Preparation and Use of a Polymer Supported BINAP Hydrogenation Catalyst

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Introduction

Asymmetric hydrogenation by chiral transition-metal species is one of the fundamental strategies for the synthesis of optically active organic molecules.[1] Of the many catalysts developed in this area, bis(diphenylphosphino)-1,1′-binaphthyl-Ru (BINAP-Ru) complexes have become one of the most extensively applied, both academically and in industry. Their ability to promote highly enantioselective transformations over a wide range of substrates with high substrate-to-catalyst ratios provides continuing interest in this area.[2] However, this catalytic system does have drawbacks; first, both BINAP itself and the ruthenium precatalyst are expensive materials, and second, the product must be purified after hydrogenation in order to remove the catalyst.[3] Clearly, it would be desirable to design a heterogeneous asymmetric catalyst that could be readily removed from the reaction mixture, thus easing purification and providing the possibility of reusing the catalyst. This approach has already found success in other areas such as asymmetric epoxidation[4] and dihydroxylation.[5] Although other diphosphines have previously been immobilized by attachment to a solid support, either their activity or enantioselectivity have been found wanting.[6]

We herein report our initial efforts to address these problems and thus develop a clean, reusable catalyst for asymmetric hydrogenation. Our proposal was to incorporate the BINAP framework onto an insoluble polymer and thus provide a heterogeneous catalyst that could be isolated from the reaction medium and reused if necessary. We chose to synthesize a suitably functionalized BINAP monomer derivative in solution and attach this compound to a commercially available polymer support. The issues that then need to be addressed are whether a non-C_2-symmetric ligand[6c−e] would still promote high enantioselectivities and whether the activity is still shown when bound to a polymer support.[7]

Results and Discussion

A BINAP containing an alkyl carboxylic acid functionality appeared to provide the greatest flexibility in that an ester or amide linkage would be attained by well-known peptide coupling reactions of the commercially available hydroxymethylated polystyrene or aminomethylated polystyrene. We also deemed the most suitable site of attachment of the polymer to be via the binaphthyl backbone so that the polymer is distal from the active catalytic site. We began our program by converting enantiomerically pure (*R*)-BINOL (**1**) to its dimethyl ether (Scheme 1).[8] Friedel−Crafts acylation of this substrate using 1 equiv of ethyl succinyl chloride provided acylated material **2** as the major component in 60% yield accompanied by small quantities of starting material and a bis-acylated product, which were readily separated by column chromatography. As predicted, ^{1}H NMR analysis indicated that acylation had occurred regioselectively in the 6-position of the binaphthalene skeleton and 6,6′ for the bis-acylated material.[9] Reduction of the ketone functionality was achieved by hydrogenolysis in the presence of methanesulfonic acid. Treatment with boron tribromide smoothly cleaved the methyl ethers while leaving the ethyl ester intact and furnished functionalized BINOL **3**. Compound **3** was then converted to its ditriflate, and at this point chiral HPLC indicated that no racemization had occurred during the synthesis.[10] The ditriflate was subsequently subjected to a nickel-catalyzed double phosphinylation reaction developed by Merck.[11] However, contrary to the ditriflate of BINOL itself, our system was sluggish to react and the nickel species became inactive after only two turnovers, leading to a poor 20% yield of diphosphinylated material. Hence, a stoichiometric amount of $NiCl_2$·dppe was employed and did indeed promote the phosphinylation albeit contaminated with a substantial amount of related phosphine oxide adducts. Therefore, the crude reaction mixture was treated with trichlorosilane to procure the requisite substituted BINAP **4** in a workable and reproducible 60% yield. Finally, saponification of the ethyl ester with lithium hydroxide furnished acid functionalized BINAP **5**, which was now ready to attach to a polymeric support. Aminomethylated polystyrene was chosen as the solid

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(9) ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.80 (6H, s), 7.13 (2H, d, J = 8 Hz), 7.23 (2H, dd, J = 9, 12 Hz), 7.33 (2H, t, J = 9 Hz), 7.48 (2H, d, J = 12 Hz), 7.87 (2H, d, J = 8 Hz), 8.00 (2H, d, J = 9 Hz). Acylation at any other position would produce a different coupling pattern in the aromatic region.

