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Asymmetric Catalysis |*Hot Paper*|

Asymmetric Hydrogenation of Furans and Benzofurans with Iridium–Pyridine–Phosphinite Catalysts

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Abstract: Enantioselective hydrogenation of furans and benzofurans remains a challenging task. We report the hydrogenation of 2- and 3-substituted furans by using iridium catalysts that bear bicyclic pyridine–phosphinite ligands. Excellent enantioselectivities and high conversions were obtained for monosubstituted furans with a 3-alkyl or 3-aryl group. Furans substituted at the 2-position and 2,4-disubstituted furans proved to be more difficult substrates. The best results (80–97% conversion, 65–82% enantiomeric excess) were obtained with monosubstituted 2-alkylfurans and 2-[4-(trifluoromethyl)phenyl]furan. Benzofurans with an alkyl substituent at the 2- or 3-position also gave high conversions and enantioselectivity, whereas 2-aryl derivatives showed essentially no reactivity. The asymmetric hydrogenation of a 3-methylbenzofuran derivative was used as a key step in the formal total synthesis of the cytotoxic naphthoquinone natural product (−)-thespesone.

Introduction

Chiral tetrahydrofuran and dihydrobenzofuran moieties are ubiquitous structural elements of biologically active natural products. Thus, efficient enantioselective routes to compounds of this type are of considerable interest in pharmaceutical research.[1] Typical examples of natural tetrahydrofuran derivatives are marmelo oxide A and its diastereomer marmelo oxide B,[2] or the diastereomeric calyxolanes A and B, isolated from the marine sponge *Calyx podatypa* (Figure 1).[3] Biologically active dihydrobenzofuran-derived natural products include conocarpan,[4] corsifuran A,[5] and thespesone (**1**), isolated in 1983 from the heartwood of the tree *Thespesia populnea*.[6] Recently, a first total synthesis of **1** and its non-natural enantiomer was reported, along with its cytotoxic activity against a small panel of human cancer cell lines. The tricyclic ring system of **1** was assembled by coupling a squaric acid precursor **3** with the brominated dihydrobenzofuran **2** (Figure 1), which, in turn, was prepared in eight steps in 8.3% overall yield.[7]

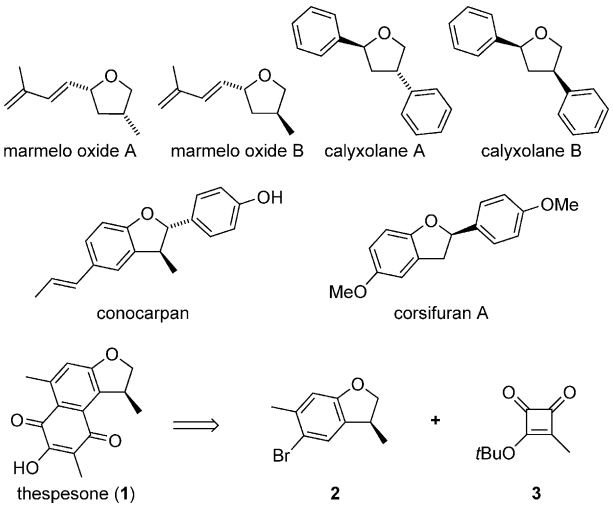

Figure 1. Selected natural products that contain a chiral tetrahydrofuran or dihydrobenzofuran moiety.

Asymmetric hydrogenation provides an attractive, very direct route to enantioenriched tetrahydrofurans and dihydrobenzofurans from aromatic precursors, which are, in general, easily accessible. For example, the reported synthesis of **1** could be considerably shortened by using enantioselective hydrogenation for the introduction of the stereocenter in precursor **2**. However, despite substantial efforts over the last two decades, enantioselective hydrogenation of furans and benzofurans is still limited in scope.[8]

After the pioneering study of the Takaya group in 1995, which reported a 50% enantiomeric excess (*ee*) for the hydrogenation of 2-methylfuran with a Ru–BINAP catalyst (BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl),[8a] further progress was rather slow. In 2003, two heterogeneous catalyst systems were disclosed that gave 77% *ee* for the hydrogenation of 2-methylfuran (catalyzed by Rh on wool)[8b] and 98% *ee* for the hydrogenation of furfuryl alcohol (catalyzed by a Pt–biopolymer complex).[8e] However, these systems were not well defined and the scope was not investigated. In 2006, Spindler and co-workers published a Rh–diphosphine catalyzed hydro-

