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# Novel Chiral Water Soluble Phosphines II. Applications in Catalytic Asymmetric Hydrogenation

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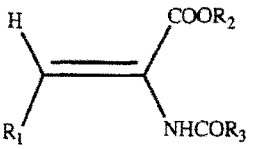
**Abstract:** The results of the homogeneous asymmetric hydrogenation of several dehydroamino acids by rhodium-diene complexes of the chiral ligands; 2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(-bis(-p-N,N-dimethylaminophenyl)phosphino)butane, **2a**; 2,4-bis(-bis(-p-N,N-dimethylaminophenyl)phosphino)pentane, **3a**; and 2,3-bis(-bis(-p-N,N-dimethylaminophenyl)phosphino) butane, **4a**; and their N-protonated and N-Me quaternized analogues are reported. The ligands comprise a versatile set which can be used both in organic and aqueous solvents. A detailed investigation of solvent and substituent effects is provided. The presence of p-$NMe_2$ groups enhances the rate of reaction in all cases. For the DIOP derivative, **2a**, the presence of the dimethylamino group causes a reversal in the observed dominant product antipode. This is attributed predominantly to a change in preferred ligand conformation rather than to a kinetic difference between the two diastereomers of a single ligand conformation.

The recently prepared tetrakis-(p-quaternary amino)phenyl derivatives of DIOP, BDPP (Skewphos) and Chiraphos (Scheme 1) represent the first examples of chiral water soluble ligands with more than one cationic functional group.[1] The presence of four ionic groups in the quaternized versions of these ligands provides unlimited water solubility to their rhodium complexes in a fashion similar to the sulfonated derivatives of chiral chelating phosphines.[2] Complexes of the cationic ligands show negligible solubility in moderately polar organic solvents such as ethyl acetate, dichloromethane, benzene, etc., and thus can serve as catalysts for the enantioselective two-phase hydrogenation of prochiral organic substrates. Water solubilization by the quaternization method is more favorable than direct sulfonation for sensitive ligands, such as DIOP, which cannot be subjected to $SO_3/H_2SO_4$.

Water soluble complexes with ionic ligands can provide significantly different enantioselectivities compared to the non-functionalized derivatives in methanol or other organic solvents.[2,3] Substitution at the aryl rings of the ligands alone is sufficient to alter the enantioselectivity in non-aqueous solvents.[4-8] The effect of water on enantioselectivity has been investigated recently and it was proposed that enantioselectivity is a function of solvent solvophobicity.[9] In many cases, however, it is difficult to separate substituent effects from solvent effects.

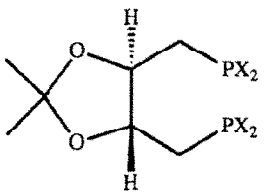
## Scheme 1
## Legend for the symbols of substrates and ligands.

**Substrates**

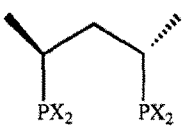



| $R_1$ | $R_2$ | $R_3$ | |
|---|---|---|---|
| Ph | H | Me | **1a** |
| Ph | Me | Me | **1b** |
| 3-OMe-4-OAc-$C_6H_3$- | H | Me | **1c** |
| Ph | Me | Ph | **1d** |
| H | H | Me | **1e** |

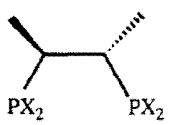
**Ligands**




2, DIOP




3, BDPP




4, Chiraphos

| X | |
|---|---|
| $C_6H_5$ | |
| [p-$C_6H_4NMe_2$] | a |
| [p-$C_6H_4NMe_3$]$^+BF_4^-$ | b |
| [p-$C_6H_4NHMe_2$]$^+BF_4^-$ | c |

With the results presented here a complete comparison of the non-substituted ligands, the p-dimethylamino (**2-4a**), and the p-dimethylammonium derivatives (**2-4c**) in methanol can be made. Furthermore the results in water for the p-trimethylammonium (**2-4b**), p-dimethylammonium (**2-4c**) and m-sulfonate derivatives can be compared. The solubility of the protonated complexes, **2-4c**, in both methanol and in water provides a link in the investigation of substituents effects between the homogeneous (MeOH) and two-phase applications. Also it is now possible to relate ligand conformational lability in DIOP derivatives to the enantioselectivities obtained with these ligands. We have previously communicated catalytic results for [Rh(**3a**)NBD]$BF_4$ and [Rh(**3b**)(NBD)]$(BF_4)_5$.[3]

## Results

The results of the homogeneous asymmetric hydrogenation of several dehydroamino acids by rhodium-diene complexes of ligands **2-4a** as catalysts in methanol are summarized in Table 1. The literature values obtained with non-functionalized DIOP,[5,10,11] BDPP,[12,13] and Chiraphos[14] in similar rhodium(I) complexes are included for comparison.

