New Class of Chiral Diphosphine Ligands for Highly Efficient Transition Metal-Catalyzed Stereoselective Reactions: The Bis(diphenylphosphino) Five-membered Biheteroaryls†

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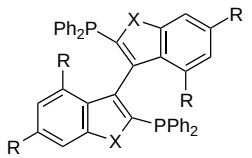
The synthesis and application of three examples of a new class of chiral (C_2) atropisomeric diphosphines characterized by two interconnected five-membered heteroaromatic rings, with hindered rotation around the interanular bond, are described. Optically pure (+)- and (−)-2,2′-bis(diphenylphosphino)-4,4′,6,6′-tetramethyl-3,3′-bibenzo[*b*]thiophene (tetraMe-bitianp) (**1a**) and the parent unsubstituted system (+)- and (−)-bitianp (**1b**) were synthesized. They were found to be optically stable at 100 °C and were successfully employed as ligands in the Ru(II)-catalyzed hydrogenation of α- and *β*-oxo esters to the corresponding α- and *β*-hydroxy esters and in the hydrogenation of olefinic substrates. The optical and chemical yields were comparable with those reported for the same Ru(II)-binap-catalyzed reactions carried out under the same experimental conditions. The 2,2′-bis(diphenylphosphino)-3,3′-bibenzo[*b*]furan (**1c**), the oxygenated analogue of bitianp, was found to be configurationally unstable at room temperature. Complete structural X-ray elucidation of the Pd complexes of **1a**−**c** is reported. The advantages of these biheteroaromatic ligands over the classical biaryl systems are discussed.

Introduction

The design and development of new chiral diphosphine ligands for transition metals to give suitable catalysts in stereoselective reactions has been consistently conditioned by binap. Binap is such a versatile and efficient ligand in many asymmetric transformations, both on the laboratory scale and in multipatented industrial processes,[1] that chemists had no incentive to develop alternative ligands. In fact dissymmetric biphenyl derivatives have attracted much less attention than the binaphthyl systems, even though the fine tuning of the basicity of phosphine groups appears to be much easier in the biphenyl series.[2] Difficulty in regioselectively introducing substituents onto the binap skeleton could explain why research on binap has been much more oriented toward finding new applications for binap itself than to functionalizing it in order to provide the ligand with new properties.

We recently published in a preliminary report[3] the first example of a new class of chiral atropisomeric diphosphines, that of diphosphino five-membered biheteroaryls: we described the synthesis of the optically pure (+)- and (−)-2,2′-bis(diphenylphosphino)-4,4′,6,6′-tetramethyl-3,3′-bibenzo[*b*]thiophene, (+)- and (−)-(**1a**) (tetraMe-bitianp) and their application as ligands in several homogeneous stereoselective reactions catalyzed by Ru(II). The chemical and optical yields of the hydrogenation experiments of five α- and *β*-oxo esters to the corresponding α- and *β*-hydroxy esters were similar to those reported in the literature for the analogous Ru(II)-binap-catalyzed reactions, carried out under the same experimental conditions.

This paper reports: (1) a general presentation of this new class of diphosphines; (2) the synthesis and the resolution of the unsubstituted ligand, the 2,2′-bis(diphenylphosphino)-3,3′-bibenzo[*b*]thiophene (**1b**) (bitianp); (3) the results of the extension of the model to the benzofuran series, with the synthesis of the 2,2′-bis(diphenylphosphino)-3,3′-bibenzo[*b*]furan (**1c**); (4) the preparation and the structural characterization of the Pd(II) complexes of the ligands **1a**−**c**; (5) the catalytic applications of enantiomerically pure **1a**- and **1b**-Ru(II) complexes in the hydrogenation of carbonyl and olefinic substrates.



1a: X = S; R = CH_3 (tetraMe-bitianp)
1b: X = S; R = H (bitianp)
1c: X = O; R = H

† This paper is dedicated to Professor Fernando Montanari, enthusiastic supporter of this research project, on the occasion of his 70th birthday.

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Bis(diphenylphosphino) five-membered biheteroaryl ligands are characterized by a backbone composed of two interconnected five-membered heteroaromatic rings. Rotation around the interanular bond is prevented by steric interaction between the *ortho* diphenylphosphino groups and bulky substituents in *ortho*′ positions [a dimethyl-substituted condensed benzene ring in the case of tetraMe-bitianp (**1a**)].

Compared with classical carbocyclic biaryls, the design of biheteroaromatic systems leads to the following structural and synthetic advantages.

(i) The electron-donor properties of the phosphorus atoms, a crucial parameter for catalytic activity, can be tuned by changing the supporting heterocyclic system. In fact, it is well known that aromatic five-membered heterocycles range from very electron-rich systems, like pyrrole, furan, and thiophene, to very electron-poor rings, like thiazole and triazole.[4] Alternatively, the electronic properties of the phosphine groups can be modulated by changing their position and/or that of the interanular bond on a given heterocycle.

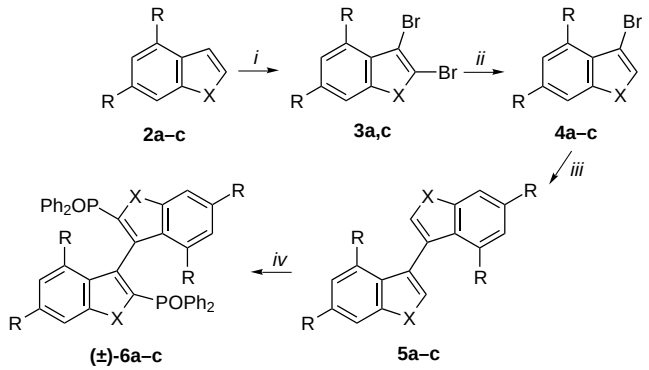
(ii) A properly substituted biheteroaryl system can easily satisfy both symmetry and configurational stability requirements, since atropisomeric biaryls with C_2 symmetry are recognized among the most efficient ligands for many transition metal-catalyzed stereoselective reactions.

(iii) The geometry associated with two interconnected five-membered rings is new, and it was interesting to compare it with the data reported in literature for known biaryl systems, all of which are derived from the connection of two six-membered rings. Furthermore, the geometry of the chelated ring in the complexes should depend on the nature of the heterocycle, since it is well documented that each heteroaromatic system shows typical internal angles and characteristic external bond directions.

(iv) The synthetic approaches to substituted pentatomic heteroaromatic rings are much more flexible than those available for carbocyclic aromatic systems. The easy and regioselective metalation of heteroaromatic pentatomic rings[5] can be a very helpful tool in introducing the phosphine functions, as well as in forming the interanular bond.

Five-membered aromatic heterocycles are gaining credit today in the design of new ligands for asymmetric homogeneous catalysis and some diphosphines containing pentatomic heteroaryls as substituents were recently described in literature. The synthesis and the resolution, achieved through fractional crystallization of diastereomeric palladium−aminato complexes, of the 2,2′-bis-(diphenylphosphino)-3,3′-biindole, were recently reported by J. M. Brown and R. Selke.[6] This compound belongs to the class of diphosphino five-membered biheteroaryls and its stucture is included in our original patent.[7] Data on the application of this ligand in asymmetric catalysis are not yet available. A few recently patented ligands

Scheme 1[a]



[a] (i) $Br_2/CHCl_3$; (ii) (1) BuLi, (2) H_2O; (iii) (1) BuLi, (2) $CuCl_2$; (iv) (1) BuLi, (2) Ph_2POCl. **a**: X = S, R = CH_3. **b**: X = S, R = H. **c**: X = O, R = H.

containing the dibenzofuran,[8] furan, thiophene, and pyrrole ring[9] do not belong to the class of five-membered biheteroaromatic diphosphines, since all of them are characterized by a biphenyl backbone.

