# MODIFICATION OF THE ATROPISOMERIC *N,N*-LIGAND 2,2′-DI(PYRIDIN-2-YL)-1,1′-BINAPHTHALENE AND ITS APPLICATION TO THE ASYMMETRIC ALLYLATION OF BENZALDEHYDE

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*Dedicated to the memory of Professor Otakar Červinka.*

The atropisomeric compound 2,2′-di(pyridin-2-yl)-1,1′-binaphthalene (**1**) has been chlorinated, *via* its bis-*N*-oxide **2**, at the 4 and 6 pyridine ring positions so as to generate the three isomeric species: 2,2′-bis(6-chloropyridin-2-yl)- (**3a**), 2-(4-chloropyridin-2-yl)-2′-(6-chloropyridin-2-yl)- (**3b**) and 2,2′-bis(4-chloropyridin-2-yl)-1,1′-binaphthalene (**3c**). The dichlorinated compounds underwent Ni-catalysed Kumada cross-coupling with MeMgI to give the methylated pyridine isomers: 2,2′-bis(6-methylpyridin-2-yl)- (**4a**), 2-(4-methylpyridin-2-yl)-2′-(6-methylpyridin-2-yl)- (**4b**) and 2,2′-bis(4-methylpyridin-2-yl)-1,1′-binaphthalene (**4c**). The enantiomerically pure forms of the six novel ligands (**3a**–**3c** and **4a**–**4c**), prepared from enantiomerically pure 2,2′-di(pyridin-2-yl)-1,1′-binaphthalene (**1**), were tested in asymmetric catalysis, but proved to be no better and in most cases poorer than parent **1**. The coordination of the ligands to Zn and Pd fragments has been explored and compared with the parent compound **1** so as to rationalise the negative effect of pyridine substitution on asymmetric induction in the zinc-catalysed allylation of benzaldehyde.

**Keywords**: Atropisomerism; Axially chiral ligands; Asymmetric catalysis; Pyridines; Resolution; Biaryls; Binaphthyls; Zinc complexes; Kumada cross-coupling reaction.

The field of ligand design for asymmetric catalysis is expanding at an ever increasing pace[1] and the synthesis and application of novel axially chiral didentate ligands, such as binaphthalene based ligands, continues to be an area that attracts much attention[2]. We recently reported the synthesis and resolution of the binaphthalene-based bipyridine ligand system **1** which is chiral due to atropisomerism caused by restricted rotation about the 1,1′ bond[3]. The chelating nature of the ligand was confirmed by preparing pal-

ladium allyl and zinc dichloride complexes which were characterised in detail by NMR and also by X-ray crystallography. The palladium allyl complexes displayed a number of unusual stereodynamic processes that were investigated by 2D NMR techniques. These investigations, in which key experiments were performed with racemic samples, revealed that (i) the ligand undergoes rapid didentate–monodentate equilibrium (favouring the didentate mode) and (ii) rapid migration of the ligand between palladium centres, mediated by traces of free ligand. Herein we report on derivatisation of enantiomerically pure ligand **1** by installing methyl groups at either the 4 or the 6 positions of both of the pyridine rings so as to generate new ligands **4a**–**4c**. The synthesis of these ligands proceeded *via* 4/6-chloropyridyl compounds (**3a**–**3c**) which can also act as modified ligand analogues of **1**. We also report on the application of the novel ligands to asymmetric catalysis and a study of their coordination to Zn- and Pd-centres.

## RESULTS AND DISCUSSION

Preliminary tests with ligand **1** in catalytic asymmetric reactions, *vide infra*, proved to be disappointing. Study of the crystal structure of the zinc chloride complex of **1**[3] (Fig. 1) suggested to us that substitution of the pyridine rings would influence the coordination sphere in two ways.

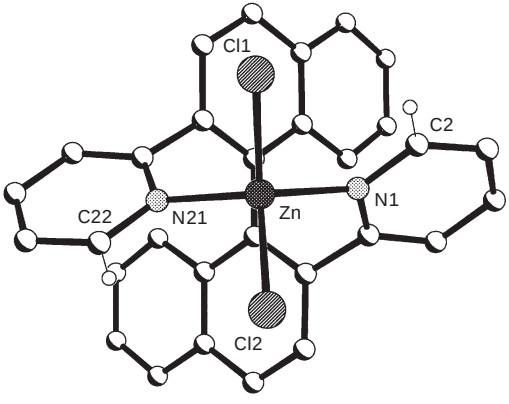


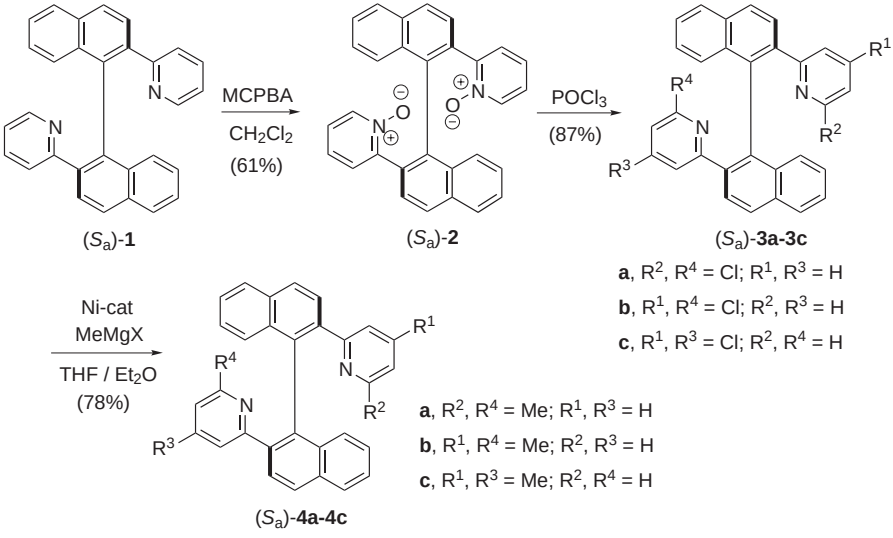

FIG. 1

The structure of the $ZnCl_2$ complex of **1**[3] showing the "canting" in the two pyridine rings caused by the fusion to the chiral 1,1-binaphthalene fragment. All protons, apart from those at pyridine C(2), have been omitted for clarity

Substitution at the 6-position of the pyridine rings would enhance the $C_2$-symmetric desymmetrisation of the coordination plane defined by N–Zn–N, whilst substitution at the 4-position of the pyridine rings would have minimal steric interaction with the two other ligands at the tetrahedral site, but may exert remote electronic effects. Both interactions appeared interesting to study and we thus chose to install methyl groups so that we could exploit the relative ease of functionalisation of the picoline moiety at a later date.

*Ligand Synthesis*

In our earlier work, the development of effective conditions for the resolution of **1** had proven rather time-consuming. Consequently, we opted to functionalise the resolved ligand **1** rather than, for example, homocoupling of a 1-halo-2-(2-picolyl)naphthalene species which would then require a subsequent resolution step and assignment of absolute configuration. In preliminary experiments we attempted to directly methylate **1** by employing procedures known to be effective with simple pyridines. However, Chichibabin-type reactions (*e.g.* MeLi, toluene, –78 to –40 °C, then air), N-




SCHEME 1

The synthesis of enantiomerically enriched (>96% ee) ligands **4a**–**4c** proceeding *via* the oxidation of >96% ee **1** to bis-*N*-oxide **2**, chlorodeoxygenation to dichlorides **3a**–**3c** and Kumada cross-coupling

activation[4] (*e.g.* methyl chloroformate and then MeMgI), radical methylation ($Ag^+$, $H^+$, AcOH)[5] and anionic methylation (BuLi, DMAE then MeI)[6] all failed to proceed to give any of the desired 6,6′-doubly methylated species (**4a**), or indeed any monomethylation[7]. The conversion of a pyridine to its *N*-oxide facilitates new modes of reactivity and we then resorted to exploration of this strategy this with **1**, Scheme 1.

Oxidation of **1** with excess MCPBA in dichloromethane at 25 °C gave bis-*N*-oxide **2** in 61% yield after column chromatography. With substoichiometric quantities of MCPBA, we were able to isolate mixtures of the mono- and bis-*N*-oxide which could be separated on column chromatography, but did not pursue the mono-oxidised system further. In an analogous manner to **1** and its complexes[3], we were unable to crystallize the enantiomerically pure samples of **2**. However, racemic samples of the bis-*N*-oxide **2** crystallized in the monoclinic space-group *C*2/*c* and the single-crystal X-ray structure was obtained (Fig. 2). None of the bond lengths or angles in **2** proved to be unusual, however it is of note that the bis-*N*-oxide rings lie in an antiparallel arrangement to each other.

