rates of conversion of 1 were calculated on this basis.

Kinetic Study of the Ni(cod)$_2$-Catalyzed Reaction of 1 and Methyl Acrylate. This experiment is illustrative for kinetic measurements of Ni(0)-catalyzed reaction of bicyclobutanes and methyl acrylate at 25 °C. Twelve 20-mL reaction ampules were equipped with serum caps and flushed with argon for 2.5 min. Into each tube was placed Ni(cod)$_2$ (14.3 ● 0.3 mg, 5.18×10^{-2} mmol), and the vessel was again flushed with argon for 2 min at −50 °C. To this were added methyl acrylate (5.0 mL) and a solution (5 mL) of 1 (7.10×10^{-2} M) and cyclohexane (5.87×10^{-2} M) in methyl acrylate by using hypodermic syringes. The reaction tube was flushed with argon for 1 min at −50 °C and sealed. The reaction vessels were placed in a constant-temperature bath kept at 25.0 ± 0.1 °C for a time and shaked vigorously for 1.5 min to dissolve the catalysts. The resulting orange-yellow solutions were kept at this temperature for a specified time and then cooled to −60 °C. After each tube was opened, bis(diphenylphosphino)-ethane (diphos; 40 mg, 0.10 mmol) was added to the mixture to quench the reaction. It was then exposed to air at −30 °C for 2 h, and the pale yellow solution was subjected to GLC analysis (column F, 35 °C, 15 mL/min, t_R = 3.8 (1) and 15.2 min (cyclohexane)) to determine the quantity of the unchanged 1. The rate constant calculated on the basis of the experiments is given in Table I.

Kinetic measurements of Ni(cod)$_2$-catalyzed reaction of 1-methylbicyclo[1.1.0]butane (**35**) and methyl acrylate were carried out in a similar manner by using initial bicyclobutane and catalyst concentrations of 6.05×10^{-2} and 5.25×10^{-3} M, respectively. The quantity of the unreacted **35** was determined by GLC (column F, 35 °C, t_R = 5.1 (**35**) and 15.0 min (cyclohexane)). For the trimethyl derivative **7**, lower concentrations of **7** (2.24×10^{-2} M) and the catalyst (2.65×10^{-3} M) were used because of the high reaction rate. Methyl laurate was added after the workup as a GLC standard (column G, 130 °C, t_R = 14.3 (**8**), 15.3 (**9**), and 24.3 min (methyl laurate)). Relatively high initial concentrations were employed for less reactive 1-(carbomethoxy)bicyclo[1.1.0]butane (**36**; 6.00×10^{-2} M, and a catalyst concentration of 1.41×10^{-2} M) and 1-(carbomethoxy)-3-methylbicyclo[1.1.0]butane (**37**; 6.37×10^{-2} M, and a catalyst concentration of 1.43×10^{-2} M). GLC analysis (column H, 65 °C) of **36**: t_R = 5.4 (methyl caproate), 13.3 min (**36**). GLC analysis (column H, 65 °C) of **37**: t_R = 7.6 (methyl caproate), 17.4 min (**37**).

Acknowledgment. The authors are indebted to the Ministry of Education of the Japanese Government for support of this work through Grants 303023 and 911511. They also acknowledge partial financial support by the Matsunaga Science Foundation, the Takeda Science Foundation, the Kurata Science Foundation, and the Ito Science Foundation.

Registry No. **1**, 157-33-5; **2**, 34529-09-4; **3**, 34529-10-7; **4**, 77462-53-4; **5**, 77462-54-5; **7**, 28569-96-2; **8**, 34529-12-9; **9**, 34561-59-6; **10**, 34058-24-7; **11**, 77462-55-6; **12**, 77462-56-7; **16**, 77462-57-8; **17**, 77519-47-2; **18**, 34529-13-0; **19**, 34529-14-1; **20**, 34529-15-2; **21**, 34529-16-3; **22**, 77462-58-9; **23**, 77519-48-3; **24**, 77519-49-4; **25**, 22664-28-4; **26**, 29569-87-7; **35**, 30494-08-7; **36**, 4935-01-7; **37**, 30493-92-6; methyl acrylate, 96-33-3; methyl (*Z*)-β-deuterioacrylate, 18910-51-5; dimethyl fumarate, 624-49-7; dimethyl 3,4-bis(carbomethoxy)adipate, 24261-13-0; dimethyl maleate, 624-48-6; Ni(an)$_2$, 12266-58-9; Ni(cod)$_2$, 1295-35-8.

Supplementary Material Available: NMR spectra for compounds **2**, **3**, **8**, **9**, **11**, **12**, **16**, and **17** taken with or without added Eu(fod)$_3$ (4 pages). Ordering information is given on any current masthead page.

Synthesis of Functional Chelating Diphosphines Containing the Bis[2-(diphenylphosphino)ethyl]amino Moiety and the Use of These Materials in the Preparation of Water-Soluble Diphosphine Complexes of Transition Metals[1]

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Received March 19, 1981

Acylation of bis[2-(diphenylphosphino)ethyl]amine provides a flexible synthesis of functionalized chelating diphosphines. This reaction offers a route to diphosphine complexes of transition metals having a wide range of structures and physical properties and especially to water-soluble complexes. The aqueous solubility of the free ligands and of the complexes prepared from them depend on the ligand, on the metal, and on other materials (especially surfactants) present in the solution. We describe typical preparations of ligands and outline the properties of their complexes with certain transition metals.

Homogeneous catalysis and asymmetric synthesis increasingly require complex organic structures incorporating ligands capable of coordinating a transition-metal center. In earlier papers,[2-4] we described a flexible synthesis of functionalized, water-soluble, chelating diphosphines and presented examples of applications of these materials. This paper provides experimental procedures for these syntheses and outlines factors affecting the properties of the resulting materials in aqueous solutions.

Results and Discussion

All syntheses are based on bis[2-(diphenylphosphino)-ethyl]amine 1 (Scheme I).[5] This compound, isolated as a crystalline, air-stable hydrochloride, can be acylated at

(1) Supported by the National Science Foundation (Grants 7711282CHE and 8012722-CHE). R.G.N. held a predoctoral traineeship from the National Cancer Institute (CA 09112 CT) and S.L.H. an HEW predoctoral fellowship.

(2) Wilson, M. E.; Whitesides, G. M. *J. Am. Chem. Soc.* **1978**, *100*, 306-307.