Results for enantioselective hydrogenation with the protonated ligands, **2-4c**, in MeOH are presented in Table 2. When the values in Table 2 are compared to the entries for **2-4a** in Table 1 it can be seen that protonation at the amine nitrogens has little effect on the enantioselectivity of these catalyst systems.

The hydrogenation results with the quaternized ligands, **2-4b** and **2-4c**, under two-phase conditions are summarized in Table 3. The optical yields for the ester derivatives (**1b, 1d**) were obtained in a two-phase system (water/ethylacetate/benzene = 2/1/1) while the acid substrates (**1a, 1c**) were hydrogenated as slurries in water.

The effect of solvent and pressure on the activity with **3c** as the ligand is summarized in Table 4. It can be seen that both an increase in pressure and a gradual change from methanol to water causes a significant drop in enantioselectivity. However,

Table 1. Homogeneous Asymmetric Hydrogenation of Substrates **1a-d** with rhodium-diene complexes of the non-substituted and p-dimethylamino derivatives in MeOH.[a]

| Ligand / Substrate | (-)**2a** ee. | t.o.f.(1/s) | (-)DIOP ee. | t.o.f.(1/s) | (S,S)-**3a** ee. | t.o.f.(1/s) | (S,S)-BDPP ee. | t.o.f.(1/s) | (S,S)-**4a** ee. | t.o.f.(1/s) | (S,S)-Chiraphos ee. | t.o.f.(1/s) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **1a** | 59(S) | 0.75 | 82(R)[c] | 0.3 | 92(R)[f] | 0.33 | 96(R) | 0.1-0.2[g] | 87(R) | 0.006 | 89 | 0.02-0.0006[i] |
| **1b** | 44(S) | 1.10 | 66(R)[d] | - | 76(R)[f] | 0.57 | 72(R) | 0.1-0.2[g] | 75(R) | 0.008 | - | |
| **1c**[b] | 88(S) | 0.40 | 84(R)[e] | - | 95(R)[f] | 0.08 | - | - | 88(R)[h] | 0.009 | 80 | 0.02-0.0006[i] |
| **1d** | 7(S) | 1.20 | - | - | 56(R)[f] | 0.44 | 79(R) | 0.1-0.2[g] | 49(R)[h] | 0.03 | | |
| **1e** | 8(S) | 1.75 | 73(R)[e] | - | 88(R) | 0.44 | 90(R) | 0.1-0.2[g] | | | | |

a. Catalyst concentration: 0.025 mmol in 10 ml of MeOH; Substrate/Rh=100, 1 bar $H_2$, 25°C. Conversion: 100%. Optical yields for (-)-(R,R)-DIOP, (S,S)-BDPP and (S,S)-Chiraphos from references 5, 10-14.
b. Hydrogenation starts as a slurry in MeOH.
c. Reference 5, 10, 11,
d. Reference 10.
e Reference 11.
f Reference 4.
g Reference 12, 13.
h 14 bar $H_2$.
i. Reference 14.

by increasing the water content in the solvent composition the system becomes more resistant to increased pressure. Thus at 14 bar of $H_2$ pressure the enantioselectivity is significantly higher in water than in MeOH. Importantly, an increase of the water concentration lowers the hydrogenation rates by two orders of magnitude.

The effect of pressure on asymmetric hydrogenation is summarized in Table 5. Not only is the enantioselectivity obtained with the Chiraphos derivative, **4b**, unaffected by switching from methanol to water as the solvent (Tables 1 and 3) its derivatives are also resistant to changes in pressure in both solvents (Table 5). A change in dominant product configuration is observed with the DIOP derivative, **2a**; with substrate **1d** the enantiomeric

Table 2. Homogeneous Asymmetric Hydrogenation of Substrates **1a, b, d** with "in situ" Protonated Complexes.

| Ligand | (-)-**2c** | | (S,S)-**3c** | | (S,S)-**4c** | |
|---|---|---|---|---|---|---|
| Substrate | ee. | t.o.f. (1/s) | ee. | t.o.f. (1/s) | ee. | t.o.f. (1/s) |
| 1a | -- | | 91(R) | 0.2 | 90(R) | 0.009[c] |
| 1b | 48(S) | 0.7 | 72(R)[b] | 0.4 | 75(R) | 0.03[c] |
| 1d | -- | | 57(R)[b] | 0.3 | 53(R) | 0.03[c] |

a. Rhodium concentration 0.025 mmol (in the form of [Rh(diene)(**2-4a**)]$BF_4$) in 10 ml MeOH containing 0.1 ml of 48% aqueous $HBF_4$. Substrate/Rh=100. 25°C, 1 bar $H_2$.

b Reference 23.

c 14 bar $H_2$.

