Platinum-Catalyzed Enantioselective Hydroformylation with (*R*,*R*)-[Bicyclo[2.2.2]octane-2,3-diylbis(methylene)]bis(5*H*-benzo[*b*]phosphindole) and Related Chiral Ligands

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[(*R*,*R*)-Bco-dpp]$PtCl_2$ (**3**; Bco-dpp is (*R*,*R*)-[bicyclo[2.2.2]octane-3,4-diylbis(methylene)]bis(diphenylphosphine)) and [(*R*,*R*)-Bco-dbp]$PtCl_2$ (**4**; Bco-dbp is (*R*,*R*)-[bicyclo[2.2.2]octane-3,4-diylbis(methylene)]bis(5*H*-benzo[*b*]phosphindole)) have been synthesized and used as the catalyst precursors in the presence of $SnCl_2$ for the enantioselective hydroformylation of some olefinic substrates. The catalytic activity of these systems is very high. The level of asymmetric induction caused by **3** remains rather low. However, the capacity for enantioface discrimination displayed by **4** is the highest reported for the hydroformylation of styrene to hydratropaldehyde (best optical yield ~86.3%) and 1-butene (best optical yield ~67%). In the case of styrene this high enantioselectivity is accompanied by an excellent regioselectivity (80% of the branched isomer). The enantioselectivity shown by **4** was not improved by carrying out the reaction in the presence of triethyl orthoformate. The results are compared with those obtained by using [(*R*,*R*)-Diop-dbp]$PtCl_2$ (**2**; Diop-dbp is [(2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(methylene)]bis(5*H*-benzo[*b*]phosphindole)) as the catalyst precursor and with those already published obtained with [(*R*,*R*)-Diop]$PtCl_2$ (**1**; Diop is [(2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(methylene)]bis(diphenylphosphine)). The systems **2** and **4** (which contain the 5*H*-benzo[*b*]phosphindole substituents) are characterized by a lower isomerizing activity and by a higher regioselectivity toward the branched isomer than systems **1** and **3** (which contain the bis(diphenylphosphino) substituents).

Introduction

The enantioselective hydroformylation of olefinic substrates has attracted much attention due to the usefulness of optically active aldehydes as intermediates for organic synthesis.[1-5] Rhodium or platinum catalysts modified by optically active phosphines and diphosphines have been mostly used as the catalysts.[6-18] These investigations have been invaluable for a better understanding of the reaction mechanism.[6,19] However, the results have been disappointing from a preparative point of view in most cases. Common features of the abovementioned catalyst precursors are (a) the cis stereochemistry of the reaction[20,21] and (b) the fact that the 2-methylbutanal produced with either linear butene (1-butene and (*E*)- and (*Z*)-2-butene) shows enantiomeric compositions that depend on the starting substrate.[6] This implies, on the basis of the commonly accepted catalytic cycle for the reaction,[22] that the asymmetric induction is determined before or during the formation of the alkyl complex.[6] Therefore, the observed dependence of the optical yield upon the carbon monoxide and hydrogen partial pressure[9,23-27] might be due

Chart I

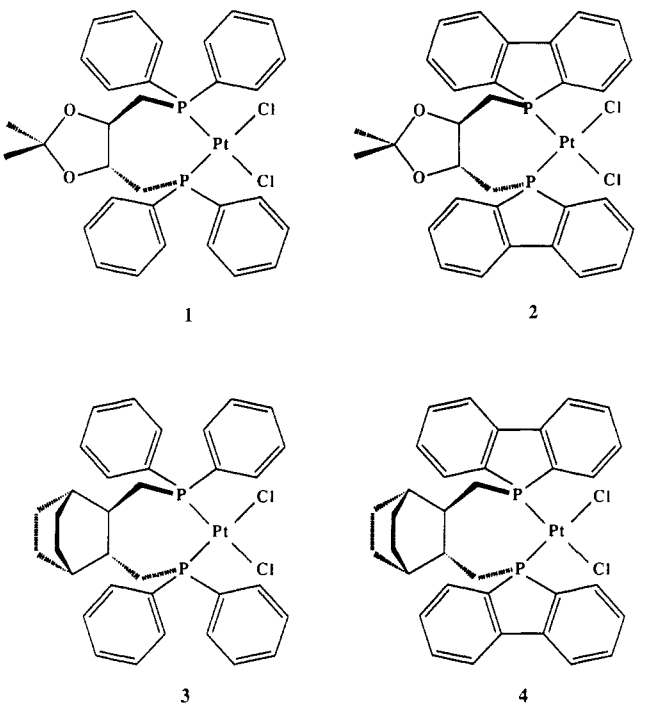

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Table I. Enantioselective Hydroformylation of Olefinic Substrates with [(*R*,*R*)-Bco-dpp]$PtCl_2/SnCl_2$[a]

