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Novel enantiopure non-C_2-symmetric NCN-pincer palladium complexes with L-proline chiral auxiliaries: *mer* η^3-*N*,*C*,*N* versus square planar η^4-*N*,*C*,*N*,*O* coordination

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This paper is dedicated to Professor Jack Halpern on the occasion of his 80th birthday

Abstract—New chiral NCN-pincer palladium complexes containing proline ester moieties as chiral auxiliaries have been synthesized. The parent ligands 2,6-bis{[(*S*)-2-(methoxycarbonyl)-1-pyrrolidinyl]methyl}-1-bromobenzene $\mathbf{L^{Me}}$ and 2,6-bis{[(*S*)-2-(benzoxycarbonyl)-1-pyrrolidinyl]methyl}-1-bromobenzene $\mathbf{L^{Bn}}$ were prepared in a single synthetic step and were obtained enantiomerically pure. Neutral arylpalladium bromide complexes **1a** and **1b**, formed upon treatment of the respective ligands $\mathbf{L^{Me}}$ and $\mathbf{L^{Bn}}$ with $[Pd_2(dba)_3]\cdot CHCl_3$, were isolated as mixtures of three stereoisomers ($S_NS_NS_CS_C$, $R_NS_NS_CS_C$ and $R_NR_NS_CS_C$). The ratio of stereoisomers is approximately 1:1:0.6 in the case of methyl ester derivative **1a**, whereas the bulkier benzyl ester derivative **1b** predominantly forms the ($S_NS_NS_CS_C$)-stereoisomer. Upon abstraction of the bromide ion from unresolved mixtures of **1a** and **1b**, cationic complexes **2** and **3**, respectively, form as single diastereoisomers in which one of the ester prolinate carbonyl groups is coordinated to palladium according to X-ray crystal structure determination. This coordination of a carbonyl group to the metal has a substantial influence on the stereochemistry and results in the formation of a single diastereoisomer, having the ($R_NR_NS_CS_C$)-configuration, regardless of the stereochemistry or ratio of stereoisomers of the starting bromide compound. The structures of compounds **2** and **3** were somewhat unexpected since formation of the corresponding cationic $[Pd(NCN)(OH_2)]^+$ complexes was anticipated. In preliminary tests of these cationic complexes as catalysts in the enantioselective aldol condensation of benzaldehyde with methyl isocyanoacetate, modest selectivities were observed.

1. Introduction

Enantioselective synthesis is one of the major research topics in both academic and industrial laboratories. The combination of a transition metal and chiral ligands as a homogeneous catalyst is one of the methods for the synthesis of optically active materials. Since Knowles[1] and Kagan[2] successfully applied chiral rhodium phosphine complexes in asymmetric hydrogenation, a large number of asymmetric coordination complexes, of mostly phosphine[3] or nitrogen containing[4] ligands, have been synthesized and applied in enantioselective catalysis. However, most of these homogeneous catalysts have a rather low stability and cannot be reused in catalysis. Catalyst deactivation can occur by metal leaching from the chiral ligand environment, as the metal is held in place solely by the dative bonding of the P- or N-donor atoms of the ligand to the metal centre. One way to increase the stability of the catalyst is to bind the metal to the ligand by a direct metal-to-carbon σ-bond. In this respect, organometallic complexes containing terdentate, monoanionic $[2,6\text{-}(ECH_2)_2C_6H_3]^-$ ligands (ECE; E = NR_2, PR_2, SR, OR), so-called 'pincer' ligands (Chart 1, structure **A**) were first reported in the late 1970s.[5] Due to the versatility and special properties of

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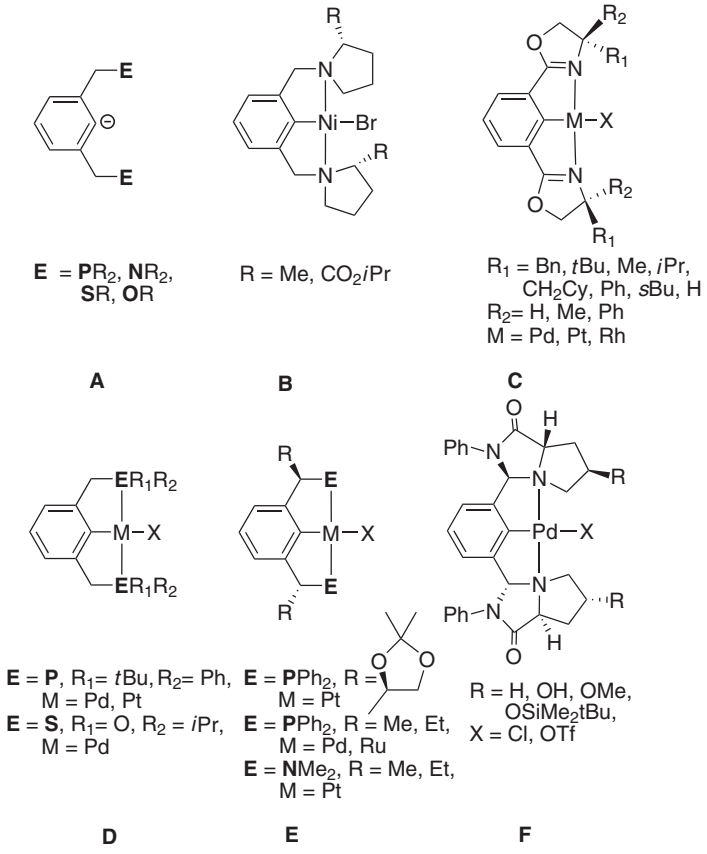


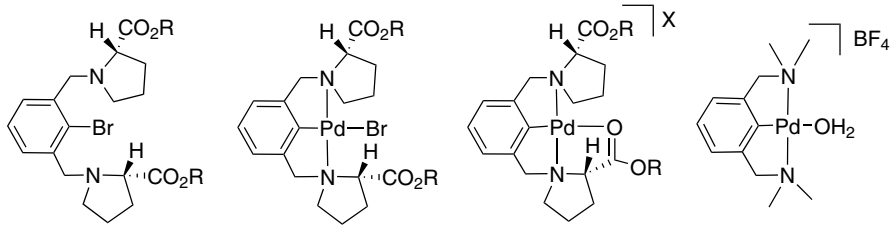
Chart 1.

these systems, they have been the subject of intensive research.[6] The catalytic deactivation of these compounds is negligible due to the very rigid coordination of the donor atoms to the metal centre, which efficiently protects the M–C σ-bond from being cleaved. The construction of nanosize structures by the attachment of active pincer catalysts to macromolecular supports, for example dendrimers or cartwheel-type macromolecules, allows the facile separation of the catalyst through nanofiltration membranes and their reuse or continuous use in catalysis.[7] Furthermore, the selective and reversible binding of SO_2 by NCN-pincer platinum and nickel complexes suggests their use as biosensors and markers in biochemical and medicinal applications.[8]

There are, however, relatively few asymmetric pincer complexes known. They contain either a chiral auxiliary, such as pyrrolidines (structure **B**),[9] oxazolines (structure **C**),[10] phosphines or sulfoxides (structure **D**),[11,12] or a stereogenic centre at the benzylic groups of the pincer backbone (structure **E**).[13] Takenaka et al. recently published pincer palladium complexes bearing pyrroloimidazolone auxiliaries (structure **F**) with stereogenic centres present on the proline rings as well as at the benzylic groups of the pincer backbone.[14] Depending on the metal of choice, these complexes have been applied in different catalytic reactions, such as aldol condensations,[10b,g,h,11,13a,c] Michael additions,[10f,14] Diels–Alder reactions,[10b] cyclopropanation,[10a] allylation of aldehydes,[12d] allylic alkylation,[10b] alkylation of aldimines,[10e] hydrogen transfer,[13f] and the Kharasch addition.[9] The enantioselectivities obtained vary from moderate (ee's below 35%)[9,10a,b,f,11,13a,f] to high (ee's up to 80%).[10d,e,g,h,13b,c,14]

We have now incorporated ester derivatives of the natural amino acid L-proline (Chart 2) as N-donor groups into the NCN-pincer backbone. These are commercially available and enantiomerically pure building blocks for the synthesis of chiral ligands and their stereogenic information can be maintained by choosing the appropriate reaction conditions during the synthesis and purification of the organometallic complexes. The stereogenic centre (S_C) at the ester prolinate ring plays an important role, together with the bulkiness of the ester group, in the introduction of stereogenicity on the nitrogen atoms (S_N or R_N) upon coordination to the metal centre.

Herein, we report the synthesis and study of the coordination behaviour of the palladium complexes of the chiral NCN-pincer ligands $\mathbf{L^{Me}}$ and $\mathbf{L^{Bn}}$ in the solid state and in solution. Cationic complexes **2** and **3** were tested in the aldol reaction between benzaldehyde and methyl isocyanoacetate (Scheme 1). In this reaction, optically active oxazolines, that is, protected β-hydroxy α-amino acids, are formed.[15] In addition, it involves the formation of a C–C bond with the simultaneous creation of two stereogenic centres. To perform this reaction in a regio- and stereoselective manner, it seems necessary to



L^{Me} R = Me
L^{Bn} R = Bn

1a R = Me
1b R = Bn

2a R = Me, X = BF_4
3a R = Me, X = PF_6
2b R = Bn, X = BF_4
3b R = Bn, X = PF_6

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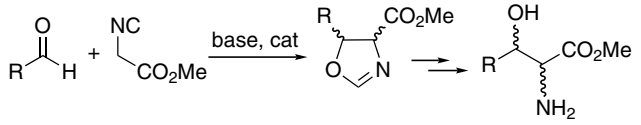
Chart 2.



