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Iridium-Catalyzed Asymmetric Hydrogenation Yielding Chiral Diarylmethines with Weakly Coordinating or Noncoordinating Substituents

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Abstract: Diarylmethine-containing stereocenters are present in pharmaceuticals and natural products, making the synthetic methods that form these chiral centers are important in industry. We have applied iridium complexes with novel N,P-chelating ligands to the asymmetric hydrogenation of trisubstituted olefins, forming diarylmethine chiral centers in high conversions and excellent enantioselectivities (up to 99% ee) for a broad range of substrates. Our results support the hypothesis that steric hindrance in one specific area of the catalyst is playing a key role in stereoselection, as the hydrogenation of substrates differing little at the prochiral carbon occurred with high enantioselectivity. As a result, excellent stereodiscrimination was obtained even when the prochiral carbon bore, for example, phenyl and *p*-tolyl groups.

Introduction

Asymmetric synthesis plays an important role in drug-discovery processes and materials design as it provides methods to selectively produce the diverse compounds required in these areas,[1] and asymmetric catalysis enables the rapid development of new methodologies.[2] Today many types of chiral centers can be formed highly enantioselectively, but the search for new synthetic methods and new chiral compounds remains relevant. Diarylmethine chiral centers are pharmaceutically interesting because they are present in marketed drugs like tolterodine[3] and sertraline[4] (Figure 1), and in natural products (e.g., podophyllotoxin[5]). The asymmetric syntheses of tolterodine[6] and sertraline[7] have been reported by a number of groups, using several synthetic methods.

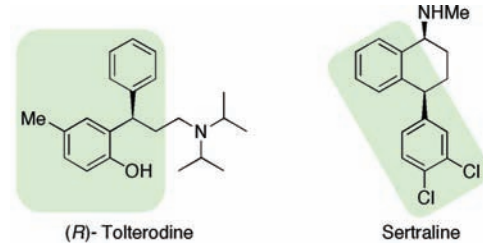

Figure 1. Diarylmethine stereogenic centers in two pharmaceuticals.

However, the existing approaches to diarylmethine chiral centers are often limited in substrate scope. Both the Pd-catalyzed[8] and Rh-catalyzed[9] asymmetric 1,4-additions of metallic and nonmetallic aryl reagents to α,β-unsaturated carbonyls have produced these compounds. Ir-catalyzed asymmetric allylic substitution with arylzinc reagents can be highly enantioselective, but is often not regioselective.[7a] The Ru-catalyzed enantioselective propargylation of aromatic compounds with propargylic alcohols also gives good

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(7) (a) Alexakis, A.; El Hajjaji, S.; Polet, D.; Rathgeb, X. *Org. Lett.* **2007**, *9*, 3393–3395. (b) Davies, H. M. L.; Stafford, D. G.; Hansen, T. *Org. Lett.* **1999**, *1*, 233–236. (c) Quallich, G. J.; Woodall, T. M. *Tetrahedron* **1992**, *48*, 10239–10248. (d) Welch, W. M.; Kraska, A. R.; Sarges, R.; Koe, B. K. *J. Med. Chem.* **1984**, *27*, 1508–1515.
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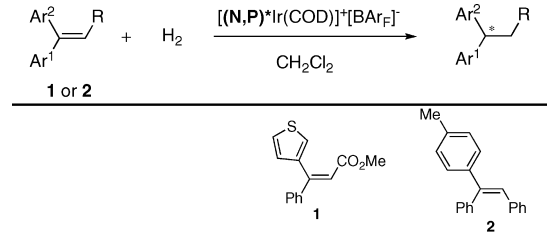
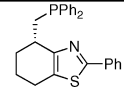
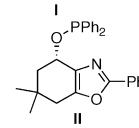
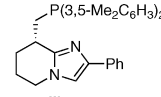
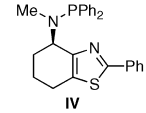
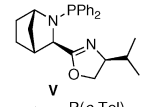
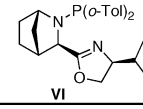
enantioselectivities, but is currently limited in its substrate scope.[10] The synthesis of unfunctionalized, optically active *gem*-diarylalkanes is especially demanding. Few reports have been published in this area,[11] and these generally yield rather low ee values. Only recently has a highly enantioselective route been reported; Carreira et al. performed the Rh-catalyzed decarbonylation of optically pure aldehydes to chiral diarylethanes.[12] New, highly selective methods to diarylmethine stereocenters are therefore still desired.