substrate	reacn time, h	conversn, %	hydrogenation, %	isomeric ratio (straight chain/branched)	chiral product optical purity, % (absolute confign)
1-butene	2.0	85	9	60/40	7.7 (*S*)
(*Z*)-2-butene	5.3	68	1	31/69	3.7 (*R*)
(*E*)-2-butene	9.8	50	1	25/75	1.6 (*S*)
styrene	1.0	~100	17	58/42	23.4 (*S*)
2,3-dimethyl-1-butene	12.5	~100	10	~100/0	18.4 (*S*)
2-phenylpropene	8.5	~100	44	~100/0	12.5 (*S*)
norbornene	0.5	~100	nd[b]	exo	29.8 (1*R*,2*R*,4*S*)

[a] Reaction conditions: 80 °C; $p(H_2)$ = 150–160 atm; $p(CO)$ = 70 atm; solvent *m*-xylene or benzene; catalyst/substrate = ~1/1000. [b] nd = not determined by GLC; the aldehyde yield was 79%.

Table II. Enantioselective Hydroformylation of Olefinic Substrates with [(*R*,*R*)-Bco-dbp]$PtCl_2/SnCl_2$[a]

substrate	reacn time, h	conversn, %	hydrogenation, %	isomeric ratio (straight chain/branched)	chiral product optical purity, % (absolute confign)
1-butene	4	34	14	86/14	67.1 (*S*)
(*Z*)-2-butene	21	67	2	13/87	30.4 (*R*)
(*E*)-2-butene	30	65	3	13/87	28.9 (*R*)
styrene	0.5	~100	33	23/77	68.1 (*S*)
2,3-dimethyl-1-butene	17	58	14	~100/0	46.1 (*S*)
2-phenylpropene	9	~100	74	~100/0	15.9 (*R*)
norbornene	0.5	~100	nd[b]	exo	7.3 (1*R*,2*R*,4*S*)

[a] For the reaction conditions see footnote *a* in Table I. [b] nd = not determined by GLC; the aldehyde yield was 63%.

to the existence of different catalytic species, each one having its own peculiarity of enantio- and regioselectivity. The chiral ligand to metallic component molar ratio also influences the optical yield in carbonylation reactions.[23-26] This is possibly related to the aforementioned influence of the carbon monoxide partial pressure. In fact, catalytic species having different carbon monoxide to phosphine ratios could be present at the same time. For the catalytic system [(*R*,*R*)-Diop]$PtCl_2$ (**1**; Chart I) (Diop is [(2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(methylene)]bis(diphenylphosphine)) modified by $SnCl_2$, an increase of the ligand to metal molar ratio, however, only brings about a decrease of the catalytic activity and has practically no influence on the enantioselectivity of the reaction.[23,24] In this case, therefore, it appears less probable that species having different metal to ligand ratios are involved in the catalytic reaction. In fact, in the platinum-catalyzed hydroformylation with **1**[12] or the related [(*R*,*R*)-Diop-dbp]-$PtCl_2$ (**2**; Chart I) (Diop-dbp is [(2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(methylene)]bis(5*H*-benzo[*b*]phosphindole)),[7] quite high optical yields have been achieved, at least for some substrates. Different complexes containing the Diop ligand have been investigated both in solution and in the solid state.[28] It has been recognized that this ligand (and probably also the related Diop-dbp ligand) can assume different conformations.[28,29] It appeared probable to us that ligands related to Diop (i.e., having C_2 symmetry and forming a seven-membered coordination ring) but with a more rigid skeleton should give improved enantioselectivities while maintaining the high catalytic activity observed for the Diop ligand in the platinum-catalyzed hydroformylation.[30] We have, therefore, synthesized the platinum dichloride complexes of Bco-dpp (Bco-dpp is (*R*,*R*)-[bicyclo[2.2.2]octane-3,4-diylbis(methylene)]bis[diphenylphosphine]; this ligand was already known[31]) and of Bco-dbp (Bco-dbp is (*R*,*R*)-[bicyclo[2.2.2]octane-3,4-diylbis(methylene)]bis[5*H*-benzo[*b*]phosphindole]) **3** and **4** (Chart I) and tested them as catalyst precursors in the presence of $SnCl_2$ in the enantioselective hydroformylation of some olefinic substrates. In this paper we compare the results obtained with those related to the use of **1** and **2** as the chiral catalyst precursors. A few results on the use of **3** and **4** as the catalyst precursors were already submitted in a preliminary form.[32]