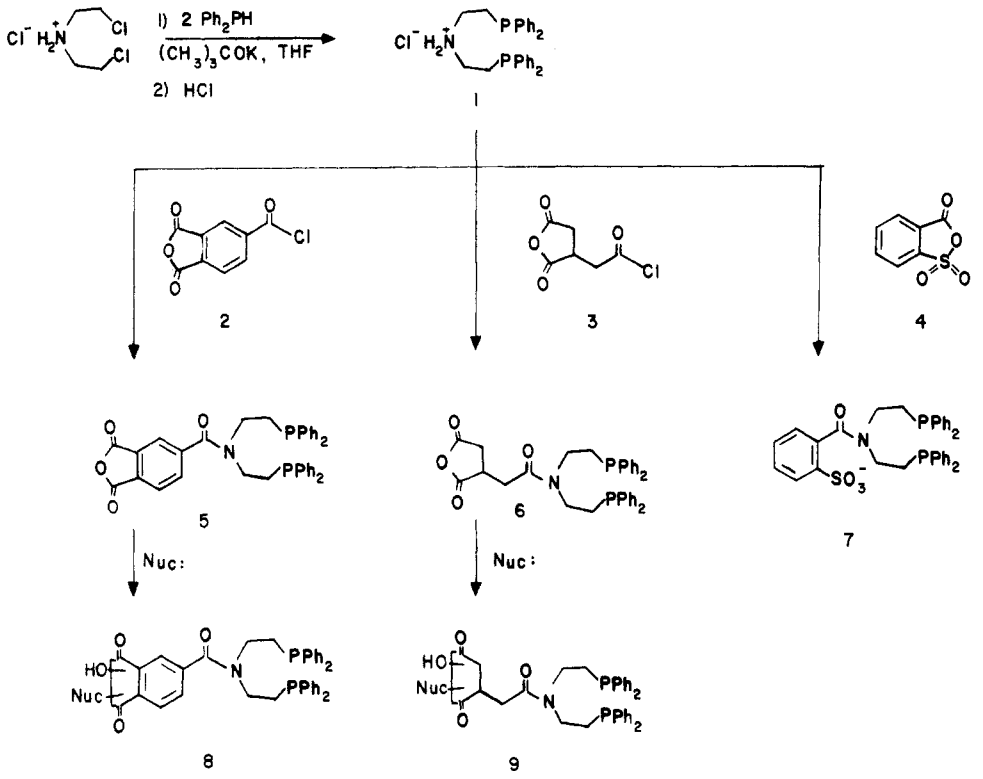
(3) Wilson, M. E.; Nuzzo, R. G.; Whitesides, G. M. *J. Am. Chem. Soc.* **1978**, *100*, 2269-2270.

(4) Nuzzo, R. G.; Feitler, D.; Whitesides, G. M. *J. Am. Chem. Soc.* **1979**, *101*, 3683-3685.

(5) Compound 1 was first prepared by: Sacconi, L.; Marassi, R. *J. Chem. Soc. A* **1968**, 2997-3002.

0022-3263/81/1946-2861$01.25/0

Scheme I. Preparation of Bis[2-(diphenylphosphino)ethyl]amine and Derivatives



nitrogen without competing reaction at phosphorus. The ability to functionalize nitrogen selectively in the presence of the phosphine centers is the basis for a method for the incorporation of 1 into complex organic structures.

The reactivity of 1 toward acid chlorides, anhydrides, isocyanates, alkyl chlorocarbonates, and *N*-hydroxysuccinimide (NHS) active esters is that expected for a sterically hindered, secondary amine. These reactions go to completion at ambient temperatures (the time necessary for reaction depends both on the coupling group employed and on the nature of additional bases present in solution; see Experimental Section). Little or no competing reactivity is observed for the phosphine groups. Only in the cases of materials capable of reactions other than acylation do competing reactions become important; special care must be exercised in using these coupling agents. Acryloyl chloride can be used to acylate 1 under the conditions described below. All attempts to acylate 1 with maleic anhydride gave only air-sensitive, red gums: although some amide formation is apparent in the IR spectra of the reaction mixtures, we have been unable to isolate a useful derivative of 1 from these mixtures. Soft electrophiles (sulfonyl chlorides, cyanogen bromide, phosphoryl halides) also seem not to demonstrate the selectivity toward nitrogen required to achieve useful functionalization.

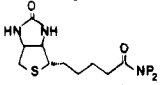
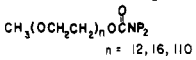
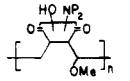
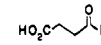
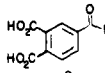
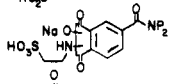
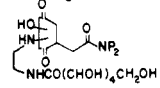
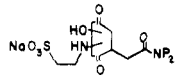
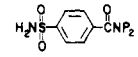
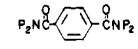
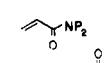
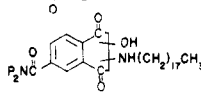
The most useful synthetic strategy to emerge from this work used a diacylating reagent [trimellitic anhydride acid chloride (2) or tricarballylic anhydride acid chloride (3)] to couple 1 to another amine-containing group which conferred the physical properties required. Thus, for example, reaction of 1 with 2 proceeds cleanly at the more reactive acid chloride site and generates 5. The effect of this transformation is to convert 1 (in which functionalization is based on the difference between the nucleophilicity of the nitrogen and phosphorus centers) to 5 (in which functionalization can be based on the electrophilic anhydride group, without competition from the phosphine centers). Compound 5 (and the analogous 6) is not isolated but is allowed to react directly with other nucleophilic groups. These groups can be designed to confer the desired physical properties to the final complex.

An alternative strategy, direct acylation of 1 (e.g., 1 → 7) is also successful. Although this procedure appears simpler, in practice we have found it to be less useful than 1 → 5 → 8 or 1 → 6 → 9 as a method for generating functionalized (especially water soluble) diphosphines. The number of readily available reactive species of the type represented by 4 (that is, species which react selectively with nitrogen in the presence of phosphorus and which introduce highly polar groups) is small. By contrast, 2 is commercially available and inexpensive, and 5 reacts with a wide range of amines. In applications in which water solubility is not an important objective, however, direct acylation can provide a convenient and useful methodology (vide infra).

Table I lists the substances prepared, the coupling agents used in their preparation, and the yields in which they were obtained. The purification and characterization of these complexes proved difficult. Many have surfactant properties; their polar functionalities are hydrated or solvated to varying extents; they are noncrystalline. Characterization often was based primarily on IR and ^{31}P and ^{1}H NMR spectroscopies and on the physical properties (water solubility, ability to complex metals) of the compounds. Only compounds 10, 12, 13, 15, 17, 21, and 22 were isolated in a form sufficiently pure to give acceptable elemental analyses. Analytical data for others are included in the Experimental Section, as an aid in judging purity. Yields given in parentheses in Table I are for *crude* compounds and are upper limits.

The proton NMR spectra of a number of the water-soluble derivatives (17–20) in aqueous solution show broad, complex resonances, suggesting micelle formation, although the presence of aggregated structures was not rigorously established. The ^{31}P NMR spectra of the free ligands are usually characterized by two lines centered at ~1.5 ppm. Control experiments demonstrated that the splitting occurs on acylation; we assume that it reflects slow rotation about

Table I. Functionalized Diphosphines from 1 [$NP_2 \equiv N(CH_2CH_2PPh_2)_2$]

	compd	reacting group	yield,[a] %
7			(98)
10		RCONHS	84
11	 n = 12, 16, 110	ROCOCl	(90)
12		RNCO	93
13		Anhydride	(85)
14		Anhydride	(95)
15	CH_3CONP_2	RCOCl	95
16		Anhydride	(95)
17		5	98
18		5	(85)
19		6	(70)
20		6	(50)
21		RCOCl	42
22		RCOCl	70
23	$Ph_2P(CH_2CH_2O)_{12}Me$	RCl	(30)
24		RCOCl	(90)
25		5	(95)

[a] Yields given in parentheses are for crude compounds and are upper limits.

the amide bond. Examination of the ^{31}P NMR data also showed that typical preparations of ligands contained <5% contamination by phosphine oxides. The physical properties of most of these compounds made purification difficult, and great care was required to prevent oxidation during manipulation or in syntheses. For similar reasons, all reagents were purified carefully prior to use. In most instances, impurities do not affect the performance of these materials as ligands for transition metals.

