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Expanded Scope of the Asymmetric Hydrogenation of Minimally Functionalized Olefins Catalyzed by Iridium Complexes with Phosphite–Thiazoline Ligands

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We have replaced the oxazoline group with a thiazoline moiety in one of the most successful of the phosphite–oxazoline ligand families for the Ir-catalyzed hydrogenation of minimally functionalized olefins. A small but structurally important library of Ir phosphite–thiazoline precatalysts (Ir-**L1**–**L2a**–**e**) has been developed by changing the substituents/configurations at the biaryl phosphite group. We found that the replacement of the oxazoline with a thiazoline moiety in the ligand design is beneficial in terms of substrate scope.

Introduction

The synthetic challenges that arise from the high degree of enantiopurity required in life-science products have stimulated the development and industrial application of asymmetric catalysis.[1] Asymmetric hydrogenation is a fundamental technique in the modern organic chemist's repertoire of reliable catalytic methods to construct optically active compounds. High enantioselectivity, low catalyst loadings, essentially quantitative yields, perfect atom economy, and mild conditions are attractive features of this transformation as is evident in the ever growing list of publications that use these methods.[1] Although the reduction of olefins that contain an adjacent polar group (i.e., dehydroamino acids) by Rh- and Ru-based catalyst precursors modified with P ligands has a long history, the asymmetric hydrogenation of minimally functionalized olefins is less developed because these substrates have no adjacent polar group to direct the reaction.[2] A breakthrough in the hydrogenation of this type of substrate was made when Pfaltz and co-workers used Ir complexes, [Ir(PHOX)(cod)]BAr_F (COD = cyclooctadiene, BAr_F = tetrakis[3,5-bis(trifluoromethyl)phenyl]-borate), modified with phosphane–oxazoline (PHOX) ligands as chiral analogues of Crabtree's catalyst ([Ir(py)(PCy_3)(cod)]PF_6) (py = pyridine, PCy_3 = tricyclohexylphosphane).[3] Since then, the composition of the ligands has been extended by introducing P-donor groups (or carbene analogues) other than phosphanes and N-donor groups other than oxazolines and varying the chiral backbone.[4] More recently, the ligand scope has also been extended to the use of other non-N-containing heterodonor ligands such as P,O and P,S ligands.[5] However, most of the chiral catalysts that have been developed are still highly substrate dependent and the development of efficient chiral ligands that tolerate a broader range of substrates, with the aim to synthesize more complex molecules, remains a challenge.[2]

Some years ago, we discovered that the presence of biaryl phosphite moieties in ligand design is highly advantageous in this process.[6] Ir phosphite–oxazoline catalytic systems provide greater substrate versatility and high activities and enantioselectivities for several largely unfunctionalized *E*- and *Z*-trisubstituted and 1,1-disubstituted olefins than previous Ir phosphinite–oxazoline systems. In this context, we have successfully used an amino-acid-derived phosphite–oxazoline ligand library ($L_{P\text{-}Ox}$, Figure 1) to reduce minimally functionalized olefins,[6b,c] and this is one of the two phosphite-containing ligand families with the broadest substrate scope.[6a–c,e] Although this phosphite–oxazoline ligand library proved to be highly efficient in the hydrogenation of unfunctionalized aryl alkyl *E*-trisubstituted and 1,1-disubstituted olefins, some substrates (such as *Z*-trisubstituted olefins, α,β-unsaturated ketones, and trifluoromethyl olefins) still need improved enantioselectivities.

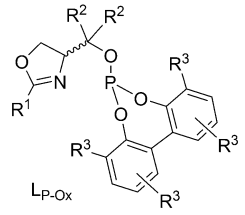

Figure 1. Basic structure of $L_{P\text{-}Ox}$.

To address this point, in this study we designed a new family of ligands in which the oxazoline group of $L_{P\text{-}Ox}$ is replaced by a thiazoline moiety to give ligands **L1**–**L2a**-**e** (Figure 2).[7] We expected the subtle variation in the basicity of the N-donor group (the thiazoline group is more basic than the oxazoline) and the steric properties[8] caused by the substituent at the N-heteroatom ring that replaces the non-coordinating heteroatom to allow the catalysts to be fine-tuned for the most challenging substrates. We report here the applica-

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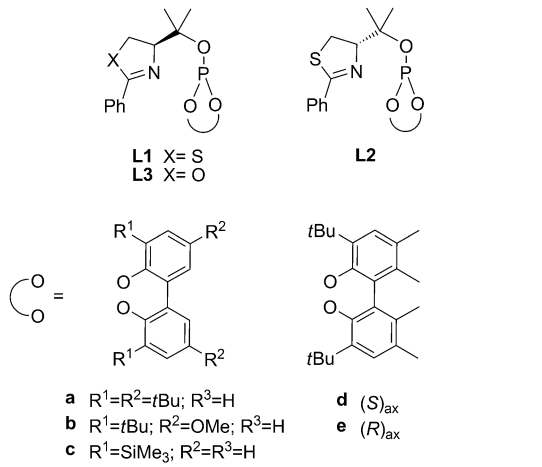


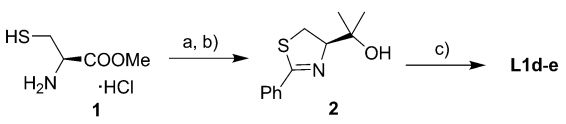
Figure 2. Phosphite–thiazoline **L1**–**L2 a**–**e** and phosphite–oxazoline **L3 a**–**e** ligands.

tion of a small but structurally relevant library of Ir phosphite–thiazoline precatalysts (Ir-**L1**–**L2 a**–**e**) in the asymmetric hydrogenation of a wide range of *E*- and *Z*-trisubstituted and 1,1-disubstituted terminal olefins, which include examples with neighboring polar groups. We have compared the effectiveness of **L1**–**L2 a**–**e** and related privileged phosphite–oxazoline ligands (**L3**, Figure 2). To this end, we have expanded our previous work on $L_{P\text{-}Ox}$[6b–c] to cover the asymmetric reduction of a wider range of challenging minimally functionalized olefins. Interestingly, we found that the reactivity and selectivity of the new Ir phosphite–thiazoline catalysts are excellent and similar to those of their phosphite–oxazoline analogues for most substrates and they performed better for the more challenging substrates.

