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# Atropisomeric N-Heterocyclic Carbene-Palladium(II) Complexes: Influence of the Backbone Substitution

Yajie Chou,<sup>[a]</sup> Mathilde Vançon,<sup>[a]</sup> Muriel Albalat,<sup>[a]</sup> Carla Deschodt,<sup>[a]</sup> Paola Nava,<sup>[a]</sup> Stéphane Humbel,<sup>[a]</sup> Nicolas Vanthuyne,<sup>\*[a]</sup> and Hervé Clavier<sup>\*[a]</sup>

In order to facilitate the synthesis of NHC precursors as well as to incorporate new moieties, the influence of the NHC backbone substitution was investigated within the concept of atropisomeric NHC-metal complexes. A series of NHC precursors was prepared from new anilines and used to synthesize the corresponding Pd(allyl)Cl(NHC) complexes, most of the time as

a mixture of diastereomers (*meso* and chiral). Chiral HPLC at preparative scale enabled to obtain enantiopure complexes in low to excellent yields. These complexes displayed good activity in the intramolecular  $\alpha$ -arylation of amides and, as a function of the structure of the chiral catalyst, excellent enantioselectivities were reached (up to 96% ee).

## Introduction

N-heterocyclic carbene (NHC) ligands are of utmost importance in homogenous catalysis as they significantly contributed, for more than two decades, to the development of a wide array of transition metal-catalyzed transformations, among them the well-known olefin metathesis, palladium-catalyzed cross couplings reactions and more recently C–H bond activation.<sup>[1,2]</sup> Hence, much attention has been paid to the development of chiral version of NHC ligands.<sup>[3]</sup> The design of chiral monodentate NHCs can be divided into three main categories: i) the use of chiral sidechain as N-substituents of the NHC,<sup>[4]</sup> including polycyclic structures;<sup>[5]</sup> ii) NHCs with chiral backbones<sup>[6]</sup> that can be associated with various *N*-substituents such as symmetric or dissymmetric *N*-aryl substituents;<sup>[7]</sup> iii) the combination of the two precedent designs,<sup>[7]</sup> including in fused polycyclic structures.<sup>[8]</sup> With these designs, fruitful researches have been accomplished. Nevertheless, to overcome the synthetic challenges of asymmetric catalysis, new designs are still needed.

Recently, we developed the concept of atropisomeric metal-NHC complexes,<sup>[9]</sup> which consists in restricted rotations of dissymmetric *N*-aryl substituents along the C–N bond of the NHC ligands (Figure 1.1). Whereas these rotations are unrestricted for the imidazolium salts, NHC precursors, the metalation step enables the generation of the axis of chirality but the corresponding complexes are obtained as racemic mixture. Due