Quéguiner *et al.*[8] have extensively studied and optimised the ortholithiation of pyridine-*N*-oxides, as first reported by Abramovitch[9], and found that LDA functions well. However, after treating bispyridine-*N*-oxide **2** with 2 equiv. LDA and then quenching with MeI, we found no evidence for methylation. Whether or not the initial lithiation had proceeded to any extent was not investigated further. We then tested activation of **2** towards nucleophilic attack by *in situ* conversion to the bis-*N*-oxide ester by reac-

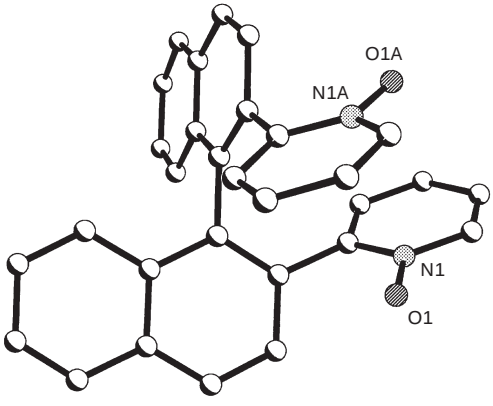



FIG. 2
The molecular structure of (racemic) bis-*N*-oxide **2** in the crystal. All protons have been omitted for clarity. See experimental section for details of X-ray diffraction and solution

tion with trimethylacetyl chloride. Neither MeLi nor MeMgI reacted satisfactorily with this species, returning only **2** (with trace side products, but not the desired **4a**) after aqueous work-up.

Consequently, we decided to prepare the corresponding halopyridines and then attempt halogen–lithium exchange and cross-coupling reactions. The *N*-oxide **2** was converted reasonably smoothly into the dichlorides **3a**–**3c** (38/42.5/19.5 ratio; 87% overall yield) by reflux in $POCl_3$. Analogous reaction with $POBr_3$ at 110 °C was not successful, giving dibromides (as **3a**–**3c** but R = H/Br) in less than 5% yield. Despite the ready conversion of 6-chloro-2,2′-bipyridine to 6-bromo-2,2′-bipyridine by reaction with $PBr_3$ at 165 °C[10], the mixture of chlorides **3a**–**3c** was not converted to the bromides, even on prolonged heating.

With chlorides **3a**–**3c** in hand, we attempted lithium-halogen exchange using the conditions developed by Yus *et al.*[11] for generation of 2-lithiopyridine from 2-choropyridine with lithium naphthalenide in THF. However, despite quenching of the green colour of the naphthalenide reagent on addition of **3a**–**3c**, we were unable to effect methylation with MeI. The presence of naphthalene rings in the substrate may of course have affected the stability of the lithium naphthalenide; however, we did not notice any lithium metal deposition. Turning then to cross-coupling reactions, we attempted to employ a variety of Pd- and Ni-based catalyst systems to react chloropyridines **3a**–**3c** with MeMgX. As we have earlier found, the chelating ligand nature of **1** and analogues can interfere with transition metal-catalysed reactions[3]. Not surprisingly then, with monodenate phosphine ($PPh_3$)-based catalyst systems, we obtained variable and non-reproducible results for Kumada coupling[12] (Ni); however, switching to [$NiCl_2$(dppf)] (dppf = 1,1′-bis(diphenylphosphino)ferrocene) as pro-catalyst provided a reliable and robust system. Ultimately, the best conditions were found to involve pre-stirring of [$NiCl_2$(dppf)] with **3a**–**3c** in THF at ambient temperature before adding a large excess of freshly prepared MeMgI in diethyl ether. Although stoichiometric quantities of [$NiCl_2$(dppf)] gave the best results (up to 83% yield of **4a**–**4c**), catalyst loadings in the range of 10 mole % still performed well on a large scale and furnished the desired bispicolinyl ligands **4a**–**4c** in 76–77% yields. The product distribution (**a**/**b**/**c**: 34/42/24) did not exactly mirror the ratio of chlorides **3a**–**3c** submitted and this indicates that the 4-chloropyridine moieties underwent cross-coupling in a slightly more efficient manner.

The 6,6′; 4,6′ and 4,4′ isomers in both the dichloro and dimethyl systems were readily separable by column chromatography and could thus be characterised individually. Unfortunately, in both of the non-symmetric

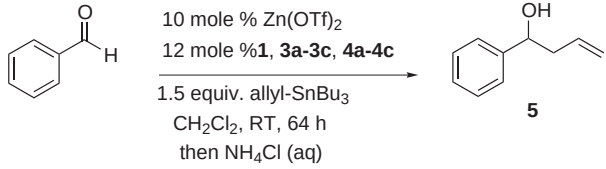
4,6-systems, most of the almost isochronous pairs of NMR signals arising from the individual naphthalene units could not be distinguished from each other, despite a number of attempts to do so by 1D NOED experiments. Interestingly, in both series, the 4,4-isomers displayed opposite signs of optical rotation (at the sodium D-line) to both the 6,6- and 6,4-isomers as well as the non-substituted system **1**. We have earlier established the absolute configuration of ligand **1**[3] and its stability towards racemisation: there is no detectable loss in ee after heating (in ethylene glycol solution) to 170 °C for 48 h. Thus enantiomeric excesses and absolute configurations of compounds **3a**–**3c** and **4a**–**4c** are assigned on the basis of stereoconservation throughout the synthetic procedure. Accordingly, in all cases, enantiomeric intermediates derived from opposite enantiomers of **1** (>96% ee) gave equal and opposite optical rotations and thus no attempt was made to confirm by other methods that the ligands were highly enantioenriched.

*Asymmetric Allylation*

Preliminary tests with ligand **1** and derivatives, in Pd-catalysed allylic substitution of cyclopentenyl esters, Kharasch–Sosnovsky oxidation of cyclopentene with *tert*-butyl perbenzoate and Cu-catalysed cyclopropanation of styrene with ethyl diazoacetate gave poor results (maximum ee's of 12, 7 and 20%, respectively) and were not studied further. Consequently, we sought an area in which pyridyl-type ligands had already proved promising[13,14] and chose to study the Lewis acid-catalysed allylation of aldehydes, an area that has seen considerable development over the past years[15]. In 1997 Cozzi *et al.*[16,17] reported on the modification of Zn halide catalysts with chiral enantiopure bisoxazoline ligands to effect the asymmetric allylation of aldehydes by allyltributyltin. Enantiomeric excesses of up to 40% were obtained with aliphatic and aromatic aldehydes and later improvements by Kwong *et al.*[18], employing chiral non-racemic bipyridine ligands, increased selectivites to up to 60% ee. We were therefore interested to test our pyridine-based ligands **1**, **3a**–**3c** and **4a**–**4c** in this reaction (Scheme 2). Following the conditions of Cozzi, we reacted benzaldehyde with allyltributyltin in $CH_2Cl_2$ at ambient temperature for 64 h before work-up, chromatography and analysis of the ee of the homoallylic alcohol **5** by chiral GC. Cozzi *et al.*[17] reported that the order of activity of $ZnX_2$/L (where L = bisoxazoline) was X = OTf > I > Br> Cl > > F (Tf = $CF_3SO_2$) and, consequently, we chose to employ 10 mole % $Zn(OTf)_2$/L (L = **1**, **3a**–**3c** and

**4a**–**4c**) which was pre-complexed for 60 min before adding the reactants. The results obtained are given in Table I.

As a comparison for the effect of the ligands **1**, **3a**–**3c** and **4a**–**4c** on the reactivity of the system, 2,2′-bipyridine was employed as a control and gave 26% conversion to (racemic) homoallylic alcohol **5**, (entry 1). Under the same conditions, the parent chiral ligand ($R_a$)-**1** gave (*S*)-**5** in 38% yield and




SCHEME 2
The Zn-catalysed, Sn-mediated allylation of benzaldehyde used to test the relative efficacy of ligands **1**, **3a**–**3c** and **4a**–**4c** (all >96% ee) as asymmetric ligands. See Table I for results

TABLE I
Zn-catalysed asymmetric allylation of benzaldehyde with allyltributyltin in $CH_2Cl_2$ at 21 °C (64 h) giving 1-phenylbut-3-en-1-ol (**5**) and employing dipyridylbinaphthalenes **1**, **3a**–**3c** and **4a**–**4c** as chiral enantioenriched (>96% ee) ligands.

| Entry[a] | Ligand | $R^1$, $R^2$ ,$R^3$ $R^4$ | Zn-source | Yield[b] of **5**, % | Selectivity[c] ee **5**, % (config.) |
|---|---|---|---|---|---|
| 1 | 2,2′-bipy | – | $Zn(OTf)_2$ | 26 | 0 |
| 2 | (–)-($S_a$)-**1** | H, H, H, H | $Zn(OTf)_2$ | 38 | 33.1 (*R*) |
| 3 | (–)-($S_a$)-**1** | H, H, H, H | Zn(OTf)Cl[d] | 3 | 0.4 (*R*) |
| 4 | (–)-($S_a$)-**1** | H, H, H, H | Zn(OTf)Cl[e] | 47 | 24.8 (*R*) |
| 5 | (–)-($S_a$)-**3a** | H, Cl, H, Cl | $Zn(OTf)_2$ | 17 | 4.6 (*R*) |
| 6 | (–)-($S_a$)-**3b** | Cl, H, H, Cl | $Zn(OTf)_2$ | 21 | 0.3 (*R*) |
| 7 | (+)-($S_a$)-**3c** | Cl, H, Cl, H | $Zn(OTf)_2$ | 11 | 19.7 (*R*) |
| 8 | (+)-($R_a$)-**4a** | H, Me, H, Me | $Zn(OTf)_2$ | 9 | 2.5 (*S*) |
| 9 | (+)-($R_a$)-**4b** | Me, H, H, Me | $Zn(OTf)_2$ | 21 | 0.3 (*R*) |
| 10 | (–)-($R_a$)-**4c** | Me, H, Me, H | $Zn(OTf)_2$ | 26 | 29.4 (*S*) |

[a] See Experimental for full details of general procedure; [b] yield of analytically pure **5** isolated after column chromatography; [c] enantiomeric excess measured by chiral GC; [d] ostensibly prepared *in situ* by abstraction of 1 equiv. chloride by AgOTf from $ZnCl_2$ prior to addition of **1**; [e] ostensibly prepared *in situ* by addition of 1 equiv. chloride $Bu_4N^+Cl^-$ to $Zn(OTf)_2$ prior to addition of **1**.