Results and Discussion

Ligand synthesis

The new phosphite–thiazoline ligands **L1 d**–**e** were synthesized straightforwardly by using the procedure described previously for **L1**–**L2 a**–**c** (Scheme 1).[7] **L1 d**–**e** were efficiently synthesized by reacting the corresponding thiazoline alcohol **2** with one equivalent of the appropriate in situ formed phosphorochloridite ($ClP(OR)_2$; $(OR)_2$ = **d**–**e**) in the presence of pyridine. Thiazoline alcohol **2** is prepared from *R*-cysteine methyl ester hydrochloride (**1**) as shown in Scheme 1. **L1 d**–**e** were stable during purification on neutral alumina under Ar and isolated in good yields as white solids. They were stable at room temperature and very stable to hydrolysis. The elemental analyses were in agreement with the assigned structures. The ^1H, ^{13}C, and ^{31}P NMR spectra were as expected for these C_1-symmetric ligands.

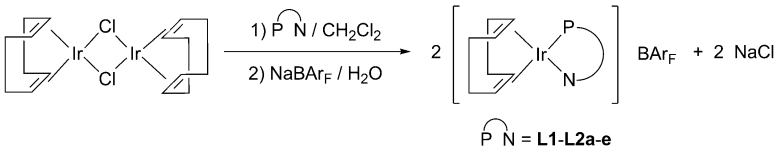


Scheme 1. Synthesis of **L1 d**–**e**. a) Ethyl benzimidate hydrochloride,[9] b) MeMgBr/THF/Et_2O,[7] c) $ClP(OR)_2$, $(OR)_2$ = **d**–**e**/Py/toluene.

Synthesis of Ir catalyst precursors

Ir complexation and subsequent chloride abstraction with $NaBAr_F$ were performed in a one-pot process using a literature procedure[6] to afford $[Ir(cod)(L)]BAr_F$ (L = **L1**–**L2 a**–**e**) complexes in almost quantitative yields in a pure form as air-stable orange solids (Scheme 2).

The complexes were characterized by elemental analysis and ^1H, ^{13}C, and ^{31}P NMR spectroscopy. The spectral assignments were based on information from ^1H-^1H and ^{13}C-^1H correlation measurements and were as expected for these C_1-symmetric Ir complexes. The variable-temperature NMR (VT-NMR) spectra indicate that only one isomer is present in solution. One singlet in the $^{31}P\{^1H\}$ NMR spectra was obtained in all cases.[10]



Scheme 2. Synthesis of $[Ir(cod)(P\text{-}N)]BAr_F$ (P-N = **L1**–**L2 a**–**e**).

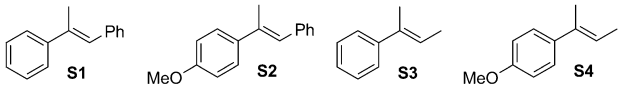
Asymmetric hydrogenation of trisubstituted olefins

Minimally functionalized E- *and* Z-*trisubstituted olefins*

To evaluate the potential of **L1**–**L2 a**–**e** in the Ir-catalyzed hydrogenation of *E*-trisubstituted olefins, a comparative study that used substrates **S1**–**S4** was performed, and the results are shown in Table 1. Excellent activities and enantioselectivities (up to 99%) were obtained. We found that the enantioselectivity is slightly affected by the substituents at the biaryl phosphite moiety (Table 1, entries 1 and 2 vs. 3). The best enantioselectivities were obtained with **L1 c**, which contains bulky trimethylsilyl groups at the *ortho* position of the biphenylphosphite moiety (Table 1, entry 3). We also found that the configuration at the biaryl phosphite moiety does not affect the enantioselectivity (Table 1, entries 4 and 5). This is in contrast with the positive effect on enantioselectivity observed in the related phosphite–oxazoline ligands if enantiopure *S* configured biaryl phosphite moieties were used.[6b]

Finally, if we compared the results obtained with **L1 a** and **L2 a** we found that the different configuration of the alkyl backbone controls the enantioselectivity (Table 1, entries 1 vs. 6). Both enantiomers of the reduced products are, therefore, accessible in high enantioselectivities. Overall, catalyst Ir-**L1 c** offers the best enantioselectivity and compares well with the

Table 1. Ir-catalyzed asymmetric hydrogenation of *E*-trisubstituted **S1**–**S4** using **L1**–**L3 a**–**e**.[a]



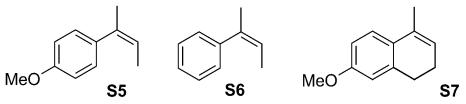
Entry	Ligand	*ee* [%][b]	*ee* [%][b]	*ee* [%][b]	*ee* [%][b]
1	**L1 a**	97 (*R*)	96 (*R*)	96 (*R*)	96 (*R*)
2	**L1 b**	98 (*R*)	97 (*R*)	96 (*R*)	96 (*R*)
3	**L1 c**	99 (*R*)	99 (*R*)	98 (*R*)	98 (*R*)
4	**L1 d**	97 (*R*)	96 (*R*)	97 (*R*)	95 (*R*)
5	**L1 e**	97 (*R*)	96 (*R*)	96 (*R*)	95 (*R*)
6	**L2 a**	97 (*S*)	96 (*S*)	95 (*S*)	96 (*S*)
7	**L3 c**	98 (*R*)[6b]	98 (*R*)	98 (*R*)	98 (*R*)

[a] Reactions performed at RT by using 0.5 mmol of substrate and 0.25 mol% of Ir catalyst precursor at 50 bar of H_2 using CH_2Cl_2 (2 mL) as solvent. Full conversions were obtained in all cases after 2 h. [b] *ee* determined by HPLC (**S1** and **S2**) or GC (**S3** and **S4**).

analogous phosphite–oxazoline catalyst (Table 1, entries 3 vs. 7).[6b]

To further assess the scope of **L1**–**L2 a**–**e**, we investigated the asymmetric hydrogenation of more demanding *Z* isomers (**S5**–**S7**), which are usually hydrogenated with a lower enantioselectivity than the corresponding *E* isomers. By carefully selecting the ligand parameters, we were able to obtain both enantiomers of the hydrogenated products in high enantioselectivities (*ee* values up to 96%) by using Ir-**L1 a** and Ir-**L2 a**. The results followed a different trend than those for *E* configured substrates (Table 2). The enantioselectivities were, therefore, affected by both the substituents and the configuration of the biaryl phosphite moiety. Unlike the hydrogenation of *E* configured substrates, the enantioselectivities improved with the introduction of bulky substituents at the *para* positions of the biaryl phosphite moiety (i.e., *t*Bu > OMe > H; Table 2, entries 1–3). We also found a cooperative effect between the configurations of the biaryl phosphite moiety and the ligand backbone that leads to a matched combination for **L1 e**, which has an *R*-biaryl configuration (Table 2, entries 4 and 5). However, the enantioselectivities were best with the tropoisomeric biphenyl-containing ligand **L1 a**, which contained *tert*-butyl groups at both the *ortho* and *para* positions. This confirms that although the configuration of the biaryl phosphite moiety affects the enantioselectivity, the presence of a *tert*-butyl group at the *para* position of the biaryl phosphite moiety is crucial if enantioselectivities are to be high.