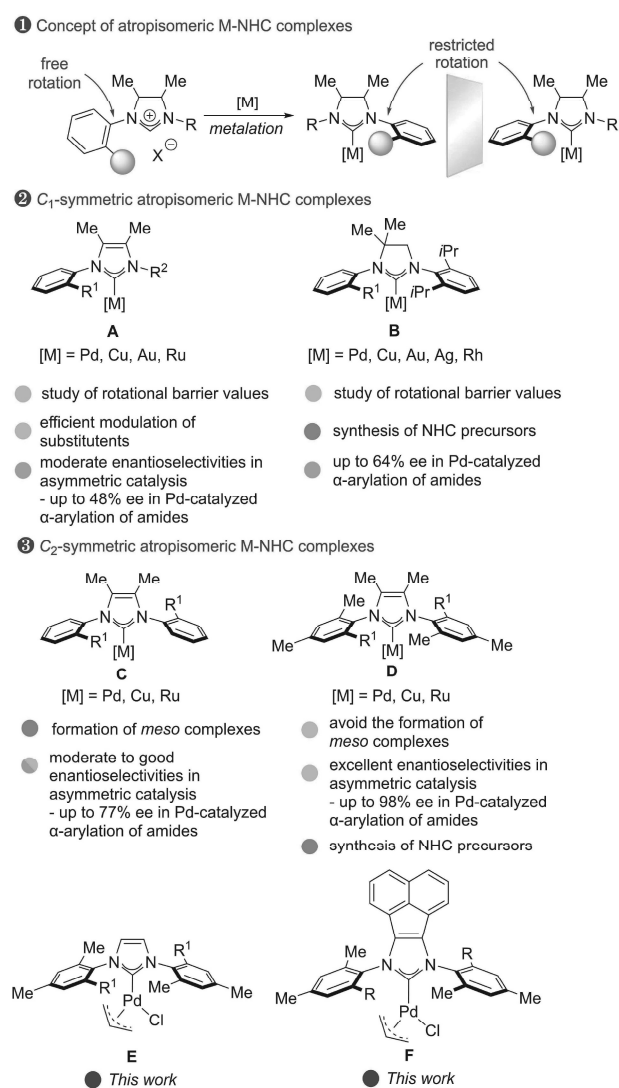


Figure 1. Concept of atropisomeric metal-NHC complexes

to the good stability of many metal-NHC complexes, a resolution by chiral HPLC at preparative scale afforded complexes with high yields and excellent enantiopurities. Conveniently, this design does not necessitate the utilization of building blocks from the chiral pool. This strategy was first developed with  $C_1$ -symmetric Pd-, Cu- and Au-NHC complexes, structure **A**, in order to thoroughly investigate the configuration stabilities and the values of the rotational barriers (Figure 1.2).<sup>[9,10]</sup> It was noticed that the presence of methyl substituents on the NHC backbone was mandatory to obtain configurationally stable metal-NHC complexes. Unfortunately, such chiral palladium complexes led to moderate enantioselectivities in the intramolecular  $\alpha$ -arylation of amides. The concept was successfully extended to NHC with a saturated backbone thanks to the presence of a *gem*-dimethyl pattern, structure **B**.<sup>[11]</sup> Unlike structure **A**, some limitations have been encountered for the synthesis of the NHC precursors. Moreover, albeit slightly higher, enantioinduction levels for the Pd-catalyzed  $\alpha$ -arylation of amides remained moderate. Better enantioselectivities were obtained with  $C_2$ -symmetric Pd-NHC complexes (Figure 1.3).<sup>[12]</sup> However, for structure **C**, a substantial formation of *meso* complexes - *cis*-conformation of the *N*-aryl substituents - was experienced. To circumvent this issue, additional *ortho*-substituents (F or Me - Structure **D**) on the *N*-aryl substituents were found to be beneficial since the corresponding imidazolium salts are conformationally stable and prepared as mainly chiral compounds (racemic). With this design and  $R^1$ =benzhydryl (CHPh<sub>2</sub>), up to 98% ee was reached in the Pd-catalyzed  $\alpha$ -arylation of amides but also in Ru-catalyzed olefin metathesis (up to 94% ee).<sup>[13]</sup> Nonetheless, some synthetic issues have been encountered such as the difficulty to prepare imidazolium salts with other  $R^1$  substituents than a benzhydryl group. For example, several attempts to prepare imidazolium salts with methyl groups on the backbone from anilines **1c** and **1f** (Figure 2) failed. In view of these results, we were wondering if

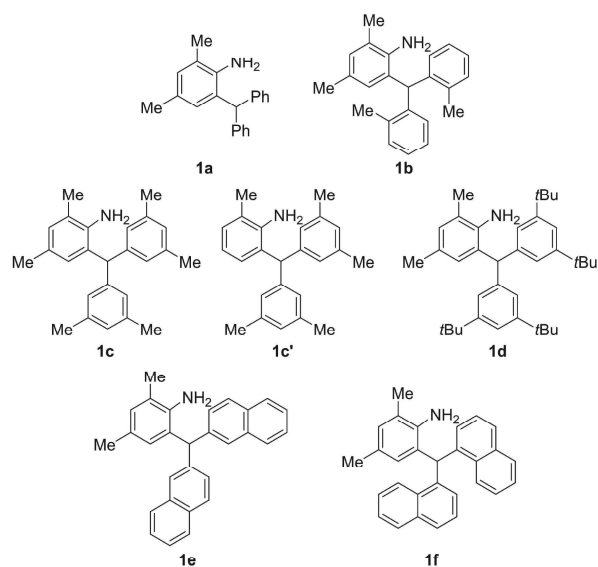


Figure 2. Anilines used in this study.

with additional *ortho*-substituents on the *N*-aryl substituents, the substitution of the NHC backbone with methyl groups was still necessary to obtain configurationally stable atropisomeric metal-NHC complexes. Of note, NHC precursors required to obtain complexes of the general structure **E** should be easier to prepare.

Therein, we also explored NHC ligands containing an acenaphthyl backbone, so-called BIAN-NHC (BIAN = bis(imino)acenaphthene), which are known to accommodate bulky *N*-substituents.<sup>[14]</sup>

## Results and Discussion

First, we decided to thoroughly investigate the rotational barriers of *N*-aryl groups along the C–N bond for PdCl(allyl)(NHC) complexes when the NHC backbone is unsubstituted. To the best of our knowledge, such data have not been reported so far.<sup>[15]</sup> Unfortunately, the synthesis of the expected dissymmetric imidazolium salts, NHC precursors, could not be achieved according to the procedure reported by Mauduit<sup>[16]</sup> or other synthetic pathways. Therefore, DFT theoretical calculations were performed as they allow to determine rotational barriers values with a good accuracy compared to experimental data.<sup>[9–11]</sup> Results of rotational barriers values are depicted in Figure 3. As expected, when the NHC backbone does not contain substituents, a single benzhydryl group in *ortho* position, structure **2a**, does not allow to restrict the rotation of the *N*-aryl substituent about the C–N bond. The calculated value of the rotation on the backbone side ( $\Delta G_{(BB)}^\ddagger$ ) is 83.3 kJ.mol<sup>-1</sup> and corresponds to a half-life of enantiomerization ( $t_{1/2}$ ) of 22 s at 25 °C. However, when the *N*-aryl group contains a second *ortho* substituent in addition of the benzhydryl, either a fluorine (**2b**) or a methyl (**2c**), the values of rotational barriers increase substantially. For both complexes, the lowest barriers account for a rotation of the benzhydryl group on the palladium side ( $\Delta G_{(Pd)}^\ddagger$ ). For complex **2b**, the  $\Delta G_{(Pd)}^\ddagger = 133.7$  kJ.mol<sup>-1</sup> correspond to  $t_{1/2} \approx 500$  years at 25 °C or 32 days at 80 °C. For complex **2c**, the  $\Delta G_{(Pd)}^\ddagger = 159.3$  kJ.mol<sup>-1</sup> correspond to  $t_{1/2} = 32$  years at 100 °C. Thus, these complexes are configurationally stable.