33% ee (entry 2). Whilst this ee compares reasonably favourably with the ee obtained by Cozzi *et al.*[17] of 35%, the reactivity of the system is somewhat lower. By consideration of the crystal structure of [$ZnCl_2$(**1**)] (Fig. 1), and the consistent (*vide infra*) sense of asymmetric induction: allylation of the *si* face of the benzaldehyde when using ligand of axial chirality $R_a$ (and of the *re* face with $S_a$), one may propose a simple model based on Lewis acid activation of the aldehyde by a tetrahedral mono- or dicationic zinc centre (Fig. 3). An alternative mechanism involving transmetallation of allyl from Sn to Zn has been discounted by Cozzi *et al.*[17]

Coordination of the zinc is expected to be through the carbonyl lone pair that is *trans* related to the benzene ring, with the aldehyde proton positioned above the coordination plane so as to minimize steric clash of the benzene ring with the pyridine rings, and of the aldehyde proton with the fourth, as yet unspecified, ligand (*i.e.*, the torsion angle L–Zn–C=O is 180°). The twist in the planes of the two pyridine rings, imparted by their connection through a 1,1′-binaphthalene linkage, results in one pyridine ring being canted above the N–Zn–N plane and the other below. In a complex bearing $R_a$-**1**, the pyridine ring that is then adjacent to the coordinated aldehyde shields the *re* face, thereby restricting attack by the allylating agent to the *si* face. If this model is correct, one might expect the steric bulk

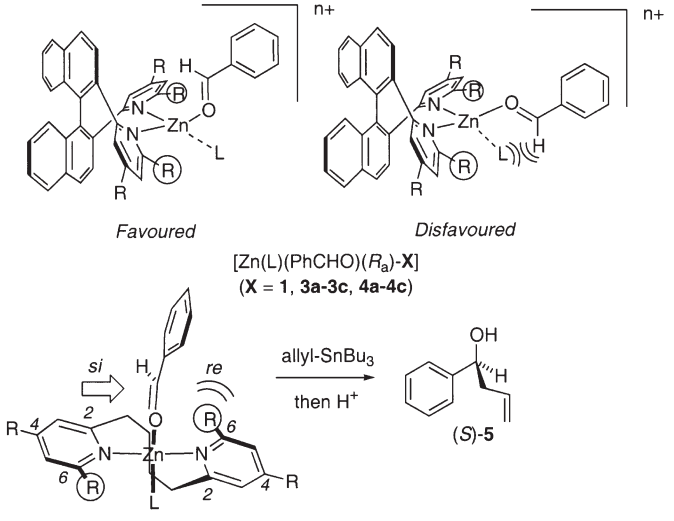



FIG. 3
A model for the asymmetric induction by Zn complexes of ligand **1** and derivatives in the allylation of benzaldehyde by allyltributyltin (Scheme 2 and Table I)

of L (see Fig. 3) to influence the torsional restriction of the L–Zn–O=C unit. When this torsional angle is 0°, which is predicted to be disfavoured over an angle of 180°, the opposite face of the aldehyde is shielded thus leading to the opposite enantiomer. On the expectation that increasing the effective bulk of L may well then lead to greater asymmetric induction, we explored the generation of a monochloro complex of the type [Zn(Cl)OTf(**1**)] *in situ* on the basis that the aldehyde would displace the more loosely coordinated triflate and that the remaining chloride, being more tightly bound than a triflate, would increase the bias towards the favoured rotamer (L in Fig. 3). There are two approaches to the generation of precursors to such species, both of which should give the same results: addition of one equivalent of a chloride source to $Zn(OTf)_2$ and removal of one equivalent chloride from $ZnCl_2$, with AgOTf. In the event, the outcomes were surprisingly different (Table I, entries 3 and 4) and neither had the desired effect. The essentially quantitative precipitation of AgCl on addition of AgOTf to $ZnCl_2$ prior to addition of ligand in principle should provide the cleanest route to the desired complex. However, this procedure negated all asymmetric induction (entry 3). One explanation of such an effect would be that disproportionation of [Zn(Cl)OTf(**1**)] to $[Zn(\mathbf{1})_2](OTf)_2$ and $[ZnCl_2L_2]$ ($L_2$ = unspecified ligand, *e.g.* solvent) occurs and that very slow catalysis then proceeds *via* the achiral $[L_2ZnCl_2]$. The effect of addition of $Bu_4N^+Cl^-$ (Table I, entry 4) is made more complex by the solubility of $Bu_4N^+TfO^-$ and thus the possibility of multiple species if halide transfer is not complete. The increased activity of the resulting catalyst system (but slightly lower selectivity) may well arise from a simple salt effect arising from the presence of $Bu_4N^+$ ions.

Returning then to the original conditions, we tested ligands **3a**–**3c** and **4a**–**4c** (Table I, entries 5–10). Considering the model outlined in Fig. 3, one might predict rather different effects on substitution of the pyridine units at position 6 *versus* position 4. The increased bulk at the 6-position (relative to **1**, R = H) would be expected to bolster steric shielding of one of the aldehyde faces and thus increase asymmetric induction. In contrast, substituents at position 4 are sterically remote and thus their influence should be predominantly electronic. Ligands **3c** and **4c** should only operate with the latter effects and the asymmetric induction is attenuated by the strongly electron-withdrawing chloro groups (ligand **3c**, Table I, entry 7) and essentially unchanged by the presence of two methyl groups (ligand **4c**, Table I, entry 10). Of ligands **3a**, **3b** and **4a**, **4b**, the symmetrically substituted pair (**3a** and **4a**) would be expected to engender the greatest asymmetric induction since in **3b** and **4b** the non-symmetric nature of the ligand–zinc as-

sembly would likely result in the aldehyde coordinating to the tetrahedral site that is closer to the least hindered pyridine ring. However, in both sets the asymmetric induction would be expected to be similar to or greater than **1**, **3c** and **4c**. In stark contrast, ligands **3a** and **4a** gave very low asymmetric induction whilst with **3b** and **4b** the product was essentially racemic (Table I, entries 5, 6, 8 and 9). The origins of these effects lie in the nature of coordination of the series of ligands to zinc which was studied by NMR.

*Coordination Modes of Ligands **1**, **3a–3c** and **4a***

We have earlier reported[3] on a study of complexation of **1** to $ZnCl_2$ in $CD_3CN$ by $^1H$ NMR and found that complexation is rapid and quantitative. Thus, titration of a solution of **1** with a solution of $ZnCl_2$ results in discrete and sharp sub-spectra arising from free **1** and complexed **1** (*i.e.*, [$ZnCl_2$(**1**)]) whose relative proportions correlate exactly with stoichiometry and thus the amount of $ZnCl_2$ added. When an excess of $ZnCl_2$ is added, there is no evidence for generation of further complexes, *e.g.* monoligated systems since the spectrum of [$ZnCl_2$(**1**)], which is consistent with a (time average) $C_2$-symmetrical structure, is the sole observable species and remains sharp and unchanged. On performing the same experiment with ligand **3c** (Fig. 4), which is less electron rich at the pyridine nitrogen donors but not significantly different in terms of steric factors at the coordination sphere, three key observations were made: (i) the stoichiometry is again, 1/1 and the complex displays (time average) $C_2$-symmetry, *i.e.*, a chelating complex of type [$ZnCl_2$(**3c**)] is formed; (ii) broad signals are observed in both the free ligand **3c** and the complex prior to addition of 1 equiv. $ZnCl_2$ and (iii) even at a ligand/zinc stoichiometry of 1/1, there is still some broadening in the signals corresponding to [$ZnCl_2$(**3c**)].

However, on addition of a further 1 equiv. $ZnCl_2$ a sharp spectrum is obtained. Overall the results demonstrate clearly that whilst the ligand is more weakly coordinating than **1** it can still function reasonably effectively as a didentate chiral ligand in competition with two monodentate $CD_3CN$ ligands. The broadening in both **3c** and [$ZnCl_2$(**3c**)] indicates that exchange of $ZnCl_2$ between complexed and free **3c** is occurring at the NMR time scale. This presumably occurs *via* the mechanism we have earlier postulated for an analogous process with Pd–allyl complexes of **1**, which involves the reversible reaction of L with [M(L)] to generate intermediates of type [$M(L)_2$] in which L is a didentate ligand in monodentate mode.

Performing an analogous experiment with non-symmetrical bispyridine **3b** gave completely different results (Fig. 5). In particular, addition of $ZnCl_2$ only had a major influence on the chemical shifts of the upfield signals arising from the protons at C(3) of each of the two pyridine rings.

