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Bis-(2,5-diphenylphospholanes) with sp^2 Carbon Linkers: Synthesis and Application in Asymmetric Hydrogenation

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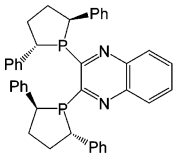
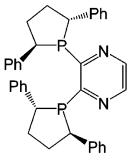
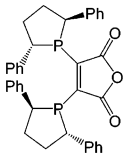


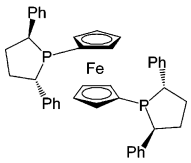
(*S*,*S*)-Ph-Quinox (**5**)



(*R*,*R*)-Ph-Pyrazine (**6**)



(*S*,*S*)-Ph-MalPhos (**7**)



(*S*,*S*)-Ph-5-Fc (**8**)

Four chiral diphosphine ligands consisting of bis(2,5-diphenylphospholan-1-yl) groups connected by the sp^2 carbon linkers 2,3-quinoxaline ((*S*,*S*)-Ph-Quinox), 2,3-pyrazine ((*S*,*S*)-Ph-Pyrazine), maleic anhydride ((*S*,*S*)-Ph-MalPhos), and 1,1′-ferrocene ((*S*,*S*)-Ph-5-Fc) were synthesized, and their cationic [rhodium-(I)(COD)] complexes were prepared. These complexes were tested in asymmetric hydrogenation of functionalized olefins. [((*S*,*S*)-Ph-Quinox)Rh(COD)]BF_4 showed high activity and selectivity against itaconate and dehydroamino acid substrates. The corresponding (*S*,*S*)-Ph-Pyrazine and (*S*,*S*)-Ph-MalPhos complexes exhibited lower activities and selectivities. [((*S*,*S*)-Ph-5-Fc)Rh(COD)]BF_4 showed high activity with low selectivity for these substrates, but high activity and selectivity against 2-C-substituted cinnamate salts, whereas rhodium complexes of (*S*,*S*)-Ph-Quinox and (*R*,*R*)-Ph-BPE showed low activity and selectivity against 2-C-substituted cinnamate salts.

Introduction

Asymmetric hydrogenation of olefins, ketones, and imines using modular phospholane-based catalysts is a powerful method to produce enantiomerically enriched products.[1−4] A subset of this class is diphosphines based on bis(2,5-diphenylphospholane) groups connected by sp^3 carbon linkers (Figure 1), which provide valuable ligands for rhodium-catalyzed asymmetric olefin hydrogenation,[2,5,6] ruthenium-catalyzed asymmetric imine hydrogenation,[6] and rhodium-catalyzed asymmetric hydroformylation.[7,8] In view of the excellent properties of the (*R*,*R*)-Ph-BPE (**1**)[5] and (*R*,*R*)-Ph-BPM (**2**)[6] ligands (Figure 1) in these reactions, we set out to extend the range of available bis(2,5-diphospholane) ligands and hence prepare asymmetric hydrogenation catalysts with novel capabilities by synthesis of a corresponding series of ligands with sp^2 carbon linkers. We intended to use the monophospholane methodology successfully applied to the synthesis of (*R*,*R*)-Ph-BPE (**1**)[5] and (*R*,*R*)-Ph-BPM (**2**)[6] ligands, in which the resolved acid **3**[9] was used as a monophospholane precursor and coupled to the linker after suitable manipulation of the phosphorus functionality. The 2,3-

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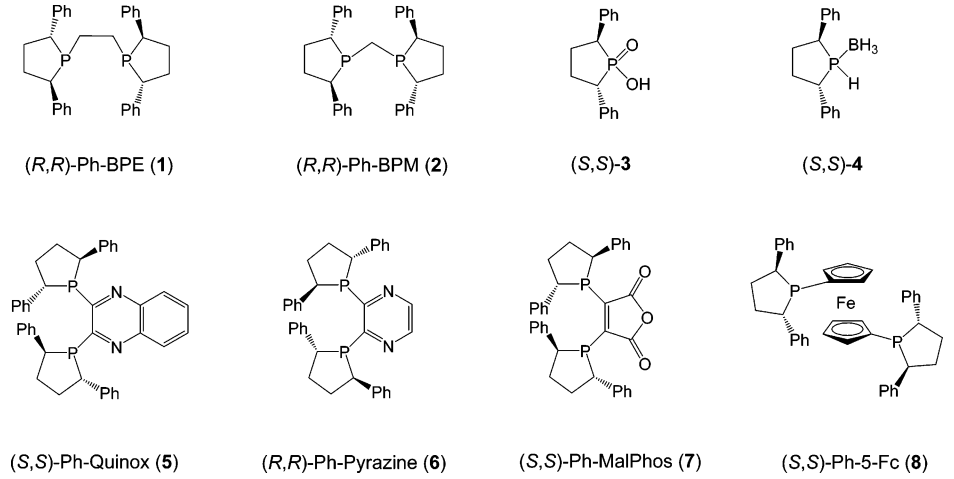
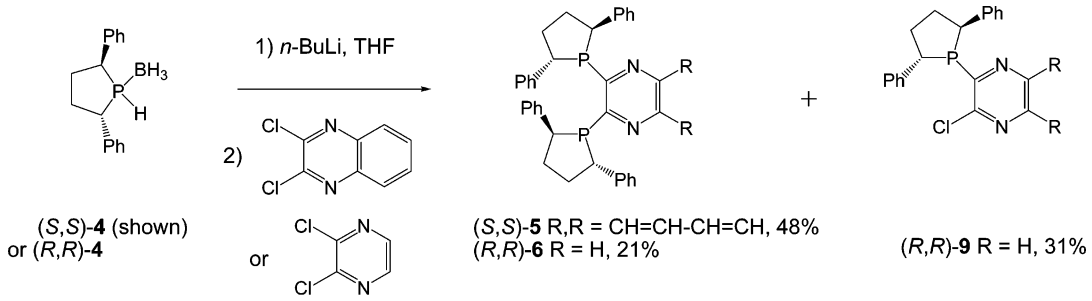


FIGURE 1. Bis(2,5-diphenylphospholane) ligands and monophospholane precursors.

SCHEME 1. Synthesis of Quinoxaline and Pyrazine Linked Ligands



quinoxalinyl group had previously been reported by Imamoto et al.[10,11] as a two-carbon linker for P-chiral diphosphine ligands exhibiting high activity and selectivity in rhodium-catalyzed asymmetric hydrogenation. Furthermore, synthesis of diphosphine ligands based on this linker was achieved by substitution using a nucleophilic phosphorus species. Hence, we anticipated that the bis(2,5-diphenylphospholane) ligand **5** based on this linker could also be valuable in asymmetric hydrogenation and that its synthesis should be achievable using the monophospolane borane adduct **4** previously employed as a P-nucleophile in the synthesis of the (*R*,*R*)-Ph-BPE (**1**)[5] and (*R*,*R*)-Ph-BPM (**2**)[6] ligands. We were also interested in making the analogous ligands with two carbon sp^2 linkers 2,3-pyrazinyl (**6**) and maleic anhydride[12] ((*S*,*S*)-Ph-MalPhos (**7**)) for comparison, which we expected to be accessible by similar nucleophilic substitution chemistry. Diphosphine ligands with a 1,1′-ferrocenyl linker have also shown high and unique selectivities in rhodium-catalyzed asymmetric hydrogenation of certain olefin substrates.[13−15] Thus, we sought to achieve the synthesis of the bis(2,5-diphospholane) ligand based on this linker, (*S*,*S*)-Ph-5-Fc (**8**). However, formation of P-ferrocenyl carbon bonds is most readily achieved by reaction of a metalated ferrocene with a phosphorus electrophile. Therefore, extension of the monophospholane strategy to this ligand would require the use of an electrophilic (2,5-diphenylphospholane) synthon.

Results and Discussion

Synthesis of 2,3-Quinoxaline and 2,3-Pyrazine Linked Ligands. The quinoxaline linked ligand **5** ((*S*,*S*)-Ph-Quinox) was prepared in a procedure analogous to that described by Imamoto et al.:[10] by reaction of the lithiated phospholane borane adduct (*S*,*S*)-**4** with 2,3-dichloroquinoxaline (Scheme 1). We observed the free phosphine rather than the borane adduct to be the product of the coupling reaction, with loss of borane occurring spontaneously during the reaction or workup, to give the free ligand **5**. This was similar to the findings of Imamoto et al. with his ligand system; however, we found that the addition of TMEDA as employed by Imamoto et al. was unnecessary. If TMEDA is added, the borane is lost from the remaining monophospholane borane adduct **4**, and the resulting free phosphine and oxidation products are difficult to separate from the product **5**. The pyrazine linked ligand **6** was prepared using the enantiomeric phospholane borane adduct (*R*,*R*)-**4**. A large amount of monophospholane **9** was also observed in this case. These procedures have not been optimized, but sufficient quantities of the target ligands **5** and **6** were obtained for our studies.

