Synthesis, Structure, and Catalytic Performance of Diastereopure Five-Coordinated NCN-Pincer Palladium(II) Complexes Bearing Bulky Amino Acid Substituents

Silvia Gosiewska,[†] Sara Martinez Herreras,[†] Martin Lutz,[‡] Anthony L. Spek,[‡,§] Remco W. A. Havenith,[⊥,△] Gerard P. M. van Klink,[†] Gerard van Koten,[†] and Robertus J. M. Klein Gebbink*[,†]

Chemical Biology & Organic Chemistry, Faculty of Science, Utrecht University, Padualaan 8, 3584 CH Utrecht, The Netherlands, Bijvoet Center for Biomolecular Research, Faculty of Science, Crystal and Structural Chemistry, Utrecht University, Padualaan 8, 3584 CH Utrecht, The Netherlands, and Theoretical Chemistry Group, Faculty of Science, Utrecht University, Padualaan 8, 3584 CH Utrecht, The Netherlands

Received February 29, 2008

New chiral NCN-pincer palladium complexes containing bulky diphenylhydroxymethyl pyrrolidinyl moieties as chiral auxiliaries have been synthesized. Oxidative palladium addition to ligand **2** (**2** = 2,6-bis{[(*S*)-2-(diphenylhydroxymethyl)-1-pyrrolidinyl]methyl}-1-bromobenzene) initially yielded neutral arylpalladium bromide complex **3** in a moderate yield as a consequence of the bulky pyrrolidinyl functional groups. Performing the palladation reaction under microwave irradiation for only 5 min gave **3** in 79% yield. Abstraction of the bromide ion from **3** subsequently yielded the cationic complexes [**4**]PF_6 and [**4**]BF_4. Palladium complexes **3**, [**4**]PF_6, and [**4**]BF_4 are all formed as single diastereoisomers with an $R_NR_NS_CS_C$ configuration. X-ray crystal structure determinations of [**4**]PF_6 and [**4**]BF_4 revealed an unusual κ^5-*N*,*C*,*N*,*O*,*O* coordination around palladium, in which the normal meridional κ^3-coordination mode of the pincer framework is complemented by two rather long Pd−O interactions (2.622(2)–2.649(2) Å). Theoretical calculations (Mulliken population analysis and "atoms in molecules" analysis) confirmed that there is a coordinative interaction between the palladium and the oxygen atoms of both hydroxyl groups despite the long Pd−O distance. Complexes [**4**]PF_6 and [**4**]BF_4 catalyze the aldol condensation between α-methyl isocyanoacetate and various aromatic aldehydes with enhanced regio- (up to 70%) and stereoselectivity (up to 42% ee) for the *cis*-oxazolines. These observations are in contrast to prior literature results on other pincer systems, where the *trans*-oxazolines were the main product, and point to a deeper chiral cavity pointing away from palladium toward the coordinated isocyanoacetate substrate.

Introduction

The transition metal complexes of pincer ligands, monoanionic $[2,6\text{-}(ECH_2)_2C_6H_3]^-$ (E,C,E) systems with E = NR_2, PR_2, AsR_2, OR, and SR (structure **A**, Chart 1), have been extensively studied, and numerous applications in material science and catalysis were reported.[1] The pincer ligands show a number of attractive characteristics: they can incorporate a wide range of transition metals and their ligand framework can be easily modified in order to tune the electronic properties of the metal and the steric hindrance around it. In addition, stereogenic centers in the ligand framework of the pincer ligand can be positioned close to the active metal site and thus can exert a direct influence on the stereochemical outcome of a reaction.

There are relatively few chiral pincer ligand known.[1f] In most of the reported systems one or more C-centered stereogenic centers are incorporated into the pincer framework via a chiral auxiliary, e.g., amino acids or other natural products (structures **B**, Chart 1).[2–6] Recently, PCP-ligands with substituents containing axial chirality have been reported (structures **C**, Chart 1).[7] The other available positions to generate stereogenic centers in

* To whom correspondence should be addressed. E-mail: r.j.m.kleingebbink@uu.nl. Tel: +31-2531889. Fax: +31-30252-3615.
[†] Chemical Biology & Organic Chemistry.
[‡] Bijvoet Center for Biomolecular Research.
[⊥] Theoretical Chemistry Group.
[§] To whom correspondence pertaining to crystallographic studies should be addressed. E-mail: a.l.spek@chem.uu.nl.
[△] To whom correspondence pertaining to theoretical calculations should be addressed. E-mail: r.havenith@science.ru.nl.

(1) (a) Rietveld, M. H. P.; Grove, D. M.; van Koten, G. *New J. Chem.* **1997**, *21*, 751–771. (b) Albrecht, M.; van Koten, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 3750–3781. (c) Singleton, J. T. *Tetrahedron* **2003**, *59*, 1837–1857. (d) van der Boom, M. E.; Milstein, D. *Chem. Rev.* **2003**, *103*, 1759–1792. (e) Szabó, K. J. *Synlett* **2006**, *6*, 811–824. (f) *The Chemistry of Pincer Compounds*; Morales-Morales, D., Jensen, C. M., Eds.; Elsevier: Amsterdam, 2007.

(2) Nishiyama, H. *Chem. Soc. Rev.* **2007**, *36*, 1133–1141.

(3) (a) Boland, N. A.; Casey, M.; Hynes, S. J.; Matthews, J. W.; Smyth, M. P. *J. Org. Chem.* **2002**, *67*, 3919–3922. (b) Hao, X.-Q.; Gong, J.-F.; Du, Ch.-X.; Wu, L.-Y.; Wu, Y.-J.; Song, M.-P. *Tetrahedron Lett.* **2006**, *47*, 5033–5036.

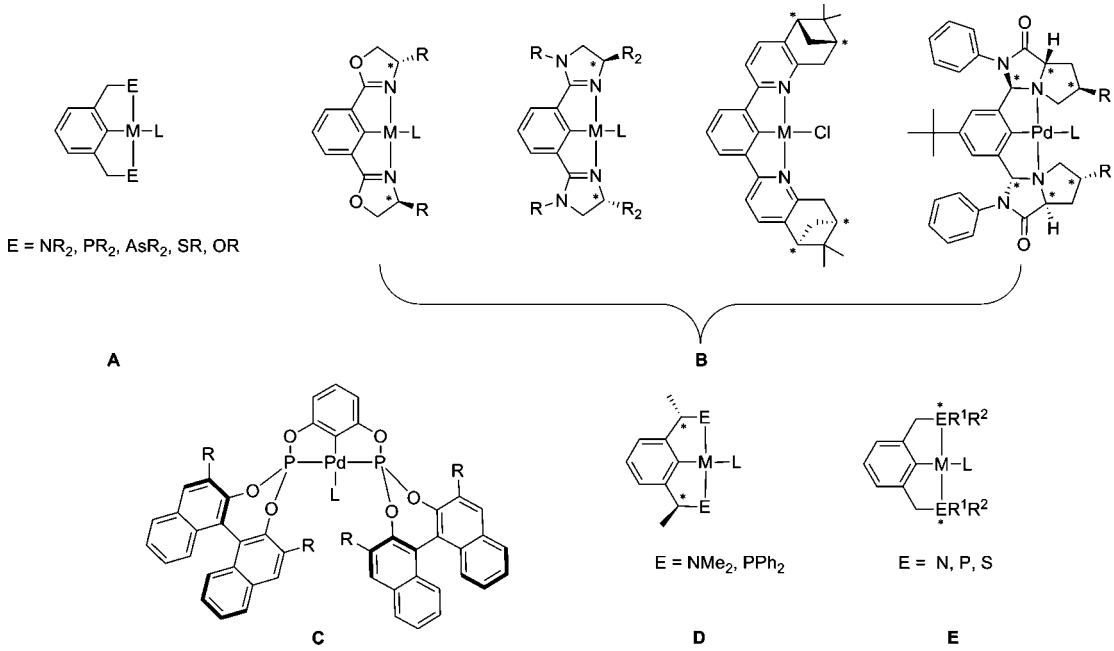
(4) (a) van de Kuil, L. A.; Veldhuizen, Y. S. J.; Grove, D. M.; Zwikker, J. W.; Jenneskens, L. W.; Drenth, W.; Smeets, W. J. J.; Spek, A. L.; van Koten, G. *Recl. Trav. Chim. Pays-Bas* **1994**, *113*, 267. (b) Gosiewska, S.; Huis in't Veld, M.; de Pater, J. J. M.; Bruijnincx, P. C. A.; Lutz, M.; Spek, A. L.; van Koten, G.; Klein Gebbink, R. J. M. *Tetrahedron: Asymmetry* **2006**, *17*, 674–686. (c) Gosiewska, S.; Herreras Martinez, S.; Lutz, M.; Spek, A. L.; van Koten, G.; Klein Gebbink, R. J. M. *Eur. J. Inorg. Chem.* **2006**, *460*, 0–4607.

(5) (a) Soro, B.; Stoccoro, S.; Minghetti, G.; Zucca, A.; Cinellu, M. A.; Manassero, M.; Gladiali, S. *Inorg. Chim. Acta* **2006**, *359*, 1879–1888. (b) Yoon, M. S.; Ramesh, R.; Kim, J.; Ryu, D.; Ahn, K. H. *J. Organomet. Chem.* **2006**, *691*, 5927–2934.

(6) (a) Takenaka, K.; Uozumi, Y. *Org. Lett.* **2004**, *6*, 1833–1835. (b) Takenaka, K.; Minakawa, M.; Uozumi, Y. *J. Am. Chem. Soc.* **2005**, *127*, 12273–12281.

10.1021/om701261q CCC: $40.75 © 2008 American Chemical Society
Publication on Web 05/02/2008

Chart 1. Examples of Chiral Pincer Metal Complexes

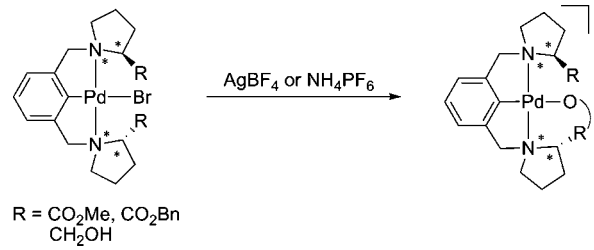


the pincer backbone are the carbon atoms of the benzylic methylene groups as depicted in structure **D** (Chart 1).[8,9] If substituents R^1 and R^2 of the E donor groups (E = P and S) of the ECE-pincer skeleton are different, chiral structures **E** (Chart 1) with E-centered stereogenic centers are formed upon introduction of the metal.[10]

Next to the octahedral geometry (Rh(III), Pt(IV), and Ni(III)), the square-planar geometry is most commonly observed for metal complexes (Ni(II), Pd(II), and Pt(II)) with chiral pincer ligands.[11] Only two examples of five-coordinated chiral pincer metal complexes were reported in the literature.[10f,12] In all examples the pincer ligand is coordinated to the metal in a tridentate meridional κ^3-*E*,*C*,*E* coordination fashion.

Previously, we reported on the synthesis and structural analysis of NCN-pincer palladium complexes with ester prolinates and prolinols as the nitrogen donor substituents (Scheme 1).[4b,c] In the cationic complexes, upon abstraction of the ancillary halide, the oxygen atoms of the ester or hydroxyl group were coordinated to the metal, yielding the κ^4-*N*,*C*,*N*,*O* coordination mode of the NCN-pincer ligand. These complexes were tested as catalysts in aldol-type reactions of aldehydes with α-methyl isocyanoacetate (reaction 1) to produce 5-aryl-2-oxazoline-4-carboxylates, which give the corresponding β-hydroxy-α-amino acids after hydrolysis. This catalytic aldol reaction is mechanistically of interest because of the simultaneous creation of two stereogenic C atoms.