Solubility of Metal Complexes and Ligands. As might be expected, the nature of the metal coordinated to a particular ligand strongly influences the solubility of the final complex. For example, 11 (n = 16) forms a stable though sparingly soluble platinum(II) dichloride complex. When coordinated to a rhodium(I) norbornadiene cation, 11·Rh(Nbd)$^+$, a much more soluble material is obtained. This same ligand in the red-brown complex 11·$NiCl_2$ decomposes to an insoluble white wax on contact with water. Similar results were also observed with nickel complexes having 7 as a ligand.[6,7] Of the several metals examined in this study, the cationic rhodium complexes were the most soluble in water.

The aqueous solubility of the free ligands seems to follow expected trends. The doubly charged species 17, 18, and 20 are much more soluble than singly charged materials such as 7, 16, and 19. The neutral polyethylene glycol system 11 shows increasing solubility with increasing molecular weight: at n = 110 the material appears to be completely soluble. In this same series similar changes were noted in the solubility of 11·$PtCl_2$ complexes.

Homogeneous Catalysis by Cationic Rhodium Complexes. The Rh(I) complexes of several of these ligands have been shown to act as effective homogeneous hydrogenation catalysts in aqueous solution for a range of water-soluble substrates.[4] The data presented below expand upon earlier observations.[4]

In general, the most soluble complexes acted as the best catalysts. Catalysts that precipitated from solution (e.g., 16·Rh(I)) gave understandably low rates of hydrogenation with α-acetamidoacrylic acid (turnover number = TN < 5 mol of olefin reduced/mol of rhodium complex/h). Solubility is, however, not the only requirement for high activity since 11·Rh(I) (n = 16, 110) was a poor catalyst despite its reasonably high solubility in water. The complex 7·Rh(I) was sparingly soluble and had low activity. Since 7 is extremely soluble, we infer that coordination of the sulfonic acid group to rhodium results in this decrease in solubility and activity.[8] In our hands, rhodium complexes of 17 and 18 formed the catalysts having the highest activity. For several reasons, we believe that the best material for most applications in homogeneous hydrogenation is 17·Rh(I). First, unlike most of these ligands, 17 is highly crystalline and is easily purified. Second, the protonated form of the acid is soluble in a wide range of organic solvents, a feature attractive for catalyst preparation. Dissolution in water is easily accomplished by transferring the catalyst preparation in a water-miscible organic solvent such as acetone, under argon, into the reaction media. In this manner, the number of manipulations necessary to prepare the catalyst can be minimized. Third, the synthesis of 17 is simple and can be easily carried out on practical scales: routine preparations gave more than 10 g of purified material in nearly quantitative yield. Fourth, hydrogenation rates with 17·Rh(I) are the highest observed for any derivative of 1: for example, TNs > 275 h^{-1} (P_{H_2} = 32 psi; ~4000 turnovers of Rh(I), 100% reduction) were found with α-acetamidoacrylic acid as a substrate.

An interesting effect is observed when hydrogenations using 16·Rh(I), a poor catalyst, are carried out in aqueous solutions containing 0.1% by weight sodium dodecyl sulfate. Under these conditions, useful rates (TN = 120 h^{-1} for α-acetamidoacrylic acid) were observed. This catalyst system was also found to be extremely stable, maintaining most of its catalytic activity even in the presence of low concentrations of substrate. At the completion of the reduction (total turnover number of Rh(I) >4000, 100% reduction) bright yellow and completely homogeneous solutions were obtained. Thus, it appears that 16·Rh(I) is incorporated into SDS micelles and that

(6) An exception was found for 11·$NiCl_2$ (n = 110). This material forms stable red solutions in water. The cause of this effect is not understood.

(7) Similar behavior was also observed with both $NiBr_2$ and NiI_2 complexes of a number of the ligands.

(8) Related effects have been observed with sulfonated triphenylphosphine complexes of Rh(I). See: Borowski, A. F.; Cole-Hamilton, D. J.; Wilkinson, G. *Nouv. J. Chim.* **1978**, *2*, 137–144.

this incorporation somehow stabilizes the complex.[9]

Rhodium complexes of **10** and **21**, themselves insoluble in water, dissolve easily in aqueous solutions containing stoichiometric amounts of avidin[3] and carbonic anhydrase,[10] respectively. In these instances, solution reflects specific binding of the diphosphine to the protein.

The catalytic activities of the rhodium complexes of **17** and **25** are dramatically influenced by the presence of α-chymotrypsin and bovine serum albumin in solution. Although the nature of the interaction of these substrates with these proteins has not been established,[11] preliminary studies indicate that albumin may influence the substrate specificity of the rhodium catalyst. The conjugate of **10**·Rh(I) with avidin is an asymmetric catalyst for the hydrogenation of α-acetamidoacrylic acid. The other rhodium–protein conjugates do not exhibit enantioselectivity in the hydrogenation of this substrate.

Complex **13**·Rh(I) is a hydrogenation catalyst which is only sparingly soluble in aqueous solution. The hydrogenation of α-acetamidoacrylic acid with **13**·Rh(I) (TN = 1000) yielded modest enantiomeric excesses of 16–18% for (*S*)-*N*-acetylalanine. The turnover number and optical yield are very sensitive to solvent and the presence of triethylamine.

Conclusions

The procedures outlined in this paper provide a synthetically straightforward route for coupling a chelating diphosphine group to independently prepared functional moieties designed to impart other physical properties (water solubility, affinity for proteins). The most practical route seems to be **1** → **5** → **8**, primarily because **2**, unlike **3**, is commercially available. The principal disadvantages of chelates derived from **8** are that they have high molecular weights and may have low solubilities, they are difficult to purify (excepting **17**), and they are probably intrinsically heterogeneous since the incoming nucleophile almost certainly attacks both carbonyl groups of the anhydride moiety.

These water-soluble diphosphines complement materials such as sulfonated triphenylphosphine, whose application in homogeneous catalysis in aqueous solution has been the subject of several papers.[12] While direct comparisons between these systems are difficult, the difference in activity and stability between them are qualitatively those expected for unidentate and bidentate phosphine complexes.