Synthesis of Maleic Anhydride Linked Ligand (*S*,*S*)-Ph-MalPhos (7). In the preparation of maleic anhydride linked bis(2,5-dialkylphospholane) ligands,[12] Börner et al. employed the reaction between dichloromaleic anhydride and a 1-trimethylsilylphospholane nucleophile. However, we found that for the 2,5-diphenylphospholane analogue, the use of the free phosphine

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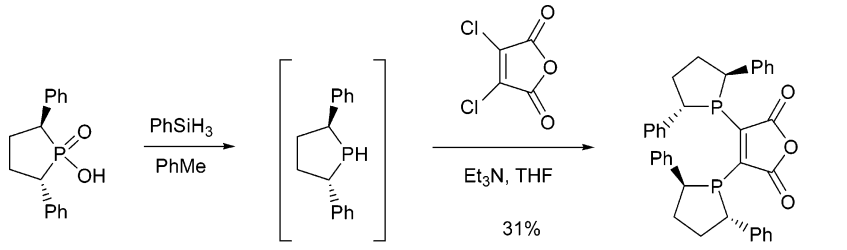
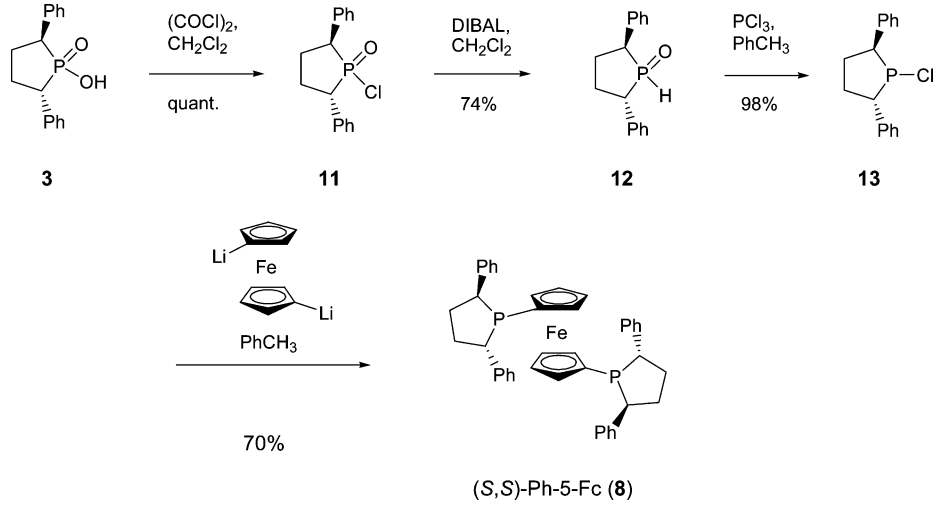
SCHEME 2. Synthesis of Maleic Anhydride Linked Ligand (*S,S*)-Ph-MalPhos (7)



SCHEME 3. Synthesis of 1-1′-Ferrocenyl Linked Ligand (*S,S*)-Ph-5-Fc (8)



10[9] was more convenient (Scheme 2). The phosphine was generated by reduction of the acid **3** with phenylsilane.[7] Subsequently, this was reacted in situ with dichloromaleic anhydride using triethylamine as a base to give the maleic anhydride linked ligand **7** ((*S,S*)-Ph-MalPhos). The yield we obtained in this process was moderate, but comparable to that reported for the parent MalPhos ligand using a more complicated procedure.[12]

Synthesis of 1,1′-Ferrocene Linked Ligand (*R,R*)-Ph-5-Fc (8). The most straightforward means of preparation of 1,1′-disubstituted ferrocenyl derivatives is by dilithiation of ferrocene followed by reaction of the dilithioferrocene with an electrophile.[13] Therefore, for the monophospholane methodology to be employed for the synthesis of the bis(2,5-diphenylphospholanyl) ligand with this linker, the preparation of a suitable 2,5-diphenylphospholane electrophile was required (Scheme 3). This required reduction from the phosphorus(V) oxidation state of the phospholanic acid **3** to the phosphorus(III) oxidation state. This was achieved in two steps: first by conversion of the phospholanic acid **3** to the phospholanoyl chloride **11**,[9] and then by reduction to the secondary phosphine oxide **12**[9] with DIBAL. Owing to the insoluble nature of the phospholanyl chloride **11** in other suitable solvents, this was carried out in dichloromethane. It remained to activate the secondary phosphine oxide **12** to an electrophile suitable for reaction with 1,1′-dilithioferrocene. This was accomplished by conversion of **12** to the 1-chlorophospholane **13**[16] using phosphorus trichloride. This reactive intermediate was characterized by ^{1}H, ^{13}C{^{1}H}, and ^{31}P{^{1}H} NMR. The ^{31}P NMR spectrum is remarkable in showing two resonances in a 3:1 ratio with a separation of 31 ppb (Figure 2). This phenomenon is ascribed to the occurrence of an isotopic chemical shift due to the presence of ^{35}Cl or ^{37}Cl attached to phosphorus and is thus analogous to the ^{35}Cl/^{37}Cl isotopic shifts previously described for carbon (observed by ^{13}C)[17] and fluorine (observed by ^{19}F).[18] To our knowledge, this is the first time this effect has been observed in ^{31}P NMR. Reaction of the chloride **13** with 1,1′-dilithioferrocene[13] gave 1,1′-bis(2,5-diphenylphospholan-1-yl)ferrocene ((*S,S*)-Ph-5-Fc) **8**. In addition to NMR, HRMS, and elemental analysis, this ligand was further characterized by single-crystal X-ray diffraction (Figure 3).

Synthesis of Rh(I)(COD)BF$_4$ Complexes of Ligands 5−8. The cationic rhodium(I)(COD) complexes of ligands **5**−**8** [L Rh(COD)]BF$_4$ were prepared in good yields by reaction of the ligand with [Rh(COD)$_2$]BF$_4$.[19] The molecular structure of the Rh complex of (*S,S*)-Ph-5-Fc (**8**) was determined by X-ray crystallography (Figure 4). This shows a Rh−P bond length of 2.3326(5)/2.3611(5) Å and a bite angle of 96.34(2)°, similar to those of [Et-Ferrotane Rh(NBD)]BF$_4$.[20]

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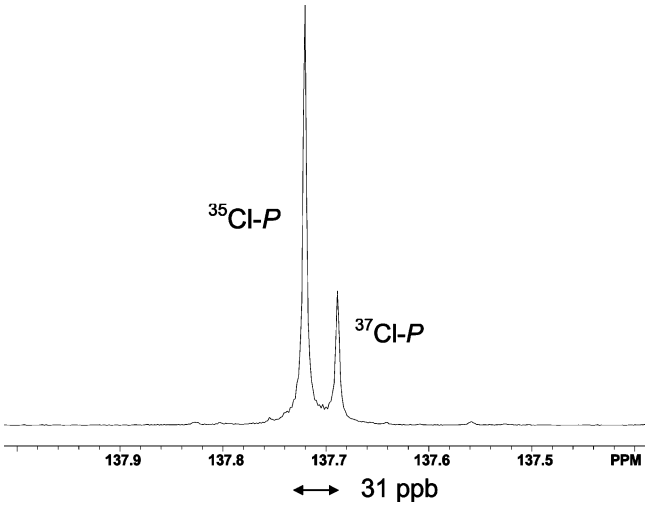


FIGURE 2. $^{31}P\{^{1}H\}$ NMR spectrum of (2*S*,5*S*)-1-chloro-2,5-diphenylphospholane (**13**) showing isotope-induced shift for the resonance arising from the chlorine-bearing phosphorus.

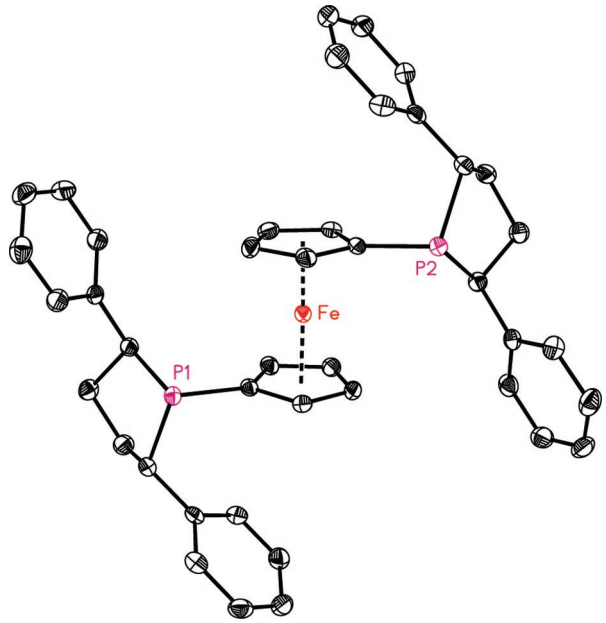


FIGURE 3. Molecular structure of (*S*,*S*)-Ph-5-Fc (**8**) at 40% probability level. Hydrogen atoms were omitted for clarity.

Rhodium-Catalyzed Asymmetric Hydrogenation with Ligands 5−8. The asymmetric hydrogenation of standard enamide and itaconate substrates **14**−**18** (Scheme 4) with rhodium complexes [L Rh(COD)]BF_4 was examined. The results are given in Table 1.

The quinoxaline catalyst [((*S*,*S*)-Ph-Quinox)Rh(COD)]BF_4 showed high selectivities (>98.7% ee) and rates for all five substrates and is clearly an excellent general asymmetric olefin hydrogenation catalyst (Table 1, entries 1−5). The pyrazine-based catalyst **6**-Rh was both less selective and much less active than **5**-Rh (entries 6−9). (*S*,*S*)-Ph-MalPhos-Rh was also much less active than **5**-Rh, but did show good selectivity with methyl acetamidomalonate **15** and methyl acetamidocinnamate **17** (entries 11 and 12). The enantiomeric excess obtained for the hydrogenation of dimethyl itaconate **14** (entry 10) was much higher than that reported for Me-MalPhos (60.2% ee at S/C 100 in MeOH and 1 bar H_2).[12] It has also been reported with Me-MalPhos that a higher ee was obtained in THF (86%).[12] However, at S/C 1000 in THF, (*S*,*S*)-Ph-MalPhos-Rh showed only 5% conversion. The Ph-Malphos-derived catalyst provided an excellent ee for methyl α-acetamidocinnamate **17**, but unexpectedly gave racemic product in hydrogenation of α-acetamidocinnamic acid **18** (entries 12 and 13).