Scheme 1.

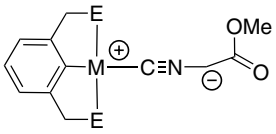


Figure 1. Structure of the enolate pincer metal complex with methyl isocyanoacetate after deprotonation with base (modified from Nishiyama et al.).[10h]

design a catalyst with a deep chiral pocket at the catalytically active metal site as the actual reaction takes place at the α-carbon which is distant from this metal centre (Fig. 1). We anticipated that by optimizing the steric bulk of the proline functional groups these systems could indeed form a deep chiral pocket at the Pd centre.

2. Results and discussion

2.1. Synthesis

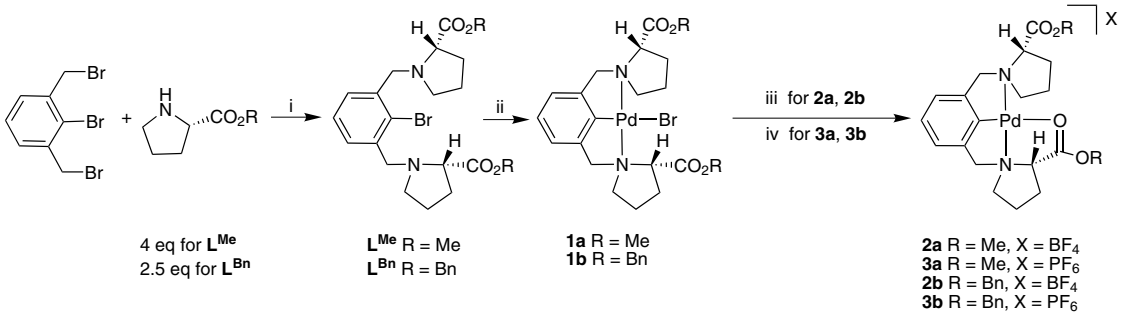
The parent ligands L^{Me} and L^{Bn} were synthesized in a one-step synthesis from the methyl and benzyl ester of L-prolinate, respectively. Reaction of 2,6-bis(bromomethyl)-1-bromobenzene with either 4 (for L^{Me}) or 2.5 (for L^{Bn}) equivalents of the appropriate L-prolinate ester in the presence of Et_3N in CH_2Cl_2 gave the aryl bromides L^{Me} and L^{Bn} in 75% and 70% yield, respectively, after purification via column chromatography (Scheme 2). The use of an excess of L-prolinate esters resulted in the formation of the desired ligands in higher yields by decreasing the amount of the monosubstituted by-product.

The arylpalladium complexes **1a** and **1b** were synthesized under an inert atmosphere via an oxidative addition reaction of the respective aryl bromides L^{Me} and L^{Bn} with $[Pd_2(dba)_3]\cdot CHCl_3$ in degassed benzene at 50 °C. These were isolated in good yields (90%, **1a** and 70%, **1b**) after purification by column chromatography (Scheme 2). In the case of complex **1a**, a mixture of three diastereoisomers was formed, whereas for complex **1b**, one diastereoisomer was formed preferentially (70%, vide infra). All attempts to separate the diastereoisomers of **1a** and **1b** via either crystallization or preparative TLC (at 0 °C) were unsuccessful. In another attempt to isolate a single diastereoisomer of **1a**, the reaction of **1a** with a chiral amine [(*S*)-dimethyl(1-phenylethyl)amine] in the presence of NH_4PF_6 yielded the corresponding cationic complex **3a**. Reaction of the complexes **1a** and **b** with either $AgBF_4$ in an acetone/water (10:1) mixture or with aqueous NH_4PF_6 in methanol yielded the cationic complexes **2a** and **2b**, and **3a** and **3b**, respectively, in good yields (68–95%) and as single diastereoisomers (Scheme 2). A disadvantage of using $AgBF_4$ as a dehalogenating agent in these reactions is that the complete removal of silver salts from the product can be troublesome. For further use of these cationic complexes as catalysts in the aldol reaction, this can be a problem, because silver(I) salts themselves can be excellent catalysts for this reaction.[16] With this in mind, we were looking for a non-silver containing dehalogenating reagent. Therefore, aqueous NH_4PF_6, which was earlier used by Bennet et al.[17] for the abstraction of chloride anions, was attempted. The driving force for the reaction of **1a** and **1b**, respectively, with the excess of aqueous NH_4PF_6 in methanol is the precipitation of the respective ionic complexes **3a** and **3b** from the reaction mixture.

All compounds were characterized by ^1H and $^{13}C\{^1H\}$ NMR, IR spectroscopy, ESI-MS and elemental analysis. The molecular structures of complexes **2a** and **3a** were confirmed by X-ray crystal structure determination (vide infra).

2.2. Structures of complexes 2a and 3a in the solid state

Single crystals suitable for X-ray analysis were obtained by slow diffusion of Et_2O into acetone solutions of the respective ionic complexes **2a** and **3a** (Table 1, see Experimental). In the crystal structure of **2a** there are two independent molecules, which differ only in the conformations of the uncoordinated ester moieties (Fig. 2). The two independent molecules of **2a** and the molecule



Scheme 2. Synthesis of ligands $\mathbf{L^{Me}}$ and $\mathbf{L^{Bn}}$, neutral palladium complexes **1** and cationic complexes **2** and **3**. Reagents and conditions: (i) Et_3N, CH_2Cl_2, rt, 16 h; (ii) $[Pd_2(dba)_3]\cdot CHCl_3$, C_6H_6, 50 °C, 3 h; (iii) $AgBF_4$, acetone/H_2O; rt; (iv) NH_4PF_6/H_2O, CH_3OH, rt.

Table 1. Experimental details of the crystal structure determinations

	2a	**3a**
Formula	$[C_{20}H_{27}N_2O_4Pd]BF_4$	$[C_{20}H_{27}N_2O_4Pd]PF_6$
fw	552.65	610.81
Crystal colour	Yellowish	Colourless
Crystal size [mm^3]	$0.27\times0.15\times0.12$	$0.38\times0.09\times0.04$
Crystal system	Monoclinic	Orthorhombic
Space group	$P2_1$ (no. 4)	$P2_12_12_1$ (no. 19)
a [Å]	7.3918(1)	9.0688(1)
b [Å]	30.2483(4)	13.0128(1)
c [Å]	10.4104(1)	20.2056(2)
β [deg.]	105.1885(6)	–
V [Å^3]	2246.35(5)	2384.47(4)
Z	4	4
D_{calc} [g/cm^3]	1.634	1.701
μ [mm^{-1}]	0.89	0.92
Abs. corr. range	0.90–0.94	0.92–0.98
Refl. measured/unique	24969/10009	32278/5461
Parameters/restraints	617/143	309/0
$R1/wR2$ [$I>2\sigma(I)$]	0.0295/0.0586	0.0251/0.0479
$R1/wR2$ [all refl.]	0.0342/0.0609	0.0298/0.0494
S	1.019	1.031
ρ(min./max.) [e/Å^3]	−0.44/0.42	−0.36/0.42
Flack × parameter	−0.030(15)	−0.026(15)

3a have essentially identical four-coordinate *N,C,N,O*-coordination geometries around the palladium centre comprising the C_{ipso}, both N atoms and the carbonyl oxygen of one of the ester groups. The coordination of the carbonyl group to palladium is somewhat unexpected since coordination of an aquo ligand was anticipated in analogy with previously synthesized cationic NCN-pincer Pd complexes.[18] As a result of the extra η^1-O coordination, the complexes lack any element of symmetry. The crystal packing of **2a** (BF_4) and **3a** (PF_6) is different. Complex **2a** crystallizes in a monoclinic crystal system, while **3a** is in an orthorhombic crystal system, which are completely unrelated. Both crystal structures are in chiral space groups and their absolute structure could be determined from the Flack parameter.[19] In all three molecules of **2a** and **3a**, the coordinated nitrogen atoms have an (R_N)-configuration, while the C_α-atoms have the expected (S_C)-configuration. The palladium centres have slightly distorted square-planar coordination environments with angles at palladium amounting to C(1)–Pd–N(1,2) 81.09(13)–84.43(9)° and N(1)–Pd–N(2) 164.82(10)–165.67(10)°. Selected bond distances, bond