Table 2. Ir-catalyzed asymmetric hydrogenation of *Z*-trisubstituted **S5**–**S7** using **L1**–**L3 a**–**e**.[a]



Entry	Ligand	*ee* [%][b]	*ee* [%][b]	*ee* [%][b]
1	**L1 a**	95 (*S*)	94 (*S*)	96 (*S*)
2	**L1 b**	83 (*S*)	84 (*S*)	83 (*S*)
3	**L1 c**	79 (*S*)	79 (*S*)	80 (*S*)
4	**L1 d**	58 (*S*)	61 (*S*)	72 (*S*)
5	**L1 e**	74 (*S*)	73 (*S*)	81 (*S*)
6	**L2 a**	94 (*R*)	94 (*R*)	95 (*R*)
7	**L3 a**	92 (*S*)[6b]	91 (*S*)	93 (*S*)

[a] Reactions performed at RT by using 0.5 mmol of substrate and 0.25 mol% of Ir catalyst precursor at 50 bar of H_2 using CH_2Cl_2 (2 mL) as solvent. Full conversions were obtained in all cases after 2 h. [b] *ee* determined by GC.

Interestingly, if the results of the reduction of *E*- and *Z*-trisubstituted olefins are compared with the enantioselectivities obtained with the corresponding Ir phosphite–oxazoline systems, we can conclude that the introduction of a thiazoline moiety into the ligand design is advantageous (Table 2, entry 1 and 6 vs. 7). Therefore, although for *E*-trisubstituted olefins comparable, excellent enantioselectivities were obtained, for *Z*-trisubstituted olefins, the enantioselectivities were improved by using phosphite–thiazoline ligands. In summary, by appropriately tuning the thiazoline-based ligands, excellent enantioselectivities were achieved in the hydrogenation of a broad range of *E*- and *Z*-trisubstituted olefins.

Trisubstituted olefins that contain a neighboring polar group

Substrates that bear a neighboring polar group need to be reduced because they are important intermediates in the synthesis of high-value chemicals and their reduced products allow further functionalization. Therefore, the development of sustainable enantioselective routes to these compounds is of great value. We decided to further study the potential of **L1**–**L2 a**–**e** in the reduction of a wide range of trisubstituted alkenes that contain several types of polar groups, and the results are summarized in Figure 3. Again, excellent enantioselectivities were obtained in both enantiomers of the reduction products (*ee* values up to 99%) for a range of substrates under mild reaction conditions by suitable tuning of the ligand parameters.

We first studied the hydrogenation of several α,β-unsaturated ketones (**S8**–**S12**) for which the related Ir phosphite–oxazoline catalytic systems were not optimal. Enantioselectivities of up to 99% for both enantiomers of the hydrogenated product were obtained by using Ir-**L1 a** and Ir-**L2 a**. Notably, the *ee* values are independent of the electronic nature of the substrate phenyl ring and the substituent in the ketone functionality. Ir-**L1 a** and Ir-**L2 a** also provided excellent enantioselectivities in the reduction of allylic alcohol **S13** and allylic acetate **S14**. If we compare all these results with those achieved by using the related Ir phosphite–oxazoline catalysts, again the introduction of a thiazoline group was beneficial for enantioselectivity (i.e., for **S8**, the *ee* improved from 93% with the related phosphite–oxazoline ligand[11] to 99%).

We then studied the hydrogenation of several α,β-unsaturated esters (**S15**–**S18**). We were pleased to find that the excellent enantioselectivities achieved with phosphite–oxazoline li-

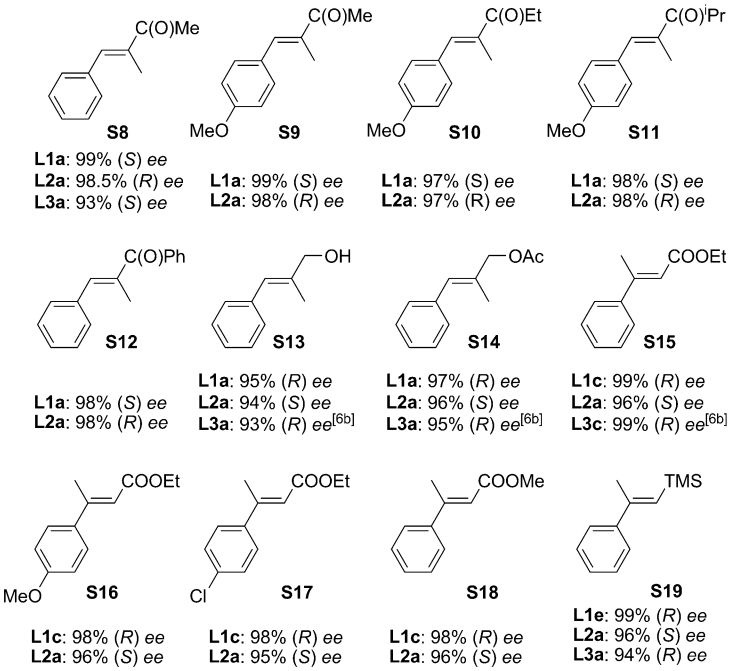


Figure 3. Selected hydrogenation results of trisubstituted olefins that bear a neighboring polar group by using [Ir(cod)(**L1**–**L2a**–**e**)]BAr_F catalyst precursors. Reaction conditions: 0.5 mol% catalyst precursor, CH_2Cl_2 as solvent, 50 bar H_2, RT, 2 h. Full conversions were achieved in all cases.

gands[6b] (i.e., 99% *ee* for **S15** using Ir-**L3c**) can be maintained with the phosphite–thiazoline analogues. Ir-**L1c**, therefore, provided enantioselectivities up to 99%. For α,β-unsaturated ketones, the enantioselectivities are highly independent of the electronic nature of the substrate phenyl ring and the substituent in the ester function, which allows the successful asymmetric reduction of a wide range of α,β-unsaturated esters.