TABLE 1. Asymmetric Hydrogenation of Substrates 14−18 with [(Ligand)Rh(COD)]BF_4[a]

entry	ligand	substrate	time to completion	ee (%)
1	(*S*,*S*)-Ph-Quinox (**5**)	**14**	15 min	99.8 (*S*)
2	(*S*,*S*)-Ph-Quinox (**5**)	**15**	10 min	99.9 (*R*)
3	(*S*,*S*)-Ph-Quinox (**5**)	**16**	10 min	98.7 (*R*)
4	(*S*,*S*)-Ph-Quinox (**5**)	**17**	20 min[b]	>99.5 (*R*)
5	(*S*,*S*)-Ph-Quinox (**5**)	**18**	25 min[b]	99.5 (*R*)
6	(*R*,*R*)-Ph-Pyrazine (**6**)	**14**	18 h	78 (*R*)
7	(*R*,*R*)-Ph-Pyrazine (**6**)	**15**	18 h	94 (*S*)
8	(*R*,*R*)-Ph-Pyrazine (**6**)	**17**	18 h[b]	96 (*S*)
9	(*R*,*R*)-Ph-Pyrazine (**6**)	**18**	18 h[b]	76 (*S*)
10	(*S*,*S*)-Ph-MalPhos (**7**)	**14**	16 h	96.6 (*S*)
11	(*S*,*S*)-Ph-MalPhos (**7**)	**15**	2 h	99.7 (*R*)
12	(*S*,*S*)-Ph-MalPhos (**7**)	**17**	6 h[b]	98.8 (*R*)
13	(*S*,*S*)-Ph-MalPhos (**7**)	**18**	4 h[b]	racemic
14	(*S*,*S*)-Ph-5-Fc (**8**)	**14**	35 min	8 (*R*)
15	(*S*,*S*)-Ph-5-Fc (**8**)	**15**	20 min	6 (*S*)
16	(*S*,*S*)-Ph-5-Fc (**8**)	**16**	10 min	49 (*R*)
17	(*S*,*S*)-Ph-5-Fc (**8**)	**17**	20 min	6 (*S*)
18	(*S*,*S*)-Ph-5-Fc (**8**)	**18**	80 min[b]	56 (*R*)

[a] Reaction conditions: 2 mmol substrate, S/C 1000:1, MeOH, 25 °C, 10 bar H_2. [b] 30 °C.

[((*S*,*S*)-Ph-5-Fc)Rh(COD)]BF_4 showed a pattern of activity and selectivity different from that of the other catalysts. This catalyst was active, but not highly selective, with the enantiomeric excess values for hydrogenation of dimethyl itaconate **14**, methyl α-acetamidoacrylate **15**, and methyl α-acetamidocinnamate **17** being near-racemic (Table 1, entries 14, 15, and 17). Moreover, the selectivities obtained for dimethyl itaconate **14** (8% ee) and methyl α-acetamidoacrylate **15** (6% ee) are much lower than those reported for Me-5-Fc-Rh (64 and 72%, respectively).[13] Under the conditions of Table 1, with these substrates, we obtained 28% ee (*S*) and 66% ee (*R*), respectively, with [((*R*,*R*)-Me-5-Fc)Rh(COD)]BF_4. We also carried out the hydrogenation of methyl α-acetamidocinnamate **17** with [((*R*,*R*)-Me-5-Fc)Rh(COD)]BF_4 under the conditions of Table 1 for comparison, obtaining complete conversion and 66% ee (*R*).

(*S*,*S*)-Ph-5-Fc-Rh showed a selectivity for the acids **16** and **18** that was higher than that of the corresponding esters **15** and **17**, which is counter to the trend seen with the other catalysts. Despite the low selectivities exhibited by Ph-5-Fc-Rh, the high activity of this catalyst encouraged us to examine the hydrogenation of other substrates. The higher enantiomeric excesses obtained with the enamide acid substrates than those of the enamide ester substrates suggested that the preferred secondary binding site of this catalyst was the carboxylate rather than the acetamide group. Therefore, we tested this catalyst against the *tert*-butylamine salts of substituted cinnamic acids, substrates **24**−**26** (Scheme 5). We were pleased to find that the catalyst exhibited both high activity and enantioselectivity against these substrates (Table 2, entries 1−3), especially the 2-aryl substrate **25** (entry 2). In contrast, Ph-phospholane ligands with other linkers, (*R*,*R*)-Ph-BPE-Rh (entries 4−6) and (*S*,*S*)-Ph-Quinox-Rh (entries 7 and 8), exhibited low activity and selectivity against these three substrates. 5-Fc ligands with alkyl instead of aryl groups exhibited high activity but much lower selectivity (entries 9−17).

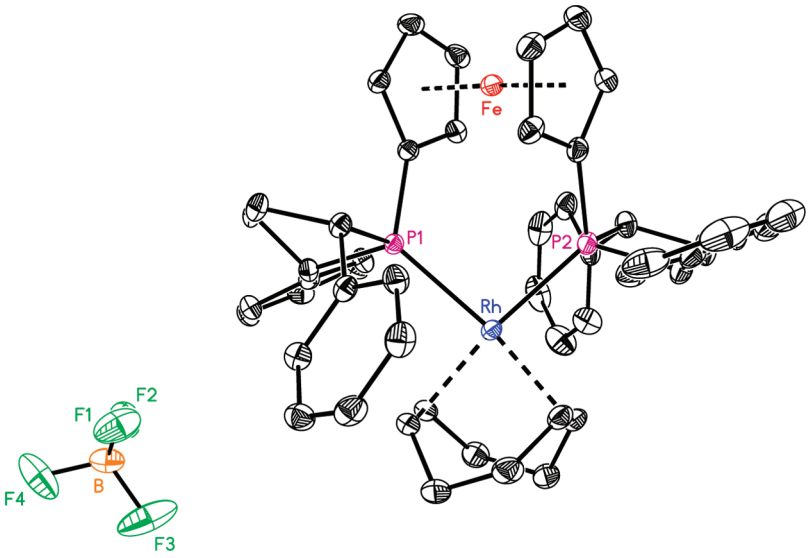
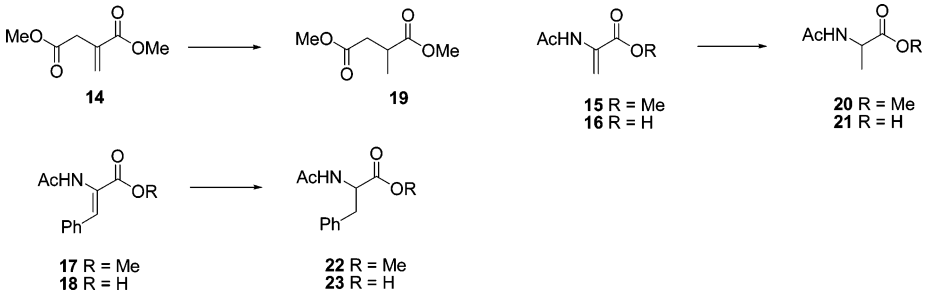
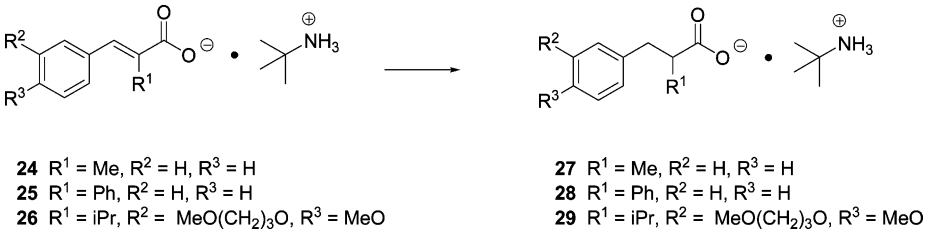


FIGURE 4. Molecular structure of [((*S*,*S*)-Ph-5-Fc)Rh(COD)]BF_4 at 40% probability level. Hydrogen atoms were omitted for clarity.

SCHEME 4. Asymmetric Hydrogenation of Itaconate and Enamides



SCHEME 5. Asymmetric Hydrogenation of α-C-Substituted Cinnamic Acid Salts



The asymmetric hydrogenation of (*E*)-2-methylcinnamic acid and (*E*)-2-phenylcinnamic acid using homogeneous rhodium catalysts has been reported, but we find that the amine salts, such as *tert*-butylamine, provide more active and reproducible reactions. Previous reports on the asymmetric hydrogenation of (*E*)-2-methylcinnamic acid provide variable enantiomeric excess values (17−92%), but all at high catalyst loadings (0.5−2 mol %).[21−23] The (*S*,*S*)-Ph-5-Fc (**8**) based catalyst gave 85% ee at a catalyst loading of 0.1 mol % for the asymmetric hydrogenation of (*E*)-2-methylcinnamic acid *tert*-butylammonium salt **24**. The asymmetric hydrogenation of (*E*)-2-phenylcinnamic acid has previously been reported to give good enantiomeric excess (95−96% ee), but again at high catalyst loading.[22−24] Here, (*S*,*S*)-Ph-5-Fc (**8**) gives outstanding results with the *tert*-butylamine salt **25** (96.5% ee, 0.075 mol %). Furthermore, the hydrogenation reaction was complete in 40 min, suggesting that even better catalyst utility can be achieved. Both free acid substrates have been hydrogenated using Ru-H_8-BINAP complexes, but lower enantiomeric excess values were obtained (74−89% ee).[25]

Asymmetric hydrogenation of the α-isopropylcinnamic acid substrate **26** provides an intermediate for the renin inhibitor aliskiren (Figure 5).[26] The enantiomeric excess achieved with the (*S*,*S*)-Ph-5-Fc (**8**) catalyst using the *tert*-butylamine salt (84.6%) is quite high, and the activity is high, with complete

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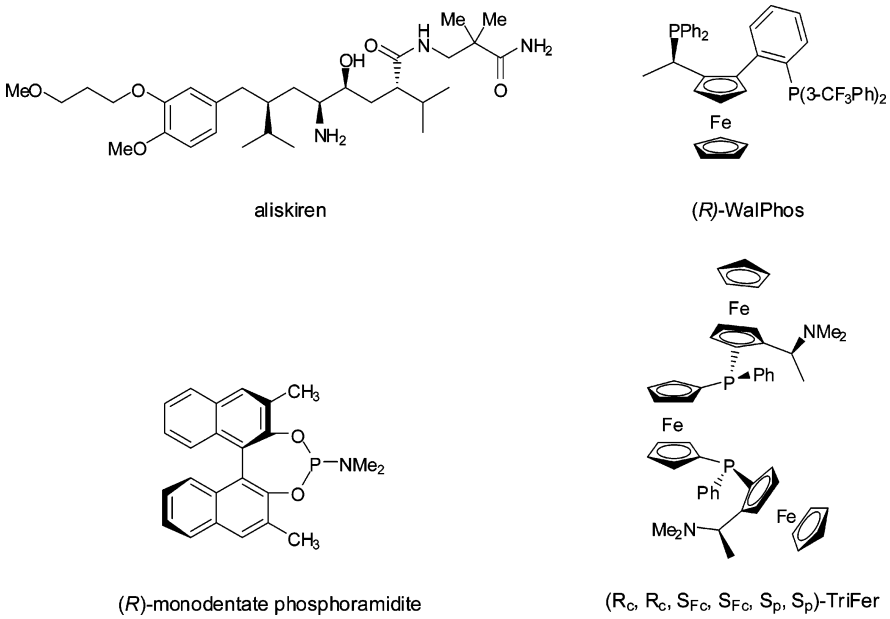

FIGURE 5. Structures of aliskiren and other ligands effective in asymmetric hydrogenation of **26**.

