Chiral Bidentate (Phosphinophenyl)benzoxazine Ligands in Asymmetric Catalysis

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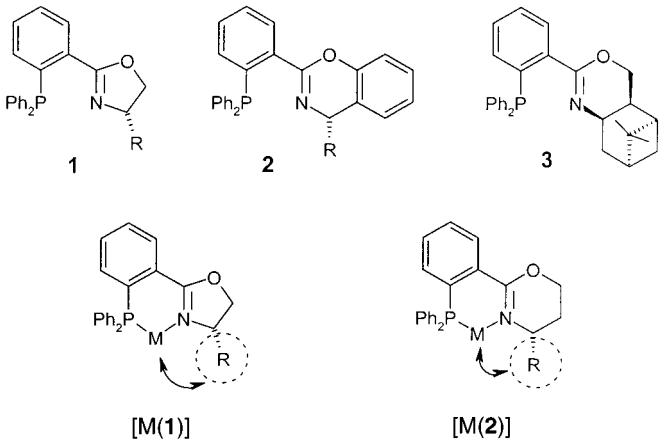
Dedicated to the memory of Prof. *Luigi M. Venanzi*

The new chiral bidentate (phosphinoaryl)benzoxazine ligands **2** were applied in asymmetric catalysis. Rhodium and copper complexes catalyzed the hydrosilylation of acetophenone and [4 + 2] cycloadditions with moderate enantioselectivity. Iridium complexes were used to hyrogenate di-, tri-, and tetrasubstituted alkenes, giving products with moderate to high enantiomer excesses. Enantioselective allylic substitution and *Heck* reactions catalyzed by [(phosphinoaryl)benzoxazine]palladium complexes occurred with high enantioselectivities. The results were similar to those obtained with the corresponding dihydro(phosphinoaryl)oxazole ligands. Comparison of the structures of (diphenylallyl)(benzoxazine)palladium and (diphenylallyl)(dihydrooxazole)-palladium complexes showed that the coordination geometries and the chiral environments of the metal centers are very similar, which explains why the enantioselectivities induced by the two ligand classes are in the same range.

1. Introduction. – Chiral bidentate dihydro(phosphinophenyl)oxazoles **1** [1] are readily obtained from 2-aminoalkan-1-ols. They have been applied successfully in a multitude of enantioselective transition-metal-catalyzed reactions, including allylic substitution [1], *Heck* reactions [2], hydrogenation [3], hydrosilylation [4], and *Diels-Alder* reactions [5]. Given the scope and popularity of ligands **1**, it is surprising that six-membered-ring analogues such as **2** are scarce [6][7]. Following our recent report on the synthesis of new members of this class of ligands, chiral bidentate (phosphinophenyl)benzoxazine ligands **2** [7], we now report the results of their application to transition-metal-catalyzed asymmetric hydrosilylation, hydrogenation, [4 + 2] cycloaddition, allylic substitution, and *Heck* reactions.

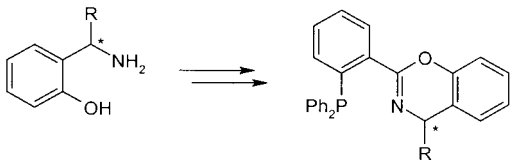
The (phosphinophenyl)benzoxazine ligands **2** differ from ligands **1** by having a benzo-fused six-membered 4*H*-1,3-oxazine ring instead of the five-membered dihydrooxazole ring. A two-dimensional drawing suggests that the R group at the stereogenic center is closer to the metal in a complex [M(**2**)] with the six-membered 5,6-dihydro-4*H*-1,3-oxazine ligand than in a complex [M(**1**)] with the dihydrooxazole ligand and, therefore, could exert a larger influence on the stereochemical course of reactions at the metal center. However, while the dihydrooxazoles are quite flat, the dihydro-(4*H*-oxazines have chair- and boat-like conformations, and this flexibility may be detrimental to their use as chiral inductors. An efficient way to reduce the number of con-



formations is ring fusion. This strategy has been used before by *Evans* and *Brandt*, who applied the pinene-derived 4*H*-oxazine ligand **3** in Pd-catalyzed asymmetric allylic substitution reactions [6a]. *Zehnder* and co-workers, on the other hand, have demonstrated that very high enantioselectivities can also be achieved with a simple 4-phenyl-substituted 5,6-dihydro-4*H*-oxazine ligand (complex [M(**2**)]; M=Pd, R=Ph) [6b].

We chose fusion to an aromatic ring to render the ring system rigid. Both the *tert*-butyl- and the isopropyl(phosphinophenyl)benzoxazine ligands **2** [7] were obtained from the chiral, enantiomerically pure 2-hydroxy-α-alkylbenzenemethanamines **4** [8] (*Scheme 1*).

Scheme 1



4a R = ^{t}Bu
b R = ^{i}Pr

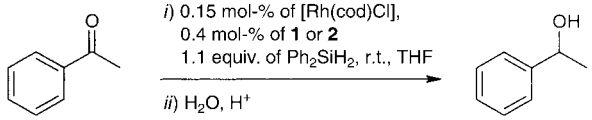
2a R = ^{t}Bu
b R = ^{i}Pr

2. Asymmetric Catalysis. – To allow comparison, the conditions for the enantioselective catalytic reactions with the benzoxazine ligands **2** were chosen so as to match those employed in analogous reactions with ligands **1**.

2.1. *Enantioselective Hydrosilylation*. Acetophenone is the standard test substrate for the enantioselective hydrosilylation of ketones. With diphenylsilane and, as catalyst, the *in-situ*-generated [(*R*)-(phosphinophenyl)benzoxazine]rhodium complexes, acetophenone afforded, after hydrolysis, (*S*)-1-phenylethanol in good yields (*Scheme 2*).

Comparing the results of the benzoxazine ligands **2** (*Entries 1* and *2*) and the dihydrooxazole ligands **1** (*Entries 3* and *4*) shows both types of ligands to produce the same sense of chiral induction, (*R*)-(phosphinophenyl)benzoxazines giving (*S*)-1-phenylethanol and (*S*)-(phosphinophenyl)dihydrooxazoles giving (*R*)-1-phenylethanol. In terms of both yields and chiral induction, ligands **1** out-perform ligands **2**. Steric

Scheme 2



5 **6**

Entry	Ligand	Yield of **6** [%]	Enantiomer excess [%] (configuration)
1	(*R*)-**2a**	56	12 (*S*)[a])
2	(*R*)-**2b**	79	66 (*S*)[b])
3[b])	(*S*)-**1a**	65	40 (*R*)
4[b])	(*S*)-**1b**	97	76 (*R*)

[a]) The absolute configuration was determined by the sign of the optical rotation and comparison with literature data [9]. [b]) Values from [10].

factors may account for this, since for both **1** and **2**, the smaller isopropyl derivatives gave higher chiral induction than the sterically more-demanding *tert*-butyl analogues.