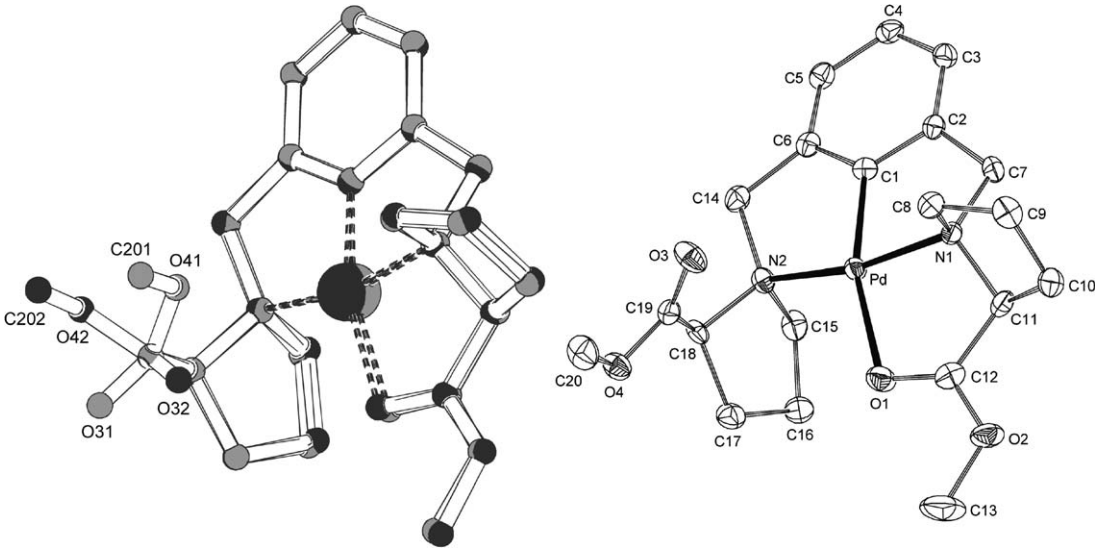


Figure 2. Quaternion fit[20] (left) of the two independent cationic molecules in the crystal structure of **2a**. Molecule 1 is drawn in grey, molecule 2 is drawn in black. The only significant difference is in the conformation of the uncoordinated ester group. On the right is depicted the displacement ellipsoid plot (50% probability) of cation **3a**; hydrogen atoms and non-coordinated BF_4 and PF_6 anions are omitted for clarity. An equivalent numbering scheme was adapted for all structures.

Table 2. Selected bond lengths (Å), angles and torsion angles (deg) of cations **2a** (X = BF_4) and **3a** (X = PF_6)

	2a		3a
	Molecule 1	Molecule 2	
Pd–C(1)	1.899(3)	1.909(3)	1.900(2)
Pd–N(1)	2.048(3)	2.063(3)	2.0493(17)
Pd–N(2)	2.113(3)	2.121(3)	2.1230(17)
Pd–O(1)	2.207(2)	2.261(2)	2.2236(17)
C(1)–Pd–O(1)	163.21(12)	161.32(12)	162.96(8)
N(1)–Pd–N(2)	165.67(10)	164.82(10)	165.26(6)
C(1)–Pd–N(1)	83.80(12)	83.77(13)	84.18(9)
C(1)–Pd–N(2)	82.15(12)	81.09(13)	81.43(9)
O(1)–Pd–N(1)	80.35(9)	78.15(10)	79.85(6)
O(1)–Pd–N(2)	113.90(9)	116.82(10)	114.08(6)
N(2)–C(18)–C(19)–O(3)	−174.6(3)	−81.1(4)	6.2(3)
C(1)–C(2)–C(7)–N(1)	−25.7(4)	−26.0(4)	−20.6(3)
C(1)–C(6)–C(14)–N(2)	−18.1(4)	−20.8(4)	−26.7(3)

angles and torsion angles of **2a** and **3a** are given in Table 2. The Pd–N distances vary depending on whether the methyl prolinate ligand is *N*,*O*- or *N*-coordinated; Pd–N(1) 2.048(3), 2.063(3) Å (**2a**) and 2.0493(17) Å (**3a**) for the *N*,*O*-coordinated proline moiety and Pd–N(2) 2.113(3) and 2.121(3) Å (**2a**), 2.1230(17) Å (**3a**) for the *N*-coordinated methyl prolinate moiety. The structurally related (achiral) cationic NCN-pincer palladium complex [Pd($C_6H_3\{CH_2NMe_2\}_2$-2,6)(OH_2)][BF_4] (**4** in Chart 2)[18] and the chiral cationic NCN–Phebox–palladium complex (Phebox = 2,6-bis(oxazolinyl)phenyl) (**C** in Chart 1)[10c] have *mer* η^3-*N*,*C*,*N* coordinated pincer ligands while the complexes are C_2-symmetric. Compared to these complexes, the Pd–N distances in **2a** and **3a** are shorter for the *N*,*O*-coordinated methyl prolinate and longer for the *N*-coordinated one. Regrettably, attempts to grow single crystals for the benzyl prolinate complexes **2b** and **3b** have failed.

The IR spectra of the solid cationic complexes **2** and **3** revealed two sharp absorptions in the region of the C=O stretching vibration. The *ν*(CO) of the carbonyl group of the N,O-chelate bonded ester prolinate is shifted to lower wavenumbers (≈1660 cm^{-1}), while the *ν*(CO) of the free ester group of the *N*-bonded ester prolinate is comparable to the *ν*(CO) values of the parent ligands **1a** and **1b** (Table 3). Solution IR spectra of **2b** and **3a** in dichloromethane also showed the presence of the two distinct carbonyl vibrations at similar wavenumbers (see Table 3).

Table 3. Solid state IR characteristics of the carbonyl groups of palladium complexes **1**–**3**[a]

Compound (R)	*ν* (CO) (cm^{-1})	
	Uncoordinated	Coordinated
1a (Me)	1736	—
2a (Me)	1740	1664
3a (Me)	1739(1739)	1662(1662)
1b (Bn)	1729	—
2b (Bn)	1740(1741)	1652(1652)
3b (Bn)	1733	1656

[a] Values measured in CH_2Cl_2 solution in parentheses.

2.3. Structures of complexes 2a and b and 3a and b in solution

The ^1H and $^{13}C\{^1H\}$ NMR spectra of the neutral complexes **1a**,**b** show three sets of distinct resonance patterns, which could be assigned to the three possible stereoisomers (see Fig. 3) by applying a number of different one- and two-dimensional NMR techniques.[22] The nature of the ester substituent (R = either Me or Bn) has a great effect on the ratio of the respective stereoisomers.

In the ^1H NMR spectra of **1a** in toluene-d_8, four singlets for the methyl ester groups (CH_3), four triplets for the hydrogens on the stereogenic carbon (Hα) and four AX patterns for the diastereotopic hydrogens (Ha and Hb) of the benzylic methylene linker are observed (for part of the aliphatic region, see Fig. 4; for the whole spectrum, see Fig. 5a). To assign the signals for each individual stereoisomer, the elements of symmetry of the three stereoisomers have to be taken into account. Since the (S_C)-configuration of the stereogenic C_α-atom was maintained, the configuration of the two nitrogen atoms is only discussed. The (R_NS_N)-isomer does not contain any element of symmetry and, therefore, all hydrogen and carbon atoms are magnetically inequivalent [the stereoisomers with (R_NS_N)- and (S_NR_N)-configurations are superimposable upon 180° rotation around the C–Pd axis and are therefore identical]. The (S_NS_N)- and (R_NR_N)-enantiomers both contain a C_2-axis and this symmetry element reduces the amount of signals by half. Based on this symmetry argument and the specific integral values, the signals corresponding to the (R_NS_N)-isomer could be recognized. The remaining signals all belong to the (S_NS_N)- and (R_NR_N)-diastereoisomers, however, the multiplicity and the number of signals are the same for both isomers. The three stereoisomers are in fact diastereoisomers due to the presence of the C_α-stereogenic centres on the L-prolinate rings. To assign the different resonances for each remaining diastereoisomer, the chemical shifts of the stereogenic hydrogen were used and compared to a structurally related NCN-pincer nickel(II) system.[9] Based on the specific integrals of identical groups of the different diastereoisomers the relative ratio of these isomers could be determined. The resonances of the methyl groups are well resolved and give a clear indication of this molar ratio, which amounts to 1(S_NS_N):1(R_NS_N):0.6(R_NR_N). The shifts of the Hα hydrogens were assigned by HETCOR, since the stereogenic carbons of all three stereoisomers are the only aliphatic tertiary carbons, which were identified by DEPT measurements. A remarkable shift difference of 2.5 ppm was observed for resonances of the Hα signal of the different stereoisomers. This shift difference is caused by the deshielding effect of palladium on the stereogenic hydrogen atoms pointing towards the metal (configuration S_N, 5.08 ppm in S_NS_N and 4.81 ppm in R_NS_N) with respect to hydrogen atoms pointing away from the metal (configuration R_N on nitrogen, 2.53 ppm in R_NR_N and 2.67 ppm in R_NS_N). In order to assign the remaining signals, 2D experiments (^1H–^1H COSY, ^1H–^{13}C HETCOR and ^1H NOESY) as well as DEPT (angle) experiments were performed