Experimental Section

General Methods. IR spectra were obtained on a Perkin-Elmer Model 598 spectrometer. ^1H and $\{^1H\}^{31}P$ NMR spectra were recorded at 60.0 and 36.4 MHz on Varian T-60 and modified Bruker HX-90 spectrometers, respectively. Phosphorus chemical shifts are relative to external 85% H_3PO_4 (downfield positive). Mass spectra were recorded on a Varian Mat 44 spectrometer. THF and diethyl ether were distilled from sodium benzophenone dianion under argon. Methylene chloride and methanol (analytical grade) were used without further purification. Taurine, bis(2-chloroethyl)amine hydrochloride, tricarballylic acid, and trimellitic anhydride acid chloride were obtained from Aldrich. *o*-Sulfobenzoic anhydride was obtained from Eastman. D-Gluconic acid δ-lactone was obtained from Sigma. A generous sample of D-biotin was a gift of the Hoffmann-La Roche Co. Polyethylene glycol monomethyl ethers (mol wt ~500, 750, 5000) were purchased from Polyscience. Gantrez AN-119, a copolymer of methyl vinyl ether and maleic anhydride, was purchased by GAF. Pyridine was distilled from calcium hydride under argon. Triethylamine was purified by treatment with benzoic anhydride followed by distillation. Ethylenediamine was distilled under argon. Reagent grade *N*,*N*-dimethylaniline (Eastman) was used without purification.

Diphenylphosphine was prepared by literature procedures.[13]

Bis[2-(diphenylphosphino)ethyl]amine (1). Diphenylphosphine (28.0 mL, 29.6 g, 160 mmol) was added by syringe to a suspension of potassium *tert*-butoxide (28 g, 250 mmol) in 500 mL of dry THF under argon. The resulting deep red solution was stirred for 5 min and bis(2-chloroethyl)amine hydrochloride (14.3 g, 80 mmol) added as a coarse powder. **Caution**: *bis(2-chloroethyl)amine hydrochloride is carcinogenic and should be handled with care in a hood.*[14] The mixture was refluxed for 16 h,[15] poured into 800 mL of hexane, and washed in succession with 300-mL portions of 10% NaOH and saturated aqueous NaCl solutions. The hexane layer was separated, filtered, and stirred vigorously with 800 mL of 2 N aqueous HCl solution, giving a dense white precipitate of **1**·HCl. Recrystallization from 300 mL of boiling acetonitrile under argon gave a 90% yield (34.4 g) of fine white needles: mp 174.5–175.5 °C; ^1H NMR ($CDCl_3$) δ 2.3–3.3 (m, 8 H), 7.0–7.6 (m, 20 H), 9.9 (s, 2 H).

Anal. Calcd for $C_{28}H_{30}ClNP_2$: C, 70.42; H, 6.33; N, 2.93. Found: C, 70.30; H, 6.27; N, 2.90.

Preparation of Compound 7. In a 25-mL flask equipped with a stirring bar were placed 0.772 g (4.19 mmol) of *o*-sulfobenzoic anhydride and 2.00 g (4.19 mmol) of **1**·HCl. The system was capped with a serum stopper and flushed with argon. A solution of 3.5 mL of triethylamine in 30.0 mL of dry THF was added by syringe. The reaction was stirred for 24 h at ambient temperature, cooled to ~−5 °C, and filtered, and the separated organic phase was evaporated under reduced pressure. Drying in vacuo (0.05 torr) for 18 h gave 3.10 g (100%, calculated for the triethylammonium salt) of a hygroscopic, solid foam: IR (neat) 1630 (s), 1235 (s) cm^{-1}. This material was dissolved in 20 mL of MeOH, the solution was cooled to 0 °C, and 2.1 mL of 2.0 M NaOH was added dropwise with vigorous stirring. The solvent was removed under reduced pressure to give a solid white foam. Drying for 1 week at 0.05 torr at ambient temperature gave 2.7 g (98%) of a white hygroscopic powder: IR (neat) 1630 (s), 1235 (s) cm^{-1}; ^{31}P NMR (D_2O) −20.1 (s), −21.4 ppm.

Anal. Calcd for $C_{35}H_{32}NNaO_4P_2S$: C, 64.90; H, 4.97; N, 2.16. Found: C, 63.28; H, 5.07; N, 2.00. Calcd for **7**·H_2O: C, 63.15; H, 5.14; N, 2.10.

***N*-Biotinoxysuccinimide** was prepared by literature procedures.[16]

***N*,*N*-Bis[2-(diphenylphosphino)ethyl]biotinamide (10).** *N*-Biotinoxysuccinimide (67 mg, 0.20 mmol), **1**·HCl (95 mg, 0.20 mmol), and triethylamine (80 mg, 0.80 mmol) were added to 3 mL of degassed DMF. The reaction mixture was stirred at ambient temperature for 60 h under argon, slowly diluted with 8 mL of degassed water, and cooled to 0 °C. The resulting white precipitate was separated by centrifugation, the solution decanted, and the remaining white waxy solid washed with 30 mL of water. Drying at reduced pressure (0.05 torr) gave 110 mg (83%) of **10**

(9) Under similar conditions, both $(Ph_3P)_3RhCl$ and (Diphos)Rh(Nbd)$^+PF_6^-$ were completely inactive as hydrogenation catalysts for α-acetamidoacrylic acid. Both complexes appear to be insoluble in aqueous SDS solutions.

(10) A typical preparation employed 5 mg of lyophilyzed protein and 0.5 μmol of catalyst dissolved in 6 mL of 0.1 M phosphate buffer (pH 7.0).

(11) No binding analyses of ligands **17** and **25** to albumin and chymotrypsin were performed. These two proteins were chosen for use in hydrogenation experiments because their natural substrates bear some resemblance to compounds **17** and **25**. Anionic benzene derivatives compete for thyroxine binding sites on serum albumin (Tabachnick, M.; Downs, F. J.; Giorgio, N. A., Jr. *Arch. Biochem. Biophys.* **1970**, *136* 467–479), and chymotrypsin exhibits strong affinity for hydrophobic and aromatic moieties (Blow, D. M. "The Enzymes"; Boyer, P., Ed., Academic Press: New York, 1973; Vol. 3, pp 189–205).

(12) Dror, Y.; Manassen, J. *J. Mol. Catal.* **1977**, *2*, 219–222.

(13) Ireland, R. E.; Wells, D. M. *Org. Synth.* **1977**, *56*, 44–48.

(14) "1978 Registry of Toxic Effects of Chemical Substances"; U.S. Department of Health, Education, and Welfare Publications: Cincinnati, OH, 1979; No. 79-100 (N105H), Entry No. IA0175000, p 452; Entry No. IA1225000 for **1**·HCl, p 452.

(15) The reaction is heterogeneous, and efficient agitation of solids is essential if longer reaction times are to be avoided. Loss of the red-orange color initially present provides a good visual indication of completion of the reaction.

(16) Bayer, E.; Wilchek, M. *Methods Enzymol.* **1974**, *34*, 265–267.

as a waxy solid: IR (Nujol) 1705, 1630 (s) cm^{-1}.

Anal. Calcd for $C_{38}H_{43}N_3O_2P_2S$: C, 68.35; H, 6.49; N, 6.29. Found: C, 68.34; H, 6.40; N, 5.99.