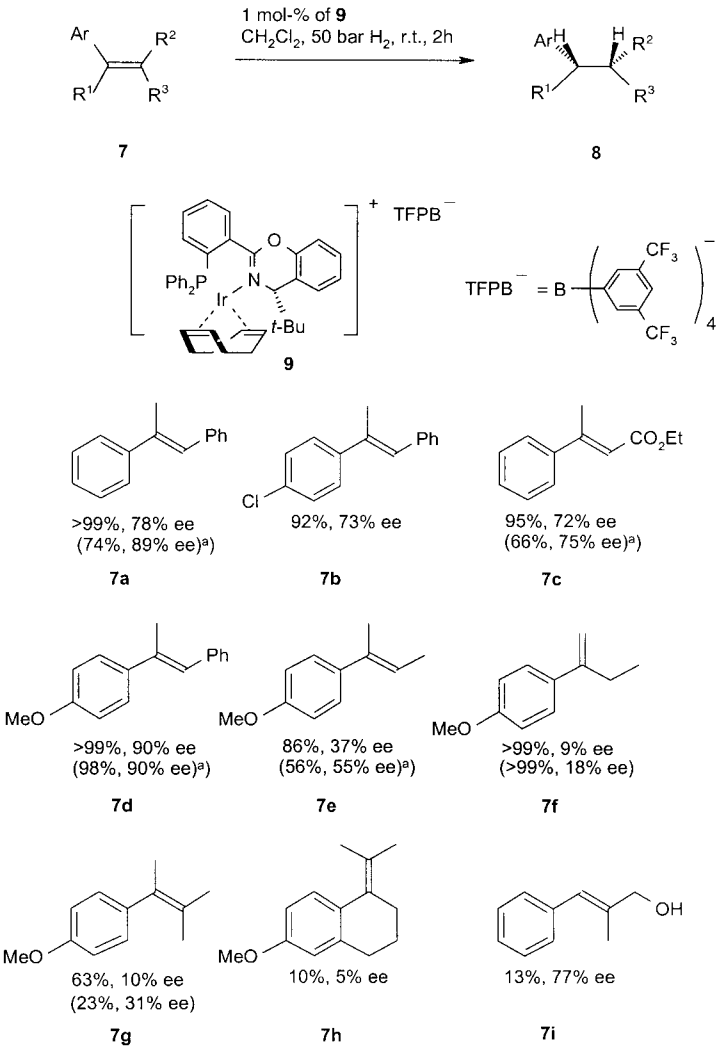
2.2. *Enantioselective Alkene Hydrogenation.* The asymmetric, highly enantioselective hydrogenation of functionalized olefins such as dehydro-amino acid derivatives, unsaturated carboxylic acids, or allylic alcohols is already well-established [11]. However, tri- and tetrasubstituted alkenes lacking heteroatom substituents near the C=C bond have been hydrogenated with high efficiency and high enantioselectivity only recently, in the presence of [dihydro(phosphinophenyl)oxazole]iridium catalysts [12]. The results of the hydrogenation of di-, tri-, and tetrasubstituted olefins **7** are shown in *Scheme 3*. These reactions were catalyzed by the [(*tert*-butyl)(phosphinophenyl)benzoxazine]iridium complex **9**, which was synthesized from $[Ir(cod)Cl]_2$ (cod = cycloocta-1,5-diene), (*tert*-butyl)(phosphinophenyl)benzoxazine, and sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (NaTFPB).

The hydrogenations of trisubstituted alkenes **7a–d** (*Scheme 3*) catalyzed by **9** gave the corresponding alkanes **8a–d** in excellent yields (90%) and with high enantioselectivities (72–90% ee), whereas that of the dialkyl-aryl-substituted alkene **7e** yielded 86% of the alkane with an enantiomer excess of only 37%. Low enantioselectivities ($\leq$10% ee) were observed with tetrasubstituted (see **7g** and **7h**) and geminally disubstituted alkenes (see **7f**). The hydrogenation of **7f** and **7g** catalyzed by the corresponding [dihydro(phosphinophenyl)oxazole]iridium catalyst showed slightly higher enantioselectivities (18 and 31% ee, resp.). However, these differences do not represent a significant energetic difference (0.3 kcal/mol). The trisubstituted allylic alcohol **7i** was hydrogenated with an enantiomer excess of 77%.

Comparing the results obtained with **9** and the analogous [dihydro(phosphinophenyl)oxazole]iridium complex bearing the PF_6^- counterion[1]), generally very similar

[1]) It has been previously shown that, although the use of $TFPB^-$ as counterion results in higher catalyst activity and stability compared to PF_6^-, the enantioselectivity is not influenced by the counterion [3].

Scheme 3



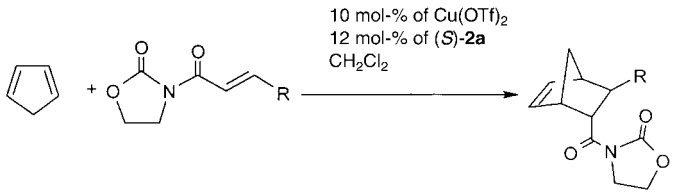
a) Values in parentheses refer to results with the corresponding -[(*tert*-butyl)dihydro(phosphinophenyl)-oxazole iridium complex having the counterion PF_6^- instead of $TFPB^-$.

enantioselectivities were observed: 78 and 89% ee, respectively, for the hydrogenation of **7a**, 72 and 75% ee, respectively, for **7c**, and 90% ee with the dihydrooxazole as well as with the oxazole complex for **7d**. The hydrogenation of alkene **7e** showed a higher selectivity with the dihydro(phosphinophenyl)oxazole complex (55% ee; 37% ee with **9**).

2.3. *Asymmetric* Diels-Alder *Reaction*. The activation of bidentate dienophiles by *Lewis* acids allows catalytic enantioselective [4+2] cycloadditions. The reaction of acryloyl-oxazolidinones **10a**,**b**,**d** with cyclopentadiene catalyzed by *in-situ*-formed

[(phosphinophenyl)benzoxazine]copper complexes gave the corresponding cycloadducts **11a**,**b**,**d** in *ca.* 90% yield (*Scheme 4*, *Entries 1*, *2*, and *4*). Only the electron-rich and therefore deactivated dienophile **10c** did not react with cyclopentadiene even on warming to 40°. The cycloadducts **11a**,**b**,**d** were obtained with high diastereoselectivities (*endo*/*exo* 94:6, 90:10, and 89:11, resp.). However, the enantioselectivities were low to moderate (48, 11, and 51% ee, resp.).