Anilines **1** were prepared by a Friedel-Crafts alkylation process<sup>[17]</sup> or a double addition of an aryl magnesium bromide reagent on an ester function and subsequent

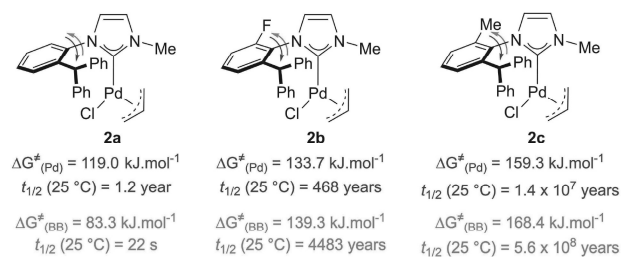


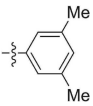


Figure 3. Values of rotational barriers of *N*-aryl substituents in  $C_1$ -symmetric Pd-NHC complexes calculated by DFT and the corresponding half-lives of enantiomerization.

dehydroxylation.<sup>[18]</sup> As depicted in Table 1, several diimines **3** were easily prepared by condensation of anilines **1** with commercially available 40% aqueous solution of glyoxal, albeit some yields were found quite moderate (53% for **3c**, entry 2 and 39% for **3e**, entry 3). The corresponding imidazolium chloride salts **4** were then synthesized through a cyclization step of diamines **3** with *para*-formaldehyde in presence of acid and ZnCl<sub>2</sub>.<sup>[19]</sup> Isolated yields are quantitative in the case of **4a** and **4f** (entries 1 and 4) but somewhat moderate for imidazolium salts **4c** and **4e** (entries 2 and 3). At room temperature, <sup>1</sup>H NMR spectra of imidazolium salts **4** displayed two signals accounting for the characteristic imidazolium proton and

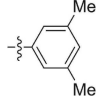
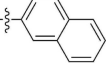
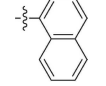
corresponding to the isomers with *cis* and *trans* configurations between *N*-aryl groups. These diastereomers behave certainly as rotamers with rotational barrier values.<sup>[10,15]</sup>

Next, imidazolium chloride salts **4** were converted into the corresponding tetrafluoroborate salts and directly used to perform the formation of PdCl(allyl)(NHC) complexes **5** by treatment with K<sub>2</sub>CO<sub>3</sub> in acetone at 60 °C in presence of [PdCl(allyl)]<sub>2</sub> (Table 2). Complexes **5** were obtained in excellent yields (83-99%) and as a mixture of diastereomers denoted as *meso* and chiral (±). Diastereomers *meso*-**5a** and (±)-**5a** were easily separated due to an important difference of polarity and solubility (entry 1).<sup>[18]</sup> Of note, the structure of complex *meso*-**5a**

**Table 1.** Preparation of imidazolium salts **4**.

Entry	Ar	<b>3</b>	<b>4</b>
1	Ph	96% ( <b>3a</b> )	97% ( <b>4a</b> )
2		54% ( <b>3c</b> )	29% ( <b>4c</b> )
3		39% ( <b>3e</b> )	56% ( <b>4e</b> )
4		99% ( <b>3f</b> )	99% ( <b>4f</b> )

**Table 2.** Synthesis of palladium complexes **5**.

Entry	Ar	Complex <i>meso</i> - <b>5</b>	Complex (±)- <b>5</b>	Overall yield (ratio <i>meso</i> /(±)) <sup>[a]</sup>
1	Ph	60%	36%	96% (1.7:1) ( <b>5a</b> )
2		49%	50%	99% (1:1) ( <b>5c</b> )
3		<i>Diastereomers not separable</i>		83% (1.8:1) ( <b>5e</b> )
4		<i>Diastereomers not separable</i>		96% (> 1:10) ( <b>5f</b> )



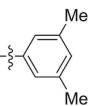
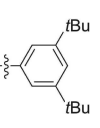
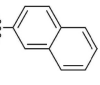
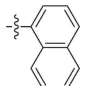
[a] Determined by <sup>1</sup>H NMR spectroscopy.

was unambiguously confirmed by single crystal X-ray diffraction studies.<sup>[18]</sup> For complex **5c**, it was possible to separate both diastereomers by silica gel chromatography (entry 2). Unfortunately, diastereomers of complexes **5e** and **5f** could not be separated by silica gel chromatography (entries 3 and 4). Diastereomeric ratios between *meso* and chiral compounds span from 1:1 to 1.8:1 in favor of the *meso* complex *meso-5* (entries 1–3), with the exception of complex **5f**, which was isolated almost as pure chiral complex (entry 4).