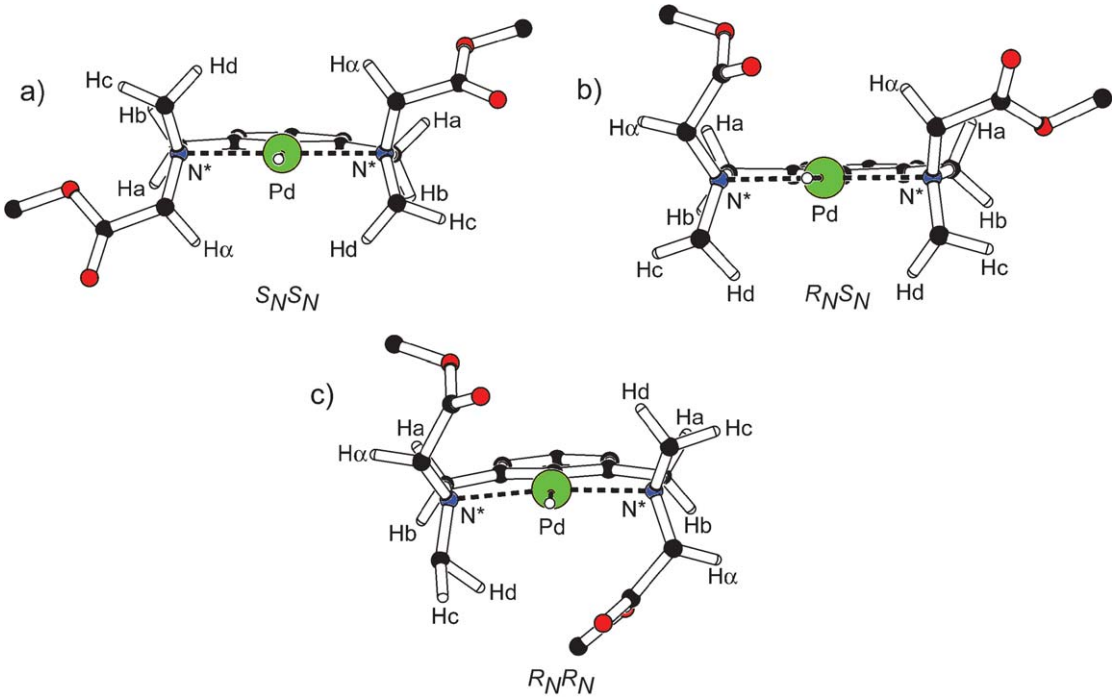


Figure 3. Molecular modelling structures (MM2) of the (a) S_NS_N, (b) R_NS_N and (c) R_NR_N stereoisomers of complexes **1a** and **1b** with selected labelling of hydrogen atoms. For simplification the configuration is assigned only for the nitrogen atoms, the configuration of the carbon stereogenic centres remained (S_C). Two methylene groups of the prolinate rings are omitted for clarity.

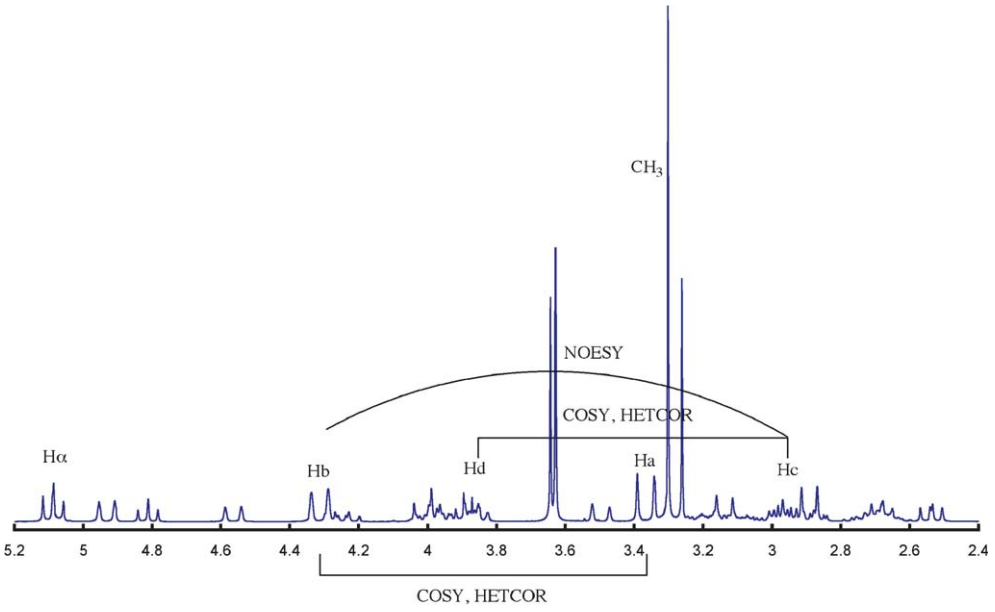


Figure 4. Part of the ^{1}H NMR spectrum of **1a** (toluene-d_8) with the assignment of the most important aliphatic protons of the (S_NS_N)-stereoisomer and the 2D NMR technique(s) used for their assignment.

(Fig. 6 depicts the ^{1}H–^{1}H COSY spectrum of **1a**). The strategy of the assignment of the most important aliphatic hydrogens is shown for the (S_NS_N)-isomer of **1a** (Fig. 4).

The hydrogen atoms belonging to the same CH_2 group were identified by COSY (Fig. 6) and HETCOR experiments. Hydrogen Hb of the benzylic methylene group interacts with one of the hydrogens of the methylene groups next to the nitrogen of the prolinate ring (Hc). This through space interaction, is observed for all stereoisomers in their NOESY spectra. For the assignment of the aromatic hydrogens we considered their multiplicity (triplet for hydrogens in *para*-position to palladium and doublet for hydrogens in *meta*-position to palladium) and intensity [according to the symmetry, for

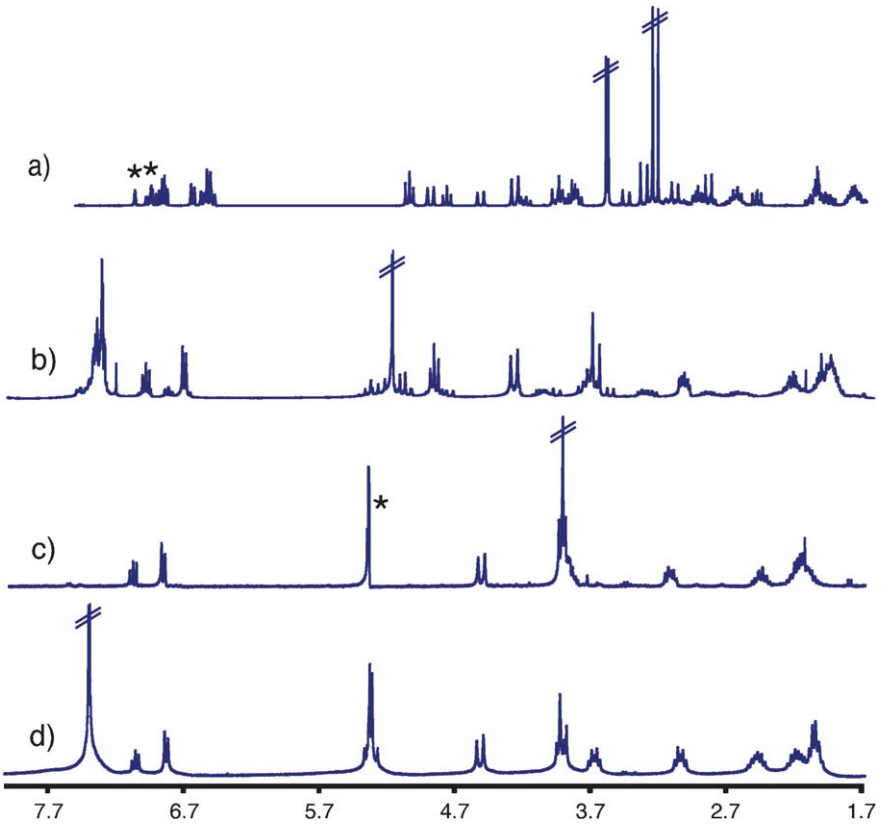


Figure 5. The ^{1}H NMR spectra of (a) **1a** in toluene-d_8, (b) **1b** in CD_2Cl_2, (c) **2a** in CD_2Cl_2 and (d) **2b** in CD_2Cl_2 (∗ represents the solvent peak).

S_NS_N and R_NR_N one triplet and one doublet (2H) is observed while for R_NS_N one triplet and two doublets were distinguished (1H)]. The hydrogens of the methylene groups of the prolinate rings were observed as an overlapping multiplet between 1.24 and 2.07 ppm.

The degree of substitution of the carbon atoms was determined by DEPT (angle) measurement and the shifts of the primary, secondary and tertiary carbons were assigned by analysis of the HETCOR spectra. The shifts of the quaternary carbons of the benzene ring (C_{ipso} and C bearing the methylene/benzylic group) were resolved by regarding the shifts and the peak intensities of the starting ligand $\mathbf{L^{Me}}$. The δ values of the hydrogen and carbon nuclei of all three stereoisomers of **1a** are listed in Tables 4 and 5.

Substitution of the methyl ester for the bulkier benzyl ester in **1b** strongly favours the formation of the least hindered (S_NS_N)-stereoisomer as the major product (approximately 70%, Fig. 5b). All the hydrogens and carbons of the S_NS_N isomer were assigned by COSY, HETCOR and NOESY experiments following a similar strategy as for **1a** (Table 6). Full assignment of the remaining two stereoisomers was not possible due to low signal intensity and signal overlapping.