Scheme 4



10a R = H
b R = Me
c R = Ph
d R = COOEt

11a R = H
b R = Me
c R = Ph
d R = COOEt

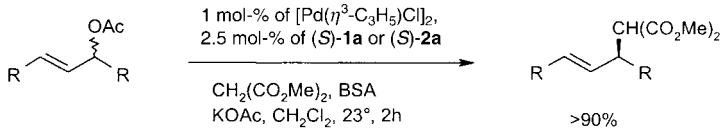
Entry	Dienophile	*T* [°]	*t* [h]	Yield [%]	*endo*/*exo*	ee [%] (*endo*)
1	**10a**	–78	7	84	94:6	48
2	**10b**	0	24	89	90:10	11
3	**10c**	40	48	–		
4	**10d**	–40	7	97	89:11	51

The comparison of the results for the cycloadduct **11a** obtained with the (phosphinophenyl)benzoxazine and the dihydro(phosphinophenyl)oxazole ligand[2]) shows a similar diastereoselectivity (*endo*/*exo* 94:6 *vs.* 95:5 [13]) but a lower enantioselectivity with the (phosphinophenyl)benzoxazine ligand (48 *vs.* 82% ee [10]).

2.4. *Enantioselective Allylic Substitutions.* Enantioselective allylic substitution [14] is one of the major applications of dihydro(phosphinophenyl)oxazole ligands [1], which is also mechanistically well-understood. Therefore, a comparison with ligands **2** appeared essential. The reactions of allylic acetates **12a**–**c** with malonic ester nucleophiles catalyzed by *in-situ*-generated [Pd{(*S*)-**2a**}] complexes led to the formation of the chiral products **13a**–**c** in excellent yields (>90%; *Scheme 5*) and with high enantioselectivities (94, 82, and 74% ee for **13a**, **13b**, and **13c**, resp.; *Entries 1–3*). Analogous results were obtained with [Pd{(*S*)-**1a**}] (*Entries 4–6*). For the methylallylic and propylallylic acetates **12b** and **12c**, the (phosphinophenyl)benz-

[2]) Modified dihydro(phosphinophenyl)oxazole ligands (*e.g.* dihydro[(dinaphthylphosphino)phenyl]oxazole) have been used in the other reactions [10].

Scheme 5



12a R = Ph
b R = Me
c R = Pr

13a R = Ph
b R = Me
c R = Pr

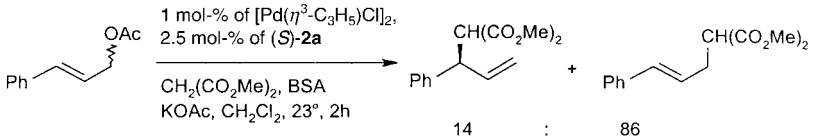
Entry	Ligand	Product	ee [%]
1	(*S*)-**2a**	**13a** (Ph)	94
2	(*S*)-**2a**	**13b** (Me)	82
3	(*S*)-**2a**	**13c** (Pr)	74
4[a])	(*S*)-**1a**	**13a** (Ph)	95
5[a])	(*S*)-**1a**	**13b** (Me)	79
6[a])	(*S*)-**1a**	**13c** (Pr)	69

[a]) Values from [1].

oxazine ligand (*S*)-**2a** induced a slightly higher enantioselectivity than the dihydro(phosphinophenyl)oxazole ligand (*S*)-**1a** (82 *vs.* 79% ee and 74 *vs.* 69% ee, resp.).

The reaction of the unsymmetrically substituted substrate **14** catalyzed by [Pd{(*S*)-**2a**}] resulted in the formation of the chiral product **15** and the linear, achiral product **16** in a ratio of 14 : 86 (*Scheme 6*). The alkylated product **15** showed an enantiomer excess of 30%. With the [dihydro(phosphinophenyl)oxazole]palladium complex, the ratio of the chiral product **15** to the linear product **16** diminished to 4 : 96, the enantiomer excess, on the other hand, was higher (78% ee [15]).

Scheme 6

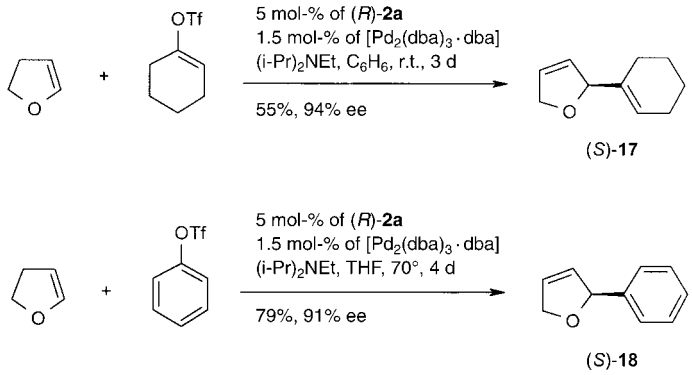


14 **15** **16**

2.5. *Enantioselective* Heck *Reactions.* It has been shown that dihydro(phosphinophenyl)oxazole ligands can induce very high enantioselectivity in Pd-catalyzed intermolecular couplings of cycloalkenes with aryl or alkyl triflates [16]. The *in-situ*-generated complex with $[Pd_2(dba)_3 \cdot dba]$ (dba = dibenzylideneacetone = 1,5-diphenylpenta-1,4-dien-3-one) and ligand (*R*)-**2a** catalyzed the coupling of 2,3-dihydrofuran

and 1-cyclohexenyl triflate or phenyl triflate to result in (*S*)-**17** or (*S*)-**18** in 55 and 79% yield with high enantiomer excesses of 94 and 91% ee, respectively (*Scheme 7*). The same reactions with the analogous dihydrooxazole ligand **1a** gave the products **17** and **18** with 99 and 97% ee [16]. Again, the (phosphinophenyl)benzoxazine and the dihydro(phosphinophenyl)oxazole ligands showed the same sense of chiral induction.

Scheme 7



Baumann and *Togni* have shown that (pyrazole)ferrocenyl-palladium-catalyzed *Heck* reactions can be accelerated by the addition of tetrabutylammonium triflate [17]. Two [Pd{(*R*)**2a**}] catalyzed coupling reactions of 2,3-dihydrofuran and phenyl triflate, run in parallel with and without tetrabutylammonium triflate, showed only a small rate difference (after 48 h, 71 yield *vs.* 60% yield of (*S*)-**18** with and without $Bu_4N(OTf)$, resp.). Both reactions occurred with the same enantioselectivity.

