Modular Bis(oxazoline) Ligands for Palladium Catalyzed Allylic Alkylation: Unprecedented Conformational Behaviour of a Bis(oxazoline) Palladium η^3-1,3-Diphenylallyl Complex

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Abstract: New families of enantiopure bis(oxazolines) with 4,5-*trans* (**5a–g**) or 4,5-*cis* (**6c**) stereochemistry at the individual rings have been prepared in high yield. Their η^3-allyl palladium complexes (**8a–g**, **9c** and **10**) have been used as catalytic precursors in allylic alkylation reactions with excellent enantioselectivities (up to 96%) for the *trans* oxazoline derivatives, while Pd/**6c** system was inactive. NMR studies on palladium η^3-1,3-diphenylallyl intermediates (**11a**, **c** and **e**) showed the presence of *syn*/*syn*- and *syn*/*anti*-allyl isomers in solution; this resembles the first example of η^3-η^1-η^3 isomerism in Pd allylic complexes containing bis(oxazolines) derived from malonic acid.

Keywords: allyl isomerism · asymmetric catalysis · bis(oxazoline) ligands · NMR spectroscopy · palladium

Introduction

Chiral ligands play a fundamental role in the complex phenomenon of asymmetric catalysis.[1] Thus, they are not only responsible for the activation of the metal atom where the catalytic activity resides, but also for the generation of a disymmetric environment around the metal atom which is in the origin of the enantioselectivity of the process.

In most cases, the molecular recognition between the metal–ligand aggregate and the reacting molecule goes beyond a simple interaction between functional groups. Even the interaction between purely skeletal regions of these species can contribute in a significant manner to the differentiation between diastereomeric transition states and, hence, to the enantioselectivity of the reactions.

Because of this, universally useful ligands are rare and optimal ligands often vary, even within a single reaction type, from one substrate to another.[2]

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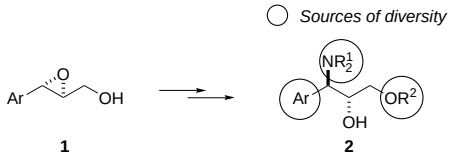
It is thus advisable that the toolkit of the synthetic chemist contains families of ligands with slightly different steric characteristics, so that enantioselectivity can be fine-tuned for a particular substrate.[3]

For historical reasons, enantiopure chiral ligands have been taken from the shelf of nature and used either directly or after some simple manipulation. Those belonging to one of the most successful types, β-amino alcohols, can be derived from amino acids by reduction protocols; however, there are some limitations due to both enantiomer availability and structural type.[4]

We have shown that synthetic yet enantiopure epoxides, readily available through well established reactions of very broad scope, such as the Sharpless[5] and the Jacobsen epoxidations,[6] are a most convenient source of structurally diverse amino alcohols through regioselective ring-opening/protection sequences (Scheme 1).[7]

These amino alcohols are devoid of the limitations encountered in those derived from *natural* amino acids, and we have succeeded in developing optimal ligands for a variety of processes and substrates through its structural fine-tuning.[8]



Scheme 1. Regioselective ring-opening/protection sequences of enantiopure epoxides.

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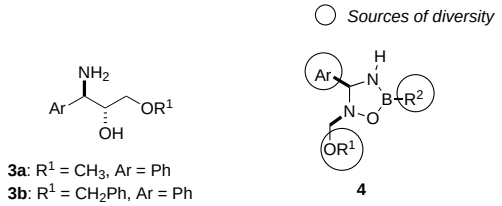
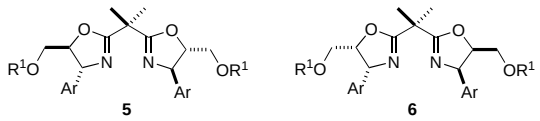
This is, in fact, greatly facilitated by the completely modular nature of **2**.

Amino alcohols **3**, bearing a free amino group, are also readily available in enantiopure form from epoxides **1** and still present two elements of structural diversity. In fact, their ruthenium complexes have been developed as efficient mediators for transfer hydrogenation,[9] while the derived oxazaborolidines **4** have been structurally optimized as ligands for the catalytic enantioselective borane reduction of prochiral ketones.[10]

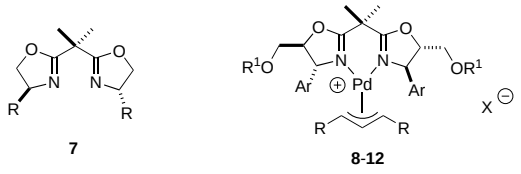


3a: $R^1 = CH_3$, Ar = Ph
3b: $R^1 = CH_2Ph$, Ar = Ph
3c: $R^1 = CHPh_2$, Ar = Ph
3d: $R^1 = CPh_3$, Ar = Ph
3e: $R^1 = (CH_2)_2OCH_3$, Ar = Ph
3f: $R^1 = CHPh_2$, Ar = mesityl
3g: $R^1 = CHPh_2$, Ar = 1-naphthyl

As a continuation of these efforts, we planned to investigate the use of amino alcohols **3** for the preparation of bis(oxazolines) **5** and **6**.



Metal complexes of bis(oxazolines) **7**, ultimately derived from amino acids, have successfully been employed as catalysts in a variety of enantioselective processes.[11] Among them, the palladium-catalyzed allylic substitution appeared as especially well suited for the purpose of this research,[12] since Ar and OR^1 groups of different steric and electronic nature in **5** and **6** could, in principle, exert a tuning of the catalytic activity and enantioselectivity of the corresponding π-allyl palladium complexes **8**–**12**.

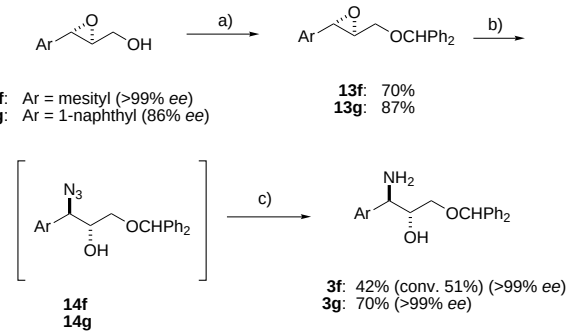


In line with these ideas, we report herein the synthesis of a diverse family of bis(oxazolines) **5** and **6**, bearing Ar and OR^1 groups of different size, from the corresponding enantiopure amino alcohols **3**. An NMR study of π-allyl palladium complexes involving symmetrically substituted allyl residues (**11**, **12**) and the use of the unsubstituted π-allyl complexes (**8**–**10**) as catalysts in the alkylation of *rac*-1,3-diphenylprop-2-enyl acetate with dimethyl malonate are also reported.

Results and Discussion

Synthesis of the bis(oxazoline) ligands: According to our synthetic plan, amino alcohols **3a**–**g** are the starting materials for the preparation of bis(oxazolines) **5**–**6**.

These amino alcohols were readily prepared from epoxyalcohols **1** through a well-documented procedure involving the initial conversion to a family of diverse epoxy ethers **13**, subsequent regioselective and stereospecific ring-opening of the epoxides with azide in the presence of lithium perchlorate[13] and final reduction of the intermediate azido alcohols **14** (Scheme 2). Whereas amino alcohols **3a**–**e** have been previously reported and used as oxazaborolidine precursors (**3f**, **g**),[10] incorporating aryl groups other than phenyl as a further source of diversity, have been designed and prepared for the purposes of this research.



Scheme 2. Synthesis of chiral amino alcohols **3** from epoxyalcohols **1**. a) NaH, DMF, $BrCHPh_2$, 0 °C, 17 h; b) NaN_3, $LiClO_4$, CH_3CN, 55 °C, 24 h; c) $NaBH_4$, THF/MeOH, 55–60 °C, 22 h.

The formation of epoxyethers **13a**–**d**, bearing alcohol protecting groups of increasing size, and **13e**, with a protecting group with chelating ability, took place uneventfully by the reported procedure.[10] For the synthesis of **13f**, **g**, in turn, the corresponding epoxyalcohols **1f**[14] and **1g**[15] were treated with benzhydryl bromide in the presence of NaH in DMF at 0 °C. This led to the formation of **13f**, **g** in 70 and 87% yield, respectively. The regioselective and stereospecific ring-opening step of these epoxyethers was carried out under Crotti's conditions, which involve the use of sodium azide in a 5 M $LiClO_4$ solution in acetonitrile. Under these conditions, the intermediate azido alcohols **14f**, **g** were obtained in quantitative yield and were further converted into the final amino alcohols **3f**, **g** without purification. The azido group in these intermediates was reduced with sodium borohydride in THF/MeOH, as these conditions turned out to be harmless to benzylic ethers. Amino alcohol **3g** was obtained in good yield (70%) and enantiomerically pure (>99%) after enantiomeric enrichment by selective crystallization of the racemate from pentane/dichloromethane (1:1). However, the reduction of **14f** leading to **3f** posed some problem. After 22 hours at 55–60 °C, conversion was only 51%, although the reaction proceeded very cleanly (83% selectivity; 42% yield). An increase in the temperature (80 °C) and in the reaction time (2 d) did not improve this result. Most probably, the difficulties observed in reduction of this azide can be attributed to the

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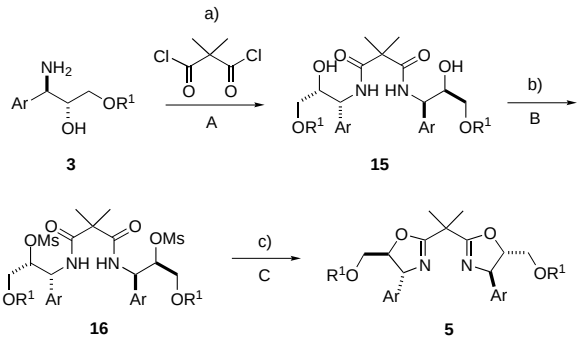
presence of the two methyl groups in the *ortho* position of the mesityl group, which could strongly hinder the approach of the nucleophile to the reacting carbon.

With the family of amino alcohols **3a–g** at hand, their conversion into bis(oxazolines) was studied next. Interestingly the substitution scheme in **3** offers the possibility of systematic variations of steric, electronic, and binding characteristics of the target ligands as well as the selection of the stereochemistry (*cis* or *trans*) in the individual oxazoline rings in order to achieve improved catalytic behaviour. Up to now, examples of bis(oxazolines) with a 4,5-disubstitution scheme in the individual rings, as those being the target of our research,[12b, 16] have been scarce. However, stereodivergent methodology for the preparation of *cis*- or *trans*-substituted derivatives from a single, stereodefined amino alcohol has already been developed.[16a]

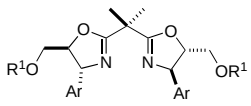
Studies directed to the conversion of amino alcohols **3a–g** into the corresponding *trans* bis(oxazolines) **5** were first undertaken. These are, in fact, the expected products in the usual preparation of mono- and bis(oxazolines) from amino alcohols, which usually involves inversion at the hydroxyl-bearing carbon atom. Thus, the usual three-step process beginning with the condensation of malonic acid derivatives with amino alcohols to form bis(hydroxyamide) intermediates **15** was followed (Scheme 3). The activation of the free hydroxy groups in **15** allows a subsequent base-induced cyclization taking place through S_N2 mechanism which leads to the target bis(oxazolines) **5**. The major variations within this general method lie in the use of diverse activating agents[17] as well as different bases[17c] to affect the ring-closure step. After some exploratory experiments, activation as mesylate[17c] and the use of 5% KOH/MeOH to induce cyclization were selected as the most appropriate for amino alcohols **3a–g**.



Scheme 3. Three-step synthesis of bis(oxazolines) **5** from amino alcohols **3**. a) Et_3N, CH_2Cl_2; RT, 20 h; b) 2.2 equiv MsCl, 4.4 equiv Et_3N, CH_2Cl_2, 0 °C → RT, 2 h; c) 5% KOH/MeOH, RT, 15 h.

The initial condensation of **3a–g** with dimethylmalonyl dichloride was carried out in the presence of triethylamine at room temperature for 20 h.[17a] The resulting bis(hydroxyamides) **15** were obtained in excellent yields in all cases (Table 1) and were used as starting materials for the next step without further purification. Next, the activation of the free hydroxyl groups in **15a–g** was studied. Neither the use of thionyl chloride[17a] nor treatment with methanesulfonic acid[17b] induced a selective reaction. Fortunately, treatment of the bis(hydroxyamides) **15a–g** with 2.2 equivalents of methanesulfonyl chloride and 4.4 equivalents of triethylamine in CH_2Cl_2 at 0 °C for two hours,[17c] afforded the corresponding bis(mesylates) **16a–g** in quantitative yield. Due to limited stability, it is advisable to perform the base-induced cyclization of **16** inmediately after its preparation. Potassium hydroxide in MeOH (5%)[17c] at room temperature provided excellent results in the cyclization of **16** leading to bis(oxazolines) **5**. Somewhat surprisingly, other bases such as NaOH in H_2O/MeOH failed to induce cyclization.

Table 1. Yields for the synthesis of *trans* **5a–g** bis(oxazolines).



5a: $R^1 = CH_3$, Ar = Ph
5b: $R^1 = CH_2Ph$, Ar = Ph
5c: $R^1 = CHPh_2$, Ar = Ph
5d: $R^1 = CPh_3$, Ar = Ph
5e: $R^1 = (CH_2)_2OCH_3$, Ar = Ph
5f: $R^1 = CHPh_2$, Ar = mesityl
5g: $R^1 = CHPh_2$, Ar = 1-naphthyl

Bis(oxazoline)	A[a] [%]	B+C[a] [%]	Overall yield [%]
5a	95	92	87
5b	80	96	77
5c	97	91	88
5d	99	96	95
5e	81	89	72
5f	100	95	95
5g	100	93	93

[a] See Scheme 3.

Quite interestingly, bis(oxazolines) **5a–g** obtained by this procedure were notably pure, so that further purification of these highly polar materials was not necessary.[18] The derived π-allyl palladium complexes could be prepared directly from the crude reaction products and, thanks to its high crystallinity (**8**, **9c**, **10**), allowed further purification whenever necessary (see below).

The relative *trans* stereochemistry of the chiral centres in the individual oxazoline rings of **5** was confirmed by means of a NOESY experiment on **5c**, where an NOE signal could be observed between C*H*-N and the single CH_2 unit (Figure 1).

Note the mean overall yield for the preparation of **5a–g** from **3a–g** by the discussed procedure is 87%.

As we have already mentioned, the *trans* stereochemistry in the individual oxazoline rings in **5a–g** arises from the fact that the cyclization step takes place with inversion of configuration at C-2, where the hydroxyl substituent has been previously activated as a mesylate. Therefore, the preparation of bis(oxazolines) **6**, with *cis* stereochemistry at the individual rings, requires a synthetic route taking place with retention of configuration at C-2. Among the different methods fulfilling this requirement,[19] the Desimoni methodology,[19d] which involves the use of a catalytic amount of Bu_2SnCl_2 to affect both the activation and the cyclization of a bis(hydroxyamide) intermediate, was selected. Starting from **15c**, heating in xylene under reflux for 48 hours in the presence of a catalytic

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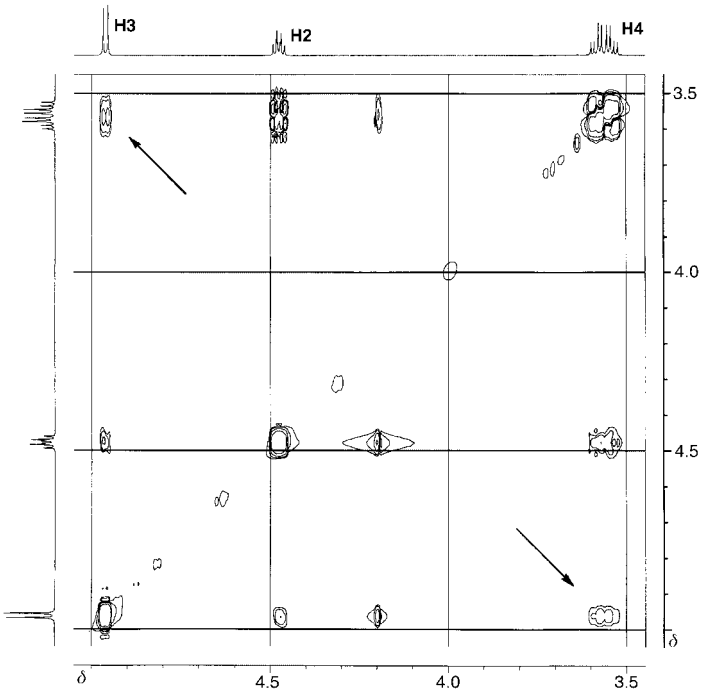
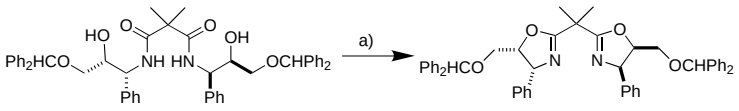


Figure 1. Part of the NOESY spectrum (3.5–5 ppm) of **5c** (arrows indicate NOE contacts between H3 and H4 protons).

amount of Bu_2SnCl_2 afforded bis(oxazoline) **6c** (Scheme 4). The preparation of its π-allyl palladium complex allowed a complete purification of the crude.