Table 3. Two-phase and slurry hydrogenations with the p-quaternary amino derivatives in water.[a]

| Ligand / Substrate | (-)-(R,R)-**2c** ee (%) . r.t. | (-)-(R,R)-**2b** ee (%) . r.t. | (S,S)-**3c** ee (%) . r.t. | (S,S)-**3b** ee (%) . r.t. | (S,S)-**4c** ee (%) . r.t. | (S,S)-**4b** ee (%) . r.t. |
|---|---|---|---|---|---|---|
| **1a** | 34(S)[b] 1 hr. | 25(S)[b] 2 hr. | 71(R)[b] 6 hr.<br>73 (R)[c] 6 hr. | 67(R)[b] 6 hr. | 90(R)[b] 6 hr. | 94(R)[b] 6 hr. |
| **1b** | 25(S)[c] 2 hr | 8(S)[b] 1 hr. | 50(R)[c] 3 hr. | 45(R)[c] 1 hr.<br>40(R)[b] 2 hr. | 74(R)[c] 2 hr. | 77(R)[c] 2 hr.<br>68(R)[b] 3 hr. |
| **1c** | 67(S)[b] 6 hr. | 42(S)[b] 2 hr. | 79(R)[b] 3 hr. | 76(R)[b] 6 hr. | 88(R)[b] 6 hr. | 93(R)[b] 6 hr. |
| **1d** | 11(S)[c] 24 hr. | 9(S)[c] 10 hr. | 67(R)[c] 12 hr. | 54(R)[c] 9 hr. | 58(R)[c] 24 hr. | 65(R)[c] 9 hr. |

a. 0.025 mmol [Rh(diene)(**2 - 4 b,c**)]$(BF_4)_5$ in 10 ml solvent, diene=NBD or COD, substrate/Rh=100/1, 25°C, 14 bar $H_2$, Conversion 100%.

b. Slurry hydrogenation; solvent 10 ml water.

c. Two-phase hydrogenation; solvent: 5 ml water/5 ml EtOAc/benzene=1/1.

Table 4. Influence of pressure and solvent change on the asymmetric hydrogenation of **1a** with **3c** ligand.[a]

| | | 1 bar $H_2$ | | 14 bar $H_2$ | |
|---|---|---|---|---|---|
| MeOH (%) | $H_2O$ (%) | e.e (%) | t.o.f. (1/s) | e.e. (%) | t.o.f. (1/s) |
| 100 | 0 | 91(R) | 0.2 | 58(R) | 0.25 |
| 50 | 50 | 73(R) | 0.1 | 64(R) | 0.1 |
| 20 | 80 | 70(R)[b] | 0.001 | 70(R) | 0.005 |
| 0 | 100 | - | - | 71(R) | 0.003 |

a 0.025 mmol $[Rh(NBD)(\mathbf{3c})]^{5+}$ in 10 ml solvent, substrate/Rh=100/1. Temperature: ambient; conversion: 100%.

b conversion: 10%.

Table 5. Influence of the pressure on the asymmetric hydrogenation of **1a-d** with various ligands.[a]

| Entry | Substrate | Ligand | 0.1 bar $H_2$[b] | | 1 bar $H_2$ | | 14 bar $H_2$ | | 91 bar $H_2$ | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | e.e | t.o.f. | e.e | t.o.f. | e.e | t.o.f | e.e | t.o.f |
| 1 | **1a** | **4a** | -- | | 87(R) | 0.006 | 82(R) | 0.05 | -- | |
| 2 | **1c** | **4a** | -- | | 93(R) | 0.0009 | 88(R) | 0.009 | -- | |
| 3 | **1b** | **4b** | -- | | 75(R) | 0.003 | 75(R) | 0.03 | -- | |
| 4 | **1a** | **3b**[c] | -- | | -- | | 67(R) | 0.005 | 65(R) | 0.01 |
| 5 | **1d** | **2b**[c] | -- | | -- | | 9(S) | 0.003 | 7(S) | 0.005 |
| 6 | **1b** | **3a** | 84(R) | 0.04[d] | 76(R) | 0.51 | 38(R) | ~0.5 | -- | |
| 7 | **1d** | **3a** | 72(R) | 0.04[e] | 56(R) | 0.44 | -- | | -- | |
| 8 | **1d** | **2a** | 14.5(S) | 0.03[f] | 7(S) | 0.75 | 1.5(R) | ~1 | 2.5(R) | ~2 |

a 0.025 mmol Rh (in NBD or COD complexes of the ligands)/10 ml solvent. Substrate/ Rh=100/1, Conversion: 100%; ambient temperature; MeOH.

b Atmospheric pressure: 10% $H_2$ , 90% $N_2$

c Solvent: water/ethylacetate/benzene = 1/0.5/0.5.