High enantioselectivities (up to 99% *ee*) were also obtained in the hydrogenation of vinylsilane **S19** by using Ir-**L1e**. Comparison with related phosphite–oxazoline catalytic systems again showed that the introduction of a thiazoline group led to higher enantioselectivities (*ee* improved from 94% using Ir-**L3** to 99%).[12]

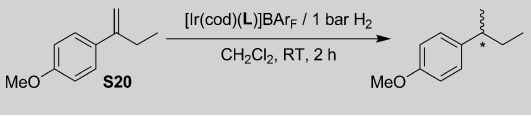
To sum up, this is one of the few catalytic systems that can hydrogenate a wide range of trisubstituted olefins, including those with a neighboring polar group, with high activities and enantioselectivities.[2]

Asymmetric hydrogenation of 1,1-disubstituted terminal olefins

To further study the potential of **L1**–**L2a**–**e**, we tested them in the asymmetric hydrogenation of more demanding terminal olefins.[13] The enantioselectivity obtained with 1,1-disubstituted terminal olefins is lower than that with trisubstituted olefins largely because of the isomerization of the terminal double bond to the more stable internal *trans*-alkene, which usually leads to the predominant formation of the opposite enantiomer of the hydrogenated product and/or to difficulty in controlling face selectivity.[2d,e] Few known catalytic systems provide high enantioselectivities for these substrates, and those that do usually have a limited substrate scope.[2d,e,12a,b,14] $L_{P\text{-}Ox}$ is one of the two most versatile ligand families for the hydrogenation of this class of substrates.[6c]

In an initial set of experiments, we used the Ir-catalyzed asymmetric hydrogenation of 2-(4-methoxyphenyl)but-1-ene (**S20**), and the results for the optimized conditions are shown in Table 3. We were again able to fine-tune the ligand parameters to produce high activities and enantioselectivities (*ee* values up to 99%) in the hydrogenation of **S20** using **L1e** at low catalyst loadings (0.25 mol%) and H_2 pressures [1 bar (100 kPa)]. Again, both enantiomers of the hydrogenated product can be obtained simply by changing the configuration of the alkyl backbone (i.e., Table 3, entries 1 vs. 6). In contrast to the reduction of *E*-trisubstituted substrates, the enantioselectivity is mainly affected by the configuration at the biaryl phosphite moiety (Table 3, entries 4 and 5). This behavior is similar to that observed in the hydrogenation of *Z*-trisubstituted olefins. However, for disubstituted **S20**, the presence of an enantiopure bulky (*R*)-biaryl phosphite moiety is crucial if the enantioselectivities of the ligand series are to be at their highest.

Table 3. Ir-catalyzed hydrogenation of **S20** using **L1**–**L2a**–**e**.[a]



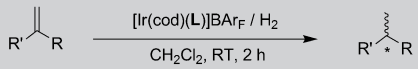
Entry	Ligand	Conversion [%][b]	*ee* [%][c]
1	**L1a**	100	94 (*S*)
2	**L1b**	100	92 (*S*)
3	**L1c**	100	95 (*S*)
4	**L1d**	100	78 (*S*)
5	**L1e**	100	99 (*S*)
6	**L2a**	100	94 (*R*)
7	**L3a**	100	91 (*S*)

[a] Reactions performed using 0.5 mmol of **S20** and 0.25 mol% of Ir catalyst precursor at 1 bar of H_2. [b] Conversion measured by GC after 2 h. [c] *ee* Values determined by chiral GC.

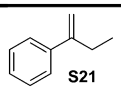
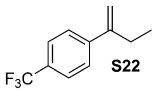
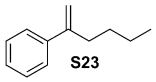
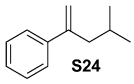
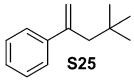
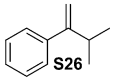
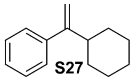
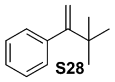
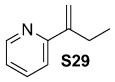
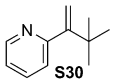
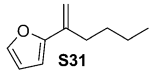
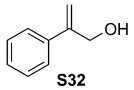
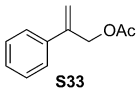
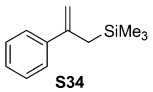
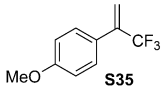
This finding contrasts with the positive effect on enantioselectivity observed if an (*S*)-binaphthylphosphite moiety was used in the related phosphite–oxazoline ligands.[6c] Again, the replacement of the oxazoline moiety by a thiazoline group is beneficial in terms of enantioselectivity (Table 3, entries 1 vs. 7).

Next, we evaluated **L1**–**L2a**–**e** in the asymmetric hydrogenation of other 1,1-disubstituted substrates, which include those that contain an heteroaromatic ring and a neighboring polar group, and notable results are shown in Table 4. The results followed the same trend as for the hydrogenation of **S20**. Again, the catalyst precursor that contained **L1e** provided the best enantioselectivities.

Table 4. Selected results for the Ir-catalyzed hydrogenation of minimally functionalized 1,1-disubstituted terminal olefins using **L1**–**L2 a**–**e**.[a]



R' = aryl, 2-pyridine, 2-thiophene
R = alkyl, CH_2OH, CH_2OAc, CH_2TMS, CF_3

Entry	Substrate	Ligand	*ee* [%][b]
1	 **S21**	**L1 e**	99 (*S*)
2	 **S22**	**L1 e**	98 (*S*)
3	 **S23**	**L1 e**	98 (*S*)
4	 **S24**	**L1 e**	97 (*S*)
5	 **S25**	**L1 e**	93 (*S*)
6	 **S26**	**L1 e**	91 (*S*)
7	 **S27**	**L1 e**	94 (*S*)
8	 **S28**	**L1 e**	99 (*S*)
9	 **S29**	**L1 e**	98 (+)
10	 **S30**	**L1 e**	99 (+)
11	 **S31**	**L1 e**	95 (−)
12[c]	 **S32**	**L1 e**	94 (*R*)
13[c]	 **S33**	**L1 e**	91 (*R*)
14[c]	 **S34**	**L1 e**	93 (*S*)
15	 **S35**	**L1 e**	99 (−)

[a] Reactions performed using 0.5 mmol of substrate and 0.25 mol% of Ir catalyst precursor at 1 bar of H_2. Full conversion were achieved after 2 h. [b] *ee* Values determined by chiral GC. [c] Reaction performed under 50 bar of H_2.

