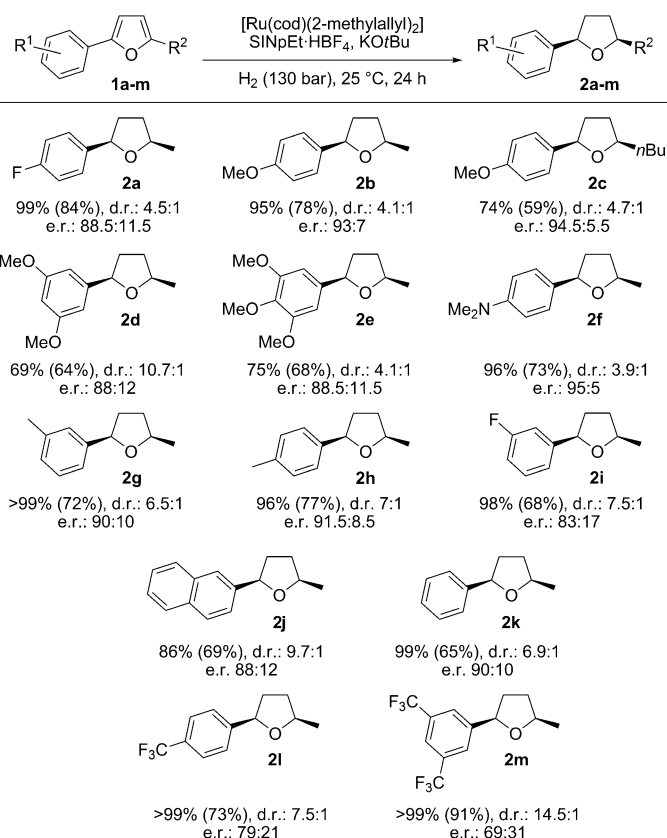
Scheme 2. Substrate scope of 2,5-disubstituted furans. General conditions: [Ru(cod)(2-methylallyl)$_2$] (0.015 mmol), SINpEt·HBF$_4$ (0.032 mmol), and KOtBu (0.045 mmol) were stirred at 70°C in *n*-hexane (0.5 mL) overnight, after which *t*-amylOH (0.5 mL) was added and the mixture was added to a vial containing a substrate (**1a–m**, 0.30 mmol). The hydrogenation reaction was performed under the shown conditions in a steel autoclave. The conversions given were estimated by ^{1}H NMR spectroscopy; the e.r. values for the *cis* products were estimated by HPLC on a chiral stationary phase.

2b in a slightly diminished conversion but with a higher e.r. value of 93:7. Modifying the alkyl substituent from a methyl to an *n*-butyl group resulted in a significantly lower conversion (**2c**). By comparing the results for **2a** and **2b**, we hypothesized that an increase in the polarity of the substrate could be beneficial for the stereochemical outcome. However, the di- and trimethoxy-substituted furans **1d** and **1e** did not follow this trend, furnishing the corresponding

tetrahydrofurans with slightly diminished enantioselectivities. A wide range of diversely substituted aryl-alkyl furans could be successively hydrogenated, and a strong correlation between the electronic properties of the aromatic substituents and the level of enantioselectivity was observed. For example, the furans **1l** and **1m** bearing strongly electron-withdrawing CF$_3$ groups were quantitatively converted into the corresponding products with diminished e.r. values. Interestingly, a simple plot of enantioselectivity (e$_1$/e$_2$) against the relevant σ Hammett parameter of the aryl substituent(s)[16] reveals an almost linear correlation ($R^2 = 0.9374$; Figure 1).
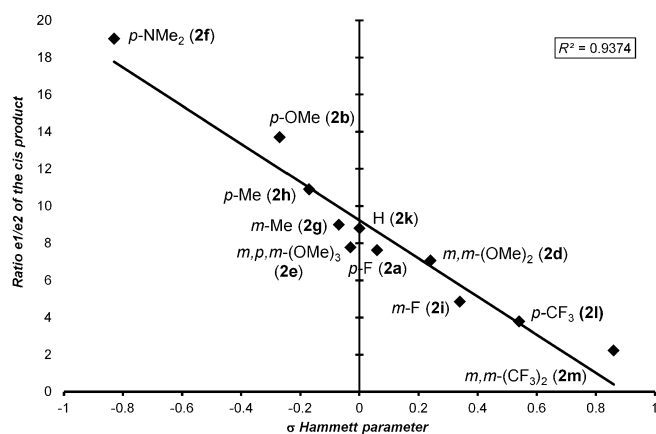