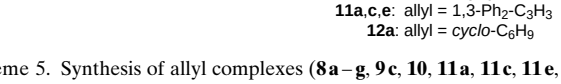


15c **6c**

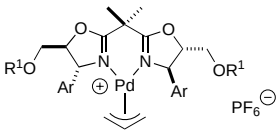
Scheme 4. Synthesis of bis(oxazoline) **6c** from bis(hydroxyamide) **15c**. a) Bu_2SnCl_2, xylene, reflux, 48 h.

The poor catalytic results obtained with **6c**, as it will be discussed later, did not warrant the continuation of synthetic efforts towards the preparation of related molecules with the same stereochemistry. They could be important, however, as catalytic ligands for different processes and, in that case, other members of the same family could be readily obtained by the same procedure.[11]

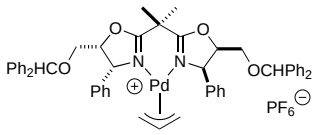
Allylic palladium complexes—NMR studies: Ionic palladium complexes containing the non-substituted allyl (**8a–g**, **9c** and **10**), 1,3-diphenylallyl (**11a**, **c** and **e**) and cyclohexenyl (**12a**) groups were prepared from standard palladium dimer materials and the appropriate chiral ligand in the presence of ammonium hexafluorophosphate (Scheme 5), following the methodology previously described.[12b, 12h] These allyl compounds were obtained as monometallic complexes of general formula $[Pd(\eta^3\text{-allyl})(\mathbf{L})]PF_6$, where the ligand is N,N-bonded to the metallic centre, see below.



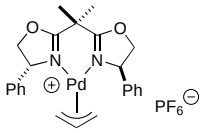
Scheme 5. Synthesis of allyl complexes (**8a–g**, **9c**, **10**, **11a**, **11c**, **11e**, **12a**) containing bis(oxazolines). a) NH_4PF_6.



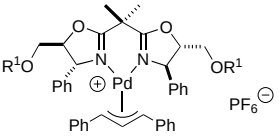
8a: $R^1 = CH_3$, Ar = Ph
8b: $R^1 = CH_2Ph$, Ar = Ph
8c: $R^1 = CHPh_2$, Ar = Ph
8d: $R^1 = CPh_3$, Ar = Ph
8e: $R^1 = (CH_2)_2OCH_3$, Ar = Ph
8f: $R^1 = CHPh_2$, Ar = mesityl
8g: $R^1 = CHPh_2$, Ar = 1-naphthyl



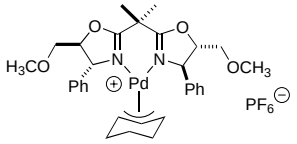
9c



10



11a: $R^1 = CH_3$
11c: $R^1 = CHPh_2$
11e: $R^1 = (CH_2)_2OCH_3$



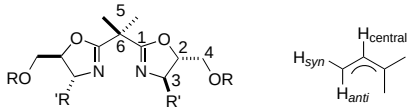
12a

Type-**11** complexes, containing the more sterically demanding 1,3-diphenylallyl ligand were obtained in low yields as oils. Only **11e** could be isolated as an orange foam and fully characterized by NMR spectroscopy and mass spectrometry (see Experimental Section). Most probably, the difficulties met in the formation of these complexes respond to an increased steric interaction between the substituents on the oxazoline rings and the allyl ligand. In this respect, it is worth noting that **6c** does not form a η^3 complex with the 1,3-diphenylallyl group, and this fact could be attributed to a conformational change in the phenyl substituents at C-4 in the oxazolines, due to the increased interaction with the alkoxyalkyl substituent at C-5, leading to an even stronger interaction with the allyl ligand.

The complexes were fully characterized by the usual techniques. The IR spectra showed a strong signal in the range 1660–1665 cm^{-1} assigned to the C=N stretching of the oxazoline moiety, in similar position to that observed in the free ligands. Positive FAB mass spectra exhibited, in all cases, the peak at highest m/z ratio for the "$[Pd(\eta^3\text{-allyl})(\mathbf{L})]$" fragment.

The NMR spectroscopy has been the most useful technique to determine the structure of these complexes in solution.[20] The relevant ^1H NMR data are summarized in Tables 2 and 3. Unfortunately, it was not possible to obtain any crystal of sufficient quality to perform X ray diffraction measurements.

Table 2. Selected ^{1}H NMR ($CDCl_3$, 298 K, 500 MHz) data[a] (δ in ppm) for complexes **8a–g**, **9c and 10**.



Complex	**2**[b]	**3**	**4**	**5**	central	*syn*	*anti*	other
8a	4.62 (m, 2H)	5.25 (d, 7.0, 1H) 5.15 (d, 7.5, 1H)	3.79 (br d, 4, 2H) 3.75 (dd, 4.5, 3.5, 2H)	1.89 (s, 3H) 1.85 (s, 3H)	4.99 (tt, 12.0, 7.5, 1H)	3.42 (br d, 6.5, 1H) 2.83 (dd, 7.0, 2.0, 1H)	2.61 (d, 13.0, 1H) 1.89 (d, 12.0, 1H)	R = CH_3: 3.50 (s, 3H) 3.47 (s, 3H)
8b[c]	4.61 (m, 2H)	5.19 (br s, 2H)	3.90 (dd, 11.1, 3.3, 2H) 3.84 (dd, 11.1, 4.5, 2H)	1.81 (s, 6H)	4.97 (tt, 12.6, 7, 1H)	3.41 (br d, 7.8, 1H) 2.83 (dd, 7, 1.9, 1H)	2.57 (d, 12.3, 1H) 1.89 (d, 12.6, 1H)	R = CH_2(Ph): 4.65 (s, 4H)
8c	4.64 (m, 2H)	5.24 (d, 6.5, 1H) 5.15 (d, 6.5, 1H)	3.92 (dd, 12, 4, 1H) 3.88 (dd, 12, 4, 1H) 3.81 (dd, 12, 4, 1H) 3.76 (dd, 12, 4, 1H)	1.82 (s, 3H) 1.75 (s, 3H)	5.02 (tt, 12.6, 6.9, 1H)	3.41 (br d, 7.2, 1H) 2.88 (dd, 6.9, 3.5, 1H)	2.61 (d, 12.5, 1H) 1.95 (d, 12.5, 1H)	R = CH(Ph)$_2$: 5.54 (s, 1H) 5.51 (s, 1H)
8d[c]	4.49 (m, 2H)	5.06 (d, 7.2, 1H) 5.03 (m, 1H)	3.69 (dd, 11.5, 3.3, 2H) 3.56 (dd, 11.5, 4.8, 2H)	1.94 (s, 7H)[d]	5.06–4.9 (m, 1H)	3.37 (br d, 6, 1H) 2.84 (br d, 6.6, 1H)	2.57 (d, 12.3, 1H)[d]	–
8e[c]	4.64 (m, 2H)	5.20 (br s, 2H) 3.87 (m, 2H)	3.89 (m, 2H)	1.87 (s, 6H)	4.98 (tt, 12.3, 6.9, 1H) 2.83 (dd, 7.2, 1.8, 1H)	3.42 (br d, 6.9, 1H) 1.89 (d, 12.6, 1H)	2.6 (d, 12.6, 1H) 3.76–3.57 (m, 8H)	R = (CH_2)$_2$OCH$_3$ (CH$_2$)$_2$OCH_3 3.37 (s, 6H)
8f[c]	4.77 (m, 1H) 4.75 (m, 1H)	5.76 (d, 8.4, 1H) 5.59 (d, 9.3, 1H)	3.90 (dd, 11, 2.5, 2H) 3.73 (dd, 11, 2.5, 2H)	1.75 (s, 3H) 1.72 (s, 3H)	5.03 (tt, 12.5, 7, 1H)	2.56 (dd, 7.0, 2, 1H) 3.35 (dd, 6.5, 2, 1H)	2.41 (d, 12.5, 1H) 1.88 (d, 12.5, 1H)	R = CHPh$_2$: 5.47 (s, 2H) mesityl *Me* 2.05, 2.12, 2.22 (each: s, 6H) CH 6.7 (s, 4H)
8g	4.73 (br d, 4.1, 2H)	6.14 (br s, 2H)	4.09 (dd, 10.5, 4.2, 2H) 3.99 (dd, 10.5, 4.2, 2H)	1.89 (s, 6H)	4.89 (tt, 12.5, 7, 1H)	2.96 (br d, 7, 1H) 2.51 (br d, 7, 1H)	2.6 (d, 12, 1H) 1.70 (d, 12, 1H)	R = CHPh$_2$: 5.67 (s, 2H)
9c[c]	5.40–5.27 (m, 2H)	5.64 (d, 10.5, 1H) 5.53 (d, 10.5, 1H)	3.25–3.20 (m, 4H)	1.84 (s, 3H) 1.77 (s, 3H)	4.88 (tt, 12.3, 7.3, 1H)	4.11 (d, 4.8, 1H) 2.72 (dd, 6.9, 1.8, 1H)	2.57 (d, 12.3, 1H) 1.72 (d, 12.6, 1H)	R = CH(Ph)$_2$ 4.97 (s, 1H) 4.94 (s, 1H)
10[e]	5.00 (m, 3H)[f] 4.30 (m, 2H)	5.53 (dd, 10.4, 7.0, 1H) 5.42 (dd, 10.4, 7.7, 1H)	–	1.88 (s, 3H) 1.84 (s, 3H)	5.00 (m, 3H)[f]	3.43 (d, 6.6, 1H) 2.85 (d, 6.0, 1H)	2.57 (d, 12.4, 1H) 1.93 (d, 12.5, 1H)	–

[a] Multiplicity (br, broad; d, doublet; m, multiplet; q, quartet; s, singlet; t, triplet), coupling constants (in Hz), and relative integration in parentheses. [b] see formala for labeling scheme.[c] 300 MHz spectrum. [d] One *anti* proton overlapped with H5 protons. [e] 250 MHz spectrum. [f] Two H2 protons and $H_{central}$ proton are overlapped.

Upon coordination of the C_2 symmetrical ligands to the metal, the loss of ligand symmetry is observed in ^{1}H NMR spectra, because some proton signals are duplicated relative to the free ligands. Therefore, methyl protons H5 appear as two singlets (**8a**, **c**, **9c**, **10**, **11a**, **c**, **e**, **12a**); protons H3, as two doublets (**8a**, **c**, **d**, **f**, **h**, **9c**, **11a**, **c**, **e**, **12a**); and diastereotopic protons H4 are split in up to four set of signals for **8c** and **11c** complexes. Obviously, this asymmetry is also shown in the allyl moiety. Therefore, two set of signals for each *syn* and/or *anti* protons are observed for each of the allyl complexes. Allyl protons of type-**11** complexes appear shifted downfield compared with the corresponding non-substituted allyl compounds, type-**8**, probably due to the presence of the phenyl substituents.

Variable temperature NMR experiments indicate a dynamic behaviour of the allyl complexes. For complex **8a**, ^{1}H NMR spectra were recorded in the temperature range -35–$55\,^\circ$C (Figure 2). Concerning the bis(oxazoline) ligand, the protons

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Table 3. Selected ^{1}H NMR (298 K, 500 MHz, $CDCl_3$) data[a] (δ in ppm) for complexes **11a**, **c**, **e** and **12**.

Complex	**2**[b]	**3**	**4**	**5**	central [$C_{central}$]	*syn* [$C_{terminal}$]	*anti* [$C_{terminal}$]	other
***syn/syn*-11a**[c]	4.37 (m, 2H)	4.26 (d, 3.5, 1H) 4.04 (d, 2, 1H)	3.57 (m, 2H) 3.42 (m, 2H)	1.98 (s, 3H) 1.67 (s, 3H)	5.73 (dd, 12.5, 10.5, 1H)	–	5.33 (d, 12.5, 1H) 3.82 (d, 10.5, 1H)	R = CH_3: 3.48 (s, 3H) 3.36 (s, 3H)
***syn/syn*-11c**	4.35 (m, 2H)	4.54 (d, 3.5, 1H) 4.22 (d, 4, 1H)	3.73 (dd, 10, 7.5, 1H) 3.58 (dd, 10, 5, 1H) 3.51 (dd, 11, 3.5, 1H) 3.31 (dd, 11, 3, 1H)	1.75 (s, 3H) 1.49 (s, 3H)	5.68 (dd, 12.5, 10.5, 1H)	–	5.31 (d, 12.5, 1H) 3.65 (d, 10.5, 1H)	R = $CH(Ph)_2$: 5.64 (s, 1H) 5.25 (s, 1H)
***syn/syn*-11e**	4.35–4.32 (m, 2H)	4.22 (d, 4.0, 1H) 3.98 (d, 4, 1H)	3.71–3.42 (m)[d]	1.87 (s, 3H) 1.58 (s, 3H)	5.66 (dd, 13, 10.5, 1H) [107.4]	–	5.25 (d, 13, 1H) [85.2] 3.70 (dd, 10.5, 1, 1H) [72.2]	R = $(CH_2)_2OCH_3$ 3.36 (s, 3H) 3.29 (s, 3H)
***syn/anti*-11e**	4.61 (ddd, 6.5, 3, 3, 1H) 4.35 (m, 1H)	5.16 (d, 6.5, 1H) 3.88 (d, 5.5, 1H)	3.82 (m, 2H) [d]	1.81 (s, 3H) 1.67 (s, 3H)	5.03 (dd, 12, 8, 1H) [105.0]	4.58 (d, 8, 1H) [80.7]	3.8 (d, 12, 1H) [76.0]	R = $(CH_2)_2OCH_3$[d] 3.29 (s, 3H) 3.26 (s, 3H)
12a	4.57 (m, 2H)	5.19 (d, 7.0, 1H) 5.13 (d, 7.0, 1H)	3.79 (t, 4.0, 2H) 3.70 (m, 2H)	1.87 (s, 3H) 1.84 (s, 3H)	5.09 (t, 6.5, 1H)	4.67 (m, 1H) 3.56 (m, 1H)	–	R = CH_3: 3.48 (s, 3H) 3.43 (s, 3H) cyclohexenyl CH_2 groups: 0.07; 0.53; 0.89; 1.18; 1.31; 1.44 (each: m, 1H)

[a] Multiplicity (d, doublet; m, multiplet; q, quartet; s, singlet; t, triplet), coupling constants (in Hz), and relative integration in parentheses. In brackets, ^{13}C chemical shifts. [b] See Table 2 for labeling. [c] 300 MHz spectrum. [d] Diastereotopic **4** and $(CH_2)_2$ protons of the R substituent of the *syn*/*syn* and *syn*/*anti* isomer appear overlapped in the 3.72–3.42 ppm range.

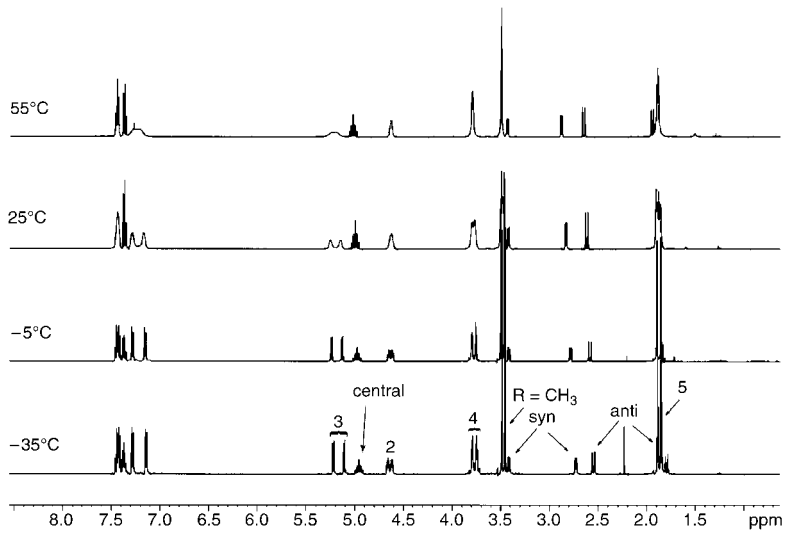

Figure 2. Variable temperature ^{1}H NMR spectra of **8a**.

of the two oxazoline rings (H2, H3, H4, H5) give rise to two sets of signals below 0 °C, but above 45 °C, only one set of broad signals is observed, indicating that the movement at high temperature in solution is fast relative to the NMR time-scale. However, the number of signals for the allyl protons is independent of the temperature and no coalescence is observed, neither between the pairs of the *syn* or *anti* protons nor among them.