Preparation of Compounds 11 (n = 11, 16, 110). All of these materials were prepared by procedures analogous to that described below for n = 110. Triethylamine (0.28 mL, 2.0 mmol) and polyethylene glycol monomethyl ether (average mol wt 5000, 2.5 g, ~0.50 mmol) were dissolved in 10 mL of dry CH_2Cl_2 at −30 °C in a 100-mL flask fitted with a dry-ice condenser. Phosgene gas (13 mL, 0.54 mmol at ambient temperature) was added by syringe, and the reaction was allowed to warm to ambient temperature over a 30-min period. **Caution**: *phosgene is toxic and should be handled only in a good hood by using appropriate procedures.*[17] The dry-ice condenser was replaced with a cold water condenser, and argon was bubbled through the solution for 5 min to remove excess phosgene. To the reaction mixture was added 0.24 g (0.50 mmol) of 1·HCl as a coarse solid. After being stirred at ambient temperature for 1 h, the reaction mixture was diluted with 16 mL of THF, cooled to 0 °C, and filtered to remove precipitated triethylamine hydrochloride. Evaporation of the solution and drying at reduced pressure (0.05 torr) gave 2.80 g (100%) of a gummy white solid. The nature of this material precluded further purification; IR (Nujol) 1695 cm^{-1}.

Anal. Calcd for $C_{250}H_{471}NO_{112}P_2$: C, 56.19; H, 8.90; N, 0.26. Found: C, 55.70; H, 8.55; N, 0.34.

The procedures employed in the preparation of the analogous materials with n = 16 and n = 11 were comparable to those described above, and the data characterizing these preparations are as follows. For 11 (n = 16): yield 97%; IR 3450 (w), 1695 (s), 1435 (s) cm^{-1}. Anal. Calcd for $C_{62}H_{95}NO_{18}P_2$: C, 61.75; H, 7.96; N, 1.15. Found: C, 60.98; H, 8.39; N, 1.12. For 11 (n = 11): yield 100%; IR 3450 (m), 1695 (s), 1435 (s) cm^{-1}. Anal. Calcd for $C_{52}H_{75}NO_{13}P_2$: C, 63.59; H, 7.65; N, 1.45. Found: C, 62.87; H, 8.23; N, 1.37.

Preparation of Compound 12. Into an argon-flushed, 100-mL, round-bottomed flask equipped with a condenser and stirring bar was placed 0.50 g (1.1 mmol) of 1·HCl. A solution of 0.22 mL of triethylamine in 20 mL of CH_2Cl_2 was added by cannula, and 0.130 g (1.09 mmol) of phenyl isocyanate in 5 mL of CH_2Cl_2 was added by syringe dropwise with stirring. The reaction was stirred for 24 h at ambient temperature, diluted with 30 mL of CH_2Cl_2, and washed with 0.2 M HCl (2 × 10 mL) and saturated aqueous $NaHCO_3$ (1 × 10 mL), and the organic phase was separated. The solution was dried over $MgSO_4$ and evaporated under reduced pressure to give an off-white solid. Recrystallization from ethyl acetate/n-hexane gave 0.5 g (93%) of white needles: mp 117.5–118.5 °C; ^1H NMR ($CDCl_3$) δ 7.23 (m, 25 H), 6.1 (s, 1 H), 3.24 (m, 4 H); IR (neat) 3450 (m), 1660 (s) cm^{-1}.

Anal. Calcd for $C_{35}H_{34}N_2OP_2$: C, 74.99; H, 6.29; N, 5.00. Found: C, 74.69; H, 6.08; N, 4.98.

Preparation of Compound 13. To a slurry of 0.478 g (1.00 mmol) of 1·HCl in 10 mL of dry THF under argon at −5 °C was slowly added 0.89 mL of a 2.2 M solution of n-butyllithium in hexane. The solution was stirred for 5 min, and 0.182 g (1.00 mmol) of D-camphoric anhydride was added to it as a solid with stirring. The reaction mixture was gradually allowed to warm to ambient temperature. After the mixture was stirred overnight, the solvent was removed under reduced pressure, the solids were redissolved in 50 mL of CH_2Cl_2, and the solution thus obtained was washed with portions (3 × 50 mL) of 2 M HCl. The organic phase was separated and dried over Na_2SO_4, and the solvent was evaporated under reduced pressure to give 0.53 g of a solidified, pale yellow foam: IR (neat) 1700 (s), 1635 (s) cm^{-1}; $[\alpha]^{25}_D$ 3.5° (c 1, EtOH).

Anal. Calcd for $C_{38}H_{43}NO_3P_2$: C, 73.18; H, 6.95; N, 2.25. Found: C, 70.75; H, 6.68; N, 2.14.

Preparation of Compound 14. The following is a typical preparation. In a 25-mL flask, under argon, were placed 0.126 g (0.792 mequiv) of Gantrez AN-119 and 0.096 g (0.200 mmol) of 1·HCl. To these materials was added a solution of 60 μL of triethylamine in 5 mL of acetonitrile. The reaction was stirred vigorously. After 1 h a pink gum began to precipitate. The reaction was stirred for an additional 3 h, by which time a significant quantity of solid had precipitated. Analysis of an aliquot of the solution by ^{31}P NMR spectroscopy indicated that little of the 1 initially present remained in solution. The reaction was diluted with 5 mL of acetonitrile and 0.5 mL of H_2O and acidified with 3 drops of concentrated HCl. The mixture was brought to reflux under argon for 30 min (sufficient to hydrolyze the remaining anhydride groups), and the resulting white solid was collected by filtration and dried under reduced pressure (0.05 torr) to give 0.21 g (95%) of product: IR (neat) 1705 (vs), 1625 (s) cm^{-1}. This material is extremely hygroscopic.

Anal. Found: C, 50.60; H, 5.63; N, 1.45; P, 4.21.

Preparation of Compound 15. In a 50-mL flask were placed 0.478 g (1.00 mmol) of 1·HCl, 0.65 mL of triethylamine, and 20 mL of CH_2Cl_2 under argon. To this mixture was added by syringe a solution of 76 μL (1.1 mmol, 83 mg) of acetyl chloride in 3 mL of CH_2Cl_2, and the reaction was stirred for 10 h at ambient temperature. The reaction was worked up by washing first with portions (2 × 10 mL) of 2 M HCl followed by 0.1 M NaOH (1 × 10 mL). Drying the separated organic phase over Na_2SO_4 and evaporating the solvent under reduced pressure gave a clear oil. The oil was dried under reduced pressure (0.05 torr) for several weeks at ambient temperature to afford 0.47 g (97%) of a solidified white glass: IR (neat) 1640 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.7 (s, 20 H), 3.5 (m, 4 H), 2.45 (m, 4 H), 1.9 (s, 3 H).

Anal. Calcd for $C_{30}H_{31}NOP_2$: C, 74.58; H, 6.47; N, 2.90. Found: C, 74.41; H, 6.32; N, 2.87.

Preparation of Compound 16. Into a 50-mL flask were weighed 0.24 g (0.50 mmol) of 1·HCl and 0.50 g (0.50 mmol) of succinic anhydride. The system was sealed with a rubber serum stopper and flushed thoroughly with argon. To the flask were added 30 mL of THF and 0.20 mL of Et_3N by syringe, and the reaction was stirred overnight at ambient temperature. The mixture was poured into 50 mL of 1.0 M HCl and extracted with portions (3 × 15 mL) of CH_2Cl_2, the organic layer was dried over $MgSO_4$, and the volatiles were removed under reduced pressure (0.05 mm) to give 0.26 g (96%) of a clear gum. Attempts to purify this material further by low-temperature recrystallization were unsuccessful: IR (neat) 3500–2500 (br, s), 1715 (s), 1635 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.4 (s, 20 H), 3.8–2.1 (complex m, 12 H).

