# New chiral diamide ligands containing redox-active hydroquinone groups. Synthesis and results in the palladium(II)-catalyzed 1,4-diacetoxylation of 1,3-dienes

Renzo C. Verboom [a], Bernd J. Plietker [b,1], Jan-E. Bäckvall [a,*]

[a] *Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, SE-106 91 Stockholm, Sweden*
[b] *Organic Chemistry II, Dortmund University, D-44221 Dortmund, Germany*

Dedicated to Professor Jean-Pierre Genêt on the occasion of his 60th birthday

## Abstract

Chiral ligands **8–11**, **22** and **23** were synthesized from different chiral diamines as a new class of ligands for the Pd(II)-catalyzed 1,4-diacetoxylation of 1,3-dienes. The synthesis from the diamines and protected benzoic acids was performed in a few simple steps and gave the ligands in high overall yields. The hydroquinone groups present in the ligands are in situ oxidized to benzoquinone to give the active ligands. Application of these ligands in the 1,4-diacetoxylation reaction afforded the oxidation product with high regio- and diastereoselectivity and an enantiomeric excess up to 42% was obtained. Possible coordination modes of the metal to the ligand are discussed, and experiments were made to investigate the coordination by varying the reaction conditions or making changes to the ligands.
© 2003 Elsevier B.V. All rights reserved.

*Keywords:* Asymmetric catalysis; Oxidation; Palladium; Ligand design; Dienes

## 1. Introduction

Reactions of carbon–carbon double bonds are of central importance in organic chemistry. A large number of processes have been developed for the transformation of carbon–carbon double bonds, and during the last two decades processes based on metal-mediated reactions have become increasingly important. Of all metals used for reactions of this kind, palladium has become one of the most diverse [1].

The palladium(II)-catalyzed 1,4-oxidation of 1,3-dienes has been shown to be useful for oxidative functionalization of conjugated dienes, thereby introducing a large variety of nucleophiles in the 1- and 4-positions of 1,3-dienes [2]. Carboxylic acids [3], alcohols

[4], halides [5], functionalized amines [6], and masked carbon nucleophiles [7] can be added to the diene to give the 1,4-oxidized products in high yields and with good control of the regio- and stereoselectivity (Scheme 1). Cyclic as well as acyclic dienes can be used, and both intermolecular and intramolecular versions of the reactions have been developed. In many cases the bis-allylic products can be used for further synthetic transformations [5,8,9]. The versatility of the 1,4-oxidation reaction has been demonstrated in the synthesis of a number of natural products [10–12]. We are currently working on an asymmetric version of the 1,4-oxidation reaction.

A catalytic amount of *p*-benzoquinone (BQ) is required in the 1,4-oxidation reaction for two reasons: (i) benzoquinone activates the intermediate (π-allyl)palladium(II) complex towards attack by the second nucleophile [13], and (ii) it reoxidizes the palladium(0) formed back to palladium(II) [14]. By the use of a stoichiometric amount of a terminal oxidant, such as manganese dioxide [3], or molecular oxygen together with a metal macrocyclic complex such as iron(II)

* Corresponding author. Fax: +46-8-154-908.
*E-mail addresses:* plietker@pop.uni-dortmund.de (B.J. Plietker), jeb@organ.su.se (J.-E. Bäckvall).
[1] Fax: +49-234-755-3884.
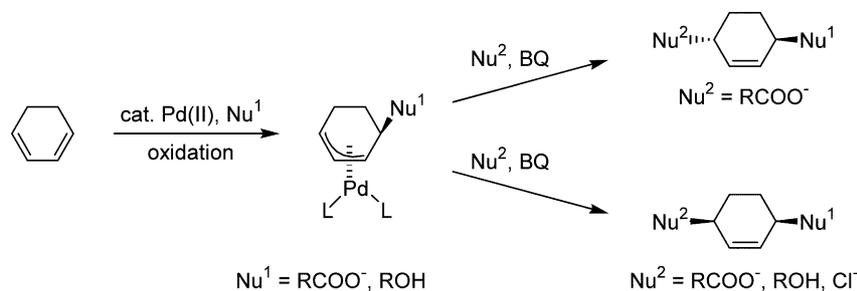
Scheme 1. 1,4-oxidation of dienes with different nucleophiles.

phthalocyanine (Fe(Pc)) [15], the hydroquinone formed in this process is reoxidized to benzoquinone. Because of the close proximity of benzoquinone to palladium, at least during the nucleophilic attack on the (π-allyl) intermediate, we have introduced the use of chiral benzoquinone ligands (BQ*) to induce enantioselectivity in the 1,4-oxidation reaction. Indeed, such ligands have been shown to generate a moderate enantioselectivity. Thus, chiral sulfoxide-substituted benzoquinone ligand **1b** (Fig. 1) gave 45% e.e. in the 1,4-diacetoxylation reaction [16], and $C_2$-symmetric chiral amide **2** afforded 54% e.e in the 1,4-dialkoxylation reaction [17].

To gain further insight into the mechanism of the 1,4-diacetoxylation reaction, we recently studied the intermediate (π-allyl)palladium complexes of this reaction in acetic acid solutions [18]. It was found that an equilibrium exists between the diene and the two enantiomeric *trans*-4-acetoxy-[$\eta^3$-(1,2,3)-cyclohexenyl]palladium complexes, and that the rate of this equilibrium is increased by the addition of either acetate or methanesulfonic acid. Treatment of racemic bis(4-acetoxy-2-phenyl-[$\eta^3$-(1,2,3)-cyclohexenyl])palladium acetate complex with a stoichiometric amount of a chiral sulfoxide ligand **1c**, in the presence of acetate, gave the 1,4-oxidation product in almost 50% enantiomeric excess in the very beginning of the reaction (at low conversion), but after full conversion the enantiomeric excess had decreased to only 28%. This shows that the nucleophilic attack on the (π-allyl)palladium(BQ*)-complex is faster than the acetate exchange reaction via the diene. It also implies that a fully dynamic system is not operative under the reactions conditions and emphasizes the need for the formation of only one of two possible diastereomeric (π-allyl)palladium(BQ*)-complexes from the diene. With the ligands used so far, it is unclear whether they

coordinate to the metal and exert their chiral information throughout the entire catalytic cycle.

It is well-known that bidentate ligands can form stable complexes upon coordination to a metal atom, and the advantage of such complexes in catalysis is illustrated by the increased use of bidentate ligands over the past decades [19]. More recently, their importance in asymmetric catalysis has increased. We envisioned that bidentate ligands in our reaction would lead to more stable palladium-ligand complexes that would not release the ligands at any stage of the reaction, and hence could provide a higher enantioselectivity. We have therefore designed and synthesized a series of new ligands, consisting of $C_2$-symmetric diamides containing redox-active hydroquinone groups. The synthesis and the results of their use in the 1,4-diacetoxylation reaction will be presented here.

## 2. Results and discussion

Amides have been used earlier as ligands for the 1,4-oxidation reaction because of their good coordinating properties to palladium [20,21]. Chiral $C_2$-symmetric diamides have a high conformational rigidity as a result of the amide bond, where rotation about the C–N bond is prohibited by the partial double bond character of this bond. For practical reasons, the hydroquinone form of the ligands was synthesized. A schematic model of the new ligands and the in situ oxidation to the benzoquinone form is given in Fig. 2.