Scheme 1. Structures of Neutral and Cationic Pyrrolidine NCN-Pincer Complexes



However, the selectivity obtained with NCN-Pd pincers with ester prolinates or prolinol substituents in the aldol reaction (eq 1) was poor (max. 16% ee for the *trans*-oxazoline). Apparently, these substituents cannot generate sufficient steric hindrance to induce a well-defined chiral pocket around the Pd center and the Pd-bound enolate intermediate. The formation of the *trans*-oxazolines as the major product was also observed for achiral NCN-pincer Pd complexes[13] and chiral PCP-pincer Pd and Pt complexes.[8b,c]

In order to increase the steric bulk close to the metal, we have investigated the introduction of pyrrolidinyl N-donor moieties with diphenylhydroxymethyl functional groups in the NCN-pincer ligand framework. Here, we report the synthesis

(7) (a) Wallner, O. A.; Olsson, V. J.; Eriksson, L.; Szabó, K. L. *Inorg. Chim. Acta* **2006**, *359*, 1767–1772. (b) Baber, A. A.; Bedford, R. B.; Betham, M.; Blake, M. E.; Coles, S. J.; Haddow, M. F.; Hursthouse, M. B.; Orpen, A. G.; Pilarski, L. T.; Pringle, P. G.; Wingad, R. L. *Chem. Commun.* **2006**, 3880–3882. (c) Aydin, J.; Kumar, K. S.; Sayah, M. J.; Wallner, O. A.; Szabó, K. L. *J. Org. Chem.* **2007**, *72*, 4689–4697.

(8) For PCP see: (a) Gorla, F.; Togni, A.; Venanzi, L. M.; Albinati, A.; Lianza, A. *Organometallics* **1994**, *13*, 1607–1616. (b) Longmire, J. M.; Zhang, X. *Tetrahedron Lett.* **1997**, *38*, 1725–1728. (c) Longmire, J. M.; Zhang, X.; Shang, M. *Organometallics* **1998**, *17*, 4374–4379. (d) Dani, P.; Albrecht, M.; van Klink, G. P. M.; van Koten, G. *Organometallics* **2000**, *19*, 4468–4476.

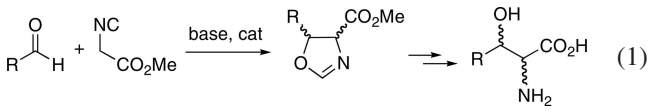
(9) For NCN see: Albrecht, M.; Kocks, B. M.; Spek, A. L.; van Koten, G. *J. Organomet. Chem.* **2001**, *624*, 271–286.

(10) (a) van Beek, J. A. M.; van Koten, G.; Dekker, G. P. C.; Wissing, E.; Zoutberg, M. C.; Stam, C. H. *J. Organomet. Chem.* **1990**, *394*, 659–678. (b) van Beek, J. A. M.; van Koten, G.; Ramp, M. J.; Coenjaarts, N. C.; Grove, D.; Goubitz, K.; Zoutberg, M. C.; Stam, C. H.; Smeets, W. J. J.; Spek, A. L. *Inorg. Chem.* **1991**, *30*, 3059–3068. (c) Dani, P.; Albrecht, M.; van Klink, G. P. M.; van Koten, G. *Organometallics* **2000**, *19*, 4468–4476. (d) Williams, B. S.; Dani, P.; Lutz, M.; Spek, A. L.; van Koten, G. *Helv. Chim. Acta* **2001**, *84*, 3519–3530. (e) Evans, D. R.; Huang, M.; Seganish, W. M.; Fettinger, J. C.; Williams, T. L. *Organometallics* **2002**, *21*, 893–900. (f) Morales-Morales, D.; Cramer, R. E.; Jensen, C. M. *J. Organomet. Chem.* **2002**, *654*, 44–50. (g) Medici, S.; Gagliardo, M.; Williams, S. B.; Chase, P. A.; Gladiali, S.; Lutz, M.; Spek, A. L.; van Klink, G. P. M.; van Koten, G. *Helv. Chim. Acta* **2005**, *88*, 694–705.

(11) Gosiewska, S.; van Koten, G.; Klein Gebbink, R. J. M. Manuscript in preparation.

(12) Gerish, M.; Krumper, J. R.; Bergman, R. G.; Tilly, T. D. *Organometallics* **2003**, *22*, 47–58.

(13) (a) Rodríguez, G.; Lutz, M.; Spek, A. L.; van Koten, G. *Chem. Eur. J.* **2002**, *8*, 46–57. (b) Mehendale, N. C.; Klein Gebbink, R. J. M.; van Koten, G. Manuscript in preparation.



(1)

and structural characterization of the novel NCN-pincer ligand and the corresponding Pd(II) complexes in the solid state and in solution. The influence of the bulky diphenylhydroxymethyl groups on the geometry and chirality of the corresponding neutral and cationic Pd complexes will be presented as well as the regio- and enantioselectivity of these compounds in the aldol condensation between α-methyl isocyanoacetate and various aromatic aldehydes (eq 1).

Results and Discussion

Synthesis. Chiral NCN-pincer ligand precursor **2** was synthesized via a Grignard reaction of the bismethyl ester compound **1** with an excess of PhMgBr (Scheme 2). This reaction yielded the desired compound **2** as the only product in 92% yield with full retention of the S_C configuration of both carbon stereogenic centers (*vide infra*).

Reaction of **2** with $[Pd_2(dba)_3 \cdot CHCl_3]$ at elevated temperatures gave complex **3** in a moderate 44% yield using a slight excess of palladium (1.5 equiv) and after reaction optimization (Scheme 2). The low-yielding palladation of **2** could result from the intrinsic bulkiness of the ligand[14] and from the concomitant decomposition of $[Pd_2(dba)_3] \cdot CHCl_3$ to palladium black due to the long reaction times and elevated temperatures. Alternatively, performing the palladation under microwave irradiation conditions (500 W) and using 2 equiv of $[Pd_2(dba)_3] \cdot CHCl_3$ at 95 °C for only 10 min yielded **3** in 79% isolated yield. Apparently, the microwave heating effects,[15] i.e., efficient internal heating, rapid attainment of high temperatures, and induced mobility by a highly polarizing field, enhanced the palladation reaction and significantly reduced the reaction time. Subsequent abstraction of the bromide anion from **3** by treatment with either NH_4PF_6 or $AgBF_4$ yielded the cationic complexes [**4**]PF_6 and [**4**]BF_4 (Scheme 2) in good yields (61 and 70%, respectively). The neutral palladium complex **3** as well as the cationic complexes [**4**]PF_6 and [**4**]BF_4 were obtained as single diastereoisomers with an $R_NR_NS_CS_C$ configuration (*vide infra*).

X-ray Crystal Structures. Single crystals suitable for X-ray crystal structure determination were obtained for ligand **2** as well as for the palladium complexes **3**, [**4**]PF_6, and [**4**]BF_4 (for crystallographic data see Experimental Section). X-ray crystal structure determination of ligand **2** revealed that it was obtained as a single enantiomer with retention of the *S* configuration of the C-stereogenic atoms (Figure 1). The crystal structure furthermore shows the presence of two independent molecules in the asymmetric unit. In both molecules the diphenyl alcohol groups are pointing above and below the phenyl bromide plane, and the pyrrolidine moieties are bent away from the bromide atom via the benzylic methylene group to yield an overall, noncrystallographic C_2 symmetry. The two independent molecules differ only in the conformation of the phenyl rings and the puckering of the pyrrolidine rings.

The structure of complex **3** as determined by X-ray crystallography shows a slightly distorted square-planar coordination environment around palladium (angles of C1−Pd−N1 81.18(11)°, C1−Pd−N2 80.84(10)°, and N1−Pd−N2 161.89(9)°), which is typical for the *mer* κ^3-*N*,*C*,*N* pincer coordination mode.[13a,16] A view of the molecular structure of **3** is presented in Figure 2, and relevant bond distances and angles are given in Table 1.[17] The five atoms of the basal plane including palladium are coplanar with a maximum deviation of 0.021(2) Å of both nitrogen atoms. The previously mentioned angles and the Pd−C1 bond length are comparable with reported structures of [PdBr(NCN)] and related complexes.[13a,16] However, the Pd−N distances in **3** are slightly longer, which can be related to the presence of the rather bulky pyrrolidine substituents. The two five-membered chelate rings which share the Pd−C1 bond have puckered conformations with the nitrogen substituents positioned on opposite sides of the aryl plane. The two diphenylmethyl groups point away from the metal center, and both hydroxyl groups form intramolecular hydrogen bonds with the halide ligand (H···Br distances of 2.38 and 2.33 Å), resulting in an overall, noncrystallographic C_2 symmetry.

Two new N stereogenic centers were generated upon coordination of ligand **2** to palladium, and therefore, three unique stereoisomers are possible.[18] In the case of the palladium halide complexes of methyl and benzyl ester NCN-prolinates and NCN-prolinols, a mixture of all three possible diastereoisomers was indeed formed.[4b,c] In the case of complex **3** the presence of the two bulky diphenylhydroxymethyl groups results in the formation of a single diastereoisomer with the $R_NR_NS_CS_C$ configuration that maintains its unique stereochemistry in solution at ambient temperature (*vide infra*).

X-ray crystal structure determination of complexes [**4**]PF_6 and [**4**]BF_4 revealed that both crystal structures are isostructural, with *mer*-κ^3-*N*,*C*,*N* pincer coordination modes at the Pd center with the N,C,N and Pd atoms perfectly in one plane, and possess an exact, crystallographic C_2 symmetry. Both complexes are formed as single diastereoisomers with $R_NR_NS_CS_C$ configuration. The cation–anion adduct of [**4**]PF_6 is represented in Figure 3, and relevant bond angles and distances for both complexes are collected in Table 2. The bond angles (e.g., N−Pd−N = 161.47(12)° and 161.10(13)° for [**4**]PF_6 and [**4**]BF_4, respectively) and Pd−C1 distances (1.918(3) and 1.916(4) Å) correspond well with those of known structures for structurally related cationic NCN-pincer Pd complexes.[19] The Pd−N distances for [**4**]PF_6 and [**4**]BF_4 (e.g., 2.142(2) and 2.137(2) Å) are similar to the Pd−N distances (2.145(2) and 2.147(2) Å) in the neutral complex **3**. Next to the normal pincer coordination mode, two additional interactions are observed between the Pd center and the ligand, i.e., interactions between Pd and the oxygen atoms

(14) Good yields (70% and 90%) were obtained in the same reaction of smaller methyl and benzyl ester NCN-Br derivatives; see ref 4b.

(15) For recent reviews on the microwave effect, see: (a) de la Hoz, A.; Díaz-Ortis, A.; Moreno, A. *Chem. Soc. Rev.* **2005**, *34*, 164–178. (b) Kappe, C. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250–6284.