In order to elucidate the solution structure of these complexes and their dynamic behaviour, some NOE NMR experiments were carried out. From NOE contacts, we could associate the allyl protons with the bis(oxazoline) protons nearby to the allyl moiety, as shown in Figure 3 for **8c**, allowing a complete correlation.

In addition to the NOE contacts, exchange signals between some protons (H3 and H3′ or H_{anti} and $H_{anti'}$) confirm the presence of two movements, a faster apparent allyl rotation around the palladium-allyl bond and a slower η^3-η^1-η^3 process.[21]

It is important to note that, type-**11** complexes containing the 1,3-diphenylallyl group, can give rise to several isomers, depending on the stereochemical relationship between the phenyl substituents of the allyl group and the central allyl

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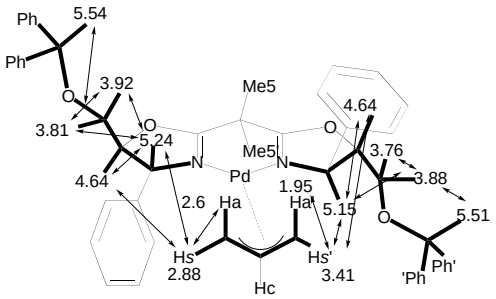
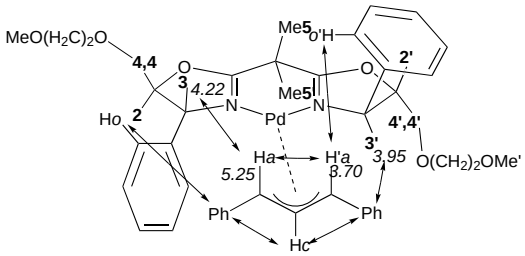
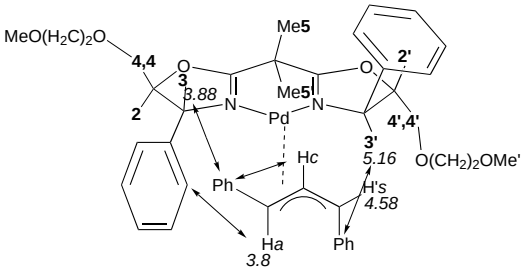


Figure 3. Relevant NOE contacts from NOESY experiment of **8c** (proton chemical shifts in ppm).



syn/syn-**11e**



syn/anti-**11e**

Figure 4. Relevant NOE contacts from NOESY experiment of **11e** isomers (proton chemical shifts in ppm).

hydrogen: *syn*/*syn*; *syn*/*anti* and *anti*/*anti*. For P-donor ligands in addition to the major *syn*/*syn* isomers, *syn*/*anti* isomers are generally observed. But for bis(oxazolines) derived malonic acids, only *syn*/*syn* isomers for (η^3-1,3-diphenylallyl)-palladium(II) complexes have been described in the literature,[12b, f] although we have recently observed *syn*/*anti* isomers for analogous complexes containing chiral biphenyl-bis(oxazolines).[12i]

Here, *syn*/*syn* and *syn*/*anti* isomers (ca. ratio 85/15, respectively) are also detected in solution by NMR spectroscopy for type-**11** complexes (**11a**, **c** and **e**), but only for **11e** the signals of both isomers could be unambigously assigned (Table 3).

The combined use of two-dimensional COSY, HSQC and NOESY experiments allows the assignment of all relevant proton signals for **11e** (Figure 4). The values of the coupling constants between central and terminal allyl protons (13.0 and 10.5 Hz) and the presence of NOE interactions between both terminal protons of the allyl group in the major isomer, allow us to assign *syn*/*syn* isomer to the major species. The minor isomer shows other values for the coupling constants (12.0 and 8.0 Hz) and no NOE contacts between terminal protons, thus suggesting a *syn*/*anti* conformation. The central allyl proton shows an NOE interaction with *ortho* hydrogens of both phenyl groups of the allyl ligand in the *syn*/*syn* isomer, while in the *syn*/*anti* isomer this interaction appears only with one phenyl substituent. Moreover, both isomers show interesting NOE contacts between allyl and oxazoline hydrogens in the 3-position. NOE contacts are observed between both methyl groups in the 5-position and *ortho* hydrogens of the oxazoline phenyl groups. Such interaction can be explained by assuming a boat-like conformation for the chelate ring with the methyl in a pseudoaxial position near the phenyl substituent and interconversion with a second conformation in which the boat-like chelate ring is inverted as reported by Pfaltz.[12b]

Interesting exchange signals between major *syn*/*syn* and minor *syn*/*anti* isomers are observed in NOESY spectra. Exchange between H_{anti} (3.70 ppm) of the major isomer and H_{syn} (4.58 ppm) of the minor one suggests η^3-η^1-η^3 movement. The fact that no other $H_{anti}-H_{syn}$ exchange is observed points to that the exchange mechanism takes place by opening selectively one of the terminal Pd–C bond, leading to the formation of the less hindered *syn*/*anti* isomer. HSQC spectrum shows correlation between H_{anti} (3.70 ppm) and terminal C (72.2 ppm), and H_{anti} (5.25 ppm) and terminal (85.5 ppm) of the major isomer. Therefore, the opened Pd–C bond belongs to the more electrophilic carbon atom containing the substituent that suffers the biggest steric hindrance with the oxazoline fragment (see below, Scheme 7). In addition, exchange signals between some protons (H3 and H3′, H2 and H2′, H4 and H4′) reveal that the well-known apparent allyl rotation around the palladium–allyl bond is also present.[21]

For **11c** an exhaustive NMR study has only been possible for the major isomer (Table 3). According to the value of the coupling constants for $H_{central}-H_{anti}$, a *syn*/*syn* configuration is suggested. NOESY experiments show correlative NOE interactions between protons of the oxazoline ligand H3 (4.54 ppm) – H4 (3.73 ppm; 3.58 ppm) – H6 (5.64 ppm), and H3′ (4.22 ppm) – H4′ (3.31 ppm; 3.51 ppm) – H6′ (5.25 ppm) as well as contacts between the allyl and the oxazoline ligands, H_{anti} (5.31 ppm) – H3 (4.54 ppm) and $H_{anti'}$ (3.65 ppm) – H3′ (4.22 ppm). Similar exchange signals between oxazoline protons as those observed for **11e** complex (H3 and H3′, H4 and H4′, H6 and H6′) suggest the presence of the allyl rotation mechanism.

^{1}H NMR spectra of the complex with cyclic allyl group, **12a**, show the same pattern as the open chain ones described above. It is noteworthy that all non allyl hydrogens of the cyclic fragment display different chemical shifts (0.07 and 0.89 ppm, 0.53 and 1.18 ppm, 1.31 and 1.44 ppm; Table 3). NOESY experiments show interactions between geminal protons, allowing to assign each pair of hydrogen atoms to one carbon. Moreover for **12a**, NOE interactions between H_{syn} (4.67 ppm) – $H_{cyclohexenyl}$ (0.07 ppm and 0.89 ppm) – H3 (5.13 ppm) as well as in the other moiety of the complex, H_{syn} (3.56 ppm) – $H_{cyclohexenyl}$ (1.31 ppm and 1.44 ppm) – H3 (3.19 ppm) allows to describe the relative position of the allyl

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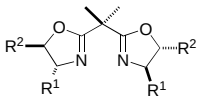
group and the phenyl substituent in the 3-position of the oxazoline ligand.

Allylic alkylations catalyzed by Pd/bis(oxazoline) complexes: When the catalytic results obtained with several bis(oxazolines) derived from dimethylmalonic acid in the alkylation of *rac*-3-acetoxy-1,3-diphenyl-1-propene with dimethyl malonate are compared (Table 4), it is readily observed that among ligands unsubstituted at C-5 ($R^2 = H$, entries 1–5), the best asymmetric induction is achieved with the phenyl and the isopropyl substituted ligands (entries 1 and 2, respectively), while more conformationally flexible substituents (entries 3–5) lead to lower enantiomeric excesses. These results warrant the specification of the chain substituent in our acyclic amino alcohol precursors **3** as aryl groups, while suggesting that the enantioselectivity of the reaction is (at least partially) controlled by steric interactions between the R^1 group in the bis(oxazoline) and the phenyl substituents on the allyl ligands in the palladium intermediate species. These interactions would induce a desymmetrization of the allyl termini with respect to palladium and ultimately determine the more electrophilic terminal allylic carbon towards which the external nucleophilic attack is directed.

Table 4. Asymmetric allylic alkylation of *rac*-3-acetoxy-1,3-diphenyl-1-propene with dimethyl malonate catalyzed by Pd/bis(oxazoline) systems.

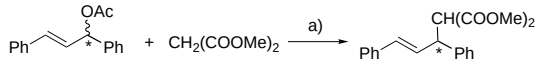


Entry	Ligand[a]	ee (%)	Ref.
1	$R^2 = H$, $R^1 = Ph$	95[b]	this work
2	$R^2 = H$, $R^1 = i$Pr	94[c]	[12b]
3	$R^2 = H$, $R^1 = CH_2Ph$	88[c]	[12b]
4	$R^2 = H$, $R^1 = CH(Ph)(OCOPh)$	90[c]	[12g]
5	$R^2 = H$, $R^1 = CH(Ph)(OH)$	92[c]	[12f]
6	$R^2 = Ph$, $R^1 = CH_2OSi(t\text{Bu})Me_2$	97[c]	[12b]

[a] See formula. [b] Determined by HPLC on a chiral column. [c] Determined by ^{1}H NMR spectroscopy with shift reagent [Eu(hfc)$_3$].

Concerning the effect of substituents at the sterogenic C-5, only one system is reported in the literature (entry 6, Table 4). When the results in entries 3, 4 and 5 are compared with those in entry 6, a benefitial contribution on enantioselectivity of the substituent at C-5 is observed, despite of the rather long distance between this part of the molecule and the region where the reaction events take place. The high enantioselectivity observed with the bis(oxazoline) developed by Pfaltz suggested that the alkoxyalkyl substituent (CH_2OR^1) in the bis(oxazolines) **5a–g** (i.e., the R^2 substituent in Table 4), could also exert an important influence on the reactivity and enantioselectivity of the derived η^3-allylpalladium complexes, so that its study is a matter of interest.

To test the effect of structural variation (CH_2OR^1 group) in the modular amino alcohol precursors **3** on the catalytic activity and enantioselectivity induced by the derived bis(oxazoline) ligands **5–6**, palladium complexes (**8a–g**, **9c** and **10**) containing an unsubstituted allyl moiety were used as catalytic precursors in model asymmetric allylic alkylation reactions. Thus, *rac*-3-acetoxy-1,3-diphenyl-1-propene was alkylated in dichloromethane at room temperature in the presence of **8a–g**, **9c** or **10** (Scheme 6), the nucleophile being generated from dimethyl malonate, BSA, and a catalytic amount of potassium acetate.[22] The results of the enantioselective allylic alkylation are collected in Table 5.



Scheme 6. Asymmetric allylic alkylation catalyzed by **8a–g**, **9c** and **10**. a) **8a–g**, **9c**, **10**, BSA, KOAc, CH_2Cl_2, RT.

Table 5. Results of asymmetric allylic alkylation of *rac*-3-acetoxy-1,3-diphenyl-1-propene with dimethyl malonate catalyzed by type-**8**, **9c** and **10** complexes.[a]

Entry	Precursor	Conv.[b]	*ee* [%][c]
1	**8a**	26	94 (*R*)
2	**8b**	16	95 (*R*)
3	**8c**	60	96 (*R*)
4	**8d**	94	96 (*R*)
5[d]	**8e**	81	93 (*R*)
6	**8f**	8	50 (*R*)
7	**8g**	100	96 (*R*)
8	**9c**	0	–
9	**10**	23	95 (*R*)

[a] Catalytic conditions: 0.02 mmol of complex **8**, **9c**, or **10**, 1 mmol *rac*-1,3-diphenyl-2-propenyl acetate, 3 mmol dimethyl malonate, 3 mmol BSA and a catalytic amount of KOAc in 4 mL CH_2Cl_2 at rt for 48 h. [b] Conversion percentage based on the substrate. [c] *ee* values determined by HPLC on a Chiralcel-OD column. Absolute configuration, in parentheses, determined by optical rotation: U. Leutenegger, G. Umbricht, C. Fahrni, P. V. Matt, A. Pfaltz, *Tetrahedron* **1992**, *48*, 2143–2156. [d] 160 h.

When 2 mol% of catalyst was used, the conversion of the allylic acetate to the desired product was complete after 48–240 h at room temperature. The amount of catalyst could be lowered to 1 mol%, but the required reaction times correspondingly increased. To compare the activities of the different bis(oxazolines), data on conversion and enantioselectivity recorded with the studied ligands after 48 h are provided. As it can be readily seen, catalytic activity notably increases (conversion varies from 16 to 94%) with the size of the C-5 substituent on the oxazoline fragment in cases where the C-4 substituent is phenyl: $CH_2Ph < CH_3 < CHPh_2 < CPh_3$ (entries 1–4). All these catalytic systems induced high enantioselectivities (94–96%) and, while the highest values are recorded with ligands containing the bulkier alkoxy groups, the differences are probably not significative. In line with these results, when the ligand derived from phenylglycinol, bearing no substituent at C-5 is studied (precursor **10**, entry 9), the recorded enantioselectivity is similar to that recorded with **8a–d** and the catalytic activity lies among those of **8a** and **8b**.[23] This tends to indicate the existence of a threshold value in the bulk of the C-5 substituent for its translation into increased activity.

For the study of the influence of the aryl substituent in the amino alcohol skeleton (C-4 substituent in the oxazoline ring), the alkoxymethyl substituent at C-5 was specified as benzhydryloxymethyl since, in this way, our starting point (**8c**) depicts an intermediate value of activity, likely to be sensitive

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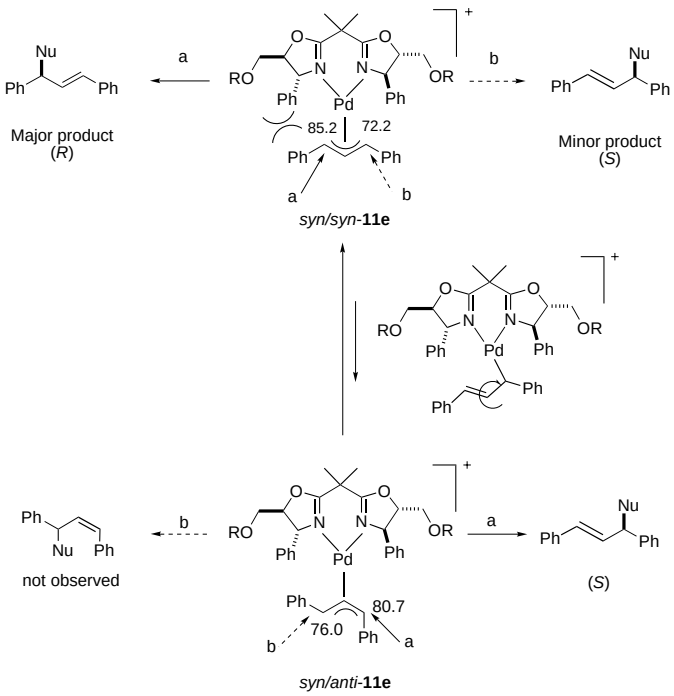
to structural variation. When the results for **8c** are compared with those recorded for **8f** (Ar = mesityl) and **8g** (Ar = 1-naphthyl), the 1-naphthyl substituted ligand gave complete conversion in 48 hours, and 96% *ee* (entry 7), while the mesityl substituted ligand was the less active and the poorest in inducing enantioselectivity (entry 6). Presumably in this case, other palladium species are formed, because of the palladium assisted C–H activation of the *ortho*-methyl groups of the mesityl moiety.[24] Thus, the aryl groups which are slightly more sterically demanding than phenyl are beneficial in the considered catalytic system; however, the sterically crowded aryls probably prevent the achievement of the transition state geometry in the enantioselective reaction path.

Somewhat surprisingly, **9c** turned out to be inactive. In this case, where the substituents on the two stereogenic centres are in *cis* arrangement, decomposition towards palladium metal was immediately observed. In order to understand the different behaviour of *trans*-**5c** and *cis*-**6c** ligands, and since [Pd(η^3-1,3-diphenylallyl)(**6c**)]PF_6 could not be isolated experimentally, the diphenylallyl intermediate complexes derived from these bis(oxazolines) were studied by means of theoretical calculations, at the PM3 (tm) level.[25] The calculated formation enthalpy of both complexes (80.97 kcal mol^{-1} for the *trans* complex and 85.47 kcal mol^{-1} for the *cis* complex) shows that the *cis* is significantly less stable than the *trans* arrangement, because of the steric interactions between the oxazoline substituents. In practice, these interactions are probably responsible for the observed decomposition in solution when using **9c**.