The asymmetric hydrogenation of olefins is among the most powerful methods in asymmetric synthesis.[13] Since Pfaltz et al.[14] reported the first chiral mimic of Crabtree's hydrogenation catalyst,[15] many groups have contributed to the development of new N,P-ligated iridium catalysts,[16,17] and recent work has focused on expanding their substrate scope.[18,19] We reasoned that applying Ir-catalyzed asymmetric hydrogenation to form diarylmethine stereogenic centers would expand the available methods for their synthesis. At first glance, this task appeared difficult; two aryl groups often have very similar steric and electronic properties. When reducing olefins bearing almost identical groups at the prochiral carbon, we must rely on other steric interactions to induce selectivity. Here, we describe a method of making diarylmethine chiral centers from substrates whose geminal olefin substituents differ very little. In one example, these differ by only a single atom in the *para*-position. These results support the hypothesis that steric hindrance in one specific quadrant is playing a key role in directing the transformation.[13a,17f,i,25]

Table 1. Screening of Ir Catalysts in the Asymmetric Hydrogenation of 1,1-Diaryl-Substituted Olefins **1** and **2**[a]



entry	(N,P)*	conv[b] (%)	ee[c] (%)	conv[b] (%)	ee[c] (%)
1	 I	29	71 (+)	**>99** (>95)[d]	**>99** (-)
2	 II	38	30 (+)	11	94 (-)
3	 III	51	67 (+)	**>99**	**>99** (+)
4	 IV	**83**	**87** (-)	57	>99 (+)
5	 V	66	68 (-)	8	50 (-)
6	 VI	>99	77 (-)	81	80 (-)

[a] Reaction conditions: 25 mg of **1** or **2**, 1 mol % catalyst, 1 mL of CH_2Cl_2. Hydrogenation of **1**: 40 °C, 100 bar of H_2, 24 h. Hydrogenation of **2**: 25 °C, 50 bar of H_2, 24 h. [b] Conversion to alkane determined by ^{1}H NMR spectroscopy. [c] Determined by chiral HPLC. For details see Supporting Information. [d] Isolated yield.

Results and Discussion

Substrate Synthesis. The present technique for producing diarylmethine stereocenters, like most methods for their synthesis, relies on the efficient synthesis of olefins in isomerically pure form. Most of the olefins discussed in this paper can easily be purified by recrystallization or chromatography, and many of them are synthesized according to literature procedures, which accentuates the usefulness of this method. Substrates (*Z*)-**1**, (*Z*)-**10** and (*Z*)-**11** (Tables 1 and 4) were synthesized using the Heck arylation of (*E*)-methyl cinnamate and isolated via standard flash