[d]Conversion: 72%.

[e]Conversion: 80%.

[f]Conversion: 50%.

excess of the product changes from 14.5 S at 0.1 bar to 2.5 R at 91 bar $H_2$. Catalysts with the amine functionalized ligands are conveniently recycled.

The aqueous catalyst solutions with ligands **2-4b,c** can be readily recycled.[3,23] A set of recycling data with **4a** and **4b** is shown in Table 6. Generally, the recycling in two-phase applications can be accomplished with very little rhodium loss; larger quantities of rhodium are entrained in the crystalline product when the reaction is done as a slurry.

Table 6. Catalyst Recycling [a]

| Catalyst | Substrate | Cycle | Reaction Time | (e.e.%) | Solvent | Rh-Loss |
|---|---|---|---|---|---|---|
| [Rh(NBD)(**4a**)]$^+$ | **1 b** | 1[b] | 4 hrs. | 75[a] | MeOH | 2.3% |
| | | 2 | 2 hrs | 74 | two-phase[c] | 2.7% |
| | | 3 | 2 hrs | 76 | two-phase[c] | 2.5% |
| [Rh(NBD)(**4b**)]$^{5+}$ | **1 c** | 1 | 3 hr | 93 | water, slurry | 3.7% |
| | | 2 | 6hr. | 95 | water, slurry | 4.4% |
| | | 3 | 6 hr. | 90 | water, slurry | 4.0% |
| [Rh(NBD)(**4b**)]$^{5+}$ | **1 b** | 1 | 2 hr. | 75 | two-phase[d] | < 0.1% |
| | | 2 | 2 hr. | 77 | two-phase[d] | < 0.1% |
| | | 3 | 2 hr. | 77 | two-phase[d] | < 0.1% |

a 20°C, 14 bar $H_2$, Substrate/Rh=100/1; 0.025 mmol Rh in 10 ml of solvent.

b 1 bar $H_2$

c Water/ethylacetate/benzene=1/0.5/0.5 containing 0.1 ml of concentrated $HBF_4$.