An additional aspect of these alkylation reactions deserve comment. It is well known that the enantioselectivity in the Pd-catalyzed allylic alkylation with soft reagents is controlled by the nucleophilic attack to the more electrophilic terminal carbon of the allyl ligand in the Pd^{II} intermediates such as **11**. As described above, **11a**, **c** and **e** are, in solution, mixtures of two isomers (*syn*/*syn* and *syn*/*anti*) and this isomerism is observed at the more electrophilic carbon (the one exhibiting the highest ^{13}C chemical shifts). For **11e** in particular, if both species reacted at the same rate, the enantiomeric excess of the reaction product would be lower (the *de* of the active species is 70%) than the observed one (*ee* 93%), because the nucleophilic attack on the more electrophilic carbon atoms leads to opposite enantiomers: *R* configuration for *syn*/*syn*-**11e** and *S* for *syn*/*anti*-**11e** (Scheme 7). The high enantioselectivity observed with our ligands provides an indication that *syn*/*anti* to *syn*/*syn* interconversion should be faster than nucleophilic attack to the *syn*/*anti* stereoisomer.



Scheme 7. Selectivity of the dimethyl malonate attack on the terminal allylic carbon atoms of type-**11** species.

Conclusion

In summary, a new family of bis(oxazolines) (**5a–g**, **6c**) derived from modular, enantiopure amino alcohol has been prepared.

Pd-allyl complexes with **5a–g** and **6c** ligands have been fully studied by means of NMR spectroscopy. For the first time, *syn*/*anti* allyl isomers for type-**11** compounds, containing the disubstituted 1,3-diphenylallyl group and bis(oxazolines) derived from dimethylmalonyl dichloride, have been detected in solution. Two-dimensional NMR experiments have shown that the π-σ-π isomerization process takes place by opening selectively the Pd–C bond containing the carbon atom which suffers the biggest steric hindrance with the oxazoline fragment.

According to the results reported here, both the alkoxymethyl moiety in the starting amino alcohols (the oxazoline C-5 substituent) and the aryl substituent in the amino alcohol skeleton (the oxazoline C-4 substituent) are important in determining the catalytic activity of the palladium complexes of *trans*-disubstituted oxazolines. Thus, the recorded order of reactivity indicates that when the steric bulk of the alkoxy methyl group increases, the aryl substituent on the same oxazoline ring experiences a conformational change in order to minimize the increased steric hindrance. The conformational change in the C-4 substituent, in turn, probably provokes an increased interaction with the allyl moiety. In response to that, the allyl group desymmetrizes with respect to palladium, leading to a more electrophilic carbon atom more efficiently attacked by the malonate anion.

This interpretation also explains the behaviour of the *cis*-substituted bis(oxazoline) **6c**. In response to the increased steric interaction, the type-**11** complex containing **6c** cannot be isolated nor generated under catalytic conditions.

In spite of the existence of *syn*/*syn* and *syn*/*anti* isomerism in the intermediate 1,3-diphenylallyl palladium complexes, very high enantioselectivities have been reported and this fact provides an indication that: a) the *syn*/*syn* isomer reacts much faster than the *syn*/*anti* one, and b) the isomerization of the *syn*/*anti* isomer is fast relative to its alkylation.

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Experimental Section

CAUTION: *Tin compounds are highly toxic. Azide salts are toxic and may explode if heated.*

General methods: All compounds were prepared under a purified nitrogen atmosphere using standard Schlenk and vacuum-line techniques. The solvents were purified by standard procedures[26] and distilled under nitrogen. $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$,[27] $[Pd(\eta^3\text{-}1,3\text{-}Ph_2\text{-}C_3H_3)(\mu\text{-}Cl)]_2$,[12b] and $[Pd(\eta^3\text{-cyclohexenyl})(\mu\text{-}Cl)]_2$[28] were prepared as previously described. Ligand **7** (R = Ph), 2,2-bis[2-(4*S*-phenyl-3,4-dihydrooxazol-2-yl)]propane was prepared as described by Corey et al.[17a] Hydrogen peroxide additions were carried out by a authomatic Metrohm 665 Dossimat syringe. NMR spectra were recorded on Varian XL-500 (^{1}H, standard $SiMe_4$), Bruker DRX 500 (^{1}H, standard $SiMe_4$), Varian Gemini (^{13}C, 50 MHz, standard $SiMe_4$) and Bruker DRX 250 spectrometers in $CDCl_3$ unless otherwise cited. IR spectra were recorded on a Nicolet 520 FT-IR, Nicolet 510 FT-IR and FTIR Nicolet Impact 400 spectrometers. FAB mass spectra were obtained on a Fisons V6-Quattro instrument. The GC analysis were performed on a Hewlett–Packard 5890 Series II gas chromatograph (50 m Ultra 2 capillary column 5% phenylmethylsilicone and 95% dimethylsilicone) with a FID detector. The GC/MS analysis were performed on a Hewlett–Packard 5890 Series II gas chromatograph (50 m Ultra 2 capillary column) interfaced to a Hewlett–Packard 5971 mass selective detector. Optical rotations were measured on a Perkin–Elmer 241MC spectropolarimeter. Enantiomeric excess were determined by HPLC on a Hewlettt–Packard 1050 Series chromatograph (Chiralcel-OD chiral column) with a UV detector, and by GC on a Hewlett–Packard 5890 Series II gas chromatograph (25 m FS-cyclodex-β-I/P column: heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin/polysiloxan) with a FID detector. Elemental analyses were carried out by the Serveis Científico-Tècnics de la Universitat de Barcelona in an Eager 1108 microanalyzer.

3-Acetoxy-1-cyclohexene: This product was prepared following the method described in the literature with minor modifications.[29] To a stirred mixture of cyclohexene (15.0 g, 183 mmol), palladium acetate (42 mg, 0.18 mmol), and benzoquinone (0.59 g, 5.5 mmol) dissolved in 150 mL of acetic acid, hydrogen peroxide (33%, 22.5 mL) was added within 6 h at 50 °C by a automatic syringe (0.25 mL each 4 minutes). Then, the mixture was kept at the same temperature for 6 h. At room temperature, the mixture was filtered over celite and extracted three times with pentane/diethyl ether 1:1 (50 mL). The organic phases were washed with 2 M NaOH solution (3 × 50 mL), dried over anhydrous Na_2SO_4, filtered off, and the solvent removed at room temperature, under reduced pressure. The colourless oil was purified by flash chromatography (silica gel, hexane/diethyl ether 1:1) to yield the title compound (11.5 g, 45%).

(2*S*,3*S*)-3-(1-Naphthyl)-2-diphenylmethoxymethyloxirane (13 g): A solution of (2*S*,3*S*)-2,3-epoxy-3-(1-naphthyl)propanol **1 g** (1.87 g, 9.3 mmol) in DMF (11.2 mL) was added through a cannula to a suspension of sodium hydride (0.477 g, ca. 10.9 mmol) in DMF (11.2 mL) at 0 °C under N_2. The mixture was stirred for 20 min, and diphenylmethylbromide (2.93 g, 11.9 mmol) was added into the mixture with a syringe. The mixture was stirred for 17 h at 0 °C. MeOH (116 mL) and brine (116 mL) were added. The aqueous solution was extracted with Et_2O. The combined organic extracts were dried and concentrated under vacuum. The residual oil was chromatographed using hexane/EtOAc (100:0/98:2) as eluent to give **13 g** (2.96 g, 87%)as an oil. $[\alpha]_D^{23} = +38.3$ ($c = 1.4$ g mL^{-1} in $CHCl_3$); ^{1}H NMR (200 MHz): $\delta = 8.12-8.08$ (m, 1H), 7.90–7.85 (m, 1H), 7.79 (dd, $J = 7$, 2.2 Hz, 1H), 7.54–7.24 (m, 14H), 5.56 (s, 1H), 4.44 (d, $J = 2.2$ Hz, 1H), 3.91 (dd, $J = 11$, 3.7 Hz, 1H), 3.82 (dd, $J = 11$, 5 Hz, 1H), 3.29–3.24 (m, 1H); ^{13}C NMR (50 MHz): $\delta = 142.5$ (C), 133.5 (C), 131.9 (C), 129.2 (CH), 129.0 (CH), 128.6 (CH), 128.1 (CH), 127.6 (CH), 127.5 (CH), 126.8 (CH), 126.4 (CH), 123.4 (CH), 122.8 (CH), 84.5 (CH), 69.3 (CH_2), 60.7 (CH), 55.0 (CH); IR (film): $\tilde{\nu} = 3062$, 3029, 2861, 2825, 1511, 1493, 1453, 1098, 1030, 801, 780, 743, 702 cm^{-1}; MS (CI, NH_3): *m*/*z* (%): 384 (100) $[M+NH_4]^+$, 367 (25) $[M+H]^+$; HRMS (EI): calcd for $C_{26}H_{22}O_2$: 366.1620; found: 366.1635 $[M]^+$.

(2*S*,3*S*)-3-(2,4,6-Trimethylphenyl)-2-diphenylmethoxymethyloxirane (13 f): Compound **1 f** (2.5 g, 13 mmol) in DMF (15.7 mL), sodium hydride (0.665 g, ca. 15.2 mmol) in DMF (15.7 mL), and diphenylmethylbromide (4.08 g, 16.5 mmol) were treated as described for **13 g** with stirring 17 h at 0 °C to give **13 f** (3.28 g, 70%) as an oil after chromatography using hexane/EtOAc (99:1/98:2). $[\alpha]_D^{23} = -2.2$ ($c = 0.75$ g mL^{-1} in $CHCl_3$); ^{1}H NMR (200 MHz): $\delta = 7.40-7.24$ (m, 10H), 6.81 (s, 2H), 5.50 (s, 1H), 3.87–3.80 (m, 2H), 3.69 (dd, $J = 10.9$, 5.1 Hz, 1H), 3.25–3.19 (m, 1H), 2.35 (s, 6H), 2.25 (s, 3H); ^{13}C NMR (50 MHz): $\delta = 142.5$ (C), 133.5 (C), 131.9 (C), 129.2 (CH), 129.0 (CH), 128.6 (CH), 128.1 (CH), 127.6 (CH), 127.5 (CH), 126.8 (CH), 126.4 (CH), 123.4 (CH), 122.8 (CH), 84.5 (CH), 69.3 (CH_2), 60.7 (CH), 55.0 (CH); IR (film): $\tilde{\nu} = 3029$, 2923, 1493, 1451, 1096, 741, 702 cm^{-1}; MS (CI, NH_3): *m*/*z* (%): 376 (18) $[M+NH_4]^+$, 359 (22) $[M+H]^+$, 358 (80) $[M]^+$, 167 (100) $[Ph_2CH]^+$; HRMS (EI): calcd for $C_{25}H_{25}O_2$: 357.1855; found: 357.1863 $[M-H]^+$.

(1*R*,2*R*)-1-Amino-1-(1-naphthyl)-3-diphenylmethoxy-2-propanol (3 g): A solution of **13 g** (2.94 g, 8.0 mmol), $LiClO_4$ (21.0 g, 0.198 mol), and NaN_3 (2.6 g, 40 mmol) in acetonitrile (40 mL) was stirred at 55 °C for 24 h under N_2. H_2O (480 mL) was added, and the aqueous layer was extracted with Et_2O. The combined organic extracts were dried and concentrated under vacuum to give **14 g** (3.24 g) as an oil that was used in the next step without further purification. A solution of **14 g** (3.24 g, 7.91 mmol) and sodium borohydride (954 mg, 23.5 mmol) in THF (18.7 mL) was heated at 55–60 °C under N_2. MeOH (3.9 mL) was added during 1 h. After the mixture was heated at this temperature for 22 h, H_2O (345 mL) was added, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried and concentrated under vacuum. The residual oil was chromatographed through a short silica gel column using hexane/EtOAc (60:40) as eluent to give **3 g** (2.12 g, 70%) and the starting product **14 g** (0.3 g, 9%). Product **3 g** was obtained enantiomerically pure (>99%, HPLC OD: 1 mL min^{-1}, hexane/isopropanol 80:20; t_R (1*R*,2*R*) = 11.5 min; t_R = (1*S*,2*S*) = 20.8 min) after enantiomeric enrichment by selective crystallization of the racemate from pentane/dichloromethane 1:1. $[\alpha]_D^{23} = -77.4$ ($c = 1.05$ g mL^{-1} in $CHCl_3$); ^{1}H NMR (200 MHz): $\delta = 8.11$ (dd, $J = 6.2$, 3.4 Hz, 1H), 7.85 (dd, $J = 6.2$, 3.4 Hz, 1H), 7.75 (d, $J = 8$ Hz, 1H), 7.63 (d, $J = 6.8$ Hz, 1H), 7.49–7.19 (m, 13H), 5.22 (s, 1H), 5.08 (d, $J = 5.2$ Hz, 1H), 4.23 (ddd, $J = 5.2$, 5.2, 5.2 Hz, 1H), 3.52 3.37 (m, 2H), 2.29 (br s, 3H); ^{13}C NMR (50 MHz): $\delta = 141.8$ (C), 138.0 (C), 133.7 (C), 131.1 (C), 128.9 (CH), 128.4 (CH), 128.3 (CH), 127.7 (CH), 127.6 (CH), 127.4 (CH), 127.0 (CH), 126.6 (CH), 126.1 (CH), 125.5 (CH), 125.4 (CH), 123.6 (CH), 122.9 (CH), 84.4 (CH), 72.8 (CH), 70.2 (CH_2), 53.7 (CH); IR (film): $\nu =$ 3371, 3062, 3029, 2921, 2867, 1598, 1493, 1453, 1077, 1028, 781, 741, 702 cm^{-1}; MS (CI, NH_3): *m*/*z* (%): 401 (1) $[M+NH_4]^+$, 384 (100) $[M+H]^+$; HRMS (EI): calcd for $C_{26}H_{25}NO_2$: 383.1885, found: 383.1892 $[M]^+$.

(1*R*,2*R*)-1-Amino-1-(2,4,6-trimethylphenyl)-3-diphenylmethoxy-2-propanol (3 f): Compound **1 f** (3.0 g, 8.4 mmol), $LiClO_4$ (22.0 g, 0.207 mol), and NaN_3 (2.7 g, 41.8 mmol) in acetonitrile (42 mL) were treated as described for **3 g** during 24 h. The workup was identical to the one described for **3 g** to give **14 f** (3.36 g) as an oil that was used in the next step without further purification.

A solution of **14 f** (3.36 g, 8.4 mmol), and sodium borohydride (1.01 g, 25.2 mmol) in THF (19.2 mL) was heated at 55–60 °C under N_2. MeOH (4.2 mL) was added during 1 h, and the mixture was heated at this temperature for 22 h. A workup identical to the one described for **3 g** followed by chromatography through a short silica gel column using hexane/EtOAc (60:40) as eluent yielded the starting product **14 f** (1.65 g, 49%) and **3 f** (1.2 g, 42%). $[\alpha]_D^{23} = -2.53$ ($c = 0.95$ g mL^{-1} in $CHCl_3$); ^{1}H NMR (200 MHz): $\delta = 7.39-7.25$ (m, 10H), 6.83 (s, 2H), 5.47 (s, 1H), 4.52 (d, $J = 6.4$ Hz, 1H), 4.20 (ddd, $J = 8.8$, 5.4, 3 Hz, 1H), 3.83 (dd, $J = 10.2$, 3 Hz, 1H), 3.72 (dd, $J = 9.9$, 5.4 Hz, 1H), 2.41 (s, 6H), 2.24 (s, 3H), 1.64 (br s, 3H); ^{13}C NMR (75 MHz): $\delta = 142.1$ (C), 142.0 (C), 136.9 (C), 136.5 (C), 135.4 (C), 130.4 (C), 128.5 (CH), 128.4 (CH), 127.6 (CH), 127.5 (CH), 127.0 (CH), 126.8 (CH), 84.3 (CH), 73.3 (CH), 71.4 (CH_2), 53.5 (CH), 21.2 (CH_3), 20.7 (CH_3); IR (KBr): $\nu = 3303$, 3029, 2925, 1493, 1455, 1117, 1069, 1030, 743, 706 cm^{-1}; MS (CI, NH_3): *m*/*z* (%): 376 (100) $[M+H]^+$; elemental analysis calcd (%) for $C_{25}H_{29}NO_2$: C 79.96, H 7.78, N 3.73; found: C 79.85, H 7.81, N 3.81.