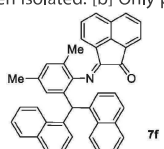
Acenaphthoimidazolium salts **8** were prepared according to the procedure reported by Liu.<sup>[14g]</sup> As depicted in Table 3, the condensation of anilines **1** with acenaphthenequinone was carried out in acetic acid at 120 °C in the presence of zinc(II) chloride. Whereas the expected diimine **6a** was isolated in good yield (entry 1), yields were found significantly lower for diimines **6b** and **6c'** (entries 2 and 3). Starting from anilines **1d** and **1e** containing 3,5-di-*tert*-butylphenyl and 2-naphthyl groups, respectively, the purification to afford pure diimine was unsuccessful (entries 4 and 5). With aniline **1f** containing 1-

naphthyl substituents, only imine **7f** was isolated in an almost quantitative yield (entry 6). To prepare acenaphthoimidazolium salts **8**, diimines **6** were heated at 100 °C in chloromethyl ethyl ether for 20 h. Subsequently, the treatment with KBF<sub>4</sub> enabled to obtain the corresponding tetrafluoroborate salts, which were more convenient to purify by silica gel chromatography. Under these conditions, salts **8a** and **8c'** were isolated in excellent yields and with diastereomeric ratios between *cis* and *trans* isomers close to equimolar (entries 1 and 3). Of note, diastereomers could be partially separated by silica gel chromatography and it was possible to obtain **8c'** with dr > 10:1.<sup>[18]</sup> With diimine **6b**, the cyclization did not take place (entry 2), probably due to an important steric congestion. Acenaphthoimidazolium salts **8d** and **8e** were also obtained, albeit in low quantities (entries 4 and 5). For **8d**, only one diastereomer was formed, unfortunately, its configuration could not be attributed at this stage. Due to the low yield of **8d**, it cannot be stated that the cyclization was diastereoselective. **8e** was isolated with dr = 1:1. Following the same protocol as for complexes **4**, com-

Table 3. Preparation of acenaphthoimidazolium salts **8**.

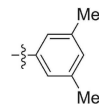
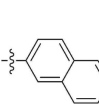
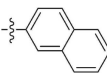
Entry	Ar	R	<b>6</b>	<b>8</b> (dr)
1		Me	71% ( <b>6a</b> )	91% (1.2:1) ( <b>8a</b> )
2		Me	37% ( <b>6b</b> )	NR
3		H	37% ( <b>6c'</b> )	98% (1.3:1) ( <b>8c'</b> )
4		Me	— <sup>[a]</sup>	6% (2 steps) (>20:1) ( <b>8d</b> )
5		Me	— <sup>[a]</sup>	7% (2 steps) (1:1) ( <b>8e</b> )
6		Me	— <sup>[b]</sup>	

[a] Pure product could not be isolated. [b] Only product **7f** was isolated (96%).



**7f**

Table 4. Synthesis of palladium complexes 9.

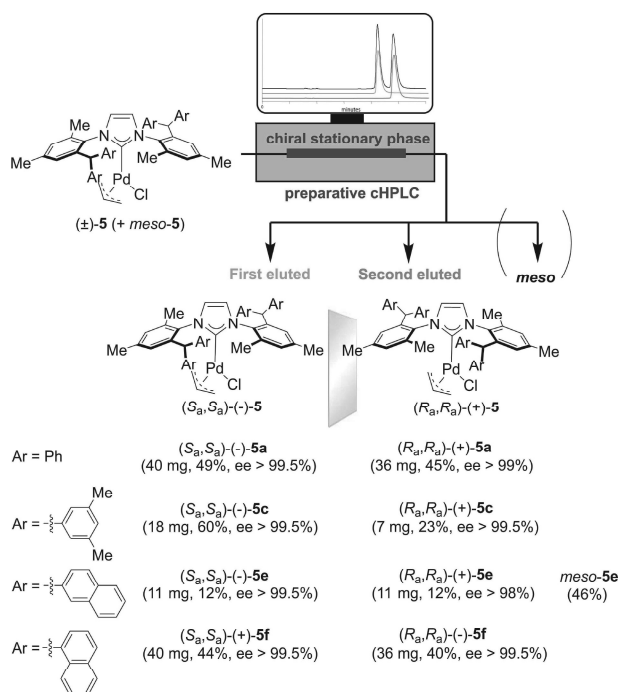
Entry	Ar	R	Diastereomeric ratio of 8	<i>meso</i> -9	(±)-9	Overall yield (ratio <i>meso</i> /(±)) <sup>[a]</sup>
1	Ph	Me	1:1.3	Diastereomers not separable		95 % (1:1) (9a)
2		H	> 10:1	–	93 %	93 % (< 10:1) (9c')
3		Me	> 20:1	–	99 %	93 % (< 20:1) (9d)
4		Me	1:1	Diastereomers not separable		99 % (1:1) (9e)

[a] Determined by <sup>1</sup>H NMR spectroscopy.

plexes 9 bearing the acenaphthoimidazolylidene NHC were prepared in excellent yields (Table 4). Since acenaphthoimidazolium salts 8 are configurationally stable,<sup>[12]</sup> the metalation step led to complexes 9 with the same dr than NHC precursors. Thus, complexes 9a and 9e were isolated with one-to-one ratios between *meso* and chiral diastereomers that could not be separated by silica gel chromatography (entries 1 and 4). On the contrary, 9c' and 9d were prepared as almost one single diastereomer (entries 2 and 3). It is worth pointing out that PEPPSI-type palladium complexes bearing similar NHCs ligands containing dissymmetric *N*-aryl substituents, have been previously reported.<sup>[14g]</sup> Unfortunately, the stereochemistry (diastereomers *meso*/chiral) was not specifically described.

