Platinum-Catalyzed Asymmetric Hydroformylation of Olefins with (–)-BPPM/$SnCl_2$-Based Catalyst Systems

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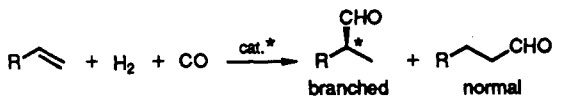
Three complexes of Pt(II) containing the chiral ligands 1-(*tert*-butoxycarbonyl)-(2*S*,4*S*)-2-[(diphenylphosphino)methyl]-4-(dibenzophospholyl)pyrrolidine (6′), 1-(*tert*-butoxycarbonyl)-(2*S*,4*S*)-2-[(dibenzophospholyl)methyl]-4-(diphenylphosphino)pyrrolidine (7′), and 1-(*tert*-butoxycarbonyl)-(2*S*,4*S*)-4-(dibenzophospholyl)-2-[(dibenzophospholyl)methyl]pyrrolidine (8′) were synthesized. Asymmetric hydroformylation of styrene was examined with use of platinum complexes of these three ligands, as well as Pt^{II}BPPM (5′), in the presence of stannous chloride as catalyst. Various branched/normal (*b*/*n*) ratios (0.5–3.2) and enantiomeric excess (ee) values (12–77%) were obtained. When the reactions were carried out in the presence of triethyl orthoformate, all four catalysts gave virtually complete enantioselectivity (ee > 96%) and similar *b*/*n* ratios. Complex 8′, with which the highest *b*/*n* (3.3) was obtained, was used for the asymmetric hydroformylation of diverse vinyl aromatic compounds that are the precursors to antiinflammatory agents. The ee's were low because of in situ racemization, and the *b*/*n* ratios depended strongly on the structure of the aromatic substituent. However, when the reactions were carried out in the presence of triethyl orthoformate, enantiomerically pure acetals were obtained.

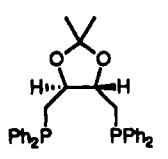
Introduction

Efficient asymmetric hydroformylation of olefins requires the ability to control both the regiochemistry (branched/normal ratio) and the absolute stereochemistry of the carbon–carbon bond-forming step (eq 1). A great deal of effort has been invested in this problem, and reasonable progress has been made.[1]



(1)

Until recently, only moderate enantiomeric excesses (ee's) of branched aldehydes had been realized in hydroformylation reactions with rhodium and platinum catalysts. Utilizing the chelating ligand (4*R*,5*R*)-2,2-dimethyl-4,5-bis[(diphenylphosphino)methyl]-1,3-dioxolane [(–)-DIOP; 1] in the presence of the appropriate rhodium



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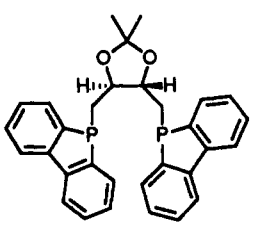

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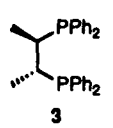

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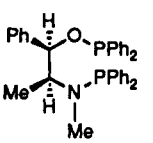

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complex generates HRh(CO)[(–)-DIOP], which catalyzes the hydroformylation of styrene to hydratropaldehyde in 25% ee.[2] Replacing the diphenylphosphino groups with dibenzophosphole gives the (–)-DBP-DIOP ligand (2), which yields a rhodium catalyst that hydroformylates styrene in 33% ee.[3] Other chelating ligands such as phosphinites, phosphines, and phospholes of 1,2-dimethylenecyclohexane and cyclobutane gave lower ee's (2–30%).[4] Low ee's (~25%) also have been obtained with the use of CHIRAPHOS (3)[5] and EPHOS (4).[6] A variety of other olefin substrates have been hydroformylated, but ee's have never been higher than about 50% with rhodium as a catalyst,[2b,7] the highest ee being achieved in the hydroformylation of vinyl acetate with Rh/(–)DBP-DIOP.[8] In a number of reactions, the optical yields were observed to be dependent on the temperature, as expected, and on the partial pressures of carbon monoxide and hydrogen.[5b,9]

Until recently, the use of platinum complexes in asymmetric hydroformylation has been less encouraging because of the lower reaction rates and the tendency for the substrate to undergo competitive hydrogenation. In addition, relatively low branched to normal (*b*/*n*) ratios have been observed in the hydroformylation of monosubstituted alkenes. (Hydroformylation of 1- and 2-butenes in the presence of [(–)-DIOP]$PtCl_2$/$SnCl_2$ was reported by two groups to give nonreproducible (and sometimes contradictory) results.[10] In contrast, the use of the preformed [(–)-DIOP]Pt($SnCl_3$)Cl complex as a catalyst precursor did give reproducible results.[11])

Although the ee's, selectivity, and *b*/*n* ratios are dependent on such variables as the H_2/CO ratio, the total

† Deceased July 19, 1989.

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Table I. Asymmetric Hydroformylation of Styrene: Influence of Ligand Structure

catalyst	conversn, %	*b/n*	ee, %
5′	40	0.55	77
6′	65	1.35	12
7′	22	1.0	74
8′	20	3.2	40
8′	42 (48 h)	2.8	7

Table II. Hydroformylation of Styrene in the Presence of $HC(OEt)_3$: Influence of Ligand Structure

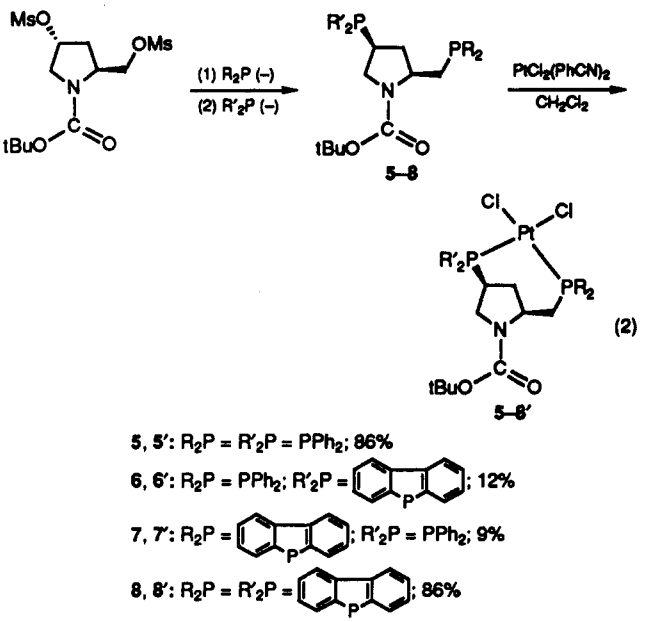
catalyst	reacn time, h	conversn, %	*b/n*	ee, %
5′	150	100	0.5	>96
6′	114	26	1.2	>96
7′	115	90	0.9	>96
8′	95	56	3.3	>96

pressure, the substrate concentration, and the ratio of phosphorus to platinum, no consistent pattern emerges to reveal much information as to the reaction mechanism.[12] The hydroformylation of a variety of substrates has been carried out, with enantiomeric excesses ranging from 20 to 44%.[13] The highest enantiomeric excesses (73% and 85%, respectively) obtained from the hydroformylation of styrene were with [(-)-DBP-DIOP]$PtCl_2/SnCl_2$ at 40–60 °C, 3200 psi, and H_2/CO = 2.4[14] and (*R,R*)-2,3-bicyclo-[2.2.2]oxetanediylbis(methylene)bis(diphenylphosphine)-$PtCl_2/SnCl_2$.[15]