Anal. Calcd for $C_{32}H_{33}NO_3P_2$: C, 70.97; H, 6.14; N, 2.59. Found: C, 68.18; H, 6.60; N, 2.19.

Preparation of *N*,*N*-Bis[2-(diphenylphosphino)ethyl]trimellitamide 3,4-Anhydride (5). Into a 250-mL, three-necked, round-bottomed flask equipped with a stirring bar and addition funnel was placed 1.83 g (8.69 mmol) of trimellitic anhydride acid chloride, and the system was flushed thoroughly with argon. To the flask was transferred 150 mL of dry, degassed THF containing 8.0 mL of pyridine. The system was cooled to 0 °C, and a solution of 4.15 g (8.69 mmol) of 1·HCl dissolved in 50 mL of THF was added dropwise with vigorous stirring over a period of ~2 h. The reaction was allowed to warm slowly to ambient temperature, stirred for an additional 4 h, and cooled to −10 °C, and the precipitated solids were removed by rapid filtration under argon. The volatiles were removed under reduced pressure. Drying in vacuo (0.05 torr) gave a quantitative yield of the anhydride amide 5: IR (CH_2Cl_2) 1855 (m), 1780 (s), 1640 (s) cm^{-1}; NMR ($CDCl_3$) δ 7.3 (m, 23 H), 3.5 (br m, 4 H), 2.4 (br m, 4 H). This material was used directly in the preparations of 17 and 18 that follow and was stored under vacuum.

Preparation of Compound 17. In an argon flushed, 250-mL Erlenmeyer flask containing 100 mL of distilled water was suspended 3.00 g (4.90 mmol) of 5, and 10.0 mL of 1.0 M NaOH was added by syringe. The reaction was stirred vigorously for 1 h, before addition of 50 mL of n-pentane and acidification to an aqueous phase pH of ~1.0 by addition of concentrated HCl to the rapidly stirred mixture. The dense, white, microcrystalline precipitate was collected by filtration and dried under reduced pressure (0.05 torr) to give 3.12 g (101%) of product: IR (neat) 3500–2500 (s), 1710 (vs), 1630 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.3 (m, 23 H), 11.1 (s, 2 H), 3.5 (m, 4 H), 2.4 (m, 4 H); $\{^1H\}$ ^{31}P NMR (H_2O, pH ~8.0) −19.1 (s), −21.1 (s) ppm.

(17) Phosgene is highly toxic and can cause severe pulmonary edema. Lethal doses may be inhaled without initially noticing irritation of tissues and eyes during exposure. A hood with adequate ventilation must be used in all procedures. Excess reagent in solution can be destroyed by using aqueous KOH.

(18) Malachowski, R. *Bull. Int. Acad. Pol. Sci. Lett, Cl. Sci. Math. Nat., Ser. A* **1929**, 265–273.

Anal. Calcd for $C_{37}H_{33}N_1O_5P_2$: C, 70.13; H, 5.25; N, 2.21. Found: C, 69.89; H, 5.31; N, 2.32. This material was extremely hygroscopic and was stored under vacuum to prevent hydration.

Sodium Taurinate. In a 1-L flask was suspended 55.0 g (440 mmol) of taurine in 550 mL of absolute methanol. To the vigorously stirred mixture was slowly added 23.0 g (426 mmol) of solid sodium methoxide. After the mixture was stirred at ambient temperature for 24 h, the residual solids were removed by filtration, and the solvent was removed under reduced pressure to give the product in quantitative yield.

Preparation of Compound 18. In a 100-mL flask, under an argon stream, were placed 1.00 g (1.63 mmol) of **5**, a stirring bar, and several glass beads. Into this mixture, with vigorous stirring, was poured a solution of 1.00 g (6.80 mmol) of sodium taurinate dissolved in 30 mL of degassed, absolute methanol. The sudsy solution and white precipitate that formed were stirred for 20 h at ambient temperature. The methanol was removed under reduced pressure, and the white solids produced were extracted with portions (6 × 100 mL) of $CHCl_3$ under argon. The combined organic phases were filtered and the volatiles removed under reduced pressure to give 1.2 g (95%) of **18**: IR (CH_2Cl_2) 1712 (w), 1625 (vs), 1595 (vs), 1200 (vs), 1050 (s) cm^{-1}. The ^1H NMR spectra were difficult to interpret due to extremely broad line widths found in all solvents in which **6** dissolved. In general, aromatic and aliphatic resonances showing little structure are observed. In D_2O low levels of taurine are observed: ^{31}P NMR (H_2O) −21.4 (s), −23.1 (s) ppm.

Anal. Calcd for $C_{39}H_{36}N_2Na_2O_7P_2S_1$: C, 59.69; H, 4.62; N, 3.57. The data suggest sodium taurinate (<0.2 molar equiv) to be the major impurity present [Found: C, 58.17; H, 4.51; N, 3.87].

Tricarballylic α,β-Anhydride. In a 500-mL flask protected from atmospheric moisture was placed 76.6 g (0.435 mmol) of tricarballylic acid. Acetic anhydride (41.0 mL, 44.4 g, 0.435 mmol) was added, with stirring, in one portion. The reaction mixture was heated to 45 °C and became homogeneous after 20 min at this temperature. After 1 h the reaction solidified. A 150-mL portion of glacial acetic acid was added and the mixture heated to 65 °C for 1 h to give a homogeneous solution. Slow cooling to ambient temperature gave a copious, white, microcrystalline powder. The solid was collected by filtration, washed with portions (4 × 100 mL) of ether, and dried in vacuo to give 60.4 g (87%) of product: mp 133–135 °C (lit.[18] mp 133–134 °C); IR (Fluorolube) 1855 (m), 1780 (vs), 1700 (s) cm^{-1}.

Tricarballylic α,β-Anhydride Acid Chloride. In a 100-mL flask containing 50 mL of thionyl chloride was suspended 11.1 g (70.2 mmol) of tricarballylic α,β-anhydride under argon. To the gently stirred mixture was added 6 drops of dimethylformamide, and the reaction was heated to 45 °C. A vigorous reaction ensued, and heating was applied intermittently to maintain evolution of gasses over an ~2-h period, giving a homogeneous yellow solution. The excess thionyl chloride was removed under reduced pressure, and portions (3 × 30 mL) of CH_2Cl_2 were sequentially added and evaporated under reduced pressure to complete its removal. The white paste obtained was recrystallized twice from a minimum of hot CH_2Cl_2 to give 7.5 g (61%) of white crystals. This compound was stored in a desiccator at −10 °C when not in use: IR (CH_2Cl_2) 1865 (m), 1790 (vs) with a shoulder at 1780 (s) cm^{-1}; mass spectrum, m/e 41 (M^+ − Cl, 2 CO, CO_2, base peak), 141 (M^+ − Cl), 132 (M^+ − CO_2), 113, 99, 76, 69, 63, 55 (no molecular ion is observed).