*Figure 1.* Hammett plot for selected 2,5-disubstituted products.

Consequently, furan **1f** with a strongly electron-donating NMe$_2$ group ($\sigma = -0.82$) was synthesized and subjected to the standard hydrogenation conditions. As predicted, the corresponding product **2f** was delivered with an excellent e.r. value of 95:5 in a yield of 73% of the isolated product. The absolute configuration of all three stereoisomers formed (major and minor enantiomer of *cis* product together with the one *trans* enantiomer; see Scheme 2) has been assigned by comparison with the literature optical rotation data for compound **2k**.[17] The absolute configuration of all other compounds was assigned by analogy.

A tentative mechanistic pathway for the hydrogenation of 2,5-disubstituted furans is shown in Scheme 3. Keeping in mind the absolute configuration of the major *cis* enantiomer formed and the enantioinduction of the related asymmetric hydrogenation of 2-substituted benzofurans with a similar catalyst system,[10c] it seems likely that the hydrogenation sequence starts at the alkyl-substituted double bond. Thus, in a stepwise process, the coordination of the substrate to the chiral Ru-NHC catalyst is followed by the enantiodetermining hydrometalation by a Ru-hydride species at the less sterically hindered side of the furan ring, thereby leading to two dihydrofuran stereoisomers (**I1** and **I2**). It is unclear if the major product enantiomer (2*R*,5*R*-*cis*) is then formed by a sequence of hydrodemetalation (reductive elimination) of **I1**, recoordination at the remaining double bond, hydrometalation, and hydrodemetalation. Naturally, recoordination from the other face of the heterocycle would lead to the 2*S*,5*R*-*trans* isomer. Alternatively, the hydrogenation to the
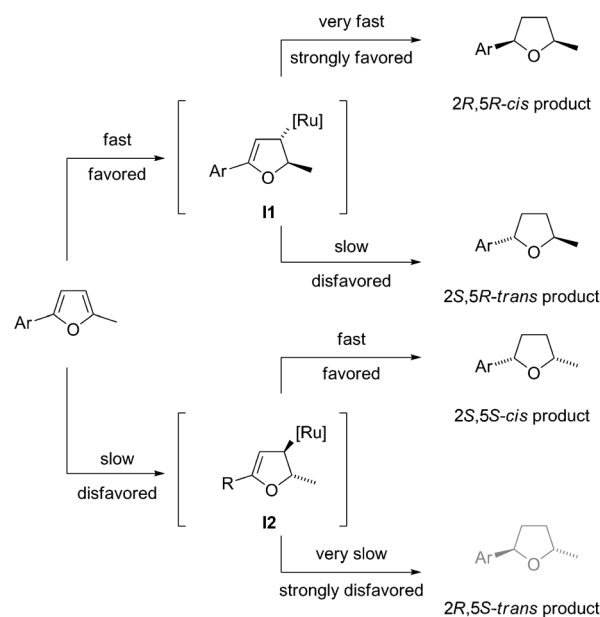
*Scheme 3.* Possible mechanistic pathways (shortened) for the asymmetric hydrogenation of 2,5-disubstituted furans.