The nature of the signal(s) observed in the ^{1}H NMR for the benzylic hydrogens of the pincer metal complexes gives information about the conformational changes of the pincer skeleton. The dynamic behaviour of NCN-pincer metal complexes [MX(NCN)] (M = Ni, Pd, Pt; X = Cl, Br, I) in solution has been studied earlier by our group.[6a,7,13f,21] In the case of achiral square-planar NCN-pincer metal complexes, these benzylic hydrogens, which are in principle diastereotopic, display a single resonance at ambient temperature due to the fast intramolecular 'wagging' of the two non-planar five-membered chelate rings with a shared M–C bond (Fig. 7). However, at low temperature, exchange processes are slowed down and an AB pattern is observed.[13g] NCN-pincer metal complexes with chirality present at the nitrogen atoms show AB patterns at ambient temperature for these benzylic protons.[21]

The ^{1}H NMR spectra of **1a** and **1b** are temperature independent in the range between −80 °C to 95 °C. The presence of three isomers for neutral complexes **1** is a consequence of the interconversion between the different diastereoisomers, caused by dissociation of the Pd–N bond, followed by pyramidal inversion at nitrogen, rotation and re-coordination. This interconversion between the stereoisomers could be observed in 2D-EXSY experiments on **1a**, but only at a temperature of 45 °C using long mixing times (2 s). In fact, the 2D-EXSY spectrum of **1a** shows cross-peaks between the Hα hydrogen atoms of two pairs of diastereoisomers, indicating the interconversion between the S_NS_N and R_NS_N, and the R_NS_N and R_NR_N diastereoisomers. The interconversion of the stereogenic nitrogen atoms is even slower for the bulkier **1b** compound, since the (S_NS_N)-stereoisomer was formed preferentially.

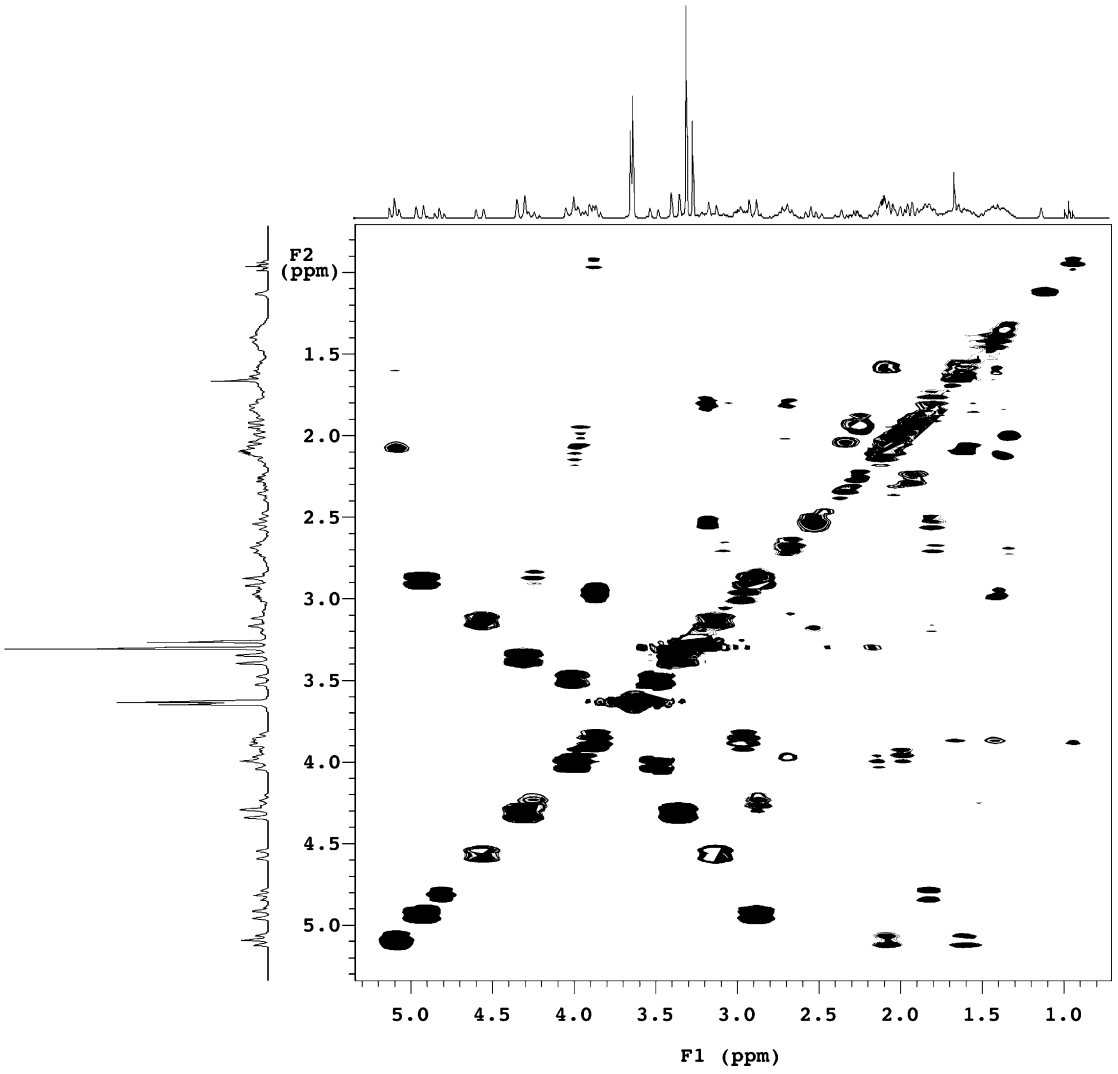


Figure 6. Aliphatic part of the ^{1}H–^{1}H COSY spectrum of **1a**.

Table 4. ^{1}H NMR data of complex **1a** in toluene-d_8

Selected H, multiplicity	S_NS_N			R_NR_N			R_NS_N			
	δ (ppm)	Type of H	J (Hz)	δ (ppm)	Type of H	J (Hz)	δ (ppm)	Type of H	J (Hz)	
CH_2 ring, m	1.24–2.07			1.24–2.07			1.24–2.07			
NCH_2, m	2.97	Hc		4.23	Hc		1.82	Hc		S_N
							3.2	Hd		S_N
	3.85	Hd		2.88	Hd		2.12	Hc		R_N
							1.64	Hd		R_N
C_α^*H, t	5.08	Hα	9.3	2.53	Hα	10.2	4.81	Hα	8.7	S_N
							2.67	Hα	8.1	R_N
CH_3, s	3.30			3.63			3.26			S_N
							3.64			R_N
CH_2 benzylic	3.36	Ha	14.7	2.89	Ha	13.8	3.14	Ha	14.1	S_N
AX pattern	4.31	Hb	14.7	4.92	Hb	13.8	4.56	Hb	13.8	S_N
							4.01	Ha	15	R_N
							3.5	Hb	15.3	R_N
CH arom, para, t	6.88		7.5	6.90		7.5	6.97		7.5	
CH arom, meta, d	6.56		7.5	6.67		7.2	6.53		7.5	S_N
							6.60		7.5	R_N

The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra obtained for the cationic complexes **2** and **3** (for ^{1}H NMR spectra of **2a** and **2b** see Fig. 5c and d), showed the presence of only one set of signals for each compound. The presence of only

Table 5. $^{13}C\{^1H\}$ NMR data for complex **1a** in toluene-d_8 (δ ppm)

Selected C	S_NS_N	R_NR_N	R_NS_N	
			S_N	R_N
CH_2 ring, γ	22.82	23.92	22.56	23.70
CH_2 ring, β	26.49	28.75	25.76	28.35
NCH_2	61.95	65.33	63.46	65.20
C^*_α	71.36	71.49	70.70	72.16
CH_3	52.10	52.58	52.06	52.68
CH_2 benzylic	64.91	73.57	66.82	73.18
C ortho	146.33	145.82	146.87	145.45
C meta	119.54	119.04	119.23	118.92
C para	124.01	124.01	124.01	124.01
C ipso	158.09	157.52	157.36	157.36
CO	171.12	171.85	170.87	171.29

one species in NMR and the information obtained from the solid state analysis leads to the conclusion that a single stereoisomer with an (R_NR_N)-configuration is present, regardless of the stereochemistry and ratio of stereoisomers in the starting material in its synthesis. Only in the (R_NR_N)-conformer, both carbonyl groups are pointing towards the palladium centre and are within suitable distance for coordination to the metal according to the X-ray crystal structure. In the stereoisomers with (R_NS_N)- and (S_NS_N)-configuration either one or both ester moieties are pointing away from palladium, thus lacking the dual intramolecular coordination ability and these stereoisomers are apparently less favoured. In solution, the fast exchange of the carbonyl group coordinating to the palladium centre was anticipated in **2** and **3**. Indeed, at ambient temperature, **2a** and **3a** display only one singlet for the ester methyl group. Upon cooling the sample to −35 °C (in CD_2Cl_2), two singlet resonances with equal intensity were detected. Coalescence of these signals is observed at 10 °C (283 K) upon increasing the temperature, representing a free energy change ($\Delta G^{\ddagger}$) of 66 kJ/mol. In the case of the benzyl ester derivatives **2b** and **3b**, the methylene diastereotopic hydrogen atoms of both ester moieties appear as one AB pattern with a ^2J value of 12.3 Hz in their ^1H NMR spectrum at ambient temperature. Samples of **2b** and **3b** were cooled to −80 °C (in CD_2Cl_2 or acetone-d_6) but no further splitting of the signals was observed.