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(16) (a) Schrems, M. G.; Neumann, E.; Pfaltz, A. *Heterocycles* **2008**, *76*, 771–781. (b) Zhou, J.; Ogle, J. W.; Fan, Y.; Banphavichit(Bee), V.; Zhu, Y.; Burgess, K. *Chem.—Eur. J.* **2007**, *13*, 7162–7170. (c) Cheemala, M. N.; Knochel, P. *Org. Lett.* **2007**, *9*, 3089–3092. (d) Wang, C. J.; Sun, X.; Zhang, X. *Angew. Chem., Int. Ed.* **2005**, *44*, 4933–4935. (e) Bunlaksananusorn, T.; Polburn, K.; Knochel, P. *Angew. Chem., Int. Ed.* **2003**, *42*, 3941–3943. (f) Tang, W.; Wang, W.; Zhang, X. *Angew. Chem., Int. Ed.* **2003**, *42*, 943–946. (g) Perry, M. C.; Cui, X.; Powell, M.; Hou, D.; Reibenspies, J.; Burgess, K. *J. Am. Chem. Soc.* **2003**, *125*, 113–123. (h) Cozzi, P. G.; Menges, F.; Kaiser, S. *Synlett* **2003**, *6*, 833–836. (i) Hou, D. R.; Reibenspies, J.; Colacot, T. J.; Burgess, K. *Chem.—Eur. J.* **2001**, *7*, 5391–5400. (j) Blankenstein, J.; Pfaltz, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 4445–4447. (k) Cozzi, P. G.; Zimmermann, N.; Hilgraf, R.; Schaffner, S.; Pfaltz, A. *Adv. Synth. Catal.* **2001**, *343*, 450–454.
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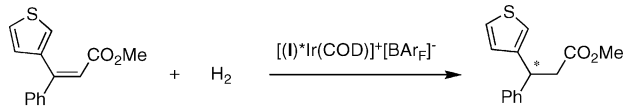
Table 2. The Effects of Solvent, Temperature and Hydrogen Pressure in the Asymmetric Hydrogenation of **1** with $[(\mathbf{I})Ir(COD)]^+[BAr_F]^{-a}$



1

entry	solvent	hydrogen pressure (bar)	temp (°C)	conv[b] (%)	ee[c] (%)
1	α,α,α-trifluorotoluene	100	25	39	82 (+)
2	2,2,4-trimethylpentane	100	25	17	78 (+)
3	CH_2Cl_2	100	25	31	75 (+)
4	CH_2Cl_2	50	25	0	–[d]
5	CH_2Cl_2	50	40	46	71 (+)

[a] Reaction conditions: 25 mg of **1**, 1 mol % catalyst, 1 mL of solvent, 24 h. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by chiral HPLC. See Supporting Information for details. [d] Not applicable.

chromatography.[20] The Suzuki cross-coupling reaction was used to selectively produce substrates **2**−**6**, which were obtained in pure *E* form following flash chromatography.[21] Substrates **12**, **14**, and **15** were derived from isomerically pure **10** or **1** without loss of isomeric purity. Substrate **13** was synthesized in analogy to **12** and **14**, and was also obtained as a single isomer from flash chromatography (see Supporting Information for details). Substrates **7**−**9** were synthesized via the Wittig reaction and separated from their isomers using preparative HPLC.

Reaction Optimization. Olefins **1** and **2** were screened against various chiral Ir complexes of ligands **I**−**VI** (Table 1). Ligands were synthesized according to published procedures: **I**,[17f] **II**,[17i] **III**,[17c] **IV**,[18d] and **V**−**VI**.[17g,h] In the asymmetric hydrogenation of α,β-unsaturated ester **1**, both conversion and enantioselectivity were very catalyst-dependent; the best result was obtained with a catalyst based on ligand **IV** (Table 1, entry 4). Contrary to the α,β-unsaturated methyl ester **1**, the unfunctionalized olefin **2** could be reduced at ambient temperature. Catalysts containing thiazole-based ligand **I** and the imidazole-based ligand **III** fully reduced **2** and gave excellent enantioselectivities (Table 1, entries 1 and 3), whereas the other catalysts were less active and/or less selective.

The effects of solvent, temperature and hydrogen pressure on the asymmetric hydrogenation of **1** by $[(\mathbf{I})Ir(COD)]^+[BAr_F]^-$ were studied (Table 2). The reaction time was limited to 24 h to keep conversions comparable.

The best enantioselectivity and activity were measured in α,α,α-trifluorotoluene and dichloromethane, respectively (Table 2, entries 1 and 5). Less activity was obtained in 2,2,4-trimethylpentane (entry 2), possibly due to lower catalyst solubility in the less-polar solvent. At least 40 °C or at least 100 bar of H_2 pressure was required for the reaction; the latter was preferred because it afforded slightly higher enantioselectivity (compare entries 3 and 5). Based on the optimization study and catalyst screening, we decided to apply ligands **I** and **IV** to further substrates. Though catalyst optimization studies were performed using 1 mol % catalyst, substrate **2** could be fully reduced in 99% ee after 18 h using only 0.5 mol % $[(\mathbf{I})Ir(COD)]^+[BAr_F]^-$ at 25 °C under 50 bar of H_2 pressure. The best reaction conditions from Table 2 (viz. α,α,α-trifluorotoluene or CH_2Cl_2 as the solvent at 25 °C and 100 bar of hydrogen pressure) were used for the subsequent studies and optimized further when needed.