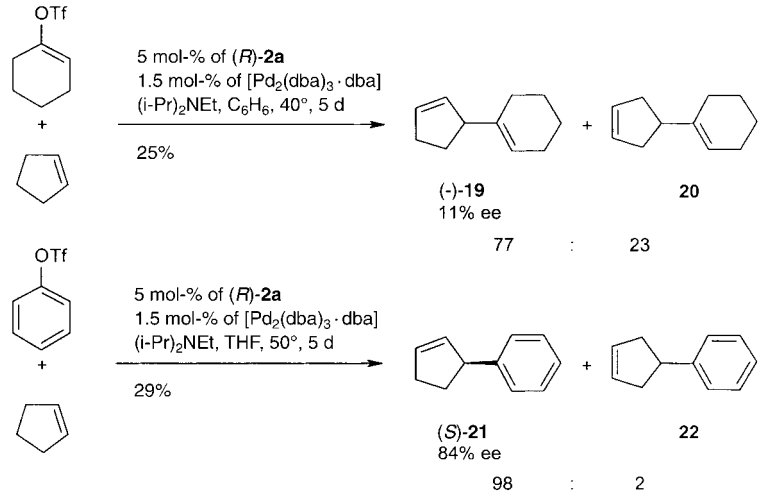
The [(phosphinophenyl)benzoxazine]palladium-catalyzed *Heck* coupling to cyclopentene led to the formation of a chiral as well as an achiral product obtained by isomerization during the reaction (*Scheme 8*). With cyclohex-1-en-1-yl triflate, the ratio of the chiral product (−)-**19** to the achiral product **20** was 77:23 with a low total yield of 25%. The reaction with phenyl triflate afforded (*S*)-**21** and **22** in a ratio of 98:2 in low yield (29%). The products (−)-**19** and (*S*)-**21** showed an enantiomer excess of 11 and 84% ee, respectively.

The same reactions with [Pd{(*R*)-**1a**}] yielded the products (−)-**19** and **20** in a ratio of 98:2 and in 70% yield and the products (*S*)-**21** and **22** in a ratio of 99:1 and in 44% yield. The products (−)-**19** and (*S*)-**21** showed significantly higer enantiomer excesses of 89 and 91%, respectively.

The enantioselectivities with the (diphenylphosphinophenyl)isopropylbenzoxazine ligand **2b** were always substantially lower than with the corresponding *tert*-butyl-substituted ligand **2a**. The same erosion of asymmetric induction was observed on going from [Pd(**1a**)] to [Pd(**1b**)] [16].

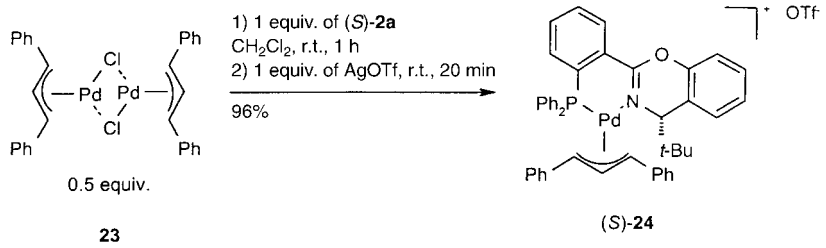
3. Structural Investigations. – (Diphenylallyl)palladium complexes of dihydro(phosphinophenyl)oxazoles have been extensively studied by X-ray crystallography and NMR spectroscopy [18], and the structural data from these studies have led to important insights into the mechanism of enantioselection. The close analogy in

Scheme 8



performance of the two ligand systems **1a** and **2a** in the Pd-catalyzed allylic substitution prompted us to analyze the structures of the corresponding (diphenylallyl)palladium complexes. The [Pd(diphenylallyl){(*S*)-**2a**}] OTf complex (*S*)-**24** was obtained as indicated in *Scheme 9*. A detailed presentation of the corresponding [Pd(diphenylallyl){(*S*)-**1a**}] PF_6 complex (*S*)-**25** is given in [19].

Scheme 9



Crystals of (*S*)-**24** have two crystallographically independent formula units per asymmetric unit. The general structural features of the two cations are very similar. A view of cation (*S*)-**24a** is shown in *Fig. 1*. The molecular structure of the corresponding dihydrooxazole complex (*S*)-**25** is given in *Fig. 2*. A comparison of (*S*)-**25** with (*S*)-**24a** and (*S*)-**24b** reveals a close similarity. Bond lengths and bond angles of the square-planar coordination geometry are in the usual range of [Pd(allyl)] complexes with P,N ligands, the Pd–C bond *trans* to the P-atom being longer than that *trans* to the N-atom (*Table*). The allyl ligands adopt the '*exo-syn-syn*' conformation. A superimposition of the N–Pd–P plane of the cations of (*S*)-**24a**,**b** and of (*S*)-**25** reveals an almost analogous conformation of the six-membered chelate ring system (*Fig. 3*).

Due to the non-planarity of the chelate ring, one of the free phenyl rings at the P-atom of (*S*)-**24a**,**b** and (*S*)-**25** adopts a pseudoaxial, the other a pseudoequatorial

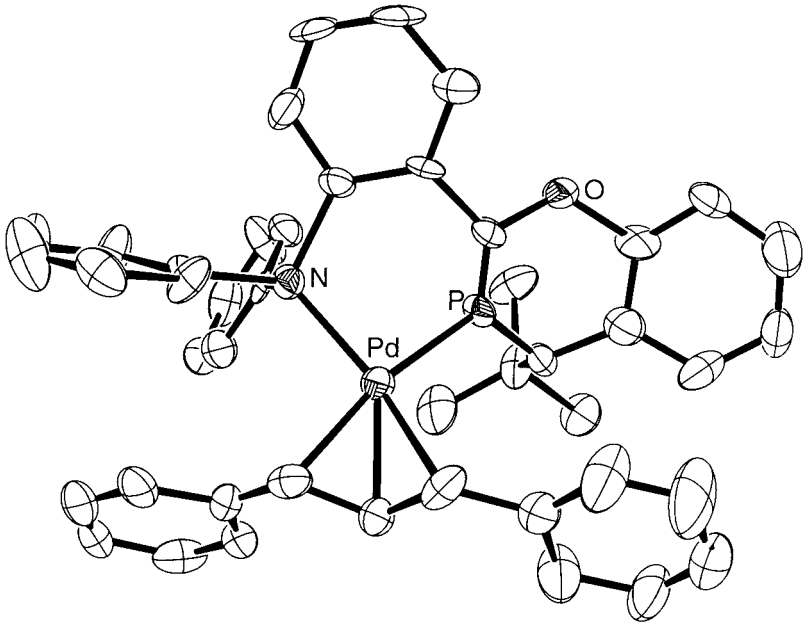
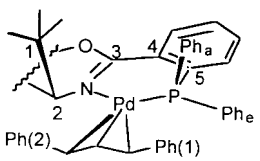


Fig. 1. *Molecular structure of the cation of* (S)-**24a**. Thermal ellipsoids at 50% probability.