(10) Enantiomeric excess of the (*R*)-ditriflate was determined to be >99% by chiral HPLC on a Chiralcel OD column by comparison with a sample of (*S*)-ditriflate synthesized by an identical route.

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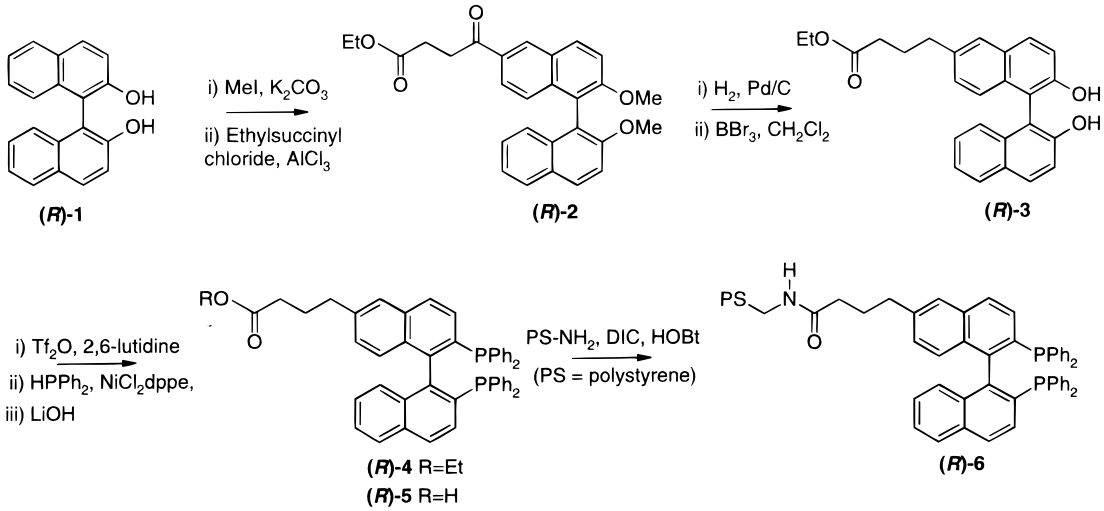
Table 1. Enantioselective Hydrogenation of Substrates (Figure 1) by Chiral Ruthenium Dibromide Complexes

entry	sub-strate	diphosphine[a]	*T*, °C	solvent	time (h)	yield (%)	ee[b] (%)
1	7	(*R*)-BINAP	40 (20 bar)	CH_2Cl_2	16	100	>99[c,12c]
2	7	4	70	THF/MeOH	18	99	99[c]
3	7	5	70	THF/MeOH	18	99	99[c]
4	7	6	70	THF/MeOH	18	99	97[c]
5	7	6[d]	70	THF/MeOH	24	99	91[c]
6	7	6[e]	70	THF/MeOH	36	82	90[c]
7	7	6[f]	70	THF/MeOH	24	99	97[c]
8	8	6	70	THF/MeOH	20	98	88[c]
9	8	(*S*)-BINAP	80 (4 bar)	MeOH	0.25	95	99[g,12c]
10	9	6	50	THF	18	95	56[g,h]
11	9	(*R*)-BINAP	50 (3 bar)	THF/EtOH	48	100	98[g,12c]
12	10	6	35	THF/MeOH	23	90	64[c,h]
13	10	(*S*)-BINAP	25 (20 bar)	THF/EtOH	48	70	75[g,12c]

[a] 2 mol % catalyst was used. All hydrogenations were carried out at 10 bar unless otherwise stated. [b] Enantiomeric excesses were determined by chiral GC on a Chiraldex G-TA (50 m × 0.32 mm) column. [c] Product was the *R* enantiomer. [d] The active resin-bound catalyst from the previous experiment was simply washed with THF and reused in this reaction. [e] Third use of catalyst. [f] 0.2 mol % catalyst was used. [g] Product was the *S* enantiomer. [h] The product was derivatized as the methyl ester before GC analysis.