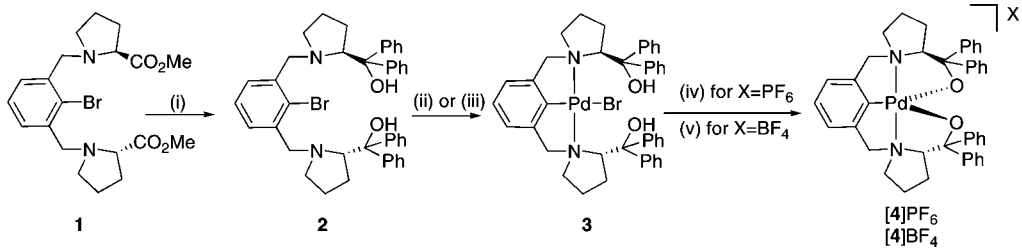
(16) (a) Dijkstra, H. P.; Meijer, M. D.; Patel, J.; Kreiter, R.; van Klink, G. P. M.; Lutz, M.; Spek, A. L.; Canty, A.; van Koten, G. *Organometallics* **2001**, *20*, 3159–3168. (b) Tsubomura, T.; Tanihata, T.; Yamakawa, T.; Ohmi, R.; Tamane, T.; Higuchi, A.; Katoh, A.; Sakai, K. *Organometallics* **2001**, *20*, 3833–3835. (c) Dijkstra, H. P.; Slagt, M. Q.; McDonald, A.; Kruithof, C. A.; Kreiter, R.; Mills, A. M.; Lutz, M.; Spek, A. L.; Klopper, W.; van Klink, G. P. M.; van Koten, G. *Eur. J. Inorg. Chem.* **2003**, *5*, 830–838. (d) Slagt, M. Q.; Rodríguez, G.; Gutters, M. M. P.; Klein Gebbink, R. J. M.; Klopper, W.; Jenneskens, L. W.; Lutz, M.; Spek, A. L.; van Koten, G. *Chem.−Eur. J.* **2004**, *10*, 1331–1344.

(17) Halogen scrambling occurred due to the use of chlorinated solvents in the purification methods. The halogen position is occupied by 2/3 Br and 1/3 Cl.

(18) The complexes where the nitrogen atoms have an opposite configuration (R_NS_N or S_NR_N) are superimposable upon 180° rotation around the C−Pd axis and are therefore identical.

(19) (a) Stark, M. A.; Jones, G.; Richards, C. J. *Organometallics* **2000**, *19*, 1282–1291. (b) Motoyama, Y.; Kawakami, H.; Shimozono, K.; Aoki, K.; Nishiyama, H. *Organometallics* **2002**, *21*, 3408–3416. (c) van den Broeke, J.; Heeringa, J. J. H.; Chuchuryukin, A. V.; Kooijman, H.; Mills, A. M.; Spek, A. L.; van Lenthe, J. H.; Ruttink, P. J. A.; Deelman, B. J.; van Koten, G. *Organometallics* **2004**, *23*, 1287–1294.

Scheme 2. Synthesis of Chiral NCN-Pincer Palladium Complexes 3 and 4[a]



[a] Conditions: (i) 8 equiv of PhMgBr, THF, rt, 3 h; (ii) $[Pd_2(dba)_3 \cdot CHCl_3]$, benzene/acetone, 1:1 (v/v), 60 °C, 24 h; (iii) $[Pd_2(dba)_3 \cdot CHCl_3]$, MW, benzene/acetone, 1:1(v/v), 95 °C, 10 min, 500 W; (iv) NH_4PF_6, CH_3OH/H_2O, 1:1 (v/v), rt; (v) $AgBF_4$, acetone/H_2O (v/v), rt.

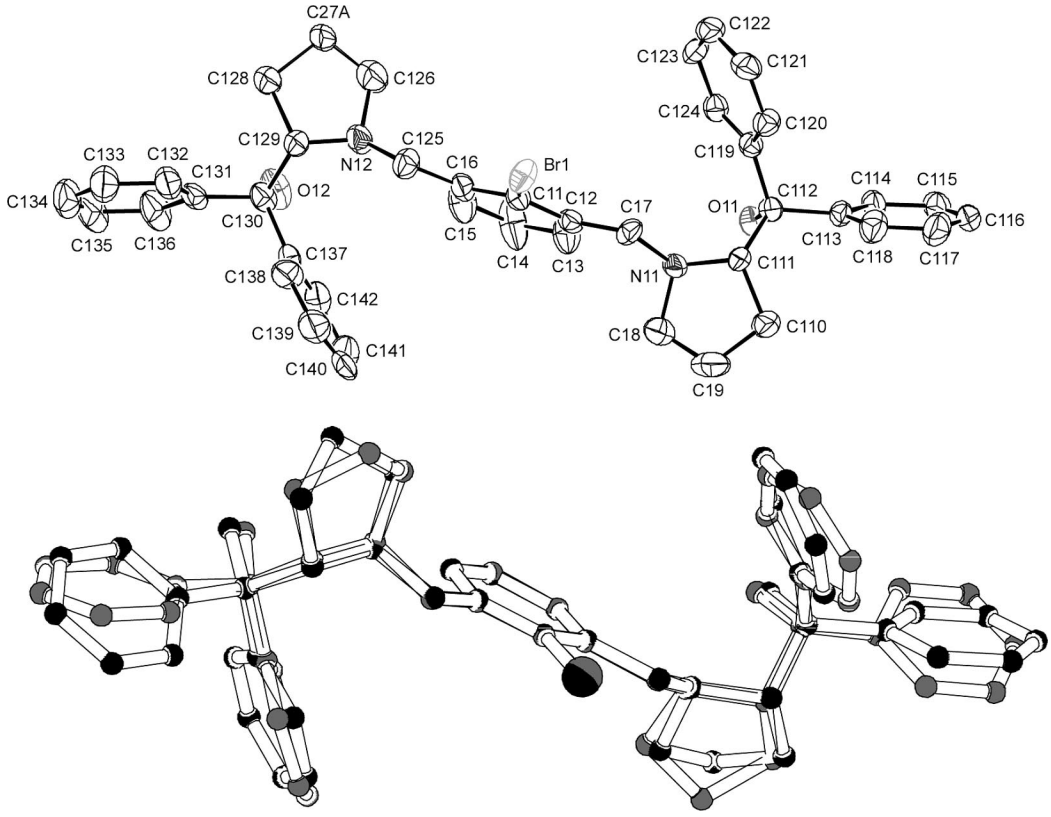


Figure 1. (Top) Displacement ellipsoid plot (50% probability) for the first of two independent molecules of **2** in the crystal; hydrogen atoms are omitted for clarity. Only the major disorder component is shown. (Bottom) Quaternion fit of the two independent molecules of ligand **2** in the crystal structure. Only the major disorder components are shown.

of the two hydroxyl groups. These Pd−O distances amount to 2.622(2) and 2.649(2) Å in [**4**]PF_6 and [**4**]BF_4, respectively, which is beyond the sum of the atomic radii (2.18 Å) and is much longer than the Pd−O distances reported for palladium complexes with neutral oxygen-containing ligands (in the range 2.097–2.220 Å).[20]

The description of the structures of [**4**]PF_6 and [**4**]BF_4, as determined by X-ray diffraction, is supported by theoretical calculations, which revealed that the interactions between the palladium atom and the oxygen atoms of both hydroxyl groups in [**4**]PF_6 are best described as coordinative interactions despite the long Pd−O distances (vide infra). Following this description, the Pd atom in [**4**]PF_6 and [**4**]BF_4 is five-coordinate with an irregular geometry. While a τ-value[21] of 0.34 indicates a geometry around Pd between square pyramidal and trigonal bipyramidal, such a description based on a Berry pseudorotation is not appropriate due to the very inequivalent bond lengths in the Pd coordination environment. According to the long Pd−O distances, we consider this interaction as weak, the formation of which may, however, be favored because the counteranion (PF_6 or BF_4) stabilizes and fixes the positions of the hydroxyl groups via hydrogen bonding. The latter hydrogen bonding involves the hydrogen atoms of both hydroxyl groups and fluorine atoms of the "noncoordinating" counteranion (H···F distance of 2.42(4) Å in [**4**]PF_6 and 2.04(4) Å in [**4**]BF_4, Table 2), forming an interesting model for a contact ion pair. An eight-membered ring is created defining a cavity at the metal (Pd···P distance = 5.5667(7) Å in [**4**]PF_6 and Pd···B = 5.431(3) Å in [**4**]BF_4) and protecting it from coordination of other ligands in the solid state. In this arrangement one of the lone pairs of each of the oxygen atoms points toward Pd (C10−O1−Pd1 angles of 103.61(14)° and 102.78(14)°, respectively), which may add

(20) For palladium aqua complexes see: Vicente, J.; Arcas, A. *Coord. Chem. Rev.* **2005**, *249*, 1135–1154.

(21) Addison, A. W.; Rao, T. N.; Reedijk, J.; van Rijn, J.; Verschoor, G. C. *J. Chem. Soc., Dalton Trans.* **1984**, *134*, 5–1349.

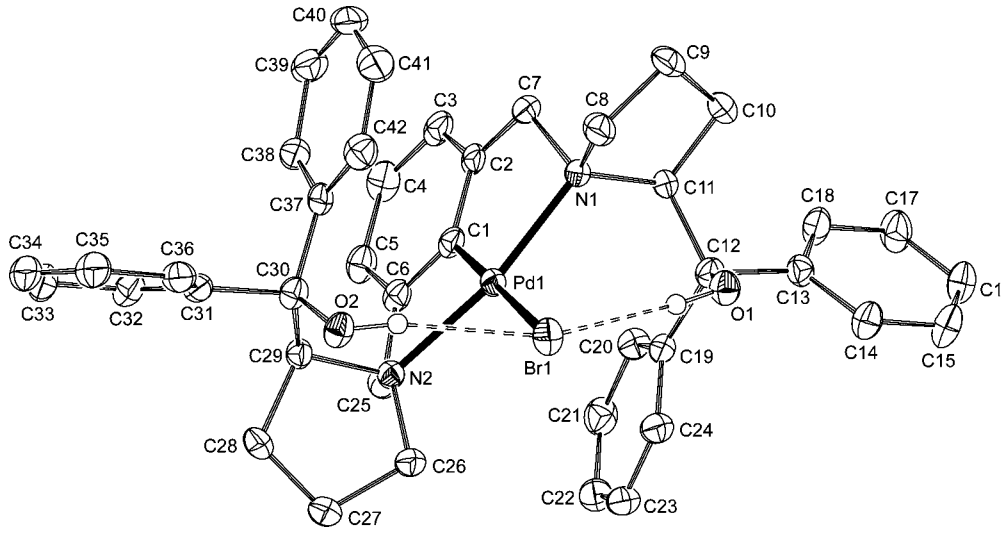


Figure 2. Displacement ellipsoid plot (50% probability) of complex **3** with depicted intramolecular hydrogen bonds. Remaining hydrogen atoms and solvent molecules are omitted for clarity.[17]

Table 1. Selected Bond Lengths (Å), Angles (deg), and Torsion Angles (deg) for 3

Pd1−C1	1.919(3)	C1−Pd1−N1	81.18(11)
Pd1−N1	2.147(2)	C1−Pd1−N2	80.84(10)
Pd1−N2	2.145(2)	Br1−Pd1−N1[a]	99.23(7)
Pd1−Br1[a]	2.5877(4)	Br1−Pd1−N2[a]	98.74(6)
C12−O1	1.418(3)	C1−Pd1−Br1[a]	179.47(8)
C30−O2	1.418(3)	N1−Pd1−N2	161.89(9)
O1−H1O	0.90	Pd1−N1−C7-C2	−35.4(2)
O2−H2O	0.92	Pd1−N2−C25-C6	−37.6(2)
H1O···Br1[a]	2.38	O1−H1O···Br1[a]	175
H2O···Br1[a]	2.33	O2−H2O···Br1[a]	168
O1···Br1[a]	3.2736(19)	O2···Br1[a]	3.230(2)
O2···Br1[a]	3.230(2)		

[a] The halogen position is occupied by 2/3 Br and 1/3 Cl.