Table. *Selected Parameters of the X-Ray Structures of* (S)-**24** *and* (S)-**25**

	(*S*)-**24a**	(*S*)-**24b**	(*S*)-**25**
Pd–N	2.118(18)	2.003(17)	2.105(6)
Pd–P	2.267(5)	2.274(5)	2.275(2)
Pd–C(*trans* to N)	2.163(30)	2.116(18)	2.141(8)
Pd–C(central)	2.173(19)	2.208(17)	2.185(8)
Pd–C(*trans* to P)	2.303(30)	2.345(17)	2.318(7)
Pd–N–C(2)–C(1)	87.9(17)	84.7(16)	75.7(8)
C(1)–C(2)–N–C(3)	– 90.5(30)	– 98.1(18)	– 107.4(9)
P–Pd–N–C(2)	– 139.4(13)	– 146.4(14)	– 148.6(7)

position with respect to the N–Pd–P plane. The pseudoaxial phenyl ring at the P-atom and the axially positioned *tert*-butyl substituent lie on the same side of the coordination plane (see **A**).The stereogenic center of (*S*)-**24a**,**b** and (*S*)-**25** adopts nearly the same position with respect to the N–Pd–P plane. Slight conformational differences can be observed with respect to the orientation of the phenyl rings. The almost identical



A

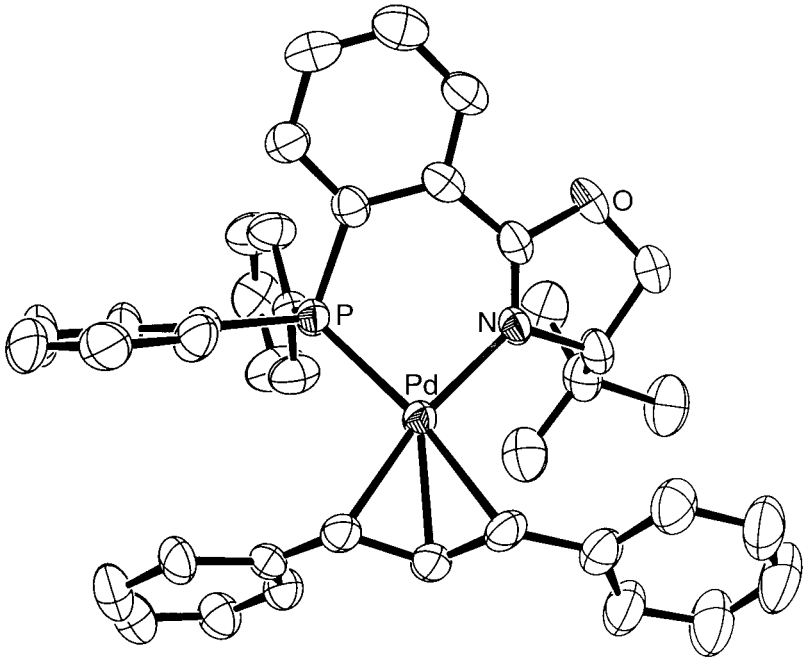


Fig. 2. *Molcular structure of the cation of* (S)-**25**. Thermal ellipsoids at 30% probability.

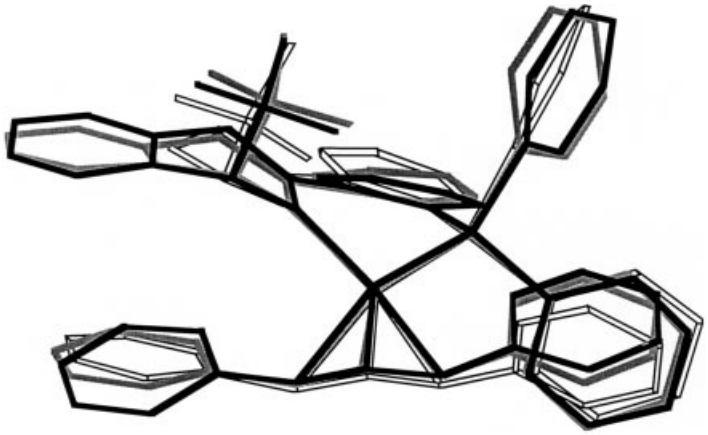


Fig. 3. *Superposition of the cations of* (S)-**24a**,**b** (black) *and of* (S)-**25** (white).

conformations of the allyl groups reflects the similar interaction between the allylic system and the P,N ligands.

Conclusions. – The (diphenylphosphinophenyl)benzoxazine ligands **2** gave moderate enantioselectivities in hydrosilylation (up to 66% ee) and *Diels-Alder* reactions (up

to 51% ee). In Ir-catalyzed hydrogenations of alkenes, allylic substitutions, and *Heck* reactions, these ligands induced enantiomer excesses of up to 94% ee. The enantioselectivities were usually in the same range as those obtained with analogous dihydro(phosphinophenyl)oxazole ligands **1**. Comparison of the crystal structures of (diphenylallyl)palladium complexes bearing these ligands showed very similar geometries of the core structures (coordination geometry, orientation of the substituents at the stereogenic center, geometry of the *P*-phenyl groups), which explains the similar performance of these two classes of ligands in various metal-catalyzed processes.

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Experimental Part

General. THF was distilled from sodium/benzophenone under N_2 before use. CH_2Cl_2 was freshly distilled from CaH_2 under N_2. All other chemicals were purchased from *Aldrich* or *Fluka* and were purified by standard procedures [20]. Flash column chromatography (FC): in air, as described by *Still* [21]; (silica gel *Merck 60*) HPLC and GC: t_R in min. M.p.: *Büchi 510* apparatus; not corrected. IR Spectra: NaCl cells; *Perkin-Elmer 1650-FT-IR* spectrometer in cm^{-1}. NMR Spectra (^1H: 200, 300, or 400 MHz; ^{13}C: 50, 75, or 100 MHz; ^{19}F: 376 MHz; ^{31}P: 162 MHz): at r.t.; *Varian XL 200* or *-300* spectrometer or *Bruker* 400-MHz spectrometer; chemical shifts δ in ppm rel. to SiM_4 (= 0 ppm) as the internal standard and referenced to the signal of the residual solvent ($CHCl_3$: δ(H) 7.24, δ(C) 77.2; C_6D_6; δ(H) 7.15, δ(C) 128.0, *J* in Hz. MS: *Varian CH4* or *SM1* spectrometer; in *m/z* (intensities in %). HR-MS: *VG-7070E* analytical instrument, data system *11250*, resolution 7000). Elemental analyses were performed by *H. Eder*, Service de Microchimie, Institut de Chimie Pharmaceutique, Université de Genève.