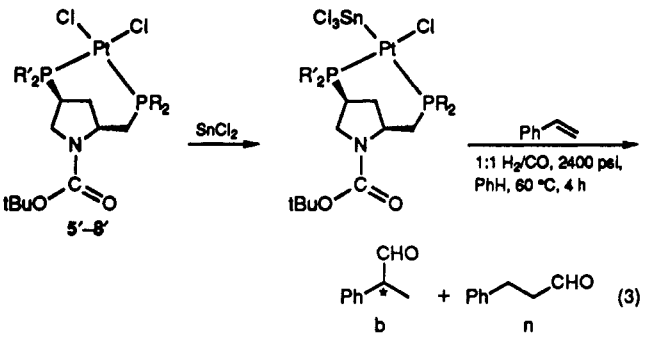
Recently, we have obtained some of the highest enantiomeric excesses in hydroformylation reactions of styrenes (~70–80% ee) with a platinum catalyst containing the chiral ligand (2*S*,4*S*)-4-(diphenylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine, [(-)BPPM]$PtCl_2$·$SnCl_2$ (5′·$SnCl_2$).[16] Even higher enantiomeric excesses (>96%) were achieved by trapping the aldehyde with triethyl orthoformate. However, there are three problems with the asymmetric hydroformylation of monosubstituted olefins in triethyl orthoformate catalyzed by 5′ that detract from its usefulness: (1) The branched to normal ratio is low; (2) The reaction has been limited thus far to a relatively small number of olefin substrates; thus, the scope of the reaction has not been fully probed. (3) The rates are somewhat slow. The research described will address these problems.

Results and Discussion

Development of the Catalyst System. Previous experience in these[17] and other laboratories[14] indicated that the substitution of diphenylphosphino groups by dibenzophosphole groups in chiral, chelating diphosphine ligands often resulted in higher stereoselectivity in hydroformylation reactions. To systematically examine the generality of this observation, 4-hydroxy-L-proline-derived ligands 5–8 were synthesized by the general approach shown in eq 2. (Because ligands 6 and 7 proved to be



inefficient in the asymmetric hydroformylation reaction, the yields of these were not optimized.) Treatment of ligands 5–8 with $PtCl_2(PhCN)_2$ in dichloromethane produced the platinum hydroformylation catalyst precursors 5′–8′. After addition of 1 equiv of anhydrous stannous chloride, complexes 5′–8′ were compared as catalysts for the asymmetric hydroformylation of styrene under a standard set of reaction conditions (1:1 H_2/CO, 2400 psi, PhH, 60 °C, 4 h, [substrate]/Pt = 400; eq 3). Enantiom-



eric excesses were determined by ^1H NMR spectroscopy with Eu(hfc)$_3$ as the chiral shift reagent. The results of this comparison are presented in Table I.

Several features warrant comment. Although the highest enantiomeric excess was obtained with the bis(phosphine) catalyst 5′,[16c] the conversion was only fair, and the branched to normal ratio (*b/n*) was impractically low. Mixed complex 6′, with a 2-phosphine–4-phosphole substitution pattern, gave both higher conversion and a better *b/n* but very low enantiomeric excess. The reverse 2-phosphole–4-phosphine complex 7′ gave low conversion and modest *b/n* but excellent enantiomeric excess, while the bis(phosphole) complex 8′ gave low conversion and excellent *b/n* but only modest enantiomeric excess. It is important to note that the *observed* enantiomeric excesses are not necessarily indicative of the *intrinsic* enantioselectivity of the catalysts, since the product aldehydes are not stereochemically inert and may be racemized after formation either by the catalyst itself or by the Lewis acidic stannous chloride present under the reaction conditions. Indeed, when the reaction with 8′ as the catalyst was run for longer times and higher conversion (48 h, 42% conversion), very low enantiomeric excess was observed, in-

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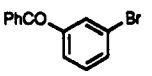
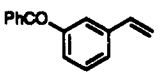
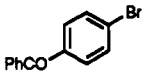
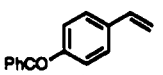
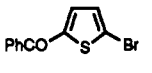
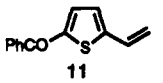
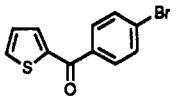
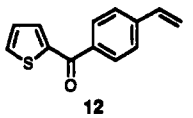
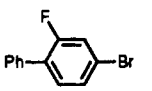
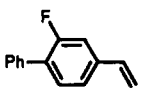
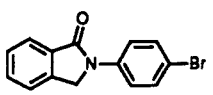
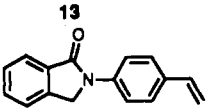
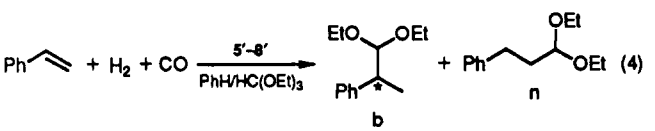
Table III. Synthesis of Vinyl Aromatic Compounds

ArBr	time, h	product	yield, %
	6	 **9**	86
	3	 **10**	72
	3	 **11**	60
	6	 **12**	79
	24	 **13**	74
	2	 **14**	37

dicating that racemization of the product branched aldehyde was probably occurring as the reaction proceeded.

To prevent this loss of optical activity by competitive racemization, the above experiments were repeated in the presence of triethyl orthoformate (2–4 equiv/equiv of styrene) to trap the aldehyde as the acetal upon formation (eq 4). Again, a standard set of conditions (except for

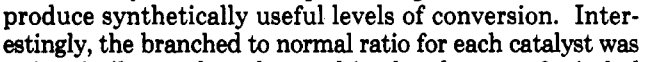


(4)

reaction time; 1:1 H_2/CO, 2400 psi, 60 °C, PhH solvent, [substrate]/Pt = 400) was used to allow comparisons to be made. The results are summarized in Table II.

Under these conditions, all four catalysts gave virtually complete enantioselectivity, although the reactions were considerably slower and required longer reaction times to produce synthetically useful levels of conversion. Interestingly, the branched to normal ratio for each catalyst was quite similar to that observed in the absence of triethyl orthoformate and probably reflects the intrinsic regioselectivity of the catalyst. Since it is the optically active branched aldehyde that is of use for the synthesis of nonsteroidal antiinflammatory 2-arylpropionic acids,[18] complex 8′, with its high (3.3) selectivity for formation of branched aldehydes, was studied as an asymmetric hydroformylation catalyst for a number of vinyl aromatic compounds.