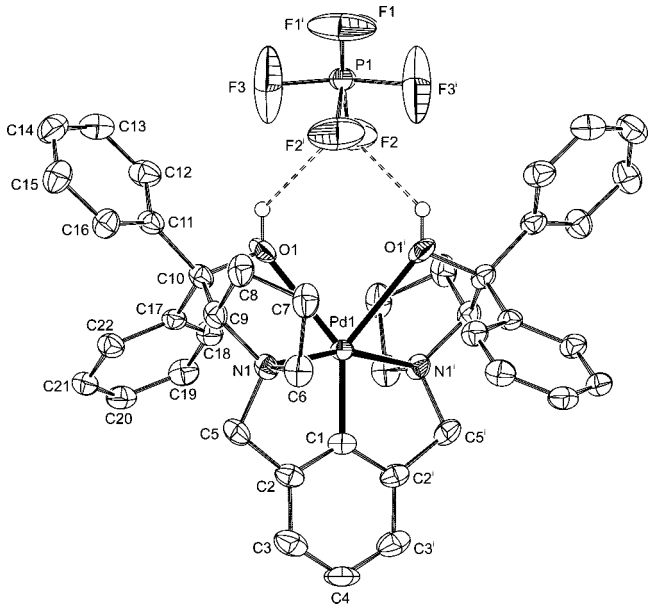


Figure 3. Displacement ellipsoid plot (50% probability) of complex [**4**]PF_6 with depicted intermolecular hydrogen bonds. Remaining hydrogen atoms are omitted for clarity. Symmetry operation i: *y*, *x*, −*z*.

to the stabilization of a bonding Pd−O interaction. A further stabilizing factor for the observed anion−cation contact are the diphenyl groups which are pointing away from the metal to lower steric interference. As a consequence, the hydroxyl groups are pointing toward the metal (R_N configuration), hence making the O-donor atoms predisposed for coordination to the metal and the hydroxyl hydrogens for intramolecular hydrogen bonding. A similar five-coordinate stereochemistry at the palladium center could occur as a sort of transition state of a process in which one hydroxyl oxygen atom is front-side "attacking" the cationic palladium center and the second one being the leaving group. This process is than assisted by the anion in the contact ion pair. That the hydrogen bonding motifs in [**4**]PF_6 and [**4**]BF_4 are crucial for the formation of the five-coordinate structures is supported by the fact that in the corresponding methyl and benzyl ester prolinate complexes (lacking the possibility for H-bonding) cationic complexes with a N,C,N,O four-coordination are formed through coordination of one of the ester carbonyl groups to the metal.[4b]

Table 2. Selected Bond Lengths (Å), Angles (deg), and Torsion Angles (deg) for the Isostructural Complexes [4]PF_6 and [4]BF_4

	[**4**]PF_6	[**4**]BF_4
Pd1−C1	1.918(3)	1.916(4)
Pd1−N1	2.142(2)	2.137(2)
Pd1−O1	2.622(2)	2.649(2)
C10−O1	1.449(3)	1.441(3)
O1−H1O	0.88(4)	0.79(4)
H1O···F2[i]	2.42(4)	2.04(4)[b]
O1···F2[i]	3.113(3)	2.773(5)[b]
C1−Pd1−N1	80.73(6)	80.55(6)
N1−Pd1−N1[i]	161.47(12)	161.10(13)
C1−Pd1−O1	141.25(5)	140.85(5)
N1−Pd1−O1	73.31(7)	73.40(7)
N1−Pd1−O1[i]	122.57(7)	122.69(7)
C10−O1−Pd1	103.61(14)	102.78(14)
O1−H1O···F2[i]	136(3)	153(4)[b]
Pd1−N1−C5-C2	35.2(2)	35.6(2)

[a] Symmetry operation i: *y*, *x*, −*z*. [b] The BF_4 anion was refined with a disorder model.

In theory, the combination of a cationic Pd fragment capable of being a hydrogen bond donor with a hydrogen bond accepting anion, like in the case of complexes **3**, [**4**]PF_6, and [**4**]BF_4, can result in the structures depicted in Figure 4. In structure A the ancillary anionic ligand is bonded to the metal, resulting in the formation of a neutral Pd complex. Structures B and C represent cationic Pd complexes in which the palladium cation and anion X are held together via hydrogen bonds forming a contact ion pair. In structure B, the hydroxyl groups are coordinated to the

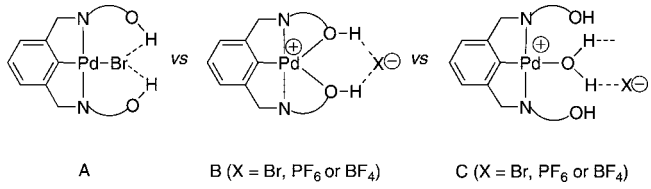


Figure 4. Schematic representation of possible structures A−C for complexes **3**, [**4**]PF_6, and [**4**]BF_4.

metal *and* form hydrogen bonds with X, while in structure C an ancillary aqua ligand is coordinated to the metal and connected with X through hydrogen bonds, as is often observed for cationic Pd complexes with noncoordinated anions.[19c,22] For palladium bromide complex **3**, a neutral complex with structure A is formed. Apparently, the formation of the Pd−Br and two H···Br bonds is energetically more favorable than the formation of two Pd−O bonds and two H···Br hydrogen bonds (structure B). For the cationic complexes [**4**]PF_6 and [**4**]BF_4, no coordinated water was found in the crystal structures. Apparently, the formation of two Pd−O bonds and H···F hydrogen bonds of the anion with both hydroxyl groups of the ligand (structure B) is energetically more favorable than the formation of the corresponding aqua complex with structure C.

A search of the Cambridge crystallographic database (CSD version 5.28, may 2007)[23] revealed that [**4**]PF_6 and [**4**]BF_4 are the first examples of pentacoordinate Pd structures involving two coordinating hydroxyl oxygen donor atoms with Pd−O distances beyond 2.4 Å. Several palladium complexes with one long Pd−O distance of approximately 2.7 Å are known, but in these cases palladium is coordinated to four donor atoms in one plane with the relatively distant oxygen atom in the apical position of a square-pyramidal type of arrangement.[24]

Theoretical Calculations. In order to study the nature of the Pd−O interactions in complexes **4** in more detail, DFT calculations were performed on complex [**4**]PF_6 (relevant distances and angles calculated for [**4**]PF_6 are reported in Table 3). These were followed by a Mulliken population analysis[25] and an "atoms in molecules" (AIM) analysis.[26] For comparison, similar calculations were carried out on **3**, which lacks the palladium oxygen-bonding interactions (structure A) and on [Pd(NCN)(OH_2)]BF_4 (structure C),[19c] which does contain a Pd−O bond (2.192 Å). Optimized geometries of **3** and [**4**]PF_6 obtained via these DFT calculations compare favorably with the structures determined experimentally by X-ray crystallography (Figure 5).

The DFT calculations revealed a more pronounced *trans* effect of the ancillary ligand on the length of Pd−C1 distance in **3** and [**4**]PF_6, which is, however, not reflected in the distances

Table 3. Selected Bond Lengths (Å) and Angles (deg) for 3 and [4]PF_6 Calculated at the B3LYP/LANL2-DZ Level

	3	[**4**]PF_6
Pd−C1	1.994	1.934
Pd−N	2.197/2.197	2.173/2.175
Pd−X	2.589 (X = Br)	2.534/2.550 (X = O)
O−H···Z	2.286/2.289 (Z = Br)	1.7256/1.7420 (Z = F)
N−Pd−N	162.00	162.82
C1−Pd−N	80.98/81.02	81.40/81.43
C1−Pd-X	179.49 (X = Br)	
O−H···F		174.64/176.94

obtained from X-ray crystallography, where these have almost identical values (Tables 1 and 2). The Pd−O distances obtained from the DFT calculation of [**4**]PF_6 are slightly shorter than the distances obtained from the X-ray structural determination (2.5501, 2.5342 vs 2.622(2), 2.649(2) Å). The differences may arise from crystal-packing effects and by the fixed hydrogen bonding motif of the hydroxyl groups and the PF_6 anion in the solid state, as compared to the larger conformational freedom of the contact ion pair in the gas phase considered in the calculations.

The Mulliken population analysis (Table 4) revealed very similar values for the palladium oxygen overlap in [**4**]PF_6 and [Pd(NCN)(OH_2)]BF_4 (0.065/0.062 and 0.059 e^-, respectively). The calculated values for the Pd−N and Pd−C1 population overlap are comparable for these complexes.

The AIM theory, developed by Bader,[26] defines bonding by the presence of bond critical points (BCPs) between atoms. The sign of the Laplacian ($\nabla^2\rho(r_P)$) at the BCP is then indicative for the type of interaction; a negative sign represents a covalent bond and a positive sign indicates closed-shell interactions as in ionic (or coordination bonds), hydrogen bonded, and van der Waals complexes. The calculations show that in [**4**]PF_6 five BCPs are located around the palladium atom and between the Pd and the C1 atom, the two nitrogen atoms, and two oxygen atoms, all possessing a positive Laplacian at the BCPs. As expected in [Pd(NCN)(OH_2)]BF_4 and **3**, only four BCPs are located around the palladium atom. In these complexes the BCPs are found between Pd and the C1 atom, the two nitrogens, and the fourth ligand, which is the oxygen atom of the water molecule in [Pd(NCN)(OH_2)]BF_4 and the bromide center in **3**. Important for our analysis is that the electron densities at the BCPs of the Pd−O bonds in [**4**]PF_6 and [Pd(NCN)(OH_2)][BF_4] amount to values of the same magnitude (0.223/0.216 and 0.318). Furthermore, the small value of the Mulliken population overlap between Pd and oxygen in [**4**]PF_6 is indicative of closed-shell interactions, which is also supported by the finding of positive values of the Laplacian at the BCPs. On the basis of

(22) (a) Leoni, P.; Sommovigo, M.; Pasqualli, M.; Midollino, S.; Braga, D.; Sabatino, P. *Organometallics* **1991**, *10*, 1038–1044. (b) Sheehan, J. P.; Spalding, T. R.; Ferguson, G.; Gallagher, J. F.; Kaitner, B.; Kennedy, J. D. *J. Chem. Soc., Dalton Trans.* **1993**, 35–42. (c) Maassarani, F.; Davidson, M. F.; Wehman-Ooyevaar, I. C. M.; Grove, D. M.; van Koten, M. A.; Smeets, W. J. J.; Spek, A. L.; van Koten, G. *Inorg. Chim. Acta* **1995**, *235*, 327–338. (d) Sodeoka, M.; Tokunoh, R.; Miyazaki, F.; Hagiwara, E.; Shibasaki, M. *Synlett* **1997**, 463–466. (e) Lindner, E.; Schmid, M.; Wegner, P.; Nachtigal, C. Steimann, M.; Fawzi, R. *Inorg. Chim. Acta* **1999**, *296*, 103–113. (f) Canty, A. J.; Patel, J.; Skelton, B. W.; White, A. H. *J. Organomet. Chem.* **2000**, *607*, 194–202. (g) Ma, J.-F.; Kojima, Y.; Yamamoto, Y. *J. Organomet. Chem.* **2000**, *616*, 149–156. (h) Nakai, H.; Ogo, S.; Watanabe, Y. *Organometallics* **2002**, *21*, 1674–1678. (i) Shi, P.-Y.; Liu, Y.-H.; Peng, S.-M.; Liu, S.-T. *Organometallics* **2002**, *21*, 3203–3207. (j) Motoyama, Y.; Kawakami, H.; Shimozono, K.; Aoki, K.; Nishiyama, H. *Organometallics* **2002**, *21*, 3408–3416. (k) Kimmich, B. F. M.; Marshall, W. J.; Fagan, P. J.; Hauptman, E.; Bullock, R. M. *Inorg. Chim. Acta* **2002**, *330*, 52–58.