Results and Discussion

Preparation and Characterization of the Ligands. We synthesized the tetraMe-bitianp (**1a**) first and then unsubstituted bitianp (**1b**), since we did not know whether or not it was necessary to have the two methyl groups in position 4 and 4′ in order to hinder rotation around the interanular bond and thus ensure good configurational stability to the ligand. In fact, the steric interference of the *ortho* substituents to the interanular bond of two interconnected five-membered planar rings is lower than that expected for two six-membered arene units.

The synthetic sequence to achieve tetraMe-bitianp (**1a)** is reported in Scheme 1: the starting product was the known 4,6-dimethylbenzo[*b*]thiophene (**2a**).[10] Three regioselective metalation steps of the thiophene ring and the resolution step of the bis-phosphine oxide **6a** (tetraMe-bitianpo), according to a known methodology,[11] are outlined. Optically pure (+)- and (−)-tetraMe-bitianpo (**6a**) were obtained by a single crystallization of their adducts with (+)- and (−)-dibenzoyltartaric acids. Alkaline decomplexation followed by trichlorosilane reduction gave enantiomerically pure (+)- and (−)-tetraMe-bitianp (**1a**).

The synthesis of (+)- and (−)-2,2′-bis(diphenylphosphino)-3,3′-bibenzo[*b*]thiophene (**1b**) (bitianp) is much simpler than that of **1a**, since thianaphthene (**2b)** is commercially available, and its bromination is highly regioselective in position 3 and directly produces **4b** with good yields.[12] The resolution process was again achieved through a single crystallization of bitianpo (**6b**)−dibenzoyltartaric acid adducts. The enantiomerically pure

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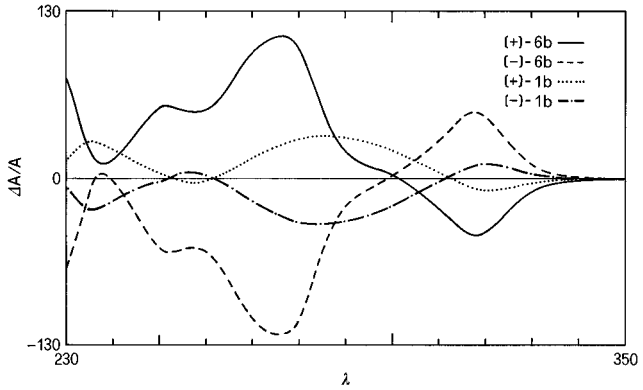


Figure 1.

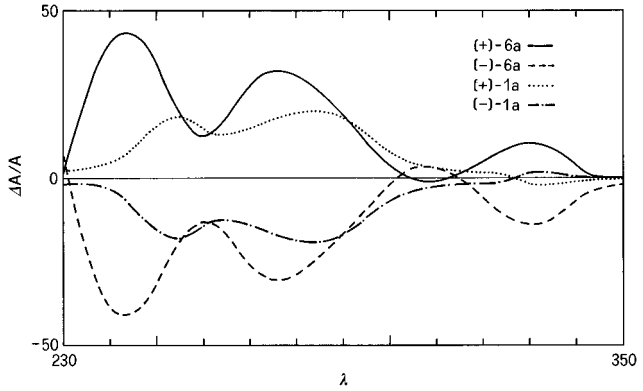


Figure 2.

phosphines (+)- and (−)-**1b** were obtained by trichlorosilane reduction of enantiomerically pure phosphinoxides (+)- and (−)-**6b**, respectively, and were found configurationally stable at 100 °C in DMF solution.

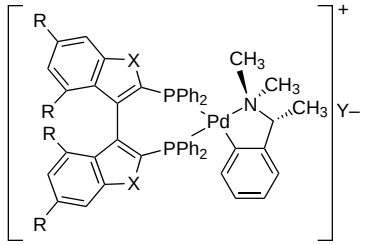
The oxygenated analogue of bitianpo, the 2,2′-bis(diphenylphosphinyl)-3,3′-bibenzo[*b*]furan (**6c**), was obtained through the same synthetic sequence described for **6a**. We were not able to resolve racemic **6c** through the adducts with dibenzoyltartaric acids, but resolution was found to be possible through chiral HPLC. However this technique was unsuccessful in the case of the corresponding phosphine **1c**; proof will be given later that diphenylphosphino-3,3′-bibenzo[*b*]furan (**1c**) is not configurationally stable at room temperature.

The optical purity of (+)- and (−)-tetraMe-bitianp (**1a**), (+)- and (−)-bitianp (**1b**), and that of the corresponding oxides (+)- and (−)-**6a** and (+)- and (−)-**6b,** was determined by HPLC on a chiral stationary phase and confirmed by the CD spectra.

The CD spectra of the phosphine enantiomers and of the corresponding phosphorus oxides showed almost perfect mirror-image shapes; (+)-tetraMe-bitianp (**1a**) was characterized by three positive CD effects at 245, 276, and 330 nm, while (−)-tetraMe-bitianp (**1a**) gave a mirror-image spectra. (+)- and (−)-tetraMe-bitianpo (**6a**) showed two maxima of the same sign at 255 and 284 nm and one maximum of minor intensity and opposite sign at 332 nm (Figure 1). Analogously, (+)- and (−)-bitianpo (**6b**) gave two maxima of the same sign at 251 and 276 nm and a third maximum of opposite sign at 318 nm; (+)- and (−)-bitianp (**1b**) gave simpler spectra, with an intense maximum at 285 nm and a minor one of opposite sign at 320 nm (Figure 2).

In the absence of an X-ray structural determination of the absolute configuration and in analogy with the results found with binap (and related phosphines)[11] and with bichemp,[13] the sign of the specific optical rotation at 589 nm, the sign of the Cotton effect, at least in the 230−300 nm region, and the results of the enantioselective catalytic reduction of various substrates with the ruthenium phosphine complexes (vide infra) strongly suggested that positive CD and $[\alpha]_D$ correspond to the *R* configuration and, of course, negative CD and $[\alpha]_D$ correspond to the *S* configuration of the ligand.

The configurational stability of the ligands **1a**−**c** at room temperature was also investigated by ^{31}P NMR analysis of their diastereomeric chloro or perchlorate Pd(II) complexes **7a**−**c** and **8a**−**c**.



7a: R = CH_3; X = S, Y = Cl^- **8a**: Y = ClO_4^-
7b: R = H, X = S, Y = Cl^- **8b**: Y = ClO_4^-
7c: R = H, X = O, Y = Cl^- **8c**: Y = ClO_4^-

The palladium complexes **7a**−**c** were prepared directly in an NMR tube, according to a known method.[14] Racemic tetraMe-bitianp **1a** and bitianp **1b** and **1c** quantitatively reacted with 1 equiv of di(*μ*-chloro)bis[(*R*)-dimethyl(α-methylbenzyl)aminato-C^2N]dipalladium(II), in $CDCl_3$ solution, to give the complexes **7a**−**c**. The addition of a stoichiometric amount of $AgClO_4$ in toluene solution produced the cationic complexes **8a**−**c**. The ^{31}P NMR spectra of the complexes exhibited the expected eight lines, four clustered around 30 ppm and four around 8 ppm, generated by the two nonequivalent phosphorus atoms in a cis arrangement. All the lines were of equal area, within the experimental error, in the case of the complexes derived from **1a** and **1b**, indicating that the two diastereoisomers were produced in a 1:1 ratio. We took these results as corroboration of the configurational stability of these ligands at room temperature and this was confirmed by the successful resolution of the racemates into optical antipodes. Instead, the cationic complex **8c** was obtained as a thermodynamic mixture of two diastereoisomers. The ^{31}P NMR spectrum showed the expected two sets of two doublets of doublets, but in a 3:1 ratio, indicating that flipping of the biheteroaryl frame occurred during complexation. This result is in agreement with the inability of chiral HPLC to resolve the racemic **1c**, although, as already stated, the corresponding racemic phosphine oxide **6c** was well separated by chiral HPLC, indicating its configurational stablility at room temperature. This demonstrates the crucial role played by the oxygen atoms of the phosphinyl groups in hindering rotation around the interanular bond. Our attempts to achieve total or partial resolution of the diastereomeric palladium complexes were unsuccessful.