Asymmetric Hydroformylation of Vinyl Aromatic Compounds. The palladium(0)-catalyzed coupling of aryl halides with vinyltin reagents (eq 5), recently developed in these laboratories,[19] provides ready access to a wide array of vinyl aromatic compounds (Table III) for which



(5)

the corresponding 2-arylpropionic acid has known antiinflammatory activity. These olefins, along with *p*-isobutylstyrene (**15**), *m*-phenoxystyrene (**16**), and 6-methoxy-2-vinylnaphthalene (**17**) (synthesized by literature procedures),[16c] were subjected to hydroformylation with catalyst 8′, under standard reaction conditions (1:1 H_2/CO, 2400 psi, 60 °C, PhCl solvent).

In the absence of triethyl orthoformate (Table IV) the reaction proceeded with high conversion in a reasonably short period of time. The selectivity for aldehyde was usually greater than 80%, with the remainder being hydrogenation product. In all but one case (**16**) the *b*/*n* was quite good, but the asymmetric induction (% ee) was low, again reflecting racemization problems.

Although each of these aldehydes is convertible to a commercial antiinflammatory 2-arylpropionic acid, the enantiomeric excesses were too low to be of any practical value. Hence, the above hydroformylation reactions were repeated in the presence of 4 equiv of triethyl orthoformate to trap the aldehyde before racemization. These results are summarized in Table V. As anticipated, the reaction rates and conversions were somewhat low, but the selectivity for aldehyde was excellent (>90%), as were the branched to normal ratios and the enantiomeric excesses. Since the acetals thus formed can be hydrolyzed to the free aldehydes without racemization,[16] this process offers access to precursors to Ketoprofen[18] from **9**, Tiaprofenic Acid[18] from **11**, Suprofen[18] from **12**, Flubiprofen[18] from **13**, Indoprofen[18] from **14**, Ibuprofen[18] from **15**, Fenoprofen[18] from **16**, and Naproxen[18] from **17**.

Catalyst 8′ is only effective for vinyl aromatic compounds. Allyl compounds such as *N*-allylacetamides and *o*-trimethylsilyl allyl alcohols and enol ethers such as propyl vinyl ether, *p*-nitrophenyl vinyl ether, and the trimethylsilyl enol ether of cyclopentanone failed to undergo hydroformylation. Vinyl acetate was hydroformylated, but with low conversion (24%) and *b*/*n* (0.46). Allyltrimethylsilane had similar problems (27% conversion, 0.53 *b*/*n*). However, with vinyl aromatic compounds catalyst 8′ gives among the best branched to normal ratios and the highest enantiomeric excesses yet observed in the asymmetric hydroformylation of this class of substrates.[20]

Experimental Section

All reactions involving the synthesis of phosphinated compounds were performed under an inert atmosphere of argon. Manipulations involving phosphines in solution were carried out in a glovebox or by Schlenk techniques.

The ^1H NMR spectra were recorded with a Bruker AC 300P spectrometer. The chemical shifts for ^1H NMR (300 MHz) and ^{13}C NMR (75.5 MHz) spectra are reported in units of parts per million (δ) relative to tetramethylsilane at 0.00 ppm by using, where possible, the residual proton signals or ^{13}C signals in the solvent as an internal standard (chloroform-*d* δ 7.24 or 77.00) or TMS. All ^{31}P NMR (121.5 MHz) spectra are proton-decoupled and reported in units of parts per million downfield of 85% phosphoric acid (H_3PO_4) and are referenced externally. FT-IR spectra were recorded on a Perkin-Elmer 1600 spectrophotometer. Optical rotations were measured on an Autopol III automatic polarimeter. All melting points are uncorrected.

Diethyl ether, tetrahydrofuran (THF), and toluene were distilled from sodium/benzophenone ketyl under an argon atmosphere. Benzene, chlorobenzene, and triethyl orthoformate (Aldrich) were distilled under argon prior to use. Synthesis gas

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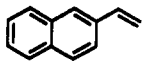
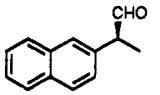
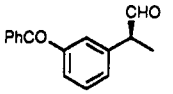
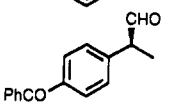
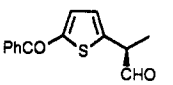
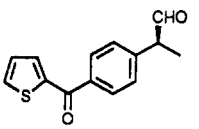
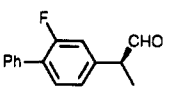
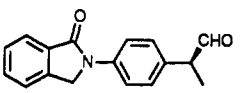
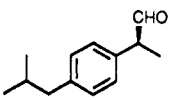
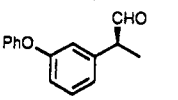
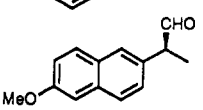
(19) McKean, D. R.; Parrinello, G.; Renaldo, A. F.; Stille, J. K. *J. Org. Chem.* **1987**, *52*, 422.

(20) For a very recent efficient *hydrocarbonylation* of the class of substrates see: Alper, H.; Hamel, N. *J. Am. Chem. Soc.* **1990**, *112*, 2803.

Table IV. Hydroformylation of Vinyl Aromatic Compounds with Catalyst 8′

substrate (substrate/8′)	reacn time, h	product	conversn, %	b/n	ee (S) %
 (334)	38		95	10	39
9 (105)	44		100	3.3	27
10 (150)	48		100	3.2	37
11 (75)	38		90[a]	5.0	≥96
12 (116)	64		65	4.0	9
13 (207)	70		95	3.8	19
14 (200)	50		70	only branched	0
15 (340)	37		45	2.0	39
16 (146)	44		25	0.8	25
17	40		100	3.3	37

[a] Selectivity for aldehyde was only 40%.

(1:1 H_2/CO) was purchased as a custom mixture from SCP Inc. and was used as received. Styrene, vinyl acetate, and trimethylallylsilane were purchased from Aldrich, freshly distilled, and stabilized with *p*-methoxyphenol before use as hydroformylation substrates. 2-Vinylnaphthalene was purchased from Aldrich and purified by sublimation before use. 2-Bromothiophene, 2-bromo-6-methoxynaphthalene, 4-bromobenzoyl chloride, benzoyl chloride, and diphenylphosphine were purchased from Aldrich and used as received. 4-Bromobenzophenone and 4-bromo-2-fluorobiphenyl were available from Lancaster Synthesis and used without further purification. The NMR shift reagent tris[3-((heptafluoropropyl)hydroxymethylene)-(+)-camphorato]europium(III) (Eu(hfc)$_3$) was purchased from Aldrich. Tetrakis(triphenylphosphine)palladium[21] and tributylethenylstannane[22] were synthesized according to literature procedures. Isobutylstyrene,[16] 3-phenoxystyrene,[23] and 2-vinyl-6-methoxynaphthalene[19,24] were prepared by following the reported procedures. Catalyst 5′ was synthesized as previously reported.[16]