(23) Allen, F. H. *Acta Crystallogr.* **2002**, *B58*, 380–388.

(24) (a) Kuzmina, L. G.; Struchkov, Y. T. *Koord. Khim. (Russ.)* **1979**, *5*, 1558. (b) Siedle, A. R.; Newmark, R. A. *J. Am. Chem. Soc.* **1981**, *103*, 4947–4948. (c) Siedle, A. R.; Newmark, R. A.; Pignolet, L. H. *J. Am. Chem. Soc.* **1982**, *104*, 6584–6590. (d) Song, R.-F.; Zhang, C.-Z.; Li, F.; Jin, S.-C.; Jin, Z.-S. *Chem. Res. Chin. Univ.* **1992**, *8*, 399. (e) Provencher, R.; Aye, K. T.; Drouin, M.; Gagnon, J.; Boudreault, N.; Harvey, P. D. *Inorg. Chem.* **1994**, *33*, 3689–3699. (f) Domhöver, B.; Hamers, H.; Kläui, W.; Pfeffer, M. *J. Organomet. Chem.* **1996**, *522*, 197–206. (g) Zuideveld, M. A.; Swennenhuis, B. H. G.; Boele, M. D. K.; Guari, Y.; van Strijdonck, G. P. F.; Reek, J. N. H.; Kamer, P. C. J.; Goubitz, K.; Fraanje, J.; Lutz, M.; Spek, A. L.; van Leeuwen, P. W. N. M. *J. Chem. Soc., Dalton Trans.* **2002**, 2308–2317. (h) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 6043–6046. (i) Goshe, A. J.; Steele, I. M.; Ceccarelli, C.; Rheingold, A. L.; Bosnich, B. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4823–4829. (j) van der Vlugt, J. I.; Sablong, R.; Mills, A. M.; Kooijman, H.; Spek, A. L.; Meetsma, A.; Vogt, D. *Dalton Trans.* **2003**, 4690–4699. (k) Grushin, V. V.; Marshall, W. J. *J. Am. Chem. Soc.* **2006**, *128*, 12644–12645.

(25) Mulliken, R. S *J. Chem. Phys.* **1955**, *23*, 1833–1840.

(26) Bader, R. F. W. *Atoms in Molecules: A Quantum Theory*; Clarendon Press: Oxford, 1990.

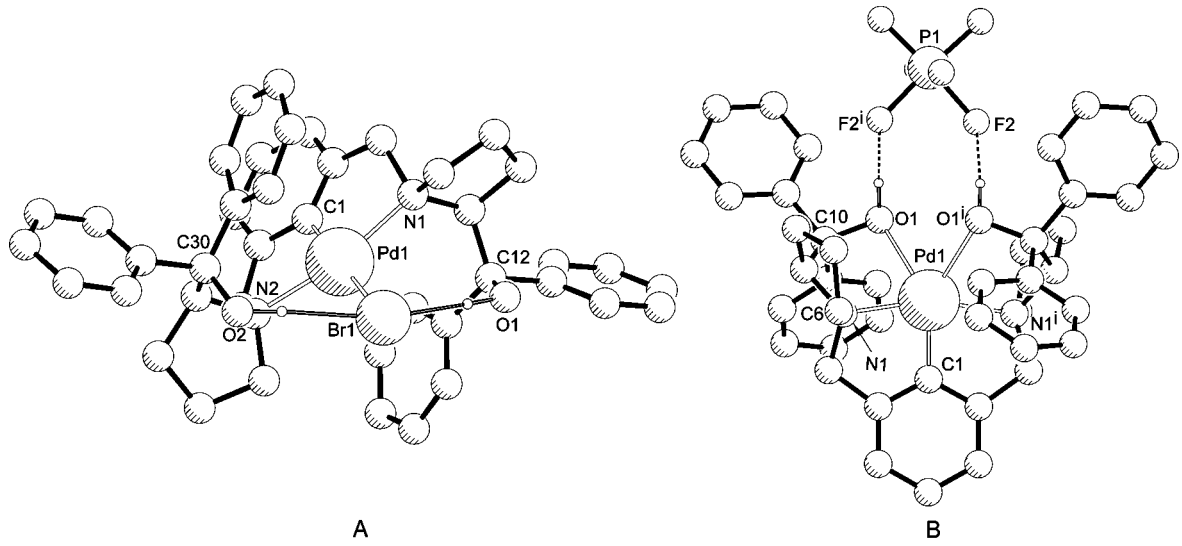


Figure 5. Optimized geometries of **3** (A) and [**4**]PF_6 (B) calculated at the B3LYP/LANL2-DZ level with depicted hydrogen bonds. Remaining hydrogen atoms are omitted for clarity.

Table 4. Values of Mulliken Population Overlap (MPO) and Properties of the BCPs and r_P[a] in Complexes [4]PF_6, [Pd(NCN)(OH_2)]BF_4, and 3

complex	bond	MPO (e^-)	$\rho(\mathbf{r}_P)$ (e Å^{-3})	$\nabla^2\rho(\mathbf{r}_P)$ (e Å^{-5})	λ_1 (e Å^{-5})	λ_2 (e Å^{-5})	λ_3 (e Å^{-5})	Pd−BCP (Å)	BCP−X (Å)
[**4**]PF_6	Pd−O1	0.065	0.233	3.855	−0.916	−0.723	5.494	1.332	1.204
	Pd−O2	0.062	0.216	3.711	−0.892	−0.699	5.277	1.341	1.211
	Pd−N1	0.145	0.554	7.181	−2.048	−1.952	11.180	1.103	1.072
	Pd−N2	0.145	0.561	7.205	−2.048	−1.976	11.229	1.102	1.071
	Pd−C1	0.458	0.999	4.337	−4.602	−4.289	13.205	1.051	0.883
[Pd(NCN)	Pd−O	0.059	0.318	6.723	−1.060	−0.867	8.651	1.174	1.120
(OH_2)]BF_4	Pd−N1	0.169	0.622	7.398	−2.386	−2.289	12.048	1.087	1.046
	Pd−N2	0.131	0.547	7.229	−2.000	−1.976	11.205	1.104	1.075
	Pd−C1	0.410	0.993	3.807	−4.647	−4.361	12.819	1.057	0.882
3	Pd−Br	0.212	0.351	3.928	−0.867	−0.747	5.518	1.124	1.375
	Pd−O1	0.013							
	Pd−O2	0.013							
	Pd−N1	0.143	0.527	6.747	−1.952	−1.904	10.578	1.116	1.082
	Pd−N2	0.143	0.527	6.771	−1.952	−1.904	10.602	1.116	1.082
	Pd−C1	0.381	0.986	4.819	−4.458	−4.193	13.494	1.048	0.897

[a] $\rho(\mathbf{r}_P)$ = charge density distribution, where **r** is a vector in crystal space; $\nabla^2\rho(\mathbf{r}_P)$ = Laplacian at the BCP, which is defined as the sum of nonzero eigenvalues λ_1, λ_2, and λ_3 of curvature (Hessian) matrix.

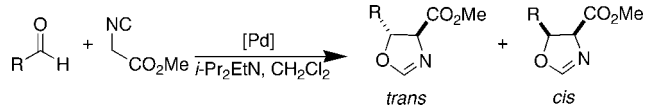
these results, we conclude that coordinative bonds exist between Pd and the two hydroxyl oxygen donor atoms in both [**4**]PF_6 and [**4**]BF_4. The long Pd−O distances of around 2.7 Å indicate that these interactions are much weaker than the Pd−OH_2 bond in [Pd(NCN)(OH_2)]BF_4.

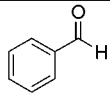
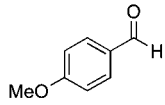
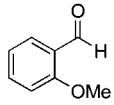
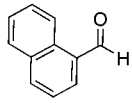
NMR Studies. The ^{1}H and ^{13}C{^{1}H} NMR spectra obtained for complexes **3**, [**4**]PF_6, and [**4**]BF_4 displayed one set of signals for each compound and indicated the presence of a single diastereoisomer in solution, as was found for these complexes in the solid state. The shifts of hydrogen and carbon atoms are rather similar for all three compounds, which points to a similar arrangement of the NCN-pincer ligand around palladium. The main difference in the coordination geometry around palladium is, however, reflected in the large shift differences in the ^{13}C{^{1}H} NMR spectra of **3** and complexes **4** observed for the C_{ipso} resonance (see Experimental Section) and the C−OH resonance. The higher C_{ipso} value in **3** as compared to **4** results from the anionic *trans* ligand in **3** resulting in a neutral complex. The upfield shift of the C−OH carbon in **4** compared to **3** reflects a combination of the deshielding effect of palladium coordination of the hydroxyl oxygen atoms and their hydrogen-bonding interaction with the counteranion. In **3**, the hydroxyl groups are further from palladium and are only involved in hydrogen bonding with the bromide ligand.

For the cationic complexes **4** and structurally related ester prolinate and prolinol complexes,[4b,c] the coordination of the oxygen donor(s) of the ligand to the metal is crucial for the formation of a single diastereoisomer. In the case of **3**, the presence of the bulky diphenylhydroxymethyl moieties in these complexes apparently prevents the formation of the other two possible diastereoisomers, since in NCN−Pd−Br complexes with smaller functional groups on the pyrrolidinyl moieties (CO_2Me[4b] or CO_2Bn[4b] and CH_2OH[4c]) the presence of three diastereoisomers was observed in their ^{1}H and ^{13}C{^{1}H} NMR spectra.

Catalysis. The results of the aldol reaction of various aromatic aldehydes with methyl α-isocyanoacetate (MIC) catalyzed by [**4**]PF_6 and [**4**]BF_4 are summarized in Table 5. In general, the oxazoline products were formed in higher yields in the reaction catalyzed by [**4**]PF_6. A relatively high regioselectivity toward the *cis* product was observed for both complexes. For instance, in the case of *o*-methoxy benzaldehyde (entries 5 and 6) the *cis*-oxazoline was formed as the major product in 70% yield. The naphthaldehyde derivative (entry 7 and 8) is an exception to this observation. For all aldehydes tested, a constant stereoselectivity around 40% ee was observed for the *cis*-oxazoline and 20% ee for the *trans*-oxazoline. Interestingly, the stereoselectivity for the *trans* products remained rather constant during

Table 5. Aldol Reaction of Methyl α-Isocyanoacetate to Aldehydes Catalyzed by [4]PF_6 and [4]BF_4[a]



Entry	Aldehyde	Complex	Conv. (%)[b]	*Trans*/*Cis* [c]	*Trans* (ee%) (4*S*, 5*R*)[d]	*Cis* (ee%) (4*R*, 5*R*)[d]
1		[**4**]PF_6	92	56/44	17	42
2		[**4**]BF_4	80	63/37	17	40
3		[**4**]PF_6	83	49/51	21	41
4		[**4**]BF_4	73	52/48	22	37
5		[**4**]PF_6	93	30/70	19	41
6		[**4**]BF_4	92	30/70	18	42
7		[**4**]PF_6	69	71/29	26	35
8		[**4**]BF_4	55	74/26	20	34

[a] Reaction conditions: aldehyde (1.6 mmol), $CNCH_2CO_2Me$ (1.6 mmol), catalyst (0.016 mmol, 1 mol %), $^iPr_2EtN$ (0.16 mmol), CH_2Cl_2 (5 mL), 20 °C, 24 h. [b]Determined by ^1H NMR analysis, each product was once isolated by bulb-to-bulb destillation to confirm the result obtained by ^1H NMR. [c]Determined by ^1H NMR analyses. [d]Determined by chiral HPLC (Daicel CHIRALCEL OD, hexane:*i*PrOH = 95:5); configuration was determined by ^1H NMR analysis using Eu(dcm)$_3$ as chiral shift reagent.[38]

the course of the reaction, while the stereoselectivity for the *cis* product increased in time with concomitant decrease of the *trans*/*cis* ratio (Table S1 shows results after 5 h). The slow addition of *o*-methoxy benzaldehyde to a reaction mixture with [**4**]PF_6 indeed led to a higher regioselectivity toward the *cis* product (76%) with 40% ee for the *cis*-oxazoline and a lower 11% ee for the *trans*-oxazoline.