Scheme 1



support, as the amide functionality should be robust under any hydrogenation conditions we were to employ. Coupling of the BINAP monomer **5** to 0.21 mmol/g of aminomethylated polystyrene was thus achieved using the standard peptide coupling reagents DIC and HOBt. Quantitative acylation was observed by mass balance, giving a loading of 0.18 mmol/g. This relatively low loading was envisaged to give the bulky ligand greater degrees of freedom and act more like a solution phase catalyst. Formation of the active hydrogenation catalyst was achieved by mixing the diphosphine, (COD)Ru(bis-methallyl), and HBr in acetone for 1 h.[12] Removal of the solvent in vacuo gave an active hydrogenation catalyst that we believe to be a ruthenium dibromide species. Preliminary results from these heterogeneous catalysts are very encouraging, as can be seen in the hydrogenation of both olefins and β-keto esters (Figure 1). The hydrogenation of methyl propionyl acetate highlights the

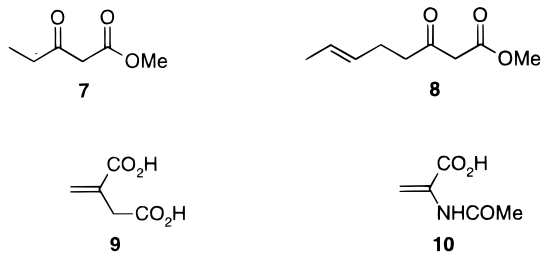


Figure 1.

capabilities of the novel polymer-bound BINAP catalyst (Table 1). First, the non-C_2-symmetric diphosphines **4** and **5** were tested as solution-phase catalysts (Table 1, entries 2 and 3). They showed similar activities to BINAP itself (Table 1, entry 1) giving ee's of 99%, indicating that the loss of C_2 symmetry is not detrimental to enantioselectivity although the break in symmetry is distal from the active catalytic site; therefore, one may consider such a ligand to be "pseudo-C_2-symmetric". The polymer-supported catalyst itself also shows high activity (Table 1, entry 4) giving the β-hydroxy ester in 97% ee, a drop of only 2% ee in going to a heterogeneous catalyst from a homogeneous catalyst. Most importantly, we have shown that the catalyst can be reused (Table 1, entries 5 and 6) by simply collecting the insoluble polymer under argon, washing with THF, and subjecting the catalyst

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once again to the hydrogenation conditions. Although reaction times are extended, the yield and enantioselectivities remain high. The hydrogenations have also been run at substrate-to-catalyst ratios of up to 500:1 with little drop in selectivity (Table 1, entry 7). Finally, it is pleasing to note that other substrates can also be hydrogenated. Thus, the unsaturated β-keto ester **8** was reduced in 88% ee, although the olefin was also hydrogenated under these conditions (Table 1, entry 8). Itaconic acid **9** was smoothly hydrogenated in 56% ee (Table 1, entry 10), and the dehydroamino acid **10** was reduced in 64% ee (Table 1, entry 12).

An impressive feature of the present catalytic system relies on the fact that the catalyst can be removed from the product by filtration. This results in significant process improvements. First, since the products contain no catalyst they are often of sufficient purity to be used in subsequent reactions without the need for further purification. This obviates the need for an otherwise costly and time-consuming process to recover a homogeneous catalyst. Furthermore, the polymer-bound catalyst itself is still an active hydrogenation catalyst. Therefore, the catalyst can be reused in another reaction without any other manipulations. This is, of course, an environmental advantage as the costly and toxic ruthenium precatalyst is also reused. Indeed, analysis of the reaction products from the solid-phase hydrogenations for ruthenium content by ICP-AES (inductively coupled plasma atomic emmision spectroscopy) show that less than 1 mol % of the total amount of ruthenium used is leached into the reaction products.[13] This indicates that the catalyst resides almost entirely on the polymer support.