For the resolution by chiral HPLC of racemate (±)-5 complexes and eventually the separation of *meso*-5 diastereomers, several chiral columns were screened and the detection of enantiomers was achieved with an UV-vis detector connected to a circular dichroism detector, giving the CD sign at 254 nm for each enantiomer. Similarly to other atropisomeric palladium-NHC complexes we previously studied,<sup>[9–12]</sup> the chiralpak IG column enabled the efficient resolution of complexes; for complex 5c, a chiralpak IE column was used.<sup>[18]</sup> The resolution at preparative scale (batches spanning from 24 mg to 90 mg) was carried out using a 1 cm diameter column (Scheme 1). Excellent yields and enantiopurities, superior to 99.5% ee, were obtained for complexes 5a and 5e as they contained no or little amount of *meso* complexes. For complex 5e that contained about 50% of *meso* complex, the separation was found more troublesome and only small quantities of enantiopure complexes were recovered.

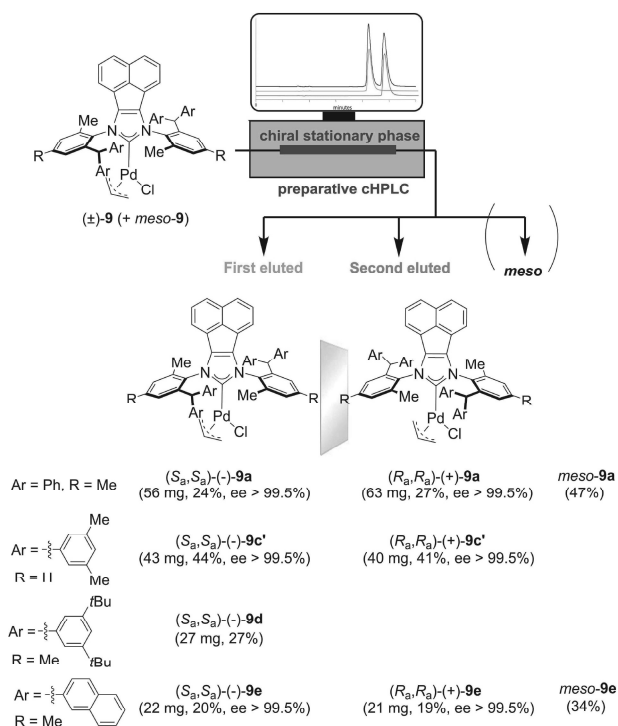
For complex 5c, the yield of the 1<sup>st</sup> eluted enantiomer superior to 50% suggests this enantiomer contains some *meso*



Scheme 1. Resolution of complexes 5 by chiral HPLC at a preparative scale.

complex, albeit this cannot be confirmed by chiral HPLC analysis.

Complexes 9 were also analyzed by chiral HPLC before performing a resolution at preparative scale with 100–230 mg batches (Scheme 2). The chiralpak IG column allowed a good separation for all the complexes as well as the chiralpak IK column for complex 9d. Nevertheless, two steps of purification



Scheme 2. Resolution of complexes **9** by chiral HPLC at a preparative scale.

were necessary for complex **9a**; a first one to isolate the second eluted enantiomer and a second one to separate the first eluted enantiomer from the *meso* complex.<sup>[18]</sup> Despite all that, isolated yields are very good taking into account the composition of the mixture to purify. Chiral HPLC analyses of complexes **9c'** and **9d** allowed to unambiguously confirm that only racemic complexes were obtained from the metalation step. Thus, it enabled us to determine that acenaphthoimidazolium salt **8d** has been prepared and isolated as the racemic diastereomer. Unfortunately, both enantiomers of **9d** could be well separated by chiral HPLC; a small amount of the first enantiomer was isolated but its enantiopurity could not be accurately measured. We assumed that the presence of *tert*-butyl groups lowers the polarity of the complexes and disfavors interactions with the chiral stationary phase.