For the ligand backbones, four different $C_2$-symmetric diamines were used: ( − )-(1R,2R)-1,2-diaminocyclohexane, ( + )-(R)-1,1′-binaphthyl-2,2′-diamine, ( + )-(11S,12S)-11,12-diamino-9,10-dihydro-9,10-ethanoanthracene and ( − )-(1S,2S)-1,2-diphenyl-1,2-ethanediamine. These diamines have dihedral angles of approximately 60, 90, 120° and a more variable angle, respectively, between the two C–N bonds (Fig. 3). The free rotation in 1,2-diphenyl-1,2-ethanediamine allows the ligand derived from it to coordinate to palladium with the optimal chelation angle. It is known that this angle can have a profound effect on the enantioselec-
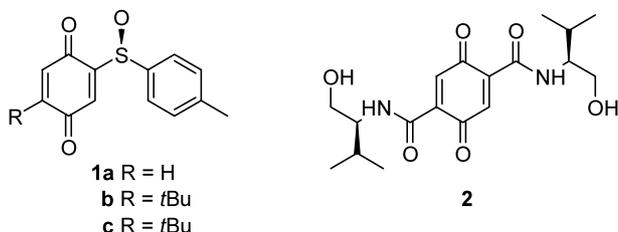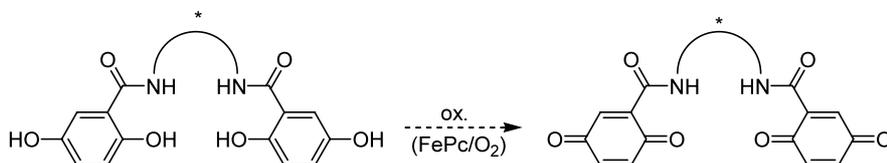


1a R = H
b R = tBu
c R = tBu

2

Fig. 1.

Fig. 2.

tivity in for instance Pd(0)-catalyzed asymmetric allylic alkylation reactions [22,23].

The synthesis of ligands **8–11** was performed in three simple steps starting from the four diamines mentioned before and commercially available 1-bromo-2,5-dimethoxybenzene (Scheme 2). Lithiation followed by carboxylation gave 68% yield of 2,5-dimethoxy-benzoic acid (**3**). Compound **3** was then transformed into the corresponding acid chloride, which was directly used for acylation of the diamines. The highest yields were obtained when the benzoic acid chloride was used in large excess relative to that of the diamine, and a 3.5:1 ratio gave diamides **4–7** in more than 90% yield. Deprotection of the methoxy groups was performed with excess boron tribromide [24] in $CH_2Cl_2$ at $-78\,^{\circ}C$, and gave ligands **8–11** in 81–93% yield.

Ligands **8–11** were tested in the 1,4-diacetoxylation reaction with 2-phenyl-1,3-cyclohexadiene (**12**) as the test substrate, using 10 mol% Pd(OAc)$_2$, 10 mol% ligand and 0.4 M LiOAc in HOAc–acetone 4:1. The above mentioned Fe(Pc)/O$_2$ system was applied for the (re)oxidation of hydroquinone. The results are shown in Table 1 (entries 1–4). The 1,4-diacetoxylation product (**13**) was formed exclusively and none of the 1,2-oxidation product was observed. The *trans*-selectivity in the 1,4-addition was in the range 88–91%. The formation of **13** was slower than in the corresponding reaction using benzoquinone, which can explain the moderate yields [25]. Except for ligand **9**, which gave racemic product only, the enantiomeric excess was moderate. Ligand **10** proved best and gave 40% yield and 39% e.e. (entry 3), very close to our 'old record' of 45% e.e. with sulfoxide ligand **1b**. However, **10** gave a much higher diastereo-

meric ratio. Ligands **8** and **11** gave an enantioselectivity of 26 and 22%, respectively (entries 1 and 4).

The higher enantioselectivity with ligand **10** when compared to ligands **8** and **11** is likely a result of the different dihedral angles between the two C–N bonds, where the larger angle of $\sim 120^{\circ}$ in **10** gives a higher enantioselectivity than the $\sim 60^{\circ}$ angle in **8**, in accordance with the results by Trost et al. [22]. In ligand **11** the angle is variable due to free rotation around the central C–C bond, which can result in good chelation of palladium, but with an angle which might be insufficient for a high enantioselectivity. The similar results with ligands **8** and **11**, however, suggest that **11** adopts a conformation to coordinate the metal center with an angle of approximately the same size as in **8**.

One of the purposes with bidentate ligands is that the formation of a chelate will guarantee a strong coordination of the ligand. Many studies have been performed on the mode and strength of coordination of metals to amides. Pd(II) is one of the most effective metal ions in the promotion of amide hydrogen ionisation in peptides [20,26–28], and a number of Pd(II)-containing amide-macrocycles have been prepared and isolated, in which the palladium ion coordinates to the amide nitrogen atoms. In some complexes containing pyridinecarboxamide groups, deprotonation occurs readily and the actual deprotonated amide nitrogens were observed [29,30]. Fig. 4 schematically shows the chelates that can be formed with the ligands discussed in this article. Complexation can in principle take place both through the amide (**A**) and the iminol (**B**) form. Based on spectroscopy data on 14-membered tetraazamacrocyclic complexes of Pd(II), where IR-measurements showed the absence of the azomethine group and the presence of
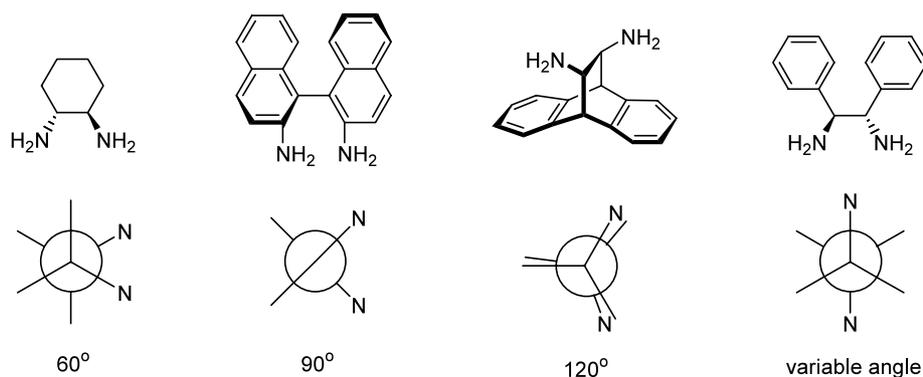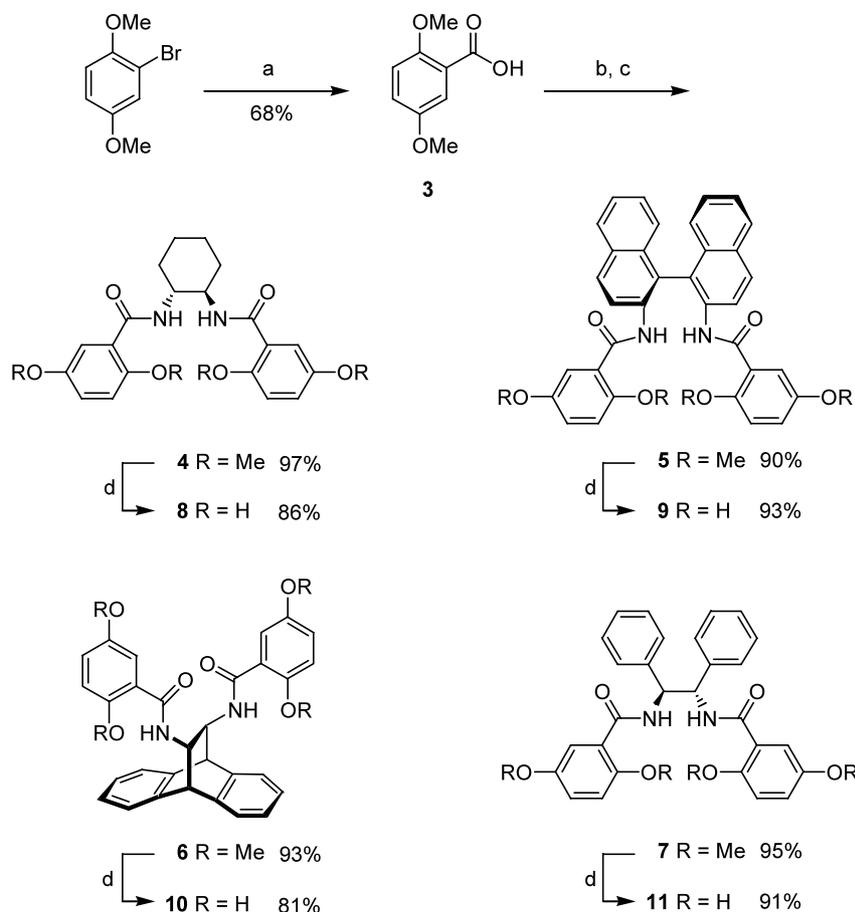