General procedure for the synthesis of compounds 8 a–g

η^3-Allyl [(4*R*,4′*R*,5*S*,5′*S*)-2,2′-(1-methylethylidene)bis(4-phenyl-5-methoxymethyl-4,5-dihydrooxazole)-*N*,*N*]-palladium(II) hexafluorophosphate (8 a): *Preparation of bis(hydroxyamide) 15 a*: A solution of dimethylmalonyl dichloride (0.47 g, 2.76 mmol) in CH_2Cl_2 (2.76 mL) was added through a cannula to a cold (0 °C) solution of (1*R*,2*R*)-1-amino-3-methoxy-1-phenyl-2-propanol (**3 a**; 1.00 g, 5.52 mmol) and Et_3N (0.77 mL, 5.52 mmol) in CH_2Cl_2 (4 mL). The reaction mixture was allowed to warm to

room temperature and stirred for 20 h. The reaction mixture was diluted with CH_2Cl_2 (18.4 mL) and washed with 2N HCl (3 × 11.5 mL) and saturated aqueous $NaHCO_3$ (3 × 11.5 mL). The organic extracts were dried (Na_2SO_4) and concentrated under vacuum to afford the crude dihydroxy diamide **15a** (1.2 g, 95%) as a yellow foam which was used in the next reaction without further purification. ^{1}H NMR (200 MHz): $\delta = 7.92$ (d, $J =$ 8.2 Hz, 2H), 7.33–7.19 (m, 10H), 5.25 (dd, $J = 8.2$, 4.6 Hz, 2H), 4.01 (ddd, $J = 4.2$, 4.2, 4.2 Hz, 2H), 3.33 (s, 6H), 3.38–3.17 (m, 4H), 1.51 (s, 6H); ^{13}C NMR (50 MHz): $\delta = 173.6$ (C=O), 138.4 (C), 128.6 (CH), 127.4 (CH), 126.7 (CH), 73.3 (CH_2), 72.0 (CH), 59.3 (CH_3), 57.1 (CH), 50.0 (C), 23.6 (CH_3); IR (film): $\tilde{\nu} = 3386$, 3033, 2929, 1663, 1517, 1455, 1106, 735, 700 cm^{-1}; MS (CI, NH_3): m/z (%): 476 (63) $[M+NH_4]^+$, 459 (100) $[M+H]^+$.

Formation of bis(oxazoline) ***5a***: Methanesulfonyl chloride (0.30 mL, 3.88 mmol, 2.2 equiv) was added dropwise to a cold (0 °C) solution of dihydroxy diamide **15a** (0.80 g, 1.74 mmol) and Et_3N (1.07 mL, 7.65 mmol) in CH_2Cl_2 (14.4 mL) was added. The reaction mixture was allowed to warm to room temperature and stirring was continued for 2 h. The reaction mixture was then poured into saturated aqueous NH_4Cl solution (16 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with brine (1 × 10 mL), dried (Na_2SO_4) and concentrated under reduced pressure to afford the crude bis(mesylate) **16a** quantitatively as a yellow oil which was used in the next reaction without further purification. The bis(mesylate) **16a** (1.05 g, 1.71 mmol) was treated with KOH (30 mL of a 5% methanolic solution in weight, 21.2 mmol, 12.4 equiv) for 15 h at room temperature. The reaction mixture was then poured into water (17 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 17 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to afford the crude bis(oxazoline) **5a** (0.66 g, 92%) as a yellow oil which was used in the next reaction without further purification. $[\alpha]_D^{23} = +132.0$ ($c = 0.9$ g mL^{-1} in $CHCl_3$); ^{1}H NMR (200 MHz): $\delta = 7.33$–7.24 (m, 10H), 4.92 (d, $J = 6.6$ Hz, 2H), 4.52 (ddd, $J =$ 5.6, 5.6, 5.6 Hz, 2H), 3.67–3.60 (m, 2H), 3.59–3.52 (m, 2H), 3.42 (s, 6H), 1.69 (s, 6H); ^{13}C NMR (50 MHz): $\delta = 169.7$ (C=N), 142.0 (C), 128.6 (CH), 127.5 (CH), 126.6 (CH), 86.2 (CH), 73.6 (CH_2), 71.8 (CH), 59.4 (CH_3), 39.0 (C), 24.3 (CH_3); IR (film): $\tilde{\nu} = 3064$, 3031, 2985, 2935, 2881, 1659, 1455, 1133, 1113, 700 cm^{-1}; MS (CI, NH_3): m/z (%): 423 (100) $[M+H]^+$.

Preparation of ***8a***: A solution of $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$ (183 mg, 0.50 mmol) and crude bis(oxazoline) **5a** (0.40 g, 0.95 mmol) in EtOH (3 mL) was stirred at room temperature for 1 h and then NH_4PF_6 (158 mg, 0.97 mmol) was added. The reaction mixture was stirred for 14 h and kept in the refrigerator, resulting in the precipitation of the complex **8a** as a white solid (0.44 g, 65%) which was filtered and washed with cold EtOH. $[\alpha]_D^{23} = +36.6$ ($c = 1.0$ g mL^{-1} in $CHCl_3$); ^{1}H NMR (500 MHz): $\delta = 7.44$–7.15 (m, 10H), 5.25 (d, $J = 7$ Hz, 1H), 5.15 (d, $J = 7.5$ Hz, 1H), 4.99 (tt, $J = 12$, 7.5 Hz, 1H), 4.66–4.59 (m, 2H), 3.79 (br d, $J = 4$ Hz, 2H), 3.75 (dd, $J = 4.5$, 3.5 Hz, 2H), 3.50 (s, 3H), 3.47 (s, 3H), 3.42 (br d, $J = 6.5$ Hz, 1H), 2.83 (dd, $J = 7$, 2 Hz, 1H), 2.61 (d, $J = 13$ Hz, 1H), 1.89 (s, 3H), 1.89 (d, $J = 12$ Hz, 1H), 1.85 (s, 3H); ^{13}C NMR (75 MHz): $\delta = 172.8$ (C=N), 139.5 (C), 139.4 (C), 129.5 (CH), 128.9 (CH), 126.6 (CH), 126.3 (CH), 116.1 (CH), 87.8 (CH), 87.6 (CH), 74.5 (CH), 74.4 (CH), 72.0 (CH_2), 71.9 (CH_2), 61.7 (CH_2), 61.1 (CH_2), 59.6 (CH_3), 40.9 (C), 26.3 (CH_3), 24.8 (CH_3); IR (KBr): $\nu = 3033$, 2838, 1663, 1455, 1127, 1096, 1032, 878, 837, 760, 704 cm^{-1}; MS (FAB): m/z (%): 570 (100) $[M - PF_6]^+$; elemental analysis calcd (%) for $C_{28}H_{35}F_6N_2O_4PPd$: C 47.04, H 4.93, N 3.92; found: C 46.81, H 4.98, N 4.08.

η^3-Allyl [(4*R*,4′*R*,5*S*,5′*S*)-2,2′-(1-methylethylidene)bis(5-benzyloxymethyl-4-phenyl-4,5-dihydrooxazole)-*N*,*N*′]-palladium(II) hexafluorophosphate (8b)

Preparation of bis(hydroxyamide) ***15b***: (1*R*,2*R*)-1-Amino-1-phenyl-3-phenylmethoxy-2-propanol (**3b**; 1.00 g, 3.89 mmol) and Et_3N (0.54 mL, 3.89 mmol) in CH_2Cl_2 (2.82 mL) were treated with dimethylmalonyl dichloride (0.33 g, 1.94 mmol) in CH_2Cl_2 (1.94 mL) as described in the general procedure. The workup was identical to the one described for **15a** to give **15b** (952 mg, 80%) as a white foam which was used in the next step without further purification. ^{1}H NMR (200 MHz): $\delta = 7.84$ (d, $J = 8.0$ Hz, 2H), 7.31–7.12 (m, 20H), 5.24 (dd, $J = 8.4$, 4.4 Hz, 2H), 4.48 (d, $J = 11.3$ Hz, 2H), 4.38 (d, $J = 11.3$ Hz, 2H), 4.00 (ddd, $J = 4.0$, 4.0, 4.0 Hz, 2H), 3.41 (dd, $J = 10.0$, 3.3 Hz, 2H), 3.28 (dd, $J = 10.0$, 4.0 Hz, 2H), 1.30 (s, 6H); ^{13}C NMR (50 MHz): $\delta = 173.6$ (C=O), 138.4 (C), 137.2 (C), 128.5 (CH), 128.3 (CH), 128.0 (CH), 127.3 (CH), 126.7 (CH), 73.8 (CH_2), 72.0 (CH), 71.0 (CH_2), 57.0 (CH), 49.9 (C), 23.4 (CH_3); IR (film): $\tilde{\nu} = 3394$, 3031, 2869, 1663, 1515, 1455, 1100, 733, 700 cm^{-1}; MS (CI, NH_3): m/z (%): 628 (3) $[M+NH_4]^+$, 611 (41) $[M+H]^+$, 610 (100) $[M]^+$.

Formation of bis(oxazoline) ***5b***: A solution of dihydroxy diamide **15b** (0.58 g, 0.95 mmol), Et_3N (0.58 mL, 4.16 mmol) and MsCl (0.165 mL, 2.12 mmol) in CH_2Cl_2 (7.8 mL) was treated as described in the general procedure. The workup was identical to the one described for **16a** to give **16b** (697 mg, 96%) as a white foam which was used in the next step without further purification. Bis(mesylate) **16b** (697 mg, 0.91 mmol) was treated with KOH (15.8 mL of a 5% methanolic solution in weight, 11.25 mmol) for 15 h as described for **5a** to afford **5b** (501 mg, 96%) as a yellow oil which was used in the next reaction without further purification. ^{1}H NMR (200 MHz): $\delta = 7.34$–7.22 (m, 20H), 4.98 (d, $J = 6.6$ Hz, 2H), 4.59–4.50 (m, 2H), 4.57 (s, 4H), 3.67–3.65 (m, 4H), 1.68 (s, 6H); ^{13}C NMR (50 MHz): $\delta = 169.6$ (C=N), 142.0 (C), 137.8 (C), 128.6 (CH), 128.5 (CH), 128.4 (CH), 127.7 (CH), 127.5 (CH), 127.4 (CH), 126.6 (CH), 86.3 (CH), 73.3 (CH_2), 71.9 (CH), 70.9 (CH_2), 39.0 (C), 24.4 (CH_3); IR (film): $\tilde{\nu} = 1659$, 1455, 1113, 737, 698 cm^{-1}; MS (CI, NH_3): m/z (%): 592 (3) $[M+NH_4]^+$, 575 (43) $[M+H]^+$, 574 (100) $[M]^+$.

Preparation of ***8b***: A solution of $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$ (44 mg, 0.12 mmol), the bis(oxazoline) **5b** (120 mg, 0.21 mmol) in EtOH (2 mL) and NH_4PF_6 (36 mg, 0.22 mmol) were treated as described in the general procedure for 14 h and then kept in the refrigerator, resulting in the separation of an orange oil. The liquid was decanted and the oil was washed with cold EtOH and dried under vacuum to give **8b** as an orange foam (96 mg, 53%). $[\alpha]_D^{23} = +64.2$ ($c = 0.85$ g mL^{-1} in $CHCl_3$); ^{1}H NMR (300 MHz): $\delta = 7.39$–7.15 (m, 20H), 5.19 (br s, 2H), 4.97 (tt, $J = 12.6$, 7.7 Hz, 1H), 4.65 (s, 4H), 4.63–4.60 (m, 2H), 3.90 (dd, $J = 11.1$, 3.3 Hz, 2H), 3.84 (dd, $J = 11.1$, 4.5 Hz, 2H), 3.41 (br d, $J = 7.8$ Hz, 1H), 2.83 (dd, $J = 7$, 1.9 Hz, 1H), 2.57 (d, $J = 12.3$ Hz, 1H), 1.89 (d, $J = 12.6$ Hz, 1H), 1.81 (s, 6H); ^{13}C NMR (75 MHz): $\delta = 172.7$ (C=N), 139.5 (C), 137.4 (C), 129.5 (CH), 128.9 (CH), 128.5 (CH), 128.0 (CH), 127.9 (CH), 126.6 (CH), 126.3 (CH), 116.1 (CH), 87.7 (CH), 87.5 (CH), 74.7 (CH), 74.5 (CH), 73.6 (CH_2), 69.6 (CH_2), 69.5 (CH_2), 61.6 (CH_2), 61.1 (CH_2), 40.9 (C), 26.2 (CH_3), 24.8 (CH_3); IR (film): $\tilde{\nu} = 3033$, 1659, 1474, 1455, 1135, 1028, 837, 739, 700 cm^{-1}; MS (FAB): m/z (%): 721 (100) $[M - PF_6]^+$.

η^3-Allyl [(4*R*,4′*R*,5*S*,5′*S*)-2,2′-(1-methylethylidene)bis(5-diphenylmethoxymethyl-4-phenyl-4,5-dihydrooxazole)-*N*,*N*′]-palladium(II) hexafluorophosphate (8c)

Preparation of bis(hydroxyamide) ***15c***: (1*R*,2*R*)-1-Amino-1-phenyl-3-diphenylmethoxy-2-propanol (**3c**; 1.5 g, 4.5 mmol) and Et_3N (0.63 mL, 4.5 mmol) in CH_2Cl_2 (3.3 mL) were treated with dimethylmalonyl dichloride (0.38 g, 2.25 mmol) in CH_2Cl_2 (2.3 mL) as described in the general procedure. After the usual workup, dihydroxy diamide **15c** was obtained as a white foam (1.67 g, 97%) which was used in the next reaction without further purification. ^{1}H NMR (200 MHz): $\delta = 7.66$ (d, $J = 8.4$ Hz, 2H), 7.30–7.12 (m, 30H), 5.26–5.2 (m, 2H), 5.21 (s, 2H), 4.08–4.00 (m, 2H), 3.33 (dd, $J = 9.7$, 3.9 Hz, 2H), 3.41 (dd, $J = 10$, 4.4 Hz, 2H), 1.18 (s, 6H); ^{13}C NMR (50 MHz): $\delta = 173.5$ (C=O), 141.1 (C), 140.8 (C), 138.1 (C), 128.4 (CH), 127.7 (CH), 127.6 (CH), 127.4 (CH), 127.2 (CH), 127.0 (CH), 126.8 (CH), 84.9 (CH), 72.1 (CH), 70.4 (CH_2), 56.6 (CH), 49.9 (C), 23.4 (CH_3); IR (film): $\tilde{\nu} = 3398$, 3031, 2921, 1663, 1495, 1453, 1098, 1028, 733, 698 cm^{-1}; MS (FAB): m/z (%): 764 (100) $[M+H]^+$.

Formation of bis(oxazoline) ***5c***: A solution of dihydroxy diamide **15c** (527 mg, 0.691 mmol), Et_3N (0.424 mL, 3.04 mmol) and MsCl (0.118 mL, 1.52 mmol) in CH_2Cl_2 (5.5 mL) was treated as described in the general procedure. After the usual workup, bis(mesylate) **16c** was obtained quantitatively as a white foam which was used in the next step without further purification. The bis(mesylate) **16c** (598 mg, 0.65 mmol) was treated with KOH (11.4 mL of a 5% methanolic solution in weight, 8.03 mmol) for 15 h as described for **5a** to afford **5c** (432 mg, 91%) as a white solid. The product was recrystallized from Et_2O. $[\alpha]_D^{23} = +143.05$ ($c =$ 0.66 g mL^{-1} in $CHCl_3$); ^{1}H NMR (500 MHz): $\delta = 7.26$–7.16 (m, 30H), 5.31 (s, 2H), 4.97 (d, $J = 6.4$ Hz, 2H), 4.48 (ddd, $J = 5$, 5, 5 Hz, 2H), 3.58 (dd, $J =$ 10, 5 Hz, 2H), 3.54 (dd, $J = 10$, 4.8 Hz, 2H), 1.59 (s, 6H); ^{13}C NMR (75 MHz): $\delta = 169.7$ (C=N), 142.2 (C), 141.8 (C), 141.7 (C), 128.6 (CH), 128.4 (CH), 128.3 (CH), 127.6 (CH), 127.5 (CH), 127.4 (CH), 127.0 (CH), 126.9 (CH), 126.6 (CH), 86.3 (CH), 83.9 (CH), 72.0 (CH), 69.6 (CH_2), 39.0 (C), 24.3 (CH_3); IR (film): $\tilde{\nu} = 3062$, 3029, 2937, 1659, 1495, 1453, 1111, 743, 698 cm^{-1}; MS (FAB): m/z (%): 727 (100) $[M]^+$; elemental analysis calcd (%) for $C_{49}H_{46}N_2O_4$: C 80.96, H 6.38, N 3.85; found: C 80.97, H 6.40, N 3.83.