Crystal Structure of Palladium(II) Dichloride Complexes of 1a−c. Since the above aminato complexes were obtained as microcrystalline compounds, but

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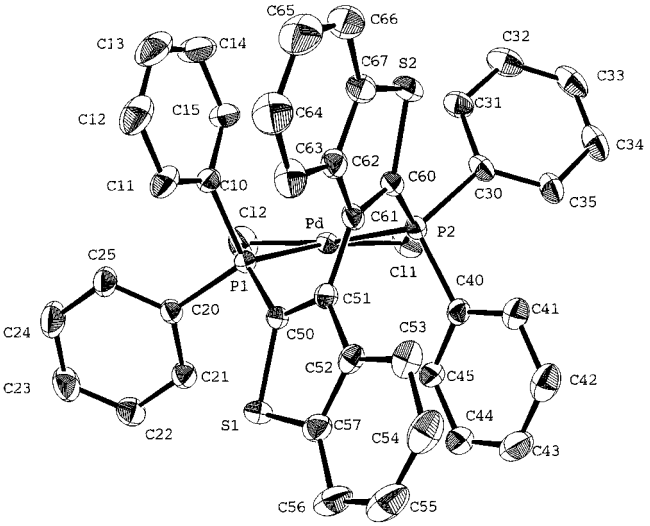

Figure 3.

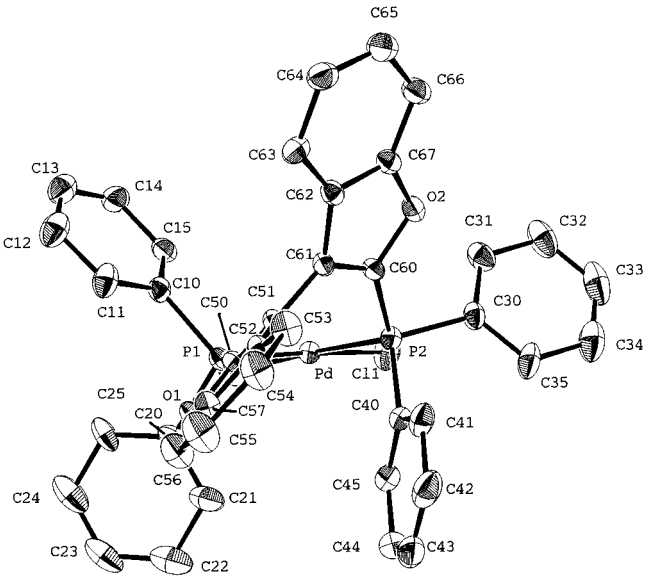

Figure 4.

unsuitable for an X-ray structural investigation, we turned to the $PdCl_2$ complexes **9a**−**c**, prepared from the ligands **1a**−**c** and $(PhCN)_2PdCl_2$.

The X-ray structure determination of the square-planar complexes shows that crystals of **9b** contain clathrated molecules of acetone and diethyl ether, whereas dichloromethane molecules are trapped in the crystals of **9a** and **9c**. Views of the molecular structure of **9b** and **9c** are reported in Figures 3 and 4, respectively. The conformational features of the tetraMe-bitianp and bitianp molecules in **9a** and **9b**, respectively, are very similar and comparable to those of the binap ligand in analogous complexes:[15] (*i*) the seven-membered diphosphine−metallacycle is highly skewed and conforms to the C_2 idealized symmetry, with the binary axis passing through the metal atom and the midpoint of the C51−C61 interanular bond; (ii) two of the four phenyl rings are oriented approximately parallel to each benzothiophene moiety thus achieving a "quasi-graphitic" interaction, as commonly observed in complexes with the triphenylphosphine ligand.[16] Instead there was severe deviation from the idealized C_2 symmetry for the diphosphine arrangement in complex **9c**; the parallelism between two of the phenyl rings and the benzofuran moiety is no longer retained, and the dihedral angle between the two moieties is 45.4°; **9a** and **9b** had values of 75.6 and 69.6°, respectively. These angles also greatly differ from binap complexes, reflecting the nature of the central metal and surrounding ligands. As the $PdCl_2$ system is common to all three complexes the different conformation of the diphosphine moiety observed in **9c** can probably be ascribed to the different geometrical features of the five-membered ring (compare the average C−O and C−S distances of 1.39 and 1.74 Å, respectively and the C−O−C and C−S−C angles of 106° and 91°, respectively).

Assuming that the variation in bond distances and angles on passing from the coordinated ligand to the free one is not substantial, a model derived from the structure solution of the palladium complexes can be computed for **1a**−**c**. Two limit conformations, where both the heteroaromatic units are coplanar, and with the interanular torsion angle of 0° or 180° respectively, should exist for the enantiomerization transition states of the free ligands. Contrary to what happens for **1a** and **1b,** both these conformations lead to such P····P and P····C distances in **1c** that rotation can be expected.

Synthesis of the Ruthenium(II) Complexes[17] of TetraMe-bitianp and Bitianp and Their Application to the Stereoselective Hydrogenation of Ketones and Alkenes. The catalysts (tetraMe-bitianp)$RuCl_2$, (+)- and (−)-**10a**, and (bitianp)$RuCl_2$, (+)- and (−)-**10b**, were prepared in DMF solution following a known procedure[18] and directly employed without further purification.

The complexes (tetraMe-bitianp)$Ru(CH_3COO)_2$, (+)- and (−)-**11a,** and (bitianp)$Ru(CH_3COO)_2$, (+)- and (−)-**11b,** were prepared from the ruthenium chloro complexes **10a** and **10b** by reaction with 1.05 equiv of silver acetate in toluene solution. Filtration of AgCl, followed by the removal of the solvent in vacuo and extractive workup with hexane, afforded crude (+)- or (−)-**11a** and (+)- or (−)-**11b** in quantitative yields. The complexes **11a** and **11b** are very soluble in hydrocarbons and moderate quantities of pure microcrystalline products were obtained only by prolonged storage of the hexane solutions at −18 °C. The complexes [(tetraMe-bitianp)$_2$Ru(*p*-cymene)I]I, (+)- and (−) **12a,** were obtained from [Ru(*p*-cimene)I_2] according to literature methods.[19]

Two classes of reactions have been investigated so far: the hydrogenation of α- and *β*-oxo esters to the corresponding α- and *β*-hydroxy esters and the hydrogenation of olefinic substrates.

Asymmetric Hydrogenation of α- and *β*-Oxo Esters. Methanol was the solvent of choice for all the catalytic reactions; temperature range was from 25 to 70 °C; the hydrogen partial pressure was 100 Kg/cm^2, unless otherwise stated; and the substrate/catalyst molar ratio varied from 300 to 1000.