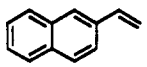
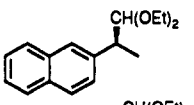
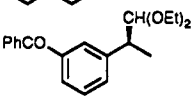
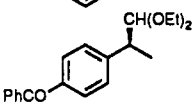
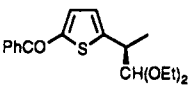
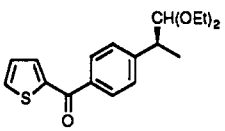
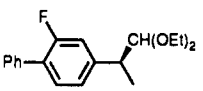
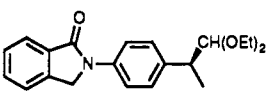
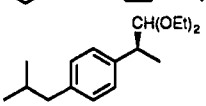
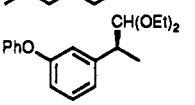
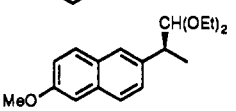
1-(*tert*-Butoxycarbonyl)-4-hydroxy-L-prolinol. To a solution of 1-(*tert*-butoxycarbonyl)-4-hydroxy-L-proline ethyl ester[16b] (16 g, 61.7 mmol) cooled to −10 °C in tetrahydrofuran (300 mL) was added lithium tetrahydroaluminate (2.0 g, 50 mmol). The mixture was stirred for 1 h at −10 °C, followed by 25 h at room temperature. The solution was cooled to 0 °C with stirring, and water (100 mL) followed by hydrochloric acid (50 mL, 6 N) was added carefully. The solution was warmed up to allow a good separation of phases. The aqueous layer was extracted with ethyl acetate (3 × 75 mL). The combined organic layers were washed with 100 mL each of solutions of sodium hydroxide (2 N), hydrochloric acid (2 N), and brine and dried over magnesium sulfate. The crude oil obtained after evaporation of the solvent was purified by flash chromatography (silica gel, eluent 50% ethyl acetate/50% hexane). After removal of the solvent, the product (11.1 g, 83%) was recovered as white crystals; mp 77–79 °C (lit.[16b] an oil). ^{1}H NMR ($CDCl_3$): δ 1.44 (s, 9 H, tBu), 1.65 (m, 1 H), 2.01 (m, 2 H), 2.29 (s, 1 H, OH), 3.39 (m, 1 H), 3.51 (m, 2 H), 3.67 (m, 1 H), 4.12 (m, 1 H), 4.33 (s, 1 H), 5.10 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$): δ 28.4, 37.2, 54.8, 55.2, 57.5, 58.4, 63.4, 65.9, 68.6, 80.2, 154.8, 156.5. IR (KBr, cm^{-1}): 3400, 1675 (C=O), 1420.

1-(*tert*-Butoxycarbonyl)-4-hydroxy-L-prolinol Dimethanesulfonate. To a solution of 1-(*tert*-butoxycarbonyl)-4-hydroxy-L-prolinol (5.4 g, 25 mmol) in dry pyridine (150 mL) at 0 °C under argon was added 4-(dimethylamino)pyridine (0.61 g, 5 mmol) and methanesulfonyl chloride (5.8 mL, 75 mmol). The mixture was stored in the refrigerator for 5 days. Methanesulfonyl chloride (4 mL, 51.7 mmol) was added to the mixture, which was kept 3 days more in the refrigerator. The mixture was cooled to 0 °C, and water (750 mL) was added dropwise over 5 h. The mixture was kept in the refrigerator an additional time of 2 days, allowing the precipitation of a crude solid, which after recrystallization from ethanol (95%) afforded the product (9.05 g, 97%) as white needles; mp 83 °C. ^{1}H NMR ($CDCl_3$): δ 1.45 (s, 9 H, tBuO), 2.24–2.35 (m, 1 H), 2.36–2.57 (m, 1 H), 2.99 (s, 3 H, $OSCH_3$), 3.03 (S, 3 H, $OSCH_3$), 3.45 (m, 1 H), 3.83 (m, 1 H), 4.25 (m, 2 H), 4.67 (m, 1 H), 5.19 (m, 1 H). ^{13}C NMR ($CDCl_3$): δ 28.3 (3 C), 34.5, 35.8, 37.0, 37.5, 38.6, 52.5, 53.1, 54.5, 69.2, 78.2, 80.9, 81.2, 154.2 (mixture of rotamers). IR (Nujol, cm^{-1}): 1692 (C=O). $[\alpha]_D^{24}$ = −59.0° (*c* = 1, benzene). Anal. Calcd for $C_{12}H_{23}NO_8S_2$: C, 38.59; H, 6.16. Found: C, 38.43; H, 6.26.

1-(*tert*-Butoxycarbonyl)-2-[(dibenzophospholyl)methyl]-4-hydroxy-L-prolinol Methanesulfonate. To liquid

(21) Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121.
(22) Seyferth, D.; Stone, F. G. A. *J. Am. Chem. Soc.* **1957**, *79*, 515.
(23) Neibercker, D.; Reau, R.; Lecolier, S. *J. Org. Chem.* **1989**, *54*, 5208.
(24) Nugent, W. A.; McKinney, R. I. *J. Org. Chem.* **1985**, *50*, 5370.

Table V. Hydroformylation of Vinyl Aromatic Compounds with Catalyst 8′ in the Presence of Triethyl Orthoformate

substrate (substrate/8′)	reacn time, h	product	conversn, %	b/n	ee (*S*), %
 (285)	145		73	3.4	≥96
9 (110)	135		34	3.3	≥96
10 (50)	170		15	3.0	≥96
11 (210)	210		38	25	≥96
12 (120)	143		15	3.4	≥96
13 (126)	138		20	3.4	≥96
14 (200)	180		60	only branched	60
15 (172)	215		7.5	2.0	≥96
16 (50)	163		33	1.3	≥96
17 (113)	182		50	3.4	≥96

ammonia (15 mL) was added sodium (271 mg, 1.18 mmol) cut into small pieces. To the resulting solution was added dropwise phenyldibenzophosphole[25] (1.53 g, 5.90 mmol) in tetrahydrofuran (10 mL) over 10 min. 2-Methyl-2-propyl chloride (0.64 mL, 5.90 mmol) was added to destroy the excess anion formed in the reaction. After the mixture was stirred at −78 °C for 30 min, the ammonia was allowed to evaporate slowly from the brown solution under a stream of argon. When it reached room temperature, the dibenzophospholide solution obtained was added dropwise over 45 min to a solution of 1-(*tert*-butoxycarbonyl)-4-hydroxy-L-prolinol dimethanesulfonate (2 g, 5.36 mmol) in tetrahydrofuran (10 mL) at −3 °C. The resulting orange-brown mixture was stirred at room temperature for 64 h; then methanol (10 mL) was added to destroy the excess anion. The oil obtained after concentration was taken up in tetrahydrofuran and the solution filtered over aluminum oxide. Elimination of the solvent afforded a crude material that, after flash chromatography over deoxygenated aluminum oxide (eluent 50% ethyl acetate/50% hexane), afforded the product (988 mg, 40%) as a white crystal (impure by ^{1}H NMR). ^{31}P NMR ($CDCl_3$): δ −22.88 and −21.96.