We attempted to grow crystals suitable for single crystal X-ray diffraction, unfortunately without success. To determine the absolute configuration of the chiral complexes, the ECD spectra that were recorded for both enantiomers, as well as Uv-vis spectra, were examined. Individual ECD spectra, showed expected mirror images for both enantiomers.<sup>[18]</sup> As depicted in Figure 4, the comparison of ECD spectrum of (+)-**5a** to the one of complex (+)-**12a** for which the absolute configuration was unambiguously assigned by X-ray crystallography – (*R*<sub>a</sub>,*R*<sub>a</sub>)-(+), shows a similar shape with a positive ECD active band around 265 nm and a negative ECD active band around 230 nm. This indicates that the substitution of NHC backbone does not influence significantly ECD spectra

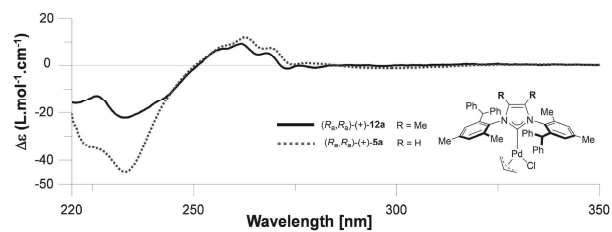


Figure 4. ECD spectra of the second eluted complexes (+)-**5a** and (+)-**12a**.

and complexes **5a** and **12a** possess the same spatial conformation.

The ECD spectra of second eluted complexes **5a**, **5e** and **5f** (Figure 5) show a more intense negative ECD active band between 225 and 230 nm for naphthyl-containing complexes. Due to the difficulty of interpreting the 240–275 nm region, we could not unambiguously attribute the configuration of **5e** and **5f**. Therefore, TD-DFT calculations were performed and the calculated ECD spectrum of (*R*<sub>a</sub>,*R*<sub>a</sub>)-**5e** matches with the experimental spectra of the second eluted enantiomer.<sup>[18]</sup>

Compared to 2<sup>nd</sup> eluted complex **12a**, ECD spectrum of 2<sup>nd</sup> eluted complex **9a** exhibits slightly different ECD active bands, certainly due to the naphthyl backbone (Figure 6). Nevertheless, we believe that both complexes possess the same spatial arrangement due to a strong positive band inferior to 210 nm and a negative band in the region 265–275 nm. This finding was corroborated by TD-DFT calculations.<sup>[18]</sup>

Second eluted complexes **9a**, **9c'** and **9e** exhibit an intense negative ECD active band between 230 and 235 nm, with a three-fold magnitude increase for **9e** containing naphthyl substituents (Figure 7). Thus, the absolute configuration (*R*<sub>a</sub>,*R*<sub>a</sub>)-(+), can be confidently attributed to the second eluted enantiomers of complexes **9**. Calculated ECD spectrum of **9e** using TD-DFT was in line with this assumption.<sup>[18]</sup>

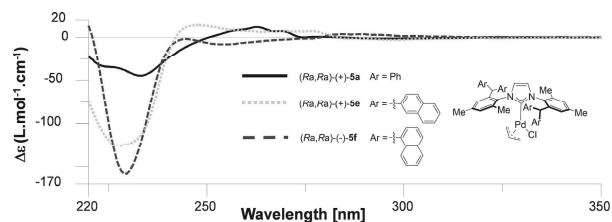


Figure 5. ECD spectra of the second eluted complexes (+)-**5a**, (+)-**5e** and (+)-**5f**.

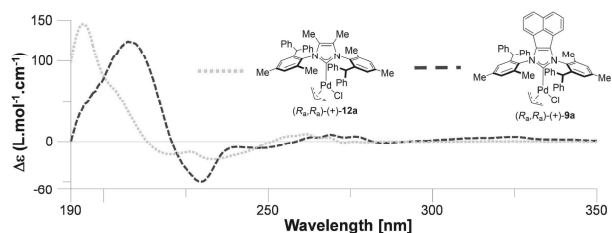


Figure 6. ECD spectra of the second eluted complexes (+)-**9a** and (+)-**12a**.

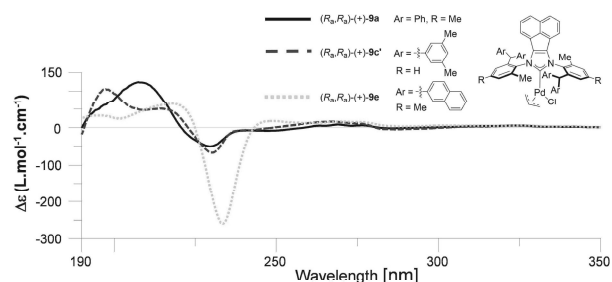


Figure 7. ECD spectra of the second eluted complexes (+)-9a, (+)-9c' and (+)-9e.

Similarly to the intensity of ECD signals, the naphthyl backbone results in a significant improvement of the optical rotation values: for 1<sup>st</sup> eluted complexes, 9a [ $\alpha_D^{25} = -375$  compared to  $-65$  and  $-116$  for 5a and 12a, respectively. Whereas the presence of 2-naphthyl substituents does not impact significantly the values of optical rotations, for 1<sup>st</sup> eluted complexes, [ $\alpha_D^{25} = -65$  for 5a,  $-17$  for 5e, 1-naphthyl groups lead to reverse the sign and increase considerably the values: [ $\alpha_D^{25} = +310$  for 5f.