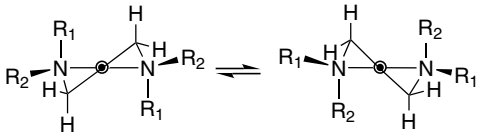


Figure 7. Interconversion of the conformation of the five-membered chelate rings of NCN-pincer metal complexes by 'wagging' about the metal–carbon covalent bond viewed along the M–C bond.

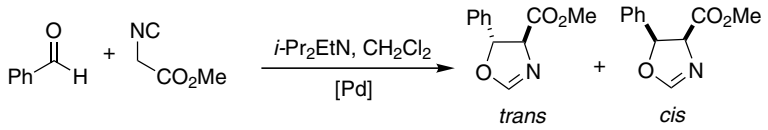
Coordination of the carbonyl group to the metal seems crucial for the overall stereochemistry and dynamic behaviour of the cationic palladium complexes. Since we did not observe any change in the number or ratio of the peaks for any of the cationic complexes upon changing the temperature, and only one set of signals was observed in each instance, we can conclude that the dissociation of the Pd–N bonds does not take place on the NMR timescale. Reaction of enantiomerically pure **2** or **3** with LiBr yielded all possible isomers of the corresponding palladium bromide complexes **1** in the same ratio as was originally observed, showing the essential influence of the carbonyl group coordination on the stereochemistry of these palladium complexes.

2.4. Preliminary catalytic results

In a preliminary investigation of the catalytic potential of complexes **2** and **3**, we tested their activity in the aldol condensation between benzaldehyde and methyl α-isocyanoacetate (MIC) in the presence of 10 mol % of *i*-Pr_2EtN (Scheme 3). Reactions were carried out in CH_2Cl_2 at ambient temperature with 1 mol % of catalyst and results obtained after 8 h are presented in Table 7. In all cases, the *trans*-oxazoline was the major product. Although higher ee's were obtained with the bulkier benzyl ester complexes **2b** and **3b** (entries 3 and 4), the enantioselectivities in general are very modest. Changing the counterion from BF_4^- to PF_6^- resulted in a slight increase in the ee's of the minor *cis* product (compare

Table 6. Selected ^1H and $^{13}C\{^1H\}$ NMR data of complex **1b** in CD_2Cl_2

Selected H, multiplicity	S_NS_N			Selected C	S_NS_N
	δ (ppm)	Type of H	J (Hz)		δ (ppm)
CH_2 ring, m	1.87–2.08			CH_2 ring, γ	23.03
	2.19–2.27			CH_2 ring, β	26.20
NCH_2, m	3.03	Hc		NCH_2	62.85
	3.75	Hd		C^*_α	72.41
$C^*_\alpha H\alpha$, t	4.87	Hs	9.9	CH_2O	68.34
CH_2O, s	5.17			CH_2 benzylic	66.50
CH_2 benzylic	4.28	Ha	15	C ortho	146.87
AX pattern	3.79	Hb	15	C meta	120.80
CH arom, meta, d	6.70		7.5	C para	125.59
CH arom, para, t	6.98		7.8	C ipso	137.12
Ph ester, m	7.27–7.37			Ph ester	157.15
					129.92
					129.73
					129.62
				CO	171.18



Scheme 3.

Table 7. Stereoselective aldol condensation of MIC and benzaldehyde[a]

Entry	Complex	Conversion[b] [%]	% trans[c]	% ee[d]	
				trans (4*R*,5*S*)	cis (4*S*,5*S*)
1	**2a**	80	65	12	3
2	**3a**	80	60	13	5
3	**2b**	60	62	16	3
4	**3b**	60	57	15	10

[a] Reaction conditions: 1 mol % catalyst, 10 mol % *i*-Pr_2EtN, methyl isocyanoacetate (1.6 mmol), benzaldehyde (1.6 mmol), CH_2Cl_2 (5 mL), 20 °C.
[b] After 8 h.
[c] Determined by GC using pentadecane as the internal standard.
[d] Determined by HPLC on Daicel Chiracel OD, *n*-hexane/*i*-propanol = 95/5%.

entries 1 and 2, and entries 3 and 4). It is important to note that in using these chiral cationic NCN-pincer palladium complexes in the aldol reaction with isocyanides, no sign of isocyanide insertion in the Pd–C_{ipso} bond was observed in contrast to observations with simple, achiral NCN-pincer palladium complexes.[16]

3. Conclusions

A family of new chiral organometallic Pd complexes was synthesized in two synthetic steps from the enantiopure ligands $\mathbf{L^{Me}}$ and $\mathbf{L^{Bn}}$ using L-prolinate esters as the chiral auxiliary. Although the precursor palladium bromide complexes **1a** and **1b** were isolated as a mixture of three stereoisomers (S_NS_N, R_NR_N and R_NS_N), the treatment of their unresolved mixtures with $AgBF_4$ or NH_4PF_6 gave the cationic complexes **2** and **3**, respectively, as diastereomerically pure species with the (R_NR_N)-configuration. The reason for this diastereospecificity is the unique coordination geometry of **2** and **3**, where one of the carbonyl groups of the ester moieties is coordinated to the palladium and the other ester moiety is in an appropriate position for coordination to Pd. Fast exchange of coordination and decoordination takes place between these ester moieties in solution. The stereoisomers (R_NS_N) and (S_NS_N), where one or both ester moieties are pointing away from palladium, lack this dual intramolecular coordination ability and are therefore less favoured. The system is entropically favoured as all four positions around the metal are occupied by potentially coordinating groups, which are part of the same molecule. Although the enantioselectivities obtained with these cationic complexes as catalysts in an aldol condensation are modest, they are promising enough to attempt further improvement by means of structural variation of the ligand. Furthermore, prompted by the high enantioselectivities obtained by bulky pyrroloimidazolone pincer complexes in the Michael addition as recently reported by Takenaka,[14] we plan to test our system in other asymmetric catalytic reactions.

4. Experimental section

4.1. General methods

All reaction were carried out using standard Schlenk techniques. The solvents were dried and freshly distilled prior to use unless stated otherwise. Methyl L-prolinate,[23] 2,6-bis(bromomethyl)-1-bromobenzene[24] and $[Pd_2(dba)_3{\cdot}CHCl_3]$[25] were prepared according to previously published procedures. L-Proline benzyl ester hydrochloride was purchased from Acros Chemical Co. and deprotected with Et_3N.[26] ^1H (300.1 MHz) and $^{13}C\{^1H\}$ (75.5 MHz) NMR spectra were recorded on a Varian Inova 300 spectrometer. The $\Delta G^{\ddagger}$ values were calculated with the Eyring equation $\Delta G^{\ddagger} = RT_c(22.96 + \ln T_c/\Delta\nu)$ (J mol^{-1}) where T_c (K) is the temperature of coalescence of two given signals and $\Delta\nu$ (Hz) their difference in chemical shift at low exchange temperature.[27] Optical rotations ($[\alpha]_D^{21}$) were measured with a Perkin polarimeter 241. Elemental microanalyses were carried out by Microanalytisches Laboratorium Dornis und Kolbe, Mulheim a.d. Ruhr, Germany. Infrared spectra were recorded on a Perkin–Elmer Spectrum One FT-IR instrument. 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 Diode Array II detector and LC pump using a Daicel Chiracel OD column. Molecular modelling was carried out using the SPARTAN 5.1.1 (UNIX) package[28] with a MMFF94 force field.

4.2. X-ray crystal structure determinations

X-ray intensities were measured on a Nonius Kappa CCD diffractometer with a rotating anode (graphite monochromator, $\lambda = 0.71073$ Å) at a temperature of 150 K. The structures were solved with automated Patterson methods[29] and refined with SHELXL-97[30] against F^2 of all reflections. One BF_4 anion of **2a** was disordered over two orientations. Structure calculations and checking for higher symmetry was performed with the PLATON[20] program. Further details are given in Table 1. CCDC 287330 (compound **2a**) and 287331 (compound **3a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.ac.uk/data_request/cif.