Asymmetric Hydrogenation of 1,1-Diarylolefins. In order to expand the scope of building blocks with chiral diarylmethine centers, we evaluated a broad range of trisubstituted olefins. Unfunctionalized olefins, in which the olefin substituent on the non-prochiral center was either alkane or phenyl, were studied first (Table 3). Overall, these were reduced highly selectively. Aryl moieties with electron-withdrawing and electron-donating groups were studied. The substrates **2** and **3**, with electron-donating substituents (−Me, −OMe), were fully and highly selectively (up to 99% ee) hydrogenated at room temperature (entries 1 and 2). Substrate **4**, which possesses an electron-withdrawing CF_3 substituent on one aromatic ring, required heating to reach 50% conversion and was hydrogenated less enantioselectively (entry 3); this might have been partially due to the higher reaction temperature. Another substrate with an electron-withdrawing substituent, bromo-substituted **8**, gave an excellent ee of 95% (entry 7). This substrate is particularly interesting because the resulting optically active product can be a useful substrate for cross-coupling reactions.[22]

The effect of substituent positioning was investigated using the methyl-substituted substrates **2**, **5** and **6** (Table 3, entries 1, 4 and 5). Both the *meta*,*meta*-dimethyl substrate **5** and *para*-substituted substrate **2** gave excellent enantioselectivities (99% ee) and full conversions, whereas the *ortho*-substituted substrate **6** required heating and was reduced in slightly lower ee. The sluggish hydrogenation of **6** is attributed to its sterically hindered carbon−carbon double bond. In the case of *para*-substituted aromatics, the substrate size did not play a crucial role; the biphenyl-substituted olefin **9** gave high conversion and excellent ee (99%; Table 3, entry 8).

Interestingly, the enantioselectivities were not affected by the steric properties of the third olefin substituent, R. Substrates having aryl or alkyl substituents in this position (Table 3), except for substrates **4** and **6** as discussed earlier, were completely reduced in high ee. On the other hand, when the R substituent on the non-prochiral carbon atom of the olefin was an ester, alcohol, or acetate, the asymmetric hydrogenation gave more varied activities and enantioselectivities (Table 4). The asymmetric hydrogenation of α,β-unsaturated esters **10** and **11** required slightly elevated temperatures to reach full conversion, and gave only moderate enantioselectivities (Table 4, entries 1 and 2).

The furan moiety of α,β-unsaturated ester **11** was untouched (Table 4, entry 2) following the reaction. Pfaltz et al. have recently hydrogenated both furans and benzofurans highly enantioselectively,[23] but have also reported some examples in which furan moieties remain intact while olefinic bonds are reduced.[24]

When the hydrogenation of the diaryl-containing allylic alcohols **12**−**14** was attempted with the catalyst formed from

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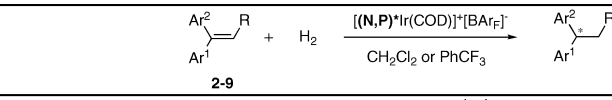
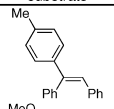
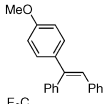
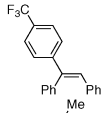
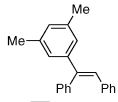
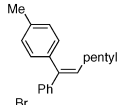
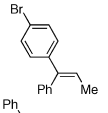
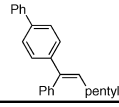
Table 3. Ir-Catalyzed Asymmetric Hydrogenation of a Range of Unfunctionalized 1,1-Diaryl-Substituted Olefins[a]