TABLE 2. Asymmetric Hydrogenation of Substrates 24−26 with [(Ligand)Rh(COD)]BF_4[a]

entry	ligand	substrate	mmol substrate	S/C	reaction time	conv %	ee (%) (config)
1	(*S*,*S*)-Ph-5-Fc (**8**)	**24**	1	1000	1 h	100	85 (*R*)
2	(*S*,*S*)-Ph-5-Fc (**8**)	**25**	1.5	1500	40 min	100	96.5 (*S*)
3	(*S*,*S*)-Ph-5-Fc (**8**)	**26**	1	1000	1 h	100	84.6 (*S*)
4	(*R*,*R*)-Ph-BPE (**1**)	**24**	2	1000	18 h	65	25 (*S*)
5	(*R*,*R*)-Ph-BPE (**1**)	**25**	1.5	1000	18 h	50	20 (*R*)
6	(*R*,*R*)-Ph-BPE (**1**)	**26**	0.4	250	16 h	100	25
7	(*S*,*S*)-Ph-Quinox (**5**)	**24**	2	1000	18 h	10	0
8	(*S*,*S*)-Ph-Quinox (**5**)	**25**	1.5	1000	18 h	5	11 (*R*)
9	(*R*,*R*)-Me-5-Fc	**24**	2	1000	18 h	100	52 (*R*)
10	(*R*,*R*)-Me-5-Fc	**25**	1.5	1000	18 h	100	46 (*S*)
11	(*S*,*S*)-Me-5-Fc	**26**	0.4	250	16 h	100	61
12	(*R*,*R*)-Et-5-Fc	**24**	2	1000	18 h	100	45 (*R*)
13	(*R*,*R*)-Et-5-Fc	**25**	1.5	1000	18 h	100	65 (*S*)
14	(*S*,*S*)-Et-5-Fc	**26**	0.4	250	16 h	100	57
15	(*R*,*R*)-*i*Pr-5-Fc	**24**	2	1000	18 h	100	69 (*S*)
16	(*R*,*R*)-*i*Pr-5-Fc	**25**	1.5	1000	18 h	65	65 (*R*)
17	(*S*,*S*)-*i*Pr-5-Fc	**26**	0.4	250	16 h	100	69
18	(*S*,*S*)-Me-DuPhos	**26**	0.4	250	16 h	34	0

[a] Reaction conditions: MeOH, 10 bar H_2, 25 °C.

conversion being achieved in 1 h at 25 °C and a catalyst loading of 0.1 mol %, but higher enantiomeric excesses have been reported with Rh-Walphos,[27] Rh-phosphoramidite,[28] and Rh-TriFer[29] catalysts using the free acid.

Conclusions

Four chiral diphosphine ligands comprising 2,5-diphenylphospholane groups connected by the sp^2 carbon linkers—2,3-quinoxaline, (*S*,*S*)-Ph-Quinox (**5**); 2,3-pyrazine, (*S*,*S*)-Ph-Pyrazine (**6**); maleic anhydride, (*S*,*S*)-Ph-MalPhos (7); and 1,1′-ferrocene, (*S*,*S*)-Ph-5-Fc (**8**)—were synthesized, and their cationic [rhodium(I)(COD)] complexes were tested in asymmetric olefin hydrogenation. The syntheses of the 2,3-quinoxaline, 2,3-pyrazine, and maleic anhydride linked ligands were achieved using the established nucleophilic 2,5-diphenylphospholane synthon[5,6,9] by displacement of chloride leaving groups from the linker. Synthesis of the 1,1′-ferrocenyl linked ligand required synthesis of an electrophilic 2,5-diphenylphospholane unit suitable for coupling with 1,1′-dilithioferrocene. Cationic rhodium complexes of these ligands exhibited contrasting activity and selectivity in asymmetric hydrogenation. Thus, [((*S*,*S*)-Ph-Quinox)Rh(COD)]BF_4 showed high activity and selectivity in asymmetric hydrogenation of standard itaconate and enamide substrates and is an excellent general asymmetric olefin hydrogenation catalyst comparable to (*R*,*R*)-Ph-BPE-Rh. The corresponding pyrazine and maleic anhydride catalysts were less active and selective. [((*S*,*S*)-Ph-5-Fc)Rh(COD)]BF_4 showed high activity but low selectivity against standard enamide and itaconate substrates, but high activity and selectivity against 2-C-

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substituted cinnamate salts, whereas rhodium complexes of (*S*,*S*)-Ph-Quinox and (*R*,*R*)-Ph-BPE showed low activity and selectivity against 2-C-substituted cinnamate salts. Thus, these ligands, especially (*S*,*S*)-Ph-Quinox and (*S*,*S*)-Ph-5-Fc, represent valuable additions to the available ligands for asymmetric hydrogenation. Yet again, this emphasizes the need for catalyst diversity when screening substrates for asymmetric hydrogenation.[2]

Experimental Section

Preparation of (*S*,*S*)-2,3-Bis(2,5-diphenylphospholan-1-yl)-quinoxaline (5). (*S*,*S*)-2,5-*trans*-Diphenylphospholane borane adduct ((*S*,*S*)-**4**)[5] (381 mg, 1.50 mmol) was dissolved in dry THF (3 mL) under nitrogen. The solution was cooled to −20 °C. A solution of *n*-BuLi (2.5 M in hexanes, 0.6 mL, 1.50 mmol) was added dropwise, and the mixture was stirred for 30 min (a yellow solution formed). 2,3-Dichloroquinoxaline (136 mg, 0.68 mmol) was added in one portion, and the residues were washed in with dry THF (1 mL) (the quinoxaline was only sparingly soluble in THF). The mixture was allowed to warm to room temperature (red/orange solution was observed). The reaction mixture was stirred overnight and then quenched with 1 M aqueous HCl (5 mL) (effervescence was observed) and extracted with ethyl acetate (10 mL). The organic solution was washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was chromatographed on silica and eluted with dichloromethane/heptane (2:3) to give (*S*,*S*)-Ph-Quinox (**5**) as a yellow solid (200 mg, 0.33 mmol, 48%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11−8.06 (m, 2H), 7.77−7.73 (m, 2H), 7.36−7.21 (m, 10H), 6.37 (t, J = 8 Hz, 2H), 6.29 (d, J = 8 Hz, 4H), 6.07 (t, J = 8 Hz, 4H), 4.53−4.46 (m, 2H), 3.83−3.73 (m, 2H), 2.58−2.45 (m, 2H), 2.09−1.99 (m, 4H), 1.87−1.75 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.2 (br d), 144.2 (t, J = 10 Hz), 141.2, 139.8, 129.4, 129.2, 129.1 (t, J = 5 Hz), 128.1, 127.4, 126.9, 125.7, 125.4, 49.6 (t, J = 10 Hz), 43.3, 37.9, 33.7. ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ 9.1. Anal. Calcd for $C_{40}H_{36}N_2P_2$: C, 79.19; H, 5.98; N, 4.62. Found: C, 79.20; H, 5.85; N, 4.73.

Preparation of 2,3-Bis[(*S*,*S*)-2,5-diphenylphospholan-1-yl]-quinoxaline-(1,5-cyclooctadiene) Rhodium(I) Tetrafluoroborate. 2,3-Bis-[(*S*,*S*)-2,5-diphenylphospholan-1-yl]-quinoxaline (**5**) (104 mg, 0.171 mmol) and $[Rh(COD)_2]BF_4$ (70 mg, 0.171 mg) were charged to a 25-mL Schlenk flask. The flask was evacuated and filled with nitrogen (×5). Degassed dichloromethane (2 mL) was added (a deep red solution formed), and the mixture was stirred for 3 h. The solvent was evaporated, and the residue was triturated with degassed ether (3 mL). The solid was filtered under nitrogen, washed with degassed ether (2 × 2 mL), and dried to give the title compound as an orange solid (119 mg, 0.13 mmol, 77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (dd, J = 6, 4 Hz, 2H), 8.15 (dd, J = 7, 4 Hz, 2H), 7.30−7.23 (m, 6H), 7.02−6.93 (m, 6H), 6.83−6.75 (m, 8H), 5.75−5.69 (m, 2H), 4.77−4.67 (m, 2H), 4.33−4.26 (m, 2H), 3.98−3.90 (m, 2H), 3.09−2.97 (m, 2H), 2.88−2.75 (m, 2H), 2.61−2.47 (m, 4H), 2.27−2.18 (m, 2H), 1.93−1.81 (m, 2H), 1.76−1.65 (m, 2H), 1.35−1.25 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 156.4 (t, J = 49 Hz), 142.6, 138.6, 135.3, 134.1, 130.4, 129.3, 128.8, 128.3, 127.8 (d, J = 11 Hz), 105.1 (m), 98.9 (m), 53.0 (t, J = 8 Hz), 49.8 (t, J = 10 Hz), 33.8, 31.9, 31.8, 28.2. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 58.6 (d, J = 151 Hz).