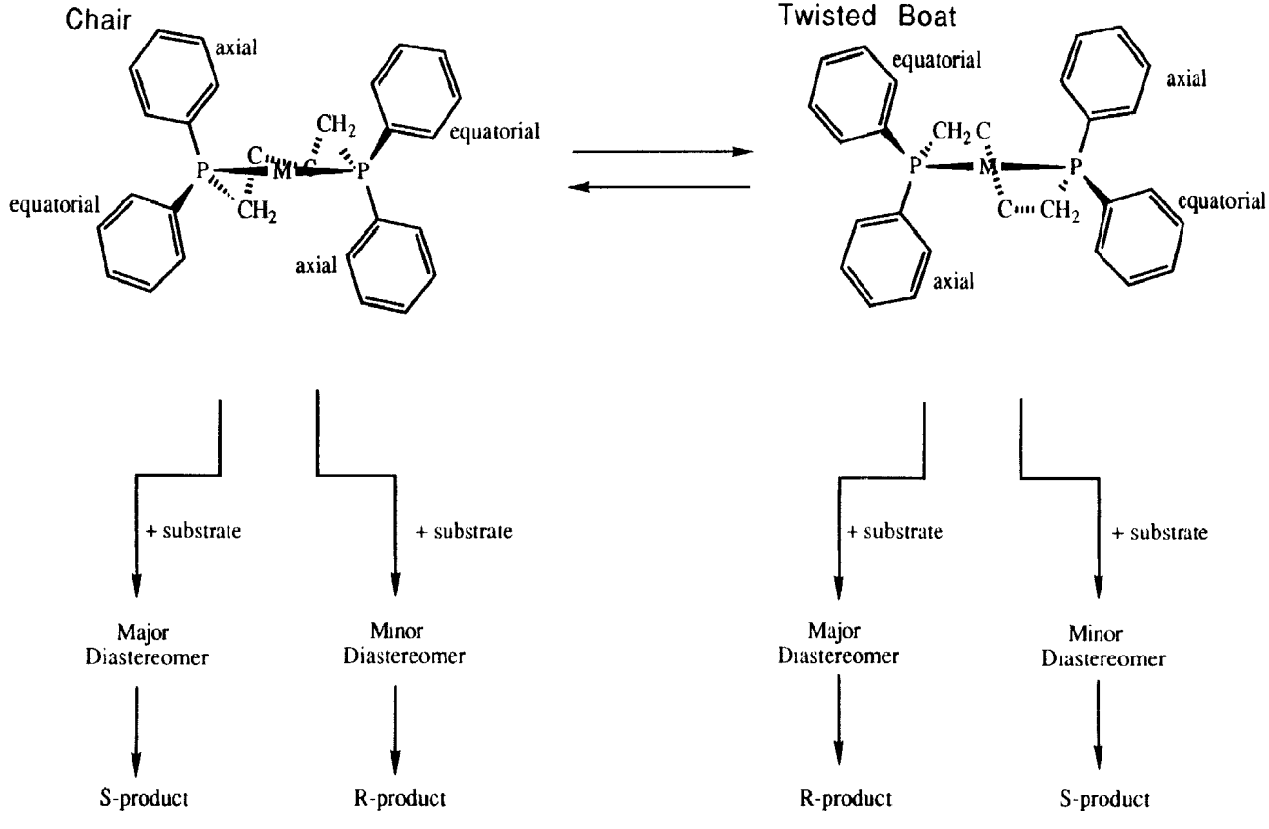
d Water/ethylacetate/benzene=1/0.5/0.5

## Discussion

Homogeneous Hydrogenation in MeOH. The optical yields provided by **3a** and BDPP, and **4a** and Chiraphos are similar; this is consistent with little change in ligand stereochemistry upon introduction of p-dimethylamino groups to the phenyl rings. In contrast, for the 7-membered chelating ring ligand, DIOP, a dramatic effect on optical yield is observed upon introduction of p-dimethylamino groups to the phenyl rings (Table 1). The presence of p-dimethylamino groups in **2a**, compared to DIOP, causes a reversal in the configuration of the prevailing product enantiomers. The nature and position of aryl substituents in DIOP analogues has previously been reported to have a significant influence on the enantioselectivity.[4-6,8] Furthermore the tetra-o-methoxy analogue,[6] like the p-dimethylamino derivative here, gives the opposite product antipodes. Since the 7-membered chelate ring of DIOP is flexible,[15] Brown and coworkers proposed that DIOP and tetra-o-methoxy-DIOP adopt different chelate conformations; the opposite conformations then lead to opposite product antipodes.[6]

Specifically, it was proposed that DIOP and its aryl substituted alkyl derivatives favor a chair conformation while the ortho-methoxy derivative prefers a twisted boat conformation. The twisted boat conformation could be stabilized by coordination of the ortho-methoxy groups of the axial phenyl groups to rhodium similar to what is observed in DIPAMP complexes.[16] This possibility was supported by the fact that, like the parent ligand and the alkyl substituted derivatives,[5] the (-)di para-methoxy derivative also gave R-dominance in the product composition[8] while the (-)tetra ortho-methoxy derivative gave products of S-configuration.[6] Both chair and twisted boat conformations provide an alternating axial-equatorial arrangement of the aryl groups. But, as shown in Scheme 2, the axial aryls in the twist-boat conformation move to equatorial sites when the chelate ring changes to the chair conformation. In principle these two conformers should lead to an opposite preference in the coordination of the two enantiotopic faces of the olefin.

**Scheme 2**


Chair
axial
equatorial
equatorial
axial
Twisted Boat
equatorial
axial
axial
equatorial
+ substrate
+ substrate
+ substrate
+ substrate
Major Diastereomer
Minor Diastereomer
Major Diastereomer
Minor Diastereomer
S-product
R-product
R-product
S-product

A more complete analysis of the mechanism of asymmetric hydrogenation shows that the ultimate success of asymmetric hydrogenation is determined by kinetic effects. Thus, the prevailing product enantiomer is derived from the diastereomeric substrate complex in which the substrate coordination is considered unfavorable, when this species reacts faster than the favored diastereomer. In principle then, both product antipodes are accessible through both ligand conformations. Many asymmetric hydrogenation systems with various ligands show kinetic control as judged by the effect of the reaction temperature[10,13,18-20] and hydrogen pressure[10,20] on enantioselectivity. In the case of rhodium DIOP complexes asymmetric hydroformylation can proceed via four different intermediates as described in Scheme 2. Furthermore the chair conformation of (-)DIOP will give products of R configuration if the reaction rate is faster through the minor diastereomeric intermediate.