4.3. 2,6-Bis[[(*S*)-2-(methoxycarbonyl)-1-pyrrolidinyl]-methyl]bromobenzene L^{Me}

A solution of methyl L-prolinate (0.036 mol, 4.7 g) in CH_2Cl_2 (15 mL) was added dropwise to a stirred solution of 2,6-bis(bromomethyl)-1-bromobenzene (8.7 mmol, 3 g) and Et_3N (0.041 mol, 5.7 mL) in CH_2Cl_2 (70 mL). The reaction mixture was stirred for 16 h at ambient temperature. Subsequently, a white precipitate was filtered off and the filtrate washed with 1 M NaOH (2×50 mL). The layers were separated and the organic layer dried over Na_2SO_4, filtrated and concentrated in vacuo. The remaining crude oil was purified via column chromatography (SiO_2, hexanes/ethylacetate = 2:1). A yellow solid was obtained in 75% yield (2.85 g). Anal. Calcd for $C_{20}H_{27}BrN_2O_4$: C, 54.68; H, 6.19; N, 6.38. Found: C, 54.56; H, 6.12; N, 6.31. ESI-MS *m/z*: 439.12 ($(M+H)^+$, calcd 439.12); $[\alpha]_D^{21} = -78.8$ (*c* 1.0, $CHCl_3$); IR *v* (cm^{-1}): 2950 (w), 2800 (w), 1729 (s), 1429 (s), 1198 (s), 1137 (s), 1008 (s), 788 (s); ^1H NMR ($CDCl_3$): δ 1.78–1.83 (m, 2H, CH_2 ring, γ to CO), 1.87–2.04 (m, 4H, CH_2 ring, β and γ to CO), 2.11–2.19 (m, 2H, CH_2 ring, β to CO), 2.45–2.53 (m, 2H, NCH_2 ring), 3.06–3.13 (m, 2H, NCH_2 ring), 3.40–3.45 (m, 2H, $C_\alpha^*H\alpha$), 3.66 (s, 6H, $2CH_3$), 3.83 and 3.99 (d, AB, 4H, $^2J = 14.1$ Hz, ArCH_2N), 7.24 (t, 1H, $^3J = 7.8$ Hz), 7.40 (d, $^3J = 7.8$ Hz, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 23.43 (*C*H_2 ring γ to CO), 29.39 (*C*H_2 ring β to CO), 51.79 ($2CH_3$), 53.43 (N*C*H_2 ring), 58.38 (Ar*C*H_2N), 65.57 (C_α^*), 126.08 (*C*Br), 126.87 (*C*p to CBr), 129.59 (*C*m to CBr), 138.41 (Ar*C*CH_2N), 174.62 (*C*O).

4.4. 2,6-Bis[[(*S*)-2-(benzyloxycarbonyl)-1-pyrrolidinyl]methyl]bromobenzene L^{Bn}

A similar synthetic route as described for L^{Me} was used, by reacting 2,6-bis(bromomethyl)-1-bromobenzene (0.017 mol, 5.69 g), Et_3N (0.05 mol, 6.94 mL), and benzyl L-prolinate (0.04 mol, 8.50 g) in CH_2Cl_2 (100 mL). The crude brown oil was purified via column chromatography (SiO_2, hexanes/ethylacetate = 4:1). A yellow oil was obtained in 70% yield (6.84 g). Anal. Calcd for $C_{32}H_{35}BrN_2O_4$: C, 64.97; H, 5.96; N, 4.74. Found: C, 65.04; H, 5.84; N, 4.77. ESI-MS *m/z*: 591.11 ($(M+H)^+$, calcd 591.18); $[\alpha]_D^{21} = -52.9$ (*c* 1.08, $CHCl_3$); IR *v* (cm^{-1}): 2956 (w), 1728 (s), 1455 (w), 1265 (w), 1163 (m), 1133 (m), 1024 (w), 732 (s), 695 (s); ^1H NMR ($CDCl_3$): δ 1.80–1.91 (m, 2H, CH_2 ring, γ to CO), 1.93–2.06 (m, 4H, CH_2 ring, β and γ to CO), 2.13–2.19 (m, 2H, CH_2 ring, β to CO), 2.48–2.56 (m, 2H, NCH_2 ring), 3.07–3.12 (m, 2H, NCH_2 ring), 3.48–3.52 (m, 2H, $C_\alpha^*H\alpha$), 3.85 and 4.01 (d, AB, 4H, $^2J = 14.1$ Hz, ArCH_2N), 5.10 and 5.14 (d, AB, 4H, $^2J = 12$ Hz, COO*C*H_2Ph), 7.19 (t, 1H, $^3J = 7.8$ Hz), 7.30–7.36 (m, 10H, Ph), 7.39 (d, 2H, $^3J = 7.5$ Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 23.46 (*C*H_2 ring γ to CO), 29.31 (*C*H_2 ring β to CO), 53.17 (N*C*H_2 ring), 58.15 (Ar*C*H_2N), 65.47 (O*C*H_2Ph), 66.28 (C_α^*), 125.83 (*C*Br), 126.82 (*C*p to CBr), 128.20 (*C*p and *C*m of OCH_2*Ph*), 128.55 (*C*m to CBr), 129.38 (*C*o of OCH_2*Ph*), 136.01 (C_{ipso} of OCH_2*Ph*), 138.42 (Ar*C*CH_2N), 173.95 (*C*O).

4.5. 2,6-Bis[[(*S*)-2-(methoxycarbonyl)-1-pyrrolidinyl]-methyl]phenylpalladium(II) bromide 1a

Solid $[Pd_2(dba)_3]\cdot CHCl_3$ (1.7 mmol, 1.76 g) was added to a solution of L^{Me} (3.4 mmol, 1.5 g) in degassed benzene (60 mL). The resulting mixture was stirred at 50 °C for 3 h, after which the solvent was evaporated in vacuo. Purification of the crude product via column chromatography (SiO_2, dba was eluted with hexanes/ethylacetate = 1:1, the product with hexanes/ethylacetate = 1:3) yielded a yellow solid in 90% yield (1.65 g). Anal. Calcd for $C_{20}H_{27}BrN_2O_4Pd$: C, 44.01; H, 4.99; N, 5.13. Found: C, 44.11; H, 4.92; N, 5.04. ESI-MS *m/z*: 465.07 ($(M-Br)^+$, calcd 465.10); $[\alpha]_D^{21} = -8.7$ (*c* 1.0, $CHCl_3$); IR *v* (cm^{-1}): 3468 (w), 2949 (s), 1736 (s), 1435 (s), 1284 (m), 1230 (s), 1178 (s), 762 (m); NMR data are presented in Tables 4 and 5.

4.6. 2,6-Bis[[(*S*)-2-(benzyloxocarbonyl)-1-pyrrolidinyl]-methyl]phenylpalladium(II) bromide 1b

The synthetic route is similar to that described for **1a** by reacting L^{Bn} (2.54 mmol, 1.5 g) with $[Pd_2(dba)_3]\cdot CHCl_3$ (1.26 mmol, 1.33 g). Purification of the crude product via column chromatography (SiO_2, dba was eluted with hexanes/ethylacetate = 4:1, the product with hexanes/ethylacetate = 1:1) yielded a yellow solid in 65% yield (1.16 g). Anal. Calcd for $C_{32}H_{35}BrN_2O_4Pd$: C, 55.07; H, 5.05; N, 4.01. Found: C, 55.16; H, 5.15; N, 3.88. ESI-MS *m/z*: 617.25 ($(M-Br)^+$, calcd 617.16); $[\alpha]_D^{21} = -88.6$ (*c* 1.0, $CHCl_3$); IR *v* (cm^{-1}): 2946 (w), 1729 (s), 1221 (s), 1172(s), 1072 (s), 1067 (m), 965 (m), 736 (m), 696 (s); NMR data are presented in Table 6.

4.7. 2,6-Bis[[(*S*)-2-(methyloxocarbonyl)-1-pyrrolidinyl]-methyl]phenylpalladium(II) tetrafluoroborate 2a

Solid $AgBF_4$ (0.18 mmol, 36 mg) was added to a solution of **1a** (0.18 mmol, 100 mg) in acetone/water (10:1, 10 mL) mixture. The reaction mixture was stirred for 30 min. The resulting suspension was filtered through Celite yielding a colourless filtrate. The solvent was removed in vacuo to leave the title compound as a white solid in 75% yield (76 mg). Crystals suitable for X-ray analysis were obtained by slow diffusion of Et_2O into acetone solution of **2a**. Anal. Calcd for $C_{20}H_{27}N_2O_4PdBF_4$: C, 43.46; H, 4.92; N, 5.07. Found: C, 43.54; H, 5.05; N, 4.88. ESI-MS *m/z*: 465.13 ($(M-BF_4)^+$, calcd 465.10); $[\alpha]_D^{21} = +42.7$ deg cm^3 g^{-1} dm^{-1} (*c* 0.5, acetone); IR *v* (cm^{-1}): 3472 (m), 2961 (m), 1740 (s), 1663 (s), 1444 (m), 1234 (m), 1057 (s, BF_4), 767 (m); ^1H NMR (CD_2Cl_2): δ 2.14–2.23 (m, 6H, CH_2 ring, γ and β to CO), 2.43–2.50 (m, 2H, CH_2 ring, β to CO), 3.10–3.15 (m, 2H, NCH_2 ring), 3.84–3.88 (m, 4H, NCH_2 ring + $C_\alpha^*H\alpha$), 3.92 (s, 6H, $2CH_3$), 3.93 and 4.54 (d, AX, 4H, $^2J = 14.1$ Hz, ArCH_2N), 6.84 (d, $^3J = 7.2$ Hz, 2H), 7.06 (t, $^3J = 7.2$ Hz, 2H); $^{13}C\{^1H\}$ NMR (CD_2Cl_2): δ 22.04 (*C*H_2 ring γ to CO), 27.26 (*C*H_2 ring β to CO), 54.36 (C_α^*), 61.59 (N*C*H_2 ring), 68.58 (Ar*C*H_2N), 70.34 (*C*H_3), 121.02 (*C*m to C_{ipso}), 125.24 (*C*p to C_{ipso}), 144.98 (Ar*C*CH_2N), 150.62 (C_{ipso}), 176.80 (*C*O).