Fig. 3.

Scheme 2. Synthesis of ligands **8–11**. Reagents and conditions: (a) *n*-BuLi, − 78 °C, then $CO_2$; (b) $SOCl_2$, reflux; (c) diamine, $Et_3N$, $CH_2Cl_2$, 0 °C to r.t.; (d) $BBr_3$, $CH_2Cl_2$, − 78 °C.

metal-bonded nitrogen atoms [31], coordination through the iminol form of the ligands can probably be ruled out. Ionization of amide hydrogens occurs at low pH with Pd(II) complexation, and complexes with $pK_a$ values as low as 3.5 have been reported [26–28]. Whether $Pd(OAc)_2$ is able to deprotonate amides in

Table 1
1,4-Diacetoxylation reactions in the presence of ligands **8–11**
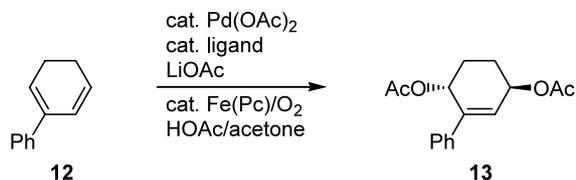


| Entry | Ligand | [LiOAc] (M) | Yield of **13** (%) [a] | *Trans*:*cis* ratio [b] | e.e. (%) [c] |
|---|---|---|---|---|---|
| 1 | **8** | 0.4 | 38 | 89:11 | 26 |
| 2 | **9** | 0.4 | 23 | 88:12 | < 5 |
| 3 | **10** | 0.4 | 40 | 91:9 | 39 |
| 4 | **11** | 0.4 | 16 | 89:11 | 22 |
| 5 | **10** | 0.25 | 45 | 88:12 | 26 |
| 6 | **10** | 1.0 | 27 | 85:15 | 42 |

Reactions were run on a 50-mg scale. See Section 4 details.
[a] Isolated yield.
[b] Determined by HPLC.
[c] Determined by HPLC. In entries 1 and 4 the major enantiomer is opposite to that of the other entries.
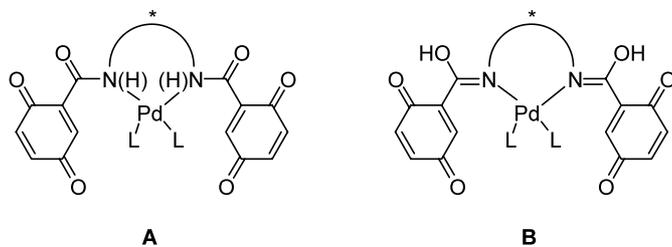
Fig. 4.

acetic acid solutions as used here is not known. A higher acetate concentration could enhance the deprotonation and promote stronger chelate formation, resulting in higher enantioselectivities. To investigate if this was the case, ligand **10** was used with varying acetate concentrations under otherwise similar reaction conditions. With 0.25 M LiOAc, the enantioselectivity was lower (26% e.e., entry 5). As mentioned before, 39% e.e. was obtained with 0.4 M LiOAc (entry 3). With 1.0 M LiOAc a slightly higher enantioselectivity was obtained (42% e.e.) but this was accompanied by a lower yield and decreased diastereoselectivity [32] (*trans*:*cis* = 85:15) (entry 6). Thus, the acetate concentration has indeed an effect on the enantioselectivity, but concentrations higher than 0.4 M are probably not beneficial for the efficiency of the reaction.

If the N–Pd–N chelate is not exclusively formed, other ways of interaction between the metal and the ligand are possible. For instance, hydrogen bonding between the amide hydrogen and the benzoquinone oxygen would make coordination of palladium to the amide nitrogen impossible, and thereby leave the outer, non-substituted C–C double bond of the benzoquinone moiety available for coordination (**C** in Fig. 5). With palladium this far from the chiral center, the role of the chiral ligand would be reduced to nothing more than a simple source of benzoquinone. The chiral information would not be transferred to the product, and this could be a possible explanation for the moderate e.e. observed. We therefore argued that steric hindrance at this outer position could prevent coordination of palladium to this C–C double bond and force the metal to the ligand center (**D**). A *tert*-butyl substituent was therefore introduced at the unsubstituted C–C double bond. Moreover, it was previously shown that such a substituent provided extra stability to the benzoquinone

ligand by protecting it against acid-catalyzed degradation [16]. This was reflected by the higher yield of diacetoxylation product **13** that was obtained with ligand **1b** (R′ = *t*Bu) compared to that with **1a** (R′ = H).

Thus, the ligands containing the *tert*-butyl substituents were synthesized as shown in Scheme 3. The protected benzoic acid **16** was prepared from *tert*-butylhydroquinone in three steps. After methylation of the two hydroxy groups, monobromination of the benzene ring gave **15** as the major isomer. Lithiation and subsequent carboxylation gave **16** in an overall yield of 43%. Following the same procedure as the acylation as described above, **17–20** were obtained in 90–98% yield. The final deprotection using excess boron tribromide gave ligands **22** and **23** in 93 and 80% yield, respectively. However, this deprotection method did not work for compounds **21** and **24**.

Deprotection of **17** and **20** with BBr₃ at −78 °C gave only partially deprotected products. Raising the temperature still gave partial deprotection (0 °C) or even led to degradation of the products to the carboxylic acid (room temperature). Dealkylation of the methyl ethers of **19** with trimethylsilyl iodide [33], prepared in situ from trimethylsilyl chloride and sodium iodide [34] in acetonitrile at 70 °C, also failed and gave only partial hydrolysis, even after longer reaction times (2 days). Oxidative dealkylation of **16** and **19** with cerium(IV) ammonium nitrate (CAN) in acetonitrile [35], a reaction that would give the benzoquinone products, indeed afforded these products according to TLC. However, they could be isolated in only low yield and were contaminated with several other products from which they could not be separated. No further efforts were made to deprotect these two compounds.