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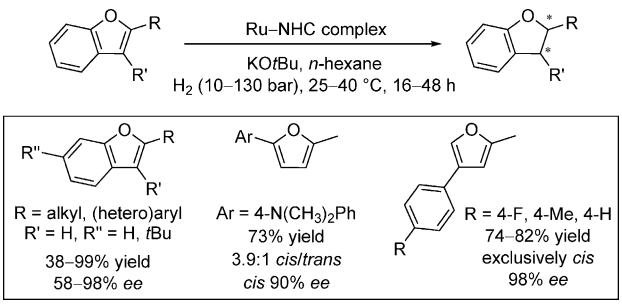
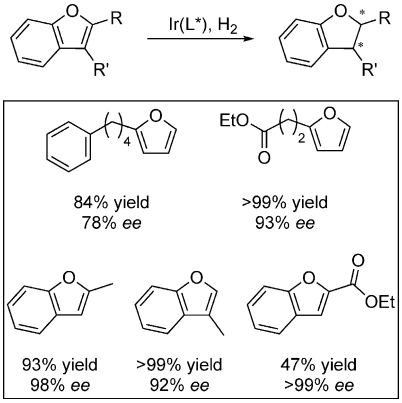
genation of a disubstituted furan with a thymine and a methoxycarbonyl group at the 2- and 5-positions to afford the corresponding tetrahydrofuran with perfect *cis* selectivity and 72% *ee*.[8f]

A very efficient catalyst for the asymmetric hydrogenation of furans and benzofurans was recently reported by Glorius and co-workers.[8i–k] With a Ru catalyst based on a chiral N-heterocyclic carbene (NHC) ligand high enantioselectivities and yields were achieved for a broad range of disubstituted furans and 2-alkyl- and 2-aryl-substituted benzofurans (Scheme 1).



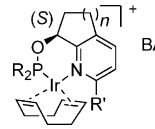
Scheme 1. Asymmetric hydrogenation of furans and benzofurans (Glorius and co-workers).[8i–k]

A systematic study of the asymmetric hydrogenation of heteroaryl-substituted alkenes carried out in our laboratory revealed that certain Ir catalysts based on N,P ligands not only reduce the olefinic C=C bond but also an attached furyl substituent.[8d] In a subsequent screening of various catalysts, bicyclic pyridine–phosphinite complexes such as **C1** and **C3**, with bulky electron-rich P(*t*Bu)$_2$ groups, emerged as the most effective catalysts for the asymmetric hydrogenation of the furan and benzofuran derivatives shown in Scheme 2.[8g] In view of



Scheme 2. Initial studies of the asymmetric hydrogenation of furans and benzofurans with Ir/N,P-ligand complexes.[8g]

these promising results, we extended our studies to a range of substituted furans and benzofurans. Here, we report the results of this work, which demonstrates the scope and limitations of catalysts **C1** and **C3** for the asymmetric hydrogenation of these challenging substrates.



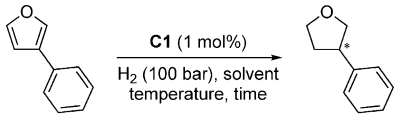
C1: *n* = 1, R= *t*Bu, R'= Ph
C2: *n* = 1, R= Ph, R'= Ph
C3: *n* = 2, R= *t*Bu, R'= CH_3
BAr_F: $B(3,5\text{-}(F_3C)_2C_6H_3)_4$

Results and Discussion

3-Substituted furans

Among the various iridium catalysts that we evaluated for the hydrogenation of 3-phenylfuran (see the Supporting Information), only catalyst **C1** showed sufficient activity and promising enantioselectivity. Therefore, optimization of the reaction conditions was focused on this catalyst (Table 1).

Table 1. Asymmetric hydrogenation of **4**.