In conclusion, we have devised a synthesis of a novel BINAP derivative that has been covalently bonded to a polymer support and used in a highly enantioselective ruthenium-catalyzed hydrogenation reaction. Moreover, we have shown that the catalyst can be isolated from the reaction mixture by filtration, leaving a product free of contamination that needs no purification. The active catalyst can then be reused with only a slight loss in effectiveness.

We are currently examining the scope and reusability of this catalytic system, as well as application to a variety of other substrates. Further results will be reported in due course.[14]

Experimental Section

General Experimental Procedures. Reaction progress was monitored with analytical thin-layer chromatography on Merck 0.2 mm aluminum-backed silica plates and visualized by ultraviolet light. Column chromatography was performed using Merck silica gel 60 (230−400 mesh) under pressure with the stated solvents. All chemicals were purchased from Aldrich, Fluka, or Acros and were used without purification.

(*R*)-2,2′-Dimethoxy-1,1′-binaphthalene. To a well-stirred solution of (*R*)-binaphthol (18.85 g, 0.0659 mol) in anhydrous acetone (600 mL) were added anhydrous K_2CO_3 (27.30 g, 0.198 mol) and methyl iodide (28.08 g, 0.198 mol). The mixture was heated at reflux under a calcium chloride guard tube for 18 h. After cooling, the volatiles were removed in vacuo and the residual solids dissolved in CH_2Cl_2 (600 mL) and H_2O (500 mL). The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were dried over anhydrous Na_2CO_3, and the solvent was removed in vacuo to leave a pale yellow solid. Purification by washing with MeOH (3 × 50 mL) and drying under reduced pressure yielded (*R*)-2,2′-dimethoxy-1,1′-binaphthalene as a white solid (18.8 g, 90%): mp 226−231 °C; $[\alpha]^{20}_D$ 112.6 (*c* 0.3, toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.80 (6H, s), 7.13 (2H, d, J = 8 Hz), 7.23 (2H, dd, J = 9, 12 Hz), 7.33 (2H, t, J = 9 Hz), 7.48 (2H, d, J = 12 Hz), 7.87 (2H, d, J = 8 Hz), 8.00 (2H, d, J = 9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.1, 134.1, 129.4, 129.3, 127.9, 126.3, 125.2, 123.5, 119.6, 114.2, 56.9; MS (ES$^+$) *m/z* 315 ($M^+ + 1$); IR (solid) ν_{max} 2926.7, 1585.9, 1500.9, 1460.5, 1244.4, 1090.0; HRMS calcd mass for $C_{22}H_{18}O_2$ 314.384, found 314.132.