The substitution position of the functional group in the substrate has a substantial influence on the *trans*/*cis* ratio. The most enhanced regioselectivity for the *cis* product was observed for the *ortho*-substituted benzaldehyde, while the *para*-substituted benzaldehyde and benzaldehyde itself gave similar results. The results obtained with *ortho*-methoxy and naphthaldehyde showed that the methoxy group is more *ortho*-hindering than the planar phenyl ring and results in a higher *cis* regioselectivity.

Our observations, i.e., increased regioselectivity as well as stereoselectivity for the *cis*-oxazoline products, are in contrast to the regioselectivity observed for the same reactions catalyzed by other achiral as well as chiral NCN- and PCP-pincer metal complexes.[5,8b,c,9,10d,13,19b,27] These complexes typically yield the *trans* product in more than 70% yield. Stereochemical models of the proposed intermediates with catalysts [**4**]PF_6 and [**4**]BF_4 show that the aldehyde can attack the enolate either from the open side of palladium (to yield the *cis* product from the *anti*-aldol adduct) or from the phenyl-Pd side of the catalyst (to yield the *trans* product from *syn*-aldol adduct) as depicted in Figure 6 (for stereochemical models for all four products, see Supporting Information, Figure S2). On the basis of the rather constant ee's (40% ee for *cis*- and 20% for *trans*-oxazolines) for all products, it seems that the bulky diphenylhydroxymethyl

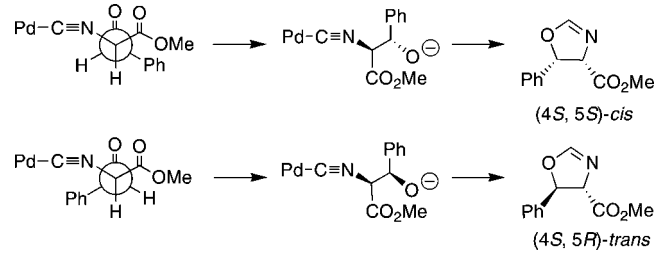


Figure 6. Stereochemical models for *anti*- and *syn*-aldol intermediates for the major *cis*- and *trans*-oxazolines.

pyrrolidine groups in complexes [**4**]PF_6 and [**4**]BF_4 form a rather deep pocket around palladium and especially in the case of an *ortho*-substituted aldehyde sterically block the phenyl-Pd side of the catalyst for the aldehyde attack on the Pd-enolate. This results in higher regio- and stereoselectivity toward the *cis*-oxazoline product.

Besides the steric effect of the bulky ligand also the presence of two potentially hydrogen bond donating hydroxyl groups can play an important role in the stereoselective outcome of the reaction. The hydroxyl groups can hydrogen bond with the palladium-bound enolate, which could induce a preferential arrangement for attack of the aldehyde. Such a secondary interaction was crucial for obtaining high stereoselectivities in aldol reaction 1 with ferrocenylphosphine ligands bearing pendant amines.[28,29] Eventually, the attack of an aldehyde can be directed by hydrogen bonds with hydroxyl groups of the ligand as recently shown by Rawal et al. and Sigman et al., who reported high enantioselectivities in the hetero-Diels–Alder reaction between aldehydes and dienes by hydrogen bond-promoted catalysis.[30] Since poor stereoselectivity was observed with pivaldehyde (not shown), $\pi-\pi$ interactions of the aromatic aldehyde ring with the phenyl rings of the catalysts might as well be involved in guiding the reactions discussed in this paper.

(27) (a) Nesper, R.; Pregosin, P. S.; Püntener, K.; Wörle, M. *Helv. Chim. Acta* **1993**, *76*, 2239–2249. (b) Stark, M. A.; Richards, C. J. *Tetrahedron Lett.* **1997**, *38*, 5881–5884. (c) Motoyama, Y.; Shimozono, K.; Aoki, K.; Nishiyama, H. *Organometallics* **2002**, *21*, 1684–1696.

Conclusions

The presence of bulky diphenylhydroxymethyl moieties in the new, chiral NCN-pincer ligand **2** results in the formation of single diastereoisomers of the corresponding neutral and cationic palladium complexes. X-ray crystal structure determination of the cationic complexes revealed an unusual κ^5-*N*,*C*,*N*,*O*,*O* coordination around the metal with very long Pd−O distances (around 2.7 Å). Although these distances are beyond what is generally considered as a Pd−O bond, theoretical calculations indicate that the Pd−O interactions are best described as a weak coordinative bond. Besides providing additional evidence for the assignment of a bonding Pd−O interaction, the theoretical calculations represent one of the first applications of AIM theory to (organometallic) Pd complexes.[31] The bulky diphenylhydroxymethyl moieties in the ligand form a cavity around palladium and sterically block the phenyl-Pd side of the complex for *ortho*-substituted substrate attack, as indicated by catalytic experiments; that is, in the aldol condensation catalyzed by these complexes an increased regio- and stereoselectivity for the *cis*-oxazoline products was observed.

Aromatic β-hydroxy-α-amino ester functionalities with the same configuration as the major *cis*-oxazoline product obtained with [**4**]PF_6 and [**4**]BF_4 are of relevance for natural product synthesis. Structural elements derived from these functionalities are, for example, found in callipeltin A, a natural compound isolated from the marine sponge *Callipelta*, which exhibits antifungal and anti-HIV activity.[32] Overall, the structural aspects and the initial catalytic results of the cationic palladium complexes reported here are promising for further investigation of their catalytic scope.

Experimental Section

General Methods. Solvents were dried and freshly distilled prior to use. All aldehydes used for catalytic reactions were distilled prior to use. Compound **1**,[4b] and $[Pd_2(dba)_3 \cdot CHCl_3]$[33] were prepared according to previously published procedures. ^{1}H (300.1 MHz) and $^{13}C\{^1H\}$ (75.5 MHz) NMR spectra were recorded on a Varian Inova 300 spectrometer at ambient temperatures. Optical rotations ($[\alpha]_D^{21}$) were measured with a Perkin polarimeter 241. Elemental microanalyses were carried out by Mikroanalytisches Laboratorium Dornis und Kolbe, Mulheim a.d. Ruhr, Germany. Infrared spectra were recorded on a Perkin-Elmer Spectrum One FT-IR instrument. Mass spectrometry was carried out on a Voyager, Biosystems, MALDI-Tof. The microwave used was an Ethos Sel, microwave solvent extraction labstation. Gas chromatography analyses were performed with a Perkin-Elmer Autosystem XL GC using a 30 m, PE-17 capillary column with a FID detector. HPLC analyses were performed with a Perkin-Elmer Series 200 machine, equipped with a diode array II detector and LC pump using a Daicel Chiracel OD column.

Computational Details. The geometries of **3** and [**4**]PF_6 were optimized at the B3LYP/LANL2-DZ level[34] using GAMESS-UK.[35] Basis sets were obtained from the Extensible Computational Chemistry Environment Basis Set Database, Version 02/25/04, as developed and distributed by the Molecular Science Laboratory, P.O. Box 999, Richland, WA 99352, and funded by the U.S. Department of Energy. The Bader AIM analysis was performed using the AIMPAC program.[36]

2,6-Bis{[(*S*)-2-(diphenylhydroxymethyl)-1-pyrrolidinyl]methyl}-1-bromobenzene (2). A THF solution of phenyl magnesium bromide (0.789 M, 47.8 mmol, 81 mL) was added via canula into a solution of **1** (7.9 mmol, 3.5 g) dissolved in dry THF (60 mL). The resulting yellow solution was stirred at ambient temperature followed by TLC analysis (SiO_2, hexanes/ethyl acetate = 2:1 (v/v)). When no starting compound **1** was present (after 3 h), the reaction mixture was quenched with NH_4Cl (40 mL). The organic layer was extracted with THF (2 × 30 mL), washed with brine (30 mL), dried with $MgSO_4$, filtrated, and evaporated *in vacuo*. Product was purified via precipitation from a CH_2Cl_2/pentane mixture and obtained as a white solid in 92% yield (5.01 g). Crystals suitable for X-ray crystal structure determination were obtained by slow vapor diffusion of pentane into a CH_2Cl_2 solution of **2**. Anal. Calcd for $C_{42}H_{43}BrN_2O_4$: C 73.35, H 6.30, N 4.07. Found: C 73.26, H 6.40, N 4.02. MALDI-tof *m*/*z*: 687.22 ($(M - Br)^+$, calc 687.26). $[\alpha]_D^{21}$ +11.4 (*c* 0.5, $CHCl_3$). IR ν (cm^{-1}): 3332 (br), 3058 (m), 3018 (m), 2967 (m), 2937 (m), 2866 (m), 2815 (m), 1596 (m), 1491 (m), 1449 (s), 1416 (m), 1365 (m), 1354 (m), 1312.1 (m), 1295 (m), 1186 (m), 1163 (m), 1138 (w), 1110(m), 1085 (m), 1060 (m), 1032 (m), 1022 (m), 996 (m), 981 (m), 893 (w), 865 (w), 764 (m), 746 (s), 706 (s), 696 (s), 655 (w). ^{1}H NMR ($CDCl_3$): δ 1.64–1.77 (m, 6H; CH_2CH_2N and CH*H*C*H ring), 1.89–2.02 (m, 2H, C*H*HC*H ring), 2.39 (q, 2H, ^2J(H,H) = 8.7 Hz, NC*H* ring), 2.84–2.89 (m, 2H, NCH*H* ring), 3.15 (d, AB, 2H, ^2J(H,H) =13.5 Hz, ArCH_2N), 3.37 (d, AB, 2H, ^2J(H,H) =13.5 Hz, ArCH_2N), 4.01 (dd, 2H,^3J(H,H) =3.9 and 5.1 Hz, C*H), 7.00–7.08 (t and d, 3H of ArBr), 7.14–7.31 (m, 12H, *m* and *p* of Ph), 7.57 (d, 4H, ^3J(H,H) = 8.1 Hz, *o* of Ph), 7.65 (d, 4H, ^3J(H,H) = 8.1 Hz, *o* of Ph) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 24.20 (*C*H_2CH_2N), 29.78 (*C*H_2C*H ring), 55.57 (N*C*H_2 ring), 60.60 (Ar*C*H_2N), 71.43 (*C**), 77.88 (*C*-OH), 125.60 (C_{ortho} of Ph), 126.45 (C_{para} of Ph), 126.69 (*C*Br), 128.14 (C_{meta} of Ph), 128.80 (C_{ipso} of Ph), 139.15 (Ar*C*CH$_2$N), 146.81 (C_{para} to CBr), 147.87 (C_{meta} to CBr) ppm.