Our results with several 1,1-disubstituted aryl alkyl substrates (**S20**–**S28**) indicated that enantioselectivity is relatively insensitive to the electronic effects in the aryl ring and to the steric properties of the alkyl substituent. Therefore, several *para*-substituted 2-phenylbut-2-enes (**S20**–**S22**; Table 3, entry 5 and Table 4, entries 1 and 2) and several α-alkyl styrenes (**S23**–**S28**; Table 4, entries 3–8) were hydrogenated, and excellent enantioselectivities were achieved (*ee* values from 91–99%). Although these results are comparable to those obtained with related chiral phosphite–oxazoline ligands,[6c] it should be noted that for **S23**–**S25** the presence of a thiazoline group led to higher enantioselectivities (i.e., for **S23**, the *ee* increased from 94 to 98%).[6c] As heterocycles are of interest to industry and as the heterocyclic part can be further modified after hydrogenation, we investigated whether phosphite–thiazoline ligands can also be used in the hydrogenation of 1,1-heteroaromatic terminal olefins (Table 4, entries 9–11). We were pleased to find that several pyridine- and thiophene-containing substrates **S29**–**S31** were also readily hydrogenated in high enantioselectivities using Ir-**L1 e** (*ee* up to 99%).

Finally, we also examined the hydrogenation of several 1,1-disubstitued terminal olefins that contain a neighboring polar group, which give rise to important intermediates for the synthesis of high-value products (e.g., derivatives of the hydrogenated product 2-phenylpropanol are frequently used in the fragrance industry).[15] Allylic alcohol **S32**, allylic acetate **S33**, and allylic silane **S34** were hydrogenated with similar high efficiencies (*ee* values from 91–94%; Table 4, entries 12–14). Ir-**L1 e** clearly outperforms complexes of related phosphite–oxazoline ligands in the asymmetric hydrogenation of trifluoromethyl olefin **S35** (99% *ee* using Ir-**L1 e** vs. 75% *ee* using related Ir phosphite–oxazoline catalysts).[6c] In addition, this result compares favorably with the best reported in the literature and opens up the possibility of using Ir hydrogenation catalysts to develop chiral organofluorine drug intermediates.[16]

Conclusion

We have replaced the oxazoline group with a thiazoline moiety in one of the most successful phosphite–oxazoline ligand families ($L_{P\text{-}Ox}$, Figure 1) for the Ir-catalyzed hydrogenation of minimally functionalized olefins. A small but structurally important library of Ir phosphite–thiazoline precatalysts (Ir-**L1**–**L2 a**–**e**) has been developed by changing the substituents/configurations at the biaryl phosphite group. By tuning these ligand parameters appropriately, we achieved excellent enantioselectivities in the hydrogenation of a wide range of *E*- and *Z*-trisubstituted and 1,1-disubstituted terminal olefins, which included examples with neighboring polar groups. We have found that replacing the oxazoline with a thiazoline moiety in the ligand design is beneficial in terms of the substrate scope. Thus, the range of substrates that can be hydrogenated with excellent enantioselectivities with the new Ir phosphite–thiazoline catalysts has been extended because more challenging *Z*-trisubstituted olefins, α,β-unsaturated ketones, and trifluoromethyl olefins have been included. These results open up a new class of ligands for the highly enantioselective Ir-catalyzed hydrogenation of a wide range of substrates, which compares favorably with the best reported in the literature.

Experimental Section

General

All reactions were performed by using standard Schlenk techniques under Ar. Solvents were purified and dried by standard procedures. Phosphorochloridites were prepared easily in one step from the corresponding biaryls.[17] **L1a–c**,[7] **L2a**,[7] and [Ir(cod)(**L3**)]BAr_F[6b,c] were prepared as reported previously. ^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra were recorded by using a 400 MHz spectrometer. Chemical shifts are reported relative to that of $SiMe_4$ (^1H and ^{13}C) as an internal standard or H_3PO_4 (^{31}P) as an external standard. ^1H, ^{13}C and ^{31}P NMR assignments were made on the basis of ^1H-^1H gradient COSY (gCOSY), ^1H-^{13}C gHSQC, and ^1H-^{31}P gHMBC experiments. All catalytic experiments were performed three times.

Preparation of the phosphite–thiazoline ligands

General procedure: The appropriate phosphorochloridite (3.0 mmol) produced in situ was dissolved in toluene (12.5 mL), and pyridine (1.14 mL, 14 mmol) was added. The corresponding hydroxylthiazoline (2.8 mmol) was dried azeotropically with toluene (3×2 mL) and then dissolved in toluene (12.5 mL) to which pyridine (1.14 mL, 14 mmol) was added. This solution was transferred slowly at 0 °C to the solution of phosphorochloridite. The reaction mixture was stirred overnight at 80 °C, and the pyridine salts were removed by filtration. Evaporation of the solvent gave a white foam, which was purified by flash chromatography on alumina to produce the corresponding ligand as a white solid.