1-(*tert*-Butoxycarbonyl)-(2*S*,4*S*)-2-[(diphenylphosphino)methyl]-4-(dibenzophospholyl)pyrrolidine (6). To liquid ammonia (15 mL) was added sodium (100 mg, 4.26 mmol) cut into small pieces. To the resulting solution was added dropwise diphenylphosphine (0.75 mL, 4.31 mmol) dissolved in tetrahydrofuran (10 mL) over 15 min. The ammonia was allowed to evaporate under a stream of argon from the clear orange solution. When the solution had reached room temperature, a solution of 1-(*tert*-butoxycarbonyl)-2-[(dibenzophospholyl)-methyl]-4-hydroxy-L-prolinol methanesulfonate (600 mg, 1.42 mmol) in tetrahydrofuran (10 mL) was added dropwise over 10 min. The mixture was stirred at room temperature for 24 h. The solution was treated with methanol to destroy the excess anion, concentrated by rotavaporation, and then taken up in benzene (30 mL) and filtered. After removal of the solvent, the residual oil was purified by flash chromatography (deoxygenated silica gel, eluent benzene) to give the white crystalline **6** as a 4:1 mixture of rotamers (190 mg, 25%); $[\alpha]_D^{24} = -17.7°$ (c = 1.05, benzene). ^{1}H NMR ($CDCl_3$): δ 1.40, 1.50 (s, 9 H), 2.03–2.12 (m, 2 H), 2.62–2.81 (m, 2 H), 3.18 (m, 1 H), 3.82 (m, 2 H), 4.25 (m, 1 H), 7.2–8.0 (m, 18 H). ^{31}P NMR ($CDCl_3$) δ −7.16, −21.08, −21.77 (the two peaks for the primary phosphorus are due to the two conformations of the tBuOC group). IR (KBr, cm^{-1}): 1685 (C=O). This intermediate was not fully characterized but instead carried on to the next step.

[1-(*tert*-Butoxycarbonyl)-(2*S*,4*S*)-2-[(diphenylphosphino)methyl]-4-(dibenzophospholyl)pyrrolidine]dichloroplatinum(II) (6′). A deoxygenated solution of **6** (150 mg, 0.27 mmol) in dichloromethane (5 mL) was added to a refluxing solution of bis(benzonitrile)dichloroplatinum(II)[26] (100 mg, 0.212 mmol) in dichloromethane (10 mL). The solution was heated at reflux for 2 h under argon. Half of the solvent volume was distilled off, and the product was precipitated with diethyl ether, filtered, washed with diethyl ether, and dried under reduced pressure to give **6′** (93 mg, 54%) as a white powder. ^{31}P NMR ($CDCl_3$): $\delta(P_{1A})$ 28.6 [d, $^2J(P_1,P_2)$ = 18.1 Hz], $\delta(P_{1B})$ 28.1 [d, $^2J(P_1,P_2)$ = 18.3 Hz], $\delta(P_2)$ 3.3 [d, $^2J(P_2,P_1)$ = 18.0 Hz] [$^1J(Pt,P_{1A})$ = 3620 Hz, $^1J(Pt,P_{1b})$ = 3600 Hz, $^1J(Pt,P_2)$ = 3430 Hz]. P_2 is the phosphorus of the secondary phosphino group, and P_1 is the phosphorus of the primary phosphino group. The two peaks P_{1A} and P_{1B} result from the two conformations of the tBuOC group at room temperature.

(25) (a) Hoffmann, H. *Chem. Ber.* **1962**, *95*, 2563. (b) Dang, T. Ph.; Poulin, J.-Cl.; Kagan, H. B. *J. Organomet. Chem.* **1975**, *91*, 105. (c) Braye, E. H.; Caplier, I.; Saussez, R. *Tetrahedron* **1971**, *27*, 5523.

(26) Uchiyama, T.; Nakmura, Y.; Miwa, T.; Kawaguchi, S.; Okeya, S. *Chem. Lett.* **1980**, 337.

Anal. Calcd for $C_{34}H_{35}Cl_2NO_2P_2Pt$: C, 49.94; H, 4.28. Found: C, 49.74; H, 4.35.

1-(*tert*-Butoxycarbonyl)-2-[(diphenylphosphino)-methyl]-4-hydroxy-L-prolinol Methanesulfonate. A solution of (diphenylphosphido)sodium[25] was prepared by addition to liquid ammonia (15 mL) of sodium (151 mg, 6.57 mmol) cut into small pieces and diphenylphosphine (1.15 mL, 6.57 mmol) in tetrahydrofuran (15 mL), which was added dropwise over 30 min. The ammonia was allowed to evaporate slowly from the clear orange solution under a stream of argon. After it reached room temperature, the phosphide solution was added dropwise to 1-(*tert*-butoxycarbonyl)-4-hydroxy-L-prolinol dimethanesulfonate (2.23 g, 5.98 mmol) in tetrahydrofuran (19 mL) over 1 h at 10 °C. The mixture was stirred for 20 h at −3 °C. Then the reaction was quenched with methanol (15 mL). The resulting mixture was concentrated, taken up in tetrahydrofuran, and filtered over aluminum oxide. The residual oil obtained after removal of the solvent was purified by flash chromatography over deoxygenated aluminum oxide (50% ethyl acetate/50% hexane as eluent), yielding the product (1.50 g, 54%) as a white oil; $[\alpha]_D^{24} = -49.3°$ (c = 1.85, chloroform). ^{1}H NMR ($CDCl_3$): δ 1.42 (s, 9 H, $(CH_3)_3$), 2.18 (m, 1 H), 2.45 (m, 1 H), 2.85 (m, 1 H), 2.98 (s, 3 H, $OSCH_3$), 3.50 (m, 1 H), 3.70–4.21 (m, 3 H), 5.17 (m, 1 H), 7.25–7.56 (m, 10 H, PhH). ^{31}P NMR ($CDCl_3$) δ −23.5 and −23.2 (two peaks due to the two conformations of the tBuOC group).

1-(*tert*-Butoxycarbonyl)-(2*S*,4*S*)-2-[(dibenzophospholyl)methyl]-4-(diphenylphosphino)pyrrolidine (7). To liquid ammonia (15 mL) was added sodium (112 mg, 4.86 mmol) cut into small pieces. Upon completion of the addition, phenyldibenzophosphole (632 mg, 2.43 mmol) in tetrahydrofuran (7 mL) was added dropwise over 10 min; then 2-methyl-2-propyl chloride (0.26 mL, 2.43 mmol) was added. This mixture was stirred for 30 min at −78 °C. The ammonia was evaporated from the clear brown suspension under a stream of argon. When the solution had reached room temperature, 1-(*tert*-butoxycarbonyl)-2-[(diphenylphosphino)methyl]-4-hydroxy-L-prolinol methanesulfonate (750 mg, 1.62 mmol) in solution in tetrahydrofuran (7 mL) was added dropwise over 10 min. The mixture was stirred at room temperature for 24 h. Deoxygenated methanol (10 mL) was added to destroy the excess anion. The resulting suspension was concentrated, taken up in tetrahydrofuran, and filtered over alumina. The crude material obtained was purified by flash chromatography over deoxygenated aluminum oxide (eluent benzene), affording 7 (200 mg, 22%) as a white viscous oil; $[\alpha]_D^{24} = -19.5°$ (c = 1.1, benzene). ^{1}H NMR ($CDCl_3$): δ 1.26 (s, 9 H, $(CH_3)_3$), 1.51–1.75 (m, 1 H), 1.80–2.10 (m, 2 H), 2.37 (m, 1 H), 2.87 (m, 1 H), 3.10 (m, 1 H), 3.71 (m, 2 H), 7.25–7.54 (m, 14 H, ArH), 7.67 (t, J = 6.6 Hz, 2 H, ArH), 7.91 (m, 2 H, ArH). ^{31}P NMR ($CDCl_3$) δ −13.45 and −21.75. This intermediate was not fully characterized but instead was carried on to the next step.