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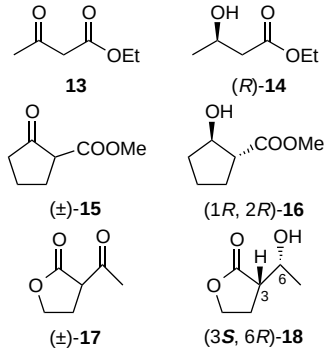
Table 1. Asymmetric Hydrogenation of α- and *β*-Keto Esters

catalyst	substrate	S/C	*T* (°C)	*t* (h)	conv (%)	de (%)	ee (%) (binap)	conf
(+)-**10a**	**13**	1000	70	2	95		99 (>99)[28]	*R*
(−)-**10b**	**13**	1000	70	2	91		99 (>99)[28]	*S*
(+)-**10a**	**15**	1000	70	2	100	86	99 (88)[27]	1*R*,2*R*
(−)-**10b**	**15**	1000	70	2	92	78	97 (88)[27]	1*S*,2*S*
(+)-**10a**	**17**	1000	70	50	100	92	91 (93)[27]	3*S*,6*R*
(−)-**10a**	**19**	1000	25	100	92		90 (85)[28]	*R*
(−)-**10a**	**21**	600	25	100	100		88 (88)[19]	*S*
(−)-**10a**	**23**	1000	25	100	90		78 (79)[19]	*S*

Table 1 reports the results of the asymmetric reduction of various ketonic substrates with the (phosphine) ruthenium complexes **10a**,**b** and **11a**. Ethyl 3-oxobutanoate (**13**) was reduced to ethyl 3-hydroxybutanoate (**14**) with enantioselectivity higher than 99% both with (+)-**10a** and (−)-**10b**. A 5% of the dimethyl acetal of methyl 3-oxo-butanoate was formed in both cases.

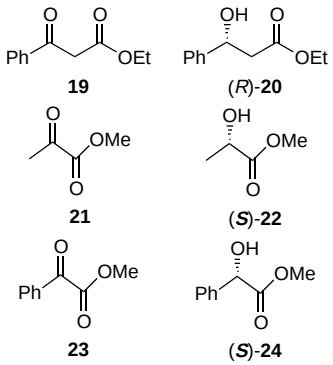


13 (*R*)-**14**

(±)-**15** (1*R*, 2*R*)-**16**

(±)-**17** (3***S***, 6*R*)-**18**

(+)-**10a** was found to quantitatively give (1*R*,2*R*)-2-(methoxycarbonyl)cyclopentanol (**16**) from 2-(methoxycarbonyl)cyclopentanone (**15**), with almost complete enantioselectivity (ee > 99%) and 86% de (GC, see Experimental Section). (−)-**10b** gave the (1*S*,2*S*) diastereoisomer of **16**, with a 97% ee and with a 78% de, together with an 8% of the dimethyl acetal of 2-(methoxycarbonyl)cyclopentanone. (+)-**10a** was able to reduce (±)-2-acetylbutyrolactone (**17**) affording (3*S*,6*R*)-3-(6-hydroxyethyl)butyrolactone (**18**), with a 91% ee and 92% de (GC, see Experimental Section). (−)-**10a** reduced methyl benzoylacetate (**19**) to (*R*)-methyl 3-hydroxy-3-phenylpropionate (**20**), with a 90% ee. The complex (−)-**10a** reduced methyl piruvate (**21**) to (*S*)-methyl lactate (**22**), with a 88% ee, and methyl phenylglyoxylate (**23**) to (*S*)-methyl mandelate (**24**), with a 78% ee.



19 (*R*)-**20**

21 (***S***)-**22**

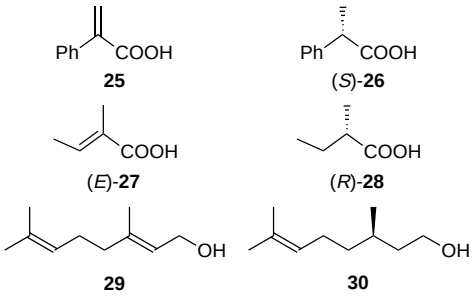
23 (***S***)-**24**

Asymmetric Hydrogenation of Olefinic Substrates. The phosphines **1a** and **1b** showed also very high stereoselectivity when used as ligands in bis(acetate)ruthenium complexes. Table 2 shows the results of the asymmetric reductions of various olefinic substrates.

Table 2. Asymmetric Hydrogenation of Olefinic Substrates

catalyst	substrate	S/C	H_2 (Kg/cm^2)	*T* (°C)	*t* (h)	conv (%)	ee (%)	conf
(−)-**11a**	**25**	300	100	25	4	100	90	*S*
(+)-**11b**	**25**	300	100	25	4	100	86	*R*
(−)-**11a**	**27**	500	10	25	85	100	89	*S*
(+)-**11b**	**27**	500	10	25	44	100	88	*R*
(−)-**12a**	**27**	500	10	25	88	100	92	*S*
(−)-**11a**	**29**	600	100	25	85	100	94	*R*

Atropic acid (**25**) was reduced to 2-phenylpropionic acid (**26**) by (−)-**11a** and (+)-**11b**, with 90% and 86% ee respectively. The same complexes were able to reduce tiglic acid (**27**) to 2-methylbutanoic acid (**28**) with 89% and 88% ee respectively. The stereoselectivity rose to 92% ee when the (*p*-cymene)ruthenium diiodide (−)-**12a** was employed. Geraniol (**29**) was reduced by (−)-**11a** to (*R*)-(−)-citronellol (**30**), with a 94% ee; only traces of dihydrocitronellol, arising from further reduction of the second double bond, were detectable.



25 (*S*)-**26**

(*E*)-**27** (*R*)-**28**

29 **30**

Conclusions

The results reported above suggest the following conclusions:

(1) The bis(diphenylphosphino)bibenzo[*b*]thiophenes **1a** and **1b** are the first examples of a new class of chiral ligands, very promising for asymmetric homogeneous catalysis: the class of the diphosphino five-membered biheteroaryls. These systems show an enantioselection ability quite similar to that exhibited by the most efficient and popular ligands, like binap, but the synthetic access is easier.

(2) The new geometry of the metallacycle in the complexes, produced by two interconnected five-membered units, has proven to be very favorable for enantioselectivity and catalytic activity.

(3) The choice of the heterocyclic system is crucial both to tune the electronic properties of the phosphine groups and to ensure good ligand configurational stability. The comparison of bibenzothiophene and bibenzofuran systems is clear: while ligand **1b** is configurationally stable at over 100 °C temperature, ligand **1c** cannot be resolved at room temperature.

We have recently synthesizes several other biheteroaromatic diphosphines of the 2,2′- and 3,3′-biindole, 3,3′-bithiophene, 1,1′-bibenzimidazole, and 2,2′-bipyrrole series and, in a few cases, we have been able to resolve them into optical antipodes.[7,20] Research is in progress to verify first their ability as ligands for transition metals, and then to establish the activity and stereoselection ability of their complexes as catalysts in homogeneous asymmetric syntheses.

Experimental Section

General. Chiral gas chromatographic (GC) analyses were perfomed with a chiral capillary column β-DEX, 25 mt, 0.25 mm, 0.4 μm film (carrier Helium). Chiral HPLC analyses were performed with a DAICEL CHIRACEL OD column (254 nm). The CD spectra were recorded in CH_2Cl_2 solution and plotted as mDeg/*A* where *A* is the UV absorption of the same solution at 300 nm. We chose this way to plot the spectra so as to be independent of the solution concentration and to avoid problems in comparing spectra when very large molar extinction coefficients are involved.