These were broadened and shifted downfield, consistent with reversible complexation to an electron-demanding Zn centre. However, no discrete signals arising from a new complex were discernable and thus equilibrium between free and complexed ligand is fast at the NMR time scale. After addition of 0.5 equiv. $ZnCl_2$ all of the other proton signals became sharp but, as addition was continued, they broadened again, becoming sharp again when a large excess (5 equiv.) of $ZnCl_2$ had been added. The identification of C(3)-H on the 2,6-substituted pyridine ring from the the 2,4-substituted

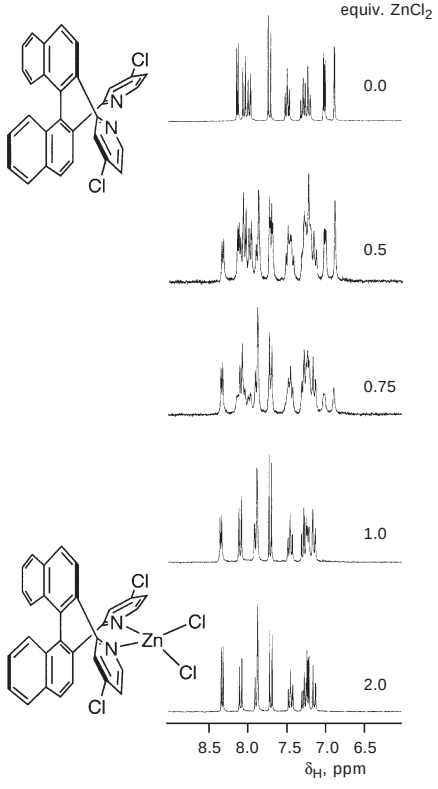



FIG. 4

$^1$H NMR sub-spectra (aromatic region) from the titration of ligand **3c** with $ZnCl_2$ in $CD_3CN$. Aliquots of a 0.23 M solution of $ZnCl_2$ in $CD_3CN$ were added to a 0.02 M solution of **3c** in $CD_3CN$

ring is simple since the former is a doublet and the latter a singlet. A plot of the difference in the chemical shift of the two signals *versus* Zn titre is given in Fig. 6.

It is clear from this (but much less so from direct inspection of the NMR titration series itself) that the ligand reacts with 1 equiv. of Zn by com-

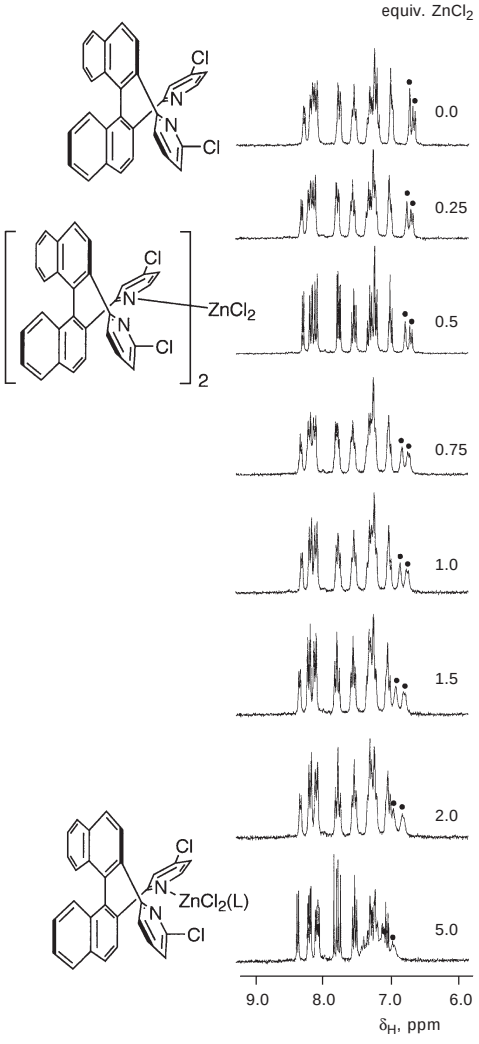



FIG. 5

$^1$H NMR sub-spectra (aromatic region) from the titration of ligand **3b** with $ZnCl_2$ in $CD_3CN$. Aliquots of a 0.23 M solution of $ZnCl_2$ in $CD_3CN$ were added to a 0.02 M solution of **3b** in $CD_3CN$

plexation through the 2,4-disubstituted pyridine ring – *i.e.*, predominantly as a monodentate ligand and thus giving a transient sharpened spectrum at 0.5 equiv. $ZnCl_2$ when [$ZnCl_2$(**3b**)$_2$] is formed. The lack of coordination of the 2,6-disubstituted ring is consistent with the higher degree of steric hindrance about the nitrogen centre. Consistent with this interpretation is the observation that there was no effect on the spectrum of the bis-2,6-disubstituted pyridine system **3a** upon addition of $ZnCl_2$, even when a large excess was employed, and thus no evidence for complexation. Thus, although the pyridinophilicity of [$ZnCl_2$(MeCN)$_2$] in MeCN is likely to be somewhat lower than that of $Zn(OTf)_2$ in $CH_2Cl_2$, these results suggest that only the non-substituted ligand **1** and the 4,4-disubstituted ligand **3c** and **4c** are able to chelate effectively. This is fully consistent with the enantioselectivities observed for these ligands as compared to the 4,6- and 6,6-systems **3a**, **3b** and **4a 4b**. To account for the small levels of induction with **3a** and **4a** and essentially no induction with **3b** and **4b**, one must consider the monodentate modes of coordination. With the non-symmetric **3b** and **4b**, the ligand will coordinate through the much less hindered 4-substituted pyridine ring, whereas with **3a** and **3b** monodentate coordination must be through a 6-substituted pyridine ring. Chirality transmission, though poor, is likely to be higher in the latter due to the steric influence of

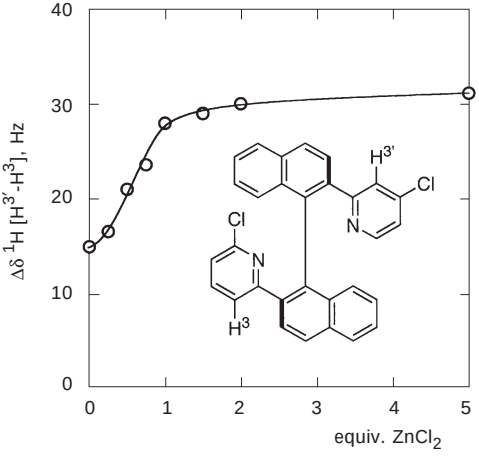



FIG. 6

Graph demonstrating the difference in $^1$H NMR chemical shift (Hz; *y*-axis) between the two C(3)-H pyridine protons on ligand structure **3b** (0.02 M solution in $CD_3CN$) during titration with a 0.23 M solution of $ZnCl_2$ in $CD_3CN$ (*x*-axis)

the 6-chloro or 6-methyl group which will be in close proximity to the coordination sphere.

To gain some evidence for the mono-coordination of **3a**/**4a**, we chose a more electrophilic complexing agent, [Pd(π-allyl)$(MeCN)_2$](OTf) and the more electron-rich 6,6′-dimethylated bispyridine system **4a**. When the less hindered parent ligand **1** is reacted with 1 equiv. [Pd(π-allyl)$(MeCN)_2$](OTf) in $CDCl_3$ at room temperature, the resulting $^1$H NMR spectrum corresponds to a single species, with a time-average $C_2$-symmetric ligand environment. In contrast, with **4a**, two species are observed in a ratio of *ca* 1/2. Each species displays time-average equivalent allyl termini within a non-symmetrical ligand environment, there is no free **4a** and no unreacted [Pd(π-allyl)$(MeCN)_2$](OTf). The $^1$H NMR chemical shifts and coupling patterns in the allyl region of new species are consistent with Pd-(π-allyl) complexes and the two species are thus tentatively assigned as the two allyl rotameric isomers of [Pd(π-allyl)(L) (**4a**)], where L = OTf or MeCN and **4a** is monodentate. However, we were unable to isolate or characterise these complexes further. Nonetheless, by reacting two equiv. of [Pd(π-allyl)$(MeCN)_2$](OTf) with **4a**, we were able to crystallise [(Pd(allyl)(OTf))$_2$(**4a**)] (**6**), a complex in which both pyridine rings act as monodentate ligands to a Pd-allyl fragment, together with the weakly coordinating triflate counter-ion. The structure of this complex (Fig. 7) was confirmed by single-crystal X-ray diffraction.