[1-(*tert*-Butoxycarbonyl)-(2*S*,4*S*)-2-[(dibenzophospholyl)methyl]-4-(diphenylphosphino)pyrrolidine]dichloroplatinum(II) (7′). The synthesis was carried out according to a procedure identical with that used for 6′, which afforded 7′ as a white powder in 74% yield. ^{31}P NMR ($CDCl_3$): $\delta(P_2)$ 20.5 (m), $\delta(P_{1A})$ 4.6 [d, $^2J(P_1,P_2)$ = 18.1 Hz], $\delta(P_{1B})$ 4.0 [d, $^2J(P_1,P_2)$ = 18.2 H] [$^1J(Pt,P_2)$ = 3460 Hz, $^1J(Pt,P_{1A})$ = 3450 Hz, $^1J(Pt,P_{1B})$ = 3500 Hz]. P_2 is the phosphorus of the secondary phosphino group, and P_1 is the phosphorus of the primary phosphino group. The two peaks P_{1A} and P_{1B} result from the two conformations of the tBuOC group at room temperature. Anal. Calcd for $C_{34}H_{35}Cl_2NO_2P_2Pt$: C, 49.94; H, 4.28. Found: C, 49.46; H, 4.30.

1-(*tert*-Butoxycarbonyl)-(2*S*,4*S*)-2-[(dibenzophospholyl)methyl]-4-(dibenzophospholyl)pyrrolidine (8). To liquid ammonia (20 mL) at −75 °C was added metallic sodium (0.46 g, 20 mmol) cut into small pieces. To the blue solution was added a solution of 5-phenyldibenzophosphole[25] (2.60 g, 10 mmol) in THF (20 mL) dropwise over 20 min. The dark blue solution was stirred for an additional 30 min. Then 2-methyl-2-propyl chloride (1.28 mL, 11 mmol) was added. The ammonia was evaporated from the solution under a stream of argon by allowing the solution to warm up to room temperature. The solution was heated at 40 °C for 10 min to allow the ammonia to evaporate completely. To the red solution was added dropwise 1-(*tert*-butoxycarbonyl)-4-hydroxy-L-prolinol dimethanesulfonate (1.24 g, 3.34 mmol) in THF (20 mL) over 30 min at room temperature. The mixture was stirred for a further 24 h. Methanol (6 mL) was added to destroy the excess sodium dibenzophosphole. The mixture was filtered, and the filter was washed with benzene. The filtrate was concentrated, and the oil obtained was chromatographed on deoxygenated silica gel under argon with benzene as the eluent. Removal of solvent under reduced pressure gave 8 as a white solid (1.57 g, 86%); mp 76 °C; $[\alpha]_D^{24} = +34.4°$ (c = 0.7, C_6H_6). ^{1}H NMR ($CDCl_3$): δ 1.27, 1.41 (s, 9 H, $(CH_3)_3$), 1.49–1.70 (m, 1 H), 1.78–2.10 (m, 3 H), 2.40–3.75 (m, 1 H), 3.12 (m, 1 H), 3.65 (m, 2 H), 7.25–7.96 (m, 16 H, ArH). ^{31}P NMR δ −13.3 (s, P_2), −20.66 (s, P_{1A}), −21.13 (s, P_{1B}). The two peaks P_{1A} and P_{1B} result from the two conformations of the tBuOC group at room temperature. Anal. Calcd for $C_{34}H_{33}NO_2P_2$: C, 74.31; H. 6.05; N, 2.55. Found: C, 74.43; H, 6.07; N, 2.57.

[1-(*tert*-Butoxycarbonyl)-(2*S*,4*S*)-2-[(dibenzophospholyl)methyl]-4-(dibenzophospholyl)pyrrolidine]dichloroplatinum(II) (8′). A deoxygenated solution of 8 (132 mg, 0.24 mmol) in dichloromethane (8 mL) was added to a refluxing solution of bis(benzonitrile)dichloroplatinum(II)[26] (94 mg, 0.2 mmol) in dichloromethane (7 mL) under an argon atmosphere. The reflux was continued for 2 h. Then, the solution volume was reduced to about 4 mL by distillation of solvent. The product was precipitated with diethyl ether, filtered, washed with diethyl ether, and dried under reduced pressure to give a white solid (149 mg, 91%); mp 220 °C dec. ^{31}P NMR ($CDCl_3$): $\delta(P_2)$ −4.65 (s) $\delta(P_1)$ −2.08 (m) [$^1J(Pt,P_2)$ = 3441 Hz, $^1J(Pt,P_1)$ = 3500 Hz]. Anal. Calcd for $C_{34}H_{33}NO_2P_2PtCl_2$: C, 50.07; H, 4.08; N, 1.72. Found: C, 50.27; H, 4.12; N, 1.75.

3-Ethenylphenyl Phenyl Ketone (Typical Coupling Procedure) (9). To a solution of 3-bromophenyl phenyl ketone (2.61 g, 10 mmol), tetrakis(triphenylphosphine)palladium (0.23 g, 0.020 mmol), and a few crystals of *p*-methoxyphenol in toluene (20 mL) was added tributylethenylstannane (3.50 g, 11 mmol). The resulting solution was heated at reflux for 3 h. The reaction completion was indicated by black precipitation of palladium and TLC analysis. The mixture was cooled to room temperature and poured into diethyl ether (250 mL). The ether solution was washed with ammonia solution (10%, 2 × 50 mL) and saturated sodium chloride solution and dried over magnesium sulfate. After removal of solvent, the crude material was purified by flash chromatography (silica gel, 10% ethyl acetate/90% hexane) to give the product as a colorless oil (1.79 g, 86%); bp 95 °C (2.7 mmHg). ^{1}H NMR ($CDCl_3$): δ 7.80 (m, 3 H), 7.60 (m, 3 H), 7.45 (m, 3 H), 6.74 (dd, ^1J = 17.5 Hz, ^2J = 10.8 Hz, 1 H, ArCH=C), 5.79 (d, J = 17.5 Hz, 1 H, *cis*-H_2C=CAr), 5.31 (d, J = 10.8 Hz, 1 H, *trans*-H_2C=CAr). ^{13}C NMR: δ 196.5, 137.8, 137.7, 137.5, 135.9, 132.4, 129.9 (2 C), 129.8, 129.3, 128.2 (2 C), 127.6, 115.2. Anal. Calcd for $C_{15}H_{12}O$: C, 86.51; H, 5.81. Found: C, 86.33; H, 5.82.