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Preparation of ***8c***: A solution of $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$ (44 mg, 0.12 mmol), bis(oxazoline) **5c** (158 mg, 0.217 mmol) in EtOH (2.5 mL) and NH_4PF_6 (36 mg, 0.22 mmol) were treated as described in the general procedure for 14 h and kept in the refrigerator, resulting in the precipitation of the complex **8c** as a white solid (115 mg, 52%). $[\alpha]_D^{23} = +96.9$ ($c = 0.5$ g mL^{-1} in $CHCl_3$); ^{1}H NMR (500 MHz): $\delta = 7.41-7.1$ (m, 30H), 5.54 (s, 1H), 5.51 (s, 1H), 5.24 (d, $J = 6.5$ Hz, 1H), 5.15, (d, $J = 6.5$ Hz, 1H), 5.02 (tt, $J = 12.6$, 6.9 Hz, 1H), 4.68–4.66 (m, 2H), 3.92 (dd, $J = 12$, 4 Hz, 1H), 3.88 (dd, $J = 12$, 4 Hz, 1H), 3.81 (dd, $J = 12$, 4 Hz, 1H), 3.76 (dd, $J = 12$, 4 Hz, 1H), 3.41 (br d, $J = 7.2$ Hz, 1H), 2.88 (dd, $J = 6.9$, 3.5 Hz, 1H), 2.61 (d, $J = 12.5$ Hz, 1H), 1.95 (d, $J = 12.5$ Hz, 1H), 1.82 (s, 3H), 1.75 (s, 3H); ^{13}C NMR (75 MHz): $\delta = 172.8$ (C=N), 141.3 (C), 139.3 (C), 129.5 (CH), 128.9 (CH), 128.5 (CH), 127.8 (CH), 127.7 (CH), 127.1 (CH), 126.9 (CH), 116.2 (CH), 87.5 (CH), 84.2 (CH), 75.0 (CH), 68.7 (CH_2), 61.6 (CH_2), 61.2 (CH_2), 40.9 (C), 26.1 (CH_3); IR (KBr): $\nu = 3031$, 1659, 1455, 1133, 839, 749, 700 cm^{-1}; MS (ESP, MeOH): m/z (%): 873 (100) $[M - PF_6]^+$; elemental analysis calcd (%) for $C_{52}H_{51}F_6N_2O_4PPd$: C 61.27, H 5.04, N 2.75; found: C 60.29, H 5.09, N 2.58.

η^3-Allyl [(4*R*,4′*R*,5*S*,5′*S*)-2,2′-(1-methylethylidene)bis(4-phenyl-5-triphenylmethoxymethyl-4,5-dihydrooxazole)-*N*,*N*]-palladium(II) hexafluorophosphate (8d)

Preparation of bis*(hydroxyamide)* ***15d***: (1*R*,2*R*)-1-Amino-1-phenyl-3-triphenylmethoxy-2-propanol (**3d**; 1.00 g, 2.44 mmol) and Et_3N (0.34 mL, 2.44 mmol) in CH_2Cl_2 (1.8 mL) were treated with dimethylmalonyl dichloride (0.206 g, 1.22 mmol) in CH_2Cl_2 (1.2 mL) as described in the general procedure for 20 h. The usual work up afforded the crude dihydroxy diamide **15d** (1.1 g, 99%) as a yellow foam which was used in the next reaction without further purification. ^{1}H NMR (200 MHz): $\delta =$ 7.37–7.0 (m, 42H), 5.12 (dd, $J = 8$, 4 Hz, 2H), 4.16–4.08 (m, 2H), 3.02–2.98 (m, 4H), 1.38 (s, 6H); ^{13}C NMR (50 MHz): $\delta = 173.0$ (C=O), 143.3 (C), 137.3 (C), 128.5 (CH), 128.2 (CH), 127.8 (CH), 127.2 (CH), 127.0 (CH), 87.1 (C), 72.1 (CH), 69.2 (CH_2), 56.1 (CH_2), 49.6 (C), 23.9 (CH_3); IR (KBr): $\nu =$ 3409, 1661, 1495, 1449, 1077, 745, 700 cm^{-1}; MS (FAB): m/z (%): 938 (100) $[M+Na]^+$.

Formation of bis(oxazoline) ***5d***: A solution of dihydroxy diamide **15d** (1.09 g, 1.19 mmol), Et_3N (0.73 mL, 5.25 mmol) and MsCl (0.2 mL, 2.63 mmol) in CH_2Cl_2 (9.8 mL) was treated as described in the general procedure. After the usual workup, bis(mesylate) **16d** was obtained quantitatively (1.27 g) as a white foam which was used in the next step without further purification. The bis(mesylate) **16d** (510 mg, 0.475 mmol) was treated with KOH (8.9 mL of a 5% methanolic solution in weight, 6.32 mmol) for 15 h as described for **5a** to afford **5d** (0.4 g, 96%) as a white foam which was recrystallized from EtOH. $[\alpha]_D^{23} = +120.85$ ($c = 1.05$ g mL^{-1} in $CHCl_3$); ^{1}H NMR (300 MHz): $\delta = 7.5-7.20$ (m, 40H), 5.0 (d, $J = 6.9$ Hz, 2H), 4.53–4.47 (m, 2H), 3.42 (dd, $J = 10.2$, 4.2 Hz, 2H), 3.31 (dd, $J = 10.2$, 4.6 Hz, 2H), 1.76 (s, 6H); ^{13}C NMR (75 MHz): $\delta = 169.8$ (C=N), 143.6 (C), 142.3 (C), 128.6 (CH), 128.5 (CH), 127.8 (CH), 127.4 (CH), 127.1 (CH), 126.7 (CH), 86.8 (CH), 86.6 (CH), 71.9 (CH), 6_4.4 (CH_2), 39.1 (C), 24.5 (CH_3); IR (film): $\tilde{\nu} = 1655$, 1449, 1117, 911, 733, 700 cm^{-1}; MS (FAB): m/z (%): 880 (100); HRMS (FAB): calcd for $C_{61}H_{55}N_2O_4$: 879.4162, found: 879.4190 $[M+H]^+$.

Preparation of ***8d***: A solution of $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$ (21.7 mg, 0.059 mmol), the bis(oxazoline) **5d** (100 mg, 0.114 mmol) in EtOH (1 mL) and NH_4PF_6 (20 mg, 0.123 mmol) were treated as described in the general procedure for 14 h and kept in the refrigerator, resulting in the precipitation of the complex **8d** as a white solid (68 mg, 51%). $[\alpha]_D^{23} =$ +72.9 ($c = 1.8$ g mL^{-1} in CH_2Cl_2); ^{1}H NMR (300 MHz): $\delta = 7.45-7.01$ (m, 40H), 5.04 (d, $J = 7.2$ Hz, 1H), 5.06–4.9 (m, 1H), 4.52–4.46 (m, 2H), 3.69 (dd, $J = 11.5$, 3.3 Hz, 2H), 3.56 (dd, $J = 11.5$, 4.8 Hz, 2H), 3.37 (br d, $J =$ 6 Hz, 1H), 2.84 (br d, $J = 6.6$ Hz, 1H), 2.57 (d, $J = 12.3$ Hz, 1H), 1.94 (s, 7H); ^{13}C NMR (75 MHz): $\delta = 172.8$ (C=N), 143.1 (C), 139.2 (C), 129.5 (CH), 129.0 (CH), 128.5 (CH), 127.5 (CH), 126.4 (CH), 126.3 (CH), 88.1 (C), 87.3 (CH), 74.8 (CH), 63.6 (CH_2), 61.7 (CH_2), 61.3 (CH_2), 41.1 (C), 25.8 (CH_3); IR (film): $\tilde{\nu} = 3060$, 1656, 1492, 1449, 1131, 839, 749, 700 cm^{-1}; MS (ESP, MeOH): m/z (%): 1025 (100) $[M - PF_6]^+$; elemental analysis calcd (%) for $C_{64}H_{59}F_6N_2O_4PPd$: C 65.62, H 5.08, N 2.39; found: C 64.24, H 5.18, N 2.70.

η^3-Allyl [(4*R*,4′*R*,5*S*,5′*S*)-2,2′-(1-methylethylidene)bis(5-methoxyethoxymethyl-4-phenyl-4,5-dihydrooxazole)-*N*,*N*]-palladium(II) hexafluorophosphate (8e)

Preparation of bis(hydroxyamide) ***15e***: (1*R*,2*R*)-1-Amino-3-[2-(methoxy)ethoxy]-1-phenyl-2-propanol (**3e**; 0.60 g, 2.66 mmol) and Et_3N (0.372 mL, 2.66 mmol) in CH_2Cl_2 (1.9 mL) were treated with dimethylmalonyl dichloride (0.225 g, 1.33 mmol) in CH_2Cl_2 (1.34 mL) as described in the general procedure for 20 h. After the usual workup, dihydroxy diamide **15e** was obtained as an orange oil (0.589 g, 81%) which was used in the next reaction without further purification. ^{1}H NMR (200 MHz): $\delta = 7.81$ (d, $J = 8.8$ Hz, 2H), 7.36–7.20 (m, 10H), 5.48 (dd, $J = 8.6$, 4.6 Hz, 2H), 3.94–3.92 (m, 2H), 3.82–3.32 (m, 12H), 3.51 (s, 6H), 1.50 (s, 6H); ^{13}C NMR (50 MHz): $\delta = 173.6$ (C=O), 139.2 (C), 128.4 (CH), 127.9 (CH), 127.0 (CH), 126.8 (CH), 126.3 (CH), 72.1 (CH), 71.8 CH_2), 71.5 (CH_2), 70.5 (CH_2), 58.6 (CH_3), 57.5 (CH), 50.3 (C), 23.7 (CH_3); IR (film): $\tilde{\nu} = 3390$, 3064, 3031, 2894, 1667, 1515, 1455, 1200, 1104, 735, 702 cm^{-1}; MS (CI, NH_3): m/z (%): 564 (19) $[M+NH_4]^+$, 547 (100) $[M+H]^+$.

Formation of bis(oxazoline) ***5e***: A solution of dihydroxy diamide **15e** (0.5 g, 0.915 mmol), Et_3N (0.559 mL, 4.0 mmol) and MsCl (0.157 mL, 2.0 mmol) in CH_2Cl_2 (7.6 mL) was treated as described in the general procedure. After the usual workup, bis(mesylate) **16e** was obtained quantitatively as an orange oil which was used in the next step without further purification. The bis(mesylate) **16e** (0.64 g, 0.915 mmol) was treated with KOH (15.9 mL of a 5% methanolic solution in weight, 11.25 mmol) for 15 h as described for **5a** to afford bis(oxazoline) **5e** (415 mg, 89%) as an orange oil which was used in the next reaction without further purification. ^{1}H NMR (200 MHz): $\delta = 7.35-7.20$ (m, 10H), 4.94 (d, $J = 6.6$ Hz, 2H), 4.54 (ddd, $J = 5$, 5, 5 Hz, 2H), 3.73–3.52 (m, 12H), 3.38 (s, 6H), 1.68 (s, 6H); ^{13}C NMR (50 MHz): $\delta = 169.6$ (C=N), 142.1 (C), 128.6 (CH), 127.5 (CH), 126.6 (CH), 86.4 (CH), 72.4 (CH_2), 72.0 (CH_2), 72.0 (CH), 71.0 (CH_2), 59.0 (CH_3), 39.0 (C), 24.4 (CH_3); IR (film): $\tilde{\nu} = 2879$, 1659, 1495, 1455, 1111, 1030, 994, 700 cm^{-1}; MS (CI, NH_3): m/z (%): 546 (100) $[M + 2\,NH_4]^+$.

Preparation of ***8e***: A solution of $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$ (137 mg, 0.37 mmol), bis(oxazoline) **5e** (362 mg, 0.71 mmol) in EtOH (4 mL) and NH_4PF_6 (122 mg, 0.75 mmol) were treated as described in the general procedure for 14 h and kept in the refrigerator, resulting in the separation of an orange oil. The liquid was decanted and the oil was washed with cold EtOH and dried under vacuum to give the complex **8e** as an orange foam (0.3 g, 53%). $[\alpha]_D^{23} = +50.9$ ($c = 1.01$ g mL^{-1} in CH_2Cl_2); ^{1}H NMR (300 MHz): $\delta = 7.42-$ 7.2 (m, 10H), 5.20 (br s, 2H), 4.98 (tt, $J = 12.3$, 6.9 Hz, 1H), 4.68–4.63 (m, 2H), 3.89–3.87 (m, 4H), 3.76–3.57 (m, 8H), 3.42 (br d, $J = 6.9$ Hz, 1H), 3.37 (s, 6H), 2.83 (dd, $J = 7.2$, 1.8 Hz, 1H), 2.6 (d, $J = 12.6$ Hz, 1H), 1.89 (d, $J = 12.6$ Hz, 1H), 1.87 (s, 6H); ^{13}C NMR (75 MHz): $\delta = 172.8$ (C=N), 139.4 (C), 129.4 (CH), 128.8 (CH), 126.4 (CH), 116.0 (CH), 87.6 (CH), 74.5 (CH), 71.7 (CH_2), 70.9 (CH_2), 70.6 (CH_2), 61.5 (CH_2), 61.0 (CH_2), 58.9 (CH_3), 40.8 (C), 25.6 (CH_3); IR (film): $\tilde{\nu} = 2927$, 1659, 1495, 1457, 1221, 1129, 839, 756, 702 cm^{-1}; MS (FAB): m/z: 658 (100) $[M - PF_6]^+$.

η^3-Allyl [(4*R*,4′*R*,5*S*,5′*S*)-2,2′-(1-methylethylidene)bis(5-diphenylmethoxymethyl-4-(2,4,6-trimethylphenyl)-4,5-dihydrooxazole)-*N*,*N*]-palladium(II) hexafluorophosphate (8f)

Preparation of bis*(hydroxyamide)* ***15f***: (1*R*,2*R*)-1-Amino-1-mesityl-3-diphenylmethoxy-2-propanol (**3f**; 0.8 g, 2.13 mmol) and Et_3N (0.297 mL, 2.13 mmol) in CH_2Cl_2 (1.54 mL) were treated with dimethylmalonyl dichloride (0.18 g, 1.065 mmol) in CH_2Cl_2 (1.1 mL) as described in the general procedure for 20 h. After the usual workup, dihydroxy diamide **15f** was obtained quantitatively as an orange foam which was used in the next reaction without further purification. ^{1}H NMR (200 MHz): $\delta = 7.41$ (d, $J =$ 8.0 Hz, 2H), 7.32–7.25 (m, 20H), 6.68 (s, 4H), 5.53–5.39 (m, 2H), 5.39 (s, 2H), 4.12–4.03 (m, 2H), 3.60 (dd, $J = 9.9$, 3.7 Hz, 2H), 3.50 (dd, $J = 10.2$, 5.2 Hz, 2H), 2.23 (s, 18H), 1.11 (s, 6H); ^{13}C NMR (50 MHz): $\delta = 172.5$ (C=O), 141.3 (C), 136.5 (C), 131.2 (C), 128.4 (CH), 127.6 (CH), 127.0 (CH), 126.9 (CH), 84.8 (CH), 71.5 (CH), 71.0 (CH_2), 52.3 (CH), 49.1 (C), 23.7 (CH_3), 20.8 (CH_3); IR (film): $\tilde{\nu} = 3408$, 3064, 3029, 1669, 1509, 1453, 1094, 735, 702 cm^{-1}; MS (FAB): m/z (%): 848 (100) $[M+H]^+$.

Formation of bis(oxazoline) ***5f***: A solution of dihydroxy diamide **15f** (0.9 g, 1.06 mmol), Et_3N (0.65 mL, 4.67 mmol) and MsCl (0.18 mL, 2.34 mmol) in CH_2Cl_2 (8.7 mL) were treated as described in the general procedure. After the usual workup, bis(mesylate) **16f** was obtained quantitatively as a yellow foam which was used in the next step without further purification. The bis(mesylate) **16f** (1.02 g, 1.02 mmol) was treated with KOH (17.7 mL of a 5% methanolic solution in weight, 12.7 mmol, 12.4) for 15 h as described for **5a** to afford bis(oxazoline) **5f** (0.78 g, 95%) as a yellow foam which was

used in the next reaction without further purification. A fraction of the crude was chromatographed through a silica gel/2.5% Et_3N column using hexane/EtOAc (95:5/90:10) as eluent to give a sample pure for the complete characterisation. $[\alpha]_D^{23} = +118.8$ ($c = 0.54$ g mL^{-1} in CH_2Cl_2); ^{1}H NMR (200 MHz): $\delta = 7.28-7.26$ (m, 20H), 6.76 (s, 4H), 5.45 (d, $J =$ 9.2 Hz, 2H), 5.33 (s, 2H), 4.70–4.63 (m, 2H), 3.64 (dd, $J = 10.8$, 3.4 Hz, 2H), 3.54 (dd, $J = 10.7$, 5.1 Hz, 2H), 2.25 (s, 12H), 2.22 (s, 6H), 1.63 (s, 6H); ^{13}C NMR (50 MHz): $\delta = 168.4$ (C=N), 141.7 (C), 141.6 (C), 137.3 (C), 136.9 (C), 132.7 (C), 130.1 (C), 128.3 (CH), 128.2 (CH), 127.5 (CH), 127.4 (CH), 127.0 (CH), 126.9 (CH), 84.0 (CH) 83.9 (CH), 69.7 (CH_2), 67.6 (CH), 39.0 (C), 24.0 (CH_3), 20.8 (CH_3), 20.5 (CH_3); IR (film): $\tilde{\nu} = 3029$, 2927, 2858, 1656, 1611, 1495, 1455, 1108, 1030, 911, 737, 702 cm^{-1}; MS (FAB): m/z (%): 812 (100) $[M+H]^+$; HRMS (FAB): calcd for $C_{55}H_{58}N_2O_4$: 811.4430, found: 811.4432 $[M]^+$.