4 **5**

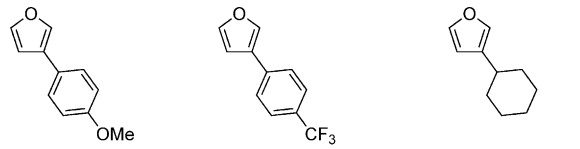
Entry	Time [h]	Solvent	Temperature [°C]	Conversion [%][a]	*ee* [%][a]
1	4	CH_2Cl_2	25	36	>98 (−)
2	24	CH_2Cl_2	25	74	>99 (−)
3	24	CH_2Cl_2	40	86	99 (−)
4	24	CH_2Cl_2	60	94	99 (−)
5	24	CH_2Cl_2	60	96	99 (−)[b]
6	24	PhCl	60	98	99 (−)[b]
7	24	PhCl	60	99	98 (+)[c]

[a] Determined by GC analysis on a chiral stationary phase. [b] Catalyst (2 mol%). [c] The *R* enantiomer of the catalyst was used.

At room temperature in dichloromethane with catalyst **C1** (1 mol%), 3-phenylfuran was cleanly reduced to the fully saturated product **5** with virtually perfect enantioselectivity (Table 1, entry 1). However, the reaction was slow and only 74% conversion was observed after 24 h (Table 1, entry 2). To drive the reaction to completion, the temperature and reaction time were increased. At 60 °C almost full conversion was achieved after 24 h (Table 1, entry 4). Gratifyingly, 99% *ee* was still reached at this temperature. Changing the solvent from dichloromethane to chlorobenzene led to an increase of conversion from 94 to 99% and the *ee* remained essentially the same (Table 1, entry 7). Because of the somewhat higher reactivity of the catalyst in chlorobenzene, further studies were carried out in this solvent.

Under these optimized conditions (60 °C, 100 bar H_2, 24 h) other 3-substituted furans were hydrogenated. Again, the best results were obtained with catalyst **C1**.

Substrates **6** and **7** with an electron-donating *para*-methoxy and an electron-withdrawing *para*-trifluoromethyl group in the phenyl substituent showed very similar conversion and enantioselectivity. The analogue **8**, with a cyclohexyl instead of a phenyl substituent, proved to be more reactive and afforded the corresponding tetrahydrofuran with full conversion and

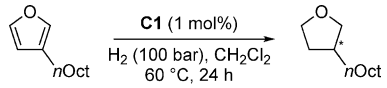


6: 83%, 95% *ee* (–) **7**: 88%, 97% *ee* (–) **8**: >99%, 98% *ee* (–)

Figure 2. Selected examples of 3-substituted furans hydrogenated with catalyst **C1**. Reaction conditions: H_2 (100 bar), PhCl, 60 °C, 24 h; **6**: catalyst (1 mol%), **7** and **8**: catalyst (2 mol%).

98% *ee* (Figure 2). On the other hand, the *n*-alkyl-substituted furan **9** reacted sluggishly under the same conditions (20% conversion), albeit with 95% *ee* (Table 2, entry 1).

Table 2. Ir-catalyzed hydrogenation of **9**.



9 **10**

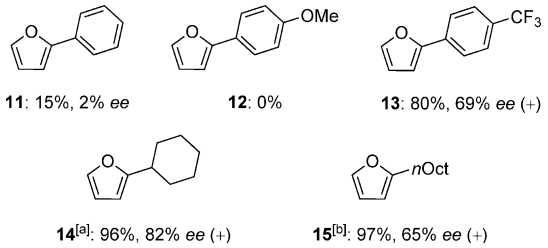
Entry	Additive	Amount [equiv]	Conversion [%][a]	*ee* [%][a]
1	–	–	20	95 (–)
2	$B(OCH_3)_3$	1.74	21	95 (–)
3	$BF_3{\cdot}O(C_2H_5)_2$	1.01	>99	59 (+)
4	$B(C_6F_5)_3$	1.01	>99	41 (+)
5	CF_3CH_2OH	2.75	17	93 (–)
6	CF_3CH_2OH	70	94	95 (–)[b]

[a] Determined by GC analysis on a chiral stationary phase. [b] Catalyst loading (2 mol%), CF_3CH_2OH as solvent.