Compounds **22** and **23** were tested as ligands in the diacetoxylation reaction using 0.4 M LiOAc, and the corresponding values for the e.e. are presented in Table 2. Contrary to the expectations, the yield of **13** was not improved when compared to the results with the ligands without the *tert*-butyl groups. The diastereomeric ratio remained unaffected and was still high, with a *trans*:*cis* ratio up to 93:7. Ligand **23** gave 24% of product **13** but with only 22% e.e., a decrease in enantioselectivity when compared to ligand **10**, indicating that the extra substituent does not have a positive influence on the
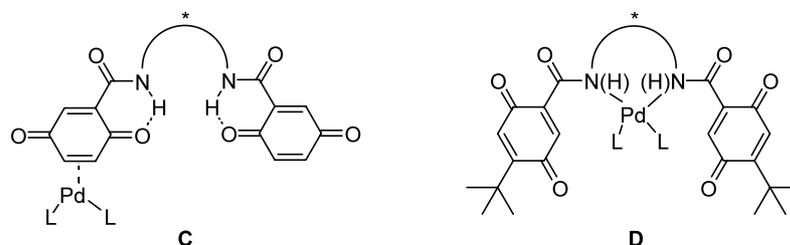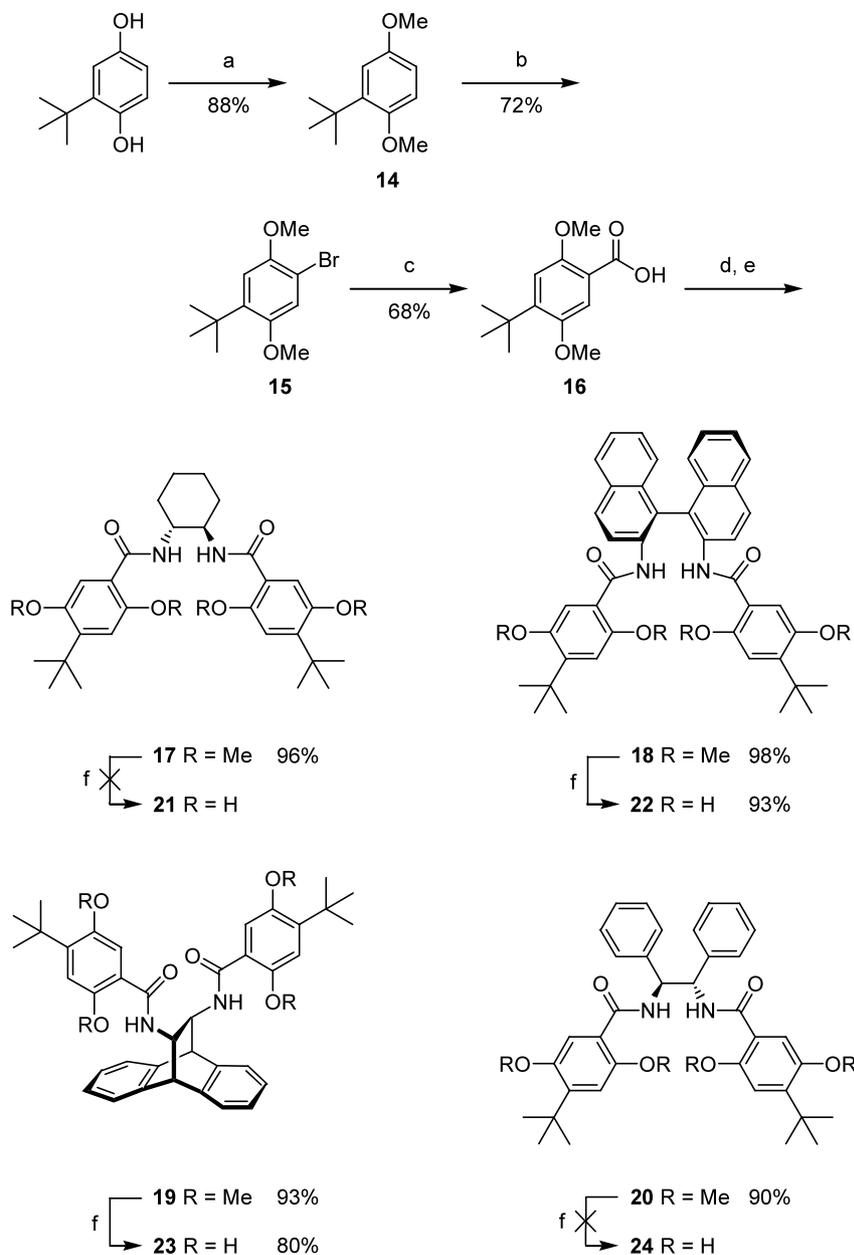


Fig. 5.

Scheme 3. (Attempted) synthesis of ligands **21–24**. Reagents and conditions: (a) K$_2$CO$_3$, MeI, DMF, 60 °C; (b) Br$_2$, HOAc, r.t.; (c) *n*-BuLi, −78 °C, then CO$_2$; (d) SOCl$_2$, reflux; (e) diamine, Et$_3$N, CH$_2$Cl$_2$, 0 °C to r.t.; (f) BBr$_3$, CH$_2$Cl$_2$, −78 °C.

enantioselectivity. Ligand **22** gave racemic product as its unsubstituted analogue **9** also did.

The lower yield and decrease in enantiomeric excess, from 39% with ligand **10** to only 22% with ligand **23**, caused by the introduction of *tert*-butyl groups to the ligand, is evidence of a less effective coordination. The extra substituents may indeed have rendered the ligands more sterically crowded, preventing palladium from coordinating to the C–C double bond away from the amide-group, but this did not lead to a more proper chelation of the metal. Instead, coordination may have become simply impossible resulting in a low yield. Moreover, the benzoquinone ring might have become

more electron-rich and the intramolecular hydrogen-bonding (as shown in **C**) might have been enhanced. This would also leave less benzoquinone available to palladium and result in both lower yield and enantios-electivity.

The lack of any enantioselectivity induced by ligands **9** and **22** could be explained by the bridge length between the two amide groups, which is two carbons longer than in the other ligands. The seven-membered chelates that could be formed with these ligands are probably weaker than their five-membered analogues, and inefficient binding of palladium with both nitrogen atoms would explain the loss of enantioselectivity.

Table 2
Diacetoxylation reactions in the presence of ligands **22** and **23**
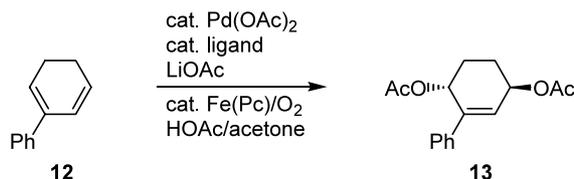


| Entry | Ligand | [LiOAc] (M) | Yield of **13** (%) [a] | *Trans*:*cis* ratio [b] | e.e. (%) [c] |
|-------|--------|-------------|--------------------------|--------------------------|---------------|
| 1 | **22** | 0.4 | 15 | 90:10 | < 5 |
| 2 | **23** | 0.4 | 24 | 93:7 | 22 |

Reactions were run on a 50-mg scale. See Section 4 for details.
[a] Isolated yield.
[b] Determined by HPLC.
[c] Determined by HPLC.

## 3. Conclusions

We have synthesized a series of new enantiopure ligands for the asymmetric palladium(II)-catalyzed 1,4-diacetoxylation of conjugated dienes. The ligands are $C_2$-symmetric diamides and contain hydroquinone groups that can be oxidized in situ to benzoquinones, which are used for the reoxidation of Pd(0) to Pd(II). The synthesis was performed in a few simple steps from 4 different chiral diamines and gave the ligands in good yields.

We have applied the ligands in the 1,4-diacetoxylation reaction where they gave a moderate chiral induction. The oxidation product was obtained with high regio- and diastereoselectivity, and an enantiomeric excess up to 42% was reached. In terms of yield and diastereoselectivity, this is a slight improvement compared to ligands that have been developed earlier.