***N*-(2-Aminoethyl)gluconamide.** Into a 100-mL Erlenmeyer flask containing 55 mL of ethylenediamine was added 2.50 g (14.0 mmol) of D-glucono-δ-lactone with vigorous stirring, and the reaction mixture was flushed quickly with argon. An exothermic reaction ensued, and eventually a homogeneous solution was formed. After stirring for 24 h at ambient temperature, the excess diamine was removed under reduced pressure (0.05 torr), and the glassy material thus obtained was dried under reduced pressure (0.05 torr) for 20 h at 60 °C. Analysis by ^1H NMR showed residual diamine in the preparation. For removal of this contaminant, the solid was extracted with portions (8 × 100 mL) of absolute diethyl ether, agitating each extraction in an ultrasonic bath for 30 min. The solids thus obtained were dried under reduced pressure (0.05 torr) for 3 days to give 3.3 g of a light yellow glass. This mixture was not purified further: ^1H NMR (D_2O) δ 2.7 (t, 2 H), 3.4 (t, 2 H), 3.5–4.3 (m, ~5 H), 4.4 (d, ~1 H); IR (neat) 3360 (vs, br), 1640 (s), 1550 (m) cm^{-1}.

Preparation of Compound 19. In an argon-flushed, 250-mL flask equipped with a stirring bar and addition funnel were placed 0.353 g (2.00 mmol) of tricarballylic anhydride acid chloride and 80 mL of dry CH_2Cl_2. The mixture was stirred until dissolution was complete. The addition funnel was charged with a solution of 0.96 g (2.00 mmol) of **1**·HCl and 0.51 mL (0.49 g, 4.0 mmol) of *N*,*N*-dimethylaniline in 20 mL of CH_2Cl_2, and this was added dropwise to the acid chloride solution at 0 °C with vigorous stirring. The reaction was warmed slowly to ambient temperature and stirred overnight. Examination of an aliquot by IR showed clean formation of the anhydride amide **6**: 1850 (m), 1780 (vs), 1635 (s) cm^{-1}. The solution was filtered under argon, the volume reduced to ~20 mL, and the resulting solution then added with vigorous stirring to a solution of 3.82 g (16.0 mmol) of *N*-(2-aminoethyl)gluconamide in 20 mL of distilled water in a thin, continuous stream (ca. 8 min to complete addition). The frothy mixture was stirred for 6 h at ambient temperature, and the methylene chloride was evaporated *carefully* (foaming) under reduced pressure. The aqueous solution was cooled to 0 °C and slowly acidified to pH ~1.0 by dropwise addition of concentrated HCl. The white solid that precipitated was collected by filtration, washed quickly with 5 mL of saturated aqueous NaCl, 1 mL of H_2O, and portions (2 × 5 mL) of 2:1 (v/v) Et_2O/CH_2Cl_2, and dried under reduced pressure (0.05 torr) for 7 days at ambient temperature to give 1.2 g (73%) of an off-white solid: IR (neat) 3300 (vs, b), 1710 (s), 1635 (vs) cm^{-1}.

Anal. Calcd for $C_{42}H_{51}N_3O_{10}P_2$: C, 61.53; H, 6.08; N, 5.13. Found: C, 60.85; H, 6.08; N, 5.34 (this material may be partially hydrated).

Preparation of Compound 20. Compound **6** was prepared by procedures similar to those described in the preparation of **19** (at half the scale described). The solution of **6** (~1.0 mmol) thus obtained was evaporated to dryness under reduced pressure and treated while being stirred vigorously with a solution of 0.75 g (5.1 mmol) of sodium taurinate in 30 mL of methanol. The reaction was stirred under argon for 24 h, the volatiles were removed under reduced pressure, and the solids were extracted with portions (8 × 100 mL) of $CHCl_3$/MeOH (2.5:1 v/v) and CH_2Cl_2 (4 × 100 mL). The combined organic extracts were evaporated under reduced pressure to give an oily material which, when washed with 50 mL of ether, gave 0.64 g of a white, hygroscopic, semicrystalline solid: IR (neat) 3450 (s), 1630 (s), 1580 (s), 1200 (s), 1050 (m) cm^{-1}; ^{31}P NMR −20.9 (s), −22.1 (s) ppm. The ^1H NMR in D_2O spectra showed a series of broad resonances and significant levels of excess taurine. Anal. Calcd for $C_{36}H_{38}N_2Na_2O_7P_2S_1$: C, 57.60; H, 5.10; N, 3.73. Found: C, 47.58; H, 4.85; N, 4.11. (These analyses indicate that slightly greater than 1 molar equiv of sodium taurinate remains in the preparation.) The mixture was purified further by dissolving the product under argon in 8 mL of H_2O, cooling to 0 °C, adding 10 mL of *n*-pentane, stirring the mixture vigorously, and precipitating the product by slow, dropwise addition of concentrated HCl. The liquids were decanted from the white gum that formed. This material was then washed with 1.0 mL of 1.0 M HCl and extracted into 10 mL of CH_2Cl_2. The organic phase was separated, concentrated, and dried under reduced pressure to give 0.36 g (49%, if pure) of a white, microcrystalline powder: IR (neat) 3400–2500 (s), 1705 (s), 1630 (vs), 1170 (vs), 1025 (s) cm^{-1}; ^{31}P NMR (H_2O, pH ~8.0) −20.8 (s), −22.2 (s) ppm.

Anal. Calcd for $C_{36}H_{39}N_2NaO_7P_2S_1$: C, 59.33; H, 5.39; N, 3.84. Found: C, 57.56; H, 5.63; N, 3.57 (this material is believed to be hydrated).

Preparation of Compound 21. A solution of *p*-sulfamylbenzoyl chloride (0.725 g, 3.30 mmol) in 20 mL of THF was added to a solution of 1.57 g (3.30 mmol) of **1**·HCl and 1.0 mL of pyridine in 20 mL of THF. After the mixture was stirred for 20 h at ambient temperature, 30 mL of H_2O was poured into the solution. The mixture was extracted with 20 mL of benzene, and the extract was washed with 100 mL of 2 N HCl and 100 mL of saturated aqueous NaCl. The solution was dried over Na_2SO_4, filtered, and evaporated to give a gummy material which recrystallized from 20% aqueous methanol as an off-white powder: 42% yield (0.79 g); ^1H NMR ($CDCl_3$) δ 1.8–2.8 (m, 4 H), 3.0–3.9 (m, 4 H), 5.7 (s, 2 H) 6.8–7.9 (m, 24 H); IR ($CDCl_3$) 3425 (s), 3340 (s), 1622 (s), 1350 (s), 1160 (m) cm^{-1}.

Anal. Calcd for $C_{35}H_{34}N_2O_3P_2S$: C, 67.30; H, 5.49; N, 4.48. Found: C, 67.28; H, 5.64; N, 4.31.