major 2*R*,5*R*-*cis* isomer could also continue without decomplexation of the Ru catalyst, through the formation of a Ru-π-allyl complex (Scheme 4) and its hydrodemetalation (reductive elimination) with formation of the second stereocenter. The second less-favored intermediate **I2** might undergo
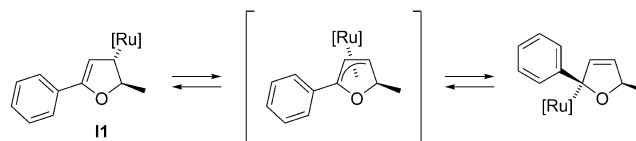
Scheme 4. Possible involvement of a hypothetical Ru-π-allyl species in the formation of the main product.

a similar sequence. In this case, the two possibilities can lead to either the corresponding 2*S*,5*S*-*cis* product or, as a very disfavored step, the 2*R*,5*S*-*trans* product. Remarkably, the 2*R*,5*S* enantiomer was not detected by HPLC with any of the substrates tested (Scheme 2).

At this stage we sought to investigate other substitution patterns of our model furan **1a**.[18] The 2,4-disubstituted furan **3a** was treated with hydrogen gas in the presence of the Ru-NHC catalyst. Although a high conversion of 98% was only observed after 48 h at the higher reaction temperature of 40°C, the corresponding tetrahydrofuran **4a** was furnished as a single *cis* diastereoisomer with an outstanding e.r. value of 99:1 (Scheme 5). Similar results were obtained for a series of 2-methyl-4-aryl-substituted furans. In all cases, the enantiomeric ratio of the obtained products was around 99:1. In contrast to the 2,5-disubstituted substrates, where the electronic properties of the aryl group had a large effect on the level on enantiocontrol, excellent e.r. values were observed
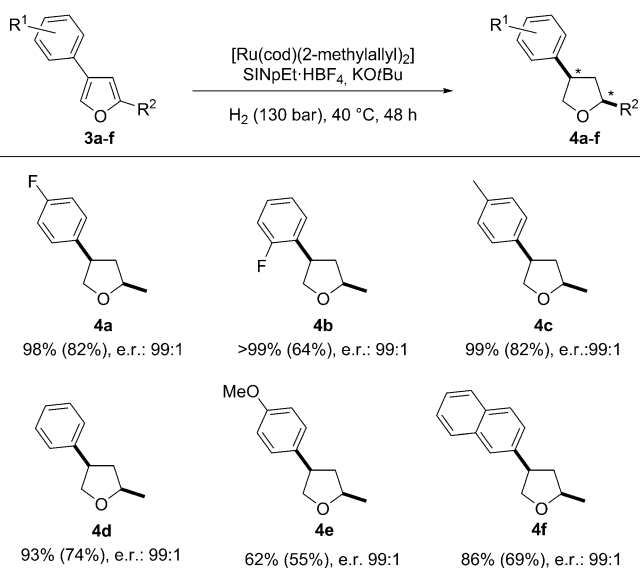
Scheme 5. Substrate scope of 2,4-disubstituted furans. General conditions: [Ru(cod)(2-methylallyl)$_2$] (0.015 mmol), SINpEt·HBF$_4$ (0.032 mmol), and KO*t*Bu (0.045 mmol) were stirred at 70°C in *n*-hexane (0.5 mL) overnight, after which *t*-amylOH (0.5 mL) was added and the mixture was added to a vial containing the substrate (**3a–f**, 0.30 mmol). The hydrogenation reaction was performed under the shown conditions in a steel autoclave. The conversions were estimated by ^{1}H NMR spectroscopy (yields of isolated product in parentheses). The e.r. values were determined by HPLC on a chiral stationary phase.

for all these furans. However, in some cases the reactivity was lower (**4e**, **4f**) and, because of the volatile character of some of the products, the yields of the isolated products lie in the range 55–82% (Scheme 5).

In conclusion we have developed an efficient procedure for the previously underexplored hydrogenation of disubstituted furans. This process gives access to biologically important tetrahydrofurans in high yields and with excellent e.r. values up to 99:1. The asymmetric hydrogenation of furans and other ubiquitous aromatic heterocycles should be of synthetic value.