The introduction of extra substituents on the ligand, thought to direct the metal to the amide nitrogen atoms in the center of the ligand, was not successful and led to a decrease in both yield and enantioselectivity.

## 4. Experimental

### 4.1. General remarks

[1]H- (400 or 300 MHz) and ^{13}C- (100 or 75 MHz) NMR spectra were recorded on a Varian spectrometer. Chemical shifts ($\delta$) are reported in ppm, using residual solvent proton resonance or tetramethylsilane as internal standard. For all characterized compounds, the ^{13}C-NMR signals correspond to two carbons due to $C_2$-symmetry. Optical rotations were obtained on a Perkin–Elmer 241 Polarimeter. Analytical high-pressure chromatography (HPLC) was performed on a Waters liquid chromatograph. Elemental analysis was performed by Analytische Laboratorien, Lindlar, Germany. MALDI-TOF spectra were recorded on a Bruker Biflex III instrument. Merck silica gel 60 (240–400 mesh) was used for flash chromatography, and analytical thin-layer chromatography was performed on Merck precoated silica gel 60-F$_{254}$ plates. Tetrahydrofuran (THF) was freshly distilled under nitrogen from sodium benzophenone ketyl prior to use. Methylene chloride (CH$_2$Cl$_2$) was distilled from calcium hydride. ( − )-(1*R*,2*R*)-1,2-Diaminocyclohexane was purchased from Fluka, (+)-(*R*)-1,1′-binaphthyl-2,2′-diamine from Aldrich and ( − )-(1*S*,2*S*)-1,2-diphenyl-1,2-ethanediamine from Lancaster in > 98% optical purity. (+)-(11*S*,12*S*)-11,12-Diamino-9,10-dihydro-9,10-ethanoanthracene [22] (96% optical purity) was prepared by a Curtius degradation of ( − )-9,10,-dihydro-9,10-ethanoanthracene-11,12-dicarboxylic acid [36]. 2,5-dimethoxybenzoic acid (**3**) [37] and 4-*tert*-butyl-2,5-dimethoxybenzoic acid (**16**) [38] were prepared following literature procedures, and the NMR data were in agreement with literature. 2-Phenyl-1,3-cyclohexadiene (**12**) was prepared by a method developed in our laboratories [39].

### 4.1.1. ( +)-(R,R)-N,N′-bis-(2′,5′-Dimethoxy-benzamido)-1,2-cyclohexane (4). General procedure

2,5-Dimethoxybenzoic acid (1.44 g, 7.9 mmol) was dissolved in 5 ml thionyl chloride and the solution was refluxed for 2 h. After cooling to room temperature (r.t.), the solvent was evaporated in vacuo, and coevaporated three times with 5 ml toluene. ( − )-(1*R*,2*R*)-1,2-Diaminocyclohexane (0.26 g, 2.3 mmol) was dissolved in 7 ml CH$_2$Cl$_2$, triethylamine (1.26 ml, 9.0 mmol) was added and the solution was cooled to 0 °C and stirred under argon. The acid chloride was dissolved in 3 ml CH$_2$Cl$_2$ and added to the solution from a syringe during five minutes. The solution was stirred for 14 h. Et$_2$O (25 ml) was added, and the organic phase was washed with water, saturated aqueous sodium bicarbonate (twice)

and water. The organic layer was dried over $Na_2SO_4$, and the solvent was removed in vacuo. The residue was purified by silica chromatography (petroleum ether–EtOAc 1:4) to give 977 mg (97%) of **4** as a beige solid. $[\alpha]_D^{25}$ +21.0° (*c* 1.76, CHCl$_3$); $^1$H-NMR (400 MHz, CDCl$_3$, 25 °C): $\delta$ 1.31–1.52 (m, 4H), 1.78–1.85 (m, 2H), 2.22–2.30 (m, 2H), 3.77 (s, 6H), 3.82 (s, 6H), 4.03–4.10 (m, 2H), 6.81–6.84 (d, *J* = 9.2 Hz, 2H), 6.91–6.95 (dd, *J* = 3.2, 9.2 Hz, 2H), 7.67 (d, *J* = 3.2 Hz, 2H), 8.10–8.16 (br d, *J* = 7.6 Hz, 2H, NH); $^{13}$C-NMR (100 MHz, CDCl$_3$, 25 °C): $\delta$ 24.92, 32.90, 53.28, 55.77, 56.37, 112.90, 115.77, 118.76, 122.18, 151.97, 153.64, 165.09. Anal. Calc. for $C_{24}H_{30}N_2O_6$: C, 65.14; H, 6.83; Found: C, 65.36; H, 6.81%.

### 4.1.2. (+)-(R)-N,N′-bis-(2′,5′-Dimethoxy-benzamido)-2,2′-binaphthalene (5)

According to the procedure for the preparation of **4**, **5** was obtained from (+)-(R)-1,1′-binaphthyl-2,2′-diamine in 90% as a beige solid. $[\alpha]_D^{24}$ +13.4° (*c* 1.08, CHCl$_3$); $^1$H-NMR (300MHz, CDCl$_3$, 25 °C): $\delta$ 2.95 (s, 6H), 3.75 (s, 6H), 6.58–6.62 (d, *J* = 9.0 Hz, 2H), 6.84–6.90 (dd, *J* = 3.3, 9.0 Hz, 2H), 7.02–7.07 (br d, 2H), 7.21–7.27 (ddd, *J* = 1.3, 6.9, 8.2 Hz, 2H), 7.38–7.44 (ddd, *J* = 1.3, 6.9, 8.2 Hz, 2H), 7.70 (d, *J* = 3.3 Hz, 2H), 7.92–7.96 (br d, 2H), 8.08–8.13 (d, *J* = 9.1 Hz, 2H), 9.02–9.07 (d, *J* = 9.1 Hz, 2H), 9.78 (br s, 2H, NH); $^{13}$C-NMR (75 MHz, CDCl$_3$, 25 °C): $\delta$ 55.57, 55.75, 112.69, 115.39, 120.01, 120.28, 121.50, 121.75, 125.27, 127.19, 128.01, 129.44, 131.05, 132.91, 136.57, 151.71, 153.60, 163.50. Anal. Calc. for $C_{38}H_{32}N_2O_6$: C, 74.49; H, 5.26; Found: C, 74.18; H, 5.37%.

### 4.1.3. (+)-(11S,12S)-N,N′-bis-(2′,5′-Dimethoxy-benzamido)-9,10-dihydro-9,10-ethanoanthracene (6)

According to the procedure for the preparation of **4**, **6** was obtained from (+)-(11S,12S)-diamino-9,10-dihydro-9,10-ethanoanthracene in 93% as a beige solid. $[\alpha]_D^{28}$ +55.9° (*c* 1.02, MeOH); $^1$H-NMR (300 MHz, CDCl$_3$, 25 °C): $\delta$ 3.52 (s, 6H), 3.79 (s, 6H), 4.34–4.40 (m, 2H), 4.52 (d, *J* = 3.0 Hz, 2H), 6.77–6.80 (d, *J* = 9.0 Hz, 2H), 6.92–6.97 (dd, *J* = 3.3, 9.0 Hz, 2H), 7.18–7.29 (m, 4H), 7.31–7.37 (m, 2H), 7.44–7.48 (m, 2H), 7.70 (d, *J* = 3.3 Hz, 2H), 7.88–7.94 (br d, *J* = 8.7 Hz, 2H, NH); $^{13}$C-NMR (75 MHz, CDCl$_3$, 25 °C): $\delta$ 49.50, 55.79, 55.99, 57.34, 112.82, 115.37, 119.37, 121.60, 124.98, 125.92, 126.38, 126.68, 139.58, 140.81, 151.79, 153.69, 164.31.