(*R*)-Ethyl 4-(2,2′-Dimethoxy-1,1′-binaphth-6-yl)-4-oxobutanoate (2). To a cooled (0 °C) solution of (*R*)-2,2′-dimethoxy-1,1′-binaphthalene (8.46 g, 0.027 mol) in CH_2Cl_2 (200 mL) under argon was added solid $AlCl_3$ (3.94 g, 0.030 mol). The red solution was stirred for 10 min, and to this was added dropwise ethyl succinyl chloride (4.88 g, 0.030 mol). The resulting brown solution was warmed to room temperature, stirred for 18 h, and poured carefully onto H_2O (200 mL). The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic fractions were dried over anhydrous Na_2SO_4, and the solvents were removed in vacuo. Purification was affected by flash column chromatography (silica gel, EtOAc−hexane, 30%) to yield the title product as a white solid (7.15 g, 60%): mp 121−125 °C; $[\alpha]^{20}_D$ 86.7 (*c* 0.3, toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (3H, t, J = 7 Hz), 2.80 (2H, t, J = 8 Hz), 3.41 (2H, t, J = 8 Hz), 3.75 (3H, s), 3.79 (3H, s), 4.18 (2H, q, J = 7 Hz), 7.10 (1H, d, J = 9 Hz), 7.20 (1H, d, J = 9 Hz), 7.24 (1H, t, J = 9 Hz), 7.33 (1H, t, J = 9 Hz), 7.48 (1H, d, J = 9 Hz), 7.52 (1H, d, J = 9 Hz), 7.80 (1H, d, J = 9 Hz), 7.89 (1H, d, J = 9 Hz), 8.00 (1H, d, J = 9 Hz), 8.12 (1H, d, J = 9 Hz), 8.57 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.9, 173.2, 157.7, 155.3, 136.8, 134.0, 131.9, 131.7, 130.3, 129.9, 129.3, 128.2, 128.1, 126.5, 125.8, 125.0, 124.1, 123.8, 119.8, 118.8, 114.3, 114.0, 60.9, 56.9, 56.5, 33.7, 28.4, 14.4; MS (ES$^+$) *m/z* 443 ($M^+ + 1$); IR (solid) ν_{max} 2933.8, 1721.5, 1689.0, 1481.0, 1247.9, 1149.0. Anal. Calcd for $C_{28}H_{26}O_5$: C, 76.00; H, 5.92. Found: C, 76.00; H, 5.89.

(*R*)-Ethyl 4-(2,2′-Dimethoxy-1,1′-binaphth-6-yl)butanoate. A flask containing ketone (*R*)-**2** (5.44 g, 0.0123 mol), Pd on carbon (0.75 g), methanesulfonic acid (1.42 g, 0.0148 mol), acetic acid (2.5 mL), EtOAc (85 mL), and EtOH (85 mL) was thoroughly purged with argon and then hydrogen. The reaction mixture was stirred under an atmosphere of hydrogen for 18 h, and filtered through Celite, and the solvents were removed in vacuo. The residue was dissolved in EtOAc (100 mL) and treated with saturated aqueous $NaHCO_3$ (100 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic extracts were dried (Na_2CO_3) and the volatiles removed in vacuo. Purification by flash column chromatography (silica gel, EtOAc−hexane, 15%) yielded the title product as a clear oil that solidified upon standing (4.20 g, 80%): mp 116−121 °C; $[\alpha]^{20}_D$ 68.8 (*c* 0.3, toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (3H, t, J = 7 Hz), 1.95−2.08 (2H, m), 2.31 (2H, t, J = 8 Hz), 2.72 (2H, t, J = 8 Hz), 3.74 (3H, s), 3.78 (3H, s), 4.12 (2H, q, J = 7 Hz), 7.01−7.08 (2H, m), 7.09 (1H, d, J = 9 Hz), 7.17−7.27 (1H, m), 7.29 (1H, t, J = 9 Hz), 7.40−7.47 (2H, m), 7.61 (1H, s), 7.84 (1H, d, J = 9 Hz), 7.92 (1H, d, J = 9 Hz), 7.98 (1H, d, J = 9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.6, 155.0, 154.7, 136.4, 134.1, 132.6, 129.4, 129.2, 128.9, 128.0, 127.8, 126.7, 126.3, 125.9, 125.4, 125.3, 123.5, 119.7, 119.6, 114.4, 114.2, 60.3, 56.9, 56.8, 35.0, 33.8, 26.4, 14.3; MS (ES$^+$) *m/z* 429 ($M^+ + 1$); IR (solid) ν_{max} 2933.5, 1725.3, 1592.7, 1461.7, 1245.2, 1146.8. Anal. Calcd for $C_{28}H_{28}O_4$: C, 78.48; H, 6.59. Found: C, 78.60; H, 6.60.