Results

The new ligand Bco-dbp was prepared according to literature procedures for analogous compounds.[31,33] The complexes [(*R*,*R*)-Bco-dpp]$PtCl_2$ (**3**) and [(*R*,*R*)-Bco-dbp]$PtCl_2$ (**4**) were synthesized by starting with $(C_6H_5CN)_2PtCl_2$[32,34] through an exchange reaction with the corresponding diphosphine ligand. In the case of **4** the use of a polar solvent and a higher temperature are necessary in order to obtain the compound in a pure form, without contamination of oligomeric material.[32] The results obtained in the enantioselective hydroformylation of some olefinic hydrocarbons with **3** in the presence of $SnCl_2$ as

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Table III. Enantioselective Hydroformylation of Styrene with either [(*R*,*R*)-Bco-dpp]$PtCl_2$/$SnCl_2$ or [(*R*,*R*)-Bco-dbp]$PtCl_2$/$SnCl_2$ as the Catalyst Precursor[a]

catalytic system	reacn time, h	*T*, °C	conversn, %	isomeric ratio (straight chain/branched)	2-phenylpropanal optical purity, % (absolute confign)
[(*R*,*R*)-Bco-dpp]$PtCl_2$/$SnCl_2$	1.0	80	~100	58/42	23.4 (*S*)
[(*R*,*R*)-Bco-dbp]$PtCl_2$/$SnCl_2$	0.5	80	~100	23/77	68.1 (*S*)
[(*R*,*R*)-Bco-dpp]$PtCl_2$/$SnCl_2$	nd[b]	50	~100	57/43	25.2 (*S*)
[(*R*,*R*)-Bco-dbp]$PtCl_2$/$SnCl_2$	2.3	50	95	20/80	84.7 (*S*)
[(*R*,*R*)-Bco-dbp]$PtCl_2$/$SnCl_2$	10	40	98	20/80	86.3 (*S*)
[(*R*,*R*)-Bco-dbp]$PtCl_2$/$SnCl_2$	190[c]	50	15	25/75	80[d] (*S*)

[a] Reaction conditions: benzene solvent (50 mL); ~0.05 mol of olefin; Cat/Ol = ~1/1000. [b] Not exactly determined; ~3 h. [c] Reaction in triethyl orthoformate. [d] Determined by NMR, with use of $Eu(dcm)_3$ as the chiral shift reagent.

Table IV. Enantioselective Hydroformylation of Olefinic Substrates with [(*R*,*R*)-Diop-dbp]$PtCl_2$/$SnCl_2$[a]

substrate	reacn time, h	conversn, %	hydrogenation, %	isomeric ratio (straight chain/branched)	chiral product optical purity, % (absolute confign)
1-butene	5.5	95	50	85/15	39.0 (*S*)
(*Z*)-2-butene	22	40	nd	12/88	12.2 (*R*)
(*E*)-2-butene	21	80	10	13/87	3.6 (*R*)
styrene	5.5	80	30	30/70	55.8 (*S*)
2,3-dimethyl-1-butene	116	70	15	~100/0	36.0 (*R*)
2-phenylpropene	110	92	78	~100/0	11.9 (*R*)
norbornene	15	~100	21	exo	0.6 (1*R*,2*R*,4*S*)

[a] For the reaction conditions see footnote *a* in Table I.

the catalyst precursor are reported in Table I, whereas in Table II the corresponding results obtained with **4** are presented. Both series of results were obtained at 80 °C under 240 atm of hydrogen and carbon monoxide (molar ratio ~2.1). The catalyst precursors used are characterized by an induction time that is different for the different substrates and varies from some minutes to a few hours. As observed with other platinum-based catalytic systems, the hydroformylation with **3** is accompanied by a competing hydrogenation, which is more extensive in the case of the aromatic substrates. Furthermore, there is some isomerization (where possible) which is revealed by the formation of 1-pentanal starting with the two internal butenes. In the case of styrene, as in the case of 1-butene, the regioselectivity favors the straight-chain isomer. The enantioselectivity achieved with this ligand is rather low in the cases examined, the best result being obtained for norbornene (~30% asymmetric induction). We note that for the 2-methylbutanal obtained from (*E*)-2-butene the same enantiomer prevails as for 1-butene. Using **4** as the catalyst precursor, we observe again competitive hydrogenation, which is rather extensive in the case of the aromatic substrates. The extent of isomerization as revealed by the formation of 1-pentanal from (*Z*)- and (*E*)-2-butene is much lower than in the case of **3**. The regioselectivity is in favor of the straight-chain isomer for 1-butene, but when styrene is the substrate, the branched product prevails. The enantioselectivity of this catalytic system is much better than with the previous catalytic systems for each substrate investigated, with the exception of norbornene. In this case the prevailing enantiomer for 2-methylbutanal is the same for (*Z*)- and (*E*)-2-butene but is opposite for 1-butene. The enantioselectivity is higher than 67% for 1-butene. A similar enantioselectivity is observed in the case of styrene (~68%), for which a high regioselectivity is also observed. The high enantioselectivity and regioselectivity obtained in the case of styrene coupled with the quite good catalytic activity of the system under investigation prompted us to test these catalyst precursors at lower temperature (Table III). In fact, styrene can be considered as a model compound for olefinic substrates that could be used for the synthesis of optically active 2-arylpropionic acid derivatives, a very important class of antiinflammatory drugs.[13,35] In the case of **3** as the catalyst precursor no essential improvement was observed in both regio- and enantioselectivity by decreasing the temperature by 30 °C. For **4**, however, the enantioselectivity was improved to ~85% and the regioselectivity to 80% (erroneously reported as 92% in ref 32). The enantioselectivity shown by **4** was not improved by carrying out the reaction in the presence of triethyl orthoformate in order to transform the optically unstable hydratropaldehyde "in situ" into the corresponding acetal. The results obtained in the hydroformylation of the same substrates with **2** as the catalyst precursor and under the same reaction conditions as for **3** and **4** are reported in Table IV. Some results with **2** under different reaction conditions have, in fact, already been reported.[7,36] Catalyst precursor **2** gives a system having a reactivity slightly lower than that of **4**. The regioselectivity of both systems appears substantially the same; however, the enantioselectivity is consistently better for **4** than for **2**. The two homochiral systems (**2** and **4**) give rise to the same prevailing enantiomer for all substrates but 2,3-dimethyl-1-butene.