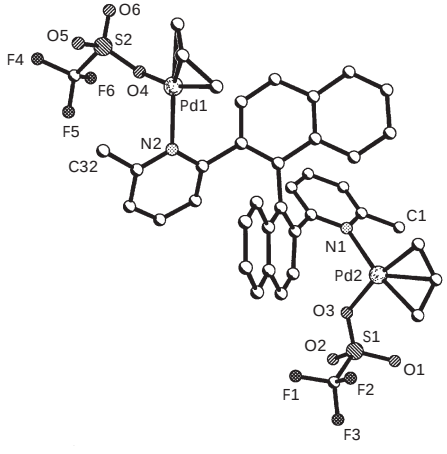



FIG. 7

The molecular structure of **6**, a bis(allyl-Pd triflate) complex of **4a** in which the ligand acts as a bis-monodentate ligand to generate [(Pd-(allyl)(OTf))$_2$**4a**], in the crystal. All protons have been omitted for clarity. See Experimental for details of X-ray diffraction and solution

## CONCLUSIONS

A fairly efficient synthetic route to enantiomerically pure methyl-substituted pyridine ligands **4a**–**4c** has been established employing enantiomerically pure **1**[3] as starting material. The major drawback to the route is that the chlorination of intermediate bis-*N*-oxide **2** is non-selective and thus mixtures of **3a**–**3c** are obtained. The modified ligands perform rather poorly in asymmetric catalysis and are outperformed by the simpler ligand structure **1** in all cases examined. NMR studies involving $ZnCl_2$ and Pd-allyl titration suggests that substitution of the pyridine rings at the 6-position severely hinders complexation in a didentate mode and that this compromises enantioselectivity by forcing the majority of turnover to proceed by Zn complexes bearing one (or two) pyridine ligands coordinated in a monodentate mode. To improve asymmetric induction, derivatisation of the binaphthalene backbone, for example at position 3, which extends over the coordination sphere, may be a viable alternative and this is currently being pursued.

## EXPERIMENTAL

### General

Reagents were purified by standard procedures. Solvents were dried by passage through an Anhydrous Technologies Drying Train. When appropriate, reactions were performed under nitrogen or argon using standard Schlenk techniques. NMR spectra: JEOL Lambda 300 instrument operating at 300 and 75 MHz ($^1$H and $^{13}$C, respectively); coupling constsmts (*J*) are given in Hz, chemical shifts (ppm) are referenced to TMS (0.00 ppm) or internally referenced to the lock signal of the deuterated solvent used. Mass spectra: Micromass Autospec. IR spectra (ν, $cm^{-1}$): Perkin–Elmer 1600 FTIR, absorptions are reported as strong (s), medium (m), weak (w). Optical rotations were measured with a Perkin–Elmer 141 instrument and are given in $10^{-1}$ deg $cm^2$ $g^{-1}$. Flash column chromatography: Merck silica gel 60 eluting with a constant gravity head of *ca* 15 cm solvent. TLC: 0.25 mm, Merck silica gel 60 F254 visualised at 254 nm. Samples of (+)-($R_a$)-2,2′-di(pyridin-2-yl)-1,1′-binaphthalene (($R_a$)-**1**) and (–)-($S_a$)-2,2′-dipyridin-2-yl)-1,1′-binaphthalene (($S_a$)-**1**) in >96% ee were prepared and resolved as previously described.[3]

### X-Ray Crystallography

X-Ray measurements were made using a Bruker SMART CCD area-detector diffractometer with MoKα radiation (λ = 0.71073 Å). Intensities were integrated from several series of exposures, each exposure covering 0.3° in ω[19]. Absorption corrections were applied, based on multiple and symmetry-equivalent measurements[20]. The structures were solved by direct methods and refined by least squares on weighted $F^2$ values for all reflections[21]. All non-hydrogen atoms were assigned anisotropic displacement parameters and refined without positional constraints. All hydrogen atoms were constrained to ideal geometries and refined

with isotropic displacement parameters riding on the equivalent isotropic displacement parameters of their parent atoms.

Crystallographic data for **2**: colourless crystals, $C_{30}H_{20}N_2O_2$, $M$ = 440.48, monoclinic, $C2/c$, $Z$ = 4, $R_1$ = 7.6% [for 753 observed data with $I > 2\sigma(I)$], $wR_2$ = 21.3% (for all 1407 data), $S$ = 0.965. Data for **2** are very weak, which probably contributes to the high value of $R_{int}$ (37.2%). No data were observed beyond 2θ = 45° and integration of data was truncated at this limit. The magnitude of $R_{int}$ was not lowered significantly by choosing a triclinic space group suggesting that the assignment of a monoclinic crystal system is correct.

Crystallographic data for **6**: colourless crystals, $C_{41}H_{36}Cl_2F_6N_2O_6Pd_2S_2$, $M$ = 1114.5, triclinic, $P$-1, $Z$ = 2, $R_1$ = 7.0% [for 4843 observed data with $I > 2\sigma(I)$], w$R_2$ = 18.9% (for all 8492 data), $S$ = 0.977. Although the data are of poor quality (the final electron density difference synthesis is noisy and a solvent accessible void of *ca* 300 Å$^3$ is present), there is no doubt about the assignment of molecular structure of the palladium complex.

CCDC 199984 (for **2**) and CCDC 199985 (for **6**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

Synthetic Chemistry

(+)-($R_a$)-2,2′-Di(pyridin-2-yl)-1,1′-binaphthalene *N*,*N*-dioxide (($R_a$)-**2**)
A solution of 3-chloroperbenzoic acid (975 mg, 2.82 mmol) in chloroform (35 cm$^3$) was added to solution of (+)-($R_a$)-2,2′-di(pyridin-2-yl)-1,1′-binaphthalene (($R_a$)-**1**) (456 mg, 1.13 mmol) in chloroform (35 cm$^3$) at 0 °C. The reaction was quenched after 16 h with aqueous $NaHCO_3$ (50 cm$^3$) and then the aqueous layer extracted with $CH_2Cl_2$ (3 × 50 cm$^3$). The combined organic layers were dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to yield ($R_a$)-**2** as a white solid (302 mg, 61%), m.p. > 300 °C. For $C_{30}H_{20}N_2O_2$ (440.5) calculated: 81.80% C, 4.58% H, 6.36% N; found: 82.05% C, 4.28% H, 6.23% N. IR (KBr): 1491 m, 1431 s, 1291 w, 1253 s, 1239 s, 1159 w, 1110 w, 1077 w, 1043 w, 940 w, 886 m, 874 m, 815 s, 767 s. $^1$H NMR (300 MHz, $CDCl_3$): 6.64 bd, 2 H, $J$(3,4) = 7.5 ($C_{pyr}{}^3$-H and $C_{pyr}{}^{3'}$-H); 6.80 dd, 2 H, $J$(3,4) = $J$(4,5) = 7.5 ($C_{pyr}{}^4$-H and $C_{pyr}{}^{4'}$-H); 7.07 dd, 2 H, $J$(4,5) = 7.5, $J$(5,6) = 5.9 ($C_{pyr}{}^5$-H and $C_{pyr}{}^{5'}$-H); 7.40 m, 4 H ($C^8$-H and $C^{8'}$-H and $C^7$-H and $C^{7'}$-H); 7.56 m, 2 H ($C^6$-H and $C^{6'}$-H); 7.71 d, 2 H, $J$(3,4) = 8.7 ($C^3$-H and $C^{3'}$-H); 7.93 d, 2 H, $J$(3,4) = 8.7 ($C^4$-H and $C^{4'}$-H); 7.95 d, 2 H, $J$(5,6) = 8.3 ($C^5$-H and $C^{5'}$-H); 8.31 d, 2 H, $J$(5,6) = 5.9 ($C_{pyr}{}^6$-H and $C_{pyr}{}^{6'}$-H). $^{13}$C NMR (75 MHz, $CDCl_3$ ): 124.7 ($C_{pyr}{}^3$ and $C_{pyr}{}^{3'}$), 124.8 ($C_{pyr}{}^5$ and $C_{pyr}{}^{5'}$), 126.7 ($C^6$, $C^{6'}$, $C^7$ and $C^{7'}$), 127.1 ($C^8$ and $C^{8'}$), 127.5 ($C^5$ and $C^5$ ), 127.6 ($C^3$ and $C^{3'}$), 127.7 ($C_{pyr}{}^4$ and $C_{pyr}{}^{4'}$), 128.3 ($C^4$ and $C^{4'}$), 131.8, 132.2, 133.7, 134.5, ($C^1$, $C^{1'}$ $C^2$, $C^{2'}$ $C^9$, $C^{9'}$, $C^{10}$ and $C^{10'}$ ), 140.2 ($C_{pyr}{}^6$ and $C_{pyr}{}^{6'}$), 147.3 ($C_{pyr}{}^2$ and $C_{pyr}{}^{2'}$). MS (EI$^+$), *m*/*z* (%): 440 ($M^+$, 37), 423 (78), 408 (25), 334 (55), 330 (46), 318 (100), 304 (47), 291 (19). $[\alpha]_D$ 45.1 (*c* 0.08, $CH_2Cl_2$, 21 °C).

Procedure for the Deoxygenative Chlorination of Bis-*N*-oxide **2** to Give **3a**, **3b** and **3c**

(–)-($S_a$)-2,2′-Di(pyridin-2-yl)-1,1′-binaphthalene *N*,*N*-dioxide (($S_a$)-**2**) (200 mg, 0.454 mmol) was refluxed in $POCl_3$ (6 cm$^3$) for 2 h. The reaction mixture was slowly added to ice/water (200 cm$^3$) and the resulting slurry was adjusted to pH 13 by addition of NaOH pellets. The aqueous mixture was extracted with dichloromethane (3 × 30 cm$^3$) and the combined or-

ganic extracts were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting brown oil was purified by column chromatography, employing an elution gradient of 5 to 50% EtOAc in hexanes, to give, in elution sequence, (–)-($S_a$)-2,2′-di(6-chloropyridin-2-yl)-1,1′-binaphthalene (($S_a$)-**3a**) as a white solid (72 mg, 33%), (–)-($S_a$)-2-(4-chloropyridin-2-yl)-2′-(6-chloropyridin-2-yl)-1,1′-binaphthalene (($S_a$)-**3b**) as a white solid (81 mg, 37%) and (–)-($S_a$)-2,2′-di(4-chloropyridin-2-yl)-1,1′-binaphthalene (($S_a$)-**3c**) as a white solid (37 mg, 17%).