Preparation of (*R*,*R*)-2,3-Bis(2,5-diphenylphospholan-1-yl)-pyrazine (6). (*R*,*R*)-2,5-*trans*-Diphenylphospholane borane adduct ((*R*,*R*)-**4**) (518 mg, 2.04 mmol) was dissolved in dry THF (3 mL) under nitrogen. The solution was cooled to −20 °C. A solution of *n*-BuLi (2.5 M in hexanes, 0.82 mL, 2.04 mmol) was added dropwise, and the mixture was stirred for 30 min (a yellow solution formed). A solution of 2,3-dichloropyrazine (137 mg, 0.92 mmol) in THF (2 mL) was added, and the solution was allowed to warm to room temperature (red/brown color was observed instantly when the pyrazine was added). After 5 h, TMEDA (0.45 mL, 3.0 mmol, 1.5 equiv) was added, and the mixture was stirred overnight. The reaction was quenched with 1 M aqueous HCl (5 mL) and extracted with ethyl acetate (10 mL). The organic solution was washed with half-saturated brine (10 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was chromatographed on silica and eluted with ethyl acetate/heptane (1:8) to give the title compound **6** as a yellow solid (105 mg, 0.19 mmol, 21%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 2H), 7.35−7.21 (m, 10H), 6.48 (t, J = 7 Hz, 2H), 6.40 (d, J = 8 Hz, 4H), 6.24 (t, J = 8 Hz, 4H), 4.27−4.20 (m, 2H), 3.80−3.69 (m, 2H), 2.54−2.43 (m, 2H), 2.07−1.99 (m, 4H), 1.80−1.66 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$,): δ 163.9 (br d), 144.6 (t, J = 10 Hz), 142.4, 139.9, 129.4 (t, J = 5 Hz), 128.5, 127.5 (m), 126.1, 125.9, 50.0 (t, J = 10 Hz), 43.8, 38.9, 33.5. ^{31}P NMR (162 MHz, $CDCl_3$): δ 7.2. HRMS (ESI, M + H)$^+$: (*m*/*z*) calcd for $C_{36}H_{34}N_2P_2$: 557.2275. Found: 557.228. Further elution with ethyl acetate/heptane (1:5) gave the monosubstituted phospholane product, 2-chloro-3-(2,5-diphenylphospholan-1-yl)-pyrazine (**9**) (100 mg, 0.28 mmol, 31%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (d, J = 2 Hz, 1H), 8.12 (d, J = 2 Hz, 1H), 7.40−7.37 (m, 2 H), 7.31 (t, J = 7 Hz, 2H), 7.22−7.17 (m, 1H), 7.06−7.03 (m, 3H), 6.82−6.78 (m, 2H), 4.87−4.80 (m, 1H), 3.96 (ddd, J = 22, 12, 6 Hz, 1H), 2.76−2.64 (m, 1H), 2.39−2.20 (m, 2H), 2.11−2.00 (m, 1H). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 14.2.

Preparation of 2,3-Bis[(*R*,*R*)-2,5-diphenylphospholan-1-yl]-pyrazine-(1,5-cyclooctadiene) Rhodium(I) Tetrafluoroborate. 2,3-Bis[(*R*,*R*)-2,5-diphenylphospholan-1-yl]-pyrazine (**6**) (50 mg, 0.09 mmol) and $[Rh(COD)_2]BF_4$ (36 mg, 0.09 mmol) were charged to a Schlenk flask. The flask was evacuated and filled with nitrogen (×5). Degassed dichloromethane (1 mL) was added (a deep red solution formed), and the mixture was stirred for 3 h. The solvent was evaporated, and the residue was washed with degassed diethyl ether (4 × 2 mL) and dried to give the title compound as an orange solid (76 mg, 0.088 mmol, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.10 (br d, 2H), 7.26−7.12 (m, 12H), 6.83 (d, J = 8 Hz, 4H), 6.76−6.73 (m, 4H), 5.67−5.60 (m, 2H), 4.56−4.46 (m, 2H), 4.26−4.19 (m, 2H), 3.85−3.78 (m, 2H), 2.97−2.84 (m, 2H), 2.79−2.65 (m, 2H), 2.56−2.41 (m, 4H), 2.24−2.14 (m, 2H), 1.89−1.78 (m, 2H), 1.73−1.62 (m, 2H), 1.30−1.20 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.3 (t, J = 49 Hz), 147.5, 138.5, 135.2, 129.3, 129.1, 128.7, 128.1, 128.0, 127.7, 104.9 (m), 98.5 (m), 52.6 (t, J = 8 Hz), 49.2 (t, J = 11 Hz), 33.7, 31.8, 31.7, 28.1. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 60.2 (d, J = 151 Hz).

Preparation of 3,4-Bis[(*S*,*S*)-2,5-diphenylphospholan-1-yl]-furan-2,5-dione [(*S*,*S*)-Ph-MalPhos] (7). (*S*,*S*)-1-Hydroxy-1-oxo-2,5-*trans*-diphenylphospholane (**3**) (600 mg, 2.20 mmol) was suspended in toluene (6 mL). The mixture was degassed by evacuation and filled with nitrogen (×5) and then heated in an oil bath at 110 °C (external temperature). Phenylsilane (0.54 mL, 4.41 mmol) was added in one portion, and the mixture was heated for 2 h (during this time vigorous effervescence was observed and a clear solution formed). The solution was cooled to room temperature, and the solvent was evaporated under reduced pressure. The crude phosphine was further dried under high vacuum (2.9 mbar, 60 °C). The residue was cooled to room temperature and dissolved in THF (3 mL) under nitrogen. Triethylamine (0.31 mL, 2.20 mmol) was added, followed by a solution of 2,3-dichloromaleic anhydride (167 mg, 1.00 mmol) in THF (2 mL). The mixture was heated in an oil bath at 60 °C (external temperature) and stirred for 18 h (dark purple solution formed). The solution was cooled to room temperature, and the solvent was evaporated under reduced pressure. The residue was chromatographed on silica and eluted with dichloromethane/heptane (2:3) to give (*S*,*S*)-Ph-MalPhos (**7**) as a deep red oil that solidified on standing (180 mg, 0.31 mmol, 31%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51−7.34 (m, 10H), 6.90 (d, J = 8 Hz, 4H), 6.80 (t, J = 7 Hz, 2H), 6.56 (t, J = 8 Hz, 4H), 4.60−4.53 (m, 2H), 4.05−3.93 (m, 2H), 2.73−2.61 (m, 2H), 2.58−2.45 (m, 2H), 2.44−2.35 (m, 2H), 1.97−1.85 (m, 2H). ^{13}C{^{1}H} NMR

(100 MHz , $CDCl_3$): δ 161.7, 156.2 (m), 141.1 (t, J = 11 Hz), 136.6, 127.1, 127.0, 126.9, 126.8, 125.0, 124.9, 124.7, 48.2 (d, J = 7 Hz), 41.1 (d, J = 5 Hz), 38.0, 31.6. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 3.5. HRMS (ESI, $[M + Na]^+$): (m/z) calcd for $C_{36}H_{32}O_3P_2$: 597.172. Found: 597.169.

Preparation of 3,4-Bis[(*S*,*S*)-2,5-diphenylphospholan-1-yl]-furan-2,5-dione-(1,5-cyclooctadiene) Rhodium(I) Tetrafluoroborate. (*S*,*S*)-Ph-MalPhos (**7**) (102 mg, 0.178 mmol) and $[Rh(COD)_2]BF_4$ (72 mg, 0.178 mg) were charged to a 25-mL Schlenk flask. The flask was evacuated and filled with nitrogen (×5). Degassed dichloromethane (2 mL) was added (a dark brown solution formed), and the mixture was stirred overnight. The solvent was evaporated, and the residue was triturated with degassed diethyl ether (3 mL). The solid was filtered under nitrogen, washed with degassed ether (2 × 2 mL), and dried to give the title compound as a brown solid (133 mg, 0.15 mmol, 86%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.41−7.36 (m, 4H), 7.30−7.26 (m, 6H), 7.22−7.18 (m, 6H), 7.11−7.07 (m, 4H), 5.68−5.62 (m, 2H), 4.51−4.36 (m, 4H), 4.00 (dd, J = 13, 6 Hz, 2H), 3.08−2.94 (m, 2H), 2.66−2.43 (m, 6H), 2.05−1.96 (m, 2H), 1.82−1.71 (m, 2H), 1.31−1.13 (m, 4H). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 62.8 (d, J = 154 Hz).

Preparation of (*S*,*S*)-2,5-Diphenyl-1-oxo-1-chlorophospholane (11).[9] (*S*,*S*)-1-Hydroxy-1-oxo-2,5-*trans*-diphenylphospholane (**3**) (5.0 g, 18.4 mmol) was placed in a flask. This was purged with nitrogen, and then anhydrous dichloromethane (50 mL) was added. The suspension was cooled to 0−5 °C, and then oxalyl chloride (3.2 mL, 36.7 mmol) was added over 20 min, the suspension was stirred at 0−5 °C for 1 h, and then allowed to warm to room temperature and stirred for 22 h. Anhydrous toluene (20 mL) was added, and the solvent was evaporated. The residue was evaporated with toluene (2 × 20 mL) to give the title compound **11** as a white solid (5.38 g, quant). Mp 133−136 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.42−7.30 (m, 10H), 3.85−3.78 (m, 1H), 3.75−3.64 (m, 1H), 2.78−2.61 (m, 1H), 2.59−2.42 (m, 1H), 2.37−2.19 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 135.1 (d, J_{C-P} = 5.9 Hz), 134.2 (d, J_{C-P} = 6.4 Hz), 129.3 (d, J_{C-P} = 2.2 Hz), 129.2, 129.2 (d, J_{C-P} = 3.5 Hz), 128.3 (d, J_{C-P} = 4.6 Hz), 128.1 (d, J_{C-P} = 4.2 Hz), 128.0 (d, J_{C-P} = 3.9 Hz), 52.5 (d, J_{C-P} = 53.7 Hz), 51.7 (d, J_{C-P} = 68.1 Hz), 30.9 (d, J_{C-P} = 14.1 Hz), 25.7 (d, J_{C-P} = 14.8 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 80.9. Anal. Calcd for $C_{16}H_{16}ClPO$: C, 66.10; H, 5.55; Cl, 12.19. Found: C, 66.21; H, 5.53; Cl, 11.93.