2,6-Bis[[(*S*)-2-(diphenylhydroxymethyl)-1-pyrrolidinyl]methyl]-phenyl palladium(II) Bromide (3). Solid $Pd_2(dba)_3 \cdot CHCl_3$ (0.11 mmol, 113 mg) was added to a solution of **2** (0.15 mmol, 100 mg) in a degassed benzene/acetone mixture (1:1, 10 mL). The resulting mixture was stirred at 60 °C for 16 h. One drop of Et_3N was added to facilitate the removal of Pd(0), and the reaction mixture was filtered through Celite. Subsequently, the solvent was evaporated

(28) (a) Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 6405–6406. (b) Pastor, S. D.; Togni, A. *J. Am. Chem. Soc.* **1989**, *111*, 2333–2334. (c) Togni, A.; Häusel, R. *Synlett* **1990**, 633–635. (d) Togni, A.; Pastor, S. D.; Rihs, G. *J. Organomet. Chem.* **1990**, *381*, C21–25. (e) Togni, A.; Pastor, S. D. *J. Org. Chem.* **1990**, *55*, 1649–1664. (f) Pastor, S. D.; Togni, A. *Helv. Chim. Acta* **1991**, *74*, 905–933. (g) Hayashi, T.; Sawamura, M.; Ito, Y. *Tetrahedron* **1992**, *48*, 1999–2012. (h) Zhou, X.-T.; Lin, Y.-R.; Dai, L.-X. *Tetrahedron:Asymmetry* **1999**, *10*, 855–862.

(29) Sawamura, M.; Hamashima, H.; Ito, Y. *J. Org. Chem.* **1990**, *55*, 5935–5936.

(30) (a) Huang, Y.; Thadani, A. N.; Rawal, V. H. *Nature* **2003**, *424*, 146. (b) Thadani, A. N.; Stankovic, A. R.; Rawal, V. H. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5846–5850. (c) Unni, A. K.; Takenaka, N.; Yamamoto, H.; Rawal, V. H. *J. Am. Chem. Soc.* **2005**, *127*, 1336–1337. (d) Rajaram, S.; Sigman, M. S. *Org. Lett.* **2005**, *7*, 5473–5475.

(31) Rimola, A.; Sodupe, M.; Ros, J.; Pons, J. *Eur. J. Inorg. Chem.* **2006**, *2*, 447–454.

(32) Zampella, A.; D'Orsi, R.; Sepe, V.; Casapullo, A.; Monti, M. C.; D'Auria, M. V. *Org. Lett.* **2005**, *7*, 3585–3588.

(33) Kanth, J. V. B.; Periasamy, M. *Tetrahedron* **1993**, *49*, 5127–5132.

(34) Komiya, S. *Synthesis of Organometallic Compounds*; Wiley: Chichester, U.K., 1997.

(35) (a) Dunning, T. H., Jr.; Hay, P. J. In *Modern Theoretical Chemistry*, Vol. 3; Schaefer, H. F., III, Ed.; Plenum Press: New York, 1977. (b) Wadt, W. R.; Hay, P. J. *J. Chem. Phys.* **1985**, *82*, 284–298. (c) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299–310.

(36) Guest, M. F.; Bush, L. J.; van Dam, H. J.; Sherwood, P.; Thomas, J. M. H.; van Lenthe, J. H.; Havenith, R. W. A.; Kendrick, J. *J. Mol. Phys.* **2005**, *103*, 719–747.

(37) (a) Bader, R. F. W., http://www.chemistry.mcmaster.ca/aimpac. (b) Biegler-König, F. W.; Nguyen-Sang, T. T.; Tal, Y.; Bader, R. F. W.; Duke, A. J. *J. Phys. B: At. Mol. Phys.* **1981**, *14*, 2739−2751. (c) Biegler-König, F. W.; Bader, R. F. W.; Tang, T.-H. *J. Comput. Chem.* **1981**, *13*, 317−328.

(38) (a) Tris(*d*,*d*-dicampholylmethanato)europium(III). McCreary, M. D.; Lewis, D. W.; Wernick, D. L.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 1038–1054. (b) Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 6405–6406.

in vacuo, and the crude mixture was purified via column chromatography (SiO_2, hexanes/ethylacetate, 4:1 (v/v)). The desired product was obtained as a white solid in 44% yield (51 mg). Crystals suitable for X-ray crystal structure determination were obtained by slow diffusion of Et_2O into an acetone solution of **3**. Anal. Calcd for $C_{42}H_{43}BrPdN_2O_4$: C 63.52, H 5.46, N 3.53. Found: C 63.41, H 5.54, N 3.39. MALDI-tof *m*/*z*: 713.22 ($(M - Br)^+$, calc 713.24). $[\alpha]_D^{21}$ –67.5 (*c* 1.0, CH_2Cl_2). IR ν (cm^{-1}): 3357 (s), 3343 (s), 3053 (w), 3013 (w), 2956 (m), 2927 (m), 2506 (w), 1593 (w), 1573 (w), 1448 (s), 1431 (m), 1331 (m), 1305 (w), 1259 (w), 1209 (w), 1181 (w), 1150 (m), 1092 (w), 1070 (m), 1032 (m), 999 (m), 956 (w), 882 (m), 824 (w), 775 (m), 740 (s), 704 (s), 688 (m), 658 (w). ^{1}H NMR (acetone-d_6): δ 1.64–1.77 (m, 6H, CH_2CH$_2$N and CH*H*C*H ring), 1.83–1.89 (m, 2H, C*H*HC*H ring), 2.66 (m, 2H, NC*H*H ring), 3.06 (d, AX, 2H, ^2J(H,H) =13.2 Hz, ArCH_2N), 3.81 (d, AX, 2H, ^2J(H,H) =13.2 Hz, ArCH_2N), 3.77 (m, 2H, NCH*H* ring), 4.60 (m, 2H, C*H), 6.77 (d, 4H, ^3J(H,H) =7.5 Hz, *o* of Ph), 6.96–2.14 (m, 15H; *m, p* of Ph and 3H of ArPdBr), 7.45 (d, 4H, ^3J(H,H) =7.8 Hz, *o* of Ph) ppm. ^{13}C{^{1}H} NMR (acetone-d_6): δ 23.47 (*C*H$_2$CH$_2$N), 25.59 (*C*H$_2$C*H ring), 63.41 (N*C*H$_2$ ring), 73.29 (Ar*C*H$_2$N), 76.30 (*C**), 80.73 (*C*-OH), 120.04 and 127.06 (C_{meta} of Ph), 123.58 and 124.86 (C_{ortho} of Ph), 125.86 (C_{para} of Ph), 143.65 (C_{ortho} of Ar), 147.09 and 148.08 (C_{ipso} of Ph), 158.64 (*C*Pd) ppm.

Reaction Performed in the Microwave. Compound **2** (0.30 mmol, 0.2 g) was dissolved in 30 mL of an acetone/benzene (1:1) mixture, and $Pd_2(dba)_3 \cdot CHCl_3$ (0.59 mmol, 0.6 g) was added to the reaction mixture. The reaction was performed in the microwave at 95 °C for 10 min at 500 W. The reaction mixture was filtered through Celite and evaporated *in vacuo*. Purification of the crude mixture was performed via flash chromatography (on a silica cartridge, 40 × 75 nm) with hexanes/acetylacetate (4:1, (v/v)) as eluent, and the desired product **3** was obtained in 79% yield (0.18 g).

2,6-Bis[[(*S*)-2-(diphenylhydroxymethyl)-1-pyrrolidinyl]methyl]-phenyl palladium(II) Hexafluorophosphate ([4]PF$_6$). An excess of NH_4PF_6 (7.6 mmol, 1.23 g) dissolved in water (13 mL) was added to a solution of **3** (0.18 mmol, 0.14 g) in mixture of methanol and CH_2Cl_2 (14 mL + 5 mL), yielding a turbid solution. The reaction mixture was stirred for 16 h at ambient temperature. The addition of water (13 mL) led to the precipitation of the product [**4**]PF$_6$. The precipitate was filtered off, redissolved in acetone, and precipitated with Et_2O. The compound was isolated as a white solid in 61% yield (95 mg). Crystals suitable for X-ray difraction were obtained by slow diffusion of Et_2O into an acetone solution of [**4**]PF$_6$. Anal. Calcd for $C_{42}H_{43}PdN_2O_4PF_6$: C 58.71, H 5.04, N 3.26. Found: C 58.74, H 4.88, N 3.34. MALDI-tof *m*/*z*: 713.09 ($(M - PF_6)^+$, calc 713.24). $[\alpha]_D^{21}$ +117.8 (*c* 1.0, CH_2Cl_2). IR ν (cm^{-1}): 3544 (s), 3347 (s), 3058 (s), 2963 (s), 2921 (s), 2861 (s), 1598 (w), 1578 (w), 1492 (m), 1446 (m), 1429 (m), 1348 (w), 1305 (w), 1259 (m), 1209 (w), 1161 (w), 1095 (m), 1067 (m), 1027 (m), 833 (s), 769 (w), 741 (m), 696 (m). ^{1}H NMR (acetone-d_6): δ 2.00–2.08 (m, 4H, CH_2CH$_2$N), 2.20–2.37 (m, 4H, C*H*HC*H ring), 3.02 (m, 2H, NC*H*H ring), 3.82 (d, AB, 2H, ^2J(H,H) =14.7 Hz, ArCH_2N), 4.02 (d, AB, 2H, ^2J(H,H) =14.7 Hz, ArCH_2N), 3.88–3.92 (m, 2H, NCH*H* ring), 4.63 (t, 2H, ^3J(H,H) =8.4 Hz, C*H), 6.56 (d, 2H, ^3J(H,H) =7.5 Hz, ArPdBr), 6.80 (t, 1H, ^3J(H,H) =7.2 Hz, ArPdBr), 7.20–7.29 (m, 4H, *p* of Ph), 7.39 (m, 8H, *m* of Ph), 7.69 (d, 4H, ^3J(H,H) = 7.8 Hz, *o* of Ph), 8.20 (d, 4H, ^3J(H,H) = 7.5 Hz, *o* of Ph) ppm. ^{13}C{^{1}H} NMR (acetone-d_6): δ 23.62 (*C*H$_2$CH$_2$N), 25.59 (*C*H$_2$C*H ring), 65.00 (N*C*H$_2$ ring), 71.06 (Ar*C*H$_2$N), 73.75 (*C**), 82.67 (*C*-OH), 119.80 (C_{meta} of Ar), 124.78 (C_{ipso} of Ph), 125.65 and 126.32 (C_{ortho} of Ph), 127.50 and 127.70 (C_{para} of Ph), 128.54 and 128.77 (C_{meta} of Ph), 144.32 (*C*Pd), 145.13 (Ar*C*CH$_2$N), 146.49 (C_{ipso} of Ph) ppm.