Discussion

Previous accurate studies with the Diop-derived catalyst precursor [(*R*,*R*)-Diop]$Pt(SnCl_3)Cl$ as the catalyst precursor for hydroformylation[9] have shown that these catalysts display a high regioselectivity toward the straight-chain product for 1-olefins coupled with a high isomerizing activity. The results concerning regio- and enantioselectivity with this catalytic system[9,24,37] are compared in Table V with those obtained with **2**–**4**. The high isomerizing activity has the consequence that in the hydroformylation of 1-butene the regioselectivity shifts more and more toward the branched isomer by increasing the conversion, whereas for (*Z*)- and (*E*)-2-butene the selectivity shifts toward the straight-chain isomer. The enantioselectivity for these catalytic systems depends on enantioface selection, as previously stated. Therefore, the differences in

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Table V. Comparison of Enantio- and Regioselectivity in the Platinum-Catalyzed Hydroformylation of Olefinic Hydrocarbons with (L-L)$PtCl_2$/$SnCl_2$ as the Catalyst Precursor[a]

	chiral ligand (L-L)							
	(*R,R*)-Diop		(*R,R*)-Bco-dpp		(*R,R*)-Diop-dbp		(*R,R*)-Bco-dbp	
substrate	R	E, %	R	E, %	R	E, %	R	E, %
1-butene	95/5	36.2 (*R*)	60/40	7.7 (*S*)	85/15	39.0 (*S*)	86/14	67.1 (*S*)
(*Z*)-2-butene	24/76	14.5 (*S*)	31/69	3.7 (*R*)	12/88	12.2 (*R*)	13/87	30.4 (*R*)
(*E*)-2-butene	23/77	24.2 (*S*)	25/75	1.6 (*S*)	13/87	3.6 (*R*)	13/87	28.9 (*R*)
styrene	69/31	28.6 (*S*)	58/42	23.4 (*S*)	30/70	55.8 (*S*)	23/77	68.1 (*S*)
2,3-dimethyl-1-butene	~100/0	19.9 (*R*)	~100/0	18.4 (*S*)	~100/0	36.0 (*R*)	~100/0	46.1 (*S*)
2-phenylpropene	~100/0	13.3 (*S*)	~100/0	12.5 (*S*)	~100/0	11.9 (*R*)	~100/0	15.9 (*R*)
norbornene	exo	29.2 (1*R*...)[b]	exo	29.8 (1*R*...)[b]	exo	0.6 (1*R*...)[b]	exo	7.3 (1*R*...)[b]

[a] The regioselectivity (R) is expressed by the molar ratio between the straight-chain and the branched product. The enantioselectivity (E) is the optical purity of the prevailing enantiomer. [b] The full description is 1*R*,2*R*,4*S*.