(*R*)-Ethyl 4-(2,2′-Dihydroxy-1,1′-binaphth-6-yl)butanoate (3). To a cooled (−78 °C) solution of (*R*)-ethyl 4-(2,2′-dimethoxy-1,1′-binaphth-6-yl)butanoate (0.99 g, 2.31 mmol) in anhydrous CH_2Cl_2 (15 mL) was added dropwise a 1.0 M CH_2Cl_2 solution of BBr_3 (5.1 mL, 5.10 mmol). The mixture was warmed over 2 h to room temperature, stirred for a further 1.5 h, and then poured carefully onto saturated aqueous $NaHCO_3$ (50 mL). The layers were separated, and the organic phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2CO_3, and the solvent was removed in vacuo. Flash column chromatography (silica gel, EtOAc−hexane, 20%) provided the title product as a white solid (0.69 g, 75%): mp 135−141 °C; $[\alpha]^{20}_D$ −76.9 (*c* 0.3, toluene); ^{1}H NMR (300 MHz,

(13) We thank AEA technology, Harwell, for their assistance with ICP-AES ruthenium content analysis.

(14) UK Patent Application No. 9619684.5.

$CDCl_3$) δ 1.23 (3H, t, J = 7 Hz), 1.98−2.03 (2H, m), 2.32 (2H, t, J = 8 Hz), 2.75 (2H, t, J = 8 Hz), 4.11 (2H, q, J = 7 Hz), 5.02 (1H, s), 5.10 (1H, s), 7.08 (1H, d, J = 9 Hz), 7.16 (2H, d, J = 9 Hz), 7.27−7.42 (4H, m), 7.58 (1H, s), 7.85−7.90 (2H, m), 7.97 (1H, d, J = 9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.9, 152.9, 152.3, 137.5, 133.8, 132.2, 131.3, 130.8, 129.8, 129.6, 128.8, 128.4, 127.4, 127.2, 124.4, 124.3, 124.0, 117.8, 117.7, 111.3, 111.2, 60.4, 34.9, 33.7, 26.4, 14.2; MS (ES^-) m/z 399 ($M^+ - 1$); IR (solid) ν_{max} 3328.3, 2934.9, 1725.8, 1594.1, 1245.5, 1143.3. Anal. Calcd for $C_{26}H_{24}O_4$: C, 77.98; H, 6.04. Found: C, 78.30; H, 6.57.

(*R*)-Ethyl 4-[2,2′-bis(trifluoromethanesulfoxy)-1,1′-binaphth-6-yl]butanoate. To a cooled (0 °C) mixture of (*R*)-**3** (0.67 g, 1.68 mmol), 2,6-lutidine (0.45 g, 4.19 mmol), and (dimethylamino)pyridine (0.020 g, 0.169 mmol) was added dropwise trifluoromethanesulfonic anhydride (1.04 g, 3.69 mmol). The resulting orange solution was warmed to room temperature, stirred for 20 h, and then poured onto saturated aqueous $NaHCO_3$ (20 mL). The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with 0.5 M aqueous HCl (20 mL) and H_2O (20 mL) and then dried over anhydrous Na_2CO_3. Removal of the solvent in vacuo and purification by flash column chromatography (silica gel, EtOAc−hexane, 15%) gave the title product as a colorless oil (0.92 g, 83%): $[\alpha]^{20}_D$ −120.5 (*c* 0.3, toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (3H, t, J = 7 Hz), 2.02−2.10 (2H, m), 2.37 (2H, t, J = 8 Hz), 2.82 (2H, t, J = 8 Hz), 4.13 (2H, q, J = 7 Hz), 7.18 (1H, d, J = 9 Hz), 7.24−7.29 (2H, m), 7.41 (1H, t, J = 9 Hz), 7.58−7.66 (3H, m), 7.79 (1H, s), 8.01 (1H, d, J = 9 Hz), 8.07 (1H, d, J = 9 Hz), 8.14 (1H, d, J = 9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.4, 145.4, 145.0, 140.8, 133.1, 132.6, 132.3, 132.0, 131.7, 131.5, 129.5, 128.4, 128.0, 127.3, 127.0, 126.8, 123.6, 123.3, 119.9, 119.4, 119.3, 116.4, 113.1, 60.4, 35.0, 33.6, 26.1, 14.2; MS (CI) m/z 664 (M^+); IR (film) ν_{max} 2935.3, 1729.2, 1418.3, 1204.4, 1135.0.