[1] For reviews on the hydrogenation of aromatic compounds, see a) P. J. Dyson, *Dalton Trans.* **2003**, 2964; b) F. Glorius, *Org. Biomol. Chem.* **2005**, *3*, 4171; c) Y.-G. Zhou, *Acc. Chem. Res.* **2007**, *40*, 1357; d) R. Kuwano, *Heterocycles* **2008**, *76*, 909; e) D.-S. Wang, Q.-A. Chen, S.-M. Lu, Y.-G. Zhou, *Chem. Rev.* **2012**, *112*, 2557; f) Z. Yu, W. Jin, Q. Jiang, *Angew. Chem.* **2012**, *124*, 6164; *Angew. Chem. Int. Ed.* **2012**, *51*, 6060; g) D. Zhao, F. Glorius, *Angew. Chem.* **2013**, *125*, 9794; *Angew. Chem. Int. Ed.* **2013**, *52*, 9616.

[2] a) J. P. Wolfe, M. B. Hay, *Tetrahedron* **2007**, *63*, 261; b) J.-Y. Pan, S.-L. Chen, M.-H. Yang, J. Wu, J. Sinkkonen, K. Zou, *Nat. Prod. Rep.* **2009**, *26*, 1251; c) A. Lorente, J. Lamariano-Merketegi, F. Albericio, M. Álvarez, *Chem. Rev.* **2013**, *113*, 4567.

[3] For selected examples of the asymmetric hydrogenation of quinolines, see a) W.-B. Wang, S.-M. Lu, P.-Y. Yang, X.-W. Han, Y.-G. Zhou, *J. Am. Chem. Soc.* **2003**, *125*, 10536; b) M. Rueping, A. P. Antonchick, T. Theissmann, *Angew. Chem.* **2006**, *118*, 3765; *Angew. Chem. Int. Ed.* **2006**, *45*, 3683; c) H.-F. Zhou, Z.-W. Li, Z.-J. Wang, T.-L. Wang, L.-J. Xu, Y.-M. He, Q.-H. Fan, J. Pan, L.-Q. Gu, A. S. C. Chan, *Angew. Chem.* **2008**, *120*, 8592; *Angew. Chem. Int. Ed.* **2008**, *47*, 8464; d) Q.-S. Guo, D.-M. Du, J. Xu, *Angew. Chem.* **2008**, *120*, 771; *Angew. Chem. Int. Ed.* **2008**, *47*, 759; e) T.-L. Wang, L.-G. Zhuo, Z.-W. Li, F. Chen, Z.-Y. Ding, Y.-M. He, Q.-H. Fan, J.-F. Xiang, Z.-X. Yu, A. S. C. Chan, *J. Am. Chem. Soc.* **2011**, *133*, 9878; f) Q.-A. Chen, K. Gao, Y. Duan, Z.-S. Ye, L. Shi, Y. Yang, Y.-G. Zhou, *J. Am. Chem. Soc.* **2012**, *134*, 2442; g) D.-Y. Zhang, C.-B. Yu, M.-C. Wang, K. Gao, Y.-G. Zhou, *Tetrahedron Lett.* **2012**, *53*, 2556; h) A. M. Maj, I. Suisse, C. Méliet, C. Hardouin, F. Agbossou-Niedercorn, *Tetrahedron Lett.* **2012**, *53*, 4747.

[4] For examples of the asymmetric hydrogenation of isoquinolines, see a) S.-M. Lu, Y.-Q. Wang, X.-W. Han, Y.-G. Zhou, *Angew. Chem.* **2006**, *118*, 2318; *Angew. Chem. Int. Ed.* **2006**, *45*, 2260; b) L. Shi, Z.-S. Ye, L.-L. Cao, R.-N. Guo, Y. Hu, Y.-G. Zhou, *Angew. Chem.* **2012**, *124*, 8411; *Angew. Chem. Int. Ed.* **2012**, *51*, 8286.