Preparation of 2,3-Dibromo-4,6-dimethylbenzo[*b*]thiophene (3a). A solution of bromine (13 mL) in $CHCl_3$ (50 mL) was dropped into a mixture of 4,6-dimethylbenzo[*b*]thiophene (**2a**)[10] (19.4 g) and AcOK (24 g) in $CHCl_3$ (300 mL). The mixture was stirred, and after 1 h, water was added. The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. Chromatography (SiO_2, eluted by petroleum ether) provided pure **3a** (25.40 g, 65%): mp 58−62 °C; ^{1}H NMR ($CDCl_3$) δ 2.4 (s, 3H), 2.84 (s, 3H), 6.9 (s, 1H), 7.35 (s, 1H).

Preparation of 3-Bromo-4,6-dimethylbenzo[*b*]thiophene (4a). BuLi (0.09 mol, 1.6 M solution in hexane) was dropped into a solution of **3a** (25.40 g) in dry THF (300 mL) at −20 °C under N_2. The mixture was stirred for 1 h, poured into water, and treated with 2 N HCl solution. The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. The residue was distilled (bp 160 °C, 1 mmHg) to give **4a** (15.30 g, 80%): mp 55 °C; ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 3H), 2.90 (s, 3H), 6.95 (s, 1H), 7.3 (s, 1H), 7.5 (s, 1H).

Preparation of 4,4′,6,6′-Tetramethyl-3,3′-bibenzo[*b*]thiophene (5a). A solution of **4a** (15.3 g) in THF (70 mL) was dropped into a solution of BuLi (0.070 mol, 1.6 M solution in hexane) in THF (150 mL) at −70 °C, under N_2. After 30 min of stirring, $CuCl_2$ (9.52 g) was added; the mixture was stirred for 6 h and then allowed to warm to 0 °C, quenched with 2N HCl solution, and stirred overnight. The mixture was concentrated and extracted with CH_2Cl_2, and the organic layer was dried (Na_2SO_4) and concentrated in vacuo. Chromatography (SiO_2, hexane) provided pure **5a** (4.5 g, 44%): mp 126 °C; ^{1}H NMR ($CDCl_3$) δ 1.9 (s, 6H), 2.4 (s, 6H), 6.9 (s, 2H), 7.2 (s, 2H), 7.5 (s, 2H); mass spectrum *m*/*z* 322 (M^+). Anal. Calcd for $C_{20}H_{18}S_2$: C, 74.49; H, 5.63. Found: C, 74.23; H, 5.57.

Preparation of (±)-2,2′-Bis(diphenylphosphino)-4,4′,6,6′-tetramethyl-3,3′-bibenzo[*b*]thiophene (1a). BuLi (0.031 mol, 1.6M solution in hexane) was dropped into a solution of **5a** (4.5 g) and TMEDA (4.5 mL) in THF (80 mL) at −50 °C under N_2, and then the temperature was allowed to warm to 0 °C. After 30 min, diphenylphosphinous chloride (5.7 mL) was added. The mixture was stirred 2 h and then concentrated in vacuo. The residue was treated with water, and the organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. The crude reaction product was tritured with isopropyl ether to give **1a** (5 g, 52%): mp 255−260 °C; ^{1}H NMR ($CDCl_3$) δ 1.6 (s, 6H), 2.4 (s, 6H), 6.7 (s, 2H), 7.2 (m, 22H); ^{31}P NMR ($CDCl_3$) δ −24.98; mass spectrum *m*/*z* 690 (M^+). Anal. Calcd for $C_{44}H_{36}P_2S_2$: C, 76.50; H, 5.25. Found: C, 76.15; H, 5.18.

Preparation of (±)-2,2′-Bis(diphenylphosphinyl)-4,4′,6,6′-tetramethyl-3,3′-bibenzo[*b*]thiophene (6a). H_2O_2 (6 mL, 35%) was dropped into a solution of (±)-**1a** (4.3 g) in CH_2Cl_2 (100 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C and for 1 h at 25 °C, and then water was added. The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. Chromatography (SiO_2, eluted by AcOEt/CH_2Cl_2/Et_3N 3:7:0.1) provided pure **6a** (4.32, 96%): mp 260 °C; ^{1}H NMR ($CDCl_3$) δ 1.5 (s, 6H), 2.4 (s, 6H), 6.7 (s, 2H), 7.4 (m, 22H); ^{31}P ($CDCl_3$) δ 20.36; mass spectrum *m*/*z* 722 (M^+). Anal. Calcd for $C_{44}H_{36}O_2P_2S_2$: C, 73.11; H, 5.02. Found: C, 73.05; H, 4.97.

Optical resolution of (±)-2,2′-bis(diphenylphosphinyl)-4,4′,6,6′-tetramethyl-3,3′-bibenzo[*b*]thiophene [(±)-6a] with (−) or (+)-2,3-*O*,*O*′-Dibenzoyltartaric Acid Monohydrate [DBTA]. A mixture of (±)-**6a** (4.32 g) and (−)-DBTA (2.27 g) was dissolved in a solution of AcOEt/$CHCl_3$ 25:4 (209 mL), refluxed for a few minutes and allowed to stand at rt for 24 h. An adduct between (−)-**6a** and (−)-DBTA was collected, and the filtrate was stored for recovery of (+)-**6a**. The above complex [2 g, mp 219 °C dec, $[\alpha]^{25}_D = -153°$ (*c* = 0.55, EtOH)] was treated with 0.75 N NaOH solution (35 mL), and the mixture was extracted with two portions of $CHCl_3$ (2 × 18 mL). The combined organic layers were washed with 0.75 N NaOH solution (11 mL) and water and then dried (Na_2SO_4). The solution, concentrated in vacuo, provided (−)-**6a** [1.3 g, mp 110−120 °C, $[\alpha]^{25}_D = -256°$ (*c* = 0.45, C_6H_6)].

The mother liquor from the first resolution was concentrated to dryness to give a solid residue (4.5 g), which was treated with 0.75N NaOH solution (81 mL) and extracted with two portions of $CHCl_3$ (2 × 81 mL). The combined organic layers were washed with 0.75 N NaOH solution (54 mL) and water (54 mL), and then they were concentrated in vacuo to give a residue **6a** enriched in the dextrorotatory enantiomer. The recovered solid and (+)-DBTA (1.46 g) were dissolved in a mixture of AcOEt/$CHCl_3$ 25:4 (135 mL) and refluxed for few minutes. After 24 h an adduct between (+)-**6a** and (+)-DBTA was collected (2.4 g) [mp 218 °C dec, $[\alpha]^{25}_D = +153°$ (*c* = 0.44, EtOH)] which was treated with 0.75 N NaOH solution (42 mL) and extracted with two portions of $CHCl_3$ (2 × 22 mL). The combined organic layers were washed with 0.75 N NaOH solution (13 mL) and water and then concentrated in vacuo to give (+)-**6a** [1.5 g, mp 110−120 °C, $[\alpha]^{25}_D = +244°$ (*c* = 0.44, C_6H_6)].