Preparation of (*S*,*S*)-2,5-Diphenyl-1-oxophospholane (12).[9] (*S*,*S*)-2,5-Diphenyl-1-oxo-1-chlorophospholane (**11**) (4.80 g, 16.5 mmol) was placed in a dry flask. This was purged with nitrogen, and then dichloromethane (38 mL) was added. The solution was cooled to −70 °C, and then diisobutylaluminum hydride (1.0 M in dichloromethane, 17.3 mL) was added over 40 min. The solution was stirred at −70 °C for 1 h, and then quenched with methanol (3.84 mL) over 15 min. The solution was allowed to warm to room temperature, and then quenched with 1 M citric acid (50 mL). The layers were separated, and then the aqueous layer was extracted with dichloromethane (2 × 20 mL). The combined organic layers were washed with brine (50 mL), and then the brine was extracted with dichloromethane (2 × 10 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was evaporated to give a white solid (4.34 g). The solid was dissolved in dichloromethane (15 mL) and precipitated by addition of heptane (60 mL). After being dried, the title compound **12** was obtained as a white solid (3.07 g, 74%). Mp 141−143 °C. $[\alpha]^{25}_D$ −61.4° (*c* 1.02, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.41−7.27 (m, 10H), 7.18 (dq, $^1J_{H-P}$ = 470.0, J_{H-H} = 2.8 Hz, 1H), 3.63−3.52 (m, 1H), 3.32−3.25 (m, 1H), 2.70−2.49 (m, 2H), 2.44−2.32 (m, 1H), 2.07−1.95 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 136.8 (d, J_{C-P} = 2.8 Hz), 135.6 (d, J_{C-P} = 5.7 Hz), 129.6, 129.5, 129.2, 127.9 (d, J_{C-P} = 5.6 Hz), 127.7 (d, J_{C-P} = 2.1 Hz), 127.6 (d, J_{C-P} = 2.1 Hz), 48.9 (d, J_{C-P} = 60.0 Hz), 45.9 (d, J_{C-P} = 59.4 Hz), 33.4 (d, J_{C-P} = 7.2 Hz), 33.4 (d, J_{C-P} = 10.9 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ +55.2. HRMS (ESI, $[M + Na]^+$): (m/z) calcd for $C_{16}H_{17}PO$: 279.091. Found: 279.087.

Preparation of (2*S*,5*S*)-1-Chloro-2,5-diphenylphospholane (13).[16] (2*S*,5*S*)-Diphenylphospholane-1-oxide (**12**) (1.83 g, 1.95 mmol) was suspended in 40 mL of toluene, and the solution was cooled to −40 °C. To this suspension was added 3.92 g (28.6 mmol) of PCl_3 dissolved in 4 mL of toluene within 1 min. The solution was warmed to room temperature and stirred overnight, resulting in formation of a white sticky solid and colorless solution. The solution was transferred into another vessel, and the solvent was removed under reduced pressure, leaving an oily residue. Toluene was added (30 mL), and the solvent was removed again under reduced pressure, leaving 1.918 g of product **13** as a colorless oil. Yield 97.8%. ^1H NMR (300 MHz, 23 °C C_6D_6): δ 6.97−715 (m, 10H), 3.75 (td, $^3J_{H-H}$ = 8.7 Hz, $^2J_{H-P}$ = 2.1 Hz, 1H), 3.11 (ddd, $^2J_{H-P}$ = 33.6 Hz, $^3J_{H-H}$ = 12.6 Hz, $^3J_{H-H}$ = 6.0 Hz, 1H), 2.24−2.49 (m, 2H), 1.97−2.08 (m, 1H), 1.50−1.65 (m, 1H). $^{13}C\{^1H\}$ NMR (75 MHz, 23 °C C_6D_6): δ 141.92 (d, $^2J_{C-P}$ = 19.8 Hz, quat), 137.09 (quat), 129.05, 128.54, 128.51 (d, $^3J_{C-P}$ = 3.8 Hz) , 128.01 (d, $^3J_{C-P}$ = 8.4 Hz), 126.82, 126.79, 58.16 (d, $^2J_{C-P}$ = 32.8 Hz), 53.64 (d, $^2J_{C-P}$ = 32.8 Hz), 34.68 (d, $^3J_{C-P}$ = 2.3 Hz), 31.91 (d, $^3J_{C-P}$ = 2.3 Hz). $^{31}P\{^1H\}$ NMR (121 MHz, 23 °C, C_6D_6): δ 137.687/137.656 in 3:1 ratio ($^{35}Cl/^{37}Cl$ isotopic shift).

Preparation of Ferrocene Dilithium TMEDA Complex. Ferrocene (5 g, 26.9 mmol) was suspended in 60 mL of hexane. TMEDA (4.5 mL) was added followed by addition (within 1 min) of 42 mL (1.6 M) of *n*-BuLi in hexane. The reaction was not exothermic. The reaction was stirred overnight. Precipitated product (orange powder) was filtered off, washed with hexane (2 × 30 mL), and dried under reduced pressure to give 6.84 g of product. Yield 81%.

Preparation of 1,1′-Bis[(2*S*,5*S*)-diphenylphospholane-1-yl]-ferrocene [(*S*,*S*)-Ph-5-Fc] (8). To a 40-mL chilled (−40 °C) solution of (2*S*,5*S*)-1-chloro-2,5-diphenylphospholane (0.900 g, 3.28 mmol) in toluene was added 0.5145 g (1.64 mmol) of ferrocene dilithium TMEDA complex as a solid. The reaction mixture was stirred at room temperature for 24 h. Methylene chloride (10 mL) was added to the mixture to dissolve some of the product that crystallized. The $^{31}P\{^1H\}$ NMR of this reaction mixture showed formation of the desired product in about 90% together with about 10% of monophosphine, (2*S*,5*S*)-diphenylphospholan-1-yl]ferrocene. The solvent was removed under reduced pressure to give a yellow-orange solid. Toluene was added (12 mL), and the suspension was stirred for 1 h. Yellow solid was collected on the frit, washed with 10 mL of hexane, and dried under reduced pressure to give 0.76 g of clean product **8**. Yield 70%. X-ray quality crystals were obtained from toluene at room temperature. ^1H NMR (300 MHz, 23 °C, C_6D_6): δ 7.47 (dm, $^3J_{H-H}$ = 8.4 Hz, 4H, *ortho*^{1}-H), 7.24 (tm, $^3J_{H-H}$ = 7.8 Hz, 4H, *meta*^{1}-H), 7.10 (tm, $^3J_{H-H}$ = 7.7 Hz, 2H, *para*^{1}-H), 6.92−6.99 (m, 4H), 6.84−6.92 (m, 6H), 4.08 (m, 2H, Cp), 4.06 (m, 2H, Cp), 3.75 (m, 2H, Cp), 3.72 (m, 2H, C*H*), 3.47 (m, 2H, Cp), 3.30 (m, 2H, C*H*), 2.47 (m, 2H, CH_2), 1.95−2.18 (m, 4H, CH_2), 1.64 (m, 2H, CH_2). $^{13}C\{^1H\}$ NMR (75 MHz, 23 °C, C_6D_6): δ 146.24 (d, $^2J_{C-P}$ = 18.9 Hz, quat), 139.16 (quat), 128.95 (*meta*-C), 128.46 (d, $^3J_{C-P}$ = 10.4 Hz, *ortho*-C), 128.09 (d, $^3J_{C-P}$ = 3.6 Hz, *ortho*-C), 127.96, 126.27 (*para*-C), 125.69 (*para*-C), 77.33 (d, J_{C-P} = 31.1 Hz, Cp), 76.02 (d, $^1J_{C-P}$ = 27.5 Hz, Cp, quat), 72.67 (d, J_{C-P} = 7.9 Hz, Cp), 71.63 (s, Cp), 69.86 (d, J_{C-P} = 4.2 Hz, Cp), 50.07 (d, $^2J_{C-P}$ = 15.9 Hz, *C*H), 48.85 (d, $^2J_{C-P}$ = 14.6 Hz, *C*H), 39.20 (s, *C*H_2), 33.73 (d, $^3J_{C-P}$ = 3.6 Hz, *C*H_2). $^{31}P\{^1H\}$ NMR (121 MHz, 23 °C, C_6D_6): δ 12.19. HSQC (23 °C, C_6D_6): δ 128.95/7.24, 128.46/7.47, 128.09/(6.92−6.99), 127.96/(6.84−6.92), 126.27/7.10, 125.69/(6.92−6.99), 77.33/3.47, 72.67/3.75, 71.63/4.08, 69.86/4.06, 50.07/3.30, 48.85/3.72, 39.20/(2.47, 1.64), 33.73/(1.95−2.18). HRMS (ESI, $[M + H]^+$): (m/z) calcd for $C_{42}H_{41}FeP_2$: 663.203. Found: 663.200. Anal. Calcd for $C_{42}H_{40}FeP_2$: C, 76.14; H, 6.09. Found: C, 76.02; H, 5.88.

Preparation of 1,1′-Bis[(2*S*,5*S*)-diphenylphospholane-1-yl]-ferrocene(1,5-cyclooctadiene) Rhodium(I) Tetrafluoroborate.