For the diene complex, (**2a**)Rh(NBD)$^+$, NMR studies are also most consistent with a preference for the chair conformation.[19] However the solvent and substrate complexes are probably fluxional, making both twisted boat and chair conformations available. The diene in the precursor complex is thought to make the chelate conformations more rigid.[19] The comparative pressure dependences for **2a** and DIOP gives some insight to the mechanism. An increase in pressure, Table 5, causes a change in product configuration from S to R with **2a** as the ligand. A pressure increase will increase the rate through the major diastereomer in solution.[17,21] Since an increase in pressure is unlikely to change the preference in ligand conformation the observed pressure dependence is consistent with increased product formation through the major diastereomer of a given ligand conformation. Alternatively if the product is already formed through the major diastereomer at atmospheric pressure then a pressure increase will not lead to a change in the dominant product antipode. Importantly a similar effect is observed with DIOP itself but the dominant product antipode changes in the opposite sense. For example.in the

hydrogenation of N-benzoylaminocinnamic acid with [((-)DIOP)Rh(COD)]$^+$.the enantioselectivity changes from ca 58 % R at 1 bar to ca 6 % S at 50 bar $H_2$.[20] It can be concluded from these results that the most active forms of the respective rhodium complexes of **2a** and DIOP have the opposite ligand conformation; most likely chair for DIOP and twisted boat for **2a**. It is likely that hydrogenation proceeds to some extent via all four reaction paths shown in Scheme 2 in all cases.

The rate of hydrogenation is faster with the p-dimethylamino derivatives than with the parent ligands. In general the higher activity of the p-dimethylamino derivatives is expected from the experience that more basic ligands give more active catalysts.[4,22] This is also consistent with the trend (Table 1) that the hydrogenation activity increases with increasing the alkyl chain length in the chelates.[21,22] It has been suggested recently that the presence of the strong electron donating groups, $NMe_2$, can change the relative rate of hydrogenation through the two diastereomeric intermediates of a single ligand conformation.[4] Observation of the opposite product antipode with **2a** as the ligand compared with DIOP was attributed to this rate difference. This explanation is inconsistent with the pressure dependence of the enantioselectivities discussed above and with the fact that not only does **2a** but also the quaternized derivatives, **2b** and **2c** give the opposite product antipode as DIOP. Quaternization significantly reduces the electron donating ability of the p-dimethylamino group.

The presence of strong electron donating groups in **3a** and **4a**, which are considered to be conformationally stable,[19] does not lead to the opposite product antipode compared to the similar complexes without the dimethylamino groups. For these reasons the unique behavior of **2a-c** and o-methoxy-DIOP derivatives is most likely conformational rather than electronic.

The p-dimethylamino derivatives were originally prepared as intermediates in the synthesis of the water soluble quaternary amino derivatives. However, the use of p-dimethylamino derivatives in place of the non-substituted derivatives has advantages under conventional homogeneous conditions. Thus, the presence of p-dimethyl amino groups in the rhodium complexes significantly eases the separation and purification of the product from the catalyst (Experimental Section).[23,24] Furthermore, the higher activity could allow the use of higher substrate/rhodium ratios or allows the use of lower hydrogen partial pressures, which results in higher enantioselectivities. The ability to work at less than 1 bar of hydrogen partial pressure with complexes of **2-3a** gives a good method for improving enantioselectivity (Table 5).

The hydrogenation rates obtained with **2-4c** in methanol are somewhat slower than with **2-4a**, but still faster than the values reported for the non-substituted ligands.[5,10-14]

The values in Table 2 were obtained in the presence of a 4 fold excess of $HBF_4$ (0.1 ml aqueous $HBF_4$). At this concentration of $HBF_4$ it is estimated that the protonation of the amino groups not complete.[23] In fact, the enantioselectivities of these catalysts are not influenced by added $HBF_4$ in the range of 0-10 fold excess. When the protonation of the complexes of **2-4a** is not complete, that is when one, two or three amino groups are protonated new chiral centers at the phosphorous atoms are formed. This leads to the formation of new optical isomers of the ligands and, in the case of diprotonated ligands, a new geometrical isomer as well. The presence of these new isomers does not influence the enantioselectivity. Thus the key stereochemistry at rhodium is generated by the chelate ring. This is consistent with the results reported for the sulfonated chiral ligands that contain less than four sulfonate groups[2,9] and also with the results obtained with the partially methyl-quaternized complexes (vide-infra).

Two-Phase Hydrogenations. As it was shown previously, the two-phase hydrogenation of dehydrocinnamic acid derivatives is a homogeneous process in the aqueous phase.[3] This is consistent with the earlier findings on other two-phase systems[25,26] and with the experimental fact that no hydrogenation is observed when water insoluble substrates are used. Additionally, the optical yields achieved in two-phase applications are close to the values obtained in the absence of organic solvents (slurry hydrogenation).