*(–)-($S_a$)-2,2′-Bis(6-chloropyridin-2-yl)-1,1′-binaphthalene* (($S_a$)-**3a**). M.p. 174 °C. IR (NaCl): 1579 s, 1434 s, 1135 m, 790 m, 763 m, 459 w. $^1$H NMR (300 MHz, $CDCl_3$): 6.42 dd, 2 H, *J*(3,4) = 7.5, *J*(3,5) = 1.1 ($C_{pyr}{}^3$-H and $C_{pyr}{}^{3'}$-H); 7.02 dd, 2 H, *J*(4,5) = 7.9, *J*(3,5) = 1.1 ($C_{pyr}{}^5$-H and $C_{pyr}{}^{5'}$-H); 7.11 dd, 2 H, *J*(4,5) = 7.9, *J*(3,4) = 7.5 ($C_{pyr}{}^4$-H and $C_{pyr}{}^{4'}$-H); 7.34 ddd, 2 H, *J*(5,6) = 8.0, *J*(6,7) = 6.5, *J*(6,8) = 1.6 ($C^6$-H and $C^{6'}$-H); 7.40 dddd, 2 H, *J*(7,8) = 8.2, *J*(6,8) = 1.6, *J*(5,8) = 0.8, *J*(4,8) = 0.8 ($C^8$-H and $C^{8'}$-H); 7.54 ddd, 2 H, *J*(7,8) = 8.2, *J*(6,7) = 6.5, *J*(5,7) = 1.5 ($C^7$-H and $C^{7'}$-H); 7.78 d, 2 H, *J*(3,4) = 8.4 ($C^3$-H and $C^{3'}$-H); 7.98 ddd, 2 H, *J*(5,6) = 8.0, *J*(5,7) = 1.5, *J*(5,8) = 0.8 ($C^5$-H and $C^{5'}$-H); 8.02 dd, 2 H, *J*(3,4) = 8.4, *J*(4,8) = 0.8 ($C^4$-H and $C^{4'}$-H). $^{13}$C NMR (75.45 MHz, $CDCl_3$): 122.3 ($C_{pyr}{}^5$ and $C_{pyr}{}^{5'}$), 122.6 ($C_{pyr}{}^3$ and $C_{pyr}{}^{3'}$), 126.9 ($C^7$ and $C^{7'}$), 127.2 ($C^6$ and $C^{6'}$), 127.6 ($C^8$ and $C^{8'}$), 128.0 ($C^3$ and $C^{3'}$), 128.6 ($C^5$ and $C^{5'}$), 129.2 ($C^4$ and $C^{4'}$), 133.6, 133.8, 134.6, 137.7 ($C^1$, $C^{1'}$ $C^2$, $C^{2'}$ $C^9$, $C^{9'}$, $C^{10}$ and $C^{10'}$), 138.1 ($C_{pyr}{}^4$ and $C_{pyr}{}^{4'}$), 150.8 ($C_{pyr}{}^6$ and $C_{pyr}{}^{6'}$), 158.8 ($C_{pyr}{}^2$ and $C_{pyr}{}^{2'}$). MS (EI), *m/z* (%): 480 ($M^+$ ($^{37}$Cl, $^{37}$Cl), 10), 478 ($M^+$ ($^{35}$Cl, $^{37}$Cl), 50), 476 ($M^+$ ($^{35}$Cl, $^{35}$Cl), 75), 366 (34), 364 (100), 328 (24), 300 (10), 252 (10), 239 (10). HR MS ($EI^+$), *m/z*: for $C_{30}H_{18}{}^{35}Cl_2N_2$ calculated 476.0847, found 476.0848; for $C_{30}H_{18}{}^{37}Cl^{35}ClN_2$ calculated 478.0818, found 478.0813. $[\alpha]_D$ –200.4 (*c* 0.225, $CH_2Cl_2$, 18 °C).

*(–)-($S_a$)-2-(4-Chloropyridin-2-yl)-2′-(6-chloropyridin-2-yl)-1,1′-binaphthalene* (($S_a$)-**3b**). M.p. 183 °C. IR (NaCl): 1579 s, 1550 s, 1433 m, 1135 w, 821 m, 802 w, 763 s, 657 w. $^1$H NMR (300 MHz, $CDCl_3$): 6.47 dd, 1 H, *J*(3,4) = 7.6, *J*(3,5) = 0.9 ($C_{pyr}{}^{3'}$); 6.53 dd, 1 H, *J*(3,5) = 2.0, *J*(3,6) = 0.7 ($C_{pyr}{}^3$); 6.95 dd, 1 H, *J*(5,6) = 5.3, *J*(3,5) = 2.0 ($C_{pyr}{}^5$); 6.97 dd, 1 H, *J*(4,5) = 7.8, *J*(3,5) = 0.9 ($C_{pyr}{}^{5'}$); 7.06 dd, 1 H, *J*(4,5) = 7.8, *J*(3,4) = 7.6 ($C_{pyr}{}^{4'}$); 7.32 ddd, 1 H, *J*(7,8) = 8.5, *J*(6,7) = 6.6, *J*(5,7) = 1.5 ($C^{7'}$-H); 7.33 ddd, 1 H, *J*(7,8) = 8.6, *J*(6,7) = 6.6, *J*(5,7) = 1.5 ($C^7$-H); 7.39 dddd, 1 H, *J*(7,8) = 8.5, *J*(6,8) = 1.5, *J*(5,8) = 0.9, *J*(4,8) = 0.7 ($C^{8'}$-H); 7.43 dddd, 1 H, *J*(7,8) = 8.6, *J*(6,8) = 1.5, *J*(5,8) = 0.9, *J*(4,8) = 0.7 ($C^8$-H); 7.50 ddd, 1 H, *J*(5,6) = 8.5, *J*(6,7) = 6.6, *J*(6,8) = 1.5 ($C^{6'}$-H); 7.51 ddd, 1 H, *J*(5,6) = 8.5, *J*(6,7) = 6.6, *J*(6,8) = 1.5 ($C^6$-H); 7.70 d, 1 H, *J*(3,4) = 8.6 ($C^3$-H); 7.77 d, 1 H, *J*(3,4) = 8.6 ($C^6$-H); 7.96 ddd, 2 H, *J*(5,6) = 8.5, *J*(5,7) = 1.5, *J*(5,8) = 0.9 ($C^5$-H and $C^{5'}$-H); 8.00 dd, 2 H, *J*(3,4) = 8.6, *J*(4,8) = 0.7 ($C^4$-H and $C^{4'}$-H); 8.24 dd, 1 H, *J*(5,6) = 5.3, *J*(3,6) = 0.7 ($C_{pyr}{}^6$-H). $^{13}$C NMR (75.45 MHz, $CDCl_3$): 121.7 ($C_{pyr}{}^{5'}$), 121.9 ($C_{pyr}{}^5$), 122.2 ($C_{pyr}{}^{3'}$), 124.1 ($C_{pyr}{}^3$), 126.4 ($C^6$ and $C^{6'}$), 126.9 ($C^7$), 126.9 ($C^{7'}$), 127.1 ($C^8$), 127.2 ($C^{8'}$), 127.3 ($C^3$), 127.5 ($C^{3'}$), 128.3 ($C^5$ and $C^{5'}$), 128.7 ($C^4$), 128.8 ($C^{4'}$), 133.2, 133.2, 133.4, 133.5, 134.1, 134.5, 137.3, 137.6, 143.1, 158.8, 159.6 ($C_{pyr}{}^{4'}$, $C_{pyr}{}^2$, $C_{pyr}{}^{2'}$, $C^1$, $C^{1'}$ $C^2$, $C^{2'}$ $C^9$, $C^{9'}$, $C^{10}$ and $C^{10'}$), 137.7 ($C_{pyr}{}^{4'}$), 149.6 ($C_{pyr}{}^6$), 150.3 ($C_{pyr}{}^{6'}$). MS (EI), *m/z* (%): 480 ($M^+$ ($^{37}$Cl, $^{37}$Cl), 14), 478 ($M^+$ ($^{35}$Cl, $^{37}$Cl), 68), 476 ($M^+$ ($^{35}$Cl, $^{35}$Cl), 88), 366 (43), 364 (100), 328 (19), 238 (15). HR MS ($EI^+$), *m/z*: for $C_{30}H_{18}{}^{35}ClN_{22}$ calculated 476.0847, found 476.0846; for $C_{30}H_{18}N_2{}^{37}Cl^{35}Cl$ calculated 478.0818, found 478.0839. $[\alpha]_D$ –65.0 (*c* 0.525, $CH_2Cl_2$, 23 °C).