Besides the loss of aromaticity during hydrogenation, coordination of the furan oxygen atom to the catalyst could be an additional factor responsible for the observed low reactivity of furans. Therefore, we decided to examine the effect of Lewis acid coordination to the oxygen atom to prevent catalyst deactivation. Addition of trimethyl borate had no notable effect on the conversion or *ee* (Table 2, entry 2). However, a strong increase in reactivity was induced by the stronger Lewis acids $BF_3{\cdot}OEt_2$ and tris(pentafluorophenyl)borane, albeit at the expense of a substantial loss of enantioselectivity (Table 2, entries 3 and 4). Trifluoroethanol, a moderately Brønsted acidic hydrogen-bond donor, but only weakly coordinating solvent, was also examined. Whereas addition of trifluoroethanol (2.75 equiv) had only a small effect, full conversion and high enantioselectivity were achieved when it was used as solvent (Table 2, entries 5 and 6). Although the origin of this surprisingly large rate increase is not entirely clear, we think that coordination of the furan oxygen atom to the catalyst is inhibited by hydrogen-bond formation with the solvent. At the same time the non-nucleophilic nature of this solvent provides a very weakly coordinating environment, which is necessary for high catalytic activity. The strong rate-enhancing effect of trifluoroethanol offers a practically useful solution to overcome reactivity problems in the hydrogenation of furans and benzofurans.

2-Substituted furans

2-Substituted furans proved to be less reactive than their 3-substituted counterparts. Low conversion and almost racemic product was observed for 2-phenylfuran (**11**), whereas 2-(*para*-methoxyphenyl)furan (**12**) did not react at all (Figure 3). On the other hand, substrate **13** with an electron-withdrawing (*para*-trifluoromethyl)phenyl substituent gave 80% conversion and a moderate *ee*, whereas analogues **14** and **15** with a 2-alkyl substituent were reduced almost completely (Figure 3). It is difficult to draw general conclusions from these results but, apparently, an electron-rich 2-aryl group strongly interferes with the reaction. Although high conversions were achieved with 2-alkylfurans, the enantioselectivity was lower than for the reactions of 3-substituted furans.



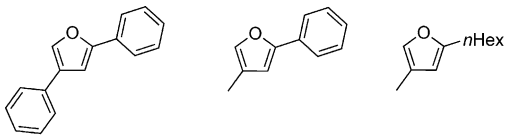
11: 15%, 2% *ee* **12**: 0% **13**: 80%, 69% *ee* (+)

14[a]: 96%, 82% *ee* (+) **15**[b]: 97%, 65% *ee* (+)

Figure 3. Selected examples of 2-substituted furans hydrogenated with catalyst **C1**. Reaction conditions: catalyst (1 mol%), H_2 (100 bar), CH_2Cl_2, 60 °C, 24 h. [a] Catalyst (2 mol%). [b] CF_3CH_2OH as solvent.

2,4-Disubstituted furans

Asymmetric hydrogenation of 2,4-disubstituted furans turned out to be very challenging, not least because of the problem of controlling *cis*/*trans* selectivity. First, 2,4-diphenylfuran (**16**), a potential precursor of calyxolanes A and B, was investigated. Only low conversion and moderate *cis*/*trans* selectivity were achieved in this case. Catalyst **C1** reduced the substrate with poor conversion (5%) and a *cis*/*trans* ratio of 66:34. Slightly better selectivity and conversion were obtained with catalyst **C2**. The *trans* isomer (calyxolane A) was obtained with 68% *ee* (Figure 4). The 2-phenyl-4-methyl analogue **17** proved to be more reactive and afforded the corresponding tetrahydrofuran with 60% conversion and good diastereoselectivity in favor of the *cis* isomer, however, the *ee* was very low. The dialkyl-substi-



16: **C2**[a]; 18%
73:27 *cis*/*trans*
cis 38% *ee*, *trans* 68% *ee*

17: **C1**; 60%
92:8 *cis*/*trans*
cis 28% *ee*

18: **C1**[b]; >99%
86:14 *cis*/*trans*
cis 55% *ee*

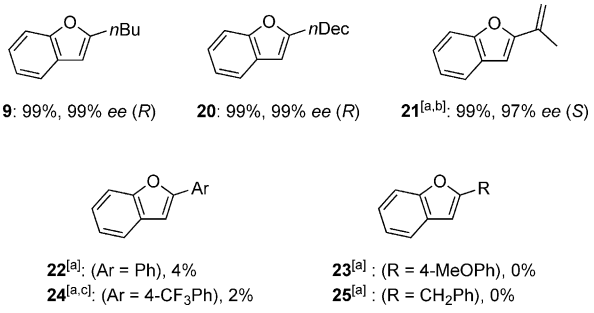
Figure 4. Hydrogenation of 2,4-disubstituted furans. Reaction conditions: catalyst (1 mol%), H_2 (100 bar), CH_2Cl_2, 60 °C, 24 h. [a] Performed at 100 °C in PhCl. [b] $B(C_6F_5)_3$ (1 equiv) as additive.