The values with the p-dimethylammonium and the p-trimethylammonium derivatives of the same ligands (that is **2b** and **2c**, **3b** and **3c**, **4b** and **4c**) are similar, as expected. Rhodium complexes of **4b** and **4c** (Chiraphos derivatives) retained their high enantioselectivity under two-phase conditions, but complexes with **2b**, **2c** and **3b**, **3c** give lower enantioselectivity in aqueous phase than those with the non-quaternized (**2a** and **3a**) derivatives in MeOH (Table 1). However, the hydrogenation rates with the Chiraphos derivatives are very slow (Table 5) and the enantioselectivity is not affected by increasing pressure.

The complexes with the p-dimethylammonium and p-trimethylammonium derivatives of DIOP and BDPP ( **2b,c**, and **3b,c**) also give slow hydrogenation rates in water (Table 3) and their enantioselectivity is not influenced by increasing $H_2$ pressures in water (entries 4 and 5 in Table 5). For example, the hydrogenation rates in water at 14 bar pressure of $H_2$ are about 60 times slower for **3c** than in methanol at atmospheric pressure (Table 4). The reaction pressure only affects the catalyst enantioselectivity when the rates are already fast at atmospheric pressure (see Table 5).

Given the similarity between **2-4a** and **2-4c** in MeOH, as well as **2-4b** and **2-4c** in water, the drop in enantioselectivity is attributed to solvent effects rather than to structural changes caused by quaternization. This is supported by the facts that a solvent change from MeOH to water causes a drop in enantioselectivity for ligand **3c** (Table 4) and that the values for the p-quaternary amino derivatives of BDPP and Chiraphos are also similar to those reported for the m-sulfonated derivatives.[2] Thus it is likely that the difference in enantioselectivity obtained in MeOH and in two-phase in water conditions is due to the reaction kinetics in the two solvents as previously indicated.[9]

The hydrogenation results with incompletely quaternized ligands (ie. **3b**, **4b** containing 30% of tri-methylquaternized derivatives) are almost identical with those obtained with the pure tetra-quaternized derivatives. Again this is consistent with the postulate that enantioselection is based on the ligand chelate ring conformation and the resulting distribution of phenyl rings.

## Conclusions

Use of the p-dimethylamine derivatives of the chiral ligands, DIOP, BDPP, and Chiraphos, simplifies reaction workup due to the chemical properties of the amine group. When protonated or methyl quaternized the rhodium complexes of these ligands are extremely water soluble which makes them convenient to recycle effectively when used in two-phase applications.

The presence of p-amino and ammonium substituents on the phenyl rings of Chiraphos and BDPP does not change the enantioselectivity compared to the parent ligands. Thus the structure is unchanged upon substitution. The drop in enantioselectivity for **3b,c** derivatives compared to the values with **3a** or BDPP in MeOH is attributed to a solvent effect.

The presence of amino and ammonium substituents on the phenyl rings of DIOP, ligands **2a,b,c**, changes the sense of the product antipode compared to DIOP. The nature and position of aryl-substituents in DIOP derivatives has an influence on the chelate conformation and thus the observed enantioselectivity.

**Experimental Section**

Complexes with **2-4a**,**2-4b** and **2-4c** were prepared as previously described.[1] Solvents for hydrogenation were purged with a stream of oxygen-free argon for at least 10 min before use. The substrates were prepared by the standard literature methods.[27-29] The conversions were checked by $^1$H NMR and the optical yields were determined by polarimetry on a Perkin-Elmer 241 polarimeter by comparison with the literature values for the optically pure compounds.[5,14,30] Rhodium analyses were performed by atomic absorption spectroscopy on a Perkin-Elmer spectrometer with an air-acetylene flame. The produce solutions were digested in 5% HCl solution and compared with standard rhodium solutions. The limit of the detection for rhodium was 0.1 ppm.

Hydrogenation experiments. Hydrogenations were performed either in glass reactors connected to gas burettes at atmospheric pressures or in 30 ml stainless steel autoclaves at pressures higher than atmospheric under the reaction conditions given in Tables 1-6. Reaction products from the hydrogenations in methanol were worked up following the manner: Methanol was removed under vacuum and replaced with 10 ml 5% HCl solution. When the catalyst was to be recycled (Table 6) aqueous 0.5% $HBF_4$ solution was used in place of HCl. The products were then extracted with $Et_2O$. The etheric extracts were washed with water and dried over $MgSO_4$. Removal of the solvent resulted in practically rhodium-free (rhodium contamination under the detection limit) products. When the hydrogenation was performed in two-phase conditions the organic ethylacetate/benzene=1/1 solutions were simply separated from the aqueous catalyst solutions. The separated organic solutions were then washed with a few ml of water and dried over $MgSO_4$. The evaporation of the solvents gave also practically rhodium-free

products in case of the methyl-quaternized complexes. When the hydrogenations were performed in aqueous $HBF_4$ solutions the rhodium contamination values were significantly higher (Table 6), probably due to the better solubility of the protonated complexes in the organic phases (dissociation equilibria[23]). Products from the slurry application could be simply filtered off from the aqueous catalyst solutions, but as the racemates have better solubility than the pure enantiomers this could lead to a resolution process.[3] Therefore, the aqueous phase should be extracted with $Et_2O$ (3 x 50 ml) to avoid the errors in the determination of optical yields.