### 4.1.4. (−)-(1S,2S)-N,N′-bis-(2′,5′-Dimethoxy-benzamido)-1,2-diphenylethane (7)

According to the procedure for the preparation of **4**, **7** was obtained from (−)-(1S,2S)-1,2-diphenyl-1,2-ethanediamine in 95% as a beige solid. $[\alpha]_D^{27}$ −50.3° (*c* 0.62, CHCl$_3$); $^1$H-NMR (400 MHz, CDCl$_3$, 25 °C): $\delta$ 3.76 (s, 6H), 3.85 (s, 6H), 5.58–5.61 (m, 2H), 6.83–6.86 (d, *J* = 8.8 Hz, 2H), 6.93–6.97 (dd, *J* = 3.2, 8.8 Hz, 2H), 7.14–

7.24 (m, 10H), 7.70 (d, *J* = 3.2 Hz, 2H), 8.89–8.95 (m, 2H, NH); $^{13}$C-NMR (100 MHz, CDCl$_3$, 25 °C): $\delta$ 55.77, 56.44, 59.00, 112.84, 115.71, 119.29, 121.72, 127.52, 127.78, 128.34, 139.49, 152.08, 153.69, 164.93. MALDI-TOF MS: Calc. for $C_{32}H_{32}N_2O_6$: 541.2334; Found: 541.2518 [M]$^+$.

### 4.1.5. (−)-(R,R)-N,N′-bis-(2′,5′-Dihydroxy-benzamido)-1,2-cyclohexane (8). General procedure

(+)-(R,R)-N,N′-bis-(2′,5′-Dimethoxy-benzamido)-1,2-cyclohexane (**4**) (856 mg, 1.93 mmol) was dissolved in $CH_2Cl_2$ (25 ml) under an argon atmosphere and cooled to −78 °C. Boron tribomide (3.7 ml, 38.7 mmol) was added dropwise from a syringe. The solution was stirred for 16 h and was allowed to slowly come to r.t. during this time. The reaction was quenched by the addition of a few ml of ether. Water and $CH_2Cl_2$ were added and the phases were separated. The organic layer was washed twice with water, dried ($Na_2SO_4$), and the solvent was removed in vacuo. Column chromatography (petroleum ether–EtOAc 1:4) gave 644 mg (86%) of **7** as a beige solid. $[\alpha]_D^{23}$ −96.4° (*c* 1.73, MeOH); $^1$H-NMR (300 MHz, acetone-$d_6$, 25 °C): $\delta$ 1.36–1.49 (m, 2H), 1.52–1.67 (m, 2H), 1.74–1.88 (m, 2H), 2.11–2.20 (m, 2H), 2.98 (s, 2H, OH), 3.98–4.12 (m, 2H), 6.66–6.70 (d, *J* = 8.7 Hz, 2H), 6.87–6.92 (dd, *J* = 2.7, 8.7 Hz, 2H), 7.14 (d, *J* = 2.7 Hz, 2H), 7.99 (s, 2H, OH), 8.02–8.08 (br d, *J* = 6.6 Hz, 2H, NH). $^{13}$C-NMR (100 MHz, acetone-$d_6$, 25 °C) $\delta$ 25.51, 30.63, 54.18, 113.05, 115.43, 119.10, 122.72, 150.01, 155.41, 170.85.

### 4.1.6. (−)-(R)-N,N′-bis-(2′,5′-Dihydroxy-benzamido)-2,2′-binaphthalene (9)

According to the procedure for the preparation of **8**, **9** was obtained from **5** in 93% as a pale brown solid. $[\alpha]_D^{23}$ −48.2° (*c* 1.77, MeOH); $^1$H-NMR (300 MHz, acetone-$d_6$, 25 °C): $\delta$ 3.04 (s, 2H, OH), 6.58-6.62 (d, *J* = 8.7 Hz, 2H), 6.78–6.83 (dd, *J* = 3.0, 8.7 Hz, 2H), 7.08–7.13 (br d, 2H), 7.15 (d, *J* = 3.0 Hz, 2H), 7.24–7.31 (ddd, *J* = 1.5, 6.9, 8.4 Hz, 2H), 7.40–7.47 (ddd, *J* = 1.5, 6.9, 8.4 Hz, 2H), 7.96–8.01 (br d, 2H), 8.09–8.14 (d, *J* = 9.0 Hz, 2H), 8.45–8.49 (d, *J* = 9.0 Hz, 2H), 9.90 (br s, 2H, OH), 10.07–10.15 (br s, 2H, NH). $^{13}$C-NMR (75 MHz, acetone-$d_6$, 25 °C): $\delta$ 114.94, 117.79, 118.82, 122.41, 124.14, 125.55, 125.90, 126.37, 127.68, 129.11, 130.24, 132.61, 133.67, 136.50, 150.75, 152.54, 167.41.

### 4.1.7. (+)-(11S,12S)-N,N′-bis-(2′,5′-dihydroxy-benzamido)-9,10-dihydro-9,10-ethanoanthracene (10)

According to the procedure for the preparation of **8**, **10** was obtained from **6** in 81% as a beige solid. $[\alpha]_D^{23}$ +117.6° (*c* 0.26, MeOH); $^1$H-NMR (300 MHz, acetone-$d_6$, 25 °C): $\delta$ 2.92 (s, 2H, OH), 4.58–4.63 (m, 4H), 6.72–6.76 (d, *J* = 9.0 Hz, 2H), 6.88–6.94 (dd, *J* = 3.0, 9.0 Hz, 2H), 7.10–7.12 (d, *J* = 3.0 Hz, 2H), 7.12–7.25 (m, 4H), 7.35–7.39 (m, 2H), 7.44–7.48 (m, 2H), 7.88 (s, 2H, OH),

7.99–8.07 (br d, $J = 6.3$ Hz, 2H, NH). $^{13}$C-NMR (75 MHz, acetone-$d_6$, 25 °C): $\delta$ 50.17, 56.56, 113.49, 115.52, 118.92, 122.66, 125.24, 126.71, 127.28, 127.30, 140.43, 142.83, 149.92, 155.25, 170.72. MALDI-TOF MS: Calc. for $C_{30}H_{24}N_2O_6$: 509.1706; Found: 509.1727 [M]$^+$.

### 4.1.8. ( − )-(1S,2S)-N,N′-bis-(2′,5′-Dihydroxy-benzamido)-1,2-diphenylethane (11)

According to the procedure for the preparation of **8**, **11** was obtained from **7** in 91% as a beige solid. $[\alpha]_D^{24}$ − 46.1° (*c* 1.77, MeOH); $^1$H-NMR (300 MHz, acetone-$d_6$, 25 °C): $\delta$ 2.95 (s, 2H, OH), 5.66–5.70 (m, 2H), 6.70–6.74 (d, $J = 9.0$ Hz, 2H), 6.89–6.95 (dd, $J = 3.0, 9.0$ Hz, 2H), 7.12–7.24 (m, 6H), 7.31–7.33 (d, $J = 3.0$ Hz, 2H), 7.35–7.40 (m, 4H), 8.03 (s, 2H, OH), 8.93–8.98 (m, 2H, NH). $^{13}$C-NMR (75 MHz, acetone-$d_6$, 25 °C): $\delta$ 59.25, 113.44, 115.68, 119.10, 122.84, 128.26, 128.75, 129.03, 140.62, 150.16, 155.09, 170.53.