tuted furan **18** gave only 6% conversion but was fully hydrogenated when the reaction was carried out in the presence of tris(pentafluorophenyl)borane (1 equiv; Figure 4). Again the *cis/trans* selectivity and *ee* were only moderate. The analogous reaction in trifluoroethanol gave 46% conversion and the same *cis/trans* ratio.

A 2,5-disubstituted analogue, 2-octyl-5-phenylfuran, was also tested. However, only very low conversion (7%) was achieved when catalyst **C1** was applied under the standard conditions.

2-Substituted benzofurans

2-Alkyl-substituted benzofurans showed high reactivity under the standard conditions and were cleanly converted to the corresponding dihydrobenzofurans with excellent enantioselectivity. In contrast, the corresponding aryl-substituted substrates **22**–**24**, as well as the benzyl-substituted analogue **25**, gave virtually no conversion (Figure 5). The reason for this lack of reactivity, which has also been observed for 2-arylfurans (Figure 3; furans **11** and **12**), is unclear. Possibly, chelation by the furan oxygen atom and the aryl π system could deactivate the catalyst. However, attempts to elucidate the nature of the inhibitory effect of these aromatic groups were unsuccessful.



19: 99%, 99% *ee* (*R*) **20**: 99%, 99% *ee* (*R*) **21**[a,b]: 99%, 97% *ee* (*S*)

22[a]: (Ar = Ph), 4%
24[a,c]: (Ar = 4-CF_3Ph), 2%

23[a] : (R = 4-MeOPh), 0%
25[a] : (R = CH_2Ph), 0%

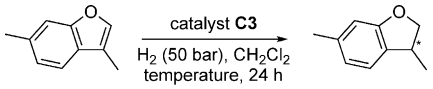
Figure 5. Hydrogenation of 2-substituted benzofurans with catalyst **C1**. Reaction conditions: catalyst (1 mol%), H_2 (50 bar), CH_2Cl_2, 60 °C, 24 h. [a] H_2 (100 bar). [b] The propenyl substituent was fully reduced. [c] Performed in PhCl.

3-Substituted benzofurans

With an enantioselective synthesis of **1** in mind with the asymmetric hydrogenation of benzofuran **31** as the key step (see Scheme 4, below), 3,6-dimethylbenzofuran (**27a**) was chosen as the test substrate for initial hydrogenation studies (Table 3). This substrate and related 3-substituted benzofurans were prepared from the corresponding acetophenone **26** by Corey–Chaykovsky reaction, followed by intramolecular epoxide opening and elimination of water (Scheme 3).[9]

Among a series of iridium catalysts, complex **C3** emerged as the catalyst of choice for the hydrogenation of benzofuran **27a** and provided the desired product with up to 93% *ee* (Table 3, entries 1 and 2). Again, low reactivity was a problem in this case. The best results were achieved at 60 °C (Table 3, entry 3); a further increase of the temperature had a negative effect on the conversion (Table 3, entry 4). An increase in catalyst loading to 2 mol% resulted in higher conversion reaching 85% at 60 °C (Table 3, entry 2 versus 3).

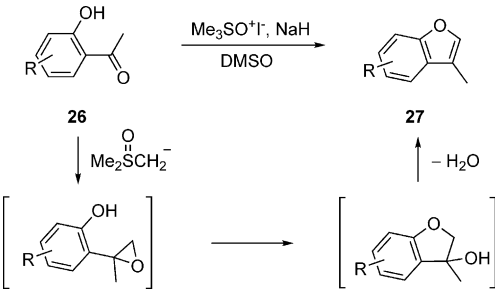
Table 3. Asymmetric hydrogenation of **27a**.