4-Ethenylphenyl Phenyl Ketone (10). Compound 10 was obtained from the coupling of 4-bromophenyl phenyl ketone and tributylethenylstannane in 72% yield by the above procedure as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.77 (m, 4 H), 7.57 (m, 1 H), 7.46 (m, 4 H), 6.75 (dd, J = 10.9, 17.5 Hz, 1 H, ArCH=C), 5.87 (dd, J = 17.5, 0.45 Hz, 1 H, *cis*-H_2C=CAr), 5.83 (dd, J = 10.9, 0.45 Hz, 1 H, *trans*-H_2C=CAr). ^{13}C NMR: δ 196.1, 141.5, 137.7, 136.6, 135.9, 132.3, 130.5, 129.9, 128.2, 126.0, 116.6. IR (film, KBr, cm^{-1}): 3061 (m), 1656 (s, C=O), 1629 (m), 1603 (s), 1578 (m), 1446 (m), 1317 (s), 1278 (s), 1177 (m), 923 (s, C=C). Anal. Calcd for $C_{15}H_{12}O$: C, 86.51; H, 5.81. Found: C, 86.35; H, 5.83.

5-Benzoyl-2-bromothiophene. A three-neck flask equipped with a mechanical stirrer and a reflux condenser was charged with aluminum trichloride (7.40 g, 0.055 mmol) and carbon disulfide (25 mL). The mixture was cooled to 0 °C, and a solution of benzoyl chloride (8.0 g, 0.056 mmol) and 2-bromothiophene (8.65 g, 0.052 mmol) in carbon disulfide (20 mL) was added dropwise over a period of 1.5 h. The red-brownish mixture was warmed to room temperature and stirred for 10 h more; TLC indicated completion of the reaction (SiO_2, 10% ethyl acetate/90% hexane). The mixture was poured on ice and extracted with diethyl ether (3 × 200 mL). The ethereal extracts were washed with sodium bicarbonate saturated solution and with sodium chloride saturated solution and dried over magnesium sulfate. Removal of the solvent under reduced pressure afforded an orange liquid, which was treated with hexane. Small quantities of red precipitate were removed by filtration. The remaining hexane solution was stored in the freezer to give pale yellow crystals (12.99 g, 93.5%); mp

38–39 °C. ^{1}H NMR ($CDCl_3$): δ 7.81 (m, 2 H), 7.58 (m, 1 H), 7.48 (m, 2 H), 7.36 (d, J = 4 Hz, 1 H, HC=C—S), 7.11 (d, J = 4 Hz, 1 H, HC=C—S). ^{13}C NMR: δ 186.9, 145.0, 137.3, 134.9, 132.5, 131.1, 131.0, 128.9, 128.5, 123.2. Anal. Calcd for $C_{11}H_7OSBr$: C, 49.45; H, 2.64; S, 12.00; Br, 29.91. Found: C, 49.48; H, 2.64; S, 12.09; Br, 30.03.

2-Ethenyl-5-benzoylthiophene (11). Compound 11 was obtained from the coupling of 5-bromo-2-thienyl phenyl ketone and tributylethenylstannane in 60.3% yield by the same procedure used for 9; yellow glue. ^{1}H NMR ($CDCl_3$): δ 7.81 (m, 2 H), 7.54 (m, 1 H), 7.48 (m, 3 H), 6.98 (d, J = 3.9 Hz), 6.79 (dd, J = 17.4, 10.8 Hz, 1 H, ArHC=C), 5.77 (d, J = 17.4 Hz, 1 H, *cis*-H_2C=CAr), 5.33 (d, J = 10.8 Hz, 1 H, *trans*-H_2C=CAr). ^{13}C NMR: δ 187.9, 151.1, 141.6, 137.9, 135.3, 132.1, 129.4, 128.9, 128.3, 126.3, 126.2, 117.3. IR (film, KBr, cm^{-1}): 3061 (m), 1657 (s, C=O), 1603 (s), 1446 (m), 1317 (s), 1278 (s), 923 (s, -C=C). Anal. Calcd for $C_{13}H_{10}OS$: C, 72.87; H, 4.70; S, 14.96. Found: C, 72.81; H, 4.70; S, 14.97.

4-Ethenylphenyl 2-Thienyl Ketone (12). Compound 12 was synthesized from the coupling of 4-bromophenyl 2-thienyl ketone and tributylethenylstannane in 78.8% yield by the procedure described above for 9: white crystals; mp 53 °C. ^{1}H NMR ($CDCl_3$): δ 7.83 (d, J = 6.7 Hz, 2 H), 7.70 (dd, J = 4.9, 1.1 Hz, 1 H), 7.63 (dd, J = 3.8, 1.1 Hz, 1 H), 7.50 (d, J = 6.7 Hz, 2 H), 7.15 (dd, J = 4.9, 3.8 Hz, 1 H), 6.77 (dd, J = 17.6, 10.9 Hz, 1 H, ArCH=C), 5.87 (d, J = 17.6 Hz, 1 H, *cis*-H_2=CAr), 5.39 (d, J = 10.9 Hz, 1 H, *trans*-H_2C=CAr). This spectrum was consistent with the previously published data.[19]

4-Ethenyl-2-fluorobiphenyl (13). To a solution of 4-bromo-2-fluorobiphenyl (2 g, 8 mmol), tetrakis(triphenylphosphine)palladium(0) (185 mg, 0.16 mmol), and a few crystals of *p*-methoxyphenol in toluene (20 mL) was added vinyltributyltin (2.80 g, 8.77 mmol). The yellow solution was heated at reflux for 26 h (1% of the catalyst was added after 4 h). The solution was cooled to room temperature, and ammonium hydroxide solution (30 mL of 10%) was added. The resulting mixture was filtered and the organic layer diluted with 200 mL of diethyl ether and worked up as described for 9. Purification by flash chromatography (silica gel, eluent hexane) gave 13 (1.2 g, 74%) as a colorless liquid. ^{1}H NMR ($CDCl_3$): δ 7.67–7.25 (m, 8 H), 6.70 (dd, J = 17.6, 10.8 Hz, 1 H, ArCH=C), 5.82 (d, J = 17.6 Hz, 1 H, *cis*-H_2C=CAr), 5.32 (d, J = 10.8 Hz, 1 H, *trans*-H_2C=CAr). Anal. Calcd for $C_{14}H_{11}F$: C, 84.81; H, 5.60. Found: C, 84.95; H, 5.63.