(*R*)-Ethyl 4-[2,2′-(Diphenylphosphino)-1,1′-binaphth-6-yl]butanoate (4). A solution of $NiCl_2$dppe (2.12 g, 4.01 mmol) in anhydrous DMF (10 mL) was degassed thoroughly using seven pump/argon cycles. $HPPh_2$ (1.24 g, 6.68 mmol) was added and the red mixture aged at 100 °C for 1 h. In a separate flask, (*R*)-ethyl 4-[2,2′-bis(trifluoromethanesulfoxy)-1,1′-binaphth-6-yl]butanoate (2.22 g, 3.34 mmol) and 1,4-diazabicyclo[2.2.2]octane (1.50 g, 0.0134 mol) were degassed in DMF (10 mL) and added to the nickel solution via cannula. The resulting deep green solution was heated at 100 °C, a further portion of $HPPh_2$ (1.24 g, 6.68 mmol) added after 4 h, and the solution continued heating for a further 16 h. After being cooled to room temperature, the mixture was diluted with EtOAc (50 mL), poured onto 50 mL of aqueous NaCN (1.64 g, 0.0334 mmol), and stirred vigorously for 1 h. The layers were separated, the organic phase was washed with H_2O (3 × 20 mL) and dried over anhydrous Na_2SO_4, and the solvents were removed in vacuo. The resulting brown solid was then dissolved in anhydrous toluene (50 mL), treated with trichlorosilane (13.42 g, 0.099 mol), and heated at reflux for 18 h. The mixture was quenched by pouring carefully onto 2.0 M aqueous NaOH (100 mL) and stirring vigorously for 30 min. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2CO_3 and the volatiles removed in vacuo. Purification was affected by flash column chromatography (silica gel, EtOAc−hexane, 10%) to give the title product as a white solid (1.64 g, 66%): mp 200 °C dec; $[\alpha]^{20}_D$ 185.2 (*c* 0.3, toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (3H, t, J = 7 Hz), 1.94−2.03 (2H, m), 2.31 (2H, t, J = 8 Hz), 2.72 (2H, t, J = 8 Hz), 4.16 (2H, q, J = 7 Hz), 6.71 (2H, s), 6.89 (1H, d, J = 9 Hz), 6.95 (1H, t, J = 9 Hz), 7.06−7.25 (10H, m), 7.37 (1H, t, J = 9 Hz), 7.48 (2H, d, J = 9 Hz), 7.62 (1H, s), 7.83−7.88 (2H, m), 7.92 (1H, d, J = 9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.9, 145.8, 145.6, 145.5, 145.0, 144.9, 139.8, 138.3, 138.0, 137.8, 137.6, 137.5, 137.4, 135.8, 135.1, 134.9, 134.8, 134.4, 134.1, 133.9, 133.7, 133.6, 133.5, 133.4, 133.3, 132.3, 132.2, 131.0, 130.6, 128.6, 128.2, 128.0, 127.9, 127.8, 127.2, 126.6, 60.4, 35.1, 33.6, 26.3, 14.3; MS (ES^+) m/z 737 ($M^+ + 1$); IR (solid) ν_{max} 2933.0, 1731.6, 1432.2, 1307.5, 1025.4.