L1d: Yield: 428 mg (71%); ^{31}P NMR (400 MHz, C_6D_6): $\delta = 150.6$ ppm (s); ^1H NMR (C_6D_6): $\delta = 1.48$ (s, 9H, CH_3, *t*Bu), 1.55 (s, 9H, CH_3, *t*Bu), 1.60 (s, 3H, CH_3), 1.62 (s, 3H, CH_3), 1.73 (s, 3H, CH_3), 1.80 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.57 (dd, 1H, $^2J_{H-H}$ = 12.0 Hz, $^3J_{H-H}$ = 8.8 Hz, CH_2–S), 2.83 (dd, 1H, $^2J_{H-H}$ = 12.0 Hz, $^3J_{H-H}$ = 10 Hz, CH_2–S), 4.53 (m, 1H, CH–N), 6.7–8.2 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): $\delta = 16.9$ (CH_3–Ar), 17.1 (CH_3–Ar), 19.2 (CH_3–Ar), 20.1 (CH_3–Ar), 23.6 (CH_3), 28.1 (d, CH_3, J_{C-P} = 7.8 Hz), 31.4 (CH_3, *t*Bu), 32.1 (CH_3, *t*Bu), 33.7 (CH_2–S), 82.1 (C), 87.3 (CH–N), 123.8 (CH=), 128.3 (CH=), 127.0 (C), 127.3 (C), 128.9 (CH=), 132.2 (CH=), 132.7 (CH=), 133.0 (C), 137.3 (C), 144.9 (C), 146.1 (C), 146.7 (C), 148.8 (C), 149.1, 167.4 ppm (C=N); elemental analysis calcd (%) for $C_{36}H_{46}NO_3PS$ (603.29): C 71.61, H 7.68, N 2.32, S 5.31; found: C 71.67, H 7.70, N 2.29, S 5.27.

L1e: Yield: 380 mg (63%); ^{31}P NMR (400 MHz, C_6D_6): $\delta = 152.1$ ppm (s); ^1H NMR (C_6D_6): $\delta = 1.46$ (s, 9H, CH_3, *t*Bu), 1.54 (s, 9H, CH_3, *t*Bu), 1.58 (s, 3H, CH_3), 1.64 (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 1.89 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.61 (dd, 1H, $^2J_{H-H}$ = 12.0 Hz, $^3J_{H-H}$ = 7.2 Hz, CH_2–S), 2.81 (dd, 1H, $^2J_{H-H}$ = 12.0 Hz, $^3J_{H-H}$ = 10 Hz, CH_2–S), 4.58 (m, 1H, CH–N), 6.7–8.2 ppm (m, 7H, CH=); ^{13}C NMR (C_6D_6): $\delta = 16.8$ (CH_3–Ar), 17.1 (CH_3–Ar), 19.8 (CH_3–Ar), 20.0 (CH_3–Ar), 23.5 (CH_3), 28.2 (d, CH_3, J_{C-P} = 7.8 Hz), 31.5 (CH_3, *t*Bu), 31.7 (CH_3, *t*Bu), 33.4 (CH_2–S), 82.0 (C), 87.3 (CH–N), 123.9 (CH=), 128.5 (CH=), 126.8 (C), 127.0 (C), 128.5 (CH=), 129.7 (CH=), 132.1 (CH=), 132.8 (CH=), 133.1 (C), 136.8 (C), 145.1 (C), 146.4 (C), 146.6 (C), 148.9 (C), 149.1, 167.2 ppm (C=N); elemental analysis calcd (%) for $C_{36}H_{46}NO_3PS$ (603.29): C 71.61, H 7.68, N 2.32, S 5.31; found: C 71.64, H 7.70, N 2.30, S 5.29.

Preparation of [Ir(cod)(L)]BAr_F

General procedure: The appropriate ligand (0.074 mmol) was dissolved in CH_2Cl_2 (2 mL), and [Ir(μ-Cl)cod]$_2$ (25 mg, 0.037 mmol) was added. The reaction was heated to reflux at 50 °C for 1 h. After 5 min at RT, $NaBAr_F$ (77.1 mg, 0.082 mmol) and water (2 mL) were added, and the reaction mixture was stirred vigorously for 30 min at RT. The phases were separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were filtered through a Celite plug, dried with $MgSO_4$, and the solvent was evaporated to give the product as an orange solid.

[Ir(cod)(**L1a**)]BAr_F: Yield: 124 mg (92%); ^{31}P NMR ($CDCl_3$): δ = 99.7 ppm (s); ^1H NMR ($CDCl_3$): $\delta = 1.11$ (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.46 (s, 9H, CH_3, *t*Bu), 1.56 (s, 9H, CH_3, *t*Bu), 1.64 (s, 9H, CH_3, *t*Bu), 1.72 (s, 9H, CH_3, *t*Bu), 2.1–2.3 (b, 5H, CH_2, cod), 2.32 (b, 1H, CH_2, cod), 2.39 (b, 2H, CH_2, cod), 3.25 (m, 1H, CH_2–S), 3.72 (m, 1H, CH_2–S), 4.32 (m, 1H, CH=cod), 4.54 (m, 1H, CH=cod), 5.09 (m, 1H, CH=cod), 5.13 (m, 1H, CH–N), 6.6–8.4 ppm (m, 21H, CH=); ^{13}C NMR ($CDCl_3$): $\delta = 24.5$ (CH_3), 27.5 (CH_2 cod), 27.7 (CH_2 cod), 28.4 (CH_3), 30.4 (CH_3), 30.6 (CH_3, *t*Bu), 30.8 (CH_3, *t*Bu), 31.0 (CH_2 cod), 32.2 (CH_3, *t*Bu), 33.3 (CH_2–S), 35.1 (C, *t*Bu), 35.3 (C, *t*Bu), 35.5 (C, *t*Bu), 35.7 (C, *t*Bu), 67.5 (CH=cod), 69.9 (CH=cod), 84.2 (CH–N), 85.5 (d, C, J_{C-P} = 4.2 Hz), 96.7 (d, CH=cod, J_{C-P} = 16.4 Hz), 104.6 (d, CH=cod, J_{C-P} = 12.0 Hz), 117.4 (b, CH=, BAr_F), 120–132 (aromatic carbon atoms), 134.7 (b, CH=, BAr_F), 135.8–157 (aromatic carbon atoms), 161.9 (q, C–B, BAr_F, $^1J_{C-B}$ = 49 Hz), 179.9 ppm (s, C=N); elemental analysis calcd (%) for $C_{80}H_{78}BF_{24}IrNO_3PS$ (1823.51): C 52.69, H 4.31, N 0.77, S 1.76; found: C 52.73, H 4.33, N 0.75, S 1.72.