1,1′-Bis-[(2*S*,5*S*)-2,5-diphenylphospholane-1-yl]ferrocene (**8**) (0.354 g, 0.53 mmol) and $Rh(COD)_2BF_4$ (0.2171 g, 0.53) were dissolved in 10 mL of CH_2Cl_2, giving rise to a red-orange solution. After being stirred for 30 min, the $^{31}P\{^1H\}$ NMR showed clean formation of the desired complex. The solvent volume was reduced to about 1 mL, and 0.5 mL of ether was added, causing formation of orange-red crystals. After 30 min more ether was added (1 mL), and solution was left standing for 2 h. The solvent was decanted, and the remaining crystals were washed with ether (2 mL) and then dried under reduced pressure to give 0.446 g of product as red-orange crystals. X-ray quality crystals were obtained from methylene chloride/ether mixture at room temperature. Crystals contained one molecule of methylene chloride. Yield 79.8%. ^1H NMR (300 MHz, 23 °C, CD_2Cl_2): δ 7.81 (m, 4H, *ortho*^{1}-H), 7.40 (m, 6H, *meta*^{1}/*para*^{1}), 7.13 (m, 6H, *meta*^{2}/*para*^{2}), 6.68 (d, $^3J_{H-H} = 7.5$ Hz, 4H, *ortho*^{2}-H), 5.59 (br t, $^3J_{H-H} = 6.9$ Hz, 2H, COD), 4.50 (br, 2H COD), 4.42 (m, 6H, Cp), 4.14 (qm, $J_{H-P} = 9.6$ Hz, 2H, PC*H*), 3.60 (m, 2H, Cp), 3.36 (dd, $J_{H-P} = 11.7$ Hz, $^3J_{H-H} = 6.3$ Hz, 2H, PC*H*), 2.61−2.80 (m, 2H, PCHCH_2), 2.24−2.46 (m, 4H, PCHCH_2), 1.70−2.50 (m, 10H, PCHCH_2/COD). $^{13}C\{^1H\}$ NMR (75 MHz, 23 °C, CD_2Cl_2): δ 140.21 (t, $J_{C-P} = 2.4$ Hz, quat), 136.29 (quat), 129.17 (*meta*^{1}), 128.89 (t, $J_{C-P} = 1.8$ Hz, *ortho*^{2}), 128.76 (t, $J_{C-P} = 3.7$ Hz, *ortho*^{1}), 128.38 (*meta*^{2}), 128.13 (*para*^{1}), 127.28 (*para*^{2}), 98.41 (dt, $J_{C-Rh} = 9.3$ Hz, $J_{C-P} = 2.4$ Hz, COD), 89.57 (q, $J = 7.2$ Hz, COD), 76.54 (dt, $J = 18.3$ Hz, $J = 7.9$ Hz, Cp), 75.38 (t, $J_{C-P} = 4.3$ Hz, Cp), 73.11 (Cp), 72.65 (t, $J_{C-P} = 1.8$ Hz, Cp), 70.92 (d, $^1J_{C-P} = 42.7$ Hz, Cp, quat), 49.72 (dt, $J = 20.7$ Hz, $J = 8.5$ Hz, P*C*H), 46.47 (dt, $J = 14.6$ Hz, $J = 10.3$ Hz, P*C*H), 35.35 (PCH*C*H_2), 33.23 (PCH*C*H_2), 33.13 (COD), 28.12 (COD). HSQC (23 °C, CD_2Cl_2): δ 129.17/7.40, 128.89/6.68, 128.76/7.81, 128.38/7.13, 128.13/7.40, 127.28/7.13, 98.41/5.59, 89.57/4.50, 76.54/3.60, 75.38/4.42, 73.11/4.42, 72.65/4.42, 49.72/4.14, 46.47/3.30, 35.35/(2.70, 2.31), 33.23/(2.38, 2.18), 33.13/1.99, 28.12/1.85. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, 23 °C, 121 MHz): δ 36.79 (d, $^1J_{P-Rh} = 146.5$ Hz). ^{19}F NMR (282 MHz, 23 °C, CD_2Cl_2): δ −153.43, HRMS (ESI, M^+): (*m*/*z*) calcd for $C_{50}H_{52}FeP_2Rh$: 873.1949. Found: 873.194. Anal. Calcd for $C_{51}H_{54}FeCl_2P_2RhBF_4$: C, 58.60; H, 5.21. Found: C, 58.76; H, 5.17.

Hydrogenation Procedure for Dimethyl Itaconate (14) Using [((*S*,*S*)-Ph-MalPhos)Rh(COD)]BF_4. An Argonaut Endeavor catalyst screening system was used. The glass liner of a vessel was charged with dimethyl itaconate **14** (316 mg, 2.0 mmol) and 3,4-bis-[(*S*,*S*)-2,5-diphenylphospholane-1-yl]-furan-2,5-dione-(1,5-cyclooctadiene) rhodium(I) tetrafluoroborate (1.7 mg, 0.002 mmol, S/C 1000). The vessel was charged to 10 bar nitrogen and vented (×5). Degassed methanol (4 mL) was added. The vessel was charged to 10 bar nitrogen and vented (×2). Stirring was commenced at 1000 rpm, and the contents were heated to 25 °C. The vessel was charged to 10 bar hydrogen. Hydrogen uptake was complete after 16 h. The mixture was vented and evaporated to give (*S*)-2-methylsuccinic acid dimethyl ester **19**, conversion 100%, 96.6% ee (Chiraldex GTA, 30 m × 0.25 mm, injector/detector 180 °C, helium 14 psi, 90 °C for 6 min then ramp at 1 °C/min to 105 °C, retention times *S* 10.11 min, *R* 10.48 min).

Hydrogenation Procedure for Methyl α-Acetamidoacrylate (15). The hydrogenation procedure for dimethyl itaconate **14** was followed: method of analysis for methyl 2-acetylaminopropionate **20** (Chirasil Dex CB, 25 m × 0.25 mm, injector/detector 200 °C, helium 20 psi, 130 °C for 10 min then ramp at 15 °C/ min to 200 °C, retention times *S* 2.91 min, *R* 2.98 min).

Hydrogenation Procedure for Methyl α-Acetamidocinnamate (17). The hydrogenation procedure for dimethyl itaconate **14** was followed: method of analysis for methyl 2-acetylamino-3-phenylpropionate **22** (Chirasil Dex CB, 25 m × 0.25 mm, injector/detector 200 °C, helium 20 psi, 150 °C for 21 min then ramp at 15 °C/min to 200 °C, hold for 5 min, retention times *R* 17.65 min, *S* 17.92 min).

Hydrogenation Procedures for α-Acetamidoacrylic Acid (16) and α-Acetamidocinnamic Acid (18). The hydrogenation procedure for dimethyl itaconate **14** was followed: analysis for 2-acetylaminopropionic acid **21** and 2-acetylamino-3-phenylpropionic acid **23** as for methyl 2-acetylaminopropionate **20** and methyl 2-acetylamino-3-phenylpropionate **22**, but samples were derivatized to the methyl ester using TMS diazomethane before analysis.

Preparation of (*E*)-2-Methylcinnamic Acid *tert*-Butylammonium Salt (24). (*E*)-2-Methylcinnamic acid (10.0 g, 61.7 mmol) and THF (100 mL) were placed in a flask. *tert*-Butylamine (6.54 mL, 61.7 mmol) was added over 30 min. The white suspension was stirred for 30 min and then filtered, and the solid was washed with THF (3 × 20 mL) and then dried to give (*E*)-2-methylcinnamic acid *tert*-butylammonium salt **24** as a fine, white solid (14.1 g, 97%). ^1H NMR (400 MHz, DMSO): δ 8.3 (br s, 3H), 7.40−7.34 (m, 5H), 7.28−7.23 (m, 1H), 2.00 (d, $J = 1.2$ Hz, 3H), 1.25 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO): δ 171.8, 138.0, 136.3, 132.1, 129.4, 128.6, 127.2, 49.9, 28.7, 15.6.

Hydrogenation Procedure for (*E*)-2-Methylcinnamic Acid *tert*-Butylammonium Salt (24) Using [((*S*,*S*)-Ph-5-Fc)Rh(COD)]-BF_4. The reaction was carried out in an Argonaut Endeavor hydrogenation vessel. The glass liner was charged with (*E*)-2-methylcinnamic acid *tert*-butylammonium salt **24** (235 mg, 1.0 mmol). The vessel was charged to 10 bar nitrogen and vented (×5). Degassed methanol (3 mL) followed by a solution of 1,1′-bis-[(2*S*,5*S*)-diphenylphospholane-1-yl]ferrocene(1,5-cyclooctadiene) rhodium(I) tetrafluoroborate in degassed methanol (1 mL of a solution of 20 mg, 0.02 mmol in methanol, 20 mL) were added. The vessel was charged to 10 bar nitrogen and vented (×2). Stirring was commenced at 1000 rpm, and the vessel was heated to 25 °C. The vessel was charged to 10 bar H_2, and hydrogen uptake was monitored. After completion, the vessel was vented, and the solvent was evaporated to give (*R*)-2-methyl-3-phenylpropionic acid *tert*-butylammonium salt **27** as a pale orange solid. ^1H NMR (400 MHz, DMSO): δ 7.6 (br s, 3H), 7.24 (t, $J = 7.0$ Hz, 2H), 7.18−7.13 (m, 3H), 2.94 (dd, $J = 13.0$, 6.2 Hz, 1H), 2.43 (dd, $J = 13.0$, 7.4 Hz, 1H), 2.39−2.34 (m, 1H), 1.17 (s, 9H), 0.93 (d, $J = 7.6$ Hz, 3H). 96.5% ee (SFC, 2 × Chiralpak AD-H columns 10% methanol, 3000 psi CO_2, 35 °C, flow rate 3 mL/min, retention times *R* 7.1 min, *S* 7.71 min, substrate 11.8 min). The salt was shaken with 2 M hydrochloric acid (5 mL) and dichloromethane (5 mL). The organic layer was separated, and the aqueous layer was extracted with dichloromethane (5 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was evaporated. The product was distilled (kugelrohr, 0.5 mbar, oven temperature 150 °C) to give (*R*)-2-methyl-3-phenylpropionic acid **27** as a colorless liquid (100 mg, 63%). $[\alpha]^{25}_D$ −22.7° (*c* 1.02, $CHCl_3$). Lit.[30] $[\alpha]^{25}_D$ −23.1° (*c* 1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 10.0 (br s, 1H), 7.31−7.28 (m, 2H), 7.25−7.17 (m, 3H), 3.08 (dd, $J = 13.2$, 6.4 Hz, 1H), 2.81 (m, 1H), 2.67 (dd, $J = 12.8$, 8.0 Hz, 1H), 1.18 (d, $J = 6.4$ Hz, 1H). 85% ee (derivatized using TMS diazomethane, Chirasil Dex CB column, 25 m × 0.25 mm, injector/detector 200 °C, helium 20 psi, 100 °C for 21 min then ramp at 15 °C/min to 200 °C, hold for 5 min, retention times *R* 30.40 min, *S* 31.06 min, (*E*)-methyl-2-methylcinnamate, 34.79 min). ^1H NMR analysis of the (*S*)-methyl mandelate ester[30] confirmed assignment of the (*R*)-configuration.