entry	substrate		(N,P)*	temp (°C)	hydrogen pressure (bar)	solvent	conv (%)	ee (%)
1		2	I	25	50	CH_2Cl_2	>99	>99 (-)
2		3	I	25	50	CH_2Cl_2	>99	95 (-)
3		4	I	40	100	CH_2Cl_2	48	76 (-)[b]
4		5	I	25	50	CH_2Cl_2	>99	>99 (+)[b]
5		6	IV	80	100	$PhCF_3$	35	92 (+)
6		7	IV	25	100	$PhCF_3$	>99	97 (-)
7		8	IV	25	100	$PhCF_3$	>99	95 (+) (*S*)[c]
8		9	IV	25	100	$PhCF_3$	99	99 (+)

[a] Reaction conditions: 0.2−0.3 M substrate in CH_2Cl_2 or α,α,α-trifluorotoluene, 1 mol % catalyst, 24 h. Conversions were determined by ^{1}H NMR spectroscopy, and ee values were determined by chiral HPLC or chiral GC. For details, see Supporting Information. Optical rotations are shown in parentheses. [b] (*R*)-**I** ligand was used. [c] Absolute configuration assigned after derivatization.

ligand **IV**, complicated mixtures with no traces of the desired product resulted. We have recently reported the asymmetric hydrogenation of the related methyl-substituted allylic alcohol **16** using [(**VII**)Ir(COD)]$^+$[BAr_F]$^-$ (Figure 2).[17c] This catalyst also proved useful in the reduction of diaryl-substituted allylic alcohols, producing the desired alkanes with high conversions and enantioselectivities (Table 4, entries 3−5).

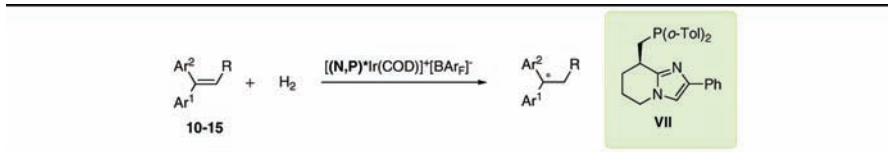
Contrary to the hydrogenation of unfunctionalized olefins, in which the electronics of the aryl rings influenced the reactivity, the asymmetric hydrogenations of substrate **12**, with an electron-donating OMe group, and substrate **13**, with an electron-withdrawing CF_3 substituent, gave the same conversions and enantioselectivities (Table 4, entries 3 and 4). The hydrogenation of the thiophene-substituted olefin **14** (Table 4, entry 5) with [(**VII**)Ir(COD)]$^+$[BAr_F]$^-$ gave higher conversion and enantioselectivity than did the corresponding hydrogenation of α,β-unsaturated ester **1** with [(**I**)Ir(COD)]$^+$[BAr_F]$^-$ (Table 2, entry 1); the ee value obtained in a synthesis can therefore be improved if alcohol **14** can be chosen as an alternative for ester **1** in a synthesis. The allylic acetate **15** was hydrogenated by with [(**VII**)Ir(COD)]$^+$[BAr_F]$^-$ (Table 4, entry 6) much like the corresponding alcohol did. Comparison of the hydrogenation of three related functionalized diarylolefins shows the enantioselectivities improving upon moving from α,β-unsaturated ester **10** to allylic alcohol **12** and allylic acetate **15**.

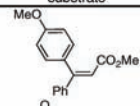
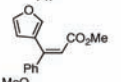
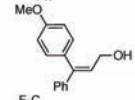
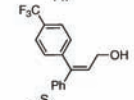
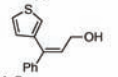
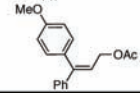
Origin of Enantiodiscrimination in the Hydrogenation Reaction. The catalysts reported here were highly enantioselective in the hydrogenation of olefins with *gem*-diaryl substituents that differed by as little as a methyl group (see Table 3, entries 1, 5, 6). We therefore suspected that the position of the "other" olefin substituent, the one at the monosubstituted olefin terminus, was pivotal to the stereochemical outcome of the reaction. To further probe this idea, we hydrogenated two sets of *cis*/*trans* isomer pairs, (*E*)- and (*Z*)-**8** and (*E*)- and (*Z*)-**9** (Figure 3). The results were striking: in each case, the two isomers were hydrogenated to opposite enantiomers in near-identical ee values. Thus the stereochemistry is dominated by the substituent on the monosubstituted terminus.