the enantiomeric composition of the chiral product arising from these substrates become smaller with increasing conversion. The poor regioselectivity observed with the linear butenes when **3** is used as the catalyst precursor and the same prevailing absolute configuration for 2-methylbutanal formed from either (*E*)-2-butene or 1-butene can be explained on the same basis. The bis[5*H*-benzo[*b*]phosphindole]-containing catalytic systems **2** and **4** are characterized by a lower isomerizing activity, as revealed by the smaller amount of 1-pentanal formed from (*Z*)- and (*E*)-2-butene. The enantioselectivity is better for **4** than for **2**. Fair enantioselectivities were obtained for the two internal butenes. The optical yield reaches a value higher than 67% for the 2-methylbutanal formed from 1-butene. This is the highest value of asymmetric induction observed in enantioselective hydroformylation of simple aliphatic olefins and one of the highest observed in asymmetric reactions catalyzed by transition-metal compounds on such types of substrates.[38,39] The high regioselectivity observed in the formation of 2-phenylpropanal and the good enantioselectivity might make the synthesis of 2-arylpropionic acids via hydroformylation[40] attractive. Another interesting aspect of the reported results is connected with the remarkable difference in the regioselectivity caused by the bis[5*H*-benzo[*b*]phosphindole]-containing catalytic systems in the hydroformylation of styrene. Similar effects with phosphole ligands have recently been observed in the rhodium-catalyzed hydroformylation[41] and seem to find a parallel in the hydrocarbalkoxylation reaction.[42]

With **4** as the catalyst precursor we did not succeed in improving the enantioselectivity of the hydroformylation of styrene by carrying out the reaction in triethyl orthoformate, contrary to what has been reported for cobalt[19] and for platinum catalysts.[13] Under these conditions the formed aldehydes are converted "in situ" to the corresponding acetals, which are expected to be optically stable.[43] This system should have allowed the achievement of an almost quantitative enantioselectivity by using [(*S,S*)-Bppm]Pt($SnCl_3$)Cl (Bppm is *N*-(*tert*-butoxycarbonyl)-4-(diphenylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine) as the catalyst precursor for the enantioselective hydroformylation of styrene and of a few other substrates.[13] However, we have been unable to reproduce these results in two different laboratories, at least in the case of styrene.[44]

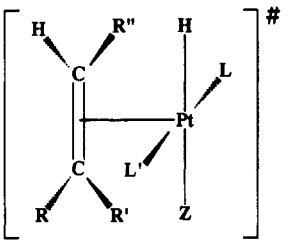

Figure 1.

Previous attempts to generalize results in the field of enantioselective hydroformylation have led to the proposal of a model for the transition state leading to the alkylmetal intermediate (Figure 1). This model allows us to predict the regio- and enantioselectivity of a particular catalytic system on the basis of a comparison of the four possible transition states for a given substrate. Once the relative size of L and L′ is identified with a first substrate, steric considerations give a high level of predictability for the other substrates.[6] In the present cases L is smaller than L′ for all ligands except for (*R,R*)-Diop. The model as described above predicts that the olefin would coordinate with its most substituted carbon atom toward the hydride ligand (as the steric hindrance around this ligand is assumed to be small), which would result in the formation of the linear aldehyde for mono- and disubstituted α-olefins. From Table V it can be seen that this prediction holds well, except for styrene with (*R,R*)-Diop-dbp and (*R,R*)-Bco-dbp as the ligand.

Comparing the direction of enantioselectivity for the four ligands (Table V) within this model, we have at least two effects to take into account: changing the carbon skeleton of the ligand ([2,2-dimethyl-1,3-dioxolane-4,5-diyl]bis(methylene) versus bicyclo[2.2.2]octane-3,4-diylbis(methylene)) and changing the nature of the substituents on the phosphine ligand (diphenylphosphine versus 5*H*-benzo[*b*]phosphindole). For instance, as one goes from Diop to Bco-dpp, the absolute configuration of the product of some of the substrates is reversed, whereas going from Diop-dbp to Bco-dbp results in a larger extent of the asymmetric induction for all of the substrates (as we had expected on going to a more rigid carbon skeleton), except for 2-phenylpropene. If we compare Diop with Diop-dbp, the absolute configurations of almost half of the products are opposite; this is reflected in the aforementioned different geometry of this model for the catalytic system containing Diop. However, as one goes from Bco-dpp to Bco-dbp, the absolute configuration of most of the products remains the same.

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When either the carbon skeleton of the diphosphine ligand is changed or the substituents on phosphorus are changed, there is apparently a strong influence on the conformation of the substituents on phosphorus. These conformations should determine the type and extent of enantioselectivity. We have not been able to ascertain the nature and magnitude of the different effects of these changes yet, despite the information obtained in this work, as the observed trends always seem to have one or more exceptions. In fact, in our model and most probably in the true catalyst the metal is a stereogenic center. Therefore, one might also have to consider attack of the olefin on the other side of the platinum complex (as both sides of the complex might not be equally sterically hindered), which would complicate the situation considerably, giving eight possible transition states. However, to be able to modify the model and predict which of the transition states would be preferred, more detailed information on the different catalytic species present in the reaction mixture and on the conformation of the phosphorus substituents in the different ligands used is required.