27a **28a**

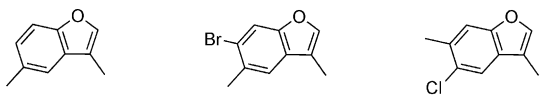
Entry	Temperature [°C]	Catalyst loading [mol%]	Conversion [%][a]	*ee* [%][b]
1	50	2	79	91 (–)
2	60	1	49	93 (–)
3	60	2	85	91 (–)
4	80	1	40	90 (–)

[a] Determined by ^{1}H NMR spectroscopy. [b] Determined by HPLC analysis on a chiral stationary phase.



Scheme 3. Synthesis of 3-methylbenzofurans.

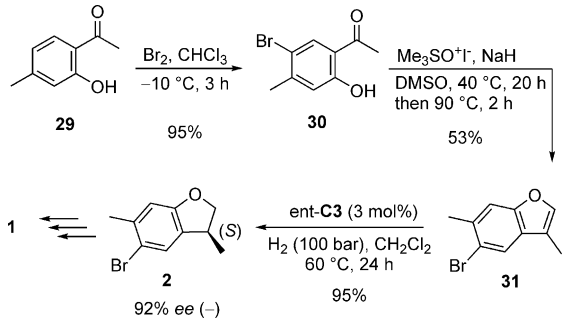
The isomeric compound 3,5-dimethylbenzofuran (**27b**) and the bromo- and chloro-substituted derivatives **27c** and **27d**, respectively, gave similar results (Figure 6). The highest conversion was achieved with **27b**, whereas the halogenated derivatives were slightly less reactive. The best enantioselectivity (95% *ee*) was observed for chlorobenzofuran **27d**; *ee* values obtained for the other derivatives ranged between 91–93%.



27b: 89%, 92% *ee* (+) **27c**: 75%, 91% *ee* (+) **27d**: 77%, 95% *ee* (+)

Figure 6. Asymmetric hydrogenation of 3-methylbenzofuran derivatives with catalyst **C3**. Reaction conditions: H_2 (50 bar), CH_2Cl_2, 60 °C, 24 h; **27b**: catalyst (1 mol%), **27c** and **d**: catalyst (2 mol%).

With optimized conditions for this substrate class at hand, the potential precursor of **1**, 5-bromobenzofuran **31** was synthesized (Scheme 4). Acetophenone **29** was brominated with perfect selectivity and excellent yield to afford bromophenol **30**.[10] Subsequent reaction with dimethyloxosulfonium methylide led to the desired benzofuran **31** in 53% yield. It was essential to perform the epoxidation at moderate temperature to prevent O-methylation of the phenol. After consumption of



Scheme 4. Formal total synthesis of **1**.

the starting material the temperature had to be increased to obtain full conversion of the intermediate tertiary alcohol to benzofuran **31**.

Screening of different iridium catalysts confirmed that complex **C3** was the most suitable catalyst for the hydrogenation of **31**. Although complex **C1** gave higher conversion under standard conditions (95%), the enantioselectivity was distinctly lower (46% *ee*). Catalyst **C3** afforded the desired product (*S*)-(−)-**2** with 89% *ee*, albeit in only 57% conversion under the standard conditions. However, increasing the hydrogen pressure to 100 bar and the catalyst loading to 3 mol% resulted in full conversion. By using this protocol, hydrogenation on a 1 mmol scale led to enantioenriched dihydrobenzofuran **2** with 92% *ee* in 95% yield after column chromatography (Scheme 4). In this way, dihydrobenzofuran **2**, which had been used as an intermediate in the total synthesis of **1** by Schobert and co-workers,[7] was prepared in an overall yield of 48% from commercially available hydroxyacetophenone **29**. This route compares favorably to the published synthesis of **2**, which required ten steps and gave an overall yield of only 7%, and illustrates the potential of Ir-catalyzed hydrogenation for the asymmetric synthesis of chiral tetrahydrofurans and dihydrobenzofurans.