The asymmetric intramolecular  $\alpha$ -arylation of amides was studied to probe chiral complexes 5 and 9 using amide 10 as benchmark substrate (Table 5).<sup>[4b,d,7c,8c,20]</sup> Reactions were carried out at 40 °C in DME using potassium *tert*-butoxide as the base. With the exception of (*R<sub>a</sub>R<sub>a</sub>*)-(+)-5c (47%, entries 4), all complexes performed well with isolated yields spanning from

70 to 99%. Precatalysts 12a, 5a and 9a containing methyl, hydrogen, and naphthyl on the backbone, respectively, can be compared to scrutinize the influence of its substitution (entries 1–3). It appears that the absence of substituents led to a slight decrease of the enantiomeric excess 79% (5a) compared to 95% ee (12a and 9a). We assumed that the substitution of the backbone brings some rigidity to the NHC structure which is beneficial for the enantiomeric induction. This observation can be related to the effect of the second ortho-substituent we previously noticed.<sup>[12]</sup> Xylyl patterns (complexes 5c and 9c') result in a slight decrease of enantiomeric excesses of product 11: 65% ee for (*R<sub>a</sub>R<sub>a</sub>*)-(+)-5c compared to 79% of (*S<sub>a</sub>S<sub>a</sub>*)-(-)-5a (entries 4 and 2) or 90% ee for (*S<sub>a</sub>S<sub>a</sub>*)-(-)-9c' versus 95% ee for (*R<sub>a</sub>R<sub>a</sub>*)-(+)-9a (entries 8 and 3). The effect of bulky 3,5-di-*tert*-butylphenyl groups does not have a benefic outcome on enantioselectivity with only 74% ee (entry 9). However, this result cannot be confidently discussed since the enantiopurity of complex (*R<sub>a</sub>R<sub>a</sub>*)-(+)-9d could not be accurately measured. Whereas 1-naphthyl substituents lead to a significant decrease of ees compared to phenyl groups (51% and 45% ee for 5f, entries 6 and 7, vs 79% ee for 5a, entry 2), 2-naphthyl-containing analogues enable to afford amide 11 with slightly better ees: 86% ee with (*S<sub>a</sub>S<sub>a</sub>*)-(-)-5e (entry 5) versus 79% ee with (*S<sub>a</sub>S<sub>a</sub>*)-(-)-5a (entry 2) or 96% ee with (*S<sub>a</sub>S<sub>a</sub>*)-(-)-9e (entry 10) versus 95% ee with (*S<sub>a</sub>S<sub>a</sub>*)-(-)-9a (entry 3).

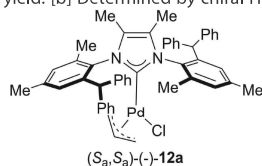
## Conclusions

In summary, we demonstrated the nature of the NHC backbone is a key parameter within the concept of atropisomeric metal-NHC complexes, and in many different respects. Compared to a 4,5-disubstituted backbone with methyl groups, unsubstituted backbone or acenaphthyl backbone enabled the synthesis of NHC precursors containing various benzhydryl derivative patterns with yields spanning from low to excellent. The corresponding Pd(allyl)Cl(NHC) complexes have been prepared in almost quantitative yields, nevertheless many complexes have been obtained in a mixture of racemic and *meso* complexes with ratios 1:1. These complexes exhibit a high chemical stability which enabled their resolution by chiral HPLC at preparative scale as well as the separation of *meso* complexes. Of note, for only one complex, both enantiomers could not be fully separated. Absolute configurations of these chiral complexes have been investigated through the comparison of the ECD spectra. The study of these complexes in the intramolecular palladium-catalyzed  $\alpha$ -arylation of amides brings some information on the relationship structure-enantioselectivity: i) substitution of the NHC backbone is necessary to reach excellent enantioselectivities, probably due to a more rigid structure; ii) the substitution of positions 3 and 5 of benzhydryl groups leads to a slight decrease of enantiomeric excesses; iii) a sharp difference of ees was observed between catalyst containing 1- and 2-naphthyl groups, the latter represents an interesting pattern for further investigations that are currently undergoing in our laboratories.

Table 5. Catalysts screening for the palladium-catalyzed intramolecular  $\alpha$ -arylation of amide 10.

Entry	Catalyst	Yield <sup>[a]</sup>	ee (%) <sup>[b]</sup>
1	( <i>S<sub>a</sub>S<sub>a</sub></i> )-(-)-12a	85 %	95 ( <i>R</i> )
2	( <i>S<sub>a</sub>S<sub>a</sub></i> )-(-)-5a	83 %	79 ( <i>R</i> )
3	( <i>R<sub>a</sub>R<sub>a</sub></i> )-(+)-9a	99 %	95 ( <i>S</i> )
4	( <i>R<sub>a</sub>R<sub>a</sub></i> )-(+)-5c	47 %	65 ( <i>S</i> )
5	( <i>S<sub>a</sub>S<sub>a</sub></i> )-(-)-5e	93 %	86 ( <i>R</i> )
6	( <i>S<sub>a</sub>S<sub>a</sub></i> )-(+)-5f	80 %	51 ( <i>R</i> )
7	( <i>R<sub>a</sub>R<sub>a</sub></i> )-(-)-5f	70 %	45 ( <i>S</i> )
8	( <i>S<sub>a</sub>S<sub>a</sub></i> )-(-)-9c'	95 %	90 ( <i>R</i> )
9	( <i>R<sub>a</sub>R<sub>a</sub></i> )-(+)-9d	85 %	74 ( <i>S</i> )
10	( <i>S<sub>a</sub>S<sub>a</sub></i> )-(-)-9e	99 %	96 ( <i>R</i> )

[a] Isolated yield. [b] Determined by chiral HPLC analysis.