Preparation of (−)-2,2′-Bis(diphenylphosphino)-4,4′,6,6′-tetramethyl-3,3′-bibenzo[*b*]thiophene [(−)-1a]. In a three-necked flask equipped with a thermometer and a reflux condenser, connected to an argon inlay tube, were placed (−)-**6a** (1.3 g), dry xilene (20 mL), trichlorosilane (1.95 g), and triethylamine (1.45 g). The mixture was heated at 100 °C under stirring, for 1 h, at 120 °C for 1 h, and finally at 140 °C for 6 h. After cooling to rt, the mixture was concentrated in vacuo, the residue was treated with water and extracted with CH_2Cl_2. The oganic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Toluene (2 mL) and methanol (10 mL) were added to the residue and the precipitate was collected to give (−)-**1a** [0.85 g, mp 320 °C dec (DSC), $[\alpha]^{25}_D = -260°$ (*c* = 0.44, C_6H_6)].

(+)-**6a** was reduced following the same procedure to give (+)-**1a** [mp 320 °C dec (DSC), $[\alpha]^{25}_D = +266°$ (*c* = 0.43, C_6H_6)].

Preparation of 3,3′-Bibenzo[*b*]thiophene (5b). A solution of 3-bromobenzo[b]thiophene (**4b**)[12] (15 g) in THF (100 mL) was dropped into a solution of BuLi (0.076 mol, 1.6 M solution in hexane) in THF (50 mL) at −90 °C under N_2. After 15 min of stirring, $CuCl_2$ (13 g) was added, and the mixture was stirred for 1 h, then allowed to warm to 0 °C, quenched with 2 N HCl solution, and stirred overnight. The mixture was concentrated under reduced pressure and extracted with CH_2Cl_2, and the organic layer was dried (Na_2SO_4) and concentrated in vacuo. Chromatography (SiO_2, eluted by hexane) provided pure **5b** (5.3 g, 56%): mp 72 °C; ^{1}H NMR ($CDCl_3$) δ 7.38 (m, 4H), 7.55 (s, 2H), 7.85 (m, 4H). Anal. Calcd for $C_{16}H_{10}S_2$: C, 74.14; H, 3.78. Found: C, 74.03; H, 3.57.

Preparation of (±)-2,2′-Bis(diphenylphosphino)-3,3′-bibenzo[*b*]thiophene (1b). BuLi (0.043 mol, 1.6M solution in hexane) was dropped into a solution of **5b** (5.3 g) and TMEDA (6.2 mL) in THF (50 mL) at −50 °C under N_2, and then the temperature was allowed to warm to 0 °C. After 30 min diphenylphosphinous chloride (8.0 mL) was added. The mixture was stirred for 2 h and concentrated in vacuo. The residue was treated with water, and the organic layer was

(20) Sannicolò, F.; et al. 15th International Congress of Heterocyclic Chemistry, 6−11 Aug, Taipei.

separated, dried (Na_2SO_4), and concentrated in vacuo. The crude reaction product was tritured with petroleum ether to give (±)-**1b** (10.35 g, 82%): mp 177 °C; ^{1}H NMR ($CDCl_3$) δ 7.25 (m, 26H), 7.78 (d, 2H); ^{31}P NMR ($CDCl_3$) δ −23; mass spectrum *m*/*z* 634 (M^+). Anal. Calcd for $C_{40}H_{28}P_2S_2$: C, 75.69; H, 4.45. Found: C, 75.47; H, 4.39.

Preparation of (±)-2,2′-Bis(diphenylphosphinyl)-3,3′-bibenzo[*b*]thiophene (6b). H_2O_2 (16 mL, 35%) was dropped into a solution of (±)-**1b** (10.35 g) in CH_2Cl_2 (200 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C and for 1 h at 25 °C and then water was added. The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. Chromatography (SiO_2, eluted by AcOEt/CH_2Cl_2/Et_3N 3:7:0.1) provided pure (±)-**6b** (10.65, 98%): mp 286 °C; ^{1}H ($CDCl_3$) δ 6.99 (d, 4H, J = 4 Hz), 7.10 (dt, 4H, J = 3.8 Hz), 7.28 (m, 4H), 7.38 (dt, 4H, J = 3.8 Hz), 7.47 (m, 2H), 7.58 (d, 2H, 7 Hz), 7.62 (d, 2H, 7 Hz), 7.69 (d, 2H, 8 Hz), 7.82 (d, 2H, 7 Hz), 7.85 (d, 2H, 7 Hz); ^{31}P ($CDCl_3$) δ 21.00; mass spectrum *m*/*z* 666 (M^+). Anal. Calcd for $C_{40}H_{28}O_2P_2S_2$: C, 72.06; H, 4.23. Found: C, 72.26; H, 4.39.

Optical resolution of (±)-2,2′-Bis(diphenylphosphinyl)-3,3′-bibenzo[*b*]thiophene (6b) with (−)- or (+)-2,3-*O*,*O*′-Dibenzoyltartaric Acid Monohydrate [DBTA]. A mixture of (±)-**6b** (2.15 g) and (−)-DBTA (1.20 g) was dissolved into a solution of AcOEt/$CHCl_3$ 9:4.3 (133 mL), refluxed for a few minutes, and allowed to stand at rt for 24 h. An adduct between (+)-**6b** and (−)-DBTA was collected, and the filtrate was stored for recovery of (−)-**6b**. Chromatography (SiO_2, eluted by AcOEt/CH_2Cl_2/Et_3N 3:7:0.1) of the above complex [0.54 g, mp 185−190 °C, $[\alpha]^{25}_D$ = +100.6° (c = 0.50, EtOH)] provided (+)-**6b** [0.2 g, mp 206 °C, $[\alpha]^{25}_D$ = +325° (c = 0.48, C_6H_6)].

The mother liquor from the first resolution was concentrated to dryness to give a solid (3 g), and chromatography (SiO_2, AcOEt/CH_2Cl_2/Et_3N 3:7:0.1) gave a residue of (−)-**6b** enriched in the dextrorotatory enantiomer. The recovered solid (1.9 g) and (+)-DBTA (1.07 g) were dissolved into a mixture of AcOEt/$CHCl_3$ 26:16 (402 mL) and refluxed for a few minutes. After 24 h an adduct between (−)-**6b** and (+)-DBTA was collected [0.8 g, mp 190 °C dec, $[\alpha]^{25}_D$ = −97.4° (c = 0.47, EtOH)]. Chromatography (SiO_2, eluted by AcOEt/CH_2Cl_2/Et_3N 3:7:0.1) of the adduct provided (−)-**6b** [0.54 g, mp 206 °C, $[\alpha]^{25}_D$ = −329° (c = 0.50, C_6H_6)].

Preparation of (−)-2,2′-Bis(diphenylphosphino)-3,3′-bibenzo[*b*]thiophene [(−)-1b]. In a three-necked flask equipped with a thermometer and a reflux condenser, which is connected to an argon inlay tube, were placed (−)-**6b** (2.7 g), dry xylene (100 mL), trichlorosilane (4 g), and triethylamine (2.9 g). The mixture was stirred and heated at 100 °C for 10 h. After cooling to rt, the mixture was concentrated in vacuo, and the residue was treated with water and extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Toluene (2 mL) and methanol (10 mL) were added to the residue, and the precipitate was collected to give (−)-**1b** (2.06 g): mp = 187−190 °C (DSC); $[\alpha]^{25}_D$ = −193° (c = 0.50, C_6H_6).

(+)-(**6b**) was reduced by following the same procedure followed for (−)-**6b**: mp = 187−189 °C (DSC); $[\alpha]^{25}_D$ = + 195° (c = 0.48, C_6H_6).