Conclusion

Iridium complexes derived from chiral pyridine–phosphinite ligands proved to be efficient catalysts for the asymmetric hydrogenation of furans and benzofurans. Catalyst **C1** with sterically demanding electron-rich P(*t*Bu)$_2$ groups, a five-membered carbocyclic ring, and a phenyl group next to the pyridine nitrogen atom emerged as the most versatile catalyst, and gave high yields and good-to-excellent enantioselectivities for a range of monosubstituted alkyl- and arylfurans and 2-alkylbenzofurans. Complex **C3**, which contains a six-membered rather than a five-membered carbocyclic ring and a methyl group next to the pyridine nitrogen atom, gave the best results for the hydrogenation of 3-methyl-substituted benzofurans. This catalyst was successfully applied in the hydrogenation of a 5-bromobenzofuran derivative to give an intermediate used in a previous synthesis of **1**.

The scope of these iridium catalysts and the ruthenium catalysts developed by Glorius and co-workers[8i–k] is complementary. Whereas the ruthenium-based catalysts have been successfully applied to the asymmetric hydrogenation of 2-arylbenzofurans, iridium-based catalysts showed only very low or no reactivity towards these substrates. For 2-alkyl-substituted benzofurans iridium complex **C1** induces higher enantioselectivities than ruthenium catalysts, whereas for disubstituted furans, ruthenium complexes are superior catalysts. On the other hand, no Ru-catalyzed hydrogenations have been reported for monosubstituted furans, a substrate class we have shown to be well suited to Ir catalysis. Taken together, these ruthenium and iridium catalysts enable asymmetric hydrogenation of a wide range of furans and benzofurans with high efficiency and enantioselectivity.

Experimental Section

Typical procedure for Ir-catalyzed hydrogenation

Catalyst screening was performed on a 0.1 mmol scale. Catalyst **C** (1.0 μmol, 1 mol%) was added to a solution of the substrate (0.1 mmol) in dry CH_2Cl_2 (0.5 mL). The reaction vial was equipped with a magnetic stirrer bar and placed in an autoclave that was pressurized to 50 or 100 bar H_2. The reaction mixture was stirred for 24 h at 60 °C before hydrogen gas was released. The solvent was removed under reduced pressure and the residue filtered through a plug of silica gel (0.5×3 cm) with a 4:1 mixture of hexane/MTBE (5 mL) as the eluent. After concentration of the filtrate, the obtained hydrogenation product was analyzed.

Bromination of 29

A 50 mL round-bottom flask was equipped with a magnetic stirrer bar and charged with a solution of **29** (1.00 g, 6.66 mmol, 1.00 equiv) in $CHCl_3$ (10 mL). At −10 °C, a solution of bromine (1.06 g, 6.66 mmol, 1.00 equiv) in $CHCl_3$ (2.5 mL) was added dropwise, so that the temperature did not exceed −5 °C. After stirring for 3 h at −5 °C, the reaction mixture was poured into water and the phases were separated. The organic layer was washed with water (10 mL), an aqueous saturated solution of sodium sulfite (2× 10 mL) and water (10 mL), dried over $MgSO_4$, and concentrated. The remaining solid was recrystallized from hot *n*-hexane (10 mL) to obtain **30** as colorless crystals (1.45 g, 6.33 mmol, 95%). R_f = 0.64 (SiO_2, 6:4 cyclohexane/EtOAc); m.p. 79–81 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$, 300 K): δ = 12.09 (s, 1H), 7.85 (s, 1H), 6.88 (s, 1H), 2.60 (s, 3H), 2.39 ppm (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K): δ = 203.2, 161.6, 147.6, 133.9, 120.6, 119.5, 113.6, 26.8, 23.8 ppm; IR: $\tilde{\nu}$ = 3075, 2964, 2360, 2342, 1700, 1635, 1616, 1475, 1371, 1331, 1312, 1264, 1252, 1215, 1023, 945, 887, 859, 784, 744, 714, 636 cm^{-1}; GCMS (EI, 70 eV, 5% polyphenylmethylsiloxane, 100 kPa, 50 °C, 2 min, 30 °C min^{-1}, 250 °C, 5 min, retention time (t_R) = 8.0 min): *m/z* (%): 230 (50), 228 (52), 215 (97), 213 (100), 106 (11), 78 (21), 77 (19), 51 (12), 43 (21).