[5] For selected examples of the asymmetric hydrogenation of quinoxalines, see a) S. Murata, T. Sugimoto, S. Matsuura, *Heterocycles* **1987**, *26*, 763; b) C. Bianchini, P. Barbaro, G. Scapacci, E. Farnetti, M. Graziani, *Organometallics* **1998**, *17*, 3308; c) C. Bianchini, P. Barbaro, G. Scapacci, *J. Organomet. Chem.* **2001**, *621*, 26; d) L. Qiu, F. Y. Kwong, J. Wu, W. H. Lam, S. Chan, W.-Y. Yu, Y.-M. Li, R. Guo, Z. Zhou, A. S. C. Chan, *J. Am. Chem. Soc.* **2006**, *128*, 5955; e) W. Tang, L. Xu, Q.-H. Fan, J. Wang, B. Fan, Z. Zhou, K.-H. Lam, A. S. C. Chan, *Angew. Chem.* **2009**, *121*, 9299; *Angew. Chem. Int. Ed.* **2009**, *48*, 9135; f) N. Mršić, T. Jerphagnon, A. J. Minnaard, B. L. Feringa, J. G. de Vries, *Adv. Synth. Catal.* **2009**, *351*, 2549; g) M. Rueping, F. Tato, F. R. Schoepke, *Chem. Eur. J.* **2010**, *16*, 2688; h) D. Cartigny, T. Nagano, T. Ayad, J. P. Genêt, T. Ohshima, K. Mashima, V. Ratovelomanana-Vidal, *Adv. Synth. Catal.* **2010**, *352*, 1886; i) D.-W. Wang, D.-S. Wang, Q.-A. Chen, Y.-G. Zhou, *Chem. Eur. J.* **2010**, *16*, 1133; j) Q.-A. Chen, D.-S. Wang, Y.-G. Zhou, Y. Duan, H.-J. Fan, Y. Yang, Z. Zhang, *J. Am. Chem. Soc.* **2011**, *133*, 6126; k) D. Cartigny, F. Berhal, T. Nagano, P. Phanasavath, T. Ayad, P. Genêt, T. Ohshima, K. Mashima, V. Ratovelomanana-Vidal, *J. Org. Chem.* **2012**, *77*, 4544.

[6] For selected examples of the hydrogenation of pyridines, see a) F. Glorius, N. Spielkamp, S. Holle, R. Goddard, C. W. Lehmann, *Angew. Chem.* **2004**, *116*, 2783; *Angew. Chem. Int. Ed.* **2004**, *43*, 2727; b) Z.-S. Ye, M.-W. Chen, Q.-A. Chen, L. Shi, Y. Duan, Y.-G. Zhou, *Angew. Chem.* **2012**, *124*, 10328; *Angew. Chem. Int. Ed.* **2012**, *51*, 10181.

[7] For recent examples of the asymmetric hydrogenation of indoles/pyrroles, see a) R. Kuwano, K. Sato, T. Kurokawa, D. Karube, Y. J. Ito, *J. Am. Chem. Soc.* **2000**, 122, 7614; b) R. Kuwano, K. Kaneda, T. Ito, K. Sato, T. Kurokawa, Y. Ito, *Org. Lett.* **2004**, *6*, 2213; c) R. Kuwano, M. Kashiwabara, *Org. Lett.* **2006**, *8*, 2653; d) R. Kuwano, M. Kashiwabara, M. Ohsumi, H. Kusano, *J. Am. Chem. Soc.* **2008**, *130*, 808–809; e) N. Mršić, T. Jerphagnon, A. J. Minnaard, B. L. Feringa, J. G. de Vries, *Tetrahedron: Asymmetry* **2010**, *21*, 7; f) A. Baeza, A. Pfaltz, *Chem. Eur. J.* **2010**, *16*, 2036; g) D.-S. Wang, Q.-A. Chen, W. Li, C.-B. Yu, Y.-G. Zhou, X. J. Zhang, *J. Am. Chem. Soc.* **2010**, 132, 8909; h) D.-S. Wang, J. Tang, Y.-G. Zhou, M.-W. Chen, Y. Duan, G.-F. Jiang, *Chem. Sci.* **2011**, *2*, 803; i) Y. Duan, M.-W. Chen, Z.-S. Ye, D.-S. Wang, Q.-A. Chen, Y.-G. Zhou, *Chem. Eur. J.* **2011**, *17*, 7193; j) Y. Duan, M.-W. Chen, Q.-A. Chen, C.-B. Yu, Y.-G. Zhou, *Org. Biomol. Chem.* **2012**, *10*, 1235; k) 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.