Conclusion

The two major problems in hydroformylation are the control of regioselectivity on one side and of enantioselectivity on the other side. We are still not able to produce the branched isomer with a fair regioselectivity, particularly in the case of aliphatic olefins. The regioselectivity and the enantioselectivity problems have been mostly approached by investigating the effect of modifying ligands, in particular phosphorus ligands. Our results in this direction may contribute to the application of the hydroformylation reaction to the synthesis of valuable optically active intermediates. In spite of the fact that the nature of the catalytic species is not yet well-known, we were able to find a catalytic system with unprecedented enantioselectivity in the platinum-catalyzed hydroformylation.

Experimental Section

Starting Materials. 1,3-Cyclohexadiene, fumaryl chloride, brucine, tosyl chloride, triphenylphosphine, $SnCl_2$, and triethyl orthoformate were purchased from Fluka. Toluene, benzene, dioxane, and methanol were dried according to normal procedures and distilled under nitrogen. All reactions involving the synthesis of phosphine compounds were performed under an inert atmosphere of nitrogen, with use of Schlenk techniques.

General Procedures. The NMR spectra were measured on a Bruker AM 300 WB or a Bruker AC 200 spectrometer with tetramethylsilane as the internal standard or 85% phosphoric acid as the external standard.

Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The optical rotations as reported below in the synthesis of the ligands were measured at room temperature. For the determination of the optical rotation of the hydroformylation products, a thermostatized cell was used. The following $[\alpha]$ values were taken as reference for the optically pure aldehydes: (*R*)-2-methylbutanal $[\alpha]_D^{25} = -35.1°$;[45] (*S*)-2-phenylpropanal, $[\alpha]_D^{25} = +238°$;[7] (*S*)-3-phenylbutanal, $[\alpha]_D^{25} = +34.8°$;[46] (*R*)-3,4-dimethylpentanal, $[\alpha]_D^{25} = +11.11°$;[47] (1*S*,2*S*,4*R*)-norbornane-2-carbaldehyde, $[\alpha]_D^{25} = +97.5°$.[48]

Gas chromatographic analyses were carried out on a Perkin-Elmer Model 990 gas chromatograph with flame ionization detector using a 2-m packed column (SF 90) or on a Shimadzu 8A GC with flame ionization detector using a 50-m (0.32 mm i.d.) fused silica (OV-1701-DF-0.25) capillary column. Helium was used as the carrier gas.

Microanalyses were carried out by the Microanalytical Laboratory of the ETH, Zürich, Switzerland.

Bicyclo[2.2.2]oct-5-ene-2,3-*trans*-dicarboxylic acid was synthesized as described in ref 49.

Resolution of Bicyclo[2.2.2]oct-5-ene-2,3-*trans*-dicarboxylic Acid.[50] In a representative experiment 22.5 g (0.11 mol) of racemic bicyclo[2.2.2]oct-5-ene-2,3-*trans*-dicarboxylic acid was dissolved in 310 mL of methanol and 150 g (0.38 mol) of brucine was added. The mixture was stirred for 3 h, after which the precipitate was filtered off, giving 60.0 g of salt. This was recrystallized from 190 mL of MeOH; yield 47.1 g of salt. A 43-g amount was again recrystallized from 110 mL of MeOH; yield 40.7 g of salt. This was treated with 60 mL of concentrated hydrochloric acid and the recovered acid was filtered off; yield 4.4 g of (*S*,*S*)-bicyclo[2.2.2]oct-5-ene-2,3-*trans*-dicarboxylic acid: $[\alpha]_{365} = -173.9°$ (c = 1.6, acetone). This sample was recrystallized from 50 mL of water: yield 2.9 g (26%); $[\alpha]_{365} = -175.2°$ (c = 1.6, acetone). To check the optical purity, part of the acid was reacted with sulfonyl chloride and methanol to give the methyl ester, which was then analyzed by NMR spectroscopy, with $Eu(dcm)_3$ as the chiral shift reagent. The optical purity thus obtained was 100%.

Through analogous experiments several other fractions of (*S*,*S*)-bicyclo[2.2.2]oct-5-ene-2,3-*trans*-dicarboxylic acid were obtained, which were combined for further reactions.