[Ir(cod)(**L1b**)]BAr_F: Yield: 122 mg (93%); ^{31}P NMR ($CDCl_3$): δ = 96.3 ppm (s); ^1H NMR ($CDCl_3$): $\delta = 1.11$ (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.46 (s, 9H, CH_3, *t*Bu), 1.56 (s, 9H, CH_3, *t*Bu), 2.1–2.3 (b, 5H, CH_2, cod), 2.29 (b, 1H, CH_2, cod), 2.39 (b, 2H, CH_2, cod), 3.23 (m, 1H, CH_2–S), 3.68 (m, 2H, CH_2–S and CH=cod), 3.76 (s, 3H, CH_3–O), 3.77 (s, 3H, CH_3–O), 4.29 (m, 1H, CH=cod), 4.51 (m, 1H, CH=cod), 5.17 (m, 1H, CH=cod), 5.22 (m, 1H, CH–N), 6.6–8.4 ppm (m, 21H, CH=); ^{13}C NMR ($CDCl_3$): $\delta = 24.5$ (CH_3), 27.5 (CH_2 cod), 27.7 (CH_2 cod), 28.4 (CH_3), 30.4 (CH_2 cod), 30.6 (CH_3, *t*Bu), 30.8 (CH_3, *t*Bu), 31.0 (CH_2 cod), 33.1 (CH_2–S), 35.1 (C, *t*Bu), 35.5 (C, *t*Bu), 55.6 (CH_3–O), 67.2 (CH=cod), 69.8 (CH=cod), 83.6 (CH–N), 85.7 (d, C, J_{C-P} = 5.4 Hz), 95.8 (d, CH=cod, J_{C-P} = 18.7 Hz), 105.8 (d, CH=cod, J_{C-P} = 12.2 Hz), 113.2 (CH=), 114.5 (CH=), 114.8 (CH=), 117.4 (b, CH=, BAr_F), 120–132 (aromatic carbon atoms), 134.7 (b, CH=, BAr_F), 135.8–157 (aromatic carbon atoms), 161.9 (q, C–B, BAr_F, $^1J_{C-B}$ = 49 Hz), 182.9 ppm (s, C=N); elemental analysis calcd (%) for $C_{74}H_{66}BF_{24}IrNO_5PS$ (1771.37): C 50.18, H 3.76, N 0.79, S 1.81; found: C 50.24, H 3.73, N 0.76, S 1.78.

[Ir(cod)(**L1c**)]BAr_F: Yield: 116 mg (90%); ^{31}P NMR ($CDCl_3$): δ = 96.3 ppm (s); ^1H NMR ($CDCl_3$): $\delta = 0.36$ (s, 9H, CH_3–Si), 0.84 (s, 9H, CH_3–Si), 1.26 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 2.0–2.4 (b, 6H, CH_2, cod), 2.44 (b, 2H, CH_2, cod), 3.22 (m, 1H, CH_2–S), 3.59 (m, 2H, CH_2–S and CH=cod), 4.11 (m, 1H, CH=cod), 4.34 (m, 1H, CH=cod), 5.01 (m, 1H, CH=cod), 5.14 (m, 1H, CH–N), 6.6–8.4 ppm (m, 23H, CH=); ^{13}C NMR ($CDCl_3$): $\delta = 0.2$ (d, CH_3–Si, J_{C-P} = 6.2 Hz), 1.2 (CH_3–Si), 24.2 (CH_3), 27.7 (CH_2 cod), 27.9 (CH_3), 28.2 (CH_2 cod), 30.3 (CH_2 cod), 33.7 (CH_2–S), 68.3 (CH=cod), 70.3 (CH=cod), 83.7 (CH–N), 85.1 (C), 97.2 (d, CH=cod, J_{C-P} = 12.6 Hz), 104.2 (d, CH=cod, J_{C-P} = 12.6 Hz), 117.4 (b, CH=, BAr_F), 120–132 (aromatic carbon atoms), 134.7 (b, CH=, BAr_F), 135.8–157 (aromatic carbon atoms), 161.9 (q, C–B, BAr_F, $^1J_{C-B}$ = 49 Hz), 181.1 ppm (s, C=N); elemental analysis calcd (%) for $C_{70}H_{62}BF_{24}IrNO_3PSSi_2$ (1743.31): C 48.22, H 3.58, N 0.80, S 1.84; found: C 48.26, H 3.61, N 0.79, S 1.81.

[Ir(cod)(**L1 d**)]BAr_F: Yield: 124 mg (95%); ^{31}P NMR ($CDCl_3$): $\delta =$ 99.1 ppm (s); ^1H NMR ($CDCl_3$): $\delta = 1.19$ (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.43 (s, 9H, CH_3, *t*Bu), 1.49 (s, 9H, CH_3, *t*Bu), 1.85 (s, 3H, CH_3), 1.92 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.12 (s, 3H, CH_3–Si), 2.1–2.5 (b, 8H, CH_2, cod), 3.19 (m, 1H, CH_2–S), 3.57 (m, 1H, CH=cod), 3.62 (m, 1H, CH_2–S), 3.99 (m, 1H, CH=cod), 4.39 (m, 1H, CH=cod), 5.04 (m, 1H, CH=cod), 5.26 (m, 1H, CH–N), 6.6–8.4 ppm (m, 19H, CH=); ^{13}C NMR ($CDCl_3$): $\delta = 16.4$ (CH_3–Ar), 16.9 (CH_3–Ar), 19.9 (CH_3–Ar), 20.4 (CH_3–Ar), 24.1 (CH_3), 27.2 (CH_2 cod), 27.4 (CH_2 cod), 27.9 (CH_3), 30.4 (CH_2 cod), 31.2 (CH_3, *t*Bu), 31.4 (CH_3, *t*Bu), 31.5 (CH_2 cod), 33.7 (CH_2–S), 35.1 (C, *t*Bu), 35.3 (C, *t*Bu), 71.1 (CH=cod), 73.2 (CH=cod), 82.9 (CH–N), 84.9 (d, C, $J_{C-P} = 4.8$ Hz), 97.1 (d, CH=cod, $J_{C-P} =$ 19.2 Hz), 103.9 (d, CH=cod, $J_{C-P} = 11.4$ Hz), 117.4 (b, CH=, BAr_F), 120–132 (aromatic carbon atoms), 134.7 (b, CH=, BAr_F), 135.8–157 (aromatic carbon atoms), 161.9 (q, C–B, BAr_F, $^1J_{C-B} = 49$ Hz), 182.4 ppm (s, C=N); elemental analysis calcd (%) for $C_{76}H_{70}BF_{24}IrNO_3PS$ (1767.42): C 51.65, H 3.99, N 0.79, S 1.81; found: C 51.71, H 4.03, N 0.76, S 1.79.