## Experimental Section

General procedure for the preparation of symmetric diimines **3**. To a solution of aniline **1** (1 equiv.) dissolved in DCM (1 mL/mmol), was added MgSO<sub>4</sub> (4.3 equiv.), glyoxal (40 wt% in H<sub>2</sub>O, 0.5 equiv.) and a catalytic amount of formic acid (5 drops). The reacting mixture was stirred at room temperature for 2 days prior to filtration. The cake was washed profusely with DCM until the filtrate became colourless. The latter was then concentrated to dryness and the residue was suspended in ethyl acetate. The slurry was finally filtered and washed with ethyl acetate (2×1 mL/mmol) to afford **3**, which was dried under high vacuum.

General procedure for the synthesis of imidazolium salts **4**. Diazabutadiene **3** (1 mmol, 1 equiv.) dissolved in dry THF (5 mL) at 60 °C was treated with paraformaldehyde (1.1 equiv.) and zinc chloride (1.1 equiv.) as a solution in 4 M HCl in dioxane (1.5 equiv.), for 14 h. The reaction mixture was then diluted with DCM, and washed with brine. The organic layer was subsequently dried over MgSO<sub>4</sub>, filtered and concentrated to dryness. The resulting residue was finally suspended in Et<sub>2</sub>O, filtered and washed thoroughly with Et<sub>2</sub>O (3×15 mL) to afford **4** as a white powder.

General procedure for the preparation of dimines **6**. Acenaphthenequinone (1 equiv.), aniline **1** (2 equiv.) and ZnCl<sub>2</sub> (2.5 equiv.) dissolved in acetic acid (2.4 mL per mmol), the resulting solution was heated at 130 °C for 16 h. The reaction mixture was cooled to room temperature. The solid was collected by filtration, washed with acetic acid and then dissolved in DCM (3 mL per mmol) with potassium oxalate (3.0 equiv.) and water (2 mL per mmol). The resulting mixture was vigorously stirred overnight before to be extracted with DCM. The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and the volatiles were removed in vacuo. Methanol was added to form a precipitate which was recovered by filtration and washed with MeOH to afford **6** an orange solid. If necessary, a second purification by silica gel chromatography was performed.

General procedure for the synthesis of acenaphthoimidazolium salts **8**. Under inert atmosphere, chloromethyl ethyl ether (37 equiv.) was added to diimine **6** (1 equiv.) and the resulting mixture heated to 100 °C for 16 h. After cooling to room temperature, Et<sub>2</sub>O (25 mL per mmol) was added and the mixture vigorously stirred for 1 h. The solid was collected and washed with Et<sub>2</sub>O and pentane to afford a yellow solid. To a solution acenaphthoimidazolium chloride (1 mmol) in H<sub>2</sub>O (20 mL), KBF<sub>4</sub> (252 mg, 2 mmol, 2 equiv.) was added as well as DCM (20 mL). The resulting mixture was vigorously stirred for 1 h at room temperature before to be extracted with DCM (2×20 mL). Combined organic phases were dried over Na<sub>2</sub>SO<sub>4</sub> and the volatiles were removed in vacuo. The product can be purified by recrystallization from DCM/pentane or by silica gel chromatography (DCM/acetone) to afford salt **8** a yellow solid.

General procedure for the preparation of NHC-palladium complexes **5** and **9**. A mixture of imidazolium or acenaphthoimidazolium tetrafluoroborate (2.3 mmol, 2.3 equiv.), [Pd(allyl)Cl]<sub>2</sub> (1.0 mmol), K<sub>2</sub>CO<sub>3</sub> (4.6 equiv.) in acetone was stirred at 60 °C for 5 h. The reaction mixture was filtered through a Celite® pad and the solvent was removed under vacuum. The crude product was purified by silica gel column (PE/Et<sub>2</sub>O = 1:1) give the NHC-palladium complex **5** or **9**.

Procedure for the palladium-catalyzed  $\alpha$ -arylation of amide. A mixture of amide **10** (0.1 mmol, 1.0 equiv.), Pd(allyl)Cl(NHC) **5** or **9** (0.005 mmol, 5 mol%) and potassium *tert*-butoxide (*t*BuOK) (0.15 mmol, 1.5 equiv.) in dry 1,2-dimethoxyethane (DME) (2 mL) was stirred at 40 °C for 20 hours under argon. The solvent was removed under reduced pressure and the residue was purified by silica gel column (petroleum ether/Et<sub>2</sub>O = 2:1).

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## Conflict of Interests

The authors declare no conflict of interest.

## Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

**Keywords:** Chirality · N-heterocyclic carbene (NHC) · Palladium · Enantioselectivity · Chiral ligand design

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