Hydrosilylation of Ketones: General Procedure. Acetophenone (**5**; 0.233 ml, 240 mg, 2.0 mmol) and Ph_sSiH_2 (0.405 ml, 405 mg, 2.2 mmol) were added to (*R*)-**2a** (3.6 mg, 0.008 mmol, 0.4 mol-%) and $[Rh(cod)Cl]_2$ (1.4 mg, 0.0028 mmol, 0.28 mol-% of Rh) in THF (0.7 ml) at 0°. The resulting soln. was stirred for 68 h at r.t. unit all **5** was consumed (TLC monitoring). Then 1N HCl (1 ml) and acetone (3 ml) were added. The resulting soln. was stirred for 1.5 h at r.t. and then extracted with Et_2O (3 × 10 ml). The combined org. phase was dried ($MgSO_4$) and evaporated and the residue purified by FC (Et_2O/pentane 1:2): (*S*)-1-phenylethanol (**6**; 137 mg, 56%; 12% ee by GC). Colorless oil. TLC (AcOEt/hexane 1:2): R_f 0.3. M.p. 19–21°. $[\alpha]_D^{21} = -5.3$ ($c = 0.37$, $CHCl_3$). GC (*Lipodex E* column, 25 m, 0.5 bar H_2, 80° isotherm): t_R 25.5 ((*S*), 56.2%), 27.4 ((*R*), 43.8%).

*{(4*S*)-4-(*tert*-Butyl)-2-[2-(diphenylphosphino-*κ*P)phenyl]-4*H*-1,3-benzoxazine-*κ*N*^{3}*}[(1,2,5,6-η)-cycloocta-1,5-diene]iridium(1+) Tetrakis[3,5-bis(trifluoromethyl)phenyl]borate* (**9**). The deep red mixture of (*S*)-**2a** (100 mg, 0.22 mmol), $[Ir(cod)Cl]_2$ (75 mg, 0.11 mmol), and CH_2Cl_2 (3 ml) was heated under Ar to reflux for 1 h (TLC (silica gel, CH_2Cl_2): no (*S*)-**2a** left). After cooling to r.t., NaTFPB (300 mg, 0.34 mmol) was added followed by H_2O (3 ml), and the resulting two-phase mixture was stirred vigorously for 10 min. TLC indicated counterion exchange from Cl^- (R_f 0) to TFPB (R_f 0.95). The aq. layer was extracted with CH_2Cl_2 (2 × 3 ml), the combined org. layer washed with H_2O (3 ml) and evaporated, and the crude product purified by FC (CH_2Cl_2): **9** (326 mg, 91%). Orange-red solid. M.p. 141–142° (dec.). $[\alpha]_D^{21} = -79$ ($c = 1.07$, $CHCl_3$). ^1H-NMR: 300 MHz, $CDCl_3$): 0.46 (*s*, 9 H); 1.18–1.35 (*m*, 1 H); 1.45–1.60 (*m*, 1 H); 1.76–1.89 (*m*, 1 H); 1.92–2.05 (*m*, 1 H); 2.18–2.32 (*m*, 2 H); 2.50–2.58 (*m*, 1 H); 3.07–3.16 (*m*, 1 H); 3.16–3.26 (*m*, 1 H); 4.38 (*s*, ^{t}Bu-C*H*); 4.63–4.72 (*m*, 1 H, cod); 4.92–5.04 (*m*, 1 H, cod); 6.94–7.13 (*m*, 4 arom. H); 7.15–7.28 (*m*, 4 arom. H); 7.29–7.40 (*m*, 4 arom. H); 7.43 (*s*, 4 H, TFPB); 7.45–7.55 (*m*, 5 arom. H); 7.65 (*s*, 8 H, TFPB); 8.51–8.58 (*m*, 1 arom. H). ^{31}P-NMR (300 MHz, $CDCl_3$): 17.4. Anal. calc. for $C_{70}H_{52}BF_{24}IrNOP$ (1582.2): C 52.12, H 3.25, N 0.87; found: C 51.96, H 3.34, N 0.89.

Ir-Catalyzed Enantioselective Hydrogenation of Alkenes: General Procedure. A mixture of **9** (3.2 mg, 0.002 mmol, 1 mol-%), alkene (0.2 mmol), and CH_2Cl_2 (0.5 mmol) in a 35-ml autoclave with magnetic stirrer was pressurized to 50 bar with H_2 and stirred at r.t. for 2 h. The CH_2Cl_2 was evaporated, heptane (3 ml) was added and the soln. passed through a short plug of silica gel (0.5 cm) to remove the precipitated metal salts. The heptane soln. containing the product alkane was analyzed by chiral GC and chiral HPLC/GC to determine the substrate conversion and the enantiomer excess of the product.

HPLC and GC analysis of the hydrogenated products from: **7a** (*Daicel-Chiralcel-OJ* column, 254 nm, 0.5 ml min^{-1}, i-PrOH/heptane 1:99): t_R 12.5 (major) and 18.6 (minor); **7b** (*Daicel-Chiralcel-OJ* column, 254 nm, 0.5 ml min^{-1}, i-PrOH/heptane 1:99): t_R 12.5 and 14.6; **7c** (*Daicel-Chiralcel-OB-H* column, 254 nm, 0.5 ml min^{-1}, i-PrOH/heptane 0.5:99.5): t_R 16.6 and 19.5; **7d** (*Daicel-Chiralcel-OJ* column, 254 nm, 0.5 ml min^{-1}, i-PrOH/heptane 5:95): t_R 15.2 and 19.9; **7e** (*Daicel-Chiralcel-OD-H* column, 254 nm, 0.5 ml min^{-1}, i-PrOH/heptane 0.01:99.99): t_R 15.3 and 13.9; **7f** (*Daicel-Chiralcel-OD-H* column, 254 nm, 0.5 ml min^{-1}, i-PrOH/heptane 0.01:99.99): t_R 13.9 and 15.3; **7g** (20% [(*tert*-butyl)dimethylsilyl]dimethyl-β-CD/80% *OV 1701*, 25 m, 0.5 bar H_2, 50°, 1° min^{-1}, 180°): t_R 51.6 (minor isomer) and 53.0 (major isomer); **7h** (20% [(*tert*-butyl)dimethylsilyl]-dimethyl-β-CD/80% *OV 1701*, 25 m, 0.5 bar H_2, 50°, 1° min^{-1}, 180°): t_R 50.1 and 51.8.