Preparation of Compound 22. The procedure and scale used were similar to that described for the preparation of **15**. The product is initially obtained as a waxy gum and can be recrystallized from ethanol to give 70 mg (70%) of a white solid: mp 213–213.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.7–2.8 (br m, 8 H), 2.8–3.9 (br m, 8 H), 6.7–7.7 (m, 44 H); IR (Nujol) 1633 cm^{-1}.

Preparation of Compound 23. Polyethylene glycol monomethyl ethyl ether (average mol wt 550; 59 g, 0.11 mol) was dissolved in 100 mL of pyridine, and thionyl chloride (10 mL, 0.14) was added dropwise over a period of 10 min. After the exothermic reaction subsided, the solution was poured into 500 mL of ether, and the ether layer was decanted from the insoluble residue that was deposited. The residue was extracted with portions (3 × 500 mL) of ether, the combined organic phases were neutralized by washing with saturated aqueous $NaHCO_3$, and the volatiles were removed under reduced pressure to give a brown oil. The oil was dissolved in methylene chloride, decolorized with activated charcoal (Fischer Darco), filtered, passed through a 1 × 8 cm column of Woelm activity I neutral alumina, and evaporated under reduced pressure to give a clear oil (20.8 g, 31%). Part of this material (12 g, 21 mmol) was dissolved in 30 mL of THF and added dropwise to a stirred solution of potassium diphenylphosphide, prepared by reaction of 3.7 g (21 mmol) of diphenylphosphine with 0.65 g (21 mmol) of potassium hydride in 30 mL of THF at 0 °C. The reaction was stirred for 1 h and quenched by addition of 2 mL of water to the reaction mixture. The reaction was diluted with 500 mL of ether, filtered through 100 g of Woelm activity I neutral alumina, and crystallized at −78 °C to give a yellow oil at room temperature. This material was dried under reduced pressure (0.05 torr, 20 h) to give 11 g of product. The ^{31}P NMR suggested that 11 (δ −22.8) comprised 85% of the phosphorus-containing species present.

Anal. Calcd for $C_{37}H_{61}O_{12}P$: C, 61.06; H, 8.46; P, 4.30. Found: C, 60.50; H, 8.45; P, 3.06.

Preparation of *N,N*-Bis[2-(diphenylphosphino)ethyl]acrylamide (24). In a 25-mL flask was dissolved **1**·HCl (465 mg, 0.975 mmol) in 15 mL of dry methylene chloride. Distilled triethylamine (0.275 mL, 2.0 mmol) was injected into the flask, and the solution was stirred for 15 min at room temperature. The reaction vessel was immersed in an acetone/dry ice bath. Acryloyl chloride (0.078 mL, 0.975 mmol) was added dropwise over a period of 3 min, and the solution was stirred for an additional 5 min before the flask was allowed to warm to ambient temperature. The solution was washed with 10% hydrogen chloride (3 × 25 mL) and distilled water (2 × 25 mL). The methylene chloride layer was dried over anhydrous sodium sulfate for 45 min under a moderate stream of argon before filtration. Solvent was removed from the filtrate under reduced pressure by rotary evaporation (20 torr) and was further dried under vacuum (0.05 torr) to a glassy oil. The oil was converted to an off-white powder by vigorous stirring in an ether–hexane solution (2:1 v/v). Washing with ether and drying under vacuum yielded 429 mg of the product: mp 124–126 °C; IR (neat, oil) 3400 (br), 3050, 2950 (s), 1640, 1610 (s), 1480, 1435 (s) cm^{-1}; NMR ($CDCl_3$) δ 7.3 (m, 8.8 H), 6.4–5.3 (m, 1 H), 3.6–3.1 (m, 2 H), 2.1–2.4 (m, 2 H). Although it is obvious from NMR and TLC analyses that **24** is not pure, this material was used without further purification.

Preparation of Compound 25. The amide anhydride **5** (162 mg, 0.264 mmol) and *n*-octadecylamine (71 mg, 0.264 mmol) were placed in separate round-bottomed flasks which were stoppered and flushed with argon for 30 min. Both solids were dissolved in 4.0 mL of dry methylene chloride and the mixtures vigorously stirred for several minutes before dropwise addition of the amine solution to the flask containing the anhydride. The yellow oily mixture was stirred for at least 2 h at room temperature under a static atmosphere of argon. The solvent was removed under reduced pressure by using a rotary evaporator (20 torr) and high vacuum (0.05 torr) to afford in quantitative yield (233 mg) a pale yellow glass. The glass was characterized by its NMR and IR spectra and was used in hydrogenation reactions without further purification: IR (neat, oil) 2980, 2900 (s), 1725 (m), 1640 (s, br), 1590 (m), 1470, 1440 (m) cm^{-1}; NMR ($CDCl_3$) δ 7.0–7.8 (m, 20 H), 2.0–3.9 (m, 1.0 H), 1.3 (m, 3.5 H).

Preparation of Metal Complexes. Nickel dichloride complexes of the phosphines described above were prepared by modification of literature procedures.[19] Platinum dichloride complexes were prepared by standard procedures by reacting $(COD)PtCl_2$[20] under argon with a slight excess of the ligand in THF for 48 h; the products were isolated as THF-insoluble precipitates by filtration. Preparation of cationic rhodium complexes and subsequent catalyses performed with them were effected by procedures analogous to those already described.[4]

Acknowledgment. We thank Dr. David Feitler, who prepared **23** and initiated our studies in homogeneous hydrogenations in aqueous solution.

Registry No. **1**·HCl, 66534-97-2; **2**, 1204-28-0; **3**, 77461-97-3; **4**, 81-08-3; **5**, 71120-43-9; **6**, 77461-98-4; **7**·Na, 77461-99-5; **10**, 66561-97-5; **11**, 66536-67-2; **12**, 66561-98-6; **13**, 77519-44-9; **15**, 66534-91-6; **16**, 66534-94-9; **17**, 77462-00-1; **18**·2Na, 77462-01-2; **19**, 77462-02-3; **20**·Na, 77462-03-4; **20**·2Na, 77462-04-5; **21**, 66534-92-7; **22**, 66534-93-8; **23**, 77461-22-4; **24**, 77462-05-6; **25**, 77462-06-7; diphenylphosphine, 829-85-6; bis(2-chloroethyl)amine HCl, 821-48-7; *N*-biotinoxysuccinimide, 35013-72-0; α-(chlorocarbonyl)-ω-methoxypoly(oxy-1,2-ethanediyl), 51023-28-0; phenyl isocyanate, 103-71-9; D-camphoric anhydride, 595-29-9; acetyl chloride, 75-36-5; succinic anhydride, 108-30-5; taurine, 107-35-7; sodium taurinate, 7347-25-3; tricarballylic α,β-anhydride, 4756-10-9; tricarballylic acid, 99-14-9; *N*-(2-aminoethyl)gluconamide, 74426-36-1; ethylenediamine, 107-15-3; D-glucono-δ-lactone, 90-80-2; *p*-sulfamylbenzoyl chloride, 51594-97-9; terephthaloyl chloride, 100-20-9; α-(2-chloroethyl)-ω-methoxypoly(oxy-1,2-ethanediyl), 52972-83-5; acryloyl chloride, 814-68-6; *n*-octadecylamine, 124-30-1.

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