(+)-Bicyclo[2.2.2]octane-2,3-*trans*-dicarboxylic Acid.[50] In a representative experiment a solution of 10.4 g of (−)-bicyclo-[2.2.2]oct-5-ene-2,3-*trans*-dicarboxylic acid ($[\alpha]_{365} = -172.4°$ (c = 1.6, acetone) in 115 mL of a 10% Na_2CO_3 solution was placed in a 150 mL stainless steel autoclave, together with 2.55 g of Pd/C (10%). The autoclave was flushed with hydrogen twice and then pressurized with hydrogen to 115 bar. The autoclave was shaken at room temperature for about 90 min, after which the gas was vented. The solution was filtered and acidified with concentrated hydrochloric acid. The white precipitate was filtered off and washed with water. Through extraction of the filtrate with diethyl ether more product could be won: total yield 10.3 g (98%); mp 186.5 °C; $[\alpha]_{365} = +258°$ (c = 0.5, acetone). From analogous experiments another 8.3 g of product was obtained. All fractions were combined and recrystallized from water: yield 16.5 g (77%) of (+)-bicyclo[2.2.2]octane-2,3-*trans*-dicarboxylic acid; mp 187.5 °C; $[\alpha]_{365} = +272°$ (c = 0.5, acetone).

(+)-*trans*-2,3-Bis(hydroxymethyl)bicyclo[2.2.2]octane.[51] A solution of 16.5 g (83 mmol) of (+)-bicyclo[2.2.2]octane-2,3-dicarboxylic acid ($[\alpha]_{365} = +272°$ (c = 0.5, acetone) in 50 mL of dry diethyl ether was added dropwise over 70 min to a suspension of 10 g (263 mmol) of $LiAlH_4$ in 50 mL of dry diethyl ether, during which the solvent refluxes. Another 50 mL of diethyl ether was added, and the mixture was stirred overnight. After workup as usual the ether fraction was dried over $MgSO_4$, filtered, concentrated, and cooled to give 5.8 g of crystals: mp 111.5 °C; $[\alpha]_{365} = +171.7°$ (c = 0.5, acetone). The filtrate was concentrated to give a second crop of crystals: yield 3.5 g; mp 111 °C; $[\alpha]_{365} = +171.7°$ (c = 0.5, acetone). The filtrate was concentrated yet again to give a third crop of crystals: yield 1.2 g; mp 110 °C; $[\alpha]_{365} = +172.7°$ (c = 0.5, acetone). Total yield: 10.5 g of (+)-2,3-bis-(hydroxymethyl)bicyclo[2.2.2]octane (74%). Anal. Calcd for $C_{10}H_{12}O_2$: C, 70.55; H, 10.66. Found: C, 70.65; H, 10.49.

(−)-*trans*-2,3-Bis((tosyloxy)methyl)bicyclo[2.2.2]octane.[52] A solution of 10.3 g (60 mmol) of (+)-bis(hydroxymethyl)bicyclo[2.2.2]octane in 40 mL of pyridine was added dropwise to a solution of 25.0 g (131 mmol) of tosyl chloride in 50 mL of pyridine, during which time the temperature was kept between 0 and 5 °C. This solution was stirred overnight at room temperature, 100 g of ice was added, and the mixture was extracted with benzene. The combined benzene fractions were washed with a 1 M NaOH solution (2 × 70 mL), water (70 mL), a 2.5 M HCl solution (400 mL), water (50 mL), a 10% $NaHCO_3$ solution (50 mL), and water

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(2 × 50 mL), respectively. The organic fraction was dried over $MgSO_4$ and filtered, after which the solvent was removed under reduced pressure. The product was recrystallized from cyclohexane (1.5 L): yield 24.2 g (84%) of (−)-*trans*-2,3-bis((tosyloxy)methyl)bicyclo[2.2.2]octane; mp 110 °C; $[\alpha]_{365} = -25.5$ (c = 0.6, acetone). Anal. Calcd for $C_{24}H_{30}S_2O_6$: C, 60.23; H, 6.32; S, 13.40. Found: C, 60.37; H, 6.43; S, 13.39.

(−)-(*R*,*R*)-[Bicyclo[2.2.2]octane-2,3-diylbis(methylene)]-bis(diphenylphosphine) (Bco-dpp).[52] Potassium (3.25 g, 83.1 mmol) and sodium (0.80 g, 34.8 mmol) were melted together in a dry 350-mL three-neck flask. A 120-mL portion of dioxane was added, after which a solution of 10.9 g (41.6 mmol) of triphenylphosphine in 30 mL of dioxane was added, with vigorous stirring. The orange-yellow suspension of potassium diphenylphosphide was stirred overnight. A solution of 10.0 g of (−)-*trans*-2,3-bis((tosyloxy)methyl)bicyclo[2.2.2]octane ($[\alpha]_{365} = -25.5°$ (c = 0.6, acetone) in 30 mL of toluene was added dropwise over about 15 min, while the mixture was cooled in an ice bath. The suspension was stirred for another 3 h at room temperature and then filtered through Celite under nitrogen; the residue was washed with toluene (3 × 10 mL). The combined filtrate and washings were concentrated under reduced pressure to give a white/yellow resin, which was treated with 10 mL of MeOH and stirred for 4 h. A 50-mL portion of ethanol was added, and the white viscous product was dissolved at 80 °C. Cooling to −70 °C was necessary to obtain the product as a white powder: yield 4.1 g; mp 73–74 °C; $[\alpha]_{365} = -99°$ (c = 0.6, $CHCl_3$). The filtrate was concentrated and cooled to give another 1.1 g of product: mp 74–75 °C; $[\alpha]_{365} = -103°$ (c = 0.6, $CHCl_3$). Total yield: 5.2 g (49%) of (−)-(*R*,*R*)-[bicyclo[2.2.2]octane-2,3-diylbis(methylene)]bis(diphenylphosphine). ^{31}P NMR: δ = −20.0 ppm ($CDCl_3$). Anal. Calcd for $C_{34}H_{36}P_2$: C, 80.61; H, 7.16. Found: C, 80.41; H, 7.26.