(*R*)-4-[2,2′-(Diphenylphosphino)-1,1′-binaphth-6-yl]butanoic acid (5). To a solution of ester (*R*)-**4** (1.48 g, 2.01 mmol) in THF (15 mL) was added 15 mL of aqueous LiOH (4.0 g, 0.10 mol) and the mixture heated at reflux for 20 h. After being cooled to room temperature, the solution was acidified to pH 3 with 2.0 M aqueous HCl and extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried over anhydrous Na_2CO_3, and the solvent was removed in vacuo. Recrystallization from methanol afforded the title compound as a white solid (1.43 g, 99%): mp 150−153 °C; $[\alpha]^{20}_D$ 179.4 (*c* 0.3, toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (3H, t, J = 7 Hz), 1.92−2.01 (2H, m), 2.35 (2H, t, J = 8 Hz), 2.72 (2H, t, J = 8 Hz), 4.16 (2H, q, J = 7 Hz), 6.71 (2H, s), 6.86 (1H, d, J = 9 Hz), 6.94 (1H, t, J = 9 Hz), 7.02−7.24 (10H, m), 7.35 (1H, t, J = 9 Hz), 7.44 (2H, d, J = 9 Hz), 7.60 (1H, s), 7.82−7.87 (2H, m), 7.90 (1H, d, J = 9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 180.0, 145.8, 145.6, 145.4, 145.0, 144.8, 139.5, 138.2, 138.1, 137.9, 137.8, 137.7, 137.5, 135.5, 135.4, 135.0, 134.9, 134.6, 134.3, 134.1, 133.5, 133.3, 133.0, 132.9, 132.1, 130.9, 130.6, 128.6, 128.5, 128.3, 128.2, 127.9, 127.7, 127.6, 127.1, 126.3, 126.0, 35.0, 33.4, 26.0; MS (ES^+) m/z 709 ($M^+ + 1$); IR (solid) ν_{max} 3049.1, 2925.7, 1703.2, 1432.4, 1239.0, 815.1. Anal. Calcd for $C_{48}H_{37}O_2P_2$: C, 81.46; H, 5.27. Found: C, 81.14; H, 5.49.

Coupling of Acid to Aminomethylpolystyrene. To a flask containing aminomethylated polystyrene resin (1.0 g, 0.21 mmol, 1% cross-linked with divinylbenzene, 75−150 μm mesh size) was added CH_2Cl_2 (10 mL). (*R*)-**5** (0.223 g, 0.315 mmol) was added as a solution in DMF (5 mL) followed by hydroxybenzotriazole (0.064 g, 0.42 mmol), diisopropylethylamine (0.030 g, 0.21 mmol), and diisopropylcarbodiimide (0.056 g, 0.44 mmol). The resulting mixture was stirred slowly for 24 h. The resin was collected by filtration and washed sequentially with DMF (2 × 5 mL), CH_2Cl_2 (2 × 5 mL), MeOH (2 × 5 mL), and Et_2O (2 × 5 mL). Drying under vacuum afforded (*R*)-**6** as a white solid (1.15 g, new loading of 0.18 mmol/g).

Asymmetric Hydrogenations, Catalyst Preparation. To a mixture of diphosphine (R)-**6** (30 mg, 0.0054 mmol) and bis(2-methylallyl)cycloocta-1,5-dieneruthenium(II) complex (1.7 mg, 0.0054 mmol) in anhydrous degassed acetone (0.5 mL) was added 0.29 M methanolic HBr (0.043 mL, 0.0125 mmol). The amber mixture was stirred at room temperature for 1 h and the solvent removed thoroughly in vacuo to leave the active catalyst, which was used immediately as a hydrogenation catalyst.

Typical Hydrogenation Procedure. A solution of methyl propionylacetate (41 mg, 0.314 mmol) in degassed THF (0.3 mL) and MeOH (0.3 mL) was added to the catalyst in a glass vial and placed into a stainless steel pressure vessel. The system was thoroughly purged with hydrogen by three cycles of pressurizing and stirred magnetically with heating at 70 °C under 10 atm of hydrogen pressure for 18 h. After cooling, the reaction mixture was filtered and the resin washed with THF (3 × 1 mL). Removal of solvent in vacuo furnished the β-hydroxy ester, which was analyzed without purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (3H, t, J = 6 Hz), 1.43−1.60 (2H, m), 2.42 (1H, dd, J = 9, 12 Hz), 2.53 (1H, dd, 4, 12 Hz), 2.96 (1H, s), 3.72 (3H, s), 3.90−4.00 (1H, m).

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