2,6-Bis[[(*S*)-2-(diphenylhydroxymethyl)-1-pyrrolidinyl]methyl]-phenyl palladium(II) Tetrafluoroborate ([4]BF$_4$). To a solution of **3** (0.16 mmol, 130 mg) in 30 mL of an acetone/water (10:1) mixture was added solid $AgBF_4$ (0.16 mmol, 31.9 mg). The reaction mixture was stirred for 90 min (protected from light). Filtration of the resulting suspension through Celite yielded a colorless filtrate. The solvent was removed *in vacuo* to leave the desired compound as a white solid in 75% yield (100 mg). Crystals suitable for X-ray crystal structure determination were obtained by slow diffusion of Et_2O into a CH_2Cl_2 solution of [**4**]BF$_4$. Anal. Calcd for $C_{42}H_{43}PdN_2O_4BF_4$: C 62.98, H 5.41, N 3.50. Found: C 62.84, H 5.30, N 3.41. MALDI-tof *m*/*z*: 713.23 ($(M - BF_4)^+$, calc 713.24). $[\alpha]_D^{21}$ +145.9 (*c* 1.0, CH_2Cl_2). IR ν (cm^{-1}): 3676 (m), 3461 (s), 2987 (s), 2901 (s), 1601 (w), 1575 (w), 1491 (m), 1429 (m), 1406 (w), 1348 (w), 1320 (w), 1285 (w), 1249 (w), 1194 (w), 1163 (m), 1087 (s), 1065 (s), 1056 (s), 1039 (s), 993 (s), 893 (m), 873 (m), 840 (w), 766 (m), 753 (s), 698 (s). ^{1}H NMR (acetone-d_6): δ 2.00–2.10 (m, 4H, CH_2CH$_2$N), 2.20–2.37 (m, 4H, C*H*HC*H ring), 3.00 (m, 2H, NC*H*H ring), 3.81 (d, AB, 2H, ^2J(H,H) = 14.7 Hz, ArCH_2N), 4.02 (d, AB, 2H, ^2J(H,H) = 14.7 Hz, ArCH_2N), 3.88–3.92 (m, 2H, NCH*H* ring), 4.62 (t, 2H, ^3J(H,H) = 8.4 Hz, C*H), 6.56 (d, 2H, ^3J(H,H) = 7.2 Hz, ArPdBr), 6.80 (t, 1H, ^3J(H,H) = 7.8 Hz, ArPdBr), 7.19–7.29 (m, 4H, *p* of Ph), 7.36–7.41 (m, 8H, *m* of Ph), 7.69 (d, 4H, ^3J(H,H) = 7.8 Hz, *o* of Ph), 8.20 (d, 4H, ^3J(H,H) = 7.5 Hz, *o* of Ph) ppm. ^{13}C{^{1}H} NMR (acetone-d_6): δ 25.03 (*C*H$_2$CH$_2$N), 25.59 (*C*H$_2$C*H ring), 66.50 (N*C*H$_2$ ring), 72.42 (Ar*C*H$_2$N), 75.60 (*C**), 84.15 (*C*-OH), 121.07 (C_{meta} of Ar), 126.11 (C_{ipso} of Ph), 127.09 and 127.73 (C_{ortho} of Ph), 128.84 and 129.00 (C_{para} of Ph), 129.90 and 130.14 (C_{meta} of Ph), 146.30 (*C*Pd), 146.62 (Ar*C*CH$_2$N), 147.93 (C_{ipso} of Ph) ppm.

General Procedure for Aldol Condensation of Methyl α-Isocyanoacetate with Aldehydes. To a solution of the palladium complex (0.016 mmol, 1 mol %) in CH_2Cl_2 (5 mL) were sequentially added methyl α-isocyanoacetate (145 μL, 1.6 mmol), aldehyde (1.6 mmol), and diisopropylethylamine (28 μl, 0.16 mmol). The reaction mixture was stirred at ambient temperature for 24 h. Subsequently, the solvent was evaporated *in vacuo*, and ^{1}H NMR samples and HPLC samples were prepared. The yield and ratio of *cis* and *trans* isomers was determined by ^{1}H NMR and the enantiomeric excess by HPLC using chiral column Daicel CHIRACEL OD, UV detector 210 nm, hexane/*i*-PrOH = 95:5. Selected products (each of the products at least once) were purified by bulb-to-bulb distillation to give the pure *trans*/*cis* mixture to confirm the result obtained by ^{1}H NMR. The configurations of the *trans* and *cis* product were determined after separation of the *trans*/*cis* mixture (column chromatography, SiO_2, ethylacetate/hexanes = 1:2 (v/v)) by ^{1}H NMR analysis using Eu(dcm)$_3$ as the chiral shift reagent.[38]

X-ray Crystal Structure Determination of *2*. $C_{42}H_{43}BrN_2O_2$, fw = 687.69, colorless block, 0.24 × 0.15 × 0.09 mm^3, monoclinic, $P2_1$ (no. 4), a = 8.3438(1) Å, b = 36.4734(4) Å, c = 11.8353(1) Å, β = 105.1480(4)°, V = 3476.65(6) Å^3, Z = 4, ρ = 1.314 g/cm^3; 33 653 reflections up to a resolution of $(\sin \theta/\lambda)_{max}$ = 0.56 Å^{-1} were measured on a Nonius KappaCCD diffractometer with rotating anode and graphite monochromator (λ = 0.71073 Å) at a temperature of 150(2) K. An absorption correction based on multiple measured reflections was applied (μ = 1.221 mm^{-1}, 0.74–0.90 correction range); 10 274 reflections were unique (R_{int} = 0.1030). The structure was solved with direct methods[39] and refined with SHELXL-97[40] on F^2 of all reflections. Non-hydrogen atoms were refined freely with anisotropic displacement parameters. Hydrogen atoms were introduced in calculated positions and refined as rigid groups. Two of the five-membered rings showed puckering disorder, and one phenyl ring was rotationally disordered; 910 parameters were refined with 149 restraints. R1/wR2 [$I > 2\sigma(I)$]: 0.0434/0.0872. R1/wR2 [all reflns]: 0.0593/0.0955. S = 1.013. Flack *x*

(39) Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G. L.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr.* **1999**, *32*, 115–119.

(40) Sheldrick, G. M. *SHELXL-97. Program for Crystal Structure Refinement*; University of Göttingen: Germany, 1997.

parameter[42] –0.012(6). Residual electron density between −0.26 and 0.39 e/Å^3. Geometry calculations, drawings, and checking for higher symmetry were performed with the PLATON[41] package.

X-ray Crystal Structure Determination of 3. $C_{42}H_{43}Br_{0.67}Cl_{0.33}N_2O_2Pd \cdot 0.35C_4H_{10}O \cdot C_3H_6O$, fw = 863.44, yellow needle, 0.42 × 0.18 × 0.06 mm^3, orthorhombic, $P2_12_12$ (no. 18), a = 17.0116(1) Å, b = 23.8755(2) Å, c = 9.9206(1) Å, V = 4029.36(6) Å^3, Z = 4, ρ = 1.423 g/cm^3; 78 778 reflections up to a resolution of $(\sin \theta/\lambda)_{max} = 0.65$ Å^{-1} were measured on a Nonius KappaCCD diffractometer with rotating anode and graphite monochromator (λ = 0.71073 Å) at a temperature of 150(2) K. An absorption correction based on multiple measured reflections was applied (μ = 1.191 mm^{-1}, 0.80–0.93 correction range); 9226 reflections were unique (R_{int} = 0.0506). The structure was solved with direct methods[39] and refined with SHELXL-97[40] on F^2 of all reflections. Non-hydrogen atoms were refined freely with anisotropic displacement parameters. All hydrogen atoms were located in the difference Fourier map. Hydroxy H atoms were kept fixed on their located positions, and the other H atoms were refined as rigid groups. The position of the coordinated halogen was occupied by 2/3 Br and 1/3 Cl. Both atom types were constrained to the same position and displacement parameters. The diethyl ether solvent molecule is located on a 2-fold axis and only partially occupied; 495 parameters were refined with 6 restraints. R1/wR2 [$I > 2\sigma(I)$]: 0.0295/0.0750. R1/wR2 [all reflns]: 0.0341/0.0772. S = 1.069. Flack x parameter[42] –0.028(8). Residual electron density between −0.58 and 1.31 e/Å^3. Geometry calculations, drawings, and checking for higher symmetry were performed with the PLATON[41] package.

X-ray Crystal Structure Determination of [4]PF$_6$. $C_{42}H_{43}N_2O_2Pd \cdot PF_6$, fw = 859.15, yellow block, 0.51 × 0.51 × 0.21 mm^3, tetragonal, $P4_12_12$ (no. 92), $a = b$ = 10.4019(1) Å, c = 34.9279(3) Å, V = 3779.18(6) Å^3, Z = 4, ρ = 1.510 g/cm^3; 20 886 reflections up to a resolution of $(\sin \theta/\lambda)_{max} = 0.65$ Å^{-1} were measured on a Nonius KappaCCD diffractometer with rotating anode and graphite monochromator (λ = 0.71073 Å) at a temperature of 150(2) K. An absorption correction based on multiple measured reflections was applied (μ = 0.603 mm^{-1}, 0.82–0.88 correction range); 4310 reflections were unique (R_{int} = 0.0332). The atomic coordinates were taken from the isostructural [**4**]BF$_4$ and refined with SHELXL-97[40] on F^2 of all reflections. Non-hydrogen atoms were refined freely with anisotropic displacement parameters. All hydrogen atoms were located in the difference Fourier map. The hydroxy H atom was refined freely with isotropic displacement parameters, and the other H atoms were refined as rigid groups; 250 parameters were refined with 21 restraints. R1/wR2 [$I > 2\sigma(I)$]: 0.0296/0.0717. R1/wR2 [all reflns]: 0.0335/0.0743. S = 1.047. Flack x parameter[42] –0.01(3). Residual electron density between −0.50 and 0.57 e/Å^3. Geometry calculations, drawings, and checking for higher symmetry were performed with the PLATON[41] package.

X-ray Crystal Structure Determination of [4]BF$_4$. $C_{42}H_{43}N_2O_2Pd \cdot BF_4$, fw = 800.99, triangular yellow plate, 0.18 × 0.18 × 0.03 mm^3, tetragonal, $P4_12_12$ (no. 92), $a = b$ = 10.3592(1) Å, c = 33.8828(2) Å, V = 3636.07(5) Å^3, Z = 4, ρ = 1.463 g/cm^3; 45 746 reflections up to a resolution of $(\sin \theta/\lambda)_{max} = 0.65$ Å^{-1} were measured on a Nonius KappaCCD diffractometer with rotating anode and graphite monochromator (λ = 0.71073 Å) at a temperature of 150(2) K. An absorption correction based on multiple measured reflections was applied (μ = 0.571 mm^{-1}, 0.85–0.98 correction range); 4178 reflections were unique (R_{int} = 0.0492). The structure was solved with direct methods[39] and refined with SHELXL-97[40] on F^2 of all reflections. Non-hydrogen atoms were refined freely with anisotropic displacement parameters. All hydrogen atoms were located in the difference Fourier map. The hydroxy H atom was refined freely with isotropic displacement parameters, and the other H atoms were refined as rigid groups. The BF$_4$ anion was refined with a disorder model; 250 parameters were refined with 3 restraints. R1/wR2 [$I > 2\sigma(I)$]: 0.0309/0.0759. R1/wR2 [all reflns]: 0.0358/0.0790. S = 1.050. Flack x parameter[42] –0.03(3). Residual electron density between −0.75 and 0.93 e/Å^3. Geometry calculations, drawings, and checking for higher symmetry were performed with the PLATON[41] package.

Crystallographic data for compounds of this paper have been deposited with the Cambridge Crystallographic Data Centre, CCDC Nos. 278929 (**2**), 278930 (**3**), 278931 ([**4**]PF$_6$), and 278932 ([**4**]BF$_4$). Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 3360333 or e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

Acknowledgment. The work described here was financially supported by the National Research School Combination-Catalysis (NRSC-C) (S.G.) and the Council for Chemical Sciences of The Netherlands Organization for Scientific Research (CW-NWO) (M. L., A.L.S.). NWO/NCF is thanked for the supercomputer time on TERAS/ASTER, SARA (The Netherlands, Project No. SG-032). R.W.A.H. acknowledges financial support from the NWO Grant 700.53.401.

Supporting Information Available: CIF files for the X-ray structural data of complexes **2**, **3**, [**4**]PF$_6$, and [**4**]BF$_4$. Table S1 displaying the results of the aldol reaction of methyl α-isocyanoacetate to aldehydes catalyzed by [**4**]PF$_6$ and [**4**]BF$_4$ after 5 h. Figure S2 displaying the stereostructures of *syn*- and *anti*-aldol intermediates for all four oxazoline products. This material is available free of charge via the Internet at http://pubs.acs.org.

OM701261Q

(41) Spek, A. L. *J. Appl. Crystallogr.* **2003**, *36*, 7–13.
(42) Flack, H. D. *Acta Crystallogr.* **1983**, *A39*, 876–881.