Preparation of (*E*)-2-Phenylcinnamic Acid *tert*-Butylammonium Salt (25). (*E*)-2-Phenylcinnamic acid (10.0 g, 44.6 mmol) and THF (100 mL) were placed in a flask. *tert*-Butylamine (4.69 mL, 44.6 mmol) was added over 30 min. The white suspension was stirred for 1 h and then filtered, and the solid was washed with THF (4 × 20 mL) and then dried to give (*E*)-2-phenylcinnamic acid *tert*-butylammonium salt **25** as a fine, white solid (11.2 g, 84.4%). ^1H NMR (400 MHz, DMSO): δ 8.0 (br s, 3H), 7.37 (s, 1H), 7.23−7.14 (m, 3H), 7.07−7.02 (m, 5H), 6.89−6.87 (m, 2H), 1.16 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO): δ 170.3, 140.3, 132.7, 129.8, 129.7, 128.3, 128.1, 127.5, 126.5, 50.1, 28.5.

(30) Tyrrell, E.; Tsang, M. W. H.; Skinner, G. A.; Fawcett, J. *Tetrahedron* **1996**, *52*, 9841−9852.

Hydrogenation Procedure for (*E*)-2-Phenylcinnamic Acid *tert*-Butylammonium Salt (25) Using [((*S,S*)-Ph-5-Fc)Rh(COD)]BF_4. The reaction was carried out as for **24** using (*E*)-2-phenylcinnamic acid *tert*-butylammonium salt **25** (448 mg, 1.51 mmol) and [(2*S*,5*S*)-diphenylphospholane-1-yl]ferrocene(1,5-cyclooctadiene) rhodium-(I) tetrafluoroborate (4 mL of a solution of 8.3 mg, 0.0086 mmol in degassed methanol, 32 mL) to give (*S*)-2,3-diphenylpropionic acid *tert*-butylamine salt **28** as a pale orange solid. ^{1}H NMR (400 MHz, DMSO): δ 7.5 (br s, 3H), 7.11 (d, J = 7.2 Hz, 2H), 7.03−6.88 (m, 8H), 3.36 (t, J = 7.4 Hz, 1H), 3.10 (d, J = 13.6, 8.8 Hz, 1H), 2.61 (dd, J = 13.4, 7.0 Hz, 1H), 0.95 (s, 9H). 96.5% ee (SFC, 2 × Chiralpak AD-H columns 10% methanol, 3000 psi CO_2, 35 °C, flow rate 3 mL/min, retention times *R* 7.1 min, *S* 7.7 min, substrate 11.8 min). The salt was shaken with 2 M hydrochloric acid (5 mL) and dichloromethane (5 mL). The organic layer was separated, and the aqueous layer was extracted with dichloromethane (5 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was evaporated to give (*S*)-2,3-diphenylpropionic acid as an orange solid (300 mg, quant). $[\alpha]^{25}_D$ +98.6° (*c* 2.03, $CHCl_3$); $[\alpha]^{25}_D$ +100.6° (*c* 0.54, acetone). $[\alpha]^{25}_D$ +103.5° (*c* 1.00, methanol). Lit.[31] +140.8° (*c* 2.04, $CHCl_3$). Lit.[31] +133.8° (*c* 0.535, acetone). Lit.[32] (enantiomer) −93.2° (*c* 1, MeOH). ^{1}H NMR (400 MHz, DMSO): δ 7.5 (br s, 3H), 7.11 (d, J = 7.2 Hz, 2H), 7.03−6.88 (m, 8H), 3.36 (t, J = 7.4 Hz, 1H), 3.10 (d, J = 13.6, 8.8 Hz, 1H), 2.61 (dd, J = 13.4, 7.0 Hz, 1H), 0.95 (s, 9H). ^{1}H NMR analysis of the (*S*)-methyl mandelate ester[30] confirmed assignment of the (*R*)-configuration.

Preparation of (*E*)-2-Isopropyl-3-{2-[3-methoxy(propyloxy)]-4-methoxyphenyl}acrylic Acid *tert*-Butylamine Salt (26). (*E*)-2-Isopropyl-3-{2-[3-methoxy(propyloxy)]-4-methoxyphenyl}-acrylic acid[33] was dissolved in MTBE (70 mL). *tert*-Butylamine (2.4 mL, 22.4 mmol) was added, and the mixture was stirred for 3 h. The dense precipitate was diluted with MTBE (20 mL) and filtered. The filter cake was washed with MTBE (30 mL) and dried to give (*E*)-2-isopropyl-3-{2-[3-methoxy(propyloxy)]-4-methoxyphenyl}acrylic acid *tert*-butylamine salt **26** as a white solid (7.43 g, 89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (s, 3H), 6.85 (m, 3H), 4.11 (t, J = 6.5 Hz, 2H), 3.87 (s, 3H), 3.57 (t, J = 6 Hz, 2H), 3.34 (s, 3H), 3.10 (m, 1H), 1.39 (s, 9H), 1.29 (d, J = 6.5 Hz, 6H).

Hydrogenation Procedure for (*E*)-2-Isopropyl-3-{2-[3-methoxy(propyloxy)]-4-methoxyphenyl}acrylic Acid *tert*-Butylamine Salt (26) Using [((*S,S*)-Ph-5-Fc)Rh(COD)]BF_4. The reaction was carried out as for **24** using (*E*)-2-isopropyl-3-{2-[3-methoxy-(propyloxy)]-4-methoxyphenyl}acrylic acid *tert*-butylamine salt **26** (382 mg, 1.00 mmol), degassed methanol (3 mL), and [(2*S*,5*S*)-diphenylphospholane-1-yl]ferrocene(1,5-cyclooctadiene) rhodium-(I) tetrafluoroborate (1 mL of a solution of 20 mg, 0.02 mmol in methanol, 20 mL) to give (*S*)-2-isopropyl-3-{2-[3-methoxy(propyloxy)]-4-methoxyphenyl}propionic acid *tert*-butylamine salt **29** as a pale orange solid. ^{1}H NMR (400 MHz, DMSO): δ ppm 6.7 (br s, 3H), 6.63−6.61 (m, 2H), 6.51 (dd, J = 8.2, 1.8 Hz, 1H), 3.78 (t, J = 3.78 Hz, 2H), 3.54 (s, 3H), 3.30 (t, J = 6.4 Hz, 2H), 3.09 (s, 3H), 2.54 (dd, J = 13.4, 10.2 Hz, 1H), 2.41 (dd, J = 13.8, 4.6 Hz, 1H), 2.05−2.00 (m, 1H), 1.76 (q, J = 6.2 Hz, 2H), 1.65−1.56 (m, 1H), 0.96 (s, 9H), 0.77 (d, J = 7.0 Hz, 3H), 0.76 (d, J = 7.2 Hz, 3H). 84.6% ee (SFC, 2 × Chiralpak AD-H columns 10% methanol, 3000 psi CO_2, 35 °C, flow rate 3 mL/min, retention times *S* 4.6 min, *R* 5.0 min, substrate 10.9 min).[34] The salt was shaken with 2 M hydrochloric acid (5 mL) and dichloromethane (5 mL). The organic layer was separated, and the aqueous layer was extracted with dichloromethane (2 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was evaporated to give (*S*)-2-isopropyl-3-{2-[3-methoxy(propyloxy)]-4-methoxyphenyl}-propionic acid as an orange oil (302 mg, 98%). $[\alpha]^{25}_D$ −33.0° (*c* 1.01, CH_2Cl_2). Lit.[26] (enantiomer) $[\alpha]^{25}_D$ +42.5° (*c* 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$,): δ 6.76 (d, J = 8.2 Hz, 1H), 6.74 (s, 1H), 6.73 (dd, J = 7.6, 1.6 Hz, 1H), 3.82 (s, 3H), 3.57 (t, J = 6.2 Hz, 2H), 3.36 (s, 3H), 2.83−2.76 (m, 1H), 2.47−2.41 (m, 1H), 2.08 (q, J = 6.4 Hz, 2H), 1.98−1.90 (m, 1H), 1.04 (d, J = 7.2 Hz, 3H), 1.01 (d, J = 7.2 Hz, 3H).

General Hydrogenation Procedure Using Multiple Vessels Used for Comparative Examples in Table 2. A Baskerville 10-well multiple pressure vessel was used. The glass liner of a vessel was charged with substrate and catalyst. The vessel was charged to 10 bar nitrogen and vented (×5). Degassed methanol (4 mL) was added, and stirring was commenced. The vessel was charged to 10 bar nitrogen and vented (×3). The vessel was charged to 10 bar H_2 and stirred for 18 h. The vessel was vented, charged with nitrogen, and vented, and then the solvent was evaporated to give the crude hydrogenation product.

X-ray Analysis of (*S,S*)-Ph-5-Fc (8) and [((*S,S*)-Ph-5-Fc)Rh-(COD)]BF_4. Data for both structures were collected at 173 K on a Siemens SMART PLATFORM equipped with a CCD area detector and a graphite monochromator utilizing Mo Kα radiation (λ = 0.71073 Å). Cell parameters were refined using up to 8192 reflections. A hemisphere of data (1381 frames) was collected using the ω-scan method (0.3° frame width) for each structure. The first 50 frames were remeasured at the end of data collection to monitor instrument and crystal stability (maximum correction on I was <1 %). Absorption corrections by integration were applied on the basis of measured indexed crystal faces.

The structures were solved by the Direct Methods in *SHELXTL5* and refined using full-matrix least-squares. The non-hydrogen atoms were treated anisotropically, whereas the methyl hydrogen atoms were calculated in ideal positions and were riding on their respective carbon atoms. For (*S,S*)-Ph-5-Fc, a total of 469 parameters were refined in the final cycle of refinement to yield R1 and wR2 of 3.25 and 6.88%, respectively. In addition to the complex, a toluene molecule in general position was found and refined. Space group *C*2 was chiral, and the Flack *x* parameter was refined to a value of −0.002(11) to confirm the correct enantiomer. For [((*S,S*)-Ph-5-Fc)Rh(COD)]BF_4, a total of 571 parameters were refined in the final cycle of refinement to yield R1 and wR2 of 2.28 and 5.83%, respectively. The Flack *x* parameter was refined to a value of −0.001(9) to confirm the correct enantiomer. Refinement was done using F^2.

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Supporting Information Available: NMR spectra of ligands **5**−**8** and their [Rh(I)(COD)]BF_4 complexes and X-ray data for ligand (*S,S*)-Ph-5-Fc and [((*S,S*)-Ph-5-Fc)Rh(COD)]BF_4. This material is available free of charge via the Internet at http://pubs.acs.org.

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