### 4.1.9. ( + )-(R,R)-N,N′-bis-(4′-tert-Butyl-2′,5′-dimethoxy-benzamido)-1,2-cyclohexane (17)

According to the procedure for the preparation of **4**, **17** was obtained from ( − )-(1R,2R)-1,2-diaminocyclohexane and 4-*tert*-butyl-2,5-dimethoxybenzoic acid in 96% as a white solid. $[\alpha]_D^{22}$ +6.5° (*c* 1.59, CHCl$_3$); $^1$H-NMR (300 MHz, CDCl$_3$, 25 °C): $\delta$ 1.35 (s, 18H), 1.35–1.52 (m, 4H), 1.76–1.83 (m, 2H), 2.21–2.29 (m, 2H), 3.82 (s, 6H), 3.86 (s, 6H), 4.01–4.10 (m, 2H), 6.85 (s, 2H), 7.65 (s, 2H), 8.13–8.19 (br d, $J = 7.8$ Hz, 2H, NH). $^{13}$C-NMR (75 MHz, CDCl$_3$, 25 °C): $\delta$ 24.94, 29.43, 32.97, 35.29, 53.12, 55.59, 56.39, 111.19, 114.30, 119.34, 143.27, 151.40, 152.63, 165.17.

### 4.1.10. ( + )-(R)-N,N′-bis-(4′-tert-Butyl-2′,5′-dimethoxy-benzamido)-2,2′-binaphthalene (18)

According to the procedure for the preparation of **17**, **18** was obtained from ( + )-(R)-1,1′-binaphthyl-2,2′-diamine in 98% as a beige solid. $[\alpha]_D^{26}$ +52.4 °(*c* 1.32, CHCl$_3$); $^1$H-NMR (300 MHz, CDCl$_3$, 25 °C): $\delta$ 1.28 (s, 18H), 2.97 (s, 6H), 3.80 (s, 6H), 6.61 (s, 2H), 7.01–7.06 (d, $J = 7.5$ Hz, 2H), 7.20–7.26 (ddd, $J = 1.5, 6.9, 8.4$ Hz, 2H), 7.37–7.43 (ddd, $J = 1.5, 6.9, 8.4$ Hz, 2H), 7.65 (s, 2H), 7.91–7.96 (d, $J = 7.5$ Hz, 2H), 8.07–8.12 (d, $J = 9.3$ Hz, 2H), 9.06–9.12 (d, $J = 9.3$ Hz, 2H), 9.78 (br s, 2H, NH). $^{13}$C-NMR (75 MHz, CDCl$_3$, 25 °C): $\delta$ 29.29, 35.32, 55.53 (two overlapping signals of non-equivalent carbons), 110.80, 114.13, 118.73, 120.08, 121.67, 125.13, 125.28, 127.12, 127.96, 129.38, 130.99, 132.98, 136.75, 144.18, 151.13, 152.57, 163.67.

### 4.1.11. ( + )-(11S,12S)-N,N′-bis-(4′-tert-Butyl-2′,5′-dimethoxy-benzamido)-9,10-dihydro-9,10-ethanoanthracene (19)

According to the procedure for the preparation of **17**, **19** was obtained from ( + )-(11S,12S)-diamino-9,10-dihydro-9,10-ethanoanthracene in 93% as a beige solid.

$[\alpha]_D^{23}$ +112.4° (*c* 1.77, CHCl$_3$); $^1$H-NMR (400 MHz, CDCl$_3$, 25 °C): $\delta$ 1.35 (s, 18H), 3.52 (s, 6H), 3.82 (s, 6H), 4.30–4.36 (m, 2H), 4.52 (d, $J = 3.2$ Hz, 2H), 6.79 (s, 2H), 7.16–7.27 (m, 4H), 7.31–7.34 (m, 2H), 7.44–7.47 (m, 2H), 7.65 (s, 2H), 7.87–7.92 (d, $J = 8.0$ Hz, 2H, NH). $^{13}$C-NMR (100 MHz, CDCl$_3$, 25 °C): $\delta$ 29.41, 35.30, 49.56, 55.58, 56.09, 57.44, 111.15, 114.18, 118.96, 124.92, 125.92, 126.35, 126.64, 139.66, 140.91, 143.51, 151.24, 152.76, 164.49.

### 4.1.12. ( − )-(1S,2S)-N,N′-bis-(4′-tert-Butyl-2′,5′-dimethoxy-benzamido)-1,2-diphenylethane (20)

According to the procedure for the preparation of **17**, **20** was obtained from ( − )-(1S,2S)-1,2-diphenyl-1,2-ethanediamine in 90% as a beige solid. $[\alpha]_D^{26}$ − 70.1° (*c* 1.26, CHCl$_3$); $^1$H-NMR (300 MHz, CDCl$_3$, 25 °C): $\delta$ 1.35 (s, 18H), 3.80 (s, 6H), 3.88 (s, 6H), 5.56–5.60 (m, 2H), 6.87 (s, 2H), 7.12–7.24 (m, 10H), 7.67 (s, 2H), 8.90–8.95 (m, 2H, NH). $^{13}$C-NMR (75 MHz, CDCl$_3$, 25 °C): $\delta$ 29.54, 35.47, 55.70, 56.52, 58.94, 111.12, 114.53, 119.04, 127.55, 127.90, 128.40, 139.79, 143.73, 151.62, 152.80, 165.12. Anal. Calc. for $C_{40}H_{48}N_2O_6$: C, 73.59; H, 7.41; Found: C, 73.78; H, 7.19%.

### 4.1.13. ( + )-(R)-N,N′-bis-(4′-tert-Butyl-2′,5′-dihydroxy-benzamido)-2,2′-binaphthalene (22)

According to the procedure for the preparation of **8**, **22** was obtained from **18** in 93% as a pale brown solid. $[\alpha]_D^{24}$ +75.2° (*c* 0.57, MeOH); $^1$H-NMR (300 MHz, acetone-$d_6$, 25 °C): $\delta$ 1.27 (s, 18H), 2.99 (s, 2H, OH), 6.61 (s, 2H), 7.03–7.08 (br d, 2H), 7.23 (s, 2H), 7.23–7.29 (ddd, $J = 1.5, 6.9, 8.3$ Hz, 2H), 7.38–7.45 (ddd, $J = 1.5, 6.9, 8.3$ Hz, 2H), 7.95–8.00 (br d, 2H), 8.08–8.12 (br d, 2H), 8.63–8.90 (d, $J = 9.0$ Hz, 2H), 9.45 (br s, 2H, OH), 9.93 (br s, 2H, NH). $^{13}$C-NMR (75 MHz, acetone-$d_6$, 25 °C): $\delta$ 29.36, 35.44, 116.11, 116.28, 116.42, 123.36, 123.82, 125.82, 126.04, 127.61, 129.09, 130.21, 132.30, 133.79, 137.12, 143.89, 149.46, 151.10, 166.20.