4.8. 2,6-Bis[[(*S*)-2-(methoxycarbonyl)-1-pyrrolidinyl]-methyl]phenylpalladium(II) hexafluorophosphate 3a

An excess of NH_4PF_6 (0.5 g) in water (5 mL) was added to a solution of **1a** (0.18 mmol, 101 mg) in methanol (7 mL) and the formation of a yellowish precipitate was observed. The reaction mixture was stirred for 30 min at ambient temperature. Subsequently, water (7 mL) was added to the reaction mixture followed by filtration. The product was redissolved in acetone, precipitated with Et_2O and dried in vacuo to give a white solid in 68% yield (77 mg). Crystals suitable for X-ray analysis were obtained by slow diffusion of Et_2O into an acetone solution. Anal. Calcd for $C_{20}H_{27}N_2O_4PdPF_6$: C, 39.32; H, 4.45; N, 4.58. Found: C, 39.18; H, 4.27; N, 4.41; ESI-MS *m*/*z*: 465.16 ($(M-PF_6)^+$, calcd 465.10); $[\alpha]_D^{21} = +48.9$ (*c* 0.5, acetone); IR *v* (cm^{-1}): 3418 (m), 2961 (m), 1740 (s), 1664 (s), 1442 (m), 1232 (m), 1095 (m), 841 (s, PF_6), 769 (m); ^1H NMR (CD_2Cl_2): δ 2.07–2.22 (m, 6H, CH_2 ring, γ and β to CO), 2.43–2.49 (m, 2H, CH_2 ring, β to CO), 3.10–3.17 (m, 2H, NCH_2 ring), 3.84–3.89 (m, 4H, NCH_2 ring + $C^*_\alpha H\alpha$), 3.92 (s, 6H, $2CH_3$), 3.93 and 4.52 (d, AX, 4H, $^2J =$ 14.7 Hz, $ArCH_2N$), 6.85 (d, $J = 7.5$ Hz, 2H), 7.07 (t, $J = 7.5$ Hz, 2H); $^{13}C\{^1H\}$ NMR (CD_2Cl_2): δ 22.50 (*C*H_2 ring γ to CO), 27.85 (*C*H_2 ring β to CO), 54.54 (C^*), 62.20 (N*C*H_2 ring), 69.46 (Ar*C*H_2N), 71.24 (*C*H_3), 121.42 (*C*m to CPd), 125.88 (*C*p to C_{ipso}), 145.57 (Ar*C*CH_2N), 150.6 (C_{ipso}), 177.2 (*C*O).

4.9. 2,6-Bis[[(*S*)-2-(benzyloxycarbonyl)-1-pyrrolidinyl]-methyl]phenylpalladium(II) tetrafluoroborate 2b

To a solution of **1b** (1.66 mmol, 1.2 g) in 30 mL of acetone/water (10:1, 30 mL) mixture was added solid $AgBF_4$ (1.66 mmol, 3.4 g). The reaction mixture was stirred for 30 min. Filtration of the resulting suspension through Celite yielded a yellow filtrate. The solvent was removed in vacuo to leave the title compound as a beige solid in 87% yield (1.02 g). Anal. Calcd for $C_{32}H_{35}N_2O_4PdBF_4$: C, 54.53; H, 5.00; N, 3.97. Found: C, 54.64; H, 4.89; N, 3.84; ESI-MS *m*/*z*: 617.12 ($(M-BF_4)^+$, calcd 617.16); $[\alpha]_D^{21} = +22.0$ (*c* 0.5, acetone); IR *v* (cm^{-1}): 2958 (w), 1740 (s), 1652 (s), 1457 (m), 1236 (m), 1185 (m), 1049 (s, BF_4), 922 (m), 748 (m), 697 (m); ^1H NMR (CD_2Cl_2): δ 2.02–2.09 (m, 4H, CH_2 ring, γ to CO), 2.11–2.21 (m, 2H, CH_2 ring, β to CO), 2.44–2.52 (m, 2H, CH_2 ring, β to CO), 2.99–3.08 (m, 2H, NCH_2 ring), 3.64–3.72 (m, 2H, NCH_2 ring), 3.92 and 4.54 (d, AX, 4H, $^2J = 14.7$ Hz, $ArCH_2N$), 3.96–3.4 (m, 2H, $C^*_\alpha H\alpha$), 5.30 and 5.35 (d, AX, 4H, $^2J = 12.3$ Hz, CO_2CH_2Ph), 6.84 (d, 2H, $^3J =$ 7.2 Hz), 7.06 (t, 1H, $^3J = 8.1$ Hz), 7.38–7.44 (m, 10H, Ph); $^{13}C\{^1H\}$ NMR (CD_2Cl_2): δ 23.51 (*C*H_2 ring γ to CO), 28.98 (*C*H_2 ring β to CO), 63.29 (N*C*H_2 ring), 70.52 (Ar*C*H_2N), 70.75 (O*C*H_2Ph), 72.47 (C^*_α), 122.367 (*C*m to C_{ipso}), 126.42 (*C*p to C_{ipso}), 130.12 (*C*m of OCH_2Ph), 130.23 (*C*o of OCH_2Ph), 130.46 (*C*p of OCH_2Ph), 135.98 (C_{ipso} of OCH_2Ph), 146.74 (Ar*C*CH_2N), 151.73 (C_{ipso}), 177.64 (*C*O).

4.10. 2,6-Bis[[(*S*)-2-(benzyloxycarbonyl)-1-pyrrolidinyl]-methyl]phenylpalladium(II) hexafluorophosphate 3b

An excess of NH_4PF_6 (0.77 g) in water (8 mL) was added to a solution of **1b** (0.17 mmol, 116 mg) in methanol (8 mL) and the formation of a yellowish precipitate was observed. The reaction mixture was stirred for 16 h at ambient temperature. Subsequently, water (8 mL) was added to the reaction mixture followed by filtration. The product was redissolved in acetone, precipitated with Et_2O and dried in vacuo. The product was isolated as a white solid in 95% yield (120 mg). Anal. Calcd for $C_{32}H_{35}N_2O_4PdPF_6$: C, 50.37; H, 4.62; N, 3.67. Found: C, 50.26; H, 4.69; N, 3.60. ESI-MS *m*/*z*: 616.97 ($(M-PF_6)^+$, calcd 617.16); $[\alpha]_D^{21} = +56.42$ (*c* 0.615, acetone); IR *v* (cm^{-1}): 2966 (m), 1734 (s), 1656 (s), 1456 (m), 1264 (m), 1223 (m), 1179 (m), 1094 (m), 831 (s, PF_6), 754 (m); ^1H NMR (CD_2Cl_2): δ 2.02–2.09 (m, 4H, CH_2 ring, γ to CO), 2.12–2.22 (m, 2H, CH_2 ring, β to CO), 2.42–2.51 (m, 2H, CH_2 ring, β to CO), 2.99–3.08 (m, 2H, NCH_2 ring), 3.64–3.72 (m, 2H, NCH_2 ring), 3.93 and 4.51 (d, AX, 4H, $^2J = 14.4$ Hz, $ArCH_2N$), 3.89–3.95 (m, 2H, $C^*_\alpha H\alpha$), 5.31 and 5.35 (d, AX, 4H, $^2J = 12.3$ Hz, CO_2CH_2Ph), 6.83 (d, 2H, $^3J = 7.8$ Hz), 7.06 (t, 1H, $^3J = 7.2$ Hz), 7.4 (m, 10H, Ph); $^{13}C\{^1H\}$ NMR (CD_2Cl_2): δ 23.54 (*C*H_2 ring γ to CO), 29.03 (*C*H_2 ring β to CO), 63.31 (N*C*H_2 ring), 70.59 (Ar*C*H_2N), 70.86 (O*C*H_2Ph), 72.51 (C^*_α), 122.64 (*C*m to C_{ipso}), 127.18 (*C*p to C_{ipso}), 130.18 (*C*m of OCH_2Ph), 130.34 (*C*o of OCH_2Ph), 130.60 (*C*p of OCH_2Ph), 135.75 (C_{ipso} of OCH_2Ph), 146.46 (Ar*C*CH_2N), 151.60 (C_{ipso}), 177.20 (*C*O).

4.11. General procedure for the decomplexation of the cationic complexes 3 and 4 with LiBr to neutral complexes 2

A solution of cationic complex in CH_2Cl_2 and excess of LiBr (10 mol equiv) was stirred for 16 h at ambient temperature. The solvent was removed in vacuo, $LiBF_4$ and the excess of LiBr was removed from the product by extraction with water. The neutral complexes were isolated in quantitative yields and analyzed by ^1H NMR spectroscopy.

4.12. General procedure for aldol condensation of methyl α-isocyanoacetate with benzaldehyde

To a solution of palladium complex (0.016 mmol, 1 mol%) in CH_2Cl_2 (5 mL) was sequentially added methyl α-isocyanoacetate (145 μl, 1.6 mmol), benzaldehyde (162 μl, 1.6 mmol) and diisopropylethylamine (28 μl, 0.16 mmol). The reaction mixture was stirred at room temperature and monitored by GC with pentadecane as the internal standard. The ratio of *cis*- and *trans*-isomers was determined by GC and ee% in the isomers by HPLC using chiral column Daicel CHIRACEL OD, UV detector 210 nm, hexane:*i*-PrOH=95:5.

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