(−)-(*R*,*R*)-[Bicyclo[2.2.2]octane-2,3-diylbis(methylene)]-bis(5*H*-benzo[*b*]phosphindole) (Bco-dbp). This compound was prepared as described above for Bco-dpp, but with phenyldibenzophosphole, synthesized according to literature methods,[53] as the reacting phosphine. After removal of toluene, the product was treated with 100 mL of methanol. An attempt to recrystallize the white powder from ethanol failed due to the low solubility of the product: yield 5.3 g (51%); $[\alpha]_{365} = +79.5°$ (c = 0.6, $CHCl_3$). ^{31}P NMR: δ = −17.6 ($CDCl_3$). Anal. Calcd for $C_{34}H_{32}P_2$: C, 81.26; H, 6.42. Found: C, 80.94; H, 6.40.

Pt(Bco-dpp)Cl_2. A 1.5-g amount of $PtCl_2(PhCN)_2$ (3.92 mmol; synthesized according to the literature)[34] was dissolved in 70 mL of refluxing benzene. Over 30 min a solution of 2.0 g (3.95 mmol) of Bco-dpp in 50 mL benzene was added dropwise under reflux, during which an off-white precipitate was formed. This mixture was refluxed for another 1.5 h. The precipitate was filtered off and washed three times with 25 mL of petroleum ether and dried in vacuo; yield 2.54 g (84%). ^{31}P NMR: δ = 9.09 ppm ($CDCl_3$); $^1J_{Pt-P}$ = 3562 Hz. Anal. Calcd for $C_{34}H_{32}P_2PtCl_2$: C, 52.86; H, 4.70; P, 8.02; Cl, 9.18. Found: C, 53.43; H, 4.65; P, 7.72; Cl, 9.05.

Pt(Bco-dbp)Cl_2. This compound was prepared as described above, but with Bco-dbp as the reacting phosphine. The product was obtained as an off-white powder, which is practically insoluble in most organic solvents; yield 2.85 g (95%). ^{31}P NMR: δ = 8.82 ppm (DMSO); $^1J_{Pt-P}$ = 3404 Hz.[54] Anal. Calcd for $C_{34}H_{32}P_2PtCl_2$: C, 53.13; H, 4.20; P, 8.06; Cl, 9.23. Found: C, 52.84; H, 4.36; P, 7.82; Cl, 8.97.

Pt(Diop)Cl_2 and Pt(Diop-dbp)Cl_2 were prepared according to literature procedures.[28a,33]

General Procedure for the Enantioselective Hydroformylation of Olefins. A 150-mL stainless steel autoclave was filled with the required amounts (see specifications in Tables I–V) of platinum catalyst and stannous chloride. The autoclave was evacuated and filled with nitrogen several times, after which the solvent and olefin were transferred into the autoclave under nitrogen. The autoclave was closed and pressurized, usually to 220 bar total pressure (H_2/CO = 2/1), placed in an oil bath, and continuously agitated by an arm shaker. The pressure was monitored throughout the reaction. After the gases were cooled and vented, the reaction mixture was removed, immediately analyzed by GC, and fractionally distilled for further characterization.

Enantioselective Hydroformylation of Styrene in the Presence of Triethyl Orthoformate. A 0.043-mmol amount of Pt(Bco-dbp)Cl_2, 0.123 mmol of $SnCl_2$, 5 mL of styrene, 20 mL of benzene, and 20 mL of triethyl orthoformate were placed in a 150-mL stainless steel autoclave. The autoclave was pressurized to 220 bar total pressure (H_2/CO = 2/1) and heated to 50 °C in an oil bath with continuous shaking. After reaction for 180 h a 20% conversion had been achieved. After removal of the solvent and most of the unreacted styrene under reduced pressure, the mixture was analyzed by NMR spectroscopy in the presence of Eu(dcm)$_3$, giving an optical purity of the acetal of approximately 80%.

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