### 4.1.14. ( + )-(11S,12S)-N,N′-bis-(4′-tert-Butyl-2′,5′-dihydroxy-benzamido)-9,10-dihydro-9,10-ethanoanthracene (23)

According to the procedure for the preparation of **8**, **23** was obtained from **19** in 80% as a beige solid. $[\alpha]_D^{27}$ + 157.7° (*c* 1.20, MeOH); $^1$H-NMR (400 MHz, CDCl$_3$, 25 °C): $\delta$ 1.31 (s, 18H), 4.21–4.26 (m, 2H), 4.40 (d, $J = 2.4$, 2H), 5.48 (s, 2H, OH), 6.43 (s, 2H), 6.45 (s, 2H, OH), 6.84 (s, 2H), 7.08–7.18 (m, 4H), 7.25–7.33 (m, 4H), 10.66 (s, 2H, NH). $^{13}$C-NMR (100 MHz, CDCl$_3$, 25 °C): $\delta$ 29.15, 35.09, 49.22, 57.01, 111.61, 112.63, 116.88, 124.84, 125.77, 127.04, 127.18, 138.23, 140.60, 145.09, 147.06, 154.02, 168.97.

## 4.2. General procedure for the asymmetric palladium(II)-catalyzed 1,4-diacetoxylation reaction

Diene **12** (50 mg, 0.32 mmol) was added to a solution of Pd(OAc)$_2$ (7.2 mg, 0.032 mmol), chiral ligand (0.032 mmol), LiOAc·2H$_2$O (51 mg, 0.50 mmol) and Fe(Pc) (4.5 mg, 0.008 mmol) in HOAc–acetone 4:1 (1.25 ml) and the solution was stirred for 18 h under an oxygen atmosphere at r.t. Et$_2$O was added, and the organic phase was extracted with 1 M NaOH ( × 3), washed with brine, dried (MgSO$_4$) and evaporated. The crude product was purified by column chromatography (pentane–Et$_2$O 3:1). The diastereomeric ratio and enantiomeric excess of *trans*-1,4-diacetoxy-2-phenyl-2-cyclohexene (**13**) was determined by HPLC analysis using a Daicel Chiralcel OD-H column (hexane–2-propanol 98/2, flow rate 0.5 ml min$^{-1}$): $t_R = 14.1$ and 16.2 min.

## Acknowledgements

## References

[1] L.S. Hegedus, Transition Metals in the Synthesis of Complex Organic Molecules, University Science Books, Sausolito, 1999.

[2] J.-E. Bäckvall, Palladium-catalyzed 1,4-additions to conjugated dienes, in: P. Stang, F. Diederich (Eds.), Metal-Catalyzed Cross Coupling Reactions, Wiley–VCH, Weinheim, 1998, pp. 339–385.

[3] J.-E. Bäckvall, S.E. Byström, R.E. Nordberg, J. Org. Chem. 49 (1984) 4619.

[4] J.-E. Bäckvall, J.O. Vågberg, J. Org. Chem. 53 (1988) 5695.

[5] J.-E. Bäckvall, J.-E. Nyström, R.E. Nordberg, J. Am. Chem. Soc. 107 (1985) 3676.

[6] J.-E. Bäckvall, P.G. Andersson, J. Am. Chem. Soc. 112 (1990) 3683.

[7] (a) A.M. Castaño, B.A. Persson, J.-E. Bäckvall, Chem. Eur. J. 3 (1997) 482;
(b) I. Dorange, J. Löfstedt, K. Närhi, J. Franzén, J.-E. Bäckvall, Chem. Eur. J. 9 (2003) 3445.

[8] J.-E. Bäckvall, R.E. Nordberg, J.E. Nyström, Tetrahedron Lett. 23 (1982) 1617.

[9] R.G.P. Gatti, A.L.E. Larsson, J.-E. Bäckvall, J. Chem. Soc. Perkin Trans. 1 (1997) 577.

[10] Y.I.M. Nilsson, A. Aranyos, P.G. Andersson, J.-E. Bäckvall, J.-L. Parrain, C. Ploteau, J.-P. Quintard, J. Org. Chem. 61 (1996) 1825.

[11] A. Palmgren, A.L.E. Larsson, J.-E. Bäckvall, J. Org. Chem. 64 (1999) 836.

[12] C. Jonasson, M. Rönn, J.-E. Bäckvall, J. Org. Chem. 65 (2000) 2122.

[13] J.-E. Bäckvall, A. Gogoll, Tetrahedron Lett. 29 (1988) 2243.

[14] H. Grennberg, A. Gogoll, J.-E. Bäckvall, Organometallics 12 (1993) 1790.

[15] J.-E. Bäckvall, R.B. Hopkins, H. Grennberg, M. Mader, A.K. Awasthi, J. Am. Chem. Soc. 112 (1990) 5160.

[16] A. Thorarensen, A. Palmgren, K. Itami, J.-E. Bäckvall, Tetrahedron Lett. 38 (1997) 8541.

[17] K. Itami, A. Palmgren, A. Thorarensen, J.-E. Bäckvall, J. Org. Chem. 63 (1998) 6466.

[18] H.K. Cotton, R.C. Verboom, L. Johansson, B.P. Plietker, J.-E. Bäckvall, Organometallics 21 (2002) 3367.

[19] P.W.N.M. van Leeuwen, P.C.J. Kamer, J.N.H. Reek, P. Dierkes, Chem. Rev. 100 (2000) 2741.

[20] H. Sigel, R.B. Martin, Chem Rev. 82 (1982) 385.

[21] F. Conti, M. Donati, G.F. Pragaglia, R. Ugo, J. Organomet. Chem. 30 (1971) 421.

[22] B.M. Trost, D.L. Van Vranken, C. Bingel, J. Am. Chem. Soc. 114 (1992) 9327.

[23] (a) B.M. Trost, J.D. Oslob, J. Am. Chem. Soc. 121 (1999) 3057;
(b) For a recent application of the optimal ligand see: B. M. Trost, J. Dudash, Jr, O. Dirat, Chem Eur. J. 8 (2002) 259.

[24] M. Demuynck, P. De Clercq, M. Vandewalle, J. Org. Chem. 44 (1979) 4863.

[25] A slower reaction usually leads to lower yields due to aromatisation as a side-reaction. The choice for this particular aromatisation-sensitive substrate is explained by the ease of separation on chiral HPLC.

[26] E.W. Wilson, Jr, R.B. Martin, Inorg. Chem. 9 (1970) 528.

[27] M.C. Lim, J. Chem. Soc. Dalton Trans. (1977) 15.

[28] J.C. Cooper, L.F. Wong, D.W. Margerum, Inorg. Chem. 17 (1978) 261.

[29] R.L. Chapman, R.S. Vagg, Inorg. Chim. Acta 33 (1979) 227.

[30] R.L. Chapman, F.S. Stephens, R.S. Vagg, Inorg. Chim. Acta 52 (1981) 161.

[31] A. Bansal, R.V. Singh, Synth. React. Inorg. Met-Org. Chem. 31 (2001) 381.

[32] A lower diastereoselectivity is not surprising, since higher acetate concentrations will favour the formation of the *cis*-addition product.

[33] M.E. Jung, M.A. Lyster, J. Org. Chem. 42 (1977) 3761.

[34] T. Morita, Y. Okamoto, H. Sakurai, J. Chem. Soc. Chem. Commun. (1978) 874.

[35] P. Jacob, III, P.S. Callery, A.T. Shulgin, N. Castagnoli, Jr, J. Org. Chem. 41 (1976) 3627.

[36] M.-J. Brienne, J. Jacques, J. Bull. Soc. Chim. Fr. 1 (1973) 190.

[37] J.S. Zweig, N. Castagnoli, Jr, J. Med. Chem. 20 (1977) 414.

[38] F.R. Hewgill, F. Legge, R.J. Webb, Aust. J. Chem. 46 (1993) 1605.

[39] S. Karlström, M. Rönn, A. Thorarensen, J.-E. Bäckvall, J. Org. Chem. 63 (1998) 2517.