Preparation of 2,3-Dibromobenzo[*b*]furan (3c). A solution of bromine (71.34 mL) in $CHCl_3$ (150 mL) was dropped into a mixture of benzo[*b*]furan (**2b**) (82 g) and AcOK (13.7 g) in $CHCl_3$ (300 mL) at rt. The mixture was heated at 50 °C, and a 5% $NaHSO_3$ solution was added after 5 h. The organic layer was separated, washed with a 5% $NaHCO_3$ solution, dried (Na_2SO_4), and concentrated in vacuo. Chromatography (SiO_2, eluted by petroleum ether) provided pure **(3c)** (115 g, 60%): ^{1}H NMR ($CDCl_3$) δ 7.3 (m, 2H), 7.45 (m, 2H).

Preparation of 3-Bromobenzo[*b*]furan (4c). BuLi (0.072 mol, 1.6 M solution in hexane) was dropped into a solution of **3c** (17.94 g) in dry THF (100 mL) at −70 °C under N_2. The mixture was stirred for 30 min, treated with methanol (2 mL), and concentrated in vacuo. The residue was treated with water and CH_2Cl_2. The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. Chromatography (SiO_2, eluted by petroleum ether) provided pure **4c** (11 g, 86%): mp 34 °C; ^{1}H NMR ($CDCl_3$) δ 7.30 (m, 2H), 7.45 (m, 2H).

Preparation of 3,3′-Bibenzo[*b*]furan (5c). A solution of **4c** (9 g) in dry THF (100 mL) was dropped into a solution of BuLi (0.055 mol, 1.6 M solution in hexane) in THF (150 mL) at −105/110 °C under N_2. After 20 min of stirring, $CuCl_2$ (7.4 g) was added, the mixture was stirred for 5 h at 105/110 °C, then allowed to warm to 0 °C, quenched with 2 M HCl solution, and stirred overnight. The mixture was concentrated and extracted with CH_2Cl_2, and the organic layer was dried (Na_2SO_4) and concentrated in vacuo. Chromatography (SiO_2, eluted by petroleum ether) provided pure **5c** (1.5 g, 26%): mp 110/115 °C; ^{1}H NMR ($CDCl_3$) δ 7.33 (t, 1H, J = 8 Hz), 7.39 (t, 1H, J = 7.3 Hz), 7.58 (d, 1H, J = 8 Hz), 7.74 (d, 1H, J = 7.3 Hz), 8 (s, 1H). Anal. Calcd for $C_{16}H_{10}O_2$: C, 82.04; H, 4.30. Found: C, 82.34; H, 4.28.

Preparation of (±)-2,2′-Bis(diphenylphosphino)-3,3′-bibenzo[*b*]furan (1c). BuLi (0.013 mol, 1.6 M solution in hexane) was dropped into a solution of **5c** (1.36 g) and TMEDA (1.94 mL) in THF (15 mL) at −50 °C under N_2, and then the temperature was allowed to warm to 0 °C. After 30 min diphenylphosphinous chloride (2.6 mL) was added. The mixture was stirred 2 h and then concentrated in vacuo. The residue was treated with water and $CHCl_3$; the organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. The residue was treated with isopropyl ether to give **1c** (0.48 g, 60%): mp 198−202 °C; ^{1}H NMR ($CDCl_3$) δ 7.20 (m, 14H), 7.35 (m, 12H), 7.50 (d, 2H); ^{31}P NMR ($CDCl_3$) δ −31.11. Anal. Calcd for $C_{40}H_{28}P_2O_2$: C, 79.73; H, 4.68. Found: C, 79.65; H, 4.65.

Preparation of 2,2′-Bis(diphenylphosphinyl)-3,3′-bibenzo[*b*]furan (6c). BuLi (0.013 mol, 1.6M solution in hexane) was dropped into a solution of **1c** (1.36 g) and TMEDA (1.94 mL) in THF (15 mL) at −50 °C under N_2, and then the temperature was allowed to warm to 0 °C. After 30 min diphenylphosphinic acid chloride (2.4 mL) was added. The mixture was stirred 2 h and then concentrated in vacuo. The residue was treated with water and $CHCl_3$; the organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. Chromatography (SiO_2, eluted by AcOEt/CH_2Cl_2 1:1) provided pure **6c** (2.3 g, 60%): mp 206−207 °C; ^{1}H NMR ($CDCl_3$) δ 6.97 (m, 4H), 7.10 (t, 2H, J = 7 Hz), 7.19 (m, 4H), 7.33 (t, 2H, J = 7 Hz), 7.45 (m, 6H), 7.53 (dd, 2H, J = 7 Hz), 7.63 (m, 4H), 7.82 (m, 4H); ^{31}P NMR ($CDCl_3$) δ 16.7; mass spectrum *m*/*z* 634 (M^+). Anal. Calcd for $C_{40}H_{28}P_2O_4$: C, 75.71; H, 4.45. Found: C, 75.67; H, 4.37.

Preparation of Pd(II) Dichloride Complexes (9a−c). General Procedure. A mixture of (±)-tetraMe-bitianp (**1a**) (0.069 g, 0.1 mmol) and $(C_6H_5CN)_2PdCl_2$ (0.038 g, 0.1 mmol) in CH_2Cl_2 (5 mL) was stirred at rt for 18 h; the solvent was removed in vacuo to leave **9a** as a yellow solid. Recrystallization of the crude product by slow diffusion of ether into a CH_2Cl_2-saturated solution afforded crystals suitable for X-ray structure analysis. An identical procedure was employed for the preparation of crystals of **9c**, while crystals of **9b** were obtained by diffusion of ether into an acetone saturated solution.

9a: ^{31}P NMR ($CDCl_3$) δ 21.22; ^{13}C NMR ($CDCl_3$) δ 19.93, 21.35, 119.25, 123.21, 124.46, 128.07, 129.68, 131.60, 133.95, 134.12, 135.15, 136.34, 137.76, 140.05, 144.38.

9b: ^{31}P NMR ($CDCl_3$) δ 19.65; ^{13}C NMR ($CDCl_3$) δ 122.49, 124.00, 124.52, 125.62, 126.99, 128.88, 128.98, 131.00, 132.34, 134.35, 135.74, 135.86, 135.90, 135.93, 136.00, 137.92, 140.00, 144.02; ^{1}H NMR ($CDCl_3$) δ 7.4 (m, 24H), 8.00 (m, 4H).

9c: ^{31}P NMR ($CDCl_3$) δ 11.19; ^{13}C NMR (DMSO) δ 11.82, 120.62, 121.44, 124.26, 125.53, 125.96, 127.30, 128.04, 128.73, 129.00, 130.06, 130.77, 131.30, 132.46, 133.36, 135.19, 135.29, 157.36; ^{1}H NMR ($CDCl_3$) δ 7.30 (m, 24H), 8.12 (m, 4H).