Diels-Alder *Reaction: General Procedure*. The dark green soln. of (*R*)-**2a** (26 mg, 0.058 mmol, 12 mol-%), $Cu(OTf)_2$ (18 mg, 0.050 mmol, 10 mol-%), and CH_2Cl_2 (1 ml) was stirred for 1 h at r.t. Then **10a** (70 mg, 0.50 mmol) in CH_2Cl_2 (0.7 ml) and freshly cracked cyclopentadiene (0.21 ml, 166 mg, 2.5 mmol) were added at −78°. The green soln. was stirred at −78° until all the starting material had been consumed (7 h; GC monitoring). The mixture was submitted as such to CC (silica gel, AcOEt/hexane 1:3).

*3-[(1*R*,2*R*,4*R*)-Bicyclo[2.2.1]hept-5-en-2-yl]oxazolidin-2-one* (**11a**; 87 mg, 84%). TLC (AcOEt/hexane 1:2): R_f 0.31. M.p. 76–78°. $[\alpha]_D^{21} = +59.4$ ($c = 0.76$, $CDCl_3$); HPLC (*Chiralcel-OD-H* column, 254 nm, 0.75 ml min^{-1}; hexane/i-PrOH 9:1): 33.2 (minor isomer), 36.2 (major isomer); 48% ee. IR ($CHCl_3$): 2982, 1780, 1697, 1481, 1384, 1338, 1278, 1247, 1220, 1184, 1110, 1041, 1004, 802, 766. ^{1}H-NMR (200 MHz, $CDCl_3$): 1.33–1.61 (*m*, 3 H); 1.88–2.03 (*m*, 1 H); 2.93 (*s*, 1 H); 3.30 (*s*, 1 H); 3.90–4.08 (*m*, 3 H); 4.39 (*t*, $J = 7.7$, 2 H); 5.86 (*dd*, $J =$ 5.7, 2.8, 1 H); 6.18, 6.24 (*dd*, $J = 3.2$, 5.6, 1 H, *exo*/*endo* 6:94). ^{13}C-NMR (100 MHz, $CDCl_3$): 29.5 (CH_2); 42.8 (CH); 42.9 (CH_2); 43.2 (CH); 46.3 (CH); 50.2 (CH_2); 61.9 (CH_2); 131.6 (CH); 138.1 (CH); 153.4 (C); 174.7 (C). EI-MS (70 eV): 207 (10, M^+), 142 (60), 120 (24), 113 (33), 100 (11), 91 (17), 88 (11), 66 (100), 55 (96). HR-MS: 207.0897 ($C_{29}H_{26}NOP^+$; calc. 207.0895).

Allylic Substitution Reaction: General Procedure. In a dry 30-ml ampoule with stirring bar, [Pd(η^3-C_3H_5)Cl]$_2$ (2.5 mg, 0.0068 mmol) and (*S*)-**2a** (7.5 mg, 0.0167 mmol) were dissolved in CH_2Cl_2 (1.5 ml) under Ar. The resulting yellow soln. was stirred for 2 h at 50°. Then **12a** (160 mg, 0.635 mmol), malonic acid dimethyl ester (252 mg, 1.9 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (BSA; 388 mg, 1.9 mmol), and KOAc (1.1 mg, 0.0013 mmol) were added. The resulting yellow soln. was stirred for 1.5 h at r.t. Et_2O was added, and the soln. was poured onto cold (0°) sat. aq. NH_4Cl soln. The aq. layer was extracted with Et_2O (3×10 ml), the combined org. phase dried ($MgSO_4$), the solvent evaporated, and the residue purified by FC (AcOEt/hexane 1:4): **13a** (203 mg, 99%). HPLC (*Daicel-Chiralcel-OD* column, 254 nm, 0.75 ml min^{-1}, hexane/i-PrOH 99:1, detection at 254 nm): 94% ee. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.52 (*s*, 3 H); 3.70 (*s*, 3 H); 3.95 (*d*, $J = 10.9$, 1 H); 4.27 (*dd*, $J = 8.6$, 10.9, 1 H); 6.33 (*dd*, $J = 15.8$, 8.6, 1 H); 6.48 (*d*, $J = 15.8$, 1 H); 7.1–7.4 (*m*, 10 H).

Heck *Reaction: General Procedure*. To [$Pd_2(dba)_3 \cdot dba$] (17.7 mg, 0.015 mol, 1.5 mol-%) and (*R*)-**2a** (22.7 mg, 0.051 mol, 5.1 mol-%) under Ar (flask with a magnetic stirring bar and a *Teflon* screw-tap), benzene (5 ml) was added and the resulting red soln. stirred for 20 min. Tridecane (73.0 mg, 0.396 mmol) as internal GC standard, $(i\text{-Pr})_2EtN$ (0.35 ml, 266 mg, 2.06 mmol), 2,3-dihydrofuran (0.23 ml, 214 mg, 3.05 mmol), and cyclohex-1-en-1-yl trifluoromethanesulfonate (222 mg, 0.982 mmol) were added, and the soln. was stirred at r.t. for 64 h. At r.t., pentane (8 ml) was added, and the solvent was evaporated after filtration over silica gel. Purification by FC (silica gel, *t*-BuOMe/pentane 1:20) afforded (*S*)-**17** (81 mg, 55%). Colorless oil. TLC (*t*-BuOMe/pentane 1:20): R_f 0.32. GC (*γ-CD-TA* capillary column, H_2, 60 kPa, 80°, 1.5° min^{-1}, 95°,15° min^{-1}, 150°): t_R 17.4 (*S*)-**17**, 97%), 19.7 ((*R*)-**17**, 3%); 94% ee. $[\alpha]_D^{21} = -165$ ($c = 0.73$, $CHCl_3$). IR ($CHCl_3$): 3078, 3052, 2927, 2839, 1667, 1620, 1447, 1437, 1379, 1349, 1328, 1283, 1260, 1227, 1175, 1136, 1082, 1063, 1044, 1022, 896, 833, 797, 779, 755, 715. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.42–1.62 (*m*, 4 H); 1.71–2.05 (*m*, 4 H); 4.58 (*dddd*, $J = 12.6$, 4.2, 2.7, 1.8, 1 H); 4.67 (*dddd*, $J = 12.6$, 5.7, 2.4, 1.5, 1 H); 5.02–5.09 (*m*, 1 H); 5.62–5.67 (*m*, 1 H); 5.87 (*ddt*, $J =$ 6.3, 2.4, 1.5, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 22.5 (CH_2); 23.7 (CH_2); 25.4 (CH_2); 27.4 (CH_2); 75.1 (CH_2); 91.0 (CH); 124.7 (CH); 127.5 (CH); 129.2 (CH); 138.4 (C). EI-MS (70 eV): 150 (100, M^+), 121 (75), 107 (35), 91 (50), 79 (91), 77 (50), 69 (50), 53 (29).