In all cases when the reactions were done as a slurry in water rhodium was present in the hydrogenated product which crystallized from solution. Repeated washing of the product with cold water was necessary to remove the rhodium. The percentage rhodium loss reported in Table 6 represents the rhodium contained in the product after filtration without washing with water.

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References

1. I. Toth, B. E. Hanson, previous paper.
2. Y. Amrani, L. Lecomte, D. Sinou, J. Bakos, I. Toth, B. Heil, Organometallics, **8**, 542 (1989).
3. I. Toth, B. E. Hanson, M. E. Davis, Cat. Lett., **5**, 183 (1990).
4. T. Morimoto, M. Chiba, K. Achiwa, Tetra. Lett., **29**, 4755 (1988).
5. T. P. Dang, J. C. Poulin, H. B. Kagan, J. Organomet. Chem., **91**, 105 (1975).
6. J. M. Brown, P. A. Chaloner, B. A. Murrer, D. Parker, A.C.S. Symposium Ser., **119**, 169 (1980).
7. W. S. Knowles, W. C. Christopher, K. E. Koenig, C. F. Hobbs, Adv. Chem., **196**, 325 (1982).
8. T. Yamagashi, M. Yaagai, H. Hatakeyama, M. Hida, Bull. Chem. Soc. Japan., **57**, 1897 (1984).
9. L. Lecomte, D. Sinou, J. Bakos, I. Toth, B.Heil, J. Organomet. Chem., **370**, 277 (1989).

10. D. Sinou, Tetra. Lett., **22**, 2987 (1981).

11. H. B. Kagan, T. P. Dang, J. Am. Chem. Soc., **94**, 6429 (1972).

12. P. A. MacNeil, N. K. Roberts, B. Bosnich; J. Am. Chem. Soc., **103**, 2273 (1981).

13. J. Bakos, I. Toth, B. Heil, L. Marko, J. Organomet. Chem., **279**, 23 (1985).

14. M. D. Fryzuk, B. Bosnich, J. Am. Chem. Soc., **99**, 6262 (1977).

15. V. Gramlich, G. Consiglio, Helv. Chim. Acta, **62**, 1016 (1979).

16. B. D. Vineyard, W. S. Knowles, J. J. Sabacky, G. L. Bachman, D. J. Weinkauff, J. Am. Chem. Soc., **99**, 5946 (1977).

17. (a) A. S. C. Chan, J. J. Plath, J. Halpern, J. Am. Chem. Soc., **102**, 5952 (1980); (b) J. M. Brown, P. A. Chaloner, J. C. S. Chem. Commun., 344, (1980); (c) J. Halpern, Science, **217**, 401 (1982).

18. (a) D. P. Riley, R. E. Shumate, J. Org. Chem., **45**, 5187 (1980). (b) J. Bakos, I. Toth, B. Heil, G. Szalontai, L. Parkanyi, V. Fulop, J. Organomet. Chem., **370**, 263 (1989).

19. I. Toth, B. E. Hanson, work in progress.

20. I. Ojima, T. Kogure, N. Yoda, J. Org. Chem., **45**, 4728 (1980).

21. J. Halpern, in 'Asymmetric Synthesis' ed. J. D. Morrison, Ac. Press, Orlando, Florida, Vol. 5, p. 41 (1985).

22. J. C. Poulin, D. P. Dang, H. B. Kagan, J. Organomet. Chem., **84**, 87 (1975).

23. I. Toth, B. E. Hanson, M. E. Davis, J. Organomet. Chem., (in press).

24. I. Toth, B. E. Hanson, M. E. Davis, J. Organomet. Chem., (in press).

25. Y. Dror, J. Manassen, J. Mol. Catal., 2, 219 (1977).

26. A. F. Borowski, D. J. Cole-Hamilton, G. Wilkinson, Nouv. J. Chim., 2, 137 (1978).

27. R. M. Herbst, D. Shemin, Org. Synth., col. vol. 2, Wiley, New York, NY, p 1 (1943).

28. H. B. Gillespie, H. R. Snyder, Org. Synth., col. vol. 1, Wiley, New York, NY, p. 489 (1941).

29. H. E. Carter, W. C. Rissert, J. Biol. Chem., **159**, 255 (1981).

30. R. Glaser, S. Geresh, Tetrahedron, **35**, 2381 (1979).