[Ir(cod)(**L1 e**)]BAr_F: Yield: 119 mg (91%); ^{31}P NMR ($CDCl_3$): $\delta =$ 98.4 ppm (s); ^1H NMR ($CDCl_3$): $\delta = 1.22$ (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.47 (s, 9H, CH_3, *t*Bu), 1.63 (s, 9H, CH_3, *t*Bu), 1.85 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 2.05 (s, 3H, CH_3–Si), 2.1–2.5 (b, 8H, CH_2, cod), 3.21 (m, 1H, CH_2–S), 3.49 (m, 1H, CH=cod), 3.53 (m, 1H, CH_2–S), 4.03 (m, 1H, CH=cod), 4.78 (m, 1H, CH=cod), 5.01 (m, 1H, CH=cod), 5.14 (m, 1H, CH–N), 6.6–8.4 ppm (m, 19H, CH=); ^{13}C NMR ($CDCl_3$): $\delta = 16.5$ (CH_3–Ar), 17.1 (CH_3–Ar), 20.1 (CH_3–Ar), 20.3 (CH_3–Ar), 24.4 (CH_3), 27.2 (CH_2 cod), 27.4 (CH_2 cod), 28.1 (CH_3), 30.0 (CH_2 cod), 31.4 (CH_3, *t*Bu), 31.7 (CH_3, *t*Bu), 32.3 (CH_2 cod), 33.2 (CH_2–S), 35.1 (C, *t*Bu), 35.3 (C, *t*Bu), 72.9 (CH=cod), 75.8 (CH=cod), 83.9 (CH–N), 84.2 (d, C, $J_{C-P} = 2.4$ Hz), 97.9 (d, CH=cod, $J_{C-P} =$ 20.4 Hz), 105.2 (d, CH=cod, $J_{C-P} = 10.4$ Hz), 117.4 (b, CH=, BAr_F), 120–132 (aromatic carbon atoms), 134.7 (b, CH=, BAr_F), 135.8–157 (aromatic carbon atoms), 161.9 (q, C–B, BAr_F, $^1J_{C-B} = 49$ Hz), 182.3 ppm (s, C=N); elemental analysis calcd (%) for $C_{76}H_{70}BF_{24}IrNO_3PS$ (1767.42): C 51.65, H 3.99, N 0.79, S 1.81; found: C 51.68, H 4.02, N 0.76, S 1.79.

[Ir(cod)(**L2 a**)]BAr_F: Yield: 124 mg (92%); ^{31}P NMR ($CDCl_3$): $\delta =$ 99.7 ppm (s); ^1H NMR ($CDCl_3$): $\delta = 1.17$ (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.49 (s, 9H, CH_3, *t*Bu), 1.54 (s, 9H, CH_3, *t*Bu), 1.69 (s, 9H, CH_3, *t*Bu), 1.71 (s, 9H, CH_3, *t*Bu), 2.1–2.3 (b, 5H, CH_2, cod), 2.34 (b, 1H, CH_2, cod), 2.43 (b, 2H, CH_2, cod), 3.21 (m, 1H, CH_2–S), 3.79 (m, 1H, CH_2–S), 4.39 (m, 1H, CH=cod), 4.63 (m, 1H, CH=cod), 5.12 (m, 1H, CH=cod), 5.24 (m, 1H, CH–N), 6.6–8.4 ppm (m, 21H, CH=); ^{13}C NMR ($CDCl_3$): $\delta = 24.7$ (CH_3), 27.6 (CH_2 cod), 27.7 (CH_2 cod), 28.9 (CH_3), 30.3 (CH_3), 30.9 (CH_3, *t*Bu), 31.2 (CH_3, *t*Bu), 31.6 (CH_2 cod), 32.2 (CH_3, *t*Bu), 32.5 (CH_3, *t*Bu), 33.3 (CH_2–S), 35.1 (C, *t*Bu), 35.3 (C, *t*Bu), 35.5 (C, *t*Bu), 35.7 (C, *t*Bu), 68.9 (CH=cod), 71.3 (CH=cod), 84.1 (CH–N), 85.2 (d, C, $J_{C-P} = 4.2$ Hz), 96.9 (d, CH=cod, $J_{C-P} = 14.4$ Hz), 105.1 (d, CH=cod, $J_{C-P} = 9.6$ Hz), 117.4 (b, CH=, BAr_F), 120–132 (aromatic carbon atoms), 134.7 (b, CH=, BAr_F), 135.8–157 (aromatic carbon atoms), 161.9 (q, C–B, BAr_F, $^1J_{C-B} = 49$ Hz), 179.9 ppm (s, C=N); elemental analysis calcd (%) for $C_{80}H_{78}BF_{24}IrNO_3PS$ (1823.51): C 52.69, H 4.31, N 0.77, S 1.76; found: C 52.71, H 4.32, N 0.75, S 1.73.

Hydrogenation of olefins

General procedure: The alkene (0.5 mmol) and Ir complex (0.25 mol%) were dissolved in CH_2Cl_2 (2 mL) in a high-pressure autoclave, which was purged four times with H_2. Then, it was pressurized at the desired pressure. After the desired reaction time, the autoclave was depressurized, and the solvent was removed by evaporation. The residue was dissolved in Et_2O (1.5 mL) and filtered through a short Celite plug. The *ee* was determined by chiral GC or chiral HPLC and the conversion was determined by ^1H NMR spectroscopy. The *ee* values of the hydrogenated products of **S1**,[4d] **S2**,[6e] **S3**,[18a] **S4**–**S5**,[4d] **S6**,[17a] **S7**,[4d] **S8**–**S12**,[4p] **S13**–**S15**,[4d] **S16**–**S18**,[4q] **S19**,[17b] **S20**,[12a] **S21**,[4d] **S22**,[12a] **S23**–**S24**,[17c] **S25**,[6c] **S26**,[4d] **S27**,[17c] **S28**–**S30**,[4d] **S31**,[6c] **S32**,[17d] **S33**,[4d] **S34**,[17b] and **S35**[6c] were determined using the conditions described previously.

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[12] Unpublished results: the hydrogenation of **S19** using the Ir complex of **L3c** afforded 100% conversion and 94% *ee* at 50 bar of H_2 using 0.5 mol% of catalyst.

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