Preparation of ***8f***: $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$ (26 mg, 0.071 mmol), bis(oxazoline) **5f** (109 mg, 0.134 mmol) in EtOH (2 mL) and NH_4PF_6 (23 mg, 0.142 mmol) were treated as described in the general procedure for 14 h and kept in the refrigerator, resulting in a poor precipitation of the complex **8f**. Then, the reaction mixture was concentrated under vacuum, CH_2Cl_2 was added. The organic phase was washed with water, separated, subsequently dried ($MgSO_4$), filtered and concentrated under reduced pressure. Hexane (2 mL) was added resulting in the precipitation of the complex **8f** as a white solid (110 mg, 74%). $[\alpha]_D^{23} = +122.2$ ($c = 0.9$ g mL^{-1} in $CHCl_3$); ^{1}H NMR (300 MHz): $\delta = 7.33-7.30$ (m, 20H), 6.79 (s, 4H), 5.76 (d, $J = 8.4$ Hz, 1H), 5.59 (d, $J = 9.3$ Hz, 1H), 5.49 (s, 2H), 5.04 (tt, $J = 12.4$, 6.9 Hz, 1H), 4.80–4.77 (m, 2H), 3.90 (dd, $J = 11$, 2.5 Hz, 2H), 3.73 (dd, $J =$ 11, 2.5 Hz, 2H), 3.35 (dd, $J = 6.5$, 2 Hz, 1H), 2.56 (dd, $J = 7.0$, 2.0 Hz, 1H), 2.41 (d, $J = 12.5$ Hz, 1H), 2.22 (s, 6H), 2.12 (s, 6H), 2.05 (s, 6H), 1.88 (d, $J =$ 12.5 Hz, 1H), 1.75 (s, 3H), 1.72 (s, 3H); ^{13}C NMR (75 MHz): $\delta = 171.4$ (C=N), 141.1 (C), 138.9 (C), 138.6 (C), 137.4 (C), 137.2 (C), 136.9 (C, 130.5 (C), 131.9 (C), 129.8 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.4 (CH), 127.3 (CH), 126.9 (CH), 116.3 (CH), 85.5 (CH), 85.1 (CH), 84.3 (CH), 70.7 (CH), 70.1 (CH), 68.5 (CH_2), 68.0 (CH_2), 60.6 (CH_2), 60.2 (CH_2), 40.9 (C), 25.8 (CH_3), 23.4 (CH_3), 20.8 (CH_3), 20.7 (CH_3), 20.6 (CH_3), 20.0 (CH_3); IR (KBr): $\nu = 3031$, 2925, 1654, 1611, 1495, 1455, 1131, 1090, 1030, 841, 733, 704 cm^{-1}; MS (FAB): m/z (%): 958 (100) $[M-PF_6]^+$; elemental analysis calcd (%) for $C_{60}H_{55}F_6N_2O_4PPd$: C 64.38, H 4.95, N 2.50; found: C 65.41, H 5.14, N 2.65.

η^3-Allyl [(4*R*,4′*R*,5*S*,5′*S*)-2,2′-(1-methylethylidene)bis(5-diphenylmethoxymethyl-4-(1-naphthyl)-4,5-dihydrooxazole)-*N*,*N*′]-palladium(II) hexafluorophosphate (8g)

Preparation of bis(hydroxyamide) ***15g***: (1*R*,2*R*)-1-Amino-1-(1-naphthyl)-3-diphenylmethoxy-2-propanol (**3g**; 0.5 g, 1.3 mmol) and Et_3N (0.182 mL, 1.3 mmol) in CH_2Cl_2 (0.95 mL) were treated with dimethylmalonyl dichloride (0.11 g, 0.65 mmol) in CH_2Cl_2 (0.65 mL) as described in the general procedure for 20 h. After the usual workup, dihydroxy diamide **15g** was obtained quantitatively as an orange foam which was used in the next reaction without further purification. ^{1}H NMR (200 MHz): $\delta = 8.13-8.08$ (m, 2H), 7.89–7.81 (m, 4H), 7.71 (d, $J = 7.8$ Hz, 2H), 7.46–7.41 (m, 8H), 7.30–7.17 (m, 20H), 6.16 (dd, $J = 8$, 4.4 Hz, 2H), 5.16 (s, 2H), 4.27–4.25 (m, 2H), 3.42 (dd, $J = 10.1$, 3.5 Hz, 2H), 3.27 (dd, $J = 10$, 3.4 Hz, 2H), 1.18 (s, 6H); ^{13}C NMR (50 MHz): $\delta = 173.6$ (C=O), 140.9 (C), 140.7 (C), 134.5 (C), 133.7 (C), 130.9 (C), 128.7 (CH), 128.4 (CH), 128.0 (CH), 127.8 (CH), 127.6 (CH), 127.4 (CH), 126.9 (CH), 126.4 (CH), 125.6 (CH), 125.2 (CH), 123.5 (CH), 122.9 (CH), 85.2 (CH), 71.1 (CH), 70.5 (CH_2), 53.4 (CH), 50.0 (C), 23.4 (CH_3); IR (film): $\tilde{\nu} = 3394$, 3062, 1663, 1513, 1453, 1100, 778, 741, 700 cm^{-1}; MS (FAB): m/z (%): 864 (100) $[M+H]^+$.

Formation of bis(oxazoline) ***5g***: A solution of dihydroxy diamide **15g** (620 mg, 0.718 mmol), Et_3N (0.435 mL, 3.12 mmol) and MsCl (0.123 mL, 1.59 mmol) in CH_2Cl_2 (5.9 mL) were treated as described in the general procedure. After the usual workup, bis(mesylate) **16g** was obtained quantitatively as a yellow foam which was used in the next step without further purification. The bis(mesylate) **16g** (0.7 g, 0.69 mmol) was treated with KOH (11.9 mL of a 5% methanolic solution in weight, 8.6 mmol) for 15 h as described for **5a** to afford bis(oxazoline) **5g** (0.53 g, 93%) as a yellow foam which was used in the next reaction without further purification. A fraction of the crude was chromatographed through a silica gel/2.5% Et_3N column using hexane/EtOAc (100:0/80:20) as eluent to give a sample pure for the complete characterisation. $[\alpha]_D^{23} = +12.0$ ($c =$ 0.63 g mL^{-1} in $CHCl_3$); ^{1}H NMR (200 MHz): $\delta = 7.97$ (d, $J = 8.8$ Hz, 2H), 7.83 (d, $J = 7.8$ Hz, 2H), 7.72 (d, $J = 8.0$ Hz, 2H), 7.45–7.23 (m, 28H), 5.92 (d, $J = 5.6$ Hz, 2H), 5.41 (s, 2H), 4.61 (ddd, $J = 4.9$, 4.9, 4.9 Hz, 2H), 3.81 (dd, $J = 10.2$, 4.8 Hz, 2H), 3.72 (dd, $J = 10.6$, 4.4 Hz, 2H), 1.82 (s, 6H); ^{13}C NMR (50 MHz): $\delta = 170.1$ (C=N), 141.7 (C), 141.6 (C), 137.3 (C), 133.8 (C), 130.7 (C), 128.7 (CH), 128.5 (CH), 128.3 (CH), 127.9 (CH), 127.7 (CH), 127.5 (CH), 127.2 (CH), 126.8 (CH), 126.0 (CH), 125.6 (CH), 125.4 (CH), 124.3 (CH), 123.1 (CH), 85.6 (CH), 84.1 (CH), 69.1 (CH_2), 67.9 (CH), 39.3 (C), 24.5 (CH_3); IR (film): $\tilde{\nu} = 3062$, 1661, 1611, 1495, 1453, 1148, 1119, 909, 778, 735, 702 cm^{-1}; MS (FAB): m/z (%): 828 (100) $[M]^+$; HRMS (FAB): calcd for $C_{57}H_{50}N_2O_4$: 827.3804; found: 827.3837 $[M]^+$.

Preparation of ***8g***: $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$ (23 mg, 0.064 mmol), bis(oxazoline) **5g** (0.1 g, 0.121 mmol) in EtOH (2 mL) and NH_4PF_6 (21 mg, 0.13 mmol) were treated as described in the general procedure for 14 h and kept in the refrigerator, resulting in the precipitation of the complex **8g** as a white solid (89 mg, 66%) which was filtered and washed with cold EtOH. $[\alpha]_D^{23} = +92.6$ ($c = 0.45$ g mL^{-1} in $CHCl_3$); ^{1}H NMR (500 MHz): $\delta =$ 7.88 (d, $J = 8.1$ Hz, 2H), 7.84 (d, $J = 8.1$ Hz, 2H), 7.72 (d, $J = 8.4$ Hz, 2H), 7.51–7.29 (m, 28H), 6.14 (br s, 2H), 5.67 (s, 2H), 4.89 (tt, $J = 12.5$, 7 Hz, 1H), 4.73 (br d $J = 4.1$ Hz, 2H), 4.09 (dd, $J = 10.5$, 4.2 Hz, 2H), 3.99 (dd, $J =$ 10.5, 4.2 Hz, 2H), 2.96 (br d, $J = 7$ Hz, 1H), 2.60 (d, $J = 12$ Hz, 1H), 2.51 (br d, $J = 7$ Hz, 1H), 1.89 (s, 6H), 1.70 (d, $J = 12$ Hz, 1H); ^{13}C NMR (75 MHz): $\delta = 172.8$ (C=N), 141.5 (C), 141.2 (C), 134.6 (C), 133.8 (C), 129.9 (CH), 129.2 (CH), 128.7 (CH), 128.5 (CH), 128.0 (CH), 127.7 (CH), 127.4 (CH), 127.1 (CH), 127.0 (CH), 126.2 (CH), 121.8 (CH), 116.3 (CH), 86.9 (CH), 84.2 (CH), 70.8 (CH), 68.5 (CH_2), 61.5 (CH_2), 60.9 (CH_2), 41.1 (C), 25.4 (CH_3); IR (KBr): $\nu = 3064$, 1661, 1474, 1455, 1133, 839, 778, 743, 702 cm^{-1}; MS (FAB): m/z (%): 974 (100) $[M-PF_6]^+$; elemental analysis calcd (%) for $C_{58}H_{63}F_6N_2O_4PPd$: C 63.13, H 5.75, N 2.59; found: C 63.48, H 5.82, N 2.69.

η^3-Allyl [(4*R*,4′*R*,5*R*,5′*R*)-2,2′-(1-methylethylidene)bis(5-diphenylmethoxymethyl-4-phenyl-4,5-dihydrooxazole)-*N*,*N*′]-palladium(II) hexafluorophosphate (9c)

Formation of bis(oxazoline) ***6c***: A solution of dihydroxy diamide **15c** (0.5 g, 0.655 mmol) in anhydrous xylene (13 mL) was heated under reflux in a Dean-Stark apparatus with dibutyl tin dichloride (13 mg) for 48 h. The solvent was distilled off and the crude bis(oxazoline) **6c** was used in the next reaction without further purification.

Preparation of ***9c***: A solution of $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$ (50 mg, 0.137 mmol), bis(oxazoline) **6c** (0.18 g, 0.248 mmol) in EtOH (3 mL) and NH_4PF_6 (44 mg, 0.27 mmol) were treated as described in the general procedure for 14 h and kept in the refrigerator, resulting in the separation of an orange oil. The liquid was decanted and the oil was washed with cold EtOH and dried under vacuum to give **9c** as an orange foam (80 mg, 32%). $[\alpha]_D^{23} =$ -48.1 ($c = 0.55$ g mL^{-1} in $CHCl_3$); ^{1}H NMR (300 MHz): $\delta = 7.33-7.13$ (m, 30H), 5.64 (d, $J = 10.5$ Hz, 1H), 5.53 (d, $J = 10.5$ Hz, 1H), 5.40–5.27 (m, 2H), 4.97 (s, 1H), 4.94 (s, 1H), 4.88 (tt, $J = 12.3$, 7.3 Hz, 1H), 4.11 (d, $J =$ 4.8 Hz, 1H), 3.25–3.20 (m, 4H), 2.72 (dd, $J = 6.9$, 1.8 Hz, 1H), 2.57 (d, $J =$ 12.3 Hz, 1H), 1.84 (s, 3H), 1.77 (s, 3H), 1.72 (d, $J = 12.6$ Hz, 1H); ^{13}C NMR (75 MHz): $\delta = 172.9$ (C=N), 141.2 (C), 141.1 (C), 134.8 (C), 134.7 (C), 128.8 (CH), 128.5 (CH), 128.3 (CH), 128.0 (CH), 127.8 (CH), 127.6 (CH), 127.5 (CH), 126.8 (CH), 126.7 (CH), 116.1 (CH), 84.3 (CH), 83.2 (CH), 83.0 (CH), 74.1 (CH), 73.9 (CH), 67.4 (CH_2), 67.3 (CH_2), 61.8 (CH_2), 60.8 (CH_2), 40.9 (C), 26.0 (CH_3), 25.1 (CH_3); IR (film): $\tilde{\nu} = 3031$, 1659, 1495, 1455, 1135, 1096, 839, 739, 702 cm^{-1}; MS (FAB): m/z (%): 873 (100) $[M-PF_6]^+$.

η^3-Allyl [(4*R*,4′*R*)-2,2′-(1-methylethylidene)bis(4-phenyl)-4,5-dihydrooxazole)-*N*,*N*′]-palladium(II) hexafluorophosphate (10): Analogous complex with SbF_6 as an outer-anion described by Rush et al.[30] Crude bis(oxazoline) **7** (R = Ph) (0.641 g, 1.92 mmol) in acetone/dichloromethane 1:1 (20 mL) was stirred and cooled to 0 °C. A solution of $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$ (0.346 g, 0.96 mmol) in 20 mL of the same mixture of solvents was added, followed by addition of NH_4PF_6 (3.12 g, 19.2 mmol) dissolved in 20 mL of the same mixture of solvents. The mixture was stirred for 1 h at room temperature. Then, the solvent was evaporated and the solid obtained was washed with water and recrystallized from absolute ethanol/pentane (0.99 g, 83%). ^{1}H NMR (250 MHz): $\delta = 7.46-7.14$ (m, 10H), 5.53 (dd, $J = 10.4$, 7.0 Hz, 1H), 5.42 (dd, $J = 10.4$, 7.7 Hz, 1H), 5.00 (m, 3H), 4.30 (m, 2H), 3.43 (d, $J = 6.6$ Hz, 1H), 2.85 (d, $J = 6.0$ Hz, 1H), 2.57 (d, $J = 12.4$ Hz, 1H), 1.93 (d, $J = 12.5$ Hz, 1H), 1.88 (s, 3H), 1.84 (s, 3H); ^{13}C NMR (50 MHz): $\delta = 173.4$ (C=N), 139.9 (C), 139.7 (C), 129.3 (CH), 128.8 (CH), 126.7 (CH), 126.4 (CH), 115.8 (CH), 76.5 (CH_2), 72.8 (CH), 72.4 (CH), 61.2 (CH_2), 60.9 (CH_2), 40.8 (C), 26.6 (CH_3), 24.7 (CH_3); IR (KBr): $\tilde{\nu} = 1566$,

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839 cm^{-1}; MS (FAB): *m/z* (%): 483 (100) $[M-PF_6]^+$; elemental analysis calcd (%) for $C_{24}H_{27}F_6N_2O_2PPd$: C 45.98, H 4.34, N 4.47; found: C 44.65, H 4.50, N 4.52.