Preparation of [(+)- and (−)-tetraMe-bitianp]$RuCl_2$ (10a).[17] To a Schlenk tube charged with (*R*)-tetraMe-bitianp (2.3×10^{-2} mmol) and red brown $[RuCl_2(C_6H_6)]_2$ (1.15×10^{-2}), prepared according to the procedure reported in the literature,[18] was added freshly distilled argon-degassed DMF. The mixture was stirred at 100 °C for 15 min. The resulting orange yellow solution was cooled to 50 °C and concentrated under reduced pressure to give **10a**. The residue was left under vacuum for 1 h and then argon pressurized. The obtained ruthenium complex, was utilized without other purification

in the enantioselective reductions of α- and β-keto esters. The ^{31}P NMR showed a complex set of signals clustered around 48 and 54 ppm, indicating that the crude catalyst was a mixture of $RuCl_2$(tetraMe-bitianp) $(DMF)_n$ with a different number of coordinated solvent molecules.[21]

Preparation of [(+)- and (−)-Bitianp]RuCl$_2$ (10b).[17] The catalyst was prepared according to the procedure described above for the preparation of **10a**: ^{31}P NMR ($CDCl_3$) δ 56.5 (d, J = 39), 54.7 (d, J = 41), 52.8 (d, J = 37), 49.2 (d, J = 39), 48.0 (d, J = 42), 47.7 (d, J = 40), 43.6 (d, J = 37), 36.1 (d, J = 63), 26.5 (d, J = 63).

Preparation of [(+)- and (−)-TetraMe-bitianp]Ru(CH$_3$COO)$_2$ (11a).[17] CH_3COOAg (0−136 mmol) and anhydrous toluene (7 mL) were added to **10a**, prepared according to the procedure above, from (−)-tetraMe-bitianp (**1a**) (0.068 mmol) and $[RuCl_2(C_6H_6)]_2$ (0.034 mmol). The mixture was stirred for 1 h and filtered through a column of microcrystalline cellulose. The solution of [(−)-tetraMe-bitianp]$Ru(CH_3COO)_2$ (**11a)** was used in catalytic reductions without further purifications: ^{31}P NMR ($CDCl_3$) δ 60.67; ^{1}H NMR ($CDCl_3$) δ 1.6 (s, 6H), 2.4 (s, 6H), 7.3 (m, 24H).

Preparation of [(+)- and (−)-Bitianp]Ru(CH$_3$COO)$_2$ (11b).[17] The catalyst was prepared according to the procedure described above for the preparation of **11a**: ^{31}P NMR ($CDCl_3$) δ 59.62; ^{1}H NMR ($CDCl_3$) δ 7.35 (m, arom).

Preparation of [(TetraMe-bitianp)$_2$Ru(*p*-cymene)I]I (12a).[17] (−)-TetraMe-bitianp (0.020g, 0.029 mmol), [Ru(p-cymene)I_2]$_2$ (0.013g, 0.013 mmol), methanol (6 mL), and CH_2Cl_2 (2 mL) were stirred in a Schlenk tube under argon at 50 °C for 1.5 h. The resulting orange solution was used in the asymmetric catalytic reductions without further purification. A sample of the solution evaporated to dryness left a deep red microcrystalline compound: ^{31}P NMR ($CDCl_3$) δ 37.0 (d, J = 58 Hz), 19.0 (d, J = 58 Hz).

Asymmetric Hydrogenation of Ethyl 3-Oxobutanoate (13). A 100 mL stainless-steel autoclave was purged five times with hydrogen; a solution of ethyl 3-oxobutanoate (23 mmol) and (+)-**10a** (0.023 mmol) in methanol, previously degassed 15 min with argon, was loaded into the autoclave with a syringe. Hydrogen was introduced (100 Kg/cm^2), and the solution was stirred at 70 °C for 2 h. The autoclave was cooled, the hydrogen pressure released, the solvent evaporated, and the residue distilled (17 mmHg) to give ethyl (*R*)-(−)-3-hydroxybutanoate (**14**) (95% yield). Enantioselectivity (99%) of the product was determined by chiral ^{1}H NMR spectroscopy [Eu(hfc)$_3$, $CDCl_3$], confirmed by ^{1}H NMR of the corresponding (*S*)-naproxen ester[22] and by GC (helium, 1.4 mL/min, oven: 80 °C isotherm).

Asymmetric hydrogenation of all α- and β-keto esters was carried out under the same conditions as employed for ethyl 3-oxobutanoate. The results are summarized in Table 1: (1*R*,2*R*)-2-(Methoxycarbonyl)cyclopentan-1-ol (**16**) [^{1}H NMR Eu(hft)$_3$ and GC (helium 1.5 mL/min, oven 105 °C isotherm)]; (3*S*,6*R*)-3-(6-hydroxyethyl)butyrolactone (**18**) (^{1}H NMR of the corresponding (*S*)-naproxen ester); methyl 3-phenyl-3-hydroxypropionate (**20**) (^{1}H NMR of the corresponding (S)-naproxen ester); methyl lactate (**22**) (^{1}H NMR of the corresponding (*S*)-naproxen ester); methyl mandelate (**24**) (HPLC, eluant hexane/isopropyl alcohol 90:10, 0.6 mL/min).

Asymmetric Hydrogenation of Geraniol. A solution of **11b** (0.015 mmol), geraniol (5.773 mmol) and methanol (10 mL), previously degassed with argon (10 min), were introduced into the autoclave, pressurized at 100 Kg/cm^3 and stirred at 25 °C for 85 h. The hydrogen pressure was released, the solvent evaporated, and the residue distilled (110 °C, 10 mmHg) to give (*R*)-(+)-β-citronellol (100%, yield). Enantioselectivity (94%) of the product was determined by GC (helium 1.5 mL/min, oven 85 °C isotherm).

Asymmetric hydrogenation of tiglic and atropic acid was carried out as for geraniol. The results are summarized in Table 2: (*S*)-2-Phenylpropionic acid (**26**) [HPLC of the corresponding anilide, eluant hexane/isopropyl alcohol 90:10, 0.6 mL/min; GC of the methyl ester (helium 1.5 mL/min, oven 78 °C isotherm)]; (*S*)-2-methylbutanoic acid (**28**) [(HPLC of the corresponding anilide, eluant hexane/isopropyl alcohol 95:5, 0.6 mL/min; GC of the methyl ester (helium 1.5 mL/min, oven 44 °C isotherm)].

X-ray Data Collection and Refinement. Details of the data collection and refinement of the structures are reported in Table 1S of the Supporting Information.[23] Crystals of compounds **9a**, **9b**, and **9c** were mounted on a glass fiber in a random orientation. Preliminary examination and data collection were performed with graphite-monochromatized Mo Kα radiation (0.71073 Å) on an Enraf-Nonius CAD4 computer controlled κ axis diffractometer for **9b** and on a Siemens P4 diffractometer for **9a** and **9c**, respectively. Cell constants and an orientation matrix for data collection were obtained from least-squares refinement, using the setting angles of 25 reflections, measured by the computer-controlled diagonal slit method of centering. The data were collected at room temperature using a variable-scan rate. The scan range (in deg) was determined as a function of θ to correct for the separation of the Kα doublet. As a check on crystal and electronic stability, three representative reflections were measured every 3 h, showing no decay of the scattering power of the crystals during the data collection.

Lorentz, polarization, and, for **9b**, an empirical absorption correction based on a series of ψ scans were applied to the data. The structure was solved by Patterson and Fourier methods and refined in full-matrix least-squares minimizing the function $\Sigma w(|F_o| - |F_c|)^2$. For **9a** the independent refinement of the two structure models related by inversion was not significant enough to establish the correct enantiomorph. Scattering factors were taken from Cromer and Waber.[24] Anomalous dispersion effects were included in F_c; the values for $\delta f'$ and $\delta f''$ were those of Cromer.[25] All calculations were performed on a 80486/33 computer using Personal SDP software.[26]

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(23) Data collection and refinement details, atomic coordinates, displacement parameters, interatomic distances, and angles of **9a**, **9b** and **9c**, and an ORTEP drawing of **9a** has been deposited at the Cambridge Crystallographic Data Centre. Structure factor tables are available on request from one of the authors (F.D.).

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