Synthesis of 31

A 250 mL three-necked round-bottom flask was charged with sodium hydride (60% *w/w* in paraffin oil; 0.38 g, 9.49 mmol, 1.50 equiv) under argon. The NaH was washed with *n*-pentane (3× 5 mL) and the flask was equipped with a magnetic stirrer bar, reflux condenser, and septum. Trimethyloxosulfonium iodide (2.08 g, 9.49 mmol, 1.50 equiv) was added and the equipment was assembled under inert atmosphere. Absolute DMSO (60 mL) was

added via syringe and the solution was stirred for 30 min at rt. Then, a solution of **30** (1.45 g, 6.33 mmol, 1.00 equiv) in absolute DMSO (30 mL) was added. The reaction mixture was stirred for 20 h at 40 °C, then at 90 °C for 2 h. After extraction with Et_2O (3× 50 mL), the combined organic layers were washed with brine (30 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 11×2 cm, cyclohexane) to obtain **31** as colorless crystals (750 mg, 3.33 mmol, 53%). R_f = 0.59 (SiO_2, 19:1 cyclohexane/EtOAc); m.p. 40–42 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$, 300 K): δ = 7.68 (s, 1H), 7.34 (q, ^4J = 1.2 Hz, 1H), 7.33 (s, 1H), 2.49 (s, 3H), 2.20 ppm (d, ^4J = 1.2 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K): δ = 154.7, 142.0, 133.5, 129.0, 122.8, 118.5, 115.2, 113.1, 22.9, 8.0 ppm; IR: $\tilde{\nu}$ = 2981, 2922, 2860, 2360, 2323, 1700, 1539, 1450, 1435, 1405, 1374, 1309, 1285, 1208, 1133, 1077, 1035, 851, 771, 676, 668 cm^{-1}; GCMS (EI, 70 eV, 5% polyphenylmethylsiloxane, 60 kPa, 100 °C, 2 min, 7 °C min^{-1}, 250 °C, 10 min, t_R = 12.2 min): *m/z* (%): 226 (67), 225 (32), 224 (71), 223 (22) 146 (11), 145 (100), 116 (13), 115 (48), 91 (10), 72 (14).

Asymmetric hydrogenation of 31

Catalyst **C3**[8g] (44.1 mg, 30.0 μmol, 3 mol%) was added to a solution of **31** (224 mg, 1.0 mmol) in dry CH_2Cl_2 (5.0 mL). The reaction vial was equipped with a magnetic stirrer bar and placed in an autoclave that was pressurized to 100 bar H_2. The reaction mixture was stirred for 24 h at 60 °C. After release of hydrogen gas and evaporation of the solvent under reduced pressure, the catalyst and starting material were removed by flash chromatography (SiO_2, 14×2 cm, cyclohexane, then 4:1 cyclohexane/MTBE). The hydrogenation product **2** was obtained as a colorless liquid (215 mg, 0.95 mmol, 95%, 92% *ee*). R_f = 0.73 (SiO_2, 9:1 cyclohexane/EtOAc); $[\alpha]_D^{20} = -8.5$ (c = 1.00 in $CHCl_3$); ^{1}H NMR (400.1 MHz, $CDCl_3$, 300 K): δ = 7.26 (s, 1H), 6.67 (s, 1H), 4.67 (dd, $^1J = {}^2J$ = 8.8 Hz, 1H), 4.06 (dd, J = 8.6, 7.4 Hz, 1H), 3.51 (ddq, J = 7.8, 7.4, 7.1 Hz, 1H), 2.33 (s, 3H), 1.30 ppm (d, ^3J = 6.8 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K): δ = 159.5, 137.4, 132.3, 127.4, 114.8, 111.8, 79.2, 36.5, 23.3, 19.5 ppm; IR: $\tilde{\nu}$ = 2960, 2923, 2870, 2356, 2342, 1698, 1482, 1457, 1448, 1395, 1375, 1249, 1230, 1135, 1116, 984, 930, 848, 668, 632 cm^{-1}; GCMS (EI, 70 eV, 5% polyphenylmethylsiloxane, 60 kPa, 100 °C, 2 min, 7 °C min^{-1}, 250 °C, 10 min, t_R = 12.3 min): *m/z* (%): 228 (26), 226 (26) [M^+], 213 (19), 211 (19), 133 (10), 132 (100), 131 (14).

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Keywords: asymmetric catalysis · benzofurans · furans · iridium · N,P ligands

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