We also examined the importance of the substituent on the nonprochiral carbon by performing the asymmetric hydrogenation of an olefin that lacked this feature, i.e. a terminal 1,1-diarylolefin. We hoped to study a terminal olefin with a phenyl and a 4-substituted-phenyl substituent. Unfortunately, although several of these olefins could be synthesized and hydrogenated, we were unable to separate the product enantiomers using chiral chroma-

(23) Kaiser, S.; Smidt, S. P.; Pfaltz, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 5194–5197.
(24) Pfaltz, A.; Blankenstein, J.; Hilgraf, R.; Hörmann, E.; McIntyre, S.; Menges, F.; Schönleber, M.; Smidt, S. P.; Wüstenberg, B.; Zimmermann, N. *Adv. Synth. Catal.* **2003**, *345*, 33–43.
(25) (a) Brandt, P.; Hedberg, C.; Andersson, P. G. *Chem.—Eur. J.* **2003**, *9*, 339–347. (b) Fan, Y.; Cui, X.; Burgess, K.; Hall, M. B. *J. Am. Chem. Soc.* **2004**, *126*, 16688–16689.

Table 4. Ir-Catalyzed Asymmetric Hydrogenation of Functionalized Olefins[a]



entry	substrate		(N,P)*	temp (°C)	conv (%)	ee (%)
1		**10**	**IV**	40	>99	69 (+) (*R*)[b]
2		**11**	**IV**	40	>99	80 (-)
3		**12**	**VII**	25	>99	**92** (-) (*R*)[c]
4		**13**	**VII**	25	>99	**92** (+)
5		**14**	**VII**	25	>99	90 (-)
6		**15**	**VII**	25	>99	**95** (-) (*R*)[c]

[a] Reaction conditions: 0.2−0.3 M substrate in α,α,α-trifluorotoluene, 1 mol % catalyst 100 bar of H_2, 24 h. Conversions were determined by ^{1}H NMR spectroscopy, and ee values were determined by chiral HPLC or chiral GC. For details, see Supporting Information. Optical rotations are shown in parentheses. [b] Absolute configuration assigned by comparing retention order in HPLC with literature data.[9a] [c] Absolute configuration assigned after converting the chiral product from substrate **10** into alcohol and acetate.

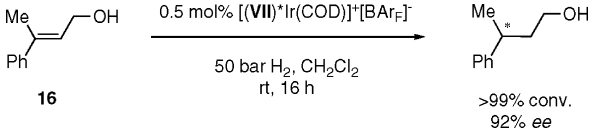


Figure 2. Iridium-catalyzed asymmetric hydrogenation of allylic alcohol **16** using ligand **VII**.

tography and thus unable to determine the selectivity of the reductions. We therefore examined the hydrogenation of **17** (Figure 4). The very bulky 2,6-dimethylphenyl group visibly affected the hydrogenation; after 60 h with 1 mol % catalyst under 100 bar of H_2, substrate **17** was only 15% hydrogenated. However, it was clear that the ee value obtained in this hydrogenation, 76%, was anomalously low compared to those obtained for unfunctionalized trisubstituted olefins using the same catalyst (92−99%, see Table 3, entries 5−8). This adds support to the idea that the geometry at the monosubstituted olefin terminus strongly influences stereoselectivity in the iridium-catalyzed asymmetric hydrogenation of 1,1-diaryl-substituted olefins.