***N*-(4-Bromophenyl)phthalimide.** To a suspension of pulverized *p*-bromoaniline (9.3 g, 53 mmol) and phthalic anhydride (7.65 g, 50 mmol) in toluene (60 mL) was added acetic acid (3 mL). The resulting mixture was heated at reflux, which became a clear solution, for 10 h. When the solution was cooled to room temperature, the product crystallized in needle form. The solid was filtered, washed with benzene, and dissolved in chloroform to remove unreacted anhydride. After removal of solvent, the product was dried under reduced pressure to give a white powder (10.2 g, 67.5%); mp 204–205 °C. ^{1}H NMR: δ 7.93 (m, 2 H), 7.77 (m, 2 H), 7.61 (m, 2 H), 7.33 (m, 2 H). ^{13}C NMR: δ 166.6, 134.3, 132.0, 131.4, 130.5, 128.1, 127.7, 123.6, 121.6. Anal. Calcd for $C_{14}H_8O_2NBr$: C, 55.66; H, 2.71; N, 4.64; Br, 26.45. Found: 55.58, H, 2.71; N, 4.57; Br, 26.52.

4-(1,3-Dihydro-1-oxo-2*H*-isoindol-2-yl)-1-bromobenzene. To tetrahydrofuran (50 mL) was added lithium aluminum hydride (188 mg, 4.96 mmol). The mixture was heated to reflux for 30 min. After the mixture was cooled to −55 °C, *N*-(4-bromophenyl)phthalimide (3 g, 9.92 mmol) dissolved in tetrahydrofuran (150 mL) was added at a rate to maintain the temperature at −55 °C. The mixture was warmed to 0 °C over 3 h. Then, when the suspension was cooled to −15 °C, hydrochloric acid (20 mL, 6 N) was added dropwise over 20 min. Once the cold bath had been removed, stirring was continued for 30 min. The aqueous layer was extracted with diethyl ether, and the combined organic layers were dried over anhydrous sodium sulfate. After evaporation of the solvent, the crude product was recrystallized in diethyl ether to give the product as a white solid (2 g, 70%). ^{1}H NMR (THF-d_8): δ 7.99 (d, J = 9.1 Hz, 2 H), 7.77 (d, J = 8.3 Hz, 1 H), 7.66 (m, 2 H), 7.53–7.50 (m, 3 H), 6.39 (d, J = 11.4 Hz, 1 H, $ArCH_2N$), 5.84 (d, J = 11.4 Hz, 1 H, $ArCH_2N$). Anal. Calcd for $C_{14}H_{10}NOBr$: C, 58.33; H, 3.50. Found: C, 58.41; H, 3.52.

4-(1,3-Dihydro-1-oxo-2*H*-isoindol-2-yl)styrene (14). To a solution of 4-(1,3-dihydro-1-oxo-2*H*-isoindol-2-yl)-1-bromobenzene (1.50 g, 5.20 mmol) and tetrakis(triphenylphosphine)palladium(0) (120 mg, 0.010 mmol) in tetrahydrofuran (20 mL) was added vinyltributyltin (1.81 g, 5.72 mmol). The solution was heated at reflux for 2 h and then cooled to room temperature and taken into diethyl ether. The solution was washed three times with a saturated solution of potassium fluoride. Then the organic layer was diluted with a 1:1 tetrahydrofuran/diethyl ether solution (200 mL), washed with sodium hydrogen carbonate and water, and dried over magnesium sulfate. Removal of the solvent, followed by flash chromatography (50% ethyl acetate/50% hexane), allowed reocvery of the product 14 (0.45 g, 37%) as a white solid. ^{1}H NMR (THF-d_8): δ 7.98 (d, J = 9.0 Hz, 2 H), 7.78 (dt, J = 7.5, 1.0 Hz, 1 H), 7.65 (m, 2 H), 7.53–7.50 (m, 3 H), 6.71 (dd, J = 17.6, 10.9 Hz, 1 H, ArCH=C), 6.39 (d, J = 11.3 Hz, 1 H, $ArCH_2N$), 5.78 (d, J = 11.3 Hz, 1 H, $ArCH_2N$), 5.72 (dd, J = 17.6, 1.1 Hz, 1 H, *trans*-ArC=CH_2), 5.14 (dd, J = 10.9, 1.1 Hz, 1 H, *cis*-ArC=CH_2).

Typical Hydroformylation Procedure. A 125-mL Parr Monel autoclave was charged with platinum catalyst (0.02 mmol), anhydrous stannous chloride (0.03 mmol), and *p*-methoxyphenol (a few crystals). The autoclave was brought into a nitrogen-filled glovebox and charged with the olefinic substrate (4–8 mmol) dissolved in an appropriate solvent (3 mL). The autoclave was sealed, pressurized, and vented three times with the synthesis gas mixture (1:1 H_2/CO) and then pressurized (usually to 2400 psi at room temperature) and heated with stirring in an oil bath at 60 °C. At the end of the reaction, the autoclave was cooled in an ice bath, the pressure was vented, and the products were isolated by the following procedures: (A) The solvent was removed by distillation. The mixture of product was vacuum-transferred from catalyst and analyzed by ^{1}H NMR spectroscopy to determine the conversion and the product composition. The ee's were determined by ^{1}H NMR spectroscopy with use of Eu(hfc)$_3$ chiral shift reagent. (B) When the product boiling point was high, diethyl ether (20 mL) was added to the reaction mixture. The catalyst was precipitated and removed by filtration over Celite. After evaporation of solvent, the mixture of the products was submitted to the ^{1}H NMR analysis. The conversions were calculated on the basis of the integrations of the starting material and product signals. The branched to normal ratios were estimated by the integrations of aldehyde proton signals (9.6–9.7 ppm for the branched and 9.7–9.8 ppm for the normal).

Typical Experiments for the Determination of Enantiomeric Excess of Aldehydes. The product mixture (~0.1 mL) containing 2-arylpropanal was diluted with deuteriochloroform and placed in an NMR tube. Eu(hfc)$_3$ was added in small portions until a neat splitting of the peak of the formyl proton (doublet at 9.6–9.7 ppm) was observed in the ^{1}H NMR spectrum. The integration of the two peaks (in the range from 11 to 20 ppm; the *S* enantiomer's peak is shifted more downfield than that of the *R* species) was used to calculate the enantiomeric excess according to the equation % ee = 100[(*S* − *R*)/(*S* + *R*)]. The accuracy by this method is ±3%.

General Procedure for Hydroformylation in the Presence of Triethyl Orthoformate. The procedure was identical with that for hydroformylation described above. Triethyl orthoformate (4 equiv to the substrate) in *o*-dichlorobenzene (3 mL) was used as solvent. At the end of the reaction, the solvent was removed by vacuum distillation and the resulting mixture was treated with diethyl ether. The precipitated catalyst was filtered over Celite. After removal of ether, the reaction mixture was analyzed by ^{1}H NMR spectroscopy to determine the conversion and the product composition. The ee's were determined directly on the acetal (or on the aldehyde obtained by hydrolysis with pyridinium *p*-toluenesulfonate in acetone[16c]) by ^{1}H NMR spectroscopy with use of Eu(hfc)$_3$ chiral shift reagent.

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