*(+)-($S_a$)-2,2′-Di(4-chloropyridin-2-yl)-1,1′-binaphthalene* (($S_a$)-**3c**). M.p. softens 68 °C, melts 218 °C. IR (NaCl): 1579 s, 1549 m, 1471 w, 1387 w, 820 m, 764 m, 739 w, 479 w. $^1$H NMR (300 MHz, $CDCl_3$): 6.65 dd, 2 H, *J*(3,5) = 1.9, *J*(3,6) = 0.6 ($C_{pyr}{}^3$-H and $C_{pyr}{}^{3'}$-H); 6.93 ddd, 2 H, *J*(5,6) = 5.3, *J*(3,5) = 1.9 ($C_{pyr}{}^5$-H and $C_{pyr}{}^{5'}$-H); 7.31 ddd, 2 H, *J*(7,8) = 8.1, *J*(6,7) = 6.8,

$J$(5,7) = 1.3 ($C^7$-H and $C^{7'}$-H); 7.40 dddd, 2 H, $J$(7,8) = 8.1, $J$(6,8) = 1.6, $J$(5,8) = 0.8, $J$(4,8) = 0.8 ($C^8$-H and $C^{8'}$-H); 7.49 ddd, 2 H, $J$(5,6) = 8.1, $J$(6,7) = 6.8, $J$(6,8) = 1.6 ($C^6$-H and $C^{6'}$-H); 7.73 d, 2 H, $J$(3,4) = 8.4 ($C^3$-H and $C^{3'}$-H); 7.94 dddd, 2 H, $J$(5,6) = 8.1, $J$(5,7) = 1.3, $J$(5,8) = 0.8 ($C^5$-H and $C^{5'}$-H); 8.00 dd, 2 H, $J$(3,4) = 8.4, $J$(4,8) = 0.8 ($C^4$-H and $C^{4'}$-H); 8.19 dd, 2 H, $J$(5,6) = 5.3, $J$(3,6) = 0.6 ($C_{pyr}{}^6$-H and $C_{pyr}{}^{6'}$-H). $^{13}$C NMR (75.45 MHz, $CDCl_3$): 121.5 ($C_{pyr}{}^5$ and $C_{pyr}{}^{5'}$), 124.2 ($C_{pyr}{}^3$ and $C_{pyr}{}^{3'}$), 126.5 ($C^6$ and $C^{6'}$), 126.9 ($C^3$ and $C^{3'}$), 127.0 ($C^8$ and $C^{8'}$), 127.0 ($C^7$ and $C^{7'}$), 128.1 ($C^5$ and $C^{5'}$), 128.7 ($C^4$ and $C^{4'}$), 133.1, 133.3, 134.4, 137.3 ($C^1$, $C^{1'}$ $C^2$, $C^{2'}$ $C^9$, $C^{9'}$, $C^{10}$ and $C^{10'}$), 143.0 ($C_{pyr}{}^4$ and $C_{pyr}{}^{4'}$), 149.4 ($C_{pyr}{}^6$ and $C_{pyr}{}^{6'}$), 159.8 ($C_{pyr}{}^2$ and $C_{pyr}{}^{2'}$). MS (EI), *m/z* (%): 480 ($M^+$($^{37}$Cl, $^{37}$Cl), 12), 478 ($M^+$ ($^{35}$Cl, $^{37}$Cl), 67), 476 ($M^+$ ($^{35}$Cl, $^{35}$Cl), 91), 441 (23), 366 (45), 364 (100), 328 (20), 300 (10), 238 (19). HR MS (EI$^+$), *m/z*: for $C_{30}H_{18}{}^{35}Cl_2N_2$ calculated 476.0847, found 476.0833; for $C_{30}H_{18}{}^{35}Cl^{37}ClN_2$ calculated 478.0818, found 478.0811. $[\alpha]_D$ 18.8 (*c* 0.538, $CH_2Cl_2$, 23 °C).

Procedure for the Kumada Cross-Coupling of **3a**–**3c** to Give Bispicolines **4a**–**4c**

A solution of a mixture of dichlorides ($R_a$)-**3a**–**3c** (38/42.5/19.5 ratio **3a**/**3b**/**3c**; 286 mg, 0.60 mmol) and [$NiCl_2$(dppf)] (40.9 mg, 0.060 mmol) in anhydrous THF (20 $cm^3$) was stirred under an atmosphere of nitrogen for 30 min at room temperature. MeMgI (1 M in $Et_2O$, 3.00 $cm^3$, 3.00 mmol) was added rapidly, initially giving a cherry red colour, which became yellow after 10 s. A precipitate was formed after 30 s. After 1 h at room temperature, the reaction was quenched with saturated $NH_4Cl$ (20 $cm^3$) and extracted with dichloromethane (3 × 30 $cm^3$). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting brown oil was purified by column chromatography, employing an elution gradient of 5 to 50% EtOAc in hexanes, to give, in elution sequence, (+)-($R_a$)-2,2′-di(6-methylpyridin-2-yl)-1,1′-binaphthalene (($R_a$)-**4a**) as a white solid (69 mg, 26%), (+)-($R_a$)-2-(6-methylpyridin-2-yl)-2′-(4-methylpyridin-2-yl)-1,1′-binaphthalene (($R_a$)-**4b**) as a white solid (83 mg, 32%) and (–)-($R_a$)-2,2′-di(4-methylpyridin-2-yl)-1,1′-binaphthalene (($R_a$)-**4c**) as a white solid (48 mg, 18%).

*(+)-($R_a$)-2,2′-di(6-methylpyridin-2-yl)-1,1′-binaphthalene* (($R_a$)-**4a**). M.p. deforms at 65 °C, decomp. at 204 °C. IR (NaCl): 1579 s, 1450 m, 1433 s, 1264 w, 1161 w, 1134 m, 986 w, 828 w, 789 s, 762 m, 737 m. $^1$H NMR (300 MHz, $CDCl_3$): 2.23 s, 6 H (2 × $CH_3$); 6.42 dd, 2 H, $J$(3,4) = 7.9, $J$(3,5) = 0.9 ($C_{pyr}{}^3$-H and $C_{pyr}{}^{3'}$-H); 6.78 dd, 2 H, $J$(4,5) = 7.9, $J$(3,5) = 0.9 ($C_{pyr}{}^5$-H and $C_{pyr}{}^{5'}$-H); 7.02 dd, 2 H, $J$(3,4) = 7.9, $J$(4,5) = 7.9 ($C_{pyr}{}^4$-H and $C_{pyr}{}^{4'}$-H); 7.28 ddd, 2 H, $J$(7,8) = 8.2, $J$(6,7) = 6.8, $J$(5,7) = 1.5 ($C^7$-H and $C^{7'}$-H); 7.40 ddd, 2 H, $J$(7,8) = 8.2, $J$(6,8) = 1.3, $J$(5,8) = 0.6 ($C^8$-H and $C^{8'}$-H); 7.46 ddd, 2 H, $J$(5,6) = 8.4, $J$(6,7) = 6.8, $J$(6,8) = 1.3 ($C^6$-H and $C^{6'}$-H); 7.78 d, 2 H, $J$(3,4) = 8.6 ($C^3$-H and $C^{3'}$-H); 7.91 ddd, 2 H, $J$(5,6) = 8.4, $J$(5,7) = 1.5, $J$(5,8) = 0.6 ($C^5$-H and $C^{5'}$-H); 7.96 d, 2 H, $J$(3,4) = 8.6 ($C^4$-H and $C^{4'}$-H). $^{13}$C NMR (75.45 MHz, $CDCl_3$): 24.2 ($CH_3$), 120.7 ($C_{pyr}{}^5$ and $C_{pyr}{}^{5'}$), 120.8 ($C_{pyr}{}^3$ and $C_{pyr}{}^{3'}$), 125.9 ($C^6$ and $C^{6'}$), 126.4 ($C^7$ and $C^{7'}$), 127.4 ($C^8$ and $C^{8'}$), 127.8 ($C^3$ and $C^{3'}$), 128.0 ($C^5$ and $C^{5'}$), 128.3 ($C^4$ and $C^{4'}$), 132.9, 133.7, 134.4, 138.7, 157.1, 157.6 ($C_{pyr}{}^1$, $C_{pyr}{}^{1'}$, $C_{pyr}{}^2$, $C_{pyr}{}^{2'}$, $C^1$, $C^{1'}$ $C^2$, $C^{2'}$ $C^9$, $C^{9'}$, $C^{10}$ and $C^{10'}$), 135.3 ($C_{pyr}{}^4$ and $C_{pyr}{}^{4'}$). MS (EI), *m/z* (%): 436 ($M^+$, 100), 422 (52), 344 (100), 330 (36), 218 (20). HR MS (EI$^+$), *m/z*: for $C_{32}H_{24}N_2$ calculated 436.1939, found 436.1944. $[\alpha]_D$ 135.8 (*c* 0.104, $CDCl_3$, 18 °C).