The strong dependence of enantioselectivity on the monosubstituted olefin terminus can be accounted for using (and can provide support to) the DFT-derived selectivity models for asymmetric, iridium-catalyzed olefin hydrogenation that have been proposed by Brandt and Andersson[17f,i,25a] and Burgess and Hall.[25b]

Calculations performed by these authors predicted that an olefin will bind to the iridium atom in the same equatorial plane as the chiral ligand, *cis* to the nitrogen atom and, most preferably, with its smallest substituent oriented toward the bulky group of the ligand. The absolute configuration of the resulting chiral hydrogenation product can be rationalized by considering the sterics about the Ir center from the perspective of the olefin, and this is the basis for the enantiofacial-selectivity models (Figure 5). Separating the space into four quadrants, labeled **I**−**IV** as in a Cartesian coordinate system, we see that quadrant **III** is occupied by a phenyl group and therefore sterically hindered. The two aryl substituents on the phosphorus atom partly occupy quadrant **I**, making it semihindered. Quadrants **II** and **IV**, which are free from bulky groups, are open. This suggests that the smallest substituent of the olefin (an H atom when the olefin is trisubstituted) should be pointing toward the hindered quadrant **III**, meaning that the configuration of the monosubstituted olefin terminus will determine the sense of selectivity in the hydrogenation reaction.

To further evaluate the utility of these models in describing the stereoselectivity in the iridium-catalyzed hydrogenation of 1,1-diarylolefins, we aimed to compare the sense of selectivity they predicted for the hydrogenations of olefins **8**, **10**, **12**, and **15** with our experimental results. The absolute configuration of the hydrogenated product from **10** has been reported,[9a] and the configuration of the products from **8**, **12**, and **15** was derived as shown in Scheme 1 (see Supporting Information for details). We therefore determined that [(**IV**)Ir(COD)]$^+$[BAr_F]$^-$ hydrogenated **8** to the *S* product and **10** to the *R* product, and [(**VII**)Ir(COD)]$^+$[BAr_F]$^-$ hydrogenated both **12** and **15** to their respective *R* products. Arranging each of these 1,1-diarylolefins on the diagram in Figure 5 with its smallest substituent (−H) pointing toward the bulky group of the ligand allows the correct prediction of the sense of stereoselectivity in its hydrogenation. Thus the models proposed by Brandt and Andersson and Burgess and Hall clearly rationalized the results of all four hydrogenations. This lends further support to these selectivity models, and demonstrates that the substituent on the non-prochiral carbon provides the high enantioselectivities observed for these substrates, which have small differences in electronic and steric properties between the two aryl groups.

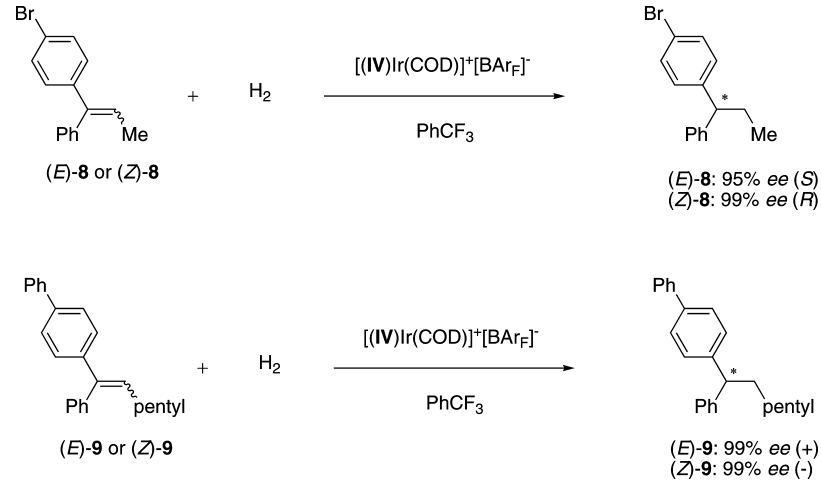


Figure 3. The asymmetric hydrogenation of the *cis*/*trans* isomer pairs **8** and **9**.

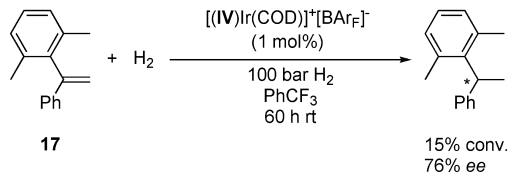


Figure 4. Asymmetric hydrogenation of the terminal 1,1-diarylolefin **17**.