*{(4*S*)-4-(*tert*-Butyl)-2-[2-(diphenylphosphino-κP)phenyl]-4*H*-1,3-benzoxazine-κN^3}[(1,2,3-η)-1,3-diphenylprop-2-enyl]palladium(1+) Trifluoromethanesulfonate* (**24**). (*S*)-**2a** (44.7 mg, 0.0994 mmol) and [Pd(η^3-{1,3-$Ph_2C_3H_3$})Cl]$_2$ (33.3 mg, 0.0497 mmol) were stirred for 20 min at r.t. in CH_2Cl_2 (3 ml). AgOTf (25.7 mg, 0.100 mmol) was added and the resulting mixture stirred for 30 min at r.t. Filtration over *Celite* and evaporation gave (*S*)-**24** (86 mg, 96%). Yellow solid. M.p. 70–72°. $[\alpha]_D^{20} = +266.7$ ($c = 0.445$, $CHCl_3$). IR ($CHCl_3$): 2962, 1771, 1631, 1460, 1241, 1210, 1117, 1030, 788, 725, 695. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.54, 0.74 (2*s*, 9 H, *endo*/*exo* 1:6); 3.66 (*s*, 1 H); 4.47 (*d*, $J = 10.3$, 1 H); 5.84 (*d*, $J = 7.4$, 1 H); 6.41 (*dd*, $J = 13.8$, 8.4, 1 H); 6.56 (*dd* $J = 11.8$, 7.5, 2 H); 6.71 (*dd*, $J = 13.7$, 10.3, 1 H); 6.82–7.80 (*m*, 24 H); 8.45 (*dd*, $J = 7.9$, 4.9, 1 H). ^{19}F-NMR (376 MHz,

$CDCl_3$): +85.6. ^{31}P-NMR (162 MHz, $CDCl_3$): +20.7. EI-MS (70 eV): 750 (71, $[M-OTf+H]^+$), 749 (13, $[M-OTf]^+$, 748 (100, $[M-OTf-H]^+$). Anal. calc. for $C_{46}H_{41}F_3NO_4PPdS\cdot 0.5\ CH_2Cl_2$ (983.22): C 59.37, H 4.50, N 1.49; found: C 58.69, H 4.63, N 1.58.

X-Ray Crystal Structure of (S)-**24**: $Pd(C_{45}H_{41}NOP)(CF_3SO_3)(CH_2Cl_2)$, M_r 983.2; $\mu = 5.670\ m^{-1}$, $d_x = 1.454\ g\cdot cm^{-3}$, triclinic, *P* 1, $Z=2$; $a=9.9206(9)$, $b=13.304(1)$, $c=17.975(1)$ Å, $\alpha=95.571(6)$, $\beta=99.949(5)$, $\gamma=103.779(6)^\circ$, $V=2245.7(4)$ Å^3; from 28 reflections ($40^\circ<2\theta<55^\circ$); yellow plate $0.126\times0.27\times0.35$ mm mounted on a quartz fibre with *RS3000* oil to prevent degradation. Cell dimensions and intensities were measured at 200 K on a *Stoe STADI4* diffractometer with graphite-monochromated CuK_α radiation (λ 1.5418 Å), ω-2θ scans; scan width $1.05^\circ+0.35$ tg θ; scan speed 0.06°/s; $-10<h<10$; $-14<k<14$; $-18<1<18$; 11183 measured reflections, 11006 unique reflections of which 10028 were observable ($|F_o|>4\sigma(F_o)$); R_{int} for equivalent reflections 0.048. Data were corrected for *Lorentz* and polarization effects and for absorption [22] ($T_{min,\ max}=0.24709$, 0.51227). The structure was solved by direct methods with MULTAN 87 [23], all other calculations used XTAL [24] system. Full-matrix least-squares refinement based on *F* with weights of $1/[\sigma^2(F_o)+0.0001(F_o^2)]$ gave final values $R=0.068$, $\omega R=0.067$, $S=2.09$, and *Flack* parameter $x=0.01(2)$ for 1080 variables and 1028 contributing reflections. Final $\Delta\rho=+1.96$, -1.80 eÅ^{-3}. H-Atoms were placed in calculated positions. Both molecules of the asymmetric unit show the same configuration and differ only by small differences of the orientation of the phenyl groups.

*X-Ray Crystal Structure of {(4*S*)-4-(*tert*-Butyl)-2-[2-(diphenylphosphino-*κ*P)phenyl]-4,5-dihydrooxazole-*κ*N^3}[(1,2,3-*η*)-1,3-diphenylprop-2-enyl]palladium(1+) Hexafluorophosphate ((*S*)-**25**)*. $Pd(C_{40}H_{39}NOP)\cdot PF_6(CHCl_3)(C_2H_5OH)$ [19], M_r 997.54; crystal size $0.20\times0.20\times0.50$ mm, monoclinic, space group $P2_1$, $D_c=1.42$ g cm^{-3}, $Z=2$; $a=12.297(1)$ Å, $b=15.564(9)$ Å, $c=13.582(1)$ Å, $\beta=116.258(6)^\circ$, $V=2331.05$ Å^3. Reflection intensities were collected at 293° K on a four-circle diffractometer (*Enraf-Nonius CAD4*, CuK_α radiation, λ 1.5418 Å, graphite monochromator) by the $\omega/2\theta$ technique; $\mu=6.08$, θ scan range $1.00<\theta<25.09^\circ$. Measured reflections 4921, independent reflections 4710, observed reflections 4051 ($I=3\sigma(I)$). The data were corrected for *Lorentz* and polarization effects. The absorption correction was determined by φ-scans [25]. The structure was solved by direct methods [26]. Anisotropic least-squares refinement against F_o was carried out on all non-H-atoms with the program CRYSTALS [27]. The positions of the H-atoms were calculated. Scattering factors were taken from [28]. The ethanol solvent was found to be disordered. The disordered atoms were refined in two positions holding the sum of their occupancies equal to one. Geometric restraints were applied to the disordered parts of the structure during the structure refinement. Final $R=0.0559$, $wR=0.0652$ (4051 reflections, 553 refined parameters, weighting scheme: *Chebychev* polynominal [29]), goodness-of-fit = 0.9682.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the *Cambridge Crystallographic Date Centre* as deposition Nos. CCDC-165229 ((*S*)-**24**) and CCDC-165905 ((*S*)-**25**). Copies of the data can be obtained, free of charge, on application to the CDCC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (1223) 336033; e-mail: deposit@ccdc.cam.ac.uk).

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