*(+)-($R_a$)-2-(6-Methylpyridin-2-yl)-2′-(4-methylpyridin-2-yl)-1,1′-binaphthalene* (($R_a$)-**4b**). M.p. 68 °C. IR (NaCl): 1580 w, 1463 s, 1291 w, 960 w, 875 m. $^1$H NMR (300 MHz, $CDCl_3$): 1.84 dd, 3 H, $J$($CH_3$) = 0.6, $J$($CH_3$) = 0.6 ($C_{pyr}{}^{4'}$-$CH_3$); 2.33 s, 3 H ($C_{pyr}{}^6$-$CH_3$); 6.42 dd, 1 H, $J$(3,4) = 7.7, $J$(3,5) = 0.8 ($C_{pyr}{}^3$-H); 6.44 ddd, 1 H, $J$(3,5) = 1.7, $J$(3,6) = 0.9, $J$($CH_3$) = 0.6 ($C_{pyr}{}^{3'}$-H);

6.77 dd, 1 H, *J*(4,5) = 7.7, *J*(3,5) = 0.8 ($C_{pyr}^{5}$-H); 6.81 ddd, 1 H, *J*(5,6) = 5.1, *J*(3,5) = 1.7, *J*(5,$CH_3$) = 0.6 ($C_{pyr}^{5'}$-H); 7.03 dd, 1 H, *J*(4,5) = 7.7, *J*(3,4) = 7.7 ($C_{pyr}^{4}$-H); 7.28 [and 7.33] ddd, 1 H, *J*(7,8) = 8.1, *J*(6,7) = 6.6, *J*(5,7) = 0.7 ($C^{7}$-H and $C^{7'}$-H); 7.46 ddd, 2 H, *J*(7,8) = 8.1, *J*(6,8) = 1.3, *J*(4,8) = 0.9, *J*(5,8) = 0.7 ($C^{8}$-H and $C^{8'}$-H); 7.49 [and 7.50] ddd, 1 H, *J*(5,6) = 8.1, *J*(6,7) = 6.6, *J*(6,8) = 1.3 ($C^{6}$-H and $C^{6'}$-H); 7.78 [and 7.80] d, 1 H, *J*(3,4) = 8.6 ($C^{3}$-H and $C^{3'}$-H); 7.94 [and 7.96] ddd, 1 H, *J*(5,6) = 8.1, *J*(5,7) = 0.7, *J*(5,8) = 0.7 ($C^{5}$-H and $C^{5'}$-H); 7.99 [and 8.01] dd, 1 H, *J*(3,4) = 8.6, *J*(4,8) = 0.9 ($C^{4}$-H and $C^{4'}$-H); 8.32 dd, 1 H, *J*(5,6) = 5.1, *J*(3,6) = 0.9 ($C_{pyr}^{6'}$-H). $^{13}$C NMR (75.45 MHz, $CDCl_3$): 20.7 ($C_{pyr}^{4'}$-**C**$H_3$), 24.1 ($C_{pyr}^{6}$-**C**$H_3$), 120.7 ($C_{pyr}^{3'}$), 120.9 ($C_{pyr}^{5'}$), 122.4 ($C_{pyr}^{5}$), 125.0 ($C_{pyr}^{3}$), 125.9 and 126.0 ($C^{6}$ and $C^{6'}$), 126.5 and 126.5 ($C^{7}$ and $C^{7'}$), 127.3 and 127.4 ($C^{8}$ and $C^{8'}$), 127.7 and 127.7 ($C^{3}$ and $C^{3'}$), 128.0 and 128.0 ($C^{5}$ and $C^{5'}$), 128.1 and 128.3 ($C^{4}$ and $C^{4'}$), 132.8, 133.0, 133.7, 134.3, 134.7, 135.3, 138.1, 138.8, 157.3, 157.4, 157.7 ($C_{pyr}^{2}$, $C_{pyr}^{6}$, $C_{pyr}^{2'}$, $C_{pyr}^{4'}$, $C^{1}$, $C^{1'}$ $C^{2}$, $C^{2'}$ $C^{9}$, $C^{9'}$, $C^{10}$ and $C^{10'}$), 146.3 ($C_{pyr}^{4}$), 148.0 ($C_{pyr}^{6'}$). MS (EI), *m/z* (%): 436 ($M^+$, 100), 422 (49), 344 (100), 330 (40), 309 (17), 218 (19). HR MS ($EI^+$), *m/z*: for $C_{32}H_{24}N_2$ calculated 436.1939, found 436.1957. $[\alpha]_D$ 31.7 (*c* 0.104, $CH_2Cl_2$, 18 °C).

*(–)-(R$_a$)-2,2′-Di(4-methylpyridin-2-yl)-1,1′-binaphthalene* ((*R*$_a$)-**4c**). M.p. decomp. 198 °C. IR (NaCl): 1602 s, 1560 m, 1504 w, 1476 m, 1321 w, 1253 w, 992 w, 815 s, 761 m, 744 m. $^1$H NMR (300 MHz, $CDCl_3$): 1.63 dd, 6 H, *J*(3,$CH_3$) = 0.8, *J*(5,$CH_3$) = 0.8 (2 × $CH_3$); 6.34 ddd, 2 H, *J*(3,5) = 1.8, *J*(3,6) = 0.8, *J*(3,$CH_3$) = 0.8 ($C_{pyr}^{3}$-H and $C_{pyr}^{3'}$-H); 6.74 ddd, *J*(5,6) = 5.0, *J*(3,5) = 1.8, *J*(5,$CH_3$) = 0.8 ($C_{pyr}^{5}$-H and $C_{pyr}^{5'}$-H); 7.33 ddd, *J*(7,8) = 8.6, *J*(6,7) = 6.7, *J*(5,7) = 1.3 ($C^{7}$-H and $C^{7'}$-H); 7.48 ddd, *J*(7,8) = 8.6, *J*(6,8) = 1.3, *J*(5,8) = 1.3 ($C^{8}$-H and $C^{8'}$-H); 7.49 ddd, *J*(5,6) = 8.2, *J*(6,7) = 6.7, *J*(6,8) = 1.3 ($C^{6}$-H and $C^{6'}$-H); 7.78 d, *J*(3,4) = 8.4 ($C^{3}$-H and $C^{3'}$-H); 7.95 ddd, *J*(5,6) = 8.2, *J*(5,7) = 1.3, *J*(5,8) = 1.3 ($C^{5}$-H and $C^{5'}$-H); 7.98 d, *J*(3,4) = 8.4 ($C^{4}$-H and $C^{4'}$-H); 8.19 dd, *J*(5,6) = 5.0, *J*(3,6) = 0.8 ($C_{pyr}^{6}$-H and $C_{pyr}^{6'}$-H). $^{13}$C NMR (75.45 MHz, $CDCl_3$): 20.7 ($CH_3$), 122.2 ($C_{pyr}^{5}$ and $C_{pyr}^{5'}$), 124.9 ($C_{pyr}^{3}$ and $C_{pyr}^{3'}$), 126.0 ($C^{6}$ and $C^{6'}$), 126.5 ($C^{7}$ and $C^{7'}$), 127.3 ($C^{8}$ and $C^{8'}$), 127.7 ($C^{3}$ and $C^{3'}$), 128.0 ($C^{5}$ and $C^{5'}$), 128.2 ($C^{4}$ and $C^{4'}$), 132.9, 133.8, 134.5, 138.7, 145.8 ($C_{pyr}^{4}$, $C_{pyr}^{4'}$,$C^{1}$, $C^{1'}$ $C^{2}$, $C^{2'}$ $C^{9}$, $C^{9'}$, $C^{10}$ and $C^{10'}$), 148.3 ($C_{pyr}^{6}$ and $C_{pyr}^{6'}$), 157.9 ($C_{pyr}^{2}$ and $C_{pyr}^{2'}$). MS (EI), *m/z* (%): 436 ($M^+$, 98), 422 (53), 344 (100), 330 (28), 218 (22). HR MS ($EI^+$), *m/z*: for $C_{32}H_{24}N_2$ calculated 436.1939, found 436.1932. $[\alpha]_D$ –7.4 (*c* 0.47, $CH_2Cl_2$, 23 °C).

Typical Procedure for the Zinc-Catalysed Allylation of Benzaldehyde with Allyltributyltin

A solution of (*S*$_a$)-2,2′-di(pyridin-2-yl)-1,1′-binaphthalene ((*S*$_a$)-**1**) (8.5 mg, 0.028 mmol) and $Zn(OTf)_2$ (8.5 mg, 0.023 mmol) in anhydrous dichloromethane (2 $cm^3$) was stirred, under $N_2$, for 1 h. Benzaldehyde (0.024 $cm^3$, 0.23 mmol) and allyltributyltin (0.108 $cm^3$, 0.35 mmol) were added and the reaction was stirred at room temperature for 44 h. Saturated aqueous $NH_4Cl$ (10 $cm^3$) was added and the aqueous layer was extracted with dichloromethane (3 × 10 $cm^3$). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting colourless oil was purified by column chromatography to give (*R*)-1-phenylbut-3-en-1-ol (absolute configuration assigned by comparison to reference sample)[22] as a colourless oil (15 mg, 38%) whose $^1$H NMR spectrum was identical to an independently prepared reference material. Chiral GC analysis: (γ-TFA 30 m × 0.25 mm, 110 °C) $t_R$ 10.7 ((*R*)-1-phenylbut-3-en-1-ol), 11.0 ((*S*)-1-phenylbut-3-en-1-ol); 33.1% ee.

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