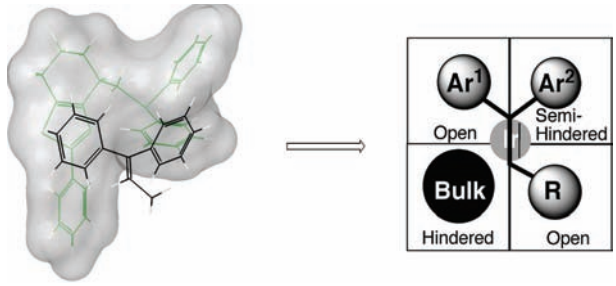


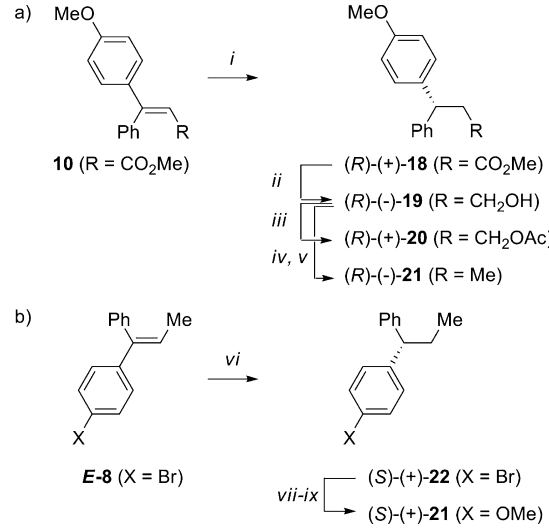
Figure 5. Schematic diagram describing the enantiodetermining substrate−ligand interactions as a trisubstituted 1,1-diarylolefin coordinates to the catalyst. The ligand (**I**) is shown in green.

The fact that high stereoselectivity can be achieved in the hydrogenation of 1,1-diarylolefins having very similar aryl groups opens up new possibilities. For example, it should in principle be possible to obtain high ee values on substrates with aryl groups differing only in isotopic substitution. The question, however, is how to evaluate the results of such a reaction; separating enantiomers can be difficult even for enantiopairs having very different substituents.

Conclusion

We have shown that Ir-catalyzed asymmetric hydrogenation using N,P-chelating ligands is a highly useful method for the formation of diarylmethine stereogenic centers. Trisubstituted olefins with aryl groups having a variety of electronic and steric properties were hydrogenated in excellent enantioselectivities and high conversions, even when the differences between the aryl groups on the prochiral carbon were very small. Notably, optically active *gem*-diarylalkanes were produced with excellent enantioselectivities; this is difficult using other synthetic methods. Allylic alcohols were also hydrogenated highly enantioselectively. These results also strengthen the hypothesis that steric hindrance in one specific quadrant of the catalyst is playing a key role in this transformation. Among the synthetic methods that form diarylmethine chiral centers, the iridium-catalyzed asymmetric hydrogenation of trisubstituted olefins is unique in that it can be applied to a wide range of olefins and can form chiral compounds that are otherwise difficult to synthesize.

Scheme 1. Preparation of Chiral 1,1-Diarylmethines with Known Absolute Configuration[a]



[a] (i) $[(\mathbf{IV})Ir(COD)]^+[BAr_F]^-$, H_2, $PhCF_3$. (ii) $LiAlH_4$, THF. (iii) Ac_2O, NEt_3, DMAP, CH_2Cl_2. (iv) MsCl, pyridine, CH_2Cl_2. (v) $NaBH_4$, DMSO. (vi) $[(\mathbf{IV})Ir(COD)]^+[BAr_F]^-$, H_2, CH_2Cl_2. (vii) B_2Pin_2, $Pd(dppf)Cl_2$, KOAc, DMF. (viii) H_2O_2, NaOH. (ix) MeI, K_2CO_3, acetone.

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Supporting Information Available: Experimental details for the hydrogenation procedures and synthesis of substrates, characterization data of new compounds, and chiral separation data. This material is available free of charge via the Internet at http://pubs.acs.org.

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