[8] T. Wang, F. Chen, J. Qin, Y.-M. He, Q.-H. Fan, *Angew. Chem.* **2013**, *125*, 7313; *Angew. Chem. Int. Ed.* **2013**, *52*, 7172.

[9] For selected examples of the hydrogenation of (benzo)thiophenes, see a) C. Bianchini, A. Meli, *Acc. Chem. Res.* **1998**, *31*, 109; b) A. F. Borowski, S. Sabo-Etienne, B. Donnadieu, B. Chaudret, *Organometallics* **2003**, *22*, 4803; c) S. Urban, B. Beiring, N. Ortega, D. Paul, F. Glorius, *J. Am. Chem. Soc.* **2012**, *134*, 15241.

[10] For selected examples of the hydrogenation of benzofurans, see a) M. Maris, W.-R. Huck, T. Mallat, A. Baiker, *J. Catal.* **2003**, *219*, 52; b) S. Kaiser, S. P. Smidt, A. Pfaltz, *Angew. Chem.* **2006**, *118*, 5318; *Angew. Chem. Int. Ed.* **2006**, *45*, 5194; c) N. Ortega, S. Urban, B. Beiring, F. Glorius, *Angew. Chem.* **2012**, *124*, 1742; *Angew. Chem. Int. Ed.* **2012**, *51*, 1710; d) N. Ortega, B. Beiring, S. Urban, F. Glorius, *Tetrahedron* **2012**, *68*, 5185.

[11] For the asymmetric hydrogenation of arenes, see a) R. Kuwano, R. Morioka, M. Kashiwabara, N. Kameyama, *Angew. Chem.* **2012**, *124*, 4212; *Angew. Chem. Int. Ed.* **2012**, *51*, 4136; b) S. Urban, N. Ortega, F. Glorius, *Angew. Chem.* **2011**, *123*, 3887; *Angew. Chem. Int. Ed.* **2011**, *50*, 3803.

[12] For selected examples of the hydrogenation of furans, see a) T. Ohta, T. Miyake, N. Seido, H. Kumobayashi, H. Takaya, *J. Org. Chem.* **1995**, *60*, 357; b) M. Studer, C. Wedemeyer-Exl, F. Spindler, H.-U. Blaser, *Monatsh. Chem.* **2000**, *131*, 1335; c) P. Feiertag, M. Albert, U. Nettekoven, F. Spindler, *Org. Lett.* **2006**, *8*, 4133.

[13] D. Zhao, B. Beiring, F. Glorius, *Angew. Chem.* **2013**, *125*, 8612; *Angew. Chem. Int. Ed.* **2013**, *52*, 8454.

[14] N. Ortega, D.-T. D. Tang, S. Urban, D. Zhao, F. Glorius, *Angew. Chem.* **2013**, *125*, 9678; *Angew. Chem. Int. Ed.* **2013**, *52*, 9500.

[15] Throughout this study, the minor *trans* isomers of 2,5-disubstituted tetrahydrofurans were observed as single enantiomers.

[16] C. Hansch, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165.

[17] M. Tiecco, L. Testaferri, L. Bagnoli, V. Purgatorio, A. Temperini, F. Marini, C. Santi, *Tetrahedron: Asymmetry* **2004**, *15*, 405.

[18] Our attempt to hydrogenate 2-phenylfuran as a representative monosubstituted furan afforded the corresponding product with full conversion, although with a low *ee* value (20%).