η^3-1,3-Diphenylallyl [(4*R*,4′*R*,5*S*,5′*S*)-2,2′-(1-methylethylidene)bis(5-methoxyethoxymethyl-4-phenyl-4,5-dihydrooxazole)-*N*,*N*]-palladium(II) hexafluorophosphate (11e): A solution of $[Pd(\eta^3\text{-}1,3\text{-}Ph_2\text{-}C_3H_3)(\mu\text{-}Cl)]_2$ (56 mg, 0.084 mmol) and crude bis(oxazoline) **5e** (0.1 g, 0.196 mmol) in CH_2Cl_2/THF/MeOH 6:5:5 (16 mL) was stirred at room temperature for 1 h and then NH_4PF_6 (32 mg, 0.198 mmol) was added. After stirring the reaction mixture for one week, it was washed with water, dried ($MgSO_4$) and concentrated under vacuum to give the crude complex. EtOH was added resulting in the separation of an oil. The liquid was decanted and the oil was washed wih cold EtOH and dried under vacuum to give the complex **11e** as an orange foam (0.1 g, 54%). $[\alpha]_D^{23} = -45.4$ ($c = 0.47$ g mL^{-1} in $CHCl_3$); ^1H NMR (500 MHz): δ (major) = 7.39–6.63 (m, 20H), 5.66 (dd, J = 13, 10.5 Hz, 1H), 5.25 (d, J = 13 Hz, 1H), 4.35–4.32 (m, 2H), 4.22 (d, J = 4 Hz, 1H), 3.98 (d, J = 4 Hz, 1H), 3.71–3.42 (m, 12H), 3.70 (dd, J = 10.5, 1 Hz, 1H), 3.36 (s, 3H), 3.29 (s, 3H), 1.87 (s, 3H), 1.58 (s, 3H); minor = 7.48–6.84 (m, 20H), 5.16 (d, J = 6.5 Hz, 1H), 5.03 (dd, J = 12, 8 Hz, 1H), 4.61 (ddd, J = 6.4, 3.1, 3.1 Hz, 1H), 4.58 (d, J = 8 Hz, 1H), 4.37–4.33 (m, 1H), 3.88 (d, J = 5.5 Hz, 1H), 3.81 (d, J = 12 Hz, 1H), 3.82–3.79 (m, 2H), 3.72–3.42 (m, 8H), 3.29 (s, 3H), 3.26 (s, 3H), 3.27–3.25 (m, 2H), 1.81 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (75 MHz): δ (major) = 173.7 (C=N), 172.7 (C=N), 139.6 (C), 139.2 (C), 138.4 (C), 135.6 (C), 129.2 (CH), 129.1 (CH), 128.9 (CH), 128.5 (CH), 128.3 (CH), 128.1 (CH), 125.3 (CH), 124.6 (CH), 107.4 (CH), 87.2 (CH), 87.0 (CH), 85.2 (CH), 72.2 (CH), 71.8 (CH_2), 71.7 (CH_2), 71.2 (CH_2), 70.9 (CH_2), 70.8 (CH_2), 70.1 (CH), 69.4 (CH), 58.9 (CH_3), 40.5 (C), 26.7 (CH_3), 24.1 (CH_3); minor = 173.2 (C=N), 139.4 (C), 138.9 (C), 137.6 (C), 129.6 (CH), 128.9 (CH), 128.2 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 126.5 (CH), 125.7 (CH), 105.0 (CH), 87.7 (CH), 86.8 (CH), 80.7 (CH), 76.0 (CH), 73.0 (CH), 70.5 (CH_2), 69.9 (CH), 58.9 (CH_3), 40.5 (C), 27.0 (CH_3), 23.6 (CH_3); IR (film): $\tilde{\nu}$ = 2925, 1655, 1492, 1451, 1123, 839, 758, 698 cm^{-1}; MS (FAB): *m/z* (%): 809 (100) $[M-PF_6]^+$.

(η^3-Cyclohexenyl)-[(4*R*,4′*R*,5*R*,5′*R*)-2,2′-(1-methylethylidene)bis(5-phenyl-4-methoxymethyl-4,5-dihydrooxazole)-*N*,*N*]-palladium(II) hexafluorophosphate (12a) *Preparation of **12a***: $[Pd(\eta^3\text{-cyclohexenyl})(\mu\text{-Cl})]_2$ (90 mg, 0.168 mmol), bis(oxazoline) **5a** (0.16 g, 0.37 mmol) in EtOH (3 mL) and NH_4PF_6 (60 mg, 0.37 mmol) were treated as described in the general procedure for 14 h and kept in the refrigerator, resulting in the precipitation of the complex **12a** as a white solid (152 mg, 70%) which was filtered and washed with cold EtOH. ^1H NMR (500 MHz): δ = 7.45–7.15 (m, 10H), 5.19 (d, J = 7 Hz, 1H), 5.13 (d, J = 7 Hz, 1H), 5.09 (t, J = 6.5 Hz, 1H), 4.67 (m, 1H), 4.57 (m, 2H), 3.79 (t, J = 4.0 Hz, 2H), 3.70 (m, 2H), 3.56 (m, 1H), 3.48 (s, 3H), 3.43 (s, 3H), 1.87 (s, 3H), 1.84 (s, 3H), 1.44 (m, 1H), 1.31 (m, 1H), 1.18 (m, 1H), 0.89 (m, 1H), 0.53 (m, 1H), 0.07 (m, 1H); ^{13}C NMR (62.9 MHz): δ = 173.1 (C=N), 172.7 (C=N), 139.7 (C), 139.4 (C), 129.7 (CH), 129.5 (CH), 129.0 (CH), 126.8 (CH), 126.4 (CH), 125.9 (C), 106.1 (CH), 88.0 (CH), 87.7 (CH), 78.8 (CH_2), 75.2 (CH_2), 74.6 (CH), 74.4 (CH), 72.0 (CH_2), 59.6 (CH_3), 40.7 (C), 28.2 (CH_2), 27.2 (CH_2), 26.7 (CH_3), 24.4 (CH_3), 19.3 (CH_2); MS (FAB): *m/z* (%): 610 (100) $[M-PF_6]^+$; elemental analysis calcd (%) for $C_{31}H_{39}F_6N_2O_4PPd$: C 49.32, H 5.21, N 3.70; found: C 48.70, H 5.60, N 3.74.

General procedure for palladium-catalyzed allylic alkylation

Allylic alkylation of rac-*3-acetoxy-1,3-diphenyl-1-propene*: The complex **8a–g**, **9c** or **10** (0.02 mmol) was dissolved in CH_2Cl_2 (2 mL). *rac*-3-Acetoxy-1,3-diphenyl-1-propene (252 mg, 1 mmol), dissolved in CH_2Cl_2 (2 mL), was added followed by dimethyl malonate (396 mg, 3 mmol), BSA (610 mg, 3 mmol), and a catalytic amount of KOAc. The mixture was stirred at room temperature for 48 h (unless stated otherwise). Then, the solution was diluted with diethyl ether, filtered over Celite, and washed with water (4 × 10 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered off, and solvent removed under reduced pressure. Purification of the product was done by column chromatography (silica gel; ethyl acetate), followed by heating treatment at 130 °C under vacuum. The enantiomeric excesses were determined by HPLC on a Chiralcel OD column, using hexane/isopropanol 9:1, in a flow of 0.5 mL min^{-1} and pressure 14 bar.

Allylic alkylation of rac-*3-acetoxy-1-cyclohexene*: The procedure was analogous to the one described for the *rac*-3-acetoxy-1,3-diphenyl-1-propene. Purification of the product was done by column chromatography (silica gel; ethyl acetate). The enantiomeric excesses were determined by GC on a FS-cyclodex-β-I/P column.

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[1] For general references on asymmetric catalysis, see: a) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**; b) *Comprehensive Asymmetric Catalysis*, *Vol. I–III* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**; c) I. Ojima, *Catalytic Asymmetric Synthesis*, Wiley, New York, **2000**.

[2] In the well-studied addition of diethylzinc to aldehydes, for instance, ligands performing very well with substrates heavily substituted at the a carbon give less satisfactory results with linear substrates, and vice versa. Compare, for instance, the results obtained with DAIB (M. Kitamura, S. Suga, K. Kawai, R. Noyori, *J. Am. Chem. Soc.* **1986**, *108*, 6071–6072) with those obtained with norephedrine derived amino alcohols (K. Soai, S. Yokoyama, T. Hayasaka, *J. Org. Chem.* **1991**, *56*, 4264–4268).

[3] For recent examples see: a) M. J. Burk, *Acc. Chem. Res.* **2000**, *33*, 363–372; b) U. Nettekoven, M. Widhalm, H. Kalchhauser, P. C. J. Kamer, P. W. N. M. van Leeuwen, M. Lutz, A. L. Spek, *J. Org. Chem.* **2001**, *66*, 759–770; c) for a review on combinatorial approaches to ligand optimization, see: K. D. Shimizu, M. L. Snapper, A. H. Hoveyda, in *Comprehensive Asymmetric Catalysis*, *Vol. III* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**, pp. 1389–1399.

[4] For compilations of natural and unnatural ligands and auxiliaries, see: a) H. U. Blaser, *Chem. Rev.* **1992**, *92*, 935–952; b) J. Seyden-Penne, *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, Wiley, New York, **1995**; c) F. Fache, E. Schulz, M. L. Tommasino, M. Lemaire, *Chem. Rev.* **2000**, *100*, 2159–2231.

[5] T. Katsuki, V. S. Martin, *Org. React.* **1996**, *48*, 1–299.

[6] E. N. Jacobsen, M. H. Wu, in *Comprehensive Asymmetric Catalysis*, *Vol. II* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**, pp. 649–677.

[7] A. Vidal-Ferran, A. Moyano, M. A. Pericàs, A. Riera, *J. Org. Chem.* **1997**, *62*, 4970–4982.

[8] a) A. Vidal-Ferran, A. Moyano, M. A. Pericàs, A. Riera, *Tetrahedron Lett.* **1997**, *38*, 8773–8776; b) A. Vidal-Ferran, N. Bampos, A. Moyano, M. A. Pericàs, A. Riera, J. K. M. Sanders, *J. Org. Chem.* **1998**, *63*, 6309–6318; c) C. Jimeno, A. Vidal-Ferran, A. Moyano, M. A. Pericàs, A. Riera, *Tetrahedron Lett.* **1999**, *40*, 777–780.

[9] M. Pastó, M. A. Pericàs, A. Riera, *Eur. J. Org. Chem.* **2002**, 2337–2341.

[10] C. Puigjaner, A. Vidal-Ferran, A. Moyano, M. A. Pericàs, A. Riera, *J. Org. Chem.* **1999**, *64*, 7902–7911.

[11] For a review, see: A. K. Ghosh, P. Mathivanan, J. Cappiello, *Tetrahedron*: *Asymmetry* **1998**, *9*, 1–45.

[12] For previous use of bis(oxazoline) ligands in palladium-catalyzed allylic alkylation, see: a) D. Muller, G. Umbricht, B. Weber, A. Pfaltz, *Helv. Chim. Acta* **1991**, *74*, 232–240; b) P. von Matt, G. C. Lloyd-Jones, A. B. E. Minidis, A. Pfaltz, L. Macko, M. Neuburger, M. Zehnder, H. Ruegger, P. S. Pregosin, *Helv. Chim. Acta* **1995**, *78*, 265–284; c) W. Zhang, T. Hirao, I. Ikeda, *Tetrahedron Lett.* **1996**, *37*, 4545–4548; d) W. Zhang, T. Kida, Y. Nakatsuji, I. Ikeda, *Tetrahedron Lett.* **1996**, *37*, 7995–7998; e) K. H. Ahn, C.-W. Cho, J. Park, S. Lee, *Tetrahedron*: *Asymmetry* **1997**, *8*, 1179–1185; f) O. Hoarau, H. Aiet-Haddou, J.-C. Daran, D. Cramailere, G. G. A. Balavoine, *Organometallics* **1999**, *18*, 4718–4723; g) O. Hoarau, H. Aït-Haddou, M. Castro, G. A. Balavoine, *Tetrahedron*: *Asymmetry* **1997**, *8*, 3755–3764; h) M. Gómez, S. Jansat, G. Muller, M. A. Maestro, J. Mahía, M. Font-Bardía, X. Solans, *J. Chem. Soc. Dalton Trans.* **2001**, 1432–1439; i) M.

Gómez, S. Jansat, G. Muller, M. A. Maestro, J. Mahía, *Organometallics* **2002**, *21*, 1077 – 1087.
[13] a) M. Chini, P. Crotti, F. Macchia, *J. Org. Chem.* **1991**, *56*, 5939 – 5942; b) M. Chini, P. Crotti, L. A. Flippin, F. Macchia, *J. Org. Chem.* **1991**, *56*, 7043 – 7048; c) M. Chini, P. Crotti, L. A. Flippin, C. Gardelli, E. Giovani, F. Macchia, M. Pineschi, *J. Org. Chem.* **1993**, *58*, 1221 – 1227.
[14] E. Medina, A. Moyano, M. A. Pericàs, A. Riera, *Helv. Chim. Acta* **2000**, *83*, 972 – 988.
[15] E. Medina, A. Vida-Ferran, A. Moyano, M. A. Pericàs, A. Riera, *Tetrahedron: Asymmetry* **1997**, *8*, 1581 – 1586.
[16] a) G. Desimoni, G. Faita, M. Mella, *Tetrahedron* **1996**, *52*, 13649 – 13654; b) I. W. Davies, L. Gerena, L. Castonguay, C. H. Senanayake, R. D. Larsen, T. R. Verhoeven, P. J. Reider, *Chem. Commun.* **1996**, 1753 – 1754.
[17] a) $SOCl_2$: E. J. Corey, N. Imai, H. Zhang, *J. Am. Chem. Soc.* **1991**, *113*, 728 – 729; D. Müller, G. Umbricht, B. Weber, A. Pfaltz, *Helv. Chim. Acta* **1991**, *74*, 232 – 240; b) CH_3SO_3H: E. J. Corey, K. Ishibara, *Tetrahedron Lett.* **1992**, *33*, 6807 – 6810; c) MsCl: S. E. Denmark, N. Nakajima, O. J. C. Nicaise, A. M. Faucher, J. P. Edwards, *J. Org. Chem.* **1995**, *60*, 4884 – 4892; d) $ZnCl_2$: C. Bolm, K. Weickhardt, M. Zehnder, T. Ranff, *Chem. Ber.* **1991**, *124*, 1173 – 1180; e) DAST: A. M. Harm, J. G. Knight, G. Stemp, *Synlett* **1996**, 677 – 678; f) triflic acid: I. W. Davies, C. H. Senayake, R. D. Larsen, T. R. Verhoeven, P. J. Reider, *Tetrahedron Lett.* **1996**, *37*, 813 – 814; g) Burgess reagent: A. J. Rippert, *Helv. Chim. Acta* **1998**, *81*, 676 – 687.
[18] Bis(oxazolines) **5c** and **5d** are crystalline and have been recrystallized from Et_2O and ethanol, respectively. Bis(oxazolines) **5f** and **5g** have been purified by column chromatography (silica gel/2.5% Et_3N) with appreciable loss of yield.
[19] a) Imidates: J. Hall, J. M. Lehn, A. DeCian, J. Fischer, *Helv. Chim. Acta* **1991**, *74*, 1 – 6; b) Me_2SnCl_2: R. E. Lowenthal, A. Abiko, S. Masamune, *Tetrahedron Lett.* **1990**, *31*, 6005 – 6008; c) $BF_3 \cdot Et_2O$: I. W. Davies, L. Gerena, N. Lu, R. D. Larsen, P. J. Reider, *J. Org. Chem.* **1996**, *61*, 9629 – 9630; d) Bu_2SnCl_2: see ref. [16a].
[20] P. S. Pregosin, R. Salzmann, *Coord. Chem. Rev.* **1996**, *155*, 35 – 68 and references therein.
[21] a) J. Sprinz, M. Kiefer, G. Helmchen, M Reggelin, G. Hutter, O. Walter, L. Zsolnai, *Tetrahedron Lett.* **1994**, *35*, 1523 – 1526; b) B. Crociani, S. Antonaroli, M. Paci, F. Di Bianca, L. Canovese, *Organometallics* **1997**, *16*, 384 – 391.
[22] a) B. M. Trost, D. J. Murphy, *Organometallics* **1985**, *4*, 1143 – 1145; b) M. T. El Gihani, H. Heaney, *Synthesis* **1998**, 357 – 375.
[23] The allylic alkylation of *rac*-3-acetoxy-1-cyclohexene with dimethyl malonate was also tested, using **8a** and **10** as catalytic precursors. After 48 h, **8a** system gave very low conversion of substrate (10%) and very low asymmetric induction (14% *ee*). Under analogous conditions, **10** was inactive.
[24] J. Albert, R. Bosque, J. M. Cadena, S. Delgado, J. Granell, G. Muller, J. I. Ordinas, M. Font-Bardia, X. Solans, *Chem. Eur. J.* **2002**, *8*, 2279 – 2287.
[25] MACSPARTAN PRO version 1.0.4. WaveFunction, Inc., 18401 Von Karman Avenue, Suite 370, Irvine, CA 92612 (USA).
[26] D. D. Perrin, W. L. F. Armarego, D. R. Perrin, *Purification of Laboratory Chemicals*, 3rd ed., Pergamon Press, Oxford, UK, **1988**.
[27] Y. Tatsuno, T. Yoshida, S. Otsuka, *Inorg. Synth.* **1990**, *28*, 342 – 345.
[28] B. M. Trost, P. E. Strege, *Tetrahedron Lett.* **1974**, *15*, 2603 – 2606.
[29] a) C. Jia, P. Muller, H. Mimoun, *J. Mol. Cat. A: Chem.* **1995**, *101*, 127 – 136; b) B. Åkermark, E. M. Larsson, J. D. Oslob, *J. Org. Chem.* **1994**, *59*, 5729 – 5733.
[30] S. Rush, A. Reinmuth, W. Risse, *Macromolecules* **1997